Washington University in St. Louis
SCHOOL OF MEDICINE

Seventh Annual

Research Training Symposium and Poster Session

October 31, 2012

Showcasing Basic, Clinical, and Translational research projects by junior faculty, fellows, residents, and training program students.

Washington University School of Medicine
Seventh Annual Research Training Symposium & Poster Session
October 31st, 2012
Farrell Learning and Teaching Center

12:30 – 12:45 pm Connor Auditorium
Welcome and Opening Remarks

Larry J. Shapiro, MD
Executive Vice Chancellor for Medical Affairs and Dean
Washington University School of Medicine

12:45 – 1:45 pm Connor Auditorium
Keynote Address

Curtis L. Lowery Jr., MD
Director of Maternal Fetal Medicine
Chairman and Director, Department of Obstetrics and Gynecology
Principal Investigator, Clinical and Translational Science Award
University of Arkansas for Medical Sciences

1:45 – 3:00 pm Connor Auditorium
Oral Presentations

1:45 – 2:00 pm	Yo-El Ju, MD
2:00 – 2:15 pm	Elaine Khoong, BS
2:15 – 2:30 pm	Peter Nagele, MD, MSc
2:30 – 2:45 pm	Cynthia Ortinau, MD
2:45 – 3:00 pm	Molly J. Stout, MD

3:00 – 5:00 pm Farrell Learning and Teaching Center Atrium
Poster Session

This symposium is made possible by the Clinical Research Training Center (CRTC), a component of the Washington University Institute of Clinical and Translational Sciences (ICTS). The ICTS is part of a national consortium of medical research institutions, funded through the Clinical and Translational Science Awards (CTSA) that includes sixty medical research institutions in thirty states and the District of Columbia, working together to improve the way biomedical research is conducted across the country. The CTSA consortium shares a common vision to reduce the time it takes for laboratory discoveries to become treatments for patients, and to engage communities in clinical research efforts. It is also fulfilling the critical need to train the next generation of clinical researchers. The CTSA initiative is led by the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health. The CRTC is supported by NCATS Grant Numbers UL1 TR000448, KL2 TR000450, and TL1 TR000449, Washington University in St. Louis School of Medicine, and Barnes-Jewish Hospital Foundation.

This symposium & poster session is co-sponsored by the Office of Medical Student Research, Washington University in St. Louis School of Medicine.

We gratefully acknowledge the support of Dr. Larry J. Shapiro, Executive Vice Chancellor for Medical Affairs and Dean, Washington University in St. Louis School of Medicine.

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Programs Represented

Clinical Research Training Center (CRTC) KL2 Career Development Awards
The KL2 Career Development Awards Program at Washington University in St. Louis provides high-quality, multidisciplinary training in clinical and translational research to promote the career development of future clinical investigators. The program is comprised of postdoctoral scholars and junior faculty committed to multidisciplinary clinical research. KL2 Career Development Awards provide financial support and benefits that allow scholars to focus on mentored, multidisciplinary research, supplemented by applicable coursework.
Program Director: Victoria Fraser, MD
Website: http://crtc.wustl.edu

CRTC KM1 Comparative Effectiveness Research (CER) Career Development Program
The KM1 CER Career Development Program is the first dedicated training program focused on CER at Washington University in St. Louis. The goal of this program is to train a new generation of highly skilled investigators with specialized expertise, who will be able to identify the best practices in prevention, treatment, and monitoring of clinical conditions and health delivery systems. The KM1 CER Program supports the development of postdoctoral scholars, junior faculty, and mid-career faculty from diverse disciplines through training, curricula, and mentored CER projects, resulting in an increased pool of CER investigators.
Program Director: Victoria Fraser, MD
Website: http://cer.wustl.edu/index.php/km1

CRTC Master of Science in Clinical Investigation (MSCI) Degree Program
The MSCI Degree Program at Washington University is designed as a one to three year full- or part-time degree program for young investigators committed to pursuing academic careers in clinical research. The unique program combines didactic coursework with mentored research and career development opportunities and provides students with the knowledge and tools to excel in the areas of clinical investigation most relevant to their careers.
Program Director: David K. Warren, MD, MPH
Website: http://crtc.wustl.edu

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
The CRTC Postdoctoral Program MTPCI provides multidisciplinary clinical and translational research training to promote the career development of junior faculty and postdoctoral fellows by helping them become clinical and translational researchers. Through didactic coursework, structured mentorship, and interactions with a diverse peer group of trainees, the CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI) enables Scholars to learn how to: develop effective research projects, utilize human subjects in clinical trials, collect, analyze and summarize data, apply epidemiologic principles and tools, consider relevant ethical and legal issues, write grants and manuscripts, and compete for research funding.
Program Director: Jane Garbutt, MBChB
Website: http://crtc.wustl.edu

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
The CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program provides career development for medical and allied healthcare students through didactic coursework, mentored training, work-in-progress research discussions, journal clubs, and conferences. This program supports a select group of trainees as they embark on patient-oriented research careers by teaching them how to: design and conduct clinical research, analyze data, consider relevant ethical and legal issues, write manuscripts and grants, develop and present scientific posters, and compete for research funding.
Program Director: Jay Piccirillo, MD, FACS
Website: http://crtc.wustl.edu

CRTC Doris Duke Clinical Research Fellowship
The Doris Duke Clinical Research Fellowship Program at Washington University is part of the Medical Research Program of the Doris Duke Charitable Foundation. One of the foundation's goals is to further the prevention and cure of disease by supporting and strengthening clinical research and by narrowing the gap between basic biomedical discoveries and their translation into the prevention, treatment and cure of human diseases. The program provides the opportunity for clinical research, individual guidance by a faculty mentor and advisory committee, stipend, health insurance and travel allowance.
Program Director: Jay Piccirillo, MD
Website: http://ddcrf.wustl.edu

David F. Silbert Summer Fellowship
In his memory, the David F. Silbert Summer Fellowship was set up to support short-term research internships for medical, graduate, or other students interested in his area of research. David's research focused on genetic biochemical and/or biophysical approaches to the study of specific membrane lipids in signal transduction pathways and in the assembly and function of eukaryotic cell membranes. Since his death from cancer in 1997, a number of biophysical techniques have been developed that address these issues. These techniques include, but are not limited to state-of-the-art fluorescence methods, structural determination using NMR or x-ray methods and computational approaches. All these techniques are directed towards understanding the role of macromolecular interactions in cellular function. It is now clear that membrane lipids and membrane proteins are functionally involved in all aspects of the regulation of cellular processes and that these processes must be studied at the level of macromolecular function.
Website: http://biochem.wustl.edu/resources/archives/awards-fellowships/silbert-fellowship/2012-david-f-silbert-summer-fellowship-research

Dean's Fellowship
This program is designed to provide medical students with a hands-on research experience. This can be a first-time experience or a project related or unrelated to research done as an undergraduate. Excellent mentors from a broad range of basic and clinical sciences are available. A Washington University Summer Research Fellowship can provide a strong background for application to the MA/MD and MD/PhD (MSTP) degree programs, can lead to abstracts at meetings and to publications, and can be important for applications for competitive residencies.
Program Director: Koong-Nah Chung, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

Forum for International Health and Tropical Medicine
The Forum for International Health and Tropical Medicine (FIHTM) brings together students and physicians at Washington University who are interested in international health. FIHTM aims to promote understanding of global health by enabling medical students to experience firsthand its locales, modes of delivery, disparities, and cultural manifestations. FIHTM organizes the Global Health Symposium each spring, as well as regular discussion lunch meetings with students and faculty. In addition, the group coordinates Spring Break community service trips for the first and second year medical classes. FIHTM offers financial and logistical assistance to students who wish to gain healthcare experience abroad and helps interested students find mentors within the university.
Program Director: Kathy Diemer, MD
Website: http://fihtm.wustl.edu

Mallinckrodt Institute of Radiology Summer Research Program
The Mallinckrodt Institute of Radiology Summer Research Program offers undergraduate and medical students an excellent introduction to the following aspects of radiological sciences research: Magnetic Resonance Imaging, Magnetic Resonance Spectroscopy, Positron Emission Tomography, X-ray Computed Tomography, Contrast Agent Development, Digital Imaging, Optical Imaging, Diagnostic Radiology, Molecular Pharmacology, Nuclear Medicine, Radiopharmaceutical Development, Neuroscience Imaging, Cardiovascular Imaging, Optical Imaging, and Ultrasound.
Program Director: Suzanne Lapi, PhD
Website: http://www.mir.wustl.edu/education

Movement Science Program (MSP)
The Program is an integral member of one of the world's largest academic biomedical research institutions; collaboration occurs with nearly every department in the School of Medicine, as well as with colleagues in biomedical engineering, psychology, and biology. Researchers lead studies in a comprehensive array of topics from the basic physiological mechanisms of tissue injury to studying health interventions at the community level. Investigations involve subjects across the life span. The Movement Science Program is supported by NIH training grant T32HD007434.
Program Director: Michael J. Mueller, PhD, PT, FAPTA
Website: https://physicaltherapy.wustl.edu/Education/DoctoralEducation/PhDinMovementScience

Office of the Provost, Diversity & Inclusion Grant
The Washington University, Office of the Provost, Diversity & Inclusion Grant helps train 5 Meharry Medical College students in the Washington University School of Medicine's Summer Research Program each summer. The benefits of the partnership include: 1) Exposing the Meharry medical students to cutting-edge science at WUSM, 2) Benefiting our WUSM faculty's research, 3) Enhancing the diversity culture of WUSM, and 4) Increasing our pipeline of under-represented medical students into our residency programs.
Program Director: Koong-Nah Chung, PhD
Website: http://provost.wustl.edu/diversity/diversity-inclusion-grants

Otolaryngology NIH T32 Physician Scientist Program (PSP)
This training program provides a pathway directing medically trained individuals toward a successful research career in academic otolaryngology. This research experience is offered at two levels. At the first level, medical students are selected to participate in this program for approximately three months during the summer. Mentored research projects for medical students are conducted by selected trainees to stimulate a general interest in research and specific interest in otolaryngological research. At the second level, residents selected into the 7-year "Advanced Physician Scholars Program" by a special residency match mechanism perform mentored research in depth, in a contiguous two-year period, free of clinical responsibilities. Funding for this program is provided by a National Institutes of Health (NIH)-National Institute on Deafness and Other Communication Disorders (NIDCD), Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Research Training Grant (T32) entitled "Development of Clinician/Researchers in Academic ENT", 5T32DC000022-22.
Program Director: Jay Piccirillo, MD, FACS
Website: http://ent.wustl.edu/oto/otoweb.nsf

Siteman Summer Opportunities Program
The Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine provides opportunities for undergraduate, pre-med and medical students enrolled at Washington University or other accredited universities to work on cancer research projects during the summer. Opportunities range from basic laboratory research to clinical research to prevention/control and population research.
Website: http://www.siteman.wustl.edu/ContentPage.aspx?id=254

T32 NIH NHLBI Cardiovascular Biology Training Program
The Training Program in Cardiovascular Biology supports Predoctoral Students conducting PhD thesis research and Postdoctoral Fellows in the early stages of post-graduate training. The goals of this Program are to provide outstanding research opportunities, well-rounded, multidisciplinary training in Modern Cardiovascular Biology, and mentoring to Predoctoral and Postdoctoral Trainees in the laboratories of one or more of the (22) participating faculty to prepare these individuals to be productive, independent scientists. The faculty derive from multiple (6) Departments (Biochemistry, Biomedical Engineering, Cell Biology and Physiology, Developmental Biology, Medicine and Radiology) and (4) Divisions (Cardiology, Chemistry, Endocrinology and Nutritional Science) within the Department of Internal Medicine, and include nationally and internationally recognized leaders in several areas of Modern Cardiovascular Biology including molecular biology, physiology, cell biology, biochemistry, modeling, imaging, pathology, genetics, and human cardiovascular disease mechanisms. The faculty are well-established, well-funded, experienced and highly productive investigators, and all are committed to providing the training, experience, resources, intellectual enthusiasm and mentoring needed to achieve the overall goals of the Training Program and to facilitate the professional development of the individual Program Trainees. In addition to research opportunities, trainees participate in weekly "Trainees in Cardiovascular Biology Series" and “Cardiovascular Research Seminar Series”. This Training Program is also actively involved in monitoring the progress and professional development, and in the mentoring of Predoctoral and Postdoctoral Trainees.
Program Director: Jeanne Nerbonne, PhD

T32 NIH NIDDK Diabetes Training Grant
The goal of the program is to expose medical students to career opportunities in basic or clinical research related to diabetes and related metabolic diseases.
Program Director: Clay Semenkovich, MD

T35 NIH NHLBI Training Grant
This program is designed to provide medical students with a hands-on research experience. This can be a first-time experience or a project related or unrelated to research done as an undergraduate. Excellent mentors from a broad range of basic and clinical sciences are available. A Washington University Summer Research Fellowship can provide a strong background for application to the MA/MD and MD/PhD (MSTP) degree programs, can lead to abstracts at meetings and to publications, and can be important for applications for competitive residencies.
Program Director: Koong-Nah Chung, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

T35 NIH NIDDK Short-Term Training Program
The goal of the trans-NIDDK Short-Term Training Program for Medical Students is to expose medical students to career opportunities in basic or clinical research related to diabetes, obesity, endocrine disorders, metabolic diseases, nutritional disorders, digestive diseases, liver diseases, kidney diseases, urologic diseases and hematological disorders.
Program Director: Thomas J. Baranski, MD, PhD

Abstracts for Oral Presentations

In the Order Presented

Ju, Yo-El, MD
CRTC KL2 Career Development Awards Program
Division of Sleep Medicine
Department of Neurology, Washington University in St. Louis School of Medicine
Mentors: David Holtzman, MD; Paul Shaw, MD

Sleep quality and preclinical Alzheimer Disease

Ju YS; McLeland JS; Toedebusch CD; Xiong C; Fagan AM; Duntley SP; Morris JS; Holtzman DM

Introduction: Sleep and circadian problems are very common in Alzheimer Disease (AD). Recent animal studies suggest there is a bidirectional relationship between sleep and amyloid-beta (Abeta), a key molecule involved in AD pathogenesis. This study tested the hypothesis that Abeta deposition in preclinical AD is associated with sleep-wake abnormalities.
Methods: Cognitively normal, middle-aged individuals (n=182) were recruited from a longitudinal study. Sleep was objectively measured using actigraphy for 2 weeks. Concurrent sleep diaries provided nap information. Cerebrospinal fluid Abeta42 levels were used to determine whether amyloid deposition was present or absent. Sleep and nap parameters were compared between the groups with and without amyloid deposition. We used multivariate logistic regression to assess whether sleep and nap characteristics are related to amyloid deposition.
Results: Participants with amyloid deposition had worse sleep efficiency compared to those without amyloid deposition (80.7% versus 83.3%, p=0.022), and also took naps more frequently (2.2 versus 1.4 days per week, p=0.037). Other sleep variables were not significantly different between the two groups. Logistic regression demonstrated sleep efficiency is a significant predictor of amyloid deposition (OR 0.942, p=0.026). Nap frequency is also a significant predictor of amyloid deposition (OR 1.271, p=0.007).
Conclusions: Amyloid deposition present in the preclinical stage of AD is associated with poor sleep efficiency and frequent napping. Since amyloid deposition as assessed by Abeta42 occurs well before symptoms of AD, our findings expand the temporal window during which sleep abnormalities are identifiable and potentially modifiable in AD.

Khoong, Elaine, BS
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Medical Student
Prevention Research Center in St. Louis
Brown School, Washington University in St. Louis School of Medicine
Mentor: Ross C Brownson, PhD

Rural-Urban Differences in Factors that Impact Physician Adherence to Clinical Preventive Service Guidelines

Khoong EC; Gibbert WS; Garbutt JM; Sumner W; Brownson RC

Introduction: Clinical preventive service guideline adherence and provision of preventive services remains low. Rural-urban disparities in the provision of preventive services have been shown, but there is sparse research on how rural, suburban, or urban differences impact physician adherence to preventive service guidelines. The purpose of this study was to qualitatively determine factors that may cause physician adherence to clinical preventive service guidelines to differ in rural, suburban, and urban outpatient settings.
Methods: Qualitative study involving semi-structured interviews with 29 purposively sampled primary care physicians (10 rural, 10 suburban, and 9 urban) who practiced in rural, suburban, and urban clinics in Missouri. Barriers and facilitators to clinical preventive service guideline adherence were elicited. Using techniques from grounded theory analysis, two coders independently conducted content analysis. The two reviewers met to reconcile any differences in coding and ensure agreement on intended meaning of transcripts.
Results: Patient descriptive epidemiology, distance to healthcare services, and care coordination were reported as prominent factors that resulted in differences in adherence to preventive service guidelines among rural, suburban, and urban physicians. Epidemiologic differences impacted all physicians, with rural physicians explicitly highlighting the importance of occupational risk factors in their patients. Reduced visit frequency resulting from increased distance to healthcare services was a more prominent barrier for rural physicians. Care coordination between multiple healthcare providers was noted to be most problematic for suburban and urban physicians. Patient resistance to all medical care and inadequate access to resources and specialists were identified as additional barriers for some rural physicians.
Conclusions: The rural, suburban, or urban context influences the likelihood of physician adherence to clinical preventive service guidelines. Future efforts to increase guideline adherence should consider the risks, barriers, and facilitators that are unique to rural, suburban, or urban areas.

Nagele, Peter, MD, MSc
CRTC Postdoctoral MTPCI Alumnus
Division of Clinical and Translational Research
Department of Anesthesiology, Washington University in St. Louis School of Medicine
Mentors: Evan Kharasch, MD, PhD; Brian Gage, MD, MSc
High-Sensitivity Cardiac Troponin T in Prediction and Diagnosis of Perioperative Myocardial Infarction
Nagele P; Brown F; Gage BF; Miller JP; Scott MG
Introduction: Newly introduced high-sensitivity cardiac troponin T (hs-cTnT) assays detect circulating plasma troponin T levels in stable patients in the absence of an acute coronary syndrome and have been associated with heart disease, cardiovascular as well as all-cause mortality. The role of hsTnT in the prediction and diagnosis of perioperative myocardial infarction and death after non-cardiac surgery, however, is unknown.
Methods: The VINO Trial involved 625 patients with or at risk for coronary artery disease undergoing major noncardiac during general anesthesia. Patients had serial blood draws and ECGs at baseline; end of surgery and on postoperative day 1-3. Plasma hs-cTnT (Roche) as well as regular troponin I (Siemens) were measured at all time-points and the change (delta) between baseline and peak troponin was calculated. Myocardial infarction was diagnosed according to the universal definition with a peak TnI increase above 0.07 ng/mL (99^{th} URL) plus ECG changes consistent with myocardial ischemia and/or clinical symptoms. Outcomes were analyzed and adjudicated by assessors blinded to treatment.
Results: Before surgery, 75% (455/606; 19 missing) of the patients had a detectable hs-cTnT concentration (median 7.4 ng/L [IQR 1.5, 15.2]). More than 70% (442/625) had a rise in hs-cTnT after surgery (median +3.1 ng/L [IQR 0, 7.8]). Thirty patients (5%) developed an MI within the first 3 days after surgery. Compared to patients with a preoperative hs-cTnT <7 ng/L (incidence rate for MI 3%), patients with a preoperative hs-cTnT >14 ng/L had an MI incidence rate of 9% (odds ratio [OR] = 3.60, 95% CI 1.49 – 8.68, p=0.004). As of July 1, 2012, 80 deaths occurred within the study population. Patients with a preoperative hs-cTnT concentration <7 ng/L had a 3-year mortality rate of 10% while patients with a preoperative hs-cTnT >14 ng/L had a 3-year mortality rate of 31% (adjusted hazard ratio 2.68; 95% CI 1.32 – 5.46, p=0.007).
Conclusions: In this cohort of high-risk patients, preoperative hs-cTnT levels were significantly associated with postoperative MI and long-term mortality after non-cardiac surgery.

Ortinau, Cynthia, MD
CRTC KL2 Career Development Awards Program
Division of Newborn Medicine
Department of Pediatrics, Washington University in St. Louis School of Medicine
Mentors: Terrie Inder, MD; Pirooz Eghtesady, MD, PhD; Jane Garbutt, MBChB
Preoperative brain imaging is associated with outcome in infants with congenital heart disease
Ortinau C; Beca J; Inder T
Introduction: Infants with congenital heart disease (CHD) are at an increased risk for developmental impairments, and brain injury and altered brain development are common on preoperative magnetic resonance imaging (MRI). This study aimed to characterize the relationship between preoperative brain MRI measures and neurodevelopment at 2 years of age.
Methods: A prospective longitudinal study was conducted in infants with CHD. Preoperative brain MRIs were performed and a scoring system was applied to assess brain injury and brain development. Infants were evaluated at 2 years of age with the Bayley Scales of Infant Development-II to assess cognitive, language, and motor function.
Results: Fifty-five infants were included in the study. On follow-up assessment, the mean composite scores for cognition were 96 (SD=11), language were 97 (SD=12), and motor function were 101 (SD=10). Head circumference at birth correlated with cognitive score (r=0.44, p=0.001). On preoperative MRI, brain injury predominantly due to focal white matter injury was present in 24 infants (44%). White matter injury did not relate to 2 year outcomes. In contrast, the volume of white matter preoperatively was decreased in 26 infants (47%) with an associated reduction in motor score at 2 years (Low volume 97 vs. normal volume 104, p=0.01). Delayed cortical gyrification preoperatively was present in 34 infants (62%) and was associated with lower language scores at 2 years (92 vs. 100, p=0.04). Increased extra-axial space, delayed myelination, and mild ventriculomegaly were common but not associated with outcome. Analysis was repeated controlling for gestational age at MRI and head circumference at birth and results were unchanged.
Conclusions: Abnormalities in white matter volume and the maturation of cortical folding on preoperative brain MRI are associated with lower developmental scores at 2 years of age, particularly motor and language outcomes. In addition, head circumference at birth is strongly correlated with cognitive outcome at 2 years of age. The use of MRI alongside clinical factors may provide insight into later outcome for infants with CHD.

Stout, Molly J, MD
CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Maternal Fetal Medicine
Department of Obstetrics and Gynecology, Washington University in St. Louis School of Medicine
Mentors: George A Macones, MD, MSCE; Allyson Zazulia, MD

Human Leukocyte Antigen-G Expression at the Maternal Fetal Interface is Increased in Preterm Birth

Stout MJ; Nelson DM; Mysorekar IU; Macones GA

Introduction: Human leukocyte antigen-G (HLAG) is a major histocompatibility complex protein expressed on extravillous trophoblast cells of the placenta. The function of HLAG is down-regulation of the maternal immune response as non-self fetal cells invade maternal uterine tissue. We aimed to test the hypothesis that HLAG tissue expression at the maternal-fetal interface (basal plate) of human placentas is altered in preterm birth (PTB).

Methods: A nested case control study within a prospective cohort investigating novel infection related pathways for PTB. Singleton pregnancies were enrolled during the antenatal course and followed to delivery. Medical history and pregnancy outcomes were collected prospectively. Women with PTB < 37 weeks were compared to those who delivered at term. Three random samples from the placental basal plate were paraffin embedded. Immunohistochemical expression of HLAG positive cells was quantified using digital brightfield microscopy. Basal plate tissue % surface area positive for HLAG was considered both continuous and dichotomous (high HLAG defined as ≥75th percentile) variables. Univariable, bivariable, and multivariable regression were used to test the association between HLAG expression and PTB.

Results: Of 135 pregnancies, 32.6% delivered <37 weeks. Basal plate HLAG positivity was significantly increased in PTB compared to term birth (36.6% vs. 32.6%, p<0.01). HLAG tissue positivity remained higher when the analysis was restricted to spontaneous labor only (37.1% spontaneous PTB vs. 30.7% spontaneous term, p<0.01). HLAG positivity was similar in patients with labor compared to cesarean section without labor (33.8% vs. 33.9%, p=0.9) suggesting that the differences noted are not due to the labor process alone. High HLAG ≥75th percentile was associated with an 8-fold increased risk for PTB (aOR 8.9, 95%CI 2.0-38.5, p<0.01) after controlling for steroid administration and prior PTB.

Conclusions: Increased HLAG tissue expression at the maternal fetal interface is associated with PTB. HLAG may alter immunotolerance and mediate the role of infection and inflammation in the pathogenesis of PTB.

Abstracts for Poster Session

Alphabetically by Training Program and Author

CRTC KL2 Career Development Awards Program

Poster Discussant

Beigelman, Avraham, MD
CRTC KL2 Career Development Awards Program
Division of Allergy, Immunology and Pulmonary Medicine
Department of Pediatrics, Washington University in St. Louis School of Medicine
Childhood Asthma Research and Education Network of the National Heart, Lung, and Blood Institute
Mentors: Leonard Bacharier, MD; Mario Castro, MD; Jane Garbutt, MBChB

Do oral corticosteroids reduce the severity of acute respiratory tract illnesses in preschool children with recurrent wheezing?

Beigelman A; King TS; Mauger D; Zeiger RS; Strunk RC; Kelly HW; Martinez FD; Lemanske RF; Rivera-Spoljaric K; Jackson DJ; Guilbert T; Covar R; Bacharier LB

Introduction: Oral corticosteroids (OCS) are recommended for severe wheezing episodes in children. However, limited evidence supports this intervention in preschool children with outpatient wheezing illnesses. Our goal was to investigate whether OCS reduce symptoms scores during acute respiratory tract illnesses in preschool children with recurrent wheeze.
Methods: We performed *post-hoc* and replication analyses in two outpatient cohorts of children aged 1-5 years with episodic wheezing participating in clinical trials. We compared symptom scores during respiratory tract illnesses that were and were not treated with OCS after adjusting for differences in disease and episode severity covariates. We stratified episodes by severity utilizing a propensity model. The primary outcome was the area under the curve (AUC) of total symptom scores among the more severe episodes.
Results: 215 participants from the Acute Intervention Management Strategy Trial experienced 798 acute respiratory tract illnesses, 106 of which were defined as severe by propensity score. The AUC of total symptom scores did not differ between the episodes that were (n=66) and were not (n=40) treated with OCS (p=0.35), nor was there an OCS treatment effect on individual symptom scores. Similar analyses of the Maintenance Versus Intermittent Inhaled Steroids in Wheezing Toddler Trial, involving 278 participants with 122 severe respiratory tract illnesses confirmed the above findings (p=0.74 for AUC of total symptoms score comparison).
Conclusions: In two separate cohorts of preschool children with episodic wheezing, OCS treatment during significant respiratory tract illnesses did not reduce symptoms severity of the acute episodes. These findings need to be confirmed in a prospective randomized controlled trial.

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Holtz, Lori, MD
CRTC KL2 Career Development Awards Program
Division of Gastroenterology and Nutrition
Department of Pediatrics, Washington University in St. Louis School of Medicine
Mentors: David Wang, PhD; Phillip Tarr, MD

Epidemiology of newly discovered astrovirus, MLB1

Holtz L; Bauer I; Rajendran P; Belshe R; Schultz-Cherry S; Kang G; Wang D

Introduction: Diarrhea is the third leading infectious cause of death worldwide. Astroviruses, noroviruses, adenoviruses, and rotaviruses are the major diarrheagenic viruses. However, ~40% of diarrhea is of unknown etiology. We have recently discovered seven highly divergent astroviruses, MLB1, MLB2, MLB3, VA1, VA2, VA3, and VA4 in stools of children with diarrhea. The purpose of this study is to define the frequency at which MLB1 infects humans and to determine if MLB1 is associated with human diarrhea.
Methods: To assess if MLB1 is associated with diarrhea, viral prevalence in a case-control cohort was determined. Stool samples were evaluated from a longitudinal birth cohort study in Vellore, India. 400 diarrhea (case) stools and 400 paired non-diarrheal (control) stools obtained from the same child at least six weeks prior were examined by RT-PCR for astrovirus MLB1 and the classic human astroviruses. To define the frequency at which MLB1 infects humans, I have developed an indirect ELISA to determine the seroprevalence of MLB1. I am currently assessing if there is cross reactivity between MLB1 and MLB2.
Results: RT-PCR of the case control stools showed that 14/400 cases were positive for the classic human astroviruses while 4/400 controls were positive (p=0.029). However, 4/400 cases and 14/400 controls were positive for MLB1 (p=0.033). From the ELISA, there appears to be a unidirectional cross reactivity between MLB1 and MLB2. Specifically, MLB1 antigen cross reacts with MLB2 antibodies.
Conclusions: The data gathered from these efforts are the first to describe if these viruses are potentially human pathogens and if they are associated with diarrhea. Results from this study suggest that MLB1 is not associated with diarrhea. The role of MLB1 in human health is still not established.

Poster Discussant

Liao, Steve, MD, MSCI

CRTC KL2 Career Development Awards Program
Division of Newborn Medicine
Department of Pediatrics, Washington University in St. Louis School of Medicine
Mentors: Jane Garbutt, MBChB; Terrie Inder, MD; Joseph Culver, PhD

Impact of head position on regional cerebral oxygen saturations in very preterm infants

Liao SM; Rao R; Mathur AM

Introduction: Cerebral autoregulation impairment is common in preterm infants in the first few days of life – a critical period associated with the highest incidence of intraventricular hemorrhage (IVH). Neonatal head position is changed frequently from side-side as part of routine clinical care. Current evidence suggests that cerebral hemodynamics correlate with changes in head position but there is currently no consensus on the appropriate positioning in very preterm infants during this critical period. We aimed to study the effect of head position changes on regional cerebral tissue oxygen saturation (SctO2) in very preterm infants in the first 2 days of life.

Methods: Preterm infants <30 weeks estimated gestational age (EGA) were recruited. Concurrent SctO2 from both sides of the forehead were obtained by near-infrared spectroscopy (NIRS) (Fore-Sight, CAS Med, Branford, CT). Data were recorded in 20-minute epochs for each position starting with the infant's head in the mid-line. The head was then turned towards one side, followed by return to mid-line and then to the opposite side. Ten minutes of data immediately before and after positioning changes were averaged to reflect acute changes in SctO2. Two-tailed paired t-tests were used to compare the averaged SctO2 from each NIRS probe measurement.

Results: All infants [n=14; mean of 26.5 (±1.8) weeks EGA; mean CRIB score of 3.5 (±3.2)] were studied on the 2nd day of life. Five infants were mechanically ventilated at the time of study but none required inotropic support. Seven infants had clinically significant patent ductus arteriosus (PDA) with 3 requiring ductal ligation after the first week of life. One infant developed IVH (grade III/IV). There was a statistically significant decrease in mean SctO2 on the left side of the brain when the head was turned towards the left (73.6% vs. 70.9%; p=0.011). No other change in regional SctO2 was observed.

Conclusions: There is a statistically significant reduction in SctO2 on the left side of the brain when the head is turned to the left during the first two days of life. While this decrease did not attain clinical significance in this cohort of relatively stable infants, the reduction in regional SctO2 with head turning may be magnified in unstable preterm infants combined with other clinical factors (e.g. higher ventilatory support, symptomatic PDA, and hemodynamic instability, etc.), leading to impaired ipsilateral venous drainage. We are currently recruiting preterm infants with higher acuity levels to further elucidate the observed finding.

Poster Discussant

Lindman, Brian R, MD, MSCI

CRTC KL2 Career Development Awards Program
Cardiovascular Division
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Douglas Mann, MD; Brian Gage, MD, MSc

Effects of phosphodiesterase type 5 inhibition on systemic and pulmonary hemodynamics and ventricular function in patients with severe aortic stenosis

Lindman BR; Zajarias A; Madrazo JA; Shah J; Gage BF; Novak E; Johnson SN; Chakinala MM; Hohn TA; Saghir M; Mann DL

Background: Patients with aortic stenosis (AS) often present with advanced heart failure symptoms and abnormal hemodynamics characterized by pulmonary venous congestion, pulmonary hypertension, afterload mismatch, and low cardiac output. Phosphodiesterase type 5 (PDE5) inhibition may help reverse this decompensated clinical state, thereby potentially reducing operative risk and improving symptoms. However, the use of PDE5 inhibitors in patients with AS is controversial because of concerns about vasodilation and hypotension.

Methods: During cardiac catheterization, we evaluated the safety and hemodynamic response of 20 subjects with severe symptomatic AS (mean aortic valve area 0.7±0.2 cm^2, ejection fraction 60±14%) who received a single oral dose of sildenafil (40mg or 80mg). Median change is reported.

Results: Compared to baseline, after 60 minutes sildenafil reduced systemic (-12%, p<0.001) and pulmonary (-29%, p=0.002) vascular resistance, mean pulmonary artery (-25%, p<0.001) and wedge (-17%, p<0.001) pressure, and increased systemic (+13%, p<0.001) and pulmonary (+45%, p<0.001) vascular compliance and stroke volume index (+8%, p=0.01). The increase in stroke volume was strongly associated with a decrease in systemic and pulmonary vascular afterload after sildenafil. The changes in hemodynamic measurements were not dose dependent. Sildenafil caused a modest decrease in mean systemic arterial pressure (-11%, p<0.001), but was well-tolerated without symptomatic hypotension.

Conclusions: This study shows for the first time that a single dose of a PDE5 inhibitor is safe and well-tolerated in patients with severe AS and is associated with acute improvements in pulmonary and systemic hemodynamics resulting in biventricular unloading. These findings support the need for longer-term studies to evaluate the role of PDE5 inhibition as adjunctive medical therapy in patients with AS.

081 **Maccotta, Luigi, MD, PhD**

CRTC KL2 Career Development Awards Program
Epilepsy Division
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Mentors: Maurizio Corbetta, MD; Edward Hogan, MD

Abnormal Functional Networks in Temporal Neocortex

Maccotta L; Hogan RE

Introduction: Mounting evidence continues to demonstrate abnormal functional connections in patients with temporal lobe epilepsy (TLE). Focus has been on the medial temporal region, as this is the typical seizure onset region and the most common site of pathology in the disease. Yet there is increasing evidence that the medial temporal region forms a functional network with other brain regions, suggesting that other nodes in the network may be affected and function as disease markers for TLE. Here we used resting state BOLD fMRI to characterize the functional network of the medial temporal region.

Methods: 32 patients with TLE were consecutively enrolled in a resting-state BOLD fMRI study. Each patient had video-EEG localization of seizures. Only patients with unilateral seizure onset were included. A group of age-, gender-, and handedness matched healthy subjects (n = 32) served as controls. Regions of interest (ROIs) were defined a priori based on anatomical segmentation, and functioned as seed in a functional connectivity analysis using typical methods.

Results: Neocortical temporal regions exhibited significantly altered functional connectivity in TLE compared to healthy controls. Specifically there was a significant decrease in the strength of the functional connections between homologous temporal regions in the inferior, medial and superior temporal gyri, mirroring the decoupling between medial temporal regions also seen with the disease ($p<.01$, post-hoc paired t-test, after cluster-level correction for multiple comparisons). Moreover, in the hemisphere ipsilateral to seizure onset, neocortical temporal regions showed increased connectivity with the ipsilateral insula and regions immediately medial to it, such as the basal ganglia ($p<.01$, post-hoc paired t-test, after cluster-level correction for multiple comparisons).

Conclusions: TLE is associated with functional network changes that go beyond the medial temporal region and involve the temporal neocortex. The observed increased coupling with the insula and basal ganglia exhibited by temporal neocortex ipsilateral to the seizure may be a correlate of a seizure propagation pathway or speculatively reflect an increased propensity of the network to generate and/or propagate seizures. The laterality it provides may have a clinical role in seizure localization and presurgical planning.

093 **Pepino, M Yanina, PhD**

CRTC KL2 Career Development Awards Program
Division of Geriatrics and Nutritional Science
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Mentors: Nada Abumrad, PhD; Todd Braver, PhD

Changes on taste perception after surgery-induced weight loss

Pepino MY; Klein S

Introduction: Bariatric surgery is the most effective weight loss therapy for obesity. However, the mechanisms responsible for decreased food intake are incompletely understood. One possible mechanism that could account for decreased food intake is changes in taste perception, which could affect energy intake by affecting food choices. The primary goal of this study was to advance our understanding of the effect of the two most common bariatric surgery-induced weight loss procedures: Roux-en-Y gastric bypass (RYGB) and laparoscopy adjustable gastric banding (LAGB) on taste perception.

Methods: Taste perception was evaluated in 27 women (RYGB; n=17 and LAGB; n=10). Subjects were studied before and after surgery, when they had lost 20% of their body weight. Taste perception, including taste sensitivity, preferences and hedonic value of sweetness was assessed by validated sensory evaluation techniques.

Results and Conclusions: Taste sensitivity was generally unchanged but lower concentrations of sucrose were preferred after both types of surgery. In addition, RYGB, but not LAGB, decreased hedonic responses to sweet taste, suggesting that gastric bypass have effects in centrally mediated reward mechanism to sweetness that are independent of weight loss.

120 **Pusic, Iskra, MD**

CRTC KL2 Career Development Awards Program
Division of Oncology
Department of Medicine, Washington University in St. Louis School of Medicine
Mentors: John DiPersio, MD, PhD; Mario Castro MD, MPH

Maintenance Therapy with Decitabine (DAC) after Allogeneic Hematopoietic Stem Cell Transplantation (alloHSCT) for Acute Myelogenous Leukemia (AML) and High-Risk Myelodysplastic Syndrome (MDS)

Pusic I; DiPersio JF

Introduction: Disease relapse is the major cause of treatment failure after alloHSCT for AML/MDS. DAC is a DNA methyltransferase inhibitor that induces DNA hypomethylation. DAC maintenance after alloHSCT may provide direct antileukemic effect, to eradicate minimal residual disease and facilitate a graft-versus-leukemia effect. Lower doses are likely to be better tolerated after alloHSCT and equally effective in inducing hypomethylation.

Methods: Patients (pts) with AML/MDS in complete remission (CR) after alloHSCT, without grade III-IV acute graft-versus-host disease (GVHD), ANC> 1,500/ mm3 and platelets> 50,000/mm3 are eligible to receive IV DAC starting between days 50-100 after alloHSCT. We are investigating 4 DAC doses: 5, 7.5, 10 and 15 mg/m2 daily x5 days of a 6 week-cycle, with a total of 8 cycles planned. Bayesian adaptive method is used to determine the maximum tolerated dose (MTD) and schedule of DAC.

Results: 16 pts were enrolled to date; median age is 69 y (22-66); 12 pts had AML and 4 MDS. 3 dose-cohorts have been completed and 4^{th} cohort is enrolling. At the time of alloHSCT 14 pts were in CR and 2 had induction failure. All conditioning regimens were myeloablative. DAC associated toxicities were grade I/II hematological toxicities, mild nausea and fatigue. 2 pts had mild acute GVHD prior to DAC and both resolved after starting DAC; 1 pt developed grade IV gut GVHD co-incidental to initiation of therapy and completely resolved while on DAC. 2 pts to date had mild chronic GVHD. 4 pts completed all 8 cycles of planed therapy, 8 pts went off study before cycle 8, and 5 pts are still in the study passed cycle 5. 3 pts have relapsed prior cycle 5. 5 pts have died, 3 from relapse and 2 from sepsis (those were off DAC at the time of infection). No MTD has been reached.

Conclusions: DAC at the dose of 10mg/m2 is safe and can be administered in heavily pretreated pts in post alloHSCT setting. The lack of toxicities and low incidence of GVHD indicate that longer period of administration and higher doses should be investigated. Correlative studies are ongoing.

108 **Riddle, David J, MD**

CRTC KL2 Career Development Awards Program
Division of Infectious Diseases
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Michael Caparon, PhD; David Hunstad, MD

Variation in S*treptococcus pyogenes* virulence genes is associated with invasive infections and tissue tropism

Riddle DJ; Hunstad DA; Caparon MG

Introduction: We hypothesize that polymorphisms in *Streptococcus pyogenes* virulence genes contribute to invasive infections or to the organism's tissue tropism. We will identify the genetic differences between strains that cause invasive and noninvasive infections and reveal patient characteristics that increase the risk of invasive streptococcal disease.

Methods: Invasive and noninvasive *S. pyogenes* strains isolated from patients at Saint Louis Children's Hospital will be matched by *emm* pattern (marker for tissue tropism), *emm* type, and housekeeping gene similarities. Polymorphisms associated with invasive diseases or tissue tropism will be uncovered. Patient characteristics associated with invasive streptococcal infections will be identified with a case control study design. Susceptibility to infections with specific virulence factor polymorphisms will also be studied.

Results: Analysis of *spn* revealed that it is diverging into NAD+ glycohydrolase (NADase)-active and -inactive subtypes. NADase activity did not correlate with invasive diseases but was associated with tissue tropism. These data, in addition to the finding that *spn* retains the characteristics of a functional gene even after the loss of NADase activity in the product, suggest that SPN has other roles in pathogenesis. Through the application of similar analyses with other virulence genes, we anticipate uncovering novel functionally significant polymorphisms that are clinically relevant.

Conclusions: This study will identify virulence factor polymorphisms and patient characteristics that are associated with invasive streptococcal disease and form a basis for the development of targeted antivirulence therapies or infection prevention techniques.

090 **Riek, Amy E, MD**

CRTC KL2 Career Development Awards Program
Division of Endocrinology, Metabolism, and Lipid Research
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Carlos Bernal-Mizrachi, MD; Victor Davila-Roman, MD

Effects of Vitamin D Supplementation on Depression in African Americans with Type 2 Diabetes

Riek AE; Hendrix R; Bruchas R; Carney RM; Bernal-Mizrachi C

Introduction: Major depressive disorder affects 340 million people globally. Depression is strongly associated with type 2 diabetes mellitus (T2DM); the RR for depression in those with T2DM is 1.15, while the RR for T2DM in those with depression is 1.60. Vitamin D deficiency is 30% more prevalent in diabetics. Low vitamin D levels nearly triple depression risk, and several interventional studies indicate vitamin D as a potential depression therapy. African Americans (AA) suffer from a disproportionately high prevalence of both T2DM and vitamin D deficiency. Analysis of 69 studies of depression and diabetes associations revealed only 11 including AA. No studies report the effects of vitamin D on depression in AA with T2DM. Therefore, we hypothesize that vitamin D supplementation in vitamin D-deficient AA with T2DM will reduce depressive symptoms.

Methods: We will investigate this using the framework of our clinical trial of vitamin D-deficient, type 2 diabetic AA, randomized to receive 600 IU/day or 4,000 IU/day of vitamin D_3 for one year. Our goal was to implement a survey tool to effectively assess depressive symptoms. Our requirements for this tool included previous validation through clinical studies, ability to diagnose depression based upon DSM-IV criteria, minimal patient burden, capability to detect changes over time, and ability to evaluate all aspects of depression (cognitive, somatic, etc.).

Results: Based upon the stated criteria, we selected the PHQ-9 (Patient Health Questionnaire) and PROMIS (Patient Reported Outcomes Measurement Information System) instruments. The PHQ-9 is frequently used in current literature, allowing for comparison to previous research. The PROMIS is relatively new, but standardized, and will facilitate evaluation of multiple aspects of depressive symptoms.

