ABSTRACT BOOK Medical Student Research Forum & Poster Day April 5, 2016



Presented by: R.S.P. Steering Committee Baxter Foundation Greos Family Office of Educational Affairs

Keck School of Medicine of USC

Keck School of Medicine of USC

HENRI R. FORD, MD, MHA Vice Dean Medical Education

Professor of Surgery

MEDICAL STUDENT RESEARCH FORUM & POSTER DAY

April 5, 2016

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 during their tenure at Keck. This week's Forum represents an important milestone for the research activities of all 2nd year students. Many of their contributions have been widely recognized at regional and national meetings as evidenced by the fact that Keck students have won numerous honors and prizes over the years.

The Dean's Research Scholars program was established for students interested in pursuing a fifth year of research during medical school. Since its inception, the program has grown exponentially. Some of our current Dean's Research Scholars are presenting at this Forum.

As you read these abstracts, I am confident you will appreciate and enjoy the remarkable accomplishments of our talented students. These research projects also represent a considerable effort on the part of the faculty mentors for each of the students. Such efforts are deeply appreciated by all of us.

Huilel-

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

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MEDICAL STUDENT RESEARCH FORUM & POSTER DAY 2016

April 5, 2016

KECK SCHOOL OF MEDICINE UNIVERSITY OF SOUTHERN CALIFORNIA

The 2016 Medical Student Research Forum and Poster Day is an annual event which allows USC medical students the opportunity to present their Required Scholarly Project (RSP) to their peers and the USC community at large. RSP is a longitudinal research experience that spans the entire four years of medical school, with projects representing a variety of disciplines, from basic science to clinical research. We are extremely appreciative of the supportive faculty who have volunteered their expertise to mentor students through this exciting research initiative. 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-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 Rohit Varma, MD, MPH, Interim Dean, Keck School of Medicine; Carmen A. Puliafito, MD, MBA; Henri R. Ford, MD, MHA, Vice Dean for Medical Education; Joyce M. Richey, PhD, Assistant Dean for Medical Education; David Hinton, MD, FARVO, Director of Dean's Research Scholars; and Sanjay Arora, MD, Director of Required Scholarly Project for their support and participation in this Forum. We are very appreciative of the faculty and student judges for reviewing poster presentations. We are extremely grateful to our benefactors, the Baxter Foundation, the Meira and Shaul G. Massry Foundation, the Wright Foundation, and the Greos Family, for their commitment and support of medical student research.

PROGRAM SCHEDULE

Welcome Address, Mayer Auditorium – Noon

Rohit Varma, MD, MPH Interim Dean, Keck School of Medicine of USC

Oral Presentations, Mayer Auditorium – 12:10-1:30 p.m.

Moderator: David Hinton, MD, FARVO Professor, Keck School of Medicine of USC

Poster Presentations, Harry & Celesta Pappas Quad – 1:45-5:00 p.m.

Dean's Research Scholars Health, Technology, and Engineering Program Class of 2018 Medical Students

2016 ORAL PRESENTATIONS

Dean's Research Scholars

Liam Harris

(Mentor: **David Skaggs**, **MD**)

Comparison of Weight Percentile Gain with Growth-Friendly Constructs in Early Onset Scoliosis (EOS)

Alice Kim, Massry Scholar (Mentor: Carmen Puliafito, MD)

Quantifying Microvascular Density and Morphology in Diabetic Retinopathy using Spectral Domain Optical Coherence Tomography Angiography (SD-OCTA)

Tymon Tai

(Mentor: Neil Segil, PhD)

Assay for specificity of Hair-cell and Supporting Cell Enhancer function in Neonatal Organ of Corti

<u>Class of 2018</u>

Aileen Baffo

(Mentor: Yuanxiang Tao, MD, PhD, MSc)

Expression of mu opioid receptor and Kv1.2 controlled by MBD1 in the dorsal root ganglion

Nipun Bhandari (Mentor: Jon-Paul Pepper, MD)

Co-Culture in microfluidic device of human induced pluripotent stem-cell derived motor neurons with muscle

Tu Wen (Kevin) Hsu

(Mentor: Kristi Clark, PhD)

Investigating the Influence of Tourette Syndrome (TS) Associated Gene COL27A1 on Cortical Thickness and Behavior in Children and Young Adults.

Christopher Pham

(Mentor: Lihua Liu, PhD)

Liver cancer incidence rates and disparities among diverse racial/ethnic populations in California, 1988-2012

REQUIRED SCHOLARLY PROJECT (RSP) STEERING COMMITTEE

We would like to extend special thanks to our 2016 Required Scholarly Project (RSP) Steering Committee members:

> Sanjay Arora, MD RSP Director, Chief, Research Division, Department of Emergency Medicine

Joyce Richey, PhD Assistant Dean of Educational Affairs, Chief Diversity Officer

> David Hinton, MD, FARVO Director, Dean's Research Scholars

Cha Chi Fung, PhD Vice-Chair, Medical Education

> Lynn Kysh, MS Library Services

Lihua Liu, PhD Assistant Professor of Clinical Preventive Medicine

> Steven Mittelman, MD Program Director, MD/PhD Program

George Tolomiczenko, PhD, MPH, MBA Co-Director, Health, Technology, and Engineering Program

> William Tseng, MD Assistant Professor of Clinical Surgery

Jane Figueiredo, PhD Assistant Professor of Preventative Medicine

William Mack, MD Associate Professor of Neurological Surgery

Fernando Fleischman, MD Assistant Professor of Clinical Surgery

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Research Categories: Alternative Medicine, Basic Science, Behavioral Science, Cardiology/Cardiovascular, Clinical, Community-Based, Dermatology, Diversity Health Disparities, Economics of Health, Education, Emergency Medicine & Trauma, Endocrinology, Epidemiology, Gastroenterology, Genetics, Imaging, Mental Health/Psychiatry; Neurology; Oncology, Ophthalmology, Orthopedics, Patient Education, Patient Quality/ Safety, Pediatrics, Public Health, Reproductive Health, Surgery, and Technology (Health, Technology & Engineering)

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DEAN'S RESEARCH SCHOLARS

Three-dimensional movement strategies during drop jump and single-leg hop in young athletes with recent anterior cruciate ligament reconstruction

<u>Christopher H. Brophy, B.A.^{a,b}</u>, Nicole M. Mueske, M.S.^a, J. Lee Pace, M.D.^{a,b}, Mia J. Katzel, D.P.T.^a, Bitte S. Healy, M.S.P.T.^a, Tishya A. L. Wren, Ph.D.^{a,b}

^aChildren's Orthopaedic Center, Children's Hospital Los Angeles, Los Angeles, CA, USA ^bKeck School of Medicine, University of Southern California, Los Angeles, CA, USA

Background: Anterior cruciate ligament (ACL) tears and reconstruction (ACLR) are increasingly prevalent in young athletes. Biomechanical deficits in landing mechanics during rehabilitation may indicate lack of return-to-sport (RTS) readiness and predict future ACL injury risk.

Purpose: To evaluate adolescent athletes with recent ACLR for biomechanical deficiencies and asymmetries during single and double-legged landing tasks.

Study Design: Retrospective cross-sectional.

Methods: 32 operative limbs with unilateral ACLR (66% female, mean age 15.8 ± 1.6 years, 5 to 12 months post-surgery), 32 contralateral non-operative limbs, and 18 control limbs (44% female, mean age 15.1 ± 1.1 years) were evaluated during a vertical drop jump and single-leg hop. Lower extremity three-dimensional kinematics and kinetics were compared among groups using ANOVA with Bonferroni adjustment and paired t-tests.

Results: During the drop jump, operative limbs demonstrated lower peak ground reaction forces (GRFs) than non-operative limbs (p=0.002). Operative limbs had lower peak knee flexion, excursion, moments, and power absorption than non-operative limbs, and lower peak knee flexion moments than controls (p \leq 0.02). Operative and non-operative limbs displayed greater peak hip flexion, moments, and power absorption than controls (p<0.05). Compared to non-operative limbs, operative limbs demonstrated lower peak ankle dorsiflexion, excursion, sagittal moments, and power absorption (p \leq 0.02). Minor differences were observed in the frontal plane.

During the hop, operative limbs jumped a shorter distance than non-operative and control limbs (p<0.05), but no differences were observed for GRF (p \ge 0.66). Compared to non-operative limbs, operative limbs displayed lower peak knee flexion and excursion, with lower knee flexion moments and power absorption (p \le 0.01). Operative and non-operative limbs trended toward higher peak hip flexion (p \le 0.06) and lower knee valgus moments (p \le 0.01) than controls. No additional differences were detected for other sagittal or frontal plane variables.

Conclusion: Adolescent patients post recent ACLR tended to offload the operative knee, which could reflect an avoidance strategy during the rehabilitation phase that could predispose patients to future injury and indicate a lack of RTS readiness.

Frailty as a predictor of complications in older patients undergoing radical cystectomy <u>Thomas G. Clifford</u>, Soroush T. Bazargani, Jie Cai, Anne K. Schuckman, Hooman Djaladat, Siamak Daneshmand

USC Institute of Urology, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California

Introduction and Objective: Frailty has been described as a medical syndrome characterized by decreased physiologic reserve causing vulnerability to adverse outcomes. There is a paucity of prospective studies on frailty in urological patients. Our goal was to determine whether established measures of frailty can identify high-risk patients undergoing radical cystectomy and predict their surgical outcomes and complication rates.

Methods: Under IRB approval, we identified patients over the age of 65 undergoing radical cystectomy. We prospectively measured frailty preoperatively using surrogates including hand dynamometry (grip strength), walking speed, shrinking (weight loss of ≥10 pounds within the past year), exhaustion, and low physical activity. The patients were also prospectively scored using the Clinical Epidemiological Survey for Depression, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists scoring system (ASA), Katz Activities of Daily Living, Karnofsky performance status (KPS), and Eastern Cooperative Oncology Group (ECOG) performance status. 30 and 90-day postoperative data was recorded. Chisquare and multivariable logistic regression were performed for analysis.

Results: A total of 62 patients were identified between 2/2014 and 6/2015 with an average age of 75 years. 42 (67.7%) and 49 (79.0%) patients had at least one postoperative complication within 30 and 90-days, respectively. 61.3% of patients underwent open radical cystectomy, with no difference in complication rates between open and robotic approach (p=0.75). On univariate analysis, shrinking was significantly associated with 30-day complications (p<0.03). There was a similar trend in patients whose grip strength was frail (accounting for sex and BMI) (p=0.06). Median number of 30 and 90-day complications was 2 (range 0-5) in those with shrinking compared to 1 (range 0-5) in those without (p<0.004, p<0.02). On multivariable analysis, frail grip strength was associated with increased number of complications after controlling for pathologic stage and albumin (OR 5.4, Cl 1.4-21.0, p<0.01). Other frailty measures (such as walking speed and activity level) and other assessment tools (such as ECOG, CCI, and KPS) were not associated with postoperative complications (p>0.05).

Conclusions: Preliminary results of this prospective study suggest that grip strength and shrinking may be useful frailty measures predictive of postoperative complications in older patients undergoing radical cystectomy. These measures may be useful for identifying patients at high risk for perioperative complications.

Lymphatic and Lymph Node Dynamics After Vascularized Lymph Node Transfer Using a Prox1-GFP Reporter Rat

Daniel Gardner, Maxwell Johnson, Zhao Zhou, MD, Brandon Pang, Kian Banks, Young-Kwon Hong, Ph.D., and Alex K. Wong, M.D.

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

Introduction: Secondary lymphedema remains an important cause of morbidity for patients undergoing surgical management of solid tumors. Vascularized lymph node transfer (VLNT) was shown to be clinically efficacious by Becker al al. in 2006, yet the procedure remains limited to resistant disease. Considering the potential widespread use of this surgical technique, it is important to understand the mechanism behind lymphatic regeneration in the transplant. To address this issue, our group developed a fluorescently labeled recombinant Prox1-GFP reporter rat making it possible to visualize lymphatic growth under UV light in the transplanted free flap.

Methods: Wild-type, syngenic superficial inferior epigastric artery (SIEA) flaps were harvested from Sprague-Dawley (SD) rats and transplanted to Prox1-GFP rats. Under the surgical microscope, the SIEA was anastomosed to the common femoral artery. After 30 days, the transplanted tissue and contralateral SIEA flaps in both Prox1-GFP and SD rats were harvested for UV and bright field microscopy.

Results: SIEA flaps from the non-transgenic wild type rats showed no fluorescence under UV light. Native SIEA flaps from the Prox1-GFP rats showed diffuse fluorescence with distinct lymph nodes and lymphatic capillaries. The transplanted free flap showed ingrowth of GFP-positive lymphatics at 30 days. **Conclusion**: VLNT is becoming an increasing common and viable option for treating unresponsive surgical lymphedema. We developed a novel rat model to examine the lymphatic connections that were thought to occur after VLNT but not experimentally proven. Our results show that host lymphatics grow into the transplanted tissue and establish connections with the donor lymph nodes.

Comparison of Weight Percentile Gain with Growth-Friendly Constructs in Early Onset Scoliosis (EOS) Liam Harris BS, Lindsay Andras MD, Paul Sponseller MD, Charles Johnston MD, John Emans MD, David Skaggs MD. MMM, Growing Spine Study Group

Design: Retrospective Multicenter

Hypothesis: We hypothesize there is no significant difference in increase in weight percentile between growth friendly constructs in the treatment of EOS.

Introduction: Previous studies demonstrate significant increases in weight percentile following treatment of early onset scoliosis (EOS) with VEPTR and Growing Rods. Our objective is to compare improvement in nutritional status seen in EOS patients following treatment with various growth friendly techniques, focusing on low-weight patients (<20th weight percentile).

Methods: Retrospective review of patients treated surgically for EOS was performed from a multicenter database. Exclusion criteria were index instrumentation at >10 yo and less than 2 year follow-up were excluded.

Results: 287 patients met the inclusion criteria and etiologies were as follows: congenital=85; syndromic=79; neuromuscular=69; and idiopathic=52. Average patient age at surgery was 5.41 years, with average follow-up of 5.8 years. Preoperatively, 55.4 % (162/287) fell below the 20^{th} percentile. There was no significant difference in preoperative weight between implants (p=0.77), or diagnoses (p=0.25). Among this group, mean change in weight percentile was 10.5% (range -16.7%-88.7%) and all implant groups increased in mean weight percentile at final follow-up (table 1). There were no significant differences in weight percentile change between the groups when divided by implant type (p=0.17).

Conclusions: Treatment of EOS with growth friendly constructs resulted in an increase in weight percentile for low-weight patients (<20th percentile) with no significant difference between constructs.

Change in Weight Percentile Among Low Weight (<20 th Percentile) Preoperative						
Patients						
Group	Patients	Preoperative	Final	Change in		
		Weight	Weight	Weight		
		Percentile	Percentile	Percentile		
Growing Rod Spine	N=101	5.03%	18.45%	13.42%		
Anchor						
Growing Rod Rib Anchor	N=16	5.30%	14.54%	9.24%		
VEPTR	N=28	5.44%	9.65%	4.21%		
Guided Growth Construct	N=17	6.59%	11.17%	4.58%		
Total	N=162	5.29%	15.78%	10.49%		

Prolonged Operative Time is Associated with 30-Day Readmission Following Shoulder Arthroscopy

<u>J. Ryan Hill¹</u>, Braden McKnight¹, William Pannell¹, Nathanael Heckmann¹, Lakshmanan Sivasundaram¹, Amir Mostofi^{1,2}, Reza Omid¹, George F. Hatch III¹

¹Keck School of Medicine of the University of Southern California, Los Angeles, CA, ²Huntington Memorial Hospital, Pasadena, CA

Introduction: Shoulder arthroscopy is a commonly performed orthopaedic procedure. Although complication rates are low, identification of risk factors associated with readmission is critical. Predictors of 30-day readmission for a cohort of knee and shoulder arthroscopy cases was previously described. The purpose of this study was to evaluate a larger cohort comprised only of shoulder arthroscopy cases to provide further insight into factors associated with 30-day readmission.

Methods: The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database was queried using Current Procedural Terminology (CPT) codes to identify all patients who had undergone shoulder arthroscopy between 2007 and 2013. Readmission data was added to NSQIP in 2011; thus, patients undergoing shoulder arthroscopy prior to 2011 were excluded. Univariate analysis using Fisher's Exact test and multivariate analysis using multinomial logistic regression were conducted. Significance was set at p<0.05.

Results: We identified 15,385 patients who underwent shoulder arthroscopy in the specified time period. The 30-day readmission rate was 1.09%. Upon multivariate analysis, operative time greater than 1.5 hours, steroid use, chronic obstructive pulmonary disease, age greater than forty years, American Society of Anesthesiologists (ASA) class three and above, disseminated cancer, and radiation therapy within ninety days were found to be independently associated with readmission (Table II). **Conclusion:** Shoulder arthroscopy is a frequently performed orthopaedic procedure; thus, minimizing readmission rates is essential. These findings identify several patient characteristics associated with 30-day readmission following shoulder arthroscopy. While risk factor modification is often out of the

surgeon's control, operative time is an exception. Prolonging operative time beyond 1.5 hours may increase the risk of readmission in patients undergoing shoulder arthroscopy.

TABLE I Univariate An Non-Rea	alysis of Rea dmitted Patie	admitted and ents		TABLE I (Cont.) Univariate Analysis of Readmitted TABLE II Multivariate Analysis of Risk Fact and Non-Readmitted Patients for Readmission after Shoulder Arthrosoc		sis of Risk Factors oulder Arthroscopy	ors opy			
	Readmitted	Non-Readmitted	P-value*	F	Readmitted	Non-Readmitted	P-value*		Adjusted Odds	P-Value*
Variable	n=168	n=15,217		Variable	n=168	n=15,217		Risk Factors	Ratio (95% CI)	
Age (%)			<0.001	Steroid use (%)	6.55	1.40	<0.001	Age		
< 40 years	2.98	16.04		Bleeding disorder (%)	4.76	1.52	0.005	< 40 years	Ref.	
40 to 65 years	64.29	61.37		Dialysis (%)	0.60	0.11	0.179	40 to 65 years	3.40 (1.35-8.55)	0.009
> 65 years	32.74	22.59		Chemotherapy ≤ 30 days (%)	0.00	0.02	1.000	> 65 years	3.26 (1.23-8.65)	0.017
Sex (%)			0.544	Radiation therapy ≤ 90 days (%)	0.60	0.01	0.022	BMI	0.93 (0.63-1.36)	0.697
Male	55.95	58.57		Prior operation ≤ 30 days (%)	0.00	0.04	1.000	Smoking	1.40 (0.96-2.05)	0.082
Female	44.05	41.41		ASA Classification (%)			<0.001	Preoperative dyspnea	0.81 (0.41-1.60)	0.535
Unkown	0.00	0.02		1	4.17	16.43		COPD	2.70 (1.60-4.56)	<0.001
Race (%)			0.280	2	40.48	57.64		CHF	3.44 (0.83-14.17)	0.087
Black	7.74	6.89		3	51.19	25.16		Hypertension	1.11 (0.78-1.58)	0.568
White	79.76	76.11		4	4.17	0.76		Diabetes	1.13 (0.76-1.68)	0.533
Other	12.50	17.00		Blood transfusion (%)	0.60	0.04	0.074	Disseminated cancer	10.17 (2.02-51.11)	0.005
BMI (%)			0.089	Operative time (%)			0.001	Steroid use	3.17 (1.66-6.07)	<0.001
<35 kg/m ²	76.19	81.49		≤1.5 hours	58.93	70.85		Bleeding disorder	1.56 (0.71-3.45)	0.267
≥35 kg/m ²	23.81	18.51		>1.5 hours	41.07	29.15		Radiation therapy ≤ 90 days	45.62 (2.52-825.34)	0.010
Alcohol abuse (%)	0.00	0.75	0.639	Functional status (%)			0.002	ASA Classification		
Smoking (%)	24.40	17.70	0.032	Independent	95.24	98.63		1	Ref.	
Recent weight loss (%)	0.60	0.07	0.123	Totally or partially dependent	2.38	0.43		2	1.85 (0.83-4.15)	0.133
Preoperative dyspnea (%)	6.55	2.86	0.010	Unknown	2.38	0.95		3	3.91 (1.67-9.12)	0.002
COPD (%)	12.50	2.60	<0.001	*Calculated using Fisher's Ex	act with sigr	nificance set at p	< 0.05	4	6.70 (2.01-22.29)	0.002
CHF (%)	1.79	0.12	0.002	2				Blood transfusion	5.13 (0.44-59.76)	0.192
Hypertension (%)	57.74	38.56	<0.001					Operative time >1.5 h	1.68 (1.23-2.30)	0.001
Diabetes(%)	23.21	13.31	0.001					Functional Status		
PVD (%)	0.60	0.11	0.179					Independent	0.37 (0.13-1.05)	0.061
Disseminated cancer (%)	1.19	0.05	0.005					Totally or Partially Depender	nt 0.85 (0.19-3.86)	0.836
*Calculated using Fisher's	s Exact with s	ignificance set at	p < 0.05					*Calculated using multinomial	logistic regression with	Hosmer-
								Lamaahaw aaadaaaa of fitu	ith algorificance act at a	O OF

Using Actigraphy to Assess The Effects of Sleep On Cognition and Injury Rate in Adolescent Athletes <u>Angela Hsu, B.S^{1,2}</u>, Iris Perez, M.D.^{1,2}, Tishya A. L. Wren, Ph.D.^{1,2}, Akash Patel², Bianca Edison, M.D.^{1,2} ¹Keck School of Medicine of University of Southern California ²Children's Hospital Los Angeles

Rationale: Insufficient sleep has been associated with a myriad of negative effects, including impaired psychomotor achievement, cognitive dysfunction, decreased reaction time, and poorer athletic performance. The National Sleep Foundation's new recommendation for sleep duration for teenagers (Ages 14-17) is between 8 and 10 hours per night. The purpose of this study is to evaluate the potential effects of sleep on factors that can affect a student athlete's scholastic success, to include sports injury rate, academic, and cognitive performance. We hypothesized that participants who slept less than the threshold of expert recommendation were more likely to a) be injured more frequently b) demonstrate poorer academic performance and c) have lower scores on neurocognitive testing than their peers. **Methods:** 16 high school cross country athletes (9M, 7F, mean age 15.6 years old) were asked to wear an ActiGraph watch for two weeks (14 nights). Subjects were also asked to complete a sleep diary for 7 days, fill out a sleep and activity survey, and undergo a computerized neurocognitive assessment with the NIH Toolbox Cognition Domain. Academic/attendance information, injury data, and athletic performance data were collected from the school registrar.

Results: During the study period, 208 nights of nocturnal sleep data were analyzed. According to ActiGraph analysis, Total Minutes in Bed averaged 455 minutes (7 hours and 35 minutes), Total Sleep Time (TST) averaged 361 minutes (6 hours and 1 minute), and Wake After Sleep Onset (WASO) averaged 91 minutes (1 hour and 31 minutes). Average sleep efficiency, calculated as the percentage of sleep time divided by the total minutes in bed, was 79.89%. There was a statistically significant correlation observed between average number of hours in bed and results of the Dimensional Change Card Sort test, a sub-test within the NIH toolbox that assesses for cognitive flexibility (0.73, p= 0.01). There was no significant correlation between academic scores and sleep time. Of the 16 participants, there were 3 athletes who had injuries during the 2 week study period window. These 3 participants were within the bottom 4 participants with the lowest average total sleep time (5.0, 5.5, 5.6 hours). **Conclusion:** In high school cross country athletes, decreased sleep is associated with increased injury rate and poorer neurocognitive performance.

Decreased colony forming capacity in mesenchymal stromal cells derived from irradiated human skin.

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Purpose: Radiotherapy results in increased complications during post-oncologic reconstructive surgery. Skin-derived mesenchymal stromal cells (SMSCs) are a heterogeneous population of cells with the capacity for self-renewal and are critically involved in skin homeostasis, but little is known about the *in situ* effect of irradiation on these cells. This study aimed to characterize functional alterations in SMSCs derived from irradiated and normal human skin.

Methods: Four pairs of irradiated and normal human skin samples were harvested from patients. SMSCs were isolated from these samples and cultured according to standard protocol. SMSC function was assessed using a colony forming unit-fibroblast (CFU-F) and WST-1 proliferation assay. Gene expression was evaluated using RNA-Seq and confirmed with quantitative polymerase chain reaction (qPCR). **Results**: SMSCs from irradiated skin had a 5.6-fold decrease in colony formation capacity and significantly lower proliferation *in vitro* (p < 0.05). Analysis of RNA-Seq data was restricted to genes with reads per kilobase of transcript per million mapped reads (RPKM) greater than 0.3. Forty-nine genes were differentially expressed in irradiated SMSCs. Three candidate genes—DACT1, FMN1, and IL32—were selected on the basis of their involvement in skin function or pathology, and the directionality of their differential expression confirmed with qPCR.

Conclusion: SMSCs from irradiated skin have significant defects in colony formation and proliferative capacity *in vitro* that are associated with a distinct pattern of altered gene expression. The investigation of these differentially expressed genes may aid in the development of targeted therapies to improve skin healing after radiotherapy.

High Resolution Reconstruction of the Central Auditory Pathway <u>Alexandra Kammen¹</u>, Rick Friedman², Arthur Toga³, Yonggang Shi³

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Objective: Automated high-resolution reconstruction of the auditory radiations using diffusion MRI data.

Background: The central auditory pathway connects the cochlear nerve to the brainstem and cerebral cortex through an intricate sequence of neurons and relay stations. While its anatomy has been fairly well-studied in other species, a robust investigation of the pathway in health and disease has not been conducted in humans. Recent advances in diffusion MRI technology, such as those seen with the Human Connectome Project, allow for the study of the central auditory pathway in vivo with an unprecedented level of detail and accuracy.

Method: Using data from five subjects obtained through the Human Connectome Project (HCP), we reconstructed the auditory radiations using our own recently-developed fiber-orientation distribution (FOD) probabilistic tractography technique. The primary auditory cortex was chosen as the seed region for the probabilistic tractography algorithm and was located by linearly and non-linearly warping postmortem data onto our subjects' brains. The other region-of-interest (ROI) included in the algorithm was the medial geniculate nucleus (MGN), which was located manually on T2-weighted images. **Results:** Our method successfully reconstructed the auditory radiations from the medial geniculate

nucleus to the primary auditory cortex. The resultant fiber bundles are consistent with the patterns seen in post-mortem studies as shown in the figure below.

Conclusion: This proof-of-concept study demonstrated the feasibility of reconstructing the human

auditory radiations using in vivo diffusion MRI and a FOD-based tractography technique. In the future, we will make the method entirely automated by generating an atlas of the MGN in all HCP subjects' brains. Additionally, we plan to use the fully-automated method to perform large-scale studies examining how the anatomy of the central auditory pathway is affected by common genetic variants and hearing ability.



Quantifying Microvascular Density and Morphology in Diabetic Retinopathy using Spectral Domain Optical Coherence Tomography Angiography (SD-OCTA)

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Background/Purpose/ Goal/ Hypothesis: Diabetic retinopathy (DR) is characterized by retinal microvasculopathy and remains a leading cause of visual impairment and blindness in the world. SD-

OCTA is a novel imaging modality that non-invasively provides high-resolution images of the retinal capillaries. Quantification of OCTA data will likely be useful in the future as an objective marker for progression of retinal vascular disease such as diabetic retinopathy (DR). In this study, we quantified changes in the retinal microvasculature affected by different severities of diabetic retinopathy (DR) using SD-OCTA and compared these results to healthy eyes.

Methods: A total of 8 healthy subjects (14 eyes) and 50 diabetic subjects (84 eyes) were imaged using SD-OCTA. A semi-automated program was used to calculate indices of microvascular density and morphology in non-segmented and segmented SD-OCTA images in a 3x3mm² area over the fovea. Microvascular density was quantified using skeleton density (SD) and vessel density (VD), while vessel morphology was quantified as fractal dimension (FD) and vessel diameter index (VDI). Statistical analyses were performed using the Student's t-test or analysis of variance with post hoc Tukey Honest Significant Difference tests for multiple comparisons.

Results: Spearman's rank test demonstrated a significant negative correlation in SD, VD, and FD and significant positive correlation in VDI between healthy and DR eyes (rho = -0.767, -0.7166, -0.768, and +0.5051, respectively; P < 0.0001). All parameters showed high repeatability ($\kappa > 0.99$) and reproducibility between graders (ICC > 0.93).

Summary/ Conclusion: Vascular changes in DR can be objectively and reliably characterized using OCTA. In general, decreasing capillary density (SD and VD), branching complexity (FD), and increasing average vascular caliber (VDI) were associated with worsening DR. While conventional methods of categorizing DR severity (indirect ophthalmoscopy, fluorescein angiography, optical coherence tomography, etc.) remain clinically relevant, they are subjective assessments and may fail to catch small but clinically important changes in the capillary networks that are reliably detected with OCTA and evaluated with these types of quantitative algorithms.

> Fractal Viewpoint of Renal Masses: A Quantitative Technique Kwon M, Varghese B, Hwang D, Desai B, Duddalwar VA

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Background: Shape complexity has been increasingly used to quantitatively describe tumors, by scoring the variation of structural detail by fractal analysis (FA). FA quantifies the self-similar structural patterns in tumors by calculating the fractal dimension (FD). Currently, FA has not yet been applied to renal tumors. There is a need to discriminate between malignant and benign renal tumors as 20%-30% of surgeries removing renal tumors involved unnecessary removal of benign renal masses. **Objective**: To develop a quantitative technique to analyze the structural complexities of renal tumors by calculating FD values, which quantifies self-similar structural properties of renal tumor ROI images. FD values of benign and malignant renal tumors will be calculated and analyzed to assess the relationships between FD values and different renal tumor types. Fractal analysis is one of many methods of quantifying renal tumor images. Alone fractal analysis cannot conclusively diagnose, but it could potentially assist radiologists by providing quantifiable information during the clinical decision-making process.

Methods: Multiphase abdominal CT images of patients with renal masses with proven pathology were retrospectively queried from our surgical database and used for this study. CECT images from 20

patients with malignant and benign renal masses underwent fractal analysis using FracLac, a plugin tool on ImageJ software (NIH, Bethesda, MD). Tumor regions of interests (ROIs) were manually selected and processed by FracLac to calculate fractal dimension values for each of the ROIs. Fractal dimension values of malignant (all subtypes of RCCs) and benign (oncocytomas and lipid poor angiomyolipomas) renal masses were then compared and statistically analyzed to assess if there is a relationship between fractal dimension and different renal tumor types.

Results: With increasing number of detection of renal lesions, it is important for radiologists to discriminate benign from malignant. Fractal analysis is one of many methods of quantification of renal lesions. Preliminary data shows that it may be possible to distinguish renal cell carcinoma from oncocytoma. clear cell RCC FD is 0.10, papillary RCC is 0.71, and oncocytoma FD is 0.32. Nevertheless, fractal analysis alone cannot conclusively diagnose renal tumors, but with more research and optimization, in the future, it could potentially help assist radiologists' diagnoses. Fractal analysis has potential, but its diagnostic capability is currently non-conclusive.

Surgical Fixation of Nonunion of Clavicle Fractures is Associated with Higher Rates of Short Term Complications Compared to Primary Fixation

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Purpose: When selecting patients for primary surgical fixation of midshaft clavicle fractures physicians must weigh the risks of surgery against the risk of nonunion following nonoperative management. Relatively little is known about the perioperative complication rates following open reduction internal fixation (ORIF) of acute fractures or nonunions. The purpose of the current study was to establish perioperative complication rates of surgical fixation for nonunion of midshaft clavicle fractures and compare them to complication rates of surgical management of acute fractures using a population cohort.

Methods: The American College of Surgeons National Surgical Quality Improvement Program (ASC NSQIP) database was queried in order to identify patients who had undergone ORIF of midshaft clavicle fractures. Patients were stratified by operative indication: acute fracture or nonunion. Patient characteristics and 30-day complication rates were compared between the two groups using univariate and multivariate analyses.

Results: A total of 1,215 patients who underwent ORIF of a midshaft clavicle fracture were included in our analysis. Of these, 1,006 (82.8%) were acute fractures and 209 (17.2%) were nonunions. Patients undergoing ORIF for nonunion had a higher rate of total complications compared to acute fractures (5.3% versus 2.3%; p=0.035). After correcting for age, sex, BMI, smoking status, diabetes and other comorbidities, patients with a nonunion were twice as likely to experience any complication (OR, 2.29; [95% CI, 1.05 to 5.00]; p=0.037) and three times as likely to experience a wound complication (OR, 3.22 [95% CI, 1.02 to 10.20]; p=0.046) compared to acute fractures.

Conclusion: Patients undergoing ORIF for a midshaft clavicle nonunion are at an increased risk of 30-day total complications and wound complications compared to primary surgical fixation. This provides

additional evidence supporting primary surgical fixation in patients with a high likelihood of nonunion, as it may obviate the risk of surgical complications.

Multivariate Analysis of Postoperative Complications by Operative Indication*					
	Odds Ratio (95% CI)	P Value			
Total complications					
Acute Fracture	Ref.				
Nonunion	2.29 (1.05-5.00)	0.037			
Wound complication					
Acute Fracture	Ref.				
Nonunion	3.22 (1.02-10.20)	0.046			
Reoperation					
Acute Fracture	Ref.				
Nonunion	0.84 (0.21-3.25)	0.797			
*Variables with P < .20 on univariate analyses were included					
in each respective multivariate analysis.					

Epidemiological Profile of Out-of-Hospital Cardiac Arrest Presenting to the Emergency Department in Chile

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Introduction: Chile lacks of out-of-hospital cardiac arrest (OHCA) data. Most of the Chilean guidelines and protocols are based on international data.

Methods: We conducted a retrospective chart review of all OHCA presenting to a major metropolitan hospital in Chile over 3 years. This center is the primary provider of emergency services for roughly 10% of the entire Chilean population. Descriptive statistics and OR were reported.

Results: We analyzed a total of 337 OHCA, corresponding to 0.4% of all visits. Most patients were brought in by family. Mean age of patients was 62 years (SD 16). Forty two percent of patients were female. Sixty-seven of the patients died in the ED. The most common presenting rhythm was asystole (67%), followed by shockable rhythms (16%) and PEA (15%). Asystole (OR=10, p<0.05) and age greater than 70 years were highly associated with failure to achieve ROSC in the emergency department (p<0.05). We were unable to retrieve reliable data regarding outcomes beyond the ED stay. **Discussion**: This is the first study that describes the characteristics of OHCA in Chile from the ED perspective. In Chile, as compared to international literature, OHCAs are rarely managed and transferred by EMS but rather are usually brought in by bystanders without cardiopulmonary resuscitation. We are currently conducting a prospective registry to better describe the characteristics, management and outcomes of OHCA. This will be the first out-of-hospital cardiopulmonary arrest registry in our country. citation: Neill E, Aguilera P, Clausdorff H, Navea O, Lara B. Epidemiologic profile of out-of-hospital cardiac arrest presenting to the emergency department in Chile. Abstract presented at: the International Conference on Emergency Medicine, April 2016, Cape Town, South Africa.

Regulated Gene Therapy for Bone Repair Using Inducible Caspase-9 (iC9) Suicide Gene System

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Introduction: Gene therapy using viral vectors encoding for BMP-2 has been successfully used to heal critical sized bone defects in murine models. Since gene therapy would be used to treat non-lethal conditions, any increase in morbidity or mortality would not be acceptable. Thus, developing a system to regulate BMP-2 production would be a useful and desirable tool. The iC9 system has the potential to serve this exact purpose. This system uses a chemical inducer of dimerization (CID) to selectively induce apoptosis in cells expressing iC9. By combining iC9 to another protein, such as BMP-2 or Luciferase (Luc), one can regulate protein expression by using CID to kill cells expressing this new fusion protein. Therefore, to increase the safety of gene therapy, we created lentiviral (LV) vectors expressing iC9/BMP-2 and iC9/Luc. Our hypothesis is that production of BMP-2 and Luc can be regulated using CID to induce apoptosis in cells expressing iC9/BMP-2 and iC9/Luc.

Methods: To enhance BMP-2 and Luc production, our LV vector was modified to a two-step transcriptional amplification (TSTA) system. This system requires a transactivator vector (LV-iC9/GAL4) and a transgene expression vector (LV-G5-iC9/BMP-2 or LV-G5-iC9/Luc). Rat bone marrow cells (RBMCs) and human adipose derived stem cells (hADSCs) were each transduced with both vectors using a multiplicity of infection (MOI) of 25. After overnight transduction, cells were washed to remove extracellular viruses and treated with two doses of CID (one dose every 24 hours). BMP-2 production of transduced cells was quantified using ELISA after the second dose of CID. Luc activity of transduced cells was evaluated using a luciferase assay after the second dose of CID. The luminescence was analyzed using a microplate reader. Non-transduced and transduced cells without exposure to CID served as our controls.

Results: We created LV vectors that express iC9 with either BMP-2 or Luc. RBMCs and hADSCs transduced with the LV-TSTA-iC9/BMP vector produced 13.1 ± 0.4 and 4.6 ± 0.1 ng of BMP-2 per 24-Hr per 100,000 cells, respectively. Exposure to CID decreased expression of BMP-2 by 85-87% in RBMCs compared to 73-82% in hADSCs. RBMCs and hADSCs transduced with the LV-TSTA-iC9/Luc vector produced a Luc signal that also declined with CID. Exposure to CID decreased the relative Luc activity by 97-99% in RBMCs and greater than 99% in hADSCs. Cytotoxicity of CID was only seen in cells expressing iC9; CID had no effect on non-transduced cells.

Conclusion: We have demonstrated that CID could be used to selectively induce apoptosis in cells transduced with a double-gene vector. Overall, by regulating the gene expression of BMP-2, we can enhance the safety of gene therapy to make it a more suitable treatment modality for non-lethal conditions, such as bone repair. Further experiments are needed to determine if gene expression using these LV vectors can also be regulated in-vivo.

Continued Delay in Diagnosis of Slipped Capital Femoral Epiphysis

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Objectives: More than a decade ago, Skaggs and Kocher et al. reported significant delays in the diagnosis of slipped capital femoral epiphysis (SCFE). The purpose of this study was to identify if the time to diagnosis has improved.

Study Design: Retrospective review of 481 patients admitted with a diagnosis of SCFE at three large pediatric hospitals between 01/2003-12/2012.

Results: The average time from symptom onset to diagnosis was 17 weeks (range 0-169). There were no significant differences in time from symptom onset to diagnosis across two year intervals of the study period (p=0.94). Time from presentation to first provider to diagnosis was significantly shorter for patients presenting to an orthopaedic clinic (mean 0 weeks, range 0-0) versus PCP (mean 4 weeks, 0-52) (p=0.003, r=0.24) or ED (mean 6 weeks, range 0-104) (p=0.008, r=0.36). 52 patients (10.8%) developed a second SCFE after treatment of the first. Time from symptoms to diagnosis for the second SCFE was significantly shorter (p<0.001, r=0.19) with mean delay in diagnosis of 11 weeks (range 0-104). The number of second SCFE patients diagnosed while mild in severity as defined by Wilson classification was significantly larger (p=0.001, OR=4.44) than those with a first SCFE.

Conclusions: Despite reports documenting a lag in the diagnosis of SCFE over a decade ago, there has been no improvement in the delay in diagnosis. Decreased delay and severity for the second SCFE suggests that the education of at risk children and their families may be of benefit in improving this delay.

Assay for Specificity of Hair-cell and Supporting Cell Enhancer Function in Neonatal Organ of Corti <u>Tymon Tai</u>, Juan Llamas, Litao Tao, Vincent Haoze Yu, Neil Segil, Department of Otolaryngology Head & Neck Surgery, KSOM

Background/Purpose/ Goal/ Hypothesis: Death of the sensory hair cells in the inner ear, and their failure to regenerate, is a major cause of permanent hearing loss. Regenerative medicine approaches to this problem require a thorough understanding of the transcriptional mechanisms that characterize the cell types of the inner ear – namely hair cells and supporting cells. This study focuses on testing the DNA regulatory elements in the genome (aka enhancers or cis-regulatory sequences), that determine gene expression in a tissue- and cell type-specific fashion.

To this end, we designed an in vitro culture method for high-throughput validation of enhancer activity in hair cells and supporting cells of the murine organ of Corti. This culture system maintains the survival of dissociated hair cells and supporting cells for two weeks and beyond. Enhancers linked to fluorescent reporters are tested for their ability to direct cell type-specific expression in these cells following infection with a lentivirus gene targeting vector..

Methods: Potential enhancer sequences predicted to be active in a particular cell types were identified by bioinformatic analysis of a combination of transcriptome analysis (RNAseq), open-chromatin configuration (ATACseq), active epigenetic modifications (H3K27ac ChIPseq) carried out in the Segil lab, as well as by cross-species conservation. Predicted sequences were then amplified from human DNA by PCR and cloned into appropriate reporter vectors for viral preparation.

Lentiviruses containing reporter constructs driven by predicted enhancer inserts of interest were generated. These constructs also encode a ubiquitously expressing fluorescent reporter. By design then, all cells infected by this virus should express a red fluorescent protein, while green fluorescent protein should also be expressed in infected cells where the enhancers are active.

We then introduced this lentivirus into our in vitro cell culture system where organ of Corti explants are first enzymatically-dissociated into a single cell suspension and then grown at high density in 96-well plates. Cell culture conditions were optimized to enhance hair cell and supporting cell infection as previously described (White et al.,). Important variables considered include: timing of infection, cell density, surface treatments for cellular adherence, and composition of the cell culture growth media, as well as validation of hair cell and supporting cell survival by immunofluorescence.

Manual and automated fluorescent microscopy were used to quantify expression. Immunohistochemical staining of cell-specific molecular markers (MyoVII, Sox1, Prox1, etc) were used to confirm hair cell and supporting cell identities. In certain experiments, transgenic mice with fluorescent reporters were also used for this purpose.

Results: We observe that organ of Corti cells form characteristic "epithelial islands" when they are plated following enzymatic dissociation. These islands of hair cells and supporting cells survive beyond 14 days and are amenable to lentiviral infection. Our results suggest that this system sustains cells that are dissociated from mouse cochlea from either embryonic (day 14.5) through postmitotic (postnatal day 3).

Furthermore, lentiviral administration at the time of cell plating yields the highest percentage of infected cells. Optimal cell density at time of plating is also an important factor to maximize cell survival and infection. After fixation of the cells, surfaces treated with poly-D-lysine and fibronectin result in retention of more cells compared to that of the standard gelatin coating, which is important for immunohistochemical applications. We also find that addition of an anti-apoptotic agent (ROCK inhibitor) to the standard defined cell culture media improves cell survival.

Preliminary data indicates that lentivirus is a feasible vector delivery system for dissociated hair cells and supporting cells, infecting ~ 10% of the supporting cell and hair cell populations, respectively. We have tested the system using a known hair cell-specific enhancer from the Atoh1 gene, and observed cell type specificity. Testing of predicted enhancers driving hair cell- and supporting cell-specific expression will be tested.

Summary/ Conclusion: We present a system for the viable, low-input, efficient method of enhancer validation for the cells in the organ of Corti. With it, we can verify the relevance of bioinformatically-predicted cis-acting DNA regulatory elements in an appropriate biological setting. Identifying these enhancer elements is crucial to our understanding of the genetic cues of cellular identity, and can potentially be manipulated in the context of cellular reprogramming. This culture system with its low requirements for biological material, and retained cellular characteristics also serves as a platform for low throughput inner ear drug screening and drug discovery.

Human induced pluripotent stem cell-derived motor neuron transplantation as a potential treatment for neuromuscular atrophy in a mouse model of sciatic nerve injury

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Objectives: After injury to peripheral motor nerves, pre-injury function may be incompletely restored. The reasons for this are multifactorial, but a significant limitation is that motor fibers regenerate slowly (about 1 millimeter per day), and regenerating axons frequently take weeks to months to reach target motor endplates. During this time, there is significant neuromuscular atrophy of both the target musculature and the distal nerve. Currently, several groups have shown that mouse induced pluripotent stem cell-derived motor neurons (iPSCMNs), when grafted into a transected mouse tibial nerve, form functional neuromuscular junctions and reduce the muscular atrophy that occurs following denervation. However, there has been no published data to date demonstrating successful transplantation and engraftment of human iPSCMNs into peripheral motor nerves. There may be clinically important differences between human and mouse iPSCs, and so our aim is to repeat these experiments using human iPSCMNs to evaluate the translational potential of iPSC technology in this setting.

Study Design: Using established protocols from a collaborator, we created functional motor neurons from human iPSCs that were themselves derived from mature human fibroblasts. In both immunodeficient mice and immunosuppressed mice, we induced sciatic nerve injury (suture ligation and division), with subsequent injection of these human iPSCMNs distal to the injury site. These surgeries were performed under varying transplantation conditions.

Methods: Using immunohistochemistry, we quantified the number of viable iPSCMNs present in the distal sciatic nerve at various time points after implant (ranging from immediately after implant to 6 weeks later). Successful transplants will be further characterized in terms of neuromuscular junction formation and electrophysiological function of the triceps surae muscle (in response to bipolar electrode stimulation of the sciatic nerve distal to the site of injury).

Results: In our mice implanted with iPSCMNs, we have shown successful motor neuron survival and extension of axons on immunohistochemistry. We have also shown preservation of muscle mass (on the side of nerve injury) in implanted mice as compared to negative controls. However, the survival of the cellular transplants appears to be unpredictable.

Conclusions: Human iPSCMNs can successfully survive and engraft in a mouse experimental model, and may have a protective effect on muscular atrophy after denervation. We are now trying to determine the transplantation conditions that will yield optimal engraftment and functional neuromuscular junction formation.

The Role of the Nervous System in the Pathophysiology of Psoriasis: A Review of Cases of Psoriasis Remission or Improvement Following Denervation Injury <u>Tian Hao Zhu¹</u>, Mio Nakamura², John Koo,² Tina Bhutani²

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Background: As most efforts in the last decade have focused on the immunologic basis of inflammatory skin disease, there has been less emphasis on the role of the nervous system in the disease process of psoriasis. Evidence in support of the neurocutaneous pathway has come from observations of patients experiencing unilateral improvement and even complete remission following nerve damage in the affected dermatomal region. The aim of this review was to investigate the role of neuropeptides in the intricate pathophysiology of psoriasis.

Study Design: The PubMed database was searched for individual case reports or case series that reported clearance or significant improvement in psoriatic disease in patients following documented nerve injury.

Results: A total of 11 cases were found that reported improvement of psoriatic lesions in areas afflicted by central or peripheral nerve injury. The most common causes of denervation were inadvertent surgical interruption, cerebrovascular accident, and poliomyelitis. In four cases the patients eventually regained neurologic function, which was associated with a recurrence of skin lesions. In cases of permanent nerve damage, there was remission of psoriasis.

Conclusion: The cases reported in the literature to date provide clinical evidence that absence of neural input leads to psoriasis improvement, suggesting a crucial role of the nervous system in the pathophysiology of psoriatic disease. In fact, neuropeptides such as nerve growth factor, substance P, calcitonin gene-related peptide, and vasoactive intestinal peptide may be important contributors of psoriatic disease and potential targets for future therapies.

ALTERNATIVE MEDICINE

The Effect of Acupuncture on Somatization and Pain in Pediatric Chronic Pain Patients. Ena Nielsen, B.A., Jeffrey Gold, PhD, Department of Anesthesiology, KSOM

Goal: Recent studies have shown that somatization in young chronic pain patients is a strong predictor of pain intensity and quality of life. In addition, there is evidence that the chronic pain population is increasingly turning to integrative treatment modalities to manage their pain symptomatology. In light of these findings, the current study aims to determine the efficacy of acupuncture treatment in reducing somatization and pain in a population of pediatric chronic pain patients. It is predicted that acupuncture will be more effective than the standard of care therapy alone in reducing somatization and pain. **Method:** 38 children (8-12 years) and adolescents (13-18 years) with chronic pain completed measures assessing somatization (Child Somatization Inventory) and pain (Brief Pain Inventory and Visual Analog Scale) before beginning treatment, after each treatment session, and 1 month after ending treatment. Patients were assigned to either 6 weeks of acupuncture, acupuncture plus massage, or standard of care treatment.

Results: The reduction in somatization scores after 6 weeks of treatment and 1-month post-treatment were not statistically significant for any of the treatment groups. In addition, patients showed no improvement in VAS scores. Interestingly, acupuncture treatment did result in a significant change in patient's BPI scores at 1-month post-treatment (p=0.041).

