Sladen Libraries
Great Research · Great Care · Start Here
Henry Ford Hospital
Henry Ford Macomb Hospital
Henry Ford Wyandotte Hospital
2799 W Grand Blvd
Detroit, MI 48202
313 916-2550, 313 874-4730 Fax
sladen@hfhs.org
henryfordconnect.com/sladen
M-Th 8:00a-7:30p, F 8:00a-5:00p

Henry Ford Health System Publication List – March 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 April, and then imported into EndNote for formatting. There are 120 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.

Click the "Full Text" link to view the articles to which Sladen Library provides access. If the full-text of the article is not available, you may request it through ILLiad by clicking on the "Article Request Form," or calling us at 313-916-2550. If you would like to be added to the monthly email distribution list to automatically receive a PDF of this bibliography, or you have any questions or comments, please contact Angela Sponer at asponer1@hfhs.org. Click here to notify us of your published work.

Allergy

Fonseca W, Lucey K, Jang S, Fujimura KE, Rasky A, Ting HA, Petersen J, **Johnson CC**, Boushey HA, **Zoratti E**, Ownby DR, **Levine AM**, **Bobbit KR**, Lynch SV, and Lukacs NW. Lactobacillus johnsonii supplementation attenuates respiratory viral infection via metabolic reprogramming and immune cell modulation *Mucosal Immunol* 2017;PMID: 28295020. Article Request Form

Department of Pathology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Medicine, University of California San Francisco, San Francisco, California, USA.
Henry Ford Health System, Detroit, Michigan, USA.
Department of Pediatrics, Augusta University, Augusta, Georgia, USA.

Regulation of respiratory mucosal immunity by microbial-derived metabolites has been a proposed mechanism that may provide airway protection. Here we examine the effect of oral Lactobacillus johnsonii supplementation on metabolic and immune response dynamics during respiratory syncytial virus (RSV) infection. L. johnsonii supplementation reduced airway T helper type 2 cytokines and dendritic cell (DC) function, increased regulatory T cells, and was associated with a reprogrammed circulating metabolic environment, including docosahexanoic acid (DHA) enrichment. RSV-infected bone marrow-derived DCs (BMDCs) from L. johnsonii-supplemented mice had altered cytokine secretion, reduced expression of co-stimulatory molecules, and modified CD4+ T-cell cytokines. This was replicated upon co-incubation of wild-type BMDCs with either plasma from L. johnsonii-supplemented mice or DHA. Finally, airway transfer of BMDCs from L. johnsonii-supplemented mice or with wild-type derived BMDCs pretreated with plasma from L. johnsonii-supplemented mice reduced airway pathological responses to infection in recipient animals. Thus L. johnsonii supplementation mediates airway mucosal protection via immunomodulatory metabolites and altered immune function.Mucosal Immunology advance online publication 15 March 2017. doi:10.1038/mi.2017.13.

Allergy

Sitarik AR, **Bobbitt KR**, **Havstad SL**, Fujimura KE, **Levin AM**, **Zoratti EM**, **Kim H**, **Woodcroft KJ**, **Wegienka G**, Ownby DR, **Joseph CL**, Lynch SV, and **Johnson CC**. Breast milk tgfbeta is associated with neonatal gut microbial composition *J Pediatr Gastroenterol Nutr* 2017;PMID: 28362692. Full Text

*Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA daggerDivision of Gastroenterology, University of California, San Francisco, California, USA double daggerDivision of Allergy and Immunology, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA section signDepartment of Pediatrics, Georgia Regents University, Augusta, Georgia, USA.

OBJECTIVES: Breast milk is a complex bioactive fluid that varies across numerous maternal and environmental conditions. While breastfeeding is known to impact neonatal gut microbiome, the milk components responsible for this effect are not well-characterized. Given the wide range of immunological activity breast milk cytokines engage in, we investigated three essential breast milk cytokines and their association with early life gut microbiota. METHODS: A total of 52 maternal-child pairs were drawn from a racially diverse birth cohort based in Detroit, Michigan. Breast milk and neonatal stool specimens were collected at 1-month postpartum. Breast milk TGFbeta1, TGFbeta2, and IL-10 were assayed using ELISAs, while neonatal gut microbiome was profiled using 16S rRNA sequencing. RESULTS:

Individually, immunomodulators TGFbeta1 and TGFbeta2 were significantly associated with neonatal gut microbial composition (R = 0.024, p = 0.041; R = 0.026, p = 0.012, respectively) and increased richness, evenness, and diversity, but IL-10 was not. However, the effects of TGFbeta1 and TGFbeta2 were not independent of one another, and the effect of TGFbeta2 was stronger than that of TGFbeta1. Higher levels of TGFbeta2 was associated with the increased relative abundance of several bacteria, including members of Streptococcaceae and Ruminococcaceae, and lower relative abundance of distinct Staphylococcaceae taxa. CONCLUSIONS: Breast milk TGFbeta concentration explains a portion of variability in gut bacterial microbiota composition among breastfed neonates. Whether TGFbeta acts in isolation or jointly with other bioactive components to alter bacterial composition requires further investigation. These findings contribute to an increased understanding of how breastfeeding affects the gut microbiome-and potentially immune development-in early life.

Anesthesiology
McCormick ZL, DeFrancesch F, **Loomba V**, Moradian M, Bathina R, and Rappard G. Diagnostic value, prognostic value, and safety of provocation discography *Pain Med* 2017;PMID: 28340253. Full Text

Department of Orthopaedic Surgery, University of California, San Francisco, California.
Interventional Spine Specialists, Kenner, Louisiana.
Henry Ford Health System, Detroit, Michigan.
Risser Orthopaedic Group, Pasadena, California.
Aurora Pain Clinic, Aurora, Illinois.
Los Angeles Minimally Invasive Spine Institute, Los Angeles, California, USA.

Anesthesiology
Walha S, and **Penning D**. Spurious hypoxemia during craniotomy *J Neurosurg Anesthesiol* 2017;PMID: 28288035. Full Text

*Department of Anesthesiology University of Colorado School of Medicine, Denver, CO daggerDepartment of Anesthesiology, Henry Ford Health System, Detroit, MI.

Behavioral Health
Rossom RC, Coleman KJ, **Ahmedani BK**, Beck A, Johnson E, Oliver M, and Simon GE. Suicidal ideation reported on the PHQ9 and risk of suicidal behavior across age groups *J Affect Disord* 2017; 215:77-84. PMID: 28319695. Full Text

HealthPartners Institute, Minneapolis, MN, United States. Electronic address: Rebecca.C.Rossom@HealthPartners.com.
Kaiser Permanente Southern California Department of Research and Evaluation, Pasadena, CA, United States.
Henry Ford Health System, Behavioral Health Services and Center for Health Policy and Health Services Research, Detroit, MI, United States.
Kaiser Permanente Colorado Institute for Health Research, Denver, CO, United States.
Kaiser Permanente Washington Health Research Institute, Seattle, WA, United States.

OBJECTIVE: The Joint Commission recommends all patients be screened for suicide. However, differences in suicide attempt and death rates may affect how well tools predict risk across age groups. Our objective was to determine whether item 9 of the Patient Health Questionnaire (PHQ9) predicts risk for suicide attempts and deaths across age groups. METHODS: PHQ9s completed by adult outpatients treated for mental health conditions in 2010-2012 at four Mental Health Research Network-affiliated healthcare systems were used to measure depression severity and suicidal ideation. Suicide attempts were identified via ICD-9 codes and suicide deaths via ICD-10 codes and state death certificates. RESULTS: In all, 939,268PHQ9s were completed by 297,290 outpatients. Compared to those without, those with nearly daily suicidal ideation were 5-to-8 times more likely to attempt suicide and 3-to-11times more likely to die by suicide within 30 days, and 2-to-4times more likely to attempt suicide and 2-to-6 times more likely to die by suicide within 365 days. The increased risk of suicide death for those with any level of suicidal ideation persisted over two years. The relationships between suicide thoughts and attempts and deaths were similar across age groups. LIMITATIONS: Our sample was limited to outpatients completing a PHQ9 and relied on pre-existing clinical and administrative data. CONCLUSIONS: Suicidal ideation reported on the PHQ9 was a robust predictor of suicide attempts and deaths regardless of age, and this increased risk persisted for two years. Healthcare systems should address both the immediate and sustained risk for suicide for patients of all ages.

Cardiology / Cardiovascular Research

Ahmed HM, **Al-Mallah MH**, **Keteyian SJ**, **Brawner CA**, **Ehrman JK**, Zhao D, Guallar E, Blaha MJ, and Michos ED. Sex-specific maximum predicted heart rate and its prognosis for mortality and mi *Med Sci Sports Exerc* 2017;PMID: 28350713. Full Text

1Preventive Cardiology and Rehabilitation, Cleveland Clinic, Cleveland, OH; 2Ciccarone Center for the Prevention of Heart Disease, Johns Hopkins University School of Medicine, Baltimore, MD; 3Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI; 4King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King Abdulaziz Cardiac Center, Ministry of National Guard, Health Affairs, Kingdom of Saudi Arabia; 5Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

PURPOSE: Maximum predicted heart rate (MPHR) is traditionally calculated by (220-Age). However, this formula's validity has been questioned in women. The purpose of this study was to derive sex-specific formulas for MPHR in a clinical population, and compare their prognostic significance to the traditional formula. METHODS: This was a retrospective cohort of adults referred for exercise treadmill testing (ETT) between 1991 and 2009. Peak heart rate versus age was plotted by sex, and linear regression analysis was used to derive sex-specific MPHR formulas. Cox models were used to calculate risk of death and MI based on attainment of 85% MPHR using both formulas. RESULTS: Of 31,090 patients (mean age 55+/-10 years), there were 2,824 deaths over mean 11+/-5 years. MPHR was best estimated by 197-0.8xAge for women and 204-0.9xAge for men (P-interaction<0.001). Compared to the sex-specific formulas, the traditional formula overestimated peak heart rate by mean 12+/-2 bpm in women and 11+/-1 bpm in men. There were 1,868 patients (6%) who achieved target heart rate using the sex-specific formulas but not with the traditional formula. Achievement of >/=85% MPHR was similarly associated with lower risk of death [adjusted hazard ratio 0.76 (95% confidence interval 0.60-0.97) vs. 0.75 (0.62-0.90)] and MI [0.71 (0.47-1.06) vs. 0.79 (0.57-1.10)] for the sex-specific vs. traditional formula. CONCLUSIONS: In patients referred for ETT, sex-specific formulas more accurately estimated peak heart rate than the traditional MPHR formula, reclassified 6% of stress tests from inadequate to adequate, and were similarly associated with risk of MI and death.

Cardiology / Cardiovascular Research

Basir MB, Karatasakis A, **Alqarqaz M**, Danek B, Rangan BV, Brilakis ES, **Kim H**, **O'Neill WW**, and **Alaswad K**. Further validation of the hybrid algorithm for CTO PCI; difficult lesions, same success *Cardiovasc Revasc Med* 2017;PMID: 28314674. Full Text

Henry Ford Hospital and Wayne State University, Detroit, MI.
VA North Texas Healthcare System and UT Southwestern Medical Center, Dallas, TX.
Henry Ford Hospital and Wayne State University, Detroit, MI. Electronic address: kalaswa1@hfhs.org.

OBJECTIVES: To evaluate the success rates and outcome of the hybrid algorithm for chronic total occlusion (CTO) percutaneous coronary intervention (PCI) by a single operator in two different clinical settings. METHODS: We compared 279 consecutive CTO PCIs performed by a single, high-volume operator using the hybrid algorithm in two different clinical settings. Data were collected through the PROGRESS CTO Registry. We compared 145 interventions performed in a community program (cohort A) with 134 interventions performed in a referral center (cohort B). RESULTS: Patient in cohort B had more complex lesions with higher J-CTO (3.0 vs. 3.41; p<0.001) and Progress CTO (1.5 vs.1.8, P=0.003) scores, more moderate to severe tortuosity (38% vs. 64%; p<0.001), longer total occlusion length (25 vs. 40mm; p<0.001) and higher prevalence of prior failed CTO PCI attempts (15% vs. 35%; p=0.001). Both technical (95% vs. 91%; p=0.266) and procedural (94% vs. 88%; p=0.088) success rates were similar between the two cohorts despite significantly different lesion complexity. Overall major adverse cardiovascular events were higher in cohort B (1.4% vs. 7.8%; p=0.012) without any significant difference in mortality (0.7% vs. 2.3%, p=0.351). CONCLUSIONS: In spite of higher lesion complexity in the setting of a quaternary-care referral center, use of the hybrid algorithm for CTO PCI enabled similarly high technical and procedural success rates as compared with those previously achieved by the same operator in a community-based program at the expense of a higher rate of MACE.

Cardiology / Cardiovascular Research

Butler J, Hamo CE, Udelson JE, O'Connor C, **Sabbah HN**, Metra M, Shah SJ, Kitzman DW, Teerlink JR, Bernstein HS, Brooks G, Depre C, DeSouza MM, Dinh W, Donovan M, Frische-Danielson R, Frost RJ, Garza D, Gohring UM, Hellawell J, Hsia J, Ishihara S, Kay-Mugford P, Koglin J, Kozinn M, Larson CJ, Mayo M, Gan LM, Mugnier P, Mushonga S, Roessig L, Russo C, Salsali A, Satler C, Shi V, Ticho B, van der Laan M, Yancy C, Stockbridge N, and Gheorghiade M. Reassessing Phase II Heart Failure Clinical Trials: Consensus Recommendations *Circ Heart Fail* 2017; 10(4)PMID: 28356300. Full Text

From the Department of Medicine, Stony Brook University, NY (J.B., C.E.H.); Division of Cardiology and the CardioVascular Center, Tufts Medical Center, Boston, MA (J.E.U.); Division of Cardiology, Inova Heart & Vascular Institute, Falls Church, VA (C.O'C.); Department of Medicine, Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI (H.N.S.); Division of Cardiology, University of Brescia and Civil Hospital, Italy (M.M.); Division of Cardiology, Northwestern University Feinberg School of Medicine, Chicago, IL (S.J.S., C.Y.); Section on Cardiovascular Medicine, Wake Forest School of Medicine, Winston-Salem, NC (D.W.K.); Division of Cardiology, University of California San Francisco (J.R.T.); Merck & Co., Kenilworth, NJ (H.S.B., J.K.); Gilead Sciences, Foster City, CA (G.B., J.H., C.S.); Amgen Inc., Thousand Oaks, CA (C.D., M.K.); Bristol-Myers Squibb, Princeton, NJ (M.M.D., M.D., R.J.F., P.M., S.M., C.R.); Bayer, Wuppertal, Germany (W.D., M.v.d.L.); Department of Cardiology, HELIOS Clinic Wuppertal, University Hospital Witten/Herdecke, Germany (W.D.); AstraZeneca, Gaithersburg, MD (R.F.-D., J.H., L.-M.G.); AstraZeneca, Gothenburg, Sweden (R.F.-D., J.H., L.-M.G.); Relypsa Inc., Redwood City, CA (D.G., M.M.); Vifor Pharma, Opfikon, Switzerland (U.-M.G.); Department of Cardiology, Nippon Medical School Musashi-Kosugi Hospital, Kawasaki, Japan (S.I.); Novartis Pharmaceuticals Inc., East Hanover, NJ (P.K.-M., V.S.); Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA (C.J.L.); Bayer Pharma AG, Wuppertal, Germany (L.R.); Cardiology Division, Columbia University Medical Center, New York, NY (C.R.); Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT (A.S.); Moderna Therapeutics, Cambridge, MA (B.T.); Division of Cardiovascular and Renal Products, United States Food and Drug Administration, Silver Spring, MD (N.S.); Center for Cardiovascular Innovation, Feinberg School of Medicine, Northwestern University, Chicago, IL (M.G.). javed.butler@stonybrook.edu.
From the Department of Medicine, Stony Brook University, NY (J.B., C.E.H.); Division of Cardiology and the CardioVascular Center, Tufts Medical Center, Boston, MA (J.E.U.); Division of Cardiology, Inova Heart & Vascular Institute, Falls Church, VA (C.O'C.); Department of Medicine, Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, MI (H.N.S.); Division of Cardiology, University of Brescia and Civil Hospital, Italy (M.M.); Division of Cardiology, Northwestern University Feinberg School of Medicine, Chicago, IL (S.J.S., C.Y.); Section on Cardiovascular Medicine, Wake Forest School of Medicine, Winston-Salem, NC (D.W.K.); Division of Cardiology, University of California San Francisco (J.R.T.); Merck & Co., Kenilworth, NJ (H.S.B., J.K.); Gilead Sciences, Foster City, CA (G.B., J.H., C.S.); Amgen Inc., Thousand Oaks, CA (C.D., M.K.); Bristol-Myers Squibb, Princeton, NJ (M.M.D., M.D., R.J.F., P.M., S.M., C.R.); Bayer, Wuppertal, Germany (W.D., M.v.d.L.); Department of Cardiology, HELIOS Clinic Wuppertal, University Hospital Witten/Herdecke, Germany (W.D.); AstraZeneca, Gaithersburg, MD (R.F.-D., J.H., L.-M.G.); AstraZeneca, Gothenburg, Sweden (R.F.-D., J.H., L.-M.G.); Relypsa Inc., Redwood City, CA (D.G., M.M.); Vifor Pharma, Opfikon, Switzerland (U.-M.G.); Department of Cardiology, Nippon Medical School Musashi-Kosugi Hospital, Kawasaki, Japan (S.I.); Novartis Pharmaceuticals Inc., East Hanover, NJ (P.K.-M., V.S.); Sanford Burnham Prebys Medical Discovery Institute, La Jolla, CA (C.J.L.); Bayer Pharma AG, Wuppertal, Germany (L.R.); Cardiology Division, Columbia University Medical Center, New York, NY (C.R.); Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, CT (A.S.); Moderna Therapeutics, Cambridge, MA (B.T.); Division of Cardiovascular and Renal Products, United States Food and Drug Administration, Silver Spring, MD (N.S.); Center for Cardiovascular Innovation, Feinberg School of Medicine, Northwestern University, Chicago, IL (M.G.).

The increasing burden and the continued suboptimal outcomes for patients with heart failure underlines the importance of continued research to develop novel therapeutics for this disorder. This can only be accomplished with successful translation of basic science discoveries into direct human application through effective clinical trial design and execution that results in a substantially improved clinical course and outcomes. In this respect, phase II clinical trials play a pivotal role in determining which of the multitude of potential basic science discoveries should move to the large and expansive registration trials in humans. A critical examination of the phase II trials in heart failure reveals multiple shortcomings in their concept, design, execution, and interpretation. To further a dialogue on the challenges and potential for improvement and the role of phase II trials in patients with heart failure, the Food and Drug Administration facilitated a meeting on October 17, 2016, represented by clinicians, researchers, industry members, and regulators. This document summarizes the discussion from this meeting and provides key recommendations for future directions.

Cardiology / Cardiovascular Research

Deseive S, Shaw LJ, Min JK, Achenbach S, Andreini D, **Al-Mallah MH**, Berman DS, Budoff MJ, Callister TQ, Cademartiri F, Chang HJ, Chinnaiyan K, Chow BJ, Cury RC, DeLago A, Dunning AM, Feuchtner G, Kaufmann PA, Kim YJ, Leipsic J, Marques H, Maffei E, Pontone G, Raff G, Rubinshtein R, Villines TC, Hausleiter J, and Hadamitzky M. Improved 5-year prediction of all-cause mortality by coronary CT angiography applying the CONFIRM score *Eur Heart J Cardiovasc Imaging* 2017; 18(3):286-293. PMID: 28363203. Full Text

Medizinische Klinik I der Ludwig-Maximilians-Universitat Munchen, Munich, Germany.
Division of Cardiology, Emory University School of Medicine, Atlanta, GA, USA.
Department of Radiology, New York Presbyterian Hospital and the Weill Cornell Medical College, New York, NY, USA.

Department of Medicine, University of Erlangen, Erlangen, Germany.
Department of Clinical Sciences and Community Health, University of Milan, Centro Cardiologico, Monzino, IRCCS Milan, Milano, Italy.
Department of Medicine, Wayne State University, Henry Ford Hospital, Detroit, MI, USA.
Department of Imaging, Cedars Sinai Medical Center, Los Angeles, CA, USA.
Department of Medicine, Harbor UCLA Medical Center, Los Angeles, CA, USA.
Tennessee Heart and Vascular Institute, Hendersonville, TN, USA.
Cardiovascular Imaging Unit, Giovanni XXIII Hospital, Monastier, Treviso, Italy.
Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands.
Division of Cardiology, Severance Cardiovascular Hospital and Severance Biomedical Science Institute, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea.
William Beaumont Hospital, Royal Oaks, MI, USA.
Department of Medicine and Radiology, University of Ottawa, Ottawa, ON, Canada.
Baptist Cardiac and Vascular Institute, Miami, FL, USA.
Capitol Cardiology Associates, Albany, NY, USA.
Duke Clinical Research Institute, Durham, NC, USA.
Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria.
University Hospital, Zurich, Switzerland.
Seoul National University Hospital, Seoul, South Korea.
Department of Medicine and Radiology, University of British Columbia, Vancouver, BC, Canada.
Hospital da Luz, Lisbon, Portugal.
Department of Cardiology at the Lady Davis Carmel Medical Center, The Ruth and Bruce Rappaport School of Medicine, Technion-Israel, Institute of Technology, Haifa, Israel.
Department of Medicine, Walter Reed Medical Center, Washington, DC, USA.
Division of Radiology, Deutsches Herzzentrum Muenchen, Lazarettstr. 36, Munich 80636, Germany.

Aims: To investigate the long-term performance of the CONFIRM score for prediction of all-cause mortality in a large patient cohort undergoing coronary computed tomography angiography (CCTA). Methods and results: Patients with a 5-year follow-up from the international multicentre CONFIRM registry were included. The primary endpoint was all-cause mortality. The predictive value of the CONFIRM score over clinical risk scores (Morise, Framingham, and NCEP ATP III score) was studied in the entire patient population as well as in subgroups. Improvement in risk prediction and patient reclassification were assessed using categorical net reclassification index (NRI) and integrated discrimination improvement (IDI). During a median follow-up period of 5.3 years, 982 (6.5%) of 15 219 patients died. The CONFIRM score outperformed the prognostic value of the studied three clinical risk scores (c-indices: CONFIRM score 0.696, NCEP ATP III score 0.675, Framingham score 0.610, Morise score 0.606; c-index for improvement CONFIRM score vs. NCEP ATP III score 0.650, P < 0.0001). Application of the CONFIRM score allowed reclassification of 34% of patients when compared with the NCEP ATP III score, which was the best clinical risk score. Reclassification was significant as revealed by categorical NRI (0.06 with 95% CI 0.02 and 0.10, P = 0.005) and IDI (0.013 with 95% CI 0.01 and 0.015, P < 0.001). Subgroup analysis revealed a comparable performance in a variety of patient subgroups. Conclusions: The CONFIRM score permits a significantly improved prediction of mortality over clinical risk scores for >5 years after CCTA. These findings are consistent in a large variety of patient subgroups.

Cardiology / Cardiovascular Research

Ehrman JK, **Brawner CA**, **Al-Mallah MH**, Qureshi WT, Blaha MJ, and Keteyian SJ. Cardiorespiratory fitness change and mortality risk among black and white patients: Henry ford exercise testing (fit) project *Am J Med* 2017;PMID: 28344150. Full Text

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan. Electronic address: jehrman1@hfhs.org.
Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan.
Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan; King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King Abdul-Aziz Cardiac Center, King Abdul-Aziz Medical City, Riyadh, Saudi Arabia.
Cardiology, Wake Forest University, Winston-Salem, North Carolina.
Ciccarone Center for the Prevention of Heart Disease, Johns Hopkins Medicine, Baltimore, Maryland.

BACKGROUND: Little is known about the relationship of change in cardiorespiratory fitness and mortality risk in Black patients. This study assessed change in cardiorespiratory fitness and its association with all-cause mortality risk in Black and White patients. METHODS: This is a retrospective, longitudinal, observational cohort study of 13,345 patients (age = 55 +/- 11 y; 39% women; 26% Black) who completed two exercise tests, at least 12 months apart at Henry Ford Hospital, Detroit MI. All-cause mortality was identified through April 2013. Data were analyzed in

2015-16 using Cox regression to calculate hazard ratios (HR) for risk of mortality associated with change in sex specific cardiorespiratory fitness. RESULTS: Mean time between the tests was 3.4 y (IQR 1.9-5.6 y). During 9.1 y (IQR 6.3-11.6 y) follow-up there were 1,931 (14%) deaths (16.5% black, 13.7% white). For both races change in fitness from Low to the Intermediate/High category resulted in a significant reduction of death risk (HR=0.65 [95% CI, 0.49-0.87] for Black; HR=0.41 [95% CI, 0.34-0.51] for White). Each 1 MET increase was associated with a reduced mortality risk in Black (HR=0.84 [95% CI, 0.81-0.89]) and White (HR=0.87 [95% CI, 0.82-0.86]) patients. There was no interaction by race. CONCLUSIONS: Among Black and White patients change in cardiorespiratory fitness from Low to Intermediate/High fitness was associated with a 35% and 59% lower risk of all-cause mortality, respectively.

Cardiology / Cardiovascular Research

Frisoli TM, **Jain T**, Swadia T, **Hong X**, and Guerrero M. Cardiac tamponade due to pyopneumopericardium from malignant bronchopericardial fistula *Neth Heart J* 2017;PMID: 28349347. Article Request Form

Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA. tfrisol1@hfhs.org.
Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Cardiology, Michigan Heart, St Joseph Mercy Health System, Livonia, MI, USA.
Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Cardiology, Evanston Hospital, North Shore University Health System, Evanston, IL, USA.

Cardiology / Cardiovascular Research

Greenbaum AB, and **Frisoli TM**. Surgical paravalvular leak closure: No more second chances *JACC Cardiovasc Interv* 2017; 10(5):508-509. PMID: 28279318. Full Text

Center for Structural Heart Disease, Henry Ford Hospital, Detroit, Michigan. Electronic address: agreenb1@hfhs.org.

Cardiology / Cardiovascular Research

Guerrero M, **Wang DD**, Himbert D, Urena M, Pursnani A, Kaddissi G, Iyer V, Salinger M, Chakravarty T, **Greenbaum A**, Makkar R, Vahanian A, Feldman T, and **O'Neill W**. Short-term results of alcohol septal ablation as a bail-out strategy to treat severe left ventricular outflow tract obstruction after transcatheter mitral valve replacement in patients with severe mitral annular calcification *Catheter Cardiovasc Interv* 2017;PMID: 28266162. Full Text

Department of Medicine, Division of Cardiology, Evanston Hospital, Evanston, Illinois.
Department of Medicine Division of Cardiology, Henry Ford Hospital, Detroit, Michigan.
Cardiology Department, Bichat-Claude Bernard Hospital, Paris, France.
Division of Cardiology, Cooper University Hospital, Camden, New Jersey.
Division of Cardiology, Buffalo General Medical Center, Buffalo New York.
Department of Medicine, Division of Cardiology, Cedars Sinai Medical Center, Los Angeles, California.

OBJECTIVES: To evaluate the outcomes of the early experience of percutaneous alcohol septal ablation in patients with severe left ventricular outflow tract (LVOT) obstruction post transcatheter mitral valve replacement (TMVR). BACKGROUND: Severe LVOT obstruction with hemodynamic compromise is a complication of TMVR associated with high mortality. Percutaneous alcohol septal ablation has recently been described as a therapeutic option in this setting. METHODS: Multicenter retrospective review of clinical outcomes of patients undergoing alcohol septal ablation to treat LVOT obstruction after TMVR for severe mitral stenosis with severe mitral annular calcification. RESULTS: Six patients underwent percutaneous alcohol septal ablation to treat LVOT obstruction post-TMVR at six different centers. Five patients had immediate significant reduction in LVOT obstruction with improvement in hemodynamic status while one had persistent LVOT gradient but hemodynamic instability improved. The first patient died on postoperative day 4 due to complete heart block. One patient had initial improvement in LVOT gradient with recurrence on postoperative day 1 thought to be secondary to septal edema, was treated with surgical removal of the transcatheter valve and resection of the anterior mitral leaflet followed by transatrial TMVR and died 3 weeks later due to multi-organ failure. The remaining four patients improved clinically after alcohol septal ablation, were discharged from the hospital and were clinically stable at 30-day follow-up. CONCLUSIONS: Percutaneous alcohol ablation provides acute relief of TMVR-induced LVOT obstruction when septal hypertrophy is a contributing factor. This may be a safer alternative to bail-out surgery in this extremely high-risk patient population. (c) 2017 Wiley Periodicals, Inc.