Conclusions: This assessment will enable us to evaluate the effects of treatment of vitamin D deficiency on a variety of depressive symptoms in diabetic AA, which could identify vitamin D as a simple adjunctive treatment for depression in this high-risk population.

014 **Rogers, Cynthia E, MD**

CRTC KL2 Career Development Awards Program
Division of Child and Adolescent Psychiatry
Department of Psychiatry, Washington University in St. Louis School of Medicine
Mentors: Terrie Inder, MD; Joan Luby, MD; Jane Garbutt, MBChB

Social and Emotional Development in Very Preterm Children at Age 2

Rogers C; Wallendorf M; Pineda B; Inder T

Introduction: Preterm birth is a significant public health problem associated with altered neonatal brain development and social and emotional disorders, particularly autism and ADHD. The aim of this study is to evaluate social and emotional development in a racially diverse cohort of very preterm infants at age 2 years. The relationship of cerebral injury and development at term equivalent to these outcomes will be explored.

Methods: Sixty-eight infants (<30 weeks gestation) recruited from the Neonatal Intensive Care Unit at St. Louis Children's Hospital had an MRI at term-equivalent age. At age 2 years, mothers completed the Infant Toddler Social and Emotional Assessment (ITSEA) and the Modified Checklist for Autism in Toddlers (M-CHAT) and reported on symptoms of maternal depression, anxiety and parenting stress.

Results: Difficulties in social and emotional scales were common with infants frequently failing (ITSEA domains lowest 10^{th}%) in Competence – 33%, Externalizing – 29%, Dysregulation 19%, and Internalizing 10%. Twenty-six percent of infants failed autism screening (M-CHAT). Preliminary analyses indicate that maternal depressive symptoms were associated with increased child Externalizing symptoms ($p<.05$), and total parenting stress was associated with increased child Externalizing ($p<.001$), Internalizing ($p<.05$), Dysregulation ($p<.001$) symptoms and lower child Competence ($p<.01$). Maternal psychosocial functioning was not associated with child autism screening.

Conclusions: Among very preterm infants maternal depression and mother-child dyadic interactions are key factors associated with a child's social and emotional development. The direction of these associations remains unclear, but regardless neonatal follow-up programs and pediatricians should routinely assess caregiver psychosocial functioning to aid interventions for these infants at risk of poor social-emotional outcomes. Future analyses will evaluate the impact of altered brain development on the child psychiatric symptoms and interactions between altered brain development and psychosocial risk in this cohort.

051 **Seifert, Michael, MD**

CRTC KL2 Career Development Awards Program
Division of Pediatric Nephrology
Department of Pediatrics, Southern Illinois University and Washington University in St. Louis School of Medicine
Mentors: Daniel Brennan, MD; Dwight Towler, MD, PhD; Keith Hruska, MD

VEGF-C, VEGF-A and Related Angiogenesis Factors as Biomarkers of Chronic Allograft Injury

Seifert ME; Daly KP; Givertz MM; Nohria A; Chandraker A; Karumanchi SA; Briscoe DM

Introduction: Chronic Allograft Injury (CAI) is the major cause of late allograft loss after solid organ transplantation. CAI develops insidiously following transplantation and is well established to be dependent on the donor directed alloimmune response. Since graft vascular endothelial cells (EC) are characteristic primary targets of alloimmunity, we hypothesize that factors associated with endothelial targeting will serve as biomarkers of CAI.

Methods: We performed a cross sectional cohort study of 17 adult heart transplant recipients with angiographically documented CAI and 16 age and sex matched controls, all of whom were more than 2 years post heart transplant. The patients were 75% male with a mean age of 61.5 ± 11.3 years. On average they were 11.8 ± 4.6 years post heart transplantation. We measured serum levels of 55 proteins involved in angiogenesis using a protein profiler array. Median levels of each protein were compared between groups using the Mann-Whitney U-test. Classification and regression tree analysis was used to determine the optimal components of a biomarker panel for CAI.

Results: We found that VEGF-C, VEGF-A, Angiopoietin-2, Artemin, Urokinase-type Plasminogen Activator, and Vasohibin showed the strongest univariable associations with CAV (all $P<0.01$). Receiver-operator characteristic curves identified VEGF-C, VEGF-A, and Platelet Factor-4 as powerful biomarkers of CAI in multivariable analysis.

Conclusions: Our data indicate that serum levels of VEGF-C and VEGF-A have high specificity as biomarkers of CAI, and together with related angiogenesis factors may serve a reliable non-invasive diagnostic test for CAI. Monitoring serum proteins associated with EC injury and repair responses also have potential to predict CAI development.

Poster Discussant **Stamatakis, Katherine A, PhD, MPH**

CRTC KL2 Career Development Awards Program
Division of Public Health Sciences
Department of Surgery, Washington University in St. Louis School of Medicine
Mentors: Ross C Brownson, PhD; Graham A Colditz, MD, DrPH

The influence of community health improvement planning on prioritizing obesity prevention in US local health departments

Stamatakis KA; Marx C; Brownson RC

Introduction: Obesity prevention may not be a priority programmatic area in local health departments (LHD) in many localities with high obesity prevalence. We examined whether developing integrated community health improvement plans (CHIP) moderated the likelihood that LHDs had obesity prevention programming in the highest prevalence localities.

Methods: We conducted a descriptive, cross-sectional study by merging organizational data on LHDs from the 2005 National Profile of LHDs Study with county-level estimates of obesity prevalence from the Behavioral Risk Factor Surveillance System (n=2,300). Multi-level logistic regression models were used to examine the moderating effect of CHIP on the relationship between obesity program implementation and local obesity prevalence; the impact on estimates of adjustment for other organizational characteristics and state-level clustering was also assessed.

Results: LHDs who developed CHIPs that were integrated with state health improvement plans were more likely to have obesity prevention programs in the highest prevalence counties (odds ratio [OR]=2.0, 95% confidence interval [CI] 1.0-4.1); there was no association among LHDs with no CHIP ($p<.0001$ for interaction). The relationship persisted after adjusting for organizational characteristics (e.g., size of service population).

Conclusions: This study suggests that development of CHIPs may be a useful strategy for LHDs to improve prioritization of local obesity prevention efforts, particularly when integrated with state plans. The findings were strongest in LHDs that were self-governed (ie, not under state health department governance), suggesting the importance of formal and informal links with other public health entities. Further work should aim to improve assessment of specific activities and processes through which CHIP and other strategies employed by LHDs may bolster local obesity prevention efforts.

No poster displayed

Wang-Gillam, Andrea, MD, PhD
CRTC KL2 Career Development Awards Program
Division of Oncology
Department of Medicine, Washington University in St. Louis School of Medicine
Mentors: Lee Ratner, MD, PhD; Jason Weber, PhD; Jane Garbutt MBChB

A pilot study of pancreatic cancer tumor phosphorylation signatures

Wang-Gilliam A

Introduction: The development of targeted therapy in pancreatic cancer has been hindered by minimal biomaterial available for molecular analysis from diagnostic endoscopic ultrasound-guided fine-needle aspirations (EUS/FNA). Revealing the phosphorylation status of key pathway mediators would allow optimal selection of patients for kinase inhibitor clinical trials. We launched a pilot study to evaluate the feasibility of detecting phosphorylation signatures from FNA samples using an ultrasensitive multiplexed protein microarray platform (CEER, Prometheus).

Methods: Patients who underwent routine diagnostic EUS/FNA for a suspicious lesion in the pancreas underwent two additional EUS passes. Tumor burden was evaluated by CK. Activation of key signaling pathways was evaluated by assessing the phosphorylated form of pathway mediators including HER1/EGFR, HER2, HER3, IGF-IR, AKT, MEK, ERK, et al by CEER. The expression level of individual biomarkers was compared among different cytology groups, and the prognostic value of individual biomarkers was determined.

Results: Between January 2011 and June 2012, 99 patients with a median age of 67.5 years were enrolled in this study. Fifty-seven subjects (58.2%) had lesions in the head of the pancreas, and the median mass size was 29 mm. Seventy-three patients had carcinoma cytology, 8 had indeterminate cytology, 13 had negative cytology and 5 had neuroendocrine tumors. Significant levels of CK were seen in the positive cytology group compared to the negative cytology group ($p=0.01$). A wide range of phosphorylation signatures detected in this analysis suggests the feasibility of this approach in clinical setting. The average correlation of individual biomarkers between 2 passes was 0.56 (0.62-0.26) based on the Spearman Correlation. The prognostic significance of individual biomarkers is forthcoming.

Conclusions: Profiling the phosphorylation status of pancreatic cancer pathways from FNA samples is feasible. If further validated, phosphorylation signatures could be used to select targeted therapies and provide prognostic information.

CRTC KM1 Comparative Effectiveness Research Career Development Awards

071 **Chang, Su-Hsin, PhD**

CRTC KM1 Comparative Effectiveness Research Career Development Awards
Division of Public Health Sciences
Department of Surgery, Washington University in St. Louis School of Medicine
Mentors: Graham Colditz, MD DrPH; Christopher Eagon, MD

Bariatric surgery: an updated systematic review and meta-analysis, 2003-2012

Chang SH; Stoll CRT; Song J; Varela JE; Eagon CJ; Colditz GA

Introduction: The analyses of the impact of bariatric surgery have not been updated and comprehensively analyzed since 2003. The goal of this study is to generalize the risks and effectiveness of bariatric surgery using updated data and sophisticated meta-analysis techniques to compare different types of surgery.

Methods: Surgeries considered were Roux-en-Y gastric bypass (RYGB), adjustable gastric banding (AGB), and sleeve gastrectomy (SG). Literature searches of Medline, Embase, Scopus, Current Contents, Cochrane Library, and the Clinicaltrials.gov databases between 2003 and 2012 were performed. Articles were screened for exclusion and inclusion criteria before data extraction. Change in body mass index (BMI) was synthesized by random-effects (RE) and mixed treatment comparison meta-analyses. For mortality, complication, reoperation rates, and percentage of remission of obesity-related diseases, we used meta-analyses of Bayesian RE and simple averaging to deal with rare binary event data. Randomized controlled trials (RCTs) and observational studies were analyzed separately.

Results: We only report the mean estimates and the 95% confidence intervals (in brackets) for RCTs. Peri- (<30 days) and post-operative (≥30 days) mortality rates were 8 [1-23] and 16 [2-47] deaths out of 10,000 patients, respectively. Complication rates were 16 [10-23]%. Reoperation rates were 8 [4-13]%. RYGB had the lowest peri-operative mortality and reoperation rates. AGB had the lowest post-operative mortality and complication rates. The first 3-year BMI loss were 14 [13-16], 13 [10-17], and 9 [1-17] kg/m^2. RYGB was the most effective in terms of weight loss, followed by SG and AGB. Comorbidities remission rates were high: type 2 diabetes–92 [85-97]%; hypertension–74 [69-85]%; and dyslipidemia–76 [56-92]%.

Conclusions: This study provides evidence suggesting bariatric surgery has a low risk of mortality and is effective with regards to weight loss and improvement of comorbidities. Compared with RYGB, AGB has lower weight loss efficacy and less effective comorbidity remission outcomes, but also leads to a lower rate of complications.

CRTC Master of Science in Clinical Investigation (MSCI) Degree Program

045 **Anyaegbu, Elizabeth, MD**

CRTC Master of Science in Clinical Investigation (MSCI) Degree Program
Division of Pediatric Nephrology
Department of Pediatrics, Washington University in St Louis School of Medicine
Mentors: Michael Seifert, MD; Stanley Paul Hmiel, MD, PhD

Ambulatory blood pressure monitoring to identify cardiovascular risk factors in pediatric transplantation

Anyaegbu E; Hmiel SP; Seifert ME

Introduction: Hypertension is common following renal transplantation, and is an important risk factor for cardiovascular disease and chronic allograft injury. Chronic allograft injury is characterized by microvascular injury/fibrosis, which leads to vascular stiffness and worsening hypertension. Ambulatory blood pressure (BP) monitoring is superior to casual BP monitoring in diagnosing hypertension, but the value of other ambulatory BP metrics such as BP load and nocturnal dipping in detecting early vascular injury/stiffness is unclear. We hypothesized that elevated BP load and abnormal nocturnal dipping reflect a state of chronic microvascular injury/stiffness, and may therefore serve as biomarkers of chronic allograft injury.

Methods: We analyzed ambulatory BP data from 30 pediatric renal transplant recipients. Mean 24-hour BP, systolic/diastolic BP load, and nocturnal dipping were calculated for each subject. Allograft function (iGFR) was estimated at 1 year post-transplant in 27 subjects using iothalamate clearance.

Results: 17/30 (57%) were being treated for hypertension at the time of the study. 9/30 (30%) still had ambulatory hypertension, with elevated mean systolic BP. 16/30 (53%) had systolic BP load > 25%. 23/29 (79%) had an abnormal nocturnal dipping pattern. 10/27 (74%) had an iGFR < 75 mL/min/1.73m2 at 1 year post-transplant.

Conclusions: Ambulatory BP monitoring identified abnormal nocturnal dipping, and therefore increased cardiovascular risk, in the majority of our pediatric renal transplant recipients, including many receiving anti-hypertensive therapy. Abnormal nocturnal dipping patterns were associated with allograft dysfunction at 1 year post-transplant, and may serve as a biomarker for early chronic allograft injury. These trends should be further explored in a larger prospective study.

009 **Garg, Gunjal, MD**

CRTC Master of Science in Clinical Investigation (MSCI) Degree Program
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology, Washington University in St. Louis School of Medicine
Mentors: Matthew A Powell, MD; David G Mutch, MD

Positive Peritoneal Cytology is an Independent Risk-Factor Among Women Diagnosed with Endometrial Cancer Confined to the Uterus

Garg G; Gao F; Hagemann AR; Mutch DG; Powell MA

Introduction: In light of the recent changes in the International Federation of Gynecology and Obstetrics (FIGO) staging criteria, the objective of this study was to determine the prognostic significance of positive peritoneal cytology (PPC) among patients with endometrial cancer apparently confined to the uterus.

Methods: Data were extracted from the Surveillance, Epidemiology, and End Results database between 1988 and 2005. Only those patients with endometrial cancer grossly confined to the uterus who had undergone a complete staging procedure (lymph-node removal) were included. Statistical analyses used Kaplan-Meier log rank, logistic regression, and Cox proportional hazards models.

Results: A total of 22,947 patients were identified. PPC was present in 3.5% of patients. The majority of patients had endometrioid adenocarcinoma (60.0%), while other histologies included adenocarcinoma not otherwise specified (NOS)(29.3%), clear cell/serous carcinoma (6.4%), and carcinosarcoma (4.4%). Survival was computed for those patients with negative lymph nodes. When compared to patients with negative peritoneal cytology, survival was significantly poorer among patients with positive peritoneal cytology ($p<0.0001$): 5-year overall survival 90.4%vs. 75.1% in endometrioid adenocarcinoma; 88.3%vs.64.6% in adenocarcinoma NOS; 71.9% vs. 46.6% in clear cell/serous cancer; and 57.2%vs. 23.6% in carcinosarcoma. We also examined the incidence of lymph node metastasis, which was significantly higher among patients with PPC compared to those with negative peritoneal cytology for all histologic types examined ($p<0.0001$): endometrioid adenocarcinoma: 28.7% vs. 14.4% adenocarcinoma NOS: 35.4% vs. 20%, clear cell/serous carcinoma: 41.4% vs. 25%, and carcinosarcoma: 38.4% vs. 28%. After adjusting for other contributing factors in the multivariable model, PPC remained an independent predictor of lymph node metastasis and poor survival ($p<0.0001$).

Conclusions: PPC confers an increased risk of lymph node metastasis and poorer survival among those patients with endometrial cancer confined to the uterus. This indicates that PPC alone is an independent risk factor and despite changes in the FIGO staging criteria, should still be considered in the assessment of patients with endometrial cancers.

107 **Iskandar, Heba N, MD**

CRTC Master of Science in Clinical Investigation (MSCI) Degree Program
Division of Gastroenterology
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Gregory Sayuk, MD, MPH; Matthew Ciorba, MD

Tricyclic antidepressants in the management of IBD patients with functional GI symptoms

Iskandar HN; Cassell B; Ciorba MA; Sayuk GS

Introduction: Irritable bowel syndrome (IBS) is common, including in inflammatory bowel disease (IBD) patients. Antidepressants (ADs), including tricyclic antidepressants (TCAs) are a mainstay of IBS therapy. In IBD in remission or with mild disease activity, functional symptoms may dominate the clinical presentation. Our aim is to assess whether TCA therapy provides benefit by reducing these IBS-type symptoms.

Methods: A retrospective study of TCA treatment was done in two cohorts: 1) IBD patients in clinical remission or with mild inflammation and GI symptoms, and 2) symptomatic IBS patients. Inclusion required a follow-up visit after TCA therapy. Baseline symptoms were assessed on a 4-point scale (0=no symptoms, 3=severe symptoms). AD responses were graded using a 4-point scale (0=no improvement; 3=complete satisfaction).

Results: 81 IBD patients (41.3±1.7yrs, 56F/25M; 58 CD/23 UC) without overt evidence of disease activity were started on a TCA. A comparator group of 65 IBS patients (43.9±1.6 yrs, 51F/14M) was identified. Abdominal pain and diarrhea were equal in both cohorts. Baseline symptom scores were moderate-severe in both IBD and IBS (2.06±0.03 vs. 2.07±0.05, p=0.73), and both groups experienced slight-moderate improvements with AD therapy (1.37±0.09 and 1.45±0.12, p=0.56). A similar number of IBD and IBS patients achieved at least moderate improvement (Likert ≥2) on AD treatment [40/81 (49.4%) vs.34/65(52.3%); p=0.73]. Among the IBD patients, UC patients had a better response than CD patients (1.78±0.14vs1.17±0.11, p=0.002). A subset of each group (47/81, 58% IBD and 54/65, 83% IBS) were followed for a second visit; with further symptom improvement (1.38 ±0.13 and 1.57±0.15, respectively, p=0.35).

Conclusions: AD therapies are effective in managing moderately-severe functional symptoms among IBD populations without overt disease activity, similar to their IBS counterparts. UC patients respond better than CD patients in our retrospective cohort. While prospective validation is needed, this study suggests that ADs are an option in the management of functional symptoms in IBD patients.

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)

133 **Alvarez, Enrique, MD, PhD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Neuroimmunology
Department of Neurology, Washington University in St. Louis School of Medicine
Mentors: Anne H Cross, MD; David K Warren, MD, MPH

Myelin basic protein and neurofilament as biomarkers of treatment response in a phase II add-on trial of rituximab for relapsing multiple sclerosis

Alvarez E; Piccio L; Tutlam NT; Mikesell RJ; Parks BJ; Naismith RT; Cross AH

Introduction: Myelin basic protein (MBP) and neurofilament (NF) levels are markers of tissue destruction to myelin sheaths and axons, respectively. We evaluated these biomarkers in predicting outcomes in multiple sclerosis (MS) subjects treated with rituximab, a B cell depleting monoclonal antibody, in combination with platform agents.

Methods: Clinical and imaging data were evaluated from a phase II trial of rituximab as an add-on agent. Patients were categorized into ideal responders (n=10), intermediate responders (n=11), and non-responders (n=9) based on clinical measures and contrast enhancing lesions (CEL) after treatment. Ideal responders had no CEL and stable or improved clinical exams after treatment. Levels of MBP and phosphorylated heavy chain NF were determined at weeks 0 and 24 using ELISA (Beckman Coulter and BioVendor, respectively). Statistical analyses were conducted using nonparametric Kruskal-Wallis rank tests and Spearman correlation coefficient (r_s) by rank.

Results: CSF MBP levels correlated strongly with the number of CEL [Spearman r (r_s)=0.609, p=0.002] and volume of CEL (r_s=0.520, p=0.009), but did not correlate with clinical markers (p=0.784 with EDSS). CSF NF correlated with EDSS (r_s=0.479, p=0.018), but not with MRI (p=0.187 with number of CEL; p=0.436 for volume of CEL). CSF levels of MBP trended towards correlating with NF (r_s=0.405, p=0.050). Serum levels of MBP and NF were mostly below detection limits. At week 24 after treatment, subjects had lower levels of CSF MBP (p=0.046) and NF (p=0.067; not significant). These differences were driven by subjects who had been pre-identified to be ideal responders to treatment with rituximab; changes were not significant in the intermediate responders or non-responders. Baseline CSF levels of MBP (p=0.191) and NF (p=0.629) at week 0 did not predict treatment response to rituximab. Subjects that responded best to treatment had more CEL (p=0.037) and lower EDSS scores (p=0.036).

Conclusions: A significant drop at 24 weeks in the CSF levels of MBP and NF was associated with good response to treatment with rituximab and may warrant future study. CSF MBP correlated with inflammatory CEL, while NF correlated with clinical measures, as has been reported previously. In this add-on study, treatment with rituximab was most beneficial in patients who were less disabled and with greater numbers of inflammatory lesions.

050 **Barone, Amy, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Hematology/Oncology
Department of Pediatrics, Washington University in St Louis School of Medicine.
Mentrors: Joshua Rubin, MD, PhD; David Wilson, MD, PhD; Jeffrey Peipert, MD, PhD

Evaluation of a CXCR4 antagonist for the treatment of glioblastoma multiforme *in vivo*

Barone A; Piwnica-Worms D; Rubin JB

Introduction: Despite advances in surgery, radiation and chemotherapy children diagnosed with glioblastoma (GBM) still have just over 10% chance for 10-year survival. The vasculature within GBMs is very abnormal; this perivascular space is thought to have properties that maintain and promote the spread of GBM. Disruption of perivascular space formation and function could be an important therapeutic target. Previously, we showed that CXCL12, acting on CXCR4, is required for recruitment of GBM cells to the perivascular space and will mediate a direct trophic effect of endothelial cells on GBM cells leading to tumor growth. Anti-angiogenic therapy, such as vascular endothelial growth factor (VEGF) inhibitors, disrupts the formation of the perivascular space, however, nearly all patients treated with a VEGF inhibitor will eventually relapse. In this study, we hypothesized that using a CXCR4 antagonist to disrupt the perivascular niche function in combination with a VEGF inhibitor to disrupt perivascular formation would result in a decrease in tumor growth. We investigated a new CXCR4 antagonist (POL5551) in a xenograft GBM model alone and in combination with a VEGF inhibitor (mcr84).

Methods: To determine the effect on tumor growth, POL5551 was tested in intracranial U87 mouse xenografts (n=5 per group) with and without mcr84. Tumor size was imaged weekly with bioluminescence imaging (BLI). Survival data was analyzed using Kaplan-Meyer log-rank analysis.

Results: Those treated with POL5551, in comparison to placebo, had a longer median (13 days vs 22 days after starting treatment) trending towards statistical significance (p=0.08). Those treated with both POL5551 and mcr85 were the first group to die with a median survival of only 13 days.

Conclusions: POL5551 may have an effect on survival in patients with glioblastoma multiforme by inhibiting CXCR4, potentially by disrupting perivascular niche function. It is interesting that the combination of POL5551 with mcr84 may have a toxic effect on the mice. Further investigation with larger treatment groups will be necessary to validate these findings.

054 **Chinta, Sri, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Emergency Medicine
Department of Pediatrics, Washington University in St Louis School of Medicine
Mentors: Robert Kennedy, MD; John McAllister, MD; Charles Schrock, MD

Minimum Effective Dose of Rapidly Administered Ketamine for Brief Pediatric Procedural Sedation

Chinta SS; McAllister J; Schrock C; Jaffe D; Kennedy R

Introduction: Ketamine is routinely used for procedural sedation in children for brief painful procedures. The standard method of ketamine administration (1.5-2 mg/kg infused intravenously over 30-60 seconds) results in prolonged recovery time (60-120min). We hypothesized that rapid bolus (over <5 seconds) of a small dose of ketamine achieves brief periods of deep sedation (3-5 min) and results in rapid recovery without increased adverse effects. The purpose of the study was to find the minimum dose and recovery time of rapidly infused ketamine that achieves effective sedation in 95% of children (ED_{95}) undergoing abscess incision and drainage (I&D).

Methods: 10 healthy 2-5 years old children (ASA 1-2) requiring deep sedation for abscess I&D at St Louis Children's Hospital Emergency Department were recruited. Using the Up-Down method, we determined the *median effective dose or* ED_{50} (dose effective in 50% participants). ED_{95} was calculated from ED_{50}.

A predetermined ketamine dose was given as a bolus. Sedation efficacy was based on participant's response to stimulation after the first dose administered. More ketamine was given as needed. Aldrete recovery scores and participant response to standard verbal command determined time of recovery. The participant and physiologic parameters were video-recorded throughout the sedation and recovery. Three faculty reviewers blinded to the dose independently review the first 5 minutes of video recording after ketamine infusion to determine sedation efficacy and the dose of next participant.

Results: ED_{50} is 0.986 mg/kg and ED_{95} is 1.148 mg/kg for 2-5 year old children for abscess I&D. No participant experienced a serious adverse event; one experienced vomiting after discharge. Mean recovery time to Aldrete score 10 (full recovery) was 22.5 minutes. Parent satisfaction with the procedural sedation was high (9 out of 9).

Conclusions: The ED_{95} for rapidly infused ketamine in 2-5 year old children undergoing abscess I&D is 1.148 mg/kg. This technique results in rapid recovery with no apparent increase in adverse events.

114 **Dickinson, John, MD, PhD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Pulmonary & Critical Care Medicine
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Steve Brody, MD; Thad Stappenbeck, MD, PhD

Role of autophagy in airway epithelial cell differentiation and function

Dickinson JD; Malvin N; Stappenbeck T; Brody S

Introduction: Autophagy is a highly conserved cellular function that regulates macromolecule recycling, immune responses, apoptosis, and protein trafficking. In prior studies, we found that autophagy is associated with epithelial cell differentiation and function in the serous and mucous cells of intestinal epithelia. We hypothesized that there are parallel functions of autophagy in the regulation of airway epithelial differentiation function that are important in normal and diseased airways.

Methods: We examined autophagy activity in a primary culture system for human tracheobronchial epithelial cell (hTEC) differentiation and used the air-liquid interface condition to generate ciliated and secretory airway epithelial cells. Treatment of cells with the cytokine, IL-13 was used as an in vitro asthma model. Autophagy proteins were examined by western blot and immunostaining. Cilia function was monitored whole field analysis of cultured airway cells using microscopy.

Results: We found that autophagy ATG5, a member of the autophagy membrane complex was expressed at a constant level throughout the course of differentiation as determined using protein blot analysis. In contrast, expression of p62, a marker of autophagy that is consumed during autophagy activity, decreased during airway epithelial differentiation. hTEC were continuously treated with recombinant IL-13 which decreased ciliated cells and increased mucous secretory cells in a model of the asthma environment. This high IL-13 condition also resulted in a lack of decline of p62 expression at ALI day 21. Furthermore, the autophagy protein, Lc3, was found to be located in ciliated cells by immunostaining. This staining was accentuated by IL-13 and chloroquine, a known drug inhibitor of autophagy. Finally chloroquine treatment in vitro induced decrease cilia beat frequency ($p<0.0001$) in cultured human airway epithelial.

Conclusions: These findings suggest that autophagy was related to ciliated cell differentiation and function. Furthermore, autophagy in airway epithelial cells was blocked with treated with of IL-13 an important cytokine in the pathogenesis of asthma.

031 **Fuller, Brian M, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Emergency Medicine, Division of Critical Care
Department of Anesthesiology, Washington University in St. Louis School of Medicine
Mentors: Richard S Hotchkiss, MD; Marin Kollef, MD

Does lower tidal volume ventilation prevent acute lung injury in mechanically ventilated patients? A systematic review

Fuller B; Mohr N; Drewry A; Carpenter C

Introduction: The most appropriate tidal volume in mechanically ventilated patients without acute lung injury (ALI) is controversial. The objective was to determine whether mechanical ventilation with lower tidal volume is associated with decreased incidence of progression to ALI when compared to higher tidal volume.

Methods: A systematic search of MEDLINE, EMBASE, CINAHL, the Cochrane Library, conference proceedings, and clinical trial registration using a comprehensive strategy. Main inclusion criteria included tidal volume studied or analyzed independently as a predictor variable, and development of ALI as a primary or secondary outcome measure.

Results: 1,704 potentially relevant publications were reviewed. 13 studies were included in the final analysis. There was significant heterogeneity with respect to patient population studied and diagnoses leading to respiratory failure, which prevented a meta-analysis from being conducted. In the only randomized controlled trial (RCT), a tidal volume of 6mL/kg ideal body weight (IBW) was associated with a lower risk for developing ALI compared to 10mL/kg IBW (2.6% vs. 13.5%, p = 0.01). Nine observational studies were performed in an ICU (n=8,165), six of which showed tidal volume to be an independent predictor for ALI development. ALI occurred between days two and four (5 hours-3.7 days), and had an incidence ranging from 6.2% to 44% in ICU patients. In studies comparing secondary outcomes between ALI and non-ALI groups, the development of ALI increased mortality, lengths of stay, duration of mechanical ventilation, and non-pulmonary organ failure.

Conclusions: No definitive recommendations can be made on the most appropriate tidal volume for mechanically ventilated patients without ALI. Data suggest an increased incidence of ALI with higher tidal volume, but data is limited by heterogeneity and high variability in baseline ALI risk amongst patients included. Given increased mortality and morbidity associated with progression to ALI, a focus on prevention should remain a high priority for future research and clinical practice.

No poster displayed

Fuller, Brian M, MD

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Emergency Medicine, Division of Critical Care
Department of Anesthesiology, Washington University in St. Louis School of Medicine
Mentors: Richard S Hotchkiss, MD; Marin Kollef, MD

Acute lung injury in the emergency department and progression after intensive care unit admission

Fuller B; Mohr N; McCammon C

Introduction: The incidence of acute lung injury (ALI) in mechanically ventilated emergency department (ED) patients, and progression to ALI after admission from the ED has not been studied extensively. The purpose of this study was to describe the incidence of ALI in the ED, the incidence of progression to ALI after admission, and to explore the mechanical ventilation parameters used in these patients.

Methods: Retrospective observational cohort study of 251 mechanically ventilated patients with severe sepsis, presenting to an urban academic ED with >95,000 annual visits (June 2005-May 2010). The primary outcome variables were ALI at ED presentation, and progression to ALI after admission. Descriptive statistics, Chi-square and Fisher's exact test were used where appropriate.

Results: Median tidal volume was 8.8mL/kg ideal body weight (7.8-10.0) and did not differ between ALI status in the ED or progression after admission. Inspiratory plateau pressure was recorded in only 76 (30.3%) patients. 22 (8.8%) patients had ALI in the ED and 65 (28.4%) patients progressed to ALI within 4 days of ICU admission. Patients progressing to ALI after admission had an increase in mechanical ventilation hours (132.7 vs. 42.0, p<0.001), vasopressor hours (57.8 vs. 19.6, p<0.001), and longer hospital length of stay (7.6 vs. 3.4 days, p<0.001). Comparing ALI vs. no-ALI patients, there was no difference in the use of lung-protective ventilation in the ED (18.2% vs. 24.9%, p=0.63).

Conclusions: ALI is relatively common in mechanically ventilated septic patients in the ED, and the rate of progression to ALI after admission is high. Lung protective ventilation is not uniformly applied in the emergency department, regardless of ALI status. Patients progressing to ALI after admission have worse outcome. Future studies should examine the role of ED mechanical ventilation for ALI prevention.

062 **McAndrew, Christopher, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Orthopaedic Trauma
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentors: William Ricci, MD; Jeffrey Peipert, MD, MPH, MHA; Richard Gelberman, MD

Risk factors associated with rehospitalization after hip fracture

McAndrew CM; Gardner MJ; Binder EF; Ricci WM; Lenze EJ

Introduction: Hip fractures are an epidemic, with $10 billion spent on inpatient care alone. Thirty percent of patients remain in some form of assisted living at 4 months, with 8% of previous independent livers still in a nursing home at one year. A significant burden to both the patient and society is associated with rehospitalization, which occurs at a rate of 10-18%.

Methods: A prospective cohort study of 500 patients followed for one year will be evaluated for rehospitalization, reason for rehospitalization, and timing of rehospitalization relative to injury date. Data from these patients regarding pre-injury status, injury type and treatment, complications, and discharge disposition will be collected. Correlations will be analyzed with Mann-Whitney U test for ranked data, and Chi-Square Independent Samples testing for nominal data. Logistic regression models will be fit to analyze risk and predict rehospitalization.

Results: Five hundred twenty-one patients were enrolled, with 500 completing 1-year follow up. Thirty-three (6.6%) enrollees died by the end of the study. Eighty-three percent lived independently, 92.2% were ambulatory outside the home, and 68.9% walked without an assistive device prior to their fracture. Sixty-three percent were discharged from the hospital to a skilled nursing facility with rehabilitation. Thirteen percent were rehospitalized in the first 30 days, with 19.7% by 90 days.

Conclusions: Rehospitalization rate following hip fracture in this cohort is consistent with previously published data from the Medicare database. The U.S. Department of Health and Human Services, through the Partnership for Patients program, has teamed with private health care entities to work toward a goal of decreased 30-day rehospitalization rates across the nation by 20% by the end of 2013. Knowledge of risk factors for rehospitalization and their relative effects should drive resource allocation and further research into novel therapies and interventions.

008 **McNicholas, Colleen, DO**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Family Planning
Department of Obstetrics and Gynecology, Washington University in St. Louis School of Medicine
Mentors: Tessa Madden, MD, MPH; Allyson Zazulia, MD; Jeffrey F Peipert, MD, MPH, MHA

CLIIP: Cervical lidocaine for IUD insertional pain

McNicholas C; Madden T; Zhao Q; Secura G; Allsworth JE; Peipert JF

Introduction: Anticipated pain with intrauterine device (IUD) insertion may be a barrier to more wide-spread use. Previous research evaluating nonsteroidal anti-inflammatory medications, paracervical block, and cervical ripening agents has not shown improvement in pain scores. Our objective was to evaluate the efficacy of 2% lidocaine gel for pain relief with IUD insertion.

Methods: We performed a single site, double-blind, randomized control trial of women undergoing intrauterine device insertion. Participants were assigned to 2% lidocaine gel or placebo water-based lubricant and received 3cc's of study gel 3 minutes prior to IUD insertion. Using a 10 point visual analog scale, pain scores were assessed at multiple time points.

Results: Of the 200 women enrolled and randomized, 199 completed the study. Pain scores in the lidocaine and placebo arms were similar at tenaculum placement (lidocaine and placebo; median score 4; range 0-10; p=0.15) and with insertion (lidocaine: median score 5; range 1-10; placebo: median score; range 0-10; p=0.16), regardless of parity.

Conclusions: In our study, topical or intracervical 2% lidocaine gel prior to IUD insertion did not decrease pain scores.

115 **Sheshadri, Ajay, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Pulmonary and Critical Care Medicine
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentor: Mario Castro, MD, MPH

Predictors of Airway Remodeling and Decline in Lung Function in Severe Asthma

Sheshadri A; Witt C; Gierada D; Kozlowski J; Hoffman EA; Cook-Granroth J; Fain SB; Busse WW; Zheng J; Wilson B; Schechtman K; Castro M

Introduction: Previous studies have demonstrated an increased decline in lung function over time in patients with asthma. This study investigates predictors of airway remodeling measured by chest CT and change in lung function over time.

Methods: In the Severe Asthma Research Program, 47 well-characterized subjects (24 severe asthma, 14 mild-to-moderate asthma, 9 normal controls) underwent volumetric lung CT (supine, maximum inspiration, post-bronchodilator) at baseline and 2.6 ± 1.1 yrs (Yr2). Using Pulmonary Workstation software (VIDA Diagnostics, Iowa City, IA), the airway wall area % (WA%) was measured at generations 3-6 in pathways 1, 4, and 10 of the right and left lungs at both time points. Multivariable linear regression analysis was used to identify predictors of WA% at Yr 2 and lung function decline as measured by change in FEV1% predicted post-bronchodilator/year.

Results: WA% Yr2 was associated with the following baseline measurements: WA% baseline (all gen, r=0.41 to 0.68, p<0.01), asthma severity (gen 3&4, r=0.32 to 0.45, p< 0.04), race (gen 3,4&6, r=0.36 to 0.43, p<0.05), and BMI (gen 3, r=0.33, p=0.025). Multivariable analysis revealed WA% baseline (all gen, p<0.02) and race (gen 6, p=0.01) predicted WA% Yr2. In asthmatics, WA% Yr2 was associated with WA% baseline (all gen, r=0.47 to 0.70, p<0.009), severity (gen 3&4, r=0.33, 0.46, p<0.05), BMI (gen 3, r=0.33, p=0.04), and healthcare utilization (gen 3&4, r=0.51, 0.55, p<0.002). Multivariable analysis revealed WA% baseline (all gen, p<0.03) predicted WA% Yr2. Change in lung function (FEV1% pred postBD/yr) trended with WA% baseline (gen 3&4, r=-0.275,-0.27, p<0.10) and WA% Yr2 (gen 3, r=0.26, p<0.10). Stepwise linear regression revealed only WA% Yr2 was associated with decline in FEV1% pred postBD/yr (gen 4, r=0.39, p=0.008).

Conclusions: Airway wall thickness measured by chest CT at baseline is associated with subsequent airway remodeling and trended to predict decline in lung function. Larger longitudinal studies are needed to confirm these findings and to identify those at risk of progressive loss of lung function.

061 **Smith, Matthew V, MD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Sports Medicine
Department of Orthopaedics, Washington University in St. Louis School of Medicine
Mentor: Rick Wright, MD

A retrospective analysis of injury patterns in youth fastpitch softball pitchers

Smith MV; Davis R; Aggrey GK; Brophy RH; Wright RW

Introduction: Fast-pitch softball is one of the most popular female sports in the United States. The pitching motion in fastpitch softball is felt to be safe compared to the overhead pitching motion in baseball. There are no studies reporting the incidence of injury in youth fastpitch softball pitchers. As a result, there are no injury prevention guidelines for fastpitch softball pitchers. The purpose of this study is to competition habits and player-reported injuries in fastpitch softball pitchers

Methods: 28 fastpitch softball players were asked to complete an online survey retrospectively cataloging their previous season participation in fastpitch softball, the average number of games played per week, the maximum number of games played per day, pain a result of pitching and the number of games missed due to the pain.

Results: Of the 28 pitchers, 26 were select level pitchers. 18 pitchers reported pitching up to 3 games per week, 7 pitched 4-6 games per week, 1 pitched 7-9 games per week and 2 pitched 10 or more games per week. 70% of pitchers reported pitching in multiple games in a day (2 pitched 4 games in a day). 17 of the 28 pitchers (60%) reported pain related to pitching during last season. 10 of the 17 injured pitchers missed competition (3 missed 1-3 days, 2 missed 4-7 days, 2 missed 1-2 weeks, 3 missed 3-6 weeks). The breakdown of injury by site was: 10 shoulder; 2 elbow; 1 wrist; 1 knee; 4 back.

Conclusions: 60% fastpitch softball pitchers reported pain from pitching last season, many of whom lost playing time to due to pain. Pitching in fastpitch softball may not be as safe as previously assumed. Guidelines for injury prevention, including pitch count limitations, improved training, and changes in competition habits are needed for these athletes.

089 **Wenger, Philip, PharmD**

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
Division of Pharmacy Practice, St. Louis College of Pharmacy
Mentors: Jeffrey Crippin, MD; Jeffrey Peipert, MD

Assessment of hepatitis C risk factors and infection prevalence in a jail population

Wenger PJ; Crippin J; Rottnek F; Parker T; Greaser S

Introduction: The prevalence of hepatitis C virus (HCV) infection in the United States (US) general population is lower at 1.3-1.9% than that of the US incarcerated population at 15-40%. HCV infections cause significant morbidity including cirrhosis, hepatocellular carcinoma, liver failure, and liver transplantation. The cost to treat HCV morbidity is in excess of $1 billion. About 12,000 annual deaths are attributed to chronic HCV. Most studies of HCV in incarcerated populations have been done in prisons, rather than jails, which are generally more dynamic. Most inmates in jails return to local communities after brief incarcerations, creating situations where untreated communicable diseases have opportunity to spread to the surrounding community. Our aims are to identify HCV risk factors in inmates at the St. Louis County Jail using a standardized risk factor assessment questionnaire and assess the prevalence of HCV infection using a screening blood test for anti-HCV antibodies.

Methods: We plan to assess risk factors with a tool recommended by the Centers for Disease Control and draw blood for an anti-HCV antibody screening test in 300 inmates. We will then assess the correlation between risk factors (single and multiple) and the antibody results.

Anticipated Results and Conclusions: This project has been approved by the Saint Louis County Department of Health, the St. Louis College of Pharmacy IRB and is awaiting review by the Washington University IRB. We anticipate that the prevalence of HCV in our population will be between the general population and the low end of the prison population. We expect the most prevalent risk factors to be injection drug use and tattoos from non-inspected/unlicensed providers and that injection drug use will be the risk factor most strongly correlated with HCV positivity.

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

025 **Adams, Tiffany**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Obstetrics & Gynecology, Washington University in St. Louis School of Medicine
Mentors: Gina Secura PhD, MPH; Jeff Peipert MD, MPH, MHA

Change in Sexual Behavior with the Provision of No Cost Contraception

Adams TK; Secura GM; Peipert JF

Introduction: A concern that has been expressed regarding whether to provide free contraception is that it may result in increased sexual risk behavior. We sought to determine if access to free contraception changes sexual behavior among women enrolled in the Contraceptive CHOICE Project.

Methods: We performed a secondary analysis of data from the CHOICE Project, a prospective cohort study of 9,256 women aged 14-45 years in the Saint Louis region. Study participants are interviewed using standardized questionnaires at baseline, 3 months, 6 months, and every 6 months for the duration of follow up. Survey questions include number of sexual partners, type of partners, and frequency of sexual intercourse. We evaluated changes in sexual behavior from baseline to 6-months as measured by the number of male sexual partners in the past 30 days. Descriptive statistics included paired t-tests for continuous variables, and McNemar's test for categorical data. All analyses were conducted using SAS Version 9.2.

Results: Among the 9,256 women enrolled in CHOICE, 8,478 had completed the baseline and 6-month questionnaires and were included in this analysis. Overall, women reported no change in the mean number of sexual partners from baseline to 6-month ($p=0.08$). We observed a notable decrease in the proportion of women who reported no male sexual partners from 20.7% to 16.8 % and an increase in the proportion of women who reported one male sexual partner from 74.2% to 79.7% ($p<0.001$). Women who reported more than one sexual partner in the last 30 days, a measure of risky sexual behavior, decreased from 5.1% to 3.5% ($p<0.001$).

Conclusions: We found that providing contraception at no cost to a large group of reproductive-aged women does not lead to a clinically meaningful increase in their sexual behavior. In fact, the proportion of women that reported more than one sexual partner decreased over time.

