# ABSTRACT BOOK Medical Student Research Forum & Poster Day April 4, 2018



Presented by: Required Scholarly Project (RSP) Program Steering Committee Dean's Research Scholar Program Office for Medical Student Research Programs Office for Curriculum

Keck School of Medicine of USC

# Keck School of Medicine of USC

Professor of Surgery

## MEDICAL STUDENT RESEARCH FORUM & POSTER DAY

April 4, 2018

The Keck School of Medicine of the University of Southern California is committed to training the future leaders of academic medicine. To this end, all KSOM medical students are required to participate in hypothesis-driven research as part of the Required Scholarly Project (RSP) program during their tenure at Keck. In addition, KSOM offers select students the opportunity to participate in the Dean's Research Scholars program, a fifth-year option of intensive mentoring and immersion in research.

This week's Forum represents an important milestone in the current research activities of all second-year students and our Dean's Research Scholars. The works of many of our students have garnered awards at regional and national meetings over the years. As you read these abstracts, we are confident that you will appreciate and enjoy the remarkable efforts and accomplishments of our talented students.

To further promote and foster medical student research activities, KSOM established an Office for Medical Student Research Programs in 2017 to oversee the RSP and Dean's Research Scholars Programs, as well as medical student research electives and summer research fellowships. KSOM looks forward to continuing to enhance and expand the training, mentoring and scope of research opportunities provided to our students, and we deeply appreciate the considerable effort, skill and passion with which our faculty support and develop our students *into skilled* scientists and future leaders.

Huile fl-

Henri R. Ford, MD, MHA Vice Dean for Medical Education

University of Southern California 1975 Zonal Avenue, Keith Administration 218, Los Angeles, California 90089-9024 • Tel: 323 442 1875 • Fax: 323 442 1876 • hford@chla.usc.edu



## MEDICAL STUDENT RESEARCH FORUM & POSTER DAY 2018

## April 4, 2018

## KECK SCHOOL OF MEDICINE UNIVERSITY OF SOUTHERN CALIFORNIA

The 2018 Medical Student Research Forum and Poster Day is an annual event which allows Keck School of Medicine of USC medical students the opportunity to present their Required Scholarly Projects (RSP) and Dean's Research Scholar (DRS) projects to their peers and the USC community at large. RSP is a longitudinal research experience that spans the duration of medical school, in which all students are required to participate. DRS is a distinguished opportunity for an optional fifth year of medical school dedicated to research. The projects presented by our students represent a wide variety of disciplines, from basic science to clinical and translational research.

We are extremely appreciative of the supportive faculty who have volunteered their expertise to mentor students through these exciting research initiatives. We also thank faculty who have volunteered their time teaching the key principles required to successfully conduct research. To the incredibly dedicated staff, we thank you for your outstanding coordination of all RSP and DRS-related activities.

The Office of Educational Affairs would like to thank all of those involved with organizing this Forum. We also extend special thanks to Laura Mosqueda, MD, Interim Dean, Keck School of Medicine; Henri R. Ford, MD, MHA, Vice Dean for Medical Education; Nuria Pastor-Soler, MD, PhD, Assistant Dean for Research Mentoring & Director of Required Scholarly Project, David Hinton, MD, FARVO, Director of Dean's Research Scholars, and Stephanie Zia, MD, MACM, Assistant Dean for Career Advising for their support and participation in this Forum. We are very appreciative of the faculty and student judges for reviewing poster presentations. Finally, we are incredibly grateful to our benefactors, the Baxter Foundation, the Wright Foundation, the Medical Faculty Assembly, the Medical Faculty Family and Friends, and Dr. Frank A. Sinicrope for their commitment and support of medical student research.

## **PROGRAM SCHEDULE**

Welcome Address, Aresty Auditorium – 1:00 p.m. Laura Mosqueda, MD Interim Dean, Keck School of Medicine of USC

## Oral Presentations, Aresty Auditorium – 1:10-2:30 p.m.

Moderator: Nuria Pastor-Soler, MD, PhD Assistant Dean of Research Mentoring, Keck School of Medicine of USC Director, Required Scholarly Project Program

Poster Presentations, Harry & Celesta Pappas Quad – 2:45-5:00 p.m.

Dean's Research Scholars Health, Technology, and Engineering Program Class of 2020 Medical Students

## 2018 ORAL PRESENTATIONS

**Dean's Research Scholars** 

Kyle Green

(Mentor: Amir Kashani, MD, PhD)

Suspended Scattering Particles in Motion: A Novel Feature of OCT Angiography in Exudative Maculopathies

Madeleine Burg, Wright Research Scholar

## (Mentor: Siamak Daneshmand, MD)

Objective Measures of Frailty as Predictors of Postoperative Complications After Radical Cystectomy

Michael Chow

(Mentor: **Joseph Rodgers, PhD**) Enhancement of Peripheral Nervous System Regeneration in Response to Priming Stimulus

Alison Yu, Wright Research Scholar

(Mentor: Uttam Sinha, MD, MS, FACS)

Saliva-Based Detection of Human Papillomavirus Related Head and Neck Cancer using Droplet Digital PCR

### <u>Class of 2020</u>

## Kacie Amacher

(Mentor: Andrew Yoon, MD) Perceived Benefits and Barriers to Consuming a Plant-Based Diet Among Patients with Heart Failure

**Carmen Cueto** 

(Mentor: **Sigita Cahoon, MD**) Attitudes Toward Contraception Use in a Rural Ugandan Community

Douglass Tucker

(Mentor: Gabriel Zada, MD)

Aberrant DNA Methylation and Osteogenic Growth Factors in Pituitary Adenomas

### Andrea Banuelos-Mota and Jennifer Perdomo (Mentors: Jo Marie Reilly, MD, MPH; Michael Hochman, MD, MPH)

Barriers and Potential Solutions to Improve Medication Adherence Amongst Latino Patients with Diabetes at FQHCs in Los Angeles, CA / Perceived Ethnic and Linguistic Barriers to Medication Adherence in the Diabetic Latino Community

### Jonathan Sadik

(Mentor: Bradley Peterson, MD)

A Longitudinal, Prospective Study of DTI-Based White Matter Disturbances in Young Adults Born Prematurely

## REQUIRED SCHOLARLY PROJECT (RSP) PROGRAM STEERING COMMITTEE

#### Nuria Pastor-Soler, MD, PhD

Assistant Dean of Research Mentoring Director, Required Scholarly Project Program

#### Ron Ben-Ari, MD, FACP

Associate Dean for Curriculum Associate Dean for Continuing Medical Education Vice Chair, LAC+USC Affairs, Department of Medicine

Jennifer Dinalo, PhD, MLIS Library Liaison to Keck School of Medicine

**Fernando Fleischman, MD** Assistant Professor of Clinical Surgery

### Cha Chi Fung, PhD

Vice-Chair, Medical Education Assistant Dean of Medical Education

#### David Hinton, MD, FARVO

Vice Chair, Department of Pathology Director of Dean's Research Scholars Co-Director, USC-Caltech MD-PhD Program

> Lynn Kysh, MS Clinical & Research Librarian

Lihua Liu, PhD Associate Professor of Clinical Preventive Medicine

William Mack, MD Associate Professor of Neurological Surgery

#### Kevin Nash, PhD

Assistant Dean for Curriculum Associate Professor of Clinical Pathology

#### Joyce Richey, PhD

Associate Dean for Diversity and Inclusion Chief Diversity Officer, Educational Affairs

Christopher Russell, MD Assistant Professor of Clinical Pediatrics

#### George Tolomiczenko, PhD, MPH, MBA

Co-Director, Health, Technology, and Engineering Program

#### Anne Vo, PhD

Director, Educational Research Assistant Professor of Clinical Medical Education

## OFFICE FOR MEDICAL STUDENT RESEARCH PROGRAMS

## Nuria Pastor-Soler, MD, PhD

Assistant Dean of Research Mentoring Director, Required Scholarly Project Program

## Han Chang

Associate Director for Medical Student Research Programs

## MEDICAL STUDENT RESEARCH CHAIRS

Mark Landau, MSIII MSIII Research Chair

Acacia Hori, MSII MSII Research Chair

## **Pranav Bhamidipati, MSI** MSI Research Chair

## **KECK MEDICAL STUDENT RESEARCH BENEFACTORS**

The Keck School of Medicine of USC is sincerely grateful to our benefactors who generously support our student research programs.

Donald E. and Delia B. Baxter Foundation Wright Foundation Medical Faculty Assembly Medical Faculty, Family, and Friends Dr. Frank A. Sinicrope Office of the Dean

## TABLE OF CONTENTS

## **Research Categories**

Anesthesiology	38
Basic Science	42
Biokinesiology and Physical Therapy	45
Cardiology and Cardiovascular Disease	48
Dean's Research Scholars	13
Dermatology	52
Education	56
Emergency Medicine & Trauma	58
Family Medicine	61
Health Disparities	69
Health, Technology & Engineering	71
Imaging and Radiology	75
Internal Medicine	79
Mental Health and Psychiatry	91
Nephrology and Urology	95
Neurology	103
Neurosurgery	105
Oncology	115
Ophthalmology	122
Orthopaedic Surgery	128
Otolaryngology	139
Palliative Care	144
Patient Care Quality and Safety	146
Pediatrics	148
Plastic Surgery	170
Preventive Medicine	172
Reproductive Health	174
Surgery	179

## **Dean's Research Scholars**

Barbaro, Michael	14
Burg, Madeleine	14
Choi, Katherine	15
Chow, Michael	16
Christian, David	17
Danielian, Arman	17
Engle, Joshua	18
Feinstein, Shera	19
Ford, Adam	20
Gor, Vadim	20
Green, Kyle	21
Hill, Colin	23
Hwang, Eric	24
Jung, Eric	24
Kogachi, Kaitlin	25
Lang, Paul	25
Lau, Christopher	26
Lin, Michelle	26
Lin-Brande, Michael	27
Maxim, Tom	28
Murgai, Rajan	29
Nazareth, Alexander	29
Oh, Paul	30
Olengue, Ketetha	31
Patel, Arati	32
Rosario, Santano	33
Rounds, Alexis	34
Samaan, Jamil	35
Yu, Alison	36
Yuen, Kaeli	37

## MD/PhD Program Medical Student Researchers

Blumenfeld, Zachary	
Grisafe, Dominic	
Hodara, Emmanuelle	116
Hori, Acacia	
Shahrestani, Shane	114

Abdelhalim, Ahmed	.72
Agari, Kimiko (MD/DDS)	.180
Alling, Torey	.180
Amacher, Kacie	. 80
Angajala, Varun Teja	.72
Azam, Saif	. 49
Bains, Sukhraj	.129
Banuelos Mota, Andrea	. 62
Basin, Michael	. 181
Bechler, Kameron	. 149
Beckler, Carlee	. 80
Campen, Natalie	.76
Cardona, Hugo	. 149
Cardoza, Giancarlo	.151
Chai, Audrey	. 49
Chang, Angela	. 39
Chappell, Zariah	.106
Chen, Anthony	.92
Chen, Ellison	.175
Chen, Erin	. 62
Chen, Xiao	.129
Cheng, Kai Wen	.96
Chu, Emily	.81
Clemesha, Chase	.96
Cline, Jared	. 50
Cueto, Carmen	.175
Curtis, William	.138
Cyprich, Janelle	.107
Dasgupta, Shruti	.176
De Coster, Mika	.81
DeClouette, Brittany	.76
Dickey, Brian	. 82
Duvalyan, Angela	.151
Ebner, Peggy	.181
Eka, Aleeson	.182
Etzel, Michael	.152
Fei, Shangnon	. 59
Feldsher, Jacob	.130
Feliz Sala, Emilio	.63

## **Class of 2020 Medical Student Researchers**

Fischer, Briah	183
Frieden, Piers	82
Friedricks, Natalie	184
Fugere, Tyler	184
Fullenkamp, Austin	97
Gallo, Matthew	130
Garapati, Hemanth	185
Garcia, Erick	140
Gaur, Kush	153
Gogia, Angad	107
Goodman, Morgan	63
Guller, Jodie	153
Guzman, Ruben	185
Hao, Michelle	53
Hardley, Macy	176
Hsiao, Victor	59
Huang, Polly	140
Hung, Alan	39
Hutchason, Alec	77
Ireland, Robert	186
Iyawe, Aisa	116
Jackanich, Anna	108
Jahr, Amy	64
Jiang, Daniel	132
Jimenez, Angelo	154
Joyner, Kyle	70
Kassardjian, Ari	83
Khan, Sara	155
Kim, Jae	133
Kolawa, Adam	43
Korber, Shane	133
Korn, Electra	177
Kuo, William	40
Kushner-Lenhoff, Samuel	156
Lai, Peter	73
Larsen, Travis	84
Lashkari, Nassim	156
Laughlin, Alice	123
Lebovitz, Lucas	109
Lee, Daniel	186
Lin, Andrew	84

Ling, Melissa	85
Liu, Alice	187
Lui, Christopher	141
Madrigal, Anna	57
Maniar, Kevin	134
Margolin, Emily	104
Masood, Maryam	53
Mathalikunnel, Alisha	157
Mattox, Jacob	141
Mayfield, Cory	134
Montgomery, Simone	147
Naicker, Seethim	64
Naman, Luke	74
Nguyen, Catherine	85
Njenga, Betty	86
Novatt, Hilary	188
Nusbaum, David	157
Nwokedi, Josephine	158
Obremskey, Alexandra	89
Olvera, Vanessa	159
O'Meara, Kyle	119
Ontiveros, Nicole	189
Or, Maya	109
Padilla, Gabriel	54
Panchal, Viraj	189
Patel, Divya	160
Patel, Krishan	160
Patel, Sagar	110
Patel, Tanu	145
Perdomo, Jennifer	65
Perese, Joshua	50
Perez, Madelyn	86
Petrosyan, Nina	87
Pierson, Natalie	110
Polski, Ashley	126
Posell, Alexander	87
Raman, Ganesh	46
Rayes, Rawad	161
Reddy, Ravali	190
Roberson, Ashlee	162
Rodrigues, Sonia	178

Rolle, Lawrence	.65
Rubalcava, Andrea	.88
Ryu, Christine	.124
Sadik, Jonathan	.162
Sadlik, Gal	.119
Salazar Adame, Matthew	.77
Sampath, Maya	.163
Sanchez, Anthony	.92
Schooner, Lauren	.111
Scott, Elizabeth	.164
Seo, Hyun Jae	.124
Serrano, Sabrina	.135
Shah, Ishan	.136
Shaw, Brian	. 190
Sheth, Parthiv	.191
Shiffler, Kyle (MD/DDS)	.192
Shirvani, Borna	.98
Shrivastava, Sharonya	.164
Shue, Lisa.	.88
Sierro, Tiffany	.192
Singer, Maxwell	.112
Situ, Betty	.125
Solis, Joel	.66
Solorzano, Walter	.67
Spitzberg, Andrew	.40
Sterris, Jason	.93
Stiers, Katharine	.165
Stone, Michael	.60
Stoneburner, Jacqueline	.171
Streeter, Hillary	.165
Tabares, Diego	.99
Tam, Courtney	.166
Tavakol, Sherwin	.112
Te, Silena	.93
Thiagarajan, Kavitha	.136
Titus, Micha	.99
Torres Pinzon, Diana	.101
Tran, Kristi	.142
Trinidad, Marissa	.166
Tucker, Douglass	.113
Tung, Andrew	.46

Vo, Sydnie	67
Vogt, Kyle	
Wang, Catherine	54
Wang, Christopher	
Wang, Jennifer	
Wang, Theodore	
Wayman, Connor	
Weller, Robert	
Wingerson, Andrew	
Wong, Victor	
Woods, Aria	
Xu, Willem	
Yanamandra, Meghana	194
Yao, Mimi	194
Yu, Valerie	
Zang, Peter	
Zargarian, Ariana	169
Zhao, Johnathan	

# DEAN'S RESEARCH SCHOLARS

#### Functional Frequency Discrimination from Cortical Somatosensory Stimulation in Humans

<u>Michael F. Barbaro BA</u>, Angad S. Gogia BS <angadgog@usc.edu>, Daniel R. Kramer MD <drk\_431@usc.edu>, Zachary Blumenfeld BS <zblumenf@usc.edu>, Dominic J Grisafe II BS <dgrisafe@usc.edu>, Charles Y. Liu MD PhD < cliu@usc.edu>, Spencer Kellis PhD <skellis@usc.edu>, Brian Lee MD PhD <brianlee@med.usc.edu>

**Introduction**: The restoration of function through brain computer interface (BCI) will require responsive somatosensory feedback for both closed-loop motor-sensory integration, and for restoration of sensory information from the body. Work in closed-loop BCI for non-human primates has shown improved motor outcomes from sensory feedback, and recent work in human sensory feedback, through somatosensory stimulation, yields consistent sensory feedback. Continuing with this prior work, our group sought to evaluate frequency as a variable for delivering different somatosensory precepts. **Methods**: Two epilepsy patients, a right-handed female and male, were implanted with a subdural electrocorticography grid over the hand region of somatosensory cortex (left-sided and right-sided, respectively). While in the intensive care unit, they performed a frequency discrimination target acquisition task consisting of the subject exploring two targets with their hand contralateral to the implant, without physically touching the targets. Over each target, the primary somatosensory cortex was stimulated randomly at either 50 or 100 Hz frequencies, with stable current, pulse width, and pulse duration. The subject had to determine which target had the higher frequency. Post-processing and statistics were done using custom Matlab software.

**Results**: The ventral surface of the tip of digit two was chosen for testing for the female subject and the medial surface of the palm and digit 5 were chosen for the male subject. Each subject performed 25 trials. Accuracy was 98% among the two subjects. The difference in sensation was described as "more intense" and "faster" by the female subject, and "stronger" and a "faster buzzing" by the male subject. No adverse events occurred.

**Conclusion**: The high degree of accuracy in discriminating between two frequencies while holding other variables of stimulation constant makes this a usable component to manipulate in future somatosensory BCI systems. Future work will require elucidation of more detailed discrimination among frequencies to establish just noticeable differences and the upper and lower limits of functional adjustment.

## Objective Measures of Frailty as Predictors of Postoperative Complications After Radical Cystectomy

Madeleine L. Burg, Thomas G. Clifford, Soroush T. Bazargani, Jie Cai, Anne K. Schuckman, Hooman Djaladat, Siamak Daneshmand Los Angeles, CA (Presentation to be made by Madeleine L. Burg)

**Objective:** Frailty has been defined as a syndrome of physiological decline causing vulnerability to adverse outcomes. As bladder cancer is diagnosed at an average age of 70 years, these patients are more likely to be frail. Prospective studies on frailty and postoperative outcomes in urological patients are lacking. We aimed to determine whether established measures of frailty can identify high-risk patients undergoing radical cystectomy and predict their surgical outcomes.

**Materials and Methods:** Patients included those 65 years and older undergoing radical cystectomy. Under IRB approval, we prospectively recorded preoperative grip strength, gait speed, weight loss of  $\geq 10$  pounds in the past year, exhaustion, and low physical activity. Patients were also prospectively scored using the Clinical Epidemiological Survey for Depression (CES-D), Charlson Comorbidity Index (CCI), Katz Index of Independence in Activities of Daily Living (Katz ADL), Karnofsky Performance Scale (KPS), and Eastern Cooperative Oncology Group (ECOG) performance status. 90-day postoperative complications were recorded. Chi-square, Kruskal-Wallis, and multivariable logistic regression analysis were performed. **Results:** A total of 91 patients were identified between 2/2014 and 2/2016 with an average age of 74.7 years. 68 (74.7%) patients had at least one postoperative complication within 90-days with no difference in age (p=0.8). 67.0% of patients underwent open radical cystectomy, with no difference in complication rates between open and robotic (p=0.08). On univariate analysis, gait speed (p<0.001), CCI (p<0.02), physical activity (p<0.02), and weight loss (p<0.03) were significantly associated with 90-day complications. On multivariable analysis, physical activity level (OR 0.73, CI 0.53-0.94, p<0.04) and CCI (OR 3.36, CI 1.14-10.56, p<0.04) were associated with increased risk of 90-day complications after controlling for pathologic stage, urinary diversion, blood transfusions, and age. Grip strength and subjective assessment tools (CES-D, Katz ADL, KPS, ECOG) were not associated with 90-day postoperative complications (p>0.05).

**Conclusion:** Objective measures of frailty, such as preoperative physical activity level or CCI, may be better predictors of postoperative complications than subjective assessments. These measures may be useful for identifying older patients at increased risk for complications after radical cystectomy who may need higher acuity care in the perioperative period.

An On-Demand Ride Service Solution for Better Healthcare Outcomes Among Older Adults <u>Katherine J. Choi</u>, Rebecca M. Ebert, Xuejiao (Catherine) Che, Mona Sobhani Ph.D., Leslie A. Saxon M.D., USC Center for Body Computing, Department of Cardiovascular Medicine, Keck School of Medicine of USC

**Background**: Transportation limitations have been shown to seriously impact senior patient access to required healthcare resources, as well as their independence and self-confidence. We will study how access to a ride requesting service (Lyft) can improve metrics of overall healthcare in a senior population, including ease of healthcare utilization and levels of social activity. The USC Center for Body Computing and AARP Foundation are conducting a study to address social isolation in the elderly. **Methods**: We are recruiting patients from the USC Healthcare Clinics and providing unlimited Lyft rides. Patients are given surveys, log books, and wrist-worn activity sensors (Fitbit) to assess baseline use of technology and transportation, as well as health and wellness. A 2 week baseline is followed by the intervention where patients are given unlimited rides via either a concierge call-in service (research coordinator uses web-based tool to dispatch rides) or the Lyft mobile application, based on their preference, for 3 months.

**Results**: Thus far, 40 patients were enrolled. Mean age of all participants is 72 years, and 653 Lyft rides have been taken. Thus far, 50% of rides are utilized to access health care services.



**Figure 1**: Aggregate ride usage data from 5 patients in preliminary analysis. Rides originating from/ending at home excluded. A total of 264 rides were examined for this figure.

**Conclusions**: This preliminary data on the methods and conduct of the study demonstrates that seniors can be trained to use app-based ride sharing services for medical appointments and other daily activities.

## Enhancement of Peripheral Nervous System Regeneration in Response to Priming Stimulus

<u>**Chow M<sup>1,3</sup>**</u>, Kochhar A<sup>2</sup>, Rodgers J<sup>1,3</sup>

- 1. Keck School of Medicine of USC
- 2. USC Department of Otolaryngology, Head and Neck Surgery
- 3. USC Department of Stem Cell Biology and Regenerative Medicine

**Goal:** Previous work in our lab found that subjecting animals to a priming stimulus before tissue injury led to accelerated tissue healing in mice. We found that this effect was due to transitioning stem and progenitor cells (cells responsible for tissue healing) into an "Alert" state in which they more rapidly respond to tissue injury. We identified hepatocyte growth factor activator (HGFA) as a biologic factor that mediates, and is sufficient to induce, the effect of a priming stimulus on the kinetics of tissue repair. This suggests that HGFA may have therapeutic value to improve healing. To this end, the overarching goal of our study is to develop a pre-clinical model to test and translate the effect of HGFA/priming stimuli on aspects of recovery from nerve injury and neurodegeneration.

**Methods:** We developed a mouse model to study the initial phases of nerve regeneration following injury. To do this, we treated mice with a priming stimulus (hindlimb muscle injury) or administered HGFA 2 days prior to isolation of the dorsal root ganglion (DRG) neurons from T1-T10 vertebral levels. Isolation of DRG neurons severs axonal processes and upon culturing, they immediately begin regrowth. We analyzed the rate and efficiency of neurite growth by DRG neurons by immunostaining for Tuj-1 and DAPI. ANOVA was used to determine significance between experimental groups.

**Results:** DRG neurons isolated from animals that were primed, 2 days earlier, by a muscle injury grew significantly quicker, 18 microns per hour, than their control, non-primed, counterparts. The ratio of cells that initiated neurite development to those which remained quiescent was improved by 3 fold when the neurons were primed. We hypothesize that HGFA mediates the effect of a priming injury on the rate of DRG growth.

**Conclusions:** Peripheral neurons display a similar alert response as previously established in a stem progenitor cell model. This suggests priming neurons for regenerative response may carry clinical significance in scenarios of peripheral nerve compromise or dysfunction.

## **Return to Sport After Meniscus Allograft Transplant**

David R. Christian<sup>1,2</sup>, BS; Gregory L. Cvetanovich<sup>1</sup>, MD; Michael L. Redondo<sup>1,3</sup>, MA, BS; Grant Garcia<sup>1</sup>, MD; Adam B. Yanke<sup>1</sup>, MD; Brian J. Cole<sup>1</sup>, MD, MBA

 Rush University Medical Center, Chicago, IL 60612
 Keck School of Medicine of USC, Los Angeles, CA 90033
 University of Illinois at Chicago Medical School, Chicago, IL 60612

**Background:** Approximately 50% of patients undergoing meniscectomy develop arthritic changes and the treatment options for young meniscus deficient patients are limited. Meniscus allograft transplant (MAT) provides successful long-term clinical outcomes, though return to sport has not been described in detail.

**Methods:** After Institutional Review Board approval, patients undergoing MAT between 2013-2015 were retrospectively identified. Patient demographics, surgical details, and complications were recorded. Patients were contacted regarding reoperation and failure. Patients were asked to complete a survey evaluating their pre- and post-operative activity level.

**Results:** Retrospective review identified 115 patients who underwent MAT. Follow-up and return to sport data has been collected for 68 (59%) patients (38 female, 30 male). Concomitant cartilage procedures were performed in 52 (76%) patients. Six (11%) patients underwent concomitant realignment procedures. Failure occurred in 7 (10%) patients while 17 (25%) patients underwent reoperation. Fifty-nine (87%) patients participated in sports prior to MAT and 40 (60%) patients returned to sport following surgery. Pre-operatively, the most common sports were running (n=32), heavy weight lifting (n=28), cycling (n=22), and basketball (n=21). Post operatively, the most common sports were light weight lifting, heavy weight lifting, cycling, and yoga (n=21, 21, 17, and 17, respectively). Higher impact sports such as running, basketball, and football were frequently discontinued following MAT. The most common reasons for discontinuing sports were to prevent damage (n=41), fear (n=28), and pain (n=25). The majority of patients (66%) were satisfied with their ability to return to sport. **Conclusion:** MAT provides is a safe and effective treatment option with high reoperation, but low failure

rates. The majority of patients are able to return sport after MAT, although low impact activities are more common while higher impact activities are discontinued for reasons such as preventing further knee damage, fear, and pain.

## Zoonotic Staphylococcus Pseudintermedius Sinonasal Infections: Risk Factors And Resistance Patterns <u>Arman Danielian<sup>1</sup></u>, MS, Elisabeth H. Ference<sup>1</sup>, MD MPH, Fredrick Yoo<sup>2</sup>, MD, Edward C. Kuan<sup>3</sup>, MD, and

- Jeffrey D. Suh<sup>2</sup>, MD
- 1. Rick and Tina Caruso Department of Otolaryngology-Head and Neck Surgery, Keck School of Medicine of the University of Southern California, Los Angeles
- 2. Department of Otolaryngology-Head and Neck Surgery, David Geffen School of Medicine of the University of California, Los Angeles, Los Angeles
  - 3. Department of Otorhinolaryngology-Head and Neck Surgery, University of Pennsylvania, Philadelphia

**Introduction**: Staphylococcus pseudintermedius is a gram-positive bacteria that colonizes the skin and orifices of healthy canines and felines. Although S. pseudintermedius commonly causes opportunistic ear and soft tissue infections in dogs and cats, it only recently was identified as a cause of infections in humans. This study is a follow up of Kuan et al.'s 2015 study, which described 4 cases of S. pseudintermedius-mediated sinonasal infections, and reports an additional 29 cases.

**Methods**: Retrospective review of 33 chronic rhinosinusitis patients with S. Pseudintermeidus positive sinonasal cultures and comparison to a prospectively collected control sample of patients undergoing culture due to acute or chronic sinusitis

**Results**: Thirty three patients with CRS had nasal cultures positive for S. pseudintermedius. Of the thirty three positive cultures, 82% demonstrated resistance to penicillin, 58% to clindamycin, 33% to doxycycline, and 27% to oxacillin. 52% of patients had a S. pseudintermedius infection within 8 weeks of endoscopic sinus surgery, and 36% had either immunosuppression due to CVID, diabetes, history of transplant or an autoimmune disease. 97% of patients with Staph pseudintermedius owned a dog, 3% owned a cat, and 3% had no pets.

**Conclusion**: Although a rare cause of infection in humans, S. pseudintermedius should be considered in post-operative sinonasal infections or those refractory to standard medical management, especially if the patient has regular contact with dogs. S. pseudintermedius is not readily identified with routine laboratory diagnostic testing and often demonstrates multi-drug resistance, making it a pathogen that is commonly misdiagnosed and difficult to treat.

## Epilepsy Monitoring and Creating a Seizure Monitor Joshua Engle, MD Candidate; George Tolomiczenko, PhD

**Goal/Background:** Epilepsy is the most common neurological disease, effecting 65 million people worldwide, with 3 million people affected in the US alone. Seizures can lead to injury, intellectual delay, and SUDEP (Sudden Unexpected Death in Epileptic Patients), which kills more than 50,000 people per year. Our goal is to assess current methods for monitoring seizures and create a better seizure monitor. **Methods:** The study methodology will be to survey participants about their epilepsy diagnosis, their knowledge about their diagnosis, and their current use of seizure monitors. Questions will be sourced from the American Academy of Neurology and formatted in the Likert Scale. The study will end when 50 patients are interviewed and their responses analyzed. We will use the data to create a linear regression model with a Pearson correlation coefficient to demonstrate the relationship (if any) between epilepsy/SUDEP education and seizure monitor use. We will also use the likert scale to assess overall attitudes towards seizure monitors.

For creating the monitor, we took a list of metrics that could be used to detect seizures: EEG, motion detection, sympathetic activation of heart rate, muscular contraction (detection via EMG, stretch receptors, or a RF sensor), HRV, and fall analysis. We then catalogue a list of 50 commercially available sensors that could easily be worn or positioned in the home that track one or more of the above metrics. Then we narrow down the above list to the minimum metrics needed to detect tonic-clonic seizures and tonic seizures that could also be detected by the sensors in our catalogue. From there we assemble the best sensor system to detect tonic-clonic/tonic seizures.

**Results:** We have catalogued 50 sensors. We determined the best sensor system would be a smart watch and RF bedside sensor. The metrics detected will be motion in excess of 7 seconds, a heart rate (HR) delta greater than 30% in either direction (based on published research on HR delta during seizure activity), an software algorithm that can distinguish between a standing and non-standing state, and

muscle contraction (measured via a bedside RF sensor). We have started software development for our sensor system, with the coding process continuing. After we complete our software code for our sensor system, we will validate our system via clinical testing in an epilepsy monitoring unit (EMU). Our survey is still ongoing.

Recurrence status and lymphovascular invasion are independent risk factors for lymph node metastasis in cutaneous squamous cell carcinoma of the head and neck: A matched case-control study <u>Shera Feinstein, BA<sup>1</sup></u>; Shauna Higgins, MD<sup>1</sup>; Omeed Ahadiat, BS<sup>1,2</sup>; Makenzie Hawkins, MSPH<sup>3</sup>; Myles Cockburn, PhD<sup>1,3</sup>; Ashley Wysong, MD, MS<sup>1</sup>

<sup>1</sup>Department of Dermatology, Keck Medicine of USC, Los Angeles, CA; <sup>2</sup>Chicago Medical School, Rosalind Franklin University of Medicine and Science, Chicago, IL; <sup>3</sup>University of Colorado Cancer Center, Denver, CO

**Importance**: Cutaneous squamous cell carcinoma (SCC) is generally characterized by low morbidity and mortality, however a subset of cases can be high-risk with increased rates of recurrence, metastasis, and death. The single most important prognostic indicator for mortality in patients with SCC is the development of lymph node metastasis. While recent staging systems continue to refine high-risk criteria, there remain low-staged tumors demonstrating high-risk behavior, highlighting gaps in current staging models. Further study is needed to identify features most likely to place a tumor at higher risk of lymphatic spread.

**Objective**: To identify key risk factors for cutaneous SCC lymph node metastasis and to characterize the predictive strength of these factors.

**Design**: An institution-based, matched case-control study of 30 cutaneous SCC tumors that resulted in lymph node metastasis and 30 cutaneous SCC tumors that did not result in lymph node metastasis. **Methods**: Patient medical records from a single tertiary academic medical center were retrospectively reviewed from 2006-2017 and we identified 30 cutaneous SCC tumors with lymph node metastasis. These cases were matched with cutaneous SCC tumors with no evidence of lymph node metastasis during a minimum follow-up period of 12 months (median 21.0, range 12-60). The cases and controls were matched by Brigham and Women's Hospital (BWH) stage of the tumor, patient age (+/- 10 years) and gender. Relevant patient and tumor data was extracted. Chi-square tests were performed and odds ratios and their 95%CIs were generated to determine the association between various risk factors and lymph node metastasis.

**Results**: Sixty tumors were included in this study with four T1, three T2a, 16 T2b, and seven T3 tumors included in both the case and control groups. Median follow-up time for tumors without lymph node metastasis was 14.5 months (range 0-70). Perineural invasion (OR 5.00, 95% CI 1.10-22.82), lymphovascular invasion (p<0.001), and recurrent status (OR 3.25, 95% CI 1.06-9.97) were significantly more common in the lymph node metastasis cohort.

**Conclusion and Relevance**: The current study suggests that perineural invasion, lymphovascular invasion and characterization of the primary tumor as recurrent are risk factors for lymph node metastasis in cutaneous squamous cell carcinoma of the head and neck. Lymphovascular invasion and characterization of primary tumor as recurrent are known high-risk features that are not utilized in current staging criteria. The results of this study may be used to refine the current staging systems for cutaneous SCC, improving early detection and optimizing management for these aggressive tumors.

## What is your time worth? Comparison of distance travelled and waiting time between online and inperson care models from a randomized controlled trial

AR Ford<sup>1</sup>, CM Gibbons<sup>1</sup>, S Boddu<sup>2</sup>, AG Florek<sup>3</sup> and AW Armstrong<sup>1</sup>

<sup>1</sup> Keck School of Medicine, University of Southern California, Los Angeles, CA; <sup>2</sup> Department of Dermatology, University of California Davis, Sacramento, CA and <sup>3</sup> Department of Dermatology, Anschutz Medical Campus, University of Colorado Denver, Aurora, CO

**Background:** Online models of specialty-care delivery have the potential to improve access to care in chronic skin diseases.

**Methods:** To determine whether an online model provides easier access to dermatologic care as compared to in-person management, we conducted a 12-month, multi-centered, pragmatic, randomized controlled trial. Psoriasis patients were randomized to online or in-person care for their psoriasis management.

**Results:** Of the 300 participants, 50% were women and 63% were white; the mean age was 49. At baseline, there were no differences in access to specialty-care between the two groups. Over the 12-month study period, the in-person group had a total of 315 in-person visits; the online group had 161 online visits. At the request of the treating provider, the online group also had eight in-person visits that were deemed best managed in-person. Over 12 months, the in-person group traveled a total of 16,075 miles (25,870 km) (mean 108.6 miles/person, 174.8 km/person) to get to and from their appointments; the online group travelled a total of 203 miles (327 km) (mean 1.4 miles/person, 2.2 km/person), p=0.0003. This represents a total reduction of 15,872 miles (25,544 km) traveled for the online group, or 64% of the circumference of Earth. With regard to time spent traveling and waiting in the office over 12 months, the in-person group spent a total of 591.1 hours (24 days, 15.1 hours) (mean 4.0 hours/person); the online group spent a total 12.6 hours (mean 0.1 hours/person), p=0.0001. This equates to an elimination of approximately 4 hours of traveling and waiting for each online patient over 12 months. **Conclusion:** In conclusion, compared to in-person care, the online model leads to significant reductions for psoriasis patients in the distance travelled and time spent traveling and waiting in providers' offices.

## Gentamicin Induces Premature Termination Codon Readthrough and Restores Laminin 332 in Junctional Epidermolysis Bullosa Cells Harboring Nonsense Mutations

<u>Vadim Lincoln</u><sup>1</sup>, Michelle Hao<sup>1</sup>, Jon Cogan<sup>1</sup>, Yingping Hou<sup>1</sup>, Michaela Hirsch<sup>3</sup>, Vitali Alexeev<sup>2</sup>, David T. Woodley<sup>1</sup>, Mei Chen<sup>1</sup>

<sup>1</sup>Keck School of Medicine, 1Department of Dermatology, University of Southern California, Los Angeles, CA; <sup>2</sup>University of New South Wales, Sydney, Australia; <sup>3</sup>Barts and the London School of Medicine and Dentistry, London, UK

The Herlitz form of Junctional epidermolysis bullosa (H-JEB) is an incurable, devastating, and mostly fatal inherited skin disease for which there is only supportive care. H-JEB is caused by loss-of-function mutations in *LAMA3*, *LAMB3* and *LAMC2*, leading to complete loss of laminin 332, the major component of anchoring filaments, which mediate epidermal adherence to the dermis. *LAMB3* mutations account for 80% of H-JEB patients and approximately 95% of H-JEB associated *LAMB3* mutations are nonsense mutations leading to premature termination codons (PTC). In this study, we evaluated the ability of gentamicin to induce PTC readthrough in H-JEB laminin  $\beta$ 3-null keratinocytes transfected with expression vectors encoding 8 different *LAMB3* nonsense mutations. We found that gentamicin was capable of inducing PTC readthrough in all 8 of the nonsense mutations tested. We next used lentiviral expression vectors to generate stably transfected H-JEB cells with the R635X and C290X nonsense mutations. Incubation of these cell lines with various concentrations of gentamicin resulted in the synthesis and secretion of full-length, 140kDa, laminin  $\beta$ 3 in a dose-dependent and sustained manner.

Importantly, the gentamicin-induced laminin  $\beta$ 3 led to the restoration of laminin 332 assembly, secretion, and deposition within the dermal-epidermal junction, as well as proper polarization of  $\alpha$ 6 $\beta$ 4 integrin in basal keratinocytes, as assessed by immunoblot analysis, immunofluorescent microscopy, and an *in vitro* three-dimensional skin equivalent model. Lastly, newly restored laminin 332 was able to improve the abnormal cellular phenotype of H-JEB cells by reversing abnormal cell morphology, poor growth potential, poor cell-substratum adhesion, and hypermotility. Therefore, gentamicin may offer a novel therapy for H-JEB and other inherited skin diseases caused by PTC mutations.

# Quantification of longitudinal changes in microvascular density and morphology among subjects with diabetic retinopathy using SD-OCT angiography.

Kyle M. Green, Xuejuan Jiang, Zhongdi Chu, Ruikang K. Wang, Amir H. Kashani.

**Purpose:** To quantify longitudinal changes in retinal capillary density and morphology among diabetic subjects imaged with spectral-domain optical coherence tomography angiography. **Methods:** This is an IRB approved, retrospective study of subjects with history of diabetic retinopathy who underwent SD-OCTA at 2 or more clinic visits over a period of >3 months. Images with signal strength <7 or significant motion artifacts were excluded. A semi-automated algorithm was used to calculate OCTA metrics of microvascular density and morphology in non- segmented SD-OCTA images. Some OCTA metrics have been previously reported (Kim AY et al., IOVS 2016) and include: vessel skeleton density (VSD) and vessel diameter index (VDI). A novel parameter, flux, was also used to estimate relative changes in blood flow. Data analysis was performed using linear regression and Student's t-tests comparing values from initial and last follow-ups.

**Results:** 34 eyes from 24 subjects (14 male) were included in this study with a mean age of 62  $\pm$  14. There were 7 mild, 6 moderate, 7 severe NDPR, and 14 PDR eyes. 82% of eyes were treated with anti-VEGF; 64% of PDR eyes received laser treatment. The median number of follow-ups per subject was 5 over a mean of 402 days (range 79-612 days). For eyes with NDPR there was a mean decrease of 4.3% in VSD from the first to last follow-up (Student's t-test; **p** = **0.028**), a 1.2% decrease in VDI (p = 0.363), and a 6.6% decrease in flux (p = 0.089). For eyes with PDR there was a mean decrease of 1.7% in VSD (p = 0.321), a 2.5% decrease in VDI (**p** = **0.020**), and a 10.8% decrease in flux (**p** = **0.009**). In our linear regression models decreasing trends were seen in 18/20 NDPR and 8/14 PDR eyes for VSD, 10/20 and 7/14 eyes for VDI, and 13/20 and 10/14 for flux respectively.

**Conclusions:** OCTA metrics of capillary density and morphology demonstrate decrease in the capillary density and size over time. Comparing metrics from first and last follow-ups, there was a significant decrease in VSD for eyes with NPDR, and in VDI and flux for eyes with PDR. OCTA metrics used over time may be useful in assessing rate of disease progression.



**Figure 1.** Linear regression of changes in vessel skeleton density overtime. Data reflects percent change from baseline at initial visit.

## Prehospital Clinical Deterioration Predicts Further Deterioration in Acute Stroke

<u>Colin M Hill</u>, Kristin Shkrikova, Jeffery L Saver, David S Liebeskind, Sidney Starkman, May Kim-Tenser, Scott Hamilton, Nerses Sanossian

**Background**: Studies of neurologic deterioration in stroke have primarily focused on the acute period 24 hours after arrival. We sought to determine whether prehospital/early ED hyper-acute deterioration portends subsequent deterioration in the 24-hour acute period.

**Methods**: All subjects were enrolled in the NIH Field Administration of Stroke Therapy-Magnesium (FAST-MAG) trial. Hyper-acute neurologic deterioration was defined as Glasgow Coma Scale (GCS) decreasing  $\geq 2$  points from paramedic to ED evaluation, acute neurologic deterioration was defined as  $\geq 4$  point increase on the NIH Stroke Scale (NIHSS) from ED evaluation to 24 hours post-arrival.

**Results:** Of 1,643 patients, 184 (11.2%) experienced acute 24-hour deterioration. Among deteriorators, 45 % were female and mean age (SD) was 70 ( $\pm$ 13.3) years. Median last-known-well time to assessments were: prehospital GCS 25 (IQR 15-46) mins, ED arrival GCS and NIHSS 149 (IQR 120-180) minutes and follow-up (24-hour) NIHSS 26 (IQR 18-30) hours. On multivariate analysis, hyper-acute deterioration increased the odds of subsequent acute neurological deterioration (OR = 2.24, p = 0.010, 95% CI 1.21-4.14). Other factors independently associated with acute 24-hour deterioration were intracerebral hemorrhage (ICH), arrival NIHSS, serum glucose level, systolic blood pressure (SBP) and body temperature (see Table 1).

**Conclusion**: Hyper-acute deterioration is associated with increased odds of acute neurological deterioration in the subsequent 24-hour period.

	P-value	Odds Ratio	Odds Ratio	95% Co	nfidence
			Unit Increase	Interval	
Hyper-acute neurologic	.010	2.241		1.212	4.143
deterioration**					
Intracerebral	<.001	2.463		1.701	3.571
hemorrhage					
NIHSS upon hospital	.007		1.030	1.008	1.053
arrival			point		
Serum glucose	.007		1.004	1.001	1.007
			(mg/dL)		
SBP at 24 hours post-	.007		1.014	1.004	1.024
arrival			mmHg		
Temperature at 24	<.001		1.645	1.419	2.559
			°C		
nours post-arrival					

## Table 1: Factors Independently Associated with Acute Neurologic Deterioration\*

\* "Acute neurologic deterioration" is defined as ≥4 point increase on the NIH Stroke Scale (NIHSS) from ED evaluation to 24 hours post-arrival

\*\* "Hyper-acute neurologic deterioration" is defined as Glasgow Coma Scale (GCS) decreasing ≥2 points from paramedic to ED evaluation

# Comparative Analysis of Scheimpflug and SD-OCT Measurements in Patients With Highly Asymmetric Keratoconus

<u>Eric S. Hwang, BS</u>, Claudia E Perez-Straziota, MD, Sang Woo Kim, MD, Marcony R. Santhiago, MD, PhD, J. Bradley Randleman, MD

Purpose: To determine optimal variables and/or variable combinations from Scheimpflug and spectral domain ocular coherence tomography (SD-OCT) imaging to distinguish the clinically unaffected eye in patients with asymmetric keratoconus (AKC) from a normal control population controls. Methods: Thirty-nine clinically unaffected eyes from 39 patients with AKC and 63 eyes from 63 normal control patients (Controls) who had undergone uneventful LASIK with at least two years of follow-up. Scheimpflug and SD-OCT imaging was obtained in all eyes, and receiver operating characteristic (ROC) curves were generated to determine area under the curve (AUC), sensitivity, and specificity for each variable and variable combination. Logistic regression analysis was used to combine variables. **Results:** No individual metric from Scheimpflug or SD-OCT technology yielded an AUC higher than 0.77. Combining 7 Scheimpflug metrics (combination of thickness and anterior curvature metrics) yielded the best Scheimpflug results (AUC 0.835, Sensitivity 87%, Specificity 73%). Combining 12 SD-OCT thickness metrics (combination of stromal and epithelial thickness) yielded the best SD-OCT results (AUC 0.948, Sensitivity 84%, Specificity 89%). Combining 19 total Scheimpflug/SD-OCT metrics yielded the best results overall (AUC 1.0, Sensitivity 100%, Specificity 100%), while Combining 12 total Scheimpflug/SD-OCT metrics yielded the best results (AUC 0.965, Sensitivity 96%, Specificity 93%) using the fewest variables.

**Conclusions:** Individual metrics from Scheimpflug and SD-OCT imaging poorly distinguished normal eyes from asymmetric keratoconus eyes. However, combining anterior curvature and asymmetry indices from Scheimpflug with reginal total thickness and epithelial thickness variability metrics from SD-OCT clearly distinguished the two populations.

# Transcription factor SP1 mediates fibrosis as a downstream target of ZEB1 induced by FGF2 in human corneal endothelium

Eric Jung, JeongGoo Lee, and Martin Heur

USC Roski Eye Institute, Keck School of Medicine of the University of Southern California, Los Angeles, California 90033, USA

**Purpose:** FGF2 induces endothelial-mesenchymal transition (EnMT) in human corneal endothelium *ex vivo*, leading to cell proliferation and fibrosis. ZEB1 plays a key role in regulation of EnMT in the corneal endothelium mediated through FGF2. Identification of putative transcriptional activator binding sites in the promoter region of EnMT-realted genes lead us to investigate the role of SP1 in regulating of Col1a1, Col1a2, Fibronectin, and Vimentin expression in *ex vivo* human corneal endothelium treated with FGF2. **Methods:** Human corneas *ex vivo* were cut into four equal sections and maintained in OptiMEM-1 culture medium with FGF2 for 7 days (n=4 per group). The control group was maintained in culture medium with no FGF2. Accell SMARTpool siRNA targeting ZEB1 and SP1 were used for gene knockdown. The endothelium was isolated from *ex vivo* corneas, and RNA and protein levels were assessed using RT-PCR and immunoblotting, respectively.

**Results:** FGF2 stimulation increased SP1 expression in *ex vivo* human corneal endothelium, which was inhibited by ZEB1 siRNA knockdown. ZEB1 expression was not affected by SP1 siRNA knockdown. However, FGF2-induced expression of fibrosis-related genes, including Fibronectin, Vimentin, Col1a1, and Col1a2, were significantly reduced by SP1 knockdown.

**Conclusions:** The induction of SP1 by FGF2 through ZEB1 promotes EnMT in human corneal endothelium *ex vivo* through expression of Fibronectin, Vimentin, Col1a1, and Col1a2.

Quantitative assessment of changes in retinal vascular density and morphology among patients with diabetic retinopathy using spectral domain optical coherence tomography angiography (SD-OCTA) <u>Kaitlin Kogachi, BA</u>; Tai-Chi Lin, MD; Anoush Shahidzadeh, MS; Xuejuan Jiang, PhD; Amir Kashani, MD, PhD; Department of Ophthalmology, USC Roski Eye Institute, Keck School of Medicine

**Purpose:** To describe and quantify SD-OCTA metrics among subjects with varying severities of diabetic retinopathy (DR) and determine correlation with disease severity.

**Methods:** Retrospective, observational, multicenter, Institutional Review Board-approved study of patients with and without DR at 3 tertiary-care centers using ZEISS AngioPlex<sup>™</sup> SD-OCTA (Cirrus, Carl Zeiss Meditec, Dublin, CA). A total of 353 eyes were included (89 normal, 113 mild non-proliferative DR (NPDR), 38 moderate NPDR, 34 severe NPDR, and 79 proliferative DR (PDR) eyes). A semi-automated segmentation algorithm was used to assess retinal microvasculature in superficial (SRL), deep (DRL), and full-thickness (RET) retinal layers with 3x3-mm scans centered on the fovea. Quantified capillary metrics included vessel skeletal density (VSD), flow impairment region (FIR), and flux. Associations between SD-OCTA metrics and DR status were analyzed with generalized estimating equations accounting for correlations between two eyes from one subject.

**Results:** When comparing normal to mild NPDR eyes, mean VSD was decreased in RET (0.160±0.007 vs 0.153±0.011) and SRL (0.154±0.006 vs 0.146±0.010) (p<0.05 for both). Mean FIR were greater in RET (0.62±0.24 mm<sup>2</sup> vs 0.94±0.54 mm<sup>2</sup>), SRL (0.78±0.27 mm<sup>2</sup> vs 1.22±0.64 mm<sup>2</sup>), and DRL (1.26±0.38 mm<sup>2</sup> vs 1.80±0.80 mm<sup>2</sup>) (p<0.05 for all). In all layers, mean VSD was decreased and FIR was increased for progressively worse DR stages (p<0.001 for all). No differences in flux were observed in normal versus mild NPDR eyes. Significant trends were also noted in other OCTA morphology parameters. **Conclusions:** There are significant differences in capillary density and morphology among normal eyes compared to mild NPDR eyes. Progressively greater changes in density and morphology are seen with worsening DR status. The OCTA-based metrics may objectively assess DR severity.

## Comparison of Outcomes with Standard and Accelerated Corneal Cross-linking Protocols in Patients with Progressive Keratoconus

Paul Lang, Nikki Hafezi, Sumitra Khandelwal, Emilio Torres, Sang Woo Kim, Farhad Hafezi, J. Bradley Randleman

**Purpose:** Corneal cross-linking is an effective treatment for progressive keratoconus, and current research efforts involve refining the procedure with accelerated protocols. This study compared and evaluated the standard corneal cross-linking (CXL) protocol with two accelerated protocols in patients with progressive keratoconus.

**Methods:** Retrospective data analysis of three groups of patients at two institutions receiving either standard 3mW/cm<sup>2</sup> for 30 minutes corneal cross-linking protocol (S-CXL) or one of two accelerated protocols: 9mW/cm<sup>2</sup> for 10 minutes (SA9-CXL) or 30mW/cm<sup>2</sup> for 4 minutes (IA30-CXL). Data was gathered using a Scheimpflug based device (Pentacam HR, Oculus, Inc.) prior to and 12 months following treatment. Group comparisons included changes in refractive astigmatism, pachymetric, topometric, keratometric, and densitometric indices.

**Results:** 92 eyes (66 patients) were evaluated, including 35 eyes (26 patients) with S-CXL, 28 eyes (18 patients) with SA9-CXL, and 29 eyes (22 patients) with IA30-CXL. Mean change in Kmax was -1.53±2.1 (adjusted mean= -1.54) for S-CXL, -0.72±1.3 (adjusted mean -0.89) for SA9-CXL, and -0.70±2.36 (adjusted mean= -0.53) for IA30-CXL (F(2, 88)=2.20, p=0.12). S-CXL reported significantly greater changes in anterior astigmatism, ISV, IVA, KI, compared to SA9-CXL and IA30-CXL. There were no differences in outcomes at 12 months for asphericity, pachymetry, CKI, IHA, IHD, and IS-Value. **Conclusion:** While all three protocols were effective at halting disease progression and improving overall outcomes, the S-CXL protocol appears to lead to greater improvements in certain variables compared to the other two accelerated protocols.

## Scoping Review of Targeted Ultrasound Contrast Agents in the Detection of Angiogenesis Christopher Lau, Marielena Rivas, Kevin King, Vinay A. Duddalwar

**Introduction:** Angiogenesis has been closely associated with cancer growth and can be mediated by various molecular pathways including vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMPs), endoglin (CD105), αvβ3 integrin and E-selectin.

Targeted ultrasound contrast agents (UCAs) have been developed by coating the surface of microbubbles with angiogenesis associated ligands. Targeted UCAs offer certain advantages over conventional imaging modalities as it allows for low cost, accessible molecular imaging with limited patient exposure to radiation.

**Methods and analysis:** A scoping review has been conducted to address the following research questions:

(1) What are the targeted ultrasound contrast agents that are currently being studied in both preclinical and clinical settings?

(2) What animal models or disease process have these targeted UCAs been applied to?

(3) What are the gaps in the literature regarding targeted UCAs and its application in cancer detection? We have conducted a comprehensive literature search in MEDLINE, EMBASE, and Cochrane Library databases, using the key words MBs, contrast-enhanced ultrasonography (CEUS), inflammation, angiogenesis, thrombosis, apoptosis, and gene and drug delivery. Review selection and characterization were performed by two independent reviewers using pretested forms.

**Results and conclusion:** The search identified 121 primary research articles from 2008 to March 2017. 15 different targeted ultrasound agents have been studied. However, 60% of primary research articles have utilized UCAs targeted to vascular endothelial growth factor (VEGF) or  $\alpha\nu\beta$ 3 integrin. Additionally, breast (21%) and colon cancer (15%) are top two most common disease processes that have been studied utilizing these contrast agents. BR55, a VEGF targeting UCA, is the first targeted UCA that has undergone and has completed Phase 0 human trials.

**Tumor-derived MMP9 facilitates colonization of the neuronal tumor microenvironment.** <u>Michelle Lin, BA</u>; Vahan Martirosian, MS; Brooke Nakamura, BA; Ling Shao, MD PhD; Josh Neman, PhD

**Goal (Background/Objective):** Presence of MMP9 (Matrix metallopeptidase 9) has previously been implicated in tumor invasion, associated with worse clinical outcomes, and served as a prognosticator for chemotherapy resistance<sup>1-4</sup>. While the canonical function of MMP9 is degradation of Type IV collagen in the extracellular membrane, recent literature suggests that MMP9 function may also be intimately associated with neuronal viability and synaptic plasticity<sup>5-7</sup>. We aimed to ascertain whether chemotherapy induced medulloblastoma secretion of MMP9 facilitates colonization of the neuronal niche.

**Methods:** Established human group 3 medulloblastoma cell lines (D425) were used as an *in vivo* model. Pure neuronal cell populations were co-cultured with D425s under trans-well conditions. Cells were treated with chemotherapy (Cisplatin). RNA expression was amplified with real-time qPCR. Protein expression and secretion was interrogated with Western Blot (WB) analysis of cell lysates, WB of concentrated D425 conditioned medium, and Immunocytochemistry on formalin-fixed cells probed with corresponding antibodies. Nonparametric one-way ANOVA and Student t-tests were performed to determine statistical significance.

**Results:** D425 cells demonstrated a 2 fold increase in MMP9 RNA expression following exposure to Cisplatin. This increase was correlated with an increase in cancer stem cell markers (*PROM1, FUT4*). No appreciable difference in neurotrophic profiles (*BDNF, NT4, NGF*), and Tyrosine receptor kinase expression (*TrkB, p75NTR*) was seen, suggesting paracrine as opposed to autocrine mechanism of action. MMP9 protein secretion was observed in D425 conditioned media and cell lysates.

**Conclusions:** MMP9 secretion from Group 3 Medulloblastomas alter the tumor microenvironment with potential resultant neuronal death and increased tumor invasion.

- 1. Al-Batran SE, Pauligk C, Wirtz R, et al. The validation of matrix metalloproteinase-9 mRNA gene expression as a predictor of outcome in patients with metastatic gastric cancer. *Ann Oncol.* 2012;23(7):1699-1705.
- Liu H, Sun Q, Zhang M, et al. Differential expression of folate receptor 1 in medulloblastoma and the correlation with clinicopathological characters and target therapeutic potential. *Oncotarget*. 2017;8(14):23048-23060.
- 3. Laios A, O'Toole SA, Flavin R, et al. An integrative model for recurrence in ovarian cancer. *Mol Cancer.* 2008;7:8.
- 4. Laios A, Mohamed BM, Kelly L, et al. Pre-Treatment of platinum resistant ovarian cancer cells with an MMP-9/MMP-2 inhibitor prior to cisplatin enhances cytotoxicity as determined by high content screening. *Int J Mol Sci.* 2013;14(1):2085-2103.
- 5. Navaratna D, Fan X, Leung W, et al. Cerebrovascular degradation of TRKB by MMP9 in the diabetic brain. *J Clin Invest.* 2013;123(8):3373-3377.
- 6. Christensen KV, Leffers H, Watson WP, Sanchez C, Kallunki P, Egebjerg J. Levetiracetam attenuates hippocampal expression of synaptic plasticity-related immediate early and late response genes in amygdala-kindled rats. *BMC Neurosci.* 2010;11:9.
- 7. Hwang JJ, Park MH, Choi SY, Koh JY. Activation of the Trk signaling pathway by extracellular zinc. Role of metalloproteinases. *J Biol Chem.* 2005;280(12):11995-12001.