Cardiology / Cardiovascular Research

Kramer F, **Sabbah HN**, Januzzi JJ, Zannad F, Peter van Tintelen J, Schelbert EB, Kim RJ, Milting H, Vonk R, Neudeck B, Clark R, Witte K, Dinh W, Pieske B, Butler J, and Gheorghiade M. Redefining the role of biomarkers in heart failure trials: expert consensus document *Heart Fail Rev* 2017;PMID: 28332132. Full Text

BAYER AG, Experimental Medicine Cardiovascular/Hematology, Aprather Weg 18a, 42133, Wuppertal, Germany. frank.kramer@bayer.com.
Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI, 48202, USA.
Cardiology Division, Massachusetts General Hospital; Clinical Trial Design, Baim Institute for Clinical Research, Boston, MA, USA.
Inserm Clinical Investigation Center 1403, Universite de Lorraine, CHU de Nancy, Institut Lorrain du Coeur et des Vaisseaux CHU and University de Lorraine, Nancy, France.
Department of Clinical Genetics, University of Amsterdam, Academic Medical Center, Amsterdam, The Netherlands.
UPMC Cardiovascular Magnetic Resonance Center, University of Pittsburgh, Pittsburgh, PA, USA.
Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, NC, USA.
Heart and Diabetes Center NRW, University Clinics of the Ruhr University, Erich and Hanna Klessmann-Institute for Cardiovascular Research and Development, Bad Oeynhausen, Germany.
BAYER, Research & Clinical Sciences Statistics, Berlin, Germany.
Medtronic Diagnostics, 8200 Coral Sea Street, MVC43, Minneapolis, MN, 55112, USA.
Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds, UK.
BAYER AG, Experimental Medicine Cardiovascular/Hematology, Aprather Weg 18a, 42133, Wuppertal, Germany.
Department of Internal Medicine and Cardiology, Charite University Medicine Berlin-Campus Virchow Klinikum, Augustenburger Platz 1, 13353, Berlin, Germany.
Department of Internal Medicine and Cardiology, German Heart Center Berlin, Augustenburger Platz 1, 13353, Berlin, Germany.
Berlin Institute of Health, Kapelle-Ufer 2, 10117, Berlin, Germany.
Division of Cardiology, Health Sciences Center, SUNY, T-16 Room 080, Stony Brook, NY, 11794, USA.
Center for Cardiovascular Innovation, Northwestern University Feinberg School of Medicine, 201 East Huron, Galter 3-150, Chicago, IL, 60611, USA.

Heart failure is a growing cardiovascular disease with significant epidemiological, clinical, and societal implications and represents a high unmet need. Strong efforts are currently underway by academic and industrial researchers to develop novel treatments for heart failure. Biomarkers play an important role in patient selection and monitoring in drug trials and in clinical management. The present review gives an overview of the role of available molecular, imaging, and device-derived digital biomarkers in heart failure drug development and highlights capabilities and limitations of biomarker use in this context.

Cardiology / Cardiovascular Research

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 *Am Heart J* 2017; 185:35-42. PMID: 28267473. Full Text

Heart and Vascular Institute, Henry Ford Hospital System, Detroit, MI.
King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King AbdulAziz Cardiac Center, Ministry of National Guard, Health Affairs, Riyadh, Kingdom of Saudi Arabia.
Wake Forest University, Winston Salem, NC.
Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, MD.
Heart and Vascular Institute, Henry Ford Hospital System, Detroit, MI; King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King AbdulAziz Cardiac Center, Ministry of National Guard, Health Affairs, Riyadh, Kingdom of Saudi Arabia. Electronic address: mouaz74@gmail.com.

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 / Cardiovascular Research

Lin J, Chudasama N, Hayashi Y, Hawk C, Ramnauth SD, Wong KY, Harxhi A, Onat D, Wakabayashi M, Uriel N, Jorde UP, LeJemtel TH, **Sabbah HN**, Demmer RT, and Colombo PC. Peripheral venous congestion causes time- and dose-dependent release of endothelin-1 in humans *Physiol Rep* 2017; 5(6)PMID: 28320895. Full Text

Columbia University Medical Center, New York, New York.
Tulane University School of Medicine, New Orleans, Louisiana.
Medicine, Henry Ford Hospital, Detroit, Michigan.
Columbia University Medical Center, New York, New York pcc2001@columbia.edu.

Endothelin-1 (ET-1) is a pivotal mediator of vasoconstriction and inflammation in congestive states such as heart failure (HF) and chronic kidney disease (CKD). Whether peripheral venous congestion (VC) increases plasma ET-1 at pressures commonly seen in HF and CKD patients is unknown. We seek to characterize whether peripheral VC promotes time- and dose-dependent increases in plasma ET-1 and whether these changes are sustained after decongestion. We used a randomized, cross-over design in 20 healthy subjects (age 30 +/- 7 years). To experimentally model VC, venous pressure was increased to either 15 or 30 mmHg (randomized at first visit) above baseline by inflating a cuff around the subject's dominant arm; the nondominant arm served as a noncongested control. We measured plasma ET-1 at baseline, after 20, 60 and 120 min of VC, and finally at 180 min (60 min after cuff release and decongestion). Plasma ET-1 progressively and significantly increased over 120 min in the congested arm relative to the control arm and to baseline values. This effect was dose-dependent: ET-1 increased by 45% and 100% at VC doses of 15 and 30 mmHg, respectively (P < 0.05), and declined after 60 min of decongestion though remaining significantly elevated compared to baseline. In summary, peripheral VC causes time- and dose-dependent increases in plasma ET-1. Of note, the lower dose of 15 mmHg (more clinically relevant to HF and CKD patients) was sufficient to raise ET-1. These findings support the potentially contributory, not merely consequential, role of VC in the pathophysiology of HF and CKD.

Cardiology / Cardiovascular Research

Luo N, Merrill P, Parikh KS, Whellan DJ, Pina IL, Fiuzat M, Kraus WE, Kitzman DW, **Keteyian SJ**, O'Connor CM, and Mentz RJ. Exercise training in patients with chronic heart failure and atrial fibrillation *J Am Coll Cardiol* 2017; 69(13):1683-1691. PMID: 28359513. Full Text

Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Duke Clinical Research Institute, Durham, North Carolina. Electronic address: nancy.luo@duke.edu.
Duke Clinical Research Institute, Durham, North Carolina.
Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Duke Clinical Research Institute, Durham, North Carolina.
Thomas Jefferson University, Philadelphia, Pennsylvania.
Montefiore-Einstein Medical Center, New York, New York.
Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina.
Wake Forest School of Medicine, Winston Salem, North Carolina.
Henry Ford Hospital, Detroit, Michigan.
Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Inova Heart and Vascular Institute, Falls Church, Virginia.

BACKGROUND: The safety and efficacy of aerobic exercise in heart failure (HF) patients with atrial fibrillation (AF) has not been well evaluated. OBJECTIVES: This study examined whether outcomes with exercise training in HF vary according to AF status. METHODS: HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) randomized 2,331 ambulatory HF patients with ejection fraction </=35% to exercise training or usual care. We examined clinical characteristics and outcomes (mortality/hospitalization) by baseline AF status (past history of AF or AF on baseline electrocardiogram vs. no AF) using adjusted Cox models and explored an interaction with exercise training. We assessed post-randomization AF events diagnosed via hospitalizations for AF and reports of serious arrhythmia caused by AF. RESULTS: Of 2,292 patients with baseline rhythm data, 382 (17%) had AF, 1,602 (70%) had sinus rhythm, and 308 (13%) had "other" rhythm. Patients with AF were older and had lower peak

Vo2. Over a median follow-up of 2.6 years, AF was associated with a 24% per year higher rate of mortality/hospitalization (hazard ratio [HR]: 1.53; 95% confidence interval [CI]: 1.34 to 1.74; p < 0.001) in unadjusted analysis; this did not remain significant after adjustment (HR: 1.15; 95% CI: 0.98 to 1.35; p = 0.09). There was no significant difference in AF event rates by randomized treatment assignment in the overall population or by baseline AF status (all p > 0.10). There was no interaction between AF and exercise training on measures of functional status or clinical outcomes (all p > 0.10). CONCLUSIONS: AF in patients with chronic HF was associated with older age, reduced exercise capacity at baseline, and a higher overall rate of clinical events, but not a differential response to exercise training for clinical outcomes or changes in exercise capacity. (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training [HF-ACTION]; NCT00047437).

Cardiology / Cardiovascular Research

Naoum C, Berman DS, Ahmadi A, Blanke P, Gransar H, Narula J, Shaw LJ, Kritharides L, Achenbach S, **Al-Mallah MH**, Andreini D, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, Chinnaiyan K, Chow B, Cury RC, DeLago A, Dunning A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Maffei E, Marquez H, Pontone G, Raff G, Rubinshtein R, Villines TC, Min J, and Leipsic J. Predictive value of age- and sex-specific nomograms of global plaque burden on coronary computed tomography angiography for major cardiac events *Circ Cardiovasc Imaging* 2017; 10(3)PMID: 28292858. Full Text

From the Department of Medicine and Radiology, University of British Columbia, Vancouver, Canada (C.N., P.B., J.L.); Department of Imaging, Cedars Sinai Medical Center, Los Angeles, CA (D.S.B., H.G.); Department of Cardiology, Mount Sinai Hospital Medical Centre, New York, NY (A.A., J.N.); Division of Cardiology, Emory University School of Medicine, Atlanta, GA (L.J.S.); Department of Cardiology, Concord Hospital and The University of Sydney, New South Wales, Australia (L.K.); Department of Medicine, University of Erlangen, Germany (S.A.); Department of Medicine, Wayne State University, Henry Ford Hospital, Detroit, MI (M.H.A.-M.); Department of Clinical Sciences and Community Health, University of Milan, Centro Cardiologico Monzino, IRCCS Milan, Italy (D.A., G.P.); Department of Medicine, Harbor University of California Los Angeles Medical Center (M.J.B.); Cardiovascular Imaging Unit, Giovanni XXIII Hospital, Monastier, Treviso, Italy (F.C., E.M.); Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands (F.C., E.M.); Tennessee Heart and Vascular Institute, Hendersonville (T.Q.C.); Division of Cardiology, Severance Cardiovascular Hospital and Severance Biomedical Science Institute, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea (H.-J.C.); William Beaumont Hospital, Royal Oaks, MI (K.C., G.R.); Department of Medicine and Radiology, University of Ottawa, Ontario, Canada (B.C.); Baptist Cardiac and Vascular Institute, Miami, FL (R.C.C.); Capitol Cardiology Associates, Albany, NY (A.D.); Duke Clinical Research Institute, Durham, NC (A.D.); Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria (G.F.); Division of Cardiology, Deutsches Herzzentrum Munchen, Munich, Germany (M.H., J.H.); Department of Nuclear Medicine, University Hospital, Zurich, Switzerland (P.A.K.); Seoul National University Hospital, South Korea (Y.-J.K.); Department of Surgery, Curry Cabral Hospital, Lisbon, Portugal (H.M.); Department of Cardiology at the Lady Davis Carmel Medical Center, The Ruth and Bruce Rappaport School of Medicine, Technion-Israel Institute of Technology, Haifa, (R.R.); Department of Medicine, Walter Reed Medical Center, Washington, DC (T.C.V.); and Department of Radiology, New York-Presbyterian Hospital and the Weill Cornell Medical College, New York (J.M.).
From the Department of Medicine and Radiology, University of British Columbia, Vancouver, Canada (C.N., P.B., J.L.); Department of Imaging, Cedars Sinai Medical Center, Los Angeles, CA (D.S.B., H.G.); Department of Cardiology, Mount Sinai Hospital Medical Centre, New York, NY (A.A., J.N.); Division of Cardiology, Emory University School of Medicine, Atlanta, GA (L.J.S.); Department of Cardiology, Concord Hospital and The University of Sydney, New South Wales, Australia (L.K.); Department of Medicine, University of Erlangen, Germany (S.A.); Department of Medicine, Wayne State University, Henry Ford Hospital, Detroit, MI (M.H.A.-M.); Department of Clinical Sciences and Community Health, University of Milan, Centro Cardiologico Monzino, IRCCS Milan, Italy (D.A., G.P.); Department of Medicine, Harbor University of California Los Angeles Medical Center (M.J.B.); Cardiovascular Imaging Unit, Giovanni XXIII Hospital, Monastier, Treviso, Italy (F.C., E.M.); Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands (F.C., E.M.); Tennessee Heart and Vascular Institute, Hendersonville (T.Q.C.); Division of Cardiology, Severance Cardiovascular Hospital and Severance Biomedical Science Institute, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea (H.-J.C.); William Beaumont Hospital, Royal Oaks, MI (K.C., G.R.); Department of Medicine and Radiology, University of Ottawa, Ontario, Canada (B.C.); Baptist Cardiac and Vascular Institute, Miami, FL (R.C.C.); Capitol Cardiology Associates, Albany, NY (A.D.); Duke Clinical Research Institute, Durham, NC (A.D.); Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria (G.F.); Division of Cardiology, Deutsches Herzzentrum Munchen, Munich, Germany (M.H., J.H.); Department of Nuclear Medicine, University Hospital, Zurich, Switzerland (P.A.K.); Seoul National University Hospital, South Korea (Y.-J.K.); Department of Surgery, Curry Cabral Hospital, Lisbon, Portugal (H.M.); Department of Cardiology at the Lady Davis Carmel Medical Center, The Ruth and Bruce Rappaport School of Medicine, Technion-Israel Institute of Technology, Haifa, (R.R.); Department of Medicine, Walter Reed Medical Center, Washington, DC (T.C.V.); and Department of Radiology, New York-Presbyterian Hospital and the Weill Cornell Medical College, New York (J.M.).
jleipsic@providencehealth.bc.ca.

BACKGROUND: Age-adjusted coronary artery disease (CAD) burden identified on coronary computed tomography angiography predicts major adverse cardiovascular event (MACE) risk; however, it seldom contributes to clinical decision making because of a lack of nomographic data. We aimed to develop clinically pragmatic age- and sex-specific nomograms of CAD burden using coronary computed tomography angiography and to validate their prognostic use. METHODS AND RESULTS: Patients prospectively enrolled in phase I of the CONFIRM registry (Coronary CT Angiography Evaluation for Clinical Outcomes) were included (derivation cohort: n=21,132; 46% female) to develop CAD nomograms based on age-sex percentiles of segment involvement score (SIS) at each year of life (40-79 years). The relationship between SIS age-sex percentiles (SIS%) and MACE (all-cause death, myocardial infarction, unstable angina, and late revascularization) was tested in a nonoverlapping validation cohort (phase II, CONFIRM registry; n=3030, 44% female) by stratifying patients into 3 SIS% groups (</=50th, 51-75th, and >75th) and comparing annualized MACE rates and time to MACE using multivariable Cox proportional hazards models adjusting for Framingham risk and chest pain typicality. Age-sex percentiles were well fitted to second-order polynomial curves (men: R2=0.86+/-0.12; women: R2=0.86+/-0.14). Using the nomograms, there were 1576, 965, and 489 patients, respectively, in the </=50th, 51-75th, and >75th SIS% groups. Annualized event rates were higher among patients with greater CAD burden (2.1% [95% confidence interval: 1.7%-2.7%], 3.9% [95% confidence interval: 3.0%-5.1%], and 7.2% [95% confidence interval: 5.4%-9.6%] in </=50th, 51-75th, and >75th SIS% groups, respectively; P<0.001). Adjusted MACE risk was significantly increased among patients in SIS% groups above the median compared with patients below the median (hazard ratio [95% confidence interval]: 1.9 [1.3-2.8] for 51-75th SIS% group and 3.4 [2.3-5.0] for >75th SIS% group; P<0.01 for both). CONCLUSIONS: We have developed clinically pragmatic age- and sex-specific nomograms of CAD prevalence using coronary computed tomography angiography findings. Global plaque burden measured using SIS% is predictive of cardiac events independent of traditional risk assessment. CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT01443637.

Cardiology / Cardiovascular Research

Sukul D, Seth M, Schreiber T, **Khandelwal A**, Cannon LA, LaLonde TA, and Gurm HS. The comparative safety and effectiveness of bivalirudin versus heparin monotherapy in patients on dialysis undergoing percutaneous coronary intervention: Insights from the Blue Cross Blue Shield of Michigan cardiovascular consortium *Catheter Cardiovasc Interv* 2017;PMID: 28303632. Full Text

Department of Internal Medicine, Division of Cardiovascular Medicine, University of Michigan, Ann Arbor, Michigan.
Detroit Medical Center-Cardiovascular Institute, Detroit, Michigan.
Division of Cardiology, Henry Ford Health System, Detroit, Michigan.
McLaren-Northern Michigan Regional Hospital, Petoskey, Michigan.
Department of Cardiovascular Medicine, St. John Hospital and Medical Center, Detroit, Michigan.
Cardiovascular Medicine, VA Ann Arbor Healthcare System, Ann Arbor, Michigan.

BACKGROUND: Dialysis patients are at a higher risk of bleeding after percutaneous coronary intervention (PCI); however, due to their exclusion from randomized clinical trials, the optimal antithrombotic regimen for this population remains unknown. We sought to evaluate the comparative safety and effectiveness of bivalirudin monotherapy versus unfractionated heparin (UFH) monotherapy in dialysis patients undergoing PCI. METHODS: We included dialysis patients who underwent PCI in a multicenter registry between January 2010 and September 2015 at 47 Michigan hospitals. We compared in-hospital outcomes between bivalirudin versus UFH; excluding those treated with glycoprotein IIb/IIIa inhibitors. Optimal full matching was used to account for the nonrandom use of these drugs. RESULTS: Of 177,963 patients who underwent PCI, 4,303 (2.4%) were on dialysis. Among those, 1,257 (29.2%) received bivalirudin monotherapy and 2,112 (49.1%) received UFH monotherapy. Patients treated with bivalirudin had fewer comorbidities. After matching, there were no significant differences in outcomes between those who received bivalirudin versus UFH: bleeding (adjusted odds ratio: 0.67; 95% confidence interval: 0.41-1.07; P = 0.093); major bleeding (0.81; 0.19-3.50; P = 0.77); transfusion (1.01; 0.77-1.33; P = 0.96); repeat PCI (0.57; 0.14-2.24; P = 0.42); stent thrombosis (0.56; 0.05-5.83; P = 0.63); and death (0.84; 0.46-1.51; P = 0.55). CONCLUSIONS: We found no significant differences in in-hospital outcomes between bivalirudin and UFH monotherapy among dialysis patients undergoing PCI. Randomized clinical trials are needed to determine the optimal anticoagulant regimen for this population. (c) 2017 Wiley Periodicals, Inc.

Dermatology

Agrawal S, **Patel D**, and **Shwayder T**. "X" marks the spot: An injection technique for alopecia areata *Pediatr Dermatol* 2017; 34(2):214-215. PMID: 28297148. Full Text

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

Children with alopecia areata often have multiple patches of hair loss. When administering intralesional steroid injections, it can be difficult to monitor which areas have already been treated. Additionally, patients and their parents may worry that we did not treat all of the affected areas. We describe a simple technique to keep track of which areas have been treated.

Dermatology

Bourcier M, **Stein Gold L**, Guenther L, Andreassen CM, Selmer J, and Goldenberg G. A dose finding trial with a novel ingenol derivative (ingenol disoxate; LEO 43204) for field treatment of actinic keratosis on full face or 250cm2 on the chest *J Dermatolog Treat* 2017:1-25. PMID: 28264612. Article Request Form

a Hop G. L. Dumont, Dermatology , 35 rue Providence , Moncton , New Brunswick , E1C 8X3 , Canada.
b Henry Ford Hospital, Dermatology , 2799 W. Grand Blvd , Detroit , MI 48202 , USA.
c Guenther Research Inc. , 835 Richmond Street , London , ON N6A 3H7 , Canada.
d LEO Pharma A/S , Industriparken 55, DK-2750 , Ballerup , Denmark.
e Icahn School of Medicine at Mount Sinai, Department of Dermatology , 5 East 98th Street, 5th Floor , NY 10029 , USA.

PURPOSE: Actinic keratoses (AKs) may progress to squamous cell carcinoma and can occur in cancerized fields as sub-clinical and clinically visible lesions. Ingenol disoxate gel is a topical field therapy for AK. This Phase I/II trial aimed to assess the safety and efficacy of ingenol disoxate on full face or chest in patients with AKs. MATERIALS AND METHODS: Part 1 was a phase-I, open-label, dose-escalation trial investigating the maximum tolerated dose of ingenol disoxate. Part 2 was a phase-II, randomized, double-blind, vehicle-controlled trial; patients were randomized 1:1:1:1 to ingenol disoxate 0.018%, 0.012%, 0.006% gel or vehicle for 2 consecutive days. RESULTS: Reduction in AK count from baseline at Week 8 was significantly higher than with vehicle for all doses of ingenol disoxate gel (0.018%, 79.0%; 0.012%, 73.4%; 0.006%, 69.7%; vehicle; 42.3%; $p < 0.001$). Local skin responses peaked at Day 3 for all doses, rapidly declined and reached mild levels at Week 2. Most adverse events were mild or moderate in intensity, and were most commonly application site pain/pruritus. CONCLUSION: Ingenol disoxate gel is efficacious and well tolerated as field treatment for AKs on the full face or chest.

Dermatology

Chung CL, Nadhan KS, Shaver CM, Ogrich LM, Abdelmalek M, Cusack CA, Malat GE, **Pritchett EN**, and Doyle A. Comparison of posttransplant dermatologic diseases by race *JAMA Dermatol* 2017;PMID: 28273280. Full Text

Department of Dermatology, Drexel University, Philadelphia, Pennsylvania.
Department of Surgery, Drexel University, Philadelphia, Pennsylvania.
Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
Department of Internal Medicine, Drexel University, Philadelphia, Pennsylvania.

Importance: The risk for skin cancer has been well characterized in white organ transplant recipients (OTRs); however, most patients on the waiting list for organ transplant in the United States are nonwhite. Little is known about cutaneous disease and skin cancer risk in this OTR population. Objective: To compare the incidence of cutaneous disease between white and nonwhite OTRs. Design, Setting, and Participants: This retrospective review of medical records included 412 OTRs treated from November 1, 2011, through April 22, 2016, at an academic referral center. Prevalence and characteristics of cutaneous disease were compared in 154 white and 258 nonwhite (ie, Asian, Hispanic, and black) OTRs. Clinical factors of cutaneous disease and other common diagnoses assessed in OTRs included demographic characteristics, frequency and type of cancer, anatomical location, time course, sun exposure, risk awareness, and preventive behavior. Main Outcomes and Measures: Primary diagnosis of malignant or premalignant, infectious, and inflammatory disease. Results: The 412 patients undergoing analysis included 264 men (64.1%) and 148 women (35.9%), with a mean age of 60.1 years (range, 32.1-94.3 years). White OTRs more commonly had malignant disease at their first visit (82 [67.8%]), whereas nonwhite OTRs presented more commonly with infectious (63 [37.5%]) and inflammatory (82 [48.8%]) conditions. Skin cancer was diagnosed in 64 (41.6%) white OTRs and 15 (5.8%) nonwhite OTRs. Most lesions in white (294 of 370 [79.5%]) and Asian (5 of 6 [83.3%]) OTRs occurred in sun-exposed areas. Among black OTRs, 6 of 9 lesions (66.7%) occurred in sun-protected areas, specifically the genitals. Fewer nonwhite than white OTRs reported having regular dermatologic examinations (5 [11.4%] vs 8 [36.4%]) and knowing the signs of skin cancer (11 [25.0%] vs 10 [45.4%]). Conclusions and Relevance: Early treatment of nonwhite OTRs should focus on inflammatory and infectious diseases. Sun protection should continue to be emphasized in white, Asian, and Hispanic OTRs. Black OTRs should be counseled to recognize the signs of genital human papillomavirus infection. Optimal posttransplant dermatologic care may be determined based on the race or ethnicity of the patients, but a baseline full-skin assessment should be performed in all patients. All

nonwhite OTRs should be counseled more effectively on the signs of skin cancer, with focused discussion points contingent on skin type and race or ethnicity.

Dermatology

Kohli I, Shafi R, **Isedeh P**, **Griffith JL**, **Al-Jamal MS**, **Silpa-Archa N**, Jackson B, Athar M, Kollias N, Elmets CA, **Lim HW**, and **Hamzavi IH**. The impact of oral Polypodium leucotomos extract on ultraviolet B response: A human clinical study *J Am Acad Dermatol* 2017;PMID: 28341348. Full Text

Multicultural Dermatology Center, Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.
Department of Dermatology, University of Alabama at Birmingham, Birmingham, Alabama.
Independent Researcher, Boston, Massachusetts.
Multicultural Dermatology Center, Department of Dermatology, Henry Ford Hospital, Detroit, Michigan. Electronic address: ihamzav1@hfhs.org.

BACKGROUND: There is a rationale for adding systemic photoprotective agents to the current photoprotection regimen. OBJECTIVE: This study was designed to objectively evaluate the molecular and photobiologic effects of oral administration of Polypodium leucotomos extract (PLE). METHODS: In all, 22 subjects with Fitzpatrick skin phototype I to III were enrolled. On day 1, subjects were irradiated with visible light, ultraviolet (UV) A1, and UVB (using 308-nm excimer laser). Evaluation was done immediately and 24 hours after irradiation. On days 3 and 4, irradiation and evaluation process was repeated after ingestion of PLE. RESULTS: Clinical assessments and colorimetry data showed a decrease in UVB-induced changes in 17 of 22 subjects post-PLE administration; histology findings demonstrated such a decrease in all 22 subjects. LIMITATIONS: Only 2 doses of PLE were given. Furthermore, subjects with skin phototypes I to III only were studied. CONCLUSION: The results suggest that PLE can potentially be used as an adjunctive agent to lessen the negative photobiologic effects of UVB.

Dermatology

Mohammad TF, and **Hamzavi IH**. Surgical therapies for vitiligo *Dermatol Clin* 2017; 35(2):193-203. PMID: 28317528. Full Text

Department of Dermatology, Henry Ford Hospital, 3031 West Grand Boulevard, Suite 800, Detroit, MI 48202, USA.
Department of Dermatology, Henry Ford Hospital, 3031 West Grand Boulevard, Suite 800, Detroit, MI 48202, USA. Electronic address: ihamzav1@hfhs.org.

Surgical management is a safe and effective treatment modality for select patients with vitiligo. Many techniques of vitiligo surgery exist, each with unique advantages and disadvantages. Preoperative screening for appropriate candidates, selection of surgical technique, and postoperative management are all key elements in enabling patients to achieve maximal repigmentation.

Dermatology

Paek SY, **Hamzavi I**, Danby FW, and Qureshi AA. Disease modification for hidradenitis suppurativa: A new paradigm *J Am Acad Dermatol* 2017; 76(4):772-773. PMID: 28325401. Full Text

Warren Alpert Medical School, Brown University, Providence, Rhode Island. Electronic address: soyeon.paek@gmail.com.
Henry Ford Hospital, Detroit, Michigan.
Geisel School of Medicine at Dartmouth, Hanover, New Hampshire.
Warren Alpert Medical School, Brown University, Providence, Rhode Island.

Dermatology

Riis PT, Saunte D, Marmol VD, Benhadou F, Guillem P, El-Domyati M, Abdel-Wahab H, Antoniou C, Dessinioti C, Gurer MA, Beksac B, Szepietowski J, Mathusiak L, Emtestam L, Lapins J, Kottb HR, Doss N, Massa AF, **Hamzavi I**, **Nicholson C**, Dolenc-Voljc M, Kim KH, Ohn J, Zouboulis C, Karagiannidis I, Durienc P, Mokos ZB, Jemec GBE, and Faster Better Study G. Clinical characteristics of low and high BMI Hidradenitis suppurativa patients *Exp Dermatol* 2017; 26:14-15. PMID: Not assigned. Abstract

[Riis, P. Theut; Saunte, D.; Jemec, G. B. E.] Roskilde Hosp, Dept Dermatol, Roskilde, Denmark. [Marmol, V. D.; Benhadou, F.] Erasmus Univ, Brussels, Belgium. [Guillem, P.] Clin Val Ouest, Ecully, France. [El-Domyati, M.; Abdel-Wahab, H.] Al Minya Univ, Al Minya, Egypt. [Antoniou, C.; Dessinioti, C.] Andreas Syggros Hosp, Athens, Greece.

[Gurer, M. Ali; Beksac, B.] Gazi Univ, Fac Med, Dept Dermatol, Ankara, Turkey. [Szepietowski, J.; Mathusiak, L.] Wroclaw Med Univ, Wroclaw, Poland. [Emtestam, L.; Lapins, J.] Huddinge Karolinska Inst, Dept Med, Sect Dermatol & Venereol, Stockholm, Sweden. [Kottb, H. Riad] Qatar Hosp & Hlth Care, Doha, Qatar. [Doss, N.] Hop Mil, Tunis, Tunisia. [Massa, A. F.] Ctr Hosp Vila Nova de Gaia Espinho, Oporto, Portugal. [Hamzavi, I.; Nicholson, C.] Henry Ford Hosp, Detroit, MI 48202 USA. [Dolenc-Voljc, M.] Univ Med Ctr Ljubljana, Ljubljana, Slovenia. [Kim, K. Han; Ohn, J.] Seoul Natl Univ, Soul, South Korea. [Zouboulis, C.; Karagiannidis, I.] Dessau Med Ctr, Dept Dermatol, Dessau, Germany. [Zouboulis, C.; Karagiannidis, I.] Dessau Med Ctr, Dept Venereol, Dessau, Germany. [Zouboulis, C.; Karagiannidis, I.] Dessau Med Ctr, Dept Allergol, Dessau, Germany. [Zouboulis, C.; Karagiannidis, I.] Dessau Med Ctr, Dept Immunol, Dessau, Germany. [Durienc, P.; Mokos, Z. Bukvic] Univ Zagreb, Zagreb, Croatia.