057 **Aufman, Elyse, OTR/L, MOT**

AAN Fellowship
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Medical Student
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Catherine Lang, PT, PhD

Predictors of return to driving after stroke

Aufman EL; Bland MD; Barco PP; Car DB; Lang CE

Introduction: Returning to driving is a major issue for many stroke survivors and their families. Driving is, however, an extremely complicated task that requires many functional abilities that may be affected by a stroke. Predicting who will return to driving is difficult for rehabilitation professionals, but would have high clinical utility. The primary aim of this study was to identify patient factors at admission to an inpatient rehabilitation facility (IRF) that can be used to predict which patients with stroke will and will not return to driving.

Methods: This retrospective cohort study used data collected by the Brain Recovery Core, a partnership between Washington University School of Medicine, Barnes-Jewish Hospital, and the Rehabilitation Institute of St. Louis. After comparing the participants who had returned to driving at six months with those who had not on demographic and clinical characteristics, candidate variables to be placed in the regression were selected based on the results of the hypothesis and correlation tests, previous research, and data availability. A binary logistic regression analysis was then run with the candidate variables using the backward stepwise method.

Results: Of the 156 participants who were drivers pre-stroke, 31% (48) had returned to driving at six months post-stroke. The final model (n=114) predicts that patients admitted to inpatient rehabilitation with a NIH Stroke Scale score of ≤ 12, a Motricity Index lower extremity score of ≥ 60, and a FIM cognition score ≥ 20 are more likely to return to driving at six months post-stroke. Overall, this model correctly identified 75% (85/114) of participants.

Conclusions: Initial stroke severity, motor deficits, and cognitive deficits were all predictors of return to driving at six months post stroke in patients who receive inpatient rehabilitation services. Using these clinical assessments, clinicians may be able to screen for patients who will and will not return to driving at an early time point in patients' IRF stay. This model may allow healthcare professionals to better counsel persons with stroke and their families, and focus treatment efforts on the areas that may be critical for a safe return to driving.

058 **Bailey, Ryan R., MS, OTR/L**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Program in Physical Therapy
Washington University in St. Louis School of Medicine
Mentor: Catherine Lang, PT, PhD

Arm use in adults: A normative study using accelerometry

Bailey RR; Lang CE

Introduction: The goal of physical rehabilitation for upper extremity (UE) impairment is functional restoration of the UE for use in daily activities. While measurement of function and performance in the clinic can be collected via observation and clinical tests, measurement outside the clinic often depends on self-report. Self report, however, can be influenced by various biases, including desire to please the clinician and memory recall. Accelerometry, a valid and reliable measure of real-world UE use, eliminates these biases. To date, accelerometry has been used to study UE use in small samples of healthy older adults between the ages of 65-78, ignoring the impact of the potential modifying effects of comorbidities on arm use. Therefore, the purpose of this study is to characterize UE use and modifiers of UE use in a comprehensive sample of adults.
Methods: 75 community-dwelling adults, ages 30-84, wore wrist accelerometers for 24 hours and completed social and medical histories as well as questionnaires on activity participation, cognition, and depression. The amount of time that the UEs were used was calculated from accelerometer data. Associations between modifiers (activity participation, cognition, depression, cohabitation status, activities of daily living status, and number of self-reported comorbidities) and UE use was determined by correlation analyses.
Results: UE use was 9.02 ± 1.94 and 8.60 ± 1.99 hours for dominant and non-dominant UEs, respectively. The ratio between non-dominant/dominant UE use was 0.95 ± 0.06. Dominant UE use was moderately associated with activity participation (ρ=0.38, p=.001).
Conclusions: The results of this study describe the typical amount of UE use in adults. Despite the variability between participants in number of hours of use, UE use was primarily bilateral, as indicated by a use ratio ≈ 1.0. These data can now be used by patients and clinicians in tracking progress during rehabilitation of the UEs in conditions such as hemiparesis, nerve injury, and arthritis.

004 **Bundy, David**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Neurological Surgery, Washington University in St. Louis School of Medicine
Mentor: Eric Leuthardt, MD

Brain-Computer Interface Applications utilizing the Unaffected Hemisphere after Stroke

Bundy DT; Wronkiewicz M; Sharma M; Moran DW; Corbetta M; Leuthardt EC

Introduction: Brain-Computer Interface (BCI) systems have emerged as a method to restore function in motor impaired patients. This has primarily been applied to patients with an intact cerebral cortex, utilizing the cortical activity associated with movement of the contralateral limb as the typical control signal. While this is ideal for patients with an intact cortex, these signals are altered or lost after hemispheric stroke. Thus, a different control signal is needed for BCI applications in hemiparetic patients after hemispheric stroke. Previous studies in motor intact subjects have shown that there is a distinct cortical physiology associated with ipsilateral limb movements; however, it was unknown if stroke survivors could use this ipsilateral motor activity from their unaffected hemisphere in a BCI. This study examined the characteristics of non-invasively recorded cortical activity in stroke survivors and determined whether these signals could be used in a BCI system.
Methods: EEG recordings were made from chronic hemispheric stroke patients as they performed movements of the affected and unaffected hands. These recordings were analyzed to identify neural activity in the unaffected hemisphere associated with movements of the affected hand that were distinct from activity during other activities. The identified neural activity was then utilized by patients to control a simple online BCI system.
Results: All of the patients demonstrated significant activations in their unaffected cortical hemisphere enabling dissociation of affected hand movement from rest and unaffected hand movements. Furthermore, in patients with more severe motor impairments, these activations were located anterior to traditional sensorimotor regions. Finally, all patients used these ipsilateral motor activations to control an online BCI system with accuracies above chance.
Conclusions: We demonstrate for the first time that EEG signals from the unaffected hemisphere that are associated with movements of the affected hand can be used by chronic stroke survivors to control a simple BCI system rapidly and effectively. These findings suggest that ipsilateral motor activity from the unaffected hemisphere in stroke survivors could provide a mechanism for BCI operation that can be further developed into a long-term assistive device or a tool for rehabilitation after stroke.

No poster displayed

Butler, Carling
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Susan B Racette, PhD

Impact of a worksite wellness program on physical activity and CVD risk factors
Butler CE; Clark BR; Burlis TL; Racette SB

Introduction: The prevalence and rising financial burden of cardiovascular disease (CVD) demonstrate the urgency for effective health promotion and disease prevention strategies. Workplaces provide ideal environments for the implementation of wellness programs. The purpose of this study was to evaluate the effects of a worksite wellness program on physical activity and CVD risk factors among employees.

Methods: A worksite wellness program was offered to 122 university employees and included: (1) pre- and post-intervention health assessments and personal health reports; (2) an 8-week pedometer-based walking program; (3) health and wellness educational sessions; and (4) participation rewards. Participants were encouraged to meet the step count recommendation of 10,000 steps/day and track daily steps utilizing the American Heart Association's MyStart! Tracker, a web-based physical activity monitoring tool. The primary outcome measure was daily step count as measured by Yamax SW-200 pedometers. Secondary outcomes included Tudor-Locke physical activity indices, resting blood pressure and heart rate, BMI, fasting blood lipid and glucose levels, waist circumference, and cardiorespiratory fitness. Analyses were performed on an intention-to-treat basis.

Results: Participants were 85% female (46 ± 11 years). At baseline, 67% of participants were overweight or obese, 39% had elevated blood pressure, and 30% were considered 'sedentary' (<5,000 steps/day). A significant increase in daily step count was observed between baseline (6617 ± 2664 steps/day) and week 8 (8705 ± 3743 steps/day), $p<.001$. Only 6% of participants were categorized as 'active' or 'highly active' (≥10,000 steps/day) upon enrollment, wheareas 30% achieved this goal by week 8. Small but significant differences were observed for body mass, triglycerides, and systolic blood pressure, $p<.001$.

Conclusions: A worksite wellness program including pedometer-based walking and health assessment components is effective for increasing physical activity volume. Pedometers are simple, cost-effective tools that may enhance health promotion initiatives. Future research should assess the long-term effects of such programs and strategies for maximizing compliance.

No poster displayed

Bylina, Alexis
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
St. Louis College of Pharmacy
Mentors: Thomas C Bailey, MD; Anne Drewry, MD

Prediction of sepsis in intensive care unit patients
Bylina AB; Drewry A

Introduction: Sepsis is a complex pathophysiologic response to infection. Despite aggressive therapy, mortality approaches 30% in critically ill patients. With each hour delay in antibiotic administration, the risk of death increases 7%, making early detection of sepsis critical. The ultimate goal is to generate a computer algorithm capable of detecting subtle changes in critically ill patients' vital signs and laboratory values to identify sepsis extremely early in its course. The specific goal of this project was to design and validate a computer query to retrospectively classify intensive care unit (ICU) patients over a two-year period into septic and non-septic groups.

Methods: The electronic medical records of patients admitted to the surgical and medical ICUs at Barnes-Jewish Hospital from January 2010 to December 2011 were queried retrospectively to identify patients who developed sepsis greater than 48 hours after admission to the ICU. For septic patients, the query included the Surviving Sepsis criteria and ICU length of stay greater than 2 days plus absence of proven or suspected infection for non-septic control patients. A random sample of the records was reviewed by two blinded investigators for validation.

Results: A total of 7,259 patients were admitted to the medical and surgical ICUs during the two-year period. Our query identified 251 patients who met the criteria for developing sepsis in the ICU and 912 patients who met the control group criteria. Of the 114 patients who were randomly sampled for review, 41 of 53 were appropriately categorized in the septic group and 51 of 61 were appropriately categorized in the control group. 22 patients were identified as being inappropriately included because they were found to have sepsis prior to their ICU admission.

Conclusions: The results of this validation study identified a large proportion of patients who were inappropriately included in both the septic and non-septic groups based on our query criteria. Eventual development of a sepsis-prediction algorithm will depend on the computer analyzing clinical data from known septic and non-septic patients. In order to avoid including septic patients in our non-septic group, we will need to revise our query criteria and repeat a validation study.

No poster displayed

Castillo, Jacqueline

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Susan B. Racette, PhD

Evaluation of in-school physical activity and cardiovascular disease risk factors in urban children

Castillo JC; Clark BR; Racette SB

Introduction: The 2008 Physical Activity Guidelines for Americans advise children to engage in ≥60 minutes of moderate or vigorous physical activity daily. Translated to pedometer steps, the President's Challenge Program recommends 12,000 steps/day. Prior studies have assessed physical activity for portions of the school day; few have reported on the entire school day. The aims of this cross-sectional study were to quantify pedometer-determined physical activity during the entire school day in urban children and determine its association with cardiovascular disease (CVD) risk factors.

Methods: In two urban public elementary schools, 219 students in grades 2 through 6 (49% female; mean age = 9.9 ± 1.2 y) wore Omron HJ-151 hip accelerometer-pedometers during the entire school day for one school week/month across four months. The primary outcome, daily in-school step count, was recorded in the 7-day memory of the pedometer. Health and fitness assessments were conducted twice to identify CVD risk factors using sex- and age-specific criteria: elevated blood pressure (BP), overweight and obesity by body mass index (BMI), abdominal obesity by waist circumference (WC), and low cardiorespiratory fitness by the PACER 20-meter shuttle run.

Results: Mean in-school step count across four months = 4131 ± 1076 steps/day. Of daily recommended steps, children achieved 34.4% within these urban schools. Health assessments revealed the following prevalence: elevated BP = 4.8%, overweight by BMI = 12.0%, obesity by BMI = 19.7%, and abdominal obesity by WC = 18.8%. In an age-eligible subsample for the PACER (n= 99), prevalence of low cardiorespiratory fitness = 29.3%. Correlations were insignificant between in-school steps and CVD risk factors.

Conclusions: In-school physical activity contributes approximately one-third of federally recommended daily steps in these urban children; this is lower than what is documented in the literature for urban American children of a different demographic. The observed low proportion of recommended daily steps in the presence of CVD risk factors necessitates enhanced physical activity opportunities within elementary curricula and after-school programs.

027 **Crittle, Kristen**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Medical Student, Meharry Medical College
Department of Obstetrics and Gynecology, Washington University in St. Louis School of Medicine
Mentor: Jeffrey F Peipert, MD, MPH, MHA

Diagnosis and treatment of pelvic inflammatory disease: A quality assessment study

Crittle K; Peipert J

Introduction: The Center for Disease Control and Prevention (CDC) publishes recommendation for the diagnosis and treatment of Pelvic Inflammatory Disease (PID) every four years; however it is unclear whether healthcare providers adhere to these guidelines.

Hypothesis: The objective of this study is to determine the rate of clinician compliance with the CDC recommendations for diagnoses and treatment of PID.

Methods: The Contraceptive CHOICE Project (CHOICE) is a prospective cohort study with 9,256 participants in the St. Louis region. CHOICE provides participants with no-cost reversible contraception for 2 -3 years, with participants responding to baseline surveys, and surveys at 3 months and every 6 months. This sub-study is a retrospective chart review of participants within CHOICE who reported a diagnosis of PID in a follow-up survey. Participants were included if they had a diagnosis of PID confirmed in their medical records, if they consented to medical record release, and records were received. Medical records were reviewed and we collected demographics characteristics, symptoms and signs at time of visit, physical exam findings, diagnostic testing, and prescribed treatment.

Results: Overall there were 112 participants who reported being diagnosed with PID on a follow-up phone interview (1% of 9,256 CHOICE participants). Eleven participants did not have a recorded diagnosis of PID, and 38 patients did not release their medical records; leaving 63 (56.3%) participants for evaluation. Abdominal pain was the most common symptom (88.9%) and most patients (77.8%) were found to have at least one of the three minimal requirements for diagnosis of PID (uterine tenderness, adnexal tenderness, or cervical motion tenderness). One-third of participants (33.3%) received treatment with the recommended 2010 CDC regimens.

Conclusions: More than three-quarters of patients met CDC minimal criteria for PID, however only one third of clinicians adhered to CDC treatment. Further education efforts should inform clinicians of evidence-based recommendation for PID therapy.

047 **Esmaeeli, Amir**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Medical Student
Division of Cardiology
Department of Pediatrics, Washington University in St. Louis School of Medicine
Mentor: Charles E. Canter, MD

Impact of liver cirrhosis on heart transplant outcomes in Fontan patients

Esmaeeli A; Simpson KE; Canter CE

Introduction: The Fontan procedure is performed as part of a staged surgical palliation for children with congenital heart disease and a single effective ventricle. Several clinical challenges have emerged as this population ages and some patients go on to require a heart transplant (HT). The presence of liver cirrhosis, not uncommon after the Fontan procedure, is considered by some cardiologists to be a contraindication for HT. The primary purpose of this study is to evaluate differences in post-HT outcomes between Fontan patients with and without cirrhosis with the primary outcome of one-year all-cause mortality. Secondary outcomes include measurements of liver health markers post-HT to determine differences between both groups.
Methods: A retrospective review of 42 Fontan patients evaluated for heart transplant at St. Louis Children's Hospital from 2004 to the present was performed. Patients were grouped into cirrhotic versus non-cirrhotic based on CT imaging score from time of listing. Post-HT one-year all-cause mortality was compared between groups. Tacrolimus dose per kilogram (1, 3, 6, 9, and 12 months), as well as AST, ALT, albumin, and total bilirubin levels (listing, 1, 3, 6, 9, and 12 months) post-HT were analyzed.
Results: Of 42 Fontan patients evaluated for HT, 19 patients had adequate CT imaging and underwent HT. Two patients were not listed for HT due to significant liver cirrhosis. Baseline pre-transplant characteristics were similar between cirrhotic (n=6) and non-cirrhotic (n=13) groups. There was no difference in one-year all-cause mortality by Kaplan-Meier analysis (log rank p=0.794). Surrogate markers of liver function did not differ at any of the serial time points after HT, including tacrolimus dose per kilogram, AST, ALT, albumin, and total bilirubin.
Conclusions: We found that presence of cirrhosis did not impact post-HT mortality or markers of liver function in Fontan patients. This suggests that heart transplants can be successfully completed on Fontan patients with liver cirrhosis without significant difference in one-year post-HT outcomes. Further, multicenter prospective studies are needed to determine possible differences in long term outcomes.

042 **Evans, Jesse**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Physical Therapy
Washington University in St. Louis School of Medicine
Mentor: Amy Eyler, PhD

How do physical therapists promote physical activity: a pilot study

Evans J; Eyler A; Finney K

Introduction: Physical activity (PA) has been shown to decrease the risk of many forms of disease and disability. In 2009, only 50% of Americans engaged in the recommended amount of PA. Despite abundant recommendations on the importance of addressing physical activity needs with patients, it is not well understand how physical therapists perceive their role in this component of preventative healthcare. The purpose of this study is to understand how physical therapists utilize their role in promoting health and wellness through PA and what barriers they perceive to being a provider of preventative services.
Methods: Currently practicing physical therapists were invited to participate in a web-based survey about their perceptions, confidence, knowledge, perceived barriers, and current practices in prescribing PA. Data was collected using Qualtrics as a survey tool and analyzed using SPSS v. 19.0. Descriptive analyses and logistic regression were conducted to determine demographic predictors of current practices and barriers.
Results: Of 300 participants recruited, 124 responded and 113 responses were analyzed. While over 90% (n=111) of respondents agree that PA can alter a person's risk for chronic disease and that it is the physical therapists' role to prescribe PA, only 67% (n=76) report prescribing general PA to patients at least most of the time. Physical therapists with 5-10 years experience were three times more likely than recent graduates (OR=3.08, CI 95% 1.09-8.69) to be familiar with the Physical Activity Guidelines for Americans. The most frequently cited barrier to prescribing general PA was lack of compliance (N=49).
Conclusions: Currently practicing physical therapists perceive that is it their role to prescribe general PA and that they have the knowledge to do it, but actual implementation of PA education and intervention is less consistent. Barriers to prescribing generally PA cited were not enough time with patient, insufficient reimbursement, and perception that patient will not comply. This pilot study can be used to inform physical therapy practice to help decrease the public health burden in physical inactivity. Future research should be aimed at strategies to improve PA promotion by physical therapists.

065 **Godzik, Jakub**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Adult and Pediatric Spinal Deformity Division
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentors: Michael Kelly, MD; Lawrence Lenke, MD

Evaluation of Outcomes in Corrective Spine Surgery in Chiari Malformation, Type I Associated Scoliosis

Godzik J; Agarwal R; Limbrick D; Lenke LG; Kelly MP

Introduction: Chiari Malformation, Type 1, (CIM) is a developmental abnormality of the craniocervical junction and skull, often associated with syringomyelia (SM) and spine abnormalities. The spinal deformities involved in 50-80% of CIM with SM associated scoliosis are often complex surgical challenges, with increased complications and postoperative economic and clinical burden. The aims of this retrospective consecutive case series were to evaluate the safety of spinal fusion procedures and assess surgical outcome following spinal reconstructive for Chiari associated deformities. This is the largest series in the literature on the surgical outcomes of these patients.

Methods: All patients treated for spinal deformity at our institution with an associated Chiari I Malformation were reviewed. Demographics, deformity morphology, treatment methods, surgical complications, and postoperative outcomes were measured and recorded. Surgical outcome was evaluated using radiographic correction criteria and change in the SRS-22 outcome instrument.

Anticipated Results: 32 patients met inclusion criteria. All patients had syringomyelia, with average syrinx width of 7.4 mm ± 3.8, and length of 12 ± 5 vertebral levels. All patients had undergone neurosurgical decompression prior to spinal reconstruction. In 13 patients with available imaging, all scoliosis curves progressed or remained unchanged following neurosurgical treatment. An average number of 10.2 ± 3.2 vertebral levels were fused posteriorly, with 12.5% (4/32) of procedures complicated by abnormality with intraoperative neurologic monitoring data. 1 procedure was aborted secondary to deteriorating signal and reattempted following 54 days of hospitalization. Based on preliminary data analysis, we anticipate an average curve percent correction of 46% and a 30% improvement in SRS-22 outcome instrument score.

Conclusions: The results from this retrospective study demonstrate that satisfactory clinical effect with posterior fusion can be achieved in Chiari Malformation, Type I patients with mild or moderate adult thoracolumbar or lumbar scoliosis. Initial surgical interventions are safe, although neurologic monitoring data abnormalities were not uncommon and surgeons should be prepared for this situation in this population.

No poster displayed

Godzik, Jakub

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Adult and Pediatric Spinal Deformity Division
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentors: Michael Kelly, MD; Lawrence Lenke, MD

Spinal Reconstructive Surgery for Poliomyelitis Associated Deformities

Godzik J; Kelly MP; Sides B; Lenke LG

Introduction: The co-occurrence of paralysis, pelvic imbalance, and spinal deformity in patients with a history of poliomyelitis is well established in the literature. Given the pathologic injury to the spinal cord, this particular etiology may predispose the patient to a different set of risks and pose a unique surgical challenge in their care. Few modern reports exist regarding the risks and results involved in the surgical care of spinal deformity in the setting of polio and post-polio syndrome.

Methods: The orthopedic surgery database was reviewed for patients with a co-morbidity of paralytic poliomyelitis who had undergone spine deformity surgery in the years between 1985 and 2012. Relevant demographic, past medical history, surgical and postoperative information were collected from the medical records. Surgical outcome was described using radiographic data and validated outcome instruments.

Anticipated Results: 17 patients with a past medical history of paralytic poliomyelitis were identified. All patients underwent instrumented spinal fusion with a median number of 12 vertebral levels involved (IQR 9 –18). 24% (4) of patients suffered a major postoperative complication within a mean follow up of 7 years ± 6. Pseudoarthrosis rate was 5% (1 patient). Complete intraoperative neuromonitoring data and surgical outcome data will be collected and analyzed further.

Conclusions: Although a rare disease in the developed world, a large number of patients with a history of poliomyelitis develop scoliosis that is only controllable by surgery. The majority of patients in our cohort underwent complex spinal deformity correction involving staged anterior and posterior intervention, attaining adequate curve correction but enduring a high complication rate.

017 **Grither, Allie**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Psychiatry, Washington University in St. Louis School of Medicine
Mentor: Denise Wilfley, PhD

Characterizing motivation for weight loss in a Family-based Behavioral Treatment program

Grither AA; Wilfley DE; Kolko RP

Introduction: Obesity and overweight weight-loss interventions are subjects of much research in current literature. Although gold standard approaches for children in the form of Family-based Behavioral Treatment (FBT) interventions exist, there is still variability in weight loss outcomes. This study aims to further the body of research by exploring characteristics predictive of treatment success. We will take a novel approach by analyzing motivation to lose weight of child-parent dyads.

Methods: Motivation on baseline enrollment in FBT will be categorized via qualitative interview, and subsequently analyzed in regression models to assess its relation to baseline relative weight and relative weight change in child and parent. Child-parent concordance of motivation, or whether the child and parent stated the same reasons for wanting to lose weight, will also be analyzed via regression models as a potential predictor of baseline relative weight and weight change. Exploratory analyses aimed at assessing the interaction of motivation and other predictor variables as predicting child relative weight change will also be examined.

Anticipated Results: We hypothesize that motivation and concordance in motivation stated by the child and parent will be related to child and parent baseline relative weight, relative weight change, and drop-out of FBT.

Conclusions: These results may aid future weight loss interventions in identifying those at risk of less success in order to tailor the program to their needs and enhance weight loss results. Bolstering the efficaciousness of the current gold-standard FBT may reduce the monetary and emotional burdens associated with overweight and obesity.

No poster displayed

Hetland, Amanda

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: David Carr, MD; Mike Wallendorf, PhD

PDI Medication Use in Medically Impaired Older Adults Referred for Driving Evaluation

Hetland A; Carr D

Introduction: 'Potentially driver impairing' (PDI) medications have been well discussed in the literature, although this definition focuses largely on motor vehicle collisions rates instead of current, measureable impairments in driving. The objective was to determine whether an association exists between driving and cognitive test performance and routine use of PDI medications in medically impaired adults referred for clinical driving assessment. A secondary aim of this study was to explore subcategories of PDI medications to determine whether any specific classes were more strongly associated with impaired clinical outcomes.

Methods: 225 medically impaired drivers (62.2% male; mean age 68 ± 12.8 years) were referred to an OT driving evaluation clinic at an academic rehabilitation center for clinical evaluation of fitness to drive. Certain medications were ascribed as being 'potentially driver impairing' based on a thorough review of the literature. PDI medication use was quantified by number of PDI medications routinely taken, and similarly, total medications were tallied as an additional predictive variable. Retrospective comparison of outcome variables in cognitive function and road test performance was done according to reported medication regimens.

Results: Subjects taking routine PDI drugs had a mean score on the ESS of 7.8, whereas subjects not taking PDI medications had a mean score of 6.0 points, indicative of a higher degree of daytime sleepiness with PDI medication use ($p = 0.007$). Total medications, regardless of PDI designation, also correlated positively with ESS scores ($p = 0.023$). Stratified assessment of PDI medications by subclass identified six drug classes most associated with impaired outcomes.

Conclusions: These findings indicate that use of PDI medications – by their current definition – is associated with hypersomnolence, a condition linked to increased motor vehicle crash risk. PDI medication use was not associated with failure of the road test, but this may suggest limitations of this outcome variable or perhaps the need for a more practical list of PDI medications based on real driving performance.

099 **Kapalka, Kristen**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Medical Student
Division of Emergency Medicine
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentor: Daniel Theodoro, MD

Checklist adherence during central venous catheter insertion in the Emergency Department

Kapalka KM; Klemisch R; Theodoro DL

Introduction: Central venous catheterization (CVC) rates are rising in US Emergency Departments (EDs), but the rate of central line-associated blood stream infections (CLABSIs) due to CVC insertion is significantly higher in the ED than in the intensive care unit (ICU). ICU CVC checklists have successfully reduced the CLABSI rate to near 0% in some ICUs. In order to ultimately determine if checklists can accomplish a similar feat in the ED, we first want to know whether or not ED physicians will use a provided checklist when placing a CVC. We aim to determine the frequency with which a provided checklist is used, as well as the frequency with which certain checklist items are performed.

Methods: Two medical students took shifts on call to observe CVC insertions in the ED at Barnes Jewish Hospital (BJH) between 6/1/2011 and 8/12/2011 and 6/1/2012 and 7/27/2012. A CVC checklist is routinely provided by BJH to ED staff for each insertion procedure. For each observed CVC placement, the observer recorded if the physician utilized this checklist, as well as if the ED team performed each of 14 specific checklist items which are known to reduce CLABSI rates.

Results: This study is ongoing, but thus far, out of 24 total observed cases, 0 checklists were used (95% confidence interval 0% to 14%). Out of 14 checklist items, 6 were performed routinely (88%-100% frequency, 95% CI from 69%-100%), 4 with intermediate frequency (45%-65% frequency, 95% CI from 27% to 82%), and 3 with very low frequency (4%-5% frequency, 95% CI from 0% to 23%).

Conclusions: The study data indicate that the ED staff uses provided CVC checklists very rarely or not at all, indicating that significant unknown barriers to using CVC checklists may exist in the ED. The data also suggest 7 items shown to reduce CLABSI rates are often neglected or ignored. If ED staff can be trained to routinely use a CVC checklist, the checklist must target these neglected items. If hospitals hope to reduce ED CLABSI rates using checklists, the reasons for the failure of ED staff to use CVC checklists as well as perform important checklist items should be studied in future research.

No poster displayed

Lang, Adam

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Marin H. Kollef, MD; Scott T. Micek, PharmD

Inappropriate Antibiotic Treatment of Patients with Pneumonia Presenting from the Community: Incidence and Risk Factors

Lang AJ

Introduction: Ceftriaxone is one of the most common antibiotics prescribed for the empiric treatment of Community Acquired Pneumonia (CAP). In the last decade, pathogens not covered by ceftriaxone have increased. The common CAP pathogens most likely not to be covered by ceftriaxone include Streptococcus pneumonia resistant to penicillin/cephalosporin and methicillin-resistant Staphylococcus aureus. The importance of identifying such pathogen-patient combinations is highlighted by the availability of new antibiotics, including ceftaroline, that are active against these antibiotic-resistant organisms.

Methods: We performed a retrospective review of all patients who presented to and were admitted to Barnes Jewish Hospital from 2008 to 2011 and were treated initially with ceftriaxone ± azithromycin or a respiratory quinolone during this time period. For the patients who meet these criteria, pneumonia screening information, CURB-65, and a number of other associated co-morbidities were collected. SPSS software was used for statistical analysis of the cohort.

Results: The cohort included 225 patients. The incidence of Inappropriate Antibiotic Therapy (IAT) has not yet been determined and other statistical tests have not yet been completed. Mortality in this patient population is expected to be between 25-35% and we estimate that at least 15% of the cohort received IAT

Conclusions: At this time, statistical analysis of the data has not been completed. We intend to report the incidence of inappropriate antibiotic therapy when a patient is admitted from the community and has an initial treatment with ceftriaxone ± azithromycin or a respiratory quinolone. Certain co-morbidities are hypothesized to increase a patient's odds of receiving inappropriate antibiotic therapy. Thus, selection of individual antibiotic agents should be based on a patient's entire clinical picture.

026 **Langhorne, Ophelia**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Obstetrics & Gynecology, Washington University in St. Louis School of Medicine
Mentor: Jeffrey Peipert, MD, MPH, MHA

Pregnancy Outcomes of Unintended and Intended Pregnancies in the Contraceptive CHOICE Project

Langhorne O; Peipert J; Secura G; McNicholas C; Zhao Q; Allsworth J; Stout M

Introduction: Unintended pregnancies are a public health problem in the United States. 49% of all U.S. pregnancies are unintended, and 82% of pregnancies in women under the age of 20 are unintended. We performed a substudy of the Contraceptive CHOICE Project to assess differences in pregnancy outcomes of intended versus unintended pregnancies. Our hypothesis was that unintended pregnancies would have more adverse outcomes (e.g. lower birthweight and greater preterm birth) than intended pregnancies.

Methods: We administered a phone survey to 16 women who experienced an unintended pregnancy, and compared this group to known outcomes of intended pregnancies within CHOICE (N=15). We included any woman who became pregnant during her enrollment period in CHOICE and had a delivery as the documented outcome of her pregnancy. We excluded any woman whose pregnancy intendedness was not documented in the CHOICE dataset (N=3), as well as multifetal gestation (N=1). We evaluated differences in responses between women with unintended and intended pregnancies using t-test and Chi-square, and when sample size permits, will adjust for demographic and reproductive factors using linear regression.

Results: We first assessed the characteristics of women experiencing an unintended pregnancy (N=338). 62.8% of these participants are black and 70.4% are low socioeconomic status. Age, race, educational achievement, SES, and history of unintended pregnancy are risk factors for unintended pregnancy. Women in the unintended pregnancy group experience their first pregnancy 1.5 years earlier than the comparison group. Compared to a group of women with intended pregnancy, newborns from the unintended pregnancy group are 1.6 oz. larger (7.0 lbs. v. 6.9 lbs.) and born earlier (38.06 wks. v. 38.13 wks.).

Conclusions: We did not find differences in birthweight or gestational age at delivery when we compared unintended to intended pregnancy outcomes. Our sample size is too small to see any significant differences. We will continue to collect data to address our research question regarding adverse outcomes associated with unintended pregnancies.

106 **Nguyen, Andrew**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Division of Gastroenterology
Departments of Internal Medicine and Psychiatry, Washington University in St. Louis School of Medicine
Mentor: Gregory Sayuk, MD, MPH

Cortical thickness and gray matter density in patients with irritable bowel syndrome

Nguyen A; Wojtalik J; Sayuk GS

Introduction: Irritable bowel syndrome (IBS) is a GI condition manifested by chronic abdominal pain. Previous work has established brain activation differences in regions known to modulate cognitive and emotional arousal responses to noxious afferent visceral signals (i.e., the homeostatic afferent processing network, HAPN). Recent evidence suggests changes in cortical thickness (CT) and gray matter volume (GMV) in HAPN subregions accompany somatic pain.
Aim: To assess for differences in CT and GMV in HAPN subregions among IBS patients and healthy controls.

Methods: T1-weighted structural MR images were collected on 77 participants (IBS=43, healthy controls=34). Established LONI software pipelines (UCLA) were applied to preprocess the T1 structural images and reconstruct cortical surfaces. General linear models were developed to assess for differences in CT and GMV in HAPN regions between study groups.

Results: IBS and healthy controls were similar in terms of gender ($\chi 2=1.94$, $p=0.16$) and age (IBS: 42.5 ±1.6, control: 40.8 ±1.4, $p=0.43$). There were no significant differences in total brain volume ($p=0.23$) or GMV ($p=0.59$) between study groups. In CT analyses, differences in the IBS and control populations were modest, with uncorrected comparisons showing trends in several HAPN regions involved in emotional arousal (L mid insula, $p=0.18$; L post insula, $p=0.058$; R mid insula, $p=0.22$, R post cingulate, $p=0.087$; R parahippocampus, $p=0.15$). In all cases, differences in CT were explained by greater CT in the IBS population. In corrected GLM models, the IBS group exhibited greater GMV in these regions: B superior and middle frontal gyri ($p=<0.01$), L OFC ($p<0.001$), B insula ($p<0.02$) and B ACC ($p<0.04$). Within primary sensory cortex and control regions, no significant group differences were observed ($p>0.10$).

Conclusions: Though overall brain and gray matter are similar in IBS, significantly greater GMV are observed, specifically among HAPN subregions. Whether these differences are of pathophysiologic relevance in IBS, or conversely result from greater afferent sensory signaling will require additional study.

No poster displayed

Nicklaus, Megan

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Division of General Medical Sciences
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentor: Brian F Gage, MD, MSc

Net stroke equivalents for antithrombotic therapy prescribed for atrial fibrillation

Nicklaus M; Hyun G; Li J; Andrade AA; Challen L; Gage BF

Introduction: Warfarin has previously been the gold standard in thromboembolism prophylaxis in atrial fibrillation patients, but the market has recently seen an increase in the number of possible alternatives. Several large, robust clinical trials looking at single agents versus warfarin or aspirin have been published, but the literature was lacking a review of all agents. This systematic analysis was designed to help guide the clinician to the most appropriate treatment choice for their individual patient.

Methods: Data sources that were searched included Pubmed, EMBASE, MEDLINE, and Clinicaltrials.gov. We conducted a systematic analysis of phase 3 clinical trials using the keywords apixaban, dabigatran, rivaroxaban, and atrial fibrillation. The primary studies of RE-LY, ROCKET-AF, ARISTOTLE, AVERROES, ACTIVE-A, and ACTIVE-W were selected for our analysis. The antithrombotics were evaluated by adjusting for the time in therapeutic range (TTR) for International Normalized Ratio (INR). The rates of stroke, intracranial hemorrhage, extracranial hemorrhage, and myocardial infarction were calculated from the relative risk of each event compared to warfarin. These adverse events were converted into stroke equivalents based on quality adjusted life years lost.

Results: The optimal antithrombotic therapy depended on risk of stroke, as estimated by $CHADS_2$ score. For patients with a $CHADS_2$ score of 1, either apixaban or dabigatran had the lowest rates of stroke and stroke equivalents, while aspirin (with or without clopidogrel) had the highest rates. For $CHADS_2$ scores of 2 or more, dabigatran 150 mg bid had the lowest rates of stroke and stroke equivalents. There was insufficient information to quantify the effect of the new antithrombotics in patients with a $CHADS_2$ score of 0. Although rivaroxaban had the advantage of once daily dosing, it was not the optimal therapy for any $CHADS_2$ score.

Conclusions: We suggest consideration of dabigatran or apixaban twice daily for stroke prophylaxis in patients with atrial fibrillation who have a $CHADS_2$ score of 1 and dabigatran 150 mg twice daily for patients with a higher $CHADS_2$ score.

No poster displayed

Noel, Camille, MS

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Biomedical Engineering, Washington University in St. Louis
Mentor: Parag Parikh, MD

Segmentation precision of abdominal anatomy for MRI–based radiotherapy planning for cancer

Noel CE; Zhu F; Lee AY; Hu Y; Parikh PJ

Introduction: The limited soft tissue visualization provided by computed tomography, the standard imaging modality for radiotherapy (RT) planning for cancer treatment, has motivated studies on the use of magnetic resonance imaging (MRI) for better characterization of treatment sites such as the prostate and head & neck. Evidence suggests that supplementing RT planning with MR images may improve delineation of abdominal targets, as well. However the utility of MRI for segmentation of abdominal tissues for RT planning purposes remains unstudied. To this end, we investigated the inter- and intra-observer precision in segmentation of abdominal organs on MR images for RT planning.

Methods: Manual segmentation of eight abdominal organs at risk (liver, stomach, duodenum, pancreas, spleen, bowel, kidneys, and spinal cord) was performed by three independent observers on MR images acquired from 14 healthy subjects. Two different MR sequences were acquired for each subject (T2-weighted and Balanced FFE), totaling to 28 image sets. Observers repeated segmentation four separate times for each image set. Inter- and intra-observer contouring precision was assessed by computing 3D overlap and distance to agreement (as indicated by the Dice coefficient (DC) and Hausdorff distance (HD)) of segmented organs. We assessed groups of subjects who did (n=7) and did not (n=7) ingest oral contrast prior to imaging. The mean and standard deviation (std) of intra- and inter-observer DC and HD values were $DC_{intra\text{-}observer}$ = 0.89 (std = 0.12), $HD_{intra\text{-}observer}$ = 3.6mm (std = 1.5), $DC_{inter\text{-}observer}$ = 0.89 (std = 0.15), and $HD_{inter\text{-}observer}$ = 3.2mm (std = 1.4).

Results: Overall, precision metrics indicated good inter-/intra-observer agreement (mean DC > 0.7, mean HD < 4mm). When precision metrics were analyzed collectively, the duodenum, pancreas, and bowel ranked poorest overall. MRI sequence and presence of contrast were significant predictors of precision metrics.

Conclusions: Results suggest that MRI can offer adequate segmentation precision for abdominal treatment planning. MRI sequence optimization and pre-imaging administration of oral contrast may be important clinical factors in maximizing optimal targeting and dosimetry.

059 **Peterson, Daniel, MS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Movement Science PhD Program
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Gammon Earhart, PT, PhD

Supra-spinal Locomotor Regions in Parkinson's Disease During Gait Imagery

Peterson DS; Pickett KA; Earhart GM

Introduction: Individuals with Parkinson's disease (PD) often exhibit gait dysfunction, particularly during complex gait tasks. Understanding how the neural control of gait differs between people with PD and healthy adults is critical for developing focused interventions including deep brain stimulation. Our purpose is to compare the neural control of gait in people with PD and healthy adults during simple (forward) and complex (turning, backward) imagined gait tasks.

Methods: Twelve people with PD (mean age +/-SD=62.6+/-9.2; 7 male) and 15 healthy adults (controls; 66.5+/-7.5; 5 male) imagined four gait tasks (forward walking, backward walking, and turning to the left and right in a small (0.6m radius) circle) during blood oxygen level dependent (BOLD) signal acquisition. Eco-planar imaging data (TR=2200ms, TE=3ms, 4.0mm^3 voxels) were acquired during alternating imagined gait tasks (approximately 15 seconds each) and rest periods (11 seconds). A region of interest (ROI) analysis was conducted on five regions suggested to be involved with locomotor control in humans: supplementary motor area (SMA), putamen, globus pallidus (GP), mesencephalic locomotor region (MLR), and cerebellar locomotor region (CLR).

Results: Imagined gait resulted in higher BOLD signal with respect to rest in PD and controls. However, relative to imagined forward walking, imagined turning resulted in a trend toward larger increase in the SMA in PD (p=0.075). PD also exhibited a trend toward a decrease in activity of the MLR during turns with respect to forward walking (p=0.16).

Conclusions: Those with PD were observed to have larger BOLD signal in the SMA, and smaller BOLD signal in the MLR during turns than controls. This shift from brainstem (MLR) to cortical (SMA) control in PD during complex gait tasks may represent a compensatory shift in activation to complete the relatively complex turning imagery task. These observations may shed light on the neural mechanisms underlying gait dysfunction in PD, and underscore the importance of testing both "simple" and "complex" tasks in those with PD.

097 **Rengarajan, Arvind**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
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Mentor: Michael Mullins, MD, FACEP, FAACT

How often do False-Positive Phencyclidine (PCP) urine screens occur with common medications?

Rengarajan A; Olatunde TO; Mullins ME

Introduction: False positive drug screens for illicit drugs can lead to an incorrect treatment, prejudice from nursing and physician staff, and adverse legal or employment action. In order to test a patient for phencyclidine (PCP), the staff collects urine and runs a urine drug screen (UDS) that performs an immunoassay for the presence of PCP. All positive urine screens undergo confirmation with gas chromatography (GC). Prior literature has shown that commonly used medications such as Tramadol, Diphenhydramine, and Dextromethorphan can result in false positive PCP urine screens. However, the incidence of these false-positives is unknown.

Methods: We collected information on patients presenting to Barnes Jewish Hospital (BJH) Emergency Department (ED) from 2007-2011 with a positive UDS for PCP. These patients were divided into those "confirmed" by GC, and those that were "not confirmed". We reviewed the charts of these patients for documented use of Tramadol, Diphenhydramine, Dextromethorphan, and calculated the proportions of these medications in both groups.

Results: From 1/1/2007 to 12/31/2009, 19,452 urine screens were performed by the laboratory at BJH on patients presenting to the ED. Of the 19,452 urine screens, 257 (1.3%) screens were positive for PCP. Of these 257, 210 (82%) were confirmed positive for PCP by GC, and 47 (18%) failed to confirm. Among the 210 confirmed positives, patient charts showed use of Tramadol in 15 patients (7.1%, 95% CI 3.7%-10.6%), Diphenhydramine in 18 patients (8.6%, 95% CI 4.8%-12.4%), and Dextromethorphan in 6 patients (2.9%, 95% CI 0.6%-5.1%). Among the 47 who failed to confirm, records reflected use of Tramadol in 9 patients (19.1%, 95% CI 7.9%-30.4%), Diphenhydramine in 8 patients (17.0%, 95% CI 6.3%-27.8%), and Dextromethorphan in 10 patients (23.1%, 95% CI 9.6%-33%).

Conclusions: As per our analysis thus far, therapeutic use of Tramadol, Diphenhydramine, or Dextromethorphan appears to be the most frequent cause of false positive UDS for PCP among our study sample, resulting in 23 of the 47 (49%) false positives. Therefore, patients and clinicians should be aware of this high false positive rate.

060 **Sorensen, Christopher J, MS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Movement Science Program
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Mentor: Linda Van Dillen, PT, PhD

The relationship between psychological factors and low back pain symptom intensity during prolonged standing in back-healthy people

Sorensen CJ; George SZ; Callaghan JP; Van Dillen LR

Introduction: Epidemiologic studies have shown jobs that involve prolonged standing are associated with increased risk of developing low back pain (LBP). Psychological factors are positively related to symptom intensity in people with LBP. We are using an induced-pain paradigm in back-healthy people to understand risk factors for developing LBP during prolonged standing. The purpose of this study was to examine the relationship between psychological factors and peak LBP symptom intensity developed during prolonged standing in this cohort. We hypothesized that peak LBP symptom intensity would be correlated with psychological factors in those who develop LBP symptoms during standing.