Conclusion: The data shows no benefit from acupuncture on somatization scores. However, there is evidence that acupuncture treatment reduced some measures of pain for up to 1 month after stopping treatment.

BASIC SCIENCE

Expression of mu opioid receptor and Kv1.2 controlled by MBD1 in the dorsal root ganglion

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Introduction: MBD1 may play a key role in the genesis of acute pain and chronic pain through changes of pain-related gene expression in nervous system. In this study, we first observed the expression of opioid receptors and potassium channels at the levels of both mRNA and protein in the dorsal root ganglia (DRG), spinal cord, midbrain and cortex in wild type and MBD1 knockout mice. We then overexpressed MBD1 in lumbar DRGs of wild type mice to determine if MBD1 overexpression alters behavioral responses and affects these pain-related gene expression. Finally, we defined if MBD1 co-localized with opioid receptors or potassium channels in individual DRG neurons.

Methods: PCR assay was carried out to detect the mRNAs of mu opioid receptor (MOR), kappa opioid receptor (KOR), delta opioid receptor (DOR), Kv1.1, Kv1.2, and Kv1.4. Western Blot assay was performed to measure MOR, KOR, Kv1.1, and Kv1.2 proteins. To overexpress MBD1 in DRGs, AAV5 virus expressing full-length MBD1 (AAV5-MBD1) was micro-injected. AAV5 virus expressing EGFP (AAV5-EGFP) was used as a control. 6 to 8 weeks after microinjection, mechanical, thermal, and cold testing took place. PCR assay was used to examine the co-localization of MBD1 with MOR and Kv1.2 in individual DRG neurons. **Results:** The levels of MOR, KOR and Kv1.2 mRNAs were significantly increased in DRG, spinal cord, and cortex of MBD1 knockout mice compared to wild type. None were changed in midbrain of MBD1 knockout mice. Only the amounts of MOR and Kv1.2 proteins were confirmed to have a remarkable increase in DRGs of MBD1 knockout mice. Wild type mice with DRG injection of AAV5-MBD1, but not AAV5-EGFP, displayed spontaneous pain and the evoked pain hypersensitivities in response to mechanical, thermal, and cold stimuli with marked reductions in amounts of MOR and Kv1.2 proteins in the injected DRGs. MBD1 mRNA was co-localized with MOR and Kv1.2 mRNAs in individual small, medium, and large DRG neurons.

Conclusion: Our findings indicate that MBD1 regulates the expression of MOR and Kv1.2 at the levels of both mRNA and protein in DRG.

Histological analysis of human acellular dermal matrix explants after joint arthroplasty

<u>Kian Banks, BS</u>, Maxwell Johnson, MS, Daniel Gardner, MS, Athanasios Bramos, MD, Lee Squitieri MD, David Kulber MD, Alex K. Wong MD

Introduction: Carpometacarpal (CMC) osteoarthritis exists in an estimated 21% of elderly individuals. Surgical bone excision and replacement by autologous tendon is the standard of care during unremitting pain. However, tendon harvest can result in donor site morbidity. Recent human trials have substituted exogenous acellular dermal matrices (ADMs) in the bone space, but there is no histological data on the outcome of ADMs after implantation to the joint. We aimed to characterize the revascularization and recellularization of ADMs in the joint space using a rabbit model. **Methods:** Bilateral surgical removal of the lunate carpal bone in New Zealand White rabbits was performed. The bone from one wrist was replaced with dermis from the rabbit's back. The other side was replaced with FlexHD ADM. As a non-joint control, the site of dermis removal received subcutaneous ADM. Samples were collected at 0, 6, or 12 weeks at which point histological and immunofluorescent analysis was performed.

Results: Semi-quantitative analysis of average cellular infiltrate at baseline, 6 weeks, and 12 weeks, respectively, revealed: 0%, 30%, and 22.5% new host cells/hpf in ADM wrist implants; <10%, 20%, and 25% new host cells/hpf in autologous dermis wrist implants; and 0%, 20%, and 10% new host cells/hpf in subcutaneous ADM implants. Immunofluorescence staining for CD31 and anti-smooth muscle actin revealed luminal structures in all samples at both the 6 and 12 week time points.

Conclusion: ADM arthroplasty led to more cellular infiltration than both autologous dermis arthroplasty and subcutaneous ADM placement at week 6 but less infiltration than the autologous dermis at week 12. All samples revealed vascularization.

Use of Recombinant DNA-based Hyaluronidase to Dissolve Fixed Amounts of Hyaluronic Acid (HA) Dermal Fillers

Stacey Barnett, Lauren Cutler, Pauline Thu Tram Phung, Nubia Fernandez and Steve Yoelin (Mentor)

Goal: Dermal filler injections have become a common cosmetic procedure in the US. If lumps, overcorrection or ischemia and impending necrosis occur, there is a need for removal of HA dermal filler. No products have been FDA approved for that purpose, and there have been no in vivo studies demonstrating the safety and efficacy of agents known to dissolve HA. We sought to determine whether various volumes of Recombinant DNA-based hyaluronidase are safe and effective for dissolving HA dermal fillers.

Methods: Human subjects (n=12) were injected with 0.2mL of HA dermal filler at 4 sites along the volar aspect of each forearm. The forearms were randomized to one filler, Voluma or Juvederm. The injection sites were photographed using a 3D camera and images were captured via 2D ultrasound. Each of the 4 dermal filler sites was then randomized to 0 units, 30 units, 60 units or 75 units of the Recombinant DNA-based Hyaluronidase (Hylenex). At 2 time points following the Hylenex injections, the sites were palpated and graded on a scale from 0-4 and imaged via 3D photography and 2D US. The subjects returned 7 days later to have the dermal filler sites palpated/graded and imaged again. Any remaining bumps were dissolved with 75 units of Hylenex. Adverse events were documented.

Results: No adverse events occurred. It is expected that the palpation grading, 3D photography and 2D US imaging will reflect a significant decrease in the amount of dermal filler present at sites injected with 60-75 units Hylenex, modest decrease at sites injected with 15-30 units Hylenex and little to no decrease in the amount of dermal filler present at sites that received no Hylenex.

Conclusion: This data demonstrates evidence that Recombinant DNA-based hyaluronidase is safe for removal of HA dermal fillers in humans. It is also expected that this data will demonstrate the efficacy of various doses of Recombinant DNA-based hyaluronidase in the removal of HA dermal fillers.

Co-Culture in microfluidic device of human induced pluripotent stem-cell derived motor neurons with muscle

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Objectives: Injury to motor nerves causing weakness or paralysis is common. Human induced pluripotent stem-cell derived motor neurons (iPSC-MNs) may be a viable form of therapy in the case of cranial or peripheral motor nerve injury. Microfluidic devices (MFDs) have been established as a specialized in vitro environment to study targeted axonal growth through microchannels connecting source wells to target wells. We describe early findings on the optimal chemical and physiological environment for rapid, targeted axonal growth of human iPSC-MNs in MFDs.

Methods: An established culture protocol was used to derive motor neurons from a line of human iPSCs. Through multiple iterations, a second protocol was established to prepare and seed MFDs with glial cells and iPSC-MNs. These findings describe four MFDs prepared with glial cells and iPSC-MNs in the source wells, of which 2 MFDs subsequently received muscle in the target wells.

Results: We established a viable co-culture protocol that allows for microfluidic analysis of human iPSC-MNs with chick myoblasts. It appears that muscle targets induce greater directional and maximal growth of the human iPSC-MNs, as well as longer in vitro viability of iPSC-MNs. When compared at equal time points of 18 days post-seeding, MFDs with muscle in the target wells exhibit a nearly three-fold increase in targeted axonal growth (number of microchannels between source and target wells with axons) and a 36% increase in maximum length achieved of axons entering microchannels ($346\pm158 \mu m vs. 254\pm138 \mu m$). MFDs receiving muscle in the target wells displayed new axonal generation from somas or axonal growth for an average of 9 days longer than in MFDs without muscle.

Conclusions: Further data will be collected analyzing the directionality and maximum axonal growth of human iPSC-MN axons toward muscle in MFDs. Findings on the significance of muscle as a target for in vitro growth of iPSC-MNs may aid development of a potential in vivo treatment for motor nerve injury.

Immune Biomarkers of Medication (bisphosphonates) related osteonecrosis of the jaws (MRONJ) Naman Desai DDS; Jettie Uyanne DDS; Anh D. Le DDS PhD; Derek Havas DDS;

Background: Medication related osteonecrosis of the jaws (MRONJ), previously known as bisphosphonate (BP) related osteonecrosis of the jaws (BRONJ) is a debilitating bone disease that has been associated with antiresorptive medications such as BP. BP remained the most commonly prescribed medication for both osteoporosis and cancer patients and subsequently the most common cause of osteonecrosis of the jaw or MRONJ. The pathophysiology or the linkage of BP to MRONJ has eluded many researchers. Studies have shown that Nitrogen containing BP can activate a subset of adaptive T-cells. Our research group have demonstrated that an altered immune homeostasis induced by BP, in part by suppressing the adaptive regulatory T-cell (Treg) and suppressing the ratio of Treg/Th17 ratio has been established as the pathogenesis of BP-related ONJ in murine model; however such linkage has not been established or confirmed in humans. **Purpose:** We propose that the altered immune homeostasis, regulated by suppressed Treg, contributes to the pathophysiology of BP associated MRONJ disease in humans. Treg levels and associated pro-inflammatory cytokines can potentially serves as determinants of MRONJ risk in BP treated patients. **Methods:** This is a cross-sectional, case-controlled study of using two well defined groups: cancer patient being treated with chemotherapy and BP use >1 year, presenting with diagnoses of MRONJ; and 2) patient being treated with BP without MRONJ. Immune profile and cytokines were evaluated in the BP treated cancer or osteoporosis patients with MRONJ (n=38) and compared to the control group without MRONJ (n=25). The case and controlled group were matched for age, sex ethnicity, and disease type; and both were compared to healthy subjects (n=57) with no history of chemotherapy and BP use. Additional outcomes were evaluated regarding comorbidities (diabetes), dental health status (periodontitis and caries) and their additional risk factors related to incidence of MRONJ. **Results:** The study groups included MRONJ (n=38), non-MRONJ (n=25), healthy control, or non-exposed subject (n=57). BP exposed group (n=63) included subjects who have been exposed to any form of BP, oral and IV, and was composed of both MRONJ and non-MRONJ subjects. The major oral BPs included

Fosamax and Actonel and the IV BP was Zometa. Of those who are on IV zometa, the order of cancer type is breast, multiple myeloma, prostate, lung, colon, and head and neck cancer.

Among other medical co-morbidities, diabetes has a strong correlation with clinical ONJ. With regards to dental diseases, periodontitis is more associated with clinical ONJ than dental caries.

Among all inflammatory cytokines, bp treatment increases the expression of IFN gamma, IL-10, IL-17, but has no significant effects on IL-6 and TNF-alpha. More importantly, the elevated of level of IL-17 is multifold as compared to the non-MRONJ group.

Conclusion: It is likely that the multiple immunosuppressant drugs given to patients undergoing chemotherapy alters their immune profile and makes them more susceptible to developing Bp related MRONJ. Elevated IFN gamma, IL-10, IL-17 have potential use as immune biomarkers for human MRONJ.

Nox3 deficiency in mice confers protection against Noise-Induced Hearing Loss.

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Goal: Data from our Genome wide association study (GWAS) of the Hybrid Mouse Diversity Panel (HMDP) showed a genome wide significant peak on Chromosome 17. Within the haplotype block at this locus, Nox3 was selected as our candidate gene to study based on its high levels of expression within the inner ear. In this study, we attempt to characterize the effects of a Nox3 knockout on noise induced hearing loss (NIHL) in mice.

Methods: C57BL/6J-Nox3^{nmf250}/J mice from the Jackson Laboratory had their pre-exposure hearing thresholds measured using auditory brainstem response (ABR) waveforms at 6 weeks of age. 1 week after pre-exposure measurements, the mice were subject to 2 hours of 10 kHz octave band noise at 108 dB SPL within our noise exposure chamber. 2 weeks after noise exposure, the post-exposure hearing threshold was measured using ABR waveforms. Hearing thresholds were measured at the frequencies of 4, 8, 12, 16, 24, and 32 kHz. Permanent Threshold Shifts (PTS) were calculated. ABR Post-exposure wave 1 amplitude was also measured and is an indicator of inner hair cell health.

Results: Analysis of Variance between Nox3^{het-4J}/Nox3^{het-4J} (homozygous), Nox3^{het-4J}/+ (heterozygous), and +/+ (wild-type) mice revealed statistically significant differences in PTS at 24 kHz and 32 kHz (p<.01 and p<.05 respectively). Post hoc tests showed homozygous mice had a significantly smaller PTS compared to heterozygous and wild-types. Comparisons of post-exposure wave 1 amplitudes also demonstrated a significant difference at 24 kHz (p<.05), with significantly higher wave 1 amplitudes in homozygous mice compared to heterozygous and wild-type mice.

Conclusion: These data indicate that the Nox3 gene is involved in susceptibility to noise-induced hearing loss and that mice lacking Nox3 are less susceptible. These findings also validate the power of HMDP in detecting genes related to susceptibility for NIHL in mice.

Effects of Metformin on the AMPK Pathway and Metabolomic Biomarkers in ADPKD Kidney Epithelial Cells

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Background: ADPKD is characterized by large-scale cystic growth resulting in kidney enlargement and progressing to end-stage renal failure in over 50% of patients. There are currently no FDA approved treatments, and no useful metabolites have been identified as specific markers for disease severity and progression. Cells with ADPKD are hyperproliferative but utilize aerobic glycolysis instead of oxidative metabolism. This is also seen in tumor cells and is called the Warburg effect. Recent work has shown that the altered metabolism in ADPKD cells demonstrates a decreased AMPK activity. Metformin, an AMPK activator, shows potential to slow cyst growth and correct the perturbed energy metabolism in ADPKD.

Methods: Both immortalized and non-immortalized primary Ad-Cre inducible Pkd2 null cells grown with or without AMPK knockdown were utilized. Through immunoblotting, AMPK pathway markers are correlated with time and dose dependent effects of metformin treatments (all treatments use 0 mM, 100 uM, 300 uM, or 1 mM metformin). 3D culturing is used to assess cyst growth after treatment with metformin and protein kinase A agonists (forskolin and IBMX). ELISAs and seahorse assays are used to correlate key glycolytic enzymes (lactate dehydrogenase A, pyruvate kinase M2 isoform, and pyruvate dehydrogenase kinase 1) enhanced by the Warburg effect. And colorimetric assays are used to assess key metabolites (lactate, succinate, pyruvate, cAMP) in urine samples using creatinine as a comparative baseline.

Results: 72 hr metformin treatment demonstrates an increase in phospho-acetyl-CoA carboxylase (pACC) and phospho-AMPKa (Thr172) expression. This indicates metformin can indeed activate AMPK in Pkd2 cells, particularly at the 300 uM concentration. 3D culturing on matrigel demonstrates treatment with 300 uM metformin results in a decrease of cyst size while avoiding the cytotoxic effects of 1mM metformin. (See attached images)

Conclusions: Data collection is still ongoing, and more data is needed to make conclusive statements on metabolomic markers and glycolytic enzymes among other things. However, it is expected that metformin will reduce cyst grown in vitro ADPKD cells by increasing AMPK activity. Metformin should be considered for a potential treatment for ADPKD. 300 uM metformin seems an ideal beginning concentration to gauge treatment concentration.



Summary of Time and Dose-dependent effect of Metformin treatment on PKD2 SV40 Cross Clone 2tc(-/-) cells Data from010816/012116/020416

022516 PKD2 C2tc 3D Matrigel culture for seeded for 9 days treated for 8 days (Forskolin 10μΜ; IBMX 100μΜ)


Comparison of De Novo Donor Specific Antibody Formation for Kidney Transplant Recipients Induced with Thymoglobulin or Basiliximab.

<u>Alexander Gong, BA</u>, Yasir Qazi, MD, Division of Transplantation, University of Southern California, Los Angeles, CA, United States.

Background: Thymoglobulin (ATG) and basiliximab (Bas) induction are commonly used therapies to prevent allograft rejection in kidney transplant recipients (KTx). Formation of donor specific antibodies (DSA) has been shown to be a reliable predictor of antibody mediated rejection (AMR). The aim of this study was to evaluate the rate of DSA formation in patients who were induced with ATG or Bas. **Methods:** We analyzed 28 cases of kidney transplant performed between August 2013 and August 2015 at our institution. All pts had at least a greater than 3 mismatch and cPRA <20. Luminex testing was used to detect DSA. DSA were tested at monthly intervals x 3 then q 3 month x 2 and if clinically indicated. We compared the rate of DSA formation between patients who received ATG (n = 18) versus Bas (n = 10). Dosing: two 20 mg doses of Bas and 3-6 mg/kg ATG were used. Triple I/S was used for maintenance [Tacrolimus (target levels 6-8), Prednisone and MMF]. For each DSA specimen, we collected information on the total number of non-DSAs formed (class I versus class II). We evaluated these parameters at two time points: < 180 or > 180 days from transplant.

Results: For DSAs performed < 180 days, the mean number of days elapsed since transplant was 58 and 29 in patients receiving ATG and Bas respectively (standard deviation 44.25 and 16.64). In the ATG group, 2/17 (11%) had a positive DSA, whereas 3/7 (42 %) of Bas had a DSA. For DSAs performed > 180 days, the mean number of days elapsed since transplant was 451 and 305 in patients receiving ATG and Bas, respectively (standard deviation 194.72 and 91.28). In the ATG group, 0 out of 5 had a positive DSA. In the Bas group, 3 out of 5 (60 %) had a positive DSA. Patients receiving Bas produced more class II DSAs compared to patients receiving ATG (p < 0.05). By contrast, patients receiving ATG produced more class I non-DSAs compared to patients receiving Bas (p < 0.05).

Conclusion: In this single center prospective study comparing the rate of de novo DSA formation, Bas was associated with a higher rate of de novo DSA formation. Data is being collected prospectively to understand the long term clinical implications of this observation.

PharmGKB Summary: Isoniazid Pathway, Pharmacokinetics (PK)

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Background: Isoniazid (isonicotinic acid hydrazide, INH; PubChem ID <u>3767</u>) is a first-line antimycobacterial agent used to treat active and latent tuberculosis (TB) infections generated by *Mycobacterium tuberculosis*. Anti-TB treatment drug-induced liver injury (ATT-DILI) and other serious adverse reactions cause discontinuation in up to 10% of patients treated with standard regimens of firstline anti-TB drugs. The underlying mechanisms for INH-specific ATT-DILI remain unclear due to their complexity and the difficulty in distinguishing drug-specific from patient-related factors that may determine susceptibility to INH toxicity. This summary outlines the basic aspects of INH absorption, distribution, metabolism and excretion in humans, with emphasis on the influence of genetic polymorphisms in genes encoding xenobiotic-metabolizing enzymes that modulate INH PK and their association with INH-induced hepatotoxicity.

Methods: Extensive review of the literature was completed.

Results: The current consensus among the literature is that a single mechanism is unlikely to explain INH-induced hepatotoxicity; numerous pathways are probably involved. Variants of enzymes involved in the INH metabolic pathway have been associated with ATT-DILI, particularly the slow acetylator variant of NAT2. However, there is no obvious underlying factor that explains why some studies found an association and others did not.

Conclusion: Polymorphisms within genes involved in the INH pharmacokinetic pathway have been investigated in order to identify possible biomarkers for hepatotoxicity risk. These associations and the possible reasons behind a lack of consensus between studies were discussed. Future investigations utilizing DNA sequencing may lead to further identification of variants contributing to ATT-DILI. Large-scale, robust analyses of these underlying genetic and environmental risk factors in clinical settings will help uncover the full picture of these important and complex adverse reactions.

RNA in situ hybridization technology in detection of CRLF2 overexpression in Philadelphia-like acute lymphoblastic leukemia

Jimmy Mao, Russell K. Brynes, and Maria Vergara-Lluri

Goal: Philadelphia-like acute lymphoblastic leukemia (Ph-like ALL) cases exhibit a gene expression profile similar to *BCR-ABL1*-positive ALL cases, but which lack *BCR-ABL1* rearrangement. Rearrangements in CRLF2 represent 50% of all Ph-like ALL cases, can result in CRLF2 overexpression, and are associated with poor clinical behavior. Identification of Ph-like ALL cases with CRLF2 alterations have potential for targeted therapy. Our goal was to investigate an RNA in-situ hybridization technology (RNAscope[™]) to detect CRLF2 overexpression in Ph-like ALL cell lines, and to identify optimal sample types and conditions required for testing patient samples

Methods: RNAscope[™] assays were performed on (a) formalin-fixed paraffin embedded (FFPE) cell lines (HeLa, CRLF2-overexpressed cell lines, and CRLF2-wild type cell lines); (b) B5-fixed decalcified trephine biopsy; (c) peripheral blood mononuclear cytospin and aspirate smear slides fixed under different conditions; and (d) patient bone marrow FFPE samples obtained from Norris Cancer Center. **Results:** RNAscope[™] assays were successfully performed on all FFPE blocks under standard pretreatment conditions with CRLF2 showing strong staining in CRLF2-overexpressed cell lines and lack of staining in CRLF2-wild type controls. Assay was unsuccessful on B5-fixed decalcified biopsy material, cytospin, and aspirate smear slides. Results of assay were variable in patient bone marrow FFPE samples, requiring optimization of pretreatment conditions between individual samples. **Conclusions:** Although a promising technology that could be applied to FFPE material, detection of CRLF2 expression by RNA in situ hybridization technology is time-consuming, labor-intensive, and costly. It requires optimization for individual archival patient samples, limiting its utility in clinical laboratory testing of diagnostic archival material.

Development of an Agent-Based Model of Angiogenesis, with Application to Liver Regeneration <u>William Matloff</u>, Brian Shaw, Paul Macklin, USC Center for Applied Molecular Medicine, KSOM

Background: Angiogenesis, the growth of new vascular networks, is a complex process driven by interactions among cells and their microenvironment and has a key role in many physiologic and pathologic processes. However, it is difficult to study how its components work together to generate vessel networks. Agent-based models, which simulate each cell as a distinct object that dynamically interacts with other cells and the microenvironment, show promise in revealing and understanding the emergent properties of multicellular systems in angiogenesis. The goal of this project is to develop a 3-D, agent-based model of angiogenesis that can be used to explore how endothelial cells with defined functionality create new vessel networks. In particular, we aim to use this model to study liver regeneration.

Methods: The *in silico* model of angiogenesis was developed by extending BioFVM, a framework for simulating biological transport. We developed a code that defines rules for directed endothelial cell division and subsequently simulates the growth of a vascular network within a microenvironment over time. Each endothelial cell and hypoperfused ECM release several diffusing substrates that influence the actions of other cells.

Results: We have successfully produced a preliminary 3-D model that simulates the division of endothelial cells over time to generate vessel networks according to a simple set of rules. We expect that through further exploration of the state space of model parameters, the model will have the ability to produce vessel networks that are quantifiably comparable to *in vivo* vessel networks.

Conclusion: Our model demonstrates that a small collection of rules governing endothelial cell division can generate vascular networks. By adjusting these rules and other model parameters, it will be possible to explore how cell function leads to the emergence of angiogenesis. This will be useful in increasing our understanding of angiogenesis, potentially revealing new therapeutic strategies for related pathology.

Differential protein expression in irradiated human skin by reverse phase protein assay

Brandon Pang, Maxwell Johnson MS, Daniel Gardner MS, Soleil Niknam-Bienia MD, Vinaya Soundararjan BA, Athanasios Bramos, MD, Mei Chen, Ph.D., Gene Kim, MD, Regina Baker MD, Lawrence Kwong, PhD, Lynda Chin M.D., and Alex K. Wong, M.D.

Introduction: Adjuvant radiation therapy after surgical resection is important to the overall management of many solid tumors; unfortunately irradiated skin is associated with poor wound healing and can complicate subsequent reconstructive procedures. This study was performed to determine the molecular basis of poor wound healing in irradiated skin.

Methods: To identify pathological differences in radiation-damaged skin, we generated protein lysates from irradiated and normal sample pairs and analyzed them with reverse phase protein array (RPPA). Differentially expressed protein candidates were determined by median/median ratios of <0.8 or >1.2. Selected candidates were confirmed by Western immunoblot.

Results: Of 211 proteins included in RPPA analysis, fibronectin was the most significantly downregulated protein. Western blot confirmed significantly reduced expression of fibronectin (up to 3 fold less) in radiation-damaged skin in 8 of 10 samples.



M: ladder

1: negative control

2: positive control

- Samples are dated according to when they were harvested; compare the fibronectin extracted form normal skin (lanes labeled "N") to fibronectin from radiation-damaged skin (lanes labeled "X") within each dated pair
- Blots aren't clean; current goal is to generate clearer Westerns for publication

Conclusion: RPPA was used to characterize protein expression differences between normal and radiation-damaged human skin. Fibronectin expression is reduced in irradiated skin and given its known role in wound healing it may be an important pathological change that warrants further investigation.

Chronic Cerebral Hypoperfusion Induced by Bilateral Carotid Artery Stenosis Induces Selective Recognition Impairment in Adult Mice

Alimohammad Moalem, Shuhan He, <u>Arati Patel</u>, Kaleena Patel, Drew M. Hodis, Deep Chandegara, Steven Cen, Qinghai Liu, William Mack

Introduction: Chronic Cerebral hypoperfusion can result in vascular dementia and small vessel white matter ischemic injury. These findings have previously been demonstrated in a murine experimental model of chronic cerebral hypoperfusion (CCH) secondary to bilateral common carotid artery stenosis (BCAS). This study sought to elucidate the effects of CCH on working memory as assessed by the novel object recognition (NOR) testing and histological analysis of the hippocampus and parahippocampal gyrus.

Methods: Studies were performed on 20 ten week old male mice using bilateral 0.18 mm microcoils to narrow the carotid arteries in accordance with prior publications. Following surgery, BCAS (n=8) and

sham (n=10) mice were evaluated using NOR and 8-arm radial maze paradigms. Tissue damage was evaluated using H&E staining.

Results: In the NOR paradigm, BCAS mice demonstrated significant deficits in short-term (p<0.05) and long-term memory (p<0.05). Consistent with prior studies, BCAS mice also performed significantly worse on 8-arm radial maze testing (p=0.02). BCAS mice exhibited significantly more neuronal damage in the anterior parahippocampal gyrus (p<0.01) when compared to sham-operated mice. However, no significant differences in neuronal damage were observed in the CA1 region of the hippocampus **Conclusion:** Experimental CCH secondary to BCAS results in working memory deficits on NOR testing. Damage to the parahippocampal gyrus, rather than to the hippocampus, may underlie this impairment in working memory.

The Effect of Standard Treatments for Autoimmune Disease on Tear Cathepsin S Activity in Patients with Sjögren's Syndrome and other Autoimmune Diseases

<u>Arunava Sarma</u>, Srikanth R. Janga, Maria C. Edman, Neha Teekappanavar, Alex Chen, Mercy Bechtold, Daniel Arkfeld, Elizabeth Ortiz, Stratos Christianakis, William Stohl, Sarah Hamm-Alvarez (PI)

Background: Sjögren's Syndrome (SS) is a chronic autoimmune disease characterized by lymphocytic infiltration and subsequent tissue destruction of the lacrimal and salivary glands, causing dry eye and dry mouth symptoms. Currently, diagnosis of SS is primarily based upon clinical symptoms but recently a study identified elevated activity of the protease Cathepsin S (CTSS) in the tears of SS patients. CTSS plays a role in antigen presentation by B cells and thus may have a role in autoimmunity. It is unknown if elevated CTSS is a driver of SS. This study explores the effect of medication groups upon patient CTSS activity levels in order to access the reliability of a CTSS assay during autoimmune therapy and assess if CTSS could be possible future drug target to modify disease progression.

Methods: Tears and medication data were collected from a cohort 71 female patients with various autoimmune conditions (SS, Osteoarthritis, and Rheumatoid Arthritis). The medications were broadly grouped into categories based on their biochemical activity. The patients were subsequently divided into subgroups based on their medication categories and their disease diagnosis. The tears were assayed for CTSS activity. A comparison was made across the different drug groups in order to identify if a particular class of medication affected tear CTSS activity levels in patients.

Results: Upon preliminary evaluation, no class of medications causes significant changes in tear CTSS activity level in patients across subgroups.

Conclusion: This data demonstrates the viability of CTSS as a diagnostic marker for SS even when the patient is being treated with current therapy for autoimmune conditions. In addition, it also opens the door for further questions on medication targets for Sjögren's syndrome-since CTSS is unaffected by drugs, is CTSS a cause of disease progression and, if so, how can we treat elevated CTSS levels to delay SS progress?

Clinical Benefits of Early Microarray-Based Identification and Resistance Determinants of Organisms Causing Gram-Negative and Gram-Positive Bacteraemia

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Background: Sepsis carries a high mortality rate, and hospitalizations due to sepsis have been increasing worldwide. Molecular tests supplementing Gram stain results from positive blood cultures provide specific organism information which may help guide therapy. More clinical impact studies, however, are still needed to assess the real-world performance and cost effectiveness of these new technologies. **Material/methods:** We retrospectively reviewed and compared records for cases of bacteraemia in hospitalized patients before and after implementation of a microarray-based early identification system called Verigene at Keck Medical Center. Prior to Verigene, peptide nucleic acid fluorescent *in situ* hybridization was used for preliminary identification of gram-positive cocci from positive blood cultures. Patient demographics, time to organism identification, time to effective antimicrobial therapy, and other key clinical parameters were compared.

Results: For gram-positive bacteraemia cases, microarray-based identifications were completed a mean of 3.6 hr after positive cultures. Adjustments to antimicrobial therapy were made sooner in the postimplementation group (p=0.026). For gram-negative bacteraemia cases, organism identifications were achieved more quickly post-microarray implementation (p<0.001). The two groups did not differ statistically in regards to source of bacteraemia, length of hospital/ICU stay, or proportions requiring ICU admission, on immunosuppressive therapy, or with absolute neutrophil count <500/ μ L (p>0.15 for all). **Conclusions:** The Verigene system provides rapid and accurate identification of organisms causing bloodstream infections and allowed more rapid initiation of effective antimicrobial therapy, particularly for multi-drug resistant organisms.

Modeling Vascular Inflammation and Atherogenicity after Inhalation of Ambient Levels of Ozone: Exploratory Lessons from Transcriptomics

Andrea Tham Medical Student, Mehrdad Arjomandi Advisor, San Francisco VA Medical Center

Background: Epidemiologic studies have linked inhalation of air pollutant such as ozone to cardiovascular mortality. Controlled human ozone exposure studies have shown that short-term inhalation of ambient levels of ozone causes acute airway inflammation, imbalance in sympathetic/parasympathetic tone, and systemic inflammation. The mechanisms that link ozone inhalation to atherosclerosis are not understood.

Methods: To explore how ozone exposure may contribute to atherosclerotic plaque development and progression, we compared gene transcriptomics data from BAL cell mRNA expression, obtained from healthy subjects after controlled exposure to ozone (200ppb) for 4h that from various cell sample gene expression data from 11 previously published atherosclerosis studies using Nextbio genomic data platform to obtain overlapping genes and relevant ontologies that may be involved in the transition from pulmonary to systemic to vascular inflammation after ozone inhalation. Active protein enzyme

levels of one of the overlapping genes, MMP-9, was analyzed in BAL fluid and serum from subjects with ozone exposure.

Results: Nextbio meta-analysis revealed a set of 24 genes that were differentially up-regulated in both the ozone study and ≥5 of the 11 atherosclerosis studies, many of which are known to contribute to atherosclerotic processes, such as cholesterol metabolism dysfunction, increased monocyte adherence, endothelial cell lesions, and matrix remodeling. These genes were also noted by Nextbio to be involved with heart failure, ischemia, and atherosclerotic occlusive disease. One gene, MMP-9, was up-regulated in the active protein form in BAL fluid of subjects after ozone exposure. Gene ontology analysis of these genes showed overlapping GO processes pertaining to response to stimulus, stress, and wounding. **Conclusions:** Comparison of mRNA expression profiling between BAL cells after ozone exposure and various cell types from atherosclerotic patients reveals a subset of commonly up-regulated genes and processes and potential mechanisms by which ozone exposure may contribute to atherosclerotic disease and its progression.

Over-expression of Periostin Is Associated with Clinical Outcomes and Poor Prognosis in Cutaneous Squamous Cell Carcinoma

<u>Vadim Gor</u>, Lyu Chao, Dedee Murrell, Minhee Kim, Edel O'Toole, David T. Woodley, Alexandre Ly, Ashley Wysong, Mei Chen. Department of Dermatology, University of Southern California, Los Angeles, CA; University of New South Wales, Sydney, Australia; Barts and the London School of Medicine and Dentistry, London, UK

Background: Cutaneous squamous cell carcinoma (cSCC), the second most common cancer in the US, is increasing in incidence globally. No specific molecular markers exist to evaluate the risk of cSCC progression and metastasis. Periostin (PN), an extracellular matrix macromolecule, is implicated in tumorigenesis and serves as a prognosis marker for many cancer types. However, there are no data on PN expression in cSCC. This study examined PN expression in patients with cSCC and explored its relationship with clinicopathologic factors and prognosis.

Methods: Using immunohistochemistry and ImageJ analysis, we compared PN expression in 103 cSCCs representing a spectrum of cSCC aggressiveness: cSCC *in situ* (SCCIS) (n=20), low-risk cSCC (LR-cSCC) (n=46), high-risk cSCC (HR-cSCC) (n=16), high-risk in immunocompromised hosts (HRIM-cSCC) (n=13) and cSCC in RDEB patients (RDEB-SCC) (n=8).

Using Transwell assays and an *in vivo* xenograft tumor model, we analyzed the effects of addition of RDEB fibroblast-derived PN or recombinant PN on SCC behavior.

Results: Immunohistochemistry demonstrated PN expression within intra-tumoral stroma but not within tumor cells. PN levels significantly (p<0.001) increased from SCCIS, LR-cSCC, HR-cSCC, HRIM-cSCC to RDEB SCC. RDEB SCCs represented the most aggressive SCC type. The high level of PN staining in RDEB cSCC was tumor specific with levels notably higher than the non-cancerous skin of the RDEB patients. In addition, the stroma of most SCCs contained cancer-associated myofibroblasts (□-SMA-positive). Transwell assays and the xenograft tumor model revealed that addition of RDEB fibroblast-derived PN or recombinant PN significantly promoted *in vitro* RDEB cSCC invasion and *in vivo* tumor formation, suggesting that the over-expression of PN in RDEB fibroblasts may play a critical permissive role for SCC development.

Conclusion: Our data show that PN expression is highly correlated with the aggressiveness of cSCC, thereby providing a molecular basis for development of novel diagnostic and therapeutic strategies targeting PN for high-risk cSCC.

BEHAVIORAL

Copy Number Variation in Autism Spectrum Disorders Christina DyBuncio, Virpi Leppa, Jennifer K. Lowe

Background: Autism Spectrum Disorder (ASD) is a heterogeneous neurodevelopmental disease in which children display restricted or repetitive behaviors and deficits in social communication. Twin and familial studies indicate a strong genetic component underlying the disorder.

It is widely recognized that specific deletions or duplications in the genome (copy number variants; CNVs) are causal for ASD. Known, syndromic forms of autism account for 10-20% of cases and allow investigators to group patients by molecular diagnoses. Genetic screening and CNV analysis is an important step towards distinguishing known syndromic forms of ASD from idiopathic autism. This study examines the genomes of all of the known cases and controls that have been collected through the Center for Autism Research and Treatment (CART) at UCLA over the past 8 years. The goal is to identify and validate CNVs that contribute to syndromic forms of ASD and to identify large novel CNVs that may contribute to syndromic forms of ASD.

Methods: Greater than 750 individuals (~300 autistic probands) from the CART cohort have been genotyped on the Illumina SNP microarray platform. These subjects will be analyzed for copy number variants using CNVision, which produces high-confidence CNV calls by integrating results from three different calling algorithms. In silico findings will be validated using both visually by plotting allele frequencies and using quantitative PCR if necessary.

Results: Final collection, genotyping and quality control on the data has just been completed. The analysis will consist of comparing affected versus non-affected individuals for differences in total CNV burden, CNVs in genic and exonic regions, CNVs by size, and CNVs with known syndromic associations. The analysis will also examine CNV events larger than 500 megabases, which is considered the threshold for clinical significance.

Conclusion: Molecular cytogenetic screening of the CART patient cohort may provide some families with a genetic diagnosis for disease. These findings also allow us to stratify the cohort based on molecular diagnosis, thereby reducing genetic heterogeneity and enhancing our ability to detect novel variants contributing to idiopathic autism.

Child Interventional Services Before Autism Diagnosis and Parenting Stress at Time of Autism Spectrum Diagnosis

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Background: Many children who are being evaluated for an autism spectrum diagnosis (ASD) have previously received early intervention services. Positive impacts on a child's language, adaptive, and social functioning have been observed, but the impact on parents' stress at the time of their child's ASD diagnosis has remained unexamined. This study investigates whether services prior to an ASD diagnosis are associated with parenting stress levels at the time of their child's ASD diagnosis. **Methods:** 98 patients, ages 3-8, assessed by a multidisciplinary team at a tertiary children's hospital clinic and meeting DSM-IV-TR and DSM-V diagnostic criteria for ASD between 2012-2015, were identified. Standardized measures of parenting stress, the Parenting Stress Index 3-Short Form, collected at the time of the team diagnostic evaluation, will be analyzed. Previous intervention services were obtained from the Medical History Intake Form and in Assessment reports.

Results: We are in the process of beginning data analysis. We expect child intervention services prior to an ASD diagnosis to reduce parenting stress levels at time of evaluation.

Conclusion: The results of this study will have important implications on recent support of early intervention services in children at high risk for ASD.

CARDIOLOGY/ CARDIOVASCULAR

Objective quantification of aortic valve leaflet and annular calcification: A predictor of outcome <u>Serena Ghanshani¹</u>, Leah Lin, MD¹, Leonardo Clavijo, MD², Mark Cunningham, MD³, Tracy Lawrence, MD², Ray Matthews, MD², Passant Mohamed, MD¹, Vaughn Starnes, MD³, Steven Cen, PhD¹, Darryl Hwang, PhD¹, Alison Wilcox, MD¹

Keck School of Medicine of USC, ¹Department of Radiology, ²Department of Cardiovascular Medicine, ³Department of Cardiothoracic Surgery

Background/Goal: The aim of this study is to determine if there is a specific location and amount of calcium that can be used to predict valvular regurgitation following Transcatheter Aortic Valve Repair. The goal is to create an objective calcium quantification scheme in order to assist pre-operative planning and improve patient outcomes.

Methods: 60 patients receiving a Medtronic Corevalve and 55 patients receiving an Edwards Sapien valve were identified. Pre-procedural contrast-enhanced, gated cardiac CT scans were reviewed. Calcium was quantified based on location, area, and percentage involvement of each leaflet. Total calcium volume of all leaflets and annulus was quantified using 3D software. These values were analyzed with echocardiograms performed immediately after the procedure, 1-2 days later, and 4-8 weeks later. **Results:** Results were demonstrated with a Spearman correlation. Statistically significant results ($p \le .03$) for the Medtronic Corevalve displayed inverse relationships between the surface area of calcium within the right coronary sinus vs. perivalvular regurgitation day 1-2 (p=0.02), 3D calcium volume vs. intravalvular regurgitation day 1-2 (p<.01), and right coronary sinus calcium vs. intravalvular regurgitation weeks 4-8 (p<.01). The Sapien valve revealed positive correlations between 3D calcium volume vs. perivalvular regurgitation day 1-2 (p=0.02) and perivalvular regurgitation weeks 4-8 (p=0.01), and an inverse relationship between volume vs. intravalvular regurgitation day 1-2 (p=0.03). **Conclusions:** These results suggest that calcium locations and amounts influence regurgitation and may affect patient outcomes. For the Medtronic Corevalve, a larger area and amount of calcium in the right coronary sinus may reduce perivalvular regurgitation, while increased calcium volume may decrease intravalvular regurgitation. For the Sapien valve, increased calcium volume may decrease intravalvular regurgitation, but may concomitantly increase perivalvular regurgitation. These results may reflect differences in valve design.

Reduced Contrast CTA for Transcatheter Aortic Valve Replacement Planning: Use of Reduced Contrast Protocol for Patients at Increased Risk of Contrast-Induced Nephropathy (CIN)

<u>Tom Liang</u>, Ashley Prosper MD, Muntasir Hoque MD, Christopher Lee MD, Cameron Hassani MD, Alison Wilcox MD

Goal: The use of IV contrast, required for the acquisition of CTAs, poses a potential risk of CIN, particularly in patients with pre-existing renal impairment and the elderly. With the aid of wide volume detector CT, contrast doses can be significantly reduced. In this study, we retrospectively reviewed reduced IV contrast TAVR CTAs and compared them to studies performed with standard IV contrast for assessment of diagnostic quality.

Methods: We examined 46 patients who underwent IV contrast ECG-gated CTAs performed for TAVR planning. All studies were acquired on a 320-row detector CT scanner with tube potential of 100 kV.

Patients were divided into reduced IV contrast (n=23) and standard IV contrast groups (n=23) for comparison. Contrast attenuation in Hounsfield units (HU) was measured in the ascending aorta, the descending aorta at the level of the aortic hiatus, the abdominal aorta above the iliac bifurcation, and both femoral arteries at the level of the mid-femoral heads. Standard deviation was included as a measurement of image noise, and Pearson Correlation Coefficients were calculated for image noise. **Results:** There were no significant differences in radiation (DLP), image noise, or image quality. Mean contrast attenuation was lower at the measured sites in the lower contrast group. Pearson correlation coefficients showed no correlation between image noise and any variable in both patient groups. **Conclusion:** Our retrospective study showed that a low-dose contrast protocol acquired with 100-kVp on 320-row CT scanners is effective in obtaining diagnostic images prior to TAVR, compared to our normal-dose contrast protocol. Image noise was not directly associated with any patient variable, suggesting that the low-contrast protocol is effective in patients with renal impairment and potentially all patients. The use of a low-dose protocol may potentially reduce the risk of CIN while still obtaining satisfactory imaging prior to TAVR.

Summary of Keck hospital patients receiving a CardioMems implantation Daniel O'Brien BS, David M. Shavelle MD

Background: Congestive heart failure (CHF) is a highly prevalent and costly medical condition that is associated with high morbidity and mortality. Nearly half of patients treated for acute decompensated heart failure are readmitted within six months. Currently, indicators for readmission are clinical symptoms such as dyspnea, orthopnea, and leg edema. However, studies have shown that pulmonary artery pressure is a much earlier indicator of worsening CHF. The CardioMems device is a pressure sensor implanted in the pulmonary artery that allows patients to measure daily pressures while at home. Managing physicians can then access these readings to predict worsening CHF before clinical symptoms are present. Management of medications can then be done remotely to manage CHF and prevent hospital readmission. The goal of our study is to describe the patient population that has received the CardioMems implant at Keck Hospital.

Methods: Since June of 2015, 33 patients have received a CardioMems implant at Keck Hospital of USC for management of CHF. Retrospective chart review was done to summarize the patient population, including demographic factors, co-morbidities, medical management, and cardiovascular diagnostics at the time of implant. The results will then be compiled and summarized to give an overview of the patients receiving the implant.

Results: Results pending.

Conclusion: Summarizing the patient population with the CardioMems sensor will provide a framework for future research on patient outcomes after being implanted with the device. These outcomes may include factors such as number of hospital readmissions after device implant, average change in pulmonary artery pressure, average changes in medication dosages per month, and device related complications. The results of these future analyses will hopefully support previous published studies showing a reduction in future heart failure related hospitalizations and improved CHF management in patients receiving the device.

Predictors of perioperative cardiac outcomes in patients undergoing liver transplant evaluation <u>Thaer Othman</u>, David Shavelle M.D., Helge Van Herle M.D., Brian Kim M.D.

Background: Cardiac evaluation is an essential component of the pre-liver transplant (pre-LT) evaluation. Cardiac events are the third leading cause of mortality in LT patients accounting for over 20% of deaths. There is wide variation among LT centers regarding the type of cardiac tests used for evaluation of LT patients. USC has an established pre-LT algorithm to risk stratify patients prior to LT. The pre-LT evaluation at USC begins with an EKG and chest X-ray of all patients, followed by a transthoracic echocardiogram (TTE) to assess cardiac function and right heart pressure. A carotid duplex is obtained in all patients at risk of atherosclerotic disease: patients over the age of 60, history of smoking, HTN, DM, or any family history of cardiac disease. Patients with 2 or more risk factors for CAD also undergo a non-invasive cardiac stress test or Left Heart Catheterization (LHC). Patients found to have coronary artery disease are either declined for liver transplant or receive preoperative treatment (medical therapy or pre-LT revascularization).

Methods: In this study, we aim to determine the performance of our pre-LT evaluation in predicting perioperative cardiac outcomes. We are retrospectively studying all patients who received a LT (340) in the past five years. Additional pre-LT factors not currently used (etiology of liver, BMI, incidental findings of arterial calcification) are also assessed to help risk stratify our LT patients.

Results: Once the data collection has been completed, the results of patient pre-LT studies will be compared to perioperative cardiac outcomes: MI, CHF, stroke arrhythmias, and reversible cardiac ischemia.

Penetrating Injury to the Cardiac Box Cyrus Rais, Luis DeLeon, Kenji Inaba MD

Goal: The management of penetrating injuries to the thoracic cavity is time sensitive and poses problems. The aim of this study is to evaluate injuries to the thoracic cavity and see if there is a difference in outcomes between patients injured within the cardiac box and those that have experienced injuries to the thoracic cavity outside the box.

Methods: The registry of LAC was queried for all patients with penetrating injuries from 2009–2015. Patient demographics and injury variables were compared by a team of two analysts to determine whether the injury fell within the cardiac box. All patients with penetrating injuries to other areas were removed from the population.

Results: During the 6-year period, 988 patients were admitted for penetrating wounds. Of these, 406 (41.1%) had penetrating injuries limited to the thoracic cavity, with 129 (31.8%) having a single or multiple GSW/s and 277 (68.2%) having a SW/s. There were 138 patients with injuries within the box, 192 patients with injuries only outside the the box and 76 patients with wounds both inside and outside the box. Overall, the mean age was 28(20-39) years, 91.1% were male, with a mean ISS of 9 (5-13). When compared without regard for mechanism of injury, box and not box groups showed no significant difference in morality (6.5% vs. 3.1%, p= .144). For stab wounds, there was also no difference in morality between box and not box groups (1.9% vs. 1.6%, p=1.0) GSWs on the other hand, did show a significantly higher rate of morality when box wounds were compared to not box wounds (21.2% vs.

6.0%, p= .022).

Conclusions: There was not sufficient evidence to assume that there is a difference in mortality between thoracic stab patients who were injured within the margins of the cardiac box and stab patients who were injured outside of the box. There was, however, enough data to suggest that there is a difference in mortality among gunshot victims. Patients with gunshot wounds within the box were less likely to survive than those with presenting wounds outside the cardiac box.

Cardiac Conduction Abnormalities in Myotonic Dystrophy: A Prospective Pilot Study

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Goal: Myotonic dystrophy (DM) is the most common inherited muscular dystrophy disorder in adults. DM has multi-systemic implications; cardiac involvement is a common manifestation and patients are at a significant increased risk of sudden cardiac death. This study investigates the relationship between conduction abnormalities, DM disease severity, and CTG (DM1) and CCTG (DM2) repeat length. Due to the progressive nature of DM cardiac conduction abnormalities, pacemaker devices have been revealed to not prevent the risk of sudden cardiac death due to ventricular tachycardia. This study will monitor patients for progression of conduction defects and determine if patients are suitable for defibrillator implantation in order to prevent arrhythmic complications.

Methods: The inclusion criteria required diagnosis of DM which is defined by clinical manifestations of myotonia with a positive family history in addition to genetic testing of CTG and CCTG expansions associated with DM1 and DM2, respectively. 20 patients are enrolled and undergoing clinical neurological and cardiac evaluations. The patients will be followed for 24-36 months. Patients with a PR interval >200 ms or EF<35% meet implantation criteria for pacemaker or AICD and will undergo pre-implantation counseling. Every 6 months, routine device interrogation will be performed on patients with implanted devices. Progression of DM as seen upon neurological and cardiac evaluations in addition to arrhythmic events will be recorded.