Dermatology

Theut Riis P, Saunte D, Marmol VD, Benhadou F, Guillem P, El-Domyati M, Abdel-Wahab H, Antoniou C, Dessinioti C, Ali Gürer M, Beksaç B, Szepietowski J, Mathusiak L, Emtestam L, Lapins J, Riad Kottb H, Doss N, Massa AF, **Hamzavi I**, **Nicholson C**, Dolenc-Voljc M, Han Kim K, Ohn J, Zouboulis C, Karagiannidis I, Durienc P, Bukvic Mokos Z, and Jemec GBE. Clinical characteristics of low and high BMI Hidradenitis suppurativa patients *Exp Dermatol* 2017; 26:14-15. PMID: Not assigned. **Abstract**

P. Theut Riis, Department of Dermatology, Roskilde Hospital, Roskilde, Denmark

Obesity, as a risk factor is a common theme in Hidradenitis Suppurativa (HS) literature. HS patients as a group have higher Body Mass Index (BMI) than control population, high BMI patients suffer more severe disease, less frequently go into remission and respond less well to laser surgery and medical treatment. It is therefore of interest to study other phenotypical differences between HS patients with normal and very high BMI, to explore the hypothesis that BMI is a marker for other underlying differences. Method: To examine this further we performed a survey and examination of 246 HS patients with a BMI under 25 and 205 patients with a BMI higher than 35. The survey include patients from 16 different centers. Results: Univariable analysis showed several differences between low BMI and high BMI patients. Patients with a high BMI were older (median age 33 vs 38, P<0.001), had a higher age at first boil (median 20 vs 23, P=0.001), had a lower alcohol consumption (P=0.007) and were less prone to Acne (P=0.007). Patients with a high BMI were more severely affected by HS as assessed by Hurley staging, physician global assessment (PGA), and Patient reported severity score (Numeric rating scale 0-10) (P<0.001 for all). There was no difference in smoking status (P=0.783) or genetic disposition towards HS (P=0.088). Logistic regression showed that an increase in 5 years in age of diagnosis was associated with an odds ratio of 0.72 and 0.67 for positive family history, for low and high BMI respectively (P>0.001). Indicating that patients with a positive family history have an earlier debut of symptoms. Disease impact, as measured by patient reported severity (PRS) on a numeric rating scale from 0-10, was associated with increased BMI for the low BMI group with an increase of 0.37 PRS per BMI (P<0.001). For patients with a high BMI disease severity was not associated with BMI, but with Pack years, with an increase of 0.38 PRS per pack year (P=0.001). Discussion: As previously reported, we find that positive family history is associated with earlier age of onset. Positive family history was however not associated with more severe disease. For high BMI patients positive family history was associated with more widespread disease, (P<0.001). For low BMI patients this association was not found (P=0.604). This suggests a synergistic relationship between BMI and genetics with regards to how wide-spread lesions are Patients with high BMI experience greater impact from their HS and more severe disease. Despite BMI being a risk factor for the development of the disease we did not find an overabundance of positive family history in the low BMI population. Interestingly disease impact if more closely linked to actual BMI in the low BMI group, whereas pack years seem the most prominent determinant for disease impact in the high BMI group. The results seemingly indicate that BMI primarily affects disease severity as distinct from onset of disease.

Diagnostic Radiology

Vega JEV, Halani SH, Yousefi S, Amrollahi F, Holder CA, **Poisson LM**, **Griffith B**, Eschbacher J, Nalisnik M, Olson JJ, Cooper LAD, and Brat DJ. Markers of progression in oligodendroglioma *Lab Invest* 2017; 97:438A-438A. PMID: Not assigned. Abstract

Emory Univ, Sch Med, Atlanta, GA USA. Henry Ford Hosp, Detroit, MI 48202 USA. St Josephs Hosp, Phoenix, AZ USA.

Endocrinology

Bhadada SK, Dhiman V, Mukherjee S, Aggarwal S, Bal A, Sukumar SP, Sood A, Sharma DC, Khandelwal N, Bhansali A, Van Hul W, and **Rao SD**. Fibrogenesis imperfecta ossium and response to human growth hormone: A potential novel therapy *J Clin Endocrinol Metab* 2017;PMID: 28323922. Full Text

Department of Endocrinology.
Orthopedics.
Histopathology.
Nuclear Medicine.
Postgraduate Institute of Medical Education and Research, Chandigarh, India. Department of Medicine, RNT Medical College, Udaipur, Rajasthan, India. Medical Genetics.
Radiodiagnosis.
University of Antwerp, Antwerp, Belgium.
Bone & Mineral Research Laboratory, Henry Ford Health System, Detroit, USA.

Context: Fibrogenesis imperfecta ossium (FIO) is a rare bone disease manifested by generalized bone pain, fragility fractures, progressive disability, and extensive mineralization defect on bone biopsy. The pathogenesis of the disease is unknown and currently there is no effective treatment. Objective: To report on the effect of recombinant human growth hormone (rhGH) therapy in FIO. Design: An observational study in two patients. Setting: Endocrinology Clinic in an Academic Institution Patients or Other Participants: Two siblings with FIO Intervention(s): rhGH was administered subcutaneously at a dose of 1U daily for one year. Main Outcome Measures: Changes in clinical, biochemical, radiological, and bone histologic (light and transmission electron microscopy, and histomorphometry) investigations. Results: Except for an elevated serum alkaline phosphatase (AP) levels routine biochemical, hematologic, and hormonal investigations were all normal in both the patients. Radiographs showed pseudo-fractures, and bone scans revealed "beheaded" tracer activity pattern (super scan without uptake in the skull). Bone biopsy showed severe mineralization defect simulating osteomalacia with disorganized collagen fibril alignment. Treatment with rhGH was followed by clinical, biochemical, and radiological improvement in both the patients with substantial improvement in the mineralization defect, most likely due to rhGH induced improvement in collagen fibril arrangement. Conclusions: We report 2 brothers with FIO and demonstrate, for the first time, clinical improvement and restoration of normal bone pathology with rhGH therapy. We suggest that rhGH offers a potential novel therapy for FIO for which no effective therapy currently exists.

Family Practice
Kwarteng JL, Schulz AJ, Mentz GB, Israel BA, Shanks TR, and **White-Perkins D**. Does perceived safety modify the effectiveness of a walking-group intervention designed to promote physical activity? *Am J Health Promot* 2017:890117117696443. PMID: 28317385. Article Request Form

1 Medical College of Wisconsin, Milwaukee, WI, USA.
2 Department of Health Behavior and Health Education, University of Michigan School of Public Health, Ann Arbor, MI, USA.
3 University of Michigan School of Social Work, Ann Arbor, MI, USA.
4 Henry Ford Health System, Institute on Multicultural Health, Detroit, MI, USA.

PURPOSE: To examine whether perceived safety modified the effectiveness of the Walk Your Heart to Health (WYHH) intervention in promoting physical activity and reducing central adiposity in predominantly non-Latino black (henceforth black) and Latino communities. DESIGN: Generalized estimation equations were used to assess modifying effects of perceived safety on the route and perceived neighborhood safety on (1) WYHH participation at 8 weeks and 32 weeks, (2) associations between participation and physical activity, and (3) associations between physical activity and central adiposity. SETTING: Community-based and faith-based organizations in black and Latino communities. PARTICIPANTS: There were 603 adults, aged 18 years and older, who were predominantly black, Latino, and female. MEASURES: Participation and physical activity (piezoelectric pedometer) were measured at each walking session. Perceived safety on the route (questionnaire), perceived neighborhood safety (questionnaire), and waist circumference were measured at baseline, 8 weeks, and 32 weeks. ANALYSIS: Secondary analysis of repeated measures using generalized estimation equations. RESULTS: Retention was 90% at 8 weeks and 64% at 32 weeks. Perceived safety on the route, but not perceived neighborhood safety, dampened participation at 8 weeks but not 32 weeks. Consistent participation in the intervention increased physical activity and reduced central adiposity irrespective of perceived safety on the walking route or perceived neighborhood safety. CONCLUSION: Efforts to improve safety in conjunction with interventions focused on increasing physical activity can work toward improving physical activity for blacks and Latinos, leading to a myriad of improved health outcomes including reduced central adiposity.

Family Practice

Park B, **Vemulapalli RC**, **Gupta A**, **Shreve ME**, and **Rees DA**. Docetaxel-induced systemic sclerosis with internal organ involvement masquerading as congestive heart failure *Case Reports Immunol* 2017; 2017:4249157. PMID: 28265474. Full Text

Department of Family Medicine, Henry Ford Hospital, Wayne State University School of Medicine, Detroit, MI 48202, USA.

Systemic sclerosis, or scleroderma, is a complex medical disorder characterized by limited or diffuse skin thickening with frequent involvement of internal organs such as lungs, gastrointestinal tract, or kidneys. Docetaxel is a chemotherapeutic agent which has been associated with cutaneous side effects. An uncommon cutaneous side effect of docetaxel is scleroderma-like skin changes that extend from limited to diffuse cutaneous systemic sclerosis. Several case reports have been published regarding the association of docetaxel and systemic sclerosis. However, those reports demonstrated the association between docetaxel and scleroderma-like skin changes without internal organ involvement. Here, we report a case of systemic sclerosis with pulmonary arterial hypertension and a microangiopathic kidney involvement induced by docetaxel chemotherapy. After an exhaustive literature review, this could be the first case of docetaxel-induced systemic sclerosis involving internal organs.

Gastroenterology

Gordon SC, Lim J, Liou I, Ozbay AB, Meyer N, Dusheiko G, and Nguyen MH. Rising prevalence of osteoporosis and bone fracture in chronic hepatitis B patients: A United States population-based study *Hepatol Int* 2017; 11(1):S272-S273. PMID: Not assigned. Abstract

S.C. Gordon, Henry Ford Hospital, Detroit, United States

Background: Older patients and those of Asian descent are of higher risk for osteoporosis. In the US, most patients with chronic hepatitis B (CHB) are Asians. The aim of this study was to characterize the longitudinal trends in osteoporosis and bone fractures and to describe comorbidities and concomitant medications use in a large diverse population of US CHB patients between 2006 and 2015. Methods: Adult patients diagnosed with CHB (ICD-9 diagnosis codes 070.22, 070.30 or 070.32) and without hepatitis delta coinfection with continuous enrollment in the 6 months before and after CHB diagnosis were identified from the MarketScan® Commercial, Medicare, and Medicaid Databases during 7/1/2004 to 6/30/2015. These CHB patients were matched to non-CHB controls by payer type, year, age, gender, and for a subset of patients with available data on geographic region and race. The prevalence (per 1000 persons) and incidence (per 1000 person-years) of osteoporosis and bone fracture were calculated for each year during 2006-2015. Comorbidities and medication use which may influence bone mineralization were also evaluated over the same period. Result: Among the 44,026 U.S. CHB patients identified for the study, the prevalence of fracture and osteoporosis increased significantly between 2006 and 2015 by nearly twofold (91-177 per 1000) overall (Figure). This trend was observed for both males (76-133 per 1000) and females (109-228 per 1000), though the prevalence were higher in females. When compared to matched non-CHB controls, fracture and osteoporosis prevalence and incidence (per 1000 person years) were also significantly higher in CHB patients in each year during study period. In CHB patients, the prevalence of osteoporosis, osteoarthritis, or vitamin D deficiency also increased nearly threefolds from 7 to 20%, all $p<0.001$. In addition, during the same period, the concomitant use of corticosteroids increased from 17 to 24%, while the use osteoporosis medications significantly decreased from 3 to 2%, $p<0.001$. Conclusion: Between 2006 and 2015, the prevalence of bone fracture and osteoporosis increased significantly in US patients with CHB, and was much higher in CHB patients than non-CHB controls. These trends were observed and significant for both male and female patients. During the same period, comorbidities related to bone mineral loss also increased and should be considered in the management of CHB patients. (Figure presented).

Gastroenterology

Hou J, Weatherly J, Sellin J, **Kaur M**, Metwally M, Vrabie R, Ali T, Kaurk N, Gasche C, Drazain N, Oberai R, Nguyen A, Weaver A, Siegel C, and Melmed G. Feasibility of screening for anemia using the crohn's and colitis foundation anemia care pathway in ibd qorus *Inflamm Bowel Dis* 2017; 23:S46-S47. PMID: Not assigned. Abstract

[Hou, Jason; Weatherly, Julie; Sellin, Joseph; Kaur, Manreet] Baylor Coll Med, Houston, TX 77030 USA. [Metwally, Mark] Saratog Schenectady Gastroenterol Associates, Burnt Hills, NY USA. [Vrabie, Raluca] Winthrop, Mineola, NY USA. [Ali, Tauseef] OIHSC, Oklahoma City, OK USA. [Kaurk, Nirmal] Henry Ford Hlth Syst, Detroit, MI USA. [Gasche, Chris] Med Univ Vienna, Vienna, Austria. [Drazain, Noam] Cedars Sinai, Beverly Hills, CA USA. [Oberai, Ridhima; Weaver, Alandra] CCFA, New York, NY USA. [Nguyen, Anne] Cedars Sinai, Los Angeles, CA USA. [Siegel, Corey] Dartmouth Hithcock Med Ctr, Lebanon, NH USA. [Melmed, Gil] Cedars Sinai Med Ctr, Los Angeles, CA 90048 USA.

Gastroenterology

Lenhart A, **Hassan M**, **Meighani A**, **Sadiq O**, and **Siddiqui Y**. A perplexing case of abdominal pain that led to the diagnosis of zollinger-ellison syndrome *Case Rep Gastrointest Med* 2017; 2017:7636952. PMID: 28321346. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI 48202, USA.

Zollinger-Ellison syndrome (ZES) is a rare clinical disorder, characterized by hypersecretion of gastric acid and multiple ulcers distal to the duodenal bulb. This occurs via the release of gastrin by neuroendocrine tumors known as gastrinomas. Patients with ZES present with nonspecific GI symptoms, which often leads to a delay in diagnosis. Our patient is a 55-year-old female with chronic abdominal pain, nausea, and diarrhea. She underwent EGD, EUS, MRCP, CT scans, and cholecystectomy, which did not reveal the cause of her symptoms. Repeat EGD showed a cratered ulcer in the second portion of the duodenum, suspicious for ZES. Serum gastrin was initially only moderately elevated while on PPI therapy, but chromogranin A was also elevated. Repeat gastrin level after stopping PPI therapy was 1639 pg/mL. Somatostatin receptor scintigraphy was obtained, which showed two small lesions in the gastrinoma triangle. She subsequently underwent a Whipple pancreaticoduodenectomy and pathology was positive for four microscopic foci of a neuroendocrine tumor. She reported improvement in her symptoms after surgery. This case highlights the need for increased awareness of ZES in patients with unexplained GI complaints and emphasizes the use of multiple modalities in the diagnosis of ZES.

Gastroenterology

Nguyen MH, Lim J, Liou I, Ozbay AB, Fraysse J, Costa L, **Gordon SC**, and Dusheiko G. Chronic hepatitis B patients have increasing prevalence and incidence of chronic kidney disease compared to matched non-chronic hepatitis B controls: Results of a real-world analysis of 1,65,594 patients in the United States *Hepatol Int* 2017; 11(1):S192-S193. PMID: Not assigned. Abstract

M.H. Nguyen, Stanford University, Stanford, United States

Background: Chronic kidney disease (CKD) is a significant comorbidity that may also be more common among patients with chronic hepatitis B (CHB). Our goal was to characterize the prevalence and incidence of CKD as well as potential changes over time during the period from 2006 to 2015 in a large, geographically and economically diverse population of CHB patients across the United States. Methods: Using the Truven Health MarketScan® Commercial (general population), Medicare (mostly older than 65), and Medicaid (low income population) insurance databases, we identified a cohort of CHB cases ≥18 years of age without hepatitis delta co-infection (ICD-9 diagnosis codes 070.22, 070.30, or 070.32) who were continuously enrolled for 6 months before and after CHB diagnosis. We then matched these CHB cases to non-CHB controls by calendar year of diagnosis date, age, gender, geographic region, and race as available. Primary outcomes were CKD prevalence (per 1000 persons) and incidence (per 1000 person-years). In addition, we analyzed CKD outcomes by age group and by presence of diabetes and hypertension for CHB patients from the most recent year 2015. Result: This matched case cohort study included 44,026 CHB patient cases (median age 47 in 2006 to 51 in 2015) and 1,21,568 non-CHB controls (median age 48 in 2006 to 53 in 2015). CKD prevalence increased significantly over time and was higher in CHB than non- CHB controls (Figure 1). CKD prevalence (per 1000 persons) increased by nearly 3-fold from 44 to 114, p<0.001. Similarly, CKD incidence per 1000 person-years increased by 56% (13-20, p = 0.003). Between 2006 and 2015, the proportion of patients with comorbidities that may predispose patients to CKD also increased: 12.2-17.7% for diabetes, 22.0-37.3% for hypertension. In addition, an analysis of CHB patients identified from the most recent study year of 2015, CKD prevalence in patients with diabetes and hypertension was 10-fold higher than those without, and 6-fold higher in patients older than 60 compared to those younger than 45 (Figure 2). Conclusion: In this large and diverse population-based US study, CKD prevalence in CHB patients has increased by almost 3-fold from 2006 to 2015 and is significantly higher than that of matched non- CHB controls and with similar trends observed for CKD incidence. CKD is particularly prevalent in older CHB patients and in those with comorbidities, affecting one-third of patients (349 per 100 persons) with diabetes and hypertension and one-quarter (237 per 1000 persons) of patients older than 60 in 2015. Whether CHB has contributed to the prevalence of CKD in the cohort requires further analysis.

Gastroenterology

Nguyen MH, Lim J, Ozbay AB, Fraysse J, Liou I, Moore-Schiltz L, Dusheiko G, and **Gordon SC**. Increasing age and comorbidities of chronic hepatitis B patients in the US: A longitudinal analysis of a diverse US populationbased cohort of 44,026 CHB patients over 10 years *Hepatol Int* 2017; 11(1):S193-S194. PMID: Not assigned. Abstract

M.H. Nguyen, Stanford University, Stanford, United States

Background: Little is known about the age, prevalence of comorbidities, and co-medications among US patients with chronic hepatitis B (CHB). Our aim was to characterize these longitudinal trends in a large diverse population of US CHB patients, between 2006 and 2015. Methods: We conducted a study of CHB patients ≥18 years of age (without hepatitis delta co-infection) (ICD-9 diagnosis codes 070.22, 070.30, or 070.32) who were continuously enrolled for 6 months before and after CHB diagnosis, using de-identified and US administrative healthcare claims extracted from the Truven Health MarketScan® Commercial (general population), Medicare (older than 65), and Multi-State Medicaid (low income population) databases between 7/1/2004 and 6/30/2015. Result: We identified a total of 44,026 US CHB patients. The median age of CHB patients increased from 47 in 2006-52 in 2015 ($p<0.001$). Deyo-Charlson comorbidity Index scores increased over time from a mean of 1.1 in 2006 to 1.4 in 2015 ($p<0.001$). The proportion of CHB patients with diabetes, hypertension, and hyperlipidemia also increased significantly between 2006 and 2015 ($p<0.001$) (Figure). Specifically, from 2006 to 2015, diabetes increased from 12.2 to 17.7%, renal impairment increased from 9.8 to 16.7%, (with glomerulonephritis, proteinuria, nephrotic syndrome, or nephropathy rates almost doubled from 6.3 to 13.2%), hypertension increased by almost two-fold from 22.0 to 37.3%, hyperlipidemia increased by almost 3-fold from 8.1 to 24.0%, and non-alcoholic fatty liver disease (NAFLD) increased over 2-folds from 1.7 to 5.2% ($p<0.001$). Concomitant medication use of cardiovascular medications and antidiabetic medications also increased significantly between 2006 and 2015 ($p<0.001$). From 2006 to 2015, use of cardiovascular medications increased from 27.0 to 37.1% and use of antidiabetic medications increased from 10.3 to 13.2%. Conclusion: In the US between 2006 and 2015, based on data from a large geographically and economically diverse patient population, the median age of patients with CHB significantly increased with increasing prevalence of associated comorbidities and concomitant medication use, up to 3-fold increase in some major comorbidities. The contribution of hepatitis B to these comorbidities in an aging population requires further analysis but advancing age and comorbidities in this group require appropriate management. (Figure Presented).

Gastroenterology
Parekh R, and **Kaur N**. Colonic dysplasia in patients with inflammatory bowel disease undergoing liver transplantation for primary sclerosing cholangitis *Inflamm Bowel Dis* 2017; 23:S56-S56. PMID: Not assigned. Abstract

[Parekh, Ravish; Kaur, Nirmal] Henry Ford Hosp, Detroit, MI 48202 USA.

Gastroenterology
Piraka C, **Saeed A**, Waljee AK, Pillai A, Stidham R, and Elmunzer BJ. Cold snare polypectomy for non-pedunculated colon polyps greater than 1 cm *Endosc Int Open* 2017; 5(3):E184-e189. PMID: 28331902. Full Text

Division of Gastroenterology, Henry Ford Hospital, Detroit, Michigan, United States.
VA Center for Clinical Management Research, VA Ann Arbor Health Care System, Ann Arbor, Michigan, United States; Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan Health System, Ann Arbor, Michigan, United States.
Division of Gastroenterology, College of Medicine, Drexel University, Philadelphia, Pennsylvania, United States.
Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan Health System, Ann Arbor, Michigan, United States.
Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, South Carolina, United States.

Background and study aims Colonic polyps > 1 cm in size are commonly managed using hot polypectomy techniques. The most frequent adverse events (delayed bleeding, post-polypectomy syndrome, and perforation) are related to electrocautery-induced injury. We hypothesized that cold resection of large polyps may have similar efficacy and improved safety compared to hot polypectomy. Our aims were to evaluate efficacy and safety of piecemeal cold snare resection of colonic polyps > 1 cm. Patients and methods Patients undergoing lift and piecemeal cold snare polypectomy of non-pedunculated colon polyps > 1 cm from October 2013 to September 2015 were identified retrospectively. Efficacy was defined by the absence of residual adenomatous tissue at endoscopic follow-up. Adverse events (AEs), including post-procedural bleeding, bowel perforation, or post-procedural pain requiring hospitalization were assessed by chart review and telephone follow-up. Results Seventy-three patients underwent piecemeal cold snare polypectomy for 94 colon polyps > 1 cm with 56 of 73 patients completing follow-up on 72 polyps. Residual or recurrent adenoma was found in 7 cases (9.7 %). Median polyp size was significantly greater in those with residual/recurrent adenoma (37.1 vs. 19.1 mm, $P < .0001$). There were no AEs among all 73 patients enrolled. Conclusions Piecemeal cold snare resection of colon polyps > 1 cm is feasible, safe and efficacious when compared to published hot polypectomy data. Additional observational and randomized comparative effectiveness studies are necessary to demonstrate comparable adenoma eradication and improved safety advantage over existing hot snare polypectomy techniques.

Gastroenterology
Younossi Z, **Gordon SC**, Ahmed A, Dieterich D, Saab S, and Beckerman R. Treating Medicaid patients with hepatitis C: clinical and economic impact *Am J Manag Care* 2017; 23(2):107-112. PMID: 28245654. Full Text

Beatty Center for Integrated Research, 3300 Gallows Rd, Falls Church, VA 22042. E-mail: zobair.younossi@inova.org.

OBJECTIVES: To estimate change in chronic hepatitis C virus (HCV) disease and the economic burden associated with comprehensive treatment of the chronic HCV-infected Medicaid population. STUDY DESIGN: Decision-analytic Markov model. METHODS: Treatment-naive patients with genotype 1 chronic HCV were followed over a lifetime horizon from the third-party payer perspective. Patients entered the model insured under Medicaid and were treated under state-specific restrictions by Metavir fibrosis stage (base case) or all treated (all-patient strategy) with an approved all-oral regimen (ledipasvir/sofosbuvir [LDV/SOF] for 8 weeks or 12 weeks, depending on cirrhosis status, viral load, and state-specific LDV/SOF restrictions). Untreated patients were assumed to age into Medicare at 65 years, where they were treated with LDV/SOF without restriction by fibrotic stage. RESULTS: The sustained virologic response (SVR) rate of the current Medicaid LDV/SOF restriction strategy was 75.2% versus 95.9% if all LDV/SOF-eligible patients were treated under Medicaid. Treating all eligible Medicaid patients with LDV/SOF, regardless of fibrotic stage, was projected to result in 36,752 fewer cases of cirrhosis; 1739 fewer liver transplants; 8169 fewer cases of hepatocellular carcinoma; 16,173 fewer HCV-related deaths; 0.84 additional life-years per patient; and 1.03 additional quality-adjusted life-years per patient. Treating all Medicaid patients with chronic HCV using LDV/SOF resulted in a 39.4% ($3.8 billion) savings and decreased the proportion of total costs attributable to downstream costs of care to 18.3%. CONCLUSIONS: A "treat all" strategy in a Medicaid population resulted in superior SVRs, substantial reductions in downstream negative clinical outcomes, and considerable cost savings. Current restrictive state policies regarding HCV treatment in Medicaid populations must be reassessed in light of these data.

Global Health Initiative
Newman LA, and **Kaljee LM**. Health disparities and triple-negative breast cancer in african american women: A review *JAMA Surg* 2017;PMID: 28355428. Full Text

Department of Surgery, Breast Oncology Program, International Center for the Study of Breast Cancer Subtypes, Henry Ford Health System, Detroit, Michigan.
Global Health Initiative, Henry Ford Health System, Detroit, Michigan.

Importance: Variation in cancer incidence and outcome has well-documented correlations with racial/ethnic identity. In the United States, the possible genetic and ancestral hereditary explanations for these associations are confounded by socioeconomic, cultural, and lifestyle patterns. Differences in the breast cancer burden of African American compared with European/white American women represent one of the most notable examples of disparities in oncology related to racial/ethnic identity. Elucidating the source of these associations is imperative in achieving the promise of the national Precision Medicine Initiative. Observations: Population-based breast cancer mortality rates have been higher for African American compared with white American women since the early 1980s, largely reflecting declines in mortality that have been disproportionately experienced among white American patients and at least partly explained by the advent of endocrine therapy that is less effective in African American women because of the higher prevalence of estrogen receptor-negative disease. The increased risk of triple-negative breast cancer in African American women as well as western, sub-Saharan African women compared with white American, European, and east African women furthermore suggests that selected genetic components of geographically defined African ancestry are associated with hereditary susceptibility for specific patterns of mammary carcinogenesis. Disentangling health care access barriers, as well as reproductive, lifestyle, and dietary factors from genetic contributions to breast cancer disparities remains challenging. Epigenetics and experiences of societal inequality (allostatic load) increase the complexity of studying breast cancer risk related to racial/ethnic identity. Conclusions and Relevance: Oncologic anthropology represents a transdisciplinary field of research that can combine the expertise of population geneticists, multispecialty oncologists, molecular epidemiologists, and behavioral scientists to eliminate breast cancer disparities related to racial/ethnic identity and advance knowledge related to the pathogenesis of triple-negative breast cancer.

Global Health Initiative
Plum A, and **Kaljee L**. Achieving sustainable, community-based health in detroit through adaptation of the UNSDGs *Ann Glob Health* 2016; 82(6):981-990. PMID: 28314500. Article Request Form

Henry Ford Health System Global Health Initiative, Detroit, MI. Electronic address: Aplum2@hfhs.org.
Henry Ford Health System Global Health Initiative, Detroit, MI.

BACKGROUND: In 2012, the Rio+20 meeting initiated the concept of the Sustainable Development Goals (SDGs) as a continuation of the Millennium Development Goals. The resulting document "The Future We Want" is best conceived as a roadmap toward poverty eradication and sustainable development. Although the SDGs were developed for low- and middle-income countries, many of these same issues face low-resource cities and communities in higher-income countries. OBJECTIVES: The aim of this study was to use the SDGs as a platform to develop health-related goals for the city of Detroit. METHODS: A 1-day workshop was convened in October 2015 including 55 representatives from government, academia, and community- and faith-based organizations. Four health-related SDGs were discussed: food security (SDG2); ensuring healthy lives at all ages (SDG3); access to potable water (SDG6); and making cities inclusive, safe, resilient, and sustainable living environments (SDG11). Workshop attendees broke into 4 groups to determine how the SDG targets for these 4 goals could be adapted for Detroit. At the end of the day, each group presented its decisions to the larger group. FINDINGS: Workshop participants expressed that the SDGs empower local communities to respond to their unique health challenges and to see themselves as part of a larger more global conversation about development and sustainability. Participants suggested that inclusive and participatory means of decision making were a significant component of the SDGs and that such a process is the direction needed to make community-focused changes in Detroit. Additionally, shortly after the workshop, a roundtable of participants representing 5 community partners began to meet monthly and has become an advocacy group for public health and addressing the city-order water shutoffs in neighborhoods throughout Detroit. CONCLUSIONS: For participants and organizers, the workshop reinforced the hypothesis that the SDGs are relevant to Detroit and other low-resource cities in the United States.

Global Health Initiative
Plum A, and **Kaljee L**. Achieving sustainable, community-based health in detroit through adaptation of the UNSDGs *Ann Glob Health* 2016; 82(6):981-990. PMID: 28314500. Article Request Form

Henry Ford Health System Global Health Initiative, Detroit, MI. Electronic address: Aplum2@hfhs.org.
Henry Ford Health System Global Health Initiative, Detroit, MI.

BACKGROUND: In 2012, the Rio+20 meeting initiated the concept of the Sustainable Development Goals (SDGs) as a continuation of the Millennium Development Goals. The resulting document "The Future We Want" is best conceived as a roadmap toward poverty eradication and sustainable development. Although the SDGs were developed for low- and middle-income countries, many of these same issues face low-resource cities and communities in higher-income countries. OBJECTIVES: The aim of this study was to use the SDGs as a platform to develop health-related goals for the city of Detroit. METHODS: A 1-day workshop was convened in October 2015 including 55 representatives from government, academia, and community- and faith-based organizations. Four health-related SDGs were discussed: food security (SDG2); ensuring healthy lives at all ages (SDG3); access to potable water (SDG6); and making cities inclusive, safe, resilient, and sustainable living environments (SDG11). Workshop attendees broke into 4 groups to determine how the SDG targets for these 4 goals could be adapted for Detroit. At the end of the day, each group presented its decisions to the larger group. FINDINGS: Workshop participants expressed that the SDGs empower local communities to respond to their unique health challenges and to see themselves as part of a larger more global conversation about development and sustainability. Participants suggested that inclusive and participatory means of decision making were a significant component of the SDGs and that such a process is the direction needed to make community-focused changes in Detroit. Additionally, shortly after the workshop, a roundtable of participants representing 5 community partners began to meet monthly and has become an advocacy group for public health and addressing the city-order water shutoffs in neighborhoods throughout Detroit. CONCLUSIONS: For participants and organizers, the workshop reinforced the hypothesis that the SDGs are relevant to Detroit and other low-resource cities in the United States.