Methods: Participants completed the Adapted Tampa Scale for Kinesiophobia (TSK-G) and Fear of Pain Questionnaire (FPQ-III). Participants then stood for 2 hours while performing 4 different simulated light work tasks randomly presented every 15 minutes. At baseline and every 15 minutes, participants rated their LBP on a 100 mm visual analog scale (VAS). Participants with a VAS score $\geq$20 mm were considered pain developers (PD). Pearson correlation coefficients were calculated for peak VAS scores and the 1) TSK-G score, and 2) FPQ-III total score, for PDs and non-pain developers (NPD) separately.

Results: There were 6 (15%) PDs and 33 (85%) NPDs. The correlations were as follows: 1) TSK-G: PDs: r = 0.62; NPDs: r = 0.07, 2) FPQ-III: PDs: r = 0.70; NPDs: r = 0.09.

Conclusions: For people who developed clinically relevant LBP ($\geq$20 mm), peak LBP intensity ratings were highly correlated with psychological measures. These data suggest that pain may have to exceed minimal levels before there is a strong psychological influence on perception of intensity. Information gained could assist in screening for risk factors for LBP development in prolonged standing, and inform preventative strategies for people frequently exposed to prolonged standing during work and daily activities.

No poster displayed

Stepan, Jeffrey

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentors: Martin Boyer, MD, FRCS; Ryan Calfee, MD, MSc

The Impact of Activity Level on Wrist Function after Distal Radius Fracture in the Elderly

Stepan J; Nelson G; Calfee R

Introduction: Distal radius fractures (DRF) are extremely common in elderly populations. Despite advances in all aspects of fracture care, universal improvements in functional outcomes have not been achieved. Several studies found no clear difference between treatment methods or achievement of anatomic alignment and functional outcomes. Some suggest that activity level following DRF may be a confounding factor in functional assessments. The purpose of this study is to use a validated self-reported activity scale to investigate differences in functional outcomes after DRF.

Methods: A retrospective review of patient records identified patients over the age of 65 treated for unilateral DRF at least one year prior. Patients were included regardless of treatment or outcome and excluded if a confounding musculoskeletal or neurological diagnoses in either upper extremity (UE) was present. Enrolled patients came to the office for a physical exam, radiographs of the wrist and completed the QuickDASH and Physical Activity Scale in the Elderly (PASE) to evaluate UE function and activity levels respectively.

Results: 57 eligible patients were enrolled. 25 (43%) met criteria for malunion (mean age 72.9 years). Of these, 10 were considered high-activity (PASE score $\geq$ 150). There was no statistically significant difference in mean QuickDASH scores between low (18.5 $\pm$ 16.3) and high-activity (8.4 $\pm$ 12.2) malunited fractures. There were no significant differences in grip strength, flexion-extension, pronosupination, or radial-ulnar deviation active range of motion. Well-united fractures (N=32, mean age 73.1 years) evaluated along the same criteria found no significant differences either. Analysis by malunion deformity; radial shortening ($\geq$ 4 mm) produced higher QuickDASH scores (22.5 $\pm$ 10.3) compared to dorsal tilt $\geq$ 10 degrees (mean 8.4 $\pm$ 4.6).

Conclusions: These results suggest functional outcomes in elderly patients after distal radius malunion do not appear to be significantly affected by activity level. A malunion subgroup analysis suggests that residual radial shortening may instead exert a greater effect on post-injury patient-rated wrist function.

063 **Stepan, Jeffrey**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentors: Martin Boyer, MD, FRCS; Ryan Calfee, MD, MSc

Reliability of Patient Recall on the QuickDASH Questionnaire

Stepan J; London D; Boyer M; Calfee R

Introduction: Orthopaedic outcomes research is increasingly emphasizing patient self-reporting questionnaires. Retrospective, case control, and cross-sectional studies often rely on patients' recall of prior function to answer these questionnaires, potentially introducing recall bias. Few prior studies have measured agreement between patients' recalled and actual prior levels of function. None have measured how recall bias is affected by time. The purpose of this study is to quantify recall bias and to determine how it changes over time using the validated QuickDASH questionnaire.

Methods: 35 patients (140 total) at 3, 6, 12, and 24 months out from initial office visit (IOV) of two Washington University orthopaedic hand surgeons were contacted and asked to recall hand function at their IOV using the QuickDASH questionnaire. These scores were then compared to the actual QuickDASH scores obtained at the IOV.

Results: Paired T-tests were used to compare actual and recalled QuickDASH scores for each group. The mean difference, 95% confidence interval, and p-value were -7.14 (-11.03 to -3.25, p=0.001) for 3 m, -0.84 (-5.24 to 3.55, p=0.699) for 6 m, -2.27 (-8.05 to 3.51, p= 0.430) for 12 m and -2.79 (-7.20 to 1.6, p=0.206) for 24 m. Only the 3 month group had statistically significant differences between actual and recalled scores, but the difference was not clinically important as the 95% confidence interval does not approach the QuickDASH MCID of +/-15. Using a Kruskal-Wallis analysis, there was no statistically significant difference in recall accuracy between the four groups (p=0.768). There was no correlation between current QuickDASH score or age and patient recall accuracy (p=0.666 and p=0.895 respectively).

Conclusions: The results show patients are able to accurately recall prior level of function up to two years prior using the QuickDASH Questionnaire. Recall accuracy is also not dependent on patient age or current level of hand function. The results suggest current and past research conducted using recalled data in this manner are valid, and future research may be conducted reliably using recalled QuickDASH scores without unacceptable levels of recall bias.

113 **Taylor, Tyler**

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Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentor: Mario Castro, MD, MPH

Impact of an Employer-based Individual and Group Smoking Cessation Program in St. Louis County

Taylor T; Ksaizek D; Castro M

Introduction: Smoking increases the risk for many disease states, increases mortality rates, and causes loss of productivity in the workplace. Nearly 1 in 4 people in Missouri currently smoke. Missouri has the lowest tax rate for cigarettes and the lowest public spending on smoking cessation. We propose to evaluate an employer based smoking cessation program sponsored by the St. Louis County Department of Health.

Methods: Group counseling sessions (n=68) were offered free of charge to six work sites in St. Louis County. Counseling was led by a trained counselor covering smoking cessation topics over 8 weeks. Individual counseling sessions (n=29) over the telephone or in person were offered free of charge to referred patients. Nicotine replacement therapy (NRT) was offered free of charge. A survey to capture self-report quit rates was administered before and after counseling and at 3 and 6 months. Participants that could not be contacted or whom did not complete subsequent group sessions were classified as relapsed.

Results: 28% (n=19) of group counseled employer-based participants quit at 3 months of follow-up compared to 54% (n=13) of individual counseled participants (p =<0.01). Group counseled patients have a higher prevalence of smoking one puff from a cigarette after quitting (84%, n=54) compared to individual counseled patients (63%, n=15) at the 3 month survey. At 6 months, individual counseling participants had a higher quit rate of 50% compared to group employer-based therapy 7%. Patients were more likely to try NRT (79%) than other prescription medication to quit smoking (21%). All data will be evaluated 6 months of follow-up (November 2012) to determine if smoking habits, NRT use, or other factors influenced quit rate among participants.

Conclusions: Employee-based smoking cessation provided on a one-on-one basis with NRT is more effective than group counseling.

043 **Williams, April**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Gammon Earhart, PT, PhD

Gait coordination in Parkinson disease: effects of altering step length and cadence

Williams AJ; Peterson DS; Earhart GM

Introduction: Freezing of Gait (FOG) is an inability to produce effective stepping during ambulation and can result in falls and decreased quality of life in people with Parkinson disease (PD). The mechanisms underlying FOG are poorly understood, but it has been proposed that cadence and step length may be important contributors. The aim of this study was to observe the effects of individually altering cadence and step length on gait coordination, which is associated with FOG. We used Phase Coordination Index (PCI), a measure of gait coordination that has been correlated with FOG severity. Our aim was to determine the effects of manipulating step length and cadence on gait coordination in those with PD who do and do not experience FOG (PD+FOG, PD-FOG), healthy older, and healthy young adults.

Methods: Participants with idiopathic PD (11 PD+FOG, 16 PD-FOG), 18 healthy older, and 19 healthy young adults walked under four conditions: Natural, Fast (+50% of preferred cadence), Small (-50% of preferred step length), and SmallFast (+50% cadence and -50% step length). Those with PD were placed in the PD+FOG group if they reported weekly or daily FOG episodes. Coordination (i.e. PCI) was measured for each participant during each condition and analyzed using a repeated measure ANOVA.

Results: No FOG episodes occurred. PCI values were different between groups ($p<0.001$), conditions ($p<0.001$), and an interaction effect was observed ($p=0.005$). Those with PD had worse coordination compared to healthy young during SmallFast ($p<0.0025$). Those with PD+FOG had worse coordination during SmallFast compared to healthy old ($p=0.0005$) and during Natural and Small compared to healthy young ($p<0.0025$). Further, those with PD+FOG had worse coordination during SmallFast compared to their Natural coordination ($p<0.0033$).

Conclusions: FOG is difficult to elicit within the laboratory or clinic and surrogate measures of FOG, such as gait coordination, are needed to facilitate research and treatment approaches. Coordination deficits can be identified in those with PD by having them walk with small steps and a fast cadence. However, further research is needed to determine if PCI is an appropriate measure to assess risk of FOG.

Doris Duke Clinical Research Fellowship

038 **London, Daniel A**

Doris Duke Clinical Research Fellowship
Department of Orthopaedic Surgery, Washington University in St. Louis School of Medicine
Mentor: Ryan Calfee, MD, MSc

Anatomic Relationships and Branching Patterns of the Ulnar Dorsal Cutaneous Nerve(s)

London DA; Root CG; Strauss N; Calfee RP

Introduction: During surgical exposure of the ulnar wrist, multiple longitudinal branches of the dorsal cutaneous ulnar nerve are expected and should be protected to avoid injury. The purpose of this study was to quantify the branching patterns of the dorsal cutaneous branches from the ulnar nerve at the wrist in relation to palpable landmarks to identify safe zones of dissection.

Methods: The dorsal cutaneous branches of the ulnar nerve were dissected in 28 unmatched fresh-frozen cadaver upper extremities. The ulnar nerve was identified in the forearm and dissection was continued distally identifying every dorsal cutaneous branch from origin to final branching at the level of the metacarpophalangeal joints. The number and location of branches were recorded, and relationships to the subcutaneous border of the ulnar head, the pisotriquetral joint, and the extensor carpi ulnaris (ECU) tendon were defined.

Results: Longitudinal branches of the dorsal cutaneous branch of the ulnar nerve coursed between the subcutaneous border of the ulnar head and the medial pisotriquetral joint in 27 of 28 specimens (96%). An average of 2 (range 1-4) branches was present at the level of the ulnocarpal joint. Only 8/28 (29%) of specimens had a single dorsal cutaneous nerve branch at the ulnocarpal joint. In 27 of 28 specimens (96%), all dorsal cutaneous branches remained volar to the subcutaneous border of the ulna. Branches crossed dorsal to the ECU tendon in 23 of 28 specimens (82%) at an average of 1.43 cm distal to the ulnocarpal joint.

Conclusions: Identification and protection of a single dorsal cutaneous nerve branch during ulnar-sided wrist surgery will not ensure nerve protection as multiple branches are frequently present at the level of the ulnocarpal joint. Certain arthroscopic portals and exposure of the ECU tendon can be expected to place dorsal cutaneous branches of the ulnar nerve at risk as the longitudinal nerve branches cross dorsally to the ECU tendon in the majority of cases. Based on our results we suggest always incising the skin only and spreading bluntly down to the capsule to avoid any damage to branches of the ulnar nerve.

David F. Silbert Summer Fellowship

122 **Aronson, Adam B**
Medical Student
David F Silbert Summer Fellowship
Summer Research Program
Section of Medical Oncology
Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentors: Ron Bose, MD, PhD; Matthew Ellis, MB, FRCP, PhD
Characterizing drug dose response curves for Her2 tyrosine kinase mutations
Aronson AB; Kavuri SM, Ellis MJ; Bose R
Introduction: Her2 tyrosine kinase gene amplification is widely recognized as a driving factor in 25% of human breast cancer cases. Cancer genome sequencing studies have led to the discovery of many mutations implicated in breast cancer, including several mutations within Her2. Tumors expressing these Her2 mutations behave like Her2-amplified tumors, despite not overexpressing Her2. The purpose of this study is to examine the pharmacological profile of these Her2 mutations with two FDA-approved anti-Her2 drugs (trastuzumab and lapatinib) and one new drug (neratinib, an irreversible inhibitor) currently in clinical trials.
Methods: Her2 mutations were inserted into MCF10A breast cells through pCFG5, a retroviral vector. Seven cell lines were made, each bearing a separate Her2 mutation. Cells were cultured in 96 well plates to grow in the presence of drug for 1 week, after which total cell metabolism was assessed via Alamar Blue assay.
Results: All of the Her2 mutations were only moderately sensitive to trastuzumab, and no significant differences in sensitivity were seen between mutations. Most of the Her2 mutations required 0.5 – 3 uM dose of lapatinib for growth inhibition, with the exception being L755S mutation, which was resistant to lapatinib and had an IC50 of >10 uM. All of the cell lines showed greater sensitivity to neratinib than lapatinib; with 4 of the mutations having IC50 of <2 nM and even the lapatinib-resistant L755S mutation having an IC50 of about 20 nM.
Conclusions: The Her2 mutations are very sensitive to neratinib, and this drug will soon be tested in a phase II clinical trial for Her2 mutation positive patients. Neratinib is an irreversible tyrosine kinase inhibitor, whereas lapatinib is a reversible tyrosine kinase inhibitor. This increased potency of neratinib is likely due to the fact that it forms a covalent adduct in the ATP binding site of Her2.

121 **Macaruso, Natalie**
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Mentor: Jason Weber, PhD
Role of nucleolin in gliomagenesis
Macaruso N; Weber J
Introduction: Human nucleolin (hNCL) is a nucleolar protein that is expressed in rapidly proliferating cells, including astrocytomas. It is a multifunctional protein that interacts with several other proteins related to cell growth and proliferation, is involved in the transcription of rDNA, and plays a role in the processing of rRNA. Although hNCL knockdown produces an anti-proliferative effect, the molecular mechanisms by which hNCL promotes cell growth are unknown. The purpose of this study is to explore those mechanisms by generating a panel of hNCL deletion mutants that target specific activities associated with different domains and measuring the ability of these mutants to rescue hNCL-knockdown glioblastoma cells.
Methods: Mutants were generated via site-directed mutagenesis in a pBabe-puro retroviral expression construct with FLAGx3-tagged hNCL inserted in the multiple cloning site. These mutants were nucleofected into U87 glioblastoma cells, and expression of the mutant proteins was examined by Western blot analysis. Mutants will be transduced into U87 cells with doxycycline-inducible hairpins that knockdown hNCL for knockdown/rescue analysis.
Results/Anticipated Results: Using site-directed mutagenesis, three deletion mutants—pBabe-ΔuPA, ΔRBD1, and ΔRBD4—were successfully created, and these were verified by sequencing. Western blot analysis indicated that these mutant constructs were capable of expressing the mutant proteins in U87 glioblastoma cells, which had noticeable deletions compared to wild-type hNCL. Knockdown/rescue analysis will indicate if these mutations are associated with changes in rates of proliferation compared to wild-type hNCL.
Conclusions: The Western blot result validates the viability of these mutants in a human cell line. The pBabe-ΔuPA mutant disrupts interaction between hNCL and urokinase, a protein associated with malignancy invasion and neovascularization. Each ΔRBD mutant deletes one of hNCL's four RNA-binding domains, through which hNCL interacts with rRNA. Knockdown/rescue analysis with these mutants and others will enhance understanding of the molecular pathways connecting hNCL to cell proliferation. Knowledge of these pathways may suggest targets for intervention in the treatment of glioblastomas and other astrocytomas.

Dean's Fellowship

No poster displayed

Anderson, Ryan
Medical Student
Dean's Fellowship
Summer Research Program
Department of Health Care Policy, Harvard Medical School
Mentor: J Michael McWilliams, MD, PhD

Relationship between quality of care and racial disparities in accountable care organizations

McWilliams JM; Anderson RE

Introduction: The Accountable Care Organization (ACO) model seeks to improve care quality and reduce cost. However, capital pressures may lead ACOs to form disproportionately in areas of affluence, limiting the ability of minorities and other vulnerable groups to benefit. This study examines who receives care from organizations eligible for ACO Shared Savings and Pioneer pilots; how does quality of care differ between racial groups; and what is the relationship between quality, racial inequity, and ACO eligibility?

Methods: A random sample of 5,457,951 Medicare beneficiaries were assigned to healthcare organizations according to ACO attribution rules using 2009 claims data. A subsample of diabetics and heart disease patients aged >=50 years was fitted to single and two-level linear regression models predicting completion of indicated disease-related screenings and AHRQ PQI measures of avoidable hospitalization.

Results: ACO-eligible beneficiaries were more female, white, and college-educated, and less likely to be on Medicaid, below the poverty line, or have multiple chronic conditions (all $p<0.001$). Racial disparities existed across all quality indicators. Disparities between blacks and whites were smaller in Pioneer-eligible vs. ineligible groups for retinal screening (1.2 vs 3.7%; $p<0.05$) and LDL-C testing (2.1 vs 4.0%; $p<0.05$), but not other measures. SSP-eligible and ineligible groups did not differ. In multilevel modeling, the disease-related PQI admission rate among whites was positively correlated ($R=0.39$; $p<0.05$) with disparity with blacks at the group level. No other measure showed group-level correlation between white quality and racial disparity.

Conclusions: Groups eligible for ACO pilots serve a smaller share of vulnerable populations, including minorities, the impoverished, and the chronically ill. Our results suggest that ACO-eligible groups have modest to no reduction in racial disparities vs. ineligible; further, little correlation was seen between improved quality and reduced disparity among ACO-eligibles. These findings suggest that ACO adoption will not necessarily improve racial disparities. This favors policies to make racial differences an explicit component of the ACO contract.

064 **Bakhsh, Wajeeh**
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Mentor: Matthew Dobbs, MD

Variables predictive of the need for extensive clubfoot surgery at a large tertiary institution

Miller N; Carry P; Graham S; Dobbs M; Bakhsh W

Introduction: Clubfoot is a prominent congenital defect with variable courses of treatment. The factors influencing the eventual need for extensive surgical correction have not yet been thoroughly explored. The purpose of this study is to correlate various aspects of a patient's course of treatment with the patient's outcome and eventual need for major surgery.

Methods: Data were gathered from clubfoot patients over the span of four years at two major tertiary institutions, including different aspects of the patient's treatment, any complications that occurred, and the eventual outcome. Kaplan Meier and Cox regression analyses were used to identify variables significantly associated with the probability of need for major surgery. Correction was made for patients with bilateral clubfoot via the Lin and Wei covariance matrix.

Anticipated Results: Given preliminary analyses, the anticipated results indicate the following variables are expected to correlate significantly with the need for major surgery: lack of percutaneous tenotomy, need for revision casting during bracing, and number of providers. Using Cox regression analyses, the first two variables show significance with [$p < 0.05$], and inverse and direct relationships respectively. The last variable, number of providers, has also shown strong, direct correlation. The number of patient visits where non-compliance was documented is marginally significant with a similar direct correlation.

Conclusions: The results of this study suggest that there are modifiable variables involved in the course of clubfoot treatment that correlate significantly with patient outcome as measured by the need for major corrective surgery. These variables have been confirmed through extensive data analysis at two major tertiary institutions, and highlight multiple possible relationships that can be exploited to improve clubfoot patient outcomes. A decrease in the number of physicians involved in treatment is associated with improved outcomes, as is a decrease in patient non-compliance during bracing or revision casting.

020 **Bayer, Chelsea**

Medical Student
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Mentor: Daniel Mamah, MD, MPE

Prevalence of psychotic and depressive symptoms in community sample of adolescents and young adults

Bayer CA; Mamah D

Introduction: It is believed by many physicians that early detection of schizophrenia risk symptoms could increase the chances of recovery, decrease the intensity of the symptoms and possibly prevent the initial psychosis warning signs from progressing to the actual disease. The Washington University Early Recognition Center Affectivity and Psychosis Screen (WERCAP Screen) was developed in order to identify youth at the highest risk for developing schizophrenia. The WERCAP Screen would be given to St. Louis youth in order to determine its validity as a psychosis risk assessment tool.

Methods: The WERCAP Screen has eight questions about depressive symptoms and eight questions about psychotic symptoms. It was administered to 173 youth ages 15-24 who were visiting the SPOT, a center that provides several services for youth in the area. The responses were translated into a numerical code and from this code, scores were calculated that determined their bipolar risk and psychosis risk. The scores were created in order to give equal weight to the severity and the frequency of the symptoms.

Results: The maximum score for both the bipolar and psychosis risk was 2. The bipolar symptoms were significantly more prevalent than the psychotic symptoms. Only 26.01% of subjects had a bipolar score of less than 0.50, indicating little to no risk, while 71.10% of subjects had psychotic scores of less than 0.50. A score that indicated high psychotic risk (greater than 1.00) was almost exclusively accompanied by a score that indicated high bipolar risk but the opposite was not true.

Conclusions: In order to better validate the WERCAP Screen and determine its success in identifying at risk youth, a Structured Interview for Psychosis-Risk Syndromes (SIPS) should be administered to the subjects. The risk determined by the SIPS should be compared to their WERCAP Screen score and used to determine a better window for low, medium and high risk scores. At this point, the scores that were designated to be high risk versus low risk were arbitrarily assigned but by using their SIPS risk, a more accurate assessment of risk could be assigned to their WERCAP score.

091 **Binagi, Samba G**

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Mentors: OrLando Yaroborough, PhD; Richard Kibbey, PhD; Philip Cryer, MD

Combining liquid chromatography, mass spectrometry, and differential Ion mobility separation for targeted metabolomics studies

Binagi NG; Yaroborough O; Kibbey RG

Introduction: Metabolomics is the study of the collection of metabolites in a cell, tissue, or organism. The metabolic state of an individual or organ sample is subject to many influences, including but not limited to genetics, behavior, disease state, and reflects what is happening on the short and long terms and at cellular and organismal levels. Among the greatest technological tools for metabolomics studies is Mass Spectroscopy. However, the technology identifies molecules by the ratio between their mass and charge. Though effective, the identification based on mass to charge ratio is insufficient in metabolic studies targeting pathways with many constitutional isomers like glycolysis and the citric acid cycle. Our lab seeks to establish a method for the combination of Liquid Chromatography/Mass Spectrometry (LC/MS) with Differential Ion Mobility Separation (DMS) to identify and quantitate metabolites for targeted metabolomics studies.

Methods: Aliquots of single compounds and of mixtures of compounds of interest were analyzed with varying LC/MS and DMS parameters. Chromatographic methods and DMS parameters were varied in the search for ways to differentiate isobaric compounds from one another.

Results: The three LC/MS methods showed reproducible identification and differentiation of most compounds of interest. However, separation of several sets of isobars was not achieved with LC/MS. Preliminary work with DMS shows that it is a promising solution to the problem of separating isomers.

Conclusions: Though incomplete, the results of this methodological research will likely improve the power of experimental targeted metabolics studies. Moreover, eventual clinical application of the LC/MS DMS methods could augment the specificity of laboratory work assessing patients' metabolomes. Moving forward, establishing and expanding a library of DMS parameters for the detection of compounds of interest is imperative.

112 **Bouchard, Brian**

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Division of Molecular and Medical Oncology
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Mentors: Hicham Baydoun, PhD; Lee Ratner, MD, PhD

Searching for determinants in HTLV-1 infection

Bouchard B; Baydoun H; Ratner L

Introduction: The Human T-Lymphotropic Virus I (HTLV-1) is the causative agent of adult T-cell lymphoma. One potential treatment of the viral infection is to stop the entry of de novo virus. However, the exact mechanism of virus attachment and entry remains elusive. Three main proteins were identified as potential receptors: glucose transporter 1 (GLUT1), neuropilin 1 (NRP1), and heparin sulfate proteoglycan (HSPG). Yet, the infection distribution of cell lines cannot be fully explained by the distribution of these three proteins alone. The purpose of this study is to explore additional protein candidates that may serve as determinants in HTLV-1 infection.

Methods: A cDNA library from a permissive cell line was tested, and a number of potential candidates were selected. We chose two established candidates (GLUT1 and NRP1), and two new candidates (FLOT1 and PRDX1) for further investigations. They were all cloned into the pIRES-GFP or p-Flag vectors and transfected into non-permissive cells for overexpression. The GFP and the flag-tag served for transfection screen and protein detection, respectively. We made pseudovirus particles with the envelope protein of three different viruses, HTLV1, MLV or VSVG. They each expressed the luciferase gene as a monitor for infection susceptibility. The pseudoviruses were used to infect the transfected cells and the luciferase activity was measured. Alternatively, we made stable permissive cells with downregulation of two transmembrane candidates (TMCO1 and TMED10) by RNA interference. These cell lines were infected with the same pseudovirus particles prepared above to assess the infection susceptibility.

Results: All overexpressed candidates showed a slight increase in luciferase activity, with NRP1 showing the greatest increase. The flag-tag vectors were successfully cloned and experiments with transfections using these clones are underway. TMED10 and TMCO1 were successfully inhibited by shRNA and luciferase activity showing a decrease in viral infection.

Conclusions: The slight changes in infectivity with TMED10 inhibition and with NRP1 and FLOT1 overexpression warrant further investigation. The new clone vector can be used to examine other candidate determinants.

052 **Bruce, Carl T**

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Mentors: Jose Pineda, MD; Dustin Ragan, PhD

Phase-contrast MRI measurement of cerebral blood flow in children: optimization and validation with arterial spin labeling

Bruce C; Pineda J; Ragan D

Introduction: Cerebral blood flow (CBF) is an important parameter to monitor in patients afflicted with central neurologic injury, but standard methods of perfusion measurement are often impractical in the critical care setting. An alternative approach estimates CBF based on the amount blood flowing through cerebral feeding arteries. The blood velocity (CBFv) and vessel size can be obtained quickly and accurately by phase-contrast MRI (PCM), but estimating CBF from CBFv also requires measuring brain volume. In this study, we investigated the accuracy of a PCM CBFv-based method of CBF measurement. We first established methods of automatic brain volume estimation by comparing three commonly used segmentation algorithms against the gold standard of manual segmentation. We then evaluated the agreement of global CBF measured using an optimized CBFv-based method with that measured directly using ASL.

Methods: Brain volume was estimated for 16 patients aged 1-18 years using three automated tools (FAST, SIENAX, and thresholding) and evaluated on the basis of agreement with manual segmentation. Flow measurements in the common carotid artery (CCA), vertebral artery (VA), and middle cerebral artery (MCA) were obtained using PCM and CBF was estimated using three different combinations of these vessels (CCA+VA; MCA+VA; MCA only). PCM CBF estimates for each vessel combination were compared with measurements obtained using ASL, which served as a reference. Agreement was assessed using Bland-Altman plots and Pearson correlation coefficients.

Results: Automated brain volume estimation using a thresholded BET method agreed best with the gold standard (R^2=0.939). Mean global CBF by ASL was 30 ± 8 mL/100g/min. Of the three vessel combinations used to estimate CBF with PCM, the one that included MCA blood flow alone showed particularly strong agreement with ASL (R^2=0.719, $p<0.001$), with mean CBF of 22 ± 7 mL/100g/min.

Conclusions: The results of this study suggest that CBFv-based methods of CBF estimation can provide information of similar quality to ASL without the encumbrances that limit the applicability of more sophisticated techniques in the critical care setting.

082 **Chollet, Madeleine B, PhD**

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Predicting PTSD in military personnel with mild traumatic brain injury

Chollet M; MacDonald CL; Brody DL

Introduction: Many military personnel who have served in the wars in Iraq and Afghanistan suffer from mild blast-related traumatic brain injury (mTBI). Individuals with mTBI may experience cognitive impairment and are nearly twice as likely to develop post-traumatic stress disorder (PTSD) as military personnel without mTBI. Previous studies using diffusion tensor imaging (DTI) have detected axonal injury in subjects with mTBI, but studies have not been completed using tract-based spatial statistics (TBSS), a methodologically rigorous whole brain approach. The purpose of this study was three-fold: (1) to determine if traumatic axonal injury in military personnel with mTBI can be detected using TBSS; (2) to verify positive TBSS findings using region-of-interest (ROI) analysis; and (3) to test for neuroanatomical correlates associated with PTSD severity using TBSS and ROI.

Methods: White matter integrity was assessed in 46 military personnel with mTBI and 18 controls using a combination of TBSS and ROI analysis.

Results: TBSS identified regions of positive fractional anisotropy (FA) in subjects with mTBI as compared to controls in diffuse regions of the brain with differences in FA most prominent in the superior frontal gyrus (SFG), temporal lobe (TL), and inferior longitudinal fasciculus (ILF). However, subsequent ROI analysis of these regions did not detect a significant difference in the relative anisotropy of these three regions between subjects with mTBI and controls. Neither TBSS nor ROI analysis found a significant correlation between CAPS score and anisotropy for subjects with mTBI.

Conclusions: Although TBSS identified differences in white matter integrity between subjects with mTBI and controls, it is unclear why FA was increased in certain regions and why differences in anisotropy were not detected using ROI analysis. The results of this study do, however, provide significant evidence that neither TBSS nor ROI analysis of the SFG, TL, or ILF can be used to predict which individuals will develop PTSD. Additional studies using a larger sample size should be completed to resolve these findings and to determine whether neuroanatomical markers for PTSD develop in the months following injury.

002 **Gamble, Paul**

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Mentor: Dennis Barbour, MD, PhD

Induced neural plasticity in the rat auditory cortex

Gamble P; Barbour D

Introduction: Neural plasticity is known to underlie cortical development and learning. However the extent to which an adult brain remains labile is not understood and methods of influencing plasticity are even less well known. Yet such methods offer promising therapies for stroke victims who often lose important motor and sensory functions as a result of cortical damage. The purpose of this study is to determine if we can affect functional connectivity changes in the rat auditory cortex using neuronally driven electrical stimulation. Changes of this sort would be an important first step towards the cortical 'rewiring' that could allow stroke victims to regain lost abilities.

Methods: Craniotomies were performed on well-anesthetized adult rats. Two tungsten electrodes were used to locate single unit signals which were confirmed to be auditory using tonal and bandwidth sound presentation protocols. Once two units with distinct receptive fields had been identified and characterized, the firing of one was used to trigger electrical stimulation through the other electrode. After a period, the stimulation was turned off and the units were re-characterized.

Anticipated Results: We expect the receptive field of the stimulated unit to come to resemble the receptive field of the driver unit. Currently, although having performed several experiments, this result has not been observed. We have however found a large transient increase in the correlation between the firing of the driver and the stimulated units.

Conclusions: This increase in correlation is a promising result. It suggests that the techniques we're using do in fact cause functional connectivity changes in the cortex. Achieving the larger goal of receptive field changes may be as simple as modifying the stimulation parameters - increasing the total stimulation period, or the temporal width or electrical amplitude of the stimulation itself. Although it is also possible that receptive field changes cannot be achieved in the acute case due to the effects of anesthesia. Relatedly, the induced correlation is observed to wash out over about an hour. To have therapeutic relevance, such changes would need to be much longer lasting. Chronic experiments using implanted electrodes should produce more permanent changes.

096 **Higgins, Stephanie**

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Sperm motility patterns: Lack of hyperactivation in sperm from SLO3 knockout mice may result from deficient Ca^{2+} entry

Higgins S; Santi C

Introduction: Mammalian sperm acquire fertilization ability only after capacitation, a maturational process occurring in the female genital tract. Capacitation results in several changes, one of which is the development of a distinctive motility pattern known as hyperactivation. Hyperactivation is characterized by asymmetrical (whip-like), high amplitude, and low frequency beating, and is required for sperm penetration of the oocyte zona pellucida. This study investigates the inability of sperm from SLO3 knockout mice to hyperactivate. SLO3 is a pH-sensitive potassium channel expressed only in mammalian testes. SLO3 -/- mice are male infertile, possibly in part because of a deficiency in hyperactivation.

Methods: Sperm from the cauda epididymis of wild type and SLO3-/- mice were collected and their motion recorded by the Hamilton-Thorne IVOS CASA machine. Sperm from both genotypes of mice were observed after three treatments: the addition of thimerosal, the addition of procaine, or exposure to capacitating conditions. Three motility parameters were analyzed to determine hyperactivation.

Results: Wild-type sperm show distinct hyperactivation after capacitation and after treatment with procaine and thimerosal. SLO3 -/- mutant sperm fail to hyperactivate after capacitation and also fail to hyperactivate after treatment with procaine. However, SLO3 mutant sperm do hyperactivate after treatment with thimerosal.

Conclusions: The results of this study show that SLO3 is necessary for hyperactivation under conditions that require calcium entry. Hyperactivation resulting from either procaine treatment or capacitating conditions requires the entry of calcium ions, and SLO3 mutants do not hyperactivate under these conditions. However, thimerosal, an agent that releases intracellular calcium, induces hyperactivation in SLO3 mutants. Thus it is likely that the SLO3 channel is crucial in the control of calcium entry. These results suggest that SLO3-controlled hyperpolarization of the sperm membrane provides an increased driving force for calcium entry that is necessary for hyperactivation. However, more studies are needed to elucidate the exact mechanism.

118 **Jiang, Allan**

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Mentor: Timothy A Graubert, MD

A next-generation sequencing panel for familial myelodysplastic syndromes and acute myeloid leukemia

Jiang A; Shen D; Graubert TA

Introduction: The occurrence of multiple cases of myelodysplastic syndromes (MDS) and/or acute myeloid leukemia (AML) among first-degree relatives is very rare. MDS and AML are known to arise from well-characterized genetic syndromes. In recent years, variants in *CEBPA*, *GATA2*, and *RUNX1* have also been found to cause familial MDS/AML. However, many affected families remain unexplained, and there is no standard procedure for genetic testing of these families. The purpose of this study is to develop and validate a robust yet cost-effective method to sequence genes that cause familial MDS/AML.

Methods: Twelve genes were selected for this panel. 196 probes spanning the coding sequences of these genes were ordered from Integrated DNA Technologies. In a pilot study, skin biopsies were taken from seven subjects belonging to three kindreds with familial MDS/AML. DNA from each sample was extracted, fragmented, and hybridized with the probes. Captured DNA was washed, amplified, and tagged with oligonucleotide sequences unique to each individual. All DNA was then combined into a single library for paired-end sequencing by MiSeq (Illumina). Reads were aligned to the reference genome; single nucleotide variants and insertion/deletion events were identified using standard tools.

Results: 125 of the 133 sequenced exons had ≥95% of base pairs with at least 20X coverage for six or seven individuals. The panel detected six distinct missense variants shared by first-degree relatives. Five were polymorphisms with allele frequencies of 1.6-62.8% in the normal population. The other variant was c.1061C>T (p.T354M) in *GATA2*, which was heterozygous in both sequenced subjects of one family. This variant has previously been reported as causative in multiple affected families.

Conclusions: This panel appears to be effective in sequencing the 12 genes, as evidenced by the coverage data and the detection of a known deleterious variant. Future plans include refinement of the panel, and whole-genome sequencing of families with no variants identified by the panel. It is hoped that these efforts will help lead to new insights on the genetic and molecular mechanisms of leukemogenesis.

No poster displayed

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Mentor: Varun Puri, MD

Vascular complications in lung transplantation–Are they avoidable? An institutional review

Johnson C; Puri V

Introduction: Lung transplantation (LTx) is a widely accepted therapy for end-stage lung disease. Vascular complications can result in catastrophic outcomes varying from intraoperative anastomoses revision, to major hemorrhage, or acute retransplantation. We hypothesized that individual case analyses could identify potentially avoidable key technical or decision points that resulted in the vascular complications.

Methods: We performed a retrospective review of patients undergoing LTx at a single institution. A prospectively maintained database was queried and missing information was extracted by chart review. A root cause analysis was performed to elucidate the cause of the complication in each individual case. Common occurrences of complication were identified and recommendations of avoidance were proposed.

Results: Between 1999 and 2012, 760 adults underwent LTx .15 of 760 patients developed major vascular complications from LTx. These were: pulmonary venous pulmonary arterial, and aortic. Root cause analysis revealed that inadequate exposure during dissection of the pulmonary veins, inadequate attention to endocardium to endocardium apposition in the venous anastomosis, and accepting and leaving the operating room with a marginally patent anastomosis were the common causes of venous complications. Pulmonary arterial complications led to major hemorrhage, and need for revision of anastomosis. Aortic injury resulted in dissection of an aorta during a reoperative situation and a cannulation for cardiopulmonary bypass.

Conclusions: Pulmonary venous anastomosis should be constructed meticulously with endocardial approximation and exclusion of atrial muscle. Anastomotic patency should be confirmed visually and with echocardiography. Exposure of the pulmonary veins must be optimized. The poor quality of pulmonary arteries must be recognized in patients on chronic steroids or with hypertension, and clamp application must be gentle.

Catastrophic vascular complications are rare in LTx. Common themes are identifiable for such complications and careful planning and attention to technical detail may prevent these complications.

036

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Mentor: Ryan Calfee, MD

Predictors of failure of surgical treatment of the ulnar nerve for cubital tunnel syndrome

Krogue JD; Calfee RP

Introduction: Cubital tunnel syndrome (CuTS) is the second most common compression neuropathy of the upper extremity, affecting 75,000 each year. Despite its incidence and the 25% failure rate of surgical treatment, there is a paucity of literature exploring predictors of surgical outcomes. In this study our aim was to identify elements of a patient's history and presentation that reliably predict surgical success.

Methods: We queried our databases for surgeries performed for CuTS surgery and categorized them as primary or revision surgeries. We then collected information about the patient's history and presentation at the time of surgery, and in the case of revision surgeries, at the time of their original surgery. Univariate analysis was conducted to pick variables that were then used in multivariate logistic regression.

Results: From January 2006-July 2011, 71 revision surgeries met our inclusion criteria, and 155 non-revision surgeries were selected as controls. After conducting logistic regression using variables that were significant in univariate analysis and those that weren't significant but would be expected clinically to be predictive, only those receiving in situ decompression ($p=.002$, $OR=4.20$) and receiving other surgery concurrently with CuTS surgery ($p=.008$, $OR=2.81$) were significantly associated with surgical failure.

Conclusions: Our study casts doubt on the predictive value of many factors commonly thought to predict surgical success, including age, sex, BMI, tobacco use, diabetes status, symptom duration, and nerve conduction velocity. Additionally, we found that patients who received in situ decompression were much more likely than those who received transposition or epicondylectomy to need revision surgery. Unfortunately, we were unable to look at pre-operative symptom type and severity as predictors because of inconsistent inclusion in our patient records. High-quality prospective studies are needed to confirm our results and to ascertain the predictive abilities of symptom type and severity.

018 **Lin, Amber**

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Mentor: Deanna Barch, PhD

Jitter orientation visual integration paradigm development for use in multi-site clinical trials

Lin A; Barch D

Introduction: Research in cognitive neuroscience has identified many promising imaging paradigms for measuring the neural correlates of cognitive deficits present in schizophrenia. The Cognitive Neuroscience Task Reliability & Clinical Applications Consortium (CNTRACs) was designed to translate these paradigms into useable clinical trial methods. This project focused on the Jitter Orientation Visual Integration (JOVI) task, which assesses visual integration, an early component of visual processing known to be impaired in schizophrenia.

Methods: Individuals with schizophrenia and healthy controls from five different sites underwent fMRI while performing the JOVI. The JOVI asks participants to decide whether a contour stimulus is pointing to the left or right. Stimuli orientation is randomly jittered + or – 0°, 7-8°, 9-10°, 11-12°, 13-14°, or 15-16°. The ability of the visual system to rapidly form the long-range, excitatory, context-dependent circuits that allow for visual integration can be probed by examining performance across these conditions. Quality control processing of the fMRI data from all 215 sessions included field map corrections, registration of each brain to a standard brain atlas, and measuring SNR and movement across sites. Maps of brain activation were created for the controls of each site and a linear contrast across levels was created for each site then compared to one for the overall group.

Results: Validation analyses in the control subjects identified a number of regions showing a linear increase in activity as a function of jitter orientation, including primary and secondary visual processing areas, as well as visual attention and top down control areas in prefrontal cortex. Analyses indicate consistent activation across sites.

Conclusions: There is a strong linear effect of activation across jitter levels in the visual cortex and areas of the parietal/frontal lobes involved with decision-making. Examination of the basic linear contrast suggests activation is consistent across all five sites. These results indicate that the JOVI task is a valid paradigm for testing early visual processing. Future analyses will focus on comparisons across diagnostic groups and reliability over time.

092 **Mah, Annelise**

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Mentor: Michael Diamond, MD, PhD

Cloning of interferon-stimulated gene IFIT1 into the TC-83 Venezuelan equine encephalitis virus

Mah A; Hyde J; Brien J; White J; Diamond MS

Introduction: Type I interferons induce a massive antiviral program that is crucial to limiting viral replication; IFIT1 (ISG56) is one of the most highly upregulated of these genes. Data suggest that viruses such as TC-83 lacking 2'O-methylation, a common cellular "self" signal, are vulnerable to the antiviral effects of IFIT1. Thus, when IFIT1 is knocked out, the pathogenicity of the usually-attenuated TC-83 is restored. To explore the role of IFIT1 in restricting viral replication and to potentially identify viral resistant mutants, we created an IFIT1-expressing TC-83 virus.

Methods: IFIT1 was inserted behind the first of two 26S subgenomic promoters in a modified TC-83 virus-expressing plasmid. Cloning was accomplished by PCR and restriction digestion techniques.

Results: Two plasmids were created: one that expresses the normal IFIT1 gene and another that is compatible with the Gateway system. This second plasmid will be used to insert tagged IFIT1 and other genes of interest into the TC-83 virus.

Conclusions: This TC-83-IFIT1 plasmid will be used to produce infectious virus, and this virus will be used to infect IFIT1 knock-out cell lines and mice. Low cytotoxicity/pathogenicity will confirm that IFIT1 is sufficient for inhibition of TC-83 replication. During the course of the infection, viruses may overcome IFIT1 inhibition—sequencing these escape mutants will reveal segments of IFIT1 necessary for antiviral action or IFIT1's interdependence with other viral replication factors. Understanding the mechanism of IFIT1 and other interferon-stimulated genes should allow development of new antiviral drugs with fewer side effects than interferon.

075 **Martin, Lauren TJ**
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Mentor: William C Chapman, MD, FACS

A novel antagonist of CD47 in reducing hepatic ischemia-reperfusion injury

Martin L; Chen C; DuBray B; Manning P; Chapman WC

Introduction: The goal of this project is to characterize a novel monoclonal antibody (400mAb) against CD47, a cell surface thrombopondin-1 (TSP1) receptor, previously implicated in mediating hepatic ischemia-reperfusion injury (IRI) during solid organ transplantation. We hypothesized specifically that in a murine model 400 CD47-mAb would result in a significant decrease in hepatocellular injury after prolonged ischemia as measured by transaminase level.