## Timely Cystectomy is Critical for Variant Histology of Urothelial Bladder Cancer

<u>Michael Lin-Brande</u>, Shane Pearce, Akbar Ashrafi, Ankeet Shah, Madeleine Burg, Gus Miranda, Hooman Djaladat, Anne Schuckman, Siamak Daneshmand

**Introduction and Objectives:** For muscle-invasive bladder cancer (MIBC), the gold standard treatment is radical cystectomy (RC). The timing of cystectomy on oncologic outcomes is poorly characterized for variant histology (VH) of urothelial carcinoma. Our objective was to compare clinical characteristics and analyze the impact of a delay in RC for pure urothelial carcinoma (PUC) and VH MIBC. **Methods:** Using our prospectively maintained bladder cancer database and after excluding patients who received neoadjuvant chemotherapy or intravesical therapy, we identified 358 patients with non-metastatic muscle invasive urothelial carcinoma (cT2-T4N0M0) who underwent radical cystectomy between 2003 and 2014. The effect of time from first diagnosis of muscle invasive cancer to RC was analyzed as a continuous variable and dichotomized at 4, 8, and 12 weeks. Histology at RC determined by genitourinary pathologists was categorized as PUC (n=292) or VH (n=71). Univariate and multivariable Cox proportional hazards models were used to analyze the impact of time to RC on overall survival (OS). **Results:** VH was more likely to present with extravesical disease (16.9% vs 7.5%, p<0.01), be upstaged at RC (60.6% vs 30.8%, p<0.01), have lymphovascular invasion (LVI) (40.8% vs 28.8%, p<0.01), and lymph node metastasis at RC (28.2% vs 14.4%, p<0.01). The median days to cystectomy did not differ between PUC and VH (55.5 vs 55, p=0.92). Median follow-up time was 3.5 years. Multivariable analysis controlling for age, comorbidities, tumor stage, lymph node status, LVI, and surgical margins confirmed worse OS for each month in delay to RC for VH (HR=1.35, p<0.01). The 5-year overall survival for VH with time to RC of less than 8 weeks was 63% compared to 34% for greater than 8 weeks (p=0.02). **Conclusions:** Variant histology portends a poor prognosis and was more likely to have LVI, be upstaged at RC, and have lymph node metastasis when compared to PUC. Delays in RC for patients with VH were associated with worse overall survival, thus highlighting the need for timely diagnosis and treatment.

## Reducing the Variability of Otoacoustic Emission Measurements in Normal-Hearing Young Adults <u>Tom Maxim</u>, Yeini Guardia, Ping Luo and Carolina Abdala

**Introduction**: Otoacoustic emissions (OAEs) provide a sensitive marker of cochlear health with many clinical uses, including neonatal hearing screening and monitoring for sensory hearing loss in patients exposed to chronic noise or ototoxic drugs. Accurate measurement of OAEs can be hindered by the presence of non-cochlear confounds. To measure evoked OAEs, stimuli presented into the external ear canal vibrate the middle ear ossicles and stimulate the cochlea, where the OAE is generated, travels back to the ear canal, and is recorded by a sensitive microphone. During this process, the presenting stimulus and outgoing OAE are both impacted by the acoustics of the ear canal; forward- and reverse-going sound waves can interact to form "standing waves" which lead to errors in OAE measurement at the recording microphone. In recent years, two calibration techniques – Forward- (FPL) and Emitted-Pressure Level (EPL) – have emerged to control for the effects of standing waves on the evoking stimulus levels and OAE levels as they travel to the recording microphone from their intracochlear generation site. This study set out to perform the first thorough test of the efficacy of these calibration methods in a group of normal-hearing young adults.

**Methods**: Two types of emissions, stimulus-frequency (SFOAE) and distortion-product otoacoustic emissions (DPOAE), were recorded at both low and high stimulus levels for a frequency range of 500 to 16,000 Hz. Stimuli were rapidly sweeping pure tones presented to 20 normal-hearing adults (aged 22-28 yrs). OAEs were measured using a conventional dB sound-pressure level (SPL) calibration, as well as the newer FPL and FPL+EPL calibration techniques. Five subjects were retested 1-3 months following the initial test to assess both inter- and intra-subject variability of OAE recordings over time. **Results**: Preliminary analysis with one of the OAEs (DPOAEs) suggests that, at frequencies impacted by

ear canal acoustics (>3-4 kHz), FPL and FPL+EPL calibrations reduce the intra- and inter-subject variability of OAE measurements relative to conventional dB SPL calibrations. A combined FPL+EPL approach appears to offer a slight improvement over FPL alone. Data analyses are ongoing and these preliminary observations will be updated.

**Conclusions**: FPL and EPL are promising calibration techniques which may improve the utility of OAEs for evaluating and monitoring cochlear health during treatment or noise exposure and enhance the early detection of sensory hearing loss.

# Neural Axis Abnormalities in Early Onset Scoliosis Patients Can Be Detected With Limited MRI Sequences

**Rajan R. Murgai BS**<sup>1</sup>, Benita Tamrazi MD<sup>2</sup>, Ken D. Illingworth MD<sup>1</sup>, David L. Skaggs MD, MMM<sup>1</sup>, Lindsay M. Andras MD<sup>1</sup>

<sup>1</sup>Children's Orthopaedic Center, Children's Hospital Los Angeles <sup>2</sup>Department of Radiology, Children's Hospital Los Angeles

Study Design: Diagnostic accuracy.

**Objective:** The purpose of this study was to determine if neural axis abnormalities in early onset scoliosis (EOS) patients can be reliably detected with limited spine MRI sequences (sagittal T1, sagittal T2, axial T2).

**Summary of Background Data:** Routine spine MRI screening is recommended for the detection of neural axis abnormalities in EOS patients. However, routine MRI's are expensive, lengthy, and in this patient population generally require sedation or general anesthesia.

**Methods:** A retrospective review of consecutive EOS patients in 2017 who received a screening cervical, thoracic, and lumbar MRI was conducted. MRI images were reviewed for pertinent neural axis abnormalities: cerebellar tonsillar ectopia, normal termination of the conus medullaris, cord signal abnormalities, and fatty filum. Three sequences (sagittal T1, sagittal T2, axial T2) of these previously reviewed MRIs were read at a separate time by an attending neuroradiologist. The imaging findings from these 3 sequences were then compared to the prior radiology report based on all of the standard MRI sequences.

**Results:** 50 patients met criteria. 20% (10/50) of patients had pertinent neural axis abnormalities detected on sagittal T1 + sagittal T2. No additional pertinent neural axis abnormalities were detected on review of the axial T2 sequence. When compared to the prior radiology report based on all sequences, all pertinent neural axis abnormalities were detected on sagittal T1 + sagittal T2 images. However, patient's required 90 ± 22 minutes of anesthesia for full MRI's. Sagittal T1 + sagittal T2 sequences lasted 21 ± 7 minutes.

**Conclusion:** Limited spine screening MRI's with sagittal T1 and T2 for EOS patients can allow for a 67% (4/6) reduction in MRI sequences and more than 50% reduction of anesthesia time without losing the ability to detect neural axis abnormalities.

## The Value of Tranexamic Acid in Children with Cerebral Palsy undergoing Proximal Femoral Varus Derotational Osteotomies

<u>Alexander Nazareth MS<sup>1,2</sup></u>, Stephen Shymon MD2 Lydia Andras MD<sup>1,2</sup>, Rachel Goldstein MD<sup>1,2</sup> <sup>1</sup>Keck School of Medicine of USC, <sup>2</sup>Children's Orthopaedic Center CHLA, Los Angeles, CA, USA

**Introduction**: Previous studies have established the safety and efficacy of tranexamic acid (TXA) in reducing blood loss after total joint arthroplasty and spinal fusion surgery. Current literature investigating the effectiveness of TXA in children with Cerebral Palsy (CP) undergoing orthopaedic procedures is limited. The aim of this study was to investigate the safety and efficacy of intra-operative TXA administration in reducing blood loss and transfusion requirements for children with CP undergoing a proximal femoral varus derotational osteotomy (VDRO).

**Methods**: A retrospective review of 237 children with CP who underwent VDRO performed at the author's institution between 2004 and 2017. 32 subjects underwent VDRO surgery with administration of intravenous TXA (mean age  $9.0 \pm 3.9$  years) and 205 subjects underwent VDRO without administration of TXA (mean age  $7.5 \pm 4.1$  years). TXA was administered at a loading dose of 50mg/kg and a maintenance dose of 5-10mg/kg/hour at the discretion of the attending anesthesiologist. Major

post-operative complications including venous thromboembolic events were recorded. Outcome measures including blood loss and transfusion requirements were compared between groups using t-tests, X<sup>2</sup> tests and multiple regression analysis.

**Results**: Significantly less patients in the TXA group required allogenic blood transfusions in the peri- and post-operative period compared to the non-TXA group (3.1% vs 16.1%, P = 0.03). Estimated intraoperative blood loss was similar between TXA and groups: averaged 121 ml for the TXA group and 143 ml for the non-TXA group (P = 0.38). Initial post-operative hemoglobin (TXA: 9.7, no TXA: 9.4, P = 0.48) and hematocrit (TXA: 29.2, no TXA: 27.9, P = 0.28) levels were similar. No major thromboembolic complications events were reported in either group.

Age at surgery (P = 0.09), feeding status (P = 0.34), seizure medication use (P = 0.13), concomitant surgeries (P = 0.17) and distribution of Gross Motor Function Classification (GMFCS) levels (P = 0.21) were similar between groups. Pre-operative hemoglobin (P = 0.39) and hematocrit levels (P = 0.85), operative time (P = 0.30) and tourniquet use (P = 0.11) did not differ between groups.

**Conclusion**: The use of tranexamic acid was effective in decreasing blood transfusion rates in children with CP undergoing VDRO and was not associated with adverse outcomes.

**Summary**: Tranexamic acid is safe and efficacious in reducing blood transfusion requirements in children with CP undergoing VDRO surgery.

# Crowdsourced versus expert evaluations of the vesico-urethral anastomosis in the robotic radical prostatectomy: Is one superior at discriminating differences in automated performance metrics?

Paul J. Oh, Jian Chen, David Hatcher, Hooman Djaladat, Andrew J. Hung Center for Robotic Simulation & Education, Catherine & Joseph Aresty Department of Urology, University of Southern California Institute of Urology, Los Angeles, California

**Purpose:** Crowdsourcing from the general population is an efficient, inexpensive method of surgical evaluation. In this study, we compared the discriminatory ability of experts and crowdsourced evaluators (the Crowd) to detect differences in robotic automated performance metrics (APMs) using Global Evaluative Assessment of Robotic Skills (GEARS) scores.

**Methods:** APMs (instrument motion tracking and system events) of anterior vesico-urethral anastomoses (VUAs) of robotic radical prostatectomies were captured by the dVLogger (Intuitive Surgical). Crowdsourced evaluators and 4 expert surgeons evaluated video footage with GEARS (individual domains and total score). Cases were stratified into performance groups (high vs. low quality) for each evaluator based on GEARS. APMs from each group were compared using the Mann-Whitney U test.

**Results:** Twenty-five VUAs performed by 8 surgeons were evaluated. The Crowd displayed moderate correlation with averaged expert scores for all GEARS domains (r>0.58, p<0.01). Bland-Altman analysis showed a narrower Total GEARS score distribution by the Crowd compared to experts. APMs compared amongst performance groups for each evaluator showed that through GEARS scoring, the most common differentiated metric by evaluators was the velocity of the dominant instrument arm. The Crowd outperformed two out of four experts by discriminating differences in 3 APMs using Total GEARS scores. **Conclusions:** The Crowd assigns a narrower range of GEARS scores compared to experts but maintains overall agreement with experts. The discriminatory ability of the Crowd at discerning differences in robotic movements through GEARS scoring is quite refined, rivaling that of expert surgeons.

## Virtual Reality – The Future Experienced by Urological Patients Undergoing Robotic-Assisted Laparoscopic Radical Prostatectomy (RALP)

<u>Ketetha Olengue</u>, Matthew Winter MD, David Nelson, David Krum PhD, Sin-hwa Kang, Mona Shobani PhD, Monish Aron MD, Leslie Saxon MD

**Background:** Surgery and invasive procedures can be an emotionally traumatic experience for patients. The process often involves physical pain, but this can be exacerbated by anxiety and stress of a process filled with unfamiliarity.

Robotic-assisted laparoscopic radical prostatectomy (RALP) is a minimally invasive technique that is used to remove the prostate gland and surrounding tissues in patients who have been diagnosed with prostate cancer (PCa) that is limited to the prostate. Research has found that RALP reduces disease-specific mortality, overall mortality, and the risk of metastasis and local progression when compared to the alternative option of watchful waiting of the cancer (Bill-Axelson et al., 2005).

**Hypothesis:** Together, the USC Institute of Urology, the USC Center for Body Computing (CBC) and the USC Institute of Creative technologies (ICT) are uniquely positioned to take a closer look at the delivery of preoperative RALP education.

We postulate that virtual reality technology can be a powerful trust-building tool in helping educate a patient undergoing an invasive procedure such as RALP and their family members in an engaging manner, thus helping form a thorough comprehension of their procedure with the ultimate impact of improving the surgical experience and post-operative quality of life.

In this randomized study, we aim to study whether medical procedure-specific preoperative education delivered through a novel technological medium, virtual reality (VR), can further improve patient satisfaction and augment patient understanding and experience.

**Methods:** The study design is a prospective randomized controlled trial. A total of 86 male Englishspeaking patients scheduled to undergo robotic assisted radical prostatectomy (RALP) at Keck Hospital of USC. Once consented, the participants will be randomized to one of two arms—the control arm and the intervention arm. The participants in the intervention arm will be given the opportunity to engage in the VR experience during their initial clinic visit and the control arm will proceed to their scheduled RALP experiencing the standard of care—*see Figure 1*.

The total timeline of this research study will span 6 months. Qualitative surveys and activity will collect data from the participants throughout the duration of the study. The control arm and intervention arm will be compared and assessed at the end of the study on the following measures: technology use, anxiety, pain, physician trust, overall satisfaction of life, physiological and physical parameters (e.g., blood pressure, heart rate, temperature, etc.) and post-operative (30-day) complication rates. Only the intervention arm will give feedback on the overall VR experience through an additional survey. The VR experience will be designed, edited, and developed by the USC Center for Body Computing with consultation from virtual reality experts at USC Institute for Creative Technologies' Mixed Reality Lab (MxR).



Figure 1 - Study Flow

# Experimental chronic cerebral hypoperfusion results in decreased pericyte coverage and increased blood-brain barrier permeability in the corpus callosum

<u>Arati Patel BS</u>, Robin Babadjouni BA, Qinghai Liu MD, Peter Baumbacher, Drew M Hodis, Zhen Zhao PhD, Berislav Zlokovic MD PhD, William Mack MD

**Background:** Murine chronic cerebral hypoperfusion (CCH) results in white matter (WM) injury and behavioral deficits. Pericytes mediate blood–brain barrier (BBB) integrity and cerebral blood flow. Under hypoxic conditions, pericytes detach from perivascular locations increasing vessel permeability and neuronal injury. This study characterizes the time course of BBB dysfunction and pericyte coverage following murine experimental CCH secondary to bilateral carotid artery stenosis (BCAS).

**Methods:** Mice underwent BCAS or sham operation. On post-procedure days 1, 3, 7 and 30, corpus callosum BBB permeability was characterized using Evans blue (EB) extravasation and IgG staining and pericyte coverage/count was calculated.

**Results:** The BCAS cohort demonstrated increased EB extravasation on postoperative days 1 (p = 0.003) 3 (p = 0.002), and 7 (p = 0.001) when compared to sham mice. Further, EB extravasation was significantly greater (p = 0.05) at day 3 than at day 30 in BCAS mice. BCAS mice demonstrated a nadir in pericyte coverage and count on post-operative day 3 (p < 0.05, compared to day 7, day 30 and sham). Decreased pericyte coverage/count and increased BBB permeability are most pronounced on postoperative day 3 following murine CCH.

**Conclusion:** CCH is disruptive to the neurovascular unit and incites morphologic changes of the angioarchitecture of the corpus callosum. Pericytes represent a potential upstream target in efforts to ameliorate white matter injury in the setting of cerebral hypoperfusion.

## When is it Safe to Return to Driving After Total Shoulder Arthroplasty?

Santano Rosario BA<sup>1</sup>, Cory Mayfield BS<sup>1</sup>, Nicholas A. Trasolini MD<sup>1</sup>, Alexis Rounds BS<sup>1</sup>, Alexander Weber MD<sup>1</sup>, Reza Omid MD<sup>1</sup>, George F. "Rick" Hatch III MD<sup>1</sup>
<sup>1</sup> Keck School of Medicine, University of Southern California, Los Angeles, CA uscortho.sports@gmail.com

Disclosures: Santano Rosario (N), Cory Mayfield (N), Nicholas A. Trasolini (N), Alexis Rounds (N),

Alexander Weber (N), Reza Omid (N), George F. "Rick" Hatch (3B - Arthrex)

**Introduction:** Patients commonly return to driving without consulting their physician following shoulder arthroplasty to keep up with activities of daily living. We aim to prospectively measure the time it takes for patients to return to their preoperative driving ability following total shoulder arthroplasty.

**Methods:** This study received approval from our institutional review board and informed consent was obtained from all patients. Licensed, adult drivers undergoing shoulder arthroplasty were prospectively enrolled. Participants used a driving simulator preoperatively and during postoperative visits to perform a series of turning and braking tasks at random in response to a visual stimulus. Each patient's turn reaction time (TRT), turn reaction distance (TRD), and brake reaction time (BRT), Disability of the Arm, Shoulder, and Hand (DASH) score, and Visual Analog Pain Scale (VAS) were measured. Postoperative performances were compared to preoperative performance and analyzed for differences in turning direction with respect to side of injury.

**Results:** Preliminary data includes a total of 7 patients (5 male, 2 female; 4 right, 3 left; av age 67.14 +/- 6.91yrs). When comparing the preoperative results to their 2-week postoperative findings, average BRT decreased while TRT, TRD, and DASH scores increased as seen below. No significant differences were seen when isolating turns toward or away from side of injury. By abstract presentation we anticipate having enrolled 30 patients and analyzed 12-week follow-up data.

**Summary/Conclusion:** All patients improved in their brake reaction time, demonstrating learning. However, the increase in mean turn reaction time, distance, and DASH scores illustrates an acute worsening in driving ability. This evidence should encourage surgeons to advise their patients refrain from driving for at least 2 weeks postoperatively. By presentation, we aim to identify the optimal time when these patients may return to driving.

#### **IMAGES AND TABLES:**

						M
	Measurements		Measurements	Modified Driv	ing (%)	Ê
Break Reaction Time (sec) Preop: 1.38sec 2wk: 1.08sec Difference: -0.30sec	Preop: 1.38sec	Disability of the Arm, Shoulder,	Preop: 60			
	2wk: 1.08sec	and Hand (DASH) Score	2wk: 69.17			
		Difference: +9.17	Number on Na	Number on Narcotics	į	
Trem Besstion Times (see)	Time (cos) Broom 0.02ccc	Viewal Amala a Carla (VAC)	Decemental 57			2v
Turn Reaction Time (sec)	Preop: 0.93sec	Visual Analog Scale (VAS)	Preop: 42.57		Number of Failures	Di
	2wk: 0.98sec		2wk: 15.67	Number of Fail		F
	Difference: +0.05sec		Difference: -26.90			1
Turn Reaction Distance (ft)	Preop: 87.85ft					
	2wk: 94.81ft	Table 2: Function and Pain Scores		Table 3: A	dditional Driv	/in
	Difference: +6.96ft					

Table 1: Reaction Times

## Proximal Humerus Fracture Conversion to Long-Term Arthroplasty by Initial Management <u>Alexis D. Rounds BS</u>\*, Michael Stone MD, Nicholas A. Trasolini MD, Santano Rosario BA, Alexander E. Weber MD, Reza Omid MD, and George F. "Rick" Hatch III MD

**Background:** Recent evidence suggests that proximal humerus fractures are on the rise, particularly with the increase in elderly population. Both operative and non-operative treatments have satisfactory functional outcomes in appropriately selected patients. However, recent studies with long-term follow-up of percutaneous fixation revealed greater posttraumatic osteoarthritis prevalence than previously reported. The purpose of this study is to determine long-term conversion of proximal humeral fractures to arthroplasty and the associated risk factors.

**Methods:** A large, statewide database was used to identify adult patients with proximal humerus fractures between 2000 and 2015. Patients with previous arthroplasty were excluded. Initial treatment within 30 days of presentation with proximal humerus fracture was recorded. Kaplan-Meier 10-year survival analysis was performed with failure defined as conversion to anatomic or reverse total shoulder arthroplasty (TSA) or revision if initial management was arthroplasty. Risk factors were identified using multivariate cox regression of variables with p<0.20 on univariate cox regression.

**Results:** We identified 172,222 (71.08% female, age 68.30+17.13) patients with proximal humerus fractures. Initial fracture management was 81.15% nonoperative, 1.15% percutaneous pinning, 11.86% open reduction and internal fixation, 4.80% hemiarthroplasty, 0.31% anatomic, and 0.70% reverse TSA. Overall survival at 2, 5, and 10 years was 98.35%, 97.63%, and 94.97% with a rate of 1.86 per 100,000 person-years with no statistical difference between initial treatment. Black and Asian race showed a significant protective effect against failure while hypertension, chronic pulmonary disease, rheumatic disease, renal disease, insurance coverage, Medicare, Medi-Cal, and Worker's Compensation were all significantly associated with failure.


**Conclusion:** Proximal humerus fractures remain a common problem. Survivorship is high at 10 years regardless of initial management. Further research into the risk factors for conversion to arthroplasty may help refine indications for initial management.

#### Characterization of Dysphagia After Magnetic Sphincter Augmentation Device Placement for Gastroesophageal Reflux Disease

J Samaan, E Alicuben, N Bildzukewicz, K Sandhu, K Samakar, C Houghton, A Dobrowolsky, J Lipham

**Introduction**: Magnetic sphincter augmentation has become an increasingly common procedure for gastroesophageal reflux disease. Dysphagia is the most common post-operative complaint and its management and outcomes are not well described.

**Methods**: All patients who underwent magnetic sphincter augmentation device placement from 2007-2017 were retrospectively reviewed. Patient characteristics including pre and post-operative symptoms, operative details and need for dilations were collected. Objective follow up was obtained via upper endoscopy, pH testing and videoesophagram.

**Results**: There were 365 patients included. 197 were male and 168 were female with median age 56 (range 17-82) and BMI 26.2 (range 16.7-44.3). 111 patients (31%) had complaints of pre-operative dysphagia. The device was placed under minimally invasive techniques in all patients and there were no major peri-operative complications. Post-operatively a total of 229 patients (63%) experienced some dysphagia. At a mean follow up of 1.3 years, most patients (82%) had improvement or complete resolution of dysphagia. Patients with smaller sized devices were more likely to have persistent dysphagia and require dilations (see table). There was no difference in reflux control. Dilations were most common in 2013-2014 but have since decreased in prevalence, possibly due to post-operative management changes and the more liberal use of steroids. Ultimately 10 patients underwent device removal for persistent dysphagia, all of which were sizes 12-15.

Device	Total	Dysphagia	Required	Percentage Requiring	Post-Op DeMeester
Size	Placed	Resolved (%)	Dilation	Dilation	Score <14.72 (%)
				(%)	
12	26	58.3	7	26.9	75.0
13	102	57.0	19	18.6	72.5
14	103	64.2	17	16.5	77.8
15	68	71.4	11	16.2	45.2
16	48	69.0	2	4.2	43.8
17	18	58.8	2	11.1	71.4

**Conclusions:** Dysphagia is common after magnetic sphincter augmentation device placement but resolves in the majority of patients. Smaller device size may be associated with increased risk for post-operative dysphagia.

### Saliva-Based Detection of Human Papillomavirus Related Head and Neck Cancer using Droplet Digital PCR

Alison Yu BA, Jae Jung PhD, Stephanie Kim BS, Niels Kokot MD, Uttam Sinha MD

**Background:** High risk HPV (HR-HPV) head and neck squamous cell carcinoma (HNSCC) has been shown to have a better prognosis than smoking-induced HNSCC. However, there is currently no method of early detection for HR-HPV HNSCC. Such tool can improve patient outcomes by reducing radiation dosages. Our goal is to investigate the utility of the droplet digital PCR (ddPCR) to detect HPV DNA in saliva.

**Methods:** Patients were classified into 4 arms: healthy control, non-aerodigestive head and neck cancer (HNC), HR-HPV -ve aerodigestive SCC, and HR-HPV +ve aerodigestive SCC. 5 ml saliva were obtained. Tumor samples from HR-HPV -ve and +ve SCC patients were collected. DNA was extracted from 50 ul saliva and 25-30 mg tumor using Qiagen Kits. DNA yield and A260/280 purity were measured using Nanodrop Spectrophotometer. HPV 16 and 18 primers amplified E6, E7, and L1 regions in endpoint PCR for saliva and tumor. Beta Globin served as internal control. Additional HPV 16 and 18 specific probes and reference probe were designed for ddPCR.

**Results:** The study cohort consisted of 30 patients: 4 healthy controls, 9 non-aerodigestive HNC, 7 HR-HPV -ve SCC, and 10 HR-HPV +ve SCC. Overall 63.3% (19/30) were male. 100% (17/17) of HR-HPV -ve and +ve SCC patients presented at stage 4. HR-HPV +ve SCC consisted of 50% (5/10) tonsillar and 50% (5/10) base of tongue. The mean DNA yield from saliva was 28.7 ng/ul. In ddPCR, 1/4 (25%) healthy controls, 1/9 (11.1%) non-aerodigestive HNC, 3/7 (42.9%) HR-HPV -ve SCC, and 5/10 (50.0%) HR-HPV +ve SCC had HPV 16 or 18 DNA detected in saliva. ddPCR detected one more saliva sample of a healthy control patient with HPV DNA than endpoint PCR.

**Summary:** ddPCR yielded a sensitivity of 50.0% and a specificity of 75.0% for detecting HR-HPV +ve SCC from saliva. ddPCR is comparable to the conventional endpoint PCR, but advantages include being more user-friendly and providing accurate quantitative data.

#### Evaluating adherence to Choosing Wisely guidelines using a rapid case simulation tool Kaeli Yuen, Seiji Hayashi, Daniella Meeker

**Background**: Unnecessary tests, treatments, and procedures are costly and potentially harmful to patients. To address this problem, the American Board of Internal Medicine (ABIM) Foundation has released "Choosing Wisely" guidelines aimed at reducing this waste. While awareness of these guidelines is widespread, critical gaps remain in their application in clinical practice.

The Human Diagnosis Project (Human Dx) is an open medical education platform that hosts brief, interactive, case simulations for assessing and potentially improving clinical knowledge. In this study, we investigated the use of this rapid case simulation tool to measure adherence to Choosing Wisely guidelines, and hypothesize that there is meaningful variation in adherence that may point to a need for targeted interventions.

**Methods**: A series of 23 peer-reviewed case simulations were authored by a group of attending-level clinical educators. Cases were disseminated to Human Dx learners via email. Cases were "solved" by learners in a step-wise process that simulates a real clinical encounter. Guideline adherence was scored manually by a clinician in training, using a rubric developed with input from three primary care physicians. Measures of diagnostic accuracy and efficiency were also captured.

**Results**: Data was collected from 1501 case solve simulations by 679 unique learners. Guideline adherence per guideline ranged from 35.1% to 100.0%, with mean adherence of 81.5%. Early analysis suggests that physicians and trainees performed more poorly on cases related to imaging, especially of the head and spine.

**Conclusion**: A clinical simulation tool such as Human Dx can be valuable for assessment of physicians' behavior. This study suggests wide variation in Choosing Wisely guideline and confirms previous findings that adherence to guidelines around back and head imaging are particularly low. This suggests that there may be a role for targeted interventions.

### ANESTHESIOLOGY

#### Patient-Inclusive Huddles Reduce Pre-operative Anxiety: A Survey Study in the Ambulatory Surgery Setting

#### Angela Chang, B.S., Jack Berger, M.D.

Department of Anesthesiology, Keck School of Medicine at USC.

**Background**: In recent years, LAC+USC Medical Center established a huddle protocol that actively involved the patient in the OR team's pre-operative huddles. The briefings are conducted at the bedside prior to surgery, and allow patients to ask for clarifications on the procedure with all team members present. Huddles have been established to improve communication between team members, increase efficiency, and reduce unanticipated problems during surgery. However, very little is known about how patients perceive the huddle. Given the broad spectrum of emotional states they are in, involvement in the huddle could directly affect patient anxiety levels.

**Methods**: This study surveyed all ambulatory surgical patients at LAC+USC Medical Center from January to April of 2017. Patients are required to participate in the huddle, and are then surveyed in post-operative recovery. The survey includes 3 questions asking for the patient's subjective response and preferences, with answers given on a 1-5 numerical scale.

**Results**: 286 patients were surveyed. Overall, participation in the huddle reduced anxiety levels. Reduction is significantly greater in patients who took the English survey compared to those who took the Spanish version. Patients also indicated significant preference to be included in pre-operative huddle, as well as a preference for the huddle to remain by the bedside.

**Conclusions**: The data suggests that patient-inclusive huddles should be adopted as a standard protocol in more ambulatory surgical settings. Inclusion of patients in pre-operative huddles is preferred by patients, and also beneficial to reducing their pre-operative anxiety, especially when the patients are able to effectively communicate with the OR team. Given the diversity of most ambulatory surgical populations, it may be effective to include a language translator for patients who do not speak English.

#### Mediastinal Masses in children: A retrospective analysis understanding the socioeconomic factors affecting the management of mediastinal masses in a tertiary care hospital. <u>Alan Hung, MS2</u>, Abhishek Karnwal, MD; Children's Hospital Los Angeles

**Background:** Health care disparities among different racial and ethnic groups have long been described in pediatric studies. The aim of this study was to assess and compare the time to diagnosis among different ethnicities, primary language, and insurance groups of pediatric patients with mediastinal masses. Specifically, we compared the symptom duration, length of stay, and mortality of these patients. We hypothesize that there is a delay in seeking diagnosis amongst minorities and non-English speaking populations.

**Methods:** A retrospective review was conducted for all patients less than 18 years of age who presented to CHLA with a mediastinal mass from 2005 to 2015. Data was collected from intraoperative reports, Cerner's KIDS database, and Synapse's radiological database and included duration and type of ventilation, socio-demographic data, race and ethnicity, diagnosis, surgical intervention types, length of stay, type of anesthesia administered, operative medications administered, and survival rate. Non-parametric data will be analyzed using the Mann-Whitney U and Chi-square statistical test. Parametric data will be analyzed using Student's T-Test analysis.

**Results:** 119 patients were identified as being diagnosed with pediatric mediastinal masses between 2005 and 2015. There were 70 (58.8%) males and 49 (41.2%) female patients in the study. The patients ranged in age from 2.4 months to 20.2 years at the time of diagnosis, with a mean of 10.1 years. Hispanics accounted for the largest ethnicity, encompassing 70 (58.8%) patients. Out of the 119

patients, 66 (55.5%) primarily spoke English, 44 (37.0%) primarily spoke Spanish, and 9 (7.5%) had a primary language other than English or Spanish. 35 (29.4%) of the patients had private insurance, 77 (64.7%) had either Medi-Cal or Medicaid, and 7 patients (5.9%) had no insurance.

**Conclusion:** We have not analyzed our results yet but we expect a delay in time to diagnosis in minority children and non-English speaking patients. This may be due in part to a lack of cultural competence among providers or difficulty in physician-patient communication. Socioeconomic status and access to care can also play a part in this delay to diagnosis.

#### Blood Lactate Levels in Adult Cancer and Non-Cancer Patients Undergoing Elective Non-Cardiac Surgery <u>William Kuo</u>, Zhongjie Cai, MS, Michael Ohebsion, Michael Tan, Allison Chambliss, PhD, Rudolfo Amaya, MD, Mary M. Joseph, MD

**Background:** Tissue lactate levels tend to be elevated in cancer patients due to the Warburg effect. However, there is little evidence regarding the relationship between cancer and blood lactate levels. Hyperlactatemia has been associated with high morbidity and mortality rates and blood lactate levels have also been used for risk stratification. To investigate a possible association between cancer and blood lactate levels, our study compared arterial blood lactate levels between cancer and non-cancer patients. **Methods:** A retrospective electronic medical record review was conducted for 699 adult cancer (n=229) and non-cancer (n=470) patients who underwent elective non-cardiac surgery at LAC+USC Medical Center between July 2015 and July 2017. Collected data included demographics, ASA PS classification, the type of procedure performed, and arterial blood lactate levels. Multivariate logistic regression was performed to investigate a possible association between cancer and elevated blood lactate levels.

**Results:** Both cancer and non-cancer patients were stratified to normal ( $\leq 1.6 \text{ mmol/L}$ ) and high (>1.6 mmol/L) lactate levels. Prior to adjustment for demographics, our data did not show a statistically significant association between blood lactate levels and cancer status for either the normal or high lactate categories (p=0.977). After adjusting for patient sex, age, and ASA level, the adjusted odds of having an higher lactate level for cancer patients is 1.076 (95% CI: 0.754-1.534) times that of non-cancer patients (p=0.688).

**Discussion:** Our data did not show statistically significant higher blood lactate levels in cancer patients. Limitations to our study included a limited sample size and the absence of co-morbidity analysis. Future studies may be conducted with a larger sample size and analyze co-morbidities that may influence blood lactate level. A prospective study may also be valuable.

#### Comprehensive pacemaker/AICD database, and its effect on perioperative care - A longitudinal health quality improvement assessment Andrew Spitzberg

**Background:** Pacemakers, automatic implantable cardioverter-defibrillators (AICDs), and combination Pacemaker/AICD devices are implanted devices that regulate the rhythms of the heart and are capable of correcting life-threatening arrhythmias. These devices come in many different models. Specific makes and models of these instruments each individually arrive with their own programming, settings, and instructions for how to manage them during surgery on a patient who has such a device implanted. Often patients with these types of devices are complicated, requiring a specific plan for perioperative management that takes into account the nuances of cardiac rhythm management devices (CRMD). This situation can prove challenging to anesthesia providers, as the specific information about each model of CRMD must be determined before that patient can be brought into the operating room. It can be difficult to find the information mentioned above, especially during an emergent surgery or at night. Calling a company's representative and asking questions related to each individual pacemaker or AICD is time consuming, and it can be difficult to get in touch with these people after hours or at night. Failure to obtain this information prior to the day of a scheduled surgery could also result in case delays as the appropriate individuals were found and information obtained. Because of the large number of pacemakers on the market, it is a near impossible task to ask a physician to be fully knowledgeable of every model's specifications and programming. We believe that having a database of pacemaker/AICD programming and specifications readily available will increase the level of comfort that the perioperative medical team feels when dealing with these devices.

**Methods:** To conduct a needs-based assessment, we plan on administering a survey to determine USC LAC Anesthesiology Department provider's current comfort levels with CRMDs and to determine their perception of the usefulness of such a database. After we make the database available for 6 months, we plan on following up with another survey to determine if the database was helpful to the practicing physicians. We will use unpaired t-testing to determine the significance of the change between the survey results.

**Results:** The research is currently ongoing, and the final data is currently not yet available. **Conclusions:** We are still waiting for the data to analyze; however, we expect a significant increase in the physician-reported comfort in working with pacemakers/AICD's. If this is the case, then having a compendium of knowledge available at all times in the emergency rooms and surgical wards of hospitals could be an easy and affordable way to increase physician comfort in dealing with pacemakers/AICD's.

## **BASIC SCIENCE**

#### AAV-Delivery of Frataxin Induces Protein Expression in Target Tissues and Modifies Behavioral Phenotypes in Mouse Models of Friedreich's Ataxia

Acacia M. Hori, B.A., Elliott Robinson, M.D., Ph.D., Ben Deverman, Ph.D., Viviana Gradinaru, Ph.D.

**Background:** Friedrich's Ataxia (FRDA) is a genetic disease characterized by progressive gait and limb ataxia and lethal cardiomyopathy. In FRDA, an intronic triplet repeat expansion (GAA) in the frataxin gene suppresses expression. The resultant deficient iron-sulfur clustering in mitochondrial respiration results in cell death. In this study, we aimed to develop AAV-mediated FXN delivery as a therapeutic strategy.

**Methods:** Three constructs of the FXN gene were packaged into AAVs and delivered to control and FRDA model mice (a GAA repeat knockin/FXN knockout model (KIKO) and an inducible shRNA-based FXN knockdown model) through IV injection. Mouse tissues were analyzed to determine FXN protein expression and localization via immunohistochemistry (IHC) and microscopy. FXN protein expression will be quantified by ELISA. A battery of mouse behavioral assays will be used to evaluate whether the AAV-FXN treatment can prevent the onset of progressive gait, neural function and coordination phenotypes. **Results:** FXN expression, as observed by IHC and microscopy, was markedly increased in the cerebellum and dorsal root ganglia of control mice transduced with all constructs. Although preliminary behavioral results show only subtle changes in gait ataxia, we anticipate that further trials and evaluation of the second mouse model, which has a more severe phenotype, will more clearly demonstrate the effects of frataxin replacement.

**Conclusions:** We have demonstrated that through gene delivery, frataxin expression can be restored in target tissues, including the peripheral nervous system. If this is sufficient to reverse the disease pathology, we expect to see reversal or inhibition of both target tissue involvement and FRDA symptomatic phenotypes in experimental animals compared to untreated FRDA model animals.

Structural Comparisons of Femoral Shafts of Several Different Human Groups <u>Adam A. Kolawa<sup>1</sup></u>; Tea Jashashvili MD, PhD<sup>2</sup>; Mark R. Dowdeswell<sup>3</sup>; Kristian J. Carlson PhD<sup>4</sup> <sup>1</sup>KSOM of Univ. of Southern California <sup>2</sup>Molecular Imaging Center, Dept. of Radiology, KSOM of Univ. of Southern California <sup>3</sup>School of Statistics and Actuarial Science, University of the Witwatersrand <sup>4</sup>Dept. of Integrative Anatomical Sciences, KSOM of Univ. of Southern California

**Background:** Relative contributions of factors to the decrease in human skeletal mass over the past several thousand years remain unclear. This study is part of a larger study that will investigate the human skeleton from the past, present, and as well as living athletes, in order to better understand how lifestyle and activity contribute to these skeletal variations we've seen develop over time. We hypothesize that there will be a difference in structure and morphology of cortical bones amongst the various populations characterized by variable lifestyles.

**Methods:** Bone samples from various populations located in unique geographic regions with unique lifestyles (e.g., hunter-gatherers, agriculturalists, foragers) were collected and scanned utilizing Computed Tomography. Image data was then converted into virtual models utilizing VG Studio Max 2.3. Femora were then standardized into anatomical position utilizing Amira 6.4 from which cross sections were generated. Heat maps were produced from the cross sections, which were then analyzed to compare femoral thickness between populations and individuals within a population.

**Results:** Preliminary results demonstrate that femoral samples taken from a population that dwelled in a forest-based ecosystem (n=2) had a thicker linea aspera compared to a population that dwelled in a

coastline-based ecosystem (n=2). Heat map generation is still ongoing, and once sample sizes reach an appropriate size, statistical analyses will be performed.

**Conclusions:** Preliminary trends indicate that the forest-based population had more developed muscles of the posterior compartment of the thigh, leading to a thicker linea aspera. This adaptation could be due to various factors including lifestyle, genetics, environment, diet, and so much more. As more samples are analyzed, it will become clearer which specific elements contributed the most to the unique femoral morphologies seen amongst the populations under study.

# BIOKINESIOLOGY & PHYSICAL Therapy

CARE Intervention in Reducing Cardiovascular Risk in Breast and Prostate Cancer Patients Ganesh Raman, BS; Christina Chow; Kyuwan Lee, MS; Christina M. Dieli-Conwright, PhD, MPH, FACSM; Division of Biokinesiology & Physical Therapy, Keck School of Medicine

**Goal:** Chemotherapy regimens can cause endothelial dysfunction and vascular injury in breast and prostate cancer survivors. As a result, cardiovascular events are a leading cause of morbidity and mortality in these patients. Two validated methods to obtain biomarkers of vascular health include carotid intima-media thickness (cIMT) and flow mediated dilation (FMD). cIMT is a measure of arterial wall thickening significantly associated with atherosclerosis. FMD refers to arterial dilation in response to increased shear stress and is a direct measure of endothelial function. The goal of this project is to assess the effect of a 16-week aerobic and resistance exercise intervention (CARE) on vascular dysfunction in breast and prostate cancer survivors. We will use ultrasound to measure cIMT and FMD. We hypothesize that CARE will reduce vascular dysfunction in breast and prostate cancer survivors. **Methods**: This randomized controlled pilot study consists of patients recruited from Norris Cancer Center and the Los Angeles County Hospital. Patients randomized to the CARE intervention participate in 3 weekly sessions for 16 weeks. High-resolution ultrasonography will be used to measure FMD (before and after a 5 min ischemic period) and cIMT of the distal part of the common carotid artery at baseline, week 8, week 17, and week 32 (follow-up).

**Results:** To date, we have enrolled 10 participants onto the study however the participants have yet to complete the study period and therefore data is not available.

**Conclusion:** We expect the 16-week CARE intervention to improve vascular function in breast and prostate cancer survivors. Further longitudinal studies will be necessary to examine long-term cardiovascular events in participants who regularly exercise.

#### Comparing Standardized and Bowed String Instrument Positions in Ulnar Nerve Conduction Studies: Pilot Study

Andrew Tung MSII, Leslie Rydberg, MD, Lauren Vernese, DO, Lauren Splittgerber, MD, Aaron Gilbert, MD

**Background:** Bowed string instrumentalists assume a playing position unique to their profession. This unnatural static position, combined with the rigorous demands they require during practice and performance likely increase their risk for compression syndromes. We propose that this may be due to a transient compressive neuropathy that only occurs when the instrumentalist assumes playing position. Therefore, our study will compare ulnar nerve conduction studies between the standard and playing positions in non-instrumentalists to asses for any changes in nerve conduction function between the two positions. Our belief is that there will be a transiently slowed conduction velocity in the playing position as compared to the standard position.

**Methods:** Residents and medical students (n=20) from Shirley Ryan AbilityLab (SRALAB) were recruited for this study. Exclusion criteria included: prior ulnar neuropathy, hand weakness, skin lesion over area to be tested, prior surgery in the upper extremities or cervical spine, and being a current bowed string instrumentalist (defined as within 5 years). Participants confirmed consent before each study. A baseline clinical strength exam was performed on ulnar nerve-innervated wrist and hand muscles to ensure no pre-existing weakness was present. Ulnar nerve motor and sensory conduction studies on the left upper extremity were then recorded in both the standard and playing positions for each participant, with the standard position tested first. All studies were performed on the same EDX machine by two PM&R residents with PI supervision.

**Results:** Not applicable. We expect our results to be consistent with our hypothesis: a transient slowed conduction velocity in the playing position as compared to the standard position. However, there is indeed possibility that there will be no significant change between the two positions.

**Summary:** Not applicable. We hope that the results of our study will elucidate the possibility of transient nerve compression in instrumentalists only during performance or practice, and serve as groundwork for future studies, including similar testing between a control (non-instrumentalist) and musician population.

# CARDIOLOGY & CARDIOVASCULAR DISEASE

#### Cardiovascular Computed Tomographic Angiography Imaging Reconstructions: Utility of Computer Generated 3D Views Versus 3D Printed Models

<u>Saif Azam, MSII</u>, Jerold Shinbane, MD, FACC, FHRS, FSCCT; Division of Cardiovascular Medicine, Keck School of Medicine of USC

**Background:** Imaging modalities such as computed tomographic angiography (CTA) and magnetic resonance (MR) acquire detailed 2D images useful for cardiovascular care. Technological advances allow 3D computer reconstructions and printed models to be created from these 2D images. The potential benefits of 3D representations for education, procedural planning, and technology design require further definition. The goal of this study is to compare the utility of these 3D printed models with that of the current standard, which includes CT and MR.

**Methods:** This is a survey-based cross-sectional study of groups' perspectives on the utility of computer generated 3D views versus 3D printed models including medical students, trainees, and staff as well as engineering students and faculty. Participants will be provided with a standardized case for which each modality has been prepared with instructions and a survey consisting of Likert-style and open-ended questions. Data will be stratified by the visualization modality evaluated and the survey participant's occupational role. Analysis of survey results will involve the application of Chi-squared analysis and multivariate/univariate student t-tests.

**Results:** We will conduct analyses for statistically significant differences between survey results for each modality based on the entire population as well as subanalyses based on participants' occupational roles. Likert-style questionnaire parameters and subjective responses will gauge surveyee understanding of cardiovascular structures and pathophysiology as well as their ability to carry out occupational tasks such as studying, patient education, surgical planning, and device design.

**Conclusions:** The ability to translate 2D cardiovascular anatomy representations into 3D computer reconstructions and physical models may provide understanding important for education, diagnosis and treatment, and technological design. The roles of these respective modalities require further investigation for practical application to cardiovascular medicine.

Incidence and Treatment of Severe Mitral Regurgitation in Contemporary Clinical Practice <u>Audrey Chai, B.A.</u>, Stephanie Wu, M.D., Anilkumar Mehra, M.D., Leonardo Clavijo, M.D., Ph.D., Ray V Matthews, M.D. and David M Shavelle, M.D.

Division of Cardiovascular Medicine, Keck School of Medicine of the University of Southern California, Los Angeles, CA

**Introduction:** Mitral regurgitation (MR) is a common valvular heart disorder present in approximately 15% of those over the age of 50 years. Surgery is established treatment for patients with primary MR, and the MitraClip device can be considered for patients at high operative risk. The purpose of this study was to determine incidence and contemporary treatment for patients with severe MR evaluated at a tertiary academic medical center.

**Methods:** The echocardiography database at Keck Medical Center of USC was searched from 2011 to 2016 to identify all patients with moderate-severe and severe MR. MR was classified as primary (valve leaflet abnormality) or secondary (left ventricular enlargement with normal leaflets). Demographics, comorbidities and echocardiographic measurements were collected, and the Society of Thoracic Surgery Adult Cardiac Surgery Risk calculator (STS score) was used to assess patients' operative risk. Treatment recommendations were classified as referral to cardiology, referral to cardiothoracic surgery (CTS) and performance of mitral valve surgery or performance of MitraClip.

**Results:** From 2011 to 2016, 1918 echocardiograms were performed and 412 patients were identified as having moderate-severe or severe MR (82 patients/year). Mean age was 67.8±17.0 years, mean ejection

fraction (EF) was 42±19%, primary MR was present in 158 (38%) and congestive heart failure (CHF) was present in 292 patients (71%). Mean STS score was 8.0±7.9 and 27% had an STS score >10. Ninety-six patients received mitral valve surgery and 16 patients received MitraClip. Most patients were referred to cardiology (359, 87%) and 227 (55%) were referred to CTS. Primary MR, lower STS score and higher EF were associated with receiving mitral valve surgery.

**Conclusion:** The incidence of moderate-severe and severe MR in patients evaluated at a tertiary academic medical center was approximately 80 patients per year. Although most patients were evaluated by cardiology, only 50% were referred to cardiothoracic surgery. Additional study investigating referral patterns may help improve access to newer therapies for MR, such as MitraClip.

#### Vascular Quality Initiative-Derived Frailty Index Effective in Risk Stratification of Patients with Critical Limb Ischemia

Jared Cline, Leonardo Clavijo MD PhD, David Armstrong MD PhD, David Shavelle MD, Vincent Rowe MD

**Background**: Frailty is increasingly used to preoperatively risk stratify patients and has become an important prognostic marker for mortality in cardiovascular disease (CVD) patients. The aim of this study was to assess the utility of the Vascular Quality Initiative (VQI) and modified Frailty Index (mFI) frailty scales in patients with CLI by correlating frailty indices to in-hospital events.

Methods: We abstracted data from 494 patient events in 329 patients with CLI. A fraction of patients experienced multiple events that were treated individually for analysis purposes. Data were analyzed on 15 criteria unique to the VQI and mFI scales and separated into 10 and 11 categories, respectively. These criteria included cardiovascular, respiratory, renal, endocrine and ambulatory risk factors that contribute to CLI risk. Patients were stratified into non-frail, pre-frail and frail statuses based on a calculated frailty index. The VQI-derived frailty index parameters were: ≥ 0.3 = 'frail', FI ≤ 0.08 = 'non-frail' and 0.08≤FI  $\geq 0.3 =$  pre-frail. The mFI scale was performed in the same manner and patients were separated similarly: mFI  $\leq$  0.08 = 'non-frail', those with mFI  $\geq$  0.25 = 'frail', 0.08 $\leq$  mFI $\geq$ 0.25 = 'pre-frail'. Indices were then correlated to rates of death, amputation and CVD endpoints using Pearson correlations. Results: Patients were 61.3% male with a mean age of 63.3 +/- 12.4 y and a BMI of 26.7 +/- 6.2 from January 2012- June 2017 with 41.8% of them frail, 52.8% pre-frail and 5.4% not frail by VQI classification. Of the total population, 18.0% received a high level (above foot) amputation. The most significant risk factors for frail status were hypertension, hypercholesterolemia, diabetes mellitus, and smoking status. Using the mFI, planned amputations correlated with frailty (p=0.01, r=-0.12). Frailty status calculated with the VQI index correlated with death and planned amputation (p=0.024, r=0.10). Death only occurred in frail patients (p=0.009, r=0.15).

**Conclusion**: Results of this study suggest that VQI frailty index may be more efficacious in stratification of amputation and mortality risk than mFI. The VQI may be used as a screening tool to identify patients who are at high risk for amputation and death. It is a tool that can assist with informed decision-making in patients with CLI.

Therapeutic Window of Clopidogrel and Ticagrelor in Patients with Critical Limb Ischemia <u>Perese, Joshua, B.A</u>.<sup>1</sup>; Clavijo, Leonardo, M.D.<sup>1</sup> <sup>1</sup>Dept. of Cardiovascular Medicine, KSOM Univ. of Southern California

**Background**: Critical Limb Ischemia (CLI) is associated with increased risk of amputations, cardiovascular events and mortality. Antiplatelet therapy is a crucial component of CLI treatment. High on-treatment platelet reactivity (HPR), defined by a platelet reactivity unit (PRU) score above 208 on the VerifyNow P2Y12 Assay, is associated with increased risk of ischemic events. Low on-treatment platelet reactivity

(LPR), defined by a PRU score below 85, is associated with increased risk of bleeding events. The goal of the current study is to investigate a therapeutic range (TR) of Clopidogrel and Ticagrelor defined by PRU scores between 85 and 208.

**Methods**: In a retrospective analysis, data from the "Switch To Ticagrelor in Critical Limb Ischemia Anti-Platelet Study 'STT-CLIPS'" study was used to assess the therapeutic window of 48 CLI patients. Data included four measurements of platelet reactivity using the VerifyNow P2Y12 Assay: baseline (before daily dose) and steady state (6 hours after daily dose) while taking Clopidogrel 75 mg daily for at least two weeks, and two weeks after switching to Ticagrelor 90 mg twice daily.

**Results:** At baseline, 47.9% of patients on Clopidogel were within TR (37.5% HPR, 14.6% LPR) compared to 10.2% on Ticagrelor (2.1% HPR, 87.5% LPR; p< 0.001). At steady state, 43.8% of patients on Clopidogel were within TR (31.3% HPR, 25.0% LPR) compared to 10.2% on Ticagrelor (2.1% HPR, 87.5% LPR; p< 0.01). HPR was more common on Clopidogrel compared to Ticagrelor at baseline (37.5% vs. 2.1%; p< 0.001) and at steady state (31.3% vs 2.1%; p< 0.001). Whereas, LPR was more common in Ticagrelor compared to Clopidogrel at baseline (87.5% vs. 14.6%, p< 0.0001) and at steady state (87.5% vs. 25%, p< 0.0001).

**Conclusion:** With only 42.9% of patients on Clopidogrel (at steady state) being in the therapeutic range of platelet inhibition, there is a reasonable concern for either bleeding or ischemic complications. Though Ticagrelor has been proposed as an antiplatelet alternative in patients with CLI, this study observes an excess of platelet inhibition, warranting concern for bleeding complications.

### DERMATOLOGY

### Gentamicin Induces Premature Termination Codon Readthrough and Restores Laminin 332 in Junctional Epidermolysis Bullosa Harboring Nonsense Mutations

Michelle Hao, Vadim Gor, Jon Cogan, Yingping Hou, Michaela Hirsch, Vitali Alexeev, David T. Woodley, Mei Chen

**Background:** The Herlitz form of Junctional epidermolysis bullosa (H-JEB) is an incurable, devastating, and mostly fatal inherited skin disease for which there is only supportive care. H-JEB is caused by loss-of-function mutations in *LAMA3*, *LAMB3* and *LAMC2*, leading to complete loss of laminin 332, the major component of anchoring filaments which mediate epidermal-dermal adherence. *LAMB3* mutations account for 80% of H-JEB patients and approximately 95% of *LAMB3* mutations are nonsense mutations leading to premature termination codons (PTC).

**Methods:** In this study, we evaluated the ability of gentamicin to induce read-through in HEK 293 cells and H-JEB laminin null keratinocytes transfected with expression vectors encoding 8 different *LAMB3* nonsense mutations. We next used lentiviral vectors to generate stably transfected H-JEB cells harboring the R635X and C290X nonsense mutations.

**Results:** We found that gentamicin was capable of inducing read-through in all 8 of the nonsense mutations in the HEK 293 cells. Incubation of the stable JEB cell lines with various concentrations of gentamicin resulted in the synthesis and secretion of a 140 kDa full-length laminin  $\beta$ 3 in a dose-dependent and sustained manner. Importantly, the gentamicin induced-laminin  $\beta$ 3 leads to the restoration of laminin 332 assembly, secretion, and deposition into the basement membrane zone as assessed by immunoblot analysis, immunofluorescent microscopy, and an *in vitro* three-dimensional skin equivalent model. Lastly, newly restored laminin 332 was able to reverse abnormal H-JEB cellular phenotypes including abnormal cell morphology, poor growth potential, and poor cell-substratum adhesion.

**Summary:** Gentamicin may offer a novel therapy for H-JEB and other inherited skin diseases caused by PTC mutations.

#### A New Leprosy Pathogen and its Relationship to Erythema Nodosum Leprosum Severity

Maryam Masood BS<sup>1</sup>, Lisa Altieri MD<sup>2</sup>, Maria Teresa Ochoa MD<sup>2</sup>

<sup>1</sup> Keck School of Medicine of the University of Southern California <sup>2</sup> University of Southern California, Department of Dermatology

**Introduction:** *Mycobacterium leprae* was the only known cause of leprosy (Hansen's disease) and its immunological reactions, including erythema nodosum leprosum (ENL), until 2008, when a new species, *Mycobacterium lepromatosis*, was found. The clinical profile of *M. lepromatosis* in comparison to *M. leprae* has yet to be fully expounded. Previous case studies have suggested that *M. lepromatosis* may cause a more severe immunological reaction than *M. leprae*.

**Objective:** To determine differences in severity of ENL among patients with Hansen's Disease caused by *M. lepromatosis* versus *M. leprae*.

**Methods:** Archived skin biopsy specimens from 20 patients with ENL were tested for both *M. leprae* and *M. lepromatosis* using polymerase chain reaction-based species-specific assays. We abstracted clinical data from patient records and used it to classify ENL severity with the recently published 16-item ENLIST ENL Severity Scale.

**Results:** Of the 20 biopsies sent for PCR analysis, 12 have results and 8 are pending analysis. 11 of the 12 specimens with PCR data were positive for *M. leprae*, while one was positive for *M. lepromatosis*. Statistical analysis for ENL severity by *Mycobacterium* species is pending.

**Discussion:** Determining the relationship between ENL severity and species of *Mycobacterium* may allow physicians to better predict a patient's clinical course when first diagnosed with either *M*.

*lepromatosis* or *M. leprae*. The information may be used to create a treatment plan that is best tailored to each patient's unique form of Hansen's Disease.

#### DRESS: A retrospective chart review of 38 cases in Los Angeles, California

**Gabriel K. Padilla, BA**, Barbara D. Lam, BA, Melanie M. Miller, BA, Ruben Guzman, BA, Adam V. Sutton MD, MBA, David Peng, MD, MPH, and Ashley B. Crew, MD, Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles, California.

**Background:** Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare and lifethreatening cutaneous hypersensitivity reaction that can occur 2-12 weeks following exposure to an offending medication. Many drugs have been documented to cause DRESS. There is no well-established standard of care for patients with DRESS. LAC+USC hospital is a tertiary care center, and therefore sees a high frequency of DRESS cases. We developed a steroid dosing algorithm and constructed a database from 38 cases of DRESS at LAC+USC hospital to investigate causes of DRESS in our patient population and assess the short and long-term outcomes of our treatment algorithm.

**Methods**: A four-year retrospective review of 38 cases of DRESS was conducted at LAC+USC hospital. All patients were diagnosed by an inpatient dermatologist using RegiSCAR criteria. Each patient's prior medication time line was carefully reviewed to identify the drug most likely to have caused DRESS. Patient demographics, organ system involvement, treatment and response, long term follow-up and other factors were recorded and a database was constructed using REDCap.

**Results:** Vancomycin was suspected in 12 of the 32 already reviewed cases of DRESS while allopurinol was the culprit in only one case. Of the 12 vancomycin-related cases, eight patients identified their race as white, and six patients also identified their ethnicity as Hispanic or Latino. We have not yet reviewed the short and long-term response to our steroid treatment algorithm.

**Conclusion:** Our findings contrast with previous literature, which suggests that allopurinol is one of the most common drug culprits implicated in DRESS, and vancomycin is a less common cause of DRESS. Interpreting our findings raises the question: was vancomycin implicated in DRESS to a greater extent than more common drug culprits due to an increased use of vancomycin at LAC+USC, or does our patient population have a greater risk of developing DRESS when treated with vancomycin?

#### Anti-tumor Necrosis Factor Agents in Sarcoidosis: A Systematic Review of Efficacy and Safety <u>Catherine J. Wang BS</u>, Brandon L. Adler MD, Thanh-Lan Bui, MA, Hannah M. Schilperoort MLIS MA, and April W. Armstrong MD MPH

**Goal:** Though tumor necrosis factor inhibitors (anti-TNFs) have been recommended as third-line therapy for sarcoidosis, the literature lacks an up-to-date systematic synthesis of their efficacy and safety. We conducted a systematic review to characterize the efficacy and safety of anti-TNFs in sarcoidosis. **Methods:** PubMed, EMBASE, CINAHL Complete, Cochrane Library, Web of Sciences, and ClinicalTrials.gov databases were searched between the inception date of each database to November 27, 2017. Observational and interventional research studies that discussed the efficacy and safety of anti-TNFs for sarcoidosis were reviewed and synthesized.