Global Health Initiative
Rowthorn V, **Plum AJ**, and **Zervos J**. Legal and regulatory barriers to reverse innovation *Ann Glob Health* 2016; 82(6):991-1000. PMID: 28314501. Article Request Form

Francis King Carey School of Law, University of Maryland, Baltimore, MD; Global Health Initiative, Henry Ford Health System, Detroit, MI. Electronic address: vrowthorn@law.umaryland.edu.
Francis King Carey School of Law, University of Maryland, Baltimore, MD; Global Health Initiative, Henry Ford Health System, Detroit, MI.

BACKGROUND: Reverse innovation, or the importation of new, affordable, and efficacious models to high-income countries from the developing world, has emerged as a way to improve the health care system in the United States. Reverse innovation has been identified as a key emerging trend in global health systems in part because low-resourced settings are particularly good laboratories for low-cost/high-impact innovations that are developed out of

necessity. A difficult question receiving scant attention is that of legal and regulatory barriers. OBJECTIVES: The objective of this paper is to understand and elucidate the legal barriers faced by innovators bringing health interventions to the United States. METHODS: Semistructured qualitative interviews were conducted with 9 key informants who have directly participated in the introduction of global health care approaches to the United States health system. A purposive sampling scheme was employed to identify participants. Phone interviews were conducted over one week in July 2016 with each participant and lasted an average of 35 minutes each. FINDINGS: Purely legal barriers included questions surrounding tort liability, standard of care, and concerns around patient-administered self-care. Regulatory burdens included issues of international medical licensure, reimbursement, and task shifting and scope of work challenges among nonprofessionals (e.g. community health workers). Finally, perceived (i.e. not realized or experienced) legal and regulatory barriers to innovative modalities served as disincentives to bringing products or services developed outside of the United States to the United States market. CONCLUSIONS: Conflicting interests within the health care system, safety concerns, and little value placed on low-cost interventions inhibit innovation. Legal and regulatory barriers rank among, and contribute to, an anti-innovation atmosphere in healthcare for domestic and reverse innovators alike. Reverse innovation should be fostered through the thoughtful development of legal and regulatory standards that encourage the introduction and scalable adoption of successful health care innovations developed outside of the US, particularly innovations that support public health goals and do not have the benefit of a large corporate sponsor to facilitate introduction to the market.

Global Health Initiative

Rowthorn V, **Plum AJ**, and **Zervos J**. Legal and regulatory barriers to reverse innovation *Ann Glob Health* 2016; 82(6):991-1000. PMID: 28314501. Article Request Form

Francis King Carey School of Law, University of Maryland, Baltimore, MD; Global Health Initiative, Henry Ford Health System, Detroit, MI. Electronic address: vrowthorn@law.umaryland.edu.
Francis King Carey School of Law, University of Maryland, Baltimore, MD; Global Health Initiative, Henry Ford Health System, Detroit, MI.

BACKGROUND: Reverse innovation, or the importation of new, affordable, and efficacious models to high-income countries from the developing world, has emerged as a way to improve the health care system in the United States. Reverse innovation has been identified as a key emerging trend in global health systems in part because low-resourced settings are particularly good laboratories for low-cost/high-impact innovations that are developed out of necessity. A difficult question receiving scant attention is that of legal and regulatory barriers. OBJECTIVES: The objective of this paper is to understand and elucidate the legal barriers faced by innovators bringing health interventions to the United States. METHODS: Semistructured qualitative interviews were conducted with 9 key informants who have directly participated in the introduction of global health care approaches to the United States health system. A purposive sampling scheme was employed to identify participants. Phone interviews were conducted over one week in July 2016 with each participant and lasted an average of 35 minutes each. FINDINGS: Purely legal barriers included questions surrounding tort liability, standard of care, and concerns around patient-administered self-care. Regulatory burdens included issues of international medical licensure, reimbursement, and task shifting and scope of work challenges among nonprofessionals (e.g. community health workers). Finally, perceived (i.e. not realized or experienced) legal and regulatory barriers to innovative modalities served as disincentives to bringing products or services developed outside of the United States to the United States market. CONCLUSIONS: Conflicting interests within the health care system, safety concerns, and little value placed on low-cost interventions inhibit innovation. Legal and regulatory barriers rank among, and contribute to, an anti-innovation atmosphere in healthcare for domestic and reverse innovators alike. Reverse innovation should be fostered through the thoughtful development of legal and regulatory standards that encourage the introduction and scalable adoption of successful health care innovations developed outside of the US, particularly innovations that support public health goals and do not have the benefit of a large corporate sponsor to facilitate introduction to the market.

Graduate Medical Education

Tatem G, **Kokas M**, **Smith CL**, and **DiGiovine B**. A feasibility assessment of behavioral-based interviewing to improve candidate selection for a pulmonary and critical care medicine fellowship program *Ann Am Thorac Soc* 2017;PMID: 28306323. Full Text

Henry Ford Hospital,Wayne State University, Internal Medicine, Pulmonary and Critical Care, Detroit, Michigan, United States ; gtatem1@hfhs.org.
Henry Ford Hospital,Wayne State University, Department of Medical Education, Henry Ford Hospital, Detroit, Michigan, United States ; mkokas1@hfhs.org.
Henry Ford Hospital,Wayne State University, Organizational Human Resource Development, Henry Ford Health System, Detroit, MI. , Detroit, Michigan, United States ; cath817@gmail.com.

Henry Ford Hospital, Wayne State University, Internal Medicine, Pulmonary and Critical Care, Detroit, Michigan, United States ; bdigiov1@hfhs.org.

Traditional interviews for residency and fellowship training programs are an important component in the selection process, but can be of variable value due to a non-standardized approach. We redesigned the candidate interview process for our large pulmonary and critical care medicine fellowship program in the United States using a behavioral-based interview structure. The primary goal of this approach was to standardize the assessment of candidates within non-cognitive domains with the goal of selecting those with the best fit for our institution's fellowship program. Eight faculty members attended two behavioral-based interview workshops. The first workshop identified our program's "best fit" criteria using the framework of the Accreditation Council for Graduate Medical Education's six core competencies and additional behaviors that fit within our programs. Behavioral-based interview questions were then selected from a national database and refined based on the attributes deemed most important by our faculty. In the second workshop, faculty practiced the behavioral-based interview format in mock interviews with third year fellows. The interview process was further refined based on feedback from the interviewees, and then applied with fellowship candidates for the 2014 recruitment season. The one-year pilot of behavioral-based interviewing allowed us to achieve consensus on the traits sought for our incoming fellows and to standardize the interview process for our program using the framework of the ACGME core competencies. Although the effects of this change on the clinical performance of our fellows have not yet been assessed, this description of our development and implementation processes may be helpful for programs seeking to redesign their applicant interviews.

Hematology / Oncology

Lin S, McCauley EP, Lorig-Roach N, Tenney K, Naphen CN, Yang AM, Johnson TA, Hernadez T, **Rattan R**, **Valeriote FA**, and Crews P. Another look at pyrroloiminoquinone alkaloids-perspectives on their therapeutic potential from known structures and semisynthetic analogues *Mar Drugs* 2017; 15(4)PMID: 28353633. Full Text

Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. linsheng2014cn@gmail.com.
State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China. linsheng2014cn@gmail.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. emccaule@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. nlorigro@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. ktenney@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. cnaphen@gmail.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. aimeiyang@163.com.
School of Life Science and Engineering, Lanzhou University of Technology, Lanzhou 730050, China. aimeiyang@163.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. tyler.johnson@dominican.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. taj_@chemistry.ucsc.edu.
Department of Internal Medicine, Division of Hematology and Oncology, Henry Ford Hospital, Detroit, MI 48202, USA. rrattan1@hfhs.org.
Department of Internal Medicine, Division of Hematology and Oncology, Henry Ford Hospital, Detroit, MI 48202, USA. FVALERI1@hfhs.org.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. pcrews@ucsc.edu.

This study began with the goal of identifying constituents from Zyzzya fuliginosa extracts that showed selectivity in our primary cytotoxicity screen against the PANC-1 tumor cell line. During the course of this project, which focused on six Z. fuliginosa samples collected from various regions of the Indo-Pacific, known compounds were obtained consisting of nine makaluvamine and three damirone analogues. Four new acetylated derivatives were also prepared. High-accuracy electrospray ionization mass spectrometry (HAESI-MS) m/z ions produced through MS(2) runs were obtained and interpreted to provide a rapid way for dereplicating isomers containing a pyrrolo[4,3,2-de]quinoline core. In vitro human pancreas/duct epithelioid carcinoma (PANC-1) cell line IC50 data was obtained for 16 compounds and two therapeutic standards. These results along with data gleaned from the literature provided useful structure activity relationship conclusions. Three structural motifs proved to be important in maximizing potency against PANC-1: (i) conjugation within the core of the ABC-ring; (ii) the presence of a positive charge in the C-ring;

and (iii) inclusion of a 4-ethyl phenol or 4-ethyl phenol acetate substituent off the B-ring. Two compounds, makaluvamine J (9) and 15-O-acetyl makaluvamine J (15), contained all three of these frameworks and exhibited the best potency with IC50 values of 54 nM and 81 nM, respectively. These two most potent analogs were then tested against the OVCAR-5 cell line and the presence of the acetyl group increased the potency 14-fold from that of 9 whose IC50 = 120 nM vs. that of 15 having IC50 = 8.6 nM.

Hospital Medicine

Gunasekaran K, and Murthi S. Unusual metallic penile foreign body *BMJ Case Rep* 2017; 2017PMID: 28348264. Full Text

Henry Ford Health System, Detroit, Michigan, USA.
Department of Internal Medicine, Bassett Healthcare, Cooperstown, New York, USA.
Sinai Grace Hospital, Detroit, Michigan, USA.

Hospital Medicine

Smith SN, Moureau N, Vaughn VM, Boldenow T, **Kaatz S**, Grant PJ, Bernstein SJ, Flanders SA, and Chopra V. Patterns and predictors of peripherally inserted central catheter occlusion: The 3p-o study *J Vasc Interv Radiol* 2017;PMID: 28292637. Full Text

Division of General Internal Medicine, Department of Medicine, University of Michigan Health System, Ann Arbor, Michigan; Quantitative Methods Program, Institute for Social Research, University of Michigan, Ann Arbor, Michigan.
PICC Excellence, Hartwell, Georgia.
Division of General Internal Medicine, Department of Medicine, University of Michigan Health System, Ann Arbor, Michigan.
St. Joseph's Health Center, Ypsilanti, Michigan.
Division of Hospital Medicine, Henry Ford Hospital, Detroit, Michigan.
Division of General Internal Medicine, Department of Medicine, University of Michigan Health System, Ann Arbor, Michigan; Center for Clinical Management Research, VA Ann Arbor Health System, Ann Arbor, Michigan.
Division of General Internal Medicine, Department of Medicine, University of Michigan Health System, Ann Arbor, Michigan; Patient Safety Enhancement Program, VA Ann Arbor Health System, Ann Arbor, Michigan. Electronic address: vineetc@umich.edu.

PURPOSE: To evaluate patterns and predictors of peripherally inserted central catheter (PICC)-related occlusion. MATERIALS AND METHODS: Data from a multihospital study were used to examine factors associated with PICC occlusion. Occlusion was defined if documented in the medical record or when tissue plasminogen activator was administered for occlusion-related concerns. Mixed-effects logistic regression was used to predict occlusion, controlling for patient-, provider-, device-, and hospital-level characteristics. RESULTS: A total of 14,278 PICCs placed in 13,408 patients were included. Of these, occlusion developed in 1,716 PICCs (12%) in 1,684 patients. The most common indications for PICC insertion were intravenous antibiotic therapy (32.7%), difficult intravenous access (21.5%), and central access (13.7%). PICCs placed in the right arm had decreased odds of occlusion compared with those in the left arm (odds ratio [OR] = 0.82; 95% confidence interval [CI] = 0.72-0.94). Verification of catheter tip position following insertion was associated with reduction in occlusion (OR = 0.75; 95% CI = 0.61-0.92). Although normal saline solution or heparin flushes did not reduce occlusion, PICCs flushed with normal saline solution and "locked" with heparin were less likely to become occluded (OR = 0.54; 95% CI = 0.33-0.88). Compared with single-lumen devices, double- and triple-lumen PICCs were associated with greater incidences of occlusion (double, OR = 3.07; 95% CI = 2.56-3.67; triple, OR = 3.72; 95% CI = 2.92-4.74). Catheter tip malposition was also associated with occlusion (OR = 1.46; 95% CI = 1.14-1.87). CONCLUSIONS: Several patient, provider, and device characteristics appear associated with PICC occlusion. Interventions targeting these factors may prove valuable in reducing this complication.

Infectious Diseases

Flynt LK, **Kenney RM**, **Zervos MJ**, and **Davis SL**. The safety and economic impact of cefazolin versus nafcillin for the treatment of methicillin-susceptible staphylococcus aureus bloodstream infections *Infect Dis Ther* 2017;PMID: 28265972. Article Request Form

Henry Ford Hospital, Detroit, MI, USA.
Henry Ford Hospital, Detroit, MI, USA. sldavis@wayne.edu.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. sldavis@wayne.edu.

INTRODUCTION: Anti-staphylococcal penicillins are generally accepted as first-line therapy for methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia, but their use may be limited by interstitial nephritis and acute kidney injury. Alternatives include first-generation cephalosporins including cefazolin. METHODS: We conducted a retrospective cohort study to compare adverse effects and clinical outcomes among patients with MSSA bacteremia treated with cefazolin or nafcillin. The primary endpoint was acute kidney injury (AKI), defined as a 0.3 mg/dL or 50% increase from baseline. RESULTS: Incidence of AKI was 27/82 (33%) versus 9/68 (13%) (p = 0.007) in the nafcillin and cefazolin arms, respectively. After adjusting for endocarditis and intensive care unit admission in multivariate logistic regression, nafcillin was an independent predictor of AKI [adj odds ratio (OR) = 2.74; 95% (CI) 1.1-6.6]. Patients who experienced AKI were more likely to have a prolonged intensive care unit stay. CONCLUSION: Risk of nephrotoxicity is increased with nafcillin compared with cefazolin. Cefazolin should considered as a safer alternative to nafcillin for select patients with MSSA bacteremia.

Internal Medicine

Grosz AM, **Gutierrez D**, Lui AA, Chang JJ, Cole-Kelly K, and Ng H. A student-led introduction to lesbian, gay, bisexual, and transgender health for first-year medical students *Fam Med* 2017; 49(1):52-56. PMID: 28166581. Full Text

Department of Family Medicine, University of California, Los Angeles.

BACKGROUND AND OBJECTIVES: Lesbian, gay, bisexual, and transgender (LGBT) individuals face significant health disparities. This is in part because many physicians are not sensitive to, and/or are underprepared to address, LGBT-specific concerns. To help meet this need, we, a group of second- and fourth-year medical students with faculty oversight, organized a session on LGBT health for first-year medical students. METHODS: The three second-year and one fourth-year student authors designed a mandatory session for the 167 first-years at Case Western Reserve University School of Medicine in Cleveland, OH. The 2-hour session consisted of a student-delivered presentation, a patient panel, and a small-group session. Students' LGBT health knowledge and confidence in providing care were assessed anonymously before and after the session, and individuals' pre- and post-session assessments were paired using student-generated identifiers. RESULTS: A total of 73 complete, matched pre-/post-session assessments were received. Students' familiarity with LGBT terminology and demographics increased significantly after the session. Students' perceived preparedness and comfort in providing LGBT-specific care significantly improved in most areas as well. Students strongly praised the session, in particular the patient panel. CONCLUSION: A student-led educational session on LGBT health can effectively improve first-year medical students' LGBT knowledge and confidence to provide care.

Internal Medicine

Lenhart A, **Hassan M**, **Meighani A**, **Sadiq O**, and **Siddiqui Y**. A perplexing case of abdominal pain that led to the diagnosis of zollinger-ellison syndrome *Case Rep Gastrointest Med* 2017; 2017:7636952. PMID: 28321346. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
Division of Gastroenterology and Hepatology, Henry Ford Hospital, Detroit, MI 48202, USA.

Zollinger-Ellison syndrome (ZES) is a rare clinical disorder, characterized by hypersecretion of gastric acid and multiple ulcers distal to the duodenal bulb. This occurs via the release of gastrin by neuroendocrine tumors known as gastrinomas. Patients with ZES present with nonspecific GI symptoms, which often leads to a delay in diagnosis. Our patient is a 55-year-old female with chronic abdominal pain, nausea, and diarrhea. She underwent EGD, EUS, MRCP, CT scans, and cholecystectomy, which did not reveal the cause of her symptoms. Repeat EGD showed a cratered ulcer in the second portion of the duodenum, suspicious for ZES. Serum gastrin was initially only moderately elevated while on PPI therapy, but chromogranin A was also elevated. Repeat gastrin level after stopping PPI therapy was 1639 pg/mL. Somatostatin receptor scintigraphy was obtained, which showed two small lesions in the gastrinoma triangle. She subsequently underwent a Whipple pancreaticoduodenectomy and pathology was positive for four microscopic foci of a neuroendocrine tumor. She reported improvement in her symptoms after surgery. This case highlights the need for increased awareness of ZES in patients with unexplained GI complaints and emphasizes the use of multiple modalities in the diagnosis of ZES.

Internal Medicine

Lin S, McCauley EP, Lorig-Roach N, Tenney K, Naphen CN, Yang AM, Johnson TA, Hernadez T, **Rattan R**, **Valeriote FA**, and Crews P. Another look at pyrroloiminoquinone alkaloids-perspectives on their therapeutic potential from known structures and semisynthetic analogues *Mar Drugs* 2017; 15(4)PMID: 28353633. Full Text

Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. linsheng2014cn@gmail.com.
State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China. linsheng2014cn@gmail.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. emccaule@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. nlorigro@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. ktenney@ucsc.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. cnaphen@gmail.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. aimeiyang@163.com.
School of Life Science and Engineering, Lanzhou University of Technology, Lanzhou 730050, China. aimeiyang@163.com.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. tyler.johnson@dominican.edu.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. taj_@chemistry.ucsc.edu.
Department of Internal Medicine, Division of Hematology and Oncology, Henry Ford Hospital, Detroit, MI 48202, USA. rrattan1@hfhs.org.
Department of Internal Medicine, Division of Hematology and Oncology, Henry Ford Hospital, Detroit, MI 48202, USA. FVALERI1@hfhs.org.
Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA. pcrews@ucsc.edu.

This study began with the goal of identifying constituents from Zyzzya fuliginosa extracts that showed selectivity in our primary cytotoxicity screen against the PANC-1 tumor cell line. During the course of this project, which focused on six Z. fuliginosa samples collected from various regions of the Indo-Pacific, known compounds were obtained consisting of nine makaluvamine and three damirone analogues. Four new acetylated derivatives were also prepared. High-accuracy electrospray ionization mass spectrometry (HAESI-MS) m/z ions produced through MS(2) runs were obtained and interpreted to provide a rapid way for dereplicating isomers containing a pyrrolo[4,3,2-de]quinoline core. In vitro human pancreas/duct epithelioid carcinoma (PANC-1) cell line IC50 data was obtained for 16 compounds and two therapeutic standards. These results along with data gleaned from the literature provided useful structure activity relationship conclusions. Three structural motifs proved to be important in maximizing potency against PANC-1: (i) conjugation within the core of the ABC-ring; (ii) the presence of a positive charge in the C-ring; and (iii) inclusion of a 4-ethyl phenol or 4-ethyl phenol acetate substituent off the B-ring. Two compounds, makaluvamine J (9) and 15-O-acetyl makaluvamine J (15), contained all three of these frameworks and exhibited the best potency with IC50 values of 54 nM and 81 nM, respectively. These two most potent analogs were then tested against the OVCAR-5 cell line and the presence of the acetyl group increased the potency 14-fold from that of 9 whose IC50 = 120 nM vs. that of 15 having IC50 = 8.6 nM.

Nephrology

Yee J. The tubulointerstitium: Dark matter *Adv Chronic Kidney Dis* 2017; 24(2):51-54. PMID: 28284378. Full Text

Henry Ford Hospital, Wayne State University, Detroit, MI.

Neurology

Ali R, Elsayed M, **Kaur M**, **Air E**, **Mahmood N**, **Constantinou J**, and **Schwalb J**. Use of social media to assess the effectiveness of vagal nerve stimulation in Dravet syndrome: A caregiver's perspective *J Neurol Sci* 2017; 375:146-149. PMID: 28320117. Full Text

Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA. Electronic address: rali1@hfhs.org.
SIU Healthcare, SIU Clinic Bldg, 751 North Rutledge, Rm 3100, Springfield, IL 62702, USA.
Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA.

BACKGROUND: Dravet syndrome (DS) is a rare genetic epilepsy syndrome which is particularly pharmacoresistant. Vagus nerve stimulation (VNS) is commonly used in the treatment of DS as an adjunct to medical therapy. A meaningful assessment of post-surgical outcomes with VNS is difficult given the rarity of the condition. OBJECTIVE: In a novel approach, we used social media to contact patients with DS to gather data on post-surgical seizure reduction and overall satisfaction with VNS. METHODS: A survey consisting of 10 questions was posted to a social media webpage for a DS support group moderated by the Dravet Syndrome Foundation. The results were analyzed and percentages reported using the integrated SurveyMonkey analytical software. RESULTS: 49 responses were received. We found that 28.5% of patients had a >50% reduction in seizure frequency after VNS placement, 55.8% felt that VNS therapy had helped to reduce seizure frequency, and 83.7% felt that seizure severity had improved. Of the respondents, 75% felt that they would undergo VNS implantation again for similar outcomes. CONCLUSIONS: We employed the novel technique of using social media to gather the largest set of self-reported outcomes of VNS therapy for Dravet syndrome. As corroborated by prior studies of VNS effectiveness in Dravet syndrome, there is significant albeit limited improvement in seizure control. Our study shows that despite this limitation, it is still considered a useful treatment adjunct from a caregiver's perspective.

Neurology
Al-Mufti F, and **Mayer SA**. Neurocritical care of acute subdural hemorrhage *Neurosurg Clin N Am* 2017; 28(2):267-278. PMID: 28325461. Full Text

Endovascular Surgical Neuroradiology Program, Rutgers University-New Jersey Medical School, Newark, NJ, USA. Department of Neurology, Henry Ford Health System, 2799 W Grand Boulevard, Detroit, MI 48202, USA. Electronic address: stephanamayer@gmail.com.

Although urgent surgical hematoma evacuation is necessary for most patients with subdural hematoma (SDH), well-orchestrated, evidenced-based, multidisciplinary, postoperative critical care is essential to achieve the best possible outcome. Acute SDH complicates approximately 11% of mild to moderate traumatic brain injuries (TBIs) that require hospitalization, and approximately 20% of severe TBIs. Acute SDH usually is related to a clear traumatic event, but in some cases can occur spontaneously. Management of SDH in the setting of TBI typically conforms to the Advanced Trauma Life Support protocol with airway taking priority, and management breathing and circulation occurring in parallel rather than sequence.

Neurology
Kassis H, **Shehadah A**, **Chopp M**, and **Zhang ZG**. Epigenetics in stroke recovery *Genes (Basel)* 2017; 8(3)PMID: 28264471. Full Text

Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA. haifa.kassis@gmail.com.
Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA. amjad.shehadah@gmail.com.
Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA. michael.chopp@gmail.com.
Department of Physics, Oakland University, Rochester, MI 48309, USA. michael.chopp@gmail.com.
Department of Neurology, Henry Ford Health System, Detroit, MI 48202, USA. zzhang1@hfhs.org.

While the death rate from stroke has continually decreased due to interventions in the hyperacute stage of the disease, long-term disability and institutionalization have become common sequelae in the aftermath of stroke. Therefore, identification of new molecular pathways that could be targeted to improve neurological recovery among survivors of stroke is crucial. Epigenetic mechanisms such as post-translational modifications of histone proteins and microRNAs have recently emerged as key regulators of the enhanced plasticity observed during repair processes after stroke. In this review, we highlight the recent advancements in the evolving field of epigenetics in stroke recovery.

Neurology
Mahajan A, and **Sidiropoulos C**. TPK1 mutation induced childhood onset idiopathic generalized dystonia: Report of a rare mutation and effect of deep brain stimulation *Journal of the Neurological Sciences* 2017; 376:42-43. PMID: Not assigned. Full Text

A. Mahajan, Detroit, United States

A genetic etiology has otherwise been described for vitamin defi-ciency induced dystonia in Biotin responsive basal ganglia disease [1–3]. Thiamine pyrophosphokinase (TPK) is a cofactor for several enzymes in the thiamine metabolism. Banka et al. reported 2 cases with a TPK 1 mutation presenting as episodic encephalopathy with

improvement after thiamine supplementation [4]. Mayr et al. reported five individuals from three families presenting with progressive dystonia, ataxia, psychomotor retardation, and lactic acidosis, among which two siblings from consanguineous parents (first cousins) of an Iraqi Christian minority [5].

Neurology
Wang L, **Chopp M**, and **Zhang ZG**. PDE5 inhibitors promote recovery of peripheral neuropathy in diabetic mice *Neural Regen Res* 2017; 12(2):218-219. PMID: Not assigned. Abstract

L. Wang, Department of Neurology, Henry Ford Hospital, Detroit, United States

Neurosurgery
Ali R, Elsayed M, **Kaur M**, **Air E**, **Mahmood N**, **Constantinou J**, and **Schwalb J**. Use of social media to assess the effectiveness of vagal nerve stimulation in Dravet syndrome: A caregiver's perspective *J Neurol Sci* 2017; 375:146-149. PMID: 28320117. Full Text

Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA. Electronic address: rali1@hfhs.org.
SIU Healthcare, SIU Clinic Bldg, 751 North Rutledge, Rm 3100, Springfield, IL 62702, USA.
Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA.
Department of Neurology, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA.

BACKGROUND: Dravet syndrome (DS) is a rare genetic epilepsy syndrome which is particularly pharmacoresistant. Vagus nerve stimulation (VNS) is commonly used in the treatment of DS as an adjunct to medical therapy. A meaningful assessment of post-surgical outcomes with VNS is difficult given the rarity of the condition. OBJECTIVE: In a novel approach, we used social media to contact patients with DS to gather data on post-surgical seizure reduction and overall satisfaction with VNS. METHODS: A survey consisting of 10 questions was posted to a social media webpage for a DS support group moderated by the Dravet Syndrome Foundation. The results were analyzed and percentages reported using the integrated SurveyMonkey analytical software. RESULTS: 49 responses were received. We found that 28.5% of patients had a >50% reduction in seizure frequency after VNS placement, 55.8% felt that VNS therapy had helped to reduce seizure frequency, and 83.7% felt that seizure severity had improved. Of the respondents, 75% felt that they would undergo VNS implantation again for similar outcomes. CONCLUSIONS: We employed the novel technique of using social media to gather the largest set of self-reported outcomes of VNS therapy for Dravet syndrome. As corroborated by prior studies of VNS effectiveness in Dravet syndrome, there is significant albeit limited improvement in seizure control. Our study shows that despite this limitation, it is still considered a useful treatment adjunct from a caregiver's perspective.

Neurosurgery
Chang V, **Basheer A**, **Baumer T**, **Oravec D**, **McDonald CP**, **Bey MJ**, **Bartol S**, and **Yeni YN**. Dynamic measurements of cervical neural foramina during neck movements in asymptomatic young volunteers *Surg Radiol Anat* 2017;PMID: 28343254. Full Text

Department of Neurosurgery, Henry Ford Hospital, K-11, 2799W. Grand Blvd, Detroit, MI, USA. vchang1@hfhs.org.
Department of Neurosurgery, Henry Ford Hospital, K-11, 2799W. Grand Blvd, Detroit, MI, USA.
Department of Orthopedic Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Mechanical Engineering, McMaster University, Hamilton, ON, Canada.

PURPOSE: Neural foraminal dimensions are considered important in nerve root compression and development of cervical radiculopathy, but baseline data regarding their range during normal motion are not available. An in vivo study of cervical foraminal motion was conducted to characterize normal 3D dynamic foraminal dimensions during physiological neck motion and compare between different tasks and intervertebral segments. METHODS: Biplane X-ray imaging and computed tomography-based markerless tracking were used to measure foraminal height (FH) and width (FW) from five asymptomatic subjects during neck axial rotation and extension. FH and FW were quantified as the minimum (SI.Min and AP.Min), range (SI.Range and AP.Range), and median (SI.Med and AP.Med) of superoinferior (SI) and anteroposterior (AP) dimensions for each trial and as the coefficient of variation of these variables from three trials (SI.Med.CV and AP.Med.CV, SI.Range.CV and AP.Range.CV) at C3-4 through C6-7 levels for each subject. Differences were analyzed using mixed model ANOVA. RESULTS: AP.Range and AP.Med.CV were greater ($P < 0.0001$) while AP.Min and AP.Range.CV were smaller ($P < 0.0006$ and $P < 0.0005$) during neck extension than rotation. SI.Range and SI.Med.CV were greater for extension than rotation at C5-6 ($P < 0.002$ and $P < 0.03$), whereas SI.Med.CV was greater for rotation than extension at C3-4 ($P < 0.03$). AP.Range ($P < 0.02$),

AP.Med.CV (P < 0.05), SI.Range (P < 0.0004), and SI.Med.CV (P < 0.02) were different between cervical levels, the latter two being during extension only. CONCLUSIONS: Patterns of FH and FW during normal motion are different between tasks and cervical levels. These findings are expected to provide a basis for future studies of spinal degeneration and surgical efficacy.