Results: Initial chart review revealed that 13 patients met the criteria for implantation while 7 patients had results within the normal range but had no updated readings within the past year. It has been difficult recruiting and scheduling patients for this study.

Conclusion: We expect to find a reduction in cardiac events upon device implantation. Additionally, we expect to see a progression of disease, number of cardiac events and neurological findings, to be associated with the CTG or CCTG repeat length in patients with DM 1 and 2, respectively.

RNAseq analysis implicates myocardial Apelin in the development of ventricular dysfunction in Hypoplastic Left Heart Syndrome patients <u>Omar Toubat BA</u>, Richard W. Kim MD, FACS

Background: Hypoplastic left heart syndrome (HLHS) is a highly lethal form of congenital heart disease characterized by left heart hypoplasia. Survival in HLHS patients requires staged reconstruction that surgically reassigns the right ventricle (RV) to serve as the major systemic pump. RV failure is a major

cause of morbidity and death in HLHS patients. It is unknown why the RV in palliated HLHS patients is prone to heart failure.

Hypothesis: We hypothesize that this susceptibility to RV failure in HLHS reflects underlying differences in gene expression when compared to controls. Our goal is to identify genetic regulators of RV function in HLHS patients.

Methods: RV myocardial specimens were collected from anatomically matched HLHS patients (n=3) during Norwood palliation, patients undergoing complete repair of Tetralogy of Fallot (TOF) (n=4), and normal fetal controls (n=9). Specimens underwent RNA extraction and purification, HiSeq2500 paired-end sequencing, alignment using the Tuxedo suite package and DeSeq2 differential gene expression analysis (FDR adjusted p<0.05).

Results:

- (1) Unsupervised clustering of RV myocardium segregates patients by anatomic diagnosis.
- (2) Apelin (APLN) and the Apelin Receptor (APLN-R) are significantly downregulated in HLHS RV myocardium as compared to TOF and normal fetal controls.



Figure 1. HLHS RVs are transcriptionally distinct from other CHD (TOF) and normal fetal controls. **Table 1.** Differential gene expression in HLHS RV myocardium.

Gene	Description	Fold Change	
		HLHS vs Normal	HLHS vs TOF
APLN-R	apelin receptor	-2.58	-2.64
Sox4	SRY-box 4	-2.74	-2.23
OIT3	oncoprotein induced transcript 3	-7.24	-4.25
APLN	apelin	-7.75	-3.78

Conclusion: APLN, APLNR, Sox4, and OIT3 define a set of differentially expressed genes in HLHS RV myocardium. Given that both APLN and APLNR are downregulated supports the validity of this finding. The APLN-APLNR axis is a powerful inotropic pathway that is downregulated in structurally normal hearts in heart failure. This work implicates myocardial Apelin in the development of ventricular dysfunction in HLHS patients.

No Acute Cardiac Effects Observed with Concurrent Trastuzumab and Breast Radiation with Low Heart Doses

Shelly X. Bian, MD, Mariam P. Korah, MD, <u>Taylor R. Whitaker, BS</u>, Lingyun Ji, MS, Susan Groshen, PhD, Eugene Chung, MD, PhD, JD

Purpose: Standard treatment for HER2+ breast cancer often includes trastuzumab (TRA), breast/chest wall (CW) radiation (RT), and anthracyclines, which may contribute additively to cardiac toxicity. Early RT-induced heart toxicity can manifest as cardiac perfusion defects or a decrease in left ventricular ejection fraction (LVEF). We aim to evaluate the relationship between heart dose and LVEF changes or cardiac events in patients receiving concurrent trastuzumab and breast/CW RT.

Methods: We retrospectively reviewed all non-metastatic breast cancer patients from 2008-2014 who received concurrent TRA and breast/CW RT as well as LVEF measurements with multiple gated acquisition (MUGA) scans at baseline and after treatment. Changes in LVEF were then correlated with tumor laterality, dosimetric parameters of the heart, and doxorubicin use.

Results: Our analysis included 88 patients with median follow-up of 45 months. 41 patients had rightsided breast cancer and 47 left-sided. Median prescribed dose to the breast/CW was 50 Gy. 31 patients received doxorubicin, 16 right-sided and 12 left-sided. Mean heart dose was 1.10 Gy and 3.63 Gy for right and left-sided patients, respectively (p<0.001).

In the entire cohort, a significant LVEF drop of 3.9% was observed pre- and post-treatment. There was a significant doxorubicin effect (p=0.013) on LVEF change. The effect of RT laterality on LVEF was not significant (p=0.083). The test of interaction between doxorubicin and laterality was not significant (p=0.73). No significant association was found between LVEF change and dosimetric values of heart RT. No cardiac events were reported.

Conclusions: With heart sparing techniques that lower cardiac doses, no significant LVEF decline or cardiac events were noted among patients who received concurrent TRA and breast/CW radiation. Statistically significant LVEF decreases were mainly attributed to doxorubicin.

Birthweight Percentiles of Fetuses with Cardiac Anomalies

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Objective: Fetuses diagnosed with congenital cardiac defects are suspected to exhibit diminished intrauterine growth, which is associated with greater medical complications. We compared the birthweight percentiles of fetuses with congenital cardiac defects to those of a population of normal fetuses.

Methods: A retrospective chart review was conducted of all patients diagnosed with a congenital heart defect at LAC+USC from 2004-2012. All anomalies were diagnosed by antepartum ultrasound and echocardiogram and confirmed postnatally. Anomalies were classified as major versus minor according to the National Birth Defect Prevention Study. Fetuses were excluded if they had aneuploidy or were born earlier than 37 weeks or later than 42 weeks gestational age. Birthweight percentiles were calculated using gender-specific mean birthweights as published by Olsen et al¹. Average birthweight

percentiles were compared to published values and the proportion of fetuses below the 10th percentile were analyzed. A p-value less than 0.05 was considered statistically significant.

Results: We evaluated a total of 267 subjects of which 249 patients (93.3%) had major anomalies. Mean birthweight percentiles of fetuses with major congenital cardiac defects were lower than the reference population for both females (38.4%, p<0.001) and males (44.8%, p<0.05). An increased number of female patients were below the 10^{th} percentile compared to the norm (16.1%, p=0.02), while the increase in male patients below the 10^{th} percentile was not significant (12.8%, p=0.3).

Conclusion: Fetuses with major cardiac anomalies demonstrate diminished growth potential compared to population norms, leading to potential over-diagnosis of fetal growth restriction and risks of unnecessary interventions.

Olsen, I. E., Groveman, S. A., Lawson, M. L., Clark, R. H. & Zemel, B. S. New intrauterine growth curves based on United States data. *Pediatrics* **125**, e214-24 (2010).

CLINICAL

Effects of Body Armor on Core Body Temperature Brian J Gandara, Cynthia Bir, Emergency Department at KSOM

Background/ Goal: Of approximately 1,200 officers killed in the line of duty since 1980, it is estimated that more than 30% could have been saved by body armor. According to the James Guelff Body Armor Act, the risk of dying from gunfire is fourteen times higher for an officer not wearing a ballistic vest. However, there is still hesitation of some Law Enforcement and Corrections Officers to routinely wearing soft body armor.

The purpose of this study is to conduct definitive research illustrating the effects of Agencyissued soft body armor (both ballistic- and stab-resistant) on core temperature during real-world operations.

Methods: Twenty law enforcement agencies were recruited to participate in the study. Each unique in size, and their capabilities. All job descriptions, and job related tasks were recorded during the data collection with exception are those positions and teams which do not wear soft body armor (tactical teams such as SWAT, bomb squad, undercover agents, air unit, etc.). Positions that have been specifically targeted include; patrol, administration, motor unit, bike unit, Marine unit, K-9 handler, Detective, mobile field force, narcotics interdiction, gang unit, etc. Using CorTemp Data Recorder to record the signal from the CorTemp sensor, a pill size device swallowed by the law enforcement officer which transmits core body temperature recordings as it travels though the digestive tract, and converts the signal into digital format.

Results: The practical implication of this project is to deliver valid data that describes the degree of heat stress as a result of wearing soft body armor. While just the first step in a series of steps that need to be taken, this initial project could have a significant impact on Agency policy, and law enforcement practices.

Summary: The data is expected to show some changes in body temperature If there is a problem identified with an increase in core body temperature while wearing body armor, various mitigating devices can be evaluated such as under armor cooling vests.

Surgical Excision and Post-operative External Beam Radiotherapy Versus HDR Interstitial Brachytherapy in the Treatment of Keloids - 10-year Single Institutional Retrospective Analysis Robert Reznik, MD, Don Hoang, MD, <u>Matthew Orgel, BA</u>, Quanlin Li, PhD, David A. Kulber, MD, Amin Mirhadi, MD

Purpose/Objectives: Excised keloids recur at reported rates of >45%. Radiotherapy (RT) has only been reserved for recalcitrant keloids due to concerns over RT-related sequelae. Post-op RT is commonly delivered via external beam RT (EBRT) and increasingly via interstitial brachytherapy techniques (high-dose rate (HDR) or low-dose rate (LDR)). Historical data has shown that post-op RT decreases keloid recurrence to 10-20%. We performed a single institution retrospective analysis to evaluate whether post-op RT reduced recurrence over excision alone, as well as to evaluate keloid recurrence rates between adjuvant EBRT and HDR brachytherapy.

Materials/Methods: 128 patients with a total of 264 keloid lesions were treated by excision alone (n = 28), excision followed by EBRT (n = 197), or excision followed by HDR (Ir-192) single-lumen interstitial

catheter brachytherapy (n = 39). Recurrence data was analyzed using mixed effect Cox regression modeling; p<0.05 was determined to be statistically significant.

Results: 54% (15/28) of keloids treated with surgery alone recurred at 9 month median follow-up; 19% (37/197) of keloids treated with adjuvant EBRT recurred at 42 month median follow-up; 23% (9/39) of keloids treated with adjuvant brachytherapy recurred at 12 month median follow-up. On multivariate analysis, adjuvant EBRT and brachytherapy each showed significant reductions in keloid recurrence compared to excision alone (HR: 0.001, p= 1.1×10^{-6} and HR: 0.08, p=0.04, respectively); adjuvant brachytherapy showed a significant increase in recurrence compared to adjuvant EBRT (HR: 54.2; p=0.0004). There were no CTCAE v4.0 grade 2+ adverse events.

Conclusions: Post-op RT continued to show significant reduction in keloid recurrence compared to excision alone. Post-op EBRT showed significant improved keloid control over adjuvant HDR interstitial brachytherapy. Our findings warrant further workup with a well-designed prospective study to help determine the optimal adjuvant RT treatment strategy.

Effect of ACL Graft Type On Side-Step Cutting in Young Athletes

<u>Ricardo A. Padilla MS ATC</u>, Nicole M. Mueske MS, J. Lee Pace MD, Mia J. Katzel DPT, Bitte S. Healy MSPT, Tishya A. L. Wren PhD

Introduction: Two of the most common Anterior Cruciate Ligament (ACL) graft sites used for surgical reconstruction are the patellar tendon (PT) and hamstring tendon (HT). Due to the slightly higher re-tear rate for ACL reconstruction (ACLR) with hamstring (HT) versus patellar tendon (PT), differences in movement strategies were assessed during side-step cutting in young athletes with recent ACLR to determine if graft type affected post-operative motion.

Methods: Dominant limbs from 19 athletes without lower extremity injury or previous surgery (age 15.2 \pm 1.8 years) and 27 limbs with recent (5.1–8.0 months post-op) unilateral ACLR were included, 17 with HT grafts (age 15.8 \pm 1.5 years) and 10 with PT (age 16.3 \pm 1.5 years). Lower extremity 3-dimensional data was recorded during the deceleration phase of a 45° cut.

Results: Both HT and PT limbs exhibited significantly lower peak ground reaction forces and significantly lower peak knee valgus moment than control limbs. HT limbs exhibited lower approach velocity than control limbs, significantly less pelvic obliquity compared to both PT and control limbs at initial contact, significantly lower pelvic obliquity excursion and significantly greater peak hip flexion, peak hip extension and power absorption at the hip than both PT and control limbs, significantly lower hip add/abduction at initial contact than PT limbs, and significantly lower average ankle dorsi/plantarflexion moment and power absorption at the ankle than control limbs. PT limbs showed significantly lower power absorption at the knee than control limbs.

Discussion: While both ACLR groups showed reduced GRFs compared with controls, the HT group demonstrated greater adaptations proximally with increased hip flexion and frontal plane pelvic and hip excursion. The lower frontal and sagittal plane hip motion in the PT group may be due to anterior knee pain associated with PT grafts. Since the HT group exhibited movement adaptations, but no observable pathologic movement patterns, factors likely account for the observed higher re-tear rate in HT vs. PT ACLR.

Systemic and Local Variations of CTSS activity in SS Patients

<u>Neha Teekappanavar</u>, Maria Edman PhD, Srikanth Janga PhD, Daniel Arkfeld MD, Stratos Christianakis MD, Elizabeth Ortiz MD, William Stohl MD, Dawn Piarulli MD, Sara Madrigal, Arunava Sarma, Mercy Bechtold, Alexander Chen, Sarah Hamm-Alvarez PhD

Background: Sjogren's Syndrome (SS) is a chronic autoimmune disease characterized by destruction of lacrimal and salivary glands leading to keratoconjunctivitis sicca and xerostomia. Diagnosis of SS is often delayed due to clinical overlap with other autoimmune diseases. Our group recently discovered SS patients exhibit elevated activity of a protease called cathepsin S (CTSS) and decreased levels of its endogenous inhibitor Cystatin C (CysC) in tears. Increasing evidence indicates an imbalance of the two exists in inflamed tissues, tears, and serum of patients with autoimmune diseases. This study explores the relationships between serum and tear levels and activity, which may indicate inflammation on both systemic and local levels in SS.

Methods: Tear samples were collected from a cohort of n=133 patients with various autoimmune conditions (SS, Rheumatoid Arthritis, and Systemic Lupus) as well as healthy controls to validate tear CTSS activity and CysC levels as potential biomarkers for SS, and parallel tear and serum samples from an additional n = 18 patients to analyze systemic and local factors. Samples were analyzed for concentration and activity of CTSS and CysC via ELISA.

Results: Median CTSS activity was confirmed to be significantly higher in patients with SS than in patients with RA (6.8-fold), other autoimmune diseases (7.8-fold), and healthy controls (21-fold) while CysC was 3.7-fold lower in SS than in RA, 5.3-fold lower than in those with other autoimmune diseases and 6.2-fold lower than in healthy controls. We also observed a shift in the ratio between CTSS and CysC in SS patients in serum, to be confirmed with a larger patient cohort.

Conclusion: Validating CTSS activity and CysC levels as biomarkers and comparing serum and tear values across multiple autoimmune diseases can help determine if imbalances in protein activity in SS is isolated to lacrimal gland inflammation or indicative of systemic inflammation as well. Defining markers or etiology distinct from lacrimal gland inflammation could suggest alternative avenues for treatment of SS.

Efficacy of the LINX[®] reflux management system in patients with large hiatal hernias

Vong, D., Rona, K., Reynolds, J., Oh, P., Zehetner, J., Sandhu, K., Samakar, K., Katkhouda, N., Bildzukewicz, N., Lipham, JC.

Background: Magnetic sphincter augmentation (MSA) has demonstrated long-term safety and efficacy in patients with gastroesophageal reflux (GERD). The purpose of our study was to evaluate the safety and efficacy of the LINX[®] device in the presence of a large hiatal hernia.

Methods: A retrospective review of all patients who underwent MSA with LINX[®] at our institutions between 05/09 and 12/15 was performed. Information obtained included: demographics, individual GERD characteristics, preoperative GERD quality-of-life (HRQL) scores, presence of intraoperative anatomic abnormalities, and details regarding the surgical procedure and LINX[®] device features. Clinical outcomes were measured using postoperative HRQL scores, proton pump inhibitor (PPI) use, and complication rate. A large hiatal hernia was defined as measuring ≥3cm by intraoperative measurement. **Results:** 192 patients were included in the study. 52 patients (27.0%) had a large hiatal hernia. GERD HRQL score decreased in patients with large hiatal hernias following LINX[®] (20.5 vs. 4.4, p < .001). When comparing outcomes in patients with large hiatal hernias to those with smaller or no hiatal hernia, there was a significant decrease in postoperative PPI requirement (10.0% vs. 24.5%, p = .040) and a higher incidence of symptom improvement or resolution (98.1% vs. 87.7%, p = .028). There was no difference in dysphagia requiring intervention (9.6% vs. 15.7%, p = 0.354) or mean postoperative GERD HRQL (4.2 vs. 6.3, p = .059) between the two groups. There were no major intraoperative or postoperative complications in either group.

Conclusion: MSA is an effective option in patients with GERD and larger hiatal hernias. MSA in patients with large hiatal hernias demonstrates improved outcomes with respect to postoperative PPI requirement and symptom improvement when compared to patients with small or no hiatal hernia. Postoperative GERD HRQL scores and the incidence of dysphagia requiring intervention is similar to patients without hiatal hernias.

Community-Based

Effects of a Hands-On Nutrition Program at a Local Public Charter School <u>Ivanova, M¹</u>. Reilly, JM¹. ¹USC Keck School of Medicine

Background: Obesity rates in the US are indicative of the need to educate our young population about nutrition and health from an early age. On average, one in three children in the US is likely to be either overweight or obese.

Purpose: This study aims to assess the effectiveness of a hands-on nutrition education program at a local charter school on improving nutrition literacy and affecting healthier eating habits.

Methods: A nutrition education curriculum was implemented to incoming 3rd-8th graders during their 2015 summer program at Renaissance Arts Academy, a charter school in Eagle Rock. Pre- and post-program surveys were administered to assess knowledge before and after the program. In addition, behavioral data collection on school lunch consumption is being implemented throughout the school year. Data consists of a record of nutrition habits (via daily tracking of whether each student ate or did not eat the federally provided school lunch and also whether each student brought lunch from home) and of knowledge progression (via standardized assessments and surveys) of all incoming students: both those that participated in the summer program and those that did not (controls). Additional stratification includes age and grade strata.

Results/Conclusions: An improvement in nutrition literacy is anticipated between the group that participated in the summer nutrition program and the one that did not. Authors anticipate finding differences in the health attitudes of participants and differences in school lunch consumption.

Effectiveness of Los Angeles County Family PACT Clinics in Southern California in Providing Long-Acting Reversible Contraceptives

<u>Christine Van Horn, MS</u>; Melissa Natavio, MD MPH, Department of Obstetrics and Gynecology, Keck School of Medicine of USC (Advisor)

Purpose: The Family Planning, Access, Care, and Treatment (Family PACT) Program in California provides no-cost family planning and related reproductive health care services to uninsured men and women. One important aspect of Family PACT is access to Long-Acting Reversible Contraception (LARC) methods. This study is intended to assess the registered Family PACT clinics in Los Angeles County and their ability to provide accessible services.

Methods: A comprehensive list of all Los Angeles County Family PACT clinics was compiled of which a random sample of 400 was generated. Students posing as potential patients are calling each clinic conducting a secret shopper survey. A scripted series of questions are asked to each clinic including acceptance of Family PACT insurance, LARC methods offered, and availability of same day insertion. **Results:** To date, 78 clinics have been successfully contacted with 65 (83%) accepting Family PACT insurance. Less than one-third (20) of those clinics offer an intrauterine device (IUD) and/or contraceptive implant. Three of those 20 clinics offer same day insertion while the other clinics required a consultation and/or physical exam prior to insertion. 16 of the 20 clinics knew that the desired method (IUD or implant) would be available at no cost. **Conclusion:** Preliminary results indicate that many of the registered Family PACT clinics may not be current providers of Family PACT services. LARC methods were only offered by 25% of all clinics surveyed. After the remaining clinics are contacted, we hope to have a better understanding of the services offered by Los Angeles County Family PACT clinics.

HHAB Tijuana Community Clinic Needs Assessment

Jeremiah Wang, MSII, KSOM; Alan Okada, MSII/PHD, KSOM; Mary Cheffers, EM RII, LAC+USC; Todd Schneberk, EM RIV, LAC+USC; John Rodarte, MD, KSOM

Goal: By collecting questionnaire data from two Healing Hearts Across Borders clinical sites in Tijuana, we hope to better understand our patients' needs so we may improve our clinics' offerings, improve clinic turnout, and ultimately better address the community's healthcare.

Methods: Needs assessment questionnaires were administered at both clinical sites in August and November 2015 by trained native Spanish-speakers. One questionnaire was done per household and asked both open-ended and quantifiable questions regarding demographics, health status, healthcare access, and HHAB accessibility. Participation was anonymous and voluntary. Data was consolidated and analyzed using Excel and Google Forms. August results helped shape edited questionnaire for November.

Results: 51 site "A" and 50 site "B" responses in August revealed both sites had poorly educated (62+% only finished primary school) and highly unemployed (78% A, 66% B) populations. Site B complained of more health issues (64% vs. 40%). 39 site A and 49 site B responses in November revealed a more specific list of suffered chronic medical issues (72% A, 78% B) with site B reporting more financial and transportation limitations to seeking clinical help outside HHAB. Site B also qualitatively reported more healthcare concerns.

Conclusions: Both clinical sites have significant healthcare needs, especially in regards to certain chronic diseases and care access. Site B, with a larger clinic turnout, exhibited a greater number of healthcare needs and perceived concerns. The data collected allows us a greater understanding of specific medical issues and needs in the community as well as support our hypothesis that a larger turnout correlates with a larger need for healthcare.

Understanding Access to Mobile Technology Among Patients and Providers in Haiti Barbara Lam, Juan Espinoza

Background: While surgical care in Haiti continues to improve, patients still face limited options for postoperative care. Telecommunication-based surveillance and health interventions have proven effective in other developing countries, but there is limited feasibility data in Haiti. A better understanding of communication paradigms can help improve patient outcomes and strengthen mentorship of local providers.

Methods: During a surgical mission trip to Haiti in 2015, a team from Hernia Repair for the Underserved worked with local surgeons to complete 56 surgeries (26 pediatric cases) at Hopital de Fort-Liberté and Hopital Universitaire de Mirebalais. All patients were approached to complete an anonymous 19-item

paper survey. Surgeons and surgical residents in the training program completed a modified 20-item survey.

Findings: 31 patients and 12 physicians completed the survey. 84% of patients did not have a regular doctor and 66% traveled more than 30 km or 30 minutes to reach their surgery. 100% of patients had access to a cell phone and 94% of patients wanted to be contacted about their health. Only 3% had regular access to a computer. Among surveyed physicians, 100% had a cell phone and used it daily for texting, social media, and the internet. Physicians accessed online medical resources regularly, and identified web resources, lectures, and group sessions as preferred methods of ongoing distance learning.

Conclusions: The overwhelming majority of patients have consistent access to mobile devices, and are receptive to using them for health-related purposes. This suggests that telecommunication-based surveillance and interventions for post-operative patients are feasible in Haiti, warranting larger studies of local telecom networks. Surveyed physicians demonstrated technological fluency across multiple devices, showing that digital platforms are primed for continued international collaboration and mentorship.

DERMATOLOGY

Ultrasound characteristics of bruises and their correlation to cutaneous appearance <u>Travis Helm</u>, Cynthia Bir, Ilene Claudius

Objective: The primary objective of this study was the comparison of size of a bruise on gross exam to the depth and height of the bruise when the subcutaneous size was ascertained by ultrasound. The hypothesis was that there will be little correlation between the apparent size of the bruise of gross exam and the actual depth when measured by ultrasound.

Methods: Adult and pediatric patients with bruising were prospectively identified in the emergency department. Photographs and ultrasound images were collected of the bruises and epidemiologic information collected from the patients. The area of the bruise cutaneously was compared with the subcutaneous characteristics.

Results: The depth and diameter of the bruises subcutaneously by ultrasound did not match with the cutaneous area. Bruises older than 48 hours were not visualized by ultrasound.

Conclusions: Cutaneous appearance of a bruise gives little indication of the depth and size of the subcutaneous fluid collection. Ultrasound can add information regarding these parameters. Capturing images early after the bruise occurs may add to the documentation of skin manifestations of abuse.

Complications of continent cutaneous diversions

<u>Eric S. Hwang</u>*, Soroush T. Bazargani M.D.*, Gus Miranda M.S.*, Jie Cai M.S.*, Siamak Daneshmand M.D.; Los Angeles, California

Purpose: To evaluate short and long term complications of continent cutaneous diversions in patients undergoing radical cystectomy for bladder cancer.

Material and Methods: Using our IRB approved institutional bladder cancer database, we reviewed the medical records of 508 patients who underwent continent cutaneous urinary diversion (CCUD) between 1972 and 2014. Patients with inadequate follow-up or incomplete medical records were excluded from this study. In order to ensure capturing all relevant data, only patients who underwent surgery after 1989 were included in the cohort.

Results: Of the 508 patients, we identified 178 of whom 62 (35%) underwent a Kock pouch, 107 (60%) a Right Colon (RC) pouch (102 with appendicoumbilicostomy, 5 Monti neoappendicoumbilicostomy) and 9 (5%) an Indiana pouch. 49 patients with Kock pouches had at least 1 complication after 90 days (79%), 69 in RC pouch (64%), and 4 in Indiana pouch (44%). Table 1 shows the breakdown of most frequent pouch-related complications in each diversion type. With Kock pouches, revision or complete conversion was required in 17 (27%), while this rate was 15 (14%) in RC and 2 (22%) in Indiana. In Kock and RC pouches, continence rate was excellent at 98.3% and 92.5% respectively, and Indiana at 77.8%. Comparison of 90-days postoperative complications between Kock and RC pouches showed that there was no significant difference in complication rate (p=0.42) or grade of complications (Clavien-Dindo) (p=0.24).

Conclusion: Results of this study suggest higher complication rates in Kock compared to RC pouch. Possible limitations of this study with very long term follow up are the follow-up and lead-time bias.

Larger comparative studies may elucidate the differences in complication rates among the various continent cutaneous diversions.

Effects of Laser Plume Evacuator on Laser in situ Keratomileusis Outcomes <u>Fiona Hoo Yeun Kim – Medical Student</u>; Gregg Feinerman M.D. – Advisor

Purpose: To evaluate the effects of laser plume evacuator on LASIK outcomes using a surgical vacuum and Nidek EC5000 Quest laser

Background/hypothesis: During excimer laser procedures, the removal of tissue creates a laser plume. In LASIK, the surgery involves ablation of the corneal stroma, producing a laser plume that contains water particles which block the ablative effects of the excimer laser. Using a plume evacuator should maintain a consistent level of surface hydration and reduce other particles that obstruct the ablation and may negatively affect outcomes. The plume evacuator will improve clinical outcomes including more accurate predicted treatment outcome and decreased complications.

Methods: Retrospective study on 3 month post-operative data for 73 eyes treated without a plume evacuator and 120 eyes with plume evacuator. All eyes were treated with the same Ziemer femtosecond laser and Nidek EC 5000 Quest excimer laser using the same nomogram. The same surgeon at a single facility performed all surgeries.

Results: Results and statistical analyses still pending. Expected results: A plume evacuator should improve clinical outcomes. Measured postoperative uncorrected visual acuity and refraction will have less deviation from predicted preoperative values with the plume evacuator. This should lead to decreased complications, including the need for Lasik enhancements.

Summary: This study should prove the efficacy of an excimer laser with functioning plume evacuator. Postoperative refractive error will be decreased leading to reduced enhancement rates, increased patient satisfaction and decreased risks.

Skeletal Muscle Tissue Microengineering on Gelatin Hydrogels

Evelyn Wang, Archana Bettadapur, Gio Suh, Clara Hua, Holly Huber, Alyssa Viscio, Kevin Kim, Julie Strickland, Megan L. McCain, Laboratory for Living Systems Engineering, Viterbi School of Engineering

Goal: *In vitro* models of skeletal muscle (SkM) are critically needed to understand mechanisms of muscle disease and to identify and test therapeutic targets. Generating SkM tissue in the lab that mimics *in vivo* muscle remains difficult, since myotubes delaminate from traditional synthetic culture substrates after 1 week. Here, we describe a new method of fabricating micromolded (µmolded) gelatin hydrogels and demonstrate improvements in SkM growth, differentiation, and long-term culture on these hydrogels vs. synthetic substrates. We determined features of hydrogels (alignment, elasticity, or composition) that improved adhesion for long-term culture.

Methods: Myotubes differentiated from C2C12 murine myoblasts were cultured on 6 substrates for 3 weeks: polydimethylsiloxane (PDMS) and soft PDMS coated isotropically or microprinted (µprinted) with lines of fibronectin (FN), and isotropic or µmolded 10% gelatin hydrogels. The elastic modulus was measured for each substrate. At weekly timepoints, cells cultured on the different substrates were fixed

and stained for sarcomeric α -actinin, a mature SkM marker, then imaged and analyzed for nuclei count, myotube thickness, and myotube alignment.

Results: µmolded gelatin hydrogels with elastic moduli similar to native tissue were engineered using a novel protocol and compared to synthetic substrates. Qualitatively, SkM tissue cultured on hydrogels was more mature with striated sarcomeres. Cell density and myotube thickness were significantly greater on hydrogels compared to PDMS and soft PDMS substrates (p<0.05). For each substrate, patterning increased myotube alignment (p<0.05).

Conclusions: We established µmolded gelatin hydrogels as substrates that sustain tissue-like, aligned myotubes in culture for 3 weeks. The elasticity and composition of hydrogels underlie improvements in myotube adhesion and differentiation. This platform enables long-term studies of SkM development and disease that were previously limited due to delamination.

Pirfenidone Inhibits RDEB Fibrosis and Scarring.

Kaitlyn Yim, Jon Cogan, Yingping Hou, Lyu Chao, David T. Woodley, Mei Chen. Dept. of Dermatology, USC.

Goal: Patients with recessive dystrophic epidermolysis bullosa (RDEB) develop skin wounds that heal with scarring, contractures, and mitten deformities. RDEB patients display increased pro-fibrotic TGF- β signaling, a distinct pro-fibrotic gene expression profile, and elevated inflammation genes. No pharmacological treatment is available for RDEB fibrosis. Pirfenidone (PFD) is an anti-fibrotic and anti-inflammatory molecule already used clinically for the treatment of idiopathic pulmonary fibrosis. In this study, we evaluated the feasibility of PFD for inhibiting RDEB fibrosis.

Methods: Fibroblasts from RDEB patients were treated with PFD, and expression of various fibrosis markers were analyzed by immunoblot analysis, RT-PCR, and ELISA. Attenuation of RDEB fibrosis phenotypes was evaluated using a RDEB mouse model.

Results: RDEB fibroblasts treated with PFD demonstrated reduced expression of fibrogenic TGF- β 2 and multiple fibrosis markers [collagen I, connective tissue growth factor, alpha smooth muscle actin (α -SMA), periostin, tenascin C] by immunolot analysis. By RT-PCR, PFD also reduced mRNA levels for fibrosis genes, as well as IL-6, an inflammation gene known to stimulate fibrosis. In addition, PFD treatment reduced the levels of pro-fibrogenic TGF- β 1 in the media of RDEB fibroblasts as assessed by ELISA. Furthermore, PFD also reversed the characteristic RDEB cellular phenotype of collagen lattice hypercontractability. Lastly, using a RDEB mouse model, PFD administered once daily subcutaneously for 4 weeks attenuated the onset of age-related fibrosis including mitten deformities and nail loss and reduced the elevated pro-fibrogenic TGF- β and its signaling [phospho-Smad2/3], as well as fibrosis markers [periostin, α -SMA, fibronectin, collagen 1, tenascin C], in RDEB mice. PFD also significantly reduced the number of cd11b-positive inflammatory cells in RDEB mice.

Conclusions: These data demonstrate that PFD may be a non-invasive, safe, and novel therapy for reducing RDEB fibrosis and scarring and improving the quality of life of RDEB patients.

Use of dermabond in pediatric patients with cerebral palsy who undergo hip surgery and its relationship to infection and antibiotic use

<u>Derek Antoku</u>¹, Nicole M. Mueske, M.S.², Deidre Ryan, M.D.^{1,2} ¹University of Southern California, Keck School of Medicine ²Children's Hospital Los Angeles

Introduction: Pediatric patients with CP often undergo surgery to correct lower extremity musculoskeletal deformities; this presents unique challenges regarding infection control in the post-op period. Many patients in this population wear diapers, and do not have full bowel and bladder control. Dermabond, which creates a waterproof seal, may be especially effective in reducing infection in these patients. While studies have analyzed the relationship between Dermabond use and infection rates in the general population, to our knowledge, no studies look specifically at the pediatric CP population. The purpose of this study was to determine if there was a relationship between the use of Dermabond and infection in the post-operative period. Infection was defined as use of antibiotics due to confirmed or suspected infection related to surgery of interest.

Methods: A retrospective review of medical records was conducted for 113 children with CP (mean ± standard deviation, 8.7 ± 4.4 years; 51% female), who underwent a total of 117 surgeries involving the thigh, hip, or inguinal region from one pediatric orthopaedic surgeon. The control (no Dermabond) group was a group of patients who underwent a surgery of interest between 2007 and 2010 while the intervention (Dermabond) group was between 2010 and 2015. Cases were followed for one year, unless they had another operation which they would have qualified for the study. In that case, they were followed for one year from the most recent surgery. Differences in infection rate between the control and intervention groups were examined using a Fisher's exact test. The patients who did have an infection in the perioperative period were also compared against those who did not for differences in gender, age, length of hospitalization, length of surgery, and estimated blood loss using the Student's t-test for continuous variables and Fisher's exact test for categorical variables.

Results: The infection rate in the control group was 18.18%, while the infection rate in the Dermabond group was 10.96% (p = 0.28). No significant differences between groups were observed for any demographic or clinical characteristic - gender (p=.79), age (p=0.46), length of hospitalization (p=0.79), length of surgery (p=0.70), and estimated blood loss (p=0.66).

Discussion: A 7.22% reduction in the use of antibiotics for actual or suspected infection in the intervention group suggests that Dermabond is indeed likely to be helpful in improving patient outcomes for children with CP undergoing surgery to correct musculoskeletal deformities of the lower extremities. However, we hypothesize that the use of prophylactic antibiotics in the perioperative period prevents many nascent infections from presenting clinically, which makes ascertaining how effective Dermabond is in reducing infection difficult to determine. A logical next step, based on the data collected here, would be a larger study which would be able to better characterize the relationship between Dermabond and patient outcomes in this population.

DIVERSITY HEALTH DISPARITIES

Justice in the U.S. Healthcare System

Dylan Atchley, Frances Pillsbury, Dr. Ankit Shah, Keck School of Medicine, Department of Medical Education, Department of Pediatrics

Background: The U.S. spends the most money per capita on healthcare in the world, but is lagging behind in many crucial health metrics. The goal of this paper is to explore the ethical roots of this incongruity. We hypothesize that a failure to address and incorporate the principle of justice into our healthcare decision-making underlies our system's many shortcomings. Furthermore, our aim is to identify policies that could create a more just system.

Methods: This paper is an ethics and policy analysis. As such, we relied on policy, ethics, and social science literature to either support or refute our hypothesis. We also utilized May's 7-step model for ethical decision-making to think through the question of how to make our healthcare system more just. **Results:** In this paper, justice is defined as an equally effective chance of receiving treatment of equal quality. Review of the literature found that our current system reflects decision-making guided primarily by non-maleficence, beneficence, and autonomy, but only limited consideration of justice. This has produced a system that excels at acute and end-of-life care for the insured. However, this comes at the expense of care for vulnerable, uninsured and underinsured populations, which are not age limited and traditionally suffer from chronic conditions. The poor return on investment we see in the healthcare system is predicated on our collective decision to only provide quality healthcare to those that can afford it.

Conclusion: Our failure to consider justice in the context of healthcare decision-making has created a system where health is closely linked to income. In order to achieve a more just system, we must begin to embrace policies that increase access to quality care for all individuals. For example, universal coverage is an obvious and important first step. However, recent analyses show that coverage alone does not ensure quality of care or improve outcomes. We discuss several additional policies that could augment the benefits of universal coverage to create a more fair and just system.

Active Surveillance: Are we failing multi-ethnic patients at safety-net hospitals?

L. K. Ballas, <u>**R. Kraus</u>**, L. Ji, R. Jennelle, and S. Groshen; *University of Southern California, Keck School of Medicine, Los Angeles, CA*</u>

Purpose/Objective(s): Active surveillance (AS) has increasingly been accepted as a safe approach for the management of favorable-risk prostate cancer (PCa) patients. AS, as opposed to observation, requires men to adhere to a defined follow-up protocol. Multiple large prospective studies have shown low rates of PCa progression, PCa mortality, and long periods without intervention 5-10 years after initiating AS. These large prospective studies evaluating safety and outcomes have, for the most part, neglected to include multi-ethnic populations. These studies have also been prospective in nature and thus have high compliance rates. Based on our experience at a large safety-net hospital with a multi-ethnic patient population, we hypothesize that many men do not comply with active surveillance and are lost to follow up.

Materials/Methods: We performed a retrospective chart review of patients with non-metastatic prostate cancer who initiated radiation therapy (RT), radical prostatectomy (RP), or active surveillance

(AS) at Los Angeles County Hospital (LAC) between 1/1/2008-1/1/2015. The AS cohort was categorized into four groups based on their AS status on 6/1/2015: 1) Still on AS, 2) Ended AS for PCa-related reasons, 3) Ended AS due to other reasons (comorbidities, moved, or transferred care), and 4) Lost to follow-up (missed two consecutive visits with no explanation).

Results: We found 116 patients who met the AS criteria of this study. The median age was 62 years (range: 47-79). The median Gleason score of men who opted for AS was 6 and their median PSA was 6.23 ng/mL. 66% of all patients seen during the study time period with Gleason 6 disease opted for AS. 59% of men who chose AS were Hispanic, and of the Latino population seen at LAC with PCa, 42% selected AS compared to 24% of non-Latinos (p < 0.001). At the time of data collection, 31/116 (27%) of men were still on AS. The majority of patients came off AS because they were lost to follow-up. 33% of patients on AS were lost to follow-up within the first year, with 50% lost to follow-up within 2 years. This pattern was seen across all ethnic groups. Interestingly, the further a patient lived from LAC, the more likely he was to continue follow-up on AS.

Conclusion: Active Surveillance is failing multi-ethnic patients in safety net hospitals. This patient population is lost to follow up at high rates within the first two years of active surveillance. More investigation is needed to evaluate the potential barriers to AS for patients in safety net hospitals.

Revisiting the Gender Gap in Orthopaedic Surgery: Can female faculty members play a role in producing more female applicants to orthopaedic surgery residencies?

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Background: Although women now account for almost half of medical students in the U.S., orthopaedic surgery continues to fall behind in its ability to recruit female applicants. Prior research has postulated that a lack of mentoring from female faculty may contribute to this trend. The objective of this study was to determine whether a higher percentage of female faculty members correlates with a higher percentage of female applicants.

Methods: Data for residents, residency applicants, medical school graduates, and full-time faculty in the U.S. from 2005-06 through 2013-14 was collected from the ACGME and AAMC. Linear regression analysis was used to compare trends between surgical specialties. Spearman rank correlation was used to assess for a correlation between female applicants and faculty members.

Results: For the 101 U.S. medical schools included in our final analysis, women accounted for 48.7% of medical school graduates but only 14.9% of orthopaedic surgery applicants. Women accounted for 13.2% of full-time faculty during this period. All surgical subspecialties had a significantly greater increase in female residents compared to orthopaedic surgery. (Figure 1) Medical schools with a higher percentage of female orthopaedic surgery faculty had a greater increase in the percentage of female applicants. (Table 1)

Conclusion: Orthopaedic surgery had the smallest increase in female residents over the nine-year period examined. U.S. medical schools with a greater percentage of female orthopaedic surgery faculty members correlated with a greater increase in the percentage of female orthopaedic surgery applicants.


Figure 1: Percentage of Female Residents in ACGME-accredited residency programs fro	m 2005-06
through 2013-14.	

Change in % of Female Applicants	Rho	P value
% of Female Instructors	0.1437	0.2510
% of Female Assistant Professors	0.1493	<0.0001
% of Female Associate Professors	0.2143	<0.0001
% of Female Professors	0.1816	<0.0001
% of Total Female Faculty	0.1457	<0.0001

Table I: Results of Spearman Rank Correlation.

Liver cancer incidence rates and disparities among diverse racial/ethnic populations in California, 1988-2012

Chris Pham, Tse-Ling Fong, M.D., and Lihua Liu, PhD.

Background: Cancer trends in Asian Americans have been studied using aggregate data but disaggregated research remains lacking, especially studies focused on hepatocellular carcinoma (HCC). Despite lower overall cancer incidence rates among Asians, incidence of HCC among Asians is significantly higher than any other race. Because of the uniquely high hepatitis B virus (HBV) prevalence

in the Asian American population, they face an increased, yet preventable risk of developing cirrhosis and, consequently, HCC, which yields a 5-year survival rate of less than 10%.

Methods: We used data from the population-based California Cancer Registry (CCR) to examine 41,177 cases of HCC cases diagnosed among California residents during 1988-2012. HCC was defined by the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), site code C220 and histology codes 8160, 8162, 8170-8172, 8174-8175, 8180, and 8190. Patient demographic and tumor information contained year of diagnosis, age at diagnosis, sex, race/ethnicity, place of birth, socioeconomic status (SES), and tumor stage at diagnosis.

We examined the trends of non-Hispanic white (NHW), black, Latino, Chinese, Filipino, Japanese, Korean, South Asian, Vietnamese, Cambodian, Laotian, Thai, and Hmong.

Results: HCC trends are heterogeneously distributed among different Asian groups with Southeast Asians having the highest risk, highest male-to-female ratios, highest cancer stage, and lowest SES when compared to any other group. While their risk remains the lowest in our study, we also saw a steady increase in HCC in NHWs, blacks, and Latinos.

Conclusion: To our knowledge, this is the largest and most diverse HCC study performed and illustrated a HCC burden that is dramatically heavier in Asians than any other race. Further efforts need to be aimed at secondary prevention in the Asian American community, with a particular emphasis on HBV screening and health literacy for Southeast Asian men and women.

Justice in the U.S. Health Care System Frances Pillsbury, Dylan Atchley, Dr. Ankit Shah

Background: The U.S. spends more money per capita on healthcare than any other nation, yet falls behind in key health metrics. We hypothesize that a failure to incorporate the principle of justice forms the bioethical root of this incongruity. Furthermore, we aim to identify policy measures that would make our system more just.

Methods: We conducted a literature review to explore how the focus of medical ethics has shifted throughout recent history and how this shift shaped current healthcare policy. Defining justice as an "equally effective chance of receiving appropriate treatment of equal quality", we then applied May's 7-step model for ethical decision-making to the question "How can we make the U.S. health care system more just?" Finally, we conducted an analysis of policies that could help achieve this goal.

Results: Review of the literature demonstrated that the bioethical principles of nonmaleficence, beneficence and patient autonomy have played a significant role in the development of our healthcare system, whereas justice has been largely overlooked. In response to the question of creating a more just system, the ethical model identified the primary stakeholders, their perspectives, and the values guiding their actions. We found that the government remains the only stakeholder bound by justice, and therefore, should play a central role in eradicating health inequities.

Conclusion: Justice is a fundamental bioethical principle, yet the U.S. healthcare system has been unsuccessful in safeguarding justice. This has created a system where health status correlates closely with income. Despite the passage of the Affordable Care Act, patients with private insurance and Medicare continue to receive better care than patients covered by Medicaid. Thus, creating a more fair

and just system requires we not only achieve universal coverage, but also take steps to eliminate disparities between insurance plans.

Gaining a better understanding of gender differences in the perceptions of ideal and less than ideal methods of communication and leadership training for trauma resuscitation.

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Background: Leadership during trauma resuscitation is critically important, as evidenced in its inclusion in Advanced Trauma Life Support. The best methods to teach leadership in a trauma setting, and the role of gender in such training is not well understood. In this study, we explore gender differences in perceptions of methods of leadership training in trauma resuscitation.

Methods: We conducted interviews with 25 attending physicians, residents, fellows, and nurses who provide care in a Level 1 trauma center. We created a coding framework using a modified grounded theory technique to identify perceptions of training methods and applied this framework to the transcripts. 8 training strategies emerged from the data: didactic, emulation of seniors and attendings, individual feedback, peer advice, formal group feedback, simulation, learning by doing, or self-reflection. The frequency that each method was coded was compared between genders.

Results: A higher proportion of codes for didactic training and emulation were from interviews with male providers (See Table 1).

"It's mostly really learning by doing, and you basically learn by watching good examples and watching bad examples, and then saying, you know, I want to be like this guy and not like that guy, and maybe have your own ideas." – Male Trauma Fellow

Perceptions of individual feedback, peer advice, formal group feedback and simulation were more often coded from interviews with female providers (See Table 1).

"We have a day where the previous class talks about assuming that role ... They'll tell you as a female that you need to be louder and more outspoken then you might normally be and to think about how you communicate things and how you might need to change your style so that you're well heard... I think, they should probably have a reflection for it after [becoming the leader in resuscitations] and ask people how do you think you're doing in that role, and have someone observe them doing it, and then give them feedback on it". – Female ED Resident

The proportion of excerpts coded as learning by doing and self-reflection were equally between interviews with male and female providers.

Conclusions: We found gender differences in provider opinions of optimal training strategies. This study highlights that the ideal methods of teaching leadership may differ between females and males, and demonstrates the value in utilizing multiple methods of training.

Training method	Total number of code applications	Code applications from interviews with female providers (%)	Codes applications from interviews with male providers (%)
Didactics	13	4 (31%)	9 (69%)
Emulation	33	12 (36%)	21 (64%)
Individual feedback	36	23 (64%)	13 (36%)
Peer advice	8	7 (88%)	1 (12%)
Formal group feedback	21	14 (67%)	7 (33%)
Simulation	33	24 (73%)	9 (27%)
Learning by doing	27	14 (48%)	13 (52%)
Self-reflection	4	2 (50%)	2 (50%)

Economics of Health

Outpatient Laparoscopic Appendectomy for Acute Appendicitis: A Feasibility Study and Cost Analysis <u>Paul Oh</u>, David Rosen MD

Background: In the United States, laparoscopic appendectomy (LA) is generally followed by 1 to 2 days of hospitalization that is believed to ensure patient safety and satisfaction. However, recent studies suggest that outpatient discharge after LAs for acute, uncomplicated appendicitis does not increase morbidity or mortality. Our study examined the safety and efficacy of discharging patients directly from the Post-Anesthesia Care Unit (PACU) at LAC+USC Medical Center following LA for uncomplicated appendicitis.

Methods: From August 2014 to June 2015, general protocol was hospitalization after LA for uncomplicated appendicitis. From June 2015 to January 2016, protocol was switched to outpatient LA unless hospitalization was deemed necessary by the surgical team. A retrospective study compared patient demographics, hospital course, and length of stay (LOS) between the two groups. **Results:** A total of 269 LA patients were included in this study with 166 control patients hospitalized

after LA and 103 protocol patients discharged from PACU after LA (unless hospitalization deemed necessary, at which point considered a failure (n = 34)). Average LOS between control patients (43.7 hr) and protocol patients excluding failures (22.5 hr) was statistically significant (P-value = 9.73×10^{-29}). Eight (5.8%) control patients (1 readmitted) and three (3.8%) of protocol patients excluding failures (none readmitted) experienced post-operative complications after being discharged. There were no mortalities in either group.

Conclusion: Outpatient LA is effective at reducing LOS at LAC+USC for acute uncomplicated appendicitis while maintaining low morbidity and readmission rates. Saving nearly one full hospital day after each LA could result in significant health care savings due to the high volume of appendectomies performed at LAC+USC. This specific financial impact of a switch to outpatient LA on LAC+USC will be analyzed as a part of this study.

EDUCATION

Student Confidence and LGBT Competence with Sexual History Taking After Peer Teaching Workshop Jennifer Franks, Justin Trop, Cha-chi Fung MD

Background: Competency in obtaining a sexual history is a requirement in medical schools, yet many students do not receive enough instruction and practice to feel confident. Evidence suggests peer practice can improve this. Given the large population that now identifies as LGBT and the special health risks members of this population face, we are in need of physicians who are clinically competent in LGBT care. This is a study of student confidence with sexual history taking and LGBT competence before and after a peer-led workshop.