Methods: Each C57BL/6 mice received either 5mg/kg (125ug/100ul for 25 g mouse) of IgG2a (control) or 400 CD47-mAb, a mouse anti-human/mouse CD47 monoclonal antibody, intravenously to block the TSP1/CD47 interaction. To simulate transplantation, an ex vivo organ culture model of liver ischemia was utilized. After circulation of the antibody for 15 minutes, liver biopsies were taken under sterile conditions, placed individually in wells containing 1 mL of hepatocyte medium, and cultured for 24 hours. Fresh medium was then added and the liver cubes were placed into an anaerobic chamber for 60 minutes (ischemia phase). The biopsies were brought to normoxic conditions for 6 hours (reperfusion phase). Conditioned media and liver tissue were then analyzed for hepatocellular injury by measuring ALT and AST.

Results: The ALT and AST values in the medium from animals treated with CD47mAb were not significantly decreased (ALT p value= 0.08, AST p value= 0.07).

Conclusions: The data suggest that 400 CD47-mAb ameliorates hepatic ischemia-reperfusion injury, however further studies should be performed.

No poster displayed

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Mentor: Susan Culican, MD, PhD

A proteomics-based search for endogenous neuroprotective proteins in retinal ganglion cells

Onyewuchi C; Lamb R; Culican S

Introduction: PHR1 is an E3 ubiquitin ligase that regulates mapping of retinal ganglion cell (RGC) axons to the brain. A proteomics-based analysis of *Phr1* RGC knockout (*Phr1-rko*) and wild-type (WT) optic nerves of mice identified proteins that were differentially expressed. One of such proteins, 14-3-3-ζ, is upregulated in both RGCs of *Phr1-rko* mice and RGCs of rats subjected to ocular hypertension, suggesting that it plays a role in RGC injury. To test whether RGCs in *Phr1-rko* mice are similarly susceptible to injury, RGCs were subjected to axotomy and survival was assessed. The revelation was that RGCs in the *Phr1-rko* group were relatively protected compared to RGCs in the WT group. This caused us to hypothesize that the loss of PHR1 in RGCs results in upregulation of neuroprotective proteins.

Methods: To identify proteins that PHR1 regulates that might account for neuroprotection following RGC injury we decided to compare *Phr1-rko* and WT mice RGCs using proteomics-based analysis. We pooled retinas from multiple mice in order to obtain ≥ 100 µg of protein necessary to resolve differences in low abundance proteins. We separated the RGCs from the other retinal cells using a postnatal neuron dissociation and cell purification system from Miltenyi Biotec. The isolated RGC fraction was subjected to cell lysis and protein extraction in a mass spectrometry compatible detergent. The extracted RGC proteins were then submitted to the Proteomics Core for analysis.

Results: Proteomics-based analysis will reveal differential protein expression between *Phr1-rko* and WT RGCs. We expect to deduce from the results the proteins that may be involved in endogenous neuroprotection of RGCs.

Conclusions: PHR1 may be implicated in endogenous neuroprotection of RGCs. Understanding the mechanisms of endogenous neuroprotection that defend neuronal cells against injury will help in efforts geared toward devising therapeutic strategies for glaucoma and other retinal degenerative disorders.

No poster displayed

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Mentor: Varun Puri, MD

Compare/Contrast adult and pediatric lung transplants in patients with cystic fibrosis: streamlining treatment and trending outcomes over time

Osunsanmi BM; Puri V

Introduction: Cystic Fibrosis (CF) is a common disease indication for lung transplant. Lung transplants can extend the life of cystic fibrosis patients with end stage lung disease. The objective of our research was to perform a retrospective analysis of patients undergoing lung transplant at Barnes-Jewish Hospital. The study contains two parts. Part 1 examined two groups of adult CF patients over a 12 year period to see whether or not outcomes are improving. Part 2 of the study will compare adult and pediatric CF patients who underwent transplant at Barnes Jewish Hospital in order to understand differences and similarities in outcomes and treatment. The goal of the study is to create recommendations to transplant programs and streamline the treatment of CF patients.

Methods: The hospital's electronic database was utilized to screen for adult and pediatric CF patients who received lung transplants between 1999 and 2012. Data and results for part 2 are to be collected and analyzed at a later date. Data collected and analyzed for part 1 included preoperative, perioperative, and postoperative variables for each patient. A total of 139 adult CF patients underwent lung transplant between 1999 and 2012. Those patients were split evenly into two groups.

Results: Preliminary data demonstrate that on average patients from Group 2 had longer stays in the intensive care unit (ICU), spent more time on a ventilator after surgery, and had more comorbidities preoperatively. This coincided with the data showing that 1, 3, and 5 year survival rates of patients in Group 2 were lower than those in Group 1.

Conclusions: Over the 12 year period, survival outcomes have seen a slight decrease. However, the data have its limitations in that not all patients had information for each variable. Future studies should investigate the effects of patient compliance to strict post operative regimen and duration of operation on survival outcomes.

127 **Perry, Andrew**
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Precision and reproducibility of hippocampal segmentations by FreeSurfer software and High Dimensional Mapping-Large Deformation (HDM-LD)-based segmentation

Perry AS; Hogan RE; Maccotta L

Introduction: Segmentations of the hippocampus based on magnetic resonance (MR) imaging are useful in diagnosis and treatment of patients with temporal lobe epilepsy, and other neuropsychiatric disorders. There are numerous automated processes to perform this segmentation, including HDM-LD and FreeSurfer based segmentations. The purpose of this study is to examine the precision and reproducibility of these techniques and the effects of acquisition protocol.

Methods: A group of five patients, with normal brain function, underwent two sets of MR scans on different dates. Each set consisted of scans using the 3 different T-1-weighted volumetric protocols, referred to as protocols A, B, and C. Acquisition parameters for protocols A, B, and C are as follows: Protocol A: TR = 14, TE = 3, flip angle = 30, voxel dimensions 0.859 x 0.859 x 1.5 mm, field of view 22 x 22 cm, matrix size 256 x 256. Protocol B: TR = 8.8, TE = 1.8, flip angle = 30, voxel dimensions 0.742 x 0.742 x 1.5mm, field of view 38 x 38 cm, matrix size 512 x 512. Protocol C: TR = 8, TE = 3, flip angle = 30, voxel dimensions 1.172 x 1.172 x 1.172, field of view 30 x 30 cm, matrix size 256x256. The hippocampi were segmented and measured using the HDM-LD technique and FreeSurfer software. Results were calculated by comparing total hippocampal volume and percentage overlap of segmentations.

Results: The average differences in volume for scans analyzed by HDM-LD segmentation are as follows: protocol A: 150 mm^3; protocol B: 80 mm^3; protocol C: 155 mm^3. The average difference in volume for scans analyzed by FreeSurfer are as follows: protocol A: 343 mm^3; protocol B: 256 mm^3; protocol C: 353 mm^3. The test-retest percent overlap was consistent across protocols; all overlapped by over 90%.

Conclusions: While both segmentation techniques isolate approximately the same volume across acquisition protocols, there is large variability in the average difference across sequences. Protocol B appears to give the most consistent results with the average hippocampal volumetric test-retest difference being the lowest among the three protocols at 80 mm^3.

100 **Shin, Nicole**

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Evaluation of a teach-back intervention with discharge instructions among emergency patients with limited health literacy

Shin N; Griffey RT

Introduction: Limited health literacy (LHL) is an increasingly recognized factor impacting health outcomes in the emergency department. It has been demonstrated that many patients with LHL have difficulty understanding their ED discharge instructions and may be unaware of their comprehension deficits. A promising approach using the teach-back method has not been studied in the ED setting for its potential impact on comprehension. The purpose of this study is to evaluate the impact of the teach-back method on the ED patients' self-reported comprehension of the discharge instructions.

Methods: 240 ED patients with LHL as determined by a score of <=6 on the REALM-R test participated in the study. They were randomized to receive either the standard or the teach-back method of discharge instructions followed by an interview covering four major domains: diagnosis, ED care, home care, and return instructions. The patient awareness of comprehension will be assessed by concordance ratings involving the self-ratings of comprehension and the objective measure of comprehension. The objective measure of comprehension will be obtained by comparing patient recall of discharge instructions and information obtained from charge review.

Anticipated Results: Preliminary results show that 52 (19%) teach-back and 95 (29%) control patients reported perceived deficit in comprehension and 24 (9%) teach-back and 40 (12%) control patients reported perceived difficulty. We anticipate that there will be higher than partial concordance between perceived and actual comprehension deficiency/difficulty among teach-back patients and partial or lower concordance between perceived and actual comprehension deficiency/difficulty among control patients.

Conclusions: The preliminary results show that patients who received the teach-back method are less likely to report that they have deficient comprehension or have difficulty understanding compared to control. Further analysis will show whether the teach-back method not only instills confidence in perceived comprehension but also helps patients accurately identify comprehension deficits and difficulty when they are present.

111 **Tien, Vivian, MS**

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Exploring the tolerability of fluoroquinolones as latent TB treatment in liver transplant candidates

Tien V; Callister D; Robilotti EV; Ho DY

Introduction: Recipients of solid organ transplants under immunosuppressive therapy are at high risk of developing opportunistic infections. In particular, reactivation of latent tuberculosis (TB) represents a unique challenge in candidates for liver transplant. Treatment of this infection is particularly challenging because standard therapies like isoniazid and rifampin are associated with significant hepatotoxicity or numerous drug interactions. Fluoroquinolones (FQs) have been shown to have anti-TB activity, but there has not been a systematic review of their use in this patient population. Thus, the purpose of this study is to examine latent TB treatment regimens of liver transplant candidates at Stanford Medical Center, focusing on the tolerability of FQ as treatment for latent TB.

Methods: Retrospective chart review of a set of 784 liver transplant candidates presenting to the Stanford University Medical Center from 2006-2012.

Results: Of 784 liver transplant candidates, 94 (12%) had documented positive Quantiferon test results suggesting latent TB infection. Infectious Diseases saw 63 of these patients and recommended treatment for 55 of them. The FQs levofloxacin or moxifloxacin were recommended for 60% of patients, generally due to severity of liver disease and surmised inability to tolerate standard therapies. Ultimately, 23 patients, 62% of those treated with any drug, pursued FQ treatment. The majority tolerated FQs well. Notably, 2 cases of C. difficile-associated diarrhea were reported. In only 3 cases were FQs discontinued due to side effects like tendonitis, GI discomfort, and general malaise.

Conclusions: While data collection and analysis is ongoing, preliminary results suggest that fluoroquinolones are well tolerated by liver transplant candidates. Due to the limitations of our data, we cannot draw any conclusions regarding the efficacy of FQ against TB reactivation post-transplant. These results make progress toward our ultimate goal of determining treatment guidelines in this special patient population.

076 **Um, Grace**

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Department of Surgery, Division of Plastic and Reconstructive Surgery, University of Washington
Mentors: Billanna Hwang, MPH; David W Mathes, MD, FACS; Scott Luhmann, MD

Upregulation of Th1-type chemokine expression in vascularized composite allograft rejection

Um G; Hwang B; Mathes DM; Storb R; Luhmann S

Introduction: Our goal is to develop more practical methods for inducing immunologic tolerance to organ transplants without the need for chronic immunosuppression, thereby significantly impacting the risk-benefit ratio of tissue transplants and allowing for more widespread use of VCA in the reconstruction of lost limbs and severe facial deformities. The role of chemokines—directors of leukocyte traffic—in the pathophysiology of transplant rejection presents an opportunity for intervention. We focused on differential expression of Th1-type chemokines associated with allograft rejection in DLA-single haplotype-mismatched canines that tolerated or rejected their VCA.

Methods: Donor peripheral blood stem cells (PBSC) were infused IV into the recipient within 4 hours of conditioning (350 cGy TBI) and VCA transplant. Two recipients were not given PBSC and were expected to reject. All dogs were treated with post-graft immunosuppression for 72 days on CSP and 56 days on MMF. Serial open biopsies of graft skin and muscle were taken from 15 dogs (6 Normal, 4 Tolerant, 5 Rejecting). Quantitative real-time RT-PCR was performed on cDNA synthesized from tissue total RNA to determine relative gene expression.

Results: Initial analysis shows higher expression of CCR5, CXCL10, and CXCR3 in dogs that rejected their grafts. CXCR3 has previously shown in the literature to be linked with cases of acute organ transplant rejection. Further statistical analysis is ongoing at this time.

Conclusions: The mechanistic findings from this study can be used to target specific chemokines known to be upregulated in the inflammatory T cell response. The presence of a Th1 chemokine in the skin such as CXCR3 could be blocked with an antibody to discourage transplant rejection, or chemokine expression profiles could be manipulated to induce donor immune cell tolerance to host tissue alloantigens. Our large animal model directly helps to address the application of this technique to a clinically relevant model for VCA transplantation.

028 **Velloze, Stephanie M**

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The impact of maternal-daughter involvement and discussions on sexual decision making

Velloze SM; Merritt DF

Introduction: The 2011 Youth Risk Behavior Surveillance Survey found that nearly half of high school students reporting having engaged in sexual intercourse. Many fail to use contraception and are prone to sexually transmitted infections. Previous studies have shown that parent-adolescent closeness and sexual communication are protective factors against adolescent sexual risk-taking. We sought to examine how parent-child communications about sexual topics and certain maternal characteristics correlate to adolescent sexual initiation.

Methods: Data were taken from a self-administered de-identified questionnaire of 282 adolescent-guardian dyads distributed in two Midwestern Obstetrics and Gynecology clinics. STATA 11 was used for all statistical analysis.

Results: 82% of dyads agreed that they had discussed sex; the majority also agreed on what topics were discussed. For those dyads that gave concordant answers, 64.66% of adolescents were abstinent; of those who did not give concordant answers, 82% of adolescents were abstinent. Of those with concordant answers, 74.39% of parents guessed correctly within two years at what age their daughters had become sexually active, whereas of those that did not agree they had discussed sex, only 44.44% of parents correctly guessed their daughters' age at sexual initiation. Additionally, 78.26% had concordant responses on parental attitudes about adolescent sexual initiation. On average, adolescents reported sexual initiation at two years younger than their mothers were at sexual initiation. Mothers with abstinent daughters were on average one year older at sexual initiation than mothers with sexually-active daughters were.

Conclusions: Contrary to expectations, in dyads where adolescents and parents agreed they had discussed sex, the adolescents were not more likely to be abstinent. If concordant answers were given, parents were more able to correctly report their daughter's age at sexual initiation, perhaps because the parent-adolescent relationship is closer and communication about sexual issues is more thorough. Daughters were overall younger than mothers at sexual initiation, but the older the mother was at sexual initiation, the older the daughter was as well.

102 **Vyhmeister, Ross**

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Reasons for incident hospitalization in adult patients with repaired tetralogy of fallot

Vyhmeister R; Cedars A

Introduction: Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart defect. It is known that patients with repaired ToF are predisposed to pulmonary and tricuspid valve dysfunction, right and left ventricular failure, and arrhythmia. The relative incidence of each of these sequelae in the repaired ToF population has not been recently studied. Identifying reasons for hospitalization in this patient group should facilitate the development of therapeutic strategies targeted to patients identified as at-risk.

Methods: The records for patients diagnosed with Tetralogy of Fallot in the existing adult congenital heart disease database at a single institution were retrospectively screened for incident hospitalizations. Multiple clinical data points were simultaneously queried.

Results: Overall, patients with ToF had an average of 0.44 admissions per patient year. The most common discharge diagnoses were pulmonary valve replacement surgery, chest pain, and labor and delivery, accounting for 12.5%, 6.0%, and 5.6% respectively. Pulmonary valve replacement surgery was performed in 34.9% of patients at an average age of 33.2 years. This procedure correlated with decreased hospitalization, with admission rates dropping from 0.75 to 0.57 admissions per patient year following surgery. Overall admission rates were highest for patients who had the procedure done between the ages of 40-49 years with an average of 0.71 admissions per patient year. In contrast, patients who had the procedure done between the ages of 20-29 years had the lowest overall admission rate of 0.30 admissions per patient year.

Conclusions: The results of this study suggest that planned admissions for either pulmonary valve replacement or pregnancy account for 18.1% of all admissions in repaired ToF. Furthermore, the present data indicate that earlier pulmonary valve replacement is beneficial in preventing future hospitalizations. This may have implications for clinical practice and timing of pulmonary valve replacement in ToF.

024 **Wichterman, Christian**

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Glaucoma severity as a predictor for driving difficulty

Wichterman CM; Bhorade AM; Wilson B; Zheng L

Introduction: Patients suffering from glaucoma report higher rates of driving difficulty and cessation. Less is known, however, about what conditions of driving are most affected by glaucoma and at what stage of disease these difficulties become most apparent.

Methods: Patients between the ages of 55 and 90 years old with bilateral glaucoma and no other major ocular diseases in addition to age and gender matched controls were recruited from Washington University School of Medicine clinics. Using the Glaucoma Staging Scale on the HVF 24-2 of their better eye, glaucoma severity was classified as mild, moderate, or advanced. ETDRS distance visual acuity, Lighthouse near visual acuity, and Pelli-Robson contrast sensitivity were also taken on each participant. A Driving Habits Questionnaire was given to current drivers asking if they have driven "During the past 3 months" in each of 8 driving conditions, and if so, whether it was with extreme, moderate, little, or no difficulty. For analysis, patient responses were dichotomized into "no difficulty" if they perform the task and report no difficulty, and "any difficulty" if they report some difficulty or avoid the condition. Analysis looked at the correlation between reported difficulty with each task and glaucoma stage. The other measures of visual function were also correlated with glaucoma severity.

Results: There was a statistically significant correlation ($p<.05$) between glaucoma severity and reported driving difficulty for all 8 driving conditions. For each driving task, reported difficulty increased with increasing glaucoma stage with the largest jump in difficulty occurring in the advanced glaucoma category. Significant correlations were also found between the other measures of vision and reported difficulty.

Conclusions: A strong correlation was found between glaucoma severity and reported difficulty with driving at night, in rain, alone, during traffic, during rush hour, on the interstate, making left hand turns, and parallel parking. Further analysis on the specific type of vision loss could provide more information on the types of driving that become difficult for each patient.

094 **Xiao, Qi**

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Structural studies of tyrosine kinases by fast photochemical oxidation of protein (FPOP) protein footprinting methodology

Xiao Q; Zhang H; Rohrs H; Gross M

Introduction: FPOP is a protein foot-printing method that modifies proteins on the microsecond time scale. Highly reactive hydroxyl radicals produced by laser photolysis of hydrogen peroxide oxidatively modify the side chains of approximately one-half the common amino acids. The short labeling exposure ensures that only solvent-accessible residues are modified. FPOP is coupled with Mass Spectroscopy (MS) to quantify modifications at the amino acid level. This information provides details about protein structure and interactions with ligands. Despite the great potential of MS, many laboratories are struggling with data analysis. The complexity of the data analysis stems from the large number of experiments that can be performed by various mass spectrometers. Her3 and Her4 are receptor tyrosine kinase of the EGFR family. Mutation affecting EGFR expression or activity could result in cancer. In this project, FPOP, MS, and a new data processing method were used to elucidate structural information of Her3 and Her4 and to test new software for speeding up data analysis.
Methods: The data used for this study were previously generated using FPOP and MS equipment in the Washington University Mass Spectrometry Resource. The data were analyzed using new software (ProtMapMS2, Neoproteomics, Cleveland, OH) and the results were compared to those obtained using the standard approach which includes database searching (Mascot, Oxford, UK) coupled with alignment procedures (Progenesis, Nonlinear Dynamics, Durham, NC).
Results: The data analysis determined the solvent-accessible and protected regions of Her3 and Her4. The new software was found to be a viable alternative to the traditional analysis method. The new software also provided higher throughput and a more straightforward data analysis workflow.
Conclusions: The results of this study confirmed that FPOP can be used to obtain structural information of proteins in relative high throughput with a new data analysis workflow. This experiment has demonstrated that ProtMapMS2 can offer a fast and straightforward way to analyze the data obtained from mass spectroscopy experiments.

032 **Xu, Wen**

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Mentors: Alex Evers, MD; Ziwei Chen, PhD

Proteomic profiling of neurosteroids-target protein

Xu WZ; Chen ZW; Evers AS

Introduction: Certain endogenous pregnane steroids and their synthetic analogues (broadly termed neurosteroids) are potent, rapidly acting intravenous anesthetics in vertebrates. The proteins currently known to specifically interact with neurosteroids have been identified by hypothesis-directed functional studies ($GABA_A$ receptors) or non-comprehensive screening (e.g. VDAC, tubulin). This study is aimed to identify neurosteroid–modified peptides from rat brain that have been labeled with neurosteroid analogue photolabeling reagents using global ("shotgun") proteomic techniques.
Methods: Rat brain membrane proteins were photolabeled with an alkyne-tagged neurosteroid analogue photolabeling reagent, KK-123, or a non-alkyne homolog, 6-AziP, as a control. The proteins were solubilized in detergent buffer. Endogenous biotinylated proteins were removed from the lysate using streptavidin-agarose affinity beads. The proteins bound to these beads were digested with trypsin to analyze the endogenously biotinylated proteins in brain. The photolabeled proteins were then coupled to an azide-biotin biolinker using a copper-catalyzed cycloaddition (click chemistry) reaction and immobilized on fresh streptavidin-agarose beads. The immobilized proteins were then extensively washed and digested with trypsin. The resulting digests were analyzed using liquid-chromatography-mass spectrometry (LC-MS). The proteins were identified by searching the sequences against a genome-derived rat protein database.
Anticipated Results: We successfully identified four endogenous carboxylases, which are known to contain biotin as cofactor. We anticipate that we will be able to identify the neurosteroid-binding proteins that were photolabeled with the click chemistry-tagged neurosteroid analogue photolabeling reagent, KK-123. The samples are under analysis in the proteomic facility.
Conclusions: The results of this experiment confirmed the known biotinylated carboxylases in rat brain. Furthermore, the use of a click chemistry-tagged neurosteroid photolabeling reagent in a shotgun proteomic approach allows the systematic identification of neurosteroid-binding proteins, and may lead to previously unknown pharmacological targets.

084 **Zantow, Emily W**

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Program development of surgical skills milestones for senior medical students matching in a surgical internship

Zantow EW; Woodhouse J; Brunt LM

Introduction: Surgical skills preparation courses given in the spring of the 4th year lead to improvements in basic suturing and knot tying skills among medical students entering a surgical internship. However, most students still do not reach proficiency goals in performance. We hypothesize that a proficiency based curriculum given at the beginning of the 4th year should enhance students' ability to achieve performance milestones in basic suturing and laparoscopic skills.

Methods: Sixteen 4th-year medical students planning to match in a surgical specialty participated in a basic suturing and fundamental laparoscopic skills curriculum. Proficiency goals were identified. Students were given access to videos for review and instruments and supplies for independent practice. Six to eight weeks later, students were evaluated using time and videotaped assessment of technical proficiency for each task and by a written exam to test knowledge. Students who failed to meet proficiency targets were given remediation training and retested. Data are mean ± SD.

Results: Thirteen students have completed the initial suturing assessment and written examination. Assessment of laparoscopic skills will occur in the next 4-6 weeks**.** Of the 13 students, 11 achieved technical proficiency in at least one task (85%), and 5 achieved technical proficiency in all 5 tasks (39%). Mean global proficiency score was 2.91 ± 0.89 (3 = proficiency), and mean total task time was 624 ± 106 seconds (700 sec = proficiency). Additionally, 10 of 13 students passed the written exam.

Conclusions: Proficiency based milestones are achievable for 4th-year medical students applying for surgical residency early in the 4th year. We anticipate using these results to work toward establishing a more comprehensive milestone-based skills curriculum offered for the 4th year of medical school.

022 **Zheng, Lida**

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Differences in intraocular pressure measured in the clinic and home in glaucoma patients

Zheng L; Wichterman CM; Bhorade AB; Wilson B

Introduction: Glaucoma is the second leading cause of blindness worldwide and the leading cause of irreversible blindness. A high intraocular pressure (IOP) is the most important risk factor for glaucoma, although as many as one in three people who have glaucoma will not have increased intraocular pressure, called Low Tension Glaucoma. Lowering IOP, using surgery and eye medication, is still the aim of all treatments for glaucoma, even for patients with Low Tension Glaucoma. The purpose of this study is to examine if patients have higher or lower IOP measures in the home and to explain this by secondary measures such as non-compliance prior to clinic visits, changes in blood pressure, or anxiety in the clinic. Accurately assessing IOP and its relationship with glaucoma progression with give us a better understanding of the multifactorial causation of glaucoma. This can help ophthalmologists determine if a patient needs more aggressive management or prevent unnecessary treatment for those who exhibit significantly higher IOP in the clinic.

Methods: This study is a prospective cohort study with home visits occurring 1-4 months after clinic visits. Patients were recruited from the Eye Clinics at Washington University. During the home and clinic visits, eye pressure and blood pressure measurements were taken. Additionally, questionnaires including demographics, medical comorbidities, glaucoma knowledge and perception of medication use were given.

Results: So far 30 patients have completed both clinic and home visits. A repeated measures analysis of variance on the preliminary data showed a significant difference (p=0.04) between home and clinic eye pressure. The mean difference showed a higher home measure by 0.895mmHg, with a 95% CI of .026 to 1.765 mmHg. In addition, home blood pressure was significantly lower.

Conclusions: This study shows that clinic measures of IOP may not be accurate measures of home IOP. The increase in home pressures may suggest increased compliance before clinic appointments. In addition, the significant drop in home blood pressures confirms studies on the well documented phenomenon of "white coat hypertension."

066 **Zozula, Alexander**
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Mentor: Susan Stark, PhD, OTR/L

Can prehospital emergency services reduce falls or fall-related morbidity in community-dwelling geriatric adults? A systematic review

Zozula A; Carpenter C; Stark S

Introduction: Whether for transport to an emergency department or simply for assistance getting up, a substantial proportion of geriatric adults utilize prehospital emergency services after falling. There is good evidence that identifying high-risk fallers and remedying specific risk factors can reduce both the total number of older adults who fall and their rates of falling at home. This study seeks to systematically review the literature to identify the effects of emergency services-based screening and referral programs on falls or fall-related morbidity in community-dwelling geriatric adults.

Methods: We will search PubMed, Embase, CINAHL, Web of Science, Scopus, OTseeker, and PEDro from 1980 to September 2012 for randomized controlled trials, non-randomized trials, and cohort studiesevaluating emergency services-based fall risk screening and referral programs. Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources will be screened by a single review team member to identify studies that potentially meet the inclusion criteria. The full text of these studies will be retrieved and independently assessed for eligibility by two review team members. A standardized, pre-piloted form will be used by two review team members to independently extract data from the included studies for assessment of study quality and evidence synthesis. Missing data will be requested from study authors. Primary outcome measures will include the risk of falling and rates of falling. Secondary outcome measures will include the probability of follow-up for further assessment/preventative measures and adverse events attributable to screening and referral.

Anticipated Results: Based on preliminary searches, we anticipate finding approximately 10-15 studies meeting the inclusion criteria. We anticipate that few studies will have evaluated the effect of emergency services-based screening and referral on the risk of falling or rates of falling.

Conclusions: The results of this systematic review will help define the role of emergency services in reducing falls or fall-related morbidity and should help guide agencies in the development of additional screening and referral programs.

Forum for International Health and Tropical Medicine

068 **Boone, Sean**
Medical Student
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Summer Research Program
Department of Surgery, Washington University in St Louis School of Medicine
Department to Public Health Sciences, Guatemala
Mentor: Joaquin Barnoya, MD, MPH
Impressions following a summer research experience in Guatemala
Boone S; Barnoya J
Introduction: Travel to the developing world, and in particular experiences that create frequent and lengthy interactions with the residents, is a transformative experience. Vastly different socioeconomic circumstances and, often, lives provide a different perspective. This travel experience can be paired with an introduction to public health research, which is incredibly useful to a future physician. This poster explores the thoughts and reactions to a summer public health research experience in Central America.
Experience: I spent a summer researching in conjunction with local fellows in Antigua and Guatemala City, Guatemala. Work consisted of visiting schools, interviewing parents, taking anthropometric measurements of parents and children, organizing the data collection for subsequent days, and data entry.
Results and Conclusions: Socioeconomic differences were anticipated, but the differences observed between the private school and public schools were of far greater magnitude than mentally predicted. The education gap of the parents was particularly dramatic, as was the subjective differences in prevalence of obesity and overweight among the parents of these schools. The frequent commute into Guatemala City on the public buses was a very colorful experience. My co-workers, who were involved in the Guatemalan healthcare system as nutritionists and medical students, also provided a very interesting perspective. Additionally, the amount of preparation work required to begin a human subject research project was also a surprise. Editing a proposal and particularly getting IRB approval to work with children was an incredibly long process. When in Guatemala, scheduling data collection times and other preparation work also was more time intensive than expected. The experience has been incredibly favorable, and I feel that I have a much better understanding of healthcare and life in the developing world, as well as the process involved in setting up a human research study.

110 **Brito, Natalia**
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Mentors: S Subash Babu, MBBS, PhD; Gary J Weil, MD
The role of IgG and IgG4 in the development of chronic pathology in filariasis patients from Tamil Nadu, South India
Brito N; Babu SS
Introduction: Lymphatic filariasis is a tropical neglected disease caused mainly by the parasite *Wuchereria bancrofti*. While most infected individuals suffer only from a subclinical infection, about one third manifest significantly debilitating clinical symptoms. The mechanisms underlying the disease's progression to chronic pathology are poorly understood. Many studies suggest damage caused by the hosts' immune response might be a major cause. Filarial parasites have been shown to down-modulate their host's immune responses and the induction of IgG4 is believed to be one of the main mechanisms through which they achieve this. IgG4 has been previously shown to have immunoregulatory properties and protective roles in various inflammatory diseases. In this study we aim to examine whether asymptomatic filariasis patients have higher IgG4 levels than chronic pathology patients that might be preventing the development of chronic pathology in this group of patients. Understanding the mechanisms underlying the progression to pathology would help develop treatments to prevent it.
Methods: IgG and IgG4 levels from asymptomatic infected and chronic pathology patients in South India were quantified by performing ELISA.
Results: Results show that IgG4 levels are significantly higher in asymptomatic patients (geometric mean of 1,922.27 pn/ml) when compared to chronic pathology patients (geometric mean of 527.32 pn/ml) (p-value= 0.002). IgG levels are also significantly higher in asymptomatic patients (geometric mean of 80,909.55 gm/ml) than in chronic pathology patients (geometric mean of 24,673.74 gn/ml) (p-value< 0.001).
Conclusions: These results suggest a protective role for IgG4 against the development of filarial-induced pathology and the possibility of a similar role for one of the remaining IgG subclasses. Further research is necessary to confirm such a protective role. If confirmed, research should aim for the development of prophylaxis treatment using IgG4 for preventing the development of pathology in filariasis-infected patients.

109 **George, Paul E**

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National Institute of Research in Tuberculosis, Chennai, India
Mentors: Subash Babu, PhD; Gary Weil, MD

Quantifying the immune response of patients with elephantiasis in Southern India

George PE; Babu S

Introduction: Lymphatic filariasis (LF), commonly known as elephantiasis, is the second leading cause of permanent disability worldwide. Currently, 120 million people are infected with LF. About one third, or 40 million, of these people are disfigured or incapacitated by the disease. And more than 1.3 billion people in 80 countries live in endemic areas and are at risk of acquiring infection. Much is known about the transmission, immunology, diagnosis and treatment of this disease. Despite this, there is a relative scarcity of information regarding the exact mechanisms behind the pathology of filariasis. In this study, we examined the hematological and immune responses of a subset of patients with chronic filarial pathology, focusing on the patients' IgG and IgG4 responses.

Methods: We studied a group of 72 patients who displayed clinical symptoms of pathology for filariasis. The patients presented with the pathology at the Communicable Diseases Hospital (Chennai, Tamil Nadu, India), and were graded by a physician on the 1-4 Scale for Pathology in Filariasis. We examined the levels of circulating filarial antigen (CFA) and levels of IgG and IgG4 specific for filarial antigen in chronic pathology patients, using enzyme-linked immunosorbent assay (ELISA) to measure the levels.

Results: In analyzing the data, we looked for trends and correlations between the following data sets: age, weeks of pathology, pathology grade, IgG levels, IgG4 levels, and IgG/IgG4 levels. We found statistically significant correlation in the following relationships: length of pathology vs. pathology grade, pathology grade vs. IgG4 levels, and age vs. IgG levels. We found statistically significant differences in the following groups: IgG4 levels in Grades 1 and 2 vs. Grades 3, 4, and hydrocele, and IgG4 levels in male vs. female patients.

Conclusions: This study examined chronic pathology patients with filariasis, a group of patients that has been historically overlooked. The results suggest, as expected, that the longer a patient has clinical symptoms of pathology, the worse the grade of pathology. Further, the results suggest that patients with higher grade of pathology have higher levels of IgG4.

069 **Lederhandler, Sarah**

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Mentor: Joaquin Barnoya, MD, MPH

Primary caregivers' educational level and childhood obesity in Guatemala

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Introduction: Low educational and health literacy skills are associated with poor understanding of health information and clinical outcomes. Guatemala, a low/middle income country, is currently in a nutrition transition, where under nutrition and obesity coexist, mostly in young family members. The objective of this study is to determine the association between primary caregivers' educational level and childhood obesity in Guatemala.

Methods: In Guatemala City and Antigua, Guatemala, 925 four-to six-year old students and their primary caregivers were invited to participate in this study. Of these, 316 chose to participate (response rate 34.16%). Primary caregivers were interviewed to assess use and knowledge of nutritional labels. Children's weights and heights were measured using standard techniques and subsequently used to calculate the BMI. Chi-square and analysis of variance tests were run to determine if there is an association between predictor and outcome variables (BMI).

Results: Regarding caregivers' nutritional status, 33.1% in public and 18.4% in private schools were classified as obese. The corresponding percentages for children were 8.3% and 21.7%, respectively ($p<0.01$). Regarding caregivers' education, in public schools and private schools, 34.3% had low educational level and 10.7% had a high educational level, and 2.6% had low educational level and 72.6% a high educational level; respectively. A significant ($p<0.05$) difference was found between the nutritional status of children stratified by caregiver educational level. Half (51.5%) of public school caregivers knew what a nutritional label was compared to 87.8% of those from private schools. Health literacy was lower in caregivers from public (6.5%) compared to private (40.1%) schools ($p<0.01$). No significant difference was found between nutritional status of children and caregivers' health literacy level.

Conclusions: Primary caregivers in Guatemala have a low educational and health literacy level, particularly in public schools. Nutritional label use and knowledge is low and therefore other strategies need to be implemented in order to help consumers make an informed decision when purchasing foods.

098 **Wesevich, Austin**

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Evaluation of community water source intervention

Wesevich A; O'Neil E

Introduction: Over fifty households in Mbale, Uganda relied on a substandard water source, exemplary of what many in the developing world endure. Humanitarian efforts seek to improve access for the world's poor. This research project evaluates intervention efforts by quantifying microbial levels and reported diarrhea rates within the context of water sanitation beliefs.

Methods: Microbial levels of total coliforms and *E. coli*, mother-reported diarrhea rates and hygiene of children ages five and younger, and beliefs held by villagers about water sanitation were all collected pre-intervention. Resources and guidance enabled Mbale villagers to transform their unprotected, open water source into a protected, covered one. Microbial levels were re-measured one month after completing construction. Microbial levels and mother-reported diarrhea levels will be measured six months post-intervention.

Results: There was a reduction in both total coliform and *E. coli* colonies one month post-intervention. It is anticipated that these microbial levels will further reduce six months post-intervention. Because diarrhea rates are mother-reported through a translated survey, the accuracy of these rates is unclear, and they may show no significant change. Villagers understood that dirty water could cause diarrhea and that boiling water was imperative but also suggested that young children might drink unboiled water when not being watched over.

Conclusions: Improving water sources for those in developing countries is an inexpensive measure that can lower microbial levels. Diarrhea rates prove more difficult to measure. Though the definition of diarrhea was affirmed with each mother, it might be unrealistic to expect a mother to know how many episodes of diarrhea each of her children under age five has had in the last month or year. Disease did not seem to be due to a lack of knowledge, as almost all villagers understood that unboiled water could cause sickness. However, some confirmed they knew that not boiling water could make their children sick, yet still did not boil their water. This was not negligent, but economic: boiling water takes time and money. Some people may not have the means to practice hygienic behaviors, even if they have been empowered by knowledge.

Mallinckrodt Institute of Radiology Summer Research Program

132 **Wooten, Lake A**
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Mentor: Suzanne E Lapi, PhD

An automated system for production of ^{89}Zr radioisotope

Wooten AL; Schweitzer III GD; Lawrence LA; Madrid E; Lapi SE

Introduction: Zirconium-89 (^{89}Zr) is a useful radioisotope for radioimmunological positron emission tomography (PET) imaging. ^{89}Zr has a half-life that is long enough ($t_{1/2}$=3.27 d) to provide time for sample preparation (purification, chelation, immunolabeling) and adequate circulation time in a patient for immunotargetting to occur. Here, we present an automated system that can be used to safely purify ^{89}Zr in a lead hot cell.

Methods: We have created a system that has automated the chemical purification of ^{89}Zr via anion exchange chromatography that has already been published. A disc was cut from yttrium foil and secured in a niobium target holder. This assembly was placed in a cyclotron where it was bombarded with 15 MeV protons. Then, this target assembly was transferred by hand to the automated system that was inside a lead hot cell. The system was controlled by a computer outside of the hot cell using a LabVIEW program that connected to a live camera and four radiation detectors. Briefly, the system dissolved the foil in acid, transferred the dissolved foil to a hydroxamate resin column, and eventually eluted the ^{89}Zr in 1 mL of oxalic acid. All liquids were moved through tubing by compressed air that was precisely controlled by a mass flow controller via the LabVIEW program.

Results: The automated system effectively purified ^{89}Zr from the ^{89}Y target foil. On separate productions, we achieved a radionuclidic purity of 99.99% with ^{88}Zr being the only contaminant, and we achieved an effective specific activity of 545 mCi/μmol, both of which are comparable to Holland, *et al,* 2009.

Conclusions: We have designed, built, and tested a new automated system that can purify ^{89}Zr inside a hot cell. This system has achieved radionuclidic purity and effective specific activity that are comparable to published results from purifications that were performed by hand. The activities used in the automated system were increased as the system was improved.

Movement Science Program

040 **Cheuy, Victor A, MS**

Movement Science Doctoral Program
Program in Physical Therapy, Washington University in St. Louis School of Medicine
Mentor: Michael J Mueller, PT, PhD

Volumetric analysis of intrinsic muscle atrophy in the diabetic neuropathic foot

Cheuy VA; Commean PK; Hastings MK; Mueller MJ

Introduction: Diabetic neuropathy and infiltration of intermuscular adipose tissue (IMAT) in the intrinsic foot muscles (IFM) may contribute to weakness, foot deformity, and subsequent amputation. However, there are no good measures of IMAT or IFM, and these relationships are not fully understood. The purposes of this study are to describe a reliable, valid, semi-automated program to quantify lean muscle and IMAT in the foot using MRI, and compare the amount of IMAT in the IFM between controls and diabetic neuropathic (DMPN) subjects with and without foot deformity.

Methods: MR images were acquired from 35 subjects (age 58.5 ± 11.4 years, BMI 37.0 ± 10.5). Two raters segmented and measured fat and lean muscle volumes from single MR slices at the forefoot, midfoot, and hindfoot at 2 times on a subset of subjects (n = 19). MR phantoms constructed of known proportions of fat and lean muscle (as determined by water displacement) were measured. Mean percent IMAT volumes in IFM were compared across three groups; 12 controls, 12 subjects with DMPN, and 11 subjects with DMPN and severe foot deformity.

Results: Indicators of measurement reliability were high (most ICC values ≥ 0.95). Indicators of measurement validity also were high; MRI estimates and water displacement measures of fat and muscle volumes were highly correlated ($r^2 \geq 0.97$) with low error (RMS error < 5%). Mean percent IMAT volumes in IFM were 51 ± 23% for DMPN with deformity, 48 ± 21% for DMPN without deformity, and 22 ± 7% for controls. The DMPN groups were not different from each other ($p > 0.05$), but were different from controls ($p < 0.02$).

Conclusions: Lean muscle and adipose tissue volumes in the foot can be quantified using this reliable and valid noninvasive MRI measure. IMAT infiltration of IFM is 2.3x higher in DMPN subjects than controls, but is not always associated with foot deformity. This program can be applied in studies investigating the relationship of these structures to the progression of foot deformity, skin breakdown, and lower extremity amputation in people with diabetes or with other musculoskeletal problems.

041 **Shah, Kshamata M**

Movement Science Program
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***Mentor*:** Michael J. Mueller, PT, PhD

Upper extremity impairments in a group of people with Diabetes Mellitus (DM)

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Introduction: The relationship of upper extremity impairments, and function in people with DM is not clearly understood. The purpose of this study was to establish the severity of shoulder problems in people diagnosed with DM attending an outpatient diabetes clinic and to compare shoulder and hand impairments in people with DM to those without DM. We hypothesized that, in people with DM, shoulder external rotation (ER) and abduction range of motion (ROM) and strength, and grip strength will explain significant variance in function measured via the Shoulder Pain and Disability Index (SPADI).

Methods: SPADI information was collected on 235 individuals with DM. A detailed shoulder and hand examination was conducted on a subgroup of 22 individuals with DM [Age 64(9.5); BMI 32.7(5.8); SPADI 36.8(26.2)] who volunteered to participate, and their measures were compared to 22 individuals without DM [Age 63(9.5); BMI 32.9(5.1); SPADI score=0].

Results: 63% of people with DM reported shoulder pain and/or disability [mean SPADI score 21.7(25.8)]. Compared to the group without DM, the group with DM had significant (*P<0.05)* decreases in passive shoulder ROM (9–19%); strength of shoulder muscles (12.5–27.5%); gross grip strength (14.8%) and lateral key pinch (11.3%); and hand dexterity. People with DM had decreased sensation (22 vs.10) and increased hand limited joint mobility (LJM) (13 vs.2) compared to the group without DM. A hierarchical regression analysis predicted 72.7% (*P<0.05*) of the variance in SPADI in people with DM using the predictors – ER and abduction ROM and strength, and grip strength.

Conclusions: In this study, people with DM had significant upper extremity ROM and strength impairments which were related to complaints of pain and disability. Further research is necessary to understand the underlying mechanisms that cause shoulder and hand LJM, and its impact on upper extremity movement and function in people with DM. LJM, thought to be caused by the accumulation of advanced glycation end-products in connective tissues, may affect multiple joints in the upper extremity in people with DM. Early detection of impairments related to LJM may help prevent functional limitations in people with DM.

Office of the Provost, Diversity & Inclusion Grant

No poster displayed

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Mentor: Richard T Griffey, MD, MPH

The impact of teach back discharge instructions on patient satisfaction of emergency patients with limited health literacy: A randomized controlled trial

Aginam N; Jones S; Shinn N; Gross M; Kinsella Y; Griffey RT

Introduction: Teach back discharge instructions will result in a higher objective satisfaction of discharge instructions among Emergency Department (ED) patients with Limited Health Literacy (LHL)

Methods: Setting: The study was performed at Barnes Jewish Hospital Emergency Dept, an urban academic level one trauma center with over 95,000 annual visits.