**Results:** We utilized data on the efficacy and safety of anti-TNFs for sarcoidosis from 1,395 patients based on 64 articles between 2003-2017. Two randomized controlled trials (RCTs) evaluated infliximab in pulmonary sarcoidosis; one found significant improvement in forced vital capacity vs placebo. In cutaneous sarcoidosis, adalimumab led to higher Physician Global Assessment response and improved target lesion area versus placebo. Golimumab was ineffective in pulmonary and cutaneous sarcoidosis, as was etanercept in ocular disease. In non-randomized studies, complete or partial remission of cutaneous, ocular, neurologic, and pulmonary disease was achieved in 83%, 73%, 69%, and 59% of

patients on any anti-TNF, respectively. In the RCTs, compared to placebo, anti-TNFs had comparable rates of overall and severe adverse events. Infections were lower for anti-TNFs than placebos (58% vs 64%), while severe infections were higher for anti-TNFs than placebo (9% vs 6%). Rates of malignancy and death were low and similar in both groups. In non-randomized studies, AEs affected 30% of patients, with 11% SAEs, 10% infection, 8% severe infection, 0.6% malignancy, and 0.5% death. **Conclusions:** Limited evidence suggests that adalimumab and infliximab are efficacious in cutaneous sarcoidosis. Anti-TNFs had comparable rates of overall and severe adverse events compared to placebo.

## Education

#### A Needs Assessment for Leadership Development Training in Undergraduate Medical Education-With a Special Focus on Underserved Medicine Leadership

Anna Madrigal, Andrea Banuelos-Mota, Stephanie K. Zia, MD, MACM, FAAP, FACP, Jehni Robinson, MD

**Goal:** Currently, there is a great need to train physicians who are passionate about practicing in underserved communities and possess the skills to effectively lead the health systems. Effective physician leaders are critical for the overall health outcomes of their patients and of our nation's health. Thus, this mixed-methods cross-sectional needs assessment aims to identify, from the student perspective, the leadership development skills that would prepare medical students for their careers as physician leaders.

**Methods:** This research project consists of an online survey that will be disseminated to medical students at the Keck School of Medicine via the class list-serves. The survey will consist of likert scale, dichotomous and open-ended questions. Additionally, students will be recruited to participate in a one-hour focus group session. The purpose of the focus groups is to identify the leadership experiences of the participants and elicit the potential leadership training that would be most beneficial for their future, as physician leaders.

**Results:** Through the survey, the KSOM students will identify the following: the characteristics of a good leader, leadership competencies that students feel least comfortable executing, and the optimal delivery for leadership training at the KSOM. Additionally, the focus group will provide qualitative data to further enhance the leadership needs assessment.

**Summary:** The information and insights obtained from this study will inform the future development of curricular or extracurricular educational programs that are designed to train future physician leaders for practice in this dynamic and changing healthcare landscape.

# EMERGENCY MEDICINE & TRAUMA

#### Effect of Advanced Practitioner Response Unit Treat & Release Program on 911 Utilization Shangnon Fei, Stephen Sanko M.D.

**Background**: The Los Angeles Fire Department (LAFD) is the sole provider of 911-response for America's second largest city, and has seen rapid growth in 911-use for non-urgent medical complaints. Such complaints are both a public health concern as well as a large component of state and national healthcare expenses. In 2016, LAFD launched an Advanced Practitioner Response Unit (APRU) with the mission of providing Mobile Urgent Care response, including on-scene treatment, release and follow-up referral for low-acuity 911-callers. Mobile Integrated Healthcare is a viable solution to the problem of low-acuity 911-use that has been piloted for over a year, but no research has yet examined the efficacy of the program. It is hypothesized that the APRU will prevent further utilization of the ED for low acuity issues, and will improve patient satisfaction with care comparative to ED care.

**Methods**: Low-acuity patients treated and released by the APRU during the first eight months of service were called back and asked to complete an uncompensated 10-minute telephone survey assessing their experience of care and perceived quality of care. Standard descriptive statistics were used to explore the disposition rate on-scene, time in service, satisfaction with care, and rate of recidivism with 911 or ED utilization.

**Results**: 159 low acuity patients were attended from January – June 2016, of which 51 answered (32.1%), and of these 33 (20.8%) agreed to complete the survey. One patient reported visiting an ED within 3 days for a follow-up wound check since he "could not get an appointment" with his PMD; and an additional three patients visited the ED for complaints unrelated to their APRU encounter – all >7 days after their APRU encounter. No patients required hospitalization within 7 days of being seen by the APRU. 32 (97.0%) strongly agreed/agreed that APRU personnel treated them with courtesy and respect, and did everything they could to treat their pain; 31 (93.9%) strongly agreed/agreed that APRU personnel listened carefully and explained their condition to them in a way they could understand. 29 stated they understood what their treatment plan was and what they were responsible for doing next (87.9%). 32 (97.0%) rated their overall quality of care as good/very good/excellent; and when asked to rate the level of care received on scale of 1 (very poor) to 10 (outstanding), the average APRU rating was 9.1. Comparatively, when asked if they went to their primary care doctor or a local ED for the same issue, what level of care would they would expect, respondents averaged 7.5 (primary care, IQR 9-10) and 6.9 (ED, IQR 6-10) for these respective sites of care.

**Conclusion**: The APRU is a cost-effective, time-efficient method of tending to low acuity medical issues. APRU personnel treat and educate patients effectively enough such that patients do not utilize ED or hospital resources for low acuity medical issues following APRU attention. Additionally, low acuity patients report superior satisfaction with APRU care compared to ED care.

#### Review of Interventions and Radiation Exposure from Chest Computed Tomography in Pediatric Blunt Trauma Patients

Victor Hsiao, BA<sup>1</sup>, Genevieve Santillanes, MD<sup>2</sup>, Daniel Malek, BA, MS<sup>3</sup>, Ilene Claudius, MD<sup>2</sup> <sup>1</sup>Keck School of Medicine of USC, Los Angeles, CA, USA <sup>2</sup>Keck School of Medicine of USC, Department of Emergency Medicine, Los Angeles, CA, USA <sup>3</sup>Eastern Virginia Medical School, Norfolk, VA, USA

**Objective**: The objective of this study was to determine the radiation risk to a child undergoing evaluation with chest CT for every clinically actionable injury identified. Currently, chest computed tomography is known to uncover injuries in both adult and pediatric trauma patients, but the likelihood of identifying an injury requiring a unique intervention in a pediatric blunt trauma patient is not well described.

**Methods**: This is an observational, cross-sectional study of all blunt trauma patients under 18 years of age undergoing chest CT in a single urban emergency department. Via a retrospective chart review, therapeutic interventions done exclusively for chest injuries identified on CT scan were identified. Effective radiation from each chest CT was calculated and averaged and the dose required to diagnose one management-changing chest injury was determined.

**Results**: Of 209 pediatric patients undergoing chest CT over a 19-month period, 168 were blunt trauma victims. Ten required an intervention specifically for a chest injury identified on chest CT (suggesting development of 1 malignancy per 37 actionable injures identified). None required an intervention for an injury exclusively noted on chest CT, as all 10 actionable injuries were apparent via other modalities (radiograph, ultrasound, clinical exam).

**Conclusion**: While 10 uniquely actionable injuries were identified of chest CT, none were found only on chest CT. Because chest CTs rarely modified management, the amount of radiation administered per management change was sufficiently high to recommend reconsideration of current imaging practice in this single-center study.

#### Out of Hospital Cardiac Arrest Evaluation in Los Angeles

<u>Michael Stone</u>, Marc Eckstein, MD, MPH, and Stephen Sanko, MD, KSOM Dept. of Emergency Medicine and the Los Angeles Fire Department.

**Background:** Out-of-hospital cardiac arrest (OHCA) is significant public health issue and a major cause of mortality and morbidity in the US. The purpose of this study was to analyze the overall survival rates for OHCA in CY2016 for the City of Los Angeles, for which the Los Angeles Fire Department is the sole EMS provider. These results will be used to assess progress when compared with survival rates from CY2000 (CARE-LA).

**Methods:** Data was collected from all LAFD-attended, non-traumatic OHCA in the City of Los Angeles where resuscitation was attempted. Patients with a return of spontaneous circulation (ROSC) in the field are transported to a STEMI-receiving center (SRC). These hospitals report survival and neurologic outcomes of all ROSC patients to a registry operated by the LA County EMS Agency. The data was analyzed and reported in accordance with the 2004 Utstein recommendations.

**Results:** Regarding OHCA measures of effectiveness, in 2016 there were 2315 LAFD-attended OHCA of non-traumatic etiology where resuscitation was attempted. Bystander CPR (categorized by field report), was noted in 1193 cases (51.5%), compared to 28% in CY2000 (CARE-LA). ROSC was obtained in 874 (37.8%), and sustained ROSC was obtained in 643 (27.8%). 213 are known to have survived to hospital discharge (9.2%), and 94 are known to have had neurologically-intact survival (CPC1-2, 4.1%). In 2000, the overall survival rate was 2.9%, and the neurologically-intact survival rate was 1.4%.

**Conclusion:** Survival and neurologically intact survival from OHCA in Los Angeles have recently improved, in spite of using a more inclusive denominator in this study (using the 2004 Utstein guidelines) compared to the original CARE-LA study (which used 1991 Utstein guidelines). Further studies are needed to clarify the relative impact of patient-, event-, dispatch-, field care- and hospital-level factors contributing to this change.

## FAMILY MEDICINE

### Barriers and Potential Solutions to Improve Medication Adherence Amongst Latino Patients with Diabetes at FQHCs in Los Angeles, CA

Andrea Bañuelos Mota<sup>1</sup>, Emilio Feliz Sala<sup>1</sup>, Jennifer Perdomo<sup>1</sup>, Joel A. Solis<sup>1</sup>, Walter Solorzano<sup>1</sup> Michael

Hochman, MD, MPH<sup>1,2</sup> Jo Marie Reilly, MD, MPH<sup>1,3</sup> <sup>1</sup>Keck School of Medicine of USC, <sup>2</sup>GEHR Family Center for Health Systems Science <sup>3</sup>Department of Family Medicine at the Keck School of Medicine, Los Angeles, CA, USA

**Background:** Diabetes is a leading cause of death in Latinos in the United States [1] and the leading cause of adult-onset blindness and kidney failure [2]. However, complications and death from diabetes are preventable outcomes. There are seven self-care behaviors, such as medication adherence, that can prevent complications from diabetes [3]. Medication adherence is a significant challenge within Latino patients with diabetes [4,5]. Interventions have been utilized to apply self-care behaviors but rarely with the sole focus of addressing medication adherence [7,8]. Thus, our study investigated three aspects of medication adherence in Latino patients: (1) demographics; (2) medication barriers (psychosocial, cognitive, disease experience) and (3) the impact of these factors on self-identified interventions. Methods: Our cross-sectional study surveyed 106 adult patients in four federally qualified health clinics in Los Angeles. The patients were Latino, with diabetes >6 months and taking medications for diabetes. Our 26-question survey had three sections: (1) demographics, (2) barriers to medication adherence and (3) potential interventions. The questions were in Likert scales, dichotomous and open-ended format. HgbA1c was also collected. Initial analysis shows that there are differences in preferences amongst patients at the clinic sites for the proposed intervention asking: "how helpful would it be if their family members understood their medication regimen" (P=0.02). Further analysis of this response will compare the patient demographics at each site with their responses.

**Conclusion:** There may be patient barriers that impact medication adherence in patients that may be site-specific. These barriers would dictate targeted, clinic-specific interventions to improve medication adherence in our Latino patients with diabetes. Future studies should consider interventions catered to the needs of our target patient population.

#### The Imbalance of Primary Care Physician Supply to Specialty Care Supply Is Associated with Increased Mortality for the Top 5 Leading Causes of Death <u>Erin Chen</u>, Gregory D. Stevens, Ph.D., MHS

**Goal:** There is growing evidence that primary care is essential to improving health outcomes. However, the association between primary care physician density and patient level health outcomes remains poorly understood. The goal of this study is to examine the relationship of physician supply with adult mortality from the top 5 leading causes of death at a fine geographic level in California. **Methods:** Data from publicly-available data sources in California were used for a cross-sectional analysis of the relationship of primary care physician supply and specialist physician supply (provider to population ratios) with mortality for the top 5 leading causes of death. California physician supply data were obtained from the Medical Board of California, which contained self-reported information for all licensed physicians. Age-adjusted mortality rates were available by special request from the California Department Health and Human Services, which included all deaths according to place of residence and cause of death. ZIP codes were used as the unit of analysis and the data was limited to 2012 for this analysis which was carried out using STATA13.

**Results:** We expect the results to show that a larger amount of primary care physicians per ZIP code will be associated with lower adult mortality rates from the top 4 causes of death, which are heart disease, cancer, cerebrovascular disease, and chronic lower respiratory disease, but no association with the top

5<sup>th</sup> cause of death, which is unintentional injuries. We also expect to see a smaller association between higher level of specialist physician supply and mortality.

**Conclusion:** We hypothesize that a higher level of primary care physician workforce will be generally associated with lower age-adjusted adult mortality rates from the top 5 leading causes of death. For future directions, we will pursue the effects of primary care physician supply on the outcomes of the geriatric population.

**Education and Residency Status, Influencing the Path to Medication Adherence in Diabetes** <u>Emilio Feliz Sala</u><sup>1</sup>, Andrea Banuelos-Mota<sup>1</sup>, Jennifer Perdomo<sup>1</sup>, Joel Solis<sup>1</sup>, Walter Solorzano<sup>1</sup>, Michael Hochman, MD MPH, Jo Marie Reilly, MD MPH, Professor of Clinical Family Medicine

<sup>1</sup> MS2

Background: The American Diabetes Association (ADA) states that medication adherence and proper self-management is key to successful disease control. Our goal is to help elucidate what patients perceive as barriers to adhering to their prescribed diabetic medications. Education and residency status are both factors and perceived barriers to medication adherence that may play an important role in health. Because of the potential impact these social determinants of health on the Latino population, it is essential to study these factors under the scope of their influence on medication adherence. Methods: At four clinics within the Los Angeles area, investigators administered a one-time, in-person survey that aided in elucidating the patient's opinions about the challenges they face in adhering to their glycemic control. Perceived barriers highlighted in the survey included education, culture, psychological, medical and demographic barriers such as age and residency status. Patients approached included individuals over the age of 18, whom identified as Latino/Hispanic/Chicano, and had been diagnosed with type 1 or type 2 diabetes for at-least six months prior to the beginning of the study. Results: 106 participants. 76.9% residents, and 23.1% non-residents. Independent T-tests performed for understanding how uncontrolled diabetes affects a person long term (medical barrier 2) and residency (p<= 0.05). Highest degree of education completed among participants: Elementary School (59, 55.7%), Middle School (17, 16.0%), Some High School (9, 8.5%), High School Diploma/GED (10, 9.4%), Some College (6, 5.7%), College Degree or Beyond (2, 1.9%), No Schooling (3, 2.8%). One-way ANOVA performed for education vs. all barriers listed (p>0.05).

**Conclusion**: These data demonstrate that there may be a statistically significant difference between residency status and (medical barrier 2). However, there seems to be no statistically significant difference between education levels and what patients perceived as barriers to medication.

#### Elder Abuse Subtypes Reported to the National Center on Elder Abuse

Morgan C. Goodman, Gali H. Weissberger, PhD, Caroline P. Nguyen, Laura Mosqueda, MD, Julie Schoen, JD, S. Duke Han, PhD

**Background:** Elder abuse is estimated to impact 1 in 10 US adults, ages 60+, and is associated with increased morbidity and mortality. Addressing this public health issue requires identifying prevalence and associated characteristics of elder abuse. This study examined the frequency of six types of elder abuse and types of abuser-victim relationships identified from calls to the National Center on Elder Abuse call center (NCEA-CC) between 08/2014-06/2017.

**Methods:** The NCEA-CC receives calls from individuals seeking assistance in report incidents or requesting general information on elder abuse. Calls were classified into six subtypes (financial, physical, sexual, emotional, neglect, and self-neglect) using the Center for Disease Control's uniform definitions for elder abuse. Frequencies of elder abuse subtype and abuser-victim relationship data were coded.

**Results:** We identified 775 calls (616 specified abuse subtype; 664 specified relationship) alleging elder abuse. Abuse subtype was coded in the following frequencies: financial (63.3%), emotional (27%), neglect (23.6%), physical (10.4%), sexual (1.4%), and self-neglect (1.1%). Abuse by a family member was most frequently alleged (49%), followed by abuse by a medical caretaker (20.1%), a non-caretaker acquaintance (16.7%), a stranger (7.8%), a non-medical caretaker (5.2%), and self-neglect (1.1%). The most commonly alleged abuse type by a family member was financial (67%). **Conclusion**: Results indicate that financial abuse is the most commonly alleged form of elder abuse to the NCEA-CC, and suggest a family member might be likely to commit this type of abuse. This supports findings from a large survey study that found financial mistreatment by family to be the most prevalent form of abuse, but is contrary to another study that found emotional abuse by family to be most prevalent. Different methodological approaches could account for divergent findings across studies.

#### Primary Care Career Interest Development in Student Interest Group Leaders <u>Amy Jahr</u>, Dr. Jo Marie Reilly

**Background:** Primary care physicians are the health professionals who are best positioned to meet the increasing demands for quality, affordable healthcare in the U.S. healthcare system. However, there is currently a shortage of primary care physicians, and this shortage is projected to grow into the future. One method of addressing this shortage in primary care capacity is by increasing the number of medical students choosing primary care careers. It is hypothesized that medical student participation in a leadership role that increases their exposure to and knowledge of career opportunities in primary care will increase those students' interest in pursuing primary care in their future careers as physicians. **Methods:** A short, 10 minute survey will be designed to assess medical students' current confidence in their knowledge of primary care career opportunities and interest in pursuing a career in primary care. This survey will be administered to student leaders of specialty interest groups with a connection to primary care careers. These interest groups include family medicine, internal medicine, pediatrics, med + peds, OBGYN, and the Primary Care Coalition. The survey will be administered twice, once at the beginning and once at the end of the term of leadership of these student officers. Results of each survey will be analyzed to determine whether students' knowledge of and interest in primary care were increased by participating in a relevant leadership experience.

Results: Results are still pending.

**Summary:** This study investigates whether leadership experiences within primary care-oriented student interest groups increases participating medical students' interest in pursuing a career in primary care.

### Understanding Preferences for Medical Decision-Making among Older Adults: Findings from the National Health and Aging Trends Study

Seethim Naicker, Annie L. Nguyen, PhD, MPH; Family Medicine, Keck School of Medicine of USC

**Purpose:** While studies have reported the positive effect of patient involvement in decision-making on health outcomes and quality of care, there is a limited understanding of the facilitators and barriers to older adults taking an active role in their own medical care. Using the National Health and Aging Trends Study (NHATS), a nationally representative survey of the older Medicare population, we investigated the factors which influence older adults' preference for involvement in medical decision-making. **Methods:** This cross-sectional study featured 1,775 community-dwelling NHATS respondents. Active decision-making preference was defined as preferring to make decisions alone or together with a physician, while passive decision-making preference left decisions entirely up to physicians. We examined the role of demographics, socioenvironmental factors, health, physical impairment, and community engagement in medical decision-making preference. Multiple logistic regression was used

with adjustment for age, ethnicity, employment, disability, mental status, participation in valued activities, number of diseases, and self-rated health.

**Results:** Overall, older adults living in a community setting preferred an active role in medical decisionmaking (83.07%). Employed individuals were more likely to prefer active decision-making (p < .01). Physical disability was linked with preference for a passive role (p < .05), as was poorer self-rating of health (p = .05). For every one year increase in age, the odds of preferring an active role decreased by 3%; younger individuals were therefore more likely to prefer active decision-making (p < .01). **Conclusion:** Older adults' involvement in health care decisions may be determined, in part, by the limitations on activity imposed by disability and increasing age. However, subjective perceptions of health may also serve as a barrier to participation in medical decisions, with lower self-ratings corresponding to preference for a passive role. Anticipation of decision-making trends among older adults can better prepare physicians to accommodate individual patient preferences while still supporting those factors that might promote active patient engagement.

**Perceived Ethnic and Linguistic Barriers to Medication Adherence in the Diabetic Latino Community** Jennifer Perdomo<sup>1</sup>, Andrea Bañuelos Mota<sup>1</sup>, Emilio Feliz Sala<sup>1</sup>, Joel A. Solis<sup>1</sup>, Walter Solorzano<sup>1</sup>, Michael Hochman, MD, MPH<sup>1,2</sup> Jo Marie Reilly, MD, MPH<sup>1,3</sup>

<sup>1</sup>Keck School of Medicine of USC, <sup>2</sup>GEHR Family Center for Health Systems Science, <sup>3</sup>Department of Family Medicine at the Keck School of Medicine, Los Angeles, CA, USA

**Background:** Increased rates of diabetes and associated complications, including death, affect the Latino population more often than the non-Latino white population. Various factors may affect these outcomes, though medication adherence is a prevailing component. Given the gap in understanding the reason for these disparities, this study aims to find the barriers and potential solutions to medication adherence. In particular, comparing varying Latino ethnicities and languages.

**Methods:** Self-identifying Latino, Hispanic or Chicano patients from four community clinics in Los Angeles, participated in a survey (n=106). The survey asked demographic questions such as age, sex and ethnicity. Likert scales were used to figure out perceptions of different barriers (e.g. cost and psychosocial) and potential solutions (e.g. picture prescriptions and family support) for medication adherence. Participants received a \$10 gift card for their participation.

**Results:** ANOVA analysis found significant differences between languages (p=0.006) and ethnicities (p=0.024) for responses to the psychosocial intervention "How helpful would it be if your family members understood your medication regimen". Further analysis is needed to associate the specific language preference and ethnicity with the responses to this intervention.

**Conclusion:** There are further analyses to be completed, but we can begin to see the potential importance of family and community regarding medication adherence. Using this data, we may be able to tailor future interventions to include family in the treatment of diabetes for Latino patients with diverse language preferences and ethnic backgrounds. Family plays a crucial role in the Latino community. Therefore, teasing out the factors that differentiate the cultures and languages within this group may help us improve their rates of medication adherence and decrease overall mortality and morbidity associated with diabetes.

#### Increasing Workflow Efficiency for Depression and Body Mass Index Screening and Follow-Up at Watts Health Center

Lawrence Rolle, Anabel Alcaraz Vargas; Assisted by: Brian Prestwich MD

**Background**: Obesity and depression are common clinical conditions affecting underserved communities. Both screening and follow-up of these clinical performance measures are largely under-

reported in Watts Health Center. With the advent of electronic health records, compliance rates for recording these conditions have decreased. As a federally qualified health center, Watts requires proper documentation of ICD-10 codes to receive funding. Our aim was to increase workflow efficiency in the Adult Medicine Department to ensure depression and BMI screenings were appropriately documented in eClinicalWorks (eCW) and patient received follow-up care if necessary.

**Methods**: PDSA cycles were developed for depression and BMI screening and follow-up in the Adult Medicine Department of Watts Health Center. This involved observing the overall protocol for screening and follow-up from multiple perspectives and assistant/provider combinations. eCW templates were created for positive/negative depression and body mass index screenings. Upon transcribing the PHQ-9, medical assistants (MA) utilized eCW templates capable of automatically generating appropriate ICD-10 codes. Outcome measurements included percentage of eligible patients screened and referred to services when indicated. Number of provider clicks and time spent reviewing and endorsing these care processes were used as a proxy for workflow efficiency.

**Results**: In addition to improving the percentage of eligible patients screened and receiving follow-up care, time was saved. With templates utilized by MAs prior to provider-patient interaction, provider time spent documenting depression screening and follow-up was reduced by approximately 37 seconds. Documentation time for BMI was reduced as follows (in seconds): 1) Underweight 35, 2) Overweight 24, 3) Obese 33, and 4) Morbidly Obese 38.

**Conclusion**: Evaluation of the entire care team's role in processes can lead to novel ideas for improvement

Age and sex differences in perceived barriers to medication adherence in Latino diabetics. Joel A. Solis, Andrea Bañuelos Mota, Emilio Feliz Sala, Jennifer Perdomo, Walter Solorzano, Michael Hochman, MD,MPH, Jo Marie Reilly, MD, MPH

**Goal:** Latino diabetics disproportionally suffer from lower glycemic control rates compared to Non-Latinos. This project aims to identify some of the particular barriers in the Latino diabetic community and potential interventions that can help address these barriers. I hypothesize that younger people and women will find interventions more helpful than their older, male counterparts.

**Methods:** Patients were given one-time survey questions on a likert scale asking about barriers to diabetes care and access and possible interventions. Patients must identify as Latino/Hispanic, be over 18 years old, and have had diabetes for at least 6 months. No identifying information was collected. We interviewed 106 patients. SPSS was used to analyze differences.

**Results:** Sixty-five (65) women and forty (41) were interviewed. The only statistically significant finding was for the possible intervention, "To what extent do you feel that meeting with community members/peer support groups would help you?" (p=0.043). The age group was divided by making the older half (above 60, n=48) one group and the younger half another group (60 and below, n=58). We found a statistically significant difference for "I understand how uncontrolled diabetes affects my health long term" (P=0.041), "How helpful would it be to have weekly conversations with a personal health coach to gain better control of your diabetes?" (P=0.035), and "How helpful would it be to attend weekly education sessions to learn more about managing your diabetes through lifestyle changes?" (P=0.036).

**Conclusions:** Data suggests differences in perceived barriers and interventions and based on age and sex. This proposal is significant for identifying specific barriers Latino patients have with managing their diabetes. These trends can provide insight into what providers and clinics/hospitals can do to bridge the gap in disparities. Hopefully, this project can collect more data and be used to help bring about change.

#### The Effects of HbA1c Control and Types of Insurance on Barriers to Medication Adherence and Potential Interventions in Latino Diabetic Patients

<u>Walter Solorzano</u>, Andrea Bañuelos Mota, Emilio Feliz Sala, Jennifer Perdomo, Joel Solis, Jo Marie Reilly, MD, MPH, Michael Hochman, MD, MPH

**Goal:** According to a 2014 American Diabetes Association report, the prevalence of diabetes in Latino communities is 16.9%. Medication adherence has been identified as an important component in proper management of diabetes. Our goal in this study is to assess the attitudes of Latino diabetic patients with regards to barriers to medication adherence and identify potential interventions to address this issue. **Methods:** A random sample of 106 eligible Latino diabetic patients completed a survey at four clinic sites in the urban Los Angeles area: White Memorial Medical Center, Universal Community Health Center, Clinica Romero-Marengo, and Edward Roybal Comprehensive Health Center. General demographic information was collected and attitudes on barriers and interventions to medication adherences in attitudes between patients with proper glycemic control (HbA1c < 7.5) versus poor glycemic control (HbA1c  $\geq$  7.5) and types of insurance.

**Results:** Latino diabetic patients with poor glycemic control have more difficulties keeping track of their medications (p=.007) and understanding the purpose of each of their medications (p=.001). They also more strongly believe that they take too many medications (p=.016). When comparing patients with public insurances and those with private insurance, the former more strongly believe that it would be helpful to attend weekly education sessions to learn about lifestyle changes (p=.035).

**Conclusion:** Latino diabetic patients with poor glycemic control would benefit from addressing cognitive gaps in their understanding of their medications. By explaining the purpose of each of their medications, it might make it easier to prioritize their medication regimen. Additionally, patients with public insurances would benefit from learning more about culturally appropriate and pragmatic lifestyle changes.

#### Impact of 4<sup>th</sup>-Year Integrative Medicine Elective on Physician Self-Care and Clinical Practice

**Sydnie Vo<sup>1</sup>**; Armaity Austin<sup>2</sup>, MD; Bonnie Olsen<sup>2</sup>, PhD <sup>1</sup>Keck School of Medicine of USC, <sup>2</sup>Department of Family Medicine

**Goal:** Symptoms of burnout and fatigue appear to peak during residency and fellowship and are also highly prevalent in medical students and early career physicians as well (Dyrbye et al., 2014). The purpose of this study is to determine how including IM in the last year of medical school benefits physician self-care practices, including physical, mental, and spiritual well-being, and clinical practice. **Methods:** An anonymous, web-based survey was sent to the 127 KSOM graduates who took the IM Elective (IME) between 2013-2017. A follow-up email was sent after 3 weeks. The survey consisted of 14 questions, addressing demographics, the impact of the IME curriculum, prior IM experience, and current Complementary and Alternative Medicine (CAM) utilization in daily life and clinical practice. Responses to Likert-style statements were categorized thematically. Current CAM utilization responses were grouped based on type of modality.

**Results:** Data analysis is still ongoing. The respondents (n=21), were predominantly female (85.71%) and white or Asian (76.19%). Most (61.90%) took the IME out of general curiosity. Most (95.24%) strongly agreed/agreed that the IME positively impacted general self-care habits, and that it introduced skills that helped them cope with residency stress (80.95%). The primary reasons for using CAM were for overall health maintenance and disease prevention (38.10%) and stress management (38.10%). Respondents utilized mind (27.86%) and body (21.01%) practices more after the IME.

**Summary:** Despite having little prior experience, students who took the course did so out of curiosity, suggesting that IM has broad appeal. The impact of this IM course during medical school on physician well-being was reportedly strongest on residents' general self-care habits and secondly on their stress coping. Further studies should be undertaken with a broader demographic so we can learn how individuals from other cultures respond to an IM course and specific CAM modalities.

## HEALTH DISPARITIES

#### Analyzing Healthcare Access in the Los Angeles Safety Net post Affordable Care Act <u>Kyle Joyner</u>, Medical Student, Sonali Saluja, MD, MPH, LAC+USC Department of Medicine and The Gehr Family Center for Health Systems Science, Lisa Shue, Medical Student.

**Goal:** The Affordable Care Act (ACA) was passed in 2012 and dramatically altered the healthcare landscape in Los Angeles, where roughly 40% of patients are now enrolled in federally-supported Medi-Cal programs. Despite this expansion, many low-income patients report difficulties navigating the healthcare system. In our study, we used a qualitative interview approach to explore unique patient perspectives on this issue.

**Methods**: 34 Patients were recruited in the Summer and Fall of 2017 from the LAC+USC Urgent Care, LAC+USC Emergency Room, White Memorial Medical Center Emergency Room, and the LAC+USC Wellness Center. Patients were grouped into three different categories: Medi-Cal patients (n=20), MyHealthLA patients (n=7) and uninsured patients (n=7) to represent a broad spectrum of coverage options for low-income patients. An interview guide was developed to emphasize aspects that enable or obstruct patients in accessing health coverage and care. The interview guide was modified and adapted with feedback from healthcare and social work professionals. Patients were interviewed in English and Spanish with interviews ranging between 25 minutes and 1 hour. Key themes from interviews were identified and grouped into a "codebook" using a program called ATLAS.ti to allow us to compare findings present throughout different interviews. Findings will be grouped into a Qualitative Coding Matrix and a Quantitative Matrix to allow us to elucidate the most powerful themes while maximizing intercoder reliability.

**Results**: Analysis is still ongoing. Early visible themes showed that patients could be broadly divided into two groups -- those that were happy with the healthcare system and benefitted from their coverage, and those that expressed frustrations and had difficulty acquiring or obtaining meaningful care with their coverage. Factors that helped patients included accessible social workers, Medi-Cal enrollment programs at large clinics, and self-education and advocacy. Barriers included difficult-to-reach social workers, lack of citizenship, problems maintaining communication, and difficulties understanding the details of their insurance coverage. Very few patients reported large medical spending -- most reported that medical expenses were completely covered by their insurance or went unpaid if they were uninsured.

**Conclusion:** While the Affordable Care Act did have profound effects in terms of increasing the number of people eligible for Medi-Cal, some patients continue to report difficulties navigating the healthcare system. However, many other patients were very satisfied with the care they received. Overall, very few reported exorbitant medical spending.
# HEALTH, TECHNOLOGY & ENGINEERING

#### Novel Method for Blood Pressure Monitoring in Patients with Left Ventricular Assist Devices Ahmed Abdelhalim, Varun Angajala

**Goal**: Patients with LVADs are in constant need of blood pressure management post-surgery, but cannot have this diagnostic measured by traditional non-invasive methods due to lack of palpable pulse. We have created a device that uses spectrophotometry to allow for both systolic and diastolic blood pressure monitoring, noninvasively, without need for palpable pulse. This technology aims to improve quality of care for patients with LVADs, as well as improve the long-term reliability of these devices and promote LVADs as a dependable alternative to heart transplants. Our first goal is to prove that the technology is functional at measurement in the range of normal blood pressures.

**Methods**: Healthy male and female patients (n=10) had blood pressure measured using a traditional noninvasive, inflating cuff that electronically calculated blood pressure via the oscillometric method. Blood pressure was collected in units of mmHg. Following a period of 2 minutes, measurement was repeated on the same arm using the created device based on the novel, spectrophotometric technique. Values were compared and analyzed to determine significance of data.

**Results**: (Our device is still being fine tuned so final data has yet to be collected).

**Conclusions**: We hope that our data shows that there is no significant difference in the measurement of blood pressure via our device when compared to the traditional oscillometer method.

#### Novel Blood Pressure Measurement Method Using Vascular Occlusion and Pulse Oximetry Varun Angajala, MS, Keck School of Medicine of USC

**Background**: Current oscillometric blood pressure measurement systems rely on high pulse pressures which some patients, particularly patients living with heart failure or continuous flow LVAD systems, lack. The presently described method utilizes the maxima and minima of a plethysmograph produced by a pulse oximeter placed distally to the site of vascular occlusion to record the timestamps of systolic and diastolic blood pressures as the applied pressure decreases continuously. Initially (at maximal applied pressure), there is no waveform in the plethysmograph. When applied pressure falls below the systolic blood pressure, a waveform is observed in the plethysmograph. When applied pressure falls below the diastolic blood pressure, a second peak and trough appear per wave on the waveform. This basic observation was used to conduct a trial to assess the reliability of the technique, compared to oscillometry.

**Methods**: 20 healthy subjects were recruited on a volunteer basis. Subjects were divided into two groups: subjects in group 1 had their blood pressures measured via oscillometry (control) first, then via the novel method after a 5 minute waiting period. Subjects in group 2 had their blood pressures measured via the novel method initially, then via the control method after a 5 minute waiting period. Omron BP742N 5 Series Upper Arm Blood Pressure Monitor was used as the oscillometric control device. The Arduino platform was used to collect data from the novel method, and Microsoft Excel 2010 was used to perform further statistical analysis. All blood pressures were compared between the two groups and between the control device and novel method.

**Results**: Average blood pressure measured via oscillometry was not significantly different in the control group or experimental group, when comparing between group 1 and group 2, thereby validating that the order of measurement (control first vs. experimental first) did not affect measurements. The experimental group blood pressure average was similar to the control group – the difference in values was not statistically different.

**Conclusion**: This data supports the hypothesis that the novel method may be a feasible method of outpatient blood pressure measurement in select patients who are not suitable for oscillometry. Further

research work needs to be undertaken to achieve the statistical rigor needed to prove differences, if any, in accuracy and precision between the two techniques.

#### Epilepsy Monitoring and Creating a Seizure Monitor Joshua Engle, MD Candidate; George Tolomiczenko, PhD

**Goal/Background:** Epilepsy is the most common neurological disease, effecting 65 million people worldwide, with 3 million people affected in the US alone. Seizures can lead to injury, intellectual delay, and SUDEP (Sudden Unexpected Death in Epileptic Patients), which kills more than 50,000 people per year. Our goal is to assess current methods for monitoring seizures and create a better seizure monitor. **Methods:** The study methodology will be to survey participants about their epilepsy diagnosis, their knowledge about their diagnosis, and their current use of seizure monitors. Questions will be sourced from the American Academy of Neurology and formatted in the Likert Scale. The study will end when 50 patients are interviewed and their responses analyzed. We will use the data to create a linear regression model with a Pearson correlation coefficient to demonstrate the relationship (if any) between epilepsy/SUDEP education and seizure monitor use. We will also use the likert scale to assess overall attitudes towards seizure monitors.

For creating the monitor, we took a list of metrics that could be used to detect seizures: EEG, motion detection, sympathetic activation of heart rate, muscular contraction (detection via EMG, stretch receptors, or a RF sensor), HRV, and fall analysis. We then catalogue a list of 50 commercially available sensors that could easily be worn or positioned in the home that track one or more of the above metrics. Then we narrow down the above list to the minimum metrics needed to detect tonic-clonic seizures and tonic seizures that could also be detected by the sensors in our catalogue. From there we assemble the best sensor system to detect tonic-clonic/tonic seizures.

**Results:** We have catalogued 50 sensors. We determined the best sensor system would be a smart watch and RF bedside sensor. The metrics detected will be motion in excess of 7 seconds, a heart rate (HR) delta greater than 30% in either direction (based on published research on HR delta during seizure activity), an software algorithm that can distinguish between a standing and non-standing state, and muscle contraction (measured via a bedside RF sensor). We have started software development for our sensor system, with the coding process continuing. After we complete our software code for our sensor system, we will validate our system via clinical testing in an epilepsy monitoring unit (EMU). Our survey is still ongoing.

#### Development of an Advanced, Discrete Asthma Spacer and Inhaler Device

Peter Lai (MSII), Austin Fullenkamp (MSII), Dr. John Bishara (advisor), Dr. Jean Michel Maarek (advisor), Steve Montgomery (advisor), Nadine Afari (advisor), George Tolomiczenko (advisor)

**Goal**: Lack of compliance with effective devices is a problem that has significantly impaired care for asthmatics, resulting in increased emergency room visits, costs, and unnecessary hospitalizations for asthmatic patients. Our device seeks to improve on the spacer + inhaler, a semi-portable but effective device, by incorporating it into a discrete design and adding additional measures to monitor and improve compliance.

**Methods**: With the help of engineers and designers, we plan to build a prototype spacer + inhaler device that has the potential to be discrete. Secondly, with the help of engineers, we will build an interface that will show doctors and patients important data to help them improve the usage of the device, as well tracking the patient's compliance.

**Results**: We anticipate that this device will help asthmatic patients increase compliance with their medication usage, and hope to find additional support from different sources for prototyping and testing.

**Summary/Conclusion:** This device will potentially help improve compliance of asthmatic patients, significantly reducing undesirable clinical events. This will be done both electronically via automatic tracking of compliance and providing instructions to improve usage, as well as by reducing the social stigma of having to use an inhaler and spacer.

#### Creating an Affordable Solution to Braille Notetakers Luke Naman

**Background**: It is estimated that there are 253 million people in the world with some type of visual impairment, with 36 million of those people being completely blind. The average cost of a braille e-reader is greater than \$10,000 USD. In light of his, we decided to create a cheaper braille e-reader. **Methods**: A new method of reading braille was developed that allowed users to use their entire hand to read a single braille cell through vibrations. Five of the six dots of a braille cell were mapped to a finger of the user's hand. The last dot was mapped to the palm of the hand. A device consisting of vibration motors connected to an Arduino and computer was created. Each motor corresponds to a dot of a braille cell. The device first translates sentences written in English into braille. Then it displays this braille sentence, one cell at a time onto the user's hand using vibrations.

**Results**: The device was created for under \$100 USD and accurately translates English to braille through vibrations. The device was tested with one blind individual at the Braille Institute of Los Angeles who was able to read using it. We hope to do more testing to prove the efficacy of reading using this device. **Conclusions**: A new braille notetaker was created for less than \$100 USD. While this initial prototype is far from ready to be in the hands of consumers, it proves the concept. A new type of braille notetakers can be created and can be inexpensive to make, lessening the financial burden placed on blind and visually impaired

## IMAGING & Radiology

#### The use of semi-manual segmentation in analysis of small lesions in brain MRI. <u>Campen, N</u>., Galarza, C., Chai Y., and Lepore, N.

**Background**: Lesions in white matter are common in those with neurological diseases, vascular and hematologic diseases, and are also part of the normal aging process. Monitoring disease progression is an integral part of forming a treatment plan. Monitoring the formation and/or growth of these white matter lesions is dependent on their detection and quantification. Traditionally, the lesions are segmented on MRI scans manually, which is prone to variability and is time consuming for the researcher. There has been a shift to use algorithms to identify the lesions, but there have been difficulties applying these methods to the detection of small lesions. This group has already applied orchestral fully convolutional neural networks, a method of machine learning, to identify small lesions in the deep white matter and in sub-cortical white matter to analyze lesions detected in the MRIs of 22 patients. The next step will be to expand the dataset and apply this machine learning based method to more patients.

**Methods**: MRI brain scans were obtained from the SIT dataset. Brain scans of children (n=21) diagnosed with sickle-cell anemia were analyzed in the axial and coronal planes by three different reviewers. Analysis was performed using a semi-manual segmentation algorithm based in MATLAB. The segmentation performed in MATLAB will be further analyzed by an on-site evaluator using the ITK-SNAP software. Following this, the lesions are sent to a neuroradiologist who will compare the quantity and location of the lesions that were segmented by the algorithm with the data provided by the SIT dataset. **Results**: The three reviewers are still in the process of analyzing the MRI brain scans using the semi-manual segmentation algorithm MATLAB in both the axial and coronal planes. We anticipate the segmentation process will be completed in the next month, which will allow us to progress to the second stage of the project.

#### Is Fractional Anisotropy of the Superior Longitudinal Fasciculus a Helpful Imaging Marker for Lateralizing the Seizure Focus? <u>Brittany DeClouette</u>, Saman Hazany, MD

**Purpose**: Localizing a seizure a focus in epileptic patients is essential to provide curative surgery. However, determination of the side of epileptogenic focus in these patients is difficult by using structural imaging and EEG. In this project, we tried to determine whether fractional anisotropy (FA) values derived from diffusion tensor imaging (DTI) could add any lateralizing information related to the seizure focus in patients with epilepsy.

**Material and methods**: The patient group consisted of 18 adult male and female epileptics with mesial temporal sclerosis. The laterality of the seizure focus was confirmed by imaging and EEG findings in all cases. DTI images were obtained using an 8 Channel Head coil, on a 1.5 Tesla General Electric magnet (GE medical system, USA). The images were analyzed using TrackVis©, where regions of interest (ROIs) in the SLF were selected. FA values were calculated in both the parietal and temporal SLF portions of each hemisphere, and compared to the contralateral side. **Results**: In the patient group as a whole, there were no significant differences in the FA values of the SLF comparing the side of the epileptogenic zone to the contralateral side in both the temporal and parietal lobes.

**Conclusion and Discussions**: While these results could be due to a lack of enough number of subjects in the patient group, lack of significant differences in white matter fiber tracts in this small group of patients can refute the idea that DTI adds any value to lateralization in epilepsy in current clinical practice. Development of more sophisticated and user friendly softwares in the future may

help determine the side of the epileptogenic focus to provide successful surgery outcomes in patients with epilepsy.

Pilot Feasibility Study of <sup>18</sup>F-FMAU PET For Diagnosing and Characterizing Prostate Cancer <u>Alec Hutchason, Medical Student</u>, Peter S Conti MD, PhD, Hossein Jadvar MD PhD MPH Keck School of Medicine

**Goal:** Overall, there exists a paucity of data in prostate cancer relevant to PET tracers in the primary disease setting—and in particular in the diagnostic setting involving men with suspected prostate cancer. Given this, there are two major goals of this research project. The first is to perform a prospective clinical imaging evaluation of <sup>18</sup>F-FMAU PET/CT in addition to mpMRI and standard TRUS-guided 12-core biopsy for detection and localization of primary tumor in 40 men with suspected prostate cancer based on elevated/rising prostate specific antigen level, abnormal digital rectal exam, or those with prior negative standard biopsy who are now returning for a standard of care follow-up. The second is to examine the associations between the PET derived imaging parameters, serum prostate specific antigen (PSA), mpMRI parameters, and the biopsy histopathology parameters.

**Methods:** This study evaluates the combination of <sup>18</sup>F-FMAU PET/CT and mpMRI, with mpMRI being the standard procedure to diagnose prostate cancer. Approximately 40 male patients with documented or suspected prostate cancer who have met all inclusion criteria and no exclusion criteria will be enrolled in the study. After IV administration of <sup>18</sup>F-FMAU, a hybrid PET-CT imaging system is used to scan the pelvic region. After reading both the PET-CT and mpMRI images, TRUS-guided prostate biopsies will be performed. The clinical pathologist then assesses the sample based on established Ki67/MIB immunostaining protocols.

**Results:** Although data collection is still underway, there are two expected results based on the two major goals listed above. With regards to goal one: <sup>18</sup>F-FMAU PET/CT will (1) identify lesions that are found with standard biopsy, and (2) will identify suspicious prostate cancer sites that might have been missed on standard biopsy and/or mpMRI. With regards to goal two: <sup>18</sup>F-FMAU PET/CT will be a reliable non-invasive imaging method, contributing significantly to mpMRI information, for determining prostate tumor characteristics.

**Conclusions:** Given the unmet need for data regarding PET tracers in the context of prostate cancer, we hope that this pilot feasibility study will maximize the utility of <sup>18</sup>F-FMAU PET/CT for improved non-invasive localization and characterization of primary prostate cancers.

#### CT Pulmonary Angiography with Reduced Contrast Dose: Does IV Location and Gauge Matter? <u>Matthew Salazar Adame</u>, BA; Steven Cen, PhD; Alison Wilcox, MD; Christopher Lee, MD

**Objectives**: We investigated whether intravenous (IV) contrast injection site, laterality, or gauge is associated with differences in image quality (IQ) of CT pulmonary angiography (CTPA) performed with reduced (65 cc) contrast dose.

**Materials/Methods**: We retrospectively reviewed CTPAs performed on a 64-slice scanner over a 3month period. 206 exams were evaluated that met the following criteria: (1) injection of 65 cc lowosmolar contrast into an upper extremity vein and (2) technologist documentation of IV site, laterality, and gauge. A cardiothoracic radiologist evaluated all studies and excluded 13 CTPAs that demonstrated transient interruption of contrast, yielding a study population of 193 exams. Objective IQ was assessed by measuring contrast attenuation within the main pulmonary artery (MPA). Subjective IQ was assessed on a 5-point scale.

**Results**: Antecubital IV was utilized 79% of the time, forearm IV 15% of the time, wrist IV 2% of the time, and hand IV 4% of the time. A right-sided IV was utilized 53% of the time. An 18-gauge IV was utilized

17% of the time, while a 20-gauge IV was utilized 83% of the time. Median contrast attenuation within the MPA was 333 HU. 31% of CTPAs were rated as excellent quality, 45% good quality, 22% fair quality, 2% diagnostic but poor quality, and 0% non-diagnostic. No statistically significant associations were found between either objective or subjective IQ and IV site, laterality, and gauge.

**Conclusions**: Over three-quarters of CTPAs performed with reduced contrast dose demonstrated excellent or good IQ. IV site, laterality, and gauge did not significantly impact IQ.

**Clinical Relevance/Application**: Adequate contrast opacification of the pulmonary arteries is essential for CTPA. Our results suggest that diagnostic exams can be obtained regardless of IV site, laterality, and/or gauge – even with reduced contrast dose. This study may validate the performance of CTPA on patients poor IV access.

## INTERNAL MEDICINE

#### Perceived Benefits and Barriers to Eating a Plant-Based Diet Among Patients with Heart Failure Kacie Amacher, Welmoed van Deen, Kurt Hong, Robert J. Ostfeld, Andrew J. Yoon.

**Background:** Heart failure (HF) is a major public health concern, and the leading cause of 30-day hospital readmission in the US. Plant-based diets, which focus on eating whole plant foods such as fruits, vegetables, whole grains, and legumes, have been shown to prevent and reverse cardiovascular disease. However, their efficacy in patients diagnosed with HF has yet to be studied. Understanding attitudes towards plant-based diets is essential for guiding future dietary interventions targeted towards HF patients.

**Methods:** We conducted a cross-sectional study of patients with HF, using a 44-item questionnaire to survey their current eating habits, as well as perceived benefits and barriers towards eating a plant-based diet. The sample consisted of 50 consecutive patients who were admitted to two academic tertiary hospital centers with acute HF exacerbation (age 57.7  $\pm$  15.9 years, 72% male, 46% Hispanic, 76% NYHA class III/IV, and LVEF 26.5%  $\pm$  13.3%). Data was analyzed for frequency of responses, and cross-tabulations by gender, age, and ethnicity were conducted in SPSS using Pearson's Chi-square test of statistical significance.

**Results:** Only 12% of patients were eating at least 2 servings of both fruits and vegetables per day. However, the majority of patients acknowledged health benefits associated with consumption of a plant-based diet, and perceived barriers were relatively low. The most commonly reported barrier was need for more information about plant-based diets (78% agreement). Gender, age, and ethnic differences were present in over a quarter of the items (Table 1). A greater proportion of Hispanic compared to non-Hispanic patients agreed that a plant-based diet would help them eat more fiber (p<0.05), keep swelling down (p<0.001), and decrease saturated fat intake (p<0.05). Younger patients (age <60 years) were more likely to agree that the plant-based diet would not be filling enough (p<0.01), would be too expensive (p<0.05), or lacked knowledge on how to prepare plant-based meals (p<0.05). Overall, 78% of patients surveyed were interested in learning more about plant-based diets. **Conclusions:** Given the high reported interest in plant-based diets, further patient education interventions centered around plant-based nutrition for managing HF are warranted. Identifying key differences in attitudes towards a plant-based diet among a demographically diverse population is important for the targeted delivery of tailored nutrition education.

#### The AltaMed Healthy Corner Store Program: Improving Access to Healthy Options Carlee Beckler, Michael Hochman

**Goal:** Residents of *food deserts*, low-income census tracts in which a significant share of people live at least one mile from the nearest supermarket, are often forced to conduct much of their grocery shopping at corner stores, and thus are at increased risk for obesity and chronic disease. The goal of this program was to improve access to, and awareness of, healthy options in eight SPA7 corner stores. **Methods:** Store reforms (signage, recipe card displays, shopping baskets promoting healthy options) were implemented in eight SPA7 corner stores. Customers (n=120) and owners (n=6) at six stores were interviewed by a research team from AltaMed and USC to assess the impact these reforms had on their perceptions regarding the availability of healthy options. Interviewees also ranked six in-store programs designed to improve community health through store purchases, and responses of the owners were compared to those of the customers.

**Results:** 91% of customers reported doing most or all of their grocery shopping at the store at which they were surveyed. Following the implementation of the store reforms, 85% of customers noticed the additional signage and 72% reported purchasing more healthy options as a result. 86% of customers expressed a desire for a larger selection of healthy options, but only 19% had expressed these desires to

a store employee. Five of six store owners reported receiving positive feedback from customers regarding the store changes, and five of six owners also reported a desire to be able to carry a larger inventory of healthy options. Despite the fact that 86% of customers desired more healthy options, only three of six store owners reported customers coming to them to express such desires. **Conclusions:** These data demonstrate that residents of certain low-income communities predominately shop for groceries in corner stores, and that both store owners and customers in the SPA7 community desire more healthy options.

Determining Variables Resulting in Insufficient Pap Smears at LAC+USC Adult Primary Care East Clinic Emily Chu, Hilary Novatt, Jaclyn Vargas, Jennifer Marks, Dept. of Research, Keck School of Medicine

**Background/Goal**: Pap smear insufficiency is a major healthcare problem because insufficient pap smears cannot be used for diagnosis of malignant or premalignant cervical cancer lesions. This causes many potential abnormalities to remain undiagnosed and puts women at risk for progression of disease without detection. It was observed that the rate of pap smear insufficiency at the LAC+USC Adult Primary Care East Clinic is significantly higher than that of the Ob/Gyn Residents' Clinic. In light of these observations, the goal of this study is to determine what factors contribute to the higher rate of insufficient pap smears at the LAC+USC Adult Primary Care East Clinic.

**Methods**: We reviewed patient charts from the Adult Primary Care East Clinic at LAC+USC, extracting data on patient age, BMI, menstrual bleeding, presence of discharge overlying the cervix, pap smear technique, specimen handling, resident performing the pap smear, chaperone present, and pathology report. Data analysis will be performed using statistical techniques which are to be determined. **Results**: We are currently in the process of data collection (see Methods section), and we have not yet begun data analysis. However, we hypothesize that one of the major causes of pap smear insufficiency is lack of experience in performing pap smears during medical training. Several other possible variable will be examined.

**Conclusions**: To be determined pending the results from data collection. It is our hope that these results will guide our development of systematic and/or educational interventions that ultimately reduce the rate of pap smear insufficiency.

Can a Simple Model of Encouraging Bed-Rest Avoidance Reduce Hospital Complications? <u>Mika De Coster</u>, Brad Spellberg MD, Gabriel Waterman MD, Michael Hochman MD MPH, Julie Tilson DPT MS NCS, Eric Wei MD, Ari Kassardjian, Andy Rubalcava, Alexander Posell

**Background/Hypothesis:** Hospitalized patients commonly spend the vast majority of their stays lying in their hospital beds, even when not on bedrest orders. The resulting deconditioning has been linked with numerous morbidities and complications. This study seeks to expand on prior studies to create an affordable and sustainable model of bed-rest avoidance widely applicable to inpatient medicine. We hypothesize that our Bed-Rest Avoidance (BRAVE) protocol will reduce hospital complications including deep vein thromboses (DVT), pressure ulcers, falls and hospital-acquired pneumonia.

**Methods:** This study was conducted on patients admitted to two Medical-Surgical wards at LAC/USC (N=1557). The BRAVE protocol involved educational handouts provided to patients/families at hospital admission accompanied by identical signs in patient rooms informing patients about the risks of excess bed-rest and encouraging them to sit, stand, and walk as much as possible. This was implemented in two intervention groups (one with recliner chairs and one without), compared to a control group with no intervention. We will compare the incidence of DVTs, pressure ulcers, falls, and hospital acquired pneumonia. Primary analysis will compare the combined intervention to the control. Secondary analysis will compare the two intervention groups. Patients on bed rest or with medical conditions precluding

leaving their bed will be excluded from analysis. We will also control for differences in disease severity among groups using the case mix index.

**Predicted Results/Summary:** We are in the early stages of data analysis. We predict that the protocol will encourage patients to spend less time in bed and be more ambulatory, leading to a reduction in hospital complications. We expect that providing recliners as an alternative to the bed will further improve outcomes. We hope for our data to be the start of a paradigm shift in hospital culture, promoting a culture of mobility where beds are simply viewed as places to sleep.

#### Glycemic Control and Resource Utilization after Introduction of Clinical Pharmacist at LAC+USC Adult Primary Care Clinics

Brian Dickey, BS; Betty Njenga, BA; Josh Banerjee, MD

**Background:** In October 2016, LAC-USC initiated a program involving the integration of a clinical pharmacist into the Adult Primary Care East and West clinic teams. Patients referred to clinical pharmacy fall into two groups: 1) "high risk" patients for consultation and 2) uncontrolled (but not high risk) patients for medication management. The objective of the study is to evaluate the program's impact on glycemic control and resource utilization among adult outpatient primary care patients with diabetes at LAC+USC during its first year of implementation.

**Methods:** We performed retrospective chart review of LAC+USC electronic medical records using Powerinsight reports. Patient inclusion criteria include LAC+USC East or West adult primary care patients with initial HbA1c  $\geq$ 7. The pharmacy intervention group includes patients with a clinical pharmacist appointment between October 2016 and October 2017. The control group includes patients with a primary care return appointment in March 2016. Clinical metrics include measures of glycemic control (Hba1c) and utilization metrics (inpatient, emergency department, and urgent care visits). Difference in Hba1c is calculated from the most recent recording within 6 months pre-baseline appointment and latest recording within 6 months post-baseline appointment, if available. Difference in resource utilization is calculated from the number of emergency department, acute care, and inpatient visits during 6-month intervals before and after baseline appointment.

**Results:** The pharmacy intervention group had greater mean reductions in HbA1c per month (-0.268 vs - 0.169) and resource utilization per patient month (-0.038 vs -0.006) compared to the historical control. Analysis was also stratified by HbA1c because 1) intervention had a higher initial HbA1c, and 2) initial HbA1c was positively correlated with change in HbA1c and resource utilization. For glycemic control, within each stratum the differences between intervention and control were mixed. For resource utilization, there were greater reductions in ED/UCC/IPT visits in intervention compared to historical control group in all strata except for HbA1c  $\ge$  12.

**Summary:** The results of the program at one year are promising, particularly with regards to reducing resource use. The greater reductions in resource utilization among patients referred to clinical pharmacist, compared to primary care return patients, suggests increased efficacy of integrating clinical pharmacists into an outpatient adult primary care setting in helping diabetic patients reduce the need for acute medical care. Further data collection is warranted to evaluate the long-term efficacy of this care model.

#### Duodenoscope Tracking Project Piers Frieden, Paul Holtom

**Goal:** Starting in 2005, several sensational stories appeared in major media outlets documenting the spread of highly-resistant organisms on duodenoscopes. It eventually became clear that the manufacturer-provided instructions for duodenoscope decontamination were inadequate, which led to

major changes in reprocessing procedure. Several major institutions in the Los Angeles County area experienced major outbreaks, with significant morbidity and mortality in patients who underwent ERCP at those facilities. The current project was designed as a QI project to ascertain whether or not a similar outbreak had occurred at the Los Angeles County Hospital at LAC + USC (LAC), and, if so, to identify the specific implicated duodenoscopes.

**Methods:** Between July of 2015 and mid-May of 2016, 406 ERCP procedures were performed at LAC using seven different duodenoscopes. The medical records of the ERCP patients were reviewed for signs of post-ERCP infection. Signs of post-ERCP infections included relevant positive cultures, physician concern for infection / initiation of new antibiotic regimen, new fever, and increase in WBC > 4.0. These findings were included only if present between 2 and 31 days post-ERCP. When culture positivity was found, organisms were separated into high and low-concern categories based on their antibiotic susceptibility pattern and status as a biliary tract pathogen (e.g. S. aureus is not a typical biliary tract pathogen and so its presence in a bile culture post-ERCP is highly suggestive of iatrogenic seeding). Evidence for alternative explanations for infection, e.g. metastatic malignancy, other non-ERCP instrumentation of the internal environment, etc. was recorded.

**Results:** 7 patient had evidence of infection with no identified organism, 26 patients had evidence of infection with low-concern organisms, and 7 had evidence of infection with high-concern organisms. Of the 7 patients with high-concern organisms, 4 were infected with MRSA and 3 were infected with ESBL E-coli. Analysis of these patients and the scopes used in their procedures revealed no pattern or clustering around a specific scope. In addition, the majority of these patients had convincing alternative explanations for their infections.