Methods: The workshop involved an interactive lecture by the LGBT medical student interest group (MedGLO)'s co-presidents that emphasized points reference participants had stated were lacking in the curriculum. These were: reasons for taking a sexual history, LGBT competence, and sample cases with specific question phrasing. MS1s were paired with MS2s who pretended to be patients. The study utilized anonymous student feedback.

Results: Of the 20 students who completed the questionnaire, 19 agreed that the workshop was valuable to them. Students' confidence with taking a sexual history increased from 6 to 8/10 after the workshop. When asked what was the most useful part of the workshop, 4/19 comments related to learning LGBT terminology, 11/19 related to the benefits of peer practice, and 4/19 related to the benefit of the specific sample questions used in the presentation. When asked to name what they learned from the workshop that they did not know before, 7/17 comments were about LGBT terminology, 3/17 were about using terminology with which the patient is familiar and comfortable, and 2/17 were about good sample question phrasing from the lecture. 4/10 MS2s stated that they now asked their ICM patients about their sexual history more frequently than they did prior to the workshop. **Conclusions**: Student confidence with sexual history taking and LGBT competence can be improved by peer workshops that emphasize: reasons for taking a sexual history, LGBT competence, and sample cases with specific question phrasing.

Comparing MS4 Suturing Performance After Proficiency-based Training Using Simulated Operative vs Inanimate Models

Tom Maxim, BS, Jennifer Yu, MD, Julie Woodhouse, RN, Andrew Kuehnle, L. Michael Brunt, MD

Background: The value of suturing skills training in senior medical students (MS4) is well-established but no studies have analyzed performance in a simulated operative setting. We hypothesized that MS4 performance on suturing and knot-tying (KT) tasks in an inanimate model would correlate with simulated operative performance. We compared video recorded with a camcorder to a GoPro camera for assessment of operative technical skills.

Methods: MS4 enrolled in a proficiency-based skills curriculum at the start of the academic year were assessed 4-7 weeks post-training by objective structured assessment of technical skills (OSATS). A dual camera video system recorded performance on a suture pad and tying board (SP/TB). A camcorder recorded testing of the same skills on fresh porcine abdominal wall (simulated operative setting). Tasks assessed were suturing (simple interrupted [SI], subcuticular [SC]), and one or two-handed KT. Total

(sum of individual scores, max score 30) and global (overall assessment, 1-5 scale) OSATS scores were analyzed using paired t-test (significance p<0.05). Data are mean \pm SD.

Results: Seven students completed SP and porcine assessments. For SI, total and global technical proficiency (TP) scores were significantly higher and times significantly faster using the SP/TB. There were no significant differences in scores for SC and KT. Recording with a camcorder provided superior lighting and magnification for technical skills assessment compared to a GoPro camera. **Summary:** MS4 suturing and KT performance on fresh tissue is comparable to SP performance. A camcorder provides comparable video quality to a commercial dual camera video system and is superior to a GoPro for assessment of performance.

Task	Total OSATS Score		Global OSATS Score		Time (sec)	
	SP/TB	Porcine	SP/TB	Porcine	SP	Porcine
SI	18.1 ± 2.2*	15.6 ± 2.2	3.0 ± 0.5*	2.4 ± 0.4	178.3± 13.6**	307.4 ± 55.8
SC	18.4 ± 3.2	16.8 ± 3.0	3.0 ± 0.6	2.6 ± 0.7		
КТ	13.2 ± 1.7	12.5 ± 2.3	2.5 ± 0.5	2.4 ± 0.6		

* p<0.05, ** p< 0.01.

The Implementation of a Curriculum-based, E-learning Program at the Keck School of Medicine of USC <u>B. Sean Nguyen</u>, Arunava Sarma, Gloria Wu, Mitch Brown, Apoorva Ananth, Donovan Roy, Anne Vo,

Department of Medical Education, KSOM

Goal: Medical education literature indicates that many medical students use memorization aid programs (MAPs), which are flashcard based study tools (e.g. Anki, Quizlet, Memorang, etc.) that test student retention. However, there is a paucity of research on institution-supported, curriculum-based MAPs. In response to these trends, the Keck Online Learning Initiative (KOLI) was created. KOLI consists of a team of second-year students who build Memorang study sets based on the first-year Keck curriculum for the first-year class.

Methods: An observational study of data collected from the FMS2 post-exam survey was performed. An observational study of Memorang-provided user data during FMS2 is pending.

Results: The FMS2 post-exam survey of the first-year class (N=186) resulted in a 59% completion rate (n=109). More than half of respondents (n=60) indicated that they used MAPs often or regularly while greater than one third indicated that they used KOLI to study (n=38). Of the students that used KOLI, a majority (>80%) agreed or strongly agreed that the program is representative of the Keck curriculum as well as a useful study resource.

Conclusions: Though other more established MAPs are heavily used (primarily Anki), KOLI Memorang usage at this single institution is robust. Future research will involve analysis of coded data amongst three data sources– post-exam surveys, KSOM-provided data (MCAT scores and exam scores), and Memorang-provided user data– in order to better understand student studying habits and performance.

Health Care for the Homeless: An Integrated Curriculum Session for First-Year Medical Students Laurie Song, BA, Ankit Shah, MD, JD, Keck School of Medicine of USC, Stephanie K. Zia, MD, FAAP, FACP, Keck School of Medicine of USC

Background: Homelessness negatively impacts a person's health and presents barriers to self-care and access to health services. Almost 8% of the nation's homeless population resides in Los Angeles County. We designed a two-hour interactive, multimodal, student-led session for MS-Is in the Professionalism and the Practice of Medicine course to address the lack of a formal curriculum surrounding health care for the homeless at the Keck School of Medicine of USC.

Methods: Session goals and objectives were provided, guest speakers shared their experiences, and a student-designed resource card was distributed for use in clinical encounters.

MS-I evaluation of session content includes Level 1 assessment of student reaction through an end-ofsession evaluation and student leader reflection pieces. MS-Is completed pre-session and post-session surveys to assess immediate and long-term Level 2 and 3 learner knowledge, attitudes, exposures, and interest. Qualitative and quantitative methods are used to analyze session impact. MS-IIs completed a survey assessing perceived need for a formal curriculum and existing knowledge, attitudes, and exposures.

Results: MS-I evaluation data (n=178) has generally been positive, with a mean 4.61 score out of 5 for overall quality of session activities. 72% (n=185) answered pre-session baseline knowledge questions correctly, and 86% (n=86) answered post-session knowledge questions correctly. Preliminary MS-I survey suggests that, after the session, 74% reported a more positive attitude toward the homeless population, and 53% reported more motivation to seek out opportunities to work with the homeless population in medical school.

Preliminary MS-II survey suggests that 83% (n=47) endorse a need for a formal curriculum addressing care of the homeless population.

Summary/Conclusion: Preliminary results show increased baseline knowledge, more positive attitudes toward the homeless population, and increased interest in working with the homeless population, demonstrating positive session impact.

Retrospective evaluation of appropriate asthma diagnosis using PFTs to guide physician education <u>Paul Yang</u>, Syeda Tun-Nisa Hamadani, M.D., Suneet Wander Dullet, M.D., Gina Rossetti, M.D.

Background: Many patients in primary care clinics are labelled with a diagnosis of asthma without having pulmonary function tests (PFT) or meeting National Asthma Education and Prevention Program: Expert Panel Report III (NAEPP) criteria. Misdiagnosis can lead to increased morbidity and mortality. **Objective**: To determine how many patients with a diagnosis of asthma in internal medicine resident primary care clinics met NAEPP criteria. To create interventions to improve knowledge surrounding the diagnosis and treatment of asthma.

Methods: A chart review was performed on 119 patients seen from July 2012 through June 2013. Each chart was reviewed for the presence of PFTs and other disease related characteristics to evaluate if the NAEPP criteria were met. A quality improvement intervention was designed and implemented based on

a survey sent to resident physicians to determine reasons for misdiagnosis and mismanagement of asthma.

Results: Among the 119 patients diagnosed with asthma, 89 did not have a PFT performed, 24 had an inconsistent PFT result, and only 6 had a confirmatory PFT. Results of the resident survey showed significant gaps in knowledge regarding asthma diagnosis and management. A didactic session was an effective method in improving residents' knowledge.

Conclusion: There was a gap in resident knowledge regarding diagnosis and management of asthma, particularly in the logistics of obtaining PFTs. This may explain the significant amount of asthma misdiagnoses made in clinic. We addressed these issues by educating residents with an interactive didactic session. Post survey analysis indicated a large improvement in housestaff knowledge.

EMERGENCY MEDICINE & TRAUMA

An Eye-tracking protocol for detecting mild traumatic brain injuries

Yom Alemante, Dan Lorenzana, Brian Robinson, Gene Yu, Alfredo Sadun, David Baron

Background/ Purpose/ Goal/ Hypothesis: While 1.4 million concussions are diagnosed in the U.S. each year, the true incidence is much higher, with estimates of sports-related concussions ranging from 1.6-3.8 million per year on their own. This study aims to establish an eye-tracking protocol that can be used by physicians as a tool in their clinical decision-making when assessing patients with potential traumatic brain injuries (TBI). To date, no such commercially-available devices exist for physician use.

Methods: Eye-tracking data from concussed subjects and controls will be collected from hospitals in Los Angeles and Turkey using the following five tasks:

- (1) smooth gaze tracking of an oscillating dot
- (2) smooth gaze tracking of an oscillating dot that pauses at each extreme
- (3) saccade
- (4) anti-saccade
- (5) vergence & accommodation

Participants will complete each task in sequence and repeat the sequence two additional times for a total of three total assessments per time point. Data will be collected in real-time by the eye-tracking software as the location of the user's gaze overlaid on the actual location of the target. From there, the mean squared error (MSE) will be calculated between the two datasets. Finally, we will ascertain the variance of the recorded errors between time points to ensure that consistent results are obtained. Statistical comparison between groups will be performed using various modalities, including Bland-Altman analysis and interclass correlation.

Results: We have not yet collected data, so there are no results yet, but preliminary data using alcohol intoxication as a stand-in for neurological impairment has shown significant differences from controls. We expect to find significant differences in a few key metrics in accordance with previous literature, in particular: saccades, anti-saccades, and vergence. Smooth pursuit has less often yielded differences according to the literature.

Summary/ Conclusion: Unfortunately, there is no current standard diagnostic tool or protocol for diagnosing and assessing concussions. Physicians continue to disagree over the diagnostic criteria for concussion, and patients habitually underreport, contributing to the difficulty of developing a universal standard. Ultimately, clinical examination remains the gold standard for concussion diagnosis and assessment.

Developing a test that can reliably distinguish between normal and concussed individuals will go a long way in providing another tool in detecting mild concussions that would otherwise go undiagnosed. Even mild concussions predispose individuals to further concussive events ("second impact" syndrome) and can cause significant morbidity in the form of post-concussive syndrome (depression, dizziness, fatigue, poor memory and concentration, sleep disturbance, headache, anxiety).

The Impact of Administration of Opiates or Benzodiazepines on Comprehension of ED Discharge Instructions

Joe Berman, Charney Burk, Nihaal Shah, Dr. Sophie Terp, Dr. Elizabeth Burner, Chun Nok Lam, Dr. Michael Menchine, Dr. Sanjay Arora **Background:** Prior research has shown that many ED patients have a poor understanding of their visit and their discharge instructions. The potential benefits of improved understanding are immense. As part of their care, some patients receive opiates and benzodiazepines, that may impair memory and recall. To date, there has been no study of how these drugs impact patients' understanding of discharge instructions.

Objective: To evaluate whether opiates or benzodiazepines impact patients understanding of their discharge instructions.

Methods: A consecutive sample of discharged ED patients were asked to complete a questionnaire, and over 90% of patients agreed to participate. The questionnaire asked about patient demographics and their discharge instructions. Two medical students independently rated patient comprehension of their discharge instructions into one of 5 different categories on a locally created scale, which were collapsed to good (score of 1 or 2) or poor understanding (score of 3-5). Kappa between reviewers was 0.97. Opiate and benzodiazepine administration were recorded directly from the patients' electronic medical record.

Results: Of 534 patients evaluated, 35% (n=189) received either a benzodiazepine or opiate prior to discharge. The proportion of patients with good understanding of their discharge instructions was lower amongst patients who received benzodiazepines or opiates when compared with patients who received neither (57.7% (95%CI 50-65%) vs. 62.6% (95%CI 50-67%)). The difference was more pronounced in the subset of patients (n=8) who received benzodiazepines only, amongst whom only 25% had good understanding.

Conclusion: Health care personnel should be cognizant of the impact that medications can have on patient comprehension of their discharge instructions. Based on our small sample, particular attention should be given to those patients who receive benzodiazepines during their ED visit.

The Impact of Rapid Patient Registration on Emergency Department Flow

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Background: The ED of LAC+USC Medical Center is one of the busiest in the country, with an annual census of >170,000. In a safety-net hospital with limited resources, waste accumulates from system inefficiencies. Delay to definitive treatment, overcrowding, and long lengths of stay lead to increased patient safety risk, decreased satisfaction, and patients leaving in nontraditional dispositions. We sought to create a new identification process to streamline patient intake and treatment.

Objectives: To determine the impact of a rapid registration protocol on operational metrics for a 12-bed fast-track pod of LAC+USC ED. We hypothesized that the new process would streamline patient flow and lead to decreased arrival to registration (ATR), arrival to orders (ATO), arrival to MD (ATMD), MD to disposition (MDDP), and length of stay (LOS) times.

Methods: Using healthcare lean tools, we created a rapid registration process where patients are identified in the electronic health record (Wellsoft) immediately upon arrival at the greeter desk. Retrospective analyses of operational metrics from a 12-week period before implementation (2/4/14-5/4/14) were compared to a 12-week period post-implementation (2/4/15-5/4/15). Patients evaluated

in the Jail ED or Urgent Care Clinic were excluded. Data analysis was completed using two-sample independent *t*-tests.

Results: Time reductions following implementation in all operational metrics in the fast-track pod were statistically significant. (*p*<0.001) (**Desai Table 1**).

Conclusions: Registration of ED patients is universally necessary for all patients entering the ED. Based on our comparative data, implementation of a rapid registration process led to increased efficiency in a fast-track pod where rapid initiation of treatment leads to prompt dispositions. These results are promising for EDs utilizing a fast-track pod (**Desai Figure 1**). This has multiple potential downstream benefits such as improved patient satisfaction and patient flow through the ED.



Desai Figure 1. Comparison of median ED patient flow metrics before and after rapid registration implementation.

	Wait time (minutes)				
2/4/14- 5/4/14	ATR	ATMD	АТО	MDDP	LOS
Average	68	216	282	329	612
SD	57	193	246	234	324
n	16051				
2/4/15- 5/4/15					
Average	9	185	253	304	591
SD	34	157	237	204	327
n	15029				
t	111.6	15.58	10.58	10.06	5.68
P-value	<.001	<.001	<.001	<.001	<.001

Desai Table 1. Mean and SD patient wait times before and after implementation of rapid registration protocol. Results of two-sample independent t-test are shown. hbyrdduncan@saem.org

Empiric Antiretroviral Therapy for Acute HIV Infection in the Emergency Department Sanjay Arora, MD, <u>Alexander Klonoff, BA</u>, Meredith Lora, MD, Michael Menchine, MD, MPH, Stephen Merjavy, MD, Kristi Stanley, MD, Kristin Walsh, MD, Kathleen Jacobson, MD.

Background: The acute phase of HIV infection is defined by high viral loads and non-specific viral symptoms, and has the greatest likelihood of transmission. Early treatment of acute HIV infection will decrease viral reserves, long-term co-morbidity, and transmission in the community. ED screening programs using 4th generation immunoassays have potential to identify cases of likely acute HIV infection who are candidates for early empiric antiretroviral therapy (ART) if positive test results are combined with pertinent clinical characteristics.

Objectives: To determine the feasibility and willingness of patients with suspected acute HIV infection to begin empiric ART in the ED.

Methods: Over the last five years we have screened over 68,000 patients identifying 852 HIV positive patients of which 274 were newly diagnosed HIV positive in the ED. In December 2014 we began offering ART to individuals with likely acute infection if they had: 1) a clinical history consistent with acute HIV infection 2) Negative HIV test in the last 6-12 months 3) No co-morbid conditions with risks that outweigh the benefits 4) 4th generation positive HIV test with pending HIV 1/2 antibody test and

HIV viral load by PCR 5) Stable baseline CBC and chemistry panel in the ED 6) Genotype and CD4 can be ordered in ED 7) Patient understands and/or agrees to: a) Confirmatory tests b) take medication c) commit to abstinence or 100% condom use d) notify partners e) follow up appointment f) provide reliable personal contact information (phone number/ email address).

Results: From December 1 2014 to October 1 2015, there have been 14 confirmed cases of acute HIV infection in the LAC+USC ED screening program. Of these, nine of the cases were identified in the ED in real time as likely acute HIV using the aforementioned criteria. All nine were offered and agreed to empiric ART in the ED. One patient withdrew prior to starting ART. The other eight were prescribed ART in the ED. Eight of the nine patients suspected to be acutely infected were ultimately confirmed to be acutely infected with HIV and one patient was chronically infected. There were no false positive tests. **Conclusion:** Prescribing empiric ART in the ED for acute HIV infection is feasible and well-received by patients. This novel approach using 4th generation immunoassays and empiric ART facilitates urgent HIV intervention, which can lead to an expanded ED role in the HIV care continuum.

The Diagnostic Yield of Commonly Used Investigations in Pelvic Gunshot Wounds

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Background: Patients who sustain pelvic gunshot wounds (GSWs) are at significant risk for injury due to the high density of visceral structures. Currently, the optimal work-up for pelvic GSWs is unclear. The aim of this study was to determine the diagnostic yield of tests commonly used in the investigation of pelvic GSWs and to develop a diagnostic algorithm.

Methods: After IRB approval, patients ≥15 years old (01/2008-01/2015) who sustained one or more GSWs with pelvic contents at risk were retrospectively identified. The diagnostic yield of CT scan, gross hematuria, urinalysis, cystogram, endoscopy, and digital rectal exam for clinically significant injuries was calculated.

Results: We identified 370 patients. Patients with peritonitis, hemodynamic instability, an unevaluable abdomen, or evisceration were taken directly to the operating room for laparotomy (n=138, 37.3%). All others (n=232, 62.7%) underwent CT scan and further investigations. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each test was as follows: For detection of injury to pelvic structures CT scan had values of 1.00, 0.98, 0.74, 1.00. For bladder injuries gross inspection of the urine and cystogram carried values of 1.00 for all parameters while urinalysis carried values of 1.00, 071, 0.17 and 1.00. For rectal injuries endoscopy had values of 1.00, 0.82, 0.75, 1.00 while digital rectal exam had values of 0.77, 0.99, 0.77, 0.99.

Conclusion: Patients not requiring emergent operation should first undergo CT scan. Patients with positive CT should be managed for their injuries while patients with negative scans should be discharged home. For equivocal scans patients should undergo endoscopy for potential rectal injury and should have urine inspected for gross hematuria if there is a possible bladder injury, with subsequent

cystogram only if there is hematuria. There is no role urinalysis or digital rectal exam in screening patients with pelvic gunshot wounds for injury.

Long Term Follow Up of Fournier's Gangrene in a Tertiary Care Center

David R. Rosen, MD; Mitchell E. Brown; Kyle G. Cologne, MD; Glenn T. Ault, MD; Aaron M. Strumwasser,

MD

Background: Fournier's Gangrene (FG) is a surgical emergency, requiring aggressive surgical debridement, antibiotics, and extensive wound care. The acute use of fecal diversion systems, (such as a rectal tube or surgical ostomy) to assist with wound healing is controversial and without clear guidelines. Little is known regarding the long term recovery of these patients after their inpatient stay. Analysis of outpatient follow up could help facilitate appropriate inpatient intervention in this physiologically altered population.

Methods: All patients treated for FG at a large, urban, safety-net hospital from 2012-2015 were retrospectively identified and reviewed from an administrative database. The database was used to identify: demographics, comorbid conditions, laboratory and physiologic data values, length of stay (LOS), number of operations, time to healing, and occurrence of any complications.

Results: 17 patients (16 males, 1 female) were treated during the study period. Average age was 49 years (range 29-68). 13 had diabetes mellitus (DM). Mean admission nutrition labs included an albumin level of 2.6 g/dL (range 2.0-3.6), and prealbumin of 6.8 mg/dL (range 3-15.4). Average admission Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was 7.4 (median 8, range 3-12) and average Fournier's Gangrene Severity Index (FSGI) score was 8.9 (median 7, range 5-18). Mean LOS was 35 days (median 31, range 2-81) and mean intensive care LOS was 7.5 days (range 1-24). There was one mortality. 11 patients underwent fecal diversion utilizing the Flexi-seal[™] fecal management system, 5 patients underwent construction of a surgical colostomy, and 1 had a preexisting colostomy. 13 of the 17 patients had long term follow up; all have completely healed their wounds. Average time to complete wound healing was 6.5 months (median 3, range 1-31). Of the five patients who received surgical ostomies, 2 have had their ostomies reversed, 2 have been unable to be reversed due to multiple admissions for comorbid conditions (uncontrolled DM and hypertension), and 1 was lost to follow up. Of the 2 patients who had their ostomies reversed, both had complications from their reversal (leak, urinary retention).

Conclusions: Fournier's Gangrene is a highly morbid illness that affects a critically ill population. Aggressive surgical debridement is necessary, and although patients may be able to heal their wounds, surgical colostomy reversal is not always performed. If possible, it may be prudent to avoid a surgical ostomy using less-invasive diversion technology. Prospective studies with larger sample sizes are needed to validate our findings.

Intraosseous Access as a Bridge to Definitive Access at LAC+USC

<u>Megan Johnson BA</u>, Kenji Inaba MD, Saskya Byerly MD, Erika Falsgraf, BA, Lydia Lam, MD, Elizabeth Benjamin, MD PhD, Aaron Strumwasser, MD, Demetrios Demetriades MD PhD

Introduction: Intraosseous (IO) infusion is an alternative access for infusion of fluids and medications in patients without sufficient venous access.

Objective: The purpose of this study was to examine the indications and outcomes associated with IO use at a Level 1 trauma center.

Methods: This is a single center retrospective study performed between 1/2008 and 5/2015. Data points extracted included demographics, time to IO insertion, other attempted venous accesses, indications, products infused, hospital and ICU length of stay and mortality.

Results: A total of 68 patients who underwent IO insertion were analyzed. Median patient age was 30, with a range of 2 weeks to 86 years. 56% were hypotensive upon arrival and 38.2% were asystolic. Mechanism of injury included 22.1% GSW, 20.6% AVP, 16.2% fall, 10.3% MVC, 7.4% medical, 7.4% stab wound, and 4.4% MCC. Indications cited were 26.5% for resuscitation, and 20.6% to facilitate rapid sequence intubation. The median time to IO access was three minutes. Peripheral IV access was established before IO in 30.9%. IO access was gained via tibia in 88.1% of patients. Through IO access, 30.9% patients received crystalloid, 29.4% received ACLS medications, 25% RSI medications, 20.6% blood products, and 2.9% seizure prophylaxis. 80.9% of patients were intubated in the ED, 26.5% had ED thoracotomy, and 20.6% had a laparotomy. Median crystalloid infused through IO was 180cc in pediatric patients and 1L in adults respectively. IO complication of extravasation was experienced by 7.4% of patients. In-hospital mortality was high at 72.9%. None of the complications or deaths could be directly attributed to IO infusion.

Conclusion: IO access should be considered when there is a need for immediate intervention requiring vascular access, particularly in patients in extremis. IO is established quickly with minor complications compared to central venous catheters.

Management of Traumatic Arterial Injuries

Reid Sakamoto, Agustin Alvarez Escalante, Dr. Kenji Inaba

Goal: Determining proper surgical intervention is important in achieving reducing morbidity and mortality in traumatic arterial injuries. The goal of this study is to determine appropriate treatment modalities measured in outcome (mortality and complications) for traumatic arterial injuries. **Design:** The LAC+USC trauma registry was examined for patients sustaining any type of arterial injury over a ten-year span (6/2005-6/2015). Injuries were grouped based upon their locations: neck, inferior limb, central and subclavian injuries. Each group was analyzed for surgical intervention and subsequent outcomes and complications.

Results: A total of 541 injuries were identified. There were 73 to the carotid, with operative management in 30. Primary repair performed in 13.7%, ligation in 20.5%, and graft in 6.8%. Death resulted in 31.5% of cases. Penetrating mechanism (OR=10.06) or ligation (OR=6.30) were risk factors for mortality. Inferior limb had 137 injuries with 76.6% repaired by graft (synthetic/tissue), ligation in 0.7% and primary repair in 18.2%. Blunt mechanism was an independent risk factor for amputation (OR=8.9). There were 320 central injuries, 168 requiring surgical intervention, primary repair was preformed in 35% and graft in 17%. 71% of aortic injuries received primary repair. Damage to the aortic, renal and iliac arteries showed mortality rates exceeding 33% for injuries requiring surgical intervention. A total of 21 subclavian injuries were identified. Of these, all patients receiving ligation (5.5%) died.

Conclusion: Ligation of the carotid artery was an independent risk factor higher mortality. Injury to the common carotid confers a higher mortality compared to other carotid injuries. In lower extremities, tissue graft was most commonly used and blunt mechanism conferred a higher risk for amputation. Primary repair was preferred for aortic injuries, however, damage to the aorta caused a high mortality regardless of treatment method. All patients receiving subclavian ligation died, however this was due to critically injured status.

Supermassive Transfusion: A 15-year Single Center Experience

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Background: Few studies have examined the survival and outcomes after large volume blood product transfusions, especially those receiving supermassive transfusions, defined as \geq 25 units of RBC within the first 24 hours of admission. Therefore, this study was designed to determine the outcomes associated with supermassive blood transfusion after trauma.

Methods: Retrospective study, level I trauma center, 1/2000-12/2014, including trauma patients who received ≥25 units of RBC within the first 24 hours. Patients were stratified based on the amount of RBC transfused in the first 6 and 12 hours of admission. Univariate analysis and multiple logistic regression were used to identify risk factors for mortality. ROC curve analysis was performed.

Results: Of 74,065 adult (≥18 years old) trauma patients, 178 patients (0.24%) received ≥25 units of RBC in the first 24 hours, 32 (0.04%) received ≥50 units, and 7 (0.01%) received ≥75 units. 93.26% male, median age 33.9 (18-82), and ISS 28.9. The overall mortality in patients receiving ≥25 units of RBC was 65.17%, ≥50 units was 71.88%, and ≥75 units was 85.71%. In multiple logistic regression, ISS and GCS were significant predictors of mortality for patients receiving ≥25 units in 6, 12, and 24 hours (p< 0.05). Female sex was protective regardless of transfusion amount (OR range 0.062-0.148, p<0.05). Survivors received fewer total units of RBC than non-survivors, and were more likely to be female. There was no difference in the amount of blood received or mortality between blunt and penetrating injuries (64.8% blunt vs. 66.1% penetrating). Higher transfusion requirements were associated with increasing mortality. Cutoff analysis identified ≥31.5 units associated with significantly higher mortality. **Conclusion:** ISS, GCS, and sex were significant predictors of mortality, with a transfusion of ≥31.5 units in 24 hours associated with significantly higher mortality.

ENDOCRINOLOGY

Diabetes Management Education and its Effect on Hispanic Diabetic Population Angelina Nieto-Rodriguez, Cesar Gonzalez, Dr. Jo Marie Reilly, Dr. Camilo Zaks

Goal: A problem among Diabetic Latino population is that of health literacy. Many individuals face a language barrier and do not have access to adequate diabetes management information. Many diabetic patients are not able to manage their diabetes outside of the hospital setting because of a lack of understanding of the lifestyle change necessary for diabetic patients. By implementing diabetic management group appointments diabetic patients will learn adequate skills to manage their diet and incorporate healthy exercises into their schedule. The knowledge gained through the diabetic management curriculum will help patients manage diabetes and improve blood glucose and HBa1c levels.

Method: Study can be defined by comparing Hba1c levels, BMI, and lipid panels of patients in the diabetes management group appointments before and after the 6 months of classes. Patients will also be asked to take a survey in which they will identify their level of confidence in the knowledge of diabetes management. Results of patients who will have attended the diabetic management group appointments will be measured against control group of patients who did not receive management education.

Results: Diabetes management education appointments have recently concluded. Collection of data is still in progress and results are pending.

Conclusion: Based on results section above, conclusion is undetermined. Data collection and analysis is still in progress.

EPIDEMIOLOGY

Epidemiology, Etiology and Treatment of Isolated Cleft Palate

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 Medicine, University of Southern California.

Purpose: The goal of this study is to distinguish the epidemiology, genetic and environmental risk factors, molecular biology, embryology, and treatment of isolated cleft palate (CPO) from cleft lip with or without palate (CL/P). We hypothesize differences in risk factors, clinical outcomes and long-term outcomes between CPO and CL/P.

Methods: Articles and data were retrieved through a systematic research of the following keywords: "cleft palate," "orofacial clefts," "environmental risk factors," "genetics," "GWAS," "molecular biology," "embryology," "syndromic" and "epidemiology" in Pubmed, OMIM, the NIH, Orphanet, and the WHO and CDC databases.

Results: Incidence of CPO varies by geography from 1.3 to 25.3 per 10,000 live births, with the highest rates in British Columbia, Canada (25.31 per 10,000) and the lowest rates in Nigeria, Africa (0.32 per 10,000). Regardless, rates of CPO are consistently higher in females than males. Fifty percent of cases occur alone; the other half occur as part of a genetic syndrome or with another malformation, with the most common being congenital heart defects (31.1%) and deformations (22.4%). Although \geq 35 syndromes with CPO have been identified with a known gene mutation, no genetic risk factors have been identified yet for solely CPO. However, genetic markers for CL/P have not been significant in CPO. Only maternal tobacco smoke has been strongly associated with CPO (highest reported OR=2.11), with inconclusive data on the role of maternal zinc, folate, and alcohol use, unlike their stronger correlation with CL/P. Treatment and long-term outcomes for children with CPO are significantly different from CL/P involving more substantive speech and dental care to preserve speech function.

Conclusions: CPO exhibits distinct risk factors, clinical care and long-term outcomes from CL/P. There is a need for larger studies of genetic and environmental risk factors (primary prevention) and determining predictors of recurrence (secondary prevention) to fully understand the etiology of CPO. **Citation:** Burg et al. Front Physiol 2016

GASTROENTEROLOGY

Redo PEH Repair is Associated with Excellent Symptomatic and Objective Outcomes Stephanie G Worrell, <u>Kyle M Green</u>, Katrin Schwameis, Steven R DeMeester

Objective: Recurrence after primary paraesophgeal hernia (PEH) repair is common. Each attempt to repair recurrent hernias at other sites such as the abdominal wall are associated with worse outcomes. The aim of this study was to evaluate the outcome with redo PEH repair.

Methods: A retrospective chart review was performed of all patients that had a re-do PEH repair from 9/2009 to 7/2015.

Results: There were 29 patients (16F:13M) that had a re-do repair for PEH recurrence. The indication for the reoperation was recurrence of symptoms (83%), persistent dysphagia (10%) and early recurrence of an intra-thoracic stomach (7%). All patients had objective evidence of a PEH. The reoperation was laparoscopic in 13 (45%) and open in 16 (55%). The laparoscopic procedure was converted to open in 4 patients. During the reoperation a Collis gastroplasty was added for esophageal shortening in 16 patients (55%) and 2 patients had diaphragmatic relaxing incisions to reduce crural tension. An absorbable mesh was placed to reinforce the crural closure in all patients. There were 2 post-operative complications, a reintubation and post-operative atrial fibrillation. There were no mortalities. At a median follow-up of 10 months symptoms were resolved or improved in all patients. Objective follow-up was available from 79% of patients and there were no recurrent hernias.

Discussion: Recurrence after PEH is common and some patients require reoperation. Re-do repair is more complicated and is more commonly done as an open procedure. During the reoperation 55% of patient had an adjunct procedure for esophageal shortening or crural tension. Early symptomatic and objective results are excellent, supporting the value of reoperation in appropriate patients.

Impact of POEM on High-Resolution Manometry Findings in Patients with Type II and Type III Achalasia

Hashemzadeh-Gargari, R., Schwameis K., Demeester S.

Background: Identification of the subytypes of achalasia has been greatly improved since the advent of High-Resolution Manometry (HRM). Type I, II, and III achalasia can all be clearly determined with HRM. The purpose of this study was to observe and quantify changes of esophageal motility using HRM after a Peroral Endoscopic Myotomy (POEM) to treat achalasia.

Methods: We did a restrospective analysis of patients who: had Type II or Type III achalasia (preoperatively determined by HRM), underwent a POEM procedure, and subsequently received a postoperative HRM, as well as an upper endoscopy and timed barium swallow (TBS).

Results: There were a total of 31 patients who had a POEM for achalasia, of those 31, 16 had Type II or Type III Achalasia (11 had Type II and 5 had Type III). All of the patients who had Type II and 2/5 of the patients who had Type III demonstrated PEP on preoperative HRM. Type II patients experienced 72.7% reduction of PEP postoperatively on HRM after POEM, but none of the patients with Type III experienced PEP reduction. The mean IRP and LES resting pressures were similar in patients with both Type II and Type III achalasia; however, IRP post-POEM was lower in patients who had resolved PEP when compared to those who had persistent PEP(9.5 vs 16.7, p=.025). There was no difference in LES among patients with resolved or persistent PEP(14.9 mmHg vs 20.7mmHg, p=.18) Patients who had

resolved PEP on HRM similarly experienced dysphagia relief (80% vs 75% p=.84), increased empyting (97% at 5 mins vs 87% at 5 mins, p=.16) and frequency of post-POEM esophagitis (60% vs 62.5%, p=.93). No patient with Type II achalasia had return of peristalsis vs 2/5 of Type III patients who did see a return of peristalsis. No Type III patient on post-POEM HRM looked like Type I or II.

Conclusions: The POEM procedure significantly relieves achalasia symptoms in most Type II achalasia patients. Persistent PEP was associated with a higher post-POEM IRP. Persistent PEP implications will be important to further research.

Optimization of the Generation of Autologous Tissue Engineered Small Intestine <u>Hilton AE</u>, Wieck MM, Grikscheit TC

Background: Pediatric patients with necrotizing enterocolitis or congenital intestinal anomalies are at significant risk for short bowel syndrome (SBS). Tissue engineered small intestine (TESI) could provide patients with autologous small intestine grown on a resorbable polymer scaffold. TESI improves outcomes of SBS in small animal models. However, no relevantly sized animal models exist to provide evidence for the effectiveness and therapeutic potential of TESI for our population. We hypothesize that through this research, our model will show successful production and growth of TESI in order to translate the technology to human patients suffering from SBS.

Methods: We surgically removed short segments of jejunum from a 6 week old, 6.4 kg Yucatan miniature swine. These segments were mechanically and enzymatically degraded and then loaded onto a biodegradable polymer to create organoid units (OU). 4 weeks after implantation into the omentum, these samples were harvested and analyzed using immunohistochemical staining for markers for epithelium, muscle, nerve, and vasculature.

Results: Resected implants from porcine omentum revealed innervated and vascularized tubular segments of TESI approximately 0.5 cm in diameter. Immunofluorescent staining for villin, e-cadherin, Muc2, and chromogranin A demonstrated all epithelial cell types seen in native tissue. Staining for Sox9 revealed progenitor cells in the base of the crypts. PDGFR α was used to stain for a thin layer of lamina propria. Staining for Tuj and α -SMA revealed neural tissue intercalated in a thin layer of muscle deep to the epithelium. H & E staining revealed structures such as crypts, villi, lamina propria, and muscularis mucosae that mimic native pig intestine.

Conclusion: Our research shows that TESI can be effectively generated from autologous tissue in a model that is more clinically relevant for our intended patient population. Future directions are to evaluate the potential for TESI to treat SBS.

Preoperative Factors Influencing Outcome of MSA Operation in Patients with GERD Justine Ko BS, Jessica Reynolds MD, John Lipham MD

Goal: Gastroesophageal reflux disease (GERD) is a common chronic disease. The current first line of treatment is proton pump inhibitors (PPIs) which provide only symptomatic relief and no reflux prevention. Up to 60% of patients on appropriate PPI therapy will continue to experience symptoms. In 2012, Magnetic Sphincter Augmentation (MSA) was approved by the FDA. A flexible band of magnetic titanium beads is placed around the gastroesphageal junction, preserving structure and function of the

native LES while preventing reflux. Because MSA is relatively new, there is little information about it available. This study was undertaken to identify pre-operative factors that may affect the outcome of MSA.

Methods: Preoperative data was collected from patients who received MSA (n=243) at 3 institutions by 3 surgeons from 6/2007-6/2015. Preoperative factors retrospectively analyzed included gender, age, BMI, preop GERD-HRWL, Demeester scores, supine reflux, Barrett's esophagus, esophagitis grade C or D, presence of hiatal hernia and repair, LPR symptoms, preoperative dysphagia, and inclusion of vagus in MSA. Post-operative EGD and pH studies were performed based on patient's symptoms at the discretion of the surgeon. Failure of MSA was defined as GERD-HRQL > 10, esophagitis of any grade, positive pH study or continued use of daily PPIs at follow up.

Results: For all preoperative variables tested, comparison between patients who failed MSA (n=65) and those that did not (n=178) was statistically insignificant (p>0.05). In MSA failure, 45 had GERD-HRQL > 10, 2 patients showed esophagitis on EGD, 10 had pH testing with 3 positive DeMeester scores, and 26 had daily PPI use. Preoperative supine reflux data was available for 146/243 patients and did not influence MSA outcome.

Conclusions: The results of the study did not yield any preoperative factors that might lead to higher risk of failure of MSA. Even with a broad definitions of failure, MSA continues to be successful and should not be withheld from individuals with uncomplicated GERD.

Is EGD Reporting Adequate: A Review of Reports from 100 Referring Gastroenterologists

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Background: Esophagogastroduodenoscopy (EGD) is a commonly performed procedure amongst patients experiencing symptoms of gastroesophageal reflux disease (GERD). Detailed EGD reporting of relevant landmarks and findings is essential in communicating with referring physicians and is particularly important in documenting a patient's baseline status. Pertinent findings include: the presence or absence of esophagitis as well as a columnar lined esophagus (CLE), the locations of the squamocolumnar junction (SCJ), gastroesophageal junction (GEJ), and crural impression and the type of hiatal hernia, if present. Our aim was to evaluate the frequency with which these pertinent findings were described in patients being evaluated for GERD.

Methods: A retrospective review was conducted of consecutive EGD in patients referred to our department from 2012-2015. In order to avoid the issue of encountering multiple reports from a single endoscopist, only the first report encountered from that endoscopist was used. Reports were subsequently reviewed for a description of the pertinent findings described.

Results: The EGD reports from different endoscopists in 100 individual patients were reviewed. Esophagitis was reported in 33 patients; however, it was graded by the endoscopist in only 14 cases (42%). The LA and Savory-Miller classifications were used equally. 15% of endoscopists characterized the esophagitis as erosive. In 28 patients a CLE was noted, but the length was only reported in 16 cases (57%), and none of the EGD reports used the Prague classification system. 61 patients presented with a hiatal hernia, but the measurement of the hernia was noted in only 31 (51%) reports. The type of hiatal hernia, sliding versus paraesophageal, was classified in only 26% of patients. One or more biopsies were taken in 93 patients. Biopsies were taken from the stomach alone in 19, esophagus/GEJ in 20 and both locations in 48 patients. The location of the biopsy was not documented in 7% of patients. In 12 patients undergoing surveillance for known Barrett's esophagus, a Seattle biopsy protocol was used in only 1 patient.

Conclusion: Only 28% of endoscopy reports contained grading systems for esophagitis or CLE when present. The type and size of hiatal hernia were reported only by 13% of endoscopists. The routine reporting of an established grading system, the measurement of hernia size and a description of the hernia subtype would greatly improve communication between the endoscopist and other intervening physicians. Moreover, these detailed descriptions are essential, invaluable assets in the assessment and treatment response or evaluation of disease progression in a patient.

Clinical outcome after laparoscopic Nissen fundoplication in PPI non-responders.

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Background: Several studies have reported that a good response to proton pump inhibitor (PPI) therapy is an important predictor of successful outcome after antireflux surgery (ARS) in GERD patients. Consequently, surgeons may be reluctant to offer ARS to patients who fail to respond. However, in the setting of typical reflux symptoms and an abnormal pH-test it is unclear how PPI response contributes to outcome. The aim of this study was to evaluate the predictive value of preoperative PPI response in these patients who had laparoscopic Nissen fundoplication.

Methods: The study population consisted of patients with typical heartburn symptoms and a positive pH-test who had a primary laparoscopic Nissen fundoplication between 01/2008-12/2014. Patients with a paraesophageal hernia or Barrett's esophagus were excluded. At their initial preoperative visit patients were asked to grade their response to PPI therapy in controlling heartburn (HB). Three patient groups were defined: good/excellent response (76-100%), fair response (26-75%) and poor/no response (0-25%). A telephone interview was conducted to assess symptomatic outcome and patient satisfaction at a minimum of 1 year after fundoplication.

Results: Of the 606 patients who underwent Nissen fundoplication, 129 met inclusion criteria, of whom 75 (M:F=38:37) were interviewed at a median follow up time of 48.4 months (12.2.-95.5). Median age at surgery was 52.8 years (20-80). There were 13 patients with a good/excellent response to preoperative PPI therapy, 36 with fair response and 26 with poor/no response. All patients were satisfied with their HB relief after fundoplication, with a mean satisfaction score of 9.5/10. There was no difference in satisfaction score or HB relief between groups (Table). All but one patient rated their HB relief better after surgery compared to on PPI therapy.

Conclusions: In patients with typical heartburn symptoms and a positive pH-test patient satisfaction after laparoscopic Nissen fundoplication was excellent and independent of their preoperative response to PPI therapy. Consequently, these patients with little or no heartburn response to PPI therapy should not be excluded from a fundoplication.

<u>Table</u> : Post-Nissen HB relief and patient satisfaction							
n (%)	n=75 NR: n=26	PR: n=36	CR: n=13	<i>p</i> -value			
	(100)	(35)	(48)	(17)			
Satisfied patients	75 (100)	26 (100)	36 (100)	13 (100)	1.0		
Mean satisfaction score (0-10)	9.5	9.6	9.6	9.2	0.19		
Degree of HB relief					0.09		
Excellent/Good	74 (98.7)	26 (100)	36 (100)	12 (92.3)			
Fair	1 (1.3)	0 (0)	0 (0)	1 (7.7)			
Poor	0 (0)	0 (0)	0 (0)	0 (0)			
Mean HB relief (%)	96.7	97.1	98.1	93.6	0.29		
	(80-100)	(90-100)	(80-100)	(80-100)			
Superior HB control by Nissen over PPI	74 (98.7)	26 (100)	36 (100)	12 (92.3)	0.09		

Table: Post-Nissen HB relief and patient satisfaction

GENETICS

First validated comprehensive chromosome screening method to routinely distinguish normal from balanced translocation carrier embryos.

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Goal: To validate a method used to distinguish a balanced translocation carrier embryo from a normal embryo in parallel with a comprehensive chromosome screening.

Methods: Phase 1 used a case with a known microdeletion near a breakpoint, allowing for determination of translocation status. Unique microdeletions within 5 Mb of the translocation on both chromosomes were identified on parental DNA and compared to that of embryos to predict normal or balanced translocation status. Phase 2 applied the method to conventional translocation patients who had already undergone IVF with PGT and embryo transfer of a balanced/normal embryo to predict translocation carrier status. Newborn karyotypes were obtained and translocation status was compared to the prediction. Phase 3 used predictions to compare implantation outcomes of balanced translocation carriers versus normal embryos.

Results:

Phase 1: There was 100% concordance between the predictive method and the genotyping analysis (10 normal, 2 carrier) of the original case embryos.

Phase 2: Phasing SNPs using unbalanced embryos allowed accurate predictions of carrier status in 10 cases. 2 patients were predicted as carriers of a, 8 as normal. Karyotyping confirmed predictions with 100% concordance.

Phase3: Implantation potential of 126 embryos was evaluated. 49% were predicted to be normal and 51% were predicted to be translocation carriers. 68% of the normal embryos and 59% of the carrier embryos implanted, not significantly different (Chi-square p-value=0.33). Maternal age and number of oocytes was not significantly different.

Conclusion: This study demonstrates the validity of the first method capable of distinguishing normal from balanced translocation carrier embryos that can be performed simultaneously with standard CCS platform and biopsy. The only prerequisite is the availability of parental DNA and an unbalanced IVF embryo which are available in most IVF couples.

Investigating the Influence of Tourette Syndrome (TS) Associated Gene COL27A1 on Cortical Thickness and Behavior in Children and Young Adults.

Tu Wen (Kevin) Hsu, Anthony Krafnick, Ph.D., Kristi Clark, Ph.D. Institute for Neuroimaging and Informatics

Background: Tourette syndrome (TS) is a neurologic developmental disorder with one of the highest familial recurrence rates among neuropsychiatric diseases with complex inheritance pattern. A genome-

wide association study (GWAS) study found multiple genetic markers with increased susceptibility to developing TS. The single nucleotide polymorphism (SNP) with the highest signal was rs7868992 which occurs in COL27A1, a fibrillary collagen gene located on chromosome 9q32-33. We undertook the current study to find correlations between the genetics, neuroanatomy and behavior.

Method: Using neuroimaging and genetic data from the Pediatric Imaging, Neurocognition and Genetics Study (PING) from 409 subjects (209 M/ 200 F; ages 8-21), cortical thickness variations with genotype for SNP rs7868992 (COL27A1) was investigated using FreeSurfer with group analysis. Post-hoc correlation with cognitive abilities as measured by the NIH toolbox Flanker and Dimensional Change Card Sort (DCCS) test were used to examine relevant behavior within regions identified by the genotype analysis (work in progress).

Results: Significant variations with genotype was found for rs7868992 (COL27A1) within females in both the left and right hemispheres. In the left lingual and parsorbitalis regions significant differences were found between GA and AA genotypes (p<0.01, cluster extent corrected). In the right superiorparietal and lateraloccipital regions significant differences were found for GG and AA (p<0.01). In the right post central gyrus regions significant differences were noted for GG and GA as well (p<0.01). **Conclusion**: The data show that genetic variation in COL27A1 are related to significant changes in cortical thickness in regions that may be relevant to the development of Tourette Syndrome. The effect was specific to females and further investigations are warranted to ascertain the cause.

Investigation of Genetic Variants in Energy Metabolism Associated with Autism Spectrum Disorder (ASD)

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Background: Autism Spectrum Disorder (ASD) is a phenotypically diverse neurodevelopmental disorder characterized by deficits in social interaction and communication, and the presence of restricted, repetitive patterns of behavior. ASD has been shown to be largely genetic, but extremely heterogeneous. The genetic architecture of ASD remains incompletely understood, although defective energy metabolism/mitochondrial disorders comprise an estimated 10-20% of ASD cases.
Purpose: This study aims to identify genetic sequence variants associated with ASD by comparing genes of approximately 150 unrelated ASD cases and 600 controls without neurodevelopmental disease.
Methods: A database of individuals undergoing clinical genetic testing for neurologic and metabolic disorders will be asked to complete an online version of the Autism Symptoms Questionnaire (ASQ). The results will be used to validate an ASD diagnosis among cases labeled as ASD by the ordering physician, and to exclude ASD and other neurodevelopmental issues among the remaining cases to serve as the control group. ASD and control groups will be compared relative to full exon sequences in about 1,200 genes, including the genes encoding for all mitochondrial proteins. Significant sequence variants will be defined as those highly predicted to alter protein number or function. Statistical testing will be performed using a Fisher exact test.

Results / Conclusions: Authors anticipate identifying one or more sequence variants associated with ASD. Discovery of such variants contributes to the understanding of ASD genetics and the eventual elucidation of mechanisms producing the disorder.

Optimizing the Threshold for Genetic Testing for Colorectal Cancer Syndromes

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Introduction: Lynch Syndrome is the most common inherited cause of colorectal cancer (CRC) and is caused by germline mismatch repair (MMR) gene mutations. The PREMM_{1.2.6} model (PREMM) predicts

the likelihood of a MMR mutations based on personal and family history. Consensus guidelines recommend germline genetic testing for those with a PREMM score of \geq 5%. We hypothesize that pathogenic MMR mutations are identifiable in a clinically meaningful fraction of patients with a PREMM score of < 5%.