Study Population: It includes all English-speaking ED patients ages 18 and older. Exclusion criteria include: too high acuity for interview as determined by the ED attending, aphasia, psychiatric chief complaint, clinical intoxication, known dementia, mental handicap, or insurmountable communication barrier.

Study Design: We consented and screened for health literacy level using the Rapid Estimate of Adult Literacy in Medicine- Revised (REALM-R) tool. Patients with LHL based on this instrument were enrolled in the study and randomized into intervention (teachback) vs. control groups. The discharge instructions were audiotaped for intervention patients. The patients were asked to complete a brief survey to assess their satisfaction with the discharge instructions during their visit at the ED.

Measurements/ Data Collection: Patient satisfaction was evaluated using a subset of questions selected from the Consumer Assessment of Healthcare Providers and Systems (CAHPS) questionnaire, a validated instrument developed by the Agency for Healthcare Research and Quality. Audiotaped discharge sessions and brief structured interviews will also be reviewed for independent assessment of satisfaction using previously described methodology.

Results: We adjusted our sample size to have 80% power to detect a 10% improvement in satisfaction in the teachback group as a result of this intervention. We will examine the effects of adjusting for health literacy, and sociodemographic and clinical factors using multivariable regression modeling to examine associations between study group assignment and patient satisfaction and comprehension.

Conclusions: There are few interventions shown to mitigate the negative effects of LHL. Teach-back is a promising intervention that may improve comprehension and may result in improved patient satisfaction with their instructions and with their ED stay.

No poster displayed

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Mentor: Steven Brandes, MD

The creation of a database to retrospectively evaluate outcomes of tandem-cuff urinary sphincter placement for stress urinary incontinence in men

Akamnonu CP; Brandes SB

Introduction: Artificial urinary sphincters (AUS) are devices used in the management of severe urinary incontinence. These devices can be used in the form of a single cuff or placed in tandem (double cuff). This study aims at evaluating the complication rates (within 90 days post AUS surgery) of patients who have received tandem cuffs, compare them to those who received single cuffs, and determine what form of complication is prevalent among these patients.

Methods: Medical records of patients seen between 1/1/1980 and 7/31/2011 were reviewed. In this retrospective study, the criteria used in determining the forms of complications were: Infection rate, mechanical failure, urinary retention, erosion and sub-cuff atrophy.

Results: Preliminary results of 155 patients analyzed showed that 20 patients received tandem cuffs. Of the 155 patients analyzed 15 patients (9.7%) had artificial urinary sphincter related complications within 90 days of the procedure. All 15 of the patients with post-operative complications had single cuff placements with none having tandem cuffs. Six of the patients had infections, 5 had erosion, 3 had urinary retention, and 1 patient had both infection and erosion. No patient had sub-cuff atrophy or mechanical failure within 90 days after surgery.

Conclusions: The analysis of the preliminary results show that infection is the most likely cause of post-operative AUS complication within 90 days of surgery, with erosion as a close second. Also the data suggest that placing of a tandem cuff does not lead to an increase in the 90 day post-operative complication when compared to patients with a single cuff. The results however may be limited by the small pool of patients with tandem cuffs when compared to single cuffs. Further analyses will compare tandem cuffs with single cuffs in terms of incontinence resolution and complications in the long term as well as to determine if other comorbid conditions play a role in increased incontinence.

No poster displayed

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Mentors: Jeremiah P Depta, MD; Yogesh Patel, MD

Increased rates of myocardial infarction associated with borderline FFR values following deferred PCI

Facey G; Depta JP; Patel Y; Patel JS; Masrani SK; Kurz HI

Introduction: FFR is an index that compares the coronary pressure distal to a stenotic lesion to the aortic pressure during maximal hyperemia. Current guidelines recommend PCI for an FFR value of $\leq$ 0.80. We hypothesize that increased adverse cardiac events occur in patients with borderline FFR values (0.81 to 0.85) following FFR-guided deferral of PCI.
Methods: From 1/1/2004 to 7/1/2010, 186 patients were deferred PCI based on FFR assessment. Patient characteristics, medical management, and long-term clinical outcomes (death, myocardial infarction [MI], and target lesion revascularization [TLR]) were compared between patients with and without borderline FFR values (0.81 to 0.85) using univariate analyses.
Results: Of the 186 patients deferred PCI based on FFR, 80 patients (43%) had borderline FFR values (0.81-0.85). No significant differences in baseline and lesion characteristics were demonstrated in patients with and without borderline FFR values, except a higher rate of chronic kidney disease in the borderline FFR group (18% vs. 5%, p = 0.0004). Patients with borderline FFR values were less likely to be on nitrates at the time of FFR assessment (19% vs. 37%, p = 0.007). Borderline FFR values were associated with significantly higher rates of MI compared with patients without borderline values (6% vs. 1%, p = 0.04). No differences were observed with cumulative death, MI, or TLR or the individual endpoints of death or TLR in patients with and without borderline FFR values.
Conclusions: Borderline FFR values of 0.81 to 0.85 were associated with increased rate of MI compared with non-borderline FFR values. Further study is warranted to fully evaluate this association using adjusted multivariate analyses.

No poster displayed

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Is health literacy and numeracy associated with medication and diet compliance in patients with hypertension?

Fletcher A; Dwyer E; Grace E; Griffey R

Introduction: Health Literacy is the capacity to obtain, process, and understand basic health information. Numeracy is the ability to reason and to apply simple numerical concepts. About 1 in 3 US adults have hypertension (HTN) with 2/3 of these being poorly controlled. Few studies have focused on the relationship between health literacy, numeracy and medication/dietary compliance in HTN.
Hypothesis: Health literacy and numeracy will be positively associated with medication and dietary compliance in patients with HTN.
Methods: Prospective observational study
Setting: A large urban adult emergency department (ED)
Subject Selection: Adults with pre-existing HTN requiring medication for control. Exclusions included severe pain, serious illness or injury, non-English speaking, or unable to give informed consent.
Protocol: Consenting subjects completed a Brief Alzheimer Screen (BAS) to test cognitive ability, and those that passed the BAS continued in the study. Subjects were administered the Short Test of Functional Health Literacy in Adults (S-TOFHLA), and the Rapid Estimate of Adult Literacy in Medicine-Revised (REALM-R) to determine Health Literacy. The Lipskus-Schwartz Numeracy Scale (LS-Numeracy Scale) was administered to determine numeracy. Subjects answered a HTN compliance questionnaire with 4 questions about diet/medication compliance. Adequate literacy was defined as a score >22 on S-TOFHLA; $\geq$ 6 on REALM-R; and >5 on LS.
Statistical Analysis: Mean compliance scores were compared between subjects with adequate vs. inadequate health literacy (comparing S-TOFHLA and REALM-R separately) using a 2-tailed t-test. We also compared mean compliance scores between subjects with adequate vs. inadequate numeracy using a 2-tailed t-test.
Results: 120 subjects were screened, 80 were enrolled and 79 had complete data. Mean compliance did not differ significantly between groups measured by S-TOFHLA nor LS (2.68 vs. 2.35, p=0.308; and 2.74 vs. 2.46, p=0.280 respectively). Mean compliance was better among literate subjects as measured by REALM-R (2.95 vs. 2.25; p=.005).
Limitations: Single Center Study; Urban Environment; HTN questionnaire not validated; Small sample size.
Conclusions: There was no association between compliance to medication/diet and numeracy, and health literacy when using LS and S-TOFLHA. There was a significant difference in compliance among those with higher literacy based on REALM-R.

No poster displayed

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The impact of teach back on comprehension of discharge instructions among emergency patients with limited health literacy: A randomized, controlled trial

Jones S; Aginam N; Shin N; Gross M; Kinsella Y; Griffey RT

Introduction: Few interventions have been demonstrated to modify the negative effects of limited health literacy on patient outcomes. The teach-back method is a promising technique to improve communication between patients and providers, where the patient is prompted to state back in their own words their comprehension of given information. The objective of this study is to measure the effect of teach-back methods on patient comprehension of discharge instructions compared to standard discharge instructions.

Methods: Setting: The study was conducted at an urban, academic emergency department, with over 95,000 annual visits. Study Population: All English-speaking ED patients >18 years old were eligible for the study. Exclusion criteria included a score of >6 (adequate) on the Rapid Estimate of Adult Literacy in Medicine- Revised (REALM-R) health literacy tool. Study Design: Enrolled patients were randomized to either standard discharge instructions or teach-back groups. Following receipt of discharge instructions, patients completed structured interviews to evaluate their comprehension in the following domains: diagnosis, ED course, medication, follow up and return visit instructions. We audiotaped patients' responses to comprehension questions and the teach-back sessions performed. Subsequent chart review was performed to compare patient comprehension against the medical record, measured on a 5-level scale of concordance. We rated the quality of the nurse's discharge instructions based on the audiotape recording to stratify results. Data Analysis: We analyzed differences between groups using the chi-squared test and multivariate modeling to examine the effect of health literacy as well as sociodemographic and clinical factors on associations between study group assignment and comprehension.

Anticipated Results: Data collection and analysis is ongoing to reach 250 patients. Preliminary data records show 137 patients were audiotaped, 65 patients randomized for teach-back. We anticipate teach-back patients to have a higher comprehension of discharge instructions.

Conclusions: Future studies should examine the impact of teach-back on patient compliance to discharge instructions. Patient outcomes are affected by health literacy; therefore, providing teach-backs will increase literacy among patients and ultimately leading to better patient care.

Otolaryngology NIH T32 Physician Scientist Program

013 **Barton, Matthew R, MD**

Otolaryngology NIH T32 Physician Scientist Program
Department of Otolaryngology, Washington University in St. Louis School of Medicine
Mentor: Mark Warchol, PhD

Characterization of Hippo signaling during development and regeneration of inner ear sensory hair cells

Barton M; Lovett M; Warchol M

Introduction: The loss of sensory hair cells (HCs) is a leading cause of deafness in humans. Although the mammalian inner ear is unable to replace lost/damaged HCs, birds and other non-mammalian vertebrates can regenerate HCs after injury. Despite promising discoveries describing the roles of Notch, FGF, and other signaling pathways during inner ear sensory epithelial development and regeneration, the critical inter- and intra-cellular communication events necessary induce mammalian HC regeneration remain elusive. The Hippo signaling pathway constitutes an evolutionarily conserved kinase cascade involved in regulation of organ size, cell proliferation, and tissue regeneration. Despite these well-documented roles in growth control, Hippo signaling remains unexplored in the ear. The purpose of this study is to begin characterization of the Hippo pathway in the context of inner ear biology, with focus on development and regeneration of sensory HCs.

Methods: Expression of key Hippo pathway constituents was carried out via RNA sequencing technology. Immunofluorescence was utilized to determine the cellular and subcellular localization of Hippo pathway components and to assess phenotypes throughout the time course of HC regeneration.

Results: RNAseq revealed that all key Hippo signaling effectors, including the core Hippo pathway components MST1/2, LATS1/2, SAV1, YAP1, and WWTR1/TAZ are robustly expressed in the inner ear sensory epithelia of both chickens and mice. The subcellular localization of several important Hippo pathway constituents suggests that Hippo signaling may be important for intercellular communication in the context of sensory epithelial damage, possibly linking extracellular damage cues to an intracellular proliferation response.

Conclusions: Despite its roles in cell proliferation and tissue regeneration in other organ systems, Hippo signaling has not been studied in the inner ear. The preliminary data presented here validates the presence of key Hippo signaling molecules within sensory epithelia of avian and murine inner ears, and provides evidence to support putative roles for Hippo signaling during sensory epithelial development and HC regeneration.

010 **Law, Jonathan H, MD**

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Mentor: Ravindra Uppaluri, MD, PhD

ERK1/2 regulation of CD44 modulates aggressiveness in a new mouse model of oral cancer

Law JH; Judd NP; Winkler AE; Murillo-Sauca O; Onken M; Sunwoo JB; Uppaluri R

Introduction: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide with an incidence of over 500,000 cases each year. Cervical lymph node metastasis is a negative prognostic factor in head and neck cancer and has been associated with a 50% reduction in 5-year survival. In order to better understand the complex interaction between host and its tumor microenvironment, our laboratory has developed a syngeneic model of oral cavity squamous cell carcinoma (OSCC) in an immunocompetent mouse that allows for manipulations of tumor growth to be evaluated in an autochthonous transplantation system.

Methods: Oral cavity DMBA application was used to generate primary tumors in C57BL/6 background mice. Individual primary tumors were cultured to establish mouse oral cancer (MOC) cell lines. Cell lines displayed either indolent or aggressive phenotypes when cultured or transplanted *in vivo*. Protein expression of pERK was evaluated by immunoblotting, and co-expression of pERK and CD44 were determined by dual immunofluorescence staining and FACs analysis. Gene expression differences were analyzed using microarray via principal component analysis (PCA) and significance analysis of microarray (SAM).

Results: Aggressive cell lines displayed increased levels of pERK, and pERK regulated CD44 cell surface expression. Knockdown of CD44 using shRNA constructs resulted in decreased migration capacity *in vitro* and decreased tumor growth *in vivo*. Microarray analysis clustered the MOC cell line gene expression in parallel to *in vivo* growth phenotypes and identified a signature for aggressive growth. Furthermore, studies of human OSCC cell lines and primary tumors revealed that CD44 expression is correlated with pERK.

Conclusions: In this new carcinogen induced cell line model of OSCC in syngeneic immunocompetent mice, pERK regulates CD44 and is associated with an aggressive/metastatic growth. This association is seen in human OSCC cell lines and primary tumors. Microarray analysis shows that gene expression parallels growth phenotypes observed *in vitro* and *in vivo*, and identifies a molecular signature associated with aggressive growth and metastasis.

012 **Lucisano, Amelia**

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Mentor: Timothy Hullar, MD

Balance improvement through haptic feedback in unbalanced individuals

Lucisano AC; Stevens M; Hullar TE

Introduction: Impaired visual, auditory, vestibular, or proprioceptive sensory function, especially in the elderly, may contribute to problems maintaining balance which can lead to an increased risk of falls. The enhancement of sensory input may contribute to an improvement in postural stability and maintenance of balance. The purpose of this study was to collect preliminary data demonstrating balance improvement in unbalanced individuals through the use of a haptic cane to enhance proprioceptive input.

Methods: Eleven subjects (three with vestibular loss and eight with hearing loss) completed computerized dynamic posturography (CDP) testing in three conditions of varying balance difficulty. The speed of their center of pressure (COP) was recorded. A 95% COP value was calculated and compared for trials with and without the use of a haptic cane.

Results: During the normal balance condition (with visual input), subjects demonstrated significantly improved balance with haptic cane use (average improvement in 95% COP velocity of 1.02 cm/s, p =0.036). Significant improvement with cane use was also observed when visual input was removed (average improvement in 95% COP velocity of 1.48cm/s, p=0.020). For the four subjects able to complete the sway-referenced condition (no proprioceptive or visual input), a dramatic improvement was documented (average improvement in 95% COP velocity of 8.65 cm/s, p=0.071).

Conclusions: These preliminary results provide evidence that haptic cane use may improve balance control in older, unbalanced individuals. Interestingly, during conditions of compromised sensory input, greater average improvement in balance was observed. This suggests that haptic feedback which provides enhanced proprioceptive input, may be especially helpful to patients who have compromised sensory pathways, a situation found frequently in elderly populations. Further investigation may show that haptic devices could improve the quality of life for unbalanced individuals, through improved balance control and avoidance of falls.

011 **Wilson, Michael**

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Mentor: Jay Piccirillo, MD

Ecological momentary assessment of tinnitus using smartphone technology

Wilson MB; Joplin C; Gorman M; Nicklaus J; Kallogjeri D; Piccirillo JF

Introduction: Tinnitus is a common clinical problem characterized by the perception of a ringing or hissing sound in the absence of external stimuli. One obstacle to the assessment of the efficacy of any intervention for bothersome tinnitus is a reliance on retrospective self-report questionnaires to assess the degree of bother patients experience from their tinnitus. One technique used to limit the biases inherent in self-report questionnaires is the use of Ecological Momentary Assessments (EMA), which assess a condition in the current moment, limiting the need for recalling past experiences. In this pilot study, we evaluated the feasibility of using Smartphone technology to collect EMAs of tinnitus bother and compared momentary assessments with data from retrospective measures.

Methods: EMA queries were delivered to Smartphones of 20 patients with severely bothersome tinnitus 4 times per day for 14 consecutive days. Each query asked, "In the last 5 minutes, how bothered have you been by your tinnitus?", with responses based on a 100 point scale, as well as other questions about their environment. The mean EMA score was compared with the following retrospective question asked at the end of the 2 weeks: "Over the last 2 weeks, how bothered have you been by your tinnitus?"

Results: The response rate to the EMAs was 81%, with an average response time of 29 minutes. Preliminary data suggest that mean EMA bother scores are significantly lower than bother reported on the retrospective questionnaire. We also expect to find associations between level of tinnitus bother and certain environmental factors, such as location, activity, stress level, etc.

Conclusions: The results of this study suggest that EMAs can feasibly be collected via Smartphone technology, and that the EMAs thus collected provide a more accurate representation of patients' tinnitus bother than traditional retrospective questionnaires. The development of a dedicated iPhone and Android App for collecting EMAs could further be scaled for use by clinicians and patients to characterize patients' individual experience with bothersome tinnitus.

034 **Yang, Lu**

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Mentors: David Ornitz, MD, PhD; Sung-Ho Huh, PhD; Mark Warchol, PhD

Role of FGF20 in hair cell regeneration in the zebrafish lateral line

Yang L; Huh S; Warchol M; Ornitz D

Introduction: Age-related hearing loss is a common problem, affecting one-third of people over the age of 65 and is commonly due to damage to outer hair cells (OHCs) in the organ of Corti. In mammals, hearing loss is irreversible because the cochlear sensory epithelium cannot regenerate. In contrast, the avian and amphibian inner ear can regenerate. We have identified the fibroblast growth factor (FGF) pathway, and specifically FGF20, as the key signaling pathway in cochlear sensory epithelium development. This pathway is present in the mature inner ears of birds, but not mammals, leading us to believe that FGF signaling may play a role in regeneration of inner ear hair cells. Previous studies have shown that FGF20 is required for fin regeneration in zebrafish. The purpose of this study is to determine whether FGF20 is involved in hair cell regeneration in neuromasts of the zebrafish lateral line.

Methods: A FGF20 knockout zebrafish strain was generated. Seventy-four 5 days-post-fertilization embryos were treated with 10 μM $CuSO_4$ for 2 hours to kill lateral line hair cells. An equal number of embryos were treated in control. The experiment is blind with respect to the genotype of the fish (wild-type, heterozygous for the FGF20 mutation, or homozygous). Hair cells in the lateral line were allowed to regenerate for 72 hours. Hair cells were stained with phalloidin and counted using confocal microscopy.

Results: Hair cells were confirmed to be gone from the lateral line 1 hour after $CuSO_4$ treatment. No significant difference in total number of hair cells or number of neuromasts was found 72 hours post $CuSO_4$ treatment among the wild-type, heterozygous for the FGF20 mutation, and homozygous genotypes.

Conclusions: The results of this study suggest that FGF20 does not play an important role in hair cell regeneration in the lateral line of zebrafish embryos. It is possible that other signaling factors in the FGF signaling pathway play a role. We have generated a zebrafish strain with the dnfgfr1 transgene, which will allow us to study the effects of FGF receptor 1 downregulation on hair cell regeneration in the zebrafish lateral line. Experiments with this strain are still ongoing.

Siteman Summer Opportunities Program

044 **Lee, Audrey**

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Mentor: Robert Hayashi, MD

Performance status of extremity tumors

Lee A; Hayashi R

Introduction: Malignant bone tumors account for approximately 6% of all annually diagnosed pediatric cancers in the US, and are the most prevalent type of extremity tumors in children. Due to advances in treatment, limb-sparing surgery has become the primary surgical intervention for extremity tumors. The purpose of this study is to evaluate the functional ability and quality of life of survivors of pediatric cancer who underwent limb-sparing surgery at St. Louis Children's Hospital.
Methods: Participants will complete two standardized questionnaires, the Toronto Extremity Salvage Score (TESS) and the Short Form Health Survey-36 (SF-36). The TESS evaluates physical function and the SF-36 assesses quality of life (QOL).
Anticipated Results: We hypothesize that the participants will have low scores on both surveys, indicating decreased physical functioning and quality of life compared to their peers.
Conclusions: Comparison of the anticipated results with the results of other studies that examine the outcomes of patients with extremity tumors will establish whether the St. Louis Children's Hospital meets the same standard of care found at other hospitals in the nation. If the TESS and SF-36 scores obtained are below the scores from other studies, it will indicate the need to reform the treatment of patients who undergo limb-sparing surgery. If indicated, further research is needed to develop a more effective post-surgical rehabilitation program to improve the functioning ability of the affected limb.

T32 NIH NHLBI Cardiovascular Biology Training Program

105 **Caputa, George**

T32 NHLBI Cardiovascular Biology Training Program
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Mentor: Jean E. Schaffer, MD, PhD

RNASET2: A novel mediator of lipotoxic cell death

Caputa G; Zhao S; Schaffer JE

Introduction: In obesity and diabetes, high levels of serum lipids can become deposited in non-adipose tissues, with serious consequence. Lipotoxic levels of free fatty acids can overwhelm cells, leading to cellular dysfunction and eventual cell death. However, the molecular mechanisms of this response are poorly understood.

Methods: In order to identify players in the lipotoxic response, a mutagenic screen was performed using Chinese hamster ovary (CHO) cells in which palmitate-resistant mutants were selected.

Results: A mutant cell line, 2B1, shows resistance to death in response to high levels of the saturated fatty acid palmitate. The provirus integrated in the locus for RNASET2, an endoribonucleases of the T2 family, causing haploinsufficiency of the RNASET2 protein. Complementation and independent shRNA knockdown confirms that RNASET2 contributes to lipotoxic response. 2B1 cells also fail to accumulate the non-canonical rpL13a small nucleolar RNAs in the cytoplasm following palmitate treatment, which have been shown to be critical to the lipotoxic response. In addition, 2B1 cells are resistant to oxidative stress and accumulate less reactive oxygen species upon palmitate- and peroxide-induced stress.

Conclusions: We conclude that RNASET2 is necessary for lipotoxic cell death, possibly through the amplification of reactive oxygen species, leading to a failure to trigger the flux of rpL13a snoRNAs into the cytoplasm. Future directions include understanding how RNASET2 triggers the production of reactive oxygen species in the context of lipotoxicity. Understanding the unique biology of RNASET2 could lead to possible preventative therapies for metabolic syndromes.

003 **Cheng, Jeffrey K**

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Mentor: Robert Mecham, PhD

Quantification of microstructural and mechanical properties of ascending aorta in elastin deficient mouse models

Cheng JK; Wagenseil JE; Mecham RP

Introduction: Decreased elastin is associated with several human genetic diseases that result in abnormal development of the vasculature. Mouse models with reduced elastin expression develop a functional vascular system with elevated blood pressure and increased arterial stiffness. Constitutive modeling identified differences in the microstructural properties in the ascending aorta of elastin deficient mice and predicted changes in collagen angle orientation and elastin contribution to stress. This study seeks to quantify collagen fiber orientation in WT and *Eln+/-* mice and to gather mechanical data from a humanized elastin mouse (hBAC-mNULL) as a model for pathological remodeling.

Methods: Ascending aorta from 1 month old WT and *Eln+/-* mice were labeled using a fluorescent probe conjugated to a collagen binding protein. Vessels were inflated to mean systolic pressure and imaged using an inverted confocal microscope. Images were flattened and collagen angles were quantified using a morphological algorithm. Inflation and extension tests were performed on ascending aorta of hBAC-mNULL mice to characterize the mechanical properties.

Results: Previous modeling results show an increase with age in the elastin contribution to wall stress in WT and *Eln+/-* mice, with elastin contribution being significantly reduced at all ages in *Eln+/-* compared to WT. This agrees with measured levels of desmosine in the ascending aorta. Collagen fibers were also predicted to reorient from a more axial to a more circumferential orientation with age. Confocal fluorescence images of ascending aorta inflated to systolic pressure showed distinct fibers, and preliminary analysis revealed two predominant orientation angles in the aorta. Mechanical testing of hBAC-mNULL aorta show significant decreases in aortic diameter compared to WT and ELN+/-.

Conclusions: Confocal microscopy was able to produce images of visible collagen fibers in the ascending aorta, and image analysis was able to quantify collagen fiber orientation. Ascending aorta from hBAC-mNULL mice showed a significantly decreased diameter compared to WT and *Eln+/-*.

103 **Jinn, Sarah**

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Mentor: Daniel S Ory, MD

Regulation of Cholesterol Homeostasis by the non-coding snoRNA U17

Jinn S; Dudley NR; Schaffer JE; Ory DS

Introduction: Cholesterol is required for the growth and viability of mammalian cells, and is a critical determinant of the structure and biochemical properties of the plasma membrane. Under physiological conditions, cellular cholesterol level is governed by sterol-regulated transcriptional pathways. The trafficking pathways responsible for cholesterol homeostasis that prevents the alteration to pathophysiological conditions, however, are poorly understood.

Methods: To gain insight into the molecular mechanisms underlying these homeostatic pathways, loss-of-function mutagenesis screen was conducted in Chinese hamster ovary (CHO) cells to select for cells with defects in transporting low-density lipoprotein (LDL)-derived cholesterol from the plasma membrane to internal membranes.

Results: One of the mutants, I5, is protected from amphotericin-induced cell death. Esterification of the plasma membrane derived cholesterol in I5 is lower than wild-type CHO cells, suggesting reduced trafficking of free cholesterol to ER membranes. Provirus had integrated into one of two expressed alleles of Snhg3, which is consistent with a model of haploinsufficiency. Within the introns we identified U17a and U17b, orphan H/ACA snoRNAs that are highly conserved. Complementation experiments and recapitulation of mutant phenotype in murine system demonstrated that U17 snoRNAs but not Snhg3 mRNA is responsible for the cholesterol trafficking defect observed in mutant I5. S1 mapping showed that deficiency of U17 snoRNA does not affect the processing of 18S rRNA, a previously characterized function of U17 homolog in yeast.

Conclusions: We conclude that the U17 snoRNAs modulate intracellular cholesterol trafficking by regulating the genes that are involved in cholesterol homeostasis. The project will further explore the targets of this novel small RNA-dependent pathway, which represents a previously unrecognized mode of regulation for cellular cholesterol homeostasis. Elucidation of the mechanism by which the U17 snoRNAs exert their effects may identify new targets for treatment of atherosclerosis and other acquired states of cholesterol pathophysiology.

001 **Laughner, Jacob, MS**

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Mentor: Igor R Efimov, PhD

A fully implantable pacemaker design for mice: from battery to wireless power

Laughner JI; Marrus SB; Shao CC; Nerbonne JM; Efimov IR

Introduction: Large and small animal models have become a popular platform for the investigation of the genetic and systemic causes of pathological cardiac physiology. Small rodent models, primarily mice, have revealed important relationships between a particular protein or gene in the heart and cardiovascular disease through genetic manipulation. In large animal models, rapid pacing of the atria or ventricles has been shown to produce useful models of heart failure and atrial fibrillation. Unfortunately, genetic engineering in large animal models is not always available or prohibitively expensive, limiting our ability to study molecular mechanisms of disease in these models. Conversely, chronic pacing studies in mice and small mammals are presently impossible due to the size of existing pacemakers.

Here, we present two designs for a fully implantable, miniature pacemaker capable of chronic (>30 days) overdrive pacing in a mouse heart based on 1) a battery powered design 2) and a wirelessly powered design.

Methods: Battery powered and wireless pacemakers were fabricated from standard electronic components at Washington University. Wild-type mice (n=21) were implanted with battery powered-devices (n=16) and wireless-powered devices (n=5). Mice were monitor for post-operative survival and device functionality for at most 6 weeks.

Results: 4 of 16 (25%) mice survived implant of battery-powered devices. Of the survivors, chronic pacing was achieved for a maximum of 6 days before device failure with the battery-powered design. Consequently, a smaller, wirelessly powered design was constructed. 4 of 5 (80%) mice survived implant of wirelessly powered devices. Acute pacing was achieved in 9 of 16 (56.3%) battery-powered devices and 5 of 5 (100%) of wirelessly powered devices. Chronic studies are currently in progress.

Conclusions: When complete, this system will allow the study of both pacemaker-specific phenomena as well as offer a novel model of heart failure. We are confident that this device will become a standard tool in the armamentarium of cardiovascular physiologists.

005 **Oladipupo, Sunday, PhD**

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Department of Developmental Biology, Washington University in St. Louis School of Medicine
Mentor: David Ornitz, MD, PhD

Endothelial FGF receptor signaling is dispensable for development, but is required for vascular response to injury and tumor growth

Oladipupo SS; Smith C; Park C; Santeford A; Apte RS; Choi K; Ornitz DM

Introduction: Despite well-established angiogenic function *in vitro,* and *in vivo* evidence suggesting that FGF signaling is important for both normal physiological and pathological responses of the vascular system, the role of FGF/FGFR signaling *in vivo* in endothelial cells is incompletely understood. The extent to which FGF signaling has direct effects on endothelial cells versus indirect effects mediated through other target cell-types and secondary signaling molecule(s) remain unresolved. Here, we determined the *in vivo* cell-autonomous loss of FGFR1/2 function in endothelial and hematopoietic cells in development, vascular response injury and tumorigenesis.

Methods: We developed and utilized a mouse model in which *Fgfr1* and *Fgfr2* were selectively deleted in cells of both endothelial and hematopoietic lineages, by inactivating conditional alleles for *Fgfr1* and *Fgfr2* (designated double flox/flox 'DFF') with *Flk1-Cre* (resultant mouse designated *Flk1-Cre* DCKO).

Results: Endothelial and hematopoietic FGFR1/2 is dispensable for vascular development under normal physiological conditions. *Flk1-Cre* DCKO mice are viable, fertile, and healthy, and have a normal life span. However, both wound healing and choroidal (following eye choroid laser injury) neovascular growth are markedly impaired in *Flk1-Cre* DCKO. Furthermore, when subjected to a two-stage skin chemical carcinogenesis protocol (DMBA/TPA), *Flk1-Cre* DCKO mice displayed significant resistance to papilloma development compared with their DFF mice counterparts.

Conclusions: These results reveal an essential requirement for FGF signaling for neovascularization following injury and epithelial tumor growth. These studies validate the endothelial cell FGFR as a potential target for enhancing wound repair and treating some cancers and diseases of the eye associated with aberrant vascular proliferation, without toxicities associated with direct manipulation of systemic FGF or VEGF activity.

104 **Olsen, Brett, PhD**

T32 NHLBI Cardiovascular Biology Training Program
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Mentor: Daniel Ory, MD

The structural basis of cholesterol activation in membranes

Olsen BN; Schlesinger PH; Baker NA; Ory DS

Introduction: Regulation of cholesterol homeostasis is essential to mammalian cell function, and multiple response pathways are responsible for detecting and maintaining cholesterol levels in different membranes. Recent work has suggested that these pathways selectively respond to an active form of cholesterol that is observed only above a threshold concentration. However, the differences between active and inactive forms of cholesterol are still poorly understood. We wish to identify structural changes in cholesterol-membrane interactions associated with activation.

Methods: We use molecular dynamics simulations of phospholipid/cholesterol membrane bilayers to obtain atomic-level detail of how the dynamic structure of membranes is perturbed as the cholesterol concentration increases that can be analyzed for changes consistent with activation.

Results: We find that at high cholesterol concentrations, cholesterol becomes significantly more exposed to solvent and partially shifts out of the membrane. This effect is seen in membranes composed of either saturated or unsaturated lipids, and shifts in experimentally measured activation thresholds with membrane composition are consistent with changes in increased cholesterol exposure in simulations.

Conclusions: We have identified several structural changes in cholesterol within membranes coincident with cholesterol activation as measured in experimental systems. These results demonstrate that the activation of cholesterol believed to be responsible for regulating cholesterol trafficking and homeostasis has a common structural basis in its interactions with the membrane. Future research will focus on validation of these simulated results with biophysical and spectroscopic experiments and an exploration of the effects of small molecules on cholesterol activation.

101 **Schugar, Rebecca C**

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Roles of ketone bodies and CoA transferase in myocardial response to pressure overload-induced remodeling

Schugar RC; D'Avignon DA; Weinheimer C; Kovacs A; Crawford PA

Introduction: Myocardial ketone body oxidation, catalyzed by the enzyme succinyl-CoA:3-oxoacid CoA transferase ('CoA transferase,' SCOT), plays a key role in the regulation of cardiac substrate selection, mitochondrial ROS generation, work, and bioenergetic efficiency. Nonetheless, the roles of CoA transferase and ketone body metabolism have never been dissected using genetic models in mammals.

Methods: Mice with cardiomyocyte-specific loss of CoA transferase (SCOT-Heart-KO) were generated. Substrate utilization was quantified in hearts of adult mice using Langendorff perfusions and ^{13}C-edited proton NMR analysis. Transverse aortic constriction (TAC) studies were performed in adult mice, followed by speckle tracking and Doppler echocardiography 4 weeks later.

Results: SCOT-Heart-KO mice tolerated starvation and ketogenic diets without developing cardiomyopathy. Hearts of SCOT-Heart-KO mice exhibit increased fatty acid utilization and reduced channeling of glucose to lactate compared to littermate controls, suggesting key roles for CoA transferase in normal substrate utilization. To determine the role of CoA transferase in pathological states that alter myocardial glucose and fatty acid metabolism, TAC studies were performed. SCOT-Heart-KO mice exhibited improved surgical mortality compared to controls, and four weeks after TAC, cardiac index was higher in the SCOT-Heart-KO cohort than in littermate controls. However, left ventricular end-diastolic volume was trending higher and ejection fraction was lower post-TAC in hearts of SCOT-Heart-KO mice compared to controls.

Conclusions: CoA transferase plays a key role in the ability of the heart to adapt to dynamic metabolic substrate availability. While myocardial loss of CoA transferase improves acute hemodynamic performance in the pressure-overloaded ventricle, CoA transferase activity may favor an adaptive remodeling course. Ongoing studies assess the roles of altered substrate metabolism on mitochondrial function and its relationship with cardiac work and efficiency.

T32 NIH NIDDK Diabetes Training Grant

088 **Wong, Angelica**

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Baseline characteristic predictors of sustained weight loss in interventions for medically vulnerable populations: Be Fit, Be Well

Wong A; Liu Y; Si X; Goodman MS; Warner ET; Bennett GG; Rosner BA; Colditz GA

Introduction: Obesity affects more than one-third of U.S. adults, disproportionately racial/ethnic minorities and socioeconomically disadvantaged persons. Evidence-based weight loss strategies are less effective in these high-risk patients who also have elevated rates of obesity-associated conditions (type 2 diabetes, hypertension, cardiovascular disease). We examine baseline characteristics that may predict sustained moderate weight loss of 2.5% and 5% at 24 months using data from the behavioral intervention, Be Fit, Be Well (BFBW).

Methods: The participants were predominantly socioeconomically disadvantaged, racial/ethnic minorities. Analysis for 2.5% and 5% weight loss was limited to the 314 of 365 participants (86.0%) completing 24-month follow-up (two patients with 24-month data were excluded because of cancer). We computed logistic regressions for successful 2.5% and 5% weight loss, controlling for predictors age, gender, baseline body mass index (BMI), treatment group, education level, income level, insurance type, ethnicity, health literacy, employment status, health center, diabetes status and hypertension control.

Results: At 24 months 119 of 316 participants (37.7%) lost more than 2.5% of their initial weight and 71 (22.5%) lost more than 5%. Intervention participants had higher odds of 2.5% weight loss (OR 1.74, 95% CI 1.07-2.83), but not statistically significant 5% weight loss (OR 1.14, 95% CI 0.65-2.01). Higher baseline BMI (weight in kg/height in m^2) was associated with increased odds of sustained 5% weight loss (OR 1.05 per 1-kg/m^2 increase, 95% CI 1.00-1.11). After multivariable control, education and employment statuses were not related to successful weight loss, though unemployed participants had a suggestive greater odds of sustained 2.5% weight loss (OR 1.61, 95% CI 0.83-3.13) and 5% weight loss (OR 1.46, 95% CI 0.67-3.19). The trend for higher health literacy and sustained weight loss was positive but not significant for either weight loss category; the lowest health literacy tertile had less sustained weight loss.

Conclusions: In this predominantly low income and ethnically diverse population education, income, and employment statuses did not emerge as strong predictors of successful weight loss of 2.5% or 5% at 24 months. Given the need to refine low cost interventions for such populations, these data, demonstrating comparable study outcomes across sociodemographic characteristics, suggest future studies can enroll a broad population, achieve high participation rates, and participants can achieve clinically meaningful sustained weight loss.

T35 NIH NHLBI Training Grant

035 **Aggrey, Gerald**
Medical Student
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Mentor: Matthew Smith, MD
A retrospective analysis of injury patterns in youth fastpitch softball players
Aggrey GK; Davis R; Brophy RH; Wright RW; Smith MV
Introduction: Fast-pitch softball is one of the most popular female sports in the United States. To date, there are no player-reported studies evaluating injury patterns in these athletes. As a result, there are no injury prevention guidelines for softball players. The purpose of this study is to evaluate player-reported injury patterns in fastpitch softball players so that injury prevention guidelines (for protective equipment, training programs, competition schedules, etc.) can be developed.
Methods: 56 fastpitch softball players were asked to complete an online survey retrospectively cataloging their level of participation in softball, the positions played, prior injury as a result of participation in fastpitch softball, and treatment for these injuries. Injury was defined as pain that prevented participation in practice or a game.
Results: Out of 56 players surveyed, 45 (80%) play at the select club level. The mean reported playing time was 6.6 years (SD = 2.7). Overall, 31 (55%) players reported injury from playing fastpitch softball. The breakdown of injury by site was: 10 shoulder (24%); 10 ankle (24%); 7 knee (17%); 5 elbow (12%); 3 wrist (7%); 3 low back (7%); 2 hip (5%), and 2 back (5%). 87% of injured players sought treatment from a physician. Only 2 (5%) injuries required surgery. 9 players (29%) out of the 31 injured reported being injured from pitching.
Conclusions: Injury from participation in fastpitch softball was reported in more than half of the players who were surveyed. Catastrophic injury (injury that requires surgery) is rare. Pitching accounted for 29% of the reported injuries. A prospective evaluation of injury patterns in these athletes is needed to identify risk factors for injury according to position.

124 **Blackett, John W**
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Mentor: Jerry Jaboin, MD, PhD
Analysis of survival and prognostic factors in aggressive meningiomas after radiosurgery
Ferraro DJ; Funk RK; Blackett JW; DeWees TA; Perrin R; Dryzmala RE; Simpson JR; Jaboin JJ
Introduction: WHO grade II and III meningiomas are aggressive brain tumors. While grade III meningiomas invariably have poor outcomes, the course of grade II tumors is less predictable. The purpose of this investigation was to identify factors associated with increased recurrence and decreased survival among patients with aggressive meningiomas so that the patients most likely to have poor outcomes might be recognized and treated appropriately.
Methods: The medical histories of 35 patients with WHO grade II and III meningiomas treated with Gamma Knife between 2000 and 2011 were retrospectively reviewed. Overall survival and progression-free survival following Gamma Knife were measured using Kaplan-Meier curves. Known and theorized prognostic factors were statistically analyzed to determine whether any were significantly associated with patient survival or tumor recurrence.
Results: Three-year overall survival (OS) and progression-free survival (PFS) rates were 78.0% and 65.0%, respectively. WHO Grade II 3-year OS and PFS were 83.4% and 70.1% respectively. WHO Grade III 3-year OS and PFS were 33.3% and 0% respectively. Three-year OS was significantly decreased by a prior history of benign meningioma, a history of previous fractionated radiation therapy, tumor volume, isocenter number and volume, increasing length of time between surgery and radiosurgery, and WHO grade III histology. Three-year PFS was significantly decreased by a prior history of benign meningioma, increasing mitotic rate, increasing margin dose, the presence of spontaneous necrosis or nuclear atypia, and WHO grade III histology.
Conclusions: WHO grade III histology and a history of previous benign meningioma were the strongest risk factors for recurrence and mortality in aggressive meningioma patients treated with surgery and Gamma Knife. The size of the tumor was a risk factor for poor survival, while nuclear atypia, necrosis, and increased mitotic rate were risk factors for recurrence. Patients with these characteristics should be closely observed and treated more aggressively.

053 **Bokshan, Steven L**

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Mentor: Jose Pineda, MD

The primary-secondary index: A novel index for quantifying primary and secondary ICP injury

Bokshan SL; Leonard JR; Mondello S; Hayes RL; Limbrick DD; Berger RP; Bruce CT; Pineda J

Introduction: Despite the current utility of biomarkers in stratifying patients with varying degrees of traumatic brain injury (TBI), researchers have yet to explore biomarkers as indicators of secondary injury in children. This study explores the clinical utility of biomarkers in quantifying both primary and secondary ICP injury after severe, pediatric TBI.

Methods: This is a prospective case-control study performed at Saint Louis Children's Hospital in Saint Louis, Missouri designed to explore the inpatient time course and clinical relevance of the biomarkers cytoplasmic ubiquitin C-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) after severe (GCS ≤ 8) TBI. Here, we created a novel index known as the primary-secondary index (PSI) to encompass both primary and secondary ICP injury. A total of n = 32 patients with severe TBI and n = 40 control subjects were enrolled.

Results: Both UCH-L1 and GFAP were latently elevated in the first few days following severe TBI. Latently elevated plasma concentrations of GFAP (measured with a standardized logarithm index) provided the highest correlation with secondary ICP insult (measured using pressure times time dose values that reflect cumulative time spent at ICP > 20 mmHg for the first 3 days following injury) with r = .77 and p = .006. The PSI correlated better with the Extended Glasgow Outcome Scale (GOS-E) than either measures of primary or secondary ICP injury alone.

Conclusions: UCH-L1 appears to be a superior indicator of primary injury shortly after pediatric TBI whereas GFAP outperforms UCH-L1 as a measure of secondary ICP injury. Taken together in the PSI, these biomarkers can potentially be used to monitor and adjust ICP treatment in real time.

078 **Brower-Lingsch, Adrienne**

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Mentor: Alexandre Carter, MD, PhD

Variability in individual response to continuous theta burst transcranial magnetic stimulation

Brower-Lingsch A; Carter A

Introduction: Transcranial magnetic stimulation has shown potentially exciting but inconsistent promise as a method of noninvasive brain stimulation. In order to build on this technique as a potential therapeutic tool, we must be able to reliably replicate the findings reported by existing protocols. Further we need to better understand and account for any individual response variability that does exist. The purpose of this study is to test a common continuous theta burst stimulation (cTBS) protocol for its ability to consistently generate corticospinal inhibition after stimulation of the primary motor cortex (M1) of healthy participants.

Methods: Motor evoked potential (MEP) responses from the first dorsal interosseous of 8 healthy participants were measured at 2 points before and at 1, 10 , 20 and 30 minutes after receiving cTBS (50Hz, 5Hz, 600 stimuli) to the contralateral M1. Participants performed an isometric muscle activation task prior to cTBS. A subset of 5 participants received an immediate second round of identical muscle activation, cTBS, and follow up MEP measures.

Results: There was no significant difference in average MEP response at any time point (Time: $F(2,15)=.94$, $p=.470$). There was a non-significant trend toward negative correlation between the participant resting motor threshold and the MEP amplitude at 10, 20, and 30 minutes (Ten: $r(6) = -.62$, $p=.099$; Twenty: $r(6) = -.62$, $p=.105$; Thirty: $r(6) = -.60$, $p=.118$). For those participants who underwent a second round of cTBS, there appeared to be little relationship between the response to the first and the second round.

Conclusions: The results of this study suggest that the current protocols do not produce reliable responses in all populations. Going forward, it may be important that we find TMS protocols which produce more consistent results. Alternatively, when incorporating this protocol into future studies or clinical applications, we must take into consideration that there may be considerable individual variability. Further, as we continue to explore this variability, we may find it in fact tells us something meaningful about differences in excitability, physiology, or malleability of individual cortices at a given time.

029 **Chen, Yulong**

Medical Student
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Summer Research Program
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Mentor: Michael Avidan, MD

Prevention of acute and persistent postoperative pain associated with surgical treatments clinical trial

Chen Y; Avidan MS

Introduction: Acute and persistent pain are common postoperative complications that have adverse effects on patients' quality of life. It is estimated that 33% of patients suffer from acute pain after major procedures, while persistent postoperative pain afflicts 5-30% of patients. While efficacy trials have suggested that supplemental administration of ketamine may reduce acute postoperative pain, the role of ketamine in preventing persistent postsurgical pain has been left unexplored, and there has been a paucity of effectiveness data analyzing the relationship between ketamine and postoperative pain. Thus, the purpose of our multi-center effectiveness trial is to assess whether supplemental administration of ketamine leads to a decrease in acute and/or persistent postoperative pain.

Methods: Patients over the age of 65, who are capable of providing informed consent and undergoing major surgeries, will be eligible for this study. After providing informed consent, patients will be randomized to receive low dose ketamine or placebo following anesthetic induction and prior to surgical incision. Aside from the supplemental administration of ketamine, the anesthetic team assigned to the patient will make all decisions regarding course of anesthesia. Once the surgery has concluded, postoperative acute pain will be assessed in the post anesthesia care unit (PACU) using the 10 point Visual Analog Scale (VAS) every 12 hours for the first 3 postoperative days. Postoperative chronic pain will be assessed with the Brief Pain Inventory Short Form (BPI-SF) and the Neuropathic Pain Symptom Inventory within 3-6 months after surgery. Quality of life will be assessed with the self-report Barthel Index within 3 months to 1 year after surgery.

Anticipated Results: We anticipate that supplemental administration of ketamine will be associated with a decrease in acute and persistent postoperative pain.

Conclusions: If, upon its conclusion, this clinical trial demonstrates that supplemental administration of ketamine decreases acute and/or persistent postoperative pain, the results may lead to a change in standard anesthetic practice that improves patients' quality of life following major surgeries.

021 **Chi, Stephen W**

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Mentor: David Beebe, PhD

Application of a double-fluorescent CreER reporter mouse to corneal epithelial lineage tracing

Chi SW; Shui YB; Bai F; Beebe DC

Introduction: Corneal epithelial homeostasis is a complex balance between stem cell proliferation, migration of differentiated cells, and mechanical loss. While past studies have examined the dynamics of corneal epithelial turnover, the inability to locate stem cells and trace their lineages has restricted our understanding of corneal maintenance and wound repair. The purpose of this study is to investigate whether the mT/mG-CreER mouse, an inducible double-fluorescent reporter line, could be used to trace corneal epithelial lineages.

Methods: mT/mG-CreER mice were divided into control, injected control, and surgical groups. To induce recombination and expression of EGFP, mice were injected subconjunctivally with Tamoxifen dissolved in corn oil. In the surgical group, stem cell proliferation was challenged by partial or whole limbal wounding using an ophthalmic burr. Mice were sacrificed over the course of six weeks and their corneas were examined under confocal microscopy.

Results: The mT/mG-CreER reporter mouse successfully produced patterns of fluorescence consistent with corneal epithelial stem cell lineages. Control mice globally expressed tdTomato and exhibited strong red fluorescence throughout the cornea. Non-induced expression of EGFP with green fluorescence was commonly noted in corneal endothelial cells and nerves, but only rarely in epithelial cells. After induction of recombination, EGFP-expressing cells were initially found stochastically throughout the epithelium, but gradually resolved into streams of green-fluorescing cells extending from the limbus to the central cornea. Surgical injury of the limbus reduced the number of streams originating from the wounded region and induced additional fluorescence in the non-surgical fellow eye.

Conclusions: The results of this study show that the mT/mG-CreER reporter mouse is an effective model for visualizing epitheli cell lineages in the cornea. The presence of streams originating in the limbus also provides additional evidence for the putative location of these stem cells. Subsequent studies with this model could be used to examine patterns of wound repair or abnorm pathologic processes.

095 **Denny, George O**

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Mentor: Arthur Loewy, PhD

Differential expression on ENaC subunits in Dahl salt-sensitive and Sprague Dawley rats

Denny GO; Miller RL; Wang MH; Loewy AD

Introduction: According to the CDC, hypertension is present in 31% of American adults and accounts for 25,000 deaths a year. High levels of sodium intake are correlated with hypertension. However, the exact molecular relationship between high sodium intake and hypertension is still not completely understood. The purpose of this study was to explore the relationship between sodium epithelial channels (ENaCs) in the regions of the brainstem and kidneys, and salt-induced hypertension in rats.

Methods: Sprague Dawley (SD) rats and Dahl salt-sensitive (DSS) rats were split into high sodium food and regular sodium food, creating four treatment groups: SD rats on regular sodium food, SD rats on high sodium food, DSS rats on regular sodium food, and DSS rats on high sodium food. DSS rats are an animal model for salt induced hypertension and develop severe hypertension following 3 weeks of high salt intake. Each animal was kept in its respective treatment group for 3 weeks, and at the 3 week time point the brain, brainstems, and kidneys were removed. The RNA was then extracted from the area postrema (AP), hypoglossal nucleus (HN), and the kidney cortex and analyzed by reverse-transcription qPCR using the 2-delta-delta-CT method. RPL4 was used as an endogenous control for the three subunits of the ENaC channel.

Results: In the SD and DSS regular sodium group there was no difference seen in the expression of any ENaC subunits in the HN or the kidney cortex. However, in the AP it was observed that the DSS rats had an expression of ENaC-beta 11% that of SD rats ($p<0.05$) and an expression of ENaC-gamma 199% that of SD rats ($p<0.05$). When subjected to a high salt diet the DSS rats had no significant change in expression of any gene in any sampled tissue. In contrast to this, the SD high sodium food rats had an AP ENaC-gamma expression 227% ($p<0.05$) that of the SD regular sodium food rats.

Conclusions: The results of this study suggest that salt induced hypertension in DSS rats may be related to a failure of the AP to up-regulate the gamma subunit of the ENaC channels in the face of high sodium levels, or perhaps to an intrinsic differential expression of ENaC subunits in the kidney cortex.

No poster displayed

Ghenbot, Rahel

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Mentors: Gary Skolnick; Kamlesh Patel, MD; Albert Woo, MD

Cranial vault volume in unoperated sagittal synostosis – a case study and comparison

Ghenbot R; Skolnick G; Patel K; Naidoo S; Smyth M; Woo A

Introduction: It has long been believed that cranial vault volume (CVV) is reduced in children with sagittal synostosis, but some studies have reported volumes within or even above normal limits. Here we present a 15 year old patient with uncorrected sagittal synostosis. Using computed tomography (CT) data we analyze his CVV and cephalic index (CI) over time and compare them to those of children with corrected sagittal synostosis and to normal controls.

Methods: CT scans of a patient with uncorrected sagittal synostosis were matched with CT scans from four age- and gender-matched patients with surgically repaired sagittal synostosis and four normal controls. CVV and CI were calculated.

Results: Our case was first seen by the craniofacial team at 21 months for untreated nonsyndromic sagittal synostosis. He was followed by the craniofacial team for the past 13 years. In that time, there has been no abnormal developmental, behavioral, or emotional functioning. At 28 months, the CVV and CI of our case were 1169.4cc and 69.9%, respectively. At 14.7 years, they were 1399.5cc and 72.0%. In the young age group, the mean CVV and CI of the operated sagittal cases were 1251cc and 70.9%, respectively. The mean CVV and CI of the normal controls were 1227cc and 89.4% respectively. In the older age group, the mean CVV and CI of the operated sagittal cases were 1428cc and 74.9%, respectively. The mean CVV and CI of the normal controls were 1634cc and 82.3%, respectively. The CVV growth was similar between our case and the patients with corrected sagittal synostosis, but well below that of the normal controls.

Conclusions: The long term effects of sagittal synostosis are not well documented as corrective surgery for sagittal synostosis is generally performed at a young age to prevent increased intracranial pressure, brain growth restriction, and for aesthetic purposes. This case demonstrates that surgical correction may not always be needed to allow normal development. Further studies are needed to determine when surgical correction is required for normal development and when it would be a strictly cosmetic, elective procedure.

131 **He, Yizheng**

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Mentor: Eric C. Leuthardt, MD

Concordance of ECOG mapping and rs-fMRI mapping in simple motor tasks

He Y; Hacker C; Leuthardt EC

Introduction: Brain-computer interfaces (BCIs) have been shown to decode electrocorticography (ECOG) signals to effect various kinds of device control, and ECoG has become increasingly important as a potential platform for clinical application in the future. A critical need exists in neurosurgery to determine the optimal location for surgical implantation of a small and minimally invasive ECoG grid for the extraction of appropriate signals. Here, we explored how well the sensorimotor network (as delineated by rs-fMRI) predicts which electrodes in an implanted grid show power changes in gamma (75-110 Hz) or beta (12-30 Hz) frequency bands during simple motor tasks.

Methods: ECOG data from four patients were analyzed, and statistically significantly activated electrodes were identified for a hand open-close task and a tongue movement task after preprocessing the data. Using these electrodes as the ground truth, a Receiver Operating Characteristic (ROC) analysis was performed on continuous values for all electrodes representing the probability of being a part of the sensorimotor network, where the probability values were generated using a perceptron classifying the rs-fMRI data for each patient.

Results: Preliminarily, there was a good correspondence (high sensitivity and specificity) between the "activated" electrodes and electrodes with high probability of belonging to the sensorimotor network. The exact values are forthcoming as more refined perceptron probability values are being developed.

Conclusions: The high concordance between the rs-fMRI and ECOG modalities in identification of the motor network is promising for the development of methods to delineate motor cortex (as well as other neural networks such as the language network) using solely rs-fMRI, which is safe and noninvasive and does not require an actively engaged patient. The current gold standard for localizing brain networks requires invasive electrophysiological monitoring. With this new technique, rs-fMRI might one day elucidate the location of brain networks non-invasively in order to accurately place electrodes for BCIs.

006 **Jagadeesan, Nhila**

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EEG through the ages

Jagadeesan N; Avidan M

Introduction: Although the electroencephalogram (EEG) has been used to monitor brain activity for nearly a century, it has not been adopted on a broad scale in operating rooms. There is much scope for its use, as many surgeries involve anesthetics, whose main target is the brain. In these cases, the use of EEG to monitor the brain activity of patients under anesthesia would afford anesthetists the opportunity to monitor more directly the therapeutic effects of general anesthesia, rather than monitoring side effects as surrogates. However, the EEG may vary with patient age and different anesthetic agents. Currently, EEG use is enjoying a resurgence in adult anesthetic practice, but its role and utility in pediatric anesthetic practice is not well defined.

Methods: Frontal single or dual channel continuous EEG recordings were obtained in the operating room from patients ranging from 4 months of age to 70 years. These data are currently being analyzed off-line for changes in brain electrical activity associated with age or administration of specific anesthetics. Different anesthetic medicines will be included as covariates in the candidate statistical models.

Results: In this ongoing study, roughly 50% of the patients were pediatric patients ranging from 12 years to 4 months. The adult 50% of the study population had more dynamic variation in age, ranging from 70 years to 32 years. In both populations, we expect to observe characteristic EEG changes (e.g., increased coherence, loss of entropy, shift to low frequency waves) after the administration of various anesthetic medications.

Conclusions: It is likely that this study will suggest that it is possible to characterize EEG changes in response to various anesthetic, sedative and analgesic medications in patients of various ages. Specifically, we anticipate that EEG patterns of patients of different ages will be characterized, and nuanced details about particular drug effects will be ascertained. This study will help to define the potential utility of limited montage EEG as a routine perioperative monitor in patients of all ages.

080 **Ji, Joyce**

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Mentors: David H Gutmann, MD, PhD; Robert C McKinstry, MD, PhD

Optic nerve tortuosity in individuals with neurofibromatosis type 1

Ji J; Shimony J; Gao F; McKinstry RC; Gutmann DH

Introduction: Increased optic nerve tortuosity is often described in children with the neurofibromatosis type 1 (NF1) brain tumor predisposition syndrome. The purpose of this study was to apply objective and subjective criteria to determine the value of this finding in individuals with NF1.

Methods: A retrospective study over a period of 8 years, from 2005 until 2012, was performed on children with NF1 with and without optic glioma compared to children without NF1 who underwent neuroimaging for headache. A tortuosity index (TI) was computed for the optic nerve in each subject using a high-resolution 3D T1-weighted magnetization prepared rapid gradient echo sequence, and the TI was averaged and compared across groups.

Results: The TI for patients with NF1, regardless of the presence of an optic glioma were greater than those without NF1 ($P<.001$). There was no correlation between subjective measures of tortuosity and the objective scoring (TI). Similarly, there was no correlation between the degree of tortuosity and patient age or sex.

Conclusions: Individuals with NF1 as a group have increased optic nerve tortuosity relative to unaffected individuals, independent of the finding of an optic glioma. In this regard, the presence of tortuosity is not predictive of optic glioma development in children with NF1.

087 **Leu, Ann**

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Mentors: Susan E Mackinnon, MD; Philip J Johnson, PhD

The effect of FK-506 on Wallerian degeneration following peripheral nerve transection

Leu A; Dvoracek LA; Johnson PJ; Mackinnon SE

Introduction: Minimizing the time to muscle re-innervation following peripheral nerve injury is a major factor that contributes to successful functional recovery. FK-506 (tacrolimus), a known immunosuppressive agent, has been shown to increase the rate of axonal regeneration after nerve injury but its effect on Wallerian degeneration (WD), a process that primes the injured nerve for axonal regrowth, is still unclear. The purpose of this study is to investigate whether FK-506 affects the rate of WD.

Methods: A chronic peroneal denervation model in Thy1-GFP transgenic rats, which express GFP in their peripheral nerves, was used to investigate the effects of FK-506 on WD. Sixteen rats were randomized into a control group receiving no injections and an experimental group receiving daily injections of FK-506 (2 mg/kg) with a 3 day pretreatment. In vivo fluorescent imaging of the injured nerve was performed on all animals on 0, 3, 7, 10, and 14 days after surgery and analyzed. The distal nerve was harvested on day 14 for histomorphometry and percent debris analysis, a measure of WD.

Results: The FK-506 treated group displayed a faster rate of decrease in fluorescence as compared to the control group, which suggests that FK-506 is potentially increasing the rate of WD after nerve transection. However, the FK-506 group started off with significantly higher baseline fluorescence than the control group on day 0, which may or may not be a contributing factor to the faster drop-off in fluorescence. The results of tissue histomorphometry and percent debris analysis are pending.

Conclusions: It has been shown that FK-506 mediates its neuroregenerative effects through a heat shock protein 90 pathway but a recent study suggests that FK-506 is also working through an additional parallel pathway that has yet to be determined. Knowing whether FK-506 has an effect on WD could help begin to elucidate other pathways that may be mediating the faster nerve regeneration and better functional recovery, with the ultimate goal of developing an FK-506 analogue that confers the benefit without the adverse immunosuppressive effects.

023 **Li, Han**

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Developing a screening test to identify psychophysical correlates of macular dysfunction

Li H; Abrams RS; Culican SM

Introduction: Hydroxychloroquine, marketed as Plaquenil, is an anti-inflammatory drug used to treat autoimmune diseases. A small percentage of patients taking Plaquenil develop retinal toxicity that leads to vision loss (bulls-eye maculopathy). Therefore, the AAO recommends screening by an ophthalmologist and ancillary testing to assess macular function for patients on Plaquenil. These recommendations are controversial due to their high cost, inaccessibility, and lack of evidence to support these tests for early detection of maculopathy. Our research aimed to develop a screening test which can be quickly and easily administered. To this end, we created a computerized visual graphic task and administered it on participants with and without macular disorders to assess efficacy in detecting macular dysfunction.

Methods: We developed and administered a visual task to two study groups: subjects with and without macular disorders. Data were collected from the task and statistical analysis was performed to compare test performance between the two groups to determine if the test has potential as a screening tool.

Results: There was a significant difference ($p=.001$) between the mean number of errors made by eyes with visual pathology compared to eyes without on the screening task. Furthermore, there is no significant difference between the first eye tested and the second eye tested, suggesting that factors such as learning curve and fatigue are negligible in our screening task. Lastly, we found only a weak correlation between visual acuity and test performance when controlling for visual pathology ($r=.320$, $p<.05$), indicating that test performance is only minimally impacted by the patient's near distance visual acuity.

Conclusions: The results of this study suggest that our visual task has potential in monitoring for retinal toxicity in patients on Plaquenil therapy. Given that it is computerized, we anticipate that this could be used as a cost effective and widely available screening tool that could reduce the burden on healthcare costs and allow a greater proportion of patients to receive screening when otherwise not available. Further research will need to be done to test toxic maculopathy patients and assess their performance on the task.

117 **Ma, Jimmy**

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Effect of indoor allergen exposure on allergic sensitization and timing of asthma diagnosis after severe respiratory syncytial virus bronchiolitis

Ma J; Bacharier LB; Schweiger T; Zheng J; Castro M

Introduction: Children who develop severe respiratory syncytial virus (RSV) bronchiolitis are at increased risk of developing childhood asthma and allergic sensitization. This study aims to examine how indoor allergen exposure affects the development of allergic sensitization and timing of asthma diagnosis in children who have had severe RSV bronchiolitis.

Methods: 206 children hospitalized for severe RSV bronchiolitis before age 1 were enrolled in the RSV Bronchiolitis in Early Life (RBEL) study. Home dust samples were collected at entry and allergen exposure histories were taken at quarterly follow-ups through age 8. Allergy testing via skin tests or RAST was done at ages 3 (n=90) and 7 (n=47). Analysis was focused on a subset of 105 children, which excluded those children lost to follow up and those with an asthma diagnosis before age 3. This allowed for a predictor analysis of those children who were diagnosed after age 3.

Results: Of the 48% diagnosed with asthma in RBEL, 19% were diagnosed with asthma after age 3. In this subset, 24% of the 90 subjects tested for allergic sensitization at age 3 were sensitized to ≥1 allergen. No specific allergen exposure (in dust or parental report) was associated with sensitization at age 3. High exposure to Can f1 (dog allergen) before age 1 was associated with sensitization at age 7 (OR=6.3, CI: 1.4-28.5) and earlier diagnosis of asthma ($p=0.022$). Sensitization to any tested allergen at age 3 was associated with subsequent asthma diagnosis (OR=3.7, CI: 1.2-11.4) and earlier timing of diagnosis ($p=0.026$).

Conclusions: In subjects diagnosed with asthma after age 3, early dog allergen exposure and sensitization at age 3 is associated with an earlier diagnosis of asthma. These are consistent with previous results in children diagnosed with asthma before age 3. Our findings suggest that those with later asthma diagnosis have similar risk factors as those diagnosed earlier. Allergen exposure and allergy testing may be helpful in understanding asthma in children of all ages who have had severe reaction to RSV.

019 **Marks, Lauren A**

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Quantitative pharmacodynamics of dopamine receptors from MRI

Marks LM; Black KJ

Introduction: Functional MRI (fMRI) is used to map which brain regions respond to a particular drug, but provides little quantitative information about its effects. This research project is part of a larger study designed to validate a novel brain imaging technique for rapidly estimating the half maximal effective dose (ED_{50}) of a drug. The purpose of this project is to provide comparative, or "true", estimates of the ED_{50} of a dopamine D1 agonist using more traditional methods.

Methods: Data were collected from 5 male baboons. A preliminary prolactin (PRL) control study was performed on each animal in order to determine the magnitude and time course of the effects of ketamine anesthesia on prolactin release. Eight BOLD sessions were then conducted on each animal with different doses of the D1 partial agonist, SKF38393. A Markov chain Monte Carlo method was used to estimate ED_{50}s from PRL plasma concentration at each dose. Similar ED_{50} estimates and dose-response curves were constructed from BOLD (fMRI) responses to SKF38393 in 4 volumes of interest (VOIs): hypothalamus, pituitary, striatum, and midbrain.

Results: Results from the prolactin time course experiments showed that PRL plasma concentrations peaked shortly after ketamine administration and decayed with a mean half-life ($t_{1/2}$) of 66.13 minutes (SD = 30.81). Dose-response curves constructed from the BOLD sessions failed to fit a predicted sigmoid shape. The ED_{50} estimated from the median plasma prolactin dose-response curve for all animals was 0.339 mg/kg. The ED_{50} estimates from group dose-response curves of BOLD data in hypothalamus, pituitary, striatum, and midbrain were 1.59, 2.74, 7.70, and 2.25 mg/kg, respectively.

Conclusions: The results from the anesthesia time course experiment suggest that ketamine causes an increase in PRL release. However, results from the BOLD experiments were inconclusive due to several limitations including a small sample size. The ED_{50} estimates obtained from the dose-response curves may not be valid comparative estimates of the half maximal dose of SKF38393 because the dose-response curves failed to fit a predicted sigmoid shaped model.

039 **Meyer, Zachary**

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Intramedullary nailing vs. spica casting in children with femoral shaft fractures ages 2-6

Meyer Z; Dobbs MB

Introduction: Historically, femoral shaft fractures in children under age 6 have been treated with spica casting with excellent outcomes. Intramedullary (IM) nailing of femoral shaft fractures in this age group has become more prevalent as operative management of pediatric fractures has become more popular and complications better predicted and avoided. The purpose of this study is to compare the outcomes, complications, and cost of spica casting vs. IM nailing of uncomplicated femoral shaft fractures in the 2-6 year old age group.

Methods: Data from consecutive patients treated by two surgeons for femoral shaft fracture between January 2001 and July 2012 were reviewed. The primary endpoints were union at six months and total cost. Secondary endpoints included time spent in the OR, follow-up length, number of follow-up visits, and clinically significant complications.

Results: Of the 183 unique records identified, 145 fractures were included in the study. Fractures were excluded if they were associated with closed head injury, extremity fracture, or chronic pathology. No patients in either group experienced non-union or malunion. 4/99 patients in the Spica group had shortening 2 cm or greater and 2/99 had skin breakdown secondary to casting. 14/46 patients in the IM group complained of painful hardware, 31/46 had the nails removed, and 6/46 retained the nails. Average OR time was significantly longer for the IM nail group (34.14 min Spica vs. 61.25 min Nails; 95% CI for difference 19.56-34.64; $p<0.0001$). Average physician cost of IM nailing was significantly higher than the Spica group ($6900 vs. $3452; 95% CI for difference $3278.15-$3617.86; $p>.0001$). Nights spent in the hospital and number of follow up visits did not differ significantly.

Conclusions: The results suggest that IM nailing for uncomplicated femoral shaft fractures in children ages 2-6 is more costly than spica casting and does not offer superior outcomes. Children in this age group have tremendous remodeling potential and the shortening seen in the spica group did not warrant additional procedures to manage. Spica casting is a cost effective treatment for uncomplicated femoral shaft fractures in the 2-6 year old age group.

134 **Molina, Sergio L**

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ApoE isoform quantitation in AD and controls

Molina SL; Bateman R

Introduction: The apolipoprotein E ε4 (ApoE4) allele is the single greatest genetic risk factor for developing Alzheimer's disease (AD). Population studies have demonstrated that ApoE4 increases the risk of developing AD (1 allele imparts a 3-fold increase while 2 alleles imparts a 12-fold increase). With a prevalence of about 22% in the general population, the E4 allele has been estimated to contribute to ~50% of AD. It is postulated that ApoE4 is a major contributing factor for AD via impaired Aβ clearance, possibly caused by impaired ApoE4 clearance or decreased amounts of ApoE. However, due to conflicting results, it is not clear if the ApoE4 isoform is decreased, increased, or unchanged in levels compared to ApoE3 in human samples. This project aims to definitively determine absolute and relative amounts of ApoE isoforms in samples of cerebrospinal fluid (CSF) from participants with AD and age-matched controls. Absolute and relative amounts of ApoE isoforms will also be measured from samples of frontal cortex from participants who were cognitively normal at the time of death.

Methods: To quantitate Apo isoforms in CSF, CSF collected from previous metabolism studies will have an isotopically-labeled internal standard of ApoE3 and 4 added to it. Affinity purification will then be performed and followed by clean up and digestion. Finally, quantitative mass spectrometry will be performed to measure each isoform amount in CSF. To quantitate isoforms in the frontal cortex, brain tissue from the frontal lobe grey matter has been collected. The tissue will be isotopically-labeled with the same internal standards, homogenized, purified, and digested. Quantitative mass spectrometry will then follow.

Predicted Results: We hypothesize that there will be at least a 25% decrease in levels of ApoE4 compared to ApoE3 in the brain and CSF within the same participant samples and between average ApoE4 and ApoE3 by group.

Conclusions: Utilizing a novel method to measure ApoE isoforms, we will measure ApoE physiology and pathophysiology in the brain and CSF of AD and control participants.

129 **Patel, Bhuvic**

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Peri-procedural complications from endovascular treatment of unruptured cerebral aneurysms: Is routine ICU observation necessary?

Patel B; Arias EJ; Derdeyn CP; Zipfel G

Introduction: Unruptured cerebral aneurysms occur in approximately 2.0% of the general population. Based on data from the Nationwide Inpatient Sample, there were 14,765 patients discharged with unruptured cerebral aneurysms between 1998 and 2007. From 2002 to 2007, 61.7% of all treated unruptured aneurysms were treated using endovascular coiling. Although endovascular coiling is now even more frequently used, there are no standards for post-procedure inpatient monitoring. However, due to the risk of potential complications, including stroke, cardiac dysfunction, intracerebral hemorrhage, and mortality, patients are often observed in an intensive care setting for at least 24 hours. The extended hospital stay significantly increases the cost associated with endovascular coiling. The purpose of this study is to analyze the rate of post procedural complications at our institution, and determine whether routine post procedure monitoring in an intensive care setting is justified.

Methods: A retrospective analysis of hospital records for 688 endovascular coiling treatments of unruptured cerebral aneurysms was performed.

Results: Overall, 505 patients underwent 688 endovascular coiling treatments of their unruptured cerebral aneurysms. In total, 33 of these treatments (4.8%) resulted in complications (6 hemorrhages, 8 strokes, 5 cardiac events, 5 retroperitoneal hematomas and 9 groin hematomas). The vast majority (72.7%) of these complications occurred within 4 hours of the end of the procedure. In contrast, 18.1% of the complications occurred between 4 to 12 hours, 3.03% occurred between 12 and 24 hours and 6.06% occurred more than 24 hour after the procedure.

Conclusions: The results of this study suggest that complications from endovascular treatment of unruptured cerebral aneurysms are not only rare, but also occur within 4 hours of the completion of the procedure in most cases. We therefore recommend that patients who awaken from the procedure at their neurologic baseline can be observed in a post-operative care setting for the first four hours before being discharged to a floor bed, thus significantly reducing the cost associated with the endovascular coiling procedure.

135 **Patel, Tirth**

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Investigation of pathologic role of microtubule associated protein tau in Alzheimer's disease

Patel T; Yamada K; Holtzman D

Introduction: Alzheimer's disease (AD) is the most common cause of dementia in the elderly. AD is characterized by two pathological hallmarks, extracellular amyloid plaques and Intracellular neurofibrillary tangles. Amyloid plaques are composed of aggregated forms of amyloid beta (A-beta) peptide. Neurofibrillary tangles (NFT) are composed of hyperphosphorylated aggregates of the microtubule associated protein tau. Under physiological conditions, tau is present as a soluble monomeric form, but loses solubility and accumulates into NFT as disease progresses. Both pathologies are detrimental and likely contribute to disease symptoms. Growing evidence suggests that NFT lead to neuronal dysfunction and cell death in AD. NFT are also hallmark of other neurodegenerative disorders. Elucidating mechanisms of tau aggregation is an extremely important step to delay/prevent not only AD but also other disorders with tau pathology. A recent in vitro study suggested that soluble tau oligomers are toxic to cells. Whether tau oligomers exist in vivo and if they do, the status of their phosphorylation state is unknown. Using mouse models, we aim to develop an immunoblot-based assay to: 1) characterize and quantify tau oligomers in brain interstitial fluid (ISF) and brain homogenates and 2) profile the phosphorylation state of these tau aggregates.
Methods: Brain homogenates are obtained from tau knockout (KO), wild-type (WT), and tau transgenic (TG) mice. ISF samples are obtained using microdialysis. To assess phosphorylation state of tau in brain homogenates, immunoblotting is performed using site-specific antibodies. Since ISF tau is of low abundance, immunoprecipitation (IP) is performed before immunoblotting. Tau oligomer-specific antibodies are used to characterize these species.
Anticipated results: The detailed steps required for the formation of NFT are not known, but studies have hinted at the presence of oligomers as an intermediate species. Abnormal phosphorylation of tau at specific sites has also been linked to increased tangle formation. Development of our assay will shed more light on the pathologic presence of specific forms of tau in AD. If present, future studies can explore the role of these species in disease.
Conclusions: Development of our assay will shed more light on the pathologic presence of specific forms of tau in AD. If present, future studies can explore the role of these species in disease.

128 **Plotzker, Alan**

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Using antisense oligonucleotides to decrease tau pathology in P301S mice

Plotzker AS; DeVos S; Miller TM

Introduction: Tauopathies are a group of neurodegenerative diseases characterized by accumulation of hyperphosphorylated tau protein, resulting in filamentous aggregates of tau in neurons. These tau aggregates form the neurofibrillary tangles found in Alzheimer's Disease, and tau pathology is the primary pathological feature in about 40% of cases of frontotemporal dementia (FTD). One particular form of tau-related FTD is frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), an autosomal dominant disease that has been linked to a variety of mutations in the gene encoding tau. One such mutation, P301S, results in early onset, rapidly lethal FTDP-17, and transgenic mice expressing the human P301S mutant form of tau have been developed as an animal model for tauopathies. These mice develop progressive motor problems and brain atrophy, and their brains show extensive tau pathology. Because tauopathies result from a build-up of undesired tau protein, a potential therapeutic strategy is to use post-transcriptional RNA interference to decrease the expression of tau. One way of doing this is to use antisense oligonucleotides (ASO), short (about 20 nucleotides) DNA-like molecules that specifically bind to the target mRNA and cause it to become degraded and/or inhibit its translation. Here, we used an ASO specific for human tau to decrease its expression in P301S transgenic mice. Our hypothesis was that P301S transgenic mice treated with tau-reducing ASO would show less tau pathology as measured by immunohistochemistry as compared to P301S mice treated with a saline control.
Methods: Five month-old P301S mice were implanted with osmotic pumps and infused with either 50μg/day of the ASO for 4 weeks, 100μg/day for 2 weeks, or saline for 4 weeks (n = 5 in each group). The mice were then sacrificed at 7 months of age and the left hemispheres of their brains were sectioned and stained immunohistochemically with AT8, an antibody to phosphorylated tau that is commonly used to identify neurofibrillary tangles in the human brain.
Results: As predicted, ASO-treated mice showed significantly decreased AT8 staining throughout the brain, including in the amygdala and cortex.
Conclusions: This ASO is effective in reducing tau pathology in an animal model of tauopathies.

037 **Raup, Valary T**

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IKDC scores for knee problems in pediatric and adolescent patients

Raup VT; Luhmann SL; Smith J

Introduction: The purpose of this study is to report the IKDC scores for a number of different pediatric and adolescent knee problems. International Knee Documentation Committee (IKDC) scores are a helpful tool to quantify patient's subjective assessment of their knee function. This study illustrates wide variability of IKDC scores in pediatric and adolescent patients with a mean IKDC score demonstrating considerable knee dysfunction.

Methods: From 7/2007 through 5/2012 IKDC scores were prospectively obtained on 313 patients with 352 affected knees who were presented to Dr. Scott Luhmann for evaluation. Scores were tabulated and the medical records and operative reports were reviewed. A list of 14 diagnoses was created into which all patients were categorized. The focus of this study is a list of 13 specific diagnoses with a minimum of 7 patients in each diagnostic category.

Results: There were 179 females and 122 males. Mean age was 14.87 years (7 to 23). There were 136 right and 124 left knees. Knee surgery was performed in 183 knees (60.6%). Mean IKDC score was 49.8. The range of IKDC scores was wide from 4.6 to 100, without any diagnosis specificity. The range of mean IKDC scores was tightly clustered between 43.9 and 61.5 with 10 of the 13 diagnoses having mean scores in the 40s. Overall of the 13 diagnoses chondromalacia had the lowest score of 43.9 and OCD lesions had the highest score of 61.5. Patellar subluxations, patellar dislocations, medial patellofemoral ligament pain, ACL tears, ACL and meniscal tears, meniscal tears, unclassified knee pain, discoid meniscus, loose bodies, and chondromalacia patients all had average IKDC scores in the 40s. OCD lesions, anterior knee pain, and Osgood Slaughters patients had average IKDC scores in the 60s. Analysis of IKDC scores failed to identify an association between the score and the need for operative management.

Conclusions: Patient perception of their knee problem, as quantified by IKDC scores, indicate a significant level of subjective knee dysfunction. Overall, the IKDC scores were remarkably similar across all diagnosis groups, regardless of the need for operative management. IKDC scores were not able to predict which patients would undergo surgery.

130 **Silver, Shawgi A**

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CSF Levels of L1CAM, NCAM1 and APP are elevated in preterm infants with post-hemorrhagic hydrocephalus

Silver SA; Morales DM; Limbrick DD

Introduction: Intraventricular hemorrhage occurs in roughly 25% of very low birth weight infants, remains the most severe neurological complication of preterm birth and post-hemorrhagic hydrocephalus develops in up to one half of those with IVH (associated with a 3-4 fold increase in the risk of cognitive and psychomotor disability). There is a need to develop new tools to improve the treatment and outcomes of infants with PHH. Recent literature suggests that the neural cell adhesion molecule L1 (L1CAM), neural cell adhesion molecule 1 (NCAM1) and amyloid-beta precursor protein (APP) are elevated in the cerebrospinal fluid of PHH infants and may represent candidate markers of PHH.

Methods: Commercially available ELISAs were used to measure concentrations of L1CAM, NCAM1 and APP in lumbar CSF of preterm infants from 5 groups: (a) no known neurological disease (n=10); (b) IVH I-II (n=10); (c) IVH III-IV (n=7); (d) PHH (n=9); and (e) ventricular enlargement without hydrocephalus (VEWOH, n=5). Datasets from the 5 groups were compared using analysis of variance modified to allow different within-group variances and examine all pairwise comparisons with a Tukey adjustment.

Results: The data show, as hypothesized, the levels of L1CAM, NCAM1 and APP were elevated significantly in the PHH preterm neonates from the 4 groups. The concentration of APP in the CSF of PHH neonates (1455.1+325.7 ng/ml) was statistically significant from the controls (608.3+102.5 ng/ml) and the VEWOHs (516.3+126.2 ng/ml). However it did not reach significance when compared to either IVH group. L1CAM concentration in PHH CSF (205.9$\pm$31.7 ng/ml) was statistically significant from controls (96.5$\pm$14.15 ng/ml), VEWOHs (85.3$\pm$35.0 ng/ml) and IVH I-II (102.9$\pm$10.3 ng/ml). However it did not reach significance with the IVH III-IV group (117.3$\pm$33.5 ng/ml). NCAM concentrations in PHH subjects (280.6$\pm$30.1) did not reach significance with any other group.

Conclusions: The results of this study suggest further research should be conducted with a broader patient range to further verify these findings. This could prove to be a diagnostic technique to alter the understanding and treatment of PHH preterm neonates.

126 **Walz, Katharine**

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Role of apolipoprotein E in a murine model of multiple sclerosis

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Introduction: Multiple Sclerosis (MS) is an autoimmune disease in which the myelin sheath of the CNS is chronically destroyed. With nearly 400,000 patients in the United States alone, MS is a leading cause of disability in young adults. A murine model, called experimental autoimmune encephalomyelitis (EAE), is used to study the pathogenesis of MS. Studies suggest that CD4 T cells are critical mediators of EAE. However, CD4 T cells rely on antigen presenting cells (APCs) in order to become activated. Previous work has demonstrated a contribution by Apolipoprotein E (ApoE) in antigen presentation. This project seeks to more fully understand the ApoE-dependent antigen presentation steps during the progression of EAE, or more specifically, to understand the role ApoE plays in EAE, and whether ApoE contributes to the antigen presentation processes.

Methods: EAE was induced in ApoE knockout and wild type mice to track and compare disease incidence and severity in the two groups. Cytokine production after immunization was measured ex vivo. APC function was tested by measuring the ability of dendritic cells (DCs) to stimulate antigen-specific T-cell responses. Cell damage in the spinal cord caused by EAE was measured ex vivo using immunohistochemistry.

Results: ApoE knockout mice exhibited reduced clinical severity of EAE compared with wild type controls. Antigen presentation of protein was equivalent between ApoE knockouts and wild type APCs, and no difference was seen in the composition of immune cell subsets after the induction of EAE. However, greater levels of antigen-specific cytokine production were observed in the ApoE knockout mice after immunization.

Conclusions: Wild type mice develop more severe EAE than ApoE knockouts, but this does not appear to be due to a deficit in APC function nor a difference in immune cell type frequency. Cytokine production appears to be elevated in ApoE knockouts at 15 days post immunization. One of the next steps in this research is to quantify the amount of axonal injury due to EAE in order to better understand the ApoE-dependent mechanisms involved in inflammatory destruction within the CNS during MS.

119 **Wang, Stephanie**

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Retrospective analysis on hematopoietic stem cell (HSC) mobilization failures

Wang S; DiPersio J

Introduction: Hematopoietic stem cell transplantation remains the current gold-standard therapy for high risk and relapsed hematological malignancies. While the minimum HSC required for stem cell transplantation is $2x10^6$ CD34/kg, an infusion of $5x10^6$ CD34/kg is associated with more rapid and less variable engraftment. Despite many advances in HSC mobilization, some patients still fail to mobilize an adequate number of HSCs needed for transplantation. Our aim is to describe the clinical features of patients who underwent mobilization for autologous transplantation and to define potential correlations between pre-mobilization clinical characteristics and mobilization outcomes. Three types of mobilization methods were used: G-CSF (n=11), G-CSF+Mozobil (n=404), and chemotherapy+ G-CSF (n=66).

Methods: A retrospective statistical analysis was performed on data from patients diagnosed with multiple myeloma (MM) or non-Hodgkin's Lymphoma (NHL) who underwent their first autologous stem cell mobilization at Siteman Cancer Center from 2009-2011.

Results: A total of 481 patients (278 MM, 203 NHL), median age 58 (range 22-74) were included in the analysis. Mobilization was measured by quantitative CD34 cell counts (10^6/kg) on day 1 of first apheresis. Failed mobilization was defined as $<2x10^6$ CD34/kg. All patients were either mobilized with G-CSF alone, G-CSF+Mozobil, or chemotherapy+G-CSF. Out of 481 patients, 85(17.7%) failed to mobilize adequate number of CD34/kg. Median CD34/kg differed among mobilization agents, with the highest in patients mobilized with chemo+G-CSF and lowest in those with G-CSF. Day 1 CD34/kg were also higher in patients with no prior history of radiation (p=0.01) but were negatively correlated with age (p=0.02). Gender, disease (MM vs NHL), and history of diabetes mellitus, hypertension, coronary artery disease, and hyperlipidemia were not significantly correlated with day 1 CD34/kg yields.

Conclusions: Despite advances, mobilization regimens still result in significant failure rates (17.7%). Determining predictors of mobilization outcome may allow for early alternative mobilization approaches to minimize the number of collections necessary for transplantation and number of patients that can proceed to transplant.

125 **Wessel, Lauren E**

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The association between hypotonia and brain tumors in children with Neurofibromatosis type 1

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Introduction: Children with the Neurofibromatosis type 1 (NF1) inherited tumor predisposition syndrome are at risk for the development of brain tumors. In addition, children with NF1 often exhibit low tone (hypotonia).

Methods: In this study, we explored the hypothesis that hypotonia may be a clinical indicator of glioma in children with NF1. Fifty-six children between 1 and 7 years of age with a confirmed diagnosis of NF1 were evaluated. Brain magnetic resonance imaging (MRI) was available for 19 of these children.

Results: Chi-square analysis demonstrated a statistically significant correlation between hypotonia and glioma in children with NF1 (90% sensitivity and 78% specificity).

Conclusions: These results suggest that hypotonia might be a clinically useful indicator of brain tumor in this at-risk population.

033 **Witt, Jacob**

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Chronic geminin depletion triggers re-replication and aneuploidy in Daoy cells and compromises cell growth in vitro

Witt J; Kroll KL; Patterson ES

Introduction: DNA replication is a tightly controlled process that occurs once per cell cycle in normal cells. Geminin is an inhibitor of DNA replication, and ensures that only one round of DNA replication takes place per cell cycle, thus maintaining genome fidelity and preventing aneuploidy. Additionally, geminin is highly expressed in many aggressive cancers, including medulloblastoma. While our previous work has shown that geminin depletion may not compromise normal somatic cell growth and viability, we and others have found that acute loss of geminin in several cancer lines has been found to trigger over-replication, cell cycle arrest, and apoptosis. Geminin has therefore been identified as a potential therapeutic target for the treatment of medulloblastoma. In this study, we evaluated the cell cycle effects of chronic geminin suppression in the Daoy cell line.

Methods: We employed several microRNA-adapted small hairpin RNAs (shRNAmirs) against geminin. These shRNAmirs were used to make lentivirus, and also inserted into the pTRIPZ inducible system (Thermo Scientific) for direct transfection or to make lentivirus for future in vivo experiments. Geminin was depleted up to 96% of control levels. Daoy cells were infected with lentivirus, selected with puromycin, and then plated repeatedly at known densities to determine growth curves. We also analyzed cell cycle profiles and corresponding geminin protein levels by taking three time points over the course of two weeks. Cells were stained with propidium iodide and analyzed using a Becton Dickinson flow cytometer with FloJo software.