Obstetrics, Gynecology and Women's Health Services

Abdulfatah E, Ghanim MT, Chaib O, Daaboul M, Alosh B, Al-Obaidy KI, Mahdi Z, Hayek K, **Sakr S**, **Munkarah AR**, Bandyopadhyay S, and Ali-Fehmi R. Ovarian granulosa cell tumors: A surveillance, epidemiology and end results (seer) data review of prognostic clinicopathological parameters in 1815 patients *Lab Invest* 2017; 97:271A-271A. PMID: Not assigned. Abstract

Wayne State Univ, Sch Med, Detroit, MI USA. Wayne State Univ, Karmanos Canc Ctr, Detroit, MI USA. Henry Ford Hlth Syst, Detroit, MI USA.

Orthopaedics

Chang V, **Basheer A**, **Baumer T**, **Oravec D**, **McDonald CP**, **Bey MJ**, **Bartol S**, and **Yeni YN**. Dynamic measurements of cervical neural foramina during neck movements in asymptomatic young volunteers *Surg Radiol Anat* 2017;PMID: 28343254. Full Text

Department of Neurosurgery, Henry Ford Hospital, K-11, 2799W. Grand Blvd, Detroit, MI, USA. vchang1@hfhs.org.
Department of Neurosurgery, Henry Ford Hospital, K-11, 2799W. Grand Blvd, Detroit, MI, USA.
Department of Orthopedic Surgery, Henry Ford Hospital, Detroit, MI, USA.
Department of Mechanical Engineering, McMaster University, Hamilton, ON, Canada.

PURPOSE: Neural foraminal dimensions are considered important in nerve root compression and development of cervical radiculopathy, but baseline data regarding their range during normal motion are not available. An in vivo study of cervical foraminal motion was conducted to characterize normal 3D dynamic foraminal dimensions during physiological neck motion and compare between different tasks and intervertebral segments. METHODS: Biplane X-ray imaging and computed tomography-based markerless tracking were used to measure foraminal height (FH) and width (FW) from five asymptomatic subjects during neck axial rotation and extension. FH and FW were quantified as the minimum (SI.Min and AP.Min), range (SI.Range and AP.Range), and median (SI.Med and AP.Med) of superoinferior (SI) and anteroposterior (AP) dimensions for each trial and as the coefficient of variation of these variables from three trials (SI.Med.CV and AP.Med.CV, SI.Range.CV and AP.Range.CV) at C3-4 through C6-7 levels for each subject. Differences were analyzed using mixed model ANOVA. RESULTS: AP.Range and AP.Med.CV were greater (P < 0.0001) while AP.Min and AP.Range.CV were smaller (P < 0.0006 and P < 0.0005) during neck extension than rotation. SI.Range and SI.Med.CV were greater for extension than rotation at C5-6 (P < 0.002 and P < 0.03), whereas SI.Med.CV was greater for rotation than extension at C3-4 (P < 0.03). AP.Range (P < 0.02), AP.Med.CV (P < 0.05), SI.Range (P < 0.0004), and SI.Med.CV (P < 0.02) were different between cervical levels, the latter two being during extension only. CONCLUSIONS: Patterns of FH and FW during normal motion are different between tasks and cervical levels. These findings are expected to provide a basis for future studies of spinal degeneration and surgical efficacy.

Otolaryngology – Head and Neck Surgery

Arden RL, and **Miller LK**. Application of trotter approach for large intralingual thyroglossal duct cyst in an 88-year-old patient *J Oral Maxillofac Surg* 2017;PMID: 28284788. Full Text

Chief of Otolaryngology-Head and Neck Surgery, Department of Surgery Division, William Beaumont Hospital, Troy, MI. Electronic address: richardlarden@aol.com.
Department of Otolaryngology-Facial Plastic Surgery, Henry Ford Macomb Hospital, Clinton Township, MI.

Thyroglossal duct cysts (TDCs) are the most common congenital cyst formations in the neck, typically occurring at midline infrahyoid positions in younger patients. Traditional management has used the Sistrunk procedure to minimize recurrence rates. Reports on elderly patients are sparse, and currently only 14 cases have been reported in patients older than 70 years and 4 patients older than 80 years. This report describes the oldest known patient with TDC who had a purely intralingual location requiring a Trotter approach and a Sistrunk procedure for symptomatic management.

Otolaryngology – Head and Neck Surgery

Smith MM, **Peterson E**, and **Yaremchuk KL**. The role of tonsillectomy in adults with tonsillar hypertrophy and obstructive sleep apnea *Otolaryngol Head Neck Surg* 2017:194599817698671. PMID: 28349770. Full Text

1 Department of Pediatric Otolaryngology-Head and Neck Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.
2 Department of Public Health Sciences, Henry Ford Hospital, Detroit, Michigan, USA.
3 Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, USA.

Objective To determine if tonsillectomy alone is an effective treatment in improving obstructive sleep apnea in adult subjects with tonsillar hypertrophy and to evaluate the effect of tonsillectomy on patient-reported quality-of-life indices. Study Design Case series with planned data collection. Setting Academic hospital. Subjects and Methods Thirty-four subjects completed enrollment and intervention from January 2011 to January 2016. Subjects completed pre- and postoperative quality-of-life questionnaires, including the Insomnia Severity Index, Epworth Sleepiness Scale, and the Functional Outcomes of Sleep Questionnaire-10. Surgical response to treatment was defined by a >50% decrease in the Apnea-Hypopnea Index and a decrease in the overall Apnea-Hypopnea Index to <20. Wilcoxon matched-pairs signed-rank tests were used to test each variable to assess for a change from pre- to postintervention. Subjects were then split into 3 BMI subgroups, with results also evaluated by Wilcoxon matched-pairs signed-rank tests. Results There was a significant difference discovered between the mean preoperative Apnea-Hypopnea Index of 31.57 and the mean postoperative value of 8.12 (P < .001). All patient-reported outcomes improved significantly following tonsillectomy. After stratifying all outcome variables (Apnea-Hypopnea Index, Epworth Sleepiness Scale, Insomnia Severity Index, and Functional Outcomes of Sleep Questionnaire-10) by sex, race, and tonsil size, no statistically significant difference was noted among any of these subgroups. There was a 78% surgical response to treatment. Conclusion Tonsillectomy appears to be an effective treatment for obstructive sleep apnea in a select population of adults with tonsillar hypertrophy.

Otolaryngology – Head and Neck Surgery

Yaremchuk K, **Darian V**, and **Williams AM**. Seasonality of auricular amputations in rabbits *Laryngoscope* 2017; 127(4):773-775. PMID: 28322456. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
Division of Plastic and Reconstructive Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.

This retrospective observational analysis hypothesizes that an increase occurs in online reports and images of auricular amputations of confectionary rabbits during the spring. Using the online search engine Google, online content and visual portrayals of confectionary rabbit auricular amputations from 2012 to 2017 were identified and trended against seasonal variations. To determine incidence, commercial availability of chocolate rabbits in retail facilities were assayed. A statistically significant increase in mention of rabbit auricular amputations occurred during the spring. Mapping techniques showed the annual peak incidence for 2012 to 2017 to be near Easter for each year studied. Human adults and children appear to be wholly responsible for the reports of rabbit auricular amputations. Reconstructive techniques are dependent on the percentage of auricular defect. Laryngoscope, 127:773-775, 2017.

Pathology

Banks P, Brown R, Laslowski A, Daniels Y, Branton P, Carpenter J, **Zarbo R**, Forsyth R, Liu YH, Kohl S, Diebold J, Masuda S, Plummer T, and Dennis E. A proposed set of metrics to reduce patient safety risk from within the anatomic pathology laboratory *Lab Med* 2017;PMID: 28340232. Full Text

Medical Affairs, Ventana Medical Systems Inc., Tucson, AZ.
Laboratory Services, Memorial Hermann Southeast Hospital, Houston, TX.
Department of Laboratory Medicine, Monash Medical Centre, Clayton, Victoria, Australia.
Department of Pathology, East Carolina University, Greenville, NC.
Biorepositories and Biospecimens Research Branch, Cancer Diagnosis Program, National Institutes of Health, Bethesda, MD.
Division of Pathology, Puget Sound Gastroenterology Medical Center, Lynnwood, WA.
Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, MI.
Department of Pathology, Universitair Ziekenhuis Brussels, Brussels, Belgium.
Department of Pathology, Guangdong General Hospital, Guangdong Academy of Medical Science Guangdong Province, China.
Anatomic & Clinical Pathology, Nebraska Methodist Health System, Inc, Omaha, NE.
Leiter Departement Institute, Luzerner Kantonsspital, Lucerne, Switzerland.

Department of Pathology, Nihon University School of Medicine, Tokyo, Japan.
Operations Division, Mayo Clinic, Mayo College of Medicine, Rochester, MN.

Background: Anatomic pathology laboratory workflow consists of 3 major specimen handling processes. Among the workflow are preanalytic, analytic, and postanalytic phases that contain multistep subprocesses with great impact on patient care. A worldwide representation of experts came together to create a system of metrics, as a basis for laboratories worldwide, to help them evaluate and improve specimen handling to reduce patient safety risk. Method: Members of the Initiative for Anatomic Pathology Laboratory Patient Safety (IAPLPS) pooled their extensive expertise to generate a list of metrics highlighting processes with high and low risk for adverse patient outcomes. Results: : Our group developed a universal, comprehensive list of 47 metrics for patient specimen handling in the anatomic pathology laboratory. Steps within the specimen workflow sequence are categorized as high or low risk. In general, steps associated with the potential for specimen misidentification correspond to the high-risk grouping and merit greater focus within quality management systems. Primarily workflow measures related to operational efficiency can be considered low risk. Conclusion: Our group intends to advance the widespread use of these metrics in anatomic pathology laboratories to reduce patient safety risk and improve patient care with development of best practices and interlaboratory error reporting programs.

Pathology
Fuller M, Gardner JM, Crane GM, **Williamson SR**, Chiosea S, Arnold CA, Arnold MA, Wasco MJ, and Jiang XYS. #pathjc: The founding and success of the first twitter pathology journal club *Lab Invest* 2017; 97:140A-140A. PMID: Not assigned. Abstract

Houston Methodist, Houston, TX USA. UAMS, Little Rock, AR USA. UTSW, Dallas, TX USA. Henry Ford Hlth, Detroit, MI USA. UPMC, Pittsburgh, PA USA. OSU, Columbus, OH USA. Nationwide Childrens Hosp, Columbus, OH USA. St Joseph Mercy Hosp, Ann Arbor, MI USA. Duke Hlth, Durham, NC USA.

Pathology
Gadde R, and **Chitale D**. "Is estrogen receptor positive (er plus) progesterone receptor negative (pr-) invasive lobular carcinoma a distinct clinicopathologic subset?" *Lab Invest* 2017; 97:41A-42A. PMID: Not assigned. Abstract

[Gadde, Ramya; Chitale, Dhananjay] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Gadde R, and **Chitale D**. Mammary and extra-mammary paget's disease-an institutional experience *Lab Invest* 2017; 97:41A-41A. PMID: Not assigned. Abstract

[Gadde, Ramya; Chitale, Dhananjay] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Gulati R, **Carey JL**, **Chitale D**, and **Sharma G**. An effective and multidisciplinary utilization framework for esoteric/referred tests in molecular pathology *Lab Invest* 2017; 97:507A-507A. PMID: Not assigned. Abstract

[Gulati, Rohit; Carey, John L.; Chitale, Dhananjay; Sharma, Gaurav] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Jamal M, **Brown R**, **Inamdar KV**, **Gomez-Gelvez J**, **Carey JL**, and **Menon MP**. Evaluation of flow cytometric variables in mycosis fungoides blood staging *Lab Invest* 2017; 97:356A-356A. PMID: Not assigned. Abstract

[Jamal, Mohsin; Brown, Ron; Inamdar, Kedar V.; Gomez-Gelvez, Juan; Carey, John L.; Menon, Madhu P.] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Jamal M, **Rayes O**, **Samuel L**, **Tibbetts R**, and **Pimentel JD**. Closing the brief case: Benign rectal polyp with schistosoma mansoni *J Clin Microbiol* 2017; 55(4):1226-1227. PMID: 28341803. Article Request Form

Department of Pathology, Henry Ford Hospital, Detroit, Michigan, USA.

Department of Pathology, Henry Ford Hospital, Detroit, Michigan, USA rtibbet1@hfhs.org.

Pathology
Jamal M, **Rayes O**, **Samuel L**, **Tibbetts R**, and **Pimentel JD**. The brief case: Benign rectal polyp with schistosoma mansoni *J Clin Microbiol* 2017; 55(4):992-995. PMID: 28341802. Article Request Form

Department of Pathology, Henry Ford Hospital, Detroit, Michigan, USA.
Department of Pathology, Henry Ford Hospital, Detroit, Michigan, USA rtibbet1@hfhs.org.

Pathology
Jebastin JAS, **Gupta NS**, **Carskadon S**, **Palanisamy N**, and **Williamson SR**. Pseudosarcomatous myofibroblastic proliferations of the urinary bladder lack the usp6 gene rearrangement common in nodular fasciitis *Lab Invest* 2017; 97:233A-233A. PMID: Not assinged. Abstract

[Jebastin, Judith A. S.; Gupta, Nilesh S.; Carskadon, Shannon; Palanisamy, Nallasivam; Williamson, Sean R.] Henry Ford Hlth Syst, Detroit, MI USA.

Pathology
Loudig O, Wang T, Ye K, Lin J, Wang Y, Ramnauth A, Liu C, **Stark A**, **Chitale D**, Greenlee R, Multerer D, Honda S, Daida Y, Spencer Feigelson H, Glass A, Couch FJ, Rohan T, and Ben-Dov IZ. Evaluation and adaptation of a laboratory-based cdna library preparation protocol for retrospective sequencing of archived micrornas from up to 35-year-old clinical ffpe specimens *Int J Mol Sci* 2017; 18(3)PMID: 28335433. Full Text

Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. Olivier.loudig@einstein.yu.edu.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. tao.wang@einstein.yu.edu.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. kenny.ye@einstein.yu.edu.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. Juan.lin@einstein.yu.edu.
Department of Pathology, Rhode Island Hospital, Providence, RI 02903, USA. ywang6@Lifespan.org.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. andrew.ramnauth12@myhunter.cuny.edu.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. christina.liu@einstein.yu.edu.
Department of Pathology and Breast Oncology Program, Henry Ford Health System, Detroit, MI 48202, USA. ASTARK1@hfhs.org.
Department of Pathology and Breast Oncology Program, Henry Ford Health System, Detroit, MI 48202, USA. dchital1@hfhs.org.
Center for Clinical Epidemiology and Population Health, Marshfield Clinic Research Foundation, Marshfield, WI 54449, USA. greenlee.robert@mcrf.mfldclin.edu.
Center for Clinical Epidemiology and Population Health, Marshfield Clinic Research Foundation, Marshfield, WI 54449, USA. multerer.deborah@mcrf.mfldclin.edu.
Department of Pathology, Center for Health Research, Kaiser Permanente, 3288 Moanalua Road, Honolulu, HI 96819, USA. Stacey.Honda@kp.org.
Department of Pathology, Center for Health Research, Kaiser Permanente, 3288 Moanalua Road, Honolulu, HI 96819, USA. Yihe.G.Daida@kp.org.
Center for Excellence in Cancer and Genomics, Kaiser Permanente Colorado, Denver, CO 80237, USA. heather.s.feigelson@kp.org.
Center for Health Research, Kaiser Permanente Northwest, Portland, OR 97227, USA. andy_5241@msn.com.
Health Sciences Research, Mayo Clinic, Rochester, NY 55902, USA. couch.fergus@mayo.edu.
Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA. thomas.rohan@einstein.yu.edu.
Montefiore Medical Center, Bronx, NY 10467, USA. thomas.rohan@einstein.yu.edu.
Laboratory of Medical Transcriptomics, Hadassah-Hebrew University Medical Center, Jerusalem 91120, Israel. Iddo@hadassah.org.il.

Formalin-fixed paraffin-embedded (FFPE) specimens, when used in conjunction with patient clinical data history, represent an invaluable resource for molecular studies of cancer. Even though nucleic acids extracted from archived FFPE tissues are degraded, their molecular analysis has become possible. In this study, we optimized a laboratory-based next-generation sequencing barcoded cDNA library preparation protocol for analysis of small RNAs recovered from archived FFPE tissues. Using matched fresh and FFPE specimens, we evaluated the robustness and reproducibility of our optimized approach, as well as its applicability to archived clinical specimens stored for up to 35 years. We then evaluated this cDNA library preparation protocol by performing a miRNA expression analysis of archived breast ductal carcinoma in situ (DCIS) specimens, selected for their relation to the risk of subsequent breast cancer development and obtained from six different institutions. Our analyses identified six miRNAs (miR-29a, miR-221, miR-375, miR-184, miR-363, miR-455-5p) differentially expressed between DCIS lesions from women who subsequently developed an invasive breast cancer (cases) and women who did not develop invasive breast cancer within the same time interval (control). Our thorough evaluation and application of this laboratory-based miRNA sequencing analysis indicates that the preparation of small RNA cDNA libraries can reliably be performed on older, archived, clinically-classified specimens.

Pathology
Lu ZC, **Gupta NS**, and **Chitale D**. Clinicopathologic characteristics and survival outcomes of small size breast carcinoma with metastasis *Lab Invest* 2017; 97:57A-58A. PMID: Not assigned. Abstract

[Lu, Zhichun; Gupta, Nilesh S.; Chitale, Dhananjay] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Lu ZC, **Noyes L**, **Cole G**, **Schultz D**, **Arthur G**, and **Zhang ZY**. Cytologic study of atypical squamous cells of unknown significance (ascus) on thinprep liquid based cytology and relationship to high risk hpv (hrhpv) status *Lab Invest* 2017; 97:106A-107A. PMID: Not assigned. Abstract

[Lu, Zhichun; Noyes, Lauren; Cole, Gary; Schultz, Daniel; Arthur, Gaba; Zhang, Ziying] Henry Ford Hlth Syst, Detroit, MI USA.

Pathology
Pagano MB, Wehrli G, Cloutier D, Galvin Karr E, **Lopez-Plaza I**, Schwartz J, Andrzejewski C, Winters JL, Wong EC, Wu Y, and Zantek ND. Apheresis medicine education in the united states of america: State of the discipline *Transfus Apher Sci* 2017; 56(1):1-5. PMID: 28089411. Full Text

Department of Laboratory Medicine, University of Washington, Seattle, WA 98195, United States. Electronic address: monibea@uw.edu.
Department of Pathology and Laboratory Medicine, University of Virginia, Charlottesville, VA, United States.
Transfusion and Apheresis Medicine Services, Department of Pathology, Baystate Medical Center, Baystate Health, Springfield, MA, United States.
Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, MI, United States.
Department of Pathology and Cell Biology, Columbia University, New York, NY, United States.
Department of Pathology, University of Massachusetts Medical School-Baystate, Springfield, MA, United States.
Department of Pathology and Laboratory Medicine, Mayo Clinic, Rochester, MN, United States.
Departments of Pediatrics and Pathology, George Washington School of Medicine and Health Sciences, Washington, DC, United States; Department of Coagulation, Quest Diagnostics Nichols Institute, Chantilly, VA, United States.
Bloodworks Northwest, Seattle, WA, United States.
Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, United States.

Apheresis Medicine is a medical discipline that involves a variety of procedures (based on the targeted component to be removed or collected), indications (therapeutic vs. donation), and personnel (operators, management, and medical oversight). Apheresis services are accredited and/or regulated by a number of agencies and organizations. Given the complexity and the heterogeneity of apheresis services, it has been particularly challenging to formulate educational goals and define curriculums that easily cover all aspects of Apheresis Medicine. This review summarizes the current state of the discipline in the United States of America, and some of the challenges, strategies, and resources that Apheresis Medicine educators have used to ensure that Apheresis Medicine educational programs meet the health care needs of the relevant population within regulatory and accrediting entity frameworks.

Pathology
Rundle A, **Wang Y**, **Sadasivan S**, **Chitale DA**, **Gupta NS**, Tang D, and **Rybicki BA**. Larger men have larger prostates: Detection bias in epidemiologic studies of obesity and prostate cancer risk *Prostate* 2017;PMID: 28349547.
Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan.
Department of Pathology, Henry Ford Health System, Detroit, Michigan.
Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York.

BACKGROUND: Obesity is associated with risk of aggressive prostate cancer (PCa), but not with over-all PCa risk. However, obese men have larger prostates which may lower biopsy accuracy and cause a systematic bias toward the null in epidemiologic studies of over-all risk. METHODS: Within a cohort of 6692 men followed-up after a biopsy or transurethral resection of the prostate (TURP) with benign findings, a nested case-control study was conducted of 495 prostate cancer cases and controls matched on age, race, follow-up duration, biopsy versus TURP, and procedure date. Data on body mass index and prostate volume at the time of the initial procedure were abstracted from medical records. RESULTS: Prior to consideration of differences in prostate volume, overweight (OR = 1.41; 95%CI 1.01, 1.97), and obese status (OR = 1.59; 95%CI 1.09, 2.33) at the time of the original benign biopsy or TURP were associated with PCa incidence during follow-up. Prostate volume did not significantly moderate the association between body-size and PCa, however it did act as an inverse confounder; adjustment for prostate volume increased the effect size for overweight by 22% (adjusted OR = 1.52; 95%CI 1.08, 2.14) and for obese status by 23% (adjusted OR = 1.77; 95%CI 1.20, 2.62). Larger prostate volume at the time of the original benign biopsy or TURP was inversely associated with PCa incidence during follow-up (OR = 0.92 per 10 cc difference in volume; 95%CI 0.88, 0.97). In analyses that stratified case-control pairs by tumor aggressiveness of the case, prostate volume acted as an inverse confounder in analyses of non-aggressive PCa but not in analyses of aggressive PCa. CONCLUSIONS: In studies of obesity and PCa, differences in prostate volume cause a bias toward the null, particularly in analyses of non-aggressive PCa. A pervasive underestimation of the association between obesity and overall PCa risk may exist in the literature.

Pathology
Shah AB, **Gupta NS**, and **Williamson SR**. Variant histologies are common in urinary tract cancers with positive polyomavirus (sv40) antigen immunohistochemistry *Lab Invest* 2017; 97:258A-259A. PMID: Not assigned. Abstract

[Shah, Alpa B.; Gupta, Nilesh S.; Williamson, Sean R.] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Tashakori M, **Sanchez J**, **Michalowski SM**, Louissaint A, **Inamdar KV**, **Gomez-Gelvez J**, **Carey JL**, and **Menon MP**. Follicular lymphoma transforming to double and triple hit lymphoma; a clinicopathologic, morphologic and cytogenetic analysis *Lab Invest* 2017; 97:380A-381A. PMID: Not assigned. Abstract

Henry Ford Hlth Syst, Detroit, MI USA. Massachusetts Gen Hosp, Boston, MA 02114 USA.

Pathology
Trpkov K, Athanazio D, Magi-Galluzzi C, Yilmaz H, Clouston D, Agaimy A, **Williamson SR**, Brimo F, Lopez JI, Ulamec M, Rioux-Leclercq N, Kassem M, Gupta NS, Al Bashir S, Hartmann A, Yilmaz A, and Hes O. Biphasic papillary renal cell carcinoma is a rare and distinct morphologic variant - clinicopathologic study of 24 novel cases *Lab Invest* 2017; 97:266A-266A. PMID: Not assigned. Abstract

Univ Calgary, Calgary, AB, Canada. Cleveland Clin, Cleveland, OH 44106 USA. Tissupath, Mt Waverley, Vic, Australia. Erlangen Univ Hosp, Erlangen, Germany. Henry Ford Hosp, Detroit, MI 48202 USA. McGill Univ, Montreal, PQ, Canada. Cruces Univ Hosp, Baracaldo, Spain. Ctr Clin, Zagreb, Croatia. CHU Pontchaillou, Rennes, France. Charles Univ Prague, Plzen, Czech Republic.

Pathology
Umar B, **Chang S**, **Ghanem T**, **Siddiqui F**, **Jacobsen G**, **Isrow D**, and **Keller CE**. Does the extent of extracapsular spread in lymph node metastases correlate with outcomes in oropharyngeal squamous cell carcinoma? - a retrospective study *Lab Invest* 2017; 97:334A-334A. PMID: Not assigned. Abstract

[Umar, Beena; Chang, Steve; Ghanem, Tamer; Siddiqui, Farzan; Jacobsen, Gordon; Isrow, Derek; Keller, Christian E.] Henry Ford Hosp, Detroit, MI 48202 USA.

Pathology
Varney RC, and **Zarbo R**. Leaning out the clinical trials process: Optimizing the last hope in cancer care *Lab Invest* 2017; 97:521A-521A. PMID: Not assigned. Abstract

[Varney, Ruan C.; Zarbo, Richard] Henry Ford Hlth Syst, Detroit, MI USA.

Pathology
Williamson SR, Cheng L, **Gadde R**, Wasco MJ, **Gupta NS**, Jorda M, and Kryvenko ON. Renal cell tumors with an entrapped papillary component: Evidence for a tumor-in-tumor collision phenomenon *Lab Invest* 2017; 97:267A-267A. PMID: Not assigned. Abstract

Henry Ford Hlth Syst, Detroit, MI USA. Indiana Univ, Indianapolis, IN 46204 USA. St Joseph Mercy Hosp, Ann Arbor, MI 48104 USA. Univ Miami, Miami, FL USA.

Pathology
Williamson SR, Gadde R, Trpkov K, Hirsch MS, Srigley JR, Reuter VE, Cheng L, Priya Kunju L, **Barod R**, **Rogers CG**, Delahunt B, Hes O, Eble JN, Zhou M, McKenney JK, Martignoni G, Fleming S, Grignon DJ, Moch H, and **Gupta NS**. Diagnostic criteria for oncocytic renal neoplasms: A survey of urologic pathologists *Hum Pathol* 2017;PMID: 28315424. Full Text

Department of Pathology and Laboratory Medicine, Detroit, MI, United States; Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States; Department of Pathology, Wayne State University School of Medicine, Detroit, MI, United States. Electronic address: seanwill@temple.edu.
Department of Pathology and Laboratory Medicine, Detroit, MI, United States.
Department of Pathology and Laboratory Medicine, Calgary Laboratory Service and University of Calgary, Calgary, AB, Canada.
Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States.
Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada.
Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, United States.
Department of Pathology and Laboratory Medicine, Indiana University, Indianapolis, IN, United States.
Department of Pathology, University of Michigan School of Medicine, Ann Arbor, MI, United States.
Vattikutti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago - Wellington, Wellington, New Zealand.
Department of Pathology, Charles University in Prague, Faculty of Medicine in Plzen, Pilsen, Czech Republic.
Department of Pathology, New York University Medical Center, New York, NY, United States.
Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA.
Department of Pathology and Diagnostics, University of Verona, Verona, Italy; Department of Pathology, Pederzoli Hospital, Peschiera del Garda, Italy.
Department of Cellular and Molecular Pathology, University of Dundee, Ninewells Hospital, Dundee, United Kingdom.
Department of Pathology, University Hospital Zurich, Zurich, Switzerland.
Department of Pathology and Laboratory Medicine, Detroit, MI, United States; Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States.

Renal oncocytoma and chromophobe renal cell carcinoma (RCC) have been long recognized as distinct tumors; however, it remains unknown if uniform diagnostic criteria are used to distinguish these tumor types in practice. A survey was distributed to urologic pathologists regarding oncocytic tumors. Responses were received from 17/26 invitees. Histologically, >1 mitotic figure was regarded as most worrisome (n=10) or incompatible (n=6) with oncocytoma diagnosis. Interpretation of focal nuclear wrinkling, focal perinuclear clearing, and multinucleation depended on extent and did not necessarily exclude oncocytoma if minor. Staining techniques most commonly used included: CK7 (94%), KIT (71%), vimentin (65%), colloidal iron (59%), CD10 (53%), and AMACR (41%). Rare CK7-positive cells (</=5%) was regarded as most supportive of oncocytoma, although an extent excluding oncocytoma was not universal. Multiple chromosomal losses were most strongly supportive for chromophobe RCC diagnosis (65%). Less certainty was reported for chromosomal gain or a single loss. For tumors with mixed or inconclusive features, many participants use an intermediate diagnostic category (82%) that does not label the tumor as unequivocally benign or malignant, typically "oncocytic neoplasm" or "tumor" with comment. The term "hybrid tumor" was used variably in several scenarios. A slight majority (65%) report outright diagnosis of oncocytoma in needle biopsies. The morphologic, immunohistochemical, and genetic characteristics that define oncocytic renal tumors remain incompletely understood. Further studies correlating genetics, behavior, and histology are needed to define which tumors truly warrant classification as carcinomas for patient counseling and follow-up strategies.

Pathology
Williamson SR, and **Palanisamy N**. Monosomy 8 as a Surrogate for TCEB1 Mutation in Renal Cell Tumors with Prominent Stroma *Lab Invest* 2017; 97:267A-268A. PMID: Not assigned. Abstract

[Williamson, Sean R.; Palanisamy, Nallasivam] Henry Ford Hlth Syst, Detroit, MI USA.

Pharmacy
Flynt LK, **Kenney RM**, **Zervos MJ**, and **Davis SL**. The safety and economic impact of cefazolin versus nafcillin for the treatment of methicillin-susceptible staphylococcus aureus bloodstream infections *Infect Dis Ther* 2017;PMID: 28265972. Article Request Form

Henry Ford Hospital, Detroit, MI, USA.
Henry Ford Hospital, Detroit, MI, USA. sldavis@wayne.edu.
Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA. sldavis@wayne.edu.