Methods: We conducted a multicenter prospective cohort study of patients undergoing cancer-risk assessment using a 25 gene-sequencing panel, which includes APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53. Patients were recruited from August 2014 at three medical centers and recruitment is ongoing. Patients are enrolled if they meet clinical criteria for genetic testing or have a ≥2.5% calculated probability of inherited susceptibility to cancer. **Results:** Multiplex gene panel (MGP) testing was performed for 933 patients of which 197 (20.4%) had clinically suspicion of Lynch Syndrome. Among the 106 (11.4%) patients who tested positive for one mutation, 19 (17.9%), patients had an MMR gene mutation with a mean PREMM score of 13.4% (95% CI: 6.72%-20.03%). 12 (63.2%) of the MMR mutation carriers had a PREMM score of 5% or higher (range: 5.5% to 47%). Importantly, 7 (36.8%) MMR carriers had a PREMM score of <5% (range 1.4% to 4.2%). Mutations found in these 7 patients were MLH1(n=2), MSH2(n=1), MSH6(n=2), PMS2(n=2). One of the patients with a PMS2 mutation had a PREMM score of <2.5%.

Conclusion: In a diverse cohort of patients undergoing 25-gene MPG testing, 37% of patients carrying an MMR mutation had a PREMM score of less than the NCCN recommended cutoff of 5%. Our results indicate enhanced sensitivity of detecting an MMR mutation at a lower probability threshold. A calculated mutation probability of 2.5% using the PREMM score should prompt germline genetic testing.

IMAGING

Accuracy of computed tomography (CT) and magnetic resonance imaging (MRI) in determining depth of invasion for squamous cell carcinoma of the oral tongue

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Introduction: It has been shown in the literature that depth of invasion (DOI) of squamous cell carcinoma (SCC) of the oral tongue is correlated with prevalence of nodal metastases. The gold standard for determining DOI is through pathological section. Preoperative knowledge of DOI through imaging would be advantageous to help make decisions about management of the neck. Our objective is to analyze DOI using imaging (CT/MRI) to determine its correlation with DOI on pathology.

Methods: We retrospectively reviewed T1 & T2 patients undergoing total or partial glossectomy for SCC of the tongue between 2012-2015 at Keck Hospital. All patients had their preoperative imaging (CT/MRI) reviewed by a senior neuroradiologist. DOI was measured as the distance from the deep-most aspect of the tumor to the mucosal junction line. DOI measurements on pathological section were confirmed by a senior head and neck pathologist.

Results: Forty-two T1-2 patients with preoperative imaging were identified with SCC of the tongue. Of these patients, 17 were excluded due to film quality which did not allow for accurate identification of the DOI. Ten of the remaining patients had MRI imaging preoperatively and 15 had CT. Linear regression comparing MRI to pathology showed a strong linear correlation that was statistically significant (r =0.798, r² = 0.637, p = 0.006). Linear regression comparing CT and pathology showed a moderate linear association that was not statistically significant. (r =0.418, r² = 0.175, p = 0.137).

Conclusion: DOI of SCC of the oral tongue on MRI is highly correlated to the DOI as measured on final pathology. MRI is a useful tool for preoperative surgical planning in patients with SCC of the oral tongue.

Correlative pre- and postnatal MR imaging of interhemispheric cysts associated with callosal abnormalities

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Purpose: Interhemispheric cysts present with varied radiological and clinical presentations, frequently appearing with callosal anomalies and other congenital CNS malformations. There is substantial debate about their etiology, development, and significance. Barkovich et al. has proposed a morphological classification scheme to better understand this complex group of disorders [1]. However, despite
increased use of fetal MRI for their prenatal evaluation, there are no studies evaluating its ability to correctly classify interhemispheric cysts. This study assesses the correlation between fetal and postnatal MR imaging features and subsequent classification of interhemispheric cysts.

Materials and Methods: We performed a retrospective institutional database search (2005-2014) and found 15 cases with fetal (EGA 21.1-36.1 wk) and postnatal (age 0-90 d) MR imaging studies diagnosing interhemispheric cysts. Studies were reviewed by two board-certified pediatric radiologists for communication with ventricles, loculation, and signal intensity compared to CSF, in addition to head size, agenesis or hypogenesis of the corpus callosum, third ventricle outflow obstruction, and other developmental abnormalities. Cysts were classified according to these features using the scheme published by Barkovich et al. and compared to postnatal MRI as the gold standard [1].

Results: Classification of cysts on fetal MRI was identical postnatally for thirteen of the fifteen cases. Fetal MRI detected twelve 1a, two 1b, and one 2a, while postnatal MRI detected ten 1a, two 1b, and three 2a. In both cases where classification changed, cysts identified as communicating on fetal MRI were non communicating postnatally.

Conclusions: Fetal MRI can accurately characterized and classify interhemispheric cysts associated with callosal anomalies. In utero classification of these malformations can improve our understanding of their development and provide prognostic information for parents.

References: [1] Barkovich et al. Neurology 2001; 56:220-7

Pre-operative breast cancer assessment with Ultrasound and MRI- Which better predicts tumor size? <u>Arman Danielian MS</u>, Sandy Lee MD¹, Lingyun Ji MS², Susan Groshen PhD², Linda Hovanessian-Larsen MD¹: Department of Radiology¹, KSOM; Department of Preventive Medicine², KSOM

Background: Size assessment of breast cancer with ultrasound (US) and MRI is important in determining the clinical stage and type of surgery needed: lumpectomy or mastectomy (usually if tumor is > 5 cm). Accurate tumor measurement is essential in avoiding radical surgery and reducing repeat surgery. It is not clear which imaging modality provides the more accurate measurement as several studies have reported different results. Our study aims to clarify the correlation by comparing the pre-operative size of breast tumors obtained on US and MRI to those on surgical pathology.

Methods: In this IRB approved study, subjects who underwent lumpectomy or mastectomy for invasive ductal or invasive lobular carcinomas at LAC+USC County Hospital or Norris Breast Center from 2005-2014, were retrospectively reviewed. Eligibility included patients who had pre-operative US and MRI, and obtainable surgical pathology. Patients who had neoadjuvant chemotherapy or whose tumors had positive margins after surgery were excluded. The largest tumor size measurements from US and MRI were compared to those from surgical pathology.

Results: A total of 592 tumors from 572 patients were analyzed. When compared to surgical pathology size, US and MRI measurements had correlations of r=0.52 (p<0.001) and r=0.57 (p<0.001), respectively. Of the 592 tumors, ultrasound under-measured by more than 2 cm a total of 62 tumors vs 28 by MRI. In contrast, MRI over-measured by more than 2 cm a total of 69 tumors vs 20 by US. For tumors smaller than 5 cm on surgical pathology, US correctly predicted 550/559 tumors, and MRI predicted 506/559. For tumors greater than 5 cm on surgical pathology, US accurately predicted 5/33, while MRI predicted 14/33.

Discussion: While neither modality demonstrated strong correlation with surgical pathology, US tended to under-measure tumor size while MRI tended to over-measure. MRI was more concordant with pathology for lesions > 5 cm, whereas US was more sensitive for lesions ≤ 5 cm.

Mental Health/ Psychiatry

Outcomes following traumatic injury in patients with preexisting psychiatric illness <u>Erika Falsgraf</u>¹, Kenji Inaba MD^{1,2}, Amory de Roulet¹, Elizabeth Benjamin MD^{1,2}, Lydia Lam MD^{1,2}, Kazuhide Matsushima MD^{1,2}, Aaron Strumwasser MD^{1,2}, Demetrios Demetriades MD PhD^{1,2} ¹Keck School of Medicine of the University of Southern California ²Division of Acute Care Surgery and Surgical Critical Care, LAC+USC Medical Center

Background: Patients with psychiatric illness have been shown to experience higher rates of traumatic injury. The objective of this study was to examine the association between psychiatric comorbidity and outcomes following traumatic injury.

Methods: This was a retrospective study of trauma patients admitted to LAC+USC Medical Center between January 2008 and March 2015. Trauma patients with psychiatric diagnoses were identified using ICD-9 diagnosis codes. Univariate and multivariate logistic regression models were then built to identify associations between psychiatric comorbidity and outcomes in patients with traumatic injury. Results: A total of 22,783 patients were identified. Of these, 2,982 (13.1%) had a documented psychiatric comorbidity. Patients with psychiatric illness were significantly less likely to undergo acute surgical intervention within 6 hours (adjusted odds ratio [AOR], 0.64; p<0.001) and no significant difference in mortality following acute surgical intervention was noted (AOR, 0.23; p = 0.09). Overall mortality was similar in both groups (AOR, 0.76; p = 0.11). Psychiatric illness was associated with a significantly higher likelihood of developing complications (AOR, 1.91; p<0.001). Patients with psychiatric illness had significantly longer hospital lengths of stay (21.2 days vs. 8.4 days, p<0.001), particularly those with diagnoses of bipolar disorder, schizophrenia, and substance use disorder (30.5 days, 31.8 days, 22.9 days respectively; p<0.001 for all subgroups). No significant difference in ICU lengths of stay was noted between the two groups. (6.5 days vs. 6.2 days, p = 0.53). Conclusions: Patients with psychiatric illness who experienced traumatic injury had lower rates of acute surgical intervention, higher complication rates, and longer hospital lengths of stay. Further studies are needed to better characterize the causative factors underlying these associations.

Participant-Informant relationship affects quality of life ratings in incipient and clinical Alzheimer's disease

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Background: Clinical trials in incipient and clinical Alzheimer's Disease (AD) typically include informantreported outcomes, since cognitive impairment may limit participant reliability. Informant reports in AD dementia may be modified by the nature of the participant-informant relationship. However, the effect of such relationships at pre-dementia stages remains uncertain. We aimed to clarify how the participant-informant relationship affects informant reports of quality of life (QOL), functional abilities, and behavioral symptoms in people with normal cognition (NC), mild cognitive impairment (MCI), and AD dementia.

Methods: We analyzed cross-sectional data from an ongoing study at the Easton Center for Alzheimer's

Disease Research at UCLA. Participants with NC (n=100), MCI (amnestic n=125, nonamnestic n=61), and AD (n=113) were subdivided by participant-informant relationship (spouse vs. non-spouse). We examined group differences in the Quality of Life-Alzheimer's Disease (QOL-AD) scale, Functional Activities Questionnaire (FAQ), and Neuropsychiatric Inventory (NPI). Multiple regression analyses were used to identify associations between informant relationship, demographics, participant Mini-Mental Status Exam (MMSE) scores, and self-rated informant QOL with informant ratings of: 1) participant QOL, 2) FAQ, and 3) NPI.

Results: After adjusting for demographics, MMSE, and self-rated informant QOL, spouses reported higher participant QOL than non-spouses in the MCI (p=0.003) and AD (p=0.04) groups. Within the MCI group, spouse informants rated QOL higher than non-spouses for participants with amnestic MCI (p<0.001). There were no differences in informant QOL ratings for participants with nonamnestic MCI or NC, or on the FAQ or NPI in any of the groups.

Conclusions: The participant-informant relationship may modulate responses on subjective measures like the QOL-AD in incipient and clinical AD. Analyses of clinical trials that use informant measures may need to address these effects, which persist after adjusting for demographics and MMSE.

Expert Perspectives On Elder Abuse Among People With Dementia Kellie Spector, Medical Student, Annie Nguyen, PhD, MPH

Goal: This study aims to explore the relationship between types of elder abuse and stages of dementia based on expert perspectives. Secondarily, this study will investigate challenges in detecting abuse in people with dementia and identify opportunities for physicians to become involved. **Methods:** Telephone interviews were conducted with elder abuse experts: prosecutors (n=4), geriatricians (n=3), and Adult Protective Services (APS) Workers (n=2). A uniform script was read to all participants, responses were audio recorded and transcribed, and personal identifiers were removed. Transcriptions were analyzed for emergent themes using a data-driven thematic coding scheme. **Results:** Interviewees estimated that 30-80% of abuse cases involve people with dementia. Cooccurrence of abuse types and risk for abuse was said to increase with worsening dementia. Financial abuse was identified by most participants as being more common in the earlier stages. Family members and caregivers were mentioned most often as the perpetrators of all forms of abuse. Challenges to investigation include difficulty assessing reliability of reports from people with dementia and some with more advanced stages are unaware or unable to communicate about the abuse and lack ability to consent to investigations. Many participants said there needs to be more general awareness of elder abuse so that victims can get help before their situation worsens. Participants stated that clinicians can play an important role in detecting abuse by being more active in screening for abuse, trusting their professional judgment of suspicions, and conducting more capacity assessments.

Conclusions: Investigating elder abuse in people with dementia may be challenging and special attention needs to be paid to this population. They may be particularly vulnerable to financial abuse in the earlier stages of dementia. Clinicians may play an important role by being more active in screening for abuse and for dementia.

Rapid Assessment of Pediatric Psychological Trauma

Joshua Tiao, Dr. Jeffrey Sugar, Department of Psychiatry, Keck School of Medicine

Introduction: The incidence of psychological trauma affecting children in the inner city is very high. For many of these families, the Emergency Room is their primary source of healthcare, so it is imperative that the medical staff can rapidly identify past or current psychological traumas that have affected these children. We have developed and are testing the Rapid Assessment of Pediatric Psychological Trauma (RAPPT) Survey in order to provide an effective tool to screen children for history of psychological trauma.

Methods: The RAPPT survey was developed using previously validated questions as well as novel questions. We are also testing whether parental responses to the same survey significantly differ from their children's responses in pediatric patients that have suffered psychological trauma. Surveys are distributed to both the patient and parent in the LAC+USC Emergency Room, but are taken while separated. If either the patient or parent indicates trauma has occurred, follow-up questions are asked to determine the validity and extent of the trauma.

Results: Data is still being collected while this abstract is being written. However, previously collected data indicated that number of trauma types experienced correlated with increased functional impairment. The number of questions patients chose to skip or pass also correlated with increased functional impairment. The data currently being collected supports these previous data trends, but not enough samples of parental surveys have been collected to analyze differences in answering the survey between the child and parent.

Conclusions: Since data has not yet been completely collected, it is too early to draw conclusions. However, previously collected data suggests that RAPPT is an effective tool for screening trauma in pediatric patients. Patients that reported trauma or chose to pass on questions had higher rates of functional impairment. We suspect that this functional impairment is related to the serious long-term consequences reported in adults who retrospectively report childhood trauma.

Mongolian Women's Experiences of Mental Health During Pregnancy and After Childbirth

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Background: Postpartum depression (PPD) is defined as depression occurring during pregnancy or within 4-6 weeks after childbirth. Understanding the culture-specific and individual aspects of PPD is critical in promoting the health of mothers, children, and families. Little information exists, however, on the ways in which PPD manifests in the Mongolian cultural context. This project aims to explore how postpartum Mongolian women experience PPD and how patients and health care providers understand, identify and treat PPD.

Methods: We conducted 3 interviews and 3 focus group discussions (FGDs) with health care providers at the Mongolian National Centre for Maternal and Child Health (N=16) in order to explore the following domains in the context of PPD: 1) awareness and views about etiology 2) clinical experience and the

impact on the patient 3) lay perspectives 4) recognition, treatment, and availability of services. Transcripts of the interviews and FGDs were transcribed and analyzed for emergent themes. **Findings:** All providers were aware of PPD, though none reported having had substantial experience working with PPD patients. Views regarding etiology ranged from unplanned pregnancy and breastfeeding difficulty to volatile emotions and family conflict, which all providers mentioned as central to PPD's etiology. When asked about symptoms, most providers focused on more observable symptoms such as crying, whereas fewer providers mentioned less observable symptoms such as anxiety. Though providers had different ideas about how women seek help for PPD, they all believed that the best way to recognize and treat PPD is to talk with women and learn about their lives.

Interpretation: Results suggest that providers have limited knowledge of PPD and minimal experience working with PPD patients. In addition, there appears to be no unified system in place for identifying and treating PPD. Thus, PPD may go unnoticed, and many women experiencing PPD may not recognize or seek help for their condition. Hence, a need exists for the following: a system to identify and treat PPD, more research about how Mongolian women experience PPD, and education of patients and providers about its etiology, symptoms, and treatment.

Recipient Hospital Responsibilities: EMTALA Citations for Deficiencies Related to Psychiatric Emergencies, 2005-2014

Bridgette Wamakima, Sophie Terp, MD, MPH, Michael Menchine, MD, MPH

Background: Under the Emergency Medical Treatment and Active Labor Act (EMTALA), recipient hospitals may not refuse to accept appropriate transfer of an individual who requires specialized capabilities if the hospital has capacity to provide treatment. In 2003, the Center for Medicare and Medicaid Services (CMS) stated that EMTALA applys to patients with psychiatric conditions. In 2009, CMS adopted changes to the regulations governing EMTALA regulations with the Inpatient Prospective Payment System (IPPS) Final Rule stating that if a patient with an unstable condition is admitted as an inpatient, EMTALA obligations ends, and receiving hospitals, including psychiatric facilities, are no longer obligated to accept inpatients in transfer.

Objective: To describe trends of citations for EMTALA deficiencies due to recipient hospital responsibilities related to psychiatric emergencies following the 2009 IPPS Final Rule. **Methods:** A list of all EMTALA citations 2005 to 2014 was obtained directly from CMS. Citations were coded according to the service that was alleged to be deficient and deficiency type Citations related to psychiatric emergencies <u>with</u> a CMS deficiency tag 2411 indicating violation for recipient hospital

responsibilities are described.

Results: Of 355 EMTALA citations related to psychiatric emergencies during the study period, 82 (23%) were related to recipient hospital responsibilities. From 2005 to 2008 there were an average of 11 citations annually, compared with an average of 6 per year from 2009 to 2014. Citations for recipient hospital responsibilities specifically accounted for 44 (29%) of 154 citations for psychiatric emergencies from 2005 to 2008, compared with 38 (19%) of 201 from 2009 to 2014. Three citations resulted in termination of CMS provider agreements and facility closure.

Conclusion: EMTALA citations related to recipient hospital responsibilities related to psychiatric emergencies decreased after the 2009 IPPS Final Rule. Whether this trend represents improved care for

psychiatric emergencies, improved EMTALA compliance, reduced requirements related to the 2009 IPPS Final Rule, or CMS enforcement fatigue remains to be determined.

Emergent Medication Administration and Physical Restraint Use in Pediatric Psychiatric Patients <u>Cassandra Wang BS</u>, Ilene Claudius MD, Y. Liza Kearl MD, Genevieve Santillanes MD, Department of Emergency Medicine, Keck School of Medicine

Background: Despite the recognized necessity of chemical and physical restraints on children and adolescents in emergency departments (ED), little has been published on their use. Our objective was to evaluate pediatric patients who demonstrated aggressive behavior or attempted elopement, resulting in the activation of the ED's "Code Gold" emergency response team.

Methods: This is a retrospective chart review of all patients in one pediatric emergency department (ED) with a Code Gold team activation. Medical records were reviewed for: involvement of social services, psychiatric/medication history, medications in the ED, non-pharmaceutical de-escalation attempts, use of physical restraints, adverse events, disposition, and final diagnosis.

Results: Code Gold Team activations were identified in 31 patients (mean age 14.3 years, 45.2% female). Most patients received one activation, four patients required two, and two patients required four. The average patient length of stay was 24 hours and 22 minutes (range: 1 hour 38 minutes to 144 hours 35 minutes), and half of patients had their first Code Gold activation within the first hour. During the Code Gold, 21 patients (74.2%) were given a medication; six received olanzapine, ten received haloperidol, and seven received a benzodiazepine with or without haloperidol. Five patients were documented to be sedated following medication, and the only adverse event was one case of rhabodomyolysis. Restraints were placed in 87.1% of cases. An attempt at verbal de-escalation was documented in 53% with oral medications offered prior to the activation in one patient.

Conclusions: The first hour of a patient's visit to the ED is a common time for agitation and elopement attempts. If the situation allows, early verbal, environmental, and chemical de-escalation should be attempted. However, in our experience, chemical restraint seems to be a safe alternative in a pediatric population when other forms of de-escalation are not successful.

Physician Attitudes on Mental Health in Santa Barbara, CA Miriam Winthrop, David Baron, DO, MSEd. Dept. of Psychiatry, Keck School of Medicine

Purpose: In recent years, numerous studies have found that non-psychiatrist physicians do not sufficiently recognize mental illness in patients and that such conditions are undertreated. However, there is a lack of research that explores physicians' feelings about their own responsibility to detect and manage patients' mental illness. This study was an exploratory survey of attitudes regarding patient mental health among non-psychiatrist physicians in Santa Barbara, CA. The goal of the study was to gain insight into the spectrum of physician attitudes and investigate the potential relationship between attitude and other physician characteristics. We hypothesized that physician perspectives on patient mental health would vary based on the physician's clinical specialty, practice setting, and the typical amount of interaction between the patient and the physician.

Methods: Participants completed a 14-question self-administered online survey. The study population

included 57 physicians in 19 different specialties. Responses were statistically analyzed using general linear model and non-parametric analysis to examine for potential relationships between demographic characteristics and attitudes.

Results: We found that physician attitudes about patient mental health varied widely. However, there were no statistically significant relationships between physician attitudes and any of the factors assessed.

Conclusion: We found no pattern linking physicians' attitudes with characteristics such as clinical specialty, practice setting, or physicians' typical amount of interaction with patients. While these results do not support our original hypothesis, they are intriguing. The broad and seemingly random variation in physician attitudes may indicate inconsistent mental health training among non-psychiatrist physicians or it may reflect the personal biases of the physicians surveyed. Understanding the factors that influence physician attitudes should remain the focus of further research, as greater insight may provide solutions to the under-treatment of mental illness.

NEUROLOGY

Comparing Endoscopic Third Ventriculostomy and Ventriculoperitoneal Shunts in the Treatment of Chiari 1 Malformations Secondary to Hydrocephalus <u>Apoorva Ananth</u>, Edward Melamed, Kevin Artiga, Mark Krieger M.D.

Introduction: Ventriculoperitoneal shunts (VPS) are commonly used for treating hydrocephalus, but in the last fifteen years endoscopic third ventriculostomy (ETV) has emerged as a viable, less invasive option. Currently, there is a paucity of work investigating the efficacy of VPS and ETV in the treatment of Chiari I malformations secondary to hydrocephalus. This project seeks to determine whether ETV or VPS might play a role in reducing tonsilar descent and syringomyelia, as well as the rate of complications such as post-operative infection, intracranial hemorrhage, and CSF leak.

Methods: This is a retrospective cohort study involving participants who received either VPS or ETV at Children's Hospital Los Angeles (CHLA) between 2000-2015.

Results: Data collection has been completed, but our group is working on the final analysis. 47 patients were identified, 22 male and 25 female. Average age at the time of first intervention was 6.1 +/- 6.1 years. Indications for treatment were elevated intracranial pressure (n=9), hydrocephalus (n=27), and the presence of a syrinx (n=11). Mean follow up was 5.9 +/- 3.7 years. Average tonsilar descent at first intervention was 9.2 +/- 2.6 mm. Patients who received ETV were more likely to have radiological findings of aqueductal stenosis (p < 0.01) and third ventriculomegaly (p < 0.05), whereas patients who received VPS were more likely to have a syrinx (p < 0.01) and trended towards having basilar invagination (p = 0.07).

Conclusion: Until data analysis is finalized, no definite conclusions can be made. From the data gathered so far, it appears that treatment of hydrocephalus and Chiari 1 malformations with VPS may demonstrate longer "survival" (ie not requiring revision or alternate treatment), but might also carry an increased risk of post-operative infections.

Preventable Complications in Epilepsy Admissions, the "Weekend Effect"

Lianne Ho, Timothy Wen, Steve Sirot, Alimohammad Moalem, Daniel Kramer, MD, Arun Amar, MD, William Mack, MD, Charles Liu, MD, PhD, Department of Neurological Surgery, KSOM

Background: In epilepsy, worse in-hospital outcomes and prolonged length of stay due to preventable causes, such as nationally identified "hospital acquired complications" (HAC), contribute significantly to the impact on patients and society. Weekend admissions have generally been found to have poorer outcomes compared to weekday admissions with increased rates of preventable complications. This study aims to assess the impact of weekend admission on HACs and mortality in the epileptic population.

Methods: Patients with epilepsy were selected from the 2000-2010 Nationwide Inpatient Sample (NIS). Poisson multivariate regression analyses assessed the effect of weekend admission on HACs and mortality. Secondary analyses assessed length of stay (LOS) and total adjusted charges for weekend admissions compared to the 50th percentile.

Results: There were 12,997,181 admissions for epilepsy with 10,106,152 (78%) weekday, 2,891,019 (22%) weekend, and 10 (<0.1%) missing admissions. Weekend epileptic admissions saw a 10% increased

likelihood of both HACs (RR=1.10,[1.09,1.11],p<0.01) and mortality (RR=1.10,[1.09,1.11],p<0.01) compared to their weekday counterparts. Weekend admissions for epilepsy also showed a small decrease in both LOS (RR=0.98,[0.98,0.98],p<0.01) and total adjusted charges (RR=0.97,[0.97,0.97],p<0.01).

Conclusion: Prior studies have shown that patients admitted on the weekends are usually associated with higher rates of adverse events and complications leading to higher costs and a longer hospital stay. Weekend admissions for epilepsy are associated with increased rates of HACs and mortality, however are also negatively associated with LOS and total charge, which may reflect the higher mortality rates. Improved quality protocols should seek to recognize the weekend epileptic population as high risk, particularly with respect to preventable causes.

Multivariate modelling of socio-economic, hospital-level, and admission-type variables predictive of "never events" after craniotomy for meningiomas.

<u>Kathleen Rowland</u>, Timothy Wen, Gabriel Zada MD, MS, FAANS, William Mack MD, Division of Neurological Surgery

Background: The Nationwide Inpatient Sample was used to sample discharges 29836 of patients who underwent craniotomies for a meningioma from 2000 to 2011 at teaching, rural, and nonteaching community hospitals across the country to evaluate how patient-level, hospital-level, and admission-level characteristics affect the incidence rates of specific hospital-acquired complications often called "Never Events."

Methods: Records for patients diagnosed with a meningioma who had a craniotomy were extracted from the Nationwide Inpatient Sample by identifying records with specified ICD9 diagnosis and procedure codes. SAS 9.4 was then used to model four multivariate mixed linear models to determine if a model that included patient; patient and hospital characteristics; patient, hospital, and admission type; or patient, hospital, admission type and admission source fit the data best.

Results: 288 out of 29,836 patients who underwent craniotomy for a meningioma had a complication included as a Never Event. The most common event was a fall. Results showed that the fourth model, which evaluated patient age, sex, race, payer, and the presence of comorbidities; the hospital region, teaching status, and size; the type of admission, and the source of the admission, fit the data better than less inclusive models. Furthermore, ages between 35 and 74, hospital in the south, transfer from another hospital, and admission from a trauma center were statistically significant factors at the 0.001 level.

Conclusions: Analysis from 29,836 patients diagnosed with a meningioma who underwent a craniotomy from 2000 to 2011 showed that the most frequent event was a fall. The second most common event was much less likely at only 22 occurrences. This shows that while surgical complications are very rare, more attention needs to be placed on perioperative care to improve patient safety.

Quality of Acute Stroke Care at Primary Stroke Centers Before and After Certification in Comparison to Never-Certified Hospitals

Lily Vartanyan, Nerses Sanossian, MD

Background: Studies show that primary stroke center (PSC) certification is associated with improvements in stroke care and outcome. However, these improvements may reflect a higher baseline level of care delivery in hospitals eventually achieving certification. This study examines whether advancements in acute stroke care at PSCs are due to certification or factors intrinsic to the hospital. Methods: Data on acute stroke care was obtained from the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) trial. Participating sites include 32 Emergency Medical System agencies, 228 ambulances, and 55 acute receiving hospitals (community hospitals, regional centers, and tertiary academic centers) in Los Angeles County. Subjects were designated as being enrolled at one of three types of centers: PSC certified hospitals (PSCs), hospitals that were not PSCs at time of enrollment but would later become certified (pre-PSCs), and hospitals that would never be certified (non-PSCs). Metrics of acute stroke care quality were time to imaging, use of intravenous tPA, and time to treatment. **Results:** Of 1700 cases, 856 (50%) were at certified PSCs, 529 (31%) were at pre-PSCs, and 315 (19%) were at non-PSCs. Mean time in minutes from Emergency Department (ED) arrival to first brain scan was 33 at PSCs, 47 at pre-PSCs, and 49 at non-PSCs (p<0.001, Mann-Whitney). Of 1223 cerebral ischemia cases, rate of tPA utilization was 43% at PSCs, 27% at pre-PSCs, and 28% at non-PSCs (p<0.001, X²). Time in minutes from ED arrival to thrombolysis in treated cases was 71 at PSC, 98 at pre-PSC, and 95 at non-PSCs (p<0.001, Mann-Whitney). PSCs had improved time to imaging (p=0.014), percent tPA use (p<0.001), and time to treatment (p=0.003). There was no difference in time to imaging, percent tPA use, and time to treatment between pre-PSCs and non-PSCs.

Conclusions: The data suggests that stroke care at hospitals prior to PSC certification is equivalent to care at non-PSCs, and that improvements in stroke care are due to certification.

Migraine response to intravenous magnesium therapy

Fanny Xu, Anush Arkelyan, Olive Nworie, Lauren Green, Anne Csere, Paul-Henri Cesar, Soma Sahai-Srivastava. USC Department of Neurology.

Purpose: Although oral magnesium has been used as prophylaxis for migraines, there is limited information regarding intravenous magnesium therapy as an acute abortive agent. The purpose of this study is to determine the effectiveness of intravenous magnesium in acute migraine relief, and characterize the patients who benefit from the therapy.

Methods: Retrospective chart review of 179 migraine patients who were treated with intravenous magnesium therapy at an academic headache infusion center from February 2014 to December 2015, in which intravenous magnesium sulfate (2 g diluted with 50-100 cc of normal saline) was administered over 1-2 hours. Patient age, gender, and self-reported pain scores (1-10) before and after infusion were recorded, as well any additional intramuscular injections that were administered for refractory pain or nausea.

Results: Of the 179 patients, the majority were female (n=135). The mean age was 45.8 ± 16.0 and the mean pre-treatment pain score was 5.57 ± 2.37 . 68 patients received intravenous magnesium only, and 111 received additional intramuscular medications after the infusion. Overall, there was a significant reduction in pain score from 5.57 ± 2.37 to 3.50 ± 2.71 (P<0.001) after intravenous therapy, with 98 (54.7%) patients experiencing a decrease of ≥ 2 in pain score, and 35 (19.6%) with a decrease of ≥ 4 . In patients who received intravenous magnesium only, pain score decreased from 4.99 ± 2.48 to 2.94 ± 2.50 (P<0.001), with 35 (51.5%) experiencing a decrease of ≥ 2 , and 10 (14.7%) experiencing a decrease of ≥ 4 . Patients with a pain reduction of ≥ 4 had a higher mean age of 50.9 ± 15.3 (P=0.037) and a higher pre-treatment pain score of 6.81 ± 1.98 (P=0.002). Response to therapy was not related to gender. **Conclusion:** Intravenous magnesium, with or without intramuscular medications, can result in significant pain relief for a subset of migraine patients. Our study suggests that the therapy is more likely to be beneficial for older patients with more severe headaches.

Exercise in the Community Setting for People with Parkinson's Disease: A 7-Year Demonstration Program 2010-2016

<u>Jason S. Chen, Medical Student</u>, Sarah Ingersoll, Clinical Assistant Professor of Neurology, Michael Jakowec, Associate Professor of Neurology

Background/ Purpose/ Goal/ Hypothesis: It is well established that people with Parkinson's disease (PD) are less active than their able-bodied counterparts, despite the fact that exercise has particular benefits for this population. In response to interest from the local PD community, the "5K Training Team" exercise program was established in 2010. The program has grown in popularity and enters its 7th year. "The challenge...is not to figure out which dose of physical activity to prescribe, but rather how to get more people to adopt the actions that researchers know work," (National Academy of Medicine). **Methods:** This community-based program emphasizes traditional team building along with principles of social cognitive theory. Modeling and social persuasion plus training for a goal race are core program components. This program is free to participants. Each weekly session, which is led by a professional coach, features tai chi-based "looseners," an aerobic walk/jog, and a light lunch. The season culminates in a chip-timed community footrace.

Results: Attendance has grown year-over-year. Numerous anecdotal reports, primarily photographic and video, attest to the appeal of this program. A recent electronic survey indicates that "socializing with other members of the team" has the most value for long-term participants with PD.

Conclusions: Participants respond to a team that involves several aspects including an engaging coach, a common goal, sociable teammates, and a shared experience. Attendance records demonstrate that this team-oriented program successfully attracts and retains participants year after year. This approach may serve as a model for community exercise programs that promote the health and wellbeing of individuals with PD.

ONCOLOGY

Hospital acquired conditions in transsphenoidal pituitary tumor surgery: the impact of age, comorbidities, and volume

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Introduction: The Centers of Medicare and Medicaid defined eleven hospital acquired conditions (HACs) as high-cost and preventable outcomes for which hospital costs are not reimbursed. Transsphenoidal surgery (TSS) is the mainstay surgical treatment for pituitary tumors. The Nationwide Inpatient Sample (NIS) a national database was leveraged to assess the effect of age, comorbidities, and hospital procedure volume on HACs in TSS patients with pituitary tumors.

Methods: Patients with pituitary tumors and TSS between 2000 and 2010 in NIS were selected. Multivariable Poisson regression evaluated patient and hospital demographics predictive for HACs. Secondary analysis evaluated effect of HAC occurrence on length of stay (LOS) and hospital charges. Results: 81,321 patients were identified with pituitary tumors and TSS, of which 171 (0.2%) experienced HACs. Patients seen at high-volume hospitals (>3 cases/year) were associated with lower risk of HAC (RR=0.38,[0.25,0.57],p<0.01). Increasing number of documented comorbidities was associated with 2.5 to 5.3-fold increasing HAC rates (1 or \geq 2 comorbidities, respectively, p<0.05). Older patients were associated with a 2.1 to 4.4-fold increased likelihood of HAC (66-80 years, RR=2.10,[1.22,3.61],p<0.01; 80+ years, RR=4.42, [1.9,10.27], p<0.01). Occurrence of HAC was associated with >90th percentile LOS (RR= 4.28,[3.59,5.12],p<0.01) and >90th percentile hospital charges (RR=2.82,[2.22,3.58],p<0.01). **Conclusions:** When evaluating HACs at a national level, high volume centers were associated with decreased likelihood of HACs. Advanced age and the presence of comorbidities were associated with increased HAC rates. HAC occurrence was a predictor of increased costs and LOS. Risk adjustment according to underlying patient factors may be warranted when considering reimbursement for costs related to HACs after TSS. The protective effect of high volume centers on HACs may support the regionalization of care into pituitary centers of excellence.

Design and Implementation of a Radiation Oncology Quality of Life and Outcomes Database for Improving Documentation and Care for Head and Neck Cancer Patients Batth, S., <u>Chan C.</u>, Trakul, N., Department of Radiation Oncology, KSOM

Goals: Analysis of electronic medical record data is often limited by its retrospective nature and the significant resources it requires. Thus, we have designed and implemented a web-based, electronic data capture (EDC) system for head and neck cancer patients receiving radiation therapy that analyzes outcomes prospectively, enhances the quality of clinical information recorded, and generates regular quality improvement (QI) and patient safety reports.

Methods: A REDCap based EDC was deployed in February 2016 at a private NCCN Comprehensive Cancer Center and a safety net hospital. It records 757 data fields which cover patient demographics, history, patient reported outcomes (PRO), cancer characteristics and treatment parameters at new patient visits, on-treatment visits (OTV) and follow-up visits. Three PRO surveys (EQ5D-3L, EORTC QLQ- C30, EORTC QLQ H&N35) were collected prior to treatment, end of treatment, and at each follow-up visit. Common Toxicity Criteria for Adverse Events v4.0 is used for observer rated toxicity scoring at all encounters.

Results: The EDC system is used by four providers and three nurses in two clinics for 35 patient encounters. Compliant data was recorded for 2 of 3 new patients, 18 of 20 follow-up patients, and 15 of 15 OTV encounters (total compliance of 92%). Preliminary feedback suggests that the EDC has streamlined OTV and follow-up documentation for providers. Only 10 of 21 (48%) quality of life questionnaires were completed. Low computer literacy rates seen in the safety net hospital setting pose a significant challenge to compliance for PRO.

Conclusion: Designing and implementing a radiation oncology quality of life and outcomes database is feasible for head and neck cancer patients. Providers and nurses were compliant with its use. This EDC can reduce the resources required to analyze patient outcomes and can enhance patient safety and QI initiatives.

Long term efficacy of endoscopic therapy for high-grade dysplasia or intramucosal esophageal adenocarcinoma

<u>Alexa Chavez, BS</u>, Katrin Schwameis MD, Steven R. DeMeester MD, University of Southern California, Los Angeles, California

Introduction: Esophageal preservation with endoscopic resection (ER) and ablation is an option for patients with high grade dysplasia (HGD) or intramucosal adenocarcinoma (IMC). The aim of this study was to review the long-term outcome of endoscopic therapy.

Methods: A retrospective chart review was performed on our initial 40 patients who had endoscopic therapy. Complete resolution of intestinal metaplasia (CRIM) was defined as two consecutive sets of endoscopic biopsies without intestinal metaplasia.

Results: There were 33 males/7 females with a median age of 66 years (44-83). Initial pathology was HGD in 22 and IMC in 18 patients. Median follow-up was 82.2 months. Four patients had an esophagectomy for persistent disease. In the remaining 36 patients 70 ER and 111 ablations were performed with ER alone in 4, ablation alone in 7 and both in 25 patients (69.4%). CRIM was achieved in 30 patients (83.3%) at a median of 21.1 months. In 18 patients (60%) CRIM was maintained, while in 12 patients there was recurrence at a median of 13.9 months. Treatment for recurrence was follow-up (n=1) or additional endotherapy (n=11) leading to CRIM again in 10 patients (83.3%). Three patients had additional recurrences. A fundoplication was performed in 16 patients. No patient died from esophageal cancer. Kaplan-Meier survival was 75% at 5 years and 66.7% at 10 years. **Conclusions:** Endotherapy is effective for HGD and IMC but recurrence is common. Most recurrences can be treated endoscopically. Endotherapy should be considered in all patients with HGD or intramucosal adenocarcinoma.

Esophageal Adenocarcinoma Stage III: Survival based on pathological response to neoadjuvant treatment.

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Background: Neoadjuvant chemo- and chemoradiotherapy (CTX and CRT) are considered the gold standard in the treatment of locally advanced adenocarcinomas of the distal esophagus (EAC) prior to surgical resection. The degree of pathological response to neoadjuvant treatment is thought to be a major prognostic factor for survival after surgical resection, however limited data exists. **Aim of the study:** To compare the survival of complete and incomplete responders to neoadjuvant chemo(radio)therapy in patients with stage III EAC. Furthermore, to determine the frequency of complete response in stage III disease.

Methods: A retrospective chart review was performed of all patients that underwent neoadjuvant therapy and esophagectomy for stage III EAC between 01/1999 and 08/2013. Demographic, clinical, histopathological and survival data were collected and analyzed. Patients were classified into complete (no residual tumor; pCR) versus incomplete responders (residual tumor; pIR) to neoadjuvant CTX/CRT based on the findings in the esophagectomy specimen.

Results: 101 EAC stage III patients (m:f=92:9) underwent esophagectomy at a mean age of 62.7 (26-84) years. 21.8% (n=22) and 78.2% (n=79) had received CXT and CRT, respectively. R0 resection was achieved in 95% (n=96). pCR and pIR was found in 19.8% (n=20) and 80.2% (n=81). Overall mean F/U time was 34.5 (0.2-172.9) months. The overall mean survival was 18.6 (0.2-111.8) months while it was 18.8 (0.2-111.8) and 17.5 (1.1-58.7) months for pIR and pCR, respectively (p=0.8). 3-year-survival in pIR and pCR was 35.5% and 52.9% respectively (p=0.18). Positive lymph node status (ypN+) was found in 54 patients (66.7%) of pIR group and none of the pCR patients. 3 year survival was 53.8% in ypN0 and 28.3% in ypN+ (p=0.02*).

Conclusion: A complete pathologic response of 20% was found in this series. Complete responders were found to have a trend toward better survival compared to incomplete responders at 3 year follow up. Residual lymph node status was a stronger prognostic factor than pathologic response with a significant survival benefit in node negative patients.

Well differentiated / dedifferentiated liposarcoma: Are patients at risk of developing a second cancer? <u>Eric E. Jung</u>, Shefali Chopra, Ann S. Hamilton, William W. Tseng

Keck School of Medicine; Department of Pathology; Department of Preventative Medicine; Department of Surgery, Section of Surgical Oncology

Background: Well differentiated / dedifferentiated (WD / DD) liposarcoma is one of the most common subtypes of soft tissue sarcomas. There are no known risk factors and a genetic predisposition has never been reported. We examined a case series of patients at our institution with WD / DD liposarcoma to determine the occurrence of a concurrent or subsequent second cancer, and also determined the risk of

second cancers among WD/DD liposarcoma cases included in the large, population-based National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database.

Methods: We selected all adult patients from 9 combined registries in the SEER database who were diagnosed with WD / DD liposarcoma between 1973-2012. Observed/expected (O/E) ratios of concurrent or subsequent primary malignancies were calculated by comparing to the age-adjusted cancer incidence in the general population using the multiple primary standardized incidence ratio session of SEER*stat software.

Results: 5 out of the 20 consecutive patients (25%) that were seen at our institution between 2014-2015 with WD / DD liposarcoma had a concurrent second cancer. Genetic testing was completed in 3 of these patients without identification of any known hereditary cancer syndromes. In the SEER database, among 1,845 patients diagnosed with WD / DD liposarcoma, 269 patients (14.6%) had 314 concurrent or subsequent second cancers with an O/E ratio of 1.33 (99% CI = 1.15-1.54). In 69 patients (3.7%), this event occurred within 2 years of the liposarcoma diagnosis with an O/E ratio of 1.81 (99% CI = 1.33-2.40). Significantly increased risks were seen for subsequent cancers of the digestive system, retroperitoneum, bones and joints, soft tissue, male genital organs, and kidney. **Conclusions:** In some patients with WD / DD liposarcoma, there appears to be an increased risk of

developing a second cancer compared to the general population. The etiology of this novel observation is unclear, however close screening for additional cancers may be indicated for these patients.

Skin Cancer Occurrence in Transplant Patients with Skin of Color vs. White Skin Igor Krivitskiy; Dr. Binh Ngo, Keck Department of Dermatology

Goal: Organ transplant patients face substantially increased rates of skin cancer due to their immunosuppressive regimens, with squamous cell carcinoma rates increasing 65-250x compared to the general population. However, several other risk factors for skin cancer impact rates, including fair skin, increasing age and cumulative sun exposure. Our study investigated the importance of skin color skin as a risk factor. Specifically, we compared the rates of basal cell carcinoma, squamous cell carcinoma and melanoma in white vs. non-white organ transplant patients.

Methods: A retrospective matched case-control study was performed, analyzing skin cancer rates, determined by comprehensive record review in lung, kidney and liver transplant recipients, occurring post-transplantation, 2005-2013 (n=1,436). Cases of white and non-white patients who developed skin cancer were matched with control patients who did not do so over that time duration in a 1:3 ratio; these rates were then compared based on patient skin color. We matched for factors including previous cancer history, family cancer history, and immunosuppressive regimen.

Results: Presently, our results are limited to analysis of lung transplant recipients (n=110). Of these, 21 of 110 patients or 19% developed skin cancer; 81% were white. Overall, 27% of White patients and 10% of Hispanic patients developed skin cancer; African-American and Asian patients had no cases. **Conclusions:** At this time, preliminary results suggest the high incidence of skin cancer associated with organ transplantation immune suppression is much more prominent in fair skinned individuals.

Correlation between age at diagnosis and survival in retinoblastoma Anna Ter-Zakarian, MS; Lihua Liu, Ph.D

Goal: Retinoblastoma (RB) is a rare cancer commonly developing in early childhood. The purpose of this study is to analyze overall survival patterns of RB based on ethnicity, age of diagnosis, and presenting stage to evaluate potential disparities in ocular outcomes. We hypothesize that due to limited access to primary and oncological care, children from minority populations who identify as Hispanic or Black ethnicity will have lower overall RB survival.

Methods: Population data was retrieved from the California Cancer Registry (CCR) of the California Department of Public Health, including information on RB demography, clinical presentation, and outcomes from 1988-2012. National data was collected from the SEER database from 2000-2012. Kaplan-Meier analysis was used to assess RB-specific mortality.

Results: Survival analyses performed from the SEER database of 994 patients found survival to be poorest among patients diagnosed between 1 to 4 years of age, with a mean survival rate at 5 years being 2.6% greater if diagnosed at 0-1 versus 1-4 years of age. Non-Hispanic Blacks diagnosed between 1-4 years of age had the greatest decline in survival by 5 years. Additional CCR database analysis of 831 patients revealed a decrease in 5-year-survival among all ethnicities if diagnosed at a later stage. However, Hispanics presented with the highest rate of undifferentiated tumors, as well as regional and remote RB metastases.

Conclusion: Patients with RB presenting at later stages have worse survival outcomes. Hispanic children in particular show an increased incidence of undifferentiated tumors and metastases. These findings provide an overview on tumor characteristics by age group and ethnicity, which may serve in developing survivorship guidelines and improved screening, monitoring and counseling protocols for RB patients.

Cisplatin and cetuximab treatment for metastatic cutaneous squamous cell carcinoma: A systematic review.

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Background: Cutaneous squamous cell carcinoma (cSCC) is the second most common form of skin cancer and metastasizes in 2% to 5% of cases.

Goal: Systematic evaluation of published cases of metastatic cSCC (mSCC) treated with cisplatin or cetuximab from 1989-2014 in order to assess the current management of this tumor.

Methods and Materials: An extensive literature search was performed to identify cases of mSCC treated with cisplatin or cetuximab. Patient demographics, tumor characteristics, response rates, and disease-free survivals were extracted.

Results: A total of 60 cases of mSCC treated with cisplatin and 9 cases treated with cetuximab reported in the literature from 1989-2014 were included in the analysis. Patients treated with cetuximab

obtained a complete response of 67%, an overall response of 78%, and a median disease-free survival of 25 months (range 3-48). Patients treated with cisplatin obtained a complete response of 22%, an overall response of 45%, and a median disease-free survival of 14.6 months (range 3-112). **Conclusion:** Cetuximab may be more effective than cisplatin in treating mSCC, though head-to-head, prospective clinical studies between the two drugs are needed to appropriately determine which is more efficacious due to the low number of reported cases in the literature. In addition, prospective tumor registries and randomized control trials should be developed in order to establish the ideal systemic regimen in cutaneous SCC.

Targeted Therapies for Human Retinoblastoma Cells Chela Wahl, Sunhye Lee, David Cobrinik

Purpose: Retinoblastoma is a pediatric ocular cancer that affects 1 in ~15,000 children from birth to ~5 year of age. The survival rate is high in developed countries though treatments are often associated with severe side effects including blindness and it can be fatal when identified late. Prominent expression of the p-53 regulator MDM2 and anti-apoptotic N-MYC in cone cell precursors renders them unusually susceptible to proliferation in the setting of pRB loss. Thus, we selected chemicals that inhibit such factors as N-MYC and MDM2, which are necessary for tumor initiation and proliferation. In this study, we aim to find more effective agents for retinoblastoma treatment and prevention.

Methods: Five retinoblastoma cell lines were treated with the chemicals (JQ1- BET inhibitor; C25 and FKA-SKP2 inhibitors; Nutlin-3a-MDM2 inhibitor; SU9516 and SNS032-CDK inhibitors) for 24 hrs at 37° C. Protein levels were assessed via Western Blot and RNA levels analyzed by quantitative reverse transcription PCR (qRTPCR). Cell numbers were counted after 4 days.

Results: JQ1 and Nutlin-3a effectively inhibited retinoblastoma cell proliferation and significantly decreased RNA and protein levels of N-MYC and MDM2 in a dose-dependent manner. SNS032 inhibited cell proliferation and decreased RNA level of N-MYC. Although FKA was a potent inhibitor of cell growth and resulted in decreased level of SKP2 and N-MYC, the high dosage required could lead to toxicity. C25 and SU9516 did not impair proliferation of the retinoblastoma cell lines.