**Conclusion:** There is no evidence of duodenoscope-associated outbreak of either high or low-concern organisms at LAC during the study period. Possible explanations include the high skill level of ERCP operators at LAC (it is a high-volume ERCP referral center), high skill of duodenoscope decontamination technicians, and plain luck.

#### Bed Rest Avoidance: The BRAVE Study

<u>Ari Kassardjian</u>, Dr. Gabriel Waterman, Dr. Nikhil Singh, Dr. Zachary Marks, Mika De Coster, David Nusbaum, Andy Rubalcava, Alexander Possell, Dr. Julie Tilson, & Dr. Brad Spellberg

**Goal:** Current inpatient models of healthcare in the United States typically rely on a bed-centered paradigm, whereby hospitalized patients may spend up to 20 to 24 hours a day in bed. By incorporating recliner chairs and encouraging patients who have the capacity to solely use the bed for sleeping, we aim to prove that patients with recliners increases their functional status and health outcomes by exhibiting decreased hospital length of stay when compared to controls.

**Methods:** Using an observational cohort study design, LAC+USC patients on an intervention ward (n=30/day) with recliners were compared with patients on a control ward (n=30/day) without recliners. Furthermore, the intervention ward incorporated n=15 rooms with recliners compared to an internal control of n=15 rooms without recliners. All patients on each ward were assessed daily by medical students using a standardized "Six Clicks" assessment. Nursing staff documented hours in bed in twice daily logs. All information and data were logged onto Redcaps Database for 6 months (180 days) duration, whereby hospital length of stay and other health outcomes could be monitored.

**Results:** Mean hospitalization times will be compared using various analyses, such as paired t-test or multivariate regression using a generalized estimating equation (GEE) with a linear link and clustering to establish significance. Preliminary results with 90% power exhibit that patients with a recliner intervention spent on average a 0.5-day reduction in length of stay (recliners mean=4.0 days; control mean=4.5 days). **Conclusions:** By demonstrating a modest reduction in length of stay between the recliner and control cohorts, we aim to prove how the addition of recliners and reminders to use the bed only for sleeping

increases patients' functional status as evidence by a decreased hospital length of stay. This not only enables patients to discharge from the hospital and return home in addition to improving their health outcomes, but also the hospital can utilize these newly available rooms for incoming patients.

#### Non-Replicating Persister Staphylococcus Aureus and It's Role in Osteomyelitis Travis Larsen, Jun Yan, Travis Nielson, Brian Luna, Brad Spelberg

**Goal:** Chronic osteomyelitis is notoriously difficult to cure with antibiotics, even when the responsible organism is classified as susceptible to the antibiotic being administered. Antibiotic treatment failure may be due to the presence of *Staphylococcus aureus* persisters; cells that have decreased cellular metabolism and exhibit antibiotic tolerance without genetic antibiotic resistance. We seek to develop a *S. aureus* osteomyelitis mouse model to support the development of effective therapeutics against persister cells.

**Methods:** The gene encoding for green fluorescent protein (GFP) was inserted via phage transduction of a plasmid containing GFP and chloramphenicol resistance into *S. aureus* JE2 (LAC derivative USA300 strain). Successful plasmid integration would confer GFP production, with the loss of functional chloramphenicol resistance.

BALB/C mice (N = 20) were infected with GFP expressing *S. aureus* intravenously. To select for and enrich for persister cells, mice will be treated with vancomycin 72 hours post infection. The tibias will be collected at days 10, 15, 25, and 30. Bone will be homogenized, and the bacterial density will be enumerated by quantitative culture of tibial homogenate on agar plates. Additionally, bone samples will be sectioned and mounted on glass slides, where GFP expression will be visualized by florescence microscopy and GFP intensity will be quantified using ImageJ.

**Results:** Successful integration of the GFP coding gene was assessed using a combination of fluorimetry to ensure plasmid uptake, and chloramphenicol susceptibility to ensure recombination of the plasmid. During the acute phase of osteomyelitis on day 10 and 15, we expect to see a low proportion of persister cells (appearing as relatively dim cells) compared to phenotypically normal (relatively bright) microbes in the bone. During the chronic phase on day 25 and 30 we expect to see this proportion increase.

**Conclusions:** If we see the projected results in our experiment, we will confirm that these persisters are driving the chronicity and the antibiotic tolerance of chronic osteomyelitis .

#### Risk Factors for Severe Post-ERCP Pancreatitis: a Multicenter Cohort Study

Andrew Lin, Han Zhang M.D., Melissa Ling, James Buxbaum, M.D.

**Background:** Endoscopic retrograde cholangiopancreatography (ERCP) is a technique that allows doctors to diagnose and treat conditions of bile and pancreatic ducts. However, the most prevalent complication of ERCP procedures is post-ERCP pancreatitis (PEP), which affects around 3-16% of patients. Currently, there are few large-scale studies (>1000 ERCPs) that investigate risk factors for severe PEP. Of these studies, very limited variables were analyzed and emphasis was placed on the length of hospitalizations, which may not properly represent the severity of PEP. This study not only analyzed more variables to determine risk factors of PEP, but also investigated the use of prophylactic rectal NSAIDs, a factor that not a single cohort previously mentioned.

**Methods:** A retrospective cohort study was conducted in LAC+USC in collaboration with multiple teaching hospitals in the Netherlands. Every ERCP performed in the LAC+USC County Hospital from 2010-2016 was first analyzed to filter out potential PEP patients. Of the PEP patients, further chart review was performed to identify potential risk factors.

**Results:** Patient chart data is still currently being analyzed. However, it is expected the use of prophylactic NSAIDs in ERCP may have a significant effect on altering baseline risk factors for severe post-ERCP pancreatitis. In addition, we predict previous pancreatitis, Sphincter of Oddi dysfunction, biliary cancer, complexity of ERCP, and self-reported difficulty of ERCP are risk factors of post-ERCP pancreatitis.

**Conclusion:** The results of this study would identify key technique-related and patient-related risk factors for post-ERCP pancreatitis.

#### **Risk Factors for Severe Post-ERCP Pancreatitis**

#### Melissa Ling, Han Zhang, MD, Andrew Lin, James Buxbaum, MD, KSOM.

**Goal**: Endoscopic retrograde cholangiopancreatography (ERCP) is an established modality for the diagnosis and treatment of pancreaticobiliary disorders. Severe post-ERCP pancreatitis (PEP) is associated with 30% of deaths in ERCP-related mortality. The objective of this study was to identify risk factors for severe PEP at LAC+USC Medical Center.

**Methods**: We performed a retrospective cohort study of 61 patients with post-ERCP pancreatitis between 2010 and 2017. All patients with new onset serum amylase/lipase >3x upper limit of normal and abdominal pain after ERCP were considered. The primary outcome was the severity of PEP according to the Cotton criteria, with the Atlanta criteria being used as a sensitivity analysis. Numerous variables were recorded for each patient, including: BMI, diabetes, hyperlipidemia, pancreatic cancer, biliary cancer, altered biliary/pancreatic anatomy, comorbidity, substance use, complexity of ERCP, trainee endoscopist involvement, number of bile duct cannulation attempts, bile duct stent placement, history of sphincterotomy, and use of pancreatic duct stents.

**Results**: Based on previous studies, we expect there to be a greater risk of severe PEP in cases with multiple cannulation attempts, history of sphincterotomy, and bile duct stent placement. **Conclusions**: We are in the process of analyzing the data. This study will help us better identify which patients are at risk for developing severe PEP.

#### Characterization of the role of the capsule in *Acinetobacter baumannii* virulence <u>Catherine Nguyen</u>, Amber Ulhaq, Brian Luna PhD, Brad Spellberg MD

**Goal**: Acinetobacter baumannii, a Gram-negative pathogen, is a significant public health concern due to emergence of extensively drug-resistant strains. Previous studies have demonstrated that the capsule is a major *A. baumannii* virulence factor. A transposon disruption of the capsule gene *gtr6* is present in the hypervirulent *A. baumannii* HUMC1 strain. In contrast, the less virulent *A. baumannii* AB 15827 lacks the transposon disruption of *gtr6*.

**Hypothesis**: Transposon disruption of *gtr6* alters the capsule structure and contributes to *A. baumannii* virulence.

**Methods**: The *gtr6::Tn* disruption and wild-type alleles were cloned from HUMC1 and ATCC 17989 genomic DNA respectively. The *gtr6:Tn* allele in HUMC1 will be repaired with the WT *gtr6* allele, while the WT *gtr6* allele in ATCC 17978 and AB15827 will be replaced with the *gtr6::Tn* allele. A capsule mutant was produced by deletion of *itrA* coding sequence. Gene replacement was done by homologous recombination using recombineering or conjugation. Antibiotic selection was used to select for successful conjugates. *In vitro* changes in virulence will be assessed by the macrophage opsonophagocytosis assay.

**Results**: ATCC 17978::ΔitrA was transformed with pABBR\_itrA by electroporation, and the complemented strain showed increased antibody binding by flow cytometry, consistent with restoration

of the capsule. Although the transposon was removed from HUMC1 *gtr6* using RecAB-mediated recombination, *sacB* negative selection was unsuccessful. Additionally, an IPTG induction assay revealed that AB 15827 does not express the RecAB machinery required for recombination. These findings prompted the use of biparental conjugation to insert the transposon into *gtr6* in AB 15827 and repair the transposon in HUMC1. This work is underway.

**Conclusion**: Construction of *A. baumannii* capsule mutants will provide insight into the specific motifs that contribute to differences in virulence.

### The effect of having a clinical pharmacist in a team on the systolic and diastolic blood pressures of adult primary care patients at LAC/USC.

Betty Njenga, Brian Dickey, Dr. Josh Banerjee, LAC/USC Adult East and West Clinics, Keck School of Medicine.

**Goals/Background**: A clinical pharmacist plays an integral role in the health care team by providing medical management services. While the utility of these services has been more extensively studied in the inpatient setting, there's increasing interest in integrating a clinical pharmacist to the patient centered medical home. This study seeks to establish the effect of introducing a clinical pharmacist to the team in the LAC/USC East and West clinics starting in October 2016.

**Methods:** This study compares changes in systolic and diastolic blood pressure of patients at the East and West clinics seen by a clinical pharmacist between October 2016 and October 2017 versus primary care patients seen in March 2016 before introduction of the clinical pharmacist. Change in blood pressure is calculated from a blood pressure reading taken before the pharmacist or return appointment and the most distal blood pressure reading taken within 6 months after the appointment. **Results:** Data collection and analysis is still ongoing. We expect our results to show whether there is a significant difference in blood pressure between the pharmacy and non-pharmacy groups. **Conclusion:** We hope that the results will better inform the use of clinical pharmacists in the patient centered medical home.

#### Health Outcomes of Implementation of an Integrated Behavioral Health Program in Adult Primary Care <u>Madelyn Pérez</u> and Barbara Rubino, MD

**Background:** Health systems are increasingly integrating mental and behavioral health into primary care. As a result, patients self-report improved well-being and functioning, inpatient stays and ED visits decrease among "high users", symptoms are often reduced in depressed patients, and diabetes management improves among diabetics.

The purpose of this study is to examine the effects of the recent integration of behavioral health (psychiatry and social work) in the LAC+USC Adult Primary Care clinics. We predict an improvement in scores and measures for depression, anxiety, blood pressure, and diabetes management among participants.

**Methods:** Participants (n=815) included those who had a psychiatry or social work encounter between December 2016 and April 2017. The following outcomes were extracted from medical records six months before and after the encounter: depression (PHQ9), anxiety (GAD7), systolic and diastolic blood pressure (SBP and DBP), and Hemoglobin A1c (HgA1c). Data analysis (paired sample t-tests and analysis of variance) was conducted using SPSS.

**Results:** Overall, 58.8% of participants were female, and mean age was 51.6 years (SD=12.8). Participants had, on average, one encounter, and 87.6% were seen by social work only. There was a significant decrease in PHQ9 score among the severely depressed,  $M_1$ =22.35,  $M_2$ =14.35, t(16)=6.15, p<.001; however, there was no significant difference in GAD7 score. Additionally, there was a significant decrease in SBP before and after initiating treatment, (*M*<sub>1</sub>=127.83, *M*<sub>2</sub>=125.75, *t*(646)=2.55, *p*<.05), as well as DBP (*M*<sub>1</sub>=73.18, *M*<sub>2</sub>=71.06, *t*(655)=4.11, *p*<.001), and HgA1c (*M*<sub>1</sub>=7.97, *M*<sub>2</sub>=7.71, *t*(206)=2.39, *p*<.05).

#### Conclusion

This preliminary data shows an improvement in PHQ9 scores among the severely depressed following the short-term integration of behavioral health treatment. Improvements were also seen in secondary health measures (SBP, DBP, HgA1c).

#### Predictors of Renal Failure in Liver Transplant Recipients Nina Petrosyan, Dr. Saro Khemichian, Department of Medicine, KSOM

**Goal**: Renal dysfunction is a common sequela for patients waiting for an orthotopic liver transplantation (OLT). A common cause for renal dysfunction in cirrhotic patients is hepatorenal syndrome (HRS), proposed to occur in the absence of other histological causes of kidney disease due to peripheral vasoconstriction. Often these kidneys will recover in function following a transplant, however, survival rates are lower among patients with HRS than patients with normal kidney function. In the model for end stage liver disease scoring era, the use of combined liver-kidney transplantation has increased but, there is still uncertainty as to which patients will recover their renal function and hence can avoid a combined transplant. It has also been demonstrated that if the kidneys do not recover after liver transplantation then the hepatic allograft function can also be affected. Given the scarcity of available organs, we undertook this study to identify qualitative predictive factors for kidney function post OLT, in order to identify when a simultaneous kidney transplant will or will not lead to better post OLT survival. Methods: We performed a longitudinal retrospective study on patients who underwent a orthotopic or live donor liver transplants, at the USC Transplant Institute at Keck Medical Center of USC in Los Angeles from the period of January 11<sup>th</sup>, 2014 to February 22<sup>nd</sup>, 2017. Data from inpatient and outpatient medical records were collected and analyzed for demographic data, family history of kidney disease, kidney predictive factors, preoperative and postoperative laboratory evaluation results and laboratory results for the time periods of one week, one month, three months, six months and one year post transplantation.

**Results**: The study is ongoing, results will be presented as they are obtained.

**Conclusions**: At the conclusion of this study, we hope to identify predictive factors to determine patients who will benefit from a simultaneous kidney transplant, and those whose kidneys will recover following a OLT.

#### The Effects of Bed Rest Avoidance in Patient Care and Outcomes

<u>Alexander Posell</u>, Ari Kassardjian, Mika De Coster, Andrea Rubalcava, Brad Spellberg, Gabriel Waterman, Julie Tilson

**Goal**: Research has shown that unnecessarily long bed rest can lead to a range of undesirable results, including muscle atrophy, fall risk, longer inpatient times, and reduction in activities of daily living. In light of this, we aimed to assess whether certain interventions may encourage patients to spend less time in bed while in the hospital, and to determine whether these techniques promote more rapid healing and/or superior healing. Our hypothesis is that these interventions should improve patients' functional status.

**Methods**: A total of 1557 patients were enrolled in this study. Intervention and control groups are being compared. A protocol was instituted with the following elements: 1) Signage was posted in "easily visible" areas in the hospital wards, encouraging patients to get out of bed and move around when possible; and 2) reclining chairs were placed in patients' rooms, with the goal of providing an alternative

location for patients to read, watch television, or engage in activities that otherwise might have been performed in bed.

Data analysis has not been finished, but will be performed using a multivariate regression using a generalized estimating equation (GEE) with a linear link and clustering.

**Results**: There is no information — yet — on whether or not functional status/debilitation was affected by our interventions. However, early analysis appears to indicate that the patients in the chair rooms were, on average, in worse condition than those in the non-chair rooms. More will be forthcoming. **Conclusions**: It is too early, at this juncture, to draw any conclusions.

#### **Bed Rest Avoidance Study**

Andrea Rubalcava, Mika De Coster, Alexander Posell, Ari Kassardjian, Brad Spellberg, MD

**Goal:** There is an extensive amount of bed rest seen in the hospitalized patient population upon admission. Functional decline is seen in up to 50% of patients because of the amount of time spent lying in bed. Even patients who are not placed on bed rest still spend a majority of their day in bed. Various things come with this deconditioning including pressure ulcers, decreased bone density, decreased muscle mass, delirium and depression among other things. The purpose of this study was to provide patients with a comfortable reclining chair and staff intervention to try and reduce the amount of time spent in bed. We hypothesized that providing this intervention would reduce the amount of time patients spend in bed.

**Methods:** This was a prospective study with 1557 enrolled patients, looking at the difference between patients admitted to intervention vs control rooms. One ward had the intervention rooms and one had the control rooms. Nurses on both wards kept track of the hours spent in bed for all their patients per shift. Patients with reasons precluding them from getting out of bed (e.g., bed rest order or medical conditions) will be excluded from the analysis. A multivariate regression will be used for statistical modeling, specifically using a generalized estimating equation with a linear link and clustering. **Expected Results:** We expect that patients who were in the intervention arm of the study will spend less time in bed compared to patients in the control arm. The reduced time in bed will also lead to shorter lengths of stay and reduced harm events by preventing the deconditioning that results from prolonged bed rest.

**Summary:** The main goal of this study is to change the culture of inpatient medicine so that beds are used as places to sleep and are not otherwise used, hence to reduce the amount of time spent in bed by hospitalized patients.

#### Understanding Access to Healthcare in the Los Angeles Safety Net Community Lisa Shue; Sonali Saluja, MD, MPH

**Goal**: 1.5 million people are still uninsured in Los Angeles County after the Affordable Care Act, with the future of the healthcare system remaining uncertain. There is an urgent need to understand how Los Angeles residents currently access care under the ACA and evaluate the impact of potential program losses. We undertook this study to identify key factors that affect patients' ability to obtain, maintain, and use health insurance in our current healthcare system.

**Methods**: 34 qualitative interviews were conducted with patients from the LAC+USC Health System and White Memorial Medical Center. Patients had Medi-Cal (n=20), My Health Los Angeles (n=7), or were uninsured (n=7). Interviews were recorded, transcribed, and coded using ATLAS.ti software to elicit themes regarding health insurance and access.

**Results**: While analysis is still in progress, the following themes have emerged from the interviews analyzed thus far: Almost all patients reported no or few medical bill expenses and have never been denied because of insurance reasons. Enrollment and re-enrollment in Medi-Cal or My Health Los Angeles is generally straightforward and social workers play an invaluable role, but patient education about coverage and plan options may have room for improvement. Most patients are highly satisfied and grateful for what these programs have enabled them to receive. There is an emerging theme of patients not fully understanding what a primary care physician is and how such a physician should be appropriately utilized; some patients either use urgent care or their specialist as a regular point of contact with the healthcare system.

**Conclusion**: These interviews demonstrate that the Medi-Cal and My Health Los Angeles programs have great importance in providing a means for healthcare for low-income individuals. Cuts to these programs would consequently lead to harmful results. There is room for improvement in patient education regarding understanding insurance coverage and properly using primary care physicians as health system navigators.

#### Generating an IBD-Specific Patient-Centric Symptom Score

<u>Alexandra Obremskey, B.S<sup>1</sup></u>.; Caroline Hwang, MD<sup>2</sup>; Jason Doctor, PhD<sup>3</sup>; Elske van den Akker-van Marle, PhD<sup>4</sup>; Welmoed van Deen, MD, PhD<sup>5</sup>

<sup>1</sup>Keck School of Medicine of USC, Los Angeles, CA, USA; <sup>2</sup>Department of Medicine/Division of Gastroenterology, Keck School of Medicine of USC, Los Angeles, CA, USA; <sup>3</sup>USC Schaeffer Center, Los Angeles, CA, USA; <sup>4</sup>Leiden University Medical Center Department of Medical Decision Making, Leiden, The Netherlands; <sup>5</sup>USC Gehr Family Center for Health Systems Sciences, Los Angeles, CA, USA

**Background**: To date, no tool exists to quantify inflammatory bowel disease (IBD) symptom burden fully based on the patient's perspective. Previous measures, such as the Mayo score, are based predominately on physician assessment. However, disease burden should be determined, in large part, by how the patient views their illness and the impact their diagnosis has on their quality of life. As healthcare reform moves towards value-based payments and patient reported outcomes, physicians will be called upon more to demonstrate the value of their care to patients and payers alike. Additionally, cost-effectiveness of current IBD medications, which drive the high cost of IBD care, remains ambiguous. Therefore, we are developing an IBD-specific, preference-weighted symptom score, which will allow for quality of care comparisons across institutions.

**Methods**: We conducted three focus groups to identify the four most important IBD-related symptoms and the variation in severity for each. We specifically asked patients about what symptoms they found most bothersome, why those symptoms were significant, and what an IBD flare looks like for them. We asked participants at the conclusion of the focus group to rank the first, second, and third "most important" symptoms to them, as they define importance. The results informed the development of a choice-based conjoint analysis survey which will quantify the relative importance of each symptom and symptom level.

**Results**: Eight patients, four Crohn's and four ulcerative colitis patients, participated in the focus groups. Patients prioritized symptoms which most disrupted their daily life and caused significant anxiety. One patient said about urgency, "Doing daily things is difficult when you always have to think, 'where is the bathroom, and can I get there?'". Urgency and abdominal pain were highly rated for both those reasons, making it into the top three important symptoms. Blood in the stool was another highly concerning symptom for patients, and usually precipitated presentation to a medical professional. Additional bothersome symptoms were stool frequency, liquid stools, and joint pain.

**Conclusion**: Symptoms for IBD patients vary widely in type and severity, but there appear to be a few key symptoms that indicate a patient's overall symptom burden. There was a consensus that urgency,

blood in stool, and abdominal pain are all highly bothersome to patients and disruptive to their lives. Based on these results, a conjoint-analysis survey was developed which will evaluate the relative importance of urgency, abdominal pain, blood in stool, and stool frequency. Stool frequency will be included as it a commonly used indicator of disease activity and severity and was mentioned, although less often, as an important symptom for patients. Interim results are expected in October, 2017.

# MENTAL HEALTH & PSYCHIATRY

#### Diffusion Tensor Imaging to Examine the Effect of Eoncussion in High School Athletes <u>Anthony F Chen</u>, Medical Student; Siddhant Sawardekar, Research Specialist II; Bradley Peterson, MD; Ravi Bansal, PhD; David Baron, MSEd, DO

**Background:** There are 3.8 million sports-related concussions in the United States per year but not much is known about their effect on human brain development. As part of a larger study, this project will use Diffusion Tensor Imaging (DTI) to examine changes at the voxel level and determine if DTI is an effective method for detecting concussion.

**Methods:** High school freshman football player subjects will be matched to track athlete controls by age, sex, ethnicity, geographical location, and socioeconomic status. Magnetic resonance imaging (MRI) brain scans will be performed before football training, once a year during high school, and within 36 hours of any concussive event. Diffusion weighted images will be examined for motion or artifacts. DSI Studio will be used to reconstruct the data and compute maps of fractional anisotropy (FA) and mean (MD), radial (RD), and axial diffusivities. Manual editing of the MD maps will remove non-brain matter voxels, and thresholding will remove high-intensity voxels that represent cerebrospinal fluid, creating a mask to process the other maps. Voxel changes will be evaluated between baseline and after concussion, and compared to changes over time in controls to determine which are statistically distinct from normal brain changes of development.

**Results:** Football subjects, but not controls, have been scanned. Previous research suggests that the corpus callosum, external capsule, and corona radiata develop white matter lesions after concussion. We predict that there will be reduced white matter organization (measured by FA and RD) in deep white matter commissures. The effectiveness of DTI at identifying changes in the brain post-concussion will be compared to other MRI modalities in the larger project.

**Conclusion:** Understanding how a developing brain reacts to concussive injury can guide treatment plans and preventative interventions for concussion in adolescents, a growing public health concern.

#### Pediatric Patient Resources in the Emergency Department

Anthony Sanchez – Medical Student, Jason Sterris – Medical Student, Dr. Erica Shoemaker – Advisor

**Goal:** Children with psychiatric concerns seen in the emergency department (ED) represent a particularly vulnerable population. They are subjected to unfamiliar and stressful environments in which they may or may not receive services or dispositions that are tailored to their needs. There is a lack of data describing children seen in the ED; therefore, this study aims to describe the pediatric patient population seen in the LAC+USC ED for mental health concerns, which may allow for improved quality of care and better provision of longitudinal support resources.

**Methods:** The study describes the number of ED visits generated by minors presenting with mental health concerns at LAC+USC during the months of October and November (~200). We will describe the age (33% 0-11 y/o; 67% 12-17 y/o) and gender of the child (49% Female; 49% Male; 2% Transgender), the number of patients per 24-hour period (8/day), their length of stay (8 hrs/day), the number of patients needing intramuscular medication and/or physical restraint (1/2 day), and whether each patient belongs to one or more vulnerable subpopulations.

**Results:** It is expected that a proportion of the pediatric patients seen in the ED for psychiatric concerns will belong to a number of vulnerable populations commonly found in LA County. Among the visits, we expect to see patients who identify as transgender (2%), have been involved with DCFS (50%) or a Regional Center (15%), have a history of PTSD (20%) or trauma (70%), and/or have a diagnosis corresponding to an Autism Spectrum Disorder (15%). We anticipate that children with involvement in the DCFS or Regional Center systems will have a longer length of stay and increased risk of receiving IM medication or physical restraint.

**Summary:** With the data in this study, we hope to show which vulnerable pediatric populations frequently visit the LAC+USC ED. The data provided in this study may allow for the ED to provide more effective outpatient resources for these patients, as well as an improved level of efficient, yet highly-tailored, emergency care.

#### Pediatric Patient Safety in the Emergency Department Jason Sterris Medical Student, Anthony Sanchez Medical Student, Dr. Erica Shoemaker Advisor

**Goal:** Children and adolescents in the emergency department with psychiatric illness represent a particularly vulnerable population. They are subjected to an unfamiliar, crowded environment receiving services, which may or may not be tailored to their individual needs. The literature lacks emergency department studies describing children with psychiatric chief complaints or the effects of ER crowding. Therefore, the study aims to describe the effects of crowding and long stay lengths for children and adolescent pediatric populations visiting the emergency department for mental health concerns. **Methods:** The study will describe the number of emergency room visits by children and adolescents with mental health concerns during the month of October at LAC+USC (~200). We will describe age (~33% 0-11y/o & 67% 12-17y/o) and gender of the child (~49% Female, 49% Male, 2% Transgender). Additionally, during 24-hour blocks, we will describe the number of patients visits (~8 children/day), their length of stay (~8 hrs./day), and if they required intramuscular medication and/or physical restraint (~1/2 day).

**Results:** A pearson-correlation will be used to compare the significance of higher children-hours (Children visits/day \* Visit hours/day) on particular-days resulting in an increased frequency of negative emergency room events (intramuscular injections administered and more events in which a child was placed in physical restraints). A pearson-correlation will be run to examine correlations of negative emergency room events on additional negative emergency room events within a 24-hour period. **Conclusion:** With the data in this study we hope to show a point of critical mass at which the pediatric psychiatric emergency department patient outcomes are significantly diminished under increased patient load. The data provided in this descriptive study may allow for emergency rooms to take actions to improve patient safety and patient experience for children with psychiatric conditions in the emergency room.

#### Circulating versus Lipopolysaccharide-Induced Inflammatory Markers as Correlates of Subthreshold Depressive Symptoms in Older Adults

<u>Silena Te</u>, Sungeun Melanie Lee, Elizabeth Breen, Richard Olmstead, Michael R. Irwin, Joshua Hyong-Jin Cho

**Background:** Inflammation is hypothesized to play a significant role in the pathophysiology of depression. Our goal was to determine whether lipopolysaccharide (LPS) induced intracellular cytokines or circulating plasma cytokines is a more sensitive biomarker of inflammation in association with subthreshold depressive symptoms.

**Methods:** A cross-sectional analysis of baseline data from a randomized trial of insomnia treatments was conducted. In 117 community dwelling adults (>55 years), plasma levels of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), and C-reactive protein (CRP) and in vitro LPS-induced peripheral monocyte production of IL-6 and TNF- $\alpha$  were assayed. Depressive symptoms were assessed by the clinician-rated Inventory of Depressive Symptomatology (IDS-C). Multivariate linear regression was conducted to test associations between inflammatory markers and depressive symptoms in the entire sample and in subgroups of higher and lower levels of inflammation, stratified by median split of each biomarker.

**Results:** None of the circulating or LPS-induced biomarkers were significantly associated with subthreshold depression in an analysis of the entire sample. In the higher inflammation subgroups, LPS-induced TNF- $\alpha$  (adjusted  $\beta$  = 0.28, p = 0.04), IL-6 (adjusted  $\beta$  = 0.29, p = 0.03), and TNF- $\alpha$ +IL-6 (adjusted  $\beta$  = 0.43, p = 0.001) significantly positively correlated with depressive symptoms. There was no association of plasma IL-6 or TNF- $\alpha$  with depressive symptoms; plasma CRP negatively correlated with depressive symptoms (adjusted  $\beta$  = -0.36, p = 0.02). In the lower inflammation subgroups, no association was found except for LPS-induced TNF- $\alpha$ , which negatively correlated with depressive symptoms (adjusted  $\beta$  = -0.30, p = 0.02).

**Conclusion:** LPS-induced cytokines appear to be more sensitive correlates than plasma cytokines of subthreshold depressive symptoms in older adults.

# NEPHROLOGY & Urology

#### Stoma Complications and Quality of Life in Indiana Pouch Urinary Diversion Kai Wen Cheng, Ankeet Shah, Gus Miranda, Anne Schuckman, Hooman Djaladat

**Background**: The Indiana Pouch (IP) is a subtype of Continent Cutaneous Urinary Diversion (CCUD) for which quality of life and CCUD-specific complications have not been well studied. We sought to evaluate the IP diversion using the aforementioned variables.

**Methods**: A retrospective review of an IRB-approved IP database was conducted for perioperative and outcome data. To assess quality of life, the EORTC QLQ-C30 questionnaire was mailed to patients who agreed to be contacted. All responses were dated >6 months after IP surgery.

**Results**: A total of 33 patients who received the IP diversion under 2 fellowship-trained urologic oncologists were included in this study (2010-2016). After a median follow up of 18 months (2.7-72.8), low-grade diversion-related Clavien complications (including related GI complications) were reported in 28 patients (85%), but high-grade in 8 patients (24%). Stoma complications were seen in 10 patients (30%), 5 low-grade and 5 high-grade; 7 had stenosis at skin/fascia level that needed outpatient dilation or superficial revision and 3 needed deeper level revision for difficult catheterization. Median time to stoma revision was 12 months (range: 5-22). A higher BMI (29 vs. 26) was associated with stoma complication (p = 0.01), but stoma size, measured as size of catheter used to taper the ileal segment, was not (p=0.4). All patients achieved continence within 90 days after surgery – coaptite injection was indicated for 1 patient. 14 responses were recorded for the EORTC questionnaire: >70% of patients reported little to no disturbance of daily functions and rated overall health and quality of life as  $\geq$ 70%. **Conclusions**: The Indiana Pouch diversion is associated with high rates of continence and patient satisfaction. Stoma complication is common; however, most of them are superficial and managed with outpatient/minor procedures.

#### Discrepancies Between the Internet and Academic Literature Regarding Vitamin Use for Male Infertility Chase G Clemesha, BS, Mary K. Samplaski, MD,

Introduction and Objective: The accuracy of online medical information may be variable. A 2014 Cochrane review looking at the effects of oral antioxidant supplementation on subfertile males did not support a robust improvement in male infertility after supplementation. Many subfertile men take antioxidant supplements in hopes of improving their fertility. We sought to evaluate the content of online information for male fertility vitamins and to compare this with the published literature. **Methods:** We searched Google to assess the online information regarding vitamins, and male infertility, using the search terms: "vitamins and sperm". Websites were evaluated for authorship, content, and validity. We then reviewed the FDA Recommended Daily Allowance (RDA), and upper tolerable intake level (UL), for each vitamin, and compared this with the supplements' actual content. **Results:** The first 100 websites were reviewed. Of these, 4 were posted by an academic source, 7 by a private clinic, 31 by industry, 8 were patient blogs and 50 by other sources. Claims made by websites regarding the effect of vitamins on male fertility included: improved sperm count in 65 (1 academic, 4 private clinic, 19 industry, 5 patient blog, 36 other), as well as improved sperm motility and morphology in a variable number of websites; Improved pregnancy rates in 42 (3 academic, 3 private clinic, 14 industry, 3 patient blog, 19 other); Improved live birth rates in 9 (1 academic, 1 private clinic, 2 industry, 0 patient blog, 5 other); Healthier offspring in 18 (1 academic, 1 private clinic, 3 industry, 1 patient blog, 12 other)). Overall, 76 websites claimed some type of improvement in semen parameters. 85 websites claimed some type of improved reproductive outcome. 15 websites mentioned the risks of taking vitamins (0 academic, 2 private clinic, 4 industry, 3 patient blog, 6 other). 26 websites referenced and

were supported by peer-reviewed literature (3 academic, 1 private clinic, 6 industry, 1 patient blog, 15 other). None of supplements had more than the tolerable upper intake levels (UL) of any of the vitamins, but several were over the RDA. The most commonly over-supplemented vitamins were zinc (16), vitamin B12 (11) and selenium (11).

**Conclusions:** Many websites currently claim improvements in a variety of male reproductive outcomes after vitamin supplementation, ranging from semen parameters to offspring outcomes. These are often not supported by the medical literature. Reassuringly, none of the supplements we surveyed had greater than the FDA UL for any individual vitamin. We need to provide evidence-based information to patients so that they can have realistic expectations of the benefits that vitamins may have on male reproductive outcomes.

### Utilizing Trained Medical Student Evaluators for Robotic Anastomosis Competency Evaluation of the Vesico-urethral Anastomosis

<u>Austin Fullenkamp</u>\*, Paul Oh, Micha Titus, Michael Lin-Brande, Jian Chen, David Hatcher, Hooman Djaladat, Andrew Hung, Los Angeles, CA

**Introduction and Objectives**: The robotic anastomosis competency evaluation (RACE) provides feedback on the vesico-urethral anastomosis (VUA) of a robotic prostatectomy. Expert surgeons were used in its validation but take extended time to complete tasks, limiting the usefulness of RACE. Crowdsourced evaluators provide rapid evaluations, but there remains skepticism due to their lack of medical knowledge. We compare trained medical students to experts to determine their reliability as evaluators. **Methods**: Five medical students (two 2nd and three 4th year students) and 3 experts (150-500 cases) evaluated 30 VUA videos performed by 20 different surgeons with expertise ranging from resident to faculty using RACE. Medical students were trained by an expert (AJH) using a sample case video. Medical student scores were compared to expert scores using Bland-Altman analysis and intra-class correlation (ICC) assuming a 2-way mixed model.

**Results**: Medical students had higher ICCs than experts for absolute agreement (0.849 vs. 0.415) and for consistency (0.895 vs. 0.744) (both p<0.001). Averaged scores by medical students compared to averaged scores by experts resulted in ICC 0.702 for absolute agreement and 0.825 for consistency (both p<0.001). Medical students completed tasks faster than experts, taking 2.6 (range 1-3) days to complete video analysis versus 8.66 (1-11) days for experts. A Bland-Altman plot (Figure) displayed a mean positive bias of 1.18 (p=0.007), indicating that medical students score slightly higher than experts on average. With lower RACE score cases, there is less consistency in grading by medical students relative to experts. However, with higher RACE scores, the variability in score differences between students and experts are minimal (circled area in Figure), indicating greater consistent agreement on high quality VUAs.

**Conclusions**: Medical students display a greater agreement in RACE scores in absolute scores and variability relative to experts. Medical students assign higher RACE scores in general compared to experts but improve in agreement with experts on cases with high RACE scores. Although medical students provide variable scores for lesser quality VUAs, they may serve as useful evaluators for high-quality VUAs.

Source of Funding: none





#### Renal function biomarkers reveal evidence of female protection from kidney injury during Angiotensin II (AngII) hypertension

<u>Borna S. Shirvani</u>\*, Luciana C. Veiras\*, Donna L. Ralph\*, and Alicia A. McDonough\* \*Department of Integrative Anatomical Sciences, Keck School of Medicine of USC

**Background**: Recent work from this lab defined sexual dimorphism in renal transporters to better understand female resistance to cardiovascular and kidney disease. This study aims to examine sexual dimorphisms in susceptibility to renal injury by assessing renal injury biomarkers. **Methods**: An Angiotensin-II (AngII) model of induced hypertension was employed. Male and female Sprague-Dawley rats were each assigned control or AngII conditions (n=6 per group). Rats were given subcutaneous infusion pumps, containing AngII (400 ng/kg/min) or a vehicle control, for 2 weeks. At the start and end of the 2 week trial, rats were placed in metabolic cages for overnight urine collection. Blood and kidney samples were also collected. End point urine and renal cortex homogenates were assayed via quantitative immunoblotting for albumin, angiotensinogen, megalin, and kidney injury molecule-1 (KIM-1). Serum and urine albumin were also quantified via ELISA. **Results**: Urine assays revealed a 10-fold increase in albuminuria in males relative to females under the AngII condition (p<0.001). Serum albumin revealed a corresponding decrease in male rats with AngII compared to controls (p=0.05), while female serum albumin levels were unaffected (p=0.86). Immunoblots revealed larger increases in injury biomarkers in renal cortices in males compared to females during AngII hypertension. Despite increased cortical albumin accumulation, male rats did not exhibit increased megalin abundance, the receptor that takes up albumin, whereas females did show significant increase in megalin abundance during AngII hypertension (p=0.01).

**Conclusions**: These data indicate male rats exhibit greater susceptibility to renal injury during hypertension compared to females. This is associated with differential regulation of megalin-reuptake mechanisms in males vs. females.

\*\*NOTE: Results and conclusions only reflect current hypotheses/projections based on data collected thus far. They do not represent final findings of this study.

#### **β1Pix Stabilizes Nedd4-2 and Plays a Critical Role in ENaC Regulation by AMPK in Kidney Epithelial Cells Diego S. Tabares**<sup>1</sup>, Pei-Yin Ho, PhD<sup>1</sup>, Hui Li, MD<sup>1</sup>, Kenneth R. Hallows, MD, PhD<sup>1</sup>.

<sup>1</sup>Medicine, Univ. of Southern California Keck School of Medicine, Los Angeles, CA, USA

**Goal**: Previous work has established that AMP-activated protein kinase (AMPK) inhibits ENaC, the epithelial Na<sup>+</sup> channel expressed in many salt-reabsorbing epithelia at apical membranes, by promoting binding of the ubiquitin ligase Nedd4-2 to ENaC. We have further demonstrated that functional  $\beta_1$ Pix, a Rho-GEF signaling protein, is required for AMPK-dependent ENaC inhibition.

**Methods**: Epithelial volt-ohmmeter measurements were performed to examine the role of  $\beta_1$ Pix in regulating ENaC currents. Lentiviral shRNA-mediated knockdown of  $\beta_1$ Pix expression in mCCD<sub>cl1</sub> collecting duct epithelial cells was performed to assess possible inhibition of AMPK activators on ENaC currents. Immunoblotting and co-immunoprecipitation (co-IP) studies were performed to explore the role of  $\beta_1$ Pix in the regulation of ENaC by AMPK and the interplay of  $\beta_1$ Pix, 14-3-3 proteins and Nedd4-2.

**Results**:  $\beta_1$ Pix expression negatively regulated ENaC-dependent Na<sup>+</sup> currents in mCCD<sub>cl1</sub> cells, and  $\beta_1$ Pix knockdown blunted the ability of AMPK to inhibit ENaC currents. Co-IP studies in mCCD<sub>cl1</sub> cells shows that the interactions between 14-3-3 proteins,  $\beta_1$ Pix, and Nedd4-2 increased with AMPK activation. Functional  $\beta_1$ Pix may promote the AMPK-dependent recruitment of these mediators into a complex.  $\beta_1$ Pix knockdown inhibited Nedd4-2 proteins expression, which was associated with a parallel reduction in Nedd4-2 phosphorylation at Ser-328, a phosphorylated site critical for cellular Nedd4-2 protein stability. **Conclusions**: Overall, our findings suggest that functional  $\beta_1$ Pix is important for Nedd4-2 Ser-328 phosphorylation and thus Nedd4-2 stability. AMPK activation promotes, potentially via AMPK-dependent  $\beta_1$ Pix phosphorylation, the association of  $\beta_1$ Pix, 14-3-3 proteins, and Nedd4-2 into a complex that inhibits ENaC by enhancing Nedd4-2 binding to ENaC followed by ENaC ubiquitination and targeting for degradation.

#### COMPARISON OF CLINICAL OUTCOMES AND AUTOMATED PERFORMANCE METRICS IN ROBOTIC-ASSISTED RADICAL PROSTATECTOMIES BETWEEN CASES WITH CARDINAL STEPS PERFORMED BY ATTENDINGS ONLY AND TEACHING CASES

Micha B. Titus<sup>1</sup>, Paul J. Oh<sup>1</sup> Jian Chen<sup>1</sup>, Michael Lin-Brande<sup>1</sup>, Austin J. Fullenkamp<sup>1</sup>, Andrew J. Hung<sup>1</sup> <sup>1</sup> Center for Robotic Simulation & Education, Catherine & Joseph Aresty Department of Urology, University of Southern California Institute of Urology, Los Angeles, California

**Introduction and Objectives:** Teaching hospitals balance resident training with optimizing patient outcomes. In this study, we determine if clinical outcomes differ with trainee involvement. We inspected whole-case automated performance metrics (APMs), patient demographics and clinical

outcome data to determine the impact of trainees' console performance in four steps of the roboticassisted radical prostatectomy (RRP) that we believe are likely to drive whole-case outcomes. These 'cardinal' steps are the prostatic pedicle dissection, apical dissection, bladder neck dissection and the vesico-urethral anastomosis.

**Methods:** Clinical data was collected prospectively. A "dVLogger" (Intuitive Surgical) recorded surgical video and APMs (kinematic movements and system events) directly from the da Vinci Si robot. Two comparisons were performed. Comparison 1 compared attending surgeons performing the whole case (Group A, n=8) to cases where attending surgeons performed all cardinal steps with trainee involvement for non-cardinal steps (Group B, n=13). Comparison 2 compared cases with an attending surgeon performing all cardinal steps (Groups A+ B= Group C, n=21) to cases with trainees performing at least one cardinal step (Group D, n=56). Kruskal-Wallis test was used to compare clinical outcomes and APMs between groups.

**Results**: Comparison 1 did not show differences in patient demographics or clinical outcomes. However, APMs between Group A and B differed. Group A had a faster camera velocity (p=0.03) and spent less time moving the dominant arm (p=0.04). Comparison 2 showed that Group C had a shorter surgical time (217 minutes vs 244 minutes, p<0.01) and a lower 24-hour abdominal drain output (262ml vs. 330ml, p=0.04). Readmission rate for Group C was higher than that of Group D (9.5% vs. 0%, p=0.02), although Group C's APMs showed greater efficiency (Table).

**Conclusion**: The APM profile differs when residents are involved in the RRP (both Groups A vs. B and Groups C vs. D), but clinical outcomes are not negatively affected when residents perform non-cardinal steps or at least one cardinal step (except for surgical time and abdominal drain output). This suggests trainee involvement does not jeopardize patient safety.

	Group C - No trainee performed cardinal steps	<b>Group D -</b> Trainees performed ≥1 cardinal step						
Automated Performance Metric	Mean (SD)	Mean (SD)	p-value					
Total Completion Time (min)	121 (40)	142 (41)	<0.01					
Path Length of All Instruments (m)	217 (71)	249 (78)	0.04					
Dominant Arm								
Dominant Arm Moving Time (min)	104 (34)	119 (29)	<0.01					
Dominant Arm Idle Time (min)	17 (7)	23 (21)	0.03					
Dominant Arm Path Length (m)	134 (43)	149 (41)	0.03					
Dominant Arm Velocity (mm/s)	47 (80)	21 (2)	0.02					
Non-Dominant Arm								
Non-Dominant Arm Moving Time (min)	109 (36)	126 (31)	< 0.01					
Non-Dominant Arm Idle Time (min)	12 (5)	16 (19)	0.03					
Non-Dominant Arm Path Length (m)	76 (26)	89 (29)	0.04					
Camera								
Camera Moving Time (min)	7 (3)	8 (2)	0.02					
Camera Idle Time (min)	115 (37)	134 (39)	<0.01					
Camera Path Length (m)	14 (5)	16 (5)	0.03					
Camera Use Count (number)	783 (387)	824 (265)	0.03					
3rd Arm								
3rd Arm Idle Time (min)	117 (38)	137 (39)	< 0.01					

**Disclosure:** Intuitive Surgical provided dVLogger for data capture.

#### Sexual Dimorphic Responses of Renal Transporters to High Salt Diet Favor More Diuresis in Females Diana L. Torres, Luciana C. Veiras, Donna L. Ralph, Alicia McDonough

**Background:** Previous studies have shown that there are distinct sexual dimorphic patterns of transporters along the nephron. Compared to males, at baseline female rats and mice have lower abundance of proximal tubule sodium transporters (NHE3, NaPi2) and higher abundance and phosphorylation (activation) of NCC as well as cleaved (activated) epithelial sodium channels' (ENaC)  $\alpha$  and  $\gamma$  subunits. Also, females (F) have shown to have a more robust pressure natriuretic response than males (M). This study aims to compare the responses of F and M mice to a high salt diet. We hypothesized that F will exhibit more robust responses to a HSD than M.

**Methods:** For two weeks, mice (n=7/group) received a normal salt diet (0.26% NaCl; MNS: males normal salt; FNS: females normal salt) or a high salt diet (4.0% NaCl; MHS: males high salt; FHS: females high salt). Urine osmolality was measured using an osmometer and urine Na<sup>+</sup> and K<sup>+</sup> were measured by flame photometry. Transporter and channel abundance in the kidneys were determined by quantitative immunoblot. Distribution of the NHE3, NHE3p, NCC, and NCCp transporters along the microvilli was examined using immunohistochemistry.These parameters were compared in MNS, MHS, FNS, FHS diet groups.

**Results:** At baseline, F exhibit lower urine output, Na<sup>+</sup> excretion and lower abundance of the PCT NHE3 and Cld2 compared to M. F had a greater diuretic response to HSD than M. NHE3p increased in MHS, but not in FHS. In FHS, the NKCC, NKCCp, NCC, and NCCp transporters were lower than FNS. In MHS vs. MNS only NCC decreased suggesting less Na<sup>+</sup> reabsorption in this nephron region in F vs. M. In the collecting duct at baseline, ENaC γ was higher in F than M and doubled in both FHS and MHS vs. NS.

**Conclusion:** This study demonstrates that the responses to a HS diet are sex dependent. Females exhibit more robust natriuresis and diuresis during HS diet which we hypothesize is due to the lower PCT NHE3 and Cld2 at baseline and reduced NKCC, NKCCp, NCC and NCCp during HS diet.

### AMP-activated protein kinase (AMPK) regulation of Sox9 expression in progenitor-like cells in models of Chronic Kidney Disease (CKD)

Connor Wayman, J. Juarez, D. Rivera, K. Ohmi, V. Mancino, K. R. Hallows and Nuria-Pastor-Soler.

**Goal:** Sox9, a transcription factor important in kidney development, is expressed in progenitor-like kidney cells at baseline, while its expression increases post-injury. Hypothesis: the metabolic sensor AMPK is necessary for kidney to express Sox9 positive progenitor-like cells at baseline and post-injury. We plan to use AMPK activators such as metformin, to upregulate AMPK, in the treatment of CKD and to help kidney donors.

**Methods**: AMPK-KO mice and wild-type mice underwent kidney reduction injury uninephrectomy (UNx), unilateral ureteral obstruction, or sham surgery. Contralateral kidneys were also examined. Posteuthanasia the kidneys were fixed and processed for immunolabeling of sections using an antibody against Sox9. Sections were imaged by confocal microscopy, and the staining pattern was compared to control sections. Sox9 levels were also evaluated in kidney tissue using qPCR. Human kidney tissue was also used to test the presence of cells positive for Sox9 expression.

**Results:** Injured kidneys showed modest differences in nuclear and peri-nuclear Sox9 expression. WT animals showed more expression of this protein compared to AMPK-KO animals as predicted. Better Sox9 labelling and the use of fluorescent-reporter Sox9 mouse models should yield better visualization of Sox9 expression. By qPCR, AMPK-KO mice had lower levels of kidney Sox9.

**Summary/Conclusion:** More work is needed to fully understand interactions between Sox9 and AMPK in kidney physiology and pathology. Our results support the hypothesis that AMPK is permissive for Sox9 expression and for survival of progenitor-like cells. We hope this will lead to a better understanding of

how metabolism interacts with regeneration, and ultimately find potential therapies for CKD patients and kidney donors.

#### Urologic Procedures in Jehovah's Witness Patients: Safety and Feasibility <u>Willem Xu, B.A</u>, Thomas Clifford, M.D., Hooman Djaladat, M.D., M.S.

**Introduction**: This study describes the safety and feasibility of performing transfusion-free urologic surgery in a patient population refusing blood transfusions due to religious conviction. **Methods**: We performed an IRB-approved retrospective review of Jehovah's Witness (JW) patients who underwent transfusion-free urological procedures at our institution between 2003 and 2016. Procedures were classified into risk groups according to transfusion rates in the literature: low, <5% risk; intermediate, 5-15%; high, >15%. Peri-operative labs, length of surgery, estimated blood loss, intraoperative fluids, blood optimization and conservation techniques used (eg. CellSaver), length of hospital stay, and 90-day complications were recorded.

**Results**: A total of 100 JW patients (median age 61, 69% male) underwent 108 urologic procedures: 12 endoscopic (11.1%), 15 low (13.9%), 56 intermediate (51.9%), and 25 high risk (23.1%). Mean pre- and postoperative hemoglobin was 13.5 (5.6-16.8) and 11.8 (5.3-15.9), respectively. EBL ranged from scant to 1600ml. There were no mortalities. LOS? Overall complication rate was 21.3%; the rate was 23.4% in intermediate and high risk procedures. Six cases were complicated by bleeding. Blood optimization and conservative techniques were occasionally used, including preoperative epoetin alfa (8.3%) and iron (4.6%), intraoperative hemostatics/procoagulants (26.0%), and CellSaver (available in 9.3%, used in 0.9%).

Risk	No of cases	Pre- op Hb	EBL (ml)	Post- op Hb	Bleeding events	Epoetin alfa/ Iron	Hemostatics/ Procoagulants	CellSaver
Overall	108	13.5	190	11.8	6 (5.6%)	14 (13%)	28 (26%)	Available- 10 (9.3%), Used-1 (0.9%)
Endosco pic	12	12.6	85	11.6	2 (16.7%)	2 (16.6%)		
Low	15	13.6	80	12.9	0	1 (6.7%)	0	0
Intermed iate	56	14	165	12.1	4 (7.15%)	1 (1.8%)	16 (28.6%)	0
High	25	12.9	356	11.1	0	10 (40%)	12 (48%)	Available- 10 (40%), Used-1 (4%)

**Conclusions**: Transfusion-free urological procedures can be safely performed in select patients and usually do not necessitate blood conservation techniques.

### NEUROLOGY

#### Serial Body Temperature Evaluation and Long-Term Clinical Outcomes in Stroke

<u>Emily Margolin</u>, Jeffrey L. Saver, Sidney Starkman, David S. Liebeskind, Nerses Sanossian for the FAST-MAG Investigators

**Background**: The relationship between acute body temperature and subsequent clinical outcome in stroke patients is unclear. Although hypothermia is effective in protecting the human brain in global ischemia following cardiac arrest, application to focal ischemia after stroke has been unsuccessful beyond the animal model. We sought to characterize the relationship of body temperature with long-term clinical outcomes by evaluating serial body temperature measurements over 24 hours. **Methods**: Within 2 hours of symptom onset, stroke patients were enrolled in the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) trial, a phase 3, randomized, placebo-controlled clinical trial. Body temperature was recorded at ED arrival, 8 hours, 16 hours and 24 hours. Long term clinical outcome was assessed using the modified Rankin Scale (mRS) at 90 days. Mean temperature at each time period was determined for subjects within each disability score on the mRS. Statistical analyses were performed using ANOVA with F-test.

**Results**: Among the 1700 enrolled patients, 1586 (93%) had temperature recorded on ED arrival, 1594 at 8 hours, 1611 at 16 hours, 1594 at 24 hours. At ED arrival, mean body temperature was higher among those experiencing better long-term outcomes (F=3.1, p=0.005). As of 8 hours, and continuing through all subsequent measures, higher body temperature was associated with poorer outcomes across the modified Rankin Scale spectrum (8-hr F=5.5, p<0.001; 16-hr F=18.7, p<0.001; 24-hr F=19.3, p<0.001). On further analyses by stroke subtype, the association of higher arrival temperatures with better long-term outcomes was seen only in cerebral ischemia and not intracerebral hemorrhage.

**Conclusions**: The association between body temperature and long-term outcome in acute stroke may be time-dependent. Decreases in body temperatures after the initial presentation may predict better long-term outcomes in acute stroke, requiring further analysis.

### NEUROSURGERY

Measurement of Cortical Stimulator Outputs in Simulated Electrode-Tissue Interface Zack Blumenfeld BS, Angad S. Gogia BS, Michael F. Barbaro BA, Dominic J Grisafe II BS, Daniel R. Kramer MD, Charles Y. Liu MD PhD, Spencer Kellis PhD, Brian Lee MD PhD

**Background**: Cortical electrical stimulators are used to map functional brain areas in epilepsy surgery. Here we measure and compare commercially-available cortical stimulator outputs using a simulated electrode-tissue interface.

**Methods**: The electrode-tissue interface was simulated using a circuit with a single 1 k $\Omega$  resistor in parallel with a 3.3  $\mu$ F capacitor to represent the tissue resistance and electrode capacitance, respectively. Cortical stimulator output was measured using a National Instruments Data Acquisition Device (USB 6343). The voltage change across a 220  $\Omega$  shunt resistor was converted to current as each stimulator is current regulated. Three cortical stimulators were tested: the Ojemann OCS-1, Natus Nicolet Cortical Stimulator, and Grass Technologies S12X. In order to collect data across a range of clinically-used stimulation parameters, we varied the current (0.2-10 mA), pulse duration (100-1000  $\mu$ s), and the pulse frequency (5-100 Hz).

**Results**: Each stimulator's measured amplitude differed from the selected amplitude. The median absolute differences were as follows: 10.7% (interquartile range = 4.83 - 42.6%, p = 0.003) for the Ojemann OCS-1, 7.1% (interquartile range = 6.11 - 12.06%, p < 0.001) for the Natus Nicolet Cortical Stimulator, and 3.8% (interquartile range = 2.50 - 4.89%, p < 0.001) for the Grass S12X. Across all stimulators and stimulation parameters, the mean negative peak value of the biphasic wave output had a greater amplitude than its corresponding positive peak (p < 0.001 for all stimulators). **Conclusions**: There are significant differences between the selected and measured output for the three commercially available cortical stimulators tested. Due to the widespread use of these cortical stimulators in clinical settings, further exploration of their outputs for the variety of clinical stimulation parameters.

#### Assessing Prognostic Factors for Patient Outcomes in Traumatic Brain Injury Zariah Chappell, Dr. Daniel Kramer, Natalie Pierson, Dr. Frank Attenello

**Background:** Traumatic brain injury (TBI) is one of the leading causes of mortality in the United States, attributed with an estimated 50,000 deaths per year. Fortunately, the last few decades have brought with it the revival of decompressive craniectomies and craniotomies, greatly improving the outcomes of TBI patients. This study aimed to query numerous variables and their association with patient outcome for TBI patients receiving craniotomies or craniectomies. We predicted that the presence of in-hospital infections, especially wound and cerebrospinal fluid (CSF) infections, would be associated with worse patient outcomes regardless of presenting GCS.

**Methods:** We conducted a retrospective chart review of patients who had undergone craniotomy or craniectomy at LAC + USC. A data collection form was created to record patient information from May 2015 to Dec 2016. Demographic information, lab values, radiographic data, injury type, length of surgery, length of stay, GSC (initially, following surgery, and on discharge), and presence of in-hospital infections were recorded.

**Results:** Of the 139 patients recorded in the study, 104 (74.8%) experienced post-operative fever, and 63 (45.3%) experienced in-hospital infection. The locations of these infections, from most to least prevalent were respiratory, urinary, blood, other, wound and CSF. The most common infections found were *Staph epidermidis* (blood), *Candida spp*. (urinary), *Klebsiella pneumoniae* and *S. aureus* (respiratory), *Acinetobacter* (CSF), and *Enterobacter spp*. (wound washout)

**Conclusion:** It has not yet been determined if the presence of in-hospital infection or fever led to deleterious outcomes for patients who underwent craniotomy and craniectomy at LAC+ USC from May
2015-Dec 2016. Results suggest that patients do experience longer hospital stay if found to have inhospital infection (esp. wound infection), however statistical analysis is required to better evaluate the role of infection in patient outcome.

#### Surgical Management of Clinically Silent Thyrotropin Pituitary Adenomas: A Single Center Series of 20 Patients

Janelle Cyprich BS<sup>1</sup>, Daniel A. Donoho MD<sup>1</sup>, Kyle Hurth MD, PhD<sup>2</sup>, John D. Carmichael MD<sup>3</sup>, Martin H. Weiss MD<sup>4</sup>, Gabriel Zada MD, MS<sup>4</sup>

<sup>1</sup>Keck School of Medicine, University of Southern California, Los Angeles, California, USA. <sup>2</sup>Department of Pathology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.

<sup>3</sup>Division of Endocrinology, Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.

<sup>4</sup>Department of Neurosurgery, Keck School of Medicine, University of Southern California, Los Angeles, California, USA.

**Introduction:** Silent thyrotropin pituitary adenomas (TSHomas) are defined by absence of hyperthyroidism despite TSH immunopositivity. The literature specific to silent TSHomas is limited and varied. We report the clinical presentation, histopathological characteristics, and surgical outcomes of our silent TSHomas.

**Methods:** A retrospective review was conducted to identify patients with histologically proven silent TSHoma who underwent transsphenoidal resection at the USC Keck Pituitary Center between 2000-2016. Patients with preoperative hyperthyroidism or those who underwent prior thyroidectomy were excluded. Patient demographics, presenting symptoms, preoperative endocrine status, surgical details, pathology, postoperative course, and follow-up outcomes were collected and analyzed.