Results: We found that chronic geminin depletion led to an accumulation of higher levels of aneuploidy and G2/M cell number, as well as a diminished capacity for growth, over time. Furthermore, these trends correlated with the level of geminin knockdown. On average, geminin depleted cells at t = 4D had no statistical differences with control cells, but at t = 7D geminin knockdown (GKD) cells began to pile up in G2/M and become aneuploid, and at t = 11D this effect was quite dramatic. On average, GKD cells at t = 7D had 38% more cells in G2/M than a control, and at t = 11D this had increased to 65%. In addition, growth curve analysis revealed that GKD cells grow at a rate that is up to 56% slower than control cells.

Conclusions: These data suggest that geminin is an important part of Daoy cell cycle regulation, and may therefore represent a useful therapeutic target in the treatment of medulloblastoma. Chronic loss of geminin led to a stunted growth rate that may be due to an increasing accumulation of cells at the G2/M checkpoint due to checkpoint arrest. This seems likely, as the G2/M buildup occurred simultaneously with an increase in cells with DNA content >4n. Future work must be done to characterize these arrested and aneuploid cells, as well as to understand geminin depletion in tumors in vivo.

030 **Wolfson, Maxim**

Medical Student
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Mentor: Michael Avidan, MD

The prevention of delirium and complications associated with surgical treatments (PODCAST) clinical trial

Wolfson M; Avidan MS; Mashour GA

Introduction: Postoperative delirium is one of the most common complications of surgery and presents as waxing and waning inattention and disorganized thinking. Besides being highly disturbing to family members, postoperative delirium is associated with longer hospital stays, long lasting cognitive deterioration, and increased mortality rate. Currently there is no accepted way of preventing or treating postoperative delirium. Ketamine is an anesthetic with a great safety profile that has been used for the last 50 years. Recent research suggests that a sub-anesthetic dose of ketamine can not only decrease postoperative pain, but delirium as well. Despite its many benefits, practitioners do not commonly administer low-dose ketamine for fear of side effects, such as delirium. The purpose of this study is to test the proposed claim that low-dose ketamine can decrease postoperative delirium in a large clinical trial. Attenuation of postoperative pain and inflammation will also be tested.
Methods: This multicenter trial will randomize 2000 elderly, surgical patients to either low-dose ketamine or placebo administered before incision. Blinded, trained observers will assess patients for delirium using the Confusion Assessment Method twice daily following surgery. Patients will also be evaluated for other postoperative neurologic and psychiatric complications such as pain, depressive symptoms, and posttraumatic stress disorder using questionnaires.
Results: This trial is expected to run for three to five years. Any of the potential outcomes of this trial will have immediate clinical implications for older surgical patients. A significant decrease in delirium would warrant the use of low-dose ketamine for prevention of delirium. A lack of significant difference between low-dose ketamine and placebo groups would show ketamine can be used to prevent pain without delirium as a side effect.
Conclusions: A large clinical trial is the only way to assess the effectiveness of low-dose ketamine at decreasing delirium. Results of this trial could definitively make low-dose ketamine the gold standard for preventing one of the most common surgical complications, delirium.

116 **Yozamp, Nicholas**

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Mentor: Steven Brody, MD

Role of c-Myb in directing airway epithelial cell fate

Yozamp N; Pan J; Huang T; Brody S

Introduction: The lung airway is lined with ciliated and secretory (Clara) cells requiring a tightly controlled program for differentiation to these cell types. Having previously identified c-Myb as an upstream regulator of ciliogenesis master gene Foxj1, we hypothesized that c-Myb also regulates Clara cell fate. Moreover, we proposed an interaction between c-Myb and Notch, a signaling pathway controlling decisions between ciliated and Clara cell fates. Finally, we examined these pathways in chronic obstructive pulmonary disease (COPD), which is characterized by abnormal airway epithelium.
Methods: We performed *in vitro* experiments in a primary culture of mouse and human airway epithelial cells, including those from normal and COPD lungs. Cells were pharmacologically treated and genes were silenced with shRNA delivered by lentivirus; analysis was via immunostaining, western blot, and RT-PCR.
Results: First, targeted silencing of c-Myb resulted in decreased expression of the early ciliogenesis factor IDAS and diminished expression of the Clara cell markers lysozyme, plunc, and CCSP. Second, targeted deletion of c-Myb decreased Notch signaling, as evidenced by diminished expression of activated Notch intracellular domain (NICD). Third, inhibition of Notch signaling with the gamma-secretase inhibitor DAPT resulted in more ciliated and fewer Clara cells in wild-type cells as expected and, more surprisingly, in c-Myb knockdown cells as well. Finally, having previously observed elevated c-Myb in the mucous-cell-rich and ciliated-cell-poor pathology of COPD, we reversed this phenotype by treating cultured human COPD cells with DAPT, resulting in fewer mucous cells and more ciliated cells.
Conclusions: Results demonstrate a role for c-Myb in commitment of airway epithelial cells to ciliated and Clara cells. Targeted deletion of c-Myb with Notch inhibition suggests that c-Myb favors the Clara cell fate by default and promotes ciliogenesis by interacting with Notch and Foxj1. Further elucidation of c-Myb's role in the developing airway and its interaction with Notch will facilitate knowledge of the normal lung and may lead to therapy to reverse the pathology in COPD.

015 **Yuen, Sonia**

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Mentor: Kelly N Botteron, MD

Neurodevelopmental differences in the cingulate cortexes of children with PO-MDD

Yuen SN; Botteron KN

Introduction: Preschool-Onset Major Depressive Disorder (PO-MDD) is associated with structural and functional changes in emotional neurocircuitry. Dr. Botteron, Dr. Luby, and Dr. Barch are studying the developmental impact of PO-MDD on the structure and function of key profrontal-limbic networks in children. One part of the study is to analyze the structure of the cingulate cortex.

Methods: 1. Psychiatric, psychosocial, and developmental data have been obtained from children with and without PO-MDD. At three time points 18 months apart, the children have structural and functional imaging. 213 children, ages 6-12 years old, have completed the first scan. 2. Via the program FreeSurfer, the first wave of MRI scans were aligned to a standardized brain image, had non-brain matter portions of the image removed, and had each volumetric pixel (voxel) classified as white or gray matter. If manual review of the scans detected errors, reference points were added to the scan, which would then be rerun through FreeSurfer. 3. Another program created Labeled Cortical Distance Maps (LCDMs) of the cingulate cortex. Among the files created, one file for each side of the cingulate cortex (left and right) had each voxel labeled as White Matter, Gray Matter, or Cerebral Spinal Fluid. Manual review determined if each file's cingulate cortex segmentation was passable, marginally passable, or bad. If necessary, additional reference points would be manually added to improve the program's segmentation accuracy.

Results: Of the 186 scans from the first wave that were manually reviewed, none were rerun through FreeSurfer. 320 of the 372 segmented cingulate cortex files were reviewed in the program BrainWorks. 27.8% of the reviewed scans were passable, 11.3% were marginally passable, and 60.9% were bad. The number of passable segmentation files is expected to increase after manually inserting reference points.

Conclusions: The cingulate cortex segmentations need manual editing to produce more accurate LCDMs. Knowledge of how PO-MDD affects the structural development of the cingulate cortex, in addition to other neurocircuitry regions, will influence the detection, treatment, and understanding of PO-MDD.

070 **Zieske, Lawrence**

Medical Student
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Department of Surgery, Washington University in St. Louis School of Medicine
Mentor: Susan Mackinnon, MD

Web-based nerve surgery education intervention

Zieske L; Mackinnon S

Introduction: I have worked on two research projects with Dr. Mackinnon. One was a study on the usage of her nerve surgery education website, and the other was a retrospective analysis of revision carpal tunnel surgeries performed by Dr. Mackinnon over the last 11 years.

Methods: The purpose of the website study was to investigate the usage patterns and user impressions of the educational website (nervesurgery.wustl.edu) and its video content. We used qualitative surveys to analyze how users felt about the website and the utility of the educational videos on the surgical management of nerve injuries. The website's content is hosted online using several websites, and we used proprietary statistical software from each website to gather and analyze data on the patterns of its use.

The purpose of the carpal tunnel study was to analyze the intraoperative findings and outcomes of patients treated by Dr. Mackinnon for carpal tunnel symptoms after a failed initial carpal tunnel release. IRB approval was obtained, and we performed a retrospective chart review of patients who received revision surgery for persistent, recurrent, or new symptoms after a primary release.

Results: I presented the results of the first study at Resident Research Day, and I am working with Dr. Ida Fox and Dr. Mackinnon on a manuscript of this study for journal submission.

The second study has a larger sample size than any retrospective analysis in the literature on secondary carpal tunnel release by a single surgeon.

Conclusions: I am working with Dr. Mackinnon to draft a manuscript for journal submission, and I will submit the paper to the Dean's Office once it is completed.

T35 NIH NIDDK Short-Term Training Program

077 **An, Tonya W**
Medical Student
T35 NIDDK Training Grant
Summer Research Program
Department of Surgery, Washington University in St. Louis School of Medicine
Mentor: Bruce Hall, MD, PhD, MBA

Summary and assessment of risk factors for gynecologic surgery

An T; Hall B; Chalas E

Introduction: Data and statistics are essential in order to better counsel patients on the risks of any surgical procedure and inform surgeons of possible complications. With directive from the Society of Gynecologic Oncologists, we analyzed the case data on a comprehensive set of gynecologic procedures. This study endeavors to quantify incidence and identify demographic and perioperative risk factors for prolonged hospitalization, morbidities and mortality after gynecologic surgery.

Methods: We stratified the ACS-NSQIP database consisting of case records from years of 2005-2010 to only select gynecologic procedures defined by CPT codes. The data were divided and evaluated in 5 classes: patient demographics, clinical risk factors, laboratory assessment values, perioperative data, and postoperative outcomes within 30 days. Certain hysterectomy procedures were isolated to compare relative rates of morbidity.

Results: We examined 37,944 cases from 263 unique institutions over the 5 year period. Out of 42 NSQIP-defined risk factors, the most prevalent risk variables were: hypertension requiring medication-31.6%, smoking-17.9%, and diabetes-8.28% of the population. 52.05% of the population of patient cases reported one or more of the 42 risk factors with an overall average of 0.8 risk factors per patient. The outcomes of surgery were measured by: length of stay (LOS)-average 2.0 (SD 3.1) days, any morbidity-8.2% and mortality-0.2%. For hysterectomy procedures, open hysterectomy was associated with longer LOS and higher rates of morbidity, including infection, than laparoscopic hysterectomy.

Conclusions: The summary of this large pool of cases provides insight into the population receiving gynecologic procedures, as well as their respective outcomes. When comparing different forms a procedure, such as hysterectomy, we see benefits in laparoscopic techniques, but the characteristics of the population must also be considered. In preliminary regression analysis, patients of minority races and suffering certain existing heath diagnoses faced significantly higher odds of post-op morbidity. The next step is to develop more robust predictive models from this data and apply it to clinical practice.

086 **Barklund, Sigrid**
Medical Student
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Summer Research Program
Division of Urologic Surgery
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Mentor: Gerald Andriole, MD

Determination of improved accuracy using the TargetScan system for prostate biopsy

Barklund JS; Vemena G; Sandhu GS; Andriole GL

Introduction: Prostate cancer is the most common cancer in men, with an estimated 214,740 new cases and 28,170 deaths in 2012. A variety of treatment options exist for prostate cancer including radical prostatectomy (RP), radiation therapy (RT) and active surveillance. Overtreatment of clinically insignificant prostate cancer is a problem, as treatments like RP and RT have undesirable side effects. To increase the number of patients being offered active surveillance for prostate cancer, a more accurate biopsy technique is needed to decrease the resistance to active surveillance. The TargetScan system creates a 3D map of the prostate, and then uses a computer algorithm to calculate and perform an optimum biopsy scheme, yielding improved performance relative to traditional ultrasound guided prostate biopsy. This study seeks to compare the results of TargetScan and conventional transrectal ultrasound-guided (TRUS) biopsies with the final pathology following RP and demonstrate the ability of the TargetScan system to perform more accurate prostate biopsies than conventional TRUS methods.

Methods: Using a retrospective chart review of patients at Washington University in St Louis who had been diagnosed with prostate cancer between 2005 and 2012, we determined the agreement between biopsy pathology and final pathology following RP for two groups of patients: one group who had TargetScan biopsies followed by RP and one group who had TRUS biopsies followed by RP. We then compared the degree of agreement between biopsy and final pathology for each biopsy technique. The variables being compared are Gleason score and tumor location and volume.

Anticipated Results: We anticipate that our results will show that the TargetScan system yields more accurate biopsy results than the conventional TRUS biopsy method.

Conclusions: Our anticipated results showing the increased accuracy of TargetScan biopsies over TRUS biopsies are significant for the large numbers of men diagnosed with prostate cancer each year. Utilization of the more accurate TargetScan system gives physicians better clinical information and patients more confidence in determining the best treatment option for their prostate cancer.

073 **Baumgartner, Kevin**
Medical Student
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Summer Research Program
Division of Cardiothoracic Surgery
Department of Surgery, Washington University in St. Louis School of Medicine
Mentor: Traves Crabtree, MD

Pyloric outlet procedures in esophagectomy for esophageal cancer

Baumgartner K; Crabtree T

Introduction: Treatment of esophageal cancer may require esophagectomy, which is associated with significant postoperative complications. Pyloric drainage procedures are often performed for esophagectomy patients to prevent aspiration, dumping syndrome, and severe reflux, but there is no consensus on the utility of these interventions. The purpose of this study is to assess and compare the postoperative outcomes of esophagectomy patients who underwent various pyloric drainage procedures, including no intervention.

Methods: Medical records for 293 patients who underwent esophagectomy for esophageal cancer from January 2007 through April 2012 were reviewed.

Results: 17.75% of patients got no pyloric intervention (N), 54.95% got a pyloromyotomy (PM), 12.29% a pyloroplasty (PP), and 15.02% pyloric dilation with Botox injection (B). Rates of surgical complications and hospital readmission were similar for all interventions. PP and B were associated with lower rates of return to the OR before discharge, (16.67% and 27.27%, against N and PM at 40.38% and 39.13%). Patients receiving N had a much lower rate of postop surgical re-intervention (9.80%, against 19.38% for all patients combined), while patients receiving PP or B had less need for anastomotic dilation, and patients receiving B had very low rates of postoperative aspiration (2.33%). B was very effective at reducing rates of reflux and dumping syndrome in the first six postoperative months, although it had little effect on dumping syndrome rates after that point. Further analysis of the data for statistical significance & possible confounding factors is forthcoming.

Conclusions: No pyloric intervention is associated with increased rates of surgical complications or hospital readmission, and results are mixed for postoperative events such as aspiration (B is most effective), surgical reintervention (N most effective), and anastomotic dilation (PP and B are both effective). B is most effective at reducing rates of reflux and dumping syndrome in the first six months after operation, but its relative efficacy declines over time, suggesting that repeated Botox injections might be necessary for maximum therapeutic benefit.

067 **Chung, Christopher**
Medical Student
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Prevention Research Center
Brown School of Social Work, Washington University in St. Louis
Mentor: Amy Eyler, PhD

Lifestyle intervention & primary care integration: a feasibility study

Chung C; Eyler A

Introduction: Our current health care system allocates limited time for physicians to offer thorough consultation in lifestyle and behavioral change. Even more difficult is providing consistent follow-up to ensure adherence to plans and goals. We propose a cost-effective plan to complement and improve adherence to treatments by using a Healthy Eating and Lifestyle Management Education (HEAL ME) curriculum to train medical students to become Health Coaches (HCs).

Methods: Five Washington University medical students were trained in Motivational Interviewing and in the Transtheoretical Model of Behavior Change to build proficiency in behavioral counseling for weight loss and chronic disease management. The training focused on behavioral modification of medication adherence, exercise, portion control, and diet. Patients with overweight, diabetes, and/or hypertension were referred by physicians to HCs immediately following their appointment. Before a 15-minute HC session, each patient completed a survey (Likert scale) to describe habits such as cooking frequency, exercise, and fruit and vegetable intake. Three weeks later, the same survey was administered over the phone.

Results: Of 100 patients enrolled, 86 completed both pre and post survey. 14 were lost to follow-up. The average response for 13 of the total 15 health behavior questions showed a positive trend towards lifestyle improvement. Physicians expressed satisfaction in offering this service to patients, and also relayed their patients' resoundingly positive reviews. Physicians report the potential of the Health Coach to improve patient satisfaction by providing a useful service to patients if the physician runs behind schedule. Health coaches report a generally appreciative sentiment from the patients whom they follow up with over the phone.

Conclusions: The HEAL ME model demonstrates feasibility of implementation in a busy primary care clinic and shows promise as an asset to clinical care. The survey results tentatively suggest a positive impact of the Health Coach intervention on health habits. We intend to perform a randomized, controlled study of weight, blood pressure, lipid panel, and hemoglobin A1C to more reliably characterize the impact of the intervention on clinical outcomes.

079 **Desanto, Cori L**

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Summer Research Program
Department of Neurology, Washington University in St. Louis School of Medicine
Mentors: Brad A Racette, MD; Allison W Willis, MD

Stability of parkinsonian and essential tremor diagnoses among the elderly in community settings

Desanto CL; Racette BA; Schootman M; Willis AW

Introduction: Parkinson Plus Syndromes (PPS) and other neurodegenerative diseases may initially mimic Parkinson's disease (PD) or Essential Tremor (ET). The stability of PD and ET diagnoses in an elderly population is unknown. This study examines the extent to which a diagnosis of another neurodegenerative disease is added to an initial diagnosis of PD and ET, and the provider and patient characteristics associated with this change.

Methods: This is a retrospective cohort study of Medicare beneficiaries first diagnosed with PD or ET in 2002 and still living in 2006. The four-year rate of diagnosis conversion from PD and ET to a Parkinson Plus Syndrome (PPS), Amyotrophic Lateral Sclerosis (ALS), Diffuse Lewy Body Disease (DLB) and Frontotemporal Dementia (FTD) was determined for the years 2002 to 2005. Interconversion of PD and ET diagnoses was also examined. Multivariable logistic regression will be used to identify predictors of diagnosis change, including patient age, sex, race and socioeconomic status, as well as provider specialty.

Results: 76,863 incident cases of PD were identified for the year 2002. The four-year rate of diagnosis conversion from PD to ET was 6.9% (6.7-7.1%). A PPS diagnosis was added in 5.8% of cases (5.7-6.0%), and DLB, ALS, and FTD diagnoses were introduced in less than 1% of cases. Analyses to determine ET diagnostic stability and predictors of diagnosis conversion are in progress.

Conclusions: A PD diagnosis is relatively stable when made in an elderly population. Conclusions regarding ET diagnosis stability and factors associated with diagnosis change are pending further analysis.

074 **Dvoracek, Lucas**

Medical Student
T35 NIDDK Training Grant
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Department of Surgery, Washington University in St. Louis School of Medicine
Mentor: Susan Mackinnon, MD

Tacrolimus induces acceleration of Wallerian degeneration in denervated peroneal nerves

Dvoracek L; Leu A; Hunter D; Johnson P; Mackinnon S

Introduction: Damaged peripheral nerves regenerate at a constant rate, but functional recovery is dependent on a timely reinnervation of neuromuscular junctions to prevent muscular fibrosis and irreversible atrophy. Axonal regrowth proximal to and Wallerian degeneration of severed axons distal to the lesion are both crucial to the process of nerve regeneration. Tacrolimus (FK-506) accelerates axonal regrowth through a heat shock protein mediated pathway, but recent evidence suggests that this immunosuppressant may also exert a calcineurin-mediated enhancement of Toll-like receptor function in macrophages, thereby speeding Wallerian degeneration and clearing the way for the regenerating axons.

Methods: Thy1-GFP Sprague Dawley rats (which express GFP in healthy nerve axons) were divided into 2 groups (n=8, IM tacrolimus injection at 0.2mg/kg/day or control) underwent chronic peroneal denervation. Fluorescent imaging of the distal stump was performed at days 0, 3, 7, 10, and 14 and evaluated for intensity changes. The distal stumps were harvested on day 14 and evaluated with histomorphologic analysis.

Results: Tacrolimus-treated rats showed a significantly greater decrease in absolute intensity at days 10 and 14 (both $p<0.01$) and in relative intensity at day 10 ($p=0.04$) compared to the control group. Histomorphologic results are still pending.

Conclusions: Wallerian degeneration must occur in order to allow growing axons to proceed through the endoneurial tube toward their targets, and tacrolimus is known to exert a neuroregenerative effect beyond simply accelerating axonal regrowth. These data suggest that tacrolimus treatment accelerates Wallerian degeneration. Further investigations to elucidate the mechanism by which this process occurs are needed, but this could ultimately support the use of tacrolimus as a nerve regeneration accelerant in patients who would otherwise experience diminished functional recovery.

072 **Forbes, Lindsay**
Medical Student
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Summer Research Program
Department of Surgery, Washington University in St. Louis School of Medicine
Mentor: Kate Wolin, ScD

Bone density in postmenopausal breast cancer survivors and its relationship with bone-related medication and exercise

Forbes L; Fagin C; Liu E; Colditz GA; Wolin KY; Ganz P

Introduction: Certain breast cancer treatments (i.e. aromatase inhibitors, glucocorticoids and tamoxifen) as well as non-cancer medications can positively or negatively impact bone health. Additionally, weight-bearing activity can stimulate bone formation. The purpose of this study is to examine the relationship between medications and activity and the bone density of postmenopausal breast cancer survivors.

Methods: Eighty-two postmenopausal women with a history of non-metastatic breast cancer participated in this study. Treatment history was obtained from medical records while non-cancer-medication use and physical activity in the past year were assessed by a detailed validated questionnaire. Activities were coded as likely, possibly or not bone-loading. Bone density was assessed by a full body DXA scan. Pearson correlation coefficients were calculated for the relationship between minutes of bone-loading activity and DXA t-score, and a t-test was used to analyze the relationship between positive- and negative-bone medications and DXA t-score.

Results: Bone-loading activity showed a correlation of 0.22 ($p=0.057$) with DXA t-score. Women who took negative medications had similar bone density to women who did not (mean difference = 0.072, $p = 0.85$), while women who took positive medications had significantly lower bone density than women who did not (mean difference = 0.75, $p = 0.045$). When women taking both positive and negative medications were excluded, neither difference was significant.

Conclusions: The results of this study suggest that weight-bearing physical activity may be associated with greater bone density in postmenopausal breast cancer survivors. Positive medications did not show the expected results in that use was actually associated with lower bone density. However, when women taking both positive and negative medications were excluded, this finding was not significant, suggesting that negative medications may impact bone density to a greater extent than positive medications. In addition, the medication variable did not account for dose or duration of use. Further analysis and research is necessary to determine the shared effect of medications and physical activity on bone density.

No poster displayed

Glawson, Keylon
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Mentor: Varun Puri, MD

A study to establish incidence, risk factors, and consequences of postoperative pneumonia after major thoracic surgery.

Glawson K; Puri V

Introduction: Postoperative pneumonia (POP) is a major complication seen after major thoracic surgery. The purpose of the study was to establish incidence, risk factors, and consequences of postoperative pneumonia after major thoracic surgery. We hypothesized that we would be able to identify potentially modifiable risk factors for POP. Additionally, we hypothesized that patients with POP suffer high levels of morbidity and mortality.

Methods: An institutional retrospective cohort study was performed using the general thoracic surgery database from 2000-2011. The patients were examined perioperatively (within 30 days of operations) for the development of postoperative pneumonia. Risk factors for POP were identified by collecting data on preoperative variables and operations. Postoperative outcomes were elucidated. Patient confidentiality was maintained by de-identifying patients. This study included patients over the age of 18 who had undergone lung or esophageal resections. The study group consisted of patients who developed POP and the control group compromised all others. Statistical analysis will be performed using SPSS 11.0 for Windows (SPSS Inc., Chicago, IL). Type 1 error will be protected at the nominal 5% level.

Results: Preliminary results have been recorded. 12.9 % of the patients who had undergone esophageal resection developed postoperative pneumonia. 3.4% of the patients who had undergone thoracic resection developed postoperative pneumonia.

Conclusions: The success of this project would allow the cardiothoracic surgery department of Washington University in St. Louis to enlist preventative measures to reduce the occurrence of postoperative pneumonia in its patient population.

048 **Graham, Cassandra**

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Department of Internal Medicine, Washington University in St. Louis School of Medicine
Mentor: Robert Heuckeroth, MD, PhD

The effect of hyperthermia on the migration of mouse enteric neural crest cells

Graham C; Heuckeroth R

Introduction: Maternal fever has been proposed as a risk factor for diverse human birth defects including Hirschsprung disease (HSCR), a problem where the enteric nervous system (ENS) is missing from the end of the bowel. There is a distinct lack of laboratory research regarding how hyperthermia affects the ENS. This project analyzed the effect of hyperthermia on the migration of enteric neural crest cells (ENCCs) in culture and of maternal fever on distal bowel aganglionosis.
Methods: Slices of embryonic day 12.5 (E12.5) mouse midgut were cultured at maternal body temperature, 37°C, or at a hyperthermic 39°C in a live imaging microscope for 16 hours. These data were used to track the cells. After fixation, migration distance of ENCCs from the edge of the slices was measured. Additionally, embryonic day 10.5 (E10.5) pregnant mice were heated to 37°C or 40°C for 10 minutes. Whole guts were obtained from the pups at E12.5 and migratory distance of ENCCs down the colon from the cecum was measured. Data were analyzed using t-tests.
Results: There was a statistically significant difference ($p=0.012$) between the farthest distance an ENCC traveled from the edge of the fixated midgut at 37°C and at 39°C. Live imaging data (not measured over the full 16 hours) showed no significant difference between 37°C and 39°C when comparing average velocity ($p=0.323$) or end displacement ($p=0.493$). Analyzing *in vivo* data showed no significant difference ($p=0.371$) in ENCC migratory distance from the cecum between 37°C and 40°C.
Conclusions: The preliminary data obtained from this project suggest that hyperthermia could affect ENCC migration both *in vitro* and *in vivo*. The small replicant number could be affecting the results. If hyperthermia is found to significantly affect ENCC migration, it would support current human epidemiologic studies that show an increased frequency of HSCR among mothers who had a fever. HSCR is a partially penetrant genetic disorder which may be influenced by environmental exposures such as hyperthermia. If hyperthermia is shown to increase the frequency of HSCR, it may be possible to reduce the disease frequency in families with genetic risk by aggressively treating fever.

083 **Ikpeama, Uzoh E**

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Summer Research Program
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Mentor: Bettina Drake, PhD, MPH

Evaluation of follow-up activities after prostate cancer screening efforts in the community

Ikpeama UE; Drake B

Introduction: Prostate cancer incidence rates are 60% higher for African-American (AA) men than for white men, and AA men have the highest prostate cancer mortality rate of any racial group in the US. Despite this, AAs remain less likely to be screened for prostate cancer, and also less likely to receive treatment for the disease. The current evaluation looks to determine the motivation behind participant initiated screening requests and to assess the nature and timing of follow-up activities among a sample of predominantly AA men who received free PSA tests as a part of community outreach events.
Methods: Men who consented to receive a PSA test at a Program for the Elimination of Cancer Health Disparities community outreach event between 2007 and 2011 were given a questionnaire that asked about participants' reasoning behind getting screened as well as follow up activity after they received the PSA tests at the community outreach event.
Results: 70% of the participants stated a major reason for receiving their PSA test was that it was free. In addition, the location of the event proved to be important for men deciding whether or not to be screened (55%), as well as the trust of the event host/sponsor (55%). With regard to follow-up activities taken, 30% of the men talked to their spouse or partner about their test result/prostate cancer, and also made an appointment to get their yearly physical. 26% of participants changed their diets and 18% modified physical activity levels. Others looked online for more information on prostate cancer (19%).
Conclusions: The results support the subsidization of PSA test costs by event hosts or sponsors as a good method for reaching men who may not otherwise be tested. The hosts associated with events also prove to be important themselves in mens' decision processes to be screened. Although the levels of follow-up activity appear bleak, they may provide an avenue for strengthening education offered at screening events. Instead of relying on participants to engage in the measures themselves, volunteers at community screenings should suggest appropriate follow-up actions for the participants in addition to providing knowledge about prostate cancer itself.

123 **Jiang, Naomi**

Medical Student
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Department of Radiation Oncology, Washington University in St. Louis School of Medicine
Mentor: Perry Grigsby, MD, MS

Sequential measurement of tumor volume during radiotherapy for outcome prediction in squamous cell carcinoma of the cervix

Jiang NY; Dyk P; Grigsby PW

Introduction: Currently, little is known about the predictive power for local recurrence of concomitant Intensity Modulated Radiotherapy (IMRT) and High-Dose-Rate (HDR) Intracavitary Brachytherapy (ICBT) induced tumor volume changes during treatment for cervical cancer. The purpose of this study was to evaluate weekly sequential and longitudinal tumor volume and regression ratio (RR) changes by magnetic resonance imaging (MRI) throughout radiotherapy as an early predictive factor for local tumor control and overall survival for patients with cervical cancer.

Methods: Concomitant IMRT and HDR ICBT were given to 103 patients with cervical cancer. Using 3D region of interest (3D ROI) contour tracing, gross tumor volumes (GTV) were measured during each weekly brachytherapy treatment, six total. Correlation of the GTV and tumor RR with local recurrence was evaluated. An algorithmic system was developed to incorporate all weekly GTV and tumor RR to predict patients' local recurrence and overall survival.

Results: The GTV during all six weeks of treatment ($p<0.001$) and the tumor RR during weeks three ($p=0.046$) and four ($p=0.022$) were significantly correlated with local recurrence. The Total Volume Score ($p<0.001$; sensitivity 88%; specificity 76%), Total RR Score ($p=0.002$; sensitivity 83%; specificity 70%), and Final Score ($p<0.001$; sensitivity 88%; specificity 76%) were all strong predictors for local recurrence. Patients with a Total Volume Score of >3 ($p<0.001$) or a Final Score of >3 ($p<0.001$) had significantly decreased overall survival.

Conclusions: A subset of cervical cancer patients with a high risk of local failure after definitive radiotherapy can be identified using tumor volume measurements, tumor regression ratios, and our algorithmic score system. These findings could have personalized therapeutic implications for patients who might benefit from a more aggressive and individualized treatment plan.

046 **Kim, Judith**

Medical Student
T35 NIDDK Training Grant
Summer Research Program
Division of Emergency Medicine
Department of Pediatrics, Washington University in St. Louis School of Medicine
Mentor: Mark Manary, MD

The impact of zinc and albendazole therapy in the treatment of environmental enteropathy

Kim J; Ryan K; Stephenson K; Shulman R; Maleta K; Manary M

Introduction: Gut dysfunction, known as environmental enteropathy (EE), affects up to 50% of children in the developing world. While EE is known to reduce nutrient absorption and significantly contribute to child stunting worldwide, there is no effective treatment. The purpose of the study is to compare the therapeutic effectiveness of high-dose zinc therapy and de-worming albendazole in restoring normal gut absorptive and immunological function in 1-3 year old rural Malawian children at high risk for environmental enteropathy.

Methods: Data were tabulated and statistically summarized from initial survey results and urinary concentration tests of 223 participants aged 1-3 in a randomized, double-blinded, placebo-controlled trial. Student t-tests were used to compare the change in participants' urinary lactulose:mannitol ratio (L:M), which is a measure of the severity of EE and was used as the primary outcome to determine the efficacy of either oral zinc administered for 14 days or a single dose of aldendazole in treating EE.

Results: The change in L:M before and after treatment with zinc ($n=73$) and placebo ($n=77$) were 0.02 ± 0.20 and 0.12 ± 0.33, respectively ($P<0.05$). The change in L:M before and after treatment with albendazole ($n=73$) and placebo ($n=77$) were 0.04 ± 0.22 and 0.12 ± 0.33, respectively ($P=0.077$). The difference in change in L:M following the zinc treatment compared to placebo is statistically significant; the difference in change in L:M following the albendazole treatment compared to placebo is not quite statistically significant.

Conclusions: In an impoverished rural African population of 1-3 year old children at risk for EE, either a 14 day course of zinc or a single albendazole dose caused a decreased change in L:M in comparison to placebo. The reduction in L:M suggests that the treatments decreased the severity of EE in the children. While further research would be useful to evaluate the significance albendazole treatments, the results of this study indicate the potential of zinc therapy as a treatment to help improve gut dysfunction.

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Changing trends in the utilization of nephron-sparing surgery at Washington University

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Introduction: Despite the demonstrated benefits of partial nephrectomy (PN) for renal tumors and the AUA's specific endorsement of PN as the standard of care for T1a renal cell carcinoma, a substantial under-utilization of nephron-sparing surgery (NSS) is present in low volume nephrectomy centers across the U.S. We report a contemporary analysis of trends in PN use at a tertiary care facility.

Methods: We reviewed Washington University's nephrectomy database, evaluating patients who underwent extirpative renal surgery for suspected renal malignancy from 2005 to 2010. Percentages of PN vs. radical nephrectomy were calculated for all renal lesions and for T1a tumors for each year. The chi-square test was used to evaluate the statistical significance of trends in relative utilization of partial vs. radical nephrectomy.

Results: Overall, 399 (45%) patients were treated with PN during this period. T1a tumors occurred in 513 patients (58%), and 66% of these patients were treated with PN during the 6-year time frame of this study. For T1a tumors, PN frequency increased 2.3-fold, from 38.4% in 2005 to 88.2% in 2010 ($p<0.0001$). For all renal lesions, PN frequency increased 2.5-fold, from 26.9% in 2005 to 66.7% in 2010 ($p<0.0001$).

Conclusions: A progressive increase in the utilization of NSS was noted at Washington University over time. More recently, approximately 88% of T1a tumors and 67% of all renal lesions are treated with PN at our institution. Our results reflect data seen at other high-volume centers and further demonstrate the disparity in the use of PN between high-volume centers and wider U.S. practice patterns.

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Detection of low concentration host mRNA sensitive and specific for environmental enteropathy

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Introduction: The term 'poor nutrition' refers to inadequate absorption of a full complement of nutrients necessary for optimum body function. Compromised function of the gut can lead to malnutrition. Specifically, gut dysfunction known as environmental enteropathy (EE) affects up to 50% of children in the developing world. EE causes no overt symptoms or signs in children. While detection of mRNA expression in human stool could help isolate biomarkers that may be indicative of the disease, the low copy numbers of mRNA in stool poses a barrier to traditional RNA isolation and PCR techniques. Our goal was to produce a non-invasive test to assess the degree of EE within patients by effectively measuring low-level mRNA expression and identifying biomarkers suggestive of disease.

Methods: Stool samples from 70 Malawian children, 34 without EE and 36 with EE, were used to develop the methodology for mRNA detection. Multiple RNA isolation techniques and PCR formats were tested to detect 38 potential mRNA biomarkers suggestive of EE. Of those 38 potential biomarkers, 6 were selected to be measured in all 70 samples.

Results: RNA isolation with magnetic bead extraction provided the most effective recovery of host mRNA from stool. Digital droplet PCR provided the most sensitive detection of low-level mRNA expression. In all 70 samples, >20 copies of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) per 200 mg of stool were detected. Copy numbers of potential biomarkers were normalized to GAPDH, to account for inter-specimen differences in concentration of human mRNA. Of the 6 selected biomarkers measured in all 70 samples, REG4 expression was the best indicator for the disease.

Conclusions: The results suggest that low-level expression of human mRNA in stool can be reliably and reproducibly quantified using magnetic bead RNA extraction and digital droplet PCR. Furthermore, REG4 has been identified as a potential biomarker indicative of EE, though further examination of other biomarkers will be conducted to improve the sensitivity and specificity of the method.

No poster displayed

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Robotic versus laparoscopic procedures: Dry lab tasks delineate sEMG differences in four bilateral muscle groups
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Introduction: Robotic platforms offer potential ergonomic benefits over laparoscopic platforms to surgeons performing large volumes of minimally-invasive procedures but these differences have not been quantified. We hypothesize that tension suturing (TS), paraesophageal hernia repair (PEHR), and bowel anastomosis (BA) will demonstrate greater differences in surface electromyography (sEMG) of 4 bilateral upper extremity muscle groups compared to standard Fundamentals of Laparoscopic Surgery (FLS) tasks [peg transfer (FLS-PT), pattern cutting (FLS-PC), and intracorporeal suturing (FLS-IS)], thus better differentiating the degree of ergonomic stress.

Methods: Four subjects performed maximum voluntary contractions (MVC) for normalization of data, followed by 3 repetitions of FLS-PT, FLS-PC, FLS-IC, TS, PEHR, and BA tasks using standard trainer boxes on laparoscopic and da Vinci Standard robotic platforms. Per task, sEMG data were collected from bilateral biceps, triceps, deltoid, and trapezius muscles using the CleveMed Biorad-150. Per individual, mean %MVC/sec ± SD for each muscle and mean total %MVC/sec ± SD were calculated. sEMG data were compared between laparoscopic and robotic approaches for each task for each subject using paired t-tests.

Results: Significant differences in mean %MVC/sec between platforms were demonstrated for the left deltoid and right trapezius on FLS-PT; right trapezius on FLS-PC; right biceps and right trapezius on FLS-IS; right biceps on TS; bilateral deltoids on PEHR; and right deltoid on BA ($p<0.05$). Significant differences in mean total %MVC/sec between platforms were demonstrated for FLS-PT and FLS-IS ($p<0.05$).

Conclusions: Robotic mean %MVC/sec were lower for all muscles except the bilateral trapezius suggesting a potential ergonomic benefit of the robotic platform. Significant differences were demonstrated during both FLS and non-FLS tasks. FLS tasks are validated components of surgical education further qualifying them for use in the larger comparative ergonomic study.

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MicroRNA may mediate the effects of retinoic acid on the maturation of enteric nervous system precursors
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Introduction: Differentiating enteric nervous system (ENS) precursors have a distinct microRNA (miRNA) profile, which could play a role in maturation**.** The Heuckeroth lab demonstrated that vitamin A is essential for normal ENS development, because retinoic acid (RA) reduces Pten protein abundance in actively migrating ENS precursors. However, Pten mRNA levels in these cells do not appear to be affected by RA. Using a microarray approach, the lab has recently identified several miRNA that appear to be preferentially expressed in the developing ENS. The investigation of miRNA expression microarray data, confirmation of miRNA levels seen in the microarray using qRT-PCR, and exploration of the miRNA profile to determine miRNAs for further examination is crucial to investigation of factors driving ENS development. By understanding factors vital to ENS maturation, there can be a better understanding of ENS diseases and their underlying pathogenesis.

Methods: RNA samples used for the microarray were analyzed using qRT-PCR for the abundance of specific miRNAs; miR-29c and miR-34a. Microarray results were also analyzed using Partek to identify potential targets for further manipulation.

Results: The Pten targeting miRNA microarray showed several miRNAs which were present in modified levels in the developing ENS. Some of these miRNAs have been linked in literature to roles in tumor suppression and cancer metastasis. However, initial runs of the qRT-PCR do not show significant differences.

Conclusions: Retinoids appear to be critical for development of the ENS because they reduce Pten protein levels in actively migrating ENS precursors. Based on work in Dr. Heuckeroth's lab, vitamin A deficiency may be a risk factor for Hirschsprung disease, a disorder where the ENS is missing from the end of the bowel. Pten deficiency is also suggested as one cause of intestinal ganglioneuromatosis. We now hypothesize that the effect of RA on Pten abundance is mediated by miRNA. If this is true, then these miRNA and the molecular mechanisms that control miRNA biogenesis and function may play critical roles in ENS development. Defining the miRNA involved and identifying potential molecular mechanisms will help us design new ways to prevent serious birth defects like Hirschsprung disease.

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Optimizing reproductive outcomes in obese women

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Introduction: Obesity is a growing problem for women of reproductive age. This population faces an increased risk of both infertility and obstetrical complications. Management of obese female patients seeking fertility treatment is difficult because it is unclear whether the benefit of weight loss outweighs the cost of delaying treatment. The purpose of this study is to systematically review the literature on the obstetrical outcomes of obese women undergoing IVF following various weight loss strategies and if appropriate, use a meta-analytic technique to compare these outcomes.

Methods: Two separate questions were developed for systematic review. Question 1 was aimed at obese women undergoing fertility treatment and the impact of lifestyle interventions for weight loss on fertility and obstetrical outcomes. Question 2 was aimed at obese women with PCOS undergoing fertility treatment and the impact of lifestyle and bariatric weight loss strategies on fertility, obstetrical outcomes, and improvement of PCOS symptoms. Searches were performed in Embase and PubMed for both questions, and are in the process of being systematically reviewed and evaluated for meta-analysis.

Anticipated Results: The search for question 1 yielded a total of 163 results. It is anticipated that 6-10 will be incorporated into a meta-analysis with results comparing outcomes of lifestyle intervention to no intervention in obese women seeking fertility treatment. The search for question 2 yielded 778 results, and is in the process of being reviewed.

Conclusions: By reviewing two distinct but related questions regarding weight loss and fertility and incorporating the population of obese women with PCOS, a broader insight to the multifactorial problem of obesity and fertility can be gained. Providing clinicians with a review of current literature on an increasingly prevalent problem and investigating the outcomes available interventions in a larger population through meta-analysis will assist in the management of a growing population of women.

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Communication about weight between medical professionals and patients: Relation to eating disorder risk

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Introduction: Communication between medical professionals and patients about obesity is suboptimal. One reported barrier is the fear that identifying obesity could lead to an eating disorder (ED). A clarified understanding of the effect of obesity communication on the development of ED pathology is needed.

Methods: 543 women (18-25 years) entered the study, *Preventing EDs and Reducing Comorbidity*. Participants answered the question, "Has a doctor, nurse, or other medical professional ever told you that you were overweight?" and completed interviews and questionnaires. Body mass index (BMI; kg/m^2) was calculated based on objectively-measured height and weight. Participants were classified into ED risk or clinical categories using DSM-5 criteria. Multiple analysis of covariance was used to assess the relation between being previously identified as overweight and eating pathology. Logistic regression was used to assess the relation between being previously identified and ED risk/symptom status.

Results: 142 (26%) women reported that they had been previously identified as overweight by a medical professional. Compared to those not identified, individuals previously identified as overweight were equally likely to report engaging in disordered eating behaviors ($p>0.05$), but were more likely to report high weight/shape concerns, a history of teasing, and a family history of being identified as overweight ($ps<0.05$). The main effect of previous identification as overweight was associated with ED risk/symptom status; however, this effect was non-significant in the full model, which took into account BMI, history of being teased, and family history of being identified as overweight.

Conclusions: Results indicate that being previously identified as overweight was not associated with an increase in disordered eating behaviors but was associated with disordered eating attitudes. Teasing, BMI, and family history of overweight drive the relation between being identified and ED risk/symptom status. Increased awareness of the importance of identifying overweight and promoting healthy attitudes about eating in the primary care setting is encouraged.

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