Conclusions: JQ1, Nutlin-3a and SNS032 all inhibited cell growth. In addition, transcription and protein levels of factors responsible for tumorigenesis were decreased. Further tests on SNS032 will need to be conducted in order to determine toxicity. Taken together, this study reveals the possibility of finding novel agents targeting oncoproteins in retinoblastoma.

Differences in the Treatment and Outcomes of Functional vs. Non-Functional Neuroendocrine Tumors of the Pancreas

Caitlin Waters (Medical Student), Dr. Rick Selby (Advisor, Chair of Hepatobiliary Surgery at Keck)

Background: Functional pancreatic neuroendocrine tumors often present with distinct and bothersome symptoms such as diarrhea, flushing, ulcers, or hypoglycemia while non-functional pancreatic neuroendocrine tumors can present incidentally or with general constitutional symptoms. I suspect that these differences in presentation contribute to the earlier diagnosis of functional pancreatic neuroendocrine tumors and more efficient treatment and outcomes as well.

Methods: I will analyze the differences between functional and non-functional pancreatic neuroendocrine tumors with respect to of age of diagnosis, method of treatment, time until resection, and outcomes while controlling for tumor stage using data from Keck's own CAFÉ database of NETs. **Results**: I strongly suspect that functional tumors will be discovered earlier, treated more swiftly, treated more often with resection, and result in better outcomes than non-functional tumors. **Conclusions**: These results have the potential to highlight the way in which we differentially treat functional and non-functional pancreatic neuroendocrine tumors and may help us provide more efficient care to patients.

A Matched Pair Cohort Study of the Effect of Neoadjuvant Chemotherapy in Stage I-III Breast Cancer

Julie Sprunt, Dany Barrak, Elise Morocco, Elizabeth Pan, <u>Gloria Wu</u>, Lily Tung, Julie Wecsler, Akshara Singareeka Raghavendra, Omar Ragab, Eugene Chung, Debu Tripathy, Naomi Schechter, Christy Russell, Stephen Sener, Julie E. Lang

Introduction: The primary aim of this study was to evaluate whether neoadjuvant chemotherapy (NAC) was associated with use of breast conserving surgery (BCS) using a matched pair cohort design. We also sought to evaluate survival outcomes in the NAC versus surgery first cohort after controlling for relevant covariates.

Methods: We performed a retrospective matched pair cohort analysis, matching NAC and surgery first cases based on tumor stage, estrogen receptor (ER) and HER2 status. We included newly diagnosed stage I-III breast cancer patients treated at our institution between 2006-2013. For univariate analysis we used Chi squared and the Kaplan Meier method. For multivariate analysis we used the Cox proportional hazards model to evaluate association with overall survival (OS).

Results: Although the cohorts were generally well matched, the NAC cohort had a significantly larger proportion of node positive, PR negative, high grade, and triple negative cases. In patients who had surgery first (n = 110), 83 (75.5%) had a mastectomy and 27 (24.5%) had BCS. In patients who received NAC (n=141), 80 (56.7%) had a mastectomy and 63 (44.7%) had BCS. The mean OS in the NAC cohort was 73.3 months (versus 61.2 months for surgery first); median follow up was 79 months in NAC cohort (versus 69 months for surgery first). Of the patients who received NAC, 46.2% had a pathologic complete response (pCR). HER2 status correlated with pCR (OR 0.64, *p*=0.048, Cl 0.54-0.88).

On multivariable analysis, the variables associated with overall survival were use of NAC (HR 0.71, p= 0.035, CI 0.69-0.99), grade (HR 3.06, p=0.021, CI 2.69-4.13), stage (HR 2.8, p=0.006, CI 1.8-3.1), ER status (HR 0.58, p=0.032, CI 0.35-0.95), HER2 status (HR 3.0, p<0.0001, CI 2.82-4.77), and nodal status (HR 2.7, p=0.037, CI 1.51-5.98). pCR nor PR status nor use of adjuvant chemotherapy were associated with OS. **Discussion:** The use of NAC was associated with higher rates of BCS in this matched cohort analysis. Use of NAC was independently associated with improved OS, even after controlling for rates of pCR, patient, tumor and treatment variables.

Evaluating presence of intestinal metaplasia in endoscopic mucosal resections of patients with esophageal adenocarcinoma

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Background: Barrett esophagus, a premalignant lesion associated with gastroesophageal reflux disease, carries increased risk of esophageal adenocarcinoma. In the US, Barrett esophagus is defined as intestinal metaplasia: goblet cells in columnar epithelium-lined esophagus (CLE). It has been recently proposed that in the absence of intestinal metaplasia, non-intestinalized CLE may also advance to adenocarcinoma. We examined the presence of intestinal metaplasia in endoscopic mucosal resection (EMR) specimens of patients with esophageal dysplasia or adenocarcinoma.

Methods: Hematoxylin and eosin-stained sections were reviewed microscopically for composition of the surface epithelium adjacent to neoplasia.

Results: In 27 EMR cases, ten (37%) did not contain residual intestinal metaplasia. For nine patients, intestinal metaplasia was subsequently identified: four in prior biopsies, three in additional EMR specimens, and two from later esophagectomies. The one remaining patient had a 20-year history of Barrett esophagus, and in the EMR specimen, goblet cells were identified within neoplastic epithelium. **Conclusion:** These findings demonstrate the presence of residual intestinal metaplasia and sustain its role as a necessary precursor lesion for the development of esophageal adenocarcinoma. An observed absence of intestinal metaplasia may arise from dysplastic loss of goblet cells; additionally, an EMR sample may not represent the entire esophageal landscape. Since expansion of the definition for Barrett esophagus would impact the diagnosis and monitoring of the patient population, any modifications to these criteria should continue to be closely evaluated.

Early-onset gastric cancer: An advanced disease with poor prognostic features Jeanney Kang, Kais Rona, Katrin Schwameis, John Lipham

Background: Early-onset gastric cancer is a rare disease, which is often advanced upon diagnosis. Previous literature suggests distinct genetic, histologic, and clinical characteristics that distinguish this disease from conventional gastric cancer. The aim of our study was to ascertain the prognostic and clinical features of early-onset gastric cancer in comparison to that seen in the elderly population. **Methods:** A retrospective review of patients 45 years and younger diagnosed with gastric adenocarcinoma at our institutions between July 1995 and August 2012 was done. Patient characteristics, tumor biology, and clinical outcomes were analyzed. These parameters were also reviewed in gastric cancer patients older than 45 years within the same time period to serve as a comparison group.

Results: There were a total of 121 patients (72M, 49F) 45 years or younger diagnosed with gastric cancer included in the study. 121 patients (86M, 35F) older than 45 years with gastric cancer served as the control. In the young group (YG), 86.8% had advanced disease upon diagnosis (stage III N=31, stage IV N=74), while in the old group (OG) 57.9% (stage III N=31, stage IV N=39) was advanced (p < .001). The YG also had a higher incidence of poorly differentiated disease (95.9% vs. 74.4%, p < .001) and signet cell type (88.4% vs. 32.2%, p < .001). The median survival was 11.7 (range 8.4-15.1) months in the YG and

41.0 (range 16.5-65.4) months in the OG (p < .001). Three-year survival in the YG was 87.1% in stage I/II, 32.2% in stage III, and 6.9% in stage IV. When comparing the two groups by stage, there was no difference in survival in stage I/II (p = 0.718), stage III (p = 0.113), or stage IV (p = 0.653) disease. **Conclusion:** Early-onset gastric adenocarcinoma is a rare and deadly disease. Our study demonstrates that it is more advanced upon diagnosis and is associated with a higher frequency of poor differentiation and signet cell type. Median survival is also decreased in younger patients although overall survival by stage is similar.

Radiographic predictors of "Second-Look Surgery" in Pediatric Intracranial Germ Cell Tumors

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Introduction: The current management of children with intracranial germ cell tumors includes chemotherapy followed by radiation therapy. Residual disease identified on radiographic images often necessitates "second-look surgery" to evaluate for persistent neoplastic elements which were nonresponsive to the up-front chemotherapy. The present study aims to evaluate radiographic features present at the time of initial diagnosis that might predict tumor recurrence or persistence, requiring the need for second-look surgery.

Methods: An IRB-approved 15-year retrospective review was performed on all patients with intracranial germ cell tumors treated at a single institution under a standardized protocol. Radiographic variables of interest were tumor location, size, calcifications, cysts, heterogeneity of enhancement, surrounding edema, and restricted diffusion of the tumor at presentation. Primary outcomes included the need for second look surgery and tumor recurrence.

Results: Thirty-seven patients with the diagnosis of germinoma were identified. Six patients with germinoma (16%) required second look surgery. Surrounding edema was associated with tumor recurrence (p=.014) and the need for second look surgery (p=0.003) while the remaining radiographic predictors were not significantly associated.

Seventeen patients with non-germinoma intracranial germ cell tumors were identified, with seven patients requiring second-look surgery (41%). Among these seventeen patients, the absence of cysts was significantly associated with the need for second look surgery (p = .03).

Conclusions: In children with intracranial germ cell tumors, radiographic features present at the time of initial diagnosis have significant prognostic value in determining disease course. This information could prove valuable in counseling patients and their families, and might help direct therapy.

Use and timing of palliative care on children with multiple relapsed or refractory Acute Lymphoblastic Leukemia (ALL) in CHLA Weili Sun, Javier Sotelo

Background/Purpose/Goal/Hypothesis: Acute lymphoblastic leukemia (ALL) is the most common malignancy in childhood. With intensive chemotherapy, the cure rate for childhood leukemia is approximately 85-90%2. However, 10-15% of children with ALL will relapse, and the outcomes for these

patients are dismal3, especially in children with multiply relapsed or refractory disease4. The patients with relapsed disease are the patients could benefit from early palliative care referral for better symptom control and psychosocial support. However, there is no guideline or consistency about when to refer those patients to palliative consult in pediatric oncologist. The time of the referral varies depending on the primary oncologist, the stage of the patient condition, and the family's attitude toward to palliative care.

As with many other healthcare facilities, specific palliative care guidelines are inconsistent when it comes to children with relapsed or refractory at Children's Hospital Los Angeles. The purpose of this study was to see how often palliative care is referred, at what stage of disease are patients with ALL referred to palliative care and determine how long after was the patient on palliative care before the time of death. Our goal is to retrieve a baseline of how palliative care is being used at CHLA and potentially improve the usage of palliative care and determine on a future study if referring to palliative care at an earlier stage of disease prolongs or improves quality of life. We hypothesize the there is a delay to refer children with multiple relapsed or refractory ALL to palliative care service in pediatric leukemia/lymphoma service in CHLA.

Methods: This is a single institution, retrospective study about the utilization of palliative service in children with relapsed/refractory ALL. I have been collecting the data for the variables from the patient's electronic medical records.

Results: Data analyses are still ongoing at this moment

Summary/Conclusion: Data analyses are still ongoing and a summary and conclusion will be drawn soon

OPHTHALMOLOGY

Rates of Orbital Recurrence and Metastasis in Patients Diagnosed with Retinoblastoma Kaitlin Kogachi, BA; Kathleen McGovern, MS; Jesse Berry, MD; Department of Ophthalmology, KSOM

Background: Retinoblastoma (Rb) is a rare cancer that develops from immature cells of the retina, generally before 6 years of age. Treatment for patients who present with advanced stage Rb generally involves enucleation of the affected eye. However, other treatment options include radiation therapy, systemic chemotherapy, and local therapies. Orbital recurrence and systemic metastasis can be devastating, so early detection is essential during follow-up. Previous studies revealed conflicting results regarding the rates of orbital recurrence and metastasis in patients primarily treated with enucleation versus those treated with globe-salvaging therapies. The purpose is to characterize the rates of metastasis and orbital recurrence in Rb patients diagnosed and treated at Children's Hospital Los Angeles (CHLA).

Methods: The study involves a retrospective chart review at a single institution and includes 343 eyes in 294 patients diagnosed between January 1995 and August 2015. All eyes were classified as either group D or E according to the International Classification System for Intraocular Retinoblastoma. Kaplan-Meier survival analysis was performed to determine the prevalence of event-free cases, with an event being defined as an orbital recurrence or metastasis.

Results: There were 181 Group E eyes and 162 Group D eyes. Unilateral Rb patients were generally treated with enucleation, while bilateral Rb patients were treated with globe-salvaging therapies. One bilateral Rb patient had an orbital recurrence. One patient had a brain metastasis, and another had a bone marrow metastasis.

Conclusions: This is the first report to assess the rates of orbital recurrence and metastasis for patients diagnosed with Group D or E Rb and treated at CHLA. The results provide insight regarding the safety of treatment modalities and appropriate follow-up time. Further data is needed to assess the risks for orbital recurrence and/or metastasis in patients evaluated, treated, and managed by CHLA.

Ocular implant outcomes in patients with Retinoblastoma

Paul Lang, Jonathan Kim, M.D., Jesse Berry, M.D., Department of Ophthalmology, Keck School of Medicine of USC

Background: Enucleation of the eye is often the best treatment option for patients with advanced retinoblastoma. Following enucleation, orbital implants made of various materials, including porous (e.g. Medpor), non-porous (e.g. silicone), and autologous (e.g. dermis fat graft) help augment the volume of the orbit and allow proper fitting of an ocular prosthesis. Benefits of using each type vary, but the ultimate goal is to minimize complications, such as exposure, extrusion, inflammation, and/or infection. The purpose of this study is to identify risk factors associated with complications in the use of the porous Medpor implant.

Methods: Retrospective review of medical records from patients between the ages of 0 to 17 years of age who have had an orbital implant placed at CHLA between January 1, 2010 through July 1, 2015. Complications, including implant exposure and extrusion, were analyzed for association with risk factors such as implant type and size, and presence of chemotherapy or external beam radiation therapy, among others.

Results: 114 enucleations were identified; 103 were porous Medpor orbital implants, and of these, 19 (18.4%) resulted in complications that included implant exposure, implant extrusion, orbital hemorrhage, and orbital hematoma. Statistical work is still being done on the data, but at first glance, it seems that possible risk factors that may affect complication rates include age at enucleation, size of orbital implant, and presence and proximity of chemotherapy therapy to enucleation.

Conclusion: Definitive conclusions can not be made until statistical analysis is complete, but early age of enucleation, larger orbital implants, and a shorter time period between chemotherapy and enucleation on first impression seem to have an association with complications. Future goals include increasing the sample size for nonporous orbital implants to be able to compare risk factors for complications between porous and nonporous implants.

Preliminary Quantification of Retinal Vascular Changes in Patients with Dry Age Related Macular Degeneration (AMD)

Christopher Lau, Alice Y. Kim, Anoush Shahidzadeh MPH, Amir H. Kashani MD, PhD.

Background: Choroidal ischemia is well accepted as a causative factor for age-related macular degeneration (AMD) (Coleman 2013). Retinal changes in dry AMD have not been as extensively studied as choroidal changes. Decreased blood flow velocities have been observed in retinal arteries of patients with dry AMD (Burgansky-Eliash 2014), so this project attempts to quantify retinal vasculature changes utilizing spectral domain optical coherence tomography angiography (SD-OCTA).

Methods: Retrospective, cross-sectional study of retinal microvasculature in 32 eyes of 18 healthy controls and 14 eyes of 10 patients with dry AMD. A prototype SD-OCTA device (Cirrus, Carl Zeiss Meditec, Dublin, CA) and optical microangiography (OMAG) decorrelation algorithm were used to obtain 3x3 mm² images of the retinal vasculature over the fovea. Images were segmented to different layers of the retina to include the superficial and deep capillary plexuses, as well as a non-segmented retinal layer which included all vascular plexuses in one image. A MATLAB program was utilized to calculated indices of retinal microvascular density (vessel and skeleton density) and morphology (fractal dimension and vessel diameter index).SAS was used to calculate Spearman correlation values and to compare healthy and AMD eyes using the generalized estimating equations model.

Results: Spearman's rank test demonstrated a significant negative correlation in SD, VD, and FD in the superficial retina between healthy and AMD eyes (rho = -0.428, -0.457, and -0.455, respectively; *P* < 0.005). SD and VD remain negatively correlated with disease state in non-segmented images (rho = -0.561 and -0.400, respectively; *P* < 0.007). No significant correlations were observed in the deep retinal layer.

Conclusion: Significant differences in SD, VD, and FD can be quantified in superficial retinal OCTA images, and non-segmented OCTA images showed significant differences in SD and VD. In general, decreasing microvascular density was significantly correlated with dry AMD. SD-OCTA can be used to quantify changes in the density and morphology of the retinal vasculature in dry AMD.

Optical Coherence Topography and the Evaluation of Coat's Disease <u>Matthew Louie</u>, Dr. Thomas Lee, Department of Ophthalmology, CHLA

Goal: Coat's disease is a rare congenital disorder that is unilateral and often effects males. Though many studies have released a small number of cases of coats, most are described as case studies with the largest study out there involving less than 20 patients. Here we present a study to categorize both the presentation and demographic characteristics of over 59 patients with Coats disease, the treatment methods, and their various clinical outcomes in an effort to better describe the clinical approach to these rare pediatric cases.

Methods: Pediatric patients with coats disease (n=59)

Results: Pediatric patients with coats disease (n=59) were treated with a combination of photocoagulation and anti-VGF as well as OCT and fluorescing angiography to diagnose and treat the rare disorders. Patients were evaluated at CHLA and diagnosed via fundoycopic exam exam and fluorescein angiography with the use of ultrasound or OCT depending on the clinical examination.

Of the patients, nearly 98% had favorable outcomes based on follow-up visual acuity measurements following operation with photocoagulation. Nearly all of them where unilateral and mostly male, with a minority of females. Two cases were treated with anti-VGF drugs. None were associated with any other familial ophthalmologic disorder. Statistical analysis of results is still in process.

Conclusions: Data reaffirms the fact that Coat's disease is usually a unilateral disease that affects predominantly males with sub retinal characteristics of exudate, telangiectasia that result in retinal detachment. It shows that photocoagulation is a highly effective method of treatment that allow patients to have great improvement on visual acuity, and in cases of retinal neovascularization anti-VEGF shows to be an effectual treatment in combination.

Coronary Fibroatheroma Cap Remodeling in Patients on Statin Therapy: An Optical Coherence Tomography Study

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Goals: Plaque characteristics associated with a greater risk of plaque rupture include the presence of a thin cap (thin cap fibroatheromas, TCFAs), and the presence of macrophages. Observational data show that plaque rupture typically occurs in the upstream shoulder (proximal to the point of maximal stenosis). In this study, IV-OCT is used to calculate the fibrous cap surface area to quantify plaque remodeling and determine if the upstream shoulder displays high-risk features.

Results: Image analysis at a single time point shows that distal, middle, and proximal subsections of the plaque are not significantly different with respect to fibrous cap area and local inflammation level. At thin cap set-point <200 μ m, plaque area decreased an average of -1.05 mm² (p=.01). Subsegment area analysis shows the middle portion (point of maximal stenosis) and the upstream shoulder display mean decreases of -0.5705 mm² (p=.045) and -0.344 mm² (p=.021) respectively; the distal segment did not

significantly decrease. Local inflammation, measured by macrophage score, significantly decreased between baseline and follow-up only in the upstream shoulder of the plaque (p=0.041). **Summary:** This study shows that the upstream shoulder of atherosclerotic plaques is not characterized by elevated levels of local inflammation or a greater thin cap surface area (when measured by OCT); both characteristics that are positively correlated with a high rupture risk. These findings may be explained by methodological differences between this IV-OCT study and historical histological studies. Analysis of plaque remodeling between baseline and follow-up revealed a decrease in thin capped area in patients on statin. The overall decrease is likely due to significant reduction in surface area in the upstream (proximal) and middle sections of the plaque. Furthermore, a decrease in local inflammation is observed in the upstream shoulder of the plaque. The correlation between decreased area and inflammation may indirectly support the concept that high levels of inflammation contribute to degeneration of the fibrous cap.

ORTHOPEDICS

An Inducible Suicide Gene to Improve the Safety of Gene Therapy in Orthopedic Applications <u>Eric Arevalo</u>, Sofia Bougloukli, KSOM.

Goal/Background: One of the most significant challenges in orthopaedic surgery involves the non-union and inadequate bone formation of fractures. Gene therapy applications employing the transduction of stem cells with viral vectors that express BMP-2 (a bone-forming agent) have been proven effective in recent years. A major safety concern, however, is that transduced cells may migrate out of the site of the bone defect and cause toxicity and/or the formation of metastases. In light of this challenge, our current study aims to test the efficacy of Caspase 9, an inducible suicide gene, in promoting the apoptosis of transduced cells in a given host after desired bone formation is achieved.

Methods: Nude rats with 6cm femoral defects will be administered either human adipose or human bone marrow stem cells transduced with a GAL4-BMP2 (control) or a GAL4-BMP2-iCasp9 vector directly into the site of the bone defect. After a period of 4 weeks, bone formation will be assessed by x-ray and a dose of CID (the chemical inducer of Caspase-9) will be administered subcutaneously to all rats. To assess the survival rate of transduced cells in response to CID, expression of BMP-2 will be quantified by PCR.

Results: We expect that adequate bone formation will be achieved in all groups containing the BMP-2 vector. In rats carrying GAL4-BMP2-iCasp9 transduced cells, BMP-2 expression following administration of CID should be reduced by 95% or greater, indicating effective apoptosis of transduced cells. We expect that BMP-2 expression in groups with the GAL4-BMP2 (control) vector will be virtually unchanged after receiving CID due to the absence of the Caspase 9 suicide gene.

Conclusions: We hope to confirm the efficacy of a stem cell killing method that provides a safety mechanism for gene therapies involving virally-transduced progenitors. Such a method will be crucial as gene therapy applications are implemented in a clinical setting.

Movement Asymmetries During Single-Leg Loading Tasks in Young Athletes Following Recent Anterior Cruciate Ligament Reconstruction

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Objectives: The objective of this study was to examine the biomechanical differences between the operative and non-operative limb during common maneuvers in young athletes after ACL reconstruction.

Methods: This retrospective study included 22 adolescent subjects (68% female, 15.8 ± 1.7 years old) with recent unilateral ACL reconstruction (7.5 \pm 1.7 months since surgery). Three-dimensional kinematic and kinetic data were collected during a single-leg hop and deceleration task. Outcome measures were evaluated at initial foot contact and during the loading phase, defined as the interval between initial foot contact and maximum knee flexion of the planting limb. Intra-subject differences between operative and contralateral limbs were evaluated using paired t-tests.

Results: In the deceleration task, the operative limbs demonstrated significantly lower peak knee flexion moments, peak ankle dorsiflexion angle, and less power absorption at the knee. In the single-leg hop, hop distance was significantly shorter in the operative limb. Lower peak knee flexion, knee flexion-extension excursion, peak and average knee flexion moment, and power absorption at the knee were also observed in the operative limb. Additionally, the ankle of the operated limb exhibited more plantarflexion at initial contact. There were no significant differences in knee frontal plane variables. **Conclusions:** Asymmetries in sagittal plane shock absorption strategies seen at 7.5 ± 1.7 months after ACL reconstruction may reflect an attempt to offload the knee during dynamic single-leg tasks. These objective measures may indicate a patient's readiness, or lack of readiness, to return to sport.

Efficacy of Intraoperative, Preharvest Morphine Injection to Iliac Crest Graft Donor Sites on Long Term Pain and Quality of Life.

Faiz Kusumo, Sona Doshi, MD, Jack Berger, MD

Goal: While the iliac crest is a common harvest site for autologous bone grafts, many patients experience long term hip pain after undergoing iliac crest bone grafting. In some cases, pain at the donor site outweighs that at the recipient site. This forces the question of whether or not the iliac crest should continue to serve as a common harvest site, and if there is an intraoperative intervention that can reduce the procedure-associated morbidity in these patients. In this study, we investigated intraoperative, preharvest morphine injection as one such intervention.

Methods: Patients were selected from those who underwent iliac crest bone graft surgery at LA County Hospital from January 2010 to May 2015. Patients who met this criteria were contacted via telephone and administered a verbal questionnaire to assess long term pain and functional status. Results will be analyzed by comparing compiled data obtained from the questionnaire between each subset of treatment options: intraoperative morphine injection, local anesthetic injection, or no injection. We will use statistical analysis to compare these three categories based on incidence of pain, chronicity of pain, severity of pain, and degree of functional impairment following surgery.

Results: Data collection/analysis is still in progress. Results from data obtained thus far are inconclusive. Out of 16 eligible patients with completed questionnaires, 1 received intraoperative morphine, 2 received local anesthetic, and 13 had no injection noted on the operative note. Because of the relative lack of patients thus far in the morphine and local anesthetic categories, a prediction of the results cannot be made from preliminary data.

Conclusions: Once data collection/analysis is complete, the results will indicate whether or not intraoperative, preharvest morphine injection is a valuable intervention to reduce long term hip pain and improve quality of life for patients undergoing iliac crest bone grafts.

Complications Associated with Proximal Tibial Traction Pins Michael Stefl, MD, **Matthew Losli, BA**, Geoffrey Marecek, MD

Background: Skeletal traction provides pain relief and temporary stability in patients anticipating surgery for femoral, pelvic or acetabular fractures. Traction may be applied through a pin placed in the distal femur or proximal tibia. Each has advantages, disadvantages, and potential complications. Recent

literature suggests that distal femoral traction provides pain relief and is safe (Bumpass, Austin). However, data regarding proximal tibial traction pins (PTTP) is limited. The purpose of this study is to document complications associated with PTTP placement.

Methods: We identified patients with PTTP placement from 1/2013-12/2015 through review of departmental databases and by CPT code. We excluded patients under age 18, patients with open fractures and patients transferred from an outside hospital. Orthopaedic residents placed pins using a standard technique. Placement was verified with post-procedure radiographs, which were reviewed for the study to identify errors. Infections were defined as any wound requiring operative debridement or antibiotic therapy within one year after placement.

Results: PTTPs were placed in 194 patients. 172 patients (89%) had femoral fractures, 8 (4%) had pelvic fractures, 10 (5%) had acetabular fractures, and 4 (2%) had combinations of femoral/acetabular fractures. One pin (0.5%) was incorrectly placed and revised. One pin site infection was identified (0.5%), which was treated with pin removal, operative irrigation, debridement, and IV antibiotics. One DVT occurred in a limb with traction in place and was treated with pharmaceutical anticoagulation. One patient did have tibial nerve deficits from their mechanism of injury (gunshot wound). No other nerve injuries, vascular injuries, or infections were identified.

Conclusions: PTTP placement for skeletal traction is an uncomplicated and safe procedure. These pins can be placed safely after appropriate training and are an important treatment modality in high volume trauma centers. Additional studies to compare PTTPs to distal femur traction pins are warranted.

The Influence of Spine-Pelvis-Hip Mobility on Acetabular Component Position in Total Hip Arthroplasty

Lawrence D. Dorr, M.D., William Lundergan, M.D., Hiroyuki Ike, M.D., Yohei Yukizawa, M.D., <u>Rajan</u> <u>Murgai</u>

Background/Purpose/Goal/Hypothesis: Optimal cup position is essential to successful total hip arthroplasty. The goals of this study were to determine how mobility of the spine and pelvis affects cup position during postural change, what spinopelvic factors create risk for impingement complications, and which implant positions were favorable or create risk in patients with at risk spineopelvic constructs.

Methods: 95 consecutive patients with 100 total hip arthroplasties were prospectively measured with preoperative and postoperative lateral standing and sitting spine-pelvis-femur and pelvis x-rays. Additionally, 23 patients with acute or late dislocation/subluxation and 23 patients with 26 hips and 10 years follow up were measured.

Results: Restricted spinopelvic mobility, a pelvis fixed in posterior tilt during standing, and excessive posterior tilt in sitting were all found to put patients at an increased risk for impingement. It was determined that cup positions in patients with spinal imbalance need to have an inclination of 45°-50° and anteversion of 20-25°. A cup inclination of <35° and anteversion <15° creates a risk for impingement in all patients.

Summary/Conclusion: This data establishes the contribution of spinopelvic mobility to cup position during postural change after total hip arthroplasty. It indicates which patients are at risk for late

dislocation. Standing and sitting lateral spine-pelvis-hip-femur x-rays are recommended prior to total hip arthroplasty. These x-rays can also be used to evaluate patients with complications.

Retrospective Analysis of Pelvic Ring Injuries Managed Non-Operatively <u>Hardik Parikh</u>, Luke Nicholson, Geoffrey Marecek

Goal: Surgical indications for managing traumatic pelvic ring injuries with minimal displacement are not well defined in the literature. The goal of this study is to analyze the value of post-ambulatory pelvic radiographs in the management of lateral compression (LC) and anterior-posterior compression (APC) injuries treated according to the pre- and post-ambulatory pelvic radiograph algorithm. We hypothesize that post-ambulatory radiographs do not significantly aid the management of such injuries. Methods: Medical records of patients that presented to LAC+USC for traumatic pelvic ring injuries between 2012-2014 were retrospectively reviewed. Patients that met the inclusion criteria – ability to weight bear for post-ambulatory films and age over 18 years at the time of admission – were included. Patients who had post-ambulatory films over 6 weeks after the date of injury, concomitant acetabular fracture, traumatic brain injury, or operative management of pelvic ring injuries were excluded. CT scans of the injuries were analyzed to classify them according to the AO/OTA pelvic ring classification. Results: Preliminary data analysis revealed 85 patients that met the inclusion criteria. 15 OTA 61-A type fractures, 49 OTA 61-B type fractures, and 21 OTA 61-C type fractures were included. Post-ambulatory radiographs were obtained an average of 8.8 days post-injury in the inpatient setting. All patients received non-operative injury management with no change of initial management after review of the post-ambulatory radiographs. Of the 85 patients, 50 patients followed up in the outpatient setting at a mean of 12.3 weeks post-injury. Non-operative care was continued for all patients at the time of followup.

Conclusion: The use of post-ambulatory pelvic radiographs does not alter the treatment of pelvic ring injuries. Fluoroscopic examination under anesthesia may be a more appropriate tool to evaluate pelvic ring injuries with physical exam findings or fracture patterns suggestive of instability.

Lateral and Syndesmotic Ankle Sprains in a Division I College Football Team

Nima Mehran, MD, Chistos Photopoulos MD, Russ Romano Ma, ATC, Seth C Gamradt MD, <u>Santano</u> <u>Rosario BA</u>

Goal: Ankle sprains are frequent, debilitating injuries in college football. The purpose of this study is to determine the differences between the incidence of injury and timing of recovery from lateral ankle sprains and syndesmotic ankle sprains in a Division I college football team.

Methods: From 2003-2014, all ankle sprains documented by the certified athletic trainers at a single division I college football team were reviewed. A comparative multivariable analysis was performed between lateral and syndesmotic ankle sprains.

Results: Of the 1155 football players analyzed, there were 204 ankle sprains recorded in 172 players (14.89%). There were 121 lateral ankle sprains (59.31%) in 99 players, and 83 syndesmotic injuries (40.69%) in 73 players. However, syndesmotic injuries were more likely to occur in games (55.6% of injuries) than lateral ankle sprains (33.3%). Players with lateral ankle sprains missed an average of 5.18

days and 0.27 games, as compared to 13.35 days and 0.72 games missed in those with syndesmotic injuries. Players with lateral ankle sprains on NSAIDs missed an average of 3.65 days, as compared to 6.02 days (p=0.05) missed for those who were not. Players with syndesmotic injuries on NSAIDs missed an average of 11.48 days, compared to 14.35 days in players who were not (p=.17). Linebackers (n=24), offensive linemen (n=23) and defensive backs (n=21) sustained the greatest number of lateral ankle sprains, while syndesmotic injuries were most common in offensive linemen (n=22), wide receivers (n=14) and defensive backs (n=12).

Conclusion: There is a high incidence of ankle sprains in college football athletes. Syndesmotic ankle sprains more commonly occurred in games and resulted in increased time lost from participation when compared to lateral ankle sprains. Certain position groups, in particular offensive linemen, sustained more syndesmotic ankle sprains. There was a trend toward the use of NSAIDs facilitating earlier return to competition in players with both types of ankle sprains

Ambulation Post Soft Tissue Reconstruction of Tibial Fractures

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Background: The lower extremity is the most common trauma injury with over 300,000 annually. Tissue transfer is standard for open fracture coverage, but functional outcomes are unclear. This study examines ambulation post-reconstruction of open tibia fracture.

Methods: Retrospective review of 115 open tibia fractures with soft tissue reconstruction between July 2007 and March 2015 was performed then analyzed with chi square $p\leq 0.05$.

Results: Of 79 patients with 3 months follow-up, 61% achieved union (average 215 days) and 11 required bone graft. Among the patients with bony union, 70% returned to full weight-bearing ambulation, 24% required an assistive device, and 6% were wheelchair dependent (average highest ambulation at 270 days). Physical therapy initiation averaged 6 days postop and 7 months duration. Age >50 years and diabetes predicted non-ambulation. Postop glucose >100mg/dL demonstrated a dose-dependent increase in wheelchair dependence. Absence of concurrent ipsilateral and/or contralateral lower extremity fracture was associated with full weight-bearing ambulation, as was use of a local flap for coverage. Initiation of dangling prior to discharge was predictive of full ambulation, while delay of dangling beyond postop day 12 demonstrated dose-dependent increase in wheelchair dependence.
Demographic			
Gender	87% male		
Age	38 <u>+</u> 15 years		
ВМІ	28 <u>+</u> 8 kg/m ²		
Smokers	37%		
Follow-up	1 year (5 days – 6 years)		
Gustilo-Anderson Grade			
I	3 (3%)		
II	35 (30%)		
Illa	2 (2%)		
IIIb	57 (49%)		
IIIc	18 (16%)		
Definitive Fixation			
Plate and screw	42 (37%)		
Intramedullary nail	44 (38%)		
External fixator	29 (25%)		
Flap			
	35% gastrocnemius		
Local (58%)	62% soleus		
	3% anterior tibialis		
	36% latissimus		
	22% rectus abdominis		
Free (42%)	25% ALT		
	14% gracilis		
	3% other		

Conclusions: Following open lower extremity fracture, return of function was high. Use of a local tissue flap and early dangling protocol were associated with ambulation while diabetes and older age were associated with wheelchair dependence.

Postoperative complications in patients undergoing minimally invasive sacroiliac fusion <u>Kyle Schoell</u>, Zorica Buser PhD, Andre Jakoi MD, Martin Pham MD, Neil N. Patel MD, Patrick C. Hsieh MD, John C. Liu MD, Jeffrey C. Wang MD

Introduction: Minimally invasive sacroiliac (SI) joint fusion has become increasingly relevant as a treatment for sacroiliac joint pathology in recent years. Previous studies have found minimally invasive SI fusion to be an effective and safe treatment option for chronic SI joint pain. However, these studies have been primarily single center, case based, or manufacturer sponsored investigations, and as such their findings are limited to their sample populations. The aim of this study was to investigate the safety of minimally invasive SI fusion using a large nationwide sample group that more accurately represents the U.S. population as a whole.

Methods: Patients undergoing minimally invasive SI fusion from 2007-2014 were identified using the Pearl Diver (Pearl Diver Technologies; PA, USA) patient records database from the nationwide insurance provider Humana. Using ICD-9 diagnosis codes, data from patient records was systematically analyzed to reveal the incidence of post-operative complications.

Results: Data from 469 patients (305 female; 165 male) showed a substantial increase in the number of minimally invasive SI fusions performed from 2007-2014 [p<.05]. Among these patients, an overall complication rate of 13.2% was seen at 90 days post-op and 16.4% at 6 months. Incidence of specific complications were as follows: infection 30 days = 3.0%, 90 days = 3.6%, 6 months = 4.1%; pain 90 days = 2.6%, 6 months = 4.1%; UTI 90 days = 3.8%, 6 months = 4.9%; nerve pathology 90 days = 4.3%, 6 months = 6.2%. The incidence of novel lumbar pathology was 3.6% at 90 days post-op and 5.3% at 6 months. Males experienced diagnoses of novel lumbar pathology at higher rates than females at both 90 days (M=6.7%; F≤3.3%) and 6 months (M=9.1%; F≤3.3%) [p<.01].

Conclusion: The results of this study show that minimally invasive SI joint fusion may carry higher risks of complications than previously stated, including a possible association with the development of lumbar pathology. These findings should be carefully considered when deciding if surgical treatment is warranted for treatment of chronic SI joint pain.

PATIENT Education

Use of a low-literacy informed consent form in Spanish to improve the understanding of sterilization: a randomized controlled trial

<u>Katharine Ciesielski</u>, Hilary Eggers, Melissa Natavio MD, Dept of OB/GYN, LAC+USC Medical Center, University of California, Los Angeles, CA, USA

Objective: To assess whether Spanish-speaking women have a better understanding of the tubal sterilization process and procedure after reading the "standard" or "low literacy" version of the Spanish Medicaid Title XIX Sterilization Consent Form (SCF).

Methods: This randomized controlled trial included women who could speak and read in Spanish and were within 21-45 years of age. The participants were patients presenting to an OB/GYN Clinic in Los Angeles. They were surveyed on their socio-demographic status . then asked three questions to establish their health literacy. They were then randomized to receive the standard or low-literacy SCF in Spanish and asked 5 questions to assess their comprehension of the form.

Results: The results of surveys from 197 women are included in this study. Women in the low-literacy group (n=102) compared to women in the standard group (n=95) better understood the length of time required between signing the form and undergoing sterilization (16.3% difference between groups, P<0.05) and the permanence of sterilization (17.0% difference between groups, P<0.05). There was no significant difference between the two groups in the understanding that a patient can chose not to undergo sterilization after signing the form, that equally effective non-permanent contraceptive options are available or of when the form expires.

Conclusion: In this randomized controlled trial, our participants had a better understanding of when they can undergo sterilization and that tubal sterilization is permanent with low literacy version of the Spanish Medicaid Title XIX SCF when compared to the standard version.

Spanish-Speaking Patient Preference Between Standard and Low-Literacy Informed Consent Forms for Sterilization

<u>Hilary Eggers</u>, Katharine Ciesielski, Melissa Natavio MD, Dept of OB/GYN, LAC+USC Medical Center, University of California, Los Angeles, CA, USA

Goal: Many of the Spanish-speaking women at LAC+USC may lack a complete understanding of the process of tubal ligation and its irreversible effects. We believe part of this arises from the highly technical and difficult to understand Medicaid Title XIX Sterilization Consent Form (SCF). This study aims to address this problem by testing a new low-literacy SCF which can provide patients with a better understanding of this procedure and its implications.

Methods: Spanish-speaking, female patients between 21 and 45 years old were approached at the LAC+USC women's clinic. The purpose of the study was explained and a written consent form was signed by each participant. Participants were randomly assigned either the original SCF or our new low-literacy SCF. After reading the assigned SCF, questions addressing the form's content were asked. Participants were then asked to read the version of the form that they did not originally receive followed by a series of questions assessing form preference. All portions of the interview were conducted in Spanish. **Results:** 193 participants completed the survey. The difference in form preference was statistically significant with 144 (75%) study participants preferring the low literacy SCF, χ^2 (1,N=193)=24.44,

p<0.001. When rating the difficulty of the low-literacy SCF, 75% of patients found it very easy or easy, 22% average, and 3% difficult. For the original SCF, 62.5% found it very easy or easy, 29% average, and 8.5% difficult or very difficult. The difference in proportions between low-literacy and original SCF is significant, $\chi^2(4,N=193)=18.98$, p<001. The most common reason for preferring the low-literacy SCF was that it was more clear and easier to understand.

Summary/Conclusion: Participants surveyed showed a significant preference for the low-literacy SCF and found this form significantly clearer and easier to understand. Implementing low-literacy consent forms for various medical procedures may benefit the medical community at large.

Patient understanding of diagnosis of infection and prescription of antibiotics in the ED Shera Feinstein, Sanjay Arora, Chun Nok Lam

Goal: In the ED, a bacterial infection is one of the few diagnoses that results in a definitive and effective treatment. Medication compliance is critical in ensuring these patients do not return to the ED with the same issue. Therefore, patient understanding of a diagnosis of infection and prescription of antibiotics is an important factor in decreasing preventable ED visits as well as controlling the spread of infectious diseases.

Methods: Over a period of 2 months, patients were interviewed to evaluate their understanding of the treatment, diagnoses and discharge instructions they were given during their visit in the LAC + USC ED. For assessment of understanding of diagnoses and prescriptions, patients were asked to answer yes/no to a list of diagnoses (including "infection") and medications (including "antibiotic," "narcotic pain medication" and "non-narcotic pain medication"). Their responses were compared to their medical record and patient concordance was evaluated.

Results: Of the patients who were diagnosed with an infection, 71.8% [Confidence Interval TBD] correctly reported receiving a diagnosis of infection. Of the patients who received a prescription for antibiotics, concordance was 76.5% [CI TBD]. The following medications were evaluated as controls: narcotic pain medication (concordance = 69.6% [CI TBD]) and non-narcotic pain medication (concordance = 54.7% [CI TBD]).

Conclusions: While patient understanding of antibiotics is higher than that of pain medications, still 28.2% of the patients who received antibiotics seemingly did not understand. In order to ensure patient compliance, prevent unnecessary visits to the ED, and control the spread of infectious diseases, further research on why patient understanding is so low as well as new methods on how to increase this understanding must be considered.

Formalizing Communication in Discharge Planning

Natalie Hartman, William Archibald, Daniel Ayala, Khloe Frank, Ryan Gamlin, Alazar Haregu, Katia Johnston, Kelly O'Connor, Emily Gottenborg MD, Read Pierce MD

Introduction: Discharge from the hospital is a complex process, requiring effective communication. Suboptimal communication may contribute to delays in discharge, in turn causing patient dissatisfaction, provider frustration, and potential for iatrogenic harm. Checklists and role standardization are tools commonly employed in quality improvement (QI) efforts, and may improve communication about discharge.

Purpose: The intervention sought to create standardized roles, processes, and tools to enhance communication about discharge planning for an inpatient ward at an academic hospital.

Program Description: Eight medical students developed a QI project to improve discharge. The team performed a current state analysis (via stakeholder interviews, process mapping, and literature-based research). Multiple communication shortcomings were identified. During three PDSA cycles, the QI team introduced tools to address common failure modes.

Interventions included articulating the estimated date of discharge (EDD) during rounds, recording the EDD within the Electronic Health Record (EHR), and using a visual indicator of EDD (VID) within patient rooms to spur conversation about potential discharge barriers. Metrics included adherence to prescribed roles during rounds, correct usage of tools (EHR and VID), number of unanticipated discharges, average length of stay (LOS), percentage of discharges by 2pm, and HCAPHS scores.

Results: The project achieved success across all chosen metrics. Audits of adherence (n = 53) to prescribed roles during discharge rounds were 96% (soliciting and articulating EDD), 92% (EDD entered in EHR), and 77% (use of VID). Unanticipated discharges decreased from four per week to two per week. Average LOS decreased by 0.4 days, and percentage of discharges by 2pm increased from 20% to 35%. HCAPHS scores are pending.

Conclusion: Formalizing roles in discharge planning is an effective method of standardizing communication between providers, staff, and patients, and can streamline discharge.

Longitudinal Evaluation of Medical Education in Abortion Services <u>Melanie Miller</u>, Emily Silverstein, Dr. Nicole Bender

Background and goals: The purpose of this longitudinal, paired study is to evaluate medical education surrounding abortion services during medical school. The aim is to track one medical student over the course of their graduate medical education. We have created a survey regarding both personal and professional attitudes, and knowledge regarding abortion to be given at three times points in their medical education. The same survey will be given before their reproductive system unit, after their reproductive system unit and again after their OB/GYN rotations.

Our hypotheses is that professional attitudes regarding circumstances for recommending an abortion will change, with more students being willing to recommend an abortion at the conclusion of their medical education. We predict that education will not change students' personal attitudes. Furthermore, we hypothesize that the biggest increase in change will occur after their clinical rotations. **Methods:** This will be a prospective cohort study of medical students at the Keck School of Medicine of the University of Southern California. First year students will be presented with a paper survey in a classroom setting before the onset of their reproductive system unit with the option to be contacted in the future.

Students who provided contact information will be emailed the same survey after the conclusion of the Reproduction unit via REDCap. The final survey will be emailed via REDCap at the end of the third year after clerkship rotations.

Results: We expect similar results to a paper done at John Hopkins, with an increase in student's willingness to refer a patient seeking an abortion.

Conclusions: Our results may help determine when in graduate medical education that educational activities will be of most benefit to medical students regarding their attitudes and knowledge around abortion.

Assessing Literacy in a Primary Care Clinic Alyssa Morse, B.A., Breck Nichols, M.D.

Goal: Illiteracy and low literacy impacts patients' abilities to access care and follow important directives for treatment, prevention and medications. It has been found that there is an illiteracy rate of 19% at Lincoln High School, just one mile away from LAC+USC Medical Center. Additionally, it has been reported that in a 2002 study done by Bass PF 3rd et al.¹, resident physicians overestimate the reading ability of their patients. Currently, all documents provided to patients at LAC+USC are written at a 6th grade reading level, as recommended by the Institute of Medicine. We hypothesized that the illiteracy rate in the LAC+USC population was higher than the United States average, and of those who can read, a significant percentage are unable to fully comprehend 6th grade reading level materials.

Methods: This study was conducted in the USC Med+Peds Outpatient Clinic via surveys of English and Spanish-speaking patients aged 18 years and older. Initially, we used the tested and validated Healthy Community Initiative computer-based decision tree that documents literacy, risk factors, and symptoms of disease. Going a step further we administered a reading level survey that assessed accuracy, fluency and comprehension.

Results: We elucidated that 2/50 patients, or 4% were illiterate. Utilizing the reading level assessment we found that thus far 4 out of 17 patients, or 23%, are unable to read at a 6th grade level, and we expect continuing assessment to reveal similar results.

Conclusions: These results support our initial hypothesis that a large percentage of LAC+USC patients do not fit within the Institute of Medicine guidelines for patient reading materials, and that literacy needs to be taken into account for each patient when providing instructions. It is anticipated that improving patient communication in this way will improve patient adherence and care.

¹ Bass PF 3rd et al. "Residents' ability to identify patients with poor literacy skills." Acad Med. 2002 Oct; 77(10):1039-41.

Offline Testing of an Automated Clinical Decision Support (CDS) System for Patients with Multiple Complex Chronic Conditions

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Background: Automated clinical decision support (CDS) systems can improve quality of care, and require extensive testing. Before CDS systems are deployed clinically, an important initial step is offline testing. The purpose of offline testing is to evaluate system function from input data to output recommendations, in relation to external specifications of "correct" function. This project applied

methods of evaluation to identify errors within a CDS system for four chronic conditions (HTN, HF, DM), with the aims of (1) improving the clinical accuracy of the CDS, and (2) reporting on experiences with error-finding in CDS system testing.

Methods: 100 test patients were selected for each of the four clinical domains (400 patients total). Recommendations from the CDS were produced and compared against the recommendations of human reviewers. Discrepancies between CDS and human reviewer output were subjected to failure analysis by a team of clinical and technical experts. The source of each error was identified and categorized, and the CDS was revised and retested accordingly.

Results: 57 discrepancies between CDS and human reviewer output were found. 34 discrepancies arose from insufficiencies of the documents describing the intended function of the CDS, known as "Rules Documents", 15 arose from errors in the CDS system programming, and 8 arose from human reviewer errors.

Conclusion: CDS systems require extensive testing to ensure safety and effectiveness; however, this important phase of development is not often described in the literature. It is important to open this area investigation by reporting on error-finding in CDS system testing. A majority of the discrepancies (34 of 57) found between CDS and human reviewer output in this study arose from insufficiencies of the Rules Documents. This points to a need for better understanding of how to specify CDS system requirements for the purpose of offline testing, which is an important issue for future investigation.

PATIENT QUALITY/ SAFETY

Does EMTALA improve Hospital Quality? The effect of EMTALA investigations and citations on hospital quality.

Michael Menchine MD MPH, Vanessa Arientyl MS II, Sophie Terp MD MPH, Chun Nok Lam MPH, Sanjay Arora MD, Seth Seabury PHD

Background: Passed in 1986, the Emergency Medical Treatment and Active Labor Act (EMTALA) was legislation aimed at improving access to quality care. EMTALA violations may result in costly corrective action plans, fines, or termination of a hospital's CMS contract. In the past decade, nearly 50% of hospitals have been investigated and 25% cited for EMTALA violations. However, little is known about the effects on hospital quality. The goal of this investigation is to quantify changes in hospital quality, if any, in response to an EMTALA investigation.