**Results:** Twenty patients were included with mean age of 51.8 years and 35% female. Median follow-up time was 18.5 months (range: 3-184 months). Presenting symptoms included vision loss (45%) and headache (40%). Preoperative pituitary dysfunction included hypothyroidism (40%), hypogonadotropic hypogonadism (30%), and panhypopituitarism (15%). Nineteen patients (95%) had macroadenomas. Extrasellar growth was identified in 17 patients (85%), consisting of suprasellar extension (80%), cavernous sinus invasion (65%), and infrasellar invasion (20%). Immunostaining for alpha-subunit was positive in 19 patients (95%), and 75% of tumors expressed immunopositivity for other pituitary hormones in addition to TSH (luteinizing hormone (LH) in 65% and follicle-stimulating hormone (FSH) in 20%). There were no deaths. Postoperative complications included delayed hyponatremia (10%), epistaxis (10%), transient diabetes insipidus (5%), cerebrospinal fluid leak (5%), hydrocephalus (5%), and meningitis (5%).

**Conclusions:** This case series describes the aggressive presentation and clinical outcomes of silent TSHoma, a distinct subtype of nonfunctioning pituitary adenomas. The majority of silent TSHomas were macroadenomas, presented with vision loss and/or headache, and expressed immunopositivity for TSH and alpha-subunit in addition to other anterior pituitary hormones, most commonly LH and FSH. Surgical complications were few considering the aggressive presentation accompanied by structural and endocrinologic abnormalities.

Integrative Analysis Implicates *MYC* and *MAX* in Functional Pituitary Adenomas <u>Angad S. Gogia, BS</u>, Douglass W. Tucker, BS, Timothy J. Triche, Jr, PhD, Charles E. Ashton, MS, Daniel J. Weisenberger, PhD, John D. Carmichael, MD, Gabriel Zada, MD **Background**: Pituitary adenomas (PAs) are common intracranial tumors that may cause endocrinopathies and neurological deterioration. Although known causal contributors include heredity, hormonal influence, and somatic mutations, the pathophysiologic mechanisms driving tumorigenesis and invasion remain unknown. Here we apply an integrative approach to elucidate regulatory differences between functional PAs (FPAs) and non-functional PAs (NFPAs).

**Methods**: DNA methylation data from 58 (40 NFPAs, 18 FPAs) surgically-resected PAs was used to identify differentially methylated regions (DMRs) between FPAs and NFPAs. We performed motif enrichment analysis on each set of DMRs to identify sequence motifs for particular transcription factors. Using RNA sequencing data available in 24 of 58 adenomas, we constructed an empirical Bayes linear model and applied gene set enrichment analysis to unearth coherent biological activities within the significantly differentially expressed genes.

**Results**: *MYC* and *MAX* emerged as leading candidates from motif enrichment analysis on the significant differentially expressed genes identified from DNA methylation data (p < 0.001). We also observed recurrent amplification of *MYC* and co-amplification of *MYC* and *MAX* on chromosomes 8 and 14. Furthermore, V\$MYCMAX\_01 and V\$MYCMAX\_03 were both among the top results (p < 0.02 and p < 0.04 respectively) of gene set analysis of the differentially expressed genes identified from RNA sequencing data.

**Conclusion**: DNA methylation and RNA sequencing data may be used to identify candidates involved in PA function such as *MYC* and *MAX*. Aberrant DNA methylation of *MYC* and *MAX* may be a mechanism of tumorigenesis in functional PAs, leading to potential loci for targeted therapy in patients with functional tumors. The younger age of presentation and higher rate of tumor relapse in functional tumors may be explained by these differences in the epigenetic and downstream changes allowing for proliferation of these lesions.

#### Silent Corticotroph Adenomas vs. Nonfunctioning Adenomas: Clinical Characteristics and Long Term Outcomes

#### Anna Jackanich, BS, Sherwin Tavakol, BA, Gabriel Zada, MD, John Carmichael, MD

**Background:** Silent corticotroph adenomas (SCA's) are pituitary tumors that stain positive for ACTH without producing clinical levels of hypercortisolemia. They are known to demonstrate aggressive behavior and have a substantial proclivity for recurrence compared to other nonfunctional pituitary adenomas. Previous studies have brought attention to SCAs, but are limited by small sample size and insufficient follow up. In addition, surgical approach, adjuvant therapy, and follow-up procedure vary from institution to institution. Through study of the current literature, it is clear there is no current gold standard for SCA management. This study from Keck Hospital is the largest single center series comparing surgically treated SCA's to NFPA.

**Method:** SCAs (60) and NFAs (381) diagnosed at Keck Hospital of USC from 2000 to 2017 were retrospectively reviewed.

**Results:** SCAs were more likely to present clinically with headache (p = 0.001), amenorrhea (p = 0.001), fatigue (p = 0.0001), cranial nerve palsy (p = 0.0001) and apoplexy (p = 0.0001) compared to NFAs. While there was no significant difference in maximal tumor diameter, SCAs were more likely to invade the cavernous sinus (p = 0.005), and recurred more frequently (p = -.0001). Patients underwent While rates of progression were statistically similar, SCA's tended to progress much quicker.

**Conclusions:** In the largest series comparing NFAs to SCAs to date, SCAs presented with more clinical symptoms, increased cavernous sinus invasion during resection and overall greater rates of recurrence. These patients were also much more likely to undergo multiple operations indicating that close follow up and adjuvant therapy may be necessary to successfully managing SCAs.

#### Psychiatric Comorbidities Predict 30-day and 90-day Readmissions in Elective Cranial Neurosurgery. <u>Lucas Lebovitz</u>, Keck School of Medicine. Frank Attenello MD, Department of Neurosurgery.

**Background:** Early readmissions following surgery are among a number of outcomes used as metrics to evaluate quality of care within surgery. The effect of psychiatric comorbidities on a number of surgical outcomes has been studied before within and across surgical specialties. Within neurosurgery the effect of psychiatric comorbidities on surgical outcomes, including 30- and 90-day readmission, including rates of readmission, has been studied in a number of procedures and groups of procedures; however, the effect of psychiatric comorbidities on readmission rates within patients undergoing elective cranial neurosurgery has not yet been studied.

**Methods:** We will utilize the Nationwide Readmission Database (NRD), which includes a large sample size from 27 geographically disparate States and verified patient identifiers to track patients across hospitals within a State to whether psychiatric comorbidities predict 30-day and 90-day readmission rates in elective cranial neurosurgery. All adult patients 18-80 years old undergoing elective cranial neurosurgery from 2013 to 2014 will be included included, and the rates of 30-day and 90-day readmission will be compared using univariate analysis between the cohort with a coexistent diagnosis of a psychiatric disorder and the rest of the sample.

**Results:** The analysis of the existent data has not yet occurred; however, we predict that psychiatric comorbidities will increase the rates of both 30-day and 90-day readmission rates in elective cranial neurosurgery.

**Conclusions:** If psychiatric comorbidities are associated with increased readmission rates from elective cranial neurosurgery, this information can be used in surgical planning and decisions.

#### Resolution of Chronic Aspiration Pneumonitis Following Endoscopic Endonasal Repair of Spontaneous Cerebrospinal Fluid Fistula of the Skull Base: A Case Series

Maya Or<sup>1</sup> Samridhi Amba<sup>3</sup> Justin Seltzer<sup>1</sup> Roozera A. Khan<sup>3</sup> Bozena B. Wrobel<sup>2</sup> Gabriel Zada<sup>1</sup>
<sup>1</sup>Department of Neurosurgery, Keck School of Medicine of USC, Los Angeles, California, United States
<sup>2</sup>Department of Otolaryngology, Keck School of Medicine of USC, Los Angeles, California, United States
<sup>3</sup>Department of Pulmonary and Critical Care, Keck School of Medicine of USC, Los Angeles, California, United States

**Objective:** Spontaneous Cerebrospinal Fluid (CSF) leaks are the rarest type of CSF leaks. Like other kinds of CSF leaks, spontaneous leaks most commonly present with CSF rhinorrhea. Persistent rhinorrhea can be confused for a symptom of rhinosinusitis or allergic rhinitis. Such misdiagnoses cause delay in treatment of the leak and lead to complications and co-morbidities. The most common complications described in the relevant literature include meningoencephalocele and meningitis. In the following retrospective case series, the authors aim to demonstrate that a CSF leak can also lead to aspiration pneumonitis, a complication that has not been previously described.

**Methods:** The authors report 5 patients presenting with pulmonary symptoms including dyspnea, aspiration, chronic cough, shortness of breath, and bilateral groundglass opacities on CT imaging, that were all found to be accompanied by a spontaneous CSF leak arising from a skull base defect. Two patients had ethmoidal CSF leaks arising from the fovea ethmoidalis, one had a lateral sphenoidal skull base defect, and one had middle fossa floor skull base dehiscence draining through the eustachian tube. Three patients underwent endoscopic endonasal approaches for skull base defect, while one required a

craniotomy. All four underwent CSF leak repair using an autologous fascia lata graft and pedicled naso-septal flap.

**Results:** All 4 patients underwent successful repair of a skull base defect and CSF leak with no complications or evidence of recurrence. Upon repair of the spontaneous CSF leak, pneumonitis symptoms were resolved and the groundglass opacities on CT imaging cleared in all four cases. **Conclusion:** The authors contend that a diagnosis of CSF leaks should be considered when a patient presents with pneumonitis symptoms that do not alleviate or worsen with treatment.

#### Prognostic factors and Outcomes in Primary Juvenile Spinal Cord Astrocytomas Sagar Patel, Nolan Rea, Mark Krieger

**Goal:** Spinal cord astrocytomas are rare intramedullary tumors without clear management consensus. We aim to identify prognostic factors and determine the outcome of treatment.

**Methods:** A retrospective review of 11 patients (2 female, 9 male, median age 11) diagnosed with primary spinal cord astrocytomas between 2002 to 2011 was performed. Data collected included patient demographic information, prognostic indicators, and treatment modalities. We utilized a multiple linear regression model to identify variables associated with postoperative outcomes.

**Results:** There were 0 deaths in the study population. Overall, 45% of patients had recurrence or progression. No Patients with grade 1 tumors had recurrence or progression. 40% of patients with grade 2 and 100% of patients with grade 3 had recurrence or progression. Only 20% of patients with a syrinx had progression or recurrence. 60% of patients with duration of symptoms of < 6 months had either progression or recurrence, whereas 25% of patients with duration of symptoms lasting  $\geq$  6 months had progression. Radiation and chemotherapy did not seem to have any independent association with progression or recurrence. Extent of resection did not have an independent association with progression or recurrence.

**Conclusions:** WHO grade and duration of symptoms were the strongest prognostic indicators in patients with primary spinal cord astrocytomas. Chemotherapy, radiotherapy, and extent of resection did not independently influence outcomes in this study.

#### Prognostic Factors Predicting Long-Term Outcomes in Traumatic Brain Injury Patients <u>Natalie Pierson</u>, Dr. Daniel Kramer, Zariah Chappell, Dr. Frank Attenello

**Background:** Traumatic brain injuries (TBI) remains one of the leading causes of mortality in the United States, with about 50,000 deaths occurring annually. Decompressive craniectomies and craniotomies have been shown to significantly reduce mortality in patients with severe TBI who have intracranial pressure which doesn't respond to medical intervention. Whether decompressive craniectomies also improve long-term outcomes, however, is still heavily debated. This study aims to evaluate the outcomes of TBI patients who received craniectomies or craniotomies and identify associated risk factors.

**Methods:** Data was collected from a retrospective chart review of patients receiving a craniotomy or craniectomy at LAC + USC after presenting with a TBI from May 2015 through December 2016. Demographic information, laboratory values, radiographic data, injury type, initial Glasgow Coma Scale (GCS), length of stay, GCS on discharge, discharge location, and length of stay were evaluated. A Modified Rankin Scale score was identified at discharge and at most recent follow-up. The incidences of various outcomes were calculated using summary statistics.

**Results:** A total of 139 patients with traumatic brain injuries that received a craniectomy or craniotomy from May 2015 – Dec 2016 were identified, 40 (28.8%) of whom died. The Modified Rankin Score at

discharge for the remaining 99 (71.2%) patients varied widely: 24 (24%) received a score of 1 or 2, signifying they could carry out all previous tasks despite some, if any, symptoms, and 28 (28.3%) patients received a score of 5, suggesting they were severely disabled, bedridden, and required constant nursing care. The rest of the patients were in between. In the 52 (62.9%) out of 89 eligible patients that returned for follow-up at LAC + USC, 20 (38.5%) had the same Modified Rankin Score as at discharge, 30 (57.8%) improved in one point or more, and 6 (11.5%) had a worse Modified Rankin Score. **Conclusion:** In the severe TBI patients receiving a decompressive craniectomy or craniotomy, morbidity and mortality rates were still high. No factors were identified yet that are associated with better or worse outcomes. Our results suggest that despite low mortality rates, many patients who do survive improve after discharge.

## Hemorrhagic Rathke's cleft cyst: Clinical presentation and transsphenoidal surgical outcomes in a series of 6 patients

<u>Lauren K Schooner, BS</u><sup>1</sup>, Phillip A Bonney, MD<sup>1</sup>, Michelle A Wedemeyer, MD/PhD<sup>1</sup>, Michelle Lin, MD<sup>1</sup>, Martin H Weiss, MD<sup>1</sup>, John D Carmichael, MD<sup>2</sup>, Gabriel Zada, MD<sup>1,2</sup> Departments of <sup>1</sup>Neurological Surgery and <sup>2</sup>Endocrinology Keck School of Medicine, University of Southern California

**Introduction:** Rathke's cleft cysts (RCCs) are benign cystic lesions of the sellar and suprasellar space, are often found incidentally and are typically asymptomatic. Due to their anatomical location, when symptomatic they can present with visual deficits, headaches, and endocrinopathies. Occasionally, RCCs can present clinically with an acute onset signs and symptoms mimicking pituitary apoplexy. The purpose of this study was to review our experience treating patients with confirmed hemorrhagic Rathke's cleft cysts.

**Methods:** We performed a single-center retrospective review and identified 6 patients presenting with acute clinical onset of hemorrhagic Rathke's cleft cysts who underwent transsphenoidal surgical management at the USC Pituitary Center. Lesions were pathologically confirmed hemorrhagic RCCs. Surgical treatment typically involved transsphenoidal fenestration and drainage. Clinical, endocrine, and imaging outcomes were reviewed.

**Results:** A total of 6 patients with a mean age of 42.5 years were identified and included. There were 3 men and 3 women with a mean follow up time was 38.4 months (range 3-66). All 6 patients were referred to for clinical symptoms of apoplexy with findings consistent with hemorrhage on outside imaging. Five of 6 patients (83.3%) presented with acute onset headaches as their presenting symptom. Two patients (33.3%) presented with vision loss. All 3 female patients presented with amenorrhea. Two patients (33.3%) presented with hypothyroidism. Two patients presented with panhypopituitarism including one with profound hyponatremia (sodium 116 mmol/L). The average RCC diameter was 16mm (range 14-20mm). Imaging typically showed a T1 hyperintense lesion consistent with internal hemorrhage. Patients were taken for elective transsphenoidal fenestration and drainage of the RCC with partial wall resection. Two patients (33.3%) had intraoperative CSF leaks that were repaired, and both showed no postoperative CSF rhinorrhea. At latest follow up, 2/5 (40%) patients with headaches had improvement and the 2 patients with vision loss had improved vision. While 3/3 women had resolution of amenorrhea, all patients who required hormone supplementation preoperatively continue on their regimens postoperatively. Follow-up MRI showed no instances of RCC recurrence.

**Conclusion:** Rathke's cleft cysts can occasionally present with internal hemorrhage and clinical signs and symptoms mimicking pituitary apoplexy. Outcomes for hemorrhagic RCCs are similar to those patients with standard RCCs. Although hyperprolactinemia tends to improve following surgery, possibly secondary to decompression of the stalk, other pituitary axes typically do not.

**Learning Objectives:** By the conclusion of this session, participants should be able to 1) Describe common presenting symptoms of Hemorrhagic Rathke's cysts, 2) Understand the uniqueness of this type of symptomatic Rathke's complicated by hemorrhage and 3) Understand the safety and success rate of surgically resecting the lesions.

Keywords: Apoplexy, Rathke's Celft Cyst, Transsphenoidal

#### Role of the Microenvironment in Medulloblastoma Development and Metastasis Maxwell Singer, Vahan Martirosian, Josh Neman

**Goal:** The medulloblastoma (MB) tumor microenvironment is critical for tumor propagation. Moreover, aggressive brain tumors are able to utilize GABA in their microenvironment as a metabolic source to gain a proliferative advantage. Our goal was to interrogate the role of GABA metabolism in the metastatic capabilities of Group 3 MBs.

**Methods**: We evaluated the presence of GABA shunt mediator mRNA in four MB cell lines using *qPCR*. We compared the mRNA expression of GABA shunt mediators in cells grown in glutamine (control) and GABA supplemented medium. Moreover, we also compared cells in adherent versus sphere conditions supplemented with GABA. Sphere conditions emulate a metastatic phenotype. Finally, to evaluate the effect of GABA on epithelial to mesenchymal transition (EMT), a gene expression phenotype indicative of metastatic cells, we interrogated 5 EMT markers (*ZEB1, TGFB3, PTP4A1, STAT3, and GSK3B*) through qPCR. We evaluated expression of these markers in control, GABA supplemented, and ABAT knockdown (KD) D283 MB cells.

**Results:** GABA shunt mediators increased in GABA supplemented cells in both G3MB cell lines (D283 and D425). Cells in floating conditions expressed higher levels of EMT markers as well as GABA shunt mediators. EMT markers also increased in GABA supplemented cells, however, in ABAT kd cells, they still increased.

**Conclusions:** GABA induces an increase in mRNA of GABA shunt mediators, providing evidence that these cells sense and seek utilization of GABA. Moreover, higher expression of EMT markers suggests this utilization of GABA may be related to a greater capacity to metastasize. Spheroids had greater expression of EMT markers and GABA shunt mediators, suggesting cells that are becoming more EMT also utilize GABA as fuel. In ABAT kd cells, expression of EMT markers still went up. This may be because GABA influences EMT but not through the GABA shunt pathway. With the GABA shunt pathway effectively closed, GABA would then be used through the pathway driving EMT.

#### Stereotactic radiosurgery for trigeminal neuralgia treatment: a retrospective review of 59 cases at the Keck Medical Center of USC

<u>Sherwin Tavakol, BA</u>, Anna Jackanich, BS, Steven Giannotta, MD, Gabriel Zada, MD, Department of Neurosurgery, Keck School of Medicine of USC

**Background/Goals:** Trigeminal neuralgia (TGN) is a debilitating disease characterized by unilateral, severe electrical shock-like pain occurring in one or more of the distributions of the trigeminal nerve (V1-V3). Stereotactic radiosurgery (SRS), also called Gamma Knife surgery (GKS), is a noninvasive form of radiotherapy that focuses gamma rays to a precise area, most typically in the brain, to treat small- to medium-sized lesions. SRS has been used in the treatment of TGN since 1951. The goal of this study is to identify the mean time of relief of symptoms after SRS, and to identify what characteristics in particular (previous SRS, previous other TGN surgery, Barrow Pain Scale (BPS) score, age, atypical TGN, etc.) effect outcomes of SRS. We hypothesize that previous successful SRS, BPS score of 4-5, and no previous intracranial surgeries are the best indicators of positive outcomes.

**Methods:** We searched through the Keck Medical Center of USC database of GKS and found 52 individuals (59 surgeries) who had received this treatment for TGN between 2007-2017. Charts were reviewed for general demographics, pain distribution, past cases of SRS, past invasive treatment for TGN, BPS scores before and after treatment, treatment dose, target volume, and complications. **Results:** We do not have analyzed results at this time, but expect that those patients with previous SRS treatments will experience statistically longer relief time. We also expect that patients with higher initial BPS scores will experience the most significant drops in pain after GKS.

**Conclusion:** These data illustrate the effectiveness of GKS for trigeminal neuralgia. Patients with the aforementioned indicators have the highest chance of experiencing the greatest and longest relief.

#### Genome Wide Methylation Analysis Reveals Novel Pathways in Functional Pituitary Adenomas Douglass W. Tucker BS, Angad A Gogia BS, Timothy Trisch Jr. PhD, Gabriel Zada MS, MD

**Introduction**: Pituitary adenomas (PAs) are common intracranial tumors that may cause endocrinopathies and neurological deterioration. Although known causal contributors include heredity, hormonal influence, and somatic mutations, the pathophysiologic mechanisms driving tumorigenesis and invasion remain unknown. Here we apply an integrative approach to elucidate regulatory differences between functional PAs (FPAs) and non-functional PAs (NFPAs).

**Methods**: DNA methylation data from 58 (40 NFPAs, 18 FPAs) surgically-resected PAs was used to identify differentially methylated regions (DMRs) between FPAs and NFPAs. We performed motif enrichment analysis on each set of DMRs to identify sequence motifs for particular transcription factors. Using RNA sequencing data available in 24 of 58 adenomas, we constructed an empirical Bayes linear model and applied gene set enrichment analysis to unearth coherent biological activities within the significantly differentially expressed genes.

**Results**: MYC and MAX emerged as leading candidates from motif enrichment analysis on the significant differentially expressed genes identified from DNA methylation data (p < 0.001). We also observed recurrent amplification of MYC and co-amplification of MYC and MAX on chromosomes 8 and 14. Furthermore, V\$MYCMAX\_01 and V\$MYCMAX\_03 were both among the top results (p &lt; 0.02 and p &lt; 0.04 respectively) of gene set analysis of the differentially expressed genes identified from RNA sequencing data.

**Conclusion**: DNA methylation and RNA sequencing data may be used to identify candidates involved in PA function such as MYC and MAX. Aberrant DNA methylation of MYC and MAX may be a mechanism of tumorigenesis in functional PAs, leading to potential loci for targeted therapy in patients with functional tumors. The younger age of presentation and higher rate of tumor relapse in functional tumors may be explained by these differences in the epigenetic and downstream changes allowing for proliferation of these lesions.

#### Glioblastoma Multiforme Treatment and Outcome Comparison Between a Public and Private Hospital

<u>Theodore Wang BS</u>, Anthony Pham MD, Stella Yoo MD, Frank Attenello MD, Richard Jennelle MD, Eric Chang MD, Gabriel Zada MD.

**Introduction**: Sociodemographic disparities negatively impact treatment and outcomes in cancer care. There is conflicting data over these factors in glioblastoma multiforme (GBM), an aggressive brain cancer. This study examines if disparities were responsible for barriers in neuro-oncological care for GBM patients.

**Methods**: We performed a retrospective review of patients diagnosed with GBM between 2010-2014 at an academic institution consisting of a public (LAC+USC) and private (Keck) hospital. Data on

demographics, clinical course, and treatment were compared using Pearson's chi-square and Mann-Whitney U-test. Kaplan-Meier analysis estimated overall survival (OS) and event free survival (EFS). Cox proportional hazards model was used for multivariable analysis.

**Results**: 48 public and 41 private patients were analyzed with a median follow up time of 13 months (range 0-62). Public hospital patients were younger, predominantly Hispanic, unmarried, lower income, and were enrolled in Medicaid or uninsured. The groups had tumors of similar size, foci number, and resection extent. Public hospital patients were less likely to receive radiation (92% vs 100%) and time from diagnosis to radiation was longer (43 vs 37 days). There was similar use of concurrent and adjuvant temozolomide as well as clinical trial enrollment. Median OS was similar between the two cohorts (19 vs 16 months), as was median EFS (7.5 vs 9 months). At the time of progression rates of salvage surgery or radiation were similar. The only factors associated with worse survival on multivariable analysis were age>50 (HR1.8) and no adjuvant chemotherapy (HR 3.68). Hospital type, income level, use and timing of radiation, and insurance status were not associated with survival. **Conclusion**: Despite clear socioeconomic differences, both patient groups had similar treatment and outcomes with GBM. Access to multidisciplinary care by academic physicians may improve the care for disadvantaged GBM patients.

**Cerebrovascular Neurosurgery in the Modern Era: Examining the Learning Curve** <u>Shane Sharestani BS<sup>1</sup></u>, Ben A. Strickland MD<sup>1</sup>, Robert Rennert MD<sup>2</sup>, Kristine Ravina MD, Joshua Bakhsheshian MD<sup>1</sup>, Vance L. Fredrickson MD<sup>1</sup>, Steven L. Gionnatta MD<sup>1</sup>, Jonathan J. Russin MD<sup>1,2</sup>

**Goal:** To date, only 8 CAST approved fellowships aimed at training open cerebrovascular neurosurgeons exist. Most aneurysms treated through endovascular surgery now, and less cases being done open. With less residency programs with faculty doing open cases, less residents are being taught these skills. **Methods:** We retrospectively reviewed the medical records of patients undergoing microsurgical intervention for aneurysm surgeries between the two senior authors (SG and JR). The 100 aneurysms treated by SG prior to June 2014 were collected for anaylsis. Similarly, the first 100 aneurysm surgeries performed by JR were included for analysis. Patient demographics, rupture status, presenting Hunt-Hess and Fisher grade, neurologic examination, aneurysm location, clip time, vasospasm status, modified Rankin Scale, and Glasgow outcome score were recorded.

**Results:** There was no significant difference between presenting Hunt Hess, Fisher, or Glasgow Coma score between the cohorts, however JR had a higher percentage of cases presenting as ruptured compared to SG [54.2% versus 45.8%, respectively] (p<0.01).

GOs at time of most recent follow up was a mean of 4.85 in JR cohort compared to 4.6 in SG cohort (p<0.01) with mRS averages of 0.86 and 1.06, respectively (p<0.01).

A significant difference in clinical vasospasm was noted between cohorts [SG -25% vs JR – 77.8%] (p<0.01).

Clip time SG – 11.6 minutes versus JR – 19.8 minutes (p<0.01)

There was no statistical significance between cohorts of reported complications.

Conclusion: The CAST approved fellowships for microsurgical neurovascular surgery.

Our data is suggestive that the CAST fellowships do lessen the learning curve, as seen by improved outcomes amongst the JR cohort.

# ONCOLOGY

## Multi-parametric liquid biopsy analysis of circulating tumor cells (CTCs), cell-free DNA (cfDNA), and cell-free RNA (cfRNA) in metastatic castration resistant prostate cancer (mCRPC)

**Emmanuelle Hodara**<sup>1</sup>, Daniel Zainfeld<sup>1</sup>, Gareth Morrison<sup>1</sup>, Alexander Cunha<sup>1</sup>, Yucheng Xu<sup>1</sup>, John Carpten<sup>2</sup>, Peter Danenberg<sup>3</sup>, Paul Dempsey<sup>4</sup>, Joshua Usher<sup>5</sup>, Kathleen Danenberg<sup>5</sup>, Farideh Bischoff<sup>6</sup>, Aditi Khurana<sup>7</sup>, Philip Cotter<sup>7</sup>, Mathew Moore<sup>7</sup>, Shelly Gunn<sup>7</sup>, Tanya Dorff<sup>1</sup>, David Quinn<sup>1</sup>, Amir

Goldkorn<sup>1</sup>

<sup>1</sup>Department of Medicine, <sup>2</sup>Department of Translational Genomics, and <sup>3</sup>Department of Biochemistry and Molecular Medicine, USC Keck School of Medicine and Norris Comprehensive Cancer Center, Los Angeles, CA; <sup>4</sup>Cynvenio Biosystems Inc., Westlake Village, CA; <sup>5</sup>Liquid Genomics, Torrance, CA; <sup>6</sup>Menarini Silicon Biosystems, San Diego, CA; <sup>7</sup>ResearchDX, Irvine, CA

**Background:** Molecular profiling of prostate cancer using liquid biopsies such as CTC capture and cellfree nucleic acid analysis yield informative yet distinct datasets. Additional insights may be gained by simultaneously interrogating multiple liquid biopsy components to construct a more comprehensive molecular disease profile. We have conducted an initial proof of principle study aimed at piloting this multi-parametric approach.

**Methods:** Blood was drawn under an IRB-approved protocol from 20 mCRPC patients. Samples were analyzed simultaneously for the following: CTC enumeration and single CTC and matched white blood cell capture for whole genome amplification and low-pass copy number variation; CTC DNA and matched cfDNA for somatic single nucleotide variant analysis; plasma cfRNA extraction and qRT-PCR for AR, AR-V7, and PCA3. When available, liquid biopsies were compared with matched tumor profiles. **Results:** Fifteen of 20 patients (75%) had detectable CTCs by CellSearch (range: 1-692/7.5mL, median: 19.5/7.5mL). Thirteen of 20 patients (65%) had detectable SSNVs in CTC DNA and/or matched cfDNA, including mutations in *TP53, PIK3CA, HRAS,* and *EGFR*. Matched CTC DNA and cfDNA demonstrated both shared and distinct SSNVs. Copy number analysis of single CTCs was performed in 6 patients, and both had CNVs in multiple cancer relevant genes. A majority of CNVs were present in matched solid tumor profiles, but some were exclusive to the liquid biopsies. Plasma PCA3 and AR transcripts were detected in 18/20 (90%) and AR-V7 in 4/20 (20%) cfRNA samples. Unique SSNVs were detected at second time points at disease progression (more are being collected).

**Conclusions:** In this pilot cohort, simultaneous multi-parametric profiling was feasible for CTC DNA mutations and CNVs, and matched plasma cfDNA mutations and cfRNA gene expression. These disease-specific molecular profiles were often concordant with tumor tissues but also contained new, potentially actionable alterations unique to CTC DNA or cfDNA. Expanded studies will build upon this approach to optimally leverage liquid biopsies for molecularly directed patient management.

#### Three-Dimensional Outline of the Hypothalamus Aisa Iyawe, Natasha Lapore

**Introduction:** Radiation therapy is universally used to treat intracranial tumors in both children and adults. Unfortunately, studies suggest that this treatment has negative long-term effects on the hypothalamus, affecting endocrine function as well as on intellectual and social behavior. The hypothalamus is part of the diencephalon and is located below the thalamus and directly above the pituitary gland. It flanks the third ventricle on either side. Despite its small size, the hypothalamus has more special nuclei than any other structure in the brain. It is involved in social behavior, ingestive behavior, and homeostatic mechanisms. Because of its many functions, it is important to avoid the hypothalamus as much as possible when treating intracranial tumors with radiation therapy.

**Goal:** The objective of this study was to determine the outer boarders of the hypothalamus.



**Methods:** Using that information, we developed a program to be able to map out the coordinates on a three-dimensional movable graph.

Figure 1



Figures 1 and 2 show the 3D MNI coordinates for all the nuclei of the hypothalamus. Figure 2 is a more superior view. The points represent the following nuclei: medial preoptic nucleus, supraoptic nucleus, periventricular hypothalamic nucleus, lateral hypothalamic area, retrochiasmatic nucleus, ventromedial nucleus, dorsomedial nucleus, infundibular nucleus (arcuate nucleus), lateral hypothalamic area (both tuberal and posterior parts), medial mammillary nucleus, and the posterior hypothalamus.



Figure 3



Figures 3 and 4 show the 3D MNI coordinates for all of the above the nuclei of the hypothalamus and also white matter. Figure 4 is a more superior view. The additional points represent the following white substance: diagonal band, anterior commissure, optic chiasm, fornix, principle mammillary fasciculus, and the mammillo-thalamic tract.

Using both the graph and the list of MNI coordinates, we removed the plot points representing inner nuclei. The remaining outer nuclei of the hypothalamus were the Medial Preoptic Nucleus (MPO), the Suprachiasmatic Nucleus (SO), the Ventromedial Nucleus (VMH), the Infundibular Nucleus (also known as the arcuate nucleus, Inf), the tuberal and medial parts of the Lateral Hypothalamic Area (LHAt and LHAp, respectively), and the Posterior Hypothalamus (PH).







Figures 5 and 6 show the 3D MNI coordinates for the outer nuclei of the hypothalamus. Figure 6 is a more superior view.

We then calculated the spaces between the nearest nuclei on the x, y, and z planes and divided that area by two to approximate the diameter of each nucleus on all three planes. We then added the diameter to the opposite side of each nucleus to approximate the coordinates of the outer boarder the nuclei. Using these coordinates, we approximated the outer boarders of the left side of the hypothalamus. In order to determine the boarders of the right side, we multiplied all the x coordinates by -1 and then subtracted 5. The 5 represents the approximate width of the third ventricle (5 mm), around which the hypothalamus is located.

**Results:** We will calculate the MNI coordinates for the outer nuclei:

Nucleus	Left Hypothalamus	Right Hypothalamus

We will calculate the MNI coordinates for the hypothalamus:

	Left Hypothalamus	Right Hypothalamus
Medial Boarder		
Lateral Boarder		

**Discussion:** We will trace the outlines of the hypothalami of children without cancer to get more of an idea of its boarders.

#### Clinical Experience with an Automated Daily EPID Exit Dose System

#### Kyle O'Meara, Medical Student; Arthur Olch, Professor of Clinical Radiation Oncology and Pediatrics, KSOM

**Purpose**: Current quality assurance in radiotherapy does not involve the use of imaging that measures the daily dose delivered to patients. This study explores the clinical use of an automated electronic portal imaging device in measuring the exit dose for daily treatments in order to identify and characterize dosimetric errors.

**Methods**: The automated PerFRACTION system was used to collect daily exit dose images from each field of 60 treatment courses. In total, 4,079 daily field values (DFV) from 855 fractions were analyzed by the system using a dose image comparison metric called Gamma. This metric measures the difference in corresponding pixel values for a pair of images, one from the first treatment day (reference) and the second from a subsequent day (fraction N). Gamma tolerance values of 2% dose, 2mm distance and 3% dose, 3% distance to agreement were used to assess accuracy of treatment. Using 93% of pixels passing the Gamma test as the cutoff, pass-fail status was categorized by treatment modality and location. An attempt was made to identify the causes of all DFV failures.

**Results**: Overall, 20.5% of DFV failed at the 2%, 2mm Gamma tolerance. However, 48% of fields experienced at least one DFV failure during the course of therapy. 3DCRT treatments failed at a higher rate than IMRT treatments. By location, chest, spine and head and neck treatments had the highest rates of failure. The most commonly identified reason for DFV failure was body position change, but this varied by location and modality, and the reason for approximately half of DFV failures could not be identified.

**Conclusion**: Analysis of exit dose imaging revealed that variations between the reference and fraction N were present in a clinically relevant percentage of treatments. While the reasons for failure were not always identifiable, approximately half were and this may facilitate improved therapy delivery. Collection of exit dose images using an automated system is a practical and effective way of monitoring dose delivery accuracy during radiotherapy.

#### Efficacy of cyclophosphamide as treatment for steroid-refractory graft versus host disease <u>Gal Sadlik</u>, Nathan Punwani MD MPH, Giridharan Ramsingh MBBS MD.

Background: Graft Versus Host Disease (GvHD) is a common and often severe complication of allogeneic hematopoietic stem cell transplantation, a treatment that has curative potential for Acute Lymphoblastic and Acute Myeloblastic Leukemia. Cyclophosphamide is commonly given as part of a myelo-ablative conditioning regimen and has also been used effectively as a prophylactic measure against GvHD. We hypothesize that cyclophosphamide will be effective at treating active GvHD that is refractory to corticosteroids, and that it will not cause significant toxicity or increased mortality.
Methods: A retrospective chart review is being conducted of patients seen at Keck Hospital for acute lymphoblastic or acute myeloblastic leukemia who have been treated for corticosteroid-refractory GvHD with cyclophosphamide. Data is being collected for transplant type, conditioning regimen, prophylaxis, cyclophosphamide regimen and dosing, GvHD stage and type, response duration, overall survival, and adverse responses including infection, toxicity, and relapse.

**Results:** Initial reports of cyclophosphamide used as a second-line treatment for corticosteroidrefractory GvHD have indicated favorable efficacy and toxicity results. We expect forthcoming data to support these findings in our patients.

**Conclusion:** A wide range of treatment modalities are currently used as second-line in corticosteroid-refractory GvHD, and further evaluation and comparison of their efficacy is needed to establish a

standard of care. This study aims to determine whether cyclophosphamide should be a candidate for second-line therapy in these cases.

Immune Related Adverse Events (irAE) in GU cancer patients receiving immune checkpoint inhibitors <u>Peter Zang</u>, Alexandra Drakaki, Betty Chan, Izak Faiena, Denise Tsao-Wei, Susan Groshen, David I. Quinn, Tanya B. Dorff

**Background:** Immune checkpoint inhibitors (ICI), mainly antibodies against PD-1 and PD-L1, prolong survival in advanced renal cell (RCC) and urothelial cancer (UC) patients. However, they can cause a wide variety of serious immune related adverse events (irAE). We sought to better describe frequency and onset of irAE at experienced centers, and evaluate whether baseline characteristics were associated with irAE in this population.

**Methods:** USC Norris Cancer Center ambulatory pharmacy identified all RCC and UC patients treated with ICI from 2014 to present. UCLA provided 26 additional patients from the same time period. Prior radiation was defined as completion within 28 days prior to ICI. Fisher's exact 2-tailed test was used to evaluate for associations of variables with irAE.

**Results:** 77 patients with median age 69 years old (49-93) received ICI between 2014-2016 for RCC and UC. 25 (32.5%) had irAE including pneumonitis (4%), myositis (3%), neurologic toxicity (1%), hepatitis (8%), colitis (1%), dermatologic toxicity (8%), endocrinopathy (6%), or hematologic toxicity (1%). 11 (14%) required steroids, 3 (4%) required more intense immunosuppression, and 1 died of complications from irAE (pneumonitis). Among the patients requiring additional immunosuppression, 5 (6%) were rechallenged after steroid tapering. Among patients who experienced irAE, median time to onset of irAEs was 15 weeks (0-112). Earliest onset of irAE (non-dermatologic) was 3 days after 1<sup>st</sup> dose, latest onset was 112 weeks. Associations of irAE with variables are listed in the table.

**Conclusions:** irAEs were more common in our experience than in published datasets, especially endocrine events and could occur after first dose. There was an association between irAE and allergy to antibiotics as well as external beam radiation therapy (EBRT) within 3 months prior to ICI therapy.

		no irAE	
	irAE n=25	n=52	p value
Gender			1.0
Male	19 (76%)	38 (73%)	
Female	6 (24%)	14 (27%)	
Ethnicity			0.69
White	15 (60%)	30(58%)	
Asian/Pacific Islander	5 (20%)	13 (25%)	
Hispanic/Latino	5 (20%)	7 (13%)	
Dosage			0.23
Low (<2 mg/kg)	5 (20%)	8 (15%)	
Medium (2-4 mg/kg)	14 (56%)	38 (73%)	
High (>4 mg/kg)	6 (24%)	6 (12%)	
Agent			0.092
PD-1 Inhibitor	9 (36%)	30 (58%)	
PD-L1 Inhibitor	16 (64%)	22 (42%)	
Prior EBRT			0.031
Yes	3 (12%)	0	
No	22 (88%)	52 (100%)	

Allergy to antibiotic		0.049	
Yes	7 (28%)	5 (10%)	
No	18 (72%)	47(90%)	

# **OPHTHALMOLOGY**

Severity of Visual Field Loss and Health Related Quality of Life in the Chinese American Eye Study <u>Dom Grisafe</u>; Roberta McKean-Cowdin, PhD; Bruce S. Burkemper, PhD, MPH; Mina Torres, MS; Alicia M. Fairbrother, MPH; Farzana Choudhury, PhD; Stanley P. Azen, PhD; XueJuan Jiang, PhD; Benjamin Y. Xu, MD, PhD; Grace M. Richter, MD; Rohit Varma, MD, MPH; for the Chinese American Eye Study Group

**Importance**: Glaucoma is the leading cause of irreversible blindness in the world. Clinical sequelae of glaucoma include repeatable visual field loss (VFL). The relationship between VFL and self-reported health related quality of life (HRQOL) has been examined in White American, Latino American, and Chinese populations.

**Objective**: To examine the association between VFL and HRQOL in Chinese Americans.

**Methods**: The Chinese American Eye Study (CHES) is a population-based cross-sectional study of 10 US census tracts within Monterey Park, California. The interview assessed HRQOL and risk factors. The eye exam tested VFL and other clinical measures. VFL was the primary exposure, and was measured using the Zeiss Humphrey Field Analyzer II 750. Severity of VFL was reported as mean deviation (MD) scores, which were stratified as no VFL (MD $\ge$  – 2 decibels [dB]), mild VFL (6dB<MD<–2dB), moderate/severe VFL (MD<–6dB). HRQOL was the main outcome studied using the Medical Outcomes Study 12-Item Short-Form Health Survey and the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25). Linear regression was used to assess the association between HRQOL and VFL. All statistical analyses were performed using SAS software 9.4 at 0.05 significance level.

**Results**: Previous results have shown an inverse, linear relationship between HRQOL and VFL in various populations. Of the 5,213 subjects studied in the Los Angeles Latino Eye Study, 1.5% had unilateral moderate/severe, 19% had bilateral mild, and 6.5% had bilateral moderate/severe VFL. A 5-point difference in the NEI-VFQ composite score was associated with a 4.5 dB difference in VFL. We suspect the direction and shape of this association in CHES will be similar, but the magnitude of the association will likely vary from previous studies. Increasing VFL had the greatest reduction in driving activities, dependency, mental health, and distance vision subscales of HRQOL. We expect similar HRQOL subscales to be most affected by VFL in the CHES population.

#### Changes observed on retinal OCT possible biomarker for brain disease Alice Laughlin, Dr. Amir Kashani

Brain disease, both cerebrovascular and neurodegenerative, is widespread and difficult to predict. With current brain imaging techniques, pathologic changes do not appear until relatively late in disease. The retina is a direct extension of the brain and is therefore likely perturbed by pathologic brain changes. OCT is a non-invasive, high-resolution imaging technique. Changes observed on retinal OCT may offer insight into brain pathology.

Prior studies have explored RNFL thinning in patients with neurodegenerative disease. Though significant, this finding is highly nonspecific. Here we explore changes in all retinal layers in search of specific findings that correlate with brain disease.

Other synaptic layers (IPL, OPL) may also show thinning. The GCL may thin or thicken due to cell dropout or swelling (chromatolysis).

All analyses will be done without knowledge of any subjects' clinical information. The data set, collected at UCSF, includes retinal scans from 20 subjects with brain disease. All scans (IR or IR-OCT) were

performed using a Heidelberg Spectralis device. Each subject visited 1-4 times for imaging (mean 1.65 visits/subject) for a collective total of 33 visits. At each visit, 3-10 scans were performed per eye.

Automated segmentation will be done using HEYEX software. Computation of layer thicknesses will be done using a MATLAB code. A rough visual inspection of HEYEX's automated segmentation of B-scans suggests that reasonably good accuracy. The quality of this study will depend highly on the accuracy and precision of segmentation. Layer thickness calculations may illuminate the quality of the automated segmentation, indicating possible need for manual adjustments.

If early cellular changes resulting from brain disease are captured on retinal OCT, this could mean earlier diagnosis and intervention. These changes could also be used to monitor disease progression and drug therapy. We investigate changes in retinal layer thicknesses as possible biomarkers.

#### Non-Invasive Clinical Ophthalmic Measurement for Stroke Risk Christine Ryu, Luke Naman, Hossein Ameri, MD, PhD

**Background:** The internal carotid arteries (ICA) are one of the major blood supplies to the brain. While some stenosis of these arteries is common with age, complications include ocular ischemic syndrome, transient ischemic attacks, and thromboembolic strokes.

ICA stenosis decreases the blood flow through its branches, including the ophthalmic artery and the retinal arteries. When blood flow through the retinal arteries is decreased, the vessel walls will be more susceptible to collapse with a rise in intraocular pressure (IOP). For patients with greatly decreased retinal artery blood flow, applying a light pressure on the eyelid increases the IOP, which can cause the retinal arteries to occlude visibly upon examination with an ophthalmoscope. In individuals without compromised blood flow to the retina, this occlusion requires much more pressure.

Carotid ultrasounds are currently used to diagnose or rule out ICA stenosis, the logistics of which can cause a significant delay in treatment. The goal of this project is to evaluate if a simple non-invasive ophthalmoscope exam with eyelid pressure could be used by healthcare providers to quickly screen for carotid stenosis in the office.

**Methods:** Patients who are receiving carotid ultrasounds at LAC+USC Hospital are eligible for this study. I use the direct ophthalmoscope to look at the optic disc and apply pressure on the upper eyelid to increase IOP. The exam is done on both eyes by two people who record if there was occlusion of the retinal arteries with light pressure or not. We then receive the results of the carotid duplex. The results of the ultrasound and ophthalmic exam will then be compared.

**Results/Conclusions:** Data collection is not complete, but we expect that patients with significant ICA stenosis (more than 80%) will have their retinal arteries occluded with light pressure. Patients with less than 50% ICA stenosis are not expected to show retinal artery occlusion with light pressure.

#### Characterization and visualization of iris lesions with Anterior Segment Optical Coherence Tomography (AS-OCT) and Ultrasound Biomicroscopy (UBM) <u>Hyun Jae Seo</u>, Jesse Berry M.D., Dept of Ophthalmology, KSOM

**Goal:** The most common diagnoses of iris lesions are iris nevus, iris pigment epithelium cyst, and iris melanoma. Iris lesions are imaged by AS-OCT and UBM. AS-OCT has limited penetration in the sclera and higher spatial resolution, while UBM has more penetration in the sclera with a lower spatial resolution. Previous literature states that AS-OCT provides better visualization for superficial lesions while UBM provides better visualization for deeper lesions. In our study, we compare the characterization and visualization of iris lesions with AS-OCT and UBM to determine which imaging modality is best indicated

for distinct types and sizes of iris lesions (nevi, cysts, and melanoma) and hope to discover whether both modalities may be informative in certain iris lesions. We hypothesize that AS-OCT will provide better visualization and resolution of thinner, hypopigmented lesions while UBM will provide superior visualization and resolution of thicker, hyperpigmented lesions.

**Methods:** We collected patients with intact iris lesions who were imaged with both modalities. We will conduct data analysis of image features (acoustic features, internal pattern, surface visibility, tumor margin visibility, posterior shadowing, and tumor dimension) and image resolution (tumor visualization, tumor surface, internal structures, pigmentation, and size and location of lesion) for both imaging modalities.

**Results:** Our preliminary results suggest that AS-OCT provides better visualization of thinner, hypopigmented lesions, whereas UBM provides superior visualization of thicker, hyperpigmented lesions. We aim to conduct a more thorough data analysis of image features going forward. **Conclusions:** Our preliminary results agree with our hypothesis and previous literature. This study can help elucidate which imaging modality is best indicated for the type and size of iris lesions.

#### Quantifying Peripapillary Microvasculature Changes Pre- and Post- Trabeculectomy Using Optical Coherence Tomography Angiography

<u>Betty Situ BA</u>, Ryuna Chang BS, Zhongdi Chu MS, Alena Reznik MD, Sahar Bedrood MD PhD, Ruikang Wang PhD, Grace Richter MD MPH

**Background/Purpose**: The only proven treatment to slow glaucoma progression is intraocular pressure (IOP) reduction. However, the mechanism by which this occurs is not fully understood. We hypothesize that IOP reduction improves ocular perfusion evident by changes in peripapillary microvasculature, measured with spectral-domain optical coherence tomography angiography (SD-OCTA). **Methods:** We analyzed 6x6-mm SD-OCTA images of the optic nerve head (ONH) in primary open-angle glaucoma (POAG) patients who underwent trabeculectomy at the USC Roski Eye Institute (n=7). Pre- and post- operative OCTA images (Zeiss AngioPlex) were manually segmented and quantified with prototype software to measure these perfusion parameters in the retinal nerve fiber layer (RNFL) globally and in clock-hour sectors (2.8mm radius annulus excluding disc): vessel area density (VAD), vessel skeletal density (VSD), vessel complexity index (VCI), flow impairment zone (FIZ), and flux. Sector data was evaluated in specific anatomic zones. Paired *t*-tests were used for statistical analysis.



Figure 1. 6x6-mm *en face* ONH image (a.); map of clock hour sectors (b.) for quantification (OD; OS sectors reflected on vertical axis).

**Results:** 7 eyes from 6 patients were analyzed. Mean IOP reduction was 56.6% at time of post-operative imaging (mean 6.5 weeks post-operatively). Combined clock-hour data showed VCI increased 7% (p=.00002), FIZ decreased 24% (p=.001), and flux increased 3% (p=.00002).

Clock-hour 1 had increased VCI (22%, p=0.02) and flux (5%, p=0.01), and decreased FIZ (24%, p=.001). Clock-hours 11 and 12 had increased VAD (12%, p=.003; 17%, p=.02), VCI (18%, p=.002; 29%, p=.002), VSD (12.9%, p=.007; 15%, p=.02), and flux (7%, p=.01; 8%, p=.02).

**Conclusions:** RNFL peripapillary perfusion improved in POAG patients after trabeculectomy and was most pronounced in the inferotemporal regions. Comparing focal anatomic regions side-by-side improved detection of perfusion changes.

#### **Clusterin from Human Clinical Tear Samples**

Valerie Yu, B.S., Dhruva Bhattacharya, Ph.D., Andrew Webster, B.S., Aditi Bauskar, Ph.D., Charles Flowers, M.D., Martin Heur, M.D., Ph.D., Shravan K. Chintala, Ph.D., Tatsuo Itakura, Ph.D., Mark R. Wilson, Ph.D., Joseph T. Barr, O.D., M.S., Shinwu Jeong, Ph.D., Mingwu Wang, M.D., Ph.D. and M. Elizabeth Fini, Ph.D.

**Background/Goal:** Dry eye syndrome is a common affliction characterized by reduced tear flow and/or increased tear evaporation. To focus on the tear film's natural protective properties, there is growing interest in exploring tear proteins, such as clusterin (CLU), as potential biomarkers and biotherapeutics. CLU, which is downregulated in dry eye, is involved in proteostasis and cytoprotection. The goal of our study was to quantify and characterize human tear CLU, and to investigate its relationship to dry eye signs and symptoms.

**Methods:** A primary (44 subjects) and replication cohort (52 subjects) were enrolled at clinical sites in Tucson and Los Angeles, respectively. Clinical tests were performed for dry eye signs and symptoms. Tear samples were collected by Schirmer strip, capillary tube and/or eye wash. CLU was quantified by immunoassay and characterized by western blotting. The correlation between tear CLU concentration and clinical test scores was determined by Pearson's correlation coefficient, followed by multiple linear regression analysis, accounting for repeated measures.

**Results:** Tear CLU concentration was 31±14 ug/mL (n=18 subjects, 33 eyes; range=7-48 ug/mL) in samples collected by capillary tube from a subset of patients with a range of dry eye signs and symptoms. A statistically significant correlation between reduced Schirmer strip head CLU amount and lower Schirmer test results was observed in the primary cohort (slope estimate=0.45, 95%CI=0.07-0.82, p=0.021) and confirmed in the replication cohort (slope estimate=0.42, 95%CI=0.09-0.75, p=0.013). Tear CLU of a normal subject appeared biochemically similar to blood plasma CLU. No consistent differences were observed in patient samples.

**Conclusions:** The results suggest that reduced tear CLU concentration could serve as a biomarker for dry eye and treatment response. The results further support the therapeutic use of topical CLU supplementation, provide information for dosage, and might be used to identify the patients who will most likely benefit.

#### Extending Far and Wide: The Role of Biopsy and Staging in the Management of Ocular Surface Squamous Neoplasia

Ashley Polski, BS, Maria Sibug Saber, MD, Jonathan W. Kim, MD, Jesse L. Berry, MD

**Purpose:** Ocular surface squamous neoplasia (OSSN) is staged based on invasiveness on biopsy as outlined by current American Joint Committee on Cancer (AJCC) staging criteria. Invasive lesions involving multiple ocular surface structures are stage T3, whereas non-invasive tumors of similar extent

are stage Tis. This retrospective study investigates the impact of staging on treatment, recurrence, and imaging features of OSSN.

**Methods:** Out of 41 eyes with OSSN, 27 cases involving multiple ocular surface structures were analyzed for demographics, anterior segment optical coherence tomography (AS-OCT) features, and outcomes. Biopsied tumors were staged as T3 or Tis; others were clinically identified but unstaged. Fisher's exact test and Student's t-test were used to compare categorical and quantitative variables, respectively. **Results:** Twelve tumors (44%) were initially treated with excisional biopsy, whereas 10 (37%) received chemotherapy without biopsy and 5 (19%) received chemotherapy and biopsy (either incisional or post-recurrence). Medically treated tumors took longer to resolve (p = 0.0056) than excised tumors, but there were no significant differences in recurrence when comparing excision and chemotherapy; however, there was a trend toward larger basal diameter in recurrent tumors regardless of initial treatment. There were no significant differences in demographic or clinical variables between stage T3 and Tis tumors, and staging was not predictive of treatment response or recurrence.

**Conclusions:** For OSSN involving multiple ocular surface structures, staging is limited in guiding or predicting response to therapy. Future staging criteria may consider the potential of largest basal dimension instead of biopsy to more accurately predict outcomes and guide management of OSSN.

# ORTHOPAEDIC Surgery

## Pre-Operative MRSA Swab Results do not Predict Surgical Site Infections in Children undergoing a Varus Derotational Osteotomy

Alexander Nazareth, MS; Rachel Goldstein, MD; Lindsay Andras, MD; Sukhraj Bains, BS; Robert M. Kay,

Children's Hospital Los Angeles

**PURPOSE:** The purpose is to determine if preoperative MRSA nasal swab results were predictive of surgical site infections (SSIs) in children undergoing a varus derotational osteotomy (VDRO). **METHODS:** We performed a retrospective chart review of patients who underwent a VDRO from 2004-2016 to determine pre-operative MRSA colonization rates, SSI rates and organisms. Patients with less than one-year follow-up, previous history of infections, or no pre-operative MRSA swab were excluded. **RESULTS:** 122 patients were studied (mean age at surgery:  $9.5 \pm 3.9$  years, 65% male). Diagnoses included Cerebral Palsy (N = 109), hip dysplasia (N = 8) and recurrent hip dislocation (N =5). 119 (97.5%) patients had a negative MRSA swab and 3 (2.5%) patients had a positive MRSA swab. 3/119 (2.5%) in MRSA swab negative patients and 0/3 (0%) in MRSA swab positive patients developed a SSI. SSIs were treated with oral antibiotics (N = 2) or surgical irrigation and debridement (N=1). 2/3 SSIs cultured isolated organisms: P. aeruginosa and MSSA. There was no significant difference in SSI rates between MRSA swab positive (0) vs. negative patients (3) (p = 0.75).

**CONCLUSION:** The results of a pre-operative MRSA nasal swab had no relationship to SSI incidence in patients undergoing VDRO surgery; therefore, pre-operative MRSA nasal swabs may be of limited benefit in routine pre-operative evaluation to predict post-op infections, although they are useful to prevent transmission of this agents to other patients.

#### The Efficacy of Platelet-Rich Plasma on Tendon and Ligament Healing: A Systematic Review and Meta-Analysis

Xiao Chen, Ian A Jones, Caron Park, Thomas Vangsness Jr., MD

**Background:** There has been a surge in high-level studies investigating platelet-rich plasma (PRP) for tendon and ligament injuries. A number of meta-analyses have been published, but few studies have focused exclusively on tendon and ligament injuries.

**Methods:** This study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A comprehensive search of the literature was carried out in April 2017 using electronic databases PubMed, MEDLINE, and the Cochrane Library. Only level 1 studies were included. The short-term and long-term efficacy of PRP was assessed using the visual analog scale (VAS) to measure pain intensity. Injury subgroups (rotator cuff, tendinopathy, anterior cruciate ligament, and lateral epicondylitis) were evaluated. Funnel plots and the Egger test were used to screen for publication bias, and sensitivity analysis was performed.

**Results:** Thirty-seven articles were included in this review, 21 (1031 participants) of which could be included in the quantitative analysis. The majority of studies published investigated rotator cuff injuries (38.1%) or lateral epicondylitis (38.1%). Overall, long-term follow-up results showed significantly less pain in the PRP group compared with the control group (weighted mean difference [WMD], -0.84; 95% CI, -1.23 to -0.44; P < .01). Patients treated with PRP for rotator cuff injuries (WMD, -0.53; 95% CI, -0.98 to -0.09; P = .02) and lateral epicondylitis (WMD, -1.39; 95% CI, -2.49 to -0.29; P = .01) reported significantly less pain in the long term. Substantial heterogeneity was reported at all timepoints. The funnel plot appeared to be asymmetric, with some missingness at the lower right portion of the plot suggesting possible publication bias.

**Conclusion:** This review shows that PRP may reduce pain associated with lateral epicondylitis and rotator cuff injuries.

MD

#### The Incidence of Plafond Impaction in OTA/AO 44C2 Ankle Fractures and the Role of Computed Tomography in Diagnosis and Surgical Planning.

J. Feldsher MSII, R. Alluri MD, P. Navo MD, G. Marecek MD

**Purpose/Goal**: The purpose of the study was to investigate and report the frequency of incidence of anterolateral plafond impaction protonation-abduction ankle fractures, and to also evaluate the use of plain radiographs vs. CT studies in the examination of these fractures.

**Methods**: Our data pool included imaging studies performed on all patients who presented at LAC + USC Medical Center (a level I trauma center) from 2005-2017, with an OTA/AO 44C2 ankle fracture. These patients were identified retrospectively and only injuries with complete preoperative radiographs were included. The total number of patients with radiographs available was 61. In part one of this study, each set of radiographs was evaluated by three fellowship-trained orthopaedic surgeons who were asked a series of questions: (1) Is there impaction of the tibial plafond? (2) Does the impaction require direct visualization and articular reduction? For the 9 patients who also had CT studies available along with their radiographs, the CT's were evaluated by the same surgeons and the same questions were asked. The incidence of plafond impaction and the preoperative plan were calculated separately for plain radiographs and CT scans. The accuracy of plain radiographs to detect impaction was calculated using responses from corresponding CT imaging in part 2 as the gold standard. Changes in the diagnosis and planned management of impaction caused by the availability of CT imaging when possible, as well as corresponding inter-observer correlation, were also measured.

**Results**: Sixty-one OTA/AO 44C2 ankle fractures were identified with preoperative radiographs, 9 of these fractures had corresponding CT imaging done as well. The average age of each subject included on this study was 38 years, with 67% of the patients being male. On plain radiographs anterolateral plafond impaction was described in 37% of fractures. This diagnosis was correct in 67% of fractures when compared to CT imaging, indicating 80% sensitivity and 75% specificity for plain radiographs. In cases where both radiographs and CT imaging studies available, direct visualization and articular reduction of plafond impaction was recommended in 18% of fractures after reviewing plain radiographs, and 40% of fractures after reviewing CT imaging. The preoperative plan was altered in 2 cases (22%) patients (P=0.07); for both changes, surgeons recommend direct visualization and articular reduction of the impacted fragments after reviewing the CT imaging. The inter-observer correlation for detecting impaction on plain radiographs and CT imaging was 0.64 and 0.67, respectively. The inter-observer correlation for planned management of impaction based on plain radiographs and CT imaging was 0.75 and 0.67, respectively.

**Conclusion**: The suspicion for the presence of anterolateral marginal impaction of the tibial plafond should be present when evaluating patients with OTA/AO 44C2 (pronation-abduction) ankle fractures. In these cases, 37% of fractures demonstrated impaction on plain radiographs. Of the fractures that demonstrated impaction on radiographs and had CT's available for comparison, the diagnosis based on radiographs was incorrect 33% of the time, and also after comparison between the two, operative planning changed in 22% of patients. In the presence of impaction on plain radiographs, CT imaging should be considered to better evaluate the fracture fragment and determine whether a direct articular reduction is the best course of management.

Risk Factors for Early Revision ACL Reconstruction: A Retrospective Database Study <u>Matthew C. Gallo<sup>1</sup> BA</u>, Santano Rosario<sup>1</sup> BA, Alexis Rounds<sup>1</sup> BS, Paul Navo<sup>1</sup> MPH, K. Soraya Heidari BA<sup>1</sup>, Erik N Mayer BS<sup>1</sup>, Nicholas A. Trasolini<sup>1</sup> MD, Alexander Weber<sup>1</sup> MD, George F. "Rick" Hatch III<sup>1</sup> MD <sup>1</sup>Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA **Background**: It is not well understood whether risk factors for early revision anterior cruciate ligament reconstruction (ACLR) are age-dependent. Therefore, the purpose of this study is to evaluate age-specific risk factors for early revision ACLR in a large, population-based cohort.

**Methods**: This study was performed using patients who underwent primary ACLR in the California Office of Statewide Health Planning and Development (OSHPD) Ambulatory Surgery Database (2005-2014). The primary endpoint was aseptic revision. Age groups were defined as <21, 21-30, 31-40, and >40 years old at the time of primary ACLR. Survival analyses were performed and risk factors including age, sex, race/ethnicity, and insurance type were assessed within each age group.

**Results**: This study evaluated 101,089 subjects who underwent primary ACLR. The overall 2-year incidence rate of revision ACLR was 1.6 (95% CI 1.6-1.7) per 100 person-years. Those aged <21 years had the highest 2-year incidence rate (2.5, 95% CI 2.3-2.6), while those aged >40 years had the lowest (1.3, 95% CI 1.2-1.4). Across all four age groups, a decreased revision risk was observed in older patients (HR, 0.84, 0.84, 0.90, 0.96, for age groups < 21, 21-30, 31-40, > 40) and in Hispanic patients compared to white patients (HR, 0.71, 0.74, 0.71, 0.71) (**Table 1**). Sex showed no association with revision. Insurance type as a risk factor for revision varied in significance by age group, but in the overall cohort, claiming Workers' Compensation was associated with a 1.40 times (95% CI 1.23-1.59) greater likelihood of revision ACLR at 2 years compared to private insurance (**Table 1**).

**Conclusion**: This study demonstrates that rates of 2-year revision ACLR are low and patient-specific risk factors for revision including age, sex, race, and insurance type are age-dependent. Our results may help physicians better identify and counsel patients that may require closer follow-up after primary ACLR.

	Age Groups				
	<b>Overall</b>	< <b>21</b>	<b>21-30</b>	<b>31-40</b>	> <b>40</b>
	n = 101,089	n = 23,342	n = 24,654	n = 25,642	n = 27,451
Age at primary ACLR	0.97 (0.97-0.97)	0.84 (0.83-0.87)	0.84 (0.82-0.87)	0.90 (0.88-0.93)	0.96 (0.95-0.97)
	p <0.001	p <0.001	p <0.001	p <0.001	p <0.001
Female	1.05 (0.97-1.13)	0.97 (0.85-1.09)	0.93 (0.79-1.11)	0.87 (0.72-1.04)	1.06 (0.91-1.25)
(reference Male)	p = 0.17	p = 0.58	p = 0.49	p = 0.14	p = 0.46
Race/Ethnicity (reference White)					
Black	0.85 (0.72 - 1.00)	0.87 (0.69-1.09)	0.86 (0.99-1.74)	0.79 (0.52-1.21)	0.66 (0.40-1.11)
	$\mathbf{p} = 0.05$	p = 0.22	p = 0.42	p = 0.29	p = 0.12
Hispanic	0.71 (0.64-0.78)	0.71 (0.61-0.83)	0.74 (0.61-0.91)	0.71 (0.57-0.87)	0.71 (0.56-0.91)
	p <0.001	p < <b>0.001</b>	<b>p</b> = 0.004	<b>p</b> = <b>0.001</b>	<b>p</b> = <b>0.006</b>
Asian/Pac Islander	0.75 (0.65-0.86)	0.74 (0.59-0.94)	0.85 (0.65-1.11)	0.82 (0.62-1.10)	0.61 (0.41-0.91)
	<b>p</b> < <b>0.001</b>	<b>p</b> = <b>0.01</b>	p = 0.19	p = 0.19	$\mathbf{p} = 0.02$
Native American	0.88 (0.49-1.60)	0.78 (0.25 - 2.43)	not enough	1.74 (0.72-4.21)	1.01 (0.32 - 3.13)
	p = 0.68	p = 0.67	observations	p = 0.22	p = 0.99
Other	0.85 (0.70-1.03)	0.99 (0.72 - 1.34)	0.71 (0.46-1.09)	0.95 (0.63-1.44)	0.78 (0.47-1.28)
	p = 0.10	p = 0.93	p = 0.12	p = 0.80	p = 0.32
Not Reported	1.00 (0.86-1.17)	0.87 (0.64-1.19)	1.31 (0.99-1.74)	0.90 (0.65-1.25)	1.01 (0.74-1.38)
	p = 0.99	p = 0.40	p = 0.06	p = 0.53	p = 0.95
Payer (reference Private)					
Public	1.07 (0.94-1.22)	0.69 (0.56-0.84)	0.94 (0.67-1.31)	1.77 (1.33-2.35)	1.91 (1.45-2.51)
	0.94	p <0.001	0.72	p <0.001	p <0.001
Workers' Comp	1.40 (1.23-1.59)	1.14 (0.65-1.97)	1.20 (0.91-1.58)	1.74 (1.40-2.17)	1.49 (1.20-1.85)
	p <0.001	0.64	0.19	p <0.001	p <0.001

Table 1. Patient-Specific Risk Factors for Revision ALCR Reported as Hazard (95% CI).

#### Radiographic Relationship Between the Lateral Tibial Plateau and Lateral Femoral Condyle in Normal Adult Knees

Daniel Jiang, Nima Kabirian, Mark Fleming, Geoffrey Marecek, USC Department of Orthopaedic Surgery

**Introduction:** Condylar width is an important measure of knee alignment in the operative treatment of tibial plateau fractures. However, a method for restoring proper condylar width has not been described. We hoped to find a "normal" relationship between the lateral tibial and femoral condyles. We also sought to determine if the contralateral knee can serve as a guide for determining a patient's "normal" alignment.

**Methods:** True anteroposterior non-weight bearing plain radiographs of 325 uninjured adult knees (including bilateral knees in 108 individuals) between 18 to 65 years old with no or minimal osteoarthritis were included. We measured the horizontal distance between the lateral end of the tibial plateau articular surface (A) and both the lateral femoral epicondyle (B) and lateral end of the femoral condyle articular surface (C). Measurements were made perpendicular to a line drawn along the articular surface of the tibial plateau, in millimeters (mm) with medial and lateral to point (A) recorded as (-) and (+), respectively. In patients with bilateral radiographs, measurements (A-B) and (A-C) were compared between right and left knees (two-tailed t-test, alpha = 0.05).

**Results:** The lateral aspect of the tibial plateau was a mean of  $0.60 \pm 2.40 \text{ mm}$  (range= -4.82 to +6.49) away from the lateral epicondyle (A-B) and -3.96  $\pm 2.07 \text{ mm}$  (range= -8.51 to +3.98) away from the lateral aspect of the femoral condyle articular surface (A-C). No significant difference was found between A-B (Right= +1.08 mm, Left= +0.90 mm, p= 0.083) and A-C (Right= -3.90 mm, Left= -4.31 mm, p= 0.56) in bilateral knee radiographs.

**Discussion and Conclusion:** There is significant variability in the relationship between the lateral tibial plateau and the lateral femoral epicondyle and the lateral femoral articular surface. However, the relationship between a patient's left and right knees is consistent; the contralateral uninjured knee is a suitable reference for restoring condylar width.



#### Analyzing Complications following Shoulder Arthroplasty utilizing a Retrospective Shoulder Registry Jae Kim Medical Student, Alexis Rounds Medical Student, Alexander Weber MD, Keck School of Medicine

**Background**: Approximately 53,000 Americans undergo a shoulder replacement each year. Despite the large volume of shoulder replacements being performed, many questions remain regarding the best surgical practices and the longevity of the implants being used. At USC, it is estimated that approximately 200-300 shoulder replacements are performed each year by our six orthopaedic sports medicine and shoulder surgeons. One of the most effective ways of studying the implants used in shoulder replacement and the clinical outcomes of the patients undergoing the procedure is to create a shoulder replacement registry. Other large national databases lack specific data on variables such as laterality or chronology of related surgeries, while single institution databases are often much smaller sample sizes. We hope to solve both those issues by having a large sample size along with the specificity that we can obtain from having direct access to patients' charts.

**Methods**: Through the use of i2b2/Cerner we will perform a database query that will extract every patient who has undergone a hemi, total, or reverse shoulder arthroplasty at Keck Medical Center from a cohort of six attending surgeons. From that initial query, we will manually enter in patient data gleaned from individual chart data in order to explore factors that affect patient health and outcomes. **Results**: We expect to build a database of approximately 1000-1500 patients from the years 2010-2016, in order to collect data with at least a 2-year minimum follow up. From this database we hope to ask a multitude of questions that will impact future patient care.

**Conclusion**: This project has the potential to become the foundation for multiple strong single institution projects involving patients undergoing shoulder arthroplasty.

Validation of PROMIS Computer Adaptive Testing for Multi-Ligament Knee Reconstruction <u>Shane Korber BS<sup>1</sup></u>, Nicholas A. Trasolini MD<sup>1</sup>, Aaron Gipsman MD<sup>1</sup>, Alexis Rounds BS<sup>1</sup>, Emily Clarke BS<sup>1</sup>, Santano Rosario BA<sup>1</sup>, Alexander Weber MD<sup>1</sup>, George F. "Rick" Hatch III MD<sup>1</sup> <sup>1</sup>Keck School of Medicine, University of Southern California, Los Angeles, CA

**Introduction:** Knee dislocations leading to multiple-ligament knee injuries (MLKI) are uncommon, but can lead to limb-threatening complications. Existing patient-reported outcome measures for MLKI are time-intensive. PROMIS Computer Adaptive Testing (CAT) is a newer metric with potential to simplify and hasten collection of patient-reported outcomes. Recent literature has validated the PROMIS score for ACL and meniscal injuries. The purpose of this study was to validate the PROMIS score relative to existing instruments for quality of life and function in patients following multiple-ligament knee reconstruction.

**Methods:** Patients who underwent multiple-ligament knee reconstruction by a single surgeon between 2014 and 2017 were retrospectively identified. The 8-item Tegner Activity Scale (TAS), 52-item Multiligament Quality of Life Questionnaire (ML-QOL), and PROMIS Computer Adaptive Testing (CAT) for Physical Function, Mobility, and Pain Interference were prospectively administered. Spearman correlations were used to assess agreement across survey instruments.

**Results:** The surveys were administered to 21 patients (19 male; aged 35.1<u>+</u>13.2 years; BMI 29.9<u>+</u>7.1). The PROMIS CAT was significantly shorter than MLQOL with an average of 15.3 questions (5.71 Pain Interference, 4.24 Physical Function, 5.38 Mobility), but still nearly twice the TAS. PROMIS Mobility and Pain Interference were significant correlated with TAS, ML-QOL Physical Impairment and Activity Limitations. Additionally, PROMIS Pain Interference was significantly correlated with all subsections of ML-QOL (Physical Impairment, Emotional Impairment, Activity Limitation, and Societal Involvement).

**Discussion and Conclusion:** The PROMIS CAT system has great correlation with existing outcome measures which supports its use for patients with multiple-ligament knee injuries. Given the concise nature of the PROMIS CAT, it may have better utility than the ML-QOL instrument. This warrants further research on patient satisfaction and time saved rather than number of questions.

#### Cost Analysis of Surgical Rotator Cuff Repair in the Worker's Compensation Population Kevin Maniar, Ian Jones, C. Thomas Vangsness, Jr., MD

**Background:** Rotator cuff tears are a highly prevalent and age-related condition associated with both wear and tear and acute trauma. Symptomatic rotator cuff tears can prove burdensome due to pain and loss of function, and surgical repair is often required. With the age-associated nature of rotator cuff tears, they will be particularly burdensome to the workforce which is projected to increase in age over the coming years. Many of these injuries will fall under the coverage of workers' compensation insurance. This study sought to analyze costs of surgical repair in a workers' compensation population compared to a non-workers' compensation population.

**Methods:** The Cerner Health Facts<sup>®</sup> database was used to generate a workers' compensation population and a non-workers' compensation population. Billed costs for surgical repair and all other costs incurred during the surgery-associated stay were compared in the two populations. Furthermore, an odds ratio analysis identified variables that were associated with the workers' compensation population. The role of these variables as causative drivers of cost were explored.

**Predicted Results:** The cost per patient is expected to be higher in the workers' compensation population compared to the general population. Specific variables that could be statistically significantly for increased cost in the workers' compensation patient include type of surgery, revision surgery status, length of hospital stay, time from initial presentation to surgery, type of hospital, age, and insurance provider.

**Desired Conclusions:** If the workers' compensation population does indeed have increased costs, the goal is to identify possible causative drivers. A discussion on the data in this study will be supported by the existing literature on rotator cuff repair surgery.

# Conversion Rates and Timing to Total Knee Arthroplasty following ACL Reconstruction: A United States Population-Based Study

<u>Cory Mayfield</u>, Jacob Bobman, Nathanael Heckmann, Alexander Weber, C. Thomas Vangsness, George. F. "Rick" Hatch

**OBJECTIVES:** Anterior cruciate ligament (ACL) injuries are extremely common and may predispose patients to post-traumatic osteoarthritis. ACL reconstruction (ACLR) is commonly performed to restore knee stability and prevent secondary meniscal and osteochondral pathology. Despite this, many patients that undergo ACLR eventually require total knee arthroplasty (TKA). However, limited data exists that explores the conversion rates between ACLR and future TKA. The purpose of this study is to investigate ACLR conversion rates and timing to TKA in a large population-based cohort study.

**METHODS:** We analyzed California's Office of Statewide Planning and Health Development (OSHPD) data from 2000-2014 who underwent primary ACLR. Exclusion criteria included prior distal femur or tibial plateau trauma, prior osteotomy, inflammatory arthroplasty, osteonecrosis, skeletal dysplasia, age <18, multi-ligamentous knee injuries, and prior patellar tendon or quadriceps tendon repair. Failure was defined as conversion to TKA. Subgroups were analyzed on the basis of concomitant procedures: osteochondral autograft, osteochondral allograft, meniscus transplant, synovectomy, chondroplasty, microfracture, meniscus debridement, and meniscus repair; and further subdivided based on age at the

time of surgery. Ten-year survival was performed using Kaplan-Meier analysis with significance defined as p < 0.05.

**RESULTS:** Preliminary data illustrates a total of 114,427 ACLR procedures (41,126 male, 73,266 female, avg age = 32.21±0.04 years) with an overall 2, 5, 10 and 15 year survival rate of 99.30%, 98.15%, 95.17% and 90.52%, respectively. As patient age increased, the survival decreased. (Figure 1) Of the patients identified, 50,427 underwent an isolated ACLR with no other concomitant procedure (20,093 male, 30,315 female, avg age = 31.03±0.05 years) with 1,748 (1.49%) eventually requiring a TKA (821 male, 927 female, avg age 54.4±0.24 years), 10-year survival of 96.07%. This isolated ACLR demonstrated worsening 15-year survival rates with increasing age (18-30yr at 99.48%; 31-40yr 97.89%; 41-50yr 89.63%; 51-60yr 83.26%; >60yr 77.42% failure rate). In regard to concomitant procedures, 616 patients underwent osteochondral autograft, 855 underwent osteochondral allograft, 63 underwent meniscal transplant, 5,945 synovectomies, 4,582 chondroplasties, 3,728 microfractures, 55,359 meniscal debridement, and 10,495 meniscal repair (Table 1). Ten-year survivorship based on concomitant procedures were computed and stratified according to age. (Table 1) Patients with an isolated ACLR and patients with a concomitant meniscal repair had the highest 10 year survival (96.07% and 98.91%, respectively), while patients undergoing microfracture or osteochondral allograft had the worst (89.83% and 89.60%, respectively). **CONCLUSION**: Patients across all age groups had good to excellent long-term survival rates following ACLR. Increasing age and patients who underwent a concomitant microfracture or allograft procedure required a TKA at higher rates. These findings will help provide surgeons with information to counsel patients about their likelihood of needing a total knee arthroplasty following their ACLR.

#### Functional Outcome Assessment Following Supination-Adduction Ankle Fractures and Open Reduction Internal Fixation Surgery

<u>Sabrina Serrano Medical Student</u>, Kiran Alluri, M.D., Geoffrey Marecek, M.D., Dept. of Orthopaedic Surgery, KSOM

**Background**: As the SAD-II ankle fracture is rare compared to other orthopaedic injuries, there is little consensus regarding their management. To determine the optimum techniques for treating SAD-II fractures, the outcomes of patients were analyzed via a telephone survey. The goal of this study is to compare outcomes of patients who had their ankle joint either opened or left closed during surgery. The hypothesis is that patients who had their ankle joint opened would have worse outcomes compared to the patients with intact joints.

**Methods:** All patients in the study population were evaluated for an isolated SAD-II fracture between 2006-2016. Patients were identified by diagnosis from the orthopaedic trauma census, located within LAC+USC's electronic medical records. Patients were telephoned to fill out a PROMIS survey to assess their functional status and pain management after their surgery. Two cohorts will be created based on if the patient's ankle joint was opened. For statistical assessment, an unpaired t-test will be used for comparison.

**Results:** The expected results are that opening the ankle joint during surgery causes increased injury and will prolong a patient's recovery time. It was predicted that patients who had their ankle joint opened had a more extensive injury prior to surgery than those whose ankle joints were left intact. Therefore, the results are predicted to show a difference between cohorts; patients with opened ankle joints will have lower scores on the PROMIS survey.

**Conclusions:** These data will demonstrate evidence for developing improved surgical techniques to repair SAD-II ankle fractures. The benefit from this study is to show the risk versus benefits for opening the ankle joint. The research study will provide additional information concerning how to address SAD-II fractures and provide a basis for future research studies to improve surgical techniques and maximize functional outcomes.

# Postoperative complications in adult spinal deformity patients with a mental illness undergoing reconstructive thoracic spine surgery

Ishan Shah, BA, Zorica Buser, PhD, Jeffrey Wang, MD

**Background:** Surgeries for adult spinal deformity patients have been steadily increasing in popularity. Previous studies have found an association between mental illness and poor outcomes in spinal surgery, but not much is known about its effect on the adult spinal deformity population. In addition, most relevant studies have focused on the lumbar spine and have a smaller patient sample size. The aim of the study was to investigate whether adult spinal deformity patients with a mental illness have an increased risk of postoperative complications and reoperation following posterior thoracic reconstructive spinal surgery.

**Methods:** Adult spinal deformity patients over 18 years of age undergoing any reconstructive thoracic spinal procedure from a posterior approach between 2007 and 2015 Q2 were identified using the Pearl Diver patient record database (Pearl Diver Technologies, West Conshohocken, PA, USA). The database includes records of approximately 18 million patients across the United States. Further selection of patients with a mental illness and their associated postoperative complications were identified using ICD-9 and ICD-10 diagnosis codes. Patients' data was analyzed for incidence of various complications and reoperative rates against a matched control group.

**Results:** The mental illness cohort (n=411) had significantly increased rates of some complications at the 90-day and/or 1-year intervals including: incision and drainage (90-days: OR 1.856, P = 0.046; 1-year: OR 1.917, P = 0.011), infection (90-days: OR 1.558, P = 0.028), and respiratory complications (90-days: OR 1.436, P = 0.015; 1-year: OR 1.438, P = 0.012).

**Conclusions:** Patients with adult spinal deformity and pre-existing depression and/or anxiety treated with a posterior thoracic or thoracolumbar reconstructive spinal surgery have significantly elevated risk of postoperative infectious and respiratory complications when compared with a control group.

#### Prevalence and Treatment of Humeral Head Avascular Necrosis in Transplant and Bariatric Surgery Patients: A Population-Based Study

<u>Kavitha Thiagarajan BA<sup>1</sup></u>, Erik N. Mayer BS<sup>1</sup>, Keemia Soraya Heidari BA<sup>1</sup>, Alexis Rounds BS<sup>1</sup>, Geoffrey S. Marecek MD<sup>1</sup>, C. Thomas Vangsness Jr. MD<sup>1</sup>, George F. "Rick" Hatch III MD<sup>1</sup>, Alexander E. Weber MD<sup>1</sup> <sup>1</sup>Keck Hospital Department of Orthopedic Surgery, Los Angeles, CA

**INTRODUCTION**: Humeral head avascular necrosis (HHAVN) is uncommon; however, the condition causes significant shoulder morbidity. The purpose of this study was to compare the rates of HHAVN and the rates of surgical treatment for HHAVN in high-risk patient populations (transplant and bariatric surgery patients) versus controls.

**METHODS**: Data from California's Office of Statewide Planning and Health Development (OSHPD) database from 2000-2014 was analyzed. ICD-9 codes were utilized to identify patients that had previously undergone an appendectomy (control group), and patients that had prior bariatric or transplant surgery. ICD-9 procedure codes for shoulder hemiarthroplasty, total shoulder arthroplasty (TSA), and reverse total shoulder arthroplasty (RTSA) were analyzed. Odds ratios were calculated to determine the risk of developing HHAVN and the need for subsequent treatment.

**RESULTS**: In a population of 793,083 patients, AVNHH was diagnosed in 0.007% of controls, 0.09% of transplant patients, and 0.02% of bariatric patients. We found that transplant patients had a twelvefold risk of HHAVN compared to controls (OR = 12.14, p < 0.001), while bariatric patients had a 1.76x risk of HHAVN compared to controls (OR = 1.76, p = 0.018). Bariatric patients with HHAVN were 3.6 times more likely to have a shoulder procedure than control HHAVN patients (OR = 3.63, p = 0.010). Transplant patients with HHAVN were 1.4 times as likely to have a shoulder procedure as control HHAVN patients,

but this was not significant (OR = 1.40, p = 0.472). The distribution of shoulder procedures was not significantly different between groups, with shoulder hemiarthroplasty being the most frequent procedure.

**DISCUSSION AND CONCLUSIONS**: Patients undergoing transplant or bariatric surgeries have a significantly increased risk of HHAVN compared to controls. In addition, bariatric patients are more likely to require shoulder arthroplasty for HHAVN. This large, population-based study provides surgeons patient-related data to aid in counseling and treating this challenging patient population.

#### The Affects of Mental Health Medications on Cervical Spine Surgery Outcomes Christopher Wang Medical Student, Zorica Buser Advisor

**Goal:** There is growing literature documenting the negative impact comorbid psychological conditions have on the outcomes of spine surgery. The confluence of a steadily increasing rate of cervical spine surgeries with the already significant prevalence of psychological conditions throughout the U.S. makes this topic one of particularly high impact. There is scarce literature involving the possible impact that medications taken for psychological conditions could be having on spine surgery outcomes. This project aims to observe mental health medications as a possible comorbidity for cervical spine surgery outcomes.

**Methods:** This will be a retrospective study utilizing Pearldiver Technologies to access the Humana insurance patient database. The program Sublime will be used to code an applicable program that will aggregate the data relevant to this study from the Humana insurance database. Statistical analysis of the data will also be achieved through coding run on the Pearldiver Technologies server.

**Results:** Adequate data has not yet been obtained to ascertain results. However, it is anticipated that mental health medications will increase the number of post-operative complications in cervical spine surgery. If this is not observed then the lack of effect on post-operative complications will also be a novel observation.

**Summary:** The data from the study will shed light on a clinical relationship that is not well understood, but clinically observed. The frequency of cervical spine surgeries is steadily increasing, so understanding a prevalent comorbidity negatively impacting the surgery's outcome will bring about safer clinical practices.

#### **Optimal Management of Long Bone Fractures Secondary to Ballistic Injury**

**Robert Weller, MS2**; Ali Azad, M.D., PGY4 Orthopedic Surgery; Geoffrey Marecek, M.D. Assistant Professor of Clinical Orthopedic Surgery

**Goal:** The treatment for gunshot injuries resulting in fractures to long bones is open reduction with internal fixation, but the benefit of simultaneous irrigation and debridement is unclear. There is a lack of data necessary to support either the use or avoidance of irrigation and debridement in the treatment of these injuries. Our goal is to compare the rates of infection, the necessity for repeated surgical intervention, and other adverse health outcomes between the two treatment options.

**Methods:** Patients presenting to LAC+USC between January 1, 2010 and January 1, 2016 with gunshot wounds resulting in fracture to long bones requiring open reduction and internal fixation are included in this retrospective chart review. Differences in health outcomes including rates of infection, return to OR, and clinical and radiographic union are compared with respect to cohort demographics, type of injury, and choice of intervention.

**Results:** The data collection is mostly complete but not all the cases have been vetted against the exclusion criteria. Rigorous statistical analysis has not yet been performed. Currently, infection rates are 0% (0/53) for wounds not treated without surgical debridement, and 2.7% (1/37) for wounds treated

with debridement. After further data analysis, the expectation is that adverse health outcomes will not differ significantly between the two groups.

**Conclusion:** Fractures secondary to GSWs are relatively common major injuries requiring intensive intervention and follow-up, so it is worthwhile to find the most appropriate treatment modality. This study will add to the body of evidence available to achieve this goal. If there is no significant difference in adverse health outcomes between the two treatment options, then differences in cost and resource effectiveness should be considered in determining a standard of care for patients with these injuries.

Effect of Pre-Operative Opioid Usage on Pain Following Total Shoulder Arthroplasty <u>William Curtis BS</u>, Alexis Rounds BS, Santano Rosario BS, Michael Stone MD, Alexander Weber MD, George F. Hatch III MD, C. Thomas Vangsness Jr MD, Reza Omid MD

**INTRODUCTION:** Opioid pain medications are a mainstay of chronic shoulder pain management. However, recent research indicates that preoperative opioid use may be associated with increased postoperative pain following arthroplasty. Furthermore, recent studies have shown increased risk of prolonged postoperative opioid use in patients after total knee arthroplasty and anterior cruciate ligament reconstruction. The purpose of this study is to evaluate the effect of preoperative usage of opioid pain medications on postoperative pain levels following total shoulder arthroplasty (TSA). **METHODS:** We conducted a retrospective review of a prospectively maintained database of patients undergoing anatomic total shoulder arthroplasty or reverse total shoulder arthroplasty by four orthopaedic surgeons at one academic institution between January 2013 and April 2017. Patients were stratified based on opioid use within four weeks prior to TSA and followed for up to two years. Pre- and postoperative pain numerical rating scale (NRS) and postoperative opioid use were assessed, with a minimal clinical important difference of 1.4 points.

**RESULTS:** We identified 138 TSAs (97 reverse, 41 anatomic), 50 (36.23%) with preoperative opioid use, and 88 (63.77%) without preoperative opioid use. The opioid cohort showed significantly greater resting and active NRS pain scores at all follow-up visits up to two years postoperatively and at final follow-up with the exception of resting NRS pain scores at one year. At three months postoperatively, the opioid cohort showed a mean resting NRS score 1.59 points greater than the non-opioid cohort (3.00±2.60 vs. 1.41±1.89, P<0.0001). The non-opioid cohort had greater improvements in pain with activity when compared to baseline at all follow-up time-points. Preoperative opioid use was the strongest predictor of postoperative opioid use at all follow-up time-points.

**DISCUSSION AND CONCLUSION:** Preoperative opioid consumption is associated with higher NRS pain scores and increased duration of opioid use following TSA.

# OTOLARYNGOLOGY

#### **Extent of microscopic disease superior to the hyoid bone in children with a thyroglossal duct remnant Erick Garcia**, Beth Osterbauer MPH, David Parham MD, Ramzi Bawab, Jared Shows, Jeffrey Koempel MD, MBA

**Background:** Despite the success of the Sistrunk procedure, recurrence of thyroglossal duct cyst, sinus or remnant (TGDR) following excision remains a clinical problem; likely due to the presence of microscopic disease in the suprahyoid region which cannot be seen or palpated at the time of surgery. As a result, the amount of tissue to be excised in this area remains unclear. To date, few studies have a specific focus on disease in the suprahyoid area. None have determined the extent of disease in this area.

**Objective:** The primary aim of this study is to determine the extent of microscopic disease in the suprahyoid area in pediatric patients with a TGDR.

**Methods:** A retrospective review was conducted of specimens from 25 children between 3 months and 16 years of age who had histopathologic confirmation of TGDR superior to the hyoid bone from either a primary or revision procedure. The distance of any TGDR from the hyoid bone in the superior direction and greatest width of any disease superior to hyoid bone were measured.

**Results:** The mean distance that disease was present above the hyoid was 11.3mm (range 0-30mm). The mean width that disease was present above the hyoid was 1.1mm(range 0.2-7mm).

**Conclusion**: This study represents the first comprehensive evaluation of the extent of microscopic disease present in the suprahyoid area in children undergoing TGDR surgery. The mean values and ranges presented will provide guidance on the amount of tissue to remove superior to the hyoid in order to avoid recurrence of disease.

#### Cochlear FLAIR Signal Intensity Changes After Hearing Preservation Surgery for Vestibular Schwannoma

Polly Huang; Gabriela Bobarnac; Nathan Tu MD; John Go MD; Rick Friedman MD, PhD

**Background:** Vestibular schwannomas (VSs) are benign, intracranial, extra-axial tumors arising from the schwann cell sheath surrounding the vestibulocochlear nerve. The T2-weighted cochlear fluidattenuated inversion recovery (FLAIR) sequence on magnetic resonance imaging (MRI) has been under investigation as a prognostic marker of hearing preservation following tumor resection. Several studies have found associations between elevated cochlear FLAIR signal and presence of VS tumor. The purpose of this study is to explore whether changes in T2-FLAIR signal intensity in vestibular schwannoma patients undergoing tumor resection are correlated with trends in hearing preservation.

**Methods:** A retrospective chart review was performed for patients who underwent vestibular schwannoma excision using the middle fossa (MF) or retrosigmoid (RS) craniotomy approach with attempted hearing preservation between January 2013 and June 2017 at the Keck Medical Center of USC. Serviceable hearing was defined as class A or B using the AAO-HNS classification system, and hearing preservation was defined as retained postoperative serviceable hearing. Mean signal intensity of the affected cochlea was evaluated by operator-determined region-of-interest technique delineating the middle and apical turns of the cochlea and normalized against the contralateral cochlea. Percent change in FLAIR signal intensity was calculated for each patient.

**Results:** Statistics to be completed. Expect difference in preoperative cochlear FLAIR signal intensity between hearing preserved and non-preserved patients, as well as improvement in abnormal cochlear FLAIR in patients who had preserved postoperative hearing.

**Summary/Conclusions:** Cochlear FLAIR MRI could have potential implications in determining the timing of surgical interventions for VS patients, as well as for research aimed at elucidating the pathophysiological mechanism behind VS induced hearing loss.

## Diffusion tensor imaging allows in vivo visualization of the facial, vestibular, and cochlear nerve bundles within the internal auditory canal.

<u>Christopher Lui</u>; Ryan Cabeen, PhD; Courtney Voelker, MD; Stefanie Bodison, OTD; Marta Kulich; Laurel Fisher, PhD

**Goal:** Children with congenital hearing loss often have abnormal inner ear anatomy involving the cochlea/semi-circular canals and the cochlear and vestibular nerve portions of the 8<sup>th</sup> cranial nerve (CN). Commonly used imaging modalities such as CT and sMRI do not provide adequate information about the integrity of the involved nerves to inform clinical decisions. In this study, we aim to demonstrate the efficacy of using diffusion tensor imaging (DTI) tractography to visualize nerve structure within the internal auditory canal (IAC).

**Methods:** Ten children (average age = 7.8 years) with a prior diagnosis of unilateral hearing loss were imaged with a Seimens 3 Tesla magnetic resonance imaging scanner using a specialized DTI acquisition protocol. Fiber tractography was performed using a multi-compartment model to reconstruct the nerves in the IAC on the normal hearing side.

**Results:** The structure of the facial, vestibular, and cochlear nerve in the IAC were reconstructed and individually visualized.



**Figure 1.** Example of an image acquired using our DTI protocol. The facial (purple), cochlear (yellow), and vestibular (blue) nerves are pictured inside the IAC coursing towards the bony labyrinth from the normal hearing side of the subject.

**Conclusions:** We used DTI to image inner ear anatomy, and to our knowledge, visualize and discriminate separate nerve structures within the IAC for the first time. The ability to assess nerve integrity is a crucial missing component of current clinical care as impaired cochlear nerve integrity may predict a poorer treatment benefit from surgical intervention such as a cochlear implant or an auditory brainstem implant. Furthermore, children with hearing loss commonly present with developmental defects secondary to vestibular dysfunction, and a reliable method of visualizing vestibular nerve structure may allow targeted early intervention in high risk patients. These results support the potential usage of DTI as an invaluable clinical tool in the treatment of children born with hearing loss.

## Zebrafish Homozygous *greb1l<sup>sa16374</sup>* Knockout Mutation Results in Aberrant Sensory and Vestibular Innervation.

Jacob Mattox<sup>1</sup>; Joanna Smeeton, PhD<sup>2</sup>; Megan Matsutani<sup>2</sup>; Lindsey Barske, PhD<sup>2</sup>; Rick A. Friedman, MD, PhD<sup>3</sup> <sup>1</sup>Keck School of Medicine of USC; <sup>2</sup>Department of Stem Cell Biology and Regenerative Medicine, Keck School of Medicine of USC; <sup>3</sup>Division of Otolaryngology, Head and Neck Surgery, Department of Surgery, University of California, San Diego

**Background:** 8<sup>th</sup> cranial nerve deficiency is a rare congenital malformation that can result in profound sensorineural hearing loss (SNHL) in newborns. These children are evaluated for cochlear implant (CI) surgery to include imaging using high resolution computed tomography and magnetic resonance imaging. Current imaging modalities are not always definitive in determining the presence of an aberrant or missing 8<sup>th</sup> cranial nerve within the internal acoustic canals. Due to imaging difficulties and the resulting reduced CI efficacy, a combined molecular and imaging-based treatment determination might aid in the determination of individual SNHL treatment modalities. To elucidate the role of *GREB1L* in early inner ear and 8<sup>th</sup> cranial nerve development and to determine its efficacy as a molecular marker for CI candidacy, the zebrafish inner ear and sensorineural innervation was evaluated in homozygous *greb11* mutant zebrafish.

**Methods:** Heterozygous *greb1l* zebrafish were mated to obtain offspring with a theoretical distribution of 25% of wild-type, 50% heterozygotes, and 25% of *greb1l* homozygotes. Embryos were anesthetized and fixed at 72 hpf, fluorescently stained and mounted in low melting point agarose and imaged on a confocal microscope to identify any inner ear or sensorineural innervation abnormalities. DNA was then extracted and animals were genotyped by PCR.

**Results:** Of the 92 embryos analyzed, 22 (24%) were homozygous for the *greb11* mutation. The mutant embryos exhibited a loss of the anterior cristae nerve (17/22 mutants, 77.3%), an abnormal innervation pathway from the occipital lateral line neuromast (2/22, 9.1%), or both abnormalities (3/22, 13.6%). No abnormalities were observed in wildtype or heterozygous animals.

**Conclusion:** *GREB1L* plays a vital role in the early inner ear development and sensory epithelia innervation and is a potential target as a molecular marker in identifying appropriate SNHL therapeutic interventions.

**CT and MRI in Determining Depth of Invasion in Squamous Cell Carcinoma of the Oral Tongue** <u>Kristi Tran BA</u>, Christopher Cheng BS, Garren M Low MS, John Go MD, Adrian Correa MD, Laurel Fischer PhD, Vaninder Dhillon MD, Uttam Sinha MD, Niels Kokot MD

**Background**: Resection of squamous cell carcinoma of the oral tongue (SCCOT) often requires neck dissection if nodal metastasis is indicated. Accurately determining the depth of invasion (DOI) would help in pre-operative planning, since tumor thickness is associated with nodal metastasis. Our study aims to look at the accuracy of two different imaging techniques, CT and MRI, in determining tumor depth of invasion by comparing pre-op imaging to post-op histological measurements. We hypothesize that MRI measurements of DOI will be more accurate than CT measurements when compared to histological measurements.

**Methods**: We retrospectively reviewed the medical records of T1 and T2 patients undergoing partial glossectomy for SCCOT between 2005-2017. DOI was measured as the perpendicular distance from the line connecting normal tongue mucosa to the deepest aspect of tumor. DOI measurements obtained from preoperative imaging (CT/MRI) and pathology were compared for accuracy using linear regression. **Results**: 80 patients who underwent glossectomy for T1 or T2 SCCOT were identified. 23 patients were excluded due to poor CT/MRI image quality. A strong correlation exists between MRI and pathology measurements (r=0.709, p=0.0002), while comparison of CT and pathology showed only a moderate linear correlation (r=0.406, p=0.0154).
**Conclusions**: Our findings demonstrate that MRI is an accurate method for measuring depth of invasion in SCCOT. MRI has the potential to serve as a useful tool in preoperative planning of surgical management of the neck.

## PALLIATIVE CARE

#### Changes in Healthcare Utilization Patterns with Palliative Care Intervention in End-Stage Liver Disease <u>Tanu A. Patel, BS</u><sup>2</sup>, Lily Chu, BS<sup>2</sup>, Carin Van Zyl, M.D.<sup>1</sup>

<sup>2</sup> Keck School of Medicine, University of Southern California, Los Angeles, California
<sup>1</sup> Section of Palliative Medicine, LAC+USC Medical Center, Keck School of Medicine, University of Southern California, Los Angeles, California

**Background/Purpose:** End-Stage Liver Disease (ESLD) patients at LAC+USC Medical Center are heavy utilizers of health care resources at the end of life. Although these patients experience as much suffering as cancer patients, they are under-referred to palliative medicine services. We aimed to understand the value of a palliative medicine approach combined with usual care on healthcare utilization in ESLD patients.

**Methods:** We performed IRB approved retrospective and prospective studies of patients seen at the LAC+USC Liver clinic. The control arm consisted of retrospectively identified patients with ESLD seen between 06/01/2015 to 05/31/2016. These patients did not have access to palliative medicine services as the clinic had not yet been started. ESLD was identified as patients with a MELD score >20 AND clinical decompensation.

Patients in the interventional arm were identified by identical ESLD criteria, and were seen by the palliative care clinic for up to one year. Interventions included case management, symptom management, and advance care planning. For each identified patient, the team collected demographic and healthcare utilization data from the medical record.

**Results:** The control group (n=65) and palliative care clinic group (n=37, data collection is ongoing) had similar MELD scores (24.7 control vs 24.6 clinic), % alcoholic liver disease (84% vs 81%) and gender (73% male vs 70%). Patients in the control group spent an average of 15.5 days inpatient and an average of 2.2 days in the ICU compared to 4.8 days inpatient and 0.8 days in the ICU with the clinic group. The control group had an average of 3.7 ED visits versus 0.9 visits for the clinic group. The number of ED visits for paracentesis was 1.8 in both groups.

**Conclusion:** Palliative care intervention reduced the number of ED visits, inpatient days, and ICU visits over the course of the program. The number of ED visits for paracentesis was unchanged suggesting that while palliative care does not impact the pathophysiology of disease, intervention influences patients' coping, and self-management.

# PATIENT CARE QUALITY & SAFETY

#### Exploring Cognitive Health Needs, Perceptions, & Barriers to Resource-Seeking Among Spanish vs. Bilingual Language in Hispanic Older Adults

**Simone Montgomery**, Semran Mann, Christopher Montgomery, Kelly Baek, Susanne Montgomery

**Background:** By 2040, the number of Americans above the age of 65 is expected to roughly estimate 20% of the population. In California, Hispanics comprise 39% of the total population, and research indicates that minorities are more adversely impacted by age-related cognitive decline due to a predominance of pre-existing, chronic conditions. As this impending demographic shift occurs, it is important for medical and public health professionals to prepare for its impact on the healthcare system. The aim of this mixed-methods study is to determine whether Spanish-language only use impacted cognitive health care needs for Hispanic adults.

**Methods:** Quantitative differences were explored by self-reported language proficiency; only speaking/reading Spanish (n=122) vs. bilingual (Spanish-English; n = 82). We used qualitative description theming and used SPSS v.24 for descriptive and bivariate analyses.

**Results:** Results suggest that Spanish-only speaking, older adults experience significantly stronger barriers to receiving cognitive-health related care. Personal barriers include transportation, health insurance/financial ability, cultural barriers, and fear of diagnosis. Importantly, provider barriers, language discordance, inconvenient hours, discrimination, and fear of deportation further contribute to the heightened vulnerability of this subgroup. Qualitative statements further describe lived experiences of affected older adults.

**Summary/Conclusion:** The findings of our study are significant for health care providers serving lowincome, older adults of diverse backgrounds, who need to be aware that not all Hispanic populations present with the same challenges and of the increased vulnerability of Spanish-only speaking populations. Primary care health care providers are on the front lines of identifying patients with early cognitive decline, and it is critical for them to identify and preventively refer these highly vulnerable populations.

## PEDIATRICS

#### Effects of a Multidisciplinary Clinic on Transitional Age Youth Who Age Out of the Foster Care System <u>Kameron Bechler</u> and Astrid Heger, M.D.

**Background:** Every year, thousands of transitional age youth (TAY) (age 16-25) age out of the foster care system without being reunited with their biological families or adopted. These TAY experience the same well-documented difficulties as younger children in foster care with the additional hardships of losing county support services, finding employment, a harsher justice system, and increased social and financial responsibilities. The Violence Intervention Program (VIP), provides a range of services to TAY in the foster care system including case management, parenting workshops, advocates, medical and dental treatment, mental health screening and clinicians, and OB-GYN services. This study examines the effects of VIP's comprehensive, multidisciplinary clinic on rates of unemployment, homelessness, incarceration, and pregnancy in TAY who age out of the foster care system.

**Methods:** This study uses data from VIP's internal records and Los Angeles County Department of Child and Family Services' automated records system that tracks all children involved in the county foster care system. A cohort of fifty TAY from VIP's records who received their range of services will be compared with a matched (based a range of variables including age, gender, and severity of medical history) cohort of fifty TAY who were assessed at other Los Angeles County affiliated facilities and not offered the same support services.

**Results:** Pending final data analysis, we expect to provide evidence that a multidisciplinary clinic focused on TAY has a significant positive impact on TAY who age out of the foster care system. We predict this study will show lower rates in all four metrics for TAY who engaged with VIP compared to those who did not.

**Conclusion:** We believe this study will provide valuable information useful for procedural and policy recommendations within the VIP clinic, other clinics involved with foster care in Los Angeles County, and state and national legislation regarding TAY in foster care.

## Portal Vein and Hepatic Artery Thrombosis in Pediatric Liver Transplantation, a 15-year retrospective study.

Hugo Cardona (Medical Student), Kevin Chu, MD, Abhishek Karnwal, MD

**Introduction:** Vascular complications are common following pediatric liver transplantation<sup>1</sup> (PLT) with an incidence of 7-10% for portal vein thrombosis (PVT) and 4-25% for hepatic artery thrombosis (HAT). <sup>2</sup> We aimed to analyze the incidence and factors associated with thrombotic complications after PLT at Children's Hospital Los Angeles.

**Methods:** After IRB approval, all patients who had PLT from 2000 to 2015 from were included in the study. We retrospectively collected demographic, perioperative and outcome data. Thrombosis was identified through chart review as well as imaging including ultrasound, doppler or CT scan up to 1 year after surgery. A univariate logistic regression was done for individual variables.

**Results:** A total of 156 PLTs were performed in the study period, of which, 14 were concurrent with kidney or small bowel transplant and 142 were solely PLTs. The average ICU length of stay was 170 hours (range 12-635) with 2 postoperative deaths. The commonest indication were cholestatic disorders n=76 (54%) followed by metabolic disorders n=21 (14.5%), Idiopathic n=21 (14.5%), Liver tumors n=17 (12%), Hepatitis n=5 (3.5%) and others 2 (1.5%). We found PVT in 5 patients 3.5% (5/142) and HAT 0.70% (1/142). Of the six patients with vascular complications, 50% (3/6) had a diagnosis of biliary atresia, 50% (3/6) had a living donor graft, and 33% (2/6) had a pre-existing vascular defect prior to transplant. (Table 1). Interestingly, length of surgery, PELD scores, amount and type of blood products given and immediate post-operative coagulation status did not show any correlation with PVT or HAT. We utilized Firth penalized logistic regression to reduce bias due to small sample size.

**Discussion:** Although thrombotic events occur less frequently than bleeding complications after PLTs, they threaten patient and graft survival<sup>3-4</sup>. In addition, biliary atresia (BA), the leading indication for transplantation in children causes portal vein sclerosis, which results in technical difficulties during vascular reconstruction. In this study, we found that 60% of PVTs (3/5) were associated with BA diagnosis. Of all thrombotic complications, 50% occurred in living donors and the other half in cadaveric donors. PVT and HAT are known to occur more commonly in children as compared to adults due to smaller caliber of vessels, split procedures, and involuntary development of high hematocrit<sup>5</sup>. Other factors associated with PVT include size discrepancy between the donor and recipient vasculature, anastomotic kinks, low portal flow, and the presence of preoperative PVT <sup>3,5</sup>. Our practice is to anticoagulate with Heparin and/or Dextran 40, when end-to-end anastomosis is performed under surgical guidance. While this could contribute to the lower incidence of PVT and HAT at our center, we also strive to maintain a post-operative hematocrit below 30 and INR between 1.5-2. In addition, consistency in surgical team and technique were other favorable factors at our center.

	Diagnosis	Type of transplant	Donor type	Complication	Type of anastomosis	Other
Patient 1	Hepatoblastom a	Split graft - left lateral segment	Cadaver	Portal vein thrombosis	End-to-end	
Patient 2	Fulminant hepatic failure	Split graft - left lateral segment	Living	Hepatic artery thrombosis	End-to-end	
Patient 3	Biliary atresia	Split graft - left lateral segment	Living	Portal vein thrombosis	End-to-end	
Patient 4	Biliary atresia	Split graft - left lateral segment	Cadaver	Portal vein thrombosis	End-to-end	
Patient 5	Hepatoblastom a	Whole organ	Cadaver	Portal vein thrombosis	End-to-end	PVT in native liver prior to transplant
Patient 6	Biliary atresia	Split graft - left lateral segment	Living	Portal vein thrombosis	Use of graft due to size discrepancy	Atretic native portal vein

#### Table 1

#### **References:**

- 1) Andrews J. Vascular Complications Following Liver Transplantation. Semin Intervent Radiol.
- 2) Orons P D, Zajko A B, Bron K M, et al. Hepatic artery angioplasty after liver transplantation: experience in 21 allografts. J Vasc Interv Radiol. 1995; 6:523–529.2004. Dec: 21(4): 221-223.
- 3) Feltracco P, Barbieri S, Cillo U. Perioperative thrombotic complications in liver transplantation. World J Gastroenterol. 2-15 Jul 14; 21(26): 8004-8013.
- 4) Neto J, Fonseca E, Feier F. Analysis of Factors Associated With Portal Vein Thrombosis in Pediatric Living Donor Liver Transplant Recipients. Liver Transplantation 2014. 20: 1157-1167.

5) Orlandini M, Feier FH, Jaeger B, Kieling C, Vieira SG, Zanotelli ML. Frequency of and factors associated with vascular complications after pediatric liver transplantation. J Pediatr (Rio J) 2014;90:169–175.

#### **HPV Documentation QI Initiative**

#### Giancarlo Cardoza - Medical Student, Dr. Susan Wu – Advisor, Children's Hospital of Los Angeles.

**Background:** HPV is the most common sexually transmitted infection in the United States. The Advisory Committee on Immunization Practices recommends routine vaccination against HPV for males and females at 11-12 years of age. However, HPV vaccination rates have remained suboptimal. The American Academy of Pediatrics recommends using every healthcare visit as an opportunity to review and update vaccine status. We hypothesize that improved documentation of HPV vaccination status at the inpatient setting may lead to increased opportunities to provide vaccines to eligible adolescents. **Methods:** From March 2016 to December 2017, 30 adolescent inpatient charts were randomly selected for audit monthly to assess resident documentation of HPV. Eligible patients were ≥ 11 years old and admitted to a resident inpatient pediatrics service. Starting August 2016, interventions were implemented via PDSA cycles to improve resident documentation of HPV vaccine status. Interventions included an educational session, implementation of EMR prompts, reminders, data feedback, and HPV vaccine order sets.

**Results:** 660 patient charts over 22 months were reviewed. HPV vaccine status was documented in 10% of charts pre-intervention. This increased to a median of 16.7% in post-intervention months, with the highest documentation immediately after a resident education session and implementation of EMR templates (23.3% documentation). Gender data was available for 450 patients. Females were more likely to have HPV vaccine documentation compared to males (B = -0.58, *p* = 0.043). Age was not significantly associated with HPV vaccine documentation.

**Conclusion:** Documentation of HPV vaccine status can be improved through low-cost interventions such as education sessions and EMR templates. Although the HPV vaccine series is recommended for both genders, significant differences in documentation exists.

#### Premature epiphyseal growth plate arrest after isotretinoin therapy in preadolescent High Risk Neuroblastoma (HR-HBL) patients

#### Angela Duvalyan (Medical Student), Araz Marachelian (Advisor)

**Background**: Isotretinoin is a Vitamin A derivative used as standard therapy for high-risk neuroblastoma given with immunotherapy. The use of Vitamin A derived synthetic retinoids have been reported to cause various skeletal abnormalities including premature epiphyseal growth plate arrest, which has severe lifelong sequelae that can greatly impact the growth of a child.

**Methods**: We identified patients at CHLA with neuroblastoma who experienced premature epiphyseal growth plate arrest. We then performed a review of the literature of this complication. Further analysis of the data was done in order to assess whether there is an association with age of isotretinoin administration and premature epiphyseal growth plate arrest. Data collection included: diagnosis age, presentation age, agent of exposure, dose, exposure range and skeletal deformity.

**Results**: 3 patients were identified all of whom had isotretinoin exposure at 7 years of age. Review of the literature identified 7 other patients who presented with isotretinoin associated skeletal abnormalities. The median age of diagnosis was 6 years old (range 1-8 years old). The median range of isotretinoin

exposure was between 6.5-7.625 years old. 8/10 showed premature growth arrest, with 6/8 experiencing asymmetric growth arrest (median age of deformity presentation was 9 years old). 2/10 patients had isotretinoin and fenretinide therapy. No case reports were found of patients whose full exposure to isotretinoin therapy occurred before the age of five.

**Conclusion**: Since all 10 patients with neuroblastoma and skeletal abnormalities had a similar age of exposure to isotretinoin that is later than the typical age of exposure to isotretinoin for neuroblastoma (more commonly in patients younger than 5 years of age), the prepubescent growth plate may be most at risk for this toxicity. We recommend special attention to this population to help prevent long term consequences.

#### Myocardial Strain Worsens Acutely After the Glenn Procedure in Infants with Univentricular Heart Defects

<u>Michael Etzel, BA</u>; Andrew L. Cheng, MD; Novel Castillo, RDCS; Hui Gao, RDCS; Pierre C. Wong, MD Department of Pediatrics, Division of Pediatric Cardiology, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA

Purpose: The Glenn procedure results in significant hemodynamic changes for the univentricular heart, the impact of which on ventricular performance has not been prospectively evaluated.
Methods: Twenty-eight patients were recruited. Transthoracic echocardiogram was performed the day of pre-Glenn cardiac catheterization and post-Glenn once stable. 2D, spectral, and tissue Doppler measurements were obtained. QLAB v.10.0 was used to calculate strain by speckle tracking. Differences pre- and post-Glenn were measured using paired Student's t-test or Wilcoxon signed-ranked test.
Results: Analysis included 20 subjects. After Glenn, indexed end diastolic area decreased significantly, accordant with reduction in preload (see Table 1). Most strain parameters decreased significantly or trended toward significant decrease, implying worsened systolic performance. Among conventional echocardiographic parameters, e' decreased and Tei index increased.

**Conclusions:** Despite volume-unloading of the single ventricle, there is slight worsening in ventricular performance acutely after the Glenn procedure. Doppler and strain data suggest diastolic dysfunction and systolic dysfunction, respectively. Further longitudinal assessment is warranted to determine if/when these parameters improve.

Parameter	Pre-Glenn	Post-Glenn	p-value			
Body Surface Area-Indexed End Diastolic Area (cm <sup>2</sup> /m <sup>2</sup> )	32.5 (27.8-38.2)	24.8 (22.2-30.1)	<0.001			
Fractional Area Change	$0.40 \pm 0.08$	0.36 ± 0.10	0.049			
e' (cm/s)	10.1 (7.5-11.8)	6.1 (5.3-7.8)	<0.001			
Tei Index	0.41 (0.28-0.57)	0.59 (0.47-0.75)	0.003			
Apical 3 Longitudinal Strain (%)	-21.7 ± 4.2	-19.3 ± 4.0	0.032			
Global Longitudinal Strain (%)	-22.5 ± 3.4	-20.9 ± 3.4	0.068			
Short-axis Base Circumferential Strain (%)	-14.4 ± 4.3	-11.5 ± 4.6	0.014			
Global Circumferential Strain (%)	-16.3 ± 4.3	-13.6 ± 5.0	0.093			
Values listed as mean ± SD (parametric)						
or median with 25-75% IQR (non-parametric)						

#### Table 1. Selected Echocardiographic and Strain Parameters

#### Validation of Transcranial Doppler Measurements Using a Flow Phantom System

Kush Gaur, MD Candidate, Marvin Nelson, MD MBA, John Wood, MD PhD, Children's Hospital Los Angeles

**Goal:** CHLA hematologists and radiologists observed an abrupt reduction in measured Transcranial Doppler velocities while assessing stroke risk in sickle cell disease patients. This change could be related to treatment effects or technical differences in the measurements. Currently, there is no systematic comparison across various vendors. This study was undertaken to provide a validation of the outputs of various machines.

**Methods:** A closed flow phantom system was built to mimic the middle cerebral artery blood flow: Fluid was water, vessel was a C-flex thermoplastic elastomeric tubing (ID 0.478 cm, OD 0.792 cm, wall thickness 0.152 cm), tissue was mimicked by 2% agar solution, and flow was generated by a submersible centrifugal aquarium pump. Constant flow was driven at flow rates of 1.22 L/min to 2.30 L/min measured by an inline ultrasonic flow probe. Velocities from 130 cm/s to 250 cm/s in 30 cm/s intervals were yielded. An 8-MHz Philips (model iE33) S8-3 and a 10 MHz Toshiba (model Aplio 500) 10C3 transducer probe were placed in a probe window on the system, and velocities were collected and compared against the flow meter. Results were analyzed using Bland-Altman statistics. **Results:** Coefficient of variation of both probes averaged 2.4% across the serial measurements, demonstrating excellent stability of the pump and ultrasound measurements. Bland-Altman analysis demonstrates that the Philips probe had nearly perfect concordance (1.2% negative bias, SD 0.4%, T=3, p=0.04) with theoretical values based upon measured mean flow. The Toshiba probe exhibited 20.4% negative bias (SD 1.4%, T=32.9, p<0.0001) compared to theoretical values.

**Conclusion:** These data demonstrate evidence that the observations of the CHLA physicians could be explained by technical differences in the two ultrasound machines. The Toshiba probe (currently used for scanning) measured consistently lower values from actual velocities, while the Philips demonstrated clinically concordant values to actual mean velocities.

## Hospital readmission and long-term morbidities in neonates treated with extracorporeal membrane oxygenation

Jodie Guller (1), Ashley Yi Song (1), Philippe Friedlich, MD, MBA, MSEPi (1), Rachel Chapman, MD (1), Ashwini Lakshmanan, MD, MPH (1,2,3)

<sup>1</sup>Fetal and Neonatal Medicine Institute, Division of Neonatal Medicine, Children's Hospital Los Angeles; Keck School of Medicine, University of Southern California, Los Angeles, CA, United States

<sup>2</sup>Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States

<sup>3</sup>Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, United States

**Goals:** Long-term studies show that neonates treated with extracorporeal membrane oxygenation (ECMO) may suffer from significant morbidities after hospital discharge, yet there is limited information on long-term morbidities and hospital readmission rates among ECMO survivors at a national level. The objectives are 1) To describe the rates of readmission and patient characteristics of neonates who were readmitted to a children's hospital after receiving ECMO at index hospital visit 2) To examine the long-term morbidities of ECMO support. We hypothesized that there would be specific predictors of hospital readmissions and long-term morbidities of ECMO support in neonates.

**Methods:** Data was obtained from the Pediatric Health Information System (PHIS) database for 2006 to 2016. All neonates (≤28 days old) who received ECMO at index hospital visit were examined.