INTRODUCTION: Anti-staphylococcal penicillins are generally accepted as first-line therapy for methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia, but their use may be limited by interstitial nephritis and acute kidney injury. Alternatives include first-generation cephalosporins including cefazolin. METHODS: We conducted a retrospective cohort study to compare adverse effects and clinical outcomes among patients with MSSA bacteremia treated with cefazolin or nafcillin. The primary endpoint was acute kidney injury (AKI), defined as a 0.3 mg/dL or 50% increase from baseline. RESULTS: Incidence of AKI was 27/82 (33%) versus 9/68 (13%) (p = 0.007) in the nafcillin and cefazolin arms, respectively. After adjusting for endocarditis and intensive care unit admission in multivariate logistic regression, nafcillin was an independent predictor of AKI [adj odds ratio (OR) = 2.74; 95% (CI) 1.1-6.6]. Patients who experienced AKI were more likely to have a prolonged intensive care unit stay. CONCLUSION: Risk of nephrotoxicity is increased with nafcillin compared with cefazolin. Cefazolin should considered as a safer alternative to nafcillin for select patients with MSSA bacteremia.

Pharmacy
Pathak RD, Schroeder EB, Seaquist ER, Zeng C, **Lafata JE**, **Thomas A**, Lawrence JM, Karter AJ, Steiner JF, Segal J, and O'Connor PJ. Response to comment on pathak et al. Severe hypoglycemia requiring medical intervention in a large cohort of adults with diabetes receiving care in u.S. Integrated health care delivery systems: 2005-2011. Diabetes care 2016;39:363-370 *Diabetes Care* 2017; 40(2):e26. PMID: 28108542. Full Text

Marshfield Clinic, Marshfield, WI pathak.ram@marshfieldclinic.org.
Kaiser Permanente Colorado, Institute for Health Research, Denver, CO.
Department of Medicine, University of Minnesota, Minneapolis, MN.
Virginia Commonwealth University, Richmond, VA.
Henry Ford Health System, Detroit, MI.
Kaiser Permanente Southern California, Pasadena, CA.
Kaiser Permanente Northern California, Oakland, CA.
Johns Hopkins University, Baltimore, MD.
HealthPartners Institute for Education and Research, Minneapolis, MN.

Pharmacy
Starosta K, **Davis SL**, **Kenney RM**, **Peters M**, **To L**, and **Kalus JS**. Creating objective and measurable postgraduate year 1 residency graduation requirements *Am J Health Syst Pharm* 2017; 74(6):389-396. PMID: 28274981. Full Text

Henry Ford Hospital, Detroit, MI.
Wayne State University, Detroit, MI.
Henry Ford Hospital, Detroit, MI jkalus1@hfhs.org.

PURPOSE: The process of developing objective and measurable postgraduate year 1 (PGY1) residency graduation requirements and a progress tracking system is described. SUMMARY: The PGY1 residency accreditation standard requires that programs establish criteria that must be met by residents for successful completion of the program (i.e., graduation requirements), which should presumably be aligned with helping residents to achieve the purpose of residency training. In addition, programs must track a resident's progress toward fulfillment of residency goals and objectives. Defining graduation requirements and establishing the process for tracking residents' progress are left up

to the discretion of the residency program. To help standardize resident performance assessments, leaders of an academic medical center-based PGY1 residency program developed graduation requirement criteria that are objective, measurable, and linked back to residency goals and objectives. A system for tracking resident progress relative to quarterly progress targets was instituted. Leaders also developed a focused, on-the-spot skills assessment termed "the Thunderdome," which was designed for objective evaluation of direct patient care skills. Quarterly data on residents' progress are used to update and customize each resident's training plan. Implementation of this system allowed seamless linkage of the training plan, the progress tracking system, and the specified graduation requirement criteria. CONCLUSION: PGY1 residency requirements that are objective, that are measurable, and that attempt to identify what skills the resident must demonstrate in order to graduate from the program were developed for use in our residency program. A system for tracking the residents' progress by comparing residents' performance to predetermined quarterly benchmarks was developed.

Public Health Sciences

Fonseca W, Lucey K, Jang S, Fujimura KE, Rasky A, Ting HA, Petersen J, **Johnson CC**, Boushey HA, **Zoratti E**, Ownby DR, **Levine AM**, **Bobbit KR**, Lynch SV, and Lukacs NW. Lactobacillus johnsonii supplementation attenuates respiratory viral infection via metabolic reprogramming and immune cell modulation *Mucosal Immunol* 2017;PMID: 28295020. Article Request Form

Department of Pathology, University of Michigan, Ann Arbor, Michigan, USA.
Department of Medicine, University of California San Francisco, San Francisco, California, USA.
Henry Ford Health System, Detroit, Michigan, USA.
Department of Pediatrics, Augusta University, Augusta, Georgia, USA.

Regulation of respiratory mucosal immunity by microbial-derived metabolites has been a proposed mechanism that may provide airway protection. Here we examine the effect of oral Lactobacillus johnsonii supplementation on metabolic and immune response dynamics during respiratory syncytial virus (RSV) infection. L. johnsonii supplementation reduced airway T helper type 2 cytokines and dendritic cell (DC) function, increased regulatory T cells, and was associated with a reprogrammed circulating metabolic environment, including docosahexanoic acid (DHA) enrichment. RSV-infected bone marrow-derived DCs (BMDCs) from L. johnsonii-supplemented mice had altered cytokine secretion, reduced expression of co-stimulatory molecules, and modified CD4+ T-cell cytokines. This was replicated upon co-incubation of wild-type BMDCs with either plasma from L. johnsonii-supplemented mice or DHA. Finally, airway transfer of BMDCs from L. johnsonii-supplemented mice or with wild-type derived BMDCs pretreated with plasma from L. johnsonii-supplemented mice reduced airway pathological responses to infection in recipient animals. Thus L. johnsonii supplementation mediates airway mucosal protection via immunomodulatory metabolites and altered immune function.Mucosal Immunology advance online publication 15 March 2017. doi:10.1038/mi.2017.13.

Public Health Sciences

Lareau CA, DeWeese CF, Adrianto I, Lessard CJ, Gaffney PM, Iannuzzi MC, **Rybicki BA**, **Levin AM**, and Montgomery CG. Polygenic risk assessment reveals pleiotropy between sarcoidosis and inflammatory disorders in the context of genetic ancestry *Genes Immun* 2017;PMID: 28275240. Article Request Form

Department of Biostatistics, Harvard University, Cambridge, MA, USA.
Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, USA.
Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA.
Department of Medicine, Staten Island University Hospital, Staten Island, NY, USA.
Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
Center for Bioinformatics, Henry Ford Health System, Detroit, MI, USA.

Sarcoidosis is a complex disease of unknown etiology characterized by the presence of granulomatous inflammation. Though various immune system pathways have been implicated in disease, the relationship between the genetic determinants of sarcoidosis and other inflammatory disorders has not been characterized. Herein, we examined the degree of genetic pleiotropy common to sarcoidosis and other inflammatory disorders to identify shared pathways and disease systems pertinent to sarcoidosis onset. To achieve this, we quantify the association of common variant polygenic risk scores from nine complex inflammatory disorders with sarcoidosis risk. Enrichment analyses of genes implicated in pleiotropic associations were further used to elucidate candidate pathways. In European-Americans, we identify significant pleiotropy between risk of sarcoidosis and risk of asthma (R2=2.03%; P=8.89 x 10-9), celiac disease (R2=2.03%; P=8.21 x 10-9), primary biliary cirrhosis (R2=2.43%; P=2.01 x 10-10) and rheumatoid arthritis (R2=4.32%; P=2.50 x 10-17). These associations validate in African Americans only after accounting for the

proportion of genome-wide European ancestry, where we demonstrate similar effects of polygenic risk for African-Americans with the highest levels of European ancestry. Variants and genes implicated in European-American pleiotropic associations were enriched for pathways involving interleukin-12, interleukin-27 and cell adhesion molecules, corroborating the hypothesized immunopathogenesis of disease.Genes and Immunity advance online publication, 9 March 2017; doi:10.1038/gene.2017.3.

Public Health Sciences

Pillai V, **Roth T**, **Roehrs T**, **Moss K**, **Peterson EL**, and **Drake CL**. Effectiveness of benzodiazepine receptor agonists in the treatment of insomnia: An examination of response and remission rates *Sleep* 2017; 40(2)PMID: 28364510. Full Text

Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, MI.
Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, MI.

Study objectives: To examine the real-world effectiveness of benzodiazepine receptor agonists (BzRAs) by quantifying response and remission rates in a clinical sample receiving chronic BzRA treatment for insomnia. Methods: Participants were outpatients (N = 193; 72% female; 55.2 +/- 11.1 year) who had an insomnia diagnosis per medical records, and who were taking a therapeutic dose of BzRA for their insomnia. Endpoints were nocturnal sleep disturbance and Insomnia Severity Index (ISI) scores. A reduction meeting the criterion for the minimally important difference in ISI scores (change >/= 6) constituted "response"; "remission" was inferred when symptoms fell below the clinical cutoff (ISI < 11). Results: Most participants (71%) used BzRAs at least 5 nights per week. Mean ISI scores were significantly lower (t = 22.31; p < .01) while on BzRAs than when untreated, but remained in the clinical range (mean = 11.0; standard deviation = 5.7). Although 76.7% responded to treatment, only 47.7% remitted. The majority (68.9%) of participants had a sleep-onset latency > 30 minutes and/or wake-time after sleep onset > 60 minutes while on BzRAs. After controlling for gender and insomnia severity when untreated, odds of insomnia persistence despite BzRA use were 2 times higher in patients with comorbid medical [odds ratio (OR) = 2.39; 95% confidence interval (CI) = 1.20% to 4.77%; p < .05] and psychiatric disorders (OR = 2.24; 95% CI = 1.21% to 4.13%; p < .05). Conclusions: This is the first study to distinguish between response and remission in insomnia patients taking BzRAs. Findings suggest that while many insomnia patients respond to chronic BzRA treatment, most do not remit. Remission rates are particularly low for comorbid insomnia, the most prevalent phenotype of the disorder.

Public Health Sciences

Rundle A, **Wang Y**, **Sadasivan S**, **Chitale DA**, **Gupta NS**, Tang D, and **Rybicki BA**. Larger men have larger prostates: Detection bias in epidemiologic studies of obesity and prostate cancer risk *Prostate* 2017;PMID: 28349547.
Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York.
Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan.
Department of Pathology, Henry Ford Health System, Detroit, Michigan.
Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York.

BACKGROUND: Obesity is associated with risk of aggressive prostate cancer (PCa), but not with over-all PCa risk. However, obese men have larger prostates which may lower biopsy accuracy and cause a systematic bias toward the null in epidemiologic studies of over-all risk. METHODS: Within a cohort of 6692 men followed-up after a biopsy or transurethral resection of the prostate (TURP) with benign findings, a nested case-control study was conducted of 495 prostate cancer cases and controls matched on age, race, follow-up duration, biopsy versus TURP, and procedure date. Data on body mass index and prostate volume at the time of the initial procedure were abstracted from medical records. RESULTS: Prior to consideration of differences in prostate volume, overweight (OR = 1.41; 95%CI 1.01, 1.97), and obese status (OR = 1.59; 95%CI 1.09, 2.33) at the time of the original benign biopsy or TURP were associated with PCa incidence during follow-up. Prostate volume did not significantly moderate the association between body-size and PCa, however it did act as an inverse confounder; adjustment for prostate volume increased the effect size for overweight by 22% (adjusted OR = 1.52; 95%CI 1.08, 2.14) and for obese status by 23% (adjusted OR = 1.77; 95%CI 1.20, 2.62). Larger prostate volume at the time of the original benign biopsy or TURP was inversely associated with PCa incidence during follow-up (OR = 0.92 per 10 cc difference in volume; 95%CI 0.88, 0.97). In analyses that stratified case-control pairs by tumor aggressiveness of the case, prostate volume acted as an inverse confounder in analyses of non-aggressive PCa but not in analyses of aggressive PCa. CONCLUSIONS: In studies of obesity and PCa, differences in prostate volume cause a bias toward the null, particularly in analyses of non-aggressive PCa. A pervasive underestimation of the association between obesity and overall PCa risk may exist in the literature.

Public Health Sciences

Sitarik AR, **Bobbitt KR**, **Havstad SL**, Fujimura KE, **Levin AM**, **Zoratti EM**, **Kim H**, **Woodcroft KJ**, **Wegienka G**, Ownby DR, **Joseph CL**, Lynch SV, and **Johnson CC**. Breast milk tgfbeta is associated with neonatal gut microbial composition *J Pediatr Gastroenterol Nutr* 2017;PMID: 28362692. Full Text

*Department of Public Health Sciences, Henry Ford Health System, Detroit, Michigan, USA daggerDivision of Gastroenterology, University of California, San Francisco, California, USA double daggerDivision of Allergy and Immunology, Department of Internal Medicine, Henry Ford Health System, Detroit, Michigan, USA section signDepartment of Pediatrics, Georgia Regents University, Augusta, Georgia, USA.

OBJECTIVES: Breast milk is a complex bioactive fluid that varies across numerous maternal and environmental conditions. While breastfeeding is known to impact neonatal gut microbiome, the milk components responsible for this effect are not well-characterized. Given the wide range of immunological activity breast milk cytokines engage in, we investigated three essential breast milk cytokines and their association with early life gut microbiota. METHODS: A total of 52 maternal-child pairs were drawn from a racially diverse birth cohort based in Detroit, Michigan. Breast milk and neonatal stool specimens were collected at 1-month postpartum. Breast milk TGFbeta1, TGFbeta2, and IL-10 were assayed using ELISAs, while neonatal gut microbiome was profiled using 16S rRNA sequencing. RESULTS: Individually, immunomodulators TGFbeta1 and TGFbeta2 were significantly associated with neonatal gut microbial composition ($R = 0.024$, $p = 0.041$; $R = 0.026$, $p = 0.012$, respectively) and increased richness, evenness, and diversity, but IL-10 was not. However, the effects of TGFbeta1 and TGFbeta2 were not independent of one another, and the effect of TGFbeta2 was stronger than that of TGFbeta1. Higher levels of TGFbeta2 was associated with the increased relative abundance of several bacteria, including members of Streptococcaceae and Ruminococcaceae, and lower relative abundance of distinct Staphylococcaceae taxa. CONCLUSIONS: Breast milk TGFbeta concentration explains a portion of variability in gut bacterial microbiota composition among breastfed neonates. Whether TGFbeta acts in isolation or jointly with other bioactive components to alter bacterial composition requires further investigation. These findings contribute to an increased understanding of how breastfeeding affects the gut microbiome-and potentially immune development-in early life.

Public Health Sciences

Smith MM, **Peterson E**, and **Yaremchuk KL**. The role of tonsillectomy in adults with tonsillar hypertrophy and obstructive sleep apnea *Otolaryngol Head Neck Surg* 2017:194599817698671. PMID: 28349770. Full Text

1 Department of Pediatric Otolaryngology-Head and Neck Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.
2 Department of Public Health Sciences, Henry Ford Hospital, Detroit, Michigan, USA.
3 Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, USA.

Objective To determine if tonsillectomy alone is an effective treatment in improving obstructive sleep apnea in adult subjects with tonsillar hypertrophy and to evaluate the effect of tonsillectomy on patient-reported quality-of-life indices. Study Design Case series with planned data collection. Setting Academic hospital. Subjects and Methods Thirty-four subjects completed enrollment and intervention from January 2011 to January 2016. Subjects completed pre- and postoperative quality-of-life questionnaires, including the Insomnia Severity Index, Epworth Sleepiness Scale, and the Functional Outcomes of Sleep Questionnaire-10. Surgical response to treatment was defined by a >50% decrease in the Apnea-Hypopnea Index and a decrease in the overall Apnea-Hypopnea Index to <20. Wilcoxon matched-pairs signed-rank tests were used to test each variable to assess for a change from pre- to postintervention. Subjects were then split into 3 BMI subgroups, with results also evaluated by Wilcoxon matched-pairs signed-rank tests. Results There was a significant difference discovered between the mean preoperative Apnea-Hypopnea Index of 31.57 and the mean postoperative value of 8.12 ($P < .001$). All patient-reported outcomes improved significantly following tonsillectomy. After stratifying all outcome variables (Apnea-Hypopnea Index, Epworth Sleepiness Scale, Insomnia Severity Index, and Functional Outcomes of Sleep Questionnaire-10) by sex, race, and tonsil size, no statistically significant difference was noted among any of these subgroups. There was a 78% surgical response to treatment. Conclusion Tonsillectomy appears to be an effective treatment for obstructive sleep apnea in a select population of adults with tonsillar hypertrophy.

Public Health Sciences

Straughen JK, Misra DP, Ernst LM, Charles AK, VanHorn S, Ghosh S, Buhimschi I, Buhimschi C, **Divine G**, and Salafia CM. Methods to decrease variability in histological scoring in placentas from a cohort of preterm infants *BMJ Open* 2017; 7(3):e013877. PMID: 28363925. http://bmjopen.bmj.com/content/7/3/e013877.long

Department of Public Health Sciences, Henry Ford Hospital, Detroit, Michigan, USA.

Department of Family Medicine & Public Health Sciences, Wayne State University School of Medicine, Detroit, Michigan, USA.
Placental Modulation Laboratory, Institute for Basic Research in Developmental Disabilities, Staten Island, New York, USA.
Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA.
Department of Anatomical Pathology, Sidra Medical and Research Center, Doha, Qatar.
Placental Analytics LLC, Larchmont, New York, USA.
Department of Women's, Gender, & Sexuality Studies & Bioethics, Emory University, Atlanta, Georgia, USA.
Center for Perinatal Research, Nationwide Children's Hospital, Columbus, Ohio, USA.
Department of Obstetrics and Gynecology, Ohio State University College of Medicine, Columbus, Ohio, USA.
Department of Pediatrics, New York Methodist Hospital, Brooklyn, New York, USA.

OBJECTIVE: Reliable semiquantitative assessment of histological placental acute inflammation is problematic, even among experts. Tissue samples in histology slides often show variability in the extent and location of neutrophil infiltrates. We sought to determine whether the variability in pathologists' scoring of neutrophil infiltrates in the placenta could be reduced by the use of 'regions of interest' (ROIs) that break the sample into smaller components. DESIGN: ROIs were identified within stained H&E slides from a cohort of 56 women. ROIs were scored using a semiquantitative scale (0-4) for the average number of neutrophils by at least two independent raters. SETTING: Preterm singleton births at Yale New Haven Hospital. PARTICIPANTS: This study used stained H&E placental slides from a cohort of 56 women with singleton pregnancies who had a clinically indicated amniocentesis within 24 hours of delivery. PRIMARY AND SECONDARY OUTCOME MEASURES: Interrater agreement was assessed with the intraclass correlation coefficient (ICC) and log-linear regression. Predictive validity was assessed using amniotic fluid protein profile scores (neutrophil defensin-2, neutrophil defensin-1, calgranulin C and calgranulin A). RESULTS: Excellent agreement by the ICC was found for the average neutrophil scores within a region of interest. Log-linear analyses suggest that even where there is disagreement, responses are positively associated along the diagonal. There was also strong evidence of predictive validity comparing pathologists' scores with amniotic fluid protein profile scores. CONCLUSIONS: Agreement among observers of semiquantitative neutrophil scoring through the use of digitised ROIs was demonstrated to be feasible with high reliability and validity.

Public Health Sciences

Straughen JK, Misra DP, Helmkamp L, and Misra VK. Preterm delivery as a unique pathophysiologic state characterized by maternal soluble fms-like tyrosine kinase 1 and uterine artery resistance during pregnancy *Reprod Sci* 2017:1933719117698574. PMID: 28335685. Full Text

1 Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
2 Department of Family Medicine and Public Health Sciences, The Wayne State University School of Medicine, Detroit, MI, USA.
3 Department of Pediatrics, Division of Genetic, Genomic, and Metabolic Disorders, The Wayne State University School of Medicine, Detroit, MI, USA.

BACKGROUND: Preterm delivery (PTD) may be characterized by altered interrelationships among angiogenic factors and measures of placental function. We analyzed the longitudinal relationship between maternal serum concentrations of soluble fms-like tyrosine kinase 1 (sFlt1), an important antiangiogenic factor, and uterine artery resistance in pregnancies resulting in preterm and term deliveries. METHODS: Data were collected in a longitudinal cohort study involving 278 women monitored at 6 to 10, 10 to 14, 16 to 20, 22 to 26, and 32 to 36 weeks of gestation. Concentrations of maternal serum sFlt1 were determined using solid-phase enzyme-linked immunosorbent assay, and uterine artery resistance indices (RI) were measured by Doppler velocimetry at each interval. Preterm delivery was defined as birth before 37-weeks completed gestation. Data analyses used multivariable repeated measures regression models. RESULTS: Uterine artery RI decreased across gestation. As pregnancy progressed, RI trajectories diverged for term and preterm deliveries; the mean RI was significantly higher in third trimester for pregnancies resulting in PTD (P = .08). sFlt1 was stable through 21 3/7 weeks of gestation and then increased rapidly; women who delivered preterm had significantly higher sFlt1 levels in the third trimester (P = .04). The relationship between uterine artery RI and sFlt1 from the prior visit was significantly different between the groups (P < .0001). For term deliveries, higher sFlt1 concentrations were associated with a smaller RI at the subsequent visit (beta = -.08, 95% confidence interval [CI]: -0.14 to -0.02). For PTD, higher sFlt1 concentrations were associated with a larger uterine artery RI (beta = .14, 95% CI: 0.06 to 0.22). CONCLUSION: PTD is characterized by altered relationships between angiogenic factors and placental vascular blood flow starting in early pregnancy.

Public Health Sciences
Vega JEV, Halani SH, Yousefi S, Amrollahi F, Holder CA, **Poisson LM**, **Griffith B**, Eschbacher J, Nalisnik M, Olson JJ, Cooper LAD, and Brat DJ. Markers of progression in oligodendroglioma *Lab Invest* 2017; 97:438A-438A. PMID: Not assigned. Abstract

Emory Univ, Sch Med, Atlanta, GA USA. Henry Ford Hosp, Detroit, MI 48202 USA. St Josephs Hosp, Phoenix, AZ USA.

Pulmonary
Cox ST, Zimmerman E, Collins D, Richmond NL, and **Simoff M**. Novel multidisciplinary management of a retropharyngeal hematoma with pulmonary stenting *J Bronchology Interv Pulmonol* 2016; 23(3):239-241. PMID: 26544077. Full Text

*Michigan State University College of Human Medicine, Grand Rapids daggerNeurosurgery Department double daggerOtolaryngology Department section signRadiology Department, Munson Medical Center, Traverse City parallelPulmonology Department, Henry Ford Health System, Detroit, MI.

Retropharyngeal hematomas (RHs) represents a rare airway obstruction that requires timely intervention to avoid a fatal outcome. Further complicating this malady, RHs of massive proportions can complicate the decision of management selection. After comprehensive literature search, there has been no mention of pulmonary stenting as an intervention for RH. The following case presentation will demonstrate the importance of multidisciplinary management of a 60-year-old presenting with a RH causing airway obstruction, with the use of a novel approach. Airway stenting is a novel, conservative approach for successfully managing patients presenting with massive RH.

Pulmonary
Tatem G, **Kokas M**, **Smith CL**, and **DiGiovine B**. A feasibility assessment of behavioral-based interviewing to improve candidate selection for a pulmonary and critical care medicine fellowship program *Ann Am Thorac Soc* 2017;PMID: 28306323. Full Text

Henry Ford Hospital,Wayne State University, Internal Medicine, Pulmonary and Critical Care, Detroit, Michigan, United States ; gtatem1@hfhs.org.
Henry Ford Hospital,Wayne State University, Department of Medical Education, Henry Ford Hospital, Detroit, Michigan, United States ; mkokas1@hfhs.org.
Henry Ford Hospital,Wayne State University, Organizational Human Resource Development, Henry Ford Health System, Detroit, MI. , Detroit, Michigan, United States ; cath817@gmail.com.
Henry Ford Hospital, Wayne State University, Internal Medicine, Pulmonary and Critical Care, Detroit, Michigan, United States ; bdigiov1@hfhs.org.

Traditional interviews for residency and fellowship training programs are an important component in the selection process, but can be of variable value due to a non-standardized approach. We redesigned the candidate interview process for our large pulmonary and critical care medicine fellowship program in the United States using a behavioral-based interview structure. The primary goal of this approach was to standardize the assessment of candidates within non-cognitive domains with the goal of selecting those with the best fit for our institution's fellowship program. Eight faculty members attended two behavioral-based interview workshops. The first workshop identified our program's "best fit" criteria using the framework of the Accreditation Council for Graduate Medical Education's six core competencies and additional behaviors that fit within our programs. Behavioral-based interview questions were then selected from a national database and refined based on the attributes deemed most important by our faculty. In the second workshop, faculty practiced the behavioral-based interview format in mock interviews with third year fellows. The interview process was further refined based on feedback from the interviewees, and then applied with fellowship candidates for the 2014 recruitment season. The one-year pilot of behavioral-based interviewing allowed us to achieve consensus on the traits sought for our incoming fellows and to standardize the interview process for our program using the framework of the ACGME core competencies. Although the effects of this change on the clinical performance of our fellows have not yet been assessed, this description of our development and implementation processes may be helpful for programs seeking to redesign their applicant interviews.

Radiation Oncology
Bagher-Ebadian H, **Siddiqui F**, **Chang L**, **Movsas B**, and **Chetty IJ**. On the impact of smoothing and noise on robustness of ct and cbct radiomics features for patients with head and neck cancers *Med Phys* 2017;PMID: 28261818. Article Request Form

Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI.
Department of Physics, Oakland University, Rochester, MI.

PURPOSE: We investigated the characteristics of radiomics features extracted from planning CT (pCT) and cone beam CT (CBCT) image datasets acquired for 18 oropharyngeal cancer patients treated with fractionated radiation therapy. Images were subjected to smoothing, sharpening, and noise to evaluate changes in features relative to baseline datasets. METHODS: Textural features were extracted from tumor volumes, contoured on pCT and CBCT images, according to the following 8 different classes: Intensity Based Histogram Features (IBHF), Gray Level Run Length (GLRL), Law's Textural information (LAWS), Discrete Orthonormal Stockwell Transform (DOST), Local Binary Pattern (LBP), Two-Dimensional Wavelet Transform (2DWT), Two Dimensional Gabor Filter (2DGF), and Gray Level Co-Occurrence Matrix (GLCM). A total of 165 radiomics features were extracted. Images were post-processed prior to feature extraction using a Gaussian noise model with different signal-to-noise-ratios (SNR= 5, 10, 15, 20, 25, 35, 50, 75, 100, and 150). Gaussian filters with different cut off frequencies (varied discreetly from 0.0458 to 0.7321 cycles-mm-1) were applied to image datasets. Effect of noise and smoothing on each extracted feature was quantified using mean absolute percent change (MAPC) between the respective values on post-processed and baseline images. The Fisher method for combining Welch p-values was used for tests of significance. Three comparisons were investigated: 1- Baseline pCT versus modified pCT (with given filter applied); 2- Baseline CBCT versus modified CBCT, and 3- Baseline and modified pCT versus baseline and modified CBCT. RESULTS: Features extracted from CT and CBCT image datasets were robust to low-pass filtering (MAPC=17.5%, pvalFisher = 0.93 for CBCT and MAPC=7.5%, pvalFisher = 0.98 for pCT) and noise (MAPC=27.1%, pvalFisher = 0.89 for CBCT, and MAPC=34.6%, pvalFisher =0.61 for pCT). Extracted features were significantly impacted (MAPC=187.7%, pvalFisher < 0.0001 for CBCT, and MAPC=180.6%, pvalFisher < 0.0001 for pCT) by LOG which is classified as a high-pass filter. Features most impacted by low pass filtering were LAWS (MAPC=11.2%, pvalFisher = 0.44), GLRL (MAPC=9.7%, pvalFisher = 0.70) and IBHF (MAPC=21.7%, pvalFisher =0.83), for the pCT datasets, and LAWS (MAPC=20.2%, pvalFisher = 0.24), GLRL (MAPC=14.5%, pvalFisher = 0.44), and 2DGF (MAPC=16.3%, pvalFisher = 0.52), for CBCT image datasets. For pCT datasets, features most impacted by noise were GLRL (MAPC=29.7%, pvalFisher = 0.06), LAWS (MAPC=96.6%, pvalFisher = 0.42), and GLCM (MAPC=36.2%, pvalFisher = 0.48), while the LBPF (MAPC=5.2%, pvalFisher = 0.99) was found to be relatively insensitive to noise. For CBCT datasets, GLRL (MAPC=8.9%, pvalFisher = 0.80) and LAWS (MAPC=89.3%, pvalFisher = 0.81) features were impacted by noise, while the LBPF (MAPC=2.2%, pvalFisher = 0.99) and DOST (MAPC=13.7%, pvalFisher = 0.98) features were noise insensitive. Apart from 15 features, no significant differences were observed for the remaining 150 textural features extracted from baseline pCT and CBCT image datasets (MAPC=90.1%, pvalFisher = 0.26). CONCLUSIONS: Radiomics features extracted from planning CT and daily CBCT image datasets for head/neck cancer patients were robust to low-power Gaussian noise and low-pass filtering, but were impacted by high-pass filtering. Textural features extracted from CBCT and pCT image datasets were similar, suggesting interchangeability of pCT and CBCT for investigating radiomics features as possible biomarkers for outcome.

Radiation Oncology

Brandner ED, **Chetty IJ**, Giaddui TG, Xiao Y, and Huq MS. Motion management strategies and technical issues associated with stereotactic body radiotherapy of thoracic and upper abdominal tumors: A review from nrg oncology *Med Phys* 2017;PMID: 28317123. Article Request Form

Department of Radiation Oncology, University of Pittsburgh Cancer Institute and UPMC CancerCenter, Pittsburgh, Pennsylvania, 15232.
Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan, 48202.
Sidney Kimmel Cancer Center, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, 19107.
Imaging and Radiation Oncology Core (IROC), University of Pennsylvania, Philadelphia, Pennsylvania, 19104.

The efficacy of stereotactic body radiotherapy (SBRT) has been well demonstrated. However, it presents unique challenges for accurate planning and delivery especially in the lungs and upper abdomen where respiratory motion can be significantly confounding accurate targeting and avoidance of normal tissues. In this paper we review the current literature on SBRT for lung and upper abdominal tumors with particular emphasis on addressing respiratory motion and its affects. We provide recommendations on strategies to manage motion for different, patient specific situations. Some of the recommendations will potentially be adopted to guide clinical trial protocols.

Radiation Oncology

Chin Snyder K, **Kim J**, **Reding A**, **Fraser C**, **Gordon J**, **Ajlouni M**, **Movsas B**, and **Chetty IJ**. Development and evaluation of a clinical model for lung cancer patients using stereotactic body radiotherapy (SBRT) within a knowledge-based algorithm for treatment planning *J Appl Clin Med Phys* 2016; 17(6):263-275. PMID: 28297307. Full Text

Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, USA.

The purpose of this study was to describe the development of a clinical model for lung cancer patients treated with stereotactic body radiotherapy (SBRT) within a knowledge-based algorithm for treatment planning, and to evaluate the model performance and applicability to different planning techniques, tumor locations, and beam arrangements. 105 SBRT plans for lung cancer patients previously treated at our institution were included in the development of the knowledge-based model (KBM). The KBM was trained with a combination of IMRT, VMAT, and 3D CRT techniques. Model performance was validated with 25 cases, for both IMRT and VMAT. The full KBM encompassed lesions located centrally vs. peripherally (43:62), upper vs. lower (62:43), and anterior vs. posterior (60:45). Four separate sub-KBMs were created based on tumor location. Results were compared with the full KBM to evaluate its robustness. Beam templates were used in conjunction with the optimizer to evaluate the model's ability to handle suboptimal beam placements. Dose differences to organs-at-risk (OAR) were evaluated between the plans generated by each KBM. Knowledge-based plans (KBPs) were comparable to clinical plans with respect to target conformity and OAR doses. The KBPs resulted in a lower maximum spinal cord dose by 1.0+/-1.6Gy compared to clinical plans, p=0.007. Sub-KBMs split according to tumor location did not produce significantly better DVH estimates compared to the full KBM. For central lesions, compared to the full KBM, the peripheral sub-KBM resulted in lower dose to 0.035 cc and 5 cc of the esophagus, both by 0.4Gy+/-0.8Gy, p=0.025. For all lesions, compared to the full KBM, the posterior sub-KBM resulted in higher dose to 0.035 cc, 0.35 cc, and 1.2 cc of the spinal cord by 0.2+/-0.4Gy, p=0.01. Plans using template beam arrangements met target and OAR criteria, with an increase noted in maximum heart dose (1.2+/-2.2Gy, p=0.01) and GI (0.2+/-0.4, p=0.01) for the nine-field plans relative to KBPs planned with custom beam angles. A knowledge-based model for lung SBRT consisting of multiple treatment modalities and lesion locations produced comparable plan quality to clinical plans. With proper training and validation, a robust KBM can be created that encompasses both IMRT and VMAT techniques, as well as different lesion locations. PACS number(s): 87.55de, 87.55kh, 87.53Ly.

Radiation Oncology

Kearney V, Huang Y, **Mao W**, Yuan B, and Tang L. Canny edge-based deformable image registration *Phys Med Biol* 2017; 62(3):966-985. PMID: 28081014. Article Request Form

Department of Radiation Oncology, University of California, San Francisco, CA, USA. Department of Bioengineering, University of Texas Arlington, Arlington, TX, USA.

This work focuses on developing a 2D Canny edge-based deformable image registration (Canny DIR) algorithm to register in vivo white light images taken at various time points. This method uses a sparse interpolation deformation algorithm to sparsely register regions of the image with strong edge information. A stability criterion is enforced which removes regions of edges that do not deform in a smooth uniform manner. Using a synthetic mouse surface ground truth model, the accuracy of the Canny DIR algorithm was evaluated under axial rotation in the presence of deformation. The accuracy was also tested using fluorescent dye injections, which were then used for gamma analysis to establish a second ground truth. The results indicate that the Canny DIR algorithm performs better than rigid registration, intensity corrected Demons, and distinctive features for all evaluation matrices and ground truth scenarios. In conclusion Canny DIR performs well in the presence of the unique lighting and shading variations associated with white-light-based image registration.

Radiation Oncology

Mahdi Z, Abdulfatah E, Pardeshi V, Hassan O, Schultz D, Morris R, Cote ML, **Elshaikh MA**, Bandyopadhyay S, and Ali-Fehmi R. The impact of androgen receptor expression on endometrial carcinoma recurrence and survival *Int J Gynecol Pathol* 2017;PMID: 28277313. Full Text

Department of Pathology, Detroit Medical Center (Z.M., E.A., V.P., O.H., S.B., R.A.-F.) Departments of Obstetrics and Gynecology (R.M.) Oncology (D.S., M.L.C.), Karmanos Cancer Institute, Wayne State University Henry Ford Hospital (M.A.E.), Detroit, MI.

Endometrial carcinomas (ECs) are the most common gynecologic cancers in the western world. The impact of androgen receptor (AR) on clinicopathologic parameters of EC is not well studied. The aim of our study is to assess

the role of AR expression in ECs and correlate its expression with estrogen (ER) and progesterone (PR). A retrospective review of 261 EC was conducted. H&E slides were reviewed and clinicopathologic parameters were analyzed. Immunohistochemical stains for AR, ER, and PR was performed on tissue microarray. The hormonal expression was evaluated and the data were analyzed using the Fisher exact test and Kaplan-Meier survival analysis. Patients' age ranged from 31 to 91 (median=65 y). Type I EC included 202 endometrioid and 7 mucinous carcinoma, whereas type II included 34 serous, 16 carcinosarcoma, and 2 clear cell carcinoma. Although not significant, AR expression showed more frequent association with type I EC, early tumor stage (I-II), and low FIGO grade (1-2) EC. AR expression significantly correlated with absence of lymphovascular invasion (P=0.041) and decreased LN involvement (P=0.048). Patients with AR expression showed increased disease-free survival (208 vs. 165 mo, P=0.008) and late disease recurrence (P=0.009). AR expression had a positive significant correlation with PR (P<0.001) and ER (P=0.037) expression. AR might play a role as a prognostic marker for ECs.

Radiation Oncology

Mao W, Rozario T, Lu W, Gu X, Yan Y, Jia X, Sumer B, and Schwartz DL. Online dosimetric evaluation of larynx SBRT: A pilot study to assess the necessity of adaptive replanning *J Appl Clin Med Phys* 2017; 18(1):157-163. PMID: 28291932. Full Text

Department of Radiation Oncology, University of Texas Southwestern School of Medicine, Dallas, TX, USA.
Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI, USA.
Department of Otolaryngology, University of Texas Southwestern School of Medicine, Dallas, TX, USA.

PURPOSE: We have initiated a multi-institutional phase I trial of 5-fraction stereotactic body radiotherapy (SBRT) for Stage III-IVa laryngeal cancer. We conducted this pilot dosimetric study to confirm potential utility of online adaptive replanning to preserve treatment quality. METHODS: We evaluated ten cases: five patients enrolled onto the current trial and five patients enrolled onto a separate phase I SBRT trial for early-stage glottic larynx cancer. Baseline SBRT treatment plans were generated per protocol. Daily cone-beam CT (CBCT) or diagnostic CT images were acquired prior to each treatment fraction. Simulation CT images and target volumes were deformably registered to daily volumetric images, the original SBRT plan was copied to the deformed images and contours, delivered dose distributions were re-calculated on the deformed CT images. All of these were performed on a commercial treatment planning system. In-house software was developed to propagate the delivered dose distribution back to reference CT images using the deformation information exported from the treatment planning system. Dosimetric differences were evaluated via dose-volume histograms. RESULTS: We could evaluate dose within 10 minutes in all cases. Prescribed coverage to gross tumor volume (GTV) and clinical target volume (CTV) was uniformly preserved; however, intended prescription dose coverage of planning treatment volume (PTV) was lost in 53% of daily treatments (mean: 93.9%, range: 83.9-97.9%). 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. CONCLUSIONS: Although GTV and CTV SBRT dose coverage is preserved with in-room three-dimensional image guidance, PTV coverage can vary significantly from intended plans and dose to critical structures may exceed tolerances. Online adaptive treatment re-planning is potentially necessary and clinically applicable to fully preserve treatment quality. Confirmatory trial accrual and analysis remains ongoing.

Radiation Oncology

Qin Y, **Zhong H**, **Wen N**, **Snyder K**, **Huang Y**, and **Chetty IJ**. Deriving detector-specific correction factors for rectangular small fields using a scintillator detector *J Appl Clin Med Phys* 2016; 17(6):379-391. PMID: 28297285. Full Text

Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, USA.

The goal of this study was to investigate small field output factors (OFs) for flattening filter-free (FFF) beams on a dedicated stereotactic linear accelerator-based system. From this data, the collimator exchange effect was quantified, and detector-specific correction factors were generated. Output factors for 16 jaw-collimated small fields (from 0.5 to 2 cm) were measured using five different detectors including an ion chamber (CC01), a stereotactic field diode (SFD), a diode detector (Edge), Gafchromic film (EBT3), and a plastic scintillator detector (PSD, W1). Chamber, diodes, and PSD measurements were performed in a Wellhofer water tank, while films were irradiated in solid water at 100 cm source-to-surface distance and 10 cm depth. The collimator exchange effect was quantified for rectangular fields. Monte Carlo (MC) simulations of the measured configurations were also performed using the EGSnrc/DOSXYZnrc code. Output factors measured by the PSD and verified against film and MC calculations were chosen as the benchmark measurements. Compared with plastic scintillator detector (PSD), the small volume ion chamber (CC01) underestimated output factors by an average of -1.0%+/-4.9%(max.=-11.7% for 0.5x0.5cm2 square field). The stereotactic diode (SFD) overestimated output factors by 2.5%+/-0.4%(max.=3.3% for 0.5x1cm2 rectangular field).

The other diode detector (Edge) also overestimated the OFs by an average of 4.2%+/-0.9%(max.=6.0% for 1x1cm2 square field). Gafchromic film (EBT3) measurements and MC calculations agreed with the scintillator detector measurements within 0.6%+/-1.8% and 1.2%+/-1.5%, respectively. Across all the X and Y jaw combinations, the average collimator exchange effect was computed: 1.4%+/-1.1% (CC01), 5.8%+/-5.4% (SFD), 5.1%+/-4.8% (Edge diode), 3.5%+/-5.0% (Monte Carlo), 3.8%+/-4.7% (film), and 5.5%+/-5.1% (PSD). Small field detectors should be used with caution with a clear understanding of their behaviors, especially for FFF beams and small, elongated fields. The scintillator detector exhibited good agreement against Gafchromic film measurements and MC simulations over the range of field sizes studied. The collimator exchange effect was found to be important at these small field sizes. Detector-specific correction factors were computed using the scintillator measurements as the benchmark. PACS number(s): 87.56.Fc.

Radiation Oncology
Song KH, **Snyder KC**, **Kim J**, **Li H**, **Ning W**, **Rusnac R**, **Jackson P**, **Gordon J**, **Siddiqui SM**, and **Chetty IJ**. Characterization and evaluation of 2.5 MV electronic portal imaging for accurate localization of intra- and extracranial stereotactic radiosurgery *J Appl Clin Med Phys* 2016; 17(4):268-284. PMID: 28296309. Full Text

Radiation Oncology, Henry Ford Health System, Detroit, MI.
Texas Oncology, Fort Worth, TX, USA.

2.5 MV electronic portal imaging, available on Varian TrueBeam machines, was characterized using various phantoms in this study. Its low-contrast detectability, spatial resolution, and contrast-to-noise ratio (CNR) were compared with those of conventional 6 MV and kV planar imaging. Scatter effect in large patient body was simulated by adding solid water slabs along the beam path. The 2.5 MV imaging mode was also evaluated using clinically acquired images from 24 patients for the sites of brain, head and neck, lung, and abdomen. With respect to 6 MV, the 2.5 MV achieved higher contrast and preserved sharpness on bony structures with only half of the imaging dose. The quality of 2.5 MV imaging was comparable to that of kV imaging when the lateral separation of patient was greater than 38 cm, while the kV image quality degraded rapidly as patient separation increased. Based on the results of patient images, 2.5 MV imaging was better for cranial and extracranial SRS than the 6 MV imaging. PACS number(s): 87.57.C.

Radiation Oncology
To DT, **Kim JP**, **Price RG**, **Chetty IJ**, and **Glide-Hurst CK**. Impact of incorporating visual biofeedback in 4D MRI *J Appl Clin Med Phys* 2016; 17(3):128-137. PMID: 28297332. Full Text

Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, USA.

Precise radiation therapy (RT) for abdominal lesions is complicated by respiratory motion and suboptimal soft tissue contrast in 4D CT. 4D MRI offers improved contrast although long scan times and irregular breathing patterns can be limiting. To address this, visual biofeedback (VBF) was introduced into 4D MRI. Ten volunteers were consented to an IRB-approved protocol. Prospective respiratory-triggered, T2-weighted, coronal 4D MRIs were acquired on an open 1.0T MR-SIM. VBF was integrated using an MR-compatible interactive breath-hold control system. Subjects visually monitored their breathing patterns to stay within predetermined tolerances. 4D MRIs were acquired with and without VBF for 2- and 8-phase acquisitions. Normalized respiratory waveforms were evaluated for scan time, duty cycle (programmed/acquisition time), breathing period, and breathing regularity (end-inhale coefficient of variation, EI-COV). Three reviewers performed image quality assessment to compare artifacts with and without VBF. Respiration-induced liver motion was calculated via centroid difference analysis of end-exhale (EE) and EI liver contours. Incorporating VBF reduced 2-phase acquisition time (4.7+/-1.0 and 5.4+/-1.5min with and without VBF, respectively) while reducing EI-COV by 43.8%+/-16.6%. For 8-phase acquisitions, VBF reduced acquisition time by 1.9+/-1.6min and EI-COVs by 38.8%+/-25.7% despite breathing rate remaining similar (11.1+/-3.8 breaths/min with vs. 10.5+/-2.9 without). Using VBF yielded higher duty cycles than unguided free breathing (34.4%+/-5.8% vs. 28.1%+/-6.6%, respectively). Image grading showed that out of 40 paired evaluations, 20 cases had equivalent and 17 had improved image quality scores with VBF, particularly for mid-exhale and EI. Increased liver excursion was observed with VBF, where superior-inferior, anterior-posterior, and left-right EE-EI displacements were 14.1+/-5.8, 4.9+/-2.1, and 1.5+/-1.0 mm, respectively, with VBF compared to 11.9+/-4.5, 3.7+/-2.1, and 1.2+/-1.4 mm without. Incorporating VBF into 4D MRI substantially reduced acquisition time, breathing irregularity, and image artifacts. However, differences in excursion were observed, thus implementation will be required throughout the RT workflow. PACS number(s): 87.55.-x, 87.61.-c, 87.19.xj.

Radiation Oncology

Umar B, **Chang S**, **Ghanem T**, **Siddiqui F**, **Jacobsen G**, **Isrow D**, and **Keller CE**. Does the extent of extracapsular spread in lymph node metastases correlate with outcomes in oropharyngeal squamous cell carcinoma? - a retrospective study *Lab Invest* 2017; 97:334A-334A. PMID: Not assigned. Abstract

[Umar, Beena; Chang, Steve; Ghanem, Tamer; Siddiqui, Farzan; Jacobsen, Gordon; Isrow, Derek; Keller, Christian E.] Henry Ford Hosp, Detroit, MI 48202 USA.

Radiation Oncology

Walker A, Metcalfe P, Liney G, Batumalai V, Dundas K, **Glide-Hurst C**, Delaney GP, Boxer M, Yap ML, Dowling J, Rivest-Henault D, Pogson E, and Holloway L. MRI geometric distortion: Impact on tangential whole-breast IMRT *J Appl Clin Med Phys* 2016; 17(5):1-13. PMID: 28297426. Full Text

Centre for Medical Radiation Physics, University of Wollongong, Wollongong, NSW, Australia.
Liverpool and Macarthur Cancer Therapy Centres, NSW, Australia.
Ingham Institute for Applied Medical Research, Liverpool Hospital, Sydney, NSW, Australia.
Institute of Medical Physics, School of Physics, University of Sydney, Sydney, NSW, Australia.
South Western Clinical School, University of New South Wales, Sydney, NSW, Australia.
Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, USA.
Collaboration for Cancer Outcomes Research and Evaluation, Liverpool Hospital, Liverpool, NSW, Australia.
School of Medicine, University of Western Sydney, Sydney, NSW, Australia.
Commonwealth Scientific and Industrial Research Organisation Computational Informatics, Australian E-Health Research Centre, Brisbane, Australia.

The purpose of this study was to determine the impact of magnetic resonance imaging (MRI) geometric distortions when using MRI for target delineation and planning for whole-breast, intensity-modulated radiotherapy (IMRT). Residual system distortions and combined systematic and patient-induced distortions are considered. This retrospective study investigated 18 patients who underwent whole-breast external beam radiotherapy, where both CT and MRIs were acquired for treatment planning. Distortion phantoms were imaged on two MRI systems, dedicated to radiotherapy planning (a wide, closed-bore 3T and an open-bore 1T). Patient scans were acquired on the 3T system. To simulate MRI-based planning, distortion maps representing residual system distortions were generated via deformable registration between phantom CT and MRIs. Patient CT images and structures were altered to match the residual system distortion measured by the phantoms on each scanner. The patient CTs were also registered to the corresponding patient MRI scans, to assess patient and residual system effects. Tangential IMRT plans were generated and optimized on each resulting CT dataset, then propagated to the original patient CT space. The resulting dose distributions were then evaluated with respect to the standard clinically acceptable DVH and visual assessment criteria. Maximum residual systematic distortion was measured to be 7.9 mm (95%<4.7mm) and 11.9 mm (95%<4.6mm) for the 3T and 1T scanners, respectively, which did not result in clinically unacceptable plans. Eight of the plans accounting for patient and systematic distortions were deemed clinically unacceptable when assessed on the original CT. For these plans, the mean difference in PTV V95 (volume receiving 95% prescription dose) was 0.13+/-2.51% and -0.73+/-1.93% for right- and left-sided patients, respectively. Residual system distortions alone had minimal impact on the dosimetry for the two scanners investigated. The combination of MRI systematic and patient-related distortions can result in unacceptable dosimetry for whole-breast IMRT, a potential issue when considering MRI-only radiotherapy treatment planning. PACS number(s): 87.61.-c, 87.57.cp, 87.57.nj, 87.55.D.

Radiation Oncology

Zaorsky NG, Showalter TN, Ezzell GA, Nguyen PL, Assimos DG, D'Amico AV, Gottschalk AR, Gustafson GS, Keole SR, Liauw SL, Lloyd S, McLaughlin PW, **Movsas B**, Prestidge BR, Taira AV, Vapiwala N, and Davis BJ. ACR Appropriateness Criteria® external beam radiation therapy treatment planning for clinically localized prostate cancer, part I of II *Adv Radiat Oncol* 2017; 2(1):62-84. PMID: Not assigned. Article Request Form

T.N. Showalter, Reston, United States

Radiology

Frisoli TM, **Jain T**, Swadia T, **Hong X**, and Guerrero M. Cardiac tamponade due to pyopneumopericardium from malignant bronchopericardial fistula *Neth Heart J* 2017;PMID: 28349347. Article Request Form

Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA. tfrisol1@hfhs.org.
Department of Cardiology, Henry Ford Hospital, Detroit, MI, USA.

Department of Cardiology, Michigan Heart, St Joseph Mercy Health System, Livonia, MI, USA.
Department of Radiology, Henry Ford Hospital, Detroit, MI, USA.
Department of Cardiology, Evanston Hospital, North Shore University Health System, Evanston, IL, USA.

Radiology

Lee C, **Flynn MJ**, Judy PF, Cody DD, Bolch WE, and Kruger RL. Body size-specific organ and effective doses of chest ct screening examinations of the national lung screening trial *AJR Am J Roentgenol* 2017:1-7. PMID: 28267354. Full Text

1 Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, 9609 Medical Center Dr, Rm 7E448, MSC 9778, Rockville, MD 20850.
2 Department of Radiology, Henry Ford Health System, Detroit, MI.
3 Department of Radiology, Brigham and Women's Hospital, Boston, MA.
4 Department of Imaging Physics, University of Texas MD Anderson Cancer Center, Houston, TX.
5 J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL.
6 System Radiology, Marshfield Clinic Health System, Marshfield, WI.

OBJECTIVE: We calculated body size-specific organ and effective doses for 23,734 participants in the National Lung Screening Trial (NLST) using a CT dose calculator. MATERIALS AND METHODS: We collected participant-specific technical parameters of 23,734 participants who underwent CT in the clinical trial. For each participant, we calculated two sets of organ doses using two methods. First, we computed body size-specific organ and effective doses using the National Cancer Institute CT (NCICT) dosimetry program, which is based on dose coefficients derived from a library of body size-dependent adult male and female computational phantoms. We then recalculated organ and effective doses using dose coefficients from reference size phantoms for all examinations to investigate potential errors caused by the lack of body size consideration in the dose calculations. RESULTS: The underweight participants (body mass index [BMI; weight in kilograms divided by the square of height in meters] < 18.5) received 1.3-fold greater lung dose (median, 4.93 mGy) than the obese participants (BMI > 30) (3.90 mGy). Thyroid doses were approximately 1.3- to 1.6-fold greater than the lung doses (6.3-6.5 mGy). The reference phantom-based dose calculation underestimates the body size-specific lung dose by up to 50% for the underweight participants and overestimates that value by up to 200% for the overweight participants. The median effective dose ranges from 2.01 mSv in obese participants to 2.80 mSv in underweight participants. CONCLUSION: Body size-specific organ and effective doses were computed for 23,734 NLST participants who underwent low-dose CT screening. The use of reference size phantoms can lead to significant errors in organ dose estimates when body size is not considered in the dose assessment.

Research Administration

Wolf B. Biotinidase deficiency masquerading as multiple sclerosis? *Mult Scler* 2017;PMID: 28337933. Full Text

Department of Research Administration, Henry Ford Hospital, Detroit, MI, USA; Center for Molecular Medicine and Genetics, Wayne State University, Detroit, MI, USA.

Rheumatology

Dozmorov MG, Coit P, **Maksimowicz-McKinnon K**, and Sawalha AH. Age-associated DNA methylation changes in naive CD4+ T cells suggest an evolving autoimmune epigenotype in aging T cells *Epigenomics* 2017;PMID: 28322571. Article Request Form

Department of Biostatistics, Virginia Commonwealth University, Richmond, VA 23298, USA.
Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109, USA.
Division of Rheumatology, Henry Ford Health System, Detroit, MI 48202, USA.
Center for Computational Medicine & Bioinformatics, University of Michigan, Ann Arbor, MI 48109, USA.

AIM: We sought to define age-associated DNA methylation changes in naive CD4+ T cells. MATERIALS & METHODS: Naive CD4+ T cells were collected from 74 healthy individuals (age 19-66 years), and age-related DNA methylation changes were characterized. RESULTS: We identified 11,431 age-associated CpG sites, 57% of which were hypermethylated with age. Hypermethylated sites were enriched in CpG islands and repressive transcription factor binding sites, while hypomethylated sites showed T cell specific enrichment in active enhancers marked by H3K27ac and H3K4me1. Our data emphasize cancer-related DNA methylation changes with age, and also reveal age-associated hypomethylation in immune-related pathways, such as T cell receptor signaling, FCgammaR-mediated phagocytosis, apoptosis and the mammalian target of rapamycin signaling pathway. The MAPK signaling

pathway was hypermethylated with age, consistent with a defective MAPK signaling in aging T cells. CONCLUSION: Age-associated DNA methylation changes may alter regulatory mechanisms and signaling pathways that predispose to autoimmunity.

Sleep Medicine
Herring WJ, Connor KM, Snyder E, Snavely DB, Zhang Y, Hutzelmann J, Matzura-Wolfe D, Benca RM, Krystal AD, Walsh JK, Lines C, **Roth T**, and Michelson D. Clinical profile of suvorexant for the treatment of insomnia over 3 months in women and men: subgroup analysis of pooled phase-3 data *Psychopharmacology (Berl)* 2017;PMID: 28265715. Full Text

Merck & Co., Inc., Kenilworth, NJ, USA. william_herring@merck.com.
Merck & Co., Inc., UG 4C-13, PO Box 1000, North Wales, PA, 19454-1099, USA. william_herring@merck.com.
Merck & Co., Inc., Kenilworth, NJ, USA.
Department of Psychiatry and Human Behavior, University of California-Irvine, Irvine, CA, USA.
Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, NC, USA.
Sleep Medicine and Research Center, St., Luke's Hospital, St. Louis, MO, USA.
Henry Ford Hospital Sleep Center, Detroit, MI, USA.

RATIONALE: Sex-related differences in the clinical profiles of some insomnia medications have been previously reported. OBJECTIVE: To evaluate the clinical profile of suvorexant, a novel orexin receptor antagonist approved for treating insomnia at doses up to 20 mg, by sex subgroups. METHODS: Efficacy analyses by sex were based on pooled data from two similar phase 3, randomized, double-blind, placebo-controlled, 3-month trials in elderly (>/=65 years) and non-elderly (18-64 years) insomnia patients. Two age-adjusted (non-elderly/elderly) dose regimes of 40/30 and 20/15 mg were evaluated, with fewer patients assigned to 20/15 mg. Efficacy was assessed by patient-reported outcomes (N = 1264 women, 707 men) and by polysomnography endpoints in ~75% of patients. Safety analyses by sex (N = 1744 women, 1065 men) included pooled data from the two 3-month trials plus 3-month data from a safety trial of 40/30 mg. RESULTS: The sex subgroup efficacy analyses mirrored the improvements seen for suvorexant 40/30 and 20/15 mg over placebo on patient-reported outcomes and polysomnography sleep maintenance and onset endpoints in the primary analyses; 95% CIs excluded zero in favor of suvorexant for most endpoints in both sexes, and similar efficacy was observed between sexes (95% CIs overlapped). Suvorexant was well-tolerated in women and men, although women in all treatment groups (including placebo) reported more adverse events than men. The most frequent adverse event was somnolence (women: 11.1% for 40/30 mg, 8.5% for 20/15 mg, 2.3% for placebo; men: 10.1% for 40/30 mg, 3.4% for 20/15 mg, 4.2% for placebo). CONCLUSION: Suvorexant was generally effective and well-tolerated in both women and men with insomnia. ClinicalTrials.gov trial registration numbers: NCT01097616, NCT01097629, NCT01021813.

Sleep Medicine
Pillai V, **Roth T**, **Roehrs T**, **Moss K**, **Peterson EL**, and **Drake CL**. Effectiveness of benzodiazepine receptor agonists in the treatment of insomnia: An examination of response and remission rates *Sleep* 2017; 40(2)PMID: 28364510. Full Text

Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, MI.
Biostatistics and Research Epidemiology, Henry Ford Hospital, Detroit, MI.

Study objectives: To examine the real-world effectiveness of benzodiazepine receptor agonists (BzRAs) by quantifying response and remission rates in a clinical sample receiving chronic BzRA treatment for insomnia. Methods: Participants were outpatients (N = 193; 72% female; 55.2 +/- 11.1 year) who had an insomnia diagnosis per medical records, and who were taking a therapeutic dose of BzRA for their insomnia. Endpoints were nocturnal sleep disturbance and Insomnia Severity Index (ISI) scores. A reduction meeting the criterion for the minimally important difference in ISI scores (change >/= 6) constituted "response"; "remission" was inferred when symptoms fell below the clinical cutoff (ISI < 11). Results: Most participants (71%) used BzRAs at least 5 nights per week. Mean ISI scores were significantly lower (t = 22.31; p < .01) while on BzRAs than when untreated, but remained in the clinical range (mean = 11.0; standard deviation = 5.7). Although 76.7% responded to treatment, only 47.7% remitted. The majority (68.9%) of participants had a sleep-onset latency > 30 minutes and/or wake-time after sleep onset > 60 minutes while on BzRAs. After controlling for gender and insomnia severity when untreated, odds of insomnia persistence despite BzRA use were 2 times higher in patients with comorbid medical [odds ratio (OR) = 2.39; 95% confidence interval (CI) = 1.20% to 4.77%; p < .05] and psychiatric disorders (OR = 2.24; 95% CI = 1.21% to 4.13%; p < .05). Conclusions: This is the first study to distinguish between response and remission in insomnia patients taking BzRAs. Findings suggest that while many insomnia patients respond to chronic BzRA treatment, most do not remit. Remission rates are particularly low for comorbid insomnia, the most prevalent phenotype of the disorder.

Surgery

Abdel Khalik H, Stevens H, **Carlin AM**, Stricklen A, Ross R, Pesta C, Finks JF, Ibrahim A, and Ghaferi AA. Site-specific approach to reducing emergency department visits following surgery *Ann Surg* 2017;PMID: 28306648. Full Text

*Department of Surgery, University of Michigan, Ann Arbor, MI daggerDepartment of Surgery, Henry Ford Health System, Detroit, MI double daggerMichigan Bariatric Surgery Collaborative, Ann Arbor, MI.

OBJECTIVE: The aim of this study was to explore the efficacy of current bariatric perioperative measures at reducing emergency department (ED) visits following bariatric surgery in the state of Michigan. SUMMARY OF BACKGROUND DATA: Many ED visits following bariatric surgery do not result in readmission and may be preventable. Little research exists evaluating the efficacy of perioperative measures aimed at reducing ED visits in this population. Therefore, understanding the driving factors behind these preventable ED visits may be a fruitful approach to prevention. Furthermore, evaluating the efficacy of current perioperative measures may shed light on how to achieve meaningful reductions in ED visits. METHODS: We studied 48,035 eligible bariatric surgery patients across 37 Michigan Bariatric Surgical Collaborative (MBSC) sites between January 2012 and October 2015. Hospitals were ranked according to their risk- and reliability-adjusted ED visit rates. For hospitals in each ED visit rate tercile, several patient, surgery, and hospital summary characteristics were compared. We then studied whether a hospital's compliance with specific perioperative measures was significantly associated with reduced ED visit rates. RESULTS: Only 3 of the 30 surgery, hospital, and patient summary characteristics studied were significant predictors of a hospital's ED visit rate: rate of sleeve gastrectomies, rate of readmissions, and rate of venous thromboembolism complications (P = 0.04, P = 0.0065, and P = 0.0047, respectively). Also, a hospital's compliance with the perioperative measures evaluated was not a significant predictor of ED visit rates (P = 0.12). CONCLUSIONS: Current practices aimed at reducing ED visits appear to be ineffective. Due to heterogeneity in patient populations and local infrastructure, a more tailored approach to ED visit reduction may be more successful.

Surgery

Catanescu I, Long G, Bove P, **Khoury M**, Brown O, Rimar S, **Rizk Y**, Uzieblo M, and **Hans S**. Rupture of abdominal aortic aneurysm in patients with and without antecedent endovascular repair *Ann Vasc Surg* 2017; 39:99-104. PMID: 27522971. Full Text

Henry Ford-Macomb Hospital, Clinton Township, MI.
William Beaumont Hospital, Royal Oak, MI.
Henry Ford-Macomb Hospital, Clinton Township, MI; St. John Macomb Hospital, Warren, MI.
Henry Ford-Macomb Hospital, Clinton Township, MI; St. John Macomb Hospital, Warren, MI. Electronic address: sshans@comcast.net.

BACKGROUND: Reported results of ruptured abdominal aortic aneurysm (rAAA) in patients with antecedent endovascular aneurysm repair (EVAR) to those presenting with de novo rupture show a similar or slightly improved outcome. The aim of this study was to compare differences in the presentation and outcomes of rAAA with and without prior EVAR. METHODS: A retrospective review of 121 patients with rAAA, ruptured identified 2 groups. Group A included 17 patients (rAAA n = 17) with antecedent EVAR and group B consisted of 104 patients (rAAA n = 104) with de novo ruptures, from January 2001 to March 2015 in 3 teaching hospitals. Patient characteristics and perioperative variables were compared; Fisher's exact test was used for categorical variables. For continuous variables, Student's t-test and Mann-Whitney U test were used. RESULTS: Both groups were similar in age, gender, the incidence of hypertension, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, and nicotine abuse. Mean time of presentation from EVAR to rupture in group A was 42 +/- 22 months. Mean preoperative transverse or anteroposterior diameter of AAA was 6.6 cm in group A and 7.1 cm in group B. Three patients of 17 (17.6%) in group A were hemodynamically unstable as compared to 47 of 104 patients (45.1%) in group B (P = 0.03). Mean red blood cells, fresh frozen plasma, and platelet transfusion were similar in both groups. Thirty-day mortality was 8 of 17 (44.7%) in group A and 44 of 104 (42.3%) in group B (P = 1.0). Postoperative complications were also similar in both groups except the incidence of postoperative respiratory failure was higher in group B (38%) as compared with 11.1% in group A (P = 0.001). CONCLUSIONS: Patients presenting with rAAA with antecedent EVAR are hemodynamically more stable as compared with patients with de novo rupture of AAA. Postoperative respiratory failure is more common in patients with de novo rupture. rAAA carry high mortality with and without prior EVAR.

Surgery

Colburn JL, **Mohanty S**, and Burton JR. Surgical guidelines for perioperative management of older adults: What geriatricians need to know *J Am Geriatr Soc* 2017;PMID: 28323335. Full Text

Division of Geriatric Medicine and Gerontology, School of Medicine, The Johns Hopkins University, Baltimore, Maryland.
Department of Surgery, Henry Ford Hospital, Detroit, Michigin.

A multidisciplinary panel of experts representing surgery, anesthesia, and geriatrics recently published guidelines for surgeons on the optimal perioperative management of older adults, including recommendations on postoperative recovery and posthospital transitions of care. Geriatricians have an important role in the care for older adults in the preoperative period as older adults consider surgical options and prepare for surgical procedures, during the perioperative period as inpatient consultants, and in the postoperative period as older adults transition to rehabilitation facilities or to home. This article outlines the perioperative surgical guidelines and describes how they apply to the role of the geriatrician in the care of older adults during the perioperative period.

Surgery
Fuzesi S, Cano SJ, Klassen AF, **Atisha D**, and Pusic AL. Validation of the electronic version of the BREAST-Q in the army of women study *Breast* 2017; 33:44-49. PMID: 28279888. Full Text

Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA. Electronic address: fuzesis@mskcc.org.
Modus Outcomes, Spirella Building, Letchworth Garden City, SG6 4ET, UK.
McMaster University, 3N27, 1200 Main Street W, Hamilton, ON L8N 3Z5, Canada.
Henry Ford Health System, 2799 W. Grand Blvd, K-16, Detroit, MI 48202, USA.
Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10065, USA.

Women undergoing surgery for primary breast cancer can choose between breast conserving therapy and mastectomy (with or without breast reconstruction). Patients often turn to outcomes data to help guide the decision-making process. The BREAST-Q is a validated breast surgery-specific patient-reported outcome measure that evaluates satisfaction, quality of life, and patient experience. It was originally developed for paper-and-pencil administration. However, the BREAST-Q has increasingly been administered electronically. Therefore, the aim of this study was to evaluate the psychometric properties of an electronic version of the BREAST-Q in a large online survey. Women with a history of breast cancer surgery recruited from the Love/AVON Army of Women program completed an electronic version of the BREAST-Q in addition to the Impact of Cancer Survey and PTSD Checklist. Traditional psychometric analyses were performed on the collected data. BREAST-Q data were collected from 6748 women (3497 Breast Conserving Therapy module, 1295 Mastectomy module, 1956 Breast Reconstruction module). Acceptability was supported by a high response rate (82%), low frequency of missing data (<5%), and maximum endorsement frequencies (<80%) in all but 17 items. Scale reliability was supported by high Cronbach's alpha coefficients (>/=0.78) and item-total correlations (range of means, 0.65-0.91). Validity was supported by interscale correlations, convergent and divergent hypotheses as well as clinical hypotheses. The electronically administered BREAST-Q yields highly reliable, clinically meaningful data for use in clinical outcomes research. The BREAST-Q can be used in the clinical setting, whether administered electronically or using paper-and-pencil, at the choice of the patient and surgeon.

Surgery
Marrocco A, and Krouse HJ. Obstacles to preventive care for individuals with disability: Implications for nurse practitioners *J Am Assoc Nurse Pract* 2017;PMID: 28266148. Full Text

Henry Ford Health System, Detroit, Michigan.
College of Nursing, Wayne State University, Detroit, Michigan.

BACKGROUND AND PURPOSE: Individuals with disabilities have been identified as a population with a significantly lower usage of preventive services. Nurse practitioners (NPs) provide a key access point in the healthcare delivery system for preventive services for vulnerable populations such as those with disabilities. It is essential to understand existing barriers that prohibit access to effective preventive care for this vulnerable population. METHODS: Systematic search and review of Cumulative Index of Nursing and Allied Health Literature (CINAHL), Medline, PubMed, Google Scholar, and government reports and World Health Organizations reports. Twenty-six articles were included in the review. CONCLUSIONS: This literature review confirmed previous notions that people with disabilities are receiving much fewer preventive services than the general population. The studies reviewed identified four major barriers that contributed to the lack of preventive care. These barriers included physical environment and system, transportation, provider knowledge and attitude, and financial. Recognition of the obstacles that this subpopulation faces in accessing preventive care services is the first step to effectively remedying this problem. IMPLICATIONS

FOR PRACTICE: Preventive services have been identified as one of the cornerstones to improving health and quality of life. By understanding the circumstances that restrict those with disabilities from accessing preventive services, NPs can provide meaningful and effective solutions.

Surgery
Newman LA. Do patterns of breast cancer surgical care reflect national voting records? *JAMA Surg* 2017;PMID: 28355435. Full Text

International Center for the Study of Breast Cancer Subtypes, Breast Oncology Program, Henry Ford Health System, Detroit, Michigan.

Surgery
Newman LA, and **Kaljee LM**. Health disparities and triple-negative breast cancer in african american women: A review *JAMA Surg* 2017;PMID: 28355428. Full Text

Department of Surgery, Breast Oncology Program, International Center for the Study of Breast Cancer Subtypes, Henry Ford Health System, Detroit, Michigan.
Global Health Initiative, Henry Ford Health System, Detroit, Michigan.

Importance: Variation in cancer incidence and outcome has well-documented correlations with racial/ethnic identity. In the United States, the possible genetic and ancestral hereditary explanations for these associations are confounded by socioeconomic, cultural, and lifestyle patterns. Differences in the breast cancer burden of African American compared with European/white American women represent one of the most notable examples of disparities in oncology related to racial/ethnic identity. Elucidating the source of these associations is imperative in achieving the promise of the national Precision Medicine Initiative. Observations: Population-based breast cancer mortality rates have been higher for African American compared with white American women since the early 1980s, largely reflecting declines in mortality that have been disproportionately experienced among white American patients and at least partly explained by the advent of endocrine therapy that is less effective in African American women because of the higher prevalence of estrogen receptor-negative disease. The increased risk of triple-negative breast cancer in African American women as well as western, sub-Saharan African women compared with white American, European, and east African women furthermore suggests that selected genetic components of geographically defined African ancestry are associated with hereditary susceptibility for specific patterns of mammary carcinogenesis. Disentangling health care access barriers, as well as reproductive, lifestyle, and dietary factors from genetic contributions to breast cancer disparities remains challenging. Epigenetics and experiences of societal inequality (allostatic load) increase the complexity of studying breast cancer risk related to racial/ethnic identity. Conclusions and Relevance: Oncologic anthropology represents a transdisciplinary field of research that can combine the expertise of population geneticists, multispecialty oncologists, molecular epidemiologists, and behavioral scientists to eliminate breast cancer disparities related to racial/ethnic identity and advance knowledge related to the pathogenesis of triple-negative breast cancer.

Surgery
Takahashi K, **Prashar R**, **Putchakayala KG**, **Kane WJ**, **Denny JE**, **Kim DY**, and **Malinzak LE**. Allograft loss from acute Page kidney secondary to trauma after kidney transplantation *World J Transplant* 2017; 7(1):88-93. PMID: 28280700. Full Text

Kazuhiro Takahashi, Krishna G Putchakayala, William J Kane, Jason E Denny, Dean Y Kim, Lauren E Malinzak, Transplant and Hepatobiliary Surgery, Henry Ford Hospital, Detroit, MI 48202, United States.

We report a rare case of allograft loss from acute Page kidney secondary to trauma that occurred 12 years after kidney transplantation. A 67-year-old Caucasian male with a past surgical history of kidney transplant presented to the emergency department at a local hospital with left lower abdominal tenderness. He recalled that his cat, which weighs 15 lbs, jumped on his abdomen 7 d prior. On physical examination, a small tender mass was noticed at the incisional site of the kidney transplant. He was producing a normal amount of urine without hematuria. His serum creatinine level was slightly elevated from his baseline. Computer tomography revealed a large subscapular hematoma around the transplant kidney. The patient was observed to have renal trauma grade II at the hospital over a period of three days, and he was finally transferred to a transplant center after his urine output significantly decreased. Doppler ultrasound demonstrated an extensive peri-allograft hypoechoic area and abnormal waveforms with absent arterial diastolic flow and a patent renal vein. Despite surgical decompression, the allograft failed to respond appropriately due to the delay in surgical intervention. This is the third reported case of allograft loss from acute Page kidney following kidney transplantation. This case reinforces that kidney care differs if the kidney is

solitary or a transplant. Early recognition and aggressive treatments are mandatory, especially in a case with Doppler signs that are suggestive of compression.

Surgery
Yaremchuk K, **Darian V**, and **Williams AM**. Seasonality of auricular amputations in rabbits *Laryngoscope* 2017; 127(4):773-775. PMID: 28322456. Full Text

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.
Division of Plastic and Reconstructive Surgery, Henry Ford Hospital, Detroit, Michigan, U.S.A.

This retrospective observational analysis hypothesizes that an increase occurs in online reports and images of auricular amputations of confectionary rabbits during the spring. Using the online search engine Google, online content and visual portrayals of confectionary rabbit auricular amputations from 2012 to 2017 were identified and trended against seasonal variations. To determine incidence, commercial availability of chocolate rabbits in retail facilities were assayed. A statistically significant increase in mention of rabbit auricular amputations occurred during the spring. Mapping techniques showed the annual peak incidence for 2012 to 2017 to be near Easter for each year studied. Human adults and children appear to be wholly responsible for the reports of rabbit auricular amputations. Reconstructive techniques are dependent on the percentage of auricular defect. Laryngoscope, 127:773-775, 2017.

Urology
Arora S. Robotic excision of a functioning hilar paraganglioma with reconstruction of renal vessels *North American Robotic Urology Symposium* 2017;PMID: Not assigned. Abstract

Urology
Arora S. Robot assisted partial nephrectomy for complex renal hilar tumors: Technical caveats *North American Robotic Urology Symposium* 2017;PMID: Not assigned. Abstract

Urology
Arora S, and Ahlawat R. A novel technique of intrafascial robotic radical prostatectomy with combined anterior-posterior approach to preserve continence mechanism - A Feasibility study *North American Robotic Urology Symposium* 2017;PMID: Not assigned. Abstract

Urology
Dalela D, Santiago-Jimenez M, Yousefi K, Karnes RJ, Ross AE, Den RB, Freedland SJ, Schaeffer EM, Dicker AP, **Menon M**, Briganti A, Davicioni E, and **Abdollah F**. Genomic classifier augments the role of pathological features in identifying optimal candidates for adjuvant radiation therapy in patients with prostate cancer: Development and internal validation of a multivariable prognostic model *J Clin Oncol* 2017:Jco2016699918. PMID: 28350520. Full Text

Deepansh Dalela, Mani Menon, and Firas Abdollah, Henry Ford Health System, Detroit, MI; Maria Santiago-Jimenez, Kasra Yousefi, and Elai Davicioni, GenomeDx Biosciences, Vancouver, British Columbia, Canada; R. Jeffrey Karnes, Mayo Clinic, Rochester, MN; Ashley E. Ross, Johns Hopkins Hospital, Baltimore, MD; Adam P. Dicker and Robert B. Den, Thomas Jefferson University, Philadelphia, PA; Stephen J. Freedland, Cedars-Sinai Medical Center, Los Angeles, CA; Edward M. Schaeffer, Northwestern University Feinberg School of Medicine, Chicago, IL; and Alberto Briganti, Vita Salute San Raffaele Hospital, Milan, Italy.

Purpose Despite documented oncologic benefit, use of postoperative adjuvant radiotherapy (aRT) in patients with prostate cancer is still limited in the United States. We aimed to develop and internally validate a risk-stratification tool incorporating the Decipher score, along with routinely available clinicopathologic features, to identify patients who would benefit the most from aRT. Patient and Methods Our cohort included 512 patients with prostate cancer treated with radical prostatectomy at one of four US academic centers between 1990 and 2010. All patients had >/= pT3a disease, positive surgical margins, and/or pathologic lymph node invasion. Multivariable Cox regression analysis tested the relationship between available predictors (including Decipher score) and clinical recurrence (CR), which were then used to develop a novel risk-stratification tool. Our study adhered to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis guidelines for development of prognostic models. Results Overall, 21.9% of patients received aRT. Median follow-up in censored patients was 8.3 years. The 10-year CR rate was 4.9% vs. 17.4% in patients treated with aRT versus initial observation (P < .001). Pathologic T3b/T4 stage, Gleason score 8-10, lymph node invasion, and Decipher score > 0.6 were independent predictors of CR (all P

< .01). The cumulative number of risk factors was 0, 1, 2, and 3 to 4 in 46.5%, 28.9%, 17.2%, and 7.4% of patients, respectively. aRT was associated with decreased CR rate in patients with two or more risk factors (10-year CR rate 10.1% in aRT v 42.1% in initial observation; P = .012), but not in those with fewer than two risk factors (P = .18). Conclusion Using the new model to indicate aRT might reduce overtreatment, decrease unnecessary adverse effects, and reduce risk of CR in the subset of patients (approximately 25% of all patients with aggressive pathologic disease in our cohort) who benefit from this therapy.

Urology
Leyh-Bannurah SR, Budaus L, Pompe R, Zaffuto E, Briganti A, Abdollah F, Montorsi F, Schiffmann J, **Menon M**, Shariat SF, Fisch M, Chun F, Huland H, Graefen M, and Karakiewicz PI. North american population-based validation of the national comprehensive cancer network practice guideline recommendation of pelvic lymphadenectomy in contemporary prostate cancer *Prostate* 2017; 77(5):542-548. PMID: 28093788. Full Text

Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada.
Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany.
Department of Urology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
Department of Urology and Division of Experimental Oncology, URI, Urological Research Institute, IRCCS San Raffaele Scientific Institute, Milan, Italy.
Department of Urology, Academic Hospital Braunschweig, Braunschweig, Germany.
Vattikuti Urology Institute and VUI Center for Outcomes Research Analytics and Evaluation (VCORE), Henry Ford Health System, Henry Ford Hospital, Detroit, Michigan.
Department of Urology, Medical University of Vienna, Vienna, Austria.
Department of Urology, University of Montreal Health Center, Montreal, Canada.

BACKGROUND: National Comprehensive Cancer Network (NCCN) guidelines recommend a pelvic lymph node dissection (PLND) in prostate cancer (PCa) patients treated with radical prostatectomy (RP) if a nomogram predicted risk of lymph node invasion (LNI) is >/=2%. We examined this and other thresholds, including nomogram validation. METHODS: We examined records of 26,713 patients treated with RP and PLND between 2010 and 2013, within the Surveillance, Epidemiology, and End Results database. Nomogram thresholds of 2-5% were tested and external validation was performed. RESULTS: LNI was recorded in 4.7% of patients. Nomogram accuracy was 80.4% and maintained minimum accuracy of 75.6% in subgroup analyses, according to age, race, and nodal yield >10. With the NCCN recommended 2% nomogram threshold, PLND could be avoided in 22.3% of patients at the expense of missing 3.0% of individuals with LNI. Alternative thresholds of 3%, 4%, and 5% yielded respective PLND avoidance rates of 60.4%, 71.0%, and 79.8% at the expense of missing 17.8%, 27.2%, and 36.6% of patients with LNI. NCCN cut-off recommendation was best satisfied with a threshold of <2.6%, at which PLND could be avoided in 13,234 patients (49.5%) versus missing 141 patients with LNI (11.2%). CONCLUSION: NCCN LNI nomogram remains accurate in contemporary patients. However, the 2% threshold appears to be too strict, since only 22.3% of PLNDs can be avoided, instead of the stipulated 47.7%. The optimal 2.6% threshold allows a higher rate of PLND avoidance (49.5%), at the cost of 11.2% missed instances of LNI, as recommended by NCCN guidelines. PATIENT SUMMARY. External validation in contemporary SEER prostate cancer patients showed that the NCCN nomogram remains accurate for predicting lymph node invasion and seems to be optimal at an alternative 2.6% threshold, with best ratio of avoided pelvic lymph node dissections (49.5%) and missed LNIs (11.2%), as recommended by NCCN guideline. Prostate 77:542-548, 2017. (c) 2017 Wiley Periodicals, Inc.

Urology
Rahbar H, and **Rogers C**. Renal tumour biopsy: let's talk about it *BJU Int* 2017; 119(4):507-508. PMID: 28319355. Full Text

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.

Urology
Spratt DE, Yousefi K, Deheshi S, Ross AE, Den RB, Schaeffer EM, Trock BJ, Zhang J, Glass AG, Dicker AP, **Abdollah F**, Zhao SG, Lam LL, du Plessis M, Choeurng V, Haddad Z, Buerki C, Davicioni E, Weinmann S, Freedland SJ, Klein EA, Karnes RJ, and Feng FY. Individual patient-level meta-analysis of the performance of the decipher genomic classifier in high-risk men after prostatectomy to predict development of metastatic disease *J Clin Oncol* 2017:Jco2016702811. PMID: 28358655. Full Text

Daniel E. Spratt and Shuang G. Zhao, University of Michigan, Ann Arbor; Firas Abdollah, Henry Ford Health System, Detroit, MI; Kasra Yousefi, Samineh Deheshi, Jingbin Zhang, Lucia L.C. Lam, Marguerite du Plessis, Voleak Choeurng, Zaid Haddad, Christine Buerki, and Elai Davicioni, GenomeDx Biosciences, Vancouver, British Columbia,

Canada; Ashley E. Ross and Bruce J. Trock, Johns Hopkins Hospital, Baltimore, MD; Robert B. Den and Adam P. Dicker, Thomas Jefferson University, Philadelphia, PA; Edward M. Schaeffer, Northwestern University, Evanston, IL; Andrew G. Glass and Sheila Weinmann, Center for Health Research, Kaiser Permanente Northwest, Portland, OR; Stephen J. Freedland, Cedars-Sinai Medical Center, Los Angeles; Felix Y. Feng, University of California, San Francisco, CA; Eric A. Klein, Cleveland Clinic, Cleveland, OH; and R. Jeffrey Karnes, Mayo Clinic, Rochester, MN.

Purpose To perform the first meta-analysis of the performance of the genomic classifier test, Decipher, in men with prostate cancer postprostatectomy. Methods MEDLINE, EMBASE, and the Decipher genomic resource information database were searched for published reports between 2011 and 2016 of men treated by prostatectomy that assessed the benefit of the Decipher test. Multivariable Cox proportional hazards models fit to individual patient data were performed; meta-analyses were conducted by pooling the study-specific hazard ratios (HRs) using random-effects modeling. Extent of heterogeneity between studies was determined with the I2 test. Results Five studies (975 total patients, and 855 patients with individual patient-level data) were eligible for analysis, with a median follow-up of 8 years. Of the total cohort, 60.9%, 22.6%, and 16.5% of patients were classified by Decipher as low, intermediate, and high risk, respectively. The 10-year cumulative incidence metastases rates were 5.5%, 15.0%, and 26.7% (P < .001), respectively, for the three risk classifications. Pooling the study-specific Decipher HRs across the five studies resulted in an HR of 1.52 (95% CI, 1.39 to 1.67; I2 = 0%) per 0.1 unit. In multivariable analysis of individual patient data, adjusting for clinicopathologic variables, Decipher remained a statistically significant predictor of metastasis (HR, 1.30; 95% CI, 1.14 to 1.47; P < .001) per 0.1 unit. The C-index for 10-year distant metastasis of the clinical model alone was 0.76; this increased to 0.81 with inclusion of Decipher. Conclusion The genomic classifier test, Decipher, can independently improve prognostication of patients postprostatectomy, as well as within nearly all clinicopathologic, demographic, and treatment subgroups. Future study of how to best incorporate genomic testing in clinical decision-making and subsequent treatment recommendations is warranted.

Urology

Territo A, Mottrie A, Abaza R, **Rogers C**, **Menon M**, **Bhandari M**, Ahlawat R, and Breda A. Robotic kidney transplantation: current status and future perspectives *Minerva Urol Nefrol* 2017; 69(1):5-13. PMID: 28009142.
Article Request Form

Puigvert Foundation, Autonoma University of Barcelona, Barcelona, Spain.
OLV Vattikuti Robotic Surgery Institute, Aalst, Belgium.
OhioHealth Dublin Methodist Hospital, Dublin, OH, USA.
Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.
Medanta Kidney and Urology Institute, Medanta, Medicity, Gurgaon, India.
Puigvert Foundation, Autonoma University of Barcelona, Barcelona, Spain - albbred@hotmail.com.

INTRODUCTION: For the treatment of patients with end-stage renal disease, kidney transplantation is preferred to renal replacement modalities such as hemodialysis and peritoneal dialysis. Although open surgery remains the gold standard, minimally invasive approaches have recently been applied in transplant kidney surgery. Despite growing enthusiasm and potential benefits of robotic kidney transplant, many aspects of this novel technique remain controversial. Aim of this study was to analyze the current status and future developments in robotic-assisted surgery for kidney transplantation. EVIDENCE ACQUISITION: A systematic PubMed search for peer-reviewed studies was performed using keywords such as "Minimally invasive surgery" or "Robotic" or "Robot assisted" AND "Kidney transplantation". Eligible articles were reviewed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria. EVIDENCE SYNTHESIS: Eleven studies evaluated reported the feasibility, safety, and reproducibility of robotic kidney transplantation using either a transperitoneal or an extraperitoneal approach. The graft kidney is usually introduced via a periumbilical or Gibson incision. The functional outcomes of the robotic approach are equivalent to those of open kidney transplantation in terms of mean serum creatinine at 6 month and delayed graft function. The benefits of robotic kidney transplantation include easier vascular anastomosis, better cosmetic results, and a lower complication rate, including in the obese population. Many concerns remain over the potential impairment of graft function due to pneumoperitoneum and warm ischemia and the technical difficulties related to the vascular anastomosis. Refinement of the robotic tactile feedback and development of a cold ischemia device may lead to further improvement in this novel technique. CONCLUSIONS: Robotic surgery allows kidney transplantation to be performed under optimal operative conditions, reducing complications while maintaining the functional results achieved by the open approach. The evolution of this technique is in progress.

Urology

Williamson SR, Gadde R, Trpkov K, Hirsch MS, Srigley JR, Reuter VE, Cheng L, Priya Kunju L, **Barod R**, **Rogers CG**, Delahunt B, Hes O, Eble JN, Zhou M, McKenney JK, Martignoni G, Fleming S, Grignon DJ, Moch H, and **Gupta NS**. Diagnostic criteria for oncocytic renal neoplasms: A survey of urologic pathologists *Hum Pathol* 2017;PMID: 28315424. Full Text

Department of Pathology and Laboratory Medicine, Detroit, MI, United States; Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States; Department of Pathology, Wayne State University School of Medicine, Detroit, MI, United States. Electronic address: seanwill@temple.edu.
Department of Pathology and Laboratory Medicine, Detroit, MI, United States.
Department of Pathology and Laboratory Medicine, Calgary Laboratory Service and University of Calgary, Calgary, AB, Canada.
Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States.
Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada.
Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, United States.
Department of Pathology and Laboratory Medicine, Indiana University, Indianapolis, IN, United States.
Department of Pathology, University of Michigan School of Medicine, Ann Arbor, MI, United States.
Vattikutti Urology Institute, Henry Ford Health System, Detroit, MI, USA.
Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago - Wellington, Wellington, New Zealand.
Department of Pathology, Charles University in Prague, Faculty of Medicine in Plzen, Pilsen, Czech Republic.
Department of Pathology, New York University Medical Center, New York, NY, United States.
Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA.
Department of Pathology and Diagnostics, University of Verona, Verona, Italy; Department of Pathology, Pederzoli Hospital, Peschiera del Garda, Italy.
Department of Cellular and Molecular Pathology, University of Dundee, Ninewells Hospital, Dundee, United Kingdom.
Department of Pathology, University Hospital Zurich, Zurich, Switzerland.
Department of Pathology and Laboratory Medicine, Detroit, MI, United States; Henry Ford Cancer Institute, Henry Ford Health System, Detroit, MI, United States.

Renal oncocytoma and chromophobe renal cell carcinoma (RCC) have been long recognized as distinct tumors; however, it remains unknown if uniform diagnostic criteria are used to distinguish these tumor types in practice. A survey was distributed to urologic pathologists regarding oncocytic tumors. Responses were received from 17/26 invitees. Histologically, >1 mitotic figure was regarded as most worrisome (n=10) or incompatible (n=6) with oncocytoma diagnosis. Interpretation of focal nuclear wrinkling, focal perinuclear clearing, and multinucleation depended on extent and did not necessarily exclude oncocytoma if minor. Staining techniques most commonly used included: CK7 (94%), KIT (71%), vimentin (65%), colloidal iron (59%), CD10 (53%), and AMACR (41%). Rare CK7-positive cells (</=5%) was regarded as most supportive of oncocytoma, although an extent excluding oncocytoma was not universal. Multiple chromosomal losses were most strongly supportive for chromophobe RCC diagnosis (65%). Less certainty was reported for chromosomal gain or a single loss. For tumors with mixed or inconclusive features, many participants use an intermediate diagnostic category (82%) that does not label the tumor as unequivocally benign or malignant, typically "oncocytic neoplasm" or "tumor" with comment. The term "hybrid tumor" was used variably in several scenarios. A slight majority (65%) report outright diagnosis of oncocytoma in needle biopsies. The morphologic, immunohistochemical, and genetic characteristics that define oncocytic renal tumors remain incompletely understood. Further studies correlating genetics, behavior, and histology are needed to define which tumors truly warrant classification as carcinomas for patient counseling and follow-up strategies.