Methods: We obtained a list of EMTALA investigations and citations completed by CMS between 2005 and 2014 and merged it with quarterly quality reports available publicly from CMS. Twenty-four core measures were available throughout the study period concerning 3 conditions: Acute myocardial infarction (AMI), congestive heart failure (CHF) and pneumonia (PNA). Performance on each measure was normalized by quarter across hospitals. Normalization set the mean score to zero (negative scores indicate lower quality). Condition-specific quality scores were created by averaging individual measure scores for that condition (e.g. AMI). An overall quality measure was created by averaging the 3 condition-specific scores. We then examined changes in hospital quality in the year before and after an investigation/citation. Paired Student's t-test was used to determine statistical significance. Results: There were 4138 investigations and 1841 citations among the 5594 hospitals that reported quality measures during the study period. Quality significantly improved following an EMTALA investigation, from a baseline normalized score of -0.04 to -0.02 (difference 0.02 (95% CI 0.01-0.05), p = 0.01). Condition-specific quality improved similarly (PNA quality improved 0.03, p<0.01, AMI quality improved 0.05, p=0.01, CHF improved 0.02, p=0.04). Improvements in quality following an EMTALA citation were similar in magnitude but were not statistically significant (possibly due to lower power). **Conclusion:** Over the past 10 years, EMTALA investigations have resulted in significant improvement in hospital quality. Research examining the specific effect of EMTALA investigation/citations on emergency care should follow.

Prior Diaphragm Plication does not Adversely Impact Hospital Course During Subsequent Stages of Palliation for Single Ventricle Physiology

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Background: Phrenic nerve injury is a known cause of morbidity following single ventricle palliation. Previous studies have shown that hemi-diaphragm plication improves short-term outcomes. However,

little is known about the effect of plication on hospital course during subsequent stages of single ventricle palliation.

Methods: Between 1997 and 2014, 962 patients underwent surgical management of single ventricle physiology at our institution. We reviewed the records of 32 patients who underwent diaphragm plication for phrenic nerve injury prior to establishment of Fontan circulation. Each patient was compared to two propensity-matched controls identified from patients who underwent Glenn or Fontan procedure and did not require diaphragm plication. Propensity matching was achieved for each test subject using nearest neighbor algorithm. Data is presented as median and interquartile range or number and percentage.

Results: The cohort includes 19 boys (59%). There were 15 Glenn patients (48%) who had undergone diaphragm plication following first stage palliation. Of these, 8 have had completion Fontan, 6 are awaiting Fontan, and 1 expired. An additional 9 patients underwent diaphragm plication after Glenn, accounting for 17 patients with diaphragm plication who underwent Fontan completion. There was no difference in pulmonary pressure or resistance between the two groups. Both groups had comparable chest tube drainage and hospital length of stay. At discharge, equal proportion of patients required sildenafil therapy and/or supplemental oxygen in both groups.

Conclusion: Prior diaphragm plication does not adversely impact course to Fontan circulation in children with single ventricle physiology. Their hospital course during subsequent stages of palliation for plicated patients is no different than that of matched controls.

Return precaution understanding: a potential target for reducing bounce backs

<u>Charney Burk</u>, Joe Berman, Nihaal Shah, Sophie Terp, Elizabeth Burner, Chun Nok Lam, Michael Menchine, Sanjay Arora

Background: In light of increasing wait times, crowding and the associated cost burden, it is vital to address deficiencies within our emergency healthcare system that could decrease preventable bounce backs. This study focused on three key variables (language preference, follow-up understanding and return precaution understanding) that might be effectively targeted in interventions to decrease bounce backs.

Methods: We surveyed a consecutive sample of patients at the time of discharge in the LAC+USC ED, recording language preference and recollection of return precautions and follow-up instructions. For return precautions two independent research assistants categorized patients into five categories by comparing patient recollection with written instructions in the medical record. Kappa concordance was 0.974. For follow-up, one research assistant categorized patients into four groups: (1) correctly identifying follow-up, (2) incorrectly indicating no follow-up, (3) correctly identifying no follow-up and (4) incorrectly indicating they received instruction. Next, using the electronic medical record, patients who returned to LAC-USC ED within 30 days of discharge were identified.

Results: Language preference (English/Spanish) and understanding of follow-up were not associated with higher bounce back rates. However, patients who incorrectly described or were unable to recall return precautions had a more than 50% relative increase in rate of bounce back.

Conclusion: Our study shows that understanding of return precautions was correlated with bounce back rates while language preference and knowledge of follow-up were not. Interventions designed to reduce

repeat visits should take this finding into account. Our results should be validated in populations of varying SES and language preferences.

Prescription Drug Monitoring Programs' Effect on Overall Opioid Prescribing <u>Matthew Georgis</u>, Michael Menchine, MD, MPH, Department of Emergency Medicine, KSOM

Goal: A dramatic increase in opioid prescribing and abuse has occurred over the last two decades. Many states have implemented Prescription Drug Monitoring Programs (PDMPs) in order to decrease the potential for prescription drug abuse. In this study, we aim to estimate PDMP effectiveness in decreasing the amounts of opioids prescribed.

Methods: We obtained the total amount of prescription opioids distributed to each state between the years of 1997-2014. Yearly opioid shipments were found using Automation of Reports and Consolidated Orders Systems (ARCOS) via a Freedom of Information Act Request to the DEA. Each opioid was converted to a 'morphine milligram equivalent' (MME) using published opioid equipotency tables (ie. 1.5 hydromorphone = 10 morphine) and then converted to per capita amount by state and year. State populations were found using intercensal estimates (1997-2009) and annual estimates (2010-2014) from the U.S. Census Bureau, Population Division. We then assessed the aggregate states' opioid prescribing response before and after PDMP implementation (Fig 1). PDMPs were also graded on whether prescribers had to mandatorily access PDMPs (in any form) and whether delegates were allowed. These characteristics were obtained from the National Alliance for Model State Drug Laws (NAMSDL). **Results:** Through the amount of opioids increased through the study period, the average increase of MMEs per capita decreased significantly after PDMP implementation. In the pre-PDMP implementation period, the rate of MME per capita increase on average by 31.5% annually. In post-PDMP

Conclusions: The data suggests PDMPs are effective in slowing the rate of increase in opioid prescribing. However, the average overall amount did not decrease after PDMP implementation. Future directions include using opioid mortality data to assess opioid abuse as well as using a "difference in differences" statistical technique.





Quality Improvement in the Administration of the Cosyntropin Stimulation Test for the Diagnosis of Adrenal-Cortisol Insufficiency in Hospitalized Patients

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Goal: The Cosyntropin Stimulation Test (CST) is a time-dependent dynamic test used to diagnose adrenal insufficiency, a condition in which the adrenal glands do not produce sufficient cortisol to support patient well-being and/or life. It has been previously observed that the medical staff at Cedars-Sinai Medical Center (CSMC) often performed this test in an inaccurate manner with variable cortisol measurements, leading to ambiguous test results and a wasting of resources. This study evaluates if the CST is performed more efficiently and consistently in hospitalized patients after the implementation of a more strict electronic medication administration record (e-MAR) protocol for the CST.

Methods: The new e-MAR protocol was implemented at CSMC in July of 2014, and directed medical staff to follow specific instructions for the proper administration of the CST. A list of inpatients that received a CST between January 2013 and May 2015 was obtained from CSMC, resulting in a total of 406 cases in which a CST was performed. Data from these cases was extracted from the CSMC patient electronic medical record database. Analysis included comparison of the 279 cases that occurred before the implementation of the new e-MAR protocol to 127 cases that occurred after the implementation of the e-MAR protocol.

Results: The results showed that the number of correct CSTs performed after the implementation of the new protocol was statistically greater than correct CSTs perform before the new protocol (z = 8.09, p = <0.0001). Furthermore, results showed that potential wasted CSTs occurred in 107 out of 279 (38%) of the before cases, amounting to a total of \$277,095 in wasted cosyntropin and cortisol measurements. In contrast, potential wasted CSTs occurred in 21 out of 127 (16%) of the cases after the protocol was initiated, amounting to a total of \$58,580.

Conclusion: The results from this study suggest that the implementation of a more strict e-MAR protocol for the administration of the CST resulted in an overall more efficient CST administration process and have implications for a more cost effective system in the test for adrenal insufficiency.

Patient satisfaction with the Diabetes Task Force and post-discharge knowledge and care

<u>Amy Komure</u>, Dr. Michael Cousineau, Dept. of Preventative Medicine KSOM, Dr. Hector Flores, White Memorial Medical Center

Goal: Diabetes management is difficult for patients, but it is unclear how to best assist them. The goal of this project was to assess patient satisfaction with their inpatient care, transition within the diabetes task force, and their understanding of diabetes management after discharge.

Methods: Patients admitted for any cause to the family medicine department with a diagnosis of diabetes mellitus were followed by the diabetes task force. This included calls from a health navigator to assist in care coordination and discharge instruction adherence. A ten question patient survey was administered via telephone seven days after discharge.

Results: There have been 61 survey responses since December 2015. The overall satisfaction score was 3.54 out of 4 with patients answering strongly agree or very satisfied (score 4 out of 4) 75.6% of the

time. The mean score of 3.34 for the first five questions related to patient knowledge at discharge was significantly lower (p < 0.01) than the mean score of 3.74 for the last five questions about satisfaction with care. The mean score of five questions varied significantly from the total mean (p < 0.05). Questions about patient satisfaction post-discharge with organization of care (mean = 3.74), assistance with appointment scheduling (mean = 3.75), and follow-up calls (mean = 3.91) all had significantly higher scores. Questions about patient knowledge of the purpose of their medications (mean = 3.80) and the HbA1C test (mean = 2.15) also varied significantly.

Conclusions: Patients are overall satisfied with the care received through White Memorial. Their higher satisfaction with post-discharge care shows how important follow-up from the task force is to patients. The health navigator is the key component of this and received the highest satisfaction score. The lower scores for questions about patient knowledge at discharge, especially about the HbA1C, shows there is still room for education. It is the hope that the task force will be able to lower readmissions and improve diabetes management and the positive satisfaction scores are the first indicators of patient benefit.

Correlates of providing assisted injections among people who inject drugs

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Background: Peer-to-peer injection (defined as giving or receiving an injection to/from someone else) has been reported to range from 19% to 49% among people who inject drugs (PWID) and has been associated with health risks. Researchers have often examined receiving injection assistance, but providing injection assistance has been less studied. In this analysis, we examine correlates of providing injection assistance.

Methods: PWID (N=777) were recruited using targeted sampling and interviewed in California (2011-2013). Multivariate analysis was used to determine correlates of providing injection assistance in the last 30 days.

Results: Injection assistance was reported by 28% of PWID. Correlates associated with providing assisted injections were poly injection drug use (Adjusted Odds Ratio [AOR] = 2.32; 95% Confidence Interval [CI] = 1.56, 3.47) and goofball injection in the last 30 days (AOR = 2.29; CI = 1.32, 3.96), having an illegal income source (AOR = 1.68; CI = 1.17, 2.42), occasionally injecting with others (AOR = 4.29; CI = 2.15, 8.55), injecting in public (AOR = 1.65; 1.13, 2.41), engaging in distributive syringe sharing (AOR = 1.90; CI = 1.19, 3.04), and having witnessed an overdose in the last six months (AOR = 1.92, CI = 1.29, 2.88) while controlling for injection frequency.

Conclusion: PWID who assist their peers with injection are at the intersection of other injection related risks such as syringe sharing and overdose. Developing interventions that enlist these individuals in efforts to reduce injection-related HIV/HCV risk, overdose, and other health ailments associated with drug injection could be beneficial.

Perioperative Quality Improvement at Keck Hospital vs. LAC+USC vs. OPSC

Amelia Lanier; Ze Di; Arash Motamed, MD, MBA; Dept. of Anesthesiology, Keck Medical Center of USC

Background: Operating rooms (ORs) generate revenue but are also one of the most expensive sites within a hospital. For USC to be able to provide beyond excellent care, a detailed examination of ORs is imperative. Through chart review, we have compared cataract procedures (LAC, OPSC) and craniotomies (LAC, Keck) as examples of typical outpatient and inpatient procedures, respectively, and noted considerable variability both within and among specialties. By gathering more data from direct observations, we systematically studied OR practices to determine causes of this variability in order to better optimize OR efficiency.

Methods: Cataract removals (LAC, OPSC) and craniotomies (LAC, Keck) were observed systematically. Time points were recorded for several events during each procedure, and a detailed case log of activity was recorded. Within each type of procedure, hospitals were compared with regard to total time in the OR, total operative and non-operative time, and total non-operative time as a percentage of total OR time. These data were compared to retrospective one-year OR metrics from the computer system. **Results:** Among the observed cataract removals, mean total OR time at LAC-USC was 112 minutes with a non-operating time of 45 minutes (40% of total OR time). Mean total OR time at OPSC was 44 minutes with a non-operating time of 24 minutes (55% of total). For craniotomies, mean total OR time at LAC was 414 minutes with a non-operating time of 144 minutes (35% of total). At Keck, total OR time was 250 minutes with a non-operating time of 96 minutes (38% of total).

Summary: This information is useful in considering OR optimization. We plan to gather and analyze more data in order to effectively reduce metric times without compromising quality of care. This allows for increasing staff flexibility while possibly allowing more operations to be performed, improving access, streamlining operations, lowering costs and improving patient outcomes.

Effect of a standardized feeding guideline on outcomes in preterm infants <u>Edward Lin</u>, Thomas Chavez, Ting-Yi Lin, MD, PhD and Arlene Garingo, MD

Background: A wide variability exists in feeding advancement practice in preterm infants. Studies have shown that adopting a standardized feeding guideline (SFG) leads to better patient outcomes. This study hypothesizes that the adoption of a SFG will reduce hospital length of stay (LOS), total parenteral nutrition (TPN) and central line (CL) days in preterm infants.

Method: The study included infants < 32 weeks of gestational age (GA) who were admitted to the Neonatal Intensive Care Unit at a single institution. A SFG was implemented in April 2014. The Pre- (P1) and post- (P2) intervention data were collected including: GA and weight at birth and at discharge (DC), LOS, TPN and CL days. Independent t-tests, Mann-Whitney tests, Fisher's Exact test, and multivariate regression were used in data analysis and to model LOS.

Results: There were 22 patients in P1 and 33 patients in P2. Between P1 and P2, there were no difference in GA at birth ($30\ 0/7\ vs.\ 30\ 0/7\ weeks,\ p=0.87$) and in birth weights ($1325\ \pm\ 258\ vs.\ 1343\ \pm\ 256\ grams,\ p=0.80$). There were 59% and 50% males in P1 and P2, respectively. There were more Hispanics in P2 ($12\ vs\ 33,\ p=0.04$). There was a non-statistical association towards decreased LOS ($55.18\ vs\ 51.03\ days,\ p=0.45$) and earlier GA at DC ($37\ 6/7\ vs.\ 37\ 0/7\ weeks,\ p=0.36$) in P2. There was no

increase in TPN days (22 vs. 20.29 days, p=0.64) or CL days (21.78 vs. 23 days, p=0.75). On multivariate regression analysis, adjusting for GA at birth, there was a trend for lower LOS in P2, however, this did not reach statistical significance (P2 β : -3.53 (95% CI: -11.48, 4.42)).

Summary: After introduction of a SFG, there was a trend towards decrease in LOS and lower GA at DC, but was not statistically significant. No increase in TPN or CL days was observed. Further research is ongoing to fully determine the SFG's effect on outcomes in preterm infants.

Risk Factors to Neurodevelopment in High Risk Infants Treated with Intensive Interventions <u>Ellen McMahon, BS</u>, Douglas Vanderbilt, MD.

Purpose: This study examines whether intensive interventions are a risk factor for maternal mental health. It will also describe if maternal mental health influences neurodevelopmental outcomes among High Risk Infant (HRI) survivors who require intensive interventions. The main outcome will be an understanding of the impact of maternal mental health on 6-month HRI neurodevelopment.
Methods: This is a prospective longitudinal study of HRI and their mothers. Assessments will occur in the HRI Follow Up clinic at CHLA. Infants and mothers will be assessed at one and at six months of the infant's corrected gestational age. The mother will complete maternal mental health surveys, and perinatal risk factors of primary diagnosis and medical severity will be collected from the medical record. Caregiving measures, using the StimQ form, and neurodevelopmental outcomes, using the Bayley Scales of Infant Development-III, will be assessed at 6 months of age. Cross-sectional comparisons will test the time-lagged and concurrent effects of maternal mental health.

Results: Data has been collected on nineteen infants at one month and on nine infants at six months corrected gestational age, and their mothers. We are continuing to enroll patients at one month and to perform six month follow up on previously enrolled infants, and then we will begin data analysis. **Summary:** Once we have enrolled a sufficient number of infants, we hope that this research will inform practice to enhance disease-free survival in HRI survivors by documenting successful practices to follow NICU survivor families and by supporting development of post-hospital early intervention strategies for infants and parents. Later studies will build upon these preliminary data in extending the age range to 12 and 24 months to obtain data on more clinically relevant long-term outcomes and observe the effect of changes to established protocols.

Perioperative Pain Management of Patients with Chronic Pain: Reducing Pain, Improving Satisfaction, and Controlling Cost

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Goal: Prior to surgical procedures risk of adverse events is reduced through suspension of all medications save for the few necessary for basic physiological functions. In patients with chronic pain (CP), suspension of their medication causes not only preop pain but their iatrogenic tolerance to analgesics results in intractable postop pain, necessitating large and frequent supplementary analgesics for pain control and resulting in an increased length of stay (LOS) and reduced satisfaction. We hypothesize that deliberate preop management of CP patients including continuation of some dosage of analgesics will reduce incidence of intractable postop pain reducing LOS.

Methods: CP patients were defined as those reliant on analgesics for daily pain management. CP patients whose surgeon had requested periop management of CP by the Pain Service (avoiding full discontinuation of analgesics) prior to intervention composed the experimental group; and patients whose surgeon had not requested such management were placed in the control group. Procedures were matched across both groups and patients with surgical complications were omitted. Using data from the medical record, the LOS, extra analgesic administrations, and where available patient-reported pain levels were compared between groups.

Results: Analysis ongoing, but we expect that for patients in the experimental group who avoided full discontinuation of analgesic medications will have a lower incidence of intractable pain leading to shorter postop LOS, fewer extra-protocol analgesic administrations, and decreased self-reported pain levels.

Conclusion: Patients without intractable postop pain are able to go home sooner, improving satisfaction and freeing a bed for another patient. Costs associated with unanticipated/extended LOS are reduced, saving man-hours and medical resources associated with inpatient care.

Procedural Variation in Management of Apparent Life Threatening Events (ALTEs) in Infants: A California Database Study

Drew Mikhail, Ermias Yebelay, Ashley Song MPH, Ashwini Lakshmanan MD MPH, Philippe Friedlich MD, MSEpi MBA and Jennifer Shepherd MD.

Background: Comprehensive descriptive information regarding management of apparent life threatening events (ALTEs) on a state or national level is limited. We postulate that the number and type of procedures differ significantly depending on the principal diagnosis of infants presenting to the emergency room With anticipated new national guidelines for management of ALTE, it is important to understand how ALTE in each diagnostic group is currently being managed.

Objective: To describe clinical procedures utilized in diagnosis and management of infants with ALTE at a state level.

Methods: We studied data from California Office of Statewide Health Planning and Development (OSHPD) Emergency Department data for years 2005–2011. Patients < 1 year old with ALTE were identified using the principal diagnoses of apnea, syncope, altered consciousness, transient loss of consciousness, cyanosis, ALTE, primary apnea, other convulsions, unspecified sleep apnea, flushing, obstructive sleep apnea, esophageal reflux, and pallor. The top 20 principal procedures were extracted by CPT code and assessed according to principal diagnosis. We used descriptive statistics to characterize procedural variation in ALTE patients according to principal diagnosis.

Results: 22015 infants <1 year old were identified with an ALTE 2005-2011. Extraction of the 20 most common CPT codes resulted in 8820 total procedures for analysis. The most common CPT code was "moderate severity ER visit" (1569 total, 7.1%) and the most common clinical procedure was lumbar puncture (506 total, 2.3%). The top diagnosis receiving a lumbar puncture was "other convulsions" (286 of 506 total). Gastroesophageal reflux disease (GERD) was the most common diagnosis (45%), and abdominal ultrasound was the most common procedure for this group (2.5%). Of the small number of patients with ALTE requiring endotracheal intubation (90 total), the most common diagnoses were apnea (36), other convulsions (25), and primary sleep apnea of newborn (24).

Conclusion: Most patients < 1 year old who presented with ALTE to the emergency department did not undergo any clinical procedures. Lumbar puncture was the most common clinical procedure. GERD was the most common principal diagnosis. It is important to determine patterns of resource utilization for these patient populations once the new guidelines (BRUE) are published.

Infection Rates Following Prolonged Time to Open Neural Tube Repair: A National Study

Frank Attenello, Alexander Tuchman, Timothy Wen, <u>Swathi Nallapa</u>, Eisha Christian, Steven Y. Cen, J. Gordon McComb, Mark D. Krieger, William J. Mack

Introduction: Newborns with a myelomeningocele are often brought to the operating room for surgical repair within the first few days of life. Wound infection in this population may represent a devastating outcome in the immature nervous system. No studies have evaluated infection as a function of surgical timing at a national level. We hypothesized an increase in wound infection in those patients with delays in myelomeningocele repair when evaluated from a national database.

Methods: Newborns with myelomeningocele and time to repair were obtained from non-overlapping abstracts of the 2000 to 2010 Kids Inpatient Database (KID) and Nationwide Inpatient Sample (NIS). Poisson multivariable regression analyses assessed the effect of time to repair on infection and routine discharge rates. Secondary outcomes of interest assessed predictive factors of >2 days until repair. Local treatment outcomes and times to transfer were evaluated at Children's Hospital of Los Angeles (CHLA) for comparison for the years 2004 to 2014.

Results: We identified 3775 cases of repaired myelomeningocele with 19% of patients receiving repair after 2 or more days. Infection was noted in 681 (18%) patients. There was no significant difference in rates of infection between same day and 1-day wait times (P = 0.22). Wait times of 2 (RR 1.65, [1.23, 2.22], P < 0.01) or more days (RR 1.88, [1.39, 2.54], P < 0.01) experienced a 65% increase in rates of infection compared with same-day procedures. Prolonged wait time was 32% less likely at facilities with increased myelomeningocele repair volume (RR 0.68, [0.56, 0.83], P < 0.01). CHLA identified 95 cases of myelomeningocele repair, with a median time from birth to treatment of 1 day. Six (6%) cases were noted to have inpatient wound breakdown or infection.

Conclusion: Myelomeningocele repair, when delayed more than 1 day after birth, is associated with increased rates of infection. High-volume centers are associated with fewer delays in procedure. Although constrained by limitations of a national coded database, results suggest that appropriate attention to timely myelomeningocele repair decreases the infection rate.

Additional Notes: This project was part of a CNS Oral Presentation and is a collaboration between the neurosurgery departments at Keck and CHLA. My final poster in March will only include the data that I have collected during my time at CHLA (the 95 cases cited in the results section).

Demographics and Surgical Treatment of Patients with Ossification of the Posterior Longitudinal Ligament in the United States: An Large Database Study from 2005-2015

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Background: There is a lack of information on the trends and demographics of Ossification of the Posterior Longitudinal Ligament (OPLL) in the United States. Although there are many studies in Japan and other East Asian countries, there has been less research done on the disease and its treatment in the US. This study aims to analyze demographics of patients and trends in surgical treatment of OPLL in the United States.

Methods: Using the PearlDiver national insurance database, we identified patients in the Humana and Medicare patient populations who had been diagnosed with OPLL using the ICD-9 code 723.7 over 2005-2015 and stratified them according to age, gender, race, and region in the United States. Patients who underwent one of seven types of surgical procedures were categorized to determine surgical treatment rates and chi square tests were performed to determine any differences in treatment modality. **Results:** A total of 2,498 patients in the Medicare database and 801 patients in the Humana database met our search criteria. Both males and females had an equal incidence rate of the disease (0.07-0.15 per 10,000) and the highest incidences were found in those between 50-65 years old (0.14-0.16 per 10,000) and in patients form the South (0.09-0.17 per 10,000). In the Humana database, we found that the majority of OPLL patients were White (51.6%). Of the seven surgical procedure types, in both databases (Medicare; Humana), anterior fusion of the cervical spine was the most common (52.8%; 26.3%), followed by posterior fusion of the cervical spine (33.5%; 17.6%), laminectomy or laminotomy (19.4%; 5.7%), and discectomy or corpectomy (18.2%; 4.7%). Male patients were treated with surgery significantly more often than female patients ($p = 4x10^{-6}$). The overall surgical rate in the two databases was 30-32%. In both databases, the Northeast had the fewest number of patients and surgeries. The type of surgery chosen did not change significantly based on gender, age, or region.

Conclusions: The incidence of OPLL in these databases is much lower than previous studies have found for the Untied States. The disease does not affect one gender more than the other and is seen in many races, with higher proportions in White and Black Americans than in Asian Americans. Anterior and posterior fusions of the cervical spine appear to be the favored approach of treatment, while laminoplasty is rare. There are differences in surgical rates between females and males, as well as by age, which is likely multifactorial due to risk factors, complications, and surgeon choices. Future research will hopefully elucidate what risk factors and complications are commonly seen in OPLL surgical patients.

Experience of Foreign Body Removal from the Ear in an ENT Office Setting Compared to Emergency Department

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Goal: Foreign bodies (FB) in the external auditory canal (EAC) are commonly seen in the pediatric population, particularly ages 2-8. Though the majority of EAC FB removals in the ED are successful, potential complications include pain, EAC lacerations, tympanic membrane perforation, bleeding, and otitis. Studies stress that the number of previous removal attempts are associated with increased rates of complications. After multiple unsuccessful attempts at removal, these patients are often referred to otolaryngologists. We hypothesize that patients seen in the ENT office will more often have led to a successful FB removal compared to those in the ED which would optimize patient care and increase overall health care efficiency with fewer complications.

Methods: Retrospective review using CHLA electronic medical records (patients ages birth-18 years-old) to extract data for the following points: patient age, length of time FB has been present in ear, type of FB, time from 1st attempt to extraction, number of extraction attempts, comorbidities prior to attempted removal, FB location, all methods employed (instrumentation, restraint, sedation etc.), complications, level of training of health care practitioners involved in attempted extraction and overall cost of visit. Simple descriptive statistics and two-by-two comparisons will be used to describe the population and outcomes.

Results: Study protocol is complete. When introduced into the CHLA computer system, data collection and analysis will begin.

Conclusion: The purpose of our study is to improve the quality of care pediatric patients with aural foreign bodies receive at Children's Hospital Los Angeles. Not only will we examine the successful removal of foreign bodies in the ear, we also hope to investigate the differences in billing costs and the impact that the level of training of the performing physician has on the outcome.

Comparing successful induction of labor with expectant management in pregnancies with congenital anomalies: A retrospective review

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Importance: Induction of labor (IOL) is a common procedure performed in obstetrics and plays a vital role in pregnancy management. In women that have pregnancies with diagnosed fetal anomalies, it is common practice to induce the pregnancy at 39 weeks for coordination purposes with the NICU and other specialty services. Induction of labor does come with potential risks that can lead to a failed induction and a subsequent cesarean.

Objective: The aim of this study is to look at the risk of a failed IOL and subsequent cesarean in women with diagnosed fetal anomalies at term as compared to those who were expectantly managed. **Design:** This study is a retrospective review of the Institute of Maternal Fetal Health (IMFH) patient data from 2011 to 2014 consisting of maternal, fetal, labor/delivery, and postpartum data.

Participants: Patients referred to the IMFH have a diagnosed fetal anomaly in their current pregnancy. **Results:** During the study period, 117 women whom had fetuses with diagnosed anomalies gave birth through the IMFH. Of the 117, 64 of these women had an IOL, while 53 were expectantly managed. Of the women who were induced, 17.2% of the pregnancies went on to be delivered via cesarean. In the expectantly managed group, 62.2% of the pregnancies ended in a cesarean. Of those patients who delivered at full term, IOL patients were 83% less likely to deliver via C-section compared to patients who were expectantly managed (95% CI [0.06, 0.48]). It appears that the induction patients, who despite having a low dilation (p=0.002) and effacement (p=0.04) on presentation, have a lower rate of C-section (OR=0.13), as compared with the patients who were expectantly managed.

Conclusions and Relevance: Historically, IOL with an "unfavorable cervix" has been associated with increased cesarean rates. In this study, the data suggests that patients with fetal anomalies who are induced at term do not have a greater risk for cesarean as compared to those who are expectantly managed. This information indicates that there is not only just less risk involved with an IOL in pregnancies complicated by fetal anomalies, but also great potential benefit as timing of the delivery can greatly improve coordination of care for mother and baby postpartum.

Quality of Life and Alimentary Satisfaction After Gastrectomy versus Esophagectomy

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Introduction: Tumors at the gastroesophageal junction can be treated by gastrectomy or esophagectomy. Oncologic outcomes are reported to be similar, therefore the aim of this study was to evaluate quality of life (QOL) and alimentary satisfaction after gastrectomy versus esophagectomy. **Methods:** A retrospective chart review was performed of patients that had gastrectomy with Roux-en-Y esophagojejunostomy or esophagectomy with gastric pull-up from 2000-2014. Symptoms, alimentary satisfaction and QOL were assessed by telephone interview and questionnaires (RAND 36-item Short Form Health Survey [SF-36], Gastrointestinal Quality of Life Index [GIQLI], and the Alimentary Satisfaction [AS] Score). In each questionnaire higher scores denote better satisfaction. Follow-up was divided into early (≤ 2years), medium (>2-5 years) and long (>5 years). Patients that could not be contacted or who refused to participate were excluded.

Results: There were 20 patients in each group (table). There were no significant differences between groups for age, gender, initial BMI, or BMI at follow-up. All but 3 patients lost weight after gastrectomy and everyone lost weight after an esophagectomy. The median weight loss after gastrectomy was 14 and after esophagectomy was 11.6 pounds. The mean number of meals a day (3) was similar between groups. There were no significant differences in symptoms but more patients used proton pump inhibitors after esophagectomy. Overall, QOL by SF-36 was similar between groups in all but the category role limitation due to physical health which was higher after esophagectomy. However, at early follow-up QOL was better after esophagectomy versus 101 after esophagectomy, p=0.685) and AS (7.5 in each group, p=0.926), but GIQLI scores were significantly higher at early follow-up after esophagectomy (78.7 for gastrectomy versus 105.6 for esophagectomy, p=0.014). The SF-36 scores were similar

between males and females after gastrectomy, but after esophagectomy scores in the categories for general health and physical function were significantly better in females (71.7 and 88.3 for females respectively versus 48.9 and 63.2 for males, p=0.043 and p=0.008). Comparing GIQOL and AS scores by gender, females tended to have higher scores for both questionnaires after a gastrectomy (100 and 8 for females respectively versus 95.4 and 7.2 for males) and an esophagectomy (116 and 9.1 for females versus 94 and 6.8 for males).

Conclusions: Overall QOL and alimentary satisfaction were similar after gastrectomy and esophagectomy, but in the first two years the scores for both SF-36 and the GIQLI questionnaires were better after an esophagectomy. Satisfaction was similar by gender, but females tended to score higher than males after both procedures.

	Gastrectomy n=20	Esophagectomy n=20	p-value
Mean age in years (range)	67.6 (41.6-87.7)	66.7 (42-83)	0.803
Gender: m/f	12/8	14/6	0.741
Mean F/U time in months (range)	37.5 (4.3-115.5)	44 (7.2-127.5)	0.541
Early F/U: n (%)	7 (35)	7 (35)	0.723
Medium F/U: n (%)	9 (45)	7 (35)	
Long F/U: n (%)	4 (20)	6 (30)	
BMI initial	29.45 (17.2-49.5)	28.2 (21.5-42.4)	0.624
BMI at follow up	24.3 (17.4-50.4)	23.8 (16.2-35.3)	0.777
Mean number of meals (range)	3 (1.5-5)	3 (2-7)	1
Dysphagia: n (%)	4 (20)	4 (20)	1
Heartburn: n (%)	3 (15)	2 (10)	1
Regurgitation: n (%)	4 (20)	5 (25)	1
Aspiration: n (%)	0	0	N/A
PPI use: n (%)	2 (10)	10 (50)	0.031
Dumping: n (%)	0	1 (5)	1
Diarrhea: n (%)	5 (25)	1 (5)	0.195

Table 1: Demographic and clinical data.

Figure 1: Early (≤ 2 years) QOL by RAND SF-36: Gastrectomy versus Esophagectomy. Esophagectomy in red and dashed line, gastrectomy in blue and solid line

Extended Hospital Stay in Patients with Radical Cystectomy on Enhanced Recovery Protocol

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Objectives: The Enhanced Recovery After Surgery (ERAS) protocol is being increasingly adopted in the postoperative care of patients following radical cystectomy (RC) and urinary diversion. It has been shown to decrease length of stay (LOS) without increasing complication and readmission rate. We have previously reported a mean LOS of 5 days in our patients. The purpose of this study is to evaluate reasons leading to extended hospital stay (EHS) in patients undergoing RC in the ERAS era. **Methods:** 250 patients underwent RC and urinary diversion for bladder cancer with USC-ERAS protocol between May 2012 and December 2014. Mean age was 70 years, and 76% were male. 50% of patients had no significant comorbidity and 29% had a charlson comorbidity index (CCI)>= 2. We defined EHS as greater than 7 days (> mean hospital stay (5) + SD (2)) postop. The examined variables included length of stay, gender, age, CCI, reasons of late discharge, insurance type, placement plan, in hospital complication (IHC), placement issues (PI), and ICU admission.

Results: 23 of the 250 (9.2%) patients had EHS and were included in this study. Mean age was 75 years, 78% were male and median CCI was 2 with 2 patients having CCI of 4. 8 patients (35%) in the EHS group were admitted to ICU; this was significantly higher than the whole ERAS cohort (4%; p<0.001). 20/23 (87.0%) patients had an extended LOS solely due to IHC. The most common IHCs were GI intolerance/ileus (19 cases), infection (9), respiratory complications (5), cardiac arrhythmia (3), and acute renal failure (3). 2/23 (8.7%) patients had an EHS due to PIs. 1/23 (4.3%) had both IHC and PI. The PIs include lack of beds at skilled nursing facilities (SNF) (2), lack of insurance for post-operative placement (1), patient indecision on placement (1), and improper coordination between healthcare stakeholders (2).

Conclusions: 9.2% of patients who underwent radical cystectomy for bladder cancer with enhanced recovery protocol had EHS, with the majority due to IHC, most commonly ileus and infection.

An Evaluation of Environmental Noise Level on the Ability to Intubate

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Background: The impact of environmental noise levels on task performance is established in Behavioral Psychology and on procedural tasks within Surgery and Radiology. However it has not yet been explored in emergent intubations. Our study aims to examine this scenario, and we hypothesize that increasing noise levels will negatively impact intubation performance.

Methods: Pediatric Emergency Department (PED) staff who were previously trained to intubate (n=20) were consented, surveyed, and underwent a crossover-randomized simulation. Each participant was asked to intubate a resuscitation mannequin at three different noise levels in randomized order (65, 75, 80 dB). Participants' heart rates (HR) were monitored as a proxy for stress. Performance was assessed by time taken to properly intubate the mannequin and depth of endotracheal tube (ET) placement. Descriptive statistics will be performed on each of the outcome variables (time, ET depth, change in HR). Additionally, the data will be analyzed with repeated measures analysis of variance tests. Data will be further stratified and analyzed by accounting for years of experience, daily caffeine intake, and amount of training.

Results: Once data are analyzed, we expect to see a dose response relationship between heart rate and noise level, as well as time taken to intubate and noise level. We also expect to see improper (deeper) ET depth with increasing noise levels. Years of experience and amount of training are postulated to reduce the impact of noise on the outcome variables. Caffeine intake is expected to be a potential confounding variable for changes in HR.

Conclusion: As louder noise is predicted to negatively affect intubation performance, our study could potentially suggest that controlling noise levels during intubation increases efficiency and safety. Additionally, it could elucidate a relationship between experience and training and the ability to cope with increasing noise levels during a simulated high stress environment.

Comparison of Outcomes in Free Flap Surgery at Keck Hospital versus LAC+USC Medical Center

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Purpose: Patients seen at LAC+USC (County) often have poorer access to healthcare and more significant disease progression, compared to patients seen at Keck hospital. This difference in patient populations, along with limited resources in a county hospital setting, may affect outcomes in head and neck surgery. We examine whether patients who underwent free flap reconstruction at County have equivalent outcomes to patients who had surgery at Keck.

Methods: Retrospective chart review of Otolaryngology patients at LAC+USC and Keck. Attending surgeons were the same at both hospitals. Patients who underwent free flap surgery for any indication in the head and neck region were included. The main outcome measure was major complications, indicated by total flap loss or unplanned re-operation within 30 days. Secondary outcome measures included partial flap loss, unplanned hospital re-admission within 30 days, and medical complications. Length of hospital stay was also noted.

Results: At our current point in data analysis, county hospital patients (n=26) had free flap failure or reoperation in 38.5% of patients, and minor complications in 54% of patients. The university hospital patients (n=31) had flap failure or re-operation in 3.2% (p=0.0008) of patients, and minor complications in 22.6% of patients (p=0.01). The mean length of hospital stay was 16 versus 10 days (p=0.006). There were no differences in rates of preoperative radiation or chemotherapy between the patient groups. **Conclusions:** Patients who had free flap reconstruction at County were more likely to have flap failure and re-operation than those at Keck. This is likely multifactorial, and may be related to poorer access to preoperative primary care, malnutrition, poorly controlled or undiagnosed medical comorbidities, and differences in hospital resources. These data suggest that the lower socioeconomic status of patients at a county hospital can result in worse outcomes for patients requiring complex head and neck surgery.

PEDIATRICS

Effectiveness of Furlow Palatoplasty with Islandization for Cleft Palate Repair <u>Christopher Chan, DDS, Medical Student</u>; Lori Howell, MD, Division of Plastic and Maxillofacial Surgery, CHLA

Background: Cleft lip and palate affects about 1:700 births in the U.S. Surgical treatment is not without complications as negative outcomes such as velopharyngeal insufficiency (VPI) and oronasal fistulas (ORF) can occur. Previous data from CHLA has demonstrated that Furlow palatoplasty with islandization of a hemipalatal flap decreases the rate of oronasal fistulas.

Purpose: This study aims to determine the impact of Furlow palatoplasty on rates of VPI in cleft palate patients postoperatively.

Methods: A ten year (2004-2014) retrospective study of medical records of patients undergoing Furlow palatoplasty at CHLA was performed (n=302). Post-operative VPI was assessed according to whether patients had a clinical diagnosis by a surgeon or by nasopharyngoscopic exam. Further analysis was then performed to determine whether additional procedures were warranted to correct the insufficiency. The data was then statistically analyzed and compared with current reported literature rates. **Results:** Preliminary data analysis form 3 years (2004, 2009 and 2010) suggests that the rate of VPI from Furlow palatoplasty that required a secondary surgical procedure for correction was 15%. The rate of ORF was 24%. Average age of repair was 26 months with equal male (n=151) and female (n=151) distribution. 68% of patients (n=206) had isolated clefts and 32% (n=96) had syndromic clefts with 60% Pierre Robin Syndrome being the most common.

Conclusions: The data demonstrates that VPI complications necessitating a secondary surgical procedure from Furlow palatoplasty occurred in 15% of patients treated at CHLA. This is a higher rate of insufficiency compared to previous studies citing rates of 5.75% and 11.4%. Further data analysis will need to be performed to determine whether these results are consistent over the 10 year period, and to evaluate the clinical significance of these findings.

Effects of Timing and Mode of Delivery on Infants with Prenatally Diagnosed Gastroschisis <u>Shannon Cooper BS</u>, Alyssa Quimby MD, Meaghan Pinheiro MD, Sara Twogood MD, Jay Pruetz MD, Tim Wen MPH, David Miller MD, Institute of Maternal-Fetal Health, University of Southern California, Los Angeles, CA

Background: Gastroschisis prevalence rates have substantially increased over the past 20 years. Though recent research has showed benefit in delaying delivery of healthy infants to at least 39 weeks, controversy remains over the appropriate timing and mode of delivery for mothers expecting infants with abdominal wall defects. The aim of this study was to evaluate associations between timing, mode of delivery, induction vs. spontaneous labor, and neonatal outcomes.

Methods: We performed a retrospective chart review of expectant mothers delivered between 2012 and 2015 at Hollywood Presbyterian Medical Center and infants subsequently managed neonatally at Children's Hospital Los Angeles.

Results: There were 22 cases of prenatally identified gastroschisis. 15 were delivered via NSVD and 7 were delivered by Cesarean section. 9 cases were induced. 10 cases were delivered prior to 37 weeks, 12 delivered at 37 weeks or greater, and 3 delivered at 39 weeks or greater.

Infants delivered via C-section were intubated for a mean of 9 days while NSVDs were intubated for a mean of 7.5 days. Mean length of ICU stay was 46.6 days for infants delivered via C-section versus a mean of 43.6 days for infants delivered NSVD. Mean length of hospital stay was 89 days for C-sections vs. 44.4 days for NSVDs.

Term deliveries were intubated for a mean of 9.7 days versus 3.7 days for infants delivered preterm. Infants delivered at term were in the ICU for an average of 31.9 days compared to preterm infants at a mean of 65.7 days. For infants delivered >39 weeks, mean intubation time was 5 days (vs. 8.3 days if <39 weeks), mean ICU length of stay 25.5 days (vs. 47.3 days), and mean hospital length of stay 27 days (vs. 60.5 days).

Conclusion: There is a clear trend toward better neonatal outcomes for infants delivered >39 weeks. Though larger studies are needed to confirm these results, our preliminary data support postponing delivery to 39 weeks if possible for infants with gastroschisis.

Neonatal Outcomes for Total Anomalous Pulmonary Venous Return in the Current Era Shelly Domadia, S. Ram Kumar, MD, PhD, Jodie Votava-Smith, MD, Jay D. Pruetz, MD

Goal: Total Anomalous Pulmonary Venous Return (TAPVR) is a failure of the pulmonary veins to connect to the left atrium during fetal development and often requires emergency neonatal surgery. This study aimed to identify factors associated with pre- and post-op outcomes in TAPVR.

Methods: This retrospective study enrolled neonates treated for TAPVR at CHLA from 2005-2014. Data were analyzed as pre-op and post-op outcomes based on presence of prenatal diagnosis, pulmonary venous obstruction, and heterotaxy syndrome. Primary pre-op outcomes were Apgar scores, days to surgery, iNO use, lowest serum pH, and highest serum lactate. Primary post-op outcomes were length of ICU and overall stay, acute renal failure (ARF), iNO use, and survival to discharge.

Results: Of 137 cases of TAPVR, there were 46% supracardiac, 28.5% infracardiac, 12.4% cardiac, and 9.5% mixed type. Neonatal surgery was done in 135 cases with 15 (10.9%) neonatal deaths (2 pre-op; 13 post-op). Total mortality was 19% (26/137). Overall, 11.7% were prenatally diagnosed, 59.8% had obstructed veins, and 21.2% had heterotaxy. In the prenatal group, 62.5% (10/16) also had heterotaxy. Prenatally diagnosed cases had shorter post-op survival (p=0.06) and more ARF (p=0.07). Heterotaxy cases had greater post-op ICU stay (p=0.03), overall stay (p=0.01), ARF (p=0.06), and mortality (p=0.02). Cases with venous obstruction had lower age at surgery (p=0.007), increased iNO use both pre-op (p=0.04) and post-op (p=0.03), lower pre-op pH (p=0.005), and higher pre-op lactate (p=0.049). Venous obstruction did not significantly affect post-op mortality.

Conclusion: TAPVR has severe neonatal morbidity and mortality independent of venous obstruction and low rates of prenatal diagnosis. Prenatal diagnosis is highly correlated with heterotaxy, likely due to associated anatomical defects which facilitate diagnosis on prenatal screening. Thus, greater complexity may underlie the higher post-op mortality and ARF seen in both prenatal diagnosis and heterotaxy.

Acupuncture and Massage Therapy for Pediatric Fibromyalgia Patients

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Background: Fibromyalgia is a chronic condition characterized by diffuse musculoskeletal pain and fatigue. Many pediatric patients rely on a combination of treatments including medication (ex. SSRI or GABA analog), psychotherapy, physical therapy, and complementary-alternative therapy (CAT). Given the lack of research supporting the efficacy of CAT, we analyzed data from a larger, randomized controlled trial (RCT) of massage and acupuncture for treatment of chronic pain at CHLA. We hypothesize that pediatric fibromyalgia patients who receive massage, acupuncture or a combination of both would achieve reductions in pain severity both in the short-term (between the start and end of individual treatment sessions) and long-term (from baseline to the last treatment).

Methods: We selected patients from the RCT at CHLA who fit the diagnosis of fibromyalgia, and analyzed 3 treatment groups: massage (n=6); acupuncture (n=3); and acupuncture and massage combined (n=3). Included patients must have received at least 4 of 6 weekly treatments. At baseline and before and after each treatment, patients completed iPad surveys that assessed pain intensity via the 10cm Visual Analog Scale (VAS) and FACES Pain Scale.

Results: In the short-term, 83% (VAS and FACES) of the massage group, 100% (VAS) and 67% (FACES) of the acupuncture group, and 100% (VAS and FACES) of the combined group achieved a reduction in pain intensity during \geq 50% of their sessions.

In the long-term, 67% (VAS) and 17% (FACES) of the massage group, 33% (VAS) and 67% (FACES) of the acupuncture group, and 67% (VAS and FACES) of the combined group achieved a reduction in pain intensity.

Conclusion: The data partially supported our hypothesis that pediatric fibromyalgia patients would achieve reductions in pain intensity due to massage and/or acupuncture. For 83% of patients studied, massage and acupuncture (administered alone or together) provided reductions in pain intensity in the short-term, during at least 50% of treatments. Results for long-term efficacy were more variable, warranting further research with a larger sample size.

Can Electronic Health Record (EHR) Data Be Used to Accurately Diagnose Pediatric Acute Respiratory Distress Syndrome (PARDS)?

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Goal: Pediatric Acute Respiratory Distress Syndrome (PARDS) is a significant cause of morbidity and mortality in children admitted to the pediatric intensive care unit (PICU). Currently, there are no automated methods to identify PARDS and diagnosis relies solely on physician recognition, which often results in PARDS diagnosis being significantly delayed or missed. We hypothesize that applying clinical PARDS criteria as determined by the Pediatric Acute Lung Injury Consensus Conference (PALICC) guidelines to data from a proprietary EHR will more accurately identify children with PARDS compared to clinical recognition alone.

Methods: We performed a retrospective cohort study to identify accuracy of PARDS diagnoses from 10/24/2012 to 4/8/2014 at an urban, free-standing children's hospital. The number of patients with clinician-recognized diagnosis of PARDS was compared with the number of children diagnosed with PARDS based on manually extracted EHR data. Percentage of patients meeting PARDS diagnosis criteria via manual data extraction vs. clinician-recognized cases of PARDS was compared.

Results: EHR records for 1600 patient encounters were screened for clinician-recognized PARDS diagnoses based on physician documentation in a PICU billing database. A total of 62 patients were recorded as having clinician-recognized PARDS (3.9%). Manual data extraction of EHR data identified 202 patients as having PARDS based on PALICC criteria (12.6%).

Conclusions: We conclude that 8.7% of children with PARDS would be missed if only clinician-recognized diagnosis of PARDS was utilized. Implementing an automated method of PARDS diagnosis by applying clinical rules to extract PARDS criteria from a proprietary EHR could identify a significantly higher number of children with PARDS. Early identification and intervention in this vulnerable patient population can greatly improve both morbidity and mortality in PARDS patients.

Delayed Sternal Closure in Pediatric Cardiac Patients

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Introduction: The standard practice in many hospitals for pediatric heart surgery is to leave the chest open after heart surgery, closing it 2 days later. However, there are ongoing concerns about the risks of morbidities with a delayed sternal closure (DSC). The goal of this study is to determine the safety of DSCs. We hypothesize that this is safe and efficacious.

Methods: 40 pediatric cardiac surgery patients' charts who had a DSC in the last 2 years were retrospectively reviewed. Complications, morbidities, and mortalities were noted.

Results: Seven patients underwent 2 open-heart surgeries followed by delayed sternal closures so that a total of 47 DSCs were reviewed. Forty-four of the operations (94%) were under the age of 12 months. In 5 of the cases (10%) the patient expired. There were a total of 16 cases (34%) that had intra-operative complications in the primary surgery. Four patients had infections on operation day (8%), 10 in the post-operation period (21%), and 5 were positive for wound cultures (10%). In 27 of the cases, the patient had morbidities but were stabilized and discharged in 22 of those cases (80%). Of the patients that expired, all had morbidities and 4 had to be placed on ECMO (80%). Three had an infection (60%), and 2 had intra-operative complications (40%).

Discussion: This data supports our hypothesis that DSC seems to be effective. While our data did show more infections than we expected, it was still the minority of patients, and of those that did, the majority were treated and discharged without problem (84%).

Predicting Height in a Pediatric Intensive Care Unit Using Ulnar Length

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¹University of Southern California, Keck School of Medicine - Los Angeles, CA/US, ²Children's Hospital Los Angeles - Los Angeles, CA/US **Background:** While height is used for pulmonary function testing, ventilator tidal volumes in pediatric intensive care units (PICU) are often weight based because height (or length for supine patients) is not routinely obtained. Ulnar length has been shown to be a surrogate for height and may be more reliable to measure. However, prior studies have been performed in healthy children with measurements by trained research personnel (Gauld 2004 ages >5 years, von Ungern-Sternberg 2009 ages <5 years). This study aims to determine if ulnar length obtained by the bedside nurse can estimate length, to compare these results to previous predictive equations, and to evaluate the performance of our equation for children with syndromes where accurate height may be difficult to obtain.

Methods: Multidisciplinary PICU in a university teaching hospital. Upon admission, bedside nurses obtained length in their typical fashion. They measured ulnar length with digital calipers for a quality improvement project. Institutional IRB approval was obtained. We used admission diagnosis codes to identify patients with syndromes which may complicate height measurements. Predictive equations were derived from half of the patients without syndromes, and performance of our equations and previously validated equations were tested on the remaining 50% without syndromes and the group with syndromes. Bland-Altman analysis used in both testing sets.

Results: Over 100 nurses measured 1177 subjects (56% males), median age 6.6 years (range, 1 mo to 23 yr). 247 had syndromes. Linear regression from derivation group: Length (cm) = 5.93*Ulnar Length (cm) +11.88, r^2 =0.94. Applied to the testing group, for children >5 years (n=264) the mean bias was -2.4 cm (95% limits of agreement -18.3 to 19.3), similar to the bias observed using Gauld's equation on the testing set: mean bias 0.5 cm (95% -15.8 to 19.7). For children <5 years (n=201) our regression mean bias was 1.9 cm (95% -15.8 to 19.7) similar to the bias observed when using von Ungern-Sternberg equation on the testing set: mean bias -1.3 cm (95% -19.2 to 16.5). Mean bias and variability was similar for patients with syndromes 0.6 cm (95% -19.0 to 20.1).

Conclusions: Ulnar length correlates well with measured length in a PICU population with minimal staff training. Our linear regression performs similarly to more complex and rigorously obtained formulas. Given large potential for error in height or length measurements in critically ill patients, ulnar length appears to be an accurate and easily measureable surrogate, including children with syndromes.



Pediatric Temporal Bone Fractures: Clinical Presentation, Radiologic Classification, and Sequelae in an Urban Setting

<u>Sarah Staley</u>, Debra Don MD, Dennis Maceri MD, Jeffrey Koempel MD, Jeffrey Upperman MD, Benita Tamrazi MD

Background: Temporal bone fractures threaten the middle and inner ear, placing patients at risk of complications such as hearing loss, facial nerve injury (FNI) and cerebrospinal fluid (CSF) leaks. Temporal bone fractures have been better characterized in adult populations; however, developmental changes and different mechanisms of injury may alter the patterns of injury in children. The goals of this study were to characterize pediatric temporal bone fractures in an urban population including mechanism of injury, signs and symptoms, complications and imaging results and to identify factors relevant to the initial presentation or radiological classification that may be useful for predicting complications in the pediatric population.

Methods: This was a retrospective chart review utilizing a trauma registry for temporal bone fractures occurring between 2004 and 2014. Computed tomography scans were reviewed by a neuroradiologist.

Results: Seventy-seven children were diagnosed with temporal bone fractures. The mean age was 6 years and falls of 5ft or less accounted for the majority of fractures (45%). Over half of patients presented with at least one additional skull fracture. Hemotympanum and bloody otorrhea were the most common presenting signs. FNI occurred in 5.2% of patients while CSF leaks developed in 15.6%. Conductive and sensorineural hearing losses developed in 12.5% and 25% of patients respectively. Otic capsule violating fractures were less common (12.5%), while transverse fractures occurred in 43.8%, longitudinal in 50% and mixed in 6%. Except for hearing loss, analysis using both classification systems demonstrate no significant predictive value for complications.

Conclusion: We present our protocol for management of pediatric temporal bone fractures. Complications are rare and radiologic classification systems do not appear to reliably predict complications such as CSF leak or FNI.

Clinical Characteristics and Outcome of Spinal Cord Glioma in Children: A Single Institution Experience.

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Background: Spinal cord glioma (SCG) is the most common intramedullary tumor in children. While pediatric intracranial gliomas are well-described, characteristics and outcomes of SCG are not well understood.

Methods: A retrospective chart review was performed on patients diagnosed with spinal cord glioma and treated at Children's Hospital Los Angeles from June 1990-June 2011. Central pathology and radiology review was performed on all patients. An institutional review board (IRB) approval was obtained to review the charts for clinical characteristics, treatment, and outcomes. **Results:** Twenty two patients were identified, including 13 with low-grade (3 diffuse astrocytoma, 4 ganglioglioma, 4 pilocytic astrocytoma, and 2 astrocytoma NOS) and 9 with high-grade glioma (8 anaplastic astrocytoma and 1 glioblastoma). Median age at diagnosis was 11.5 years (range 1.5-16 years). 5-year event-free survival (EFS) and overall survival (OS) for low-grade patients was 66.7% and 100%. Seven of nine high-grade patients died with a median EFS and OS of 8 months and 15 months. Among low-grade patients, 5 received irradiation, 6 chemotherapy, and all received surgery (2 debulking, 9 subtotal, and 2 gross-total resections). Of the high-grade patients, all received irradiation, 7 chemotherapy, and all underwent surgery (3 debulking and 6 subtotal resections).

Conclusion: Outcome of SCG is similar to their counterparts in the brain. Low-grade tumors are highly treatable and have high 5-year OS whereas high-grade tumors portend poor prognosis with most cases resulting in death despite aggressive treatment.

PUBLIC HEALTH

Local Policy Targeting Youth Tobacco Access and Prevalence of Cigarette, Electronic Cigarette, and Hookah Use Among Adolescents: A Comparison of Findings From the Children's Health Study and American Lung Association Local Tobacco Grades

<u>Roee Astor</u>, Rob S. McConnell, PhD, Robert Urman, as an initiative with the Tobacco Centers of Regulatory Science (TCORS), Department of Preventative Medicine, Keck School of Medicine

Goal: Studies analyzing local tobacco policy have shown mixed results regarding the effect on adolescent cigarette smoking behavior. Despite the recent rise in electronic cigarettes and hookah as preferred tobacco products among adolescents, few studies have examined the effect of local tobacco policy on their prevalence and incidence. With these observations in mind, we examined the relationship between various American Lung Association local tobacco policy grades with prevalence/incidence of cigarettes, e-cigarettes, and hookah among high school students. **Methods:** We used a subset of survey-based data from the ongoing Children's Health Study (CHS) collected in 2014 from 11th and 12th grade high school students in twelve communities across Southern California (N=2,072). We examined the main predictive effect of ALA local tobacco grades on prevalence and incidence of various tobacco product use including cigarettes, electronic cigarettes, and hookah. **Results:** Other than Reduced Tobacco Sales, all other policy category grades showed a lack of meaningful findings concerning incidence and prevalence of various tobacco products. However, a grade of "A" compared to "F" for Reduced Tobacco Sales indicated a statistically insignificant but notable reduction in prevalence and incidence across all tobacco products with prevalence more heavily reduced.

Conclusions: Students living in communities with a grade of "A" for Reduced Tobacco Sales may be less likely to ever use cigarettes, electronic cigarettes, and hookah use compared to students living in communities with a Reduced Tobacco Sale Grade of F, while other grades showed no effect on tobacco product incidence and prevalence. Results suggest that policies designed specifically to reduce youth access to tobacco may have an effect not only on adolescent cigarette smoking prevalence but also use of other tobacco products, yet additional research is needed in this area.

The access to healthcare for the Togolese population and its correlation with depression <u>Lloyd Camper (Student)</u>, Michael Cousineau (Advisor)

Goals: The goal of the research is to take a public health perspective on the access to care in low-income countries such as Togo in West Africa. Such countries are susceptible to a high prevalence to infectious diseases, yet the associated comorbidities such as mental health diseases are often disregarded or misdiagnosed. In that regard, the study is evaluating the correlation between the lack of access to care and the higher risks of depression in the population.

Methods: Subjects (N=64) were asked to respond to a survey that had questions giving a score based on their access, use of services, and coordination of the people's care (0-84 the higher representing the least access to care) in addition to a Beck depression scale (0-33 the higher representing more depression risks). The subjects were classified by age, gender, and rural/urban for further analysis of the data.

Results: The overall results showed a mean access to care score of 47.3 ±13.0 and a mean depression score of 7.0 ±5.0 with a positive Pearson correlation coefficient r=0.41 (p<0.001). Higher scores represent low access and higher depression risks. Therefore, a positive correlation between both variables represents higher depression risks for lower access to care subjets. Subsequently, the correlation coefficient was higher for women (N=28) than men (N=36) with r=0.50 and r=0.37 respectively. Interestingly, the positive correlation coefficient remained for the age group over 30 years old (N=48, r=55) but was not consistent for the age group under 30 years old (N=16, r=-0.1). **Conclusion:** These data demonstrate higher risks for depression in populations with lower access to care. In this way, the data supports the susceptibility for comorbidities in populations lacking care that would expose themselves to risks of infectious and mental health diseases.

The WISH Project: Advance Care Planning with the East Los Angeles Geriatric Population

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Goal: Advance care planning (ACP) provides numerous benefits to patients, families, and our healthcare system. Underserved communities are less likely to participate in ACP or discuss end-of-life (EOL) goals of care, which is alarming in a rapidly aging population. We aim to determine the role of medical students as facilitators of EOL discussions in the Latino community of East Los Angeles. We also aim to identify demographic and health factors associated with EOL decision preferences.

Methods: Pairs of bilingual medical students held private sessions with patients (n=40) and accompanying family members at the Geriatrics Clinic of LAC+USC Medical Center. The following items were completed during each session: (a) a pre-session survey to assess patient demographics, medical status, and current attitudes toward EOL care; (b) the Five Wishes advance directive document in Spanish; and (c) a post-session survey to assess satisfaction and changes in attitudes toward EOL care. We also analyzed associations between patient demographic and health factors versus EOL decisions. Results: Most patients had never previously written (95%) or discussed (75%) EOL wishes. 61% were unaware they could choose to accept or reject treatment at the EOL, but 85% felt it was important to learn about these options. Only 19% had previously heard of an advance directive and no participant had previously completed one, but 88% completed one during the session. After the session, 90% felt comfortable discussing EOL goals compared to 65% pre-session. Patients felt more comfortable discussing EOL goals with medical students (95%) than with their doctor (65%). Associations between EOL decisions and patient age, chronic disease burden, and living situation were insignificant (p > 0.05). **Conclusions:** Our results suggest that patients are willing to complete advance directives given personalized attention in their native language. Medical students may help improve ACP participation in underserved communities. More research is needed to understand associations between patient demographics and EOL preferences.
Reproductive Health

Intrapartum electronic fetal heart rate monitoring and mode of delivery for pregnancies complicated by gastroschisis.

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Background: Electronic Fetal Heart Rate Monitoring (EFM) research before 1997 demonstrated pregnancies complicated by gastroschisis have more decelerations than normal pregnancies. In 1997, the National Institute of Child Health & Human Development (NICHD) published standardized definitions for EFM. In this study, we review intrapartum EFM decelerations for pregnancies complicated by gastroschisis and normal controls using the NICHD definitions. We assess mode of delivery and indication for c-section. We hypothesize that fetuses with gastroschisis will have more decelerations than normal controls but these decelerations will not affect mode of delivery.

Methods: This is a retrospective chart review of fetuses with gastroschisis from USC Institute for Maternal-Fetal Health (IMFH) and normal controls delivered at the same hospital between 2012-2014, using REDCAP. Fetal heart rate tracings were read by USC OBGYN attendings using the NICHD nomenclature. Data analysis compared number and type of decelerations in the two groups and differences in the mode of delivery.

Results: Pending. We will evaluate the number of variable, early, late, and prolonged decelerations for pregnancies affected by gastroschisis and normal controls. We expect an increased number of decelerations in pregnancies affected by gastroschisis. We will analyze the percentage of patients who underwent vaginal versus cesarean delivery in each group and if cesarean, the indication. We do not expect to see a significant difference in mode of delivery.

Conclusions: This is the first analysis done with NICHD standardized definitions looking at intrapartum EFM patterns for pregnancies complicated by gastroschisis. These results may help with counseling and management of pregnancies complicated by gastroschisis, using EFM to help achieve the most favorable delivery and neonatal outcome.

Pregnancy Outcomes in Hypothyroid Women

Jennifer Tang MSII, Martin Montoro MD, Andrew Mayo MD, Lisa Korst PhD, Jennifer King MD

Introduction: Hypothyroid pregnant women are at risk of developing obstetrical complications while their children are at risk of developing neonatal complications, including neuro-intellectual impairments. This study aims to assess whether or not early TSH normalization can help prevent such outcomes. We predict that hypothyroid pregnant women will have a higher rate of premature deliveries as well as a higher rate of obstetrical and neonatal complications compared to euthyroid pregnant women. Methods: LAC+USC Medical Center's Thyroid Clinic followed 52 hypothyroid patients, other conditions excluded, from 2010-2014. Patients are categorized as either euthyroid or hypothyroid, which is further subdivided as "clinical" or "subclinical". Every 2-4 weeks, patients were clinically evaluated and their TSH, FT4, and FT4I values were measured to assess thyroid function. The target TSH was <2.5 in the first trimester and <3.0 thereafter. Lists of pertinent obstetrical (e.g. preeclampsia and preterm labor), fetal (e.g. meconium and macrosomia), and neonatal (e.g. NICU admission) complications have been predefined. Each hypothyroid patient's relevant medical history, demographics, outcome, and lab values as well as neonatal APGARs, birth weight, and complications have been recorded by chart review. **Results:** A preliminary 2008 study followed 73 hypothyroid women through 85 pregnancies who were divided into 2 groups: 1) 38 hypothyroid women further subdivided into clinically hypothyroid: 1a and subclinically hypothyroid: 1b 2) 35 euthyroid women. The prematurity rate was 20% in 1a, 25% in 1b, and 2.4% in 2, which was statistically significant with a p-value of .0044. The serum TSH normalized before 17 weeks in 6/10 premature deliveries in Group 1 while women who were euthyroid had no complications.

We are now finishing 2010-2014 data analysis, but expect to find group differences especially in prematurity rates.

Conclusion 138: Upon statistical analysis, we expect to advocate the need to control hypothyroidism in pregnant women prior to conception in order to improve pregnancy outcomes.

SURGERY

Surgical Outcomes and Complications of endoscopic or microscopic transsphenoidal resection of Prolactinomas in a pituitary center

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Purpose: Prolactinomas are the most frequently encountered pituitary tumors. In addition to symptoms of mass effect, namely headaches and vision loss, prolactinomas commonly presents with symptoms of hypogonadotrophic hypogonadism. Hyperprolactinemia can thus result in decreased libido, galactorrhea, amenorrhea or oligomenorrhea. Medical management with dopamine agonists is often first line therapy, however intolerance or lack of efficiency of DA therapy are indications for surgical treatment. Because of the challenging nature of sellar tumors, our goal is to analyze the safety and efficacy of surgical removal of prolactinomas within our institution to improve postoperative outcomes, while decreasing recurrence.

Methods: A retrospective analysis of 49 patients surgically treated for prolactinomas at a single center between 1995-2015 was conducted, with the majority of patients undergoing transsphenoidal endoscopic or microscopic resection. After surgery, patients were followed by clinical assessment, MRI, prolactin levels, and visual field testing. The mean follow-up time was 37.8 months.

Results: The average preoperative prolactinoma diameter was 15.2 mm. Although cavernous sinus invasion occurred in 51.1% of patients, gross total resection was achieved in 69.4%. Postoperatively 64.1% had improved endocrine status, while one patient developed new hypopituitarism. 23.7% reported improvement in their headaches, and 13.5% reported improvement in their vision. No patients died postoperatively. Prolactinomas recurred in 7% of patients, with the average time to recurrence being 23 months.

Conclusions: Although Prolactinomas have a low rate of recurrence and endocrine status improved in the majority of patients, rate of improvement in headaches and visual deficits is uncommon. Additionally, many patients require dopamine agonists or stereotactic radiosurgery after resection. A hormonal remission rate of 59.3% may indicate the need for earlier surgical intervention so that gross total resection is able to be achieved in a larger percentage of patients.

Breast Reconstruction and Adjuvant Therapy: A Systematic Review of Surgical Outcomes <u>Bassim EL-Sabawi, BS</u>, Michael Sosin, MD, Joseph N. Carey, MD, Maurice Y. Nahabedian, MD, Ketan M. Patel, MD

Purpose: The impact of adjuvant therapy on surgical outcomes following breast reconstruction is poorly understood. The purpose of this systematic review was to evaluate surgical outcomes following autologous and prosthetic reconstruction in the setting of post-mastectomy radiation therapy (PMRT) and adjuvant chemotherapy.

Methods: A systematic search of the English literature published from 2000 to 2015 in the Pubmed/MEDLINE database was performed to identify all manuscripts reporting surgical outcomes following post-mastectomy breast reconstruction in the setting of PMRT and/or adjuvant chemotherapy. Exclusion criteria included studies that contained less than 20 patients and those that

lacked relevant extractable data. A pooled analysis using study size weighted means was performed for the PMRT studies.

Results: A total of 1,825 potential titles were identified by the initial search, of which, 62 manuscripts met the criteria for inclusion. This included 56 manuscripts (5437 patients) evaluating patients treated with PMRT and 11 manuscripts (820 patients) evaluating patients treated with chemotherapy. Pooled analysis of the PMRT cohort demonstrated that prosthetic reconstruction had a significantly higher incidence of infection (13.5% v. 5.8%; p<0.0001), re-operation due to complication (37.0% v. 16.6%; p=<0.0001), total complications (41.3% v. 30.9%; p<0.0001), and reconstructive failure (16.8% v. 1.6%; p< 0.0001). Autologous reconstruction had a significantly increased incidence of wound related complications (5.8% v. 12.9%; p=0.001), hematoma (2.8% v. 6.1%; p=0.02) and seroma (6.0% v. 8.0%; p=0.02). There was little evidence to suggest that postoperative chemotherapy is associated with poorer overall outcomes.

Conclusions: PMRT is associated with a higher incidence of adverse events compared to chemotherapy. The timing of reconstruction in relation to PMRT may play a role in determining outcomes and may help to better achieve success with implant-based options.

Surgical Techniques of Melanoma In Situ

Christina S. Gainey B.S., Ashley Wysong, M.D., M.S.

Background: The current recommendation for management of melanoma in situ (MIS) is surgical excision with **5-10 mm** margins. However, the standard excision margins are often inadequate for many lesions, and there is a lack of randomized, controlled trial data to support the current recommendation. Multiple surgical techniques have been developed to achieve better margin control, but the wide variation in methods lack standardization. Currently, there is no consensus on the optimal surgical management of MIS.

Objective: To review the available literature and describe the surgical and histologic processing techniques used in the management of MIS. We sought to create an organizational framework upon which to classify each new technique and to define and clarify a set of terms that can be used to make direct comparisons.

Methods: PubMed/MEDLINE databases were utilized to identify studies pertaining to variations in both surgical and laboratory techniques used in MIS.

Results: We found that there was a large variation in the nomenclature, description of techniques, as well as outcome measures. The main methods we reviewed were wide local excision (WLE), Mohs micrographic surgery (MMS), MMS with immunohistochemistry, "slow Mohs," mapped serial excision, radial staged excision, square procedure, and the perimeter technique. We created a classification schema that organizes and classifies each technique by the method of excision technique, histological processing, and margin evaluation, with a discussion of the advantages and disadvantages of each. **Conclusion:** Numerous alternative margin-guided excision techniques have been developed, with an increasing number of new modifications of those techniques. It is difficult to interpret the results of these studies and apply them to clinical practice because there is no standardization of techniques. We suggest in the future that all groups adhere to a standard set of terms that can be applicable to the entire field.

Surgical Resection of Rathke's Cleft Cysts

Michelle Lin MSII, Daniel Bradley MS IV, Daniel Donoho M.D., Gabriel Zada M.D.

Goal: Rathke's Cleft Cysts (RCCs) are benign cysts of the sellar region that may present with vision loss, headaches, and hypopituitarism. Transsphenoidal surgery for RCC fenestration and drainage is the mainstay of treatment. We report our institutional experience on the surgical management of RCCs, relationships between patient/lesion characteristics, postoperative outcomes, cyst recurrence and complications.

Methods: A retrospective analysis of 130 patients surgically treated for RCCs at a single center between 1995-2015 was conducted. The majority of patients underwent transsphenoidal endoscopic or microscopic RCC fenestration for decompression and histopathological diagnoses were made by wall biopsy. Patients were followed with MRI, visual field tests, and clinical follow up. A mean follow-up time of 71 months was obtained over 92 patients. Analysis was conducted with Chi square testing. **Results:** The average preoperative RCC diameter was 14.42 mm. 88.9% of patient reported postoperative improvement of headaches. 86.4% had resolution of visual deficits. Prolactin levels normalized in 100% of patients. None of the patients with preoperative hypopituitarism experienced improvement in their respective pituitary axes. Transient diabetes insipidus developed in 22.6% of patients. No patients developed new neurological deficits or died postoperatively.

RCC recurrence developed in 26.1% of patients. The average time to recurrence was 33 months. Neither fat/fascial graft reconstruction, the presence of squamous metaplasia, or alcohol cauterization were associated with recurrence. Recurrence was more common in patients older than 40 years of age (p=0.0037).

Conclusions: Surgical management of RCCs is indicated for symptomatic lesions, with most patients experiencing improvement of headaches, visual field deficits, and hyperprolactinemia. Improvement in endocrinopathies is uncommon. Following fenestration, RCCs have an appreciable rate of recurrence, particularly in patients over 40 years of age necessitating diligent follow up.

Surgical Outcomes of Nonfunctioning Pituitary Macroadenomas

<u>Michael Lin-Brande</u>, Gabriel Zada, M.D., John Carmichael, M.D. Department of Neurologic Surgery, Department of Endocrinology, USC Keck SOM

Purpose: The prevalence of nonfunctioning pituitary adenoma (NFPA) is estimated at 22.2 per 100,000 people. As there are only a few studies that have analyzed NFPAs, our goal was to evaluate surgical outcomes of NFPAs.

Methods: We performed a 20-year (1994-2014) single-center retrospective review of 393 patients who underwent NFPA resection.

Results: At the time of surgery, the average max tumor diameter was 25.8 cm. Average age at surgery was 57.29 years. Microscopic transphenoidal resection was the preferred procedure (90.8%). Gross total resection was achieved in 67.9% of patients. CSF leak occurred in 52.6% of cases. Complications occurred in 105 patients (21.9% transient DI, 21.0% hyponatremia, 9.5% CSF leak, 7.6% CN palsy, 6.7% hematoma). Early readmission and reoperation were 7.1% and 5.1% respectively. The most common

reason for early readmission was hyponatremia (53.6%) and hematoma (40%) and CSF leak (35%) for reoperation.

Average hospital stay postoperatively was 3.31 days with a 2-day median. An average follow-up time of 53.0 months was achieved. In the latest MRI scans, 52.2% had no evidence of disease, 41.2% had stable disease, and 6.6% had progression. Recurrence occurred in 28 (7.1%) with average time to recurrence of 62.5 months. Progression was seen in 44 (11.2%) with average time to progression of 47.7 months.

Headache postoperatively was improved in 37.5% of patients. Vision improved in 49.8% of patients.

Conclusion: CSF leak remains a common intraoperative complication while immediately postoperatively, patients need to be monitored for hyponatremia and transient DI as the two most common complications. While 41.2% had residual tumor, only 6.6% had evidence of progression which points to the propensity of the tumor to remain unchanged over time. Our findings highlight the importance of yearly surveillance MRIs because of the long time to recurrence. Surgical intervention most noticeably improves the visual deficits caused by pressure symptoms of macroadenomas.

Effect of Non-routine Perioperative Laboratory Values on 30 day Mortality after Non-Cardiac Surgery <u>Michael Ohebsion</u>, Zhongjie Cai, Alexandra Ruan, Stephanie Biglarian, Ling Zheng, MBBS, PhD, Mary M. Joseph, MD, Departments of Neurology and Anesthesiology, KSOM

Background: It is known that certain laboratory value abnormalities may increase mortality in patient populations with specific risk factors and specific procedures. The purpose of this paper was to investigate the effect of drawing a non-routine lab (regardless of its result) on 30 day mortality and to investigate the effect of an abnormal non-routine laboratory value on 30 day mortality. **Methods:** The electronic medical records of adult patients undergoing non-cardiac surgery from 2011-2014 at LAC+USC Medical Center were reviewed retrospectively as approved by our institutional review board. Demographic data, surgical risk assessment, and routine and non-routine laboratory values (TSH, Troponin, Creatine Kinase, Hb A1c) were recorded; patients were grouped according to the single non-routine lab they had drawn. Multivariate logistic regression analysis was used to determine significant risk factors associated with increased 30 day mortality.

Results: 11,306 patients met our inclusion criteria. Drawing a non-routine lab significantly increased mortality in the Troponin group (OR=3.05, P<.001) but not in the TSH, Creatine Kinase, and Hb A1c groups. An abnormal non-routine laboratory value significantly increased in mortality in the TSH group (OR=11.07, P=.008) but not in the other three groups.

Conclusions: The 30 day mortality in adult patients undergoing non-cardiac surgery, who had clinical indications to draw Troponin, was significantly higher than in the routine only group. Next, mortality was statistically higher in patients with abnormal TSH values but not in patients with abnormal Troponin, Creatine Kinase, or Hb A1c, although elevated Troponin may be clinically significant. Routine and non-routine laboratory testing may guide perioperative patient care and result in improved post-surgical outcome.

Т	a	b	e	:

Non-Routine Lab	OR	P-Value
Draw:		
тѕн	1.24	0.466
Troponin	3.05	<.001
Creatine Kinase	0.90	0.702
Hb A1c	0.35	<.001
Abnormal:		
TSH	11.07	0.008
Troponin	0.63	0.724
Creatine Kinase	1.47	0.517
Hb A1c	0.42	0.085

Effects of Bariatric Surgery on Postprandial Amino Acid Profiles and Correlations with Insulin Sensitivity in Non-Diabetic Patients

Dennis Tsang (University of Southern California, Keck School of Medicine), Donald J. McMahon, M.S., Gerardo Ferber, M.D., Charles Burant, M.D., Ph.D. (University of Michigan), Judith Korner, M.D., Ph.D., Columbia University, College of Physicians and Surgeons

Background: Levels of select amino acids (AAs) have been previously shown to be altered in obese versus lean individuals. Bariatric surgery is among the most effective treatments for obesity, providing long-term weight loss as well as improvements in insulin sensitivity, some of which have been hypothesized to be weight loss independent. Two popular forms of bariatric surgery – Laparoscopic Adjustable Gastric Banding (LAGB) and Roux-en-Y Gastric Bypass (RYGB) – and their effects on AA profiles were explored in this study. The main objective of this study was to compare the fasting and postprandial AA profiles between lean and obese subjects before and after surgery. We predicted that lean controls would have an AA profile that differs from obese individuals and post surgery individuals would have a profile that approaches that of lean controls.

Methods: A mixed meal test (MMT) 5.8 weeks prior to surgery and an average 7.7 months post-surgery were performed in obese individuals after an overnight fast. Venous blood was drawn in the fasted state

and at 30, 60, 90 and 120 minutes after the meal. Purification and quantification of serum amino acid levels was achieved using the EZ:faast kit from Phenomenex, along with a Zebron ZB-AAA column on a 6890 GC with a 5973 MSD.

Results: Post-LAGB and post-RYGB individuals demonstrated a 15.4 \pm 1.6 percent and a 24.4 \pm 3.7 percent weight loss respectively. We found that there are distinct metabolic improvements in both LAGB (n=9) and RYGB (n=12) surgery groups post-intervention. As expected, fasting BCAA levels decrease from pre to post-op for band and bypass groups (p=0.08 band, p=0.001 bypass). Fasting levels of aromatics (Phe, Tyr, Trp) followed similar trends whereas fasting levels of glycine and serine increased from pre to post-op. Correlations of fasting amino acid levels to HOMA-IR, a measure of insulin resistance were also conducted. Fasting levels of BCAAs have a positive correlation with HOMA-IR (p=0.0009), whereas fasting levels of glycine have a negative correlation with HOMA-IR (p=0.0044). In terms of weight loss, fasting levels of BCAAs and phenylalanine (but no other aromatic amino acid) demonstrate negative correlations with % weight loss.

Conclusions: Our findings suggest that both LAGB and RYGB procedures produce similar metabolic changes that shift one's metabolic signature towards that of lean controls. Some AAs are tied to insulin sensitivity, some are tied to weight loss, and some are tied to both. The fact that RYGB individuals often have immediate, clinically different post-surgical outcomes compared to LAGB individuals could be explained by the more pronounced shift of the metabolic markers rather than the greater weight loss itself, which is often not achieved until several months after surgery. This study also elucidates several AA markers that are altered with bariatric surgery, could potentially be involved in regulation of one's overall metabolic health, and may warrant further study such as in the pursuit of pharmaceutical interventions that target their metabolism.

Complications from Surgical Excision for the Treatment of Lymphatic Malformations – a 10-year Institutional Review

Yang T, Hoang D, Schall K, Wieck M, Nowicki D, Zeinati C, Anselmo D, Howell L

Purpose: Treatment options for lymphatic malformations (LMs) include percutaneous sclerotherapy, surgical resection, or a combination thereof. The purpose of our study was to compare complication rates of surgical resection alone versus a combination of surgery and sclerotherapy in the treatment of extra-abdominal LMs at a single multidisciplinary vascular anomalies center.

Methods: A retrospective chart-review at CHLA included 177 patients diagnosed with LMs from August 2003-June 2015. LMs that were intra-abdominal or not treated with surgery were excluded. 48 total patients' complications were compared using chi-square testing based on their treatment. **Results:** Of 48 surgical patients, 48% underwent surgical resection only, 19% were treated with surgery and post-operative sclerotherapy, and 33% with pre-operative sclerotherapy and surgery. Overall complication rates were as follows: 25% of patients had a post-op seroma, 20% developed edema, 16% had a wound infection, 13% developed chronic draining wounds, and 11% resulted in wound breakdown following treatment. Wound infection rates were higher in patients undergoing surgery if combined with pre-operative sclerotherapy compared with those undergoing surgery alone (p<0.05). Post-op edema rates were higher in patients treated with surgery followed by sclerotherapy than in patients treated with surgery alone (p<0.05); however, no statistical differences were observed for other wound problems post-operatively.

Conclusion: Treatment with pre-operative sclerotherapy appears to exacerbate the rate of post-op wound infection. Treatment with surgery followed by sclerotherapy increases the rate of post-op edema. Given that the most common postsurgical complications were post-op seroma and edema, surgical drain placement and prophylactic edema compression garments should be utilized to anticipate these complications regardless of whether sclerotherapy is used as adjunctive therapy.

TECHNOLOGY (HEALTH, TECHNOLOGY & ENGINEERING)

Store-and-Forward Teledermatology: A Model of Feasibility in Rural Haiti Lauren Cutler, BS¹, <u>Katherine Ross, BS¹</u>, Melvin Chiu, MD, MPH², David Cutler, MD³

Objective: To see if implementation of TD would help increase access to dermatological care in rural Haiti with adequate concordance and turnaround time.

Study Design: At the Henri Gerard Desgranges Clinic in rural Haiti, patients with dermatological issues were recruited to be enrolled into the study. PCPs provided patients with a free skin exam, a preliminary diagnosis and a treatment plan. Dermatologic conditions were photographed on an Apple iPhone 6 Plus and uploaded into an encrypted Google Documents folder named with a de-identified patient code. PCPs completed an intake evaluation and uploaded this form into the patient folder with the photos and an accompanying blank consultation form. Board Certified Dermatologists in the U.S. completed the consultation form indicating their diagnosis and treatment plan. Clinical and TD diagnoses were reviewed and adjustments to treatment plans were reported to local Haitian physicians to carry out. If diagnoses differed, but treatment plan remained the same, no action was taken.

Results: Out of 100 patients, the mean concordance value between TD and PCPs diagnoses was 75%. The average time from patient intake to "case-closed" was 40 hours. The most prevalent disease was atopic dermatitis (31%) followed by fungal infections (25%). The mean age was 26 years old and male to female ratio was 1:2.

Conclusion: The concordance value of 75% and the turn around time of 40 hours were both within accepted ranges from previous studies. Turn around time could be improved with specific assignments to each consulting dermatologist. Incorporation of real time TD via live-feed video, such as iPhone's "FaceTime", could be considered. Future directions include implementing a sustainable telemedicine practice in rural Haiti and applying telemedicine to other specialties. In Haiti there is an unmet need for dermatological services and TD is a viable option to provide care to rural patients.

Breaking the Silence:

Analyzing the Effect of Vocal Interaction with the Virtual Standardized Patient

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Introduction: The next step in creating an authentic standardized patient (SP) interaction is to allow for vocal interaction. We know when typing to virtual standardized patients (VSPs), students somewhat agreed the system would prepare them for future SP interaction. The VSP natural language understanding system (NLU) also correctly interpreted 92% of questions. We also know students did improve after multiple attempts with the VSPs. These same parameters need to be compared against students having vocal communications with the VSPs. I hypothesize students will have a higher perceived applicability of the system and will have the same improvement patterns with vocal interaction while the NLU may correctly interpret fewer questions.

Methods: As a pilot study, 5 students will be tested with voice interactions with the VSPs. They will be given a small orientation on the use of the VSP. Students will do a series of four 5 minute interviews with the patients and will have two minutes to view the after action report for each attempt. At the end of

the series, students will be surveyed on perceived applicability and opinions on their experience with the system.

Results: We expect the score improvement to be similar to that of students when typing with the VSPs. We expect students will have a higher perceived applicability of the system and will find it more useful than those that typed. We expect the NLU to correctly interpret fewer questions than those that were typed.

Conclusion: If expected results are met, we can say incorporating vocal interactions with the VSPs leads to a more positive experience and higher perceived applicability of the system. While the score improvement on the interviews may be similar to typing, they still maintain the VSPs lead to improvement of a student's diagnostic interviewing skills. Even if the NLU interpreted fewer questions correctly, the positive increase in VSP experience would demonstrate the VSPs are great tools to improve a student's diagnostic interviewing skills.

A Novel Mobile Solution to Help Users Find Immediate Care <u>Rupan Bose, MB¹</u>; Alexa Hudnut²; <u>Joseph Juliano¹</u>; <u>Martin Shapiro¹</u>; George Tolomiczenko, PhD, MPH, MBA^{1,2}; Terry Sanger, MD, PhD^{1,2} ¹Keck School of Medicine of USC – HTE@USC ²USC Viterbi School of Engineering – HTE@USC

Background: One of the biggest challenges in healthcare is that many people do not know where to go when they need acute medical care, causing them to go straight to the emergency room. Yet, approximately 1 in 4 emergency visits could have been seen by urgent care facilities and for an average cost of \$400 less per comparable procedure. Furthermore, 90% of urgent care wait-times are less than 30 minutes while wait-times at emergency rooms can be upwards of 10 hours, indicating that many urgent cares are being underutilized. Thus, there is a need to empower patients with options to help them determine where they should go that is both fast and appropriate for the care that they need. **Proposed Solution:** Our solution to help people find quick and appropriate care, while simultaneously redistributing patient throughput to ease the burden of wait-times, is a mobile-based app called DocFindr. Based on a patient's location and insurance, DocFindr will list all the appropriate care facilities that can address their need, and also the clinic's real wait-time, location, and contact information. This allows individuals to make informed decisions of where to get medical treatment quickly and effectively, and helps them avoid facilities that may have long wait times.

Methods: Our team is currently interviewing clinicians and administrators to guide the development of our app. We will design an alpha test to iterate better interfaces for clinic integration in terms of checkins and wait-times. Our beta test will involve rolling it out to patient populations to gauge their input on user interface and functionality, as well as explore opportunities to incorporate other care modalities such as telemedicine and house calls.

Results & Conclusions: Our tests and user feedback would help expand our features such that not only could you find care that you could go to, but the it could also either address your medical concern remotely via telemedicine, or even come directly to you via house calls. In doing so, we hope to create a solution that is so complete that it ultimately becomes the first place you turn to when you need medical care.

EverDry: A Smartphone Application for Dysfunctional Elimination Syndrome

Karen Burtt, MSII; Fotos Frangoudes, PhD Candidate; Terry Sanger, MD; George Tolomiczenko, PhD

Background: Dysfunctional Elimination Syndrome consumes a substantial amount of clinical resources and physician time. Studies have shown that 40% of pediatric urology clinic visits are related to voiding dysfunction problems. Incontinence is distressing to the patient who faces social isolation and increased risk of bladder infections. Dysfunctional Elimination Syndrome is largely an acquired behavioral disorder with the current standard of care involving the use of a paper log. Compliance is poor as parents must track time, children are not engaged or motivated, and the paper log may be forgotten or lost. We propose a smartphone application that treats and tracks voiding behaviors to improve the reliability with which patients follow clinical guidelines for behavioral change.

Methods: Our methods process began with compiling a list of clinical needs observed while shadowing in the urology clinic. Customer discovery consisted of interviewing the proposed customers, users, and payers of the application by asking a series of universal questions based on segments of the Business Model Canvas. We are currently working on prototyping the product, developing a marketing plan, and obtaining seed funding through a device development competition.

Results: Development is ongoing, with a proof of concept expected in the next month. The application targets children between the ages of 4 and 15, with emphasis on the teen age group. We will digitize the reminder system, gamify pelvic floor exercises to reward compliance, and use outcomes to modify treatment plans for each child on an ongoing basis.

Conclusion: Upon prototyping, we intend to further collaborate with the urology clinic at Children's Hospital Los Angeles in order to ensure that our smartphone application meets the needs of their patient population.

GPS and Accelerometer Measurements to Predict Noncontact Injuries in College Football Athletes <u>Jessica Chen</u>, Seth Gamradt, Department of Orthopaedic Surgery, KSOM

Goal: GPS and accelerometer technology are often used in sports to assess performance. Measurements captured by the sensors are recorded during training practice and in competition. In this study, we aim to assess parameters that may predict the risk of a noncontact injury in college football athletes. Our hypothesis is that players with more explosive movements and collisions are more likely to sustain a noncontact lower extremity injury.

Methods: 46 athletes in the USC football team wore Catapult sensors, containing GPS and accelerometer, during practices and games. Catapult measurements include total yards traveled, player load, player load per yard, player load per minute, top speed, accelerations, decelerations, running yards, high speed efforts (> 18 mph), explosive movements, and collisions. Player data was compared across the 4 quarters of competition and compared to training. Data from athletes that sustained a noncontact lower extremity injury was compared to those from non-injured athletes. **Results**: Initial data analysis reveals that players have the highest output during the pre-game time and output declines with each quarter of competition. No conclusions could be drawn with respect to injured vs. noninjured athletes using the current data. **Conclusions**: GPS and accelerometer technology can be used to assess player performance but these data may not be predictive to identify athletes that are "at risk" for a noncontact lower extremity injury.

An integrated mobile device platform for real-time biofeedback and compliance improvement for athome physical therapy (PT) regimens

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Introduction: Compliance with prescribed physical therapy (PT) regimens is estimated to be approximately 40%. The reasons for the unacceptably low rates of compliance include confusion about how to do perform exercises without direct supervision and a lack of significant observable progress in the short term. Adherence to physical therapy is strongly correlated with improved short-term and longterm patient outcomes while a lack of compliance leads to a substantial decline in outcomes. **Methods:** Our solution to addressing the lack of compliance with PT is real-time biofeedback device integrated with an application for mobile devices. The physical device will be a wireless sleeve embedded with lightweight sensors. This device will be worn during exercises for real-time analysis of joint position and muscle activation using a mobile device application. Further, the application will serve as a motivational tool in facilitating patient compliance by serving as an important resource for the user in his or her recovery processes. Features such as direct clinician communication and progress reports will provide much needed support to patients while simultaneously encouraging them to comply with their PT exercise regimen.

Results: The mobile application and hardware are currently being designed in parallel. The layout and organization of the application are being designed using InVision, an online prototyping service. Some functionalities that are under exploration include progress assessment, adaptive PT regimens, direct clinician messaging, and social media integration. Initial experimentation for the device has consisted of assessing which types of sensors (e.g. bending, stretch, accelerometer) provide the most reliable biometric data for the sleeve. Further research is required before preliminary data can be collected. **Conclusions:** The development of a solution to this unmet healthcare is underway, but will require a great deal of product testing and design before it reaches consumers.

Socially assistive robotics to reduce distress in children receiving intravenous lines Adam Ford, BS; Jill Greczek, MS; Grant Christman, MD; Maja Mataric, MS, PhD; Margaret Trost, MD

Background: Socially assistive robots (SAR) can act as a powerful form of distraction leading to decreased pain during procedures such as immunizations in children. It remains unknown if SAR assistance during longer procedures such as intravenous catheter (IV) insertion (the most common source of pain in hospitalized children) could improve the experience for children in hospital settings. Preliminary work suggests SAR employing the technique of "empathy" lead to human perceptions of human-robot interactions as more positive. However, it remains unclear if empathetic interaction is more effective than simple distraction to reduce pain and anxiety. We hypothesize empathetic SAR interaction during IV insertion in children will reduce pain distress and increase IV placement success.

Methods: A prospective randomized controlled trial is underway comparing empathetic SAR, nonempathetic SAR, and current care during IV placement in 90 children age 4-12 receiving an IV prior to MRI. Currently we have finished pilot testing the equipment on 8 patients without use of the robot. To assess distress we are collecting heart rate, interaction characteristics, and self-rated pain scores using digital video recording, pulse oximeter, the validated FACES pain scale, and parent survey.

Results: 8 pilot patients have been consented and enrolled. The average age of participants was 7.63 years; the most frequent ethnicity (38%) was Hispanic. All children had experience with IVs in the past and half (4/8) had > 6 IVs in their lives. Previous IVs caused "quite a bit of pain" (5/8) and made the child "extremely" or "somewhat" anxious (5/8). No children disliked robots and 63% of parents indicated their children liked or loved robots. Almost all (6/8) children reached a FACES pain level of 4/5 or 5/5 during IV placement.

Conclusions: Most children in the pilot like robots and have pain and anxiety in relation to IV placement. Video equipment and tablet interface for recording heart rate and FACES scale are functioning. Next steps will be to finish enrolling patients and collecting data and to proceed with analysis.

Mobile Health Project

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Background: At LAC + USC Medical Center, physicians encounter many patients with health conditions which could be significantly improved by a healthier diet and more active lifestyle. After the patients leave the medical center, physicians have no way of keeping track of the patients' diet or physical activity. There needs to be an improvement of communication about the patients' lifestyles and diet between physicians and patients in between appointments, and cell phones can be a medium to the solution.

Objective: To assess the use of mobile phones in LAC + USC Medical Center's patient population, and see if the population is interested in using mobile phones as part of the medical care for their conditions.

Methods: Three people gathered 244 surveys from patients at LAC + USC Medical Center clinics regarding information such as demographics, current cellular phone usage, current mobile health application and social media usage, barriers to using cellular phones or mobile health applications, and interest in using a mobile health application.

Results: Per surveys, 91% of the population reports owning a cellular phone. Of that 91%, 75% of the patients own phones with internet capabilities. A total of 57% of the population has used a mobile phone application at least once in their life. Thirty-one percent of the population has used a mobile application relating to health. Eighty-six percent of the population said they would be interested in using a mobile application to improve their health if it were to be developed, and 39% of the population said they would use such an application daily.

Conclusion: Most of the patient population at LAC + USC Medical Center makes less than \$20,000 annually, yet still owns cellular phones. We found that the majority of the patients are Spanish speaking

and interested in using mobile phones/ applications to improve their health. Given that this socioeconomic class and culture of people have higher incidences of chronic diseases such as diabetes and hypertension, the incorporation of mobile health tools could be used to improve the health of this population.

Mobile Health Technology Use by Patients of LAC+USC Primary Care Clinics

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Background: Advances in mobile health technology may help patients with chronic conditions to improve their health outcomes. Smartphone "apps" and text messaging are simple tools that may aid patients in their daily disease management. Currently, there is limited data regarding the use of such tools among patients in lower-income communities, and their role in improving their health outcomes. **Objectives:** Determine how patients in a lower-income, culturally diverse population use cellular phones and mobile applications, and if patients are interested in using mobile health technology for chronic disease management.

Design: Observational study

Participants: 250 Patients of the Internal Medicine resident primary care clinics of LAC+USC Medical Center.

Measures: Patients answered a 26-question survey, in their primary language. Information collected included demographics, current cellular phone usage, current mobile health application and social media usage, barriers to using cellular phones or mobile health applications, and interest in using a mobile health application.

Results: The majority of patients, 91%, own a mobile phone, with 75% having internet capability. Mobile phone "apps" were used by 57% of patients, but only 31% were health-related. Most patients (86%) expressed interest in using mobile applications to improve their health, and 39% said they would use it daily. The greatest utility they would find for a mobile health application is for obtaining general information on medical conditions.

Conclusions: Despite, the lower socioeconomic status of our primary care patients, they use cellular phones with internet and applications to a large extent, and they are interested in using mobile health technology to manage and prevent chronic diseases. The correlation between cultural, educational and socioeconomic inequalities and higher rates of chronic diseases suggests that culturally and linguistically-relevant mobile health tools may help improve health outcomes in these populations.

Teledermatology: A Model of Feasibility in Rural Haiti

Lauren Cutler, B.S., Katherine Ross, B.S., Melvin Chiu, MPH, M.D., David Cutler, M.D.

Background: Dermatological ailments in Haiti contribute significantly to the health complaints, but much of the dermatological care has been provided by transient international aid groups. Our aim is to see to

see if implementation of Teledermatology (TD) would help increase access to dermatological care in rural Haiti with adequate concordance and turn around time.

Methods: At the Henri Gerard Desgranges Clinic in rural Haiti, patients with dermatological issues were recruited by to be enrolled into the study. Primary Care Practitioners (PCPs) provided patients with a free skin exam, a preliminary diagnosis and a treatment plan. Dermatologic conditions were photographed on an iPhone 6 Plus and uploaded into an encrypted Google Documents folder. PCPs completed an intake evaluation and uploaded this form into the patient folder with the photos and a blank consultation form. Board Certified Dermatologists in the U.S. completed the consultation form indicating their diagnosis and treatment plan. Clinical and TD diagnoses were reviewed and adjustments to treatment plans were reported to local Haitian physicians to implement.

Results: Out of 100 patients, the mean concordance value between TD and PCPs was 75%. The mean time from patient intake to "case-closed" was 40 hours. The most prevalent disease was atopic dermatitis (30%). The mean age was 26 years old and male to female ratio was 1:2.

Conclusion: The concordance value of 75% and the turn around time of 40 hours were both within accepted ranges from previous studies. Turn around time could be improved with specific commitments consulting dermatologist. Overall improvements could include incorporation of real time TD via live-feed video such as Skype. Future directions include implementing a sustainable TD practice in rural Haiti and applying telemedicine to other specialties.