Readmission was assessed with respect to age at readmission, diagnoses and procedures, time to

readmission, and survival at discharge. Descriptive statistics, bivariate comparisons, and multivariate regressions were used in statistical analysis.

**Results:** From 2006 to 2016, a total of 4,869 neonates received ECMO at index hospitalization. Of these, 1,252 (25.7%) had at least one readmission. Readmitted patients were more likely to have gastrointestinal (37.9% of readmitted group vs. 13.7% of no readmissions group, p<0.001; OR 2.144, p<0.001) or neuromuscular (16.1% of readmitted vs. 10.3% of no readmissions, p<0.001; OR 1.35, p=0.03) flags. Neonates with a principal diagnosis of hypoplastic left heart syndrome (HLHS) (OR 1.544, p=0.04) or conditions originating in the perinatal period (OR 2.857, p=0.001) also had a higher adjusted odds ratio of a readmission.

**Summary:** Neonates receiving ECMO support at index hospitalization suffer significant morbidity and mortality after discharge. Those who required hospital readmissions were more likely to have gastrointestinal or neuromuscular morbidities.

#### Characterization of Children Admitted to the CHLA Pediatric Intensive Care Unit for Status Asthmaticus

<u>Angelo Jimenez</u> (Keck School of Medicine of USC); Ronald Ferdman, MD (Division of Clinical Immunology and Allergy, Children's Hospital Los Angeles)

**Background/Purpose/Goal/Hypothesis:** Pediatric asthma is a serious public health concern—in 2013, nearly 500,000 American children under the age of 15 were treated in an emergency department for a primary diagnosis of asthma, which illustrates a significant medical and economic burden. Pediatric asthma prevalence in America increased at a rate of 1.4% yearly from 2001-2010. Although the increases documented prior to 2010 may have been leveling off for non-Hispanic White children, prevalence has been increasing more dramatically for children of color, especially those living in poverty. An asthma exacerbation severe enough to require a PICU admission for treatment is rare, and can be viewed as a "near fatal" asthma exacerbation. Data from 2014 confirms that Los Angeles County alone accounted for 28.6% of all pediatric asthma PICU admissions in California. In 2015, CHLA admitted the second most children with asthma in Los Angeles County, and preliminary data suggests that CHLA admits children with asthma to the PICU at a substantially higher rate than shown in historical data. This means that CHLA is uniquely qualified to characterize the sickest and most high-risk group of asthmatic children in California.

The goal of the study is to characterize pediatric patients admitted to the PICU for status asthmaticus over the last two years to identify risk factors unique to the CHLA patient population and allow for better screening of other children at risk for ICU admission, such that earlier intervention can be started. We hypothesize that the proportion of children admitted to CHLA for asthma that require PICU admission has increased compared to historical CHLA data; that despite the predominantly Latino/a population seen at CHLA, African-American children will predominate among those admitted to the PICU for asthma; that the majority of children admitted to the PICU for asthma will have a potentially modifiable risk factor that may have prevented admission; and that children admitted to the PICU for asthma will have a high rate of readmission for asthma both in general, and to the PICU, specifically. Methods: A structured retrospective chart review of all children admitted CHLA's PICU for status asthmaticus between January 1<sup>st</sup>, 2016 and December 31<sup>st</sup>, 2017 is being conducted. Specifically, we are collecting the following data: patient demographics (age, gender, race/ethnicity, insurance, ZIP code); number of hospital and PICU admissions and number of ER visits for asthma treatment prior to this PICU admission; treatment in the PICU and outcome (level of treatment received including specific medications, any oxygen therapy, ventilator support, and length of stay); estimation of asthma severity and control prior to admission; prescribed asthma medications and an estimate of medication adherence prior to admission; psychosocial factors which may have contributed to the admission (as

much as can be determined from a retrospective chart review such as financial instability, mental illness in the patient or their family, living conditions); and evidence of asthma education done prior to discharge including proper use of an inhaler and spacer and any follow-up appointments. **Results:** Pending completion of data collection and subsequent analysis, we expect to identify several unique trends among CHLA's pediatric asthma population. Preliminary data suggest a strong prevalence of adolescent patients being admitted to the PICU for acute asthma exacerbations rather than younger children. We have also begun to see a higher prevalence of Latina/o children being admitted, regardless of age or gender. Interestingly, the preliminary data suggest that the majority of patients admitted to the PICU for status asthmaticus do not routinely receive long-acting beta agonists (LABAs). Aminophylline use in PICU admissions is variable, according to preliminary data collected. Of note, the majority of pediatric patients admitted to the CHLA PICU have never met with a Pulmonologist or Allergist prior to admission; that is to say, the current PICU admission is often the first encounter the family has with an asthma or pulmonary specialist. This may present an opportunity to implement more sensitive screening protocol in the general pediatrics clinic to connect families with an asthma specialist earlier in life to reduce the number of PICU admissions later in life. Other possible results may lead to a correlation between degree of obesity and level of compliance with one's asthma medications, or a link between BMI and number of recurrent PICU admissions.

**Summary/Conclusion:** The preliminary data and trends evidenced by our data thus far illustrate unique, modifiable risk factors unique to the CHLA pediatric asthma patient population that will allow us to more effectively intervene and connect families with allergy and pulmonology earlier in life to prevent further episodes of status asthmaticus. Patient and family education earlier in life may improve adherence to medication regiments, which will ultimately reduce the frequency of ER visits and PICU admissions for acute asthma exacerbations. Given CHLA's unique, multi-ethnic patient population, completion of our data collection and thorough characterization of pediatric asthma patients admitted to the PICU will allow us to address barriers to care that perpetuate disparities in healthcare access, delivery, and patient outcomes, improving the quality of life for pediatric patients in Los Angeles, regardless of race, ethnicity, gender, or socioeconomic status.

#### A Retrospective Cohort Study of Children and Adolescents with Atypical or Complex Pineal Cysts <u>Sara Khan<sup>1</sup>, BA</u>, Benita Tamrazi<sup>2,3</sup>, MD, Nathan Robison<sup>2,4</sup>, MD <sup>1</sup>Keck School of Medicine of USC, <sup>2</sup>Children's Hospital of Los Angeles, <sup>3</sup>Division of Radiology, <sup>4</sup>Division of Hematology/Oncology, Los Angeles, CA, USA

Background: While pineal gland cysts are usually benign, atypical characteristics on MRI (e.g. solid enhancement, restricted diffusion, or other susceptibility artifact) may raise concern for a pineal malignancy. Appropriate evaluation of complex pineal cysts (CPC) is not well defined. In this retrospective study, we attempt to define the natural course of CPC in children and adolescents and to identify radiographic and clinical features associated with malignancy. We hypothesize that specific radiographic features can differentiate malignant from benign CPC with high sensitivity.
Methods: This retrospective cohort study includes all subjects aged <18 with CPC identified at Children's Hospital Los Angeles (CHLA) from 2010-2017. The study was approved by the CHLA institutional review board. Subjects were identified by an electronic search of MRI reports including terms "pineal cyst". Reports were individually screened for evidence of complex pineal features, defined as cysts that were multi-cystic, enhancing or ≥1cm in size, had a solid component, or restricted diffusion. The chief complaint, initial clinical and radiographic symptoms, tumor markers, and final diagnosis will be extracted from the medical record. Both sensitivity/specificity and multivariate analyses will be performed.</li>

**Results:** A review of 878 MRI reports identified 192 subjects with evidence of CPC at initial encounter. Mean age of included subjects was 8 years; 40% were male. Follow-up MRIs were obtained on 84 (44%). Data extraction and imaging review is ongoing.

**Summary**: We hope to identify clinical and radiographic features that can reliably differentiate patients with benign CPC from the subset of higher-risk patients requiring further diagnostic evaluation.

## Effect of Maternal Intrapartum Antibiotics and Delivery Method on Breast Milk and Infant Microbiome

<u>Sam Kushner-Lenhoff, MS2</u>. Pia Pannaraj, MD, MPH, CHLA mentor. Fan Li, PhD, CHLA Bioinformatics mentor.

**Goal:** An increasing body of evidence has demonstrated a significant relationship between an infant's microbiome and a variety of health outcomes. This project builds on a previous study investigating the relationship between breast milk communities and the establishment of the infant gut microbiome to look at the effects of intrapartum antibiotics on an infant microbiome's establishment and development.

**Methods:** The data is a collection of 16S ribosomal RNA gene sequence information from breast milk and infant stool samples collected from 107 healthy mother-infant pairs in Los Angeles, California and St Petersburg Florida between January 1, 2010 and February 28, 2015. The rRNA sequences were filtered and trimmed for errors in the quality of the read, then denoised using the DADA2 algorithm. Sequence variants were merged to reduce overlap and then classified and organized according to their taxonomy. This information was then analyzed by bacterial abundance, alpha diversity, principal coordinates analysis, PERMANOVA and ZINB.

**Results:** Although analysis is still ongoing, so far significant differences have been found among the stool and breast milk microbiome communities due to several variables of interest. Importantly, antibiotics at delivery appeared to cause about 3.1% and 2.7% of the variance in the breast milk and stool microbiome communities respectively (p<.001) over the first year of the infant's life according to Bray-Curtis distances. Future results will investigate the effect of this impact at birth and its trend through the first year as well as the interaction of a C-section/Vaginal delivery on this trend.

**Conclusion:** This research already has shown an impact of intrapartum antibiotics on the infant's microbiome. The duration and trend of this effect on the infant over the first year is currently being investigated. As further research demonstrates the importance of the infant's microbiome on pediatric health, this study and others will give mothers additional information when deciding treatment during and immediately before delivery.

## Evolution of bacterial lower respiratory tract infections and viral infections in pediatric patients with tracheostomies

#### Nassim Lashkari MSII, Christopher J.Russell MD

**Background**: Children with respiratory failure or anatomic abnormalities requiring tracheostomy are at increased risk for bacterial lower respiratory tract infections. Little is known about the effect of concomitant viral infections on patient outcomes.

**Methods**: A retrospective chart review of 146 children 18 years and younger who underwent tracheostomy at Children's Hospital Los Angeles (CHLA) between 1/1/2003 and 6/30/2014 with readmission at CHLA for bacterial infection. The following variables were recorded for each patient: comorbidities on presentation, symptoms on presentation, laboratory testing including respiratory cultures and viral DAA and/or PCR testing. Outcomes included length of stay and ICU admission.

Bivariate logistic regression will be used to identify the independent association between positive viral infection on primary outcomes.

**Results**: Of the 146 patients included, the median age at readmission was 12 months [Interquartile range (IQR) 0-4 years], primarily male (60.3%) and Hispanic (78.8%). On presentation 45.9% (n = 142) were on positive pressure ventilation at home, 37% had an upper airway obstruction/vascular anomaly, 58.9% had chronic lung disease, and 56.8% had a neuromuscular disorder. Viral testing was done in 50.7% of patients with rhinovirus as the primary infection identified (48.9%, n = 45). For patients with positive viral infection, the median length of stay was 8 days (IQR 5-13 days), 19% (n = 161) had an ICU admission, 25.2% (n= 162) had new/increased ventilator use and 71.2% (n = 162) had a new oxygen requirement.

**Conclusion**: No significant differences in length of stay and ICU admissions was found in those patients with positive viral infection and those without positive infection on our unadjusted analysis.

#### RANK-Ligand levels in pediatric bone disease

Alisha Mathalikunnel, Sara Akhtar, MD, Pisit Pitukcheewanont, MD

**Background**: Receptor activator of nuclear factor kappa-B ligand (RANKL) is a protein involved in the regulation of bone resorption. The overproduction of RANKL has been implicated in several degenerative bone diseases. However, limited research has been done on this protein's role in the pathogenesis of pediatric bone diseases.

**Goal:** This study seeks to quantify the levels of RANKL in pediatric patients with metabolic bone diseases and compare them to controls. The goal of this investigation is to determine whether there is a difference in RANKL levels in patients with bone disease.

**Hypothesis:** As RANKL levels have been shown to be increased in other degenerative bone diseases, it is expected that they will be raised in pediatric patients with metabolic bone conditions as well.

**Methods**: 150 children ages 1 to 21 who have been diagnosed with bone diseases will be recruited from the Center for Endocrinology, Diabetes and Metabolism at CHLA. As controls, 50

to 100 healthy children aged 1 to 21 with no known chronic disease or regular medications will be enrolled from AltaMed Pediatric Clinic. Two 4mL blood samples will be collected

from all patients and a RANKL ELISA assay will be performed to quantify the levels of the protein in both groups. ANOVA analysis will be used to compare various conditions and controls.

**Results** : While some samples from the experimental control group have undergone an ELISA RANKL assay, no data has been gathered from the control group. Preliminary analysis has shown that the average RANKL concentration for 16 Duchenne's Muscular Dystrophy patients is 0.289 pmol/L and is 0.264 pmol/L for 9 Osteogenesis Imperfecta patients. More data is needed for the validity of these results to be determined.

**Conclusion:** We expect to see raised levels of RANKL in pediatric metabolic bone disease patients when compared to a control population. If this is true, further research will need to be done on the role of RANKL in these conditions. As a RANKL inhibitor drug, Denosumab, is being used in patients with osteoporosis, this drug could be a potential treatment in pediatric diseases if RANKL is shown to be causative factor.

#### Convergence Toward Donor Microbial and Metabolomic Profiles After Fecal Microbiota Transplantation in Pediatric Ulcerative Colitis Patients

<u>David J. Nusbaum</u><sup>1</sup>, Nicholas Pervolarakis<sup>2</sup>, Natalie Ramsy<sup>3</sup>, Whitney England<sup>4</sup>, Sonia Michail<sup>1,5</sup>, Katrine Whiteson<sup>4</sup>

<sup>1</sup> Keck School of Medicine of the University of Southern California, Los Angeles, CA <sup>2</sup> Department of Biological Chemistry, University of California, Irvine, CA <sup>3</sup> University of Southern California, Los Angeles, CA

<sup>4</sup> Molecular Biology and Biochemistry, University of California, Irvine, CA

<sup>5</sup> Department of Pediatric Gastroenterology and Nutrition, University of Southern California, Los Angeles,

CA

**Background:** Ulcerative colitis (UC) is a chronic inflammatory disease of the colon. Due to the severity and poor outcomes of pediatric onset UC, new therapeutic approaches are required for children living with this disease. Recent studies have shown a role for the gut microbiota in the pathogenesis of UC. Fecal microbiota transplantation (FMT) provides an avenue for altering the composition of the gut microbiota, and a pilot study of FMT in children with UC found it to be a safe and potentially efficacious treatment.

**Methods:** We performed 16S rRNA gene sequencing and untargeted GC-MS/TOF metabolomic profiling on stool samples from 4 children and their respective healthy FMT donors before and four weeks after intervention.

**Results:** Alpha diversity of the gut microbiota increased after FMT, with species richness increasing from 251 ( $\pm$  125) to 358 ( $\pm$  27). The mean relative abundance of bacteria in the class Clostridia shifted toward donor levels, increasing from 33% ( $\pm$  11%) to 54% ( $\pm$  16%). Ordination by principal coordinates analysis of microbial abundance data demonstrated clustering of the post-treatment and donor samples, suggesting that FMT shifted gut microbial composition toward donor profiles. The metabolomic profiles of the subjects exhibited a similar but less pronounced shift toward donor profiles. Metabolites such as stearic acid and 1-hexadecanol increased toward donor levels after treatment. Norvaline and creatinine levels were lower in both donor and post-treatment patient samples.

**Conclusions:** These findings indicate that FMT alters gut microbial and metabolomic profiles in children who responded to this therapy. Larger studies using a similar "-omics" approach may reveal novel microbial and metabolic targets for the treatment of pediatric ulcerative colitis.

#### The management of cystic craniopharyngiomas

<u>Josephine O. Nwokedi ScB<sup>1</sup>;</u> Mark D. Krieger MD<sup>1, 2</sup>; Nolan Rea<sup>2</sup> <sup>1</sup> Keck School of Medicine, University of Southern California, Los Angeles, CA <sup>2</sup> Division of Neurosurgery, Children's Hospital of Los Angeles, Los Angeles, CA Department of Neurological Surgery

**OBJECTIVE:** To evaluate the efficacy of various initial therapies on cystic craniopharyngioma in children, upon initial presentation and at the time of first recurrence.

**METHODS:** A retrospective analysis of 48 patients (22 females, 26 males, median age 8 years) who were diagnosed with cystic craniopharyngioma between January 2003 and July 2017 was performed. Patient demographics, tumor characteristics, and surgical management were analyzed for statistically significant influences on tumor recurrence and progression.

**RESULTS:** The initial therapy was cyst aspiration in 1 patient (2.0 %), subtotal resection in 32 patients (67 %), and total resection in 15 patients (31 %). Two patients (17 %) with gross total resections and 22 patients (69 %) with subtotal tumor resections received adjuvant radiation therapy.

Patients who received adjuvant radiation therapy as initial therapy showed no significant difference in progression free survival when compared to patients who did not receive adjuvant radiation therapy (M difference = 3.70 months, SE difference = 11.79 months), t(41) = 0.31, p= 0.755.

Among the 48 patients who presented with craniopharyngiomas, 19 experienced tumor progression or recurrence (19 cystic and 0 solid). The average time to first recurrence was 24 months (SD = 22 months). Management for tumor regrowth included 3 (16 %) total resections, 10 (53 %) subtotal tumor resections

with cyst wall fenestration, 1n (5 %) subtotal resection with a cystic catheter, 3 (16 %) cystic aspirations, and 2 (11 %) radiation therapy.

Patients did not develop tumor regrowth following gross total resection of their first recurrent tumor. Five patients (50 %) who received a subtotal resection with cyst wall fenestration presented with a second tumor progression—3 (60 %) of these patients did not receive radiation therapy. All patients treated with subtotal resection and a cystic catheter for first recurrence progressed following treatment. None of these patients received radiation therapy. Two of the three patients (67 %), who received cystic aspiration, without adjunctive radiation therapy, also experienced tumor regrowth. Lastly, patients who received radiation therapy, without surgical management, for first tumor recurrence did not progress. Two patients with tumor regrowth following initial treatment received chemotherapy. The patient who received systemic chemotherapy did not present with tumor progression, while the patient who received intracystic chemotherapy experienced tumor regrowth.

**CONCLUSION:** Subtotal resection was a significant risk factor for tumor regrowth in patients and radiation therapy may play a protective role in tumor recurrence. The data in this large series did not support one treatment type over another for recurrent cystic tumors. Prospective studies comparing a larger population of recurrent craniopharyngiomas are warranted.

Increasing Discussion and Documentation of HPV Vaccine Status in the Inpatient Setting <u>Vanessa Olvera, BA</u>; Alexandra Mihalek, MD; Chelsea Garnett, MD; Nora Pfaff, MD; Giancarlo Cardoza, BS; Mary Rose Mamey, PhD, MA; Matthew Keefer, MD; Susan Wu, MD; Division of Hospital Medicine, Children's Hospital Los Angeles

**Background:** The AAP recommends updating vaccine status at every healthcare visit. There are no studies evaluating recommendation of HPV vaccination in the inpatient setting. This project aims to assess the effectiveness of hospital-based interventions on resident documentation of HPV vaccine status.

Methods: From March 2016 to December 2017, 30 adolescent inpatient charts at an urban freestanding children's hospital were randomly selected monthly to assess resident documentation of CDC recommended vaccines. Eligible patients were ≥ 11 years old and admitted to a resident inpatient pediatrics service. In August 2016, PDSA cycles were implemented to improve HPV vaccine documentation. Binary logistic regression was used to identify associations between vaccine documentation and patient age or gender. Chi-square testing was utilized to compare documentation of HPV, other vaccines and seasonal variation. Monthly data was plotted on a run chart and analyzed using Shewhart rules.

**Results:** 660 patient charts were reviewed over 22 months. HPV vaccine documentation increased from 10% to 16.7% post-interventions. This finding was not statistically significant. Documentation was highest after an education session and addition of EMR templates (23.3%).

HPV documentation was more likely to occur for females than males (B= -0.58, p=.043), and was not significantly associated with age nor seasonal variation (p=.822). There was no significant difference between documentation of HPV and influenza vaccines ( $\chi$ 2=1.76, p=.185). Influenza vaccine documentation was statistically associated with seasonal variation (pp<.001), and not with age nor gender.

**Conclusion:** Documentation of HPV vaccine status can be improved through low-cost interventions, however compliance remained poor. Although the HPV vaccine is recommended for both genders, providers are more likely to document status for females. Continued identification of sustainable interventions are needed to target these issues.

#### Prevalence of Group B *Streptococcus* in Pregnant Women in Ulaanbaatar, Mongolia <u>Divya Patel</u>, MSII, Pia Pannaraj, MD/MPH, Badarch Jargalsaikhan, MD/PhD

**Background**: The neonatal mortality rate in Mongolia remains high, at 11.1 per 1000 live births, with neonatal sepsis accounting for 5% of these deaths. The leading cause of neonatal sepsis globally is Group B streptococcus (GBS). Many healthy women are colonized with GBS, and can transmit it to their infants during childbirth. A small fraction of exposed infants go on to develop GBS disease, which often leads to death or poor neurodevelopmental outcomes. Vertical transmission of GBS is preventable through intrapartum antibiotic prophylaxis or maternal vaccination. There is currently a multivalent vaccine in clinical trials, which could become an effective preventative intervention in Mongolia. Currently, there is no information about the burden of GBS disease in neonates in Mongolia. The aim of this prospective cohort study is to measure prevalence of rectovaginal GBS colonization in pregnant women in Ulaanbaatar, to determine GBS serotype distribution, and to estimate the incidence of GBS disease in Mongolian infants.

**Methods**: Third trimester pregnant women receiving prenatal care at Urguu Maternal Hospital in Ulaanbaatar will be approached for enrolment in the study. Rectovaginal swabs will be collected and cultured for GBS. GBS positive samples will be serotyped. 300 women will be enrolled in the study. Maternal colonization prevalence data along with World Health Organization census data on annual birth rate in Mongolia will be used to estimate incidence of GBS disease, given that 1-2% of infants born to colonized mothers will develop early onset GBS disease.

**Results**: Study set up and training were initiated in Ulaanbaatar during summer, 2017. Data collection phase will be carried out by Mongolian colleagues over a period of 6 months, starting in spring, 2018. Based on previous studies, we speculate that approximately one third of the women will be colonized by GBS.

**Conclusions**: GBS is a common colonizer of healthy pregnant women. Determining GBS prevalence and serotype distribution among Mongolian women is critical for guiding maternal immunization programs to reduce infant morbidity and mortality from GBS infection in Mongolia.

#### Assessing Predictors of Morbidity and Mortality in Patients with Pulmonary Atresia with Intact Ventricular Septum

Krishan Patel, Arash Sabati, MD, Jon Detterich, MD

**Background/Hypothesis**: Pulmonary atresia with intact ventricular septum (PAIVS) is a rare congenital heart defect that affects nearly 7 in 100,000 live births. PAIVS has been treated using various surgical options that may result in: 1. Biventricular repair where continuity between the right ventricle (RV) and pulmonary artery is established, 2. One and a half ventricle palliation that establishes continuity between the RV and pulmonary artery in addition to a Glenn procedure where the superior vena cava is connected to the right pulmonary artery, or 3. Single ventricle palliation utilizing a Fontan completion, connecting the inferior vena cava to the pulmonary arteries after a Glenn with no continuity between the RV and pulmonary artery established.

Though several authorities in the field have advocated for a balanced approach that uses initial tricuspid Z-scores to predicate the type of repair, there has been an innate bias towards biventricular repairs due to the belief that it maximizes long-term functional health status. Several studies have demonstrated the advantages of single ventricle and 1.5 ventricle palliations in patients with borderline degrees of right-sided hypoplasia, with benefits including decreased mortality and increased exercise capacity. However even z-score methods can be imperfect, as the scores can be derived from different data sets, leading to inappropriate surgical pathway allocation. To our knowledge, there has not been a comprehensive review of echocardiogram and cardiac catheterization data comparing the different

treatment groups and their pre- and post-surgery anatomies and physiologies. This project aims to determine risk factors for mortality in patients with pulmonary atresia with intact ventricular septum and determine predictors of successful two ventricle repair versus single ventricle palliation versus 1.5 ventricle palliation.

**Methods**: Between January 2003 and December 2015, 161 patients were treated for PAIVS at our heart center with catheter-based interventions and/or surgery. Echocardiogram and cardiac catheterization data was retrospectively collected and reviewed. We will use multivariate logistic regression to determine predictors for survival, area under the curve analysis to determine the importance of the variables for survival, and Kaplan Meyer curves to determine whether

survival is different in the different groups (single ventricle palliation, 1.5 ventricle palliation, and two ventricle repair).

**Results**: We are still currently in the process of collecting and analyzing data. We expect that right ventricular (RV) morphology and tricuspid Z-score will be the best predictors of mortality across all groups. We expect patients with higher tricuspid Z-scores will fare better in the single ventricle palliation and 1.5 ventricle palliation groups rather than the two-ventricle repair group.

**Summary/Conclusion**: This project will give insight on the management of patients with PAIVS based on imaging findings. In the future, we hope to expand the end points of this study beyond mortality to include exercise physiology data, which objectively conveys the functional status of PAIVS children.

#### Preoperative Echocardiographic Predictors of Left Ventricular Outflow Tract Reintervention following Repair of Interrupted Aortic Arch with Ventricular Septal Defect

<u>Rawad Rayes</u>, Andrew L. Cheng MD , S. Ram Kumar MD PhD, Winfield J. Wells MD, Vaughn A. Starnes MD, Pierre C. Wong MD

**Background:** Interrupted Aortic Arch (IAA) is a rare congenital defect in the development of the aorta leading to a separation/coarctation between the ascending and descending thoracic segments, and is frequently accompanied by a Ventricular Septal Defect (VSD). The preferred treatment involves pharmacologically maintaining a patent ductus arteriosus until a surgery known as a biventricular repair can be performed (usually within the first 2 weeks of life); however a small but significant proportion of patients will require reintervention for left ventricular outflow tract (LVOT) obstruction. Several preoperative echocardiographic criteria have been proposed to predict the likelihood of subsequent development of important LVOT obstruction. We hypothesized that preoperative aortic valve (AoV) annulus diameter is the best predictor of future need for surgical reintervention.

**Methods:** We retrospectively reviewed pre and postoperative echocardiograms and medical histories of 50 infants who underwent neonatal primary biventricular repair of IAA/VSD between 2000 and 2016 at our institution (CHLA). Parameters included diameters of LVOT (anterior/posterior and lateral), AoV annulus, aortic root, ascending and descending aorta, mitral valve annulus, and pulmonary valve annulus; and cross-sectional areas (CSA) of LVOT, AoV, and pulmonary valve. Primary endpoint was surgical LVOT reintervention. Differences between reintervention and non-reintervention groups were determined with Student's t-test. Receiver operator characteristic (ROC) curves were used to determine optimal discrimination thresholds for survival analysis using Cox proportional hazard models. **Results:** Median age at surgery was 8 days (interquartile range 5-12 days). Mean weight was 3±0.6 kg. Median follow-up time was 2.2 years (interquartile range 0.1-7.1 years). Nine patients (18%) required reintervention at a median 1.9 years after initial surgery. AoV annulus diameter, AoV CSA, AoV z-score, weight-indexed AoV annulus diameter, and BSA-indexed AoV annulus diameter were significantly different between the reintervention group and non-reintervention groups (p<0.01 for all variables). By multiple regression among measured variables, AoV annulus diameter was most strongly associated with reintervention. ROC curve identified 4.5 mm as the threshold that best estimated need for

reintervention. Hazard ratio of reintervention for AoV annulus  $\leq$  4.5 mm versus > 4.5 mm was 8.2 (p=0.01).

**Conclusions:** Preoperative aortic valve annulus  $\leq$  4.5 mm was found to be the best echocardiographic determinant for LVOT reintervention following primary biventricular repair of IAA/VSD. For infants below this threshold, initial palliation with an alternative surgery (e.g. Norwood procedure), may be a preferable first-stage intervention with potential for biventricular repair in the future.

#### Opportunities to Decrease Preterm Births Among African American Women in Los Angeles County Ashlee Roberson, Medical Student, KSOM, Diana Ramos, MD, MPH, Faculty Advisor, KSOM Dept. of Obstetrics & Gynecology

**Background:** In the United States, preterm birth, or birth before 37 weeks gestation, is the leading cause of infant mortality. In 2015, the preterm birth rate in Los Angeles County (LAC) was 8.8% compared to 8.5% in California. Preterm births in LAC have declined over the past several years but ethnic disparities persist, with African Americans having the highest rates, 12.1% compared to 8.0% in Whites and 8.8% in Hispanics. Disparities in preterm birth vary between hospitals, even those within close proximity. This study will highlight differences in healthcare received by African American women with a preterm birth and best practices provided by hospitals with lower preterm birth rates.

**Methods:** African American women (n=20) with a history of preterm birth will be interviewed from two LAC hospitals in close proximity, but with disparate preterm birth rates. Participants will be recruited via email using preterm birth parent group listservs at participating hospitals. First, a brief survey will be administered to assess knowledge of select risk factors. Then, focus group discussions will be conducted to allow participants to share their pregnancy experiences along with identifying 1) what advice based on their experience participants would give to other women at risk for preterm birth and 2) preferred ways to share health information with African American women. A descriptive analysis of the collected data will be performed.

**Results:** Results have yet to be obtained. Differences in perceived prenatal care, preterm labor precautions, and when patients should present to labor and delivery are some of the differences predicted to be seen. We also predict 1) lack of social support and 2) stress stemming from racism/discrimination, physical/verbal abuse, and financial worries to be key risk factors for preterm birth in the African American community.

**Conclusions:** The findings generated in this project will be used to identify best practices within healthcare systems and to identify opportunities for education and intervention to help reduce preterm births and disparities.

## A longitudinal, prospective study of DTI-based white matter disturbances in young adults born prematurely

Jonathan Sadik, Ravi Bansal, Siddhant Sawardekar, Bradley S. Peterson. Institute for the Developing Mind, Children's Hospital Los Angeles and the University of Southern California. Stein Magus Aukland, Irene B. Elgen, Lars Ersland. Haukeland University Hospital and the University of Bergen.

**Background:** Preterm low birth weight infants tend to display neurocognitive deficits later in life. Past work has shown that deficits in numerous brain areas, in both white and grey matter, contribute to this disparity. We aim to corroborate the brain regions affected by preterm birth, and explore the nature of these deficits, using diffusion tensor imaging (DTI) of preterm and healthy cohorts assigned at birth. **Methods:** One hundred and three preterm-born individuals and 110 term-born subjects, originally recruited at birth and early childhood, had DTI images taken at 19 years of age. Neurocognitive

measures were also recorded at this time. The DTI images were processed using computer programs and numerous measures were calculated, including the fractional anisotropy (FA) and average diffusion coefficient (ADC). Statistical programs were used to compare differences in these values between the two groups.

**Results:** After removing scans with poor quality, 190 subjects remained: 101 controls and 89 preterm. The preterm cohort displayed lower FA in various white matter areas, including the external capsule, posterior and anterior internal capsule, and the splenium of the corpus callosum. Grey matter FA was also reduced, namely in the thalamus and caudate. The preterm group had higher FA in the superior longitudinal fasciculus and centrum semiovale (white matter areas), and in the lenticular nucleus and insula (grey matter). There was a higher ADC in the preterm group in the subcortical gray matter nuclei—basal ganglia and thalamus.

Birth at a younger gestational age in the preterm group likely contributed significantly to the betweengroup findings. The effects of birthweight and Apgar scores were minimal.

**Conclusion:** Preterm birth differentially affects the development of white matter pathways and reduces cell density of subcortical gray matter nuclei, and in direct proportion to gestational age at birth. Birth at a younger gestational age likely disrupts normal maturational processes in deep white matter pathways and gray matter nuclei of the fetal brain. These effects endure into young adulthood. Future work includes assessing whether abnormal brain development mediates cognitive and behavioral outcomes in individuals born preterm.

#### Delayed cord clamping (DCC) in preterm and term infants Maya Sampath, BS, Ting-Yi Lin, MD

**Background:** While recent evidence indicates that DCC can have significant benefits to neonatal outcomes, there are some concerns. The DCC protocol may need to be further modified to minimize risks. Our goals are to examine the protocol compliance rate, examine the impact of DCC, and compare the outcome measures in preterm vs. term infants after implementation of DCC. We anticipate greater benefit in infants of lower birth weight and gestational age.

Methods: Hollywood Presbyterian Medical Center implemented the DCC protocol in April 2016 based on the ACOG/AAP recommendations. Data was collected on retrospective metrics including CBC, electrolyte panels, the incidence of phototherapy, and the incidence of transfusions. Infants in pre- and post-intervention periods have been further divided into three gestational age (GA) groups: preterm (< 34 weeks GA), late preterm (34-36 6/7 weeks GA), and term (≥ 37 weeks GA) infants. The data regarding the outcome metrics was tallied and assessed using paired T-tests, chi-squared tests, and ANOVA. **Results:** Ineligible infants were eliminated from the data and compliance rates were analyzed. Of the eligible infants, compliance rates fluctuated between 68.2 and 79.9%.

The outcome measures mentioned above were compared within each gestational age group between infants who underwent DCC and those who did not. In preterm infants, there were no significant differences in outcomes. In late preterm infants, the only significant difference was calcium (p=0.023). In term infants, the only significant difference was sodium (p=0.036).

**Conclusions:** These are very preliminary results and more data will be collected before conclusions can be made. In preterm infants, DCC appears to have no significant risks or benefits. In late preterm infants, DCC appears to increase the risk for hypocalcemia. In term infants, DCC appears to decrease the risk for hyponatremia. Once more data points are collected, propensity-matched analysis will be performed and the results will be reevaluated.

#### Impact of BMI on Treatment-Related Toxicity in Pediatric Non-Hematologic Malignancies <u>Elizabeth Scott, MS2</u>; Teresa Rushing, PharmD, Etan Orgel, MD

**Background:** Understanding risk factors for toxicity is essential to promoting individualized treatment of childhood cancers. Previous studies have shown obesity increases risk for cancer-associated mortality in adults. However, scant data describes obesity's impact on treatment related toxicity (TRT) and survival for non-hematologic pediatric tumors. The purpose of this study was to determine if obesity significantly increases risk of TRT and poorer survival in pediatric patients.

Methods: A retrospective cohort study of patients ages 2-21 diagnosed with a cisplatin-treated nonhematologic malignancy (June 2008 - September 2016). Data collected included body mass index percentile (BMI%) at diagnosis and end of study (end of therapy, prior to transplant or relapse) Grade ≥3 TRT, demographic, therapy, and survival data. We examined the distribution of obesity and each endpoints (TRT, intensive care unit [ICU], dose reductions [DR], event-free survival [EFS]). TRT was analyzed using a competing risks multivariable regression model with stepwise forward selection (p<0.15) and significance set at p<0.05.

**Results:** Approximately 25% (52/221) of the cohort was overweight/obese at diagnosis, 18% (40/221) were adolescent and young adults (AYA), and the distribution of diagnoses were as expected for a pediatric cancer cohort. Two-thirds of patients (146/221) experienced ≥1 TRT and 20% a dose-reduction (51/221). BMI% was not associated with risk of TRT (sHR obese= 1.07, p=0.763). TRT and ICU use was not significantly different in obese patients (p=0.148 and p=0.364 respectively). Obesity, TRT or DR were not associated with EFS (HR=0.70, p=0.396, HR=0.92, p=0.769, and HR=0.83, p=0.510 respectively). **Conclusion:** Obesity did not significantly influence risk for overall serious toxicity or survival. Future directions will explore the impact of obesity during therapy on the development of specific toxicities.

#### Role of Age, Sex, BMI and Degree of Mindfulness in Determining Acceptability of Imagine HEALTH After-school Intervention

#### <u>Sharonya Shrivastava</u>, MSII, KSOM, Daniella Florindez, MS, Christianne Lane, PhD, Marc Weigensberg, MD

**Goal:** The Imagine HEALTH study is a lifestyle intervention that utilizes the mind-body modality of guided imagery (GI) to promote health and prevent diabetes in youth. Our objective is to examine the impact of factors such as sex, BMI status, grade in school and degree of mindfulness at baseline on acceptability of the program to the participants.

**Methods:** 24 students (11F, 13M) ages 15 to 18 participated in a 12-week program of biweekly lifestyle education classes and weekly GI sessions (use of mental images for stress reduction and motivating lifestyle behavior change). Program staff developed exit surveys to assess program acceptability. Students were asked to rate their level of agreement with statements relating to the benefit of the program to their lives as well as statements related to the ease of participating in the GI activities. **Results:** On a scale of 1 to 4, 1 being "really liked" and 4 being "really disliked the program," 73% of students 17 or older selected 1 compared with 67% of students under 17. 80% of female students selected 1 compared with 70% of male students. Differences in acceptability based on BMI status were small. 73% of students with BMI status below the group average (25.4) selected 1, versus 75% of students with above average BMI status. Degree of mindfulness data is pending.

**Summary/Conclusion:** These data show that students that are older or female may demonstrate greater acceptability of the program. More data is needed to determine if these differences in acceptability are significant.

#### HEROES: Healthy Eating Through Reduction of Excess Sugar Katharine B. Stiers; Jennifer Truong, MPH; Gregory Harlan, MD MPH; Michael Goran, PhD

**Background:** Non-alcoholic fatty liver disease (NAFLD) is a significant and under-addressed health issue in the Hispanic population. Our study aims to determine the effect of dietary sugar reduction in obese adolescents and examine differential effects based on the *PNPLA3* genotype. *PNPLA3* has 50% prevalence in Hispanics and is associated with NAFLD. The data from this intervention will potentially offer a nutrigenetic strategy that will reduce liver fat through a gene-dietary interaction. This study may impact personalized dietary recommendations for treatment and prevention of NAFLD as a function of genetic predisposition, and clarify mechanisms controlling liver fat.

Methods: This is a 12-week prospective RCT involving 180 Hispanic patients 12-18 years old with a BMI ≥ 95th percentile. The data collected include *history* (demographic information, residential history, diet recall, physical activity recall, pubertal development), *vital signs, body measurements, labs* (CBC, biomarker assays, OGTT, DNA isolation, genotype distribution, stool collection), and *imaging* (DEXA scan and Liver MRI). The intervention group has water bottles delivered weekly and 4 sessions with a dietician. The control group receives nutrition pamphlets. All participants are reevaluated at 12 weeks. **Results:** We have 30 participants recruited, 18 of which have completed the study. Data collection and analysis is ongoing. Our goal is 180 participants over 4 years. Enrollment with likely increase with the updated recruitment criteria. We anticipate the intervention group will have a greater reduction in liver fat compared to the control group.

**Conclusion:** Research on the topic of gene-diet interactions in patients with the *PNPLA3* genotype is still in the early stages. The goal of this study is to demonstrate an association between a low-sugar diet and a reduction in hepatic lipid content for Hispanic adolescents, a high-risk population for fatty liver disease. Identification of an effective intervention could have widespread relevance.

#### GnRH Analog Suppression of Puberty in Youth with Gender Dysphoria: A Comparison of Implantable Histrelin

<u>Hillary Streeter Medical Student</u>, Dr. Johanna Olson-Kennedy MD, Julie McAvoy-Banerjea MPH, Division of Young Adult and Adolescent Medicine, CHLA

**Goal:** Histrelin is a gonadotropin releasing hormone agonist commonly prescribed to suppress endogenous puberty in youth with gender dysphoria, and is brand marketed by Endo Pharmaceuticals as SupprelinLA and Vantas. SupprelinLA has FDA approval for use in treating central precocious puberty and costs \$33,741.19, whereas Vantas has FDA approval for use in treating advanced prostate cancer and costs \$4,198.32. Neither implant has been FDA approved for use in youth with gender dysphoria. The objective of this study was to determine if SupprelinLA and Vantas were equally effective in suppressing puberty in transgender youth.

**Methods:** The study is a retrospective chart review of patients with gender dysphoria at the Center for Transyouth Health and Development at CHLA who had a puberty blocking implant placed for suppression of their endogenous puberty. Patients who received injectable GnRH agonists, such as leuprolide acetate, antiandrogens, or cross gender hormones were ineligible. Participants were stratified and analyzed by assigned sex at birth and implant brand name. Sex steroid levels, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) collected at around 8 weeks and one year following insertion were abstracted from the medical record. Hormone levels were compared across cohorts to determine if participants achieved pre-pubertal hormone levels. **Results:** Gonadotropins decreased across cohorts to pre-pubertal levels within the first 8 weeks of treatment and did not change thereafter. Sex steroid levels across cohorts at 8 weeks and one year were similar in value, all of which were at pre-pubertal levels or just slightly above.

**Conclusions:** Vantas and SupprelinLA both are equally efficacious for suppressing puberty in youth with gender dysphoria. The major limitation in this study was the small sample size. Further studies are needed to include a larger number of participants to support the findings from this study.

#### Resource utilization of neonates with central line-associated bloodstream infection, ventilatorassociated pneumonia, and urinary tract infection in the US: 2009-2012

<u>Courtney W. Tam, BS, BA</u><sup>1</sup>, Ashley Y. Song, MPH<sup>1</sup>, Srikumar Nair, MD, MHA<sup>1</sup>, Ting Yi Lin, MD, PhD<sup>1</sup>, Steven Chin, MD, MSc<sup>1</sup>, Philippe Friedlich, MD, MSEpi, MBA<sup>1</sup>, Ashwini Lakshmanan, MD, MPH<sup>1,2,3</sup>
 <sup>1</sup>Fetal and Neonatal Medicine Institute, Division of Neonatal Medicine, Children's Hospital Los Angeles; Keck School of Medicine, University of Southern California, Los Angeles, CA, United States
 <sup>2</sup>Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States

<sup>3</sup>Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, United States

**Purpose:** Central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and urinary tract infection (UTI) are hospital-acquired infections (HAI) associated with increased morbidity and mortality in the neonate. Despite HAI prevalence, there exists limited knowledge regarding resource utilization in neonatal CLABSI, VAP, and UTI. This study aims to determine the difference in resource utilization patterns such as length of stay (LOS) and total hospital cost (THC) among neonates with CLABSI, VAP and UTI.

**Methods:** Data were obtained from the Kid's Inpatient Database from the Healthcare Cost and Utilization Project for 2009-2012. Admissions were identified by ICD-9 diagnosis code (CLABSI=999.31/999.32, VAP=997.31, UTI=771.82) and neonates defined as  $\leq$ 28 days. Statistical analysis included  $\chi^2$  and Kruskal-Wallis tests. Weighted variables were applied for analysis of national estimates. **Results:** We identified 1165 neonates with CLABSI, 354 neonates with VAP, and 8895 neonates with UTI from 2009-2012. Patient sex (p<0.01), race (p<0.01), payer (p=0.0005), hospital region (p<0.001), hospital teaching status (p<0.001), and mortality (p<0.001) were significantly associated with neonatal CLABSI, VAP, and UTI.

There are significant relationships between median LOS, hospital charge (HC), and THC and neonatal CLABSI, VAP, and UTI (p<0.001). For CLABSI neonates, median (IQR) LOS was 68.5 (61) days while median (IQR) LOS was 97 (57) days for VAP neonates and 16 (60) days for UTI neonates. For CLABSI neonates, median (IQR) THC was \$154,383 (\$173,558) while median (IQR) THC was \$237,410 (\$226,873) in VAP neonates and \$28,759 (\$113,418) for UTI neonates.

**Conclusions:** Neonatal CLABSI, VAP, and UTI were associated with elevated LOS, THC, and HC. Further studies on resource utilization patterns are necessary to improve management and reduce socioeconomic burden of neonatal HAIs.

**Family Perception of Barriers to Care for Improving Asthma Control in Children Marissa Trinidad**, Dr. Marielena Lara, Dr. Evie Huang, Dept. of Pediatrics at CHLA

**Background**: There is an overall need for sustained asthma prevention and control efforts in children, however racial disparities present a challenge to effective pediatric asthma care in the underserved and low-income minority populations. The purpose of this study is to understand what underserved families perceive as barriers to care for their children with asthma.

**Methods**: Participants were recruited from patients at the AltaMed Clinic in CHLA. If parents/legal guardians answered yes to at least 1 of 5 qualifying questions, they could participate in the study. A survey was given that asked about how often they experienced different barriers to care for their child with asthma and their education regarding asthma care. The final part consisted of 2 open-ended questions that required the families to identify what they need to care for their child with asthma and what they perceive as the most important barrier they face in acquiring care. This information will be analyzed to identify the most commonly experienced barrier and the area of education that is most lacking. This data will also be stratified by race/ethnicity, primary language, and whether the child has a regular doctor to look for trends in these participant subgroups.

**Results**: Recruitment for this study is still ongoing. Based on prior studies, it is expected that Black and Latino parents/legal guardians will experience disproportionately more barriers to accessing health care than participants of other races/ethnicities. It is also possible that those whose primary language is not English and those who do not have a regular pediatrician, may be less educated regarding their child's asthma care.

**Conclusion**: In order to improve pediatric asthma care, it is imperative that physicians understand what families perceive as barriers to treatment. In doing so, healthcare providers will be better able to address the patient concerns and deliver effective solutions, as well as culturally and socio-economically appropriate care.

#### CRISPR-Cas9 Correction Restores Endocrine Differentiation in NGN3-null iPSCs Kyle Vogt, Kate Millette, Senta Georgia

**Background**:  $\beta$ -cells make up 70% of the endocrine pancreatic islets and are responsible for secreting insulin, which in turn is essential for serum glucose homeostasis. Literature suggests that a transcription factor (TF) named *neurogenin3* (*ngn3*) is required for the proper development of endocrine cell lines. We have identified a patient with a *ngn3* loss of function mutation. In order to investigate the roll of this gene in development of pancreatic progenitor cells, we used iPSC's from our patient and Human H1-ESC's and sought to compare the expression of various endodermal, pancreatic, and  $\beta$ -cell genetic markers at spaced time points in a previously described differentiation protocol.

**Methods**: RNA was from cell culture at S0, S1, S3, S4, S5, and S6 checkpoints in the established 21-day pancreatic differentiation protocol. cDNA was formed from extracted. cDNA was then run on 48-well qPCR plate at a standard concentration of 15ng/uL with the stage-appropriate probe added in duplicates. CT data was obtained and compared to the standard (H1 S0) for H1, NN3 (our patient's iPSC's) and a corrected iPSC line, N3C3. In addition, qPCR's were run for another clonal expansion of our patient's stem cells, labeled N2 and a corrected N2C10.

**Results** (note: data is still not complete): Early stages (S0-1) show similar differentiation profiles and gene expression across all lines. However, NKX6.1 (a downstream target of *ngn3* and a TF essential  $\beta$ -cell development) was significantly lower in the NN3 line when compared to the H1 and corrected line in S4 data. Other, non-*ngn3* dependent markers like *PDX1* were near control levels. In later stages, there is significant decrease in definitive endocrine and  $\beta$ -cell markers in the NN3 line when compared to all other lines.

**Conclusions**: *ngn3* appears to be essential for proper  $\beta$ -cell differentiation *in vitro*. It is worth noting, however, that our patient made insulin as a child, suggesting some potential *ngn3*-bypass method of producing  $\beta$ -cells *in vivo*. Further studies are needed to elucidate the exact role of this gene and its role in pancreatic development with potential implications in various endocrine disorders as well as genetic therapy for this patient.

### Analysis of copy number aberrations, loss of heterozygosity, and somatic mutations in medulloblastoma FFPE samples using Oncoscan

<u>Jennifer Wang BA</u>, Nathan Robison MD, Ashley Margol MD, Shahab Asgharzadeh MD, Hematology, Oncology, and Bone and Marrow Transplantation, Children's Hospital Los Angeles, USC Keck School of Medicine

**Background/Goal:** Medulloblastoma is the most common malignant brain tumor of childhood. A major goal of medulloblastoma research is to decrease treatment toxicity while maintaining high cure rates. Better risk stratification of patients may allow us to tailor treatments to different patients and minimize the usage of toxic radiation therapy. In the past decade, medulloblastomas have been classified into four molecular subgroups, each with different prognoses and patient outcomes: sonic hedgehog (SHH), Wingless (WNT), group 3, and group 4. Our goal is to classify medulloblastomas into molecular subgroups using Oncoscan, as well as identify additional new biomarkers that are correlated with clinical outcomes.

Methods: FFPE tissue sections from 100 medulloblastoma tumors were sent to Affymetrix for Oncoscan assay, which amplifies DNA regions of interest using molecular inversion probes and captures them using universal tag arrays. The data received was analyzed using Nexus Express software. The medulloblastoma tumors were classified into molecular subgroups based on consensus biomarkers: CTNNB1 mutation, PTCH1/SMO/SUFU mutation, GLI2 amplification, MYCN amplification, i17g, MYC amplification, and CDK6 amplification. Then additional new biomarkers, in the form of loss of heterozygosity or homozygous deletions, were identified that may be correlated with clinical outcomes. **Results:** 63 of the medulloblastoma tumors were classified as group 3/4, 18 tumors were SHH, 4 tumors were WNT, and the remainder did not fall into one of the consensus molecular subgroups of medulloblastoma. Loss of heterozygosity was frequently found at these chromosomal regions: 8p, 8q, 9q, 10q, 11p, 11q, and 17p. Loss of heterozygosity at 9q was strongly correlated with SHH (p<0.0001), and loss of heterozygosity at 17p was strongly correlated with group 3/4 (p<0.001). Homozygous deletions of 22q11.23 and 8p11.22 were also common amongst the medulloblastoma tumors. **Conclusions:** Loss of heterozygosity at 8p, 8q, 9q, 10q, 11p, 11q, and 17p and homozygous deletions at 22q11.23 and 8p11.22 are potential new prognostic and predictive biomarkers for medulloblastoma. Next steps in our research include performing hypothesis testing and survival analysis to look for correlations between these molecular markers and clinical outcomes.

#### Physician Perspectives and Attitudes on Genetic Testing and its Role in Practice Andrew Wingerson, BS; Joseph Hacia, PhD; Sulagna Saitta, MD, PhD

**Goal:** There is an increasing prevalence of genetic testing in making diagnoses and guiding treatment in modern medicine. However, the current physician workforce does not routinely receive continued training on how to order appropriate tests, interpret the results of genetic tests, nor what actions should be taken with a given set of results. We seek to identify gaps in the knowledge of practicing physicians regarding genetic testing.

**Methods:** We are developing an anonymous survey of 20-30 questions to be emailed to physicians currently in practice at USC. Physicians will include both generalists and specialists. The questions mainly require a response on a five point Likert scale, with a subset of open-ended questions. The survey is divided into sections: a general section, a genetics section, a family impact section, an education section, and an impact section. Open response questions will be coded for qualitative themes.

**Results:** By dividing questions into specific categories, we hope to illuminate gaps in knowledge as well as barriers to providing physicians with the information they need to successfully incorporate genetics

into their practice. We also seek to determine how physicians would prefer to be further educated about genetic testing in order to guide the development of future educational modules and programs. **Conclusions:** Although we have yet send out our survey, we hypothesize that physicians are not fully comfortable discussing the results of genetic tests with patients and that they would benefit from further education. We aim to develop modules or a class in a manner directed by the results of these data.

Blood Perfusion Abnormalities in Individuals with Autism Spectrum Disorder <u>Ariana Zargarian<sup>1</sup></u>; Ravi Bansal<sup>1,2</sup>; Siddhant Sawardekar<sup>2</sup>; Bradley S. Peterson<sup>1,2</sup> <sup>1</sup>Keck School of Medicine, University of Southern California, <sup>2</sup>Institute for the Developing Mind, Children's Hospital Los Angeles

**Background:** Autism Spectrum Disorder (ASD) is characterized by impaired social interactions and communication and restricted and repetitive behaviors. Perfusion and blood flow measures are an indirect index of regional metabolism that may aid understanding of pathogenesis and the neural systems that produce the illness phenotype. Our study will use Arterial Spin Labeling (ASL) Magnetic Resonance Imaging (MRI) to compare cerebral blood flow (CBF) in ASD vs typically developing (TD) controls.

Methods: We matched the subjects (N=111) in age and sex and obtained Autism Diagnostic Observation Schedule (ADOS) scores for individuals with ASD. We acquired pulsed ASL MRI data and corrected for head motion. Using pair-wise subtraction of the control and labeled images, we calculated perfusion-weighted images and averaged across the imaging time series. We performed voxel-wise multiple linear regression comparing CBF between the groups with age and sex as covariates. **Results:** We found increased CBF in

ASD in the dorsal white matter, basal ganglia and nucleus accumbens. Increasing scores for the ADOS accompany greater perfusion in the white matter and lenticular nucleus. **Conclusion:** Though perfusion in



Figure 1: ASD vs TD differences in CBF Hyperperfusion in ASD in white matter (CR=corona radiata, CC=corpus callosum, IC=internal capsule), caudate (Cd) nucleus, lenticular (Lent) nucleus, nucleus accumbens (NA), thalamus (Th)

white matter is approximately half of gray matter perfusion, white matter still has considerable metabolic demands to support axonal processes and glial cell functioning. Increased CBF in white matter may derive from altered axonal and glial cell metabolism in ASD. Altered white matter hypermetabolism may contribute to the disruption of long-range functional connectivity that is increasingly reported in ASD. Altered basal ganglia development and connectivity, implicated in motor and cognitive dysfunction in ASD, may relate to our findings of hyperperfusion.

## PLASTIC SURGERY

#### Competency-Based Surgical Education in Low Resource Settings: Development of a Novel Training Program

#### Jacqueline Stoneburner, BS, Meghan McCullough, MD, William Magee, III, MD, DDS, Division of Plastic and Reconstructive Surgery, Keck School of Medicine

**Background:** The Lancet Commission on Global Surgery estimates that 5 billion people lack access to safe, affordable and timely surgical and anesthesia care. A critical component of the inadequacy of surgical care worldwide is the lack of trained providers. While competency-based surgical training has been advanced in high-resource countries, it is poorly understood how these training models might be applied to low resource settings to increase surgical capacity. To improve surgical training in low- and middle-income countries, the CHLA/Operation Smile collaboration created a novel competency-based surgical educational initiative and examined the efficacy of this intervention on surgeon learning. This initiative combines formalized mentor-trainee pairings, intensive intra-operative instruction, and structured evaluation to be implemented in the cleft lip and palate surgical mission setting. **Methods**: Nineteen trainees participated in a total of 32 training initiatives occurring in nine international mission sites from November 2016 to January 2018. Each trainee completed a pre- and post-mission self-evaluation, mentor evaluations and mission reflections. Each mentor assessed trainee technical and non-technical competency daily. Specific competency improvement was assessed using paired t-tests, and improvement was correlated with prior trainee experience, caseload, and mentor quality using bivariate correlational analyses.

**Results:** Trainees demonstrated significant improvement in confidence scores for surgical technique (61.0% to 68.0%, p<0.05). Significant improvement was also seen in general surgical competency (58.3% to 67.7%, p<0.01) and overall surgical competency (59.7% to 68.2%, p<0.01). Overall procedure-specific competency improvement was significant (44.7% to 61.5%, p<0.01), and specifically significant for unilateral cleft lip (45.1% to 64.2%, p<0.01) and cleft palate repairs (43.9% to 62.2%, p<0.01). A strong positive correlation was found between total cases performed prior to the mission and pre-mission confidence scores (0.61, p=0.01), while a strong negative correlation was found between pre-mission confidence scores and average change in confidence scores (-0.77, p<0.01). No significant associations were found between technical or non-technical competency improvement and mentor quality, total cases performed prior to the mission.

**Conclusion:** These data suggest evidence for the efficacy of the novel competency-based surgical educational initiative for trainees with varying skill levels and demonstrates that the quantity of cases undertaken may not impact surgeon learning. This paradoxical decrease in confidence in skill may be due to a greater self-awareness of limitations and areas of improvement as a result of increased supervision and instruction.

# **PREVENTIVE MEDICINE**

#### Correlates of non-medical use of methadone among people who inject drugs in California Johnathan Zhao, Alex H. Kral, Lynn Wenger, Ricky Bluthenthal

**Background**: Illicit use of opioid substitution medications such as methadone has been controversial. Yet, the behaviors and negative health impacts associated with methadone diversion are not wellunderstood. This study describes the prevalence of methadone diversion within a community sample of people who inject drugs (PWID) and characterizes factors associated with recent (last 30 days) use of diverted methadone.

**Methods**: PWID (N=777) were recruited using targeted sampling and interviewed in California (2011-2013). Descriptive, bivariate, and multivariate analyses were used to determine correlates of using diverted methadone in the last 30 days.

**Results**: Among PWID sampled, 21% reported recent diverted methadone use. In multivariate analysis, methadone diversion was not associated with increased odds of nonfatal overdose within the last 6. Factors associated with methadone diversion included recent methadone maintenance treatment, recent diverted buprenorphine use, higher injection frequency, schizophrenia diagnosis, both recent non-injection opiate prescription use and recent injection opiate prescription misuse, non-injection polysubstance use, and concern about arrest risk for drug paraphernalia.

**Conclusion**: PWID who divert methadone represent a vulnerable population marked by recent methadone maintenance, mental illness, frequent injection, non-injection drug use, and concerns with arrest. Yet, diverted methadone use did not increase the likelihood of nonfatal overdose. Future studies should seek to determine motivations for methadone diversion among PWID and whether they may predict readiness for treatment, response to withdrawal symptoms, and/or other medical indications.

# **Reproductive Health**

#### Late Preterm Steroids and Peripartum Maternal Infection at a Single Center

<u>Ellison Chen BS</u>, Kristen Uquillas MD, Richard H. Lee MD, Ugonna Ihenacho MPH, Victoria Cortessis PhD, Lorayne Barton MD

**Background**: Antenatal corticosteroids (ACS) are commonly administered to pregnant women at risk of delivery before 34 weeks to enhance fetal lung development. Following the Antenatal Late Preterm Steroids (ALPS) trial in 2016, this practice was extended to mothers at risk of delivering in the late preterm period (34 0/7 to 36 6/7 weeks). However, corticosteroid use is known to predispose patients to infection. This study aims to investigate whether women given late preterm ACS at our center were at increased risk of chorioamnionitis or endometritis, or had prolonged postpartum hospitalizations. **Methods**: A retrospective chart review identified all LAC+USC patients who based on the ALPS trial were eligible for late preterm ACS between February 2015 and July 2017. Maternal outcomes were compared using Student's t-test for continuous data and Pearson's chi-squared test for categorical data. Significance was defined as a P-value <0.05.

**Results**: Of 194 mothers found to eligible, 67 (34.5%) received ACS. The incidence of chorioamnionitis or endometritis was not significantly different between those who did and did not receive ACS, respectively (1.5% vs. 6.3%, p = 0.13). ACS recipients did not have significantly different postpartum length of stays compared to those who did not receive ACS ( $3.7 \pm 1.1 \text{ vs. } 3.7 \pm 1.1 \text{ days}$ , p = 0.88).

**Conclusion**: At LAC+USC, mothers who received late preterm ACS did not appear to experience greater risk of peripartum maternal infections, and ACS administration in the late preterm period did not appear to alter postpartum recovery time.

#### Attitudes Toward Contraception Use in a Rural Ugandan Community

<u>Carmen A. Cueto<sup>1</sup></u>, Sigita S. Cahoon<sup>2</sup>, Sandra Najuna<sup>3</sup>, Victoria K. Cortessis<sup>3</sup>, Laila I. Muderspach<sup>2</sup>

- 1. Keck School of Medicine, University of Southern California, Los Angeles, CA, USA
- 2. Department of Obstetrics and Gynecology, Los Angeles County Medical Center, University of Southern California, Los Angeles, CA, 90033, USA
- 3. Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, 90033, USA.

**Background**: Unmet contraceptive need remains high in low-income countries. There is a relative lack of research at the community level identifying attitudes and barriers towards contraception. This study aims to identify factors influencing contraceptive use among women in a rural Ugandan community in order to implement effective, sustainable programs to decrease unmet contraceptive need. **Methods**: A free response survey was administered to women in Mpigi District, Uganda in July of 2016 as part of a cervical cancer prevention program. Questions focused on attitudes toward contraceptive use, specifically factors and concerns surrounding contraception decision-making, future fertility desires, and thoughts on menstrual patterns. Surveys were translated into Luganda and were administered by the local study team. Free form responses were collected and qualitative themes were identified. Responses were coded by identified themes and then transferred into a REDCap software database. Data analysis was conducted using R software.

**Findings**: A total of 393 participants were surveyed and the average age of the study sample was 41 years with 73.2% (n=287) reporting pre-menopausal status. Of the 77.4% (n=222) pre-menopausal women reported sexual activity within the past 6 months, 50.5% reported they did not desire to become pregnant; however, only 35.7% of them reported current contraceptive use, while 64.3% were not using any form of contraception. The top three factors women identified when considering contraceptives were: reversibility (29.8%), convenience (16.3%) and effectiveness (13.2%). Of 179 women who reported concerns about contraceptives, the majority listed side effects (36.3%) as their main concern, followed

by irregular bleeding (35.2%), cancer (16.2%), amenorrhea (10.6%), infertility (8.4%), failure (5.6%), and decreased libido (3.9%). 59.6% (n=171) of pre-menopausal women reported no interest in forms of contraception that decreased menses. **Interpretation**: Our findings illustrate existing unmet contraception need in this rural Ugandan community and describe trends in local attitudes regarding contraception. Understanding these perspectives can guide future education targeted to specific community concerns and barriers to help improve contraception uptake where unmet need for contraception remains high.

#### Men's perspectives on and plans for contraception at the time of an abortion <u>Shruti Ria Dasgupta, MS II</u>; Sonia Rodrigues, MS II; Brian T. Nguyen, M.D. MSCP

**Goal**: A variety of factors may influence men's beliefs and behaviors surrounding contraception. While age, race/ethnicity, knowledge, and communication are known contributors to men's lack of contraceptive use, the influence of an unintended pregnancy and abortion is unclear. We aim to explore how the experience of an abortion might influence a man's perspectives and receptiveness towards contraception.

**Methods**: In 2015, we interviewed the male partners of women obtaining abortions at two facilities in a large, metropolitan city in the Midwestern United States. Participants were either present with their partner at the time of the abortion or recruited by the patient following the abortion. All interviews were conducted in private, either in-person or over the phone, following a brief demographic and screening survey. All interviews were transcribed verbatim and analyzed on NVivo; two researchers independently explored the transcripts for emergent themes related to men's perspectives on and plans for contraception. Their initial findings were consolidated into a codebook, with definitions based upon consensus, and which informed the remainder of the analysis. Coding consistency between the two was verified via early Kappa scores. Patterns were explored using queries and a coding matrix.

**Results**: We interviewed 29 men (mean: 28.5 years old), mostly minorities in a long-term relationship, within one month of their female partner's abortion. Eight themes on male partner contraceptive perspectives emerged from our analysis: "Contraceptive Responsibility", "Impact of the Relationship", "Contraception Knowledge and Attitudes", "Contraceptive Experiences and Behaviors", "Perception of Possible Pregnancy Risk", "Impact of Abortion on Contraceptive Plans", "Contraceptive and Counseling Needs", and "Thoughts on Male Contraception".

**Conclusion**: This analysis supports the notion that men's views on contraception may be influenced by their abortion experience, which may present an opportunity for contraceptive education.

### Characteristics of patients with twin-twin transfusion syndrome (TTTS) who did not undergo fetal therapy

Elizabeth B. Sasso<sup>1</sup>, <u>Macy T. Hardley<sup>2</sup></u>, Isabela Bottura<sup>3</sup>, Lisa M. Korst<sup>4</sup>, Joseph Ouzounian<sup>1</sup>, Ramen H. Chmait<sup>1</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Keck School of Medicine, University of Southern California <sup>2</sup>Keck School of Medicine, University of Southern California <sup>3</sup>Hospital Israelita Albert Einstein <sup>4</sup>Childbirth Research Associates, North Hollywood, California

**Purpose:** Research regarding treatment of TTTS predominantly focuses on the outcomes of patients who undergo treatment with various fetal therapy techniques. Treatment options include amnioreduction, selective feticide, and laser surgery. This study aims to describe the cohort of patients referred to a fetal therapy center that did not undergo treatment.

**Methods:** A retrospective chart review was performed, selecting those patients that did not receive a fetal intervention. Patients were referred between 1/2006 and 3/2017, and were between 16-26 weeks gestation at referral. The cohort was subdivided into those who were candidates for fetal surgery and those who were not. The cause for lack of intervention, degree of subsequent TTTS progression, and eventual perinatal outcomes were determined for both groups.

**Results:** Of the 734 patients referred to the fetal therapy center, 68 (9.3%) did not receive a fetal intervention. Of those, 26 (38%) were candidates for surgery while 42 (62%) were not. 11 surgical candidates chose expectant management, 8 elected for termination of pregnancy, and 7 planned for surgery but had complications prior to the procedure. Of the non-surgical candidates, 21 were ineligible due to maternal factors such as PPROM or preterm labor (12), placental abruption (7), or membrane separation (2), and 21 were ineligible due to fetal factors such as demise of one or more fetuses. Of all the patients that did not receive a fetal intervention, 10 (15.2%) developed worsening TTTS. Neonatal outcomes were available in 64 out of the 66 cases. In 41 (64%) cases, neither neonate survived. In 11 (17.2%), one neonate survived. Both neonates survived in 12 (18.8%) of cases.

**Conclusion:** Only 9% of patients at this particular fetal therapy center did not undergo fetal therapy. Despite their minority status, characterization of the outcomes of this cohort and the circumstances surrounding their lack of intervention remain significant to the study of TTTS as a whole and to its treatment.

#### Men's Access to Emergency Contraception: A Survey of Pharmacies in Los Angeles County <u>Electra KORN</u><sup>a</sup>; Brian T. NGUYEN, MD MSCP<sup>a</sup>

a: Section of Family Planning, Department of Clinical Obstetrics and Gynecology, Keck School of Medicine of the University of Southern California, Los Angeles, CA

**Background:** Ensuring access to emergency contraception (EC) has been a slow process since its FDA approval in 1999, with all single-pill methods approved for over-the-counter (OTC) sale to men and women without restrictions in 2014. By sampling pharmacies in Los Angeles (LA) County and interviewing staff involved in the sale of EC, we explore the persistence of barriers and biases, with attention to their impact on men's access to EC.

**Methods:** A list of pharmacies in LA county was obtained from the California State Board of Pharmacy website. Two pharmacies were randomly chosen as available from the 50 most populated zip codes of the 4 service planning areas with unintended pregnancy rates over 50% - areas that likely have the highest demand for EC. After removing medical center pharmacies to focus on community access, the list totaled 94 pharmacies. The survey, an adaptation of the ASEC EC Access & Price Survey (2017), will be verbally administered to staff to assess their attitudes and the availability of EC.

**Results:** Data has been collected at 41/94 of the chosen pharmacies. Of these sites, 27 (66%) never stocked EC on the shelves; 22 pharmacies keep EC behind the pharmacy and/or cashier counter or in a back room, 3 sites only offer it with prescription or preorder, and 2 locations never sell EC. The remaining 14 sites either did not have it in stock at the time (21%) or locked the EC in a display case or box (79%). Out of 60 employees surveyed, 97% knew that men could buy EC, although 13% expressed concern about selling to men and 18% either had refused or would refuse to sell to a man. The average cost of Plan B One-Step<sup>®</sup> and generic EC at the pharmacies was \$49.77 and \$42.36 respectively. **Conclusion:** Preliminary data suggests that purveyors in LA County are aware that EC can be sold without age or gender-based restrictions. However, concerns about male purchases of EC persist and may act as a barrier to men's access. Other systemic barriers are also still in place at many pharmacies, including availability, placement, and cost.

#### Immediate Postpartum Contraceptive Uptake at a Safety-Net Hospital and Factors Influencing the Final Contraceptive Obtained

Leandra Fraser MD, Melissa Natavio MD MPH, <u>Sonia Rodrigues</u>, Victoria Cortessis PhD, Ugonna Ihenacho MPH, Anita Nelson MD

**Goal:** Postpartum contraception, including long-acting reversible contraception (LARC), can improve pregnancy spacing and reduce unintended pregnancies, especially for high-risk populations with postpartum follow-up rates as low as 20%. Now that reimbursement for immediate postpartum LARC is available in 35 of 50 states, more institutions are trying to create postpartum LARC programs with fewer barriers. Since LAC+USC has had a postpartum LARC program for 5 years, it can serve as a model. The goals of the study are to ascertain the proportion of women who used immediate postpartum contraception, LARC in particular, and to describe factors that influenced the type of postpartum contraception these women initially chose and ultimately received at LAC+USC.

**Methods:** This is a retrospective chart review of all deliveries between June 1, 2015 and November 1, 2017 that were recorded in Orchid EMR at LAC+USC. The objective is to determine the proportion of women who received their desired postpartum contraceptive method, including LARC. It will provide descriptive summaries of demographic details, reproductive history and clinical course of the index pregnancy. Using prevalence odds ratios and 95% confidence intervals, associations will be made between predictive variables of contraceptive methods and the birth control that was desired and ultimately received.

**Results:** The expected results will include the proportion of women at LAC+USC who use immediate postpartum contraception and participate in the LARC program. It will reveal demographic and reproductive history factors that influence patients obtaining their desired contraceptive method. **Conclusions:** The study can help define factors that influence patients receiving their desired form of immediate postpartum contraception. Results obtained can help others who want to develop postpartum LARC programs and improve patient-centered counseling and contraception.
# SURGERY

Assessing the survival of dental implants placed in sites of previous implant failure Kimiko Agari, Bach Le, DDS, MD, FICD, FACD, Department of Oral & Maxillofacial Surgery, LAC+USC

**Background:** When dental implants fail, re-implantation is often a preferred treatment option. The purpose of this study is to investigate the survival rates of implants re-implanted in sites of previous failure (first, second, and third re-implantations) and to assess the factors that may affect re-implantation outcomes.

**Methods:** This retrospective study included implants placed from 2010 to May of 2017, during which 5,532 implants were placed in 3,597 patients. All implant failures and patients with failed implants were identified. Successive re-implantations and re-implantation failures were identified, including first, second, and third re-implantation groups. All re-implanted implants were placed by one certified oral and maxillofacial surgeon in a private practice setting. Various patient-, site-, implant-, and technique-specific factors were collected retrospectively and analyzed.

**Results:** Of 5,532 implants placed in 3,597 patients, the survival rate was 95%. All implant failures occurred in 208 patients, who had a total of 664 implants placed. Of this group, the survival rate was 62%. The survival rate of first re-implants was 77% (137/177), of second re-implants was 73% (16/22), and of third re-implants was 50% (1/2). There was a statistically significant lower survival rate in first re-implants compared to initial implants (p=0.0001). Each implant group had significantly more early failures than late failures. For each implant group, the implant failure population reported higher rates of post-operative pain compared to the implant survival population (p<0.05 for each group). **Conclusion:** This study supports existing evidence that survival rates of implants placed in sites of previous failure are lower than that of initial implants. These data also demonstrate that re-implant failures more often occur prior to abutment connection and are more likely to be associated with reports of early post-operative pain, which can help clinicians predict re-implant success.

Social Impacts of Community Tattoo Removal Program Torey Alling, Briah Fischer, Christopher Foran, MD, Damen Clark, MD

**Background/ Purpose/ Goal/ Hypothesis**: Tattoos denoting gang affiliation and chronological crimes are a continued impediment on former gang members. Many of these tattoos occupy areas of the that cannot be covered with clothing. These tattoos can compromise employment opportunities, safety, ability to leave gang life and family satisfaction. We hypothesize that completion of a tattoo removal program will help subjects overcome these barriers to social reintegration after leaving a gang. **Methods**: A retrospective review of patients completing an established tattoo removal program who have filled out at post-completion assessment of subjective improvements in safety, confidence, ability to leave gang affiliation, family satisfaction and economic opportunity.

**Results**: Results are currently pending. The subjects and data have been collected but we are waiting for approval to use the data.

**Summary/ Conclusion**: Although it is commonly accepted that removal of gang tattoos can help former gang members reintegrate into a "gang-free" life, the social impact of a removal program has not been assessed. To understand the impact of removal and advocate for community outreach and funding of these programs, the impacts must be quantitated. Feelings of safety, the ability to leave a gang, family satisfaction, and economic opportunity contribute to violence prevention and ultimately, the health of a community.

#### Effect of Hypoxia on Ventricular Growth in Children with Hypoplastic Left Heart Syndrome Michael F. Basin, Hampton Gray MD, Ram Subramanyan MD, PhD

**Background**: Cardiac regeneration is a hotly debated topic and there is no clear evidence if the human heart has any significant potential to regenerate. Murine models of cardiac regeneration suggest that mice have the capacity to regenerate their hearts during the first three to four days after birth. By extrapolation, it is believed that human hearts may still maintain some capacity to regenerate in the neonatal period. Hypoxia is a strong promoter of cardiomyocyte proliferation in animal models of myocardial regeneration. Taking these two observations together, we predict there will be a correlation between systemic oxygen saturation and ventricular mass in children with hypoplastic left heart syndrome.

**Methods**: We retrospectively reviewed the charts of 100 consecutive patients born between 1/2013 and 08/2016, who underwent a Norwood procedure. Oxygen saturation, ventricular mass, ventricular function, and ventricular volume were analyzed over three time points: pre-Norwood procedure, at discharge post-Norwood procedure and pre-Glenn procedure.

**Results**: We are in the process of obtaining ventricular measurements from echocardiography data. Results are pending.

**Conclusion**: Based on the results section above, conclusion is undetermined. We expect to find that hypoxia induces ventricular growth in neonates with hypoplastic left heart syndrome.

## The effect of socioeconomic status on treatment and mortality in patients with non-small cell lung cancer

Peggy Ebner, Li Ding, Scott M. Atay, Mimi Yao, Omar Toubat, P. Michael McFadden, Alex A. Balekian, Anthony W. Kim

**Objective:** Many factors influence the treatment options provided to patients with non-small cell lung cancer (NSCLC). In addition to patient and tumor characteristics, socioeconomic status (SES) factors may influence therapeutic decisions. The objective of this study was to assess the contribution of SES factors to therapies provided and outcome associated with these therapies among patients with stage I NSCLC. Methods: The National Cancer Database (NCDB) Participant User Data File was gueried to identify patients with stage I NSCLC, <4 cm, and with a Charlson-Deyo score of 0 or 1; a cohort for whom surgery alone would be guideline concordant therapy. This cohort was divided further into those who underwent surgery only (SURG), those who underwent chemotherapy with or without radiation therapy (CTR), and those who underwent no therapy (NT). There were six SES factors that were dichotomized: 1) income, 2) race, 3) education, 4) insurance type, 5) residence in relation to an urban area, and 6) distance to the treating facility (great circle distance). Chi-squared and Fisher-exact tests were used to compare the SES factors and multivariate logistic regression was used to test each SES factor and then consolidate them into a final model. Kaplan Meier survivals were compared using log rank tests. **Results**: A total of 69,168 patients (SURG – 51,208, CTR – 6,369, NT – 11,591) were identified as having stage I NSCLC and a number of SES factors between 0 and 5 (no patient had all 6 SES factors). SES factors that were associated with patients not undergoing surgery were: income <\$38,000 per year, nonwhite race, living in an area with >21% high school non-graduation rates, Medicaid or no insurance, residence in a rural area, and great circle distance of <12.5 miles. The presence of more than one of these factors was found to create a combined effect greater than the sum of their individual effects with respect to undergoing NT versus SURG. For each additional SES factor, the rate of rise for risk of NT increased as a guadratic function (Figure 1). A patient with 5 SES factors was at significantly higher risk of undergoing NT rather than SURG (OR=4.7; 95% CI 3.44-6.30). For CTR versus SURG, each additional SES factor conferred a more linear rate of rise, such that a patient with 5 SES factors was also at

significantly higher risk of undergoing CTR (OR=2.4; 95% CI 1.52-3.67) rather than SURG. An unadjusted analysis of survival demonstrated that SURG was associated with a significantly higher 5-year survival (71.8%) compared to CTR (22.7%) and NT (21.8%), respectively (p<0.0001).

**Conclusions:** SES factors appear to exert a strong influence over whether patients undergo guideline concordant therapy for stage I NSCLC. The receipt of treatment in NSCLC patients appears to be based not only upon factors influencing their SES, but also how many of these factors apply to an individual patient. Patients who underwent SURG as their treatment had a significantly higher survival than patients who underwent CTR or NT.



Figure 1. The relationship between number of SES factors and Odds Ratio.

### Evaluation of the Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) Instrument to Assess Psychosocial Risk in Candidates for Mechanical Circulatory Support

<u>Aleeson Eka BS</u>, Ramsey S. Elsayed MD, Jeremy O'Connor, Tammie Possemato, Amy E. Hackmann MD, Mark L. Barr MD, Vaughn A. Starnes MD and Michael E. Bowdish MD

**Objective**: The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) scoring system is a promising assessment tool for pre-transplant psychosocial evaluation. The utility of SIPAT with durable Mechanical circulatory supports (MCS) is unproven, therefore, we analyzed pre-operative SIPAT scores and one-year psychosocial and clinical outcomes in durable MCS recipients.

**Methods**: This single-center, retrospective study included patients who underwent isolated durable continuous flow ventricular assist implantation between October 2012 and July 2017 and had a SIPAT score obtained. Both bridge to transplant and destination therapy patients were included. A total of 51 patients met criteria for inclusion in this study. Preoperative characteristics, SIPAT and INTERMACS scores, readmissions, and psychosocial and clinical outcomes were analyzed. Multivariate logistic regression was used to model survival. Time to event comparisons 1ill be performed by Kaplan-Meier and cox-proportional hazard modeling.

**Results**: The mean age for our study cohort was  $58 \pm 11$  years, 36 (71%) of whom were males. Mean preoperative body mass index, left ventricular ejection fraction, and creatinine were  $30 \text{ kg/m}^2$ , 17%, and 1.3 mg/dL, respectively. Median SIPAT score was 9 (0-34). The total population (n=51) was divided into 2 groups above and below the median SIPAT score, a low-score group (n=26) with a mean SIPAT score of  $4.85 \pm 2.68$  and a high-score group (n=25) with a mean SIPAT score of  $17.83 \pm 6.24$ .

All of the pre-operative psychosocial domain scores were significantly lower in the low-score group and higher in the high-score group, with the exception of psychosocial stability, history of deceptive behavior, risk of recidivism of alcohol and illicit substance abuse, and nicotine dependence. The mean time of follow-up was 795.49 days. Outcomes including postoperative length of hospital stay, readmissions (time after initial discharge, number and duration), occurrence of adverse clinical events did not reveal any significant difference between the SIPAT score groups. Regarding post-operative psychosocial outcomes, the low-score group had a significantly incidence of support system failure than the high-score group. All other psychosocial outcomes showed no significant difference between the groups.

**Conclusion**: Psychosocial factors detected by preoperative SIPAT evaluation have some ability to predict postoperative clinical and psychosocial outcomes. Although not significant, 30-day readmissions in this study were more common with higher SIPAT scores. Additionally, failure of social support systems were significantly more common with higher SIPAT scores.

Psychosocial evaluation is critical in patients undergoing MCS device implantation. However, it remains unclear whether the SIPAT is a valid preoperative evaluation tool for these patients.

# Screening for Intimate Partner Violence in LAC+USC Medical Center Female Trauma Patients from 2015-2017

<u>Briah Fischer, MS2</u>, Chris Foran, MD, Damon Clark, MD, Department of Surgery, Keck School of Medicine of the University of Southern California

Background: In the United States, intimate partner violence (IPV) is estimated to play a role in up to 30% of emergency department visits by women, making screening an essential step in preventing further morbidity and mortality in this patient population. In compliance with the Joint Commission for Accreditation of Healthcare Organizations (JCAHO) requirement, most Level 1 Trauma Centers report having a universal IPV screening policy. However, the few studies that have evaluated execution of these policies show that screening rates consistently fall below 100% at centers nationwide.
Objective: This study aims to evaluate the rate of screening for IPV in female trauma patients at LAC+USC Medical Center, a major Level 1 Trauma Center in Los Angeles, California between 2015-2017.
Methods: A retrospective analysis of screening for intimate partner violence (IPV) in all female patients who received a trauma team consult at LAC+USC Medical Center between 2015-2017. Documentation of ICD-10 codes for adult physical, sexual and psychological abuse (T74.91XA, T76.91XA, T74.11XA, T76.31XA, T74.21XA, T76.21XA, T74.91XA, T76.91XA, Z91.410, Z91.411, Z91.419) and external cause codes for mechanisms of assault (X92-X99, Y00-Y04, Y08-Y09) will identify screening. Social work notes will be used to identify specific screening tools, if any were used.

**Results:** We hypothesize that LAC+USC Medical Center did not screen 100% of the female patients who received a trauma team consult between 2015-2017 for intimate partner violence. Based on current literature, we expect screening rates to fall between 30-55%.

**Conclusions:** Recognizing IPV is an essential first step towards providing interventional support services to women affected. If LAC+USC Medical Center falls below 100% IPV screening in female trauma patients, our results will encourage action towards improving the execution of our screening protocol. Future research may include surveying patient and provider barriers to screening, assessing screening tools currently in use and implementing a new screening tool.

#### Patient Compliance and Barriers to Mechanical VTE Prophylaxis

<u>Natalie Friedricks, M.S</u>., Jynette Querubin, B.S.N, Anupreet Singh, Welmoed Van Deen, M.D, Ph.D, Christianne Lane, Carol Peden, M.D., M.P.H, Joan Brown, M.B.A., Amy Hackmann, M.D.

**Background:** Hospital-acquired (HA) venous thromboembolism (VTE) is a common source of morbidity/mortality in surgical patients. VTEs, comprised of deep venous thrombosis (DVT) and pulmonary embolisms (PE), are prevalent in the US with an estimated 900,000 people affected each year. Many hospitalized patients have 1 or more risk factors for VTE including immobility, surgery, trauma, malignancy, etc. It is therefore very important to implement strategies to prevent these events. Both pharmacologic and mechanical prophylaxis are used to prevent VTE. Mechanical approaches such as sequential compression devices and graduated compression stockings can reduce blood clot formation by increasing blood flow in an otherwise immobile patient. However, patient compliance for mechanical prophylaxis is presumed to be quite low. This is a problem throughout Keck Hospital of USC, there are consistently low levels of mechanical VTE prophylaxis compliance.

**Methods:** This qualitative cross-sectional study aims to determine the barriers of mechanical VTE prophylaxis for patients. 35 patients who are currently hospitalized and have been prescribed either compression stocking or cuffs will be interviewed regarding their experiences with the devices, knowledge of VTE, and exposure to medical educational tools. Interviews consist of 28 open questions, and interviews should take 30min-1hr.

**Results:** We project that most patients will not be fully aware of their level of risk for VTE events. Furthermore, we predict problems with comfortability with the device leading to decreased patient compliance.

**Conclusion:** We hope to elucidate the full patient perspective to facilitate the eventual creation of better VTE educational tools and systems level interventions.

#### Clinical Outcomes of Patients with Acute Type A Aortic Dissections Complicated by Malperfusion: A Single Center Study

#### Tyler Fugere BA, Ramsey S. Elsayed MD and Michael E. Bowdish MD

**Background**: Malperfusion in acute type A aortic dissection (ATAAD) patients is a complication that arises from stenosis or occlusion of vessels after intimal tear. Surgical correction must be prompt to restore blood flow and optimize outcomes. This study aims to examine the impact of malperfusion on outcomes.

**Methods**: A retrospective cohort study of patients who underwent surgical correction of ATAAD between 2005-2017. Patient demographics, comorbidities as well as postoperative complications were collected. Survival will be analyzed using Kaplan-Meier methods.

**Results:** A total of 266 consecutive patients underwent surgical repair of ATAAD, of whom 46 patients (17%) presented with malperfusion of at least one non-aortic vessel. Mean age was 59 (±13) with 37 males (80%). All-cause In-hospital mortality was 11% (5) and overall mortality was 17% (8). Location of

malperfusion was cerebral in 8, peripheral in 28 (upper or lower extremities), renal in 8, visceral in 8, and spinal in 1 patient. While data analysis has not yet been completed, we predict that the vessel location of the malperfusion might have an impact on outcome, with some locations leading to a higher morbidity or mortality rate.

**Conclusions:** Organ malperfusion remains a severe clinical condition with strong potential for adverse outcomes in patients with ATAAD. The results of this study will compare how the location of malperfusion following the Type A Aortic Dissection affects the severity of complications and mortality. With this information, we can better predict outcomes in an attempt to mitigate morbidity and mortality of this critically ill cohort of patients.

#### The Indications for Diagnostic Peritoneal Aspiration and its Utility in Trauma <u>Hemanth Garapati</u>, Marianne Marchini Reitz, Ruben Guzman, Kazuhide Matsushima MD, FACS, Department of Acute Care Surgery, LAC+USC Medical Center

**Background:** For the evaluation of the unstable patient with abdominal trauma, the focused assessment with sonography for trauma (FAST) has been used as a primary diagnostic modality. However, the sensitivity of FAST is not known to be high enough to rule out intraabdominal hemorrhage. Currently, it remains unclear whether the use of diagnostic peritoneal aspiration (DPA) would increase the accuracy to identify the patients with ongoing intraabdominal hemorrhage. This study aims to describe the current indications for the use of DPA in modern trauma centers and to evaluate the accuracy of FAST and DPA for intraabdominal hemorrhage. It is expected that the joint use of FAST and DPA in hemodynamically unstable patients will yield the highest sensitivity and specificity in evaluating for intraabdominal fluid, which prevents the need for subsequent testing and saves valuable time in treatment.

**Methods:** This is a single center, retrospective study on trauma patients admitted at LAC+USC from January 2010-December 2016. Hemodynamically unstable patients with blunt and penetrating trauma who underwent a DPA were included. We will describe the indications for DPA in trauma patients, and the accuracy of DPA for intraabdominal hemorrhage will be reported.

**Results:** We are currently in the process of data collection. However, we expect that the combined use of FAST and DPA in hemodynamically unstable patients will yield the highest sensitivity and specificity in evaluating for intraabdominal fluid.

**Conclusion:** To our knowledge, little is known about the utility of DPA in a modern trauma center. This study will examine our hypothesis that DPA would be accurate enough to identify patients with ongoing intraabdominal hemorrhage, and therefore should be considered a necessary addition to FAST.

# The Accuracy of the Focused Assessment with Sonography for Trauma in the Setting of Resuscitative Thoracotomy

**Ruben Guzman**, Marianne Marchini Reitz, Hemanth Garapati, Kazuhide Matsushima MD, FACS, Department of Acute Care Surgery, LAC+USC Medical Center.

**Background:** After regaining spontaneous circulation in a patient following an emergent resuscitative thoracotomy, trauma surgeons have to evaluate whether the abdominal cavity needs to be surgically explored as a source of hemorrhage. Currently, little is known on the accuracy of the Focused Assessment with Sonography for Trauma (FAST) results for detecting any intraabdominal free fluid. Our hypothesis is that results of the FAST examination would be accurate enough to be used to guide the surgical management of patients with return of spontaneous circulation after resuscitative thoracotomy. **Methods:** We conducted a 3-year retrospective (2014-2017) study in patients admitted to LAC+USC Medical Center, a Level 1 Trauma Center with high trauma volume. Patients who underwent an

emergent resuscitative thoracotomy in the emergency department were included for analysis. All FAST examinations were performed by non-radiologists. Findings in the operation or on computed tomography were used as references to evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the pericardial and abdominal FAST.

**Results:** A total of 100 patients who underwent an emergent resuscitative thoracotomy were included in the preliminary analysis. Median age was 33 (IQR: 23-49) and 87% were male patients. FAST was performed in 64% of the study patients and 13 patients had positive results in the abdominal views. Exploratory laparotomy was performed in 19 patients. Of those, 6 patients (31.6%) had positive FAST results.

**Conclusions:** FAST findings could be used to determine surgical management of patients following an emergent resuscitative thoracotomy. With this, surgeons may avoid further performing invasive surgeries on the patients.

#### Predicting Injury Severity and the Need for Operative Management Based on the Number of Stab Wounds Sustained in a Traumatic Event

<u>Robert Ireland</u>; Marianne Marchini Reitz, MD; Kenji Inaba, MD Division of Trauma and Acute Care Surgery, LAC+USC Medical Center, Los Angeles, California

**Background:** There is a lack of literature addressing the severity of injury in cases of penetrating trauma from stab wounds. Most of the relevant literature on the subject addresses penetrating trauma from gunshot wounds specifically. These two types of traumatic injury differ in significant ways, making it hard to draw conclusions about one based on studies of the other. In addition, results from the most relevant gunshot trauma studies have been inconclusive. Our project aims to examine the association between the number of stab wounds sustained in a traumatic event and the severity of the injury. We hope to explore whether the number of stab wounds can be quickly used to identify the severity of the case and in turn utilized as an indicator of the need for operative intervention by the trauma team. **Methods:** A 10-year retrospective review (2006-2016) of penetrating trauma admissions to the LAC+USC Emergency Department was performed. 2722 patients were admitted for stab wound injuries during this time. 2372 of these patients were excluded due to region of injury, inaccessible patient charts, or missing data. Patients were included who had sustained stab wounds to the thorax and/or abdomen (n=350). Factors evaluated included number of stab wounds sustained, location of injury, severity of injury (AIS/ISS), treatment modality (operative vs. non-operative), and comorbidities.

**Results:** Data analysis is ongoing. On initial univariate analysis, patients with multiple stab wounds were found to be associated with an Injury Severity Score (ISS) >15 (p=0.013) when compared to those with a single stab wound. Similarly, patients with multiple stab wounds to the thorax were associated with an Abbreviated Injury Score (AIS)  $\geq$ 3 (p=0.001) when compared to those with a single stab wound to the thorax.

**Discussion**: Based on our preliminary results, it appears that there may be an association between the number of stab wounds sustained in a traumatic event and the severity of the injury. Further data analysis is needed to explore this relationship fully.

#### Comparison of Aortic Aneurysm Measurement Variation by Computed Tomography Cali E. Johnson, Gregory Magee, <u>Daniel Lee</u>, Alison Wilcox

**Background/Purpose**: Computed tomography (CT) is an essential tool for the diagnosis and management of patients with abdominal aortic aneurysms (AAA). Aortic characteristics (such as diameter and volume) captured by CT guide decisions in diagnosis, treatment, and follow-up, in addition to serving as predictors of rupture risk and other complications. However, current radiology protocols

vary across different hospitals and institutions. Our study aims to assess whether variations in CT slice thickness result in significant differences in diameter and volume measurements for AAAs.

**Methods**: A convenience sample of 37 subjects was selected from a study population of patients with an ICD9/10 diagnosis of AAA who had also received abdominal CT scans of both 1mm and 3mm slice thicknesses at Keck Hospital of USC. Based upon literature suggesting the significance of aortic diameter and volume measurements in the diagnosis, treatment, and follow-up of AAAs, the following items were selected for measurement: luminal diameter 1mm below the most distal renal artery, luminal diameter 15mm below the most distal renal artery, maximum luminal aneurysmal diameter, length of the aortic neck, length from the most distal renal artery to the aortic bifurcation, volume of the aortic neck, and volume of the aneurysm. Aortic diameter and volume measurements will be compared with paired t-test (P = 0.05).

**Results**: We hypothesize that there is no difference in aortic diameter and volume measurements using 1mm CT cuts vs 3mm CT cuts.

**Conclusion**: We expect the results of our study to shed light on the impact of radiology protocols on the measurement of the aorta via CT.

#### Hemodialysis as a Predictor of Outcomes After Isolated CABG <u>Alice Liu</u>, Ramsey S. Elsayed, Michael E. Bowdish

**Background**: Hemodialysis is a known risk factor for mortality after surgery. This retrospective cohort study evaluated outcomes after isolated CABG in hemodialysis-dependent (HDD) and non-HDD patients. **Methods**: 778 patients undergoing isolated CABG between 2006 and 2016 were placed into matched groups based on preoperative hemodialysis status (65 HDD, 65 non-HDD) using propensity scores and 1:1 Greedy matching, with median time on hemodialysis in the HD group being 78 weeks. Matched groups were then compared for primary outcomes. Multivariable logistic regression models were developed to predict thirty-day mortality and major adverse cardiac events (MACEs). Kaplan-Meier analysis was used to assess survival and multivariable Cox proportional hazard modeling was used to identify factors associated with overall mortality.

**Results**: Thirty-day mortality was 1.9 and 4.9% in the non-HDD and HD groups, respectively (OR 2.7, 95% CI 0.86-8.47, p=0.09). Kaplan-Meier estimates of survival between non-HDD and HD patients showed a significant difference in survival (figure). After multivariable adjustment for age, sex, presence of diabetes, presence of COPD, and history of previous cardiac surgery, mortality was higher in the HDD group as compared to the non-HDD group (HR 3.1, 95% CI 1.05-9.1, P=0.04). On multivariable analysis, 30-day mortality was increased in those with diabetes, COPD , on preoperative inotropes, and with increasing cross clamp times. Additionally, MACE at 30-days was more common in those with diabetes, COPD, MI within 30 days, on preoperative inotropes, and with increasing cross clamp times.



**Conclusions**: These data demonstrate that the need for preoperative hemodialysis remains a significant risk factor for long term mortality in CABG patients. While overall survival after isolated CABG remains excellent, decreased survival is observed in patients with diabetes, with COPD, needing preoperative inotropes and patients with diabetes, or with longer aortic cross clamp times.

#### Assessing the Validity of the Milestone Project in the Evaluation of Colon and Rectal Surgery Residents <u>Hilary Novatt</u> and Glenn Ault, MD, MSEd, FACS, FASCRS

**Goal:** The Colon and Rectal Surgery (CRS) Milestone Project was developed by the Accreditation Council for Graduate Medical Education (ACGME) and the American Board of Colon and Rectal Surgery in 2015 to provide a framework to evaluate colon and rectal surgery residents on several core competencies, or milestones. The General Surgery Milestone Project was also developed by the ACGME and the American Board of Surgery to evaluate general surgery residents on similar milestones. Because colon and rectal surgery residents have completed five years of general surgery residency, they have already been evaluated using the milestones prior to entry into the colon and rectal surgery residency program. The validity and utility of using the milestones to evaluate resident competency at each stage of training has yet to be established. It is therefore our goal to determine if there is a correlation between residents' milestone evaluations by general surgery residency programs and by colon and rectal surgery residency programs.

**Methods:** First, we will collect the general surgery milestone reports from ACGME for incoming colon and rectal surgery residents in August 2018. Then, within four months of beginning colon and rectal surgery residency training, residents will be evaluated by the CRS Clinical Competency Committee (CCC) using the same general surgery milestones. We will then calculate inter-rater reliability using the interclass correlation coefficient to assess whether there is a correlation between the two evaluations in each of the milestone categories. We will primarily be focusing on nonspecialty-specific milestones: systems-based practice, practice-based learning and improvement, professionalism, and interpersonal and communication skills.

**Results:** The expected result of this study is that there is a significant correlation between residents' milestone evaluations by general surgery residency programs and by colon and rectal surgery residency programs.

**Conclusions:** Based on the results of this study, we can evaluate the validity of using the Milestone Project as the primary tool to assess competency of residents progressing from general surgery to colon and rectal surgery residency. If necessary, we will seek to make recommendations for changes to the milestones to more effectively address any discrepancies in resident evaluation and education.

#### Aesthetic and Cultural Considerations in Hallux versus Second Toe-to-Thumb Transfer <u>Nicole Ontiveros, BA</u>, Erin Weber, MD, PhD, Daniel Gould, MD, PhD and Joseph Carey, MD

**Background:** Toe-to-Thumb transfer is a reconstruction modality that is best suited for patients who have suffered a traumatic loss of the thumb with an intact metacarpophalangeal joint. Though much research has focused on the indications of varying types of thumb reconstruction techniques, there is a dearth of research regarding patient preference for hallux versus second toe transfer when toe-to-thumb reconstruction is employed. Thus, the present study examines the preference of various patient populations in terms of hallux versus second toe-to-thumb transfer in order to guide clinician selection and lead to increased long-term patient satisfaction.

**Methods:** One-thousand individuals between the ages of 25 and 60 were recruited for the study via Amazon Mechanical Turk (MTurk), an online research crowd-sourcing platform. Participants were shown 10 sets of a two-image pair and asked to choose the image that was more aesthetically pleasing to them. Each set of images contained one photograph of a toe-to-thumb reconstruction utilizing a hallux and one photograph of a toe-to-thumb reconstruction using a second toe. Participants were asked to provide their age, gender, race, ethnicity, education level, income, occupation, activity level and religious preference.

**Results:** Data collection is currently underway. It is surmised that patients will prefer hallux transfer with subsequent debulking and contouring compared to second toe-to-thumb transfer due to the hook shaped appearance and smaller nail of the second toe. Additionally, it is expected that ethnic differences in preference will exist given findings from previous case reports.

**Conclusions:** These data indicate a preference for the use of the hallux in toe-to-thumb reconstruction. Future research should investigate the functional outcomes of hallux versus second toe-to-thumb transfer and long-term patient satisfaction with each technique.

### Utility of Treatment in High-Risk Trauma Patients with Subsegmental Pulmonary Embolism Viraj Panchal; Aaron Strumwasser, MD

**Background:** The surgical plan of care for adult trauma patients with subsegmental pulmonary embolism (SSPE) who have high-risk features is currently imprecise. Current therapeutic suggestions are outlined in the CHEST guidelines released by the American College of Chest Physicians, but they offer only a weak recommendation due to a lack of strong evidence relevant to SSPE. The role of treatment for SSPE patients with high-risk features, then, needs to be further elucidated to reduce negative outcomes and prevent overtreatment. In this study, we focus on the treatment of high-risk trauma patients and the subsequent mortality and hospital length of stays that follow. We hypothesize that surgeons should administer anticoagulative treatments in this subset of patients with high-risk features who have SSPE to improve outcomes.

**Methods:** A retrospective chart review of LAC+USC adult trauma patients admitted between 2004 and 2017 with demonstrated pulmonary embolism was conducted. Statistical analyses will be performed to determine associations between treatment and primary outcomes like mortality, hospital length of stay, and lung function.

**Results:** We believe the findings from this study will positively impact patient outcomes by providing evidence that high-risk trauma patients with SSPE require anticoagulation measures. Our study aims to determine an inverse association between treatment and mortality in this high-risk trauma population. **Summary/Significance:** The current CHEST guidelines do not have adequate evidential support for SSPE treatment in high risk trauma patients. If the study findings demonstrate that treatment of patients with SSPE with high-risk features is associated with better patient outcomes, the data may contribute to surgeons' approaches to such patients. Conclusions following the examination of patient data will therefore provide a cogent approach to treating patients with SSPE, leading to better outcomes.

#### Developing a surgically-induced rodent model for cervical lymphedema

**Ravali A. Reddy**, Artur Fahradyan, Alex K. Wong, Division of Plastic and Reconstructive Surgery, Department of Surgery, Keck School of Medicine of University of Southern California

**Background:** Lymphedema is a complication amongst cancer patients that results in the accumulation of tissue fluid in the affected area. Cervical lymphedema, in particular, is a side effect of treatment for head and neck cancer associated with a severe decrease in quality of life. We are developing a surgically-induced animal model for cervical lymphedema to better understand the disease and identify early signs that can predict if, when, and how it will develop. Our long-term goal is to establish a model that can guide future treatment options for human cervical lymphedema patients.

**Methods:** We are using Prox-1 GFP mice and rats for our model. All animals will have CTs and MRIs to measure baseline cervical volume. We will remove skin at the base of the head to block dermal lymphatic function, and cauterize lymph nodes in order to exacerbate lymphedema in each animal. A subset of animals will also receive radiation therapy. We will photograph and measure the animals' head and neck regions for 30 days post-op. All animals will have follow-up CTs and MRIs to determine the degree of lymphedema. Upon sacrifice, indocyanine green lymphangiography will be performed and skin will be harvested for H&E staining, immunohistochemistry, and molecular genetic analysis. **Results:** A literature search revealed no head and neck animal models of lymphedema. We are conducting pilot surgeries and have identified the superficial cervical and facial lymph nodes to be cauterized. We anticipate that CTs and MRIs taken 30 days post-op will show a significant increase in soft tissue swelling when compared to baseline. We also anticipate that post-sacrifice tissue analysis will reveal biomarkers unique to the swollen tissue.

**Conclusions:** A rodent model for cervical lymphedema will allow us to explore whether treatment options such as retinoic acid-based therapies that have been successful in tail and hind limb models can be more broadly applied, eventually resulting in new evidence-based therapies for human cervical lymphedema patients.

#### Interstitial Pressure Affects Efficiency of Lymphangiogenesis in 3D Culture

W. Jiao, G. Lee, S. Park, <u>B. Shaw</u>, C. Sung, B. Han, Y. Hong, A.K. Wong; University of Southern California, Plastic Surgery, Los Angeles, CA

**Introduction:** Lymphedema leads to progressive stiffness of soft tissue. We hypothesize that a progressive increase in interstitial pressure has an adverse effect on lymphatic endothelial cell function, thus further contributing to disease progression. To test this hypothesis, we cultured lymphatic endothelial cells (LECs) in 3D scaffolds of different stiffness conditions to determine the effect of interstitial pressure on LEC proliferation and tube formation.

**Methods:** Human primary LECs were isolated under an IRB approved protocol and cultured in Endothelial Cell Basal Medium (EBM, Lonza) with 15% FBS. LECs (1x10<sup>4</sup>) were encapsulated in a range of percentages of biomimetic collagen hydrogels with physiologically relevant pressures including: 5.25%

(3.37 kPa), 6.0% (5.57 kPa), 7.5% (12.8 kPa), and 9.0% (15.31 kPa). 3D in vitro cultures were observed for phenotypic behavior and analyzed at defined time points for three weeks. Two-way ANOVA was used for multi-group statistical analysis.

**Results:** Lymphangiogenesis and lymphatic branching and collateral structures were observed at 3 days post cell-seeding in 3D hydrogel and increased with time. Immunofluorescence demonstrated branch-like structures that positively stained for podoplanin, an LEC specific marker. The optimal percentage of gel concentration favoring formation of these structures was 6.0% gel. 6.0% and 7.5% groups were statistically different from 5.25% and 9.0% groups (p = 0.0198). There was no statistical difference between the 6.0% and 7.5% groups, and 5.25% and 9.0% groups.

**Conclusion:** In this study, we used a 3D in vitro model to demonstrate optimal/physiologic and suboptimal/pathologic ranges of interstitial pressures for lymphangiogenesis efficiency. This data may be used to guide medical/prolymphangiogenic and surgical approaches to the management of lymphedema.

#### Topical 9-cis retinoic acid for the treatment of secondary lymphedema Parthiv Sheth, Antoun Bouz, Roy Yu, Alex K. Wong, MD.

**Background/Goals:** Secondary lymphedema is an incurable condition characterized by tissue swelling after lymphatic damage, usually due to cancer treatment. Patients with lymphedema have a severely compromised quality of life as lymphedema causes debilitating chronic swelling of the affected extremity, recurrent infections, and limited mobility. Current treatment is primarily centered on relief of symptoms by compression bandages, manual lymphatic drainage, and pneumatic pumps. A recent study (Bramos et al. 2016) has revealed the efficacy of systemic injections of 9-cis retinoic acid for the prevention of postsurgical lymphedema by activating lymphangiogenesis, thereby increasing lymphatic clearance and lymphatic vessel density in mice. We have therefore sought to determine whether topical application of 9-cis retinoic acid has similar pro-lymphangiogenic effects and could serve as an effective treatment option for secondary lymphedema.

**Methods:** Lymphedema was induced in 12 mice with a 5mm circumferential tail skin excision and subsequent surgical lymphatic injury. The treatment group (n=6) were subject to twice daily application of 0.5g of Panretin gel (0.1% alitretinoin) while the control group (n=6) had a vehicle control (3% hydroxyethyl cellulose) applied at the same frequency. To determine the efficacy of the treatment, total distal tail volume measurements were taken every 7 days. At the conclusion of the 28 day treatment cycle, we conducted H&E staining for dermal and epidermal thickness measurements, immunofluorescence to screen for several lymphangiogenic markers, and indocyanine green lymphangiography using SPY fluorescence imaging to further assess effectiveness of the treatment. **Results:** Total percent change in tail volume between the control and treatment groups was insignificant

at each time point except day 14 (p<0.01). Severe dermatitis and scabbing was observed on the tails of the treatment mice, likely attributed to the 9-cis cream. This forced premature euthanasia prior to lymphangiography analysis. Histology of these tails will be completed soon.

**Conclusions:** These data demonstrate inconclusive evidence for efficacy of topical 9-cis retinoic acid for the treatment of secondary lymphedema, primarily due to the degree of dermatitis on the tails of treatment mice. Since there is some data to suggest reductions in tail volumes in the treatment group, we now plan to repeat this treatment cycle with a less aggressive, once daily topical 9-cis retinoic acid application in hopes of curbing skin reactions.

# Efficacy of Bio-Oss and recombinant bone morphogenetic protein 2 in grafting critically-sized mandibular defects in a rat model

Shiffler K, Kim I, Bahmanyar S, St. John M, Aghaloo T

**Purpose:** To compare PLGA, Bio-Oss, rhBMP-2, and nonvascular autogenous bone in the bony regeneration of a critical-sized marginal mandibular defect in a rat model.

**Methods:** Twenty-five 4-month-old male Sprague Dawley rats underwent surgical removal of a 5 x 5 x 2.5 mm section of the mandible along the inferior border, with placement of an absorbable collagen sponge (ACS), rhBMP-2 + ACS, Poly(lactic-co-glycolic acid) (PLGA), PLGA + rhBMP-2, Bio-Oss, Bio-Oss + rhBMP-2, or autogenous bone at the surgical site. At 8 weeks post-operatively, the rats were sacrificed and  $\mu$ CT and histological analysis were performed.

**Results:** One animal expired intra-operatively. The other 24 animals were included in the analysis. Little osteoid formation occurred in defects grafted with ACS, ACS + rhBMP-2, or PLGA + rhBMP-2. Bio-Oss + rhBMP-2 had the highest bone volume and bone volume fraction (22.0±1.0 mm, 0.37±0.15), followed by Bio-Oss alone (15.4±1.0 mm, 0.30±0.11), and autogenous bone (13.1±0.9 mm, 0.32±0.03). Persistence of Bio-Oss granules with little evidence of resorption was noted in the histological analysis.

**Conclusion:** The results of this study suggest that the combined use of an allogenic graft material like Bio-Oss and rhBMP-2 may serve as a viable method in treating critical-sized mandibular defects. rhBMP-2 demonstrated a synergistic, pro-osteogenic effect when combined with an osteoconductive material, such as Bio-Oss. Micro-CT bone volume and bone volume fraction at 8 weeks postoperatively were higher in the BioOss group than the autogenous bone group, suggesting that BioOss is slowly resorbed or degraded. Future studies should focus on evaluating the biomechanical properties of the healing sites when these graft materials are used.

### Equivalent Outcomes in Patients With and Without Mitral Valve Operation and Aortic Root Replacement

#### Tiffany Sierro; Daniel P. Logsdon MD

**Objective:** The combination of a mitral valve operation with an aortic root procedure is becoming increasingly common. This combined operation is more demanding than either procedure alone, and knowledge regarding clinical outcomes is limited.

**Methods:** A single center retrospective cohort study was conducted of those undergoing surgical aortic root replacement (Bentall) with concomitant mitral valve surgery. Subjects were further divided into groups by mitral valve operation (repair vs. replace). Primary endpoints were in-hospital and 30-day mortality, and re-intervention. Two sample t-tests and Fisher's exact tests were used for continuous and categorical variables respectively.

**Results:** Between 2004 and 2017, 356 patients underwent aortic root replacement surgery, Bentall procedure, of which, 51 had mitral surgery. The mean age (59.0 vs. 58.7) and BMI (26.7 vs. 28.3) were similar between patients with and without mitral surgery. Patients with mitral surgery had more endocarditis (27% vs 8%), congestive heart failure (69% vs 44%), arrhythmia (33% vs 22%), and previous heart operations (80% vs 43%). Hypertension (69% vs 71%), diabetes mellitus (10% vs 11%), renal failure (6% vs 6%), were similar between groups. No significant difference in in-hospital (9% vs 12%, p = 0.445) and 30-day mortality (10% vs 12%, p = 0.61) or re-intervention rate (6% vs 9%, p = 0.09) for patients with and without mitral surgery respectively. A total of 30 mitral replacements and 21 repairs were completed with no difference in in-hospital (10% vs. 14%, p = 0.68) and 30-day mortality (10% vs 9%, p = 0.258) for replace vs. repair respectively. **Conclusion:** Similar outcomes were seen with patients undergoing aortic root replacement with concomitant mitral valve surgery and no difference was observed between a replaced or repaired mitral.

In the proper hands, a two-valve operation with aortic root replacement can be done safely and should be standard of care when indicated.

#### Management of Penetrating Torso Injuries in Unstable Patients: Chest Tube or X-Rays First? <u>Victor Wong</u>, Jeremy Hardin, Aaron Strumwasser MD

**Background/Purpose/Goal/Hypothesis:** Although prophylactic chest tube insertion can be life-saving as a diagnostic and therapeutic maneuver in hypotensive patients with penetrating chest trauma, iatrogenic complications can result in uncontrolled trauma scenarios. This study aims to clarify whether imaging should be performed prior to chest tube placement to minimize tube-related complications or whether prophylactic placement of chest tubes should be performed first in emergent cases of penetrating chest trauma to achieve better patient outcomes because of the life-saving potential of chest tubes in severe, yet treatable thoracic pathology.

**Methods:** Data was collected retrospectively from 2011 to 2016 on 227 patients at LAC+USC who sustained penetrating torso trauma and received chest tubes. We recorded data on imaging performed, hospitalization length, additional interventions, and hospital complications from the patient records with Quantim, Synapse, Affinity, and Orchid.

**Results:** 59 of patients within criteria received a prophylactic chest tube prior imaging, while 168 patients received a chest x-ray before tube placement. A preliminary analysis showed insignificant differences among days in the hospital, in the ICU, or on a ventilator between the groups. To further elucidate the outcomes between the two management strategies, we will look into the incidence and severity of tube complications in both groups.

**Conclusions:** The original hypothesis that placing a chest tube first in certain emergent scenarios was not supported by the data on hospitalization outcomes. However, complications from chest tubes may be conceivably more frequent and severe in the group that received tubes prior to imaging. If this is supported, then our original hypothesis is contradicted and the data would support performing imaging studies prior to placing chest tubes.

### Open Healing Provides Faster Time-To-Ambulation as Compared to Closed-Wound Healing in Patients Undergoing Transmetatarsal Amputations

Aria Woods BA, Ramsey Elsayed, MD, Vincent L. Rowe, MD, Jared Cline BA

**Background/Objective**: The current standard of practice dictates TMA be performed with a closedwound method in which a dorsal and plantar skin flap are sutured together over the metatarsal stumps. This wound is then covered and allowed to heal. Open-wound healing procedures, however, do not involve sparing and suturing of dorsal and plantar skin flaps. Instead, a negative pressure wound therapy (NPWT) device or wet-to-dry wound packing is used. We believe that open wound healing will shown to improved healing outcomes for TMA wounds, particularly those in diabetes mellitus patients. We hypothesize that open healing provides for faster time-to-primary healing and time-to-ambulation, which serves to preserve patients' functional status, reduce frailty and improve quality of life. **Methods**: We retrospectively queried the Vascular surgery database for all transmetatarsal amputation cases from 2010 to present (I need a date here) to produce a cohort of (insert patient number or if not done then estimate). Survival will be assessed using Kaplan-Meier methods. Multivariable logistic regression will be used to model healing and reintervention, Kaplan-Meier methods will be used for survival. p values less than 0.05 are considered significant.

**Results:** Patients had a mean age/BMI of xx.x +/- xx.. (for however many demographic measurements you want) and were xx.x% male, xx.x% smoking, diabetes etc. (even if data analysis not done you can get

these numbers pretty easily). We expect to find that patients who underwent open TMA will demonstrate faster time-to-primary healing, shorter time-to-ambulation and wound-related complications such as infection as compared to patients who underwent closed-wound healing. We also expect that patients who underwent open TMA will be less likely to have undergone further amputations on the same limb.

**Conclusion:** We hope to demonstrate that open-wound healing methods for TMA provide better outcomes for patients reflected in (better healing/ambulation time, less subsequent amputation, less CLI, etc) and should be the method of choice for TMA procedures. The TMA procedure was developed as a technique to salvage limb functionality in patients that might otherwise undergo more radical amputations (such as below- or above-the-knee). Identifying the optimal wound-healing technique for the TMA will allow providers to better manage the needs of patients who require amputation but for whom limb-function salvage remains a possibility. Since the majority of the patients in this study suffer from ischemic complications of Diabetes Mellitus, a disease of increasing prevalence, the number of patients who are candidates for TMA will increase the demand for a safer and more efficient procedure.

#### Danger of Non-Compliance with Brain Trauma Foundation Guidelines regarding Surgical Decompression of Intracranial Hematomas <u>Meghana Yanamandra</u>, Aaron Strumasser, MD

Background: The Brain Trauma Foundation developed an evidence-based guideline on severe TBI, one of the leading causes of mortality. The guideline is loosely considered the standard-of-practice for neurosurgeons regarding medical and surgical management of TBI. However, it has been found that physicians are often not compliant with these guidelines, which may in turn impact patient outcomes. Our goal is to determine if, under current surgical practices, there are differences in patient outcomes between treatment compliant with and not compliant with BTF guidelines on surgical drainage. **Methods**: A retrospective review of patients between the ages of 16 and 50 years old ( $16 < age \le 50$ ) with intracranial hemorrhage (ICH) between 2009 and 2016 at LAC-USC was done. Patient radiological results, type of ICH, intracranial pressure, score on the Glasgow Coma Scale (GCS), physical examination, and vital signs were used to determine whether the patient met criteria for decompressive craniotomy. Outcomes obtained include all-cause mortality, hospital length-of-stay, ICU length-of-stay, ICU complications, rehabilitation length-of-stay, comorbidities, cost, delayed neurosurgical intervention, poor neurological outcomes, complications related to TBI, and need for blood transfusion. **Results**: The 71 patients who met criteria for drainage were further split into two groups based on compliance or non-compliance with guidelines. A comparison regarding all-cause mortality between the two groups showed a significant (p<0.05) increase in mortality in the non-compliant group. Summary: These data demonstrate evidence that compliance with BTF guidelines may result in lower mortality rates among patients who meet criteria for decompressive craniotomy secondary to intracranial hemorrhage. If it is found that compliance with BTF guidelines also leads to better overall outcomes, the results may impact clinical decision making and improve outcomes.

Surgical therapy as the primary modality of therapy in solitary fibrous tumors of the pleura <u>Mimi J. Yao</u>, Li Ding, Scott M. Atay, Omar Toubat, Peggy Ebner, P. Michael McFadden, Anthony W. Kim Division of Thoracic Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA

**Background:** Solitary fibrous tumors of the pleura (SFTP) are rare mesenchymal neoplasms that account for approximately 5% of all pleural tumors. There is a lack of nationally representative data that describes clinical outcomes of SFTP patients to inform therapeutic recommendations. The primary objective was to describe the most effective treatment modality for survival in SFTP patients.

**Methods:** The National Cancer Database (NCDB) was queried for patients with malignant solitary fibrous tumors of the lung using the ICD-O-3 histology code 8815/3. Variables examined included demographics, tumor characteristics, staging, and treatment type. Patients were divided into two groups, those who had surgical treatment and those who did not have surgical treatment. The primary outcome was 5-year survival, which was assessed by the Kaplan-Meier method and the log-rank test.

**Results:** From 2004 to 2014, 204 patients with SFTP were identified in the NCDB. Of those, 65% (133) patients had surgical intervention, whereas 18% (37) had no surgical intervention, and 17% (34) had unknown treatment information. Among those who underwent resection, 42% (56) had sublobar resections, 45% (60) had lobectomies, and 13% (17) had pneumonectomies. The overall 5-year survival for SFTP patients was 56%. Patients who had surgical intervention had a relative survival of 64% and no surgical intervention had 22%, p<0.001. The 5-year survival of patients who had sublobar resections and those who had anatomic resections were 65% and 64%, respectively, p=0.823.

**Conclusion:** This study demonstrates that SFTP patients managed with surgical intervention have better overall survival than those who are not. Furthermore, similar 5-year survival for sublobar resections compared with anatomic resections suggest that the latter are not always indicated.