The 2011 Medical Student Research Forum and Poster Day is an annual event which allows USC Medical Students the opportunity to present their basic science and clinical research to their peers and the USC community at large. The Office of Student Affairs would like to thank all of those involved with organizing this Forum. We also extend special thanks to Dean Carmen A. Puliafito, M.D., M.B.A., Henri R. Ford, M.D., Vice Dean for Medical Education, Joel E. Schechter, Ph.D., Assistant Dean for Student Affairs and Robert Decker, Ph.D., Director of Medical Student Research Training, for their support and participation in this event. We are extremely grateful to our benefactors, the Baxter Foundation and the General Clinical Research Center, for their commitment and support of medical student research.

PROGRAM SCHEDULE

Welcome
Dr. Joel Schechter
Mayer Auditorium

General Assembly
(Introduction of Speakers)
Dr. Henri Ford, M.D.
Vice Dean of Medical Education

Oral Presentations

Poster Presentations
Hoyt Gallery
Winners of the 2011 Medical Student Research Forum

Oral Presentations

Christopher Lee
*Dean’s Research Scholar*

Sarah Tomassetti
*RSP*

Christiane Abouzeid

Erin Blake

Luke Donnelly
# 2011 Medical Student Research Forum Participants

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ORAL PRESENTATIONS

Proximal Junctional Kyphosis in Distraction-Based Growing Rods
Christopher Lee, Karen Myung, David Skaggs

Introduction:
This study examines the rate of proximal junctional kyphosis (PJK) in distraction-based growing rods.

Methods:
A retrospective review of 32 consecutive cases with growing rods for early onset scoliosis was performed. Average age at initial surgery was 4 years (1-10), with diagnoses of congenital scoliosis (15), neuromuscular (11), idiopathic (4), and other (2) included. Minimum follow up was 24 months (mean 52, 24-88). PJK was defined as fulfilling 2 criteria:
1. An angle $\geq 10^\circ$ between the endplates of the vertebrae two levels cephalad to the upper instrumented vertebrae and two vertebrae caudal to the upper instrumented vertebrae.
2. This angle must be at least 10° greater than preoperative values. Z-test was performed to compare rates.

Results:
Of the 32 patients, 18 (56%) developed PJK. 8/18 patients (44%) with PJK had upper anchor failure, with 7 requiring unplanned operations to revise the failed implants. In comparison, 5/14 patients (36%) without PJK had upper anchor failure, which was not statistically significant (p=0.89). In the 4 patients with PJK that underwent final fusion, 3 (75%) underwent fusion and instrumentation to levels cephalad to the growing rod construct. PJK was more common in patients with dual rods (10/16; 62%) than single rods (5/13; 38%) (p=0.36), and in spine-to-spine constructs (10/17; 59%) compared to hybrid constructs (upper hooks on ribs) (5/12; 42%) (p=0.59).

Conclusion:
With a mean follow-up of 4 years, 56% of patients with distraction-based growing rods developed PJK. PJK is almost twice as common with dual rods compared to single rods, and more common if the upper anchors are spine anchors compared to rib anchors.

Significance:
PJK occurs in more than half of children treated with distraction-based growing rods, and the final fusion is likely to involve additional cephalad vertebrae than the original growing rod construct. Placement of upper anchors on ribs reduces the risk of PJK.

Delayed Diagnosis of Extremity Fractures in Pediatric Blunt Trauma is Very Low

Sarah Tomassetti, B.A., Shannon L. Castle, M.D., Hollie Jackson, M.D., Emily Willner, M.D., Mary Taylor, C.S.T.R., Henri Ford, M.D., Jeffrey S. Uperman, M.D., and James R. Pierce, M.D.

Background/Purpose: Trauma is one of the leading causes of morbidity and mortality in the pediatric population, and delayed diagnosis of injuries is a recognized problem. Tertiary survey and screening radiographs have both been used to reduce delays in diagnosis. Prior studies have indicated that extremity fractures are the most commonly missed injuries. In patients who are too young to communicate their complaints, timely identification of these injuries can be difficult and use of skeletal survey has been suggested to avoid delay. We hypothesize that the incidence of missed extremity
fractures in pediatric accidental blunt trauma is low but varies by mechanism of injury. We propose that mechanism and younger age are predictive of missed injuries. We further suggest that missed injuries are picked up effectively by tertiary survey and that additional screening radiographs are not beneficial.

**Methods:** After IRB approval, we conducted a retrospective review of all children 6 years old and younger who presented to Children’s Hospital Los Angeles with accidental blunt trauma between January 1, 2004 and January 1, 2010. Chart review was used to gather patient demographics, mechanism of injury, presence and location of extremity injuries, time of diagnosis, other injuries, serial physical examination, radiographic findings, and associated morbidity and mortality. Our main outcome measures were the presence of extremity fractures and their time of diagnosis. Delay in diagnosis was defined as diagnosis of injury twenty-four hours or more after presentation to the hospital. Secondary measures included mortality, ICU stay, length of stay, need for surgical intervention for fracture, and morbidity associated with missed injury.

**Results:** Over the study period, 2732 children were seen for blunt trauma at our institute. We identified 977 children under 6 years old with no suspicion of non-accidental trauma for inclusion in our study. The most common mechanisms of injury were fall, automobile versus pedestrian accident, and motor vehicle crash; incidences were 55%, 19%, and 16%, respectively. The most common mechanisms of falling were fall from furniture, fall greater than one story, and fall from standing, with incidences of 33%, 26%, and 18%. Associated head injury, abdominal injury, rib injury, pelvis injury, and spine injury occurred in 68%, 5%, 3%, 2%, and 0.7% of patients. Overall, 146 extremity fractures were identified in 128 patients (13%). Only five children had a delayed diagnosis of fracture. All five had their fracture identified on tertiary survey. No patients had a delayed diagnosis made at or after discharge. Of these missed fractures, 2 were upper extremity and 3 were lower extremity. This yielded an extremity fracture delayed diagnosis incidence of 0.5%, ranging from 0-2% by mechanism of injury. On univariate analysis (chi-squared), there was no increased risk of delayed diagnosis associated with age, sex, race, mechanism injury, factors associated with mechanism, or additional fracture diagnosed on admission. Multivariate analysis was not performed because no risk factors were identified. Prior to tertiary survey, 98 skeletal surveys were performed; after tertiary survey, 59 skeletal surveys were performed. No skeletal survey identified a new fracture.

<table>
<thead>
<tr>
<th>Mechanism of Injury</th>
<th>Total Number</th>
<th>Upper Extremity Fracture</th>
<th>Lower Extremity Fracture</th>
<th>Any Fracture</th>
<th>Multiple Fractures</th>
<th>Delay in Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall</td>
<td>538</td>
<td>27 (5%)</td>
<td>21 (4%)</td>
<td>48 (35%)</td>
<td>4 (0.7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Automobile Crash</td>
<td>155</td>
<td>9 (6%)</td>
<td>14 (9%)</td>
<td>23 (15%)</td>
<td>4 (3%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Automobile vs. Pedestrian</td>
<td>187</td>
<td>7 (4%)</td>
<td>48 (26%)</td>
<td>55 (29%)</td>
<td>6 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Bike vs. Pedestrian</td>
<td>13</td>
<td>0 (0%)</td>
<td>4 (31%)</td>
<td>4 (31%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bike Crash</td>
<td>15</td>
<td>1 (7%)</td>
<td>0 (0%)</td>
<td>1 (7%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Crush</td>
<td>45</td>
<td>1 (2%)</td>
<td>6 (13%)</td>
<td>7 (16%)</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Assault</td>
<td>23</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Conclusion: These data support our hypothesis that the incidence of missed extremity fracture is low, but failed to identify any predictors of missed injury. We also demonstrated that missed injuries are picked up effectively by tertiary survey. The low incidence of missed extremity fracture means that a large number of negative skeletal surveys would be needed to diagnose a single missed injury, supporting our hypothesis that additional screening radiographs are not beneficial. The limitation of this study is the low number of delayed diagnosis. Given the infrequency of delayed diagnosis, it is not surprising that there are no good predictors of missed injury. Also, we did not enough delayed diagnoses to effectively evaluate the associated morbidity. The next logical step is to develop a prospective missed-injury registry. This would help identify predictors of missed injury and clarify the degree of associated morbidity. Nevertheless, without any evidence of severe associated morbidity at this time, we advocate careful tertiary survey and acceptance of the occasional delay in diagnosis rather than widespread radiologic screening.

Fornix injury in patients with heart failure

C. M. Abouzeid¹, R. Kumar², H. L. Richardson², J. A. Ogren³, P. M. Macey³, G. C. Fonarow⁵, M.A. Hamilton⁵, R. M. Harper², M. A. Woo³.

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ABSTRACT: Short-term memory deficits are common in heart failure (HF) patients and linked to increased morbidity and mortality and diminished quality of life. Damage to important gray matter structures involved in short term memory, the hippocampus and mammillary bodies, have been reported. However, the status of the major white matter link between these structures, the fornix, is unknown. Inadequate communication between these 2 gray matter structures could be an important contribution to the cognitive abnormalities observed in HF. The integrity of the fornix can be assessed by diffusion tensor imaging (DTI)-based fiber tractography procedures. Therefore, the specific aim of this study is to examine specific regional distribution of white matter damage within the fornix tract in the brains of HF subjects and healthy controls.

METHODS: We will collect DTI series from 12 HF and 24 healthy controls using a 3.0 Tesla MRI scanner (Tim-Trio, Siemens). Inclusion criteria for the HF will be LVEF < 0.40 and systolic HF. Inclusion criteria for controls will be a lack of cardiac or other significant health problem. Two series of DTI will be performed using echoplanar-imaging with a twice-refocused spin-echo pulse sequence (TR = 10,000 ms; TE = 87 ms; FA = 90°; broadband bandwidth = 1346 Hz/ pixel; matrix size = 128x128; FOV = 230x230 mm; slice thickness = 2.0 mm; no interslice-gap; diffusion gradient directions = 64; b = 0 and 700 s/mm2). We will combine both series to increase signal-to-noise ratio. The Diffusion Toolkit software will be used to reconstruct DTI data and generate whole-brain fiber tracks and DTI indices. Diffusion tensors will be calculated using the least-squares fitting method and eigenvalues and DTI indices, including fractional anisotropy (FA), and eigenvectors derived by standard procedures. Whole brain fiber tracking was performed with the fiber assignment by a continuous tracking algorithm. A whole-brain mask, derived from averaged diffusion-weighted images of individual subjects, with a minimum signal intensity will be used to terminate fibers in non-brain regions in each subject. We will use a 35° turning angle between the principal eigenvectors of neighboring voxels to terminate tracking of fibers. Regional fiber counts between the hippocampus and fornix will be evaluated with fiber tractography procedures. Demographic data will be assessed with independent samples t-tests and Chi-square, and regional hippocampal-fornix fiber counts between groups will be determined with ANCOVA (covariates: age and gender).
RESULTS: Data collection and analyses are ongoing at this time. However, we expect that the HF subjects will have significantly damaged fornix (white matter fibers between the hippocampus and mammillary body regions) in comparison to healthy controls. A global reduction in fiber counts in HF compared to age- and gender-matched control subjects are visible in Figure 1; this evaluation represents the tractography recording method that will be used to distinguish fornix fiber integrity in HF subjects alongside healthy controls.

CONCLUSIONS: If there is fornix loss in HF, this could provide an underlying etiology of the damage in gray matter regions which impact short-term memory loss. Such site-specific fiber reduction may result from, and contribute to, characteristics found in the syndrome.

Figure 1. Global fiber tracts in Controls (Left) and HF (right).
**Incidence of Anxiety and Depression in Women Undergoing Labor and Delivery at an Urban County Hospital**

E. Blake, and A. Wittenberg, MD

Year II medical student¹, KSOM, Univ. of So. California; LACoH-USC Obstetrics and Gynecology resident²

**Goal:** Although pregnancy is traditionally conceived as a joyous time in a woman's life, depression and anxiety experienced during pregnancy can adversely affect both fetal and maternal well-being. While much research has been completed on the topic of anxiety and depression in pregnancy, few studies have focused on Latinas and African Americans living in low-income urban environments. The goal of this study is to use a standardized evaluation tool (HADS and PHQ-9) to examine depression and anxiety in these populations and to use this information to improve both screening and treatment in an urban county hospital. We hypothesize that the overall incidence of anxiety and depression will be higher in this study population when compared to incidence in the general population. We also hypothesize that women who have either unwanted or mistimed pregnancies will have higher rates of anxiety and depression compared to women who have planned pregnancies when controlling for all other factors.

**Methods:** The study design is a cross-sectional cohort study that consists of administering validated depression (PHQ-9) and anxiety (HADS) surveys to a sample of 100 women undergoing labor and delivery at LAC+USC Medical Center. Demographic data, medical history, including psychiatric and social history, and information on the wantedness of the pregnancy will also be collected. The surveys will be re-administered 2 weeks postpartum and again at 6 weeks postpartum via phone interview.

**Results:** This study was begun in November of 2009 and my role (E. Blake) has been to enroll eligible patients and conduct the follow-up interviews via telephone. Dr. Wittenberg has facilitated forward progress on the project. Once patient enrollment and follow-up is complete, I will assist Dr. Wittenberg with evaluation and analysis of the final results with the eventual goal of publishing the study. The current estimated end date for patient enrollment is March 1, 2011.

**Conclusion:** The purpose of the study is to assess the rate of anxiety and depression during pregnancy in a population that is currently underrepresented in the literature. The potential benefits include learning more about the needs of this population in order to provide better care through improved screening and treatment.

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**Can ICG-001, a novel B-Catenin/CBP antagonist, inhibit melanoma growth and suppress oncogene activity?**

L. Donnelly

Year II medical student, KSOM, Univ. of So. California.

**Goal:** ICG-001 is a novel therapeutic agent currently in clinical trials for colon cancer. The medication is involved in the Wnt signaling pathway, and works to antagonize the activity of a Beta Catenin co-activator CBP which is proposed to be active in cell proliferation pathways. ICG-001 instead favors the interaction of Beta Catenin with co-activator p300 which is instrumental in cell differentiation. The goal of this project is to look at the effect that ICG-001 has on cell proliferation of both human and mouse melanoma cell lines in the in vitro setting, and mouse melanoma cells in the in vivo setting, as well as determining how the medication affects gene transcription in both lines of cells.
Methods: B-16 mouse melanoma cells and Lu-1205 human melanoma cells were ordered and cultured in an incubator. The cells were grown out and DMSO and blank well controlled 96-well proliferation assays were performed to evaluate the effects of varying concentrations of ICG-001 on its own and in conjunction with 1st line melanoma treatments, namely serafaneb and cisplatin. For the gene expression studies, B-16 and Lu-1205 cells were plated and treated with varying concentrations ICG-001 or DMSO as a control. The cells were then lysed and RNA was isolated from the cells and reverse transcribed into DNA that then underwent real time PCR to determine gene expression.

Results: Preliminary results demonstrate that isolated ICG-001 treatment reduces cell proliferation in both human and mouse melanoma cells. Furthermore, ICG-001 in conjunction with serafaneb reduces cell proliferation to a rate lower than that attained by serafaneb treatment alone. However, ICG-001 in conjunction with cisplatin increases cell proliferation above the level attained by cisplatin treatment alone. Preliminary gene expression studies show that ICG-001 treatment lowers Survivin expression in a dose dependent manner.

Conclusion: ICG-001 provides encouraging results in treatment of melanoma, lowering cell proliferation and reducing oncogene expression. The next step is to observe the effect of ICG-001 in vivo, and it has already been determined from additional work done during the summer that Blk 6 mice should be injected with 200,000 melanoma cells to provide a suitable model for evaluating the in vivo effects of ICG-001 on the B-16 melanoma cell line. We hope that we can work to demonstrate that ICG-001 can be an effective therapeutic agent for the treatment of melanoma in the near future.

DEAN’S RESEARCH SCHOLARS POSTER PRESENTATIONS

Efficacy and Feasibility of Combination Excimer Laser Therapy, Clobetasol Spray, and Calcitriol Ointment in the Treatment of Generalized Plaque Psoriasis

Misha Heller, B.A.,1 John Koo, M.D.2
1University of Southern California, Keck School of Medicine, Los Angeles, CA
2University of California San Francisco, Department of Dermatology, San Francisco, CA

Purpose: To ascertain if a combination of the most powerful excimer laser, clobetasol spray, and calcitriol ointment is an effective and efficient treatment for generalized psoriasis.

Methods: This is a 12-week, on-going open-label, pilot trial evaluating the efficacy and safety of the combination of excimer laser therapy with clobetasol spray as the initial treatment of generalized psoriasis, followed by maintenance therapy with calcitriol ointment. All patients will receive excimer laser treatments twice weekly for the first 6 weeks. For the remaining 6 weeks, only patients who are less than or are concerned for falling below PASI 75 will continue twice weekly excimer laser treatments. In regards to topical therapies, the study will be conducted in three distinct periods (A, B, and C), each of 4 weeks duration. During Period A (weeks 1-4), patients will use clobetasol spray twice daily. During Period B (weeks 5-8), patients will use calcitriol ointment twice daily. During Period C (weeks 9-12), patients will use clobetasol spray twice daily and calcitriol ointment twice daily.

Results: Ten patients have been recruited so far. 6 out of 7 (86%) patients who completed the first 6 weeks achieved PASI 75. 4 out of 4 (100%) patients who completed all 12 weeks achieved PASI 75. More data will be available in the poster.

Conclusion: Preliminary data is promising. This proposed combination regimen for the treatment of generalized psoriasis has thus far demonstrated both outstanding efficacy and fast onset of action. Clobetasol spray may be an ideal partner to excimer laser therapy enhancing its efficacy and minimizing risk of phototoxic reaction from aggressive UVB irradiation involving many times the
Calcitriol ointment provides the required steroid holiday to prevent adrenal suppression. This approach may not be feasible for patients with generalized pustular, erythodermic, or guttate psoriasis. However, it may be feasible for a significant proportion of patients with generalized psoriasis with <20% body surface area involvement and reasonably confluent plaque configuration. Thus, an external approach with better efficacy than current treatment options and without any serious systemic risks may be within reach.

**Polarized Secretion of TGF-β and Thrombospondin from Human Fetal RPE**

Hirsch, L.

**Purpose:**
Retinal pigmented epithelium (RPE) secretes fibrogenic proteins, *e.g.* transforming growth factor β1 & β2 (TGF-β1 & TGF-β2), and thrombospondin-1 (TSP-1). These proteins contribute to the pathogenesis of macular degeneration (AMD) and proliferative vitreoretinopathy (PVR). Since RPE cell polarity may be altered in AMD and PVR, we studied effects of polarity on protein secretion.

**Methods:**
(1) Human Fetal RPE (Hf-RPE) culture: RPE from 2 donors were cultured under 3 conditions for comparison: subconfluent nonpolarized, confluent nonpolarized, and highly polarized monolayers. (2) Enzyme-linked immunosorbent assay (ELISA): TGF-β1, TGF-β2, and TSP-1 were measured in media from apical and basal compartments of polarized RPE transwell filters and from the single compartment of nonpolar RPE petri dishes. (3) Transepithelial Resistance (TER): To confirm RPE differentiation, donors had TERs of 235 & 185 Ω cm². (4) Normalization: Data normalized by total cell protein assays.

**Results:**
Comparing polarized and nonpolarized hf-RPE, nonpolarized cells secreted higher concentrations of TGF-β2 in both active and inactive isoforms. Subconfluent and confluent nonpolarized RPE secreted 21-fold (*p* < 0.001) and 399-fold (*p* < 0.001) greater concentrations respectively. Comparing apical and basal secretions from polarized hf-RPE, TGF-β2 was secreted in 5-fold greater concentrations apically (*p* = 0.004). TGF-β1 was secreted in 6-fold greater concentrations basally. TSP-1 was secreted equally in both compartments.

**Conclusions:**
Nonpolarized RPE secretes higher concentrations of TGF-β2 than polarized RPE. Additionally, differentiated RPE secretes TGF-β2 & TGF-β1 with polar distribution. These data suggest that protein over-secretion, and altered protein distribution, contribute to pathogenesis in disorders with altered RPE polarity, *e.g.* AMD and PVR.

**PROSPECTIVE EVALUATION OF THE TIME COURSE OF COAGULOPATHY IN TRAUMA ELICITED VIA THROMBOELASTOGRAPHY**

Crystal Ives, MS; Kenji Inaba, MD; Bernardino Castelo Branco, MD; Obi Okoye, MD; Stuart Swadron, MD; Demetrios Demetriades, MD, PhD.

**Background:** Thromboelastography (TEG) is a point of care test that evaluates coagulation in real time. The time-course of acute traumatic coagulopathy is not well-established.
Methods: Injured patients meeting our institution's trauma team activation (TTA) criteria had a TEG performed at admission using citrated blood. For surviving patients, additional TEegrors were performed at 1, 2 and 6 hours post-admission. Coagulopathy was defined as any TEG parameter in the hypocoagulable range.

Results: The study population (n=65) was 78.5% male, mean age of 36.4 years (range 11-91), Mean ISS was 14.0 ± 11.6, 50.8% penetrating, 4.6% had SBP < 90 mmHg on admission. In-hospital mortality was 18.5%. 53.8% required blood products in the first 24 hours. Mean amount of pRBCs transfused 6.2 ± 16.8 units range (0,127); FFP 4.5 ± 14.9 units (0,113); apheresis platelets 0.7 ± 2.4 units. 18.5% (n=12) were massively transfused (≥10 u pRBCs in 24 hours). 30.8% (n=20) of patients became coagulopathic in the first six hours post admission. 90% of massively transfused patients developed coagulopathy (see figure). Mean time to coagulopathy was 38 ± 46 minutes. All patients developing coagulopathy did so by two hours post-admission. 12.3% (n=8) of patients were coagulopathic on admission; of those, 2 were massively transfused, 1 received 9 units pRBC, 1 received 3 units pRBC, 2 were autotransfused, and 2 had no blood product requirements. In 90% of patients, coagulopathy resolved by 6 hours post-admission.

Conclusion: Trauma patients requiring increasing amounts of pRBCs have significantly greater coagulopathy on TEG profiles. 12% of patients had coagulopathy on admission. All coagulopathic patients developed coagulopathy within 2 hours of admission.

Myeloid-Derived Suppressor Cells in Head and Neck Squamous Cell Carcinoma

Russell S.M.¹, Lechner M.G. ², Megiel C.², Bass R.², and Epstein A.L.²

¹Deans Research Scholar, USC Keck School of Medicine, Los Angeles, California
²Department of Pathology, USC Keck School of Medicine, Los Angeles, California

Purpose: Recurrent and metastatic disease accounts for the vast majority of morbidity and mortality in head and neck squamous cell carcinoma (HNSCC) patients and a specific and reliable biomarker to monitor tumor growth is lacking. It is well established that HNSCC is highly immune-modulatory with frequent induction of tumor immune tolerance and Th2 cytokine shift. Myeloid-derived suppressor cells (MDSC) are a recently discovered population of immune suppressor cells that are major mediators of immune suppression in HNSCC and a significant barrier to immunotherapy. While absent in healthy individuals, MDSC accumulate and mediate expansion of regulatory T cells and
inhibit T effector responses in the tumor microenvironment. Because MDSC accumulation in patient peripheral blood correlates with tumor burden and spread, MDSC levels can be used as a minimally-invasive test for cancer monitoring in HNSCC patients. In this study, we describe the prevalence and characterization of MDSC in HNSCC both in vitro and in vivo using a unique set of markers for these cells.

Methods: As a first step, the propensity for HNSCC cell lines to generate suppressive MDSC in vitro was assessed using a newly developed MDSC induction assay followed by studies to test their ability to inhibit the proliferation and IFN-γ production of CD3/CD28 stimulated autologous T cells. To identify possible mechanisms for MDSC induction, production of immune modulatory factors by HNSCC cell lines was assessed by qRT-PCR and ELISA techniques. Suppressive and non-suppressive MDSC were then characterized phenotypically by flow cytometry. Finally, antibodies were developed for a set of three biomarkers found to identify suppressive MDSC and used in combination to identify these cells in the blood of HNSCC patients and healthy volunteers.

Results: Using this approach, 7/9 HNSCC cell lines were found to induce suppressive MDSC. qRT-PCR and ELISA studies demonstrated an increased expression of IL-6, IL-1β, GM-CSF, TNF-α, and VEGF, but subsequent experiments showed that IL-6 and GM-CSF together were sufficient to induce suppressive MDSC. Moreover, neutralization experiments showed that all five cytokines contribute to suppressor cell induction, with inhibition of GM-CSF or IL-6 sufficient to abrogate 90% of the suppressive effect. Phenotypic studies of MDSC showed that along with the common myeloid cell surface protein CD33, HIF-1α, an important transcription factor for myeloid differentiation, and low HLA-Dr expression were key biomarkers for suppressive MDSC. Preliminary data from patient and healthy volunteer samples demonstrated that these biomarkers do distinguish suppressive MDSC present in HNSCC patients.

Conclusion: In conclusion, this unique minimally-invasive bioassay could provide a new method with which to monitor tumor growth and recurrence in HNSCC. Finally, if successful, this bioassay may then be tested in patients with other types of cancers to demonstrate its universal potential as a new approach for cancer diagnosis and monitoring.

Rescue Therapy with Combined Anti-VEGF and PDT for refractory AMD

Kevin Tozer BS1, Lawrence Chong MD1,2, Srinivas Sadda MD1
1Doheny Eye Institute, University of Southern California; 2VMR Institute, Huntington Beach, CA

Purpose: Examine the efficacy of combination anti-VEGF and photodynamic therapy for the treatment of neovascular AMD refractory to anti-VEGF monotherapy.

Methods: Retrospective interventional study. Study patients consisted of a subset of all patients treated at the VMR Institute and the Doheny Eye Institute with anti-VEGF monotherapy for neovascular AMD and considered treatment failures between January 1, 2009 and December 30, 2010. Treatment failure was defined as persistent subretinal or intraretinal fluid after at least 3 anti-VEGF injections in the 7 months prior to combination treatment. Combination treatment consisted of anti-VEGF intravitreal injection followed 7 to 14 days later by half fluence photodynamic therapy. Primary outcome measure was resolution of subretinal or intraretinal fluid by spectral domain OCT. Secondary outcome measures were visual acuity and frequency of repeat treatments with anti-VEGF monotherapy or combination therapy. All patients had at least 3 months of follow-up at time of abstract submission.

Results: Nine eyes from nine patients were included in this study. Mean follow-up was 9.2 months (3-20 months). These patients received a mean of 5.3 injections (35 lucentis, 13 avastin) within the 12 months prior to declaration of treatment failure. After rescue combination therapy, a mean of 1.9 retreatments were administered (13 lucentis, 6 avastin, 4 combination retreatments). At one month
after combination treatment, subretinal or intraretinal fluid resolved completely in 4 eyes, improved in 3 eyes and was unchanged in 2 eyes. Mean visual acuity was .85 logmar (20/140) before rescue therapy, .70 (20/100) at one month, and .75 (20/100-2) at 3 months. The mean interval between injections increased from 2.3 months to 3.89 months after combination therapy. 

**Conclusion:** Rescue therapy with the combination of Anti-VEGF and PDT is effective for eyes which fail Anti-VEGF monotherapy. Most patients experienced a decrease in subretinal fluid, improvement in visual acuity, and longer period between injections after patients receive combination therapy. Larger studies are needed to confirm these results.

**Defining a Mechanism for the Initiation of Myelin-Specific Immune Responses**

Shirley L. Wang, Brett T. Lund

Multiple sclerosis is an autoimmune degenerative demyelinating disease affecting the central nervous system. Little is known about the factors that initiate the immunopathology of MS. We attempted to study to possible role of heat shock proteins in MS pathogenesis. HSP associates with myelin proteins or peptides following the death or stress of oligodendrocytes. Preliminary experiments show that Hsp70-myelin complexes are highly immunogenic and demonstrate adjuvanticity in stimulating adaptive immune responses specific for the associated myelin protein in vitro. We hypothesized that following intra-CNS administration, complexes of Hsp70 and myelin basic protein derived peptides would stimulate myelin-specific immune responses and a demyelinating course. We further hypothesized that this is a mechanism for the initiation of myelin-specific immune response, and that this initial event leads to subsequent immune-mediated destruction of myelin.

**POSTER PRESENTATIONS**

**Diagnostic Accuracy of Venous Blood Gas Electrolytes for Identifying Diabetic Ketoacidosis in the Emergency Department.**

C. Agy¹, M. Probst M.D., S. Arora M.D., M. Menchine M.D., D. Bach²  
¹Year II Medical Student, ²Year IV Undergraduate Student

**Objective:**
Diagnosing diabetic ketoacidosis (DKA) has traditionally required a venous blood gas (VBG) to obtain serum pH and a serum chemistry panel to obtain electrolyte values. Since newer blood gas analyzers have the ability to report electrolyte values in addition to pH, this diagnostic process theoretically could be reduced to just one test. However, the degree of agreement between the VBG electrolytes and the serum chemistry electrolytes, including sodium, chloride and bicarbonate, has not yet been evaluated in the context of acute hyperglycemia. The purpose of this study is to assess the accuracy of the venous blood gas as a stand-alone blood test for diagnosing diabetic ketoacidosis, and describe the correlation between VBG and serum chemistry electrolytes in a sample of hyperglycemic patients seen in the emergency department (ED).

**Methods:**
We prospectively identified a convenience sample of ED patients with serum blood glucose
The diagnosis of DKA was made by using American Diabetes Association criteria including: serum glucose $\geq 250$ mg/dL, serum anion gap $>10$ mEq/L, carbon dioxide $\leq 18$ mEq/L, serum pH $\leq 7.30$ and presence of ketosis. Serum chemistry electrolyte values were considered to be the criterion standard. Diagnostic test characteristics of VBG electrolytes including sensitivity and specificity were compared against the standard. In addition, correlation coefficients for individual electrolytes and anion gap were calculated.

**Results:**
Paired VBG and serum chemistry panels were available for 342 patients, of which 46 (13.5%) had DKA. The sensitivity and specificity of the VBG alone for diagnosing DKA was 97.8% (95%CI 88.5-99.9%) and 100% (95%CI 98.8-100%) respectively. One case of DKA was missed by the VBG. Correlation coefficients between VBG and serum chemistry were 0.90, 0.73, 0.94 and 0.81 for sodium, chloride, bicarbonate and anion gap respectively.

**Conclusions:**
The VBG electrolytes were 97.8% sensitive and 100% specific for the diagnosis of DKA in hyperglycemic patients. These results suggest that VBG electrolytes may be used in lieu of serum chemistry electrolytes for the diagnosis of DKA. These findings should be validated in a larger trial prior to widespread implementation.

**Macular Dysfunction and Structure in Macular Pucker with Good Visual Acuity**

*Khwaja A. Ahmed, 1,2 Kevin R. Tozer, 1,2 Craig D. Robison, 1,2 Michelle Wang, 1,2 Wolfgang Fink, 3,4 Alfredo A. Sadun, 2 Jerry Sebag, 1,2.*

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**Purpose:**
To characterize the functional and structural status of Macular Pucker (MP) patients who have good objective visual acuity, despite subjective distortions.

**Methods:**
10 eyes in 10 patients with MP and visual acuity of 20/32 or better underwent quantification of central field abnormalities with 3D Computer-automated Threshold Amsler Grid (3D-CTAG) testing (Fink & Sadun, J Biomed Opt, 2004). Quantitative analysis of the 3D visual field abnormalities were: Lost Area Grade (LAG = scotoma area ratio as a function of contrast sensitivity), Preserved Area Grade (PAG = intact visual field area ratio as a function of contrast sensitivity), Difference Area Grade (DAG = PAG minus LAG), and Hill-of-Vision Volume Loss (%). Results were compared to macular thickness [$\mu\text{m}$] and macular volume [$\mu\text{L}$] as measured by combined Optical Coherence Tomography/Scanning Laser Ophthalmoscopy (OCT/SLO, OPKO/OTI, Miami). Fellow eyes were normal in 5 subjects and served as controls.

**Results:**
The average macular thickness was 304.8 $\mu\text{m}$ and macular volume was 2.83 $\mu\text{L}$ in the MP eyes, compared to 272.6 $\mu\text{m}$ and 2.54 $\mu\text{L}$ in controls ($p = 0.015$ and $p=.04$; respectively). Average LAG, PAG, and DAG differed from controls by 42.95%, 25.75%, and 68.7% ($p =.0009$; $p=.071$, and $p=.00005$; respectively). Positive correlation existed between macular thickness and both LAG (Spearman $\rho$
Coefficient r = 0.74, p = 0.01) and PAG (r = 0.77, p = 0.008). The mean Hill-of-Vision Volume Loss was 1.66 % in the MP eyes, which significantly differed from controls (p = 0.005).

**Conclusions:**
3D-CTAG and OCT/SLO determined that there are significant functional and structural abnormalities in eyes with MP and good visual acuity. That there was nearly 50% loss of LAG and over 50% in DAG were striking. Since 3D-CTAG quantification of central vision correlates well with macular structure, it may be better in assessing the effects of MP on vision in patients with normal visual acuity. Furthermore, these quantitative indices of central vision might provide useful outcome measures of therapy with either surgery or pharmacologic vitreolysis (Sebag, RETINA 29:871-4, 2009).

**MR Techniques in the Evaluation of Hepatocellular Carcinoma: Gadoxetate.**

J. Shriki\(^1\), MD, J. Park\(^2\), MD and E. Allgood\(^3\)
Radiologist\(^1\), Seattle, WA; Radiologist\(^2\), USC Norris Cancer Hospital; Year II medical student\(^3\), KSOM, Univ. of So. California

**Goal:** Initial diagnosis and ongoing evaluation of hepatocellular carcinoma (HCC) is dependent on accurate measurement of tumor size and volume. Current CT imaging techniques lack precision in determining tumor size and volume, due mainly to variations in enhancement during the different vascular phases of CT with contrast. Gadoxetate contrast, however, is selectively taken up by healthy liver parenchyma, with HCC lesions negatively enhanced with precisely defined edges on MRI. This study aims to assess the precision of this Gadoxetate enhanced MRI as compared to the current CT standard, in hopes of establishing a more precise standard for measuring HCC lesions.

**Methods:** Twenty-five recent recipients of liver CTs will be asked to undergo a Gadoxetate enhanced MRI within 3 weeks of their initial CT scan. Radiologists will clinically evaluate both the CT and MRI of each patient, and assess HCC lesion volume and size. To evaluate precision, HCC lesion measurements will compared between readers to assess inter-observer variability. Twenty images will be chosen at random and read by the evaluating radiologists in order to assess intra-observer variability as well.

**Results:** This study is currently in the early recruiting phase and my role (E. Allgood) has been to screen portions of patients’ charts in order to determine eligibility of prospective subjects. Dr. Park has recently made substantial efforts to get this project moving after taking over for Dr. Shriki this past summer. Once more patients have been recruited, I will begin to compile the CT and MRI images and prepare a presentation for the reading radiologists.

**Conclusion:** Since Gadoxetate enhanced MRI provides a more defined border of HCC lesions, this study should help to establish the most precise method of evaluating HCC lesion size and volume, enabling more effective treatment and monitoring of HCC patients.
Correlation between polysomnography and questionnaire in overweight Latino adolescents

A. Amack¹ and R. Bhatia², MD

Year II medical student¹, KSOM, Univ. of So. California; CHLA pulmonology fellow²

Introduction: Polysomnography (PSG) is considered the gold-standard for diagnosing and qualifying sleep related breathing disorders (SRBD). PSG is an expensive and time-consuming test, and often it is not available at many centers. The Epworth Sleepiness Scale (ESS) is a validated self-reported questionnaire which provides a measurement of the subject's general level of daytime sleepiness. Previous studies aiming to establish a link between excessive daytime sleepiness and PSG parameters have featured children with SRBD secondary to adenotonsillar hypertrophy. None of these studies have specifically targeted our subject population, which are children with SRBD secondary to obesity. We hypothesized that the subjects' ESS score would correlate with the frequency of PSG abnormalities, and thus the severity of SRBD.

Methods: 17 overweight (BMI > 85th percentile for age/gender), otherwise healthy Latino adolescents with symptoms of SRBD were recruited from the pool of sleep study referrals from the Children's Hospital Los Angeles Sleep Laboratory. Overnight PSG was performed on all subjects to measure sleep related parameters. The questionnaire containing the ESS was completed by the patient’s parents on the same night as the PSG. Pearson correlation was used to correlate the ESS score with PSG.

Results: 17 Latino adolescents (14 males, 3 females, age range 10 - 17 yrs; 13.2 + 1.9 yrs (Mean + SD); BMI 34.9 + 8.3 (Mean + SD); BMI Z score 2.36 + 0.4 (Mean + SD)) completed the study. PSG results revealed a mean OAHI of 8.5 ± 14.5 events/hr (Mean + SD) (range 1 - 61.8 events/hr). The mean sleep efficiency was 78 ± 9.9 (Mean + SD) and TAI was 11.8 ± 5.7 events/hr (Mean + SD). On average, subjects had 15.9 ± 14.1 desaturation index (defines as >= 3% drop in oxygen saturation from baseline) per hour of sleep (Mean + SD). The mean ESS score was 8.7 with a median of 9 and 10/17 subjects reporting a score of 9 or greater. Using Pearson correlation, there was no significant correlation found between PSG parameters and the ESS.

Conclusion: In overweight Latino adolescents, the ESS does not correlate with sleep study parameters. However, sleep study parameters and sleep questionnaire parameters were abnormal independently. We speculate that the absence of correlation between these parameters in our study is due to low number of subjects.

Lifestyle Intervention on obese adolescents: Utilizing the Wilderness and other Complementary Modalities.

Ali Arastu¹, Marc Weigensberg MD², Erin Quinn³

Year II Medical Student, KSOM, Univ. of So. California¹; Director of Pediatric Endocrinology, USC-LAC²; Associate Dean of Admissions, KSOM, University of Southern California
**Goal:** Obesity and type 2 diabetes have achieved epidemic proportions that represent an enormous threat to both the personal health of young adults and future public health expenditures; this proposal addresses the urgent need for innovative, culturally and developmentally tailored, lifestyle interventions in this population to promote healthy body weight and minimize further diabetes risk.

The overall aim of this pilot is to conduct a non-randomized 2 arm (intervention and control), six-month pilot, testing the feasibility and effects of a lifestyle intervention on metabolic, behavioral, psychological, and health/well-being outcomes among obese adolescents.

**Methods:** The intervention consists of one 9-day wilderness retreat and regular maintenance sessions by the staff of Outward Bound Adventures (OBA). The content of the intervention is a series of modules that utilize the wilderness setting and Council as the mode of group communication. The modules are based on curriculums developed by the USC Childhood Obesity Research Center and are adapted to work with existing OBA trips; they Group Guided Imagery/Stress Reduction, Diet/Nutrition, and Exercise.

The pilot aims to not only demonstrate that the intervention is acceptable and enjoyable by the participants, but also to illustrate that the intervention reduces adiposity (BMI & body fat) and improves overall health and well-being (e.g. General Well-being, Self-esteem) of the participants.

**Results:** I have struggled significantly this year to work out the logistics with carrying forth this study. Liability and financial constraints complicated the initial planning of the wilderness retreats; we have now, however, reached collaboration with Outward Bound Adventures. This will allow us to implement several health modules into their existing, and successful, retreats.

**Conclusion:** With its use of multiple modalities, this intervention represents an extremely innovative, multi-disciplinary approach to the problem of adolescent obesity. If shown to be effective, this pilot would generate important preliminary data to support a larger randomized controlled trial, and may also lead to studies in other populations.

**Readmission of Trauma Patients to the Intensive Care Unit Results in Significantly Worse Outcomes**

Bechler, K.

**Background:** The burden of intensive care unit (ICU) readmissions among trauma patients has been poorly documented. The aim of this study was to characterize the incidence of ICU readmissions at a level 1 trauma center and examine outcomes and possible risk factors.
**Methods:** After IRB approval, trauma patients readmitted to the surgical ICU within the same hospitalization between the years 2006-2008 were retrospectively reviewed. Demographics, clinical data and outcomes were examined.

**Results:** During the three year study period, 1,826 patients were admitted to the ICU. Of these, 128 (6.9%) died within 48 hours. Of the remaining 1,698 patients, 49 (2.9%) were readmitted once and 11 (0.6%) were readmitted more than once during their hospital stay. The reason for the readmission of the 60 patients included respiratory failure (32%), secondary surgical interventions (30%), and infections (17%). Compared to patients who were not readmitted, readmitted patients were more likely to be over 55 years old (30% vs. 19%, p=0.03), to have AIS Abdomen ≥3 (38% vs. 23%, p=0.01), to have AIS Extremity ≥3 (38% vs. 21%, p<0.01), and to have undergone a laparotomy (38% vs. 22%, p<0.01). After adjusting for confounding factors, readmitted patients had a significantly higher mortality (17% vs. 8%; Adjusted OR (95% CI): 2.11 (1.01, 4.41); Adjusted p=0.046) and a longer overall hospital length of stay (43 ± 36 vs. 15 ± 18 days; Adjusted Mean Difference (95% CI): 19.14 (11.90, 26.38); Adjusted p<0.001). A forward logistic regression model identified laparotomy (Adjusted OR (95% CI): 2.43 (1.41, 4.20), p=0.001) and age ≥55 years (Adjusted OR (95% CI): 2.15 (1.20, 3.83), p=0.01) as independent risk factors for readmission to the ICU.

**Conclusions:** Readmission to the ICU results in a longer hospital length of stay, and a significantly higher mortality. Patients undergoing a laparotomy and patients older than 55 years are at a significantly higher risk to be readmitted to the ICU.

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**Human Capital Gains Associated with Robotic-Assisted Pyeloplasty in Children Compared to Open Pyeloplasty**

J.W. Behan¹, R.E. De Filippo², A.Y. Chang², B.E. Hardy², C.J. Koh²

KSOM, Univ. of So. California¹, CHLA / USC, Los Angeles, CA²

**Purpose:** Robotic-assisted laparoscopic pyeloplasty (RALP) is an emerging, minimally invasive alternative to open pyeloplasty in children for the treatment of ureteropelvic junction obstruction (UPJO) that has been associated with smaller incisions, shorter hospital stays, and reduced pain medication requirements. Previous outcomes analyses of these modalities have traditionally not included consideration of human capital losses in a pediatric setting, especially regarding non-work days for parents. We compared the perioperative factors at a single institution for RALP and open pyeloplasty patients, especially with regards to human capital changes in an institutional cost analysis.

**Methods:** A total of 44 patients 2 years and older from one children’s hospital underwent either robotic assisted pyeloplasty (n =37) or open pyeloplasty (n =7) from 2008 to 2010. After institutional review board approval, a retrospective chart review was performed to collect demographic and perioperative data. Cohorts were sampled from the same time period at a single institution, with exclusion of children under the age of two years from data sampling. The human capital approach was used to value productivity losses by the parents.
Results: There were no statistically significant differences regarding the demographics between the RALP group and the OPN group, including age (10.3 years vs 7.3 years; \( p = 0.251 \)). The OPN patients had a significantly longer average hospital length of stay (LOS) (2.8 days vs 1.6 days; \( p < 0.05 \)). This correlated with an average increase in lost parental wages of $90.00 and hospitalization expenses of $612.80 per patient.

Conclusion: Minimally-invasive pyeloplasty techniques in children such as RALP in our experience, are associated with human capital gains (e.g. reduction in lost wages for parents) and lower hospital per diem expenses. Future comparative outcomes analyses of minimally invasive approaches in children should include financial factors such as human capital loss / lost work-days, as these can be especially important for these families with young children.

<table>
<thead>
<tr>
<th></th>
<th>RALP (N = 37)</th>
<th>OPN (N = 7)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10.3 ± 0.9</td>
<td>7.3 ± 2.2</td>
<td>0.251</td>
</tr>
<tr>
<td>Gender (F:M)</td>
<td>15 : 22</td>
<td>3 : 4</td>
<td></td>
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<tr>
<td>Weight (kg)</td>
<td>41.5 ± 3.7</td>
<td>24.1 ± 4.8</td>
<td>0.012</td>
</tr>
<tr>
<td>Laterality (L:R)</td>
<td>26: 11</td>
<td>5: 2</td>
<td></td>
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<tr>
<td>Operative time (min)</td>
<td>203±7.7</td>
<td>164 ± 14.6</td>
<td>0.019</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>7.5 ± 2.6</td>
<td>7.3 ± 4.0</td>
<td>0.482</td>
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<tr>
<td>Length of stay (days)</td>
<td>1.6 ± 0.1</td>
<td>2.8 ± 0.5</td>
<td>0.019</td>
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</tbody>
</table>

*Data for age, weight, operative time, estimated blood loss, and length of stay represent averages ± standard error of the mean

Soluble Inflammatory Marker Higher in Subset of Obese Hispanic Patients

Bogart, A., Gilsanz, V., Sobrera, E. Aldrovandi, GM.
Year II medical student. KSOM Univ. of So. California. Children’s Hospital Los Angeles.

Goal: This study sought to determine the nature of the relationship between the soluble inflammatory marker Cluster of Differentiation 14 (sCD14) and measurements of adiposity including body mass index (BMI) and visceral and subcutaneous fat as determined by dual energy X-ray absorptiometry (DXA). CD14 is a co-receptor and mediator of bacteria-induced inflammation, and has previously been used as a marker of reduced gut epithelial integrity in the face of immune dysfunction.

Methods: Serum samples of 103 healthy female subjects (55% Hispanic, 29% white, 7% Asian, 9% multiethnic, 0% African American) between the ages of 16 and 25, (median 21.1 years) were analyzed for concentration of soluble CD14 in duplicate using a standard ELISA kit (R&D Systems Inc.) In this assay, wells are pre-coated with a monoclonal antibody which binds and immobilizes any sCD14 present in the sample serum. Following wash steps, an enzyme-linked polyclonal antibody specific for sCD14 is added. A final substrate solution induces a measurable color change in proportion to the amount of sCD14 bound to the microplate wells. The color development is stopped and the intensity of the color is measured by photometry. Concentrations of sCD14 were extrapolated using optical density by comparison to laboratory standards made separately.
for each assay. In order to remove investigator bias, the research team was blind to subject demographics until final analysis stage.

**Results:** Calculated concentrations of sCD14 were then compared to subject phenotypes including ethnicity, BMI, subcutaneous fat, visceral fat, and bone density. For the whole subject population, there did not appear to be any direct trends or correlations between any of the mentioned variables and the sCD14 levels. However, a subset of 21 Hispanic subjects had a much higher visceral fat cross-sectional area (Visceral CSA) than members of any other ethnicity, so this group was singled out for analysis. Within this group, subcutaneous fat cross-sectional area (SubQ CSA) significantly correlated with both BMI ($P = 0.0022$) and Visceral CSA ($P < 0.0001$). Although not statistically significant, there was a notable positive trend between sCD14 and BMI. In addition, sCD14 positively correlated with the ratio of SubQ CSA to Visceral SCA, but not significant at the $P < 0.05$ level. The most significant finding was the correlation between sCD14 and the ratio of SubQ CSA to total CSA ($P=0.0508$). In addition, sCD14 negatively correlated with the ratio of Visceral CSA to total CSA, but this finding was not statistically significant ($P = 0.2285$).

**Conclusion:** These findings describe a relationship between the inflammatory marker sCD14 and measurements of body composition; specifically in subjects with higher SubQ CSA than Visceral CSA. Although the subject population at large did not lend itself to this relationship, we suspect that the study was limited by demographics. In a previous study linking sCD14 and BMI, the association was attributable to effects in both male subjects and African American subjects, neither of whom were included in our study. Further, another study linking inflammatory markers to BMI reported that overweight Mexican-American children have significantly higher levels of sCD14 than their normal weight counterparts. The subjects used in this study were younger (age 13.2-13.4) than those in the present study, however they similarly found that only those subjects with the highest BMI had significantly increased levels of sCD14. It is possible that the correlations found between sCD14 and body composition are uniquely more apparent within certain ethnicities, specifically in African Americans and Hispanics. The relationship between sCD14 and obesity remains to be fully elucidated, but this study sheds light on the specific relationship of SubQ CSA versus total fat CSA as an indicator of obesity status. We also propose that a lower ratio of SubQ to total fat CSA may offer a protective factor in obese subjects, as these were shown to have reduced concentrations of the inflammatory marker sCD14.

**Simvastatin treatment and its effect on digit tip regeneration in mice**

M. Booker, and F. Mariani, PhD  
Year II medical student, KSOM, Univ. of So. California; Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research

**Goal:** Statins have been shown to enhance osteogenesis within *in vivo* models through the mevalonate pathway. Additionally, statins have been shown *in vitro* to enhance osteoblast functioning, inhibit angiogenesis, alter the expression of the BMP pathway, and alter collagen deposition. However, there have been no studies
exploring digit tip regeneration and statin treatment to date, but we believe there is cause for investigation given statins ability to alter pathways inherent in the regeneration process.

**Methods:** A digit tip resection of the terminal phalanx was performed on the 2nd, 3rd, and 4th digit of CD1 PN3 mice. Within a litter, mice were organized into three simvastatin dosage groups of 40 mg/kg/day in DMSO, 20mg/kg/day in DMSO, or vehicle-only. To compare the relative regrowth between the dosage groups, we amputated the hindlimb on the resected hand of each mouse and grouped by both litter and dosage. We then measured the terminal phalanx digit length of the 2nd, 3rd, and 4th cut digits and averaged the length for each mouse. We used this number as a measure of the average digit regeneration in each particular mouse.

**Results:** In our first trial, transdermal application between the scapulas was started the day after resection and continued for two weeks. Mice paws were collected at post-natal day 17 (PN17). They were digested, stained in Alizarin Red, and the terminal phalanx was measured using imaging software. We subsequently ran a simulation nesting for both litter and dosage, and found that there was a suggestive but statistically insignificant difference detected between the control and dosage groups ($p = .09$). Both the low and high-dose group demonstrated a decreased terminal phalanx regrowth length when compared to the control group at PN17.

**Conclusion:** Our first trial suggested that simvastatin has a negative effect on digit tip regeneration in CD1 neonatal mice. While statins have been shown to enhance osteogenesis in *in vivo* fracture models, statins reduction of terminal phalanx regeneration could be due to an inhibition of a mechanism necessary for regrowth but not fracture healing. The primary areas we’ve indicated for further exploration are 1) whether statins inhibit early wound healing and organization thus delaying osteogenesis, or 2) reducing the amount of bone deposited during the osteogenesis stage.

To take into consideration these possibilities, we suggest altering the protocol to include multiple time points for collection. This would allow better insight as to when simvastatin’s inhibitory effect on the time-course of regrowth is most pronounced. Histological examination comparing granulation tissue progression and structure would also provide further insight into any morphological changes in early wound healing. In addition, it became apparent while organizing the data that even slight variability within the resection may play a significant role in the quality of the measurement obtained. Since many of the control-dose digits grew back to within 70-80% of the uncut paired digit, the margin for error in recognizing a significant reduction from this number in the dose group is very slim considering our target was an initial 50% resection of the digit. In order to account for variability within the resection itself, we suggest measuring the resected tips when analyzing regeneration. Future experiments may confirm the results from our first trial or provide different outcome.


**Predictive Value of Chest Tube for Thoracotomy (APP-10-05777)**

Does chest tube output correlate with need for thoracotomy?

*W. Breed¹, B. Bernardino, MD², and K. Inaba, MD FRCSC FACS³*

Year II medical student¹, KSOM, Univ. of So. California; Research Fellow², LACoH-USC Dep. of Surgery - Div. of Acute Care Surgery; Assistant Professor of Surgery³, Medical Director, Surgical ICU - Div. of Trauma and Critical Care

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1. Year II medical student
2. Research Fellow, LACoH-USC Dep. of Surgery - Div. of Acute Care Surgery
3. Assistant Professor of Surgery, Medical Director, Surgical ICU - Div. of Trauma and Critical Care
**Goal:** Drainage from chest tube placement for thoracic drainage after severe chest trauma is an important indicator of patient status. Currently, chest tube output greater than 1500mL of blood upon initial placement is considered universally indicative for immediate thoracotomy. The goal is to complete a retrospective study that will provide contemporary data on the critical output levels that may predict the necessity of a thoracotomy.

**Methods:** We will perform a broad literature search on the topic, collect and analyze any relevant data. At LAC-USC we will be reviewing the chest tube output from all patients who received a chest tube following traumatic injury. We will analyze this data to determine if there is a predictive value for emergency thoracotomy.

**Results:** This study is currently underway. My role (W. Breed) has been to access patient records and record relevant hematological data, nature of injury, location and drainage from chest tube placement, if there was a thoracotomy performed, and why. Dr. Bernardino and Dr. Inaba have both facilitated the forward progress and supervised the general direction of the study. The results of the study will be published once all data has been gathered, reviewed, and analyzed. Data gathering activities for 2009 are nearly complete and will be analyzed for statistical significance before additional years are reviewed.

**Conclusion:** Due to the size of the population pool, and because data is still being collected, it is premature to draw any particular conclusions from the study. However, the general benefit of this study would be to increase the sensitivity and specificity of the current protocols governing emergency thoracotomy due to chest tube output, potentially decreasing patient mortality.

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**Estimated Risk of Acute Coronary Syndrome in Chest Pain Patients at LAC+USC**

G. Carmelli\(^1\), P. Gruber, MD\(^2\) and M. Menchine\(^3\), MD

Year II medical student\(^1\), KSOM, USC; LACoH-USC Emergency Medicine Attending\(^2\); LACoH-USC Emergency Medicine Attending\(^3\)

**Goal:** The Emergency Room at LAC+USC sees a large number of patients with the chief complaint of "chest pain." In order to rule out a dangerous Acute Coronary Syndrome (ACS), patients often require a full cardiac workup. To date, there is no single great method of determining a patient's risk of having an ACS in order to save those with low risk from having to go through this full workup. As a result, many of these "chest pain" patients, who otherwise have a low ACS risk, may be unnecessarily receiving a full cardiac workup, so that the doctors don't miss an actual ACS. The goal of this project is to assess the risk of having an ACS of over 1600 "chest pain" patients at LAC+USC over the last year. With this data we hope to open for discussion, new ways of treating future "chest pain" patients, such that those with low risk of having an ACS may not require undergoing the full cardiac workup.

**Methods:** In this observational study, I have been reviewing the charts of patients presenting with a chief complaint of "chest pain" or other similar terminology. To assess their risk of having an ACS, I will be imputing the patients' data into the four major risk
assessment devices currently used, i.e., the Grace Score, Timi, ACI Tipi, and the Attribute Score calculator. Currently, I am in the process of collecting the data from these charts in order to input it into these risk assessment tools. The data is scattered through various collection programs at the hospital (Wellsoft, Quantum, Affinity etc) and I have been using various methods of acquiring this information. To date, I have competed over 90% of the data collection and am awaiting completion of the remaining part (reviewing EKGs) by my physician associates.

**Results:** Currently I am in the data collection phase of this study and thus have not yet calculated the risk of ACS for these patients. Once all the data has been collected it is a simple manner of plugging them into the risk assessment programs and then graphing their results. Thus far I have collected over 90% of the data I need before I can begin calculating the risks. Here is some of the data:

- **Gender:** 58.1% are Male, 41.9% are Female
- **Age:** 20.9% are < 40, 56.1% are between 40-60, 23% are > 60
- **Positive Troponin T:** 4.3% of patients had a clinically significant increase in TropT
- **Positive Creatinine:** 9.5% of patients had a clinically significant increase in Cr
- **Diaphoresis:** 6.9% of patients presented with diaphoresis
- **Killip CHF classification:** 87.3% class I, 10% class II, 2% class III, 1% class IV

**Challenges/ Complications:** While doing this clinical research project, I noticed that there are many challenges that cause things to go slower then expected. Although at first it seemed like all I needed to do was collect data from patient’s charts, I learned that much of the data is not easily accessible. Furthermore, I learned that a patient’s clinical information is not in one succinct location, but rather is distributed throughout multiple data storage softwares. In order to access much of the information, I needed the help of various tech support agencies, ER attendings and residents. This also took a lot of time to do. Lastly, for certain data points, like abnormalities on EKG, we are trying to be more accurate by reading all 1600 EKGs manually, rather then using an automated EKG reader program. This requires the use of multiple residents and attendings to help out with and a good deal of time.

**Conclusion:** We are still in the process of determining the risk of ACS for these patients, and thus do not have results yet. Current data seems to correlate well with our hypothesis that most patients have very low risk. As seen from the data, less then 10% of patients had any significant sign (elevated Troponin, Killip class, elevated Creatinine..etc) of an underlying cardiac etiology. Since these are some of the major examination points for a cardiac workup, it would suggest that these patients seem to have low risk of having had an ACS.

After receiving the last bit of data, we will graph the results on a bell-shaped curve to determine the mean risk that patients complaining of chest pain have. Next we will compare this to the published data that shows that doctors tend to decide to workup a patient if they have a risk of at least 1%. We could then analyze the number of patients being worked up who have a risk 1% or greater and determine how many patients would not have to undergo a full workup, if doctors were to increase the amount of risk they will accept to at least 3%.
Evaluation of Outcomes in Breast Conservation Therapy Utilizing Accelerated Partial Breast Irradiation in Ductal Carcinoma in Situ and Early Stage Invasive Breast Cancer

Cervenka, B.

**Purpose**: The standard of care for early-stage breast cancer with breast conservation therapy consists of a 5-7 week course of whole breast irradiation. Studies have shown, however, that the vast majority (>80%) of ipsilateral breast recurrences occur in or within 1cm of the tumor bed, making a case for the use of accelerated partial breast irradiation (APBI), a radiotherapy treatment that delivers a high dose of radiation to the tumor bed and a surrounding 1cm margin. We set forth to investigate the outcome of patients treated with APBI at our institution.

**Methodology**: Statistical analysis of all definitive APBI cases performed at this institution was collected via retrospective review of charts, electronic medical records, and patient phone interviews. Data regarding patient demographics, tumor histology, and outcomes were recorded in a database. Patients were included in the statistical analysis if they had completed their definitive APBI treatment by May 16, 2010.

**Results**: A total of 132 patients were definitively treated from August 2004 to May 2010, 71 with the MammoSite catheter and 61 with the Strut-Adjusted Volume Implant (SAVI) catheter. The median follow up for this population was 27 months (range, 2-71 months), with a 99.2% overall disease-free survival rate. There was one patient with DCIS histology who recurred 25 months post-treatment. There was a subset population of 23 patients with a median follow up of 59 months. This population had no recurrences. Three patients treated with the MammoSite catheter had major adverse side effects including skin necrosis and osteoradionecrosis. The SAVI population reported no such complications.

**Conclusions**: The survival outcomes of the patients treated with definitive APBI at this institution are acceptable and comparable to outcomes at other institutions. Based on these outcomes, APBI is an alternative to conventional whole breast irradiation for carefully selected early-stage breast cancers, though longer follow up is necessary.

AGE AT ONSET OF PUBERTY PREDICTS BONE MASS IN YOUNG ADULTHOOD

Vicente Gilsanz, MD, PhD¹, James Chalfant¹, Heidi Kalkwarf, PhD², Babette Zemel, PhD³, Joan Lappe, PhD⁴, Sharon Oberfield, MD⁵, John Shepherd, PhD⁶, Tishya Wren, PhD¹, Karen Winer, MD⁷

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⁴Creighton University, Omaha, NE  
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⁷NICHD, Bethesda, MD
Goal: Although the amount of bone gained during puberty is the main contributor to peak bone mass, the influence that normal variations in sexual development have on bone acquisition has yet to be clearly defined. The goal of this study was to determine whether the age of commencement and length of puberty influences dual x-ray absorptiometry (DXA) values of bone mineral content (BMC) and bone mineral density (BMD) in the axial and appendicular skeleton at skeletal maturity.

Methods: We identified 78 girls and 85 boys who began puberty and completed sexual and skeletal development during the duration of the Bone Mineral Density in Childhood Study and examined whether the timing and length of puberty influence DXA values of BMC and BMD at skeletal maturity.

Results: Multiple linear regression analyses indicated that the age of onset of puberty was a strong negative predictor of DXA bone measurements at skeletal maturity, independent of bone values at the beginning of puberty and the length of puberty. This negative relation was observed for all BMC and BMD measurements at all skeletal sites, in both boys and girls (all P < .0001). In contrast, length of puberty had no relation to any measures of bone.

Conclusions: In healthy adolescent males and females, bone mass and bone density at skeletal maturity are inversely related to the timing of puberty.

New Biomimetic Technology for “Just-In-Time” Delivery of Anti-Convulsants Following Traumatic Brain Injury.

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² Research Lab Specialist, KSOM, USC; LAC Dept of Cell and Neurobiology  
³ Assoc Prof of Neurological Surgery, Assoc Prof of Cell and Neurobiology, KSOM, USC; LAC Dept of Neurological Surgery

Goal: Epileptic seizures are a common, unfortunate sequela of traumatic brain injury (TBI). Epileptogenic foci within the damaged tissue can be localized, but pharmacologic therapy must be given by systemic route in sufficient doses to quell excitatory activity that, by nature, spreads rapidly from the point of epileptogenesis. USC Viterbi School of Engineering has developed an implantable piezoelectric micropump capable of delivering minute dosages of antiepileptic drug (AED) directly to the seizure-inciting tissue with minimal lag time. This approach has the dual advantages of limiting adverse side effects frequent with systemic therapy and delivering AED promptly enough to correct pathologic excitation before it spreads to neighboring neural tissue. The goal of this study will therefore be to study the tissue perfusion characteristics of the micropump using micro CT and autoradiographic techniques and to implement this novel drug delivery method in a rodent model of TBI-induced epilepsy.

Methods: A pilot investigation analyzing the resolution resolving capabilities of micro CT is underway. Further testing will be conducted infusing microliter quantities of CT
contrast from the micropump cannula into rodent brain tissue to analyze pump
characteristics and tissue diffusion. The resolving capabilities of the micro CT machine
have been tested with 2.5 µl and 5 µl boluses of iopamidol (trade name IsoVue) contrast
media in 4% agarose gel, but gel crystallization artifacts necessitated a media transition to
in vitro neural tissue. Trials in rodent neural tissue were conducted with three contrast
agents: iopamidol, phosphotungstic acid (PTA), and gold nanoparticles (50 nm, 0.05
mg/ml in water) with bolus sizes of 2.5 µl and 5 µl tested for each. Perfusion
characteristics of the pump will be further analyzed using radiolabeled Phenytoin and
autoradiography in rodent brain samples.

Results: Iopamidol boluses of 2.5 µl in 4% agarose gel were distinguishable on micro CT
so this imaging modality appears to be suitable for analysis of diffusion for the fluid
volumes in the range within which the micropump operates. Follow-up trials in rodent
neural tissue with 2.5 µl and 5 µl boluses of iopamidol and PTA confirmed the previous
assessment, showing contrast agent deposition with adequate volumetric resolution for
qualitative analysis. The gold nanoparticle trial was less successful; though faintly
visible, the bolus could not be discerned in detail on the micro CT scan. Subsequent
studies using the micropump itself with iopamidol and/or PTA contrast should yield
invaluable diffusion data that can be quantified via micro CT and autoradiographic
techniques.

Conclusion: Epilepsy secondary to TBI is a condition amenable to treatment with an
implantable drug delivery device. This project will examine the drug delivery capabilities
of the Viterbi micropump and its efficacy in controlling TBI-induced epilepsy in a rodent
model. The micro CT machine is appropriate for bolus diffusion analysis in rodent neural
tissue with either iopamidol or PTA (but not with gold nanoparticles in the current
preparation) in the microliter-scale volumes we expect to be testing.

Assessing the accuracy of ultrasonography for the detection and size measurement
of rotator cuff tears

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Department of Orthopedics, Hadassah University Hospital Ein-Karem, Jerusalem, Israel

Background: The accuracy of ultrasonography for the detection and size measurement
of full and partial rotator cuff tears plays a key role in an orthopedist's decision making
when contemplating rotator cuff surgery. The accuracy, sensitivity, and specificity of
ultrasonography in the detection of rotator cuff tears have been widely studied by several
investigators. These values, as reported in the literature can be as high as 100 percent
sensitivity, 85 percent specificity, and overall accuracy of 96 percent (Teefey), or 85%
sensitivity and 92 percent specificity (de Jesus). These reported values can be much
greater than the values seen in clinical practice because these studies compared the results
of shoulder ultrasounds done in university based hospitals by dedicated musculoskeletal
ultrasonographers. For example, the Teefey study was performed at the Mallinckrodt
Institute of Radiology in St. Louis, Missouri by fellowship-trained radiologists with more
than ten years of experience with the test. Most orthopedic surgeons in the world,
however, do not work in the environment of university hospitals. These community based orthopedists often receive shoulder ultrasound studies from ultrasonographers not dedicated to musculoskeletal imaging. The accuracy of such studies is not known. The purpose of this study is to compare the results of community based ultrasounds to intraoperative findings during rotator cuff surgery. We analyzed the difference in the size measurements of full thickness rotator cuff tears seen in ultrasonography compared to what is actually found in open surgery. We also compared the overall accuracy, sensitivity and specificity of ultrasonography in the detection of rotator cuff tears as reported in the literature to those values found for ultrasonography performed in a community health care center.

**Methods:** Seventy eight consecutive patients undergoing rotator cuff surgery were evaluated preoperatively by community based ultrasonographers who performed bilateral shoulder ultrasonography. The presence of a full thickness tear, partial thickness tear, and no tear was recorded. Measurements of the size of a full thickness tear, as seen on ultrasonography, were also recorded. The intraoperative clinical findings were then compared to the ultrasound results. Statistical analysis comparing the means of the tear size as seen by ultrasound and intraoperatively was done using the student t-test.

**Results:** The mean size of a full thickness tear as seen on ultrasound was 21.1 ± 12.69, whereas the mean size of a full thickness tear as seen in surgery was 30.1 ± 8.8 (p<.05). Ultrasonography correctly identified sixty of the sixty one full thickness rotator cuff tears. Ultrasonography correctly identified four of the eleven partial thickness tears. Ultrasonography correctly identified one of three cases in which there was no tear, and falsely identified three tears as no tears. The overall accuracy of ultrasonography was found to be 83.3%, the sensitivity was found to be 85.5%, and specificity was found to be 33.3%.

**Table 1:** Measurements recorded for full thickness rotator cuff tears as detected by ultrasonography and intraoperatively:

<table>
<thead>
<tr>
<th>Case #</th>
<th>US measurements (mm)</th>
<th>OR measurements (mm)</th>
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</thead>
<tbody>
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<td>25</td>
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<tr>
<td>93</td>
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</table>
Table 2: Comparison of diagnoses of rotator cuff tears made by ultrasonography and in rotator cuff surgery (intraoperatively):

<table>
<thead>
<tr>
<th>Diagnosis with ultrasonography</th>
<th>Full thickness</th>
<th>Partial thickness</th>
<th>No tear</th>
<th>Total</th>
<th>Accuracy</th>
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</thead>
<tbody>
<tr>
<td>Full thickness</td>
<td>60</td>
<td>1</td>
<td>1</td>
<td>62</td>
<td>65/78 = 83.3%</td>
</tr>
<tr>
<td>Partial thickness</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>No tear</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
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</table>

Conclusions: A significant difference was found between the size of a full thickness rotator cuff tear detected on ultrasonography compared to what is actually seen in surgery. An orthopedic surgeon should expect about a 9mm increase in the size of the tear from what is measured in ultrasound. Knowing the size of a rotator cuff tear preoperatively is of great importance to the orthopedic surgeon because it serves as a prognostic indicator. A larger rotator cuff tear decreases the chances of surgically achieving a repair and increases the likelihood of a re-tear after surgery. Hence, accurately knowing the size of a tear helps the surgeon decide if a rotator cuff surgery is indicated. This information is especially valuable in older patients, over 60 years of age, because the decision to operate is up to the surgeon’s discretion and very much depends on the size and nature of the tear.

Additionally, the accuracy, sensitivity, and specificity of ultrasonography in the detection of rotator cuff tears as reported in the literature seems to be higher than that found by a community ultrasonographers. The values reported in the literature are based on studies done by dedicated musculoskeletal ultrasonographers in university based hospitals. Ultrasonography performed in a community based health center is typically performed by a less experienced ultrasonographer who is not dedicated to musculoskeletal imaging, and therefore the values for accuracy, sensitivity, and specificity are typically lower than those reported in the literature. A similar decrease in the accuracy of shoulder MRIs can be expected for MRI studies done with extremity MRI scanners in outpatient centers. Further studies should be done to explore the accuracy of such imaging tests.
Demographic and Clinical Characteristics of Patients Undergoing PCI at USC: Comparison of LAC+USC and University Hospital

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

Background: Percutaneous coronary interventions (PCI) are frequently performed to treat patients with stable and unstable coronary artery disease (CAD). CAD is a common health care problem associated with significant cost, morbidity and mortality. The Keck School of Medicine, University of Southern California, serves two diverse patient populations within the same geographic area—public Los Angeles County General Hospital (LAC+USC) and private USC University Hospital (UH).

Methods and Results: We performed a retrospective comparison of demographics and clinical characteristics from patients treated with PCI at either LAC+USC or UH between January 2008 and December 2010 (n=702 and n=431, respectively). Demographics show that LAC+USC patients are younger (58.17±9.2 vs. 67.91±11.3, p<0.0001) and predominantly Hispanic (52.14% vs. 22.74%, p<0.01) patients, while UH patients are older and predominantly Caucasian (53.36% vs. 15.53%, p<0.0001). PCI indications are different with more LAC+USC patients presenting with unstable angina (37.25% vs. 12.88%, p<0.0001) or primary angioplasty (28.84% vs. 7.49%, p<0.0001) compared to UH patients who more frequently undergo PCI for asymptomatic myocardial ischemia (40.05% vs. 5.13%, p<0.0001). LAC+USC patients are less likely to have prior history of PCI (36.07% vs. 46.43%, p<0.0001) or coronary artery bypass grafting (CABG) (8.43% vs. 35.03%, p<0.0001).

Conclusion: This analysis demonstrates that despite being within the same geographic area significant differences exist in patient population demographics and clinical characteristics. Further research is necessary to establish if these differences impact cardiovascular outcomes.
### Table 1: Clinical Characteristics

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>LAC+USC (n=702)</th>
<th>University Hospital (n=431)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y*</td>
<td>58.17±9.2</td>
<td>67.91±11.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male, n</td>
<td>544 (77.49)</td>
<td>323 (74.94)</td>
<td>0.36</td>
</tr>
<tr>
<td>Race</td>
<td></td>
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</tr>
<tr>
<td>African American, n (%)</td>
<td>52 (7.41)</td>
<td>14 (3.25)</td>
<td>0.0037</td>
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<tr>
<td>Asian Pacific, n (%)</td>
<td>92 (13.11)</td>
<td>42 (9.74)</td>
<td>0.089</td>
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<tr>
<td>Caucasian, n (%)</td>
<td>109 (15.53)</td>
<td>230 (53.36)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Hispanic, n (%)</td>
<td>366 (52.14)</td>
<td>98 (22.74)</td>
<td>0.01</td>
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<tr>
<td>Native American, n (%)</td>
<td>0 (0)</td>
<td>4 (0.43)</td>
<td>0.33</td>
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<tr>
<td>Other, n (%)</td>
<td>83 (11.82)</td>
<td>43 (9.98)</td>
<td>0.11</td>
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<tr>
<td>Height, cm*</td>
<td>167.70±9.57</td>
<td>168.96±13.1</td>
<td>0.097</td>
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<tr>
<td>Weight, kg*</td>
<td>81.35±17.1</td>
<td>80.89±19.9</td>
<td>0.69</td>
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<td>Co-Morbidities</td>
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<tr>
<td>HTN, n (%)</td>
<td>518 (73.79)</td>
<td>336 (77.96)</td>
<td>0.11</td>
</tr>
<tr>
<td>PUD, n (%)</td>
<td>16 (2.28)</td>
<td>43 (9.98)</td>
<td>&lt;0.0001</td>
</tr>
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<td>CVA, n (%)</td>
<td>37 (5.27)</td>
<td>37 (8.58)</td>
<td>0.02</td>
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<td>Sleep apnea, n (%)</td>
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<td>10 (2.32)</td>
<td>0.014</td>
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<tr>
<td>PVD, n (%)</td>
<td>15 (2.14)</td>
<td>54 (12.53)</td>
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<td>CKD, n (%)</td>
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<td>44 (10.21)</td>
<td>&lt;0.0001</td>
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<td>Dialysis, n (%)</td>
<td>16 (2.30)</td>
<td>40 (9.28)</td>
<td>&lt;0.0001</td>
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<td>Hypercholesterolemia, n (%)</td>
<td>372 (52.99)</td>
<td>291 (67.52)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Diet controlled, n (%)</td>
<td>8 (11.15)</td>
<td>14 (3.25)</td>
<td>0.013</td>
</tr>
<tr>
<td>Oral medication, n (%)</td>
<td>125 (19.99)</td>
<td>83 (19.26)</td>
<td>0.59</td>
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<tr>
<td>Insulin dependent, n (%)</td>
<td>146 (21.01)</td>
<td>92 (21.35)</td>
<td>0.89</td>
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<tr>
<td>Prior History</td>
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<tr>
<td>CABG, n (%)</td>
<td>36 (8.43)</td>
<td>124 (35.03)</td>
<td>&lt;0.0001</td>
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<tr>
<td>PCI, n (%)</td>
<td>176 (36.07)</td>
<td>171 (46.43)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>158 (34.27)</td>
<td>98 (29.08)</td>
<td>&lt;0.0001</td>
</tr>
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</table>

*Data are presented as mean±SD
Elucidation of the molecular mechanisms underlying invasa type of recessive dystrophic epidermolysis bullosa using site-directed mutagenesis.

Y.P. Hou, J. Cogan, E. Cua, S. Lee, D.T. Woodley, M. Chen

Year II medical student¹, KSOM; Department of Dermatology, University of Southern California, Los Angeles, CA

**Goal:** Type VII collagen (C7), composed of a central triple helical domain (TH) flanked by non-helical domains, NC1 and NC2, is the major component of anchoring fibrils. Mutations in the type VII collagen gene (COL7A1) cause dystrophic epidermolysis bullosa (DEB). Inversa recessive DEB (RDEB-I), a rare form of DEB, is associated with missense mutations involving arginine or glycine within the TH. Because the lesions in RDEB-I are mainly restricted to body sites with higher skin temperature, it has been hypothesized that the pathophysiology of RDEB-I is temperature dependent. The goal of this study is to elucidate the biological consequences of specific COL7A1 mutations leading to the unique RDEB-I phenotypes.

**Methods:** In this study, we generated 18 substitution mutations associated with RDEB-I and purified the recombinant mutant proteins. Protein precipitation and purification were performed using dialysis and Sepharose ion-exchange chromatography. Biochemical, structural and functional characterization of the purified mutant C7s were compared to that of wild type C7 under different temperatures.

**Results:** The study demonstrated the following: (1) All mutations except G1907E

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Table 2: Procedure Indication

<table>
<thead>
<tr>
<th>Procedure Indication</th>
<th>LAC+USC (n=702)</th>
<th>University Hospital (n=431)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute heart failure, n (%)</td>
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<td>16 (3.71)</td>
<td>0.0038</td>
</tr>
<tr>
<td>Arrhythmia, n (%)</td>
<td>3 (0.43)</td>
<td>4 (0.93)</td>
<td>0.30</td>
</tr>
<tr>
<td>Asymptomatic ischemia, n (%)</td>
<td>36 (5.13)</td>
<td>171 (40.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Post infarction, n (%)</td>
<td>24 (3.42)</td>
<td>11 (2.53)</td>
<td>0.40</td>
</tr>
<tr>
<td>Post infarction with recurrent ischemia, n (%)</td>
<td>9 (1.28)</td>
<td>1 (0.23)</td>
<td>0.065</td>
</tr>
<tr>
<td>Primary angioplasty, n (%)</td>
<td>199 (28.84)</td>
<td>32 (7.49)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Progressive/worsening angina, n (%)</td>
<td>92 (13.33)</td>
<td>88 (20.61)</td>
<td>0.0013</td>
</tr>
<tr>
<td>Stable angina, n (%)</td>
<td>59 (8.55)</td>
<td>47 (11.01)</td>
<td>0.17</td>
</tr>
<tr>
<td>Unstable angina, n (%)</td>
<td>257 (37.25)</td>
<td>55 (12.88)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Immediate/Rescue, n (%)</td>
<td>3 (0.43)</td>
<td>2 (0.47)</td>
<td>0.93</td>
</tr>
</tbody>
</table>
synthesized and secreted a 290 kDa mutant C7 at levels similar to the wild type C7. (2) Most RDEB-I mutations produced mutant C7s with the reduced thermal stability, as demonstrated by increased sensitivity to protease digestion and reduced ability to form trimers at higher temperature. (3) Many RDEB-I mutations generated mutated C7s with significantly reduced ability to promote keratinocyte migration and support cell adhesion at higher temperatures. Nevertheless, under lower temperature, these RDEB-I mutant C7s were as effective as wild type C7 in supporting keratinocyte adhesion and migration. (4) The R2622W and R2628W RDEB-I mutations next to NC2 reduced C7’s ability to form antiparallel dimers.

**Conclusion:** We conclude that effects of RDEB-I mutations on C7 functions such as folding, molecular stability, cell attachment, or cell motility are highly temperature dependent and are concordant with the observed clinical phenotype. This study elucidates the biological consequences of specific COL7A1 mutations which lead to RDEB-I and positively impacts the future of the clinical management of patients with RDEB-I.

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**Radionuclides in Gastrointestinal Bleeds: the usefulness of 99m-technetium red blood cell scintigraphy and dynamic cinematic displays**

Cummings, A.

**Purpose:** Gastrointestinal (GI) bleeds lead to approximately 4.7 million imaging procedures a year in the United States. While endoscopy, capsule endoscopy, and angiography are often sufficient for localization and treatment, non-diagnostic results are common and may require alternative imaging. This educational exhibit will explain and review the use of radionuclide imaging in GI bleeding, including its most recent use with single photon emission computed tomography/computed tomography (SPECT/CT). A particular emphasis will be placed on the evaluation of Technetium-99m Red Blood Cell Scintigraphy (99mTc-RBC) in comparison to alternative techniques. 1. Metter FA Jr, Bhargavan M, Faulkner K, et al. Radiographic and nuclear medicine studies in the Unites States and worldwide. Radiology. 2009 Nov;253(2):293-6.

**Methods:** Ten cases including ileal ulcers, small bowel trauma, Meckel’s diverticulum, colonic angiodysplasia, gastritis, esophageal varices and aorto-duodenal fistula were given 99mTc-RBC or 99mTc-SC as an intravenous bolus and then imaged with a gamma camera with a frame recorded every minute for 60-90 minutes to build a dynamic cinematic scintigraphy display. Three cases were also recorded with standard angiography for comparison. In two cases with initial negative scintigraphy, delayed images were taken 18-24 hours after the initial injection of 99mTc-RBC. All cases involved patients seeking treatment at LAC+USC.

**Results:** 99mTc-RBC is a highly sensitive, well-tolerated diagnostic tool used to detect acute GI bleeding. Indications for use include evidence of active bleeding with non-diagnostic endoscopy; common confounders include varices and other upper GI bleeds. Delayed views corresponding to episodic clinical bleeding are helpful when initial scintigraphy is negative and/or there has been larger transfusion requirements with lower GI bleeding.
Conclusion: Radionuclide imaging is a valuable tool in the evaluation of acute GI bleeds. Exploring this form of imaging, its indications and the anatomical findings associated with various common pathologies can be helpful for medical students interested in the area of diagnostic radiology.

Evaluation of MMPs in Wound Healing

K. Doolittle¹, Y. P. Han², PhD, W. Garner, MD

Year II medical student¹, KSOM, Univ. of So. California; Hoffman Medical Research Center

Goal: An important aspect of wound repair is remodeling of the extracellular matrix to support growth and regeneration. Breaking down the extracellular matrix allows cells and proteins to move more freely in the space, and this is a critical step in the process of wound healing. Matrix metalloproteinase 13 (MMP-13) is an enzyme that digests elements of the extracellular matrix, including collagen. My goal is to show that MMP-13 is needed for proper skin wound healing. My first aim will be to prove that MMP-13 KO mice wounds do not heal as well as wild type (WT) mice wounds. My second aim will be to prove that the wound beds of MMP-13 KO mice are different from the wound beds of WT mice. Specifically, I plan to measure the levels of inflammatory cells and mediators in the wound beds of the MMP-13 KO mice versus WT mice. Understanding the role of MMP-13 in wound repair will help us to understand the mechanism involved in normal and abnormal wound healing.

Methods: Excision wounds (6 mm) are created on the dorsal side of KO and WT mice using a 6mm punch biopsy tool. Then, we track the wound sizes with a camera and standard ruler over a 10 day period. Next, we calculate the wound area differences using Photoshop and analyze for statistical significance. Additionally, we use immunofluorescence staining to determine the different inflammatory conditions present in MMP-13 KO mice versus WT mice. We are using Hematoxylin and Eosin staining to visualize the samples we are working with.

Results: Thus far, our data shows that MMP-13 KO mice wounds heal at a slower rate than WT mice, with the most significant differences in wound size appearing at the beginning of the healing phase. This supports our belief that MMP-13 is important for proper wound healing.

Conclusion: Similar wound healing mechanisms are employed throughout our body; thus, studying MMP-13 may be significant for the proper healing of other conditions, such as cancer metastasis and liver cirrhosis. In order to maximize our ability to treat wounds, it is crucial to understand the enzymes involved in the overall process. It is clear that MMP-13 plays an important role in wound healing, and our lab is working to uncover key differences among wounds with normal levels of MMP-13 and wounds lacking MMP-13. With this knowledge, novel therapies may be created for the treatment of skin wounds, as well as other medical conditions.
Determination of critical concentrations for direct drug susceptibility testing of first and second-line anti-tuberculosis drugs in the MODS assay using survival analyses

Sean Patrick Fitzwater1,2, G. Andrew Sechler3 MD, Robert H. Gilman2 MD, David AJ Moore3-5 MD

Background: Multidrug resistant tuberculosis is a leading threat controlling tuberculosis (TB) in resource poor settings. Microscopic observation drug susceptibility assay (MODS) has emerged as a high-performance diagnostic technique for direct detection of TB and to determine resistance to first line TB drugs. However, the MODS technique has not yet been adapted to determine the sensitivity to ethambutol, streptomycin, and second line drugs.

Methods: To address this issue, samples were obtained from 94 culture positive patients with demonstrated resistance to second line in drugs. Samples were culture following standardized MODS protocols, with the addition of titrations of antimicrobial drugs. Critical concentrations were determined using a modified Kaplan Meier survival curve analysis, and the results were compared to the proportion method for determining resistance.

Results: All drugs tested except for pyrazinamide showed characteristic drug susceptible and restraint populations with drug titrations. Critical concentration were determined for capreomycin (10 µg/ml), ciprofloxacin (1.25 µg/ml), cycloserine (40 µg/ml), ethambutol (10 µg/ml), ethionamide (5 µg/ml), kanamycin (5 µg/ml), para-aminosalicylic acid (10 µg/ml), and streptomycin (10 µg/ml).

Conclusions: Our results demonstrate that MODS is a promising method for inexpensively deterring the susceptibility of Mycobacterium tuberculosis to second-line drugs. Further studies are needed expand sensitivity testing to other second line drugs and pyrazinamide.

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Selective Chest Radiography in Blunt Trauma

E. Fried, and D. Anglin2, MD
Year II medical student1, KSOM, Univ. of So. California; LA CoH-USC Emergency Attending, Site project coordinator2

Goal: The goal of this study is to validate a decision tool to predict whether or not a patient who presents to the ED with blunt chest trauma should receive a chest x-ray as part of their evaluation. Current standards of care dictate that patients presenting with blunt chest trauma receive a chest x-ray; however, very often these x-rays do not reveal
diagnostically significant information. The cost of these unnecessary x-rays is estimated to be greater than $900 million per year in addition to avoidable patient exposure to radiation. The study aims to eliminate these unwarranted x-rays in which no significant intrathoracic injury is discovered.

**Methods:** Patients presenting to the ED with blunt chest trauma will be administered a "diagnostic instrument" which is a series of questions that document the mechanism of injury in addition to several other risk factors such as if the patient has chest wall tenderness on palpation, if the patient is intoxicated, if the patient is alert and oriented, if the patient is reporting pain on their chest wall or an another distracting painful injury, among other relevant findings from the history and physical exam of the patient. After the information is recorded the patient will receive a chest x-ray. After data collection is complete the data gathered will be compared against the chest x-rays to search for a correlation between data collected purely on physical exam and patient history as directed by the diagnostic instrument with the findings on the x-ray.

**Results:** The study is currently in a validation phase validating the conclusions of the completed pilot stage which enrolled 1850 subjects. The pilot study concluded that the clinical criteria based on patient history and physical exam as directed by the diagnostic instrument were able to identify patients with a significant intrathoracic injury with 100% sensitivity and excludes injury with 100% negative predictive value. By ruling out patients with a very low chance of significant intrathoracic injury using the diagnostic instrument 38% of chest x-rays can be eliminated. My role (E. Fried) is to enroll patients who present to LA CoH-USC's emergency department with blunt chest trauma in the study by applying the diagnostic instrument on these patients. This summer I enrolled over 100 patients in the validation stage of the study. I am continuing to enroll patients throughout the last 6 months as the study continues.

**Conclusions:** Based on the very promising results of the pilot study, a two year, multi-center, 10,000+ patient validation study of the pilot's conclusions is currently in progress. If the validation study verifies the pilot's conclusion, a new standard of care evidence-based guideline for emergency medicine physicians will be created directing physicians when it is recommended and when is not advisable to take chest x-rays in the case of acute blunt chest trauma.

**Incidence of Elevated Lactate in Non-diabetic Patients Undergoing Non-cardiac Surgery.**

Ardeshir Jahanian, BA, Jason Fuhrman, BA, Kimberly Simms, BA, Naira Martirosyan MD, Zaruhi Meliksetyan MD, Mary M Joseph MD, Linda Chan PhD.

Institution: Department of Anesthesiology, Keck School of Medicine of University of Southern California, Los Angeles CA.

Corresponding Author: Ardeshir Jahanian. Medical Student Keck School of Medicine (MS-4). ardeshir.jahanian@gmail.com. 408-888-8960.

**Background:** Metabolic acidosis occurs when the body either produces too much acid or when the kidneys are no longer removing enough acid from the body. The objective of this study was to find the incidence of metabolic acidosis, especially elevated lactate
levels, in non-diabetic patients undergoing non-cardiac surgery, particularly cancer patients.

**Methods:** This is a retrospective electronic chart review study approved by the University of Southern California Health Sciences Institutional Review Board. It was approved to include all non-diabetic patients who had had non-cardiac surgery between the dates of April 2005 through May 2010. We looked at patients with acidosis for any association with cancer. We also looked for any physiologic derangements in electrolytes and ABG values in these patients.

**Results:** A total of 5495 of the 8101 patients were identified to be non-diabetic patients, with or without metabolic acidosis, between the years 2008-2010. Out of 5495 only 3344 had complete data. Out of the 3344, 534 (16%) had metabolic acidosis, 2810 (84%) did not. Therefore we reviewed patients with elevated lactate (>1.6) and anion gap (>20) as well. Elevated lactate levels were observed in patients with gastrointestinal disorders, pulmonary disease, and sepsis (P<0.05). Anion gap was elevated in patients with renal insufficiency, sepsis, and pulmonary disease (P<0.05).

3344-Total sample evaluated.
2865-Lactate measured; 46% (1331) had lactate >1.6.
3294-Anion gap measured; 2.1% (70) had anion gap >20
2910-Base deficit measured; 55% (1591) had base deficit >2
663- Cancer patients; 20%

<table>
<thead>
<tr>
<th>Acidosis parameters</th>
<th>Cancer</th>
<th>Percent (Number)</th>
<th>Adjusted Odds Ratio</th>
<th>Adjusted p-value</th>
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<tbody>
<tr>
<td>Anion gap &gt;20</td>
<td>Yes</td>
<td>1% (7/654)</td>
<td>0.27 (0.04, 3.65)</td>
<td>0.227</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2% (63/2640)</td>
<td></td>
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</tr>
<tr>
<td>Lactate &gt;1.6</td>
<td>Yes</td>
<td>35% (195/562)</td>
<td>0.61 (0.38, 0.96)</td>
<td>0.0318</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>49% (1136/2303)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base deficit &gt;2</td>
<td>Yes</td>
<td>41% (236/572)</td>
<td>1.17 (0.71, 1.98)</td>
<td>0.546</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>58% (1355/2338)</td>
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</tbody>
</table>

1) Anion gap is not statistically significant
2) Likelihood of having lactate >1.6 among cancer group is .61 times less likely than the non-cancer group.
3) Base deficit is not statistically significant.

**Conclusions:** Based on this study we found different outcomes than clinically observed and which prior research dictated. We did not find an increased incidence of metabolic or lactic acidosis amongst cancer patients. A possible reason for this is that the cancer patients in this study may not have been in advanced stages. To further investigate this physiologic anomaly a larger sample size is needed along with a larger direct sample of cancer patients.
A Review of Terminal Sterilization with Gamma Irradiation

Gregory Gomez, C. Thomas Vangsness Jr. MD
Keck School of Medicine, University of Southern California

Purpose: The use of allograft transplantation by orthopedic surgeons has increased due to the decreased morbidity and mortality issues associated with autograft transplants. With the increase popularity amongst orthopedic surgeons it has become evident that there are important issues associated with the use of donor tissue.

Goal: This article is a comprehensive review of terminal sterilization in soft tissue allografts transplants.

Methods: A broad PubMed and OVID search was completed to collect studies that discussed the issues regarding gamma irradiation of soft tissue for allograft tissue transplant. The clinical research papers cited are Level 1, Level2, and Level 3 that are based on the level of evidence referenced. Results: Currently, the safest and least detrimental protocol that ensures a soft tissue grafts SAL of $10^{-6}$ is by carrying out rigorous donor screening programs along with low dose gamma irradiation (~13kGy).

Conclusion: While this processing protocol is not perfect, many more studies need to investigate ways to preserve the biochemical and biomechanical properties of soft tissue during exposures to high dose gamma irradiation to ensure sterile grafts along with patient safety.

USC-HN2, a new model for recurrent oral cavity squamous cell carcinoma with immunosuppressive characteristics

Lucy Gong¹, Sarah Russell², Melissa Lechner², and Alan Epstein, MD, PhD²

¹Year II medical student, KSOM, University of Southern California, Los Angeles, California
²Department of Pathology, KSOM, University of Southern California, Los Angeles, California

Goal: Head and neck squamous cell carcinoma (HNSCC) is the 8th most common solid tumor malignancy worldwide. Tumors are often aggressive, with significant morbidity and mortality related to locally invasive, recurrent, and metastatic disease. Few HNSCC cell line models are available for much needed pre-clinical investigations of recurrent or metastatic disease pathogenesis and the development of systemic adjuvant therapies.

Methods: The USC-HN2 cell line was established from a patient biopsy specimen of
invasive recurrent buccal HNSCC. The immortalized cells were then further characterized by morphology, heterotransplantation, cytogenetics, immunohistochemical and flow cytometry staining, suppressor cell induction, oncogene and cytokine analysis, and gene microarray analysis.

**Results:** Characterization studies confirmed the human HNSCC origin of USC-HN2 and demonstrated a phenotype similar to the original tumor, which was typical of aggressive HNSCC (EGFR+CD44v6+FABP5+Keratin+). Gene and protein expression studies revealed USC-HN2 cells to have highly immune-modulatory cytokine production with strong suppressor cell induction capacity *in vitro* relative to a group of existing HNSCC cell lines. Compared to other well characterized HNSCC cell lines, USC-HN2 appears to represent a highly immunosuppressive phenotype and as such, is an excellent tumor model for studying interaction of HNSCC tumors with immune host defenses.

**Conclusion:** USC-HN2 has unique immunosuppressive features and is an important new model for further investigation of HNSCC and the development of new therapeutic modalities.

**Type IV collagen binding-site within type VII collagen is a pathogenic epitope for EBA autoantibodies.**

X.Y. Wang, R. Gupta, A. Garlapati, J. Cogan, D.T. Woodley, M. Chen, Department of Dermatology, University of Southern California, Los Angeles, CA.

Type VII (anchoring fibril) collagen (C7) mediates epidermal-dermal adherence and is the target for IgG autoantibodies in patients with epidermolysis bullosa acquisita (EBA). The amino-terminal non-collagenous (NC1) domain of C7 harbors the antigenic epitopes for EBA autoantibodies and contains 9 fibronectin type III-like (FNIII) homology repeats. We previously demonstrated NC1 had affinity for type IV collagen. Using a panel of recombinant NC1 deletion mutant proteins and a solid-phase ligand, antigen-to-antigen affinity assay, in this study, we further refined the type IV collagen-binding site to residues 202-360, a predicted 158 amino acid stretch with one of the FNIII. Further, EBA autoantibodies shown to bind to this subdomain by epitope mapping were capable of inhibiting C7 affinity for type IV collagen while IgG from normal human serum did not. Using a FNIII subdomain affinity column, we affinity purified FNIII-specific antibodies from a high titer rabbit polyclonal antibody against NC1, and injected these antibodies into hairless, immunocompetent mice (20-100 microgram/gm body weight) daily for 7 days. Skin bullae, erosions and nail loss developed in the injected mice and biopsies of lesional skin revealed histological, ultrastructural and immunological features of human EBA including sub-epidermal bullae formation, a sub-lamina densa blister cleavage plane and rabbit IgG and murine C3 immunodeposits at the dermal-epidermal junction. The extent of skin disease correlated with the titer of anti-FNIII antibodies circulating in the animal's plasma. In contrast, no skin pathology was observed with the injection of normal rabbit serum. We conclude that the type IV collagen binding site within one of the FNIII like sub-domains of C7 likely plays an important role in epidermal-dermal adherence and that EBA autoantibodies to this subdomain are highly
pathogenic and responsible for the induced epidermal-dermal disadherence observed in EBA.

**Penetrating craniocerebral injuries: CT prognostic indicators of postoperative survival.**

*S. He*¹, D. Hasson¹, M. Pham MD² Year I medical student¹, KSOM, Univ. of So. California; LACoH-USC Neurosurgery resident²

**Goal:** Victims with gunshot wounds (GSW) to the head have high mortality rates. This study examines patients who arrived at LAC+USC with GSW head and received an operation. **Methods:** Scans of 280 patients at the USC-LAC Hospital will be analyzed for specific variables including number of bullet wounds, through and through penetration, crossed midline, lobes traversed, cerebellar injury, penetration of geographic center, ventricular violation, midline shift distance, presence of subdural hematoma, presence of epidural hemmorhage, and non-cranial injury. The data of surgical management will be examined for survival, wound debridement, craniectomy, craniotomy, lobectomy, bullet removal, placement of extraventricular drains, and removal of necrotic tissue. Nonsurgical patients will be examined to elucidate their prognosis, whether that is brain death or functional rehabilitation. **Results:** The project is currently in progress and results will be reported and published. **Conclusion:** Initial computed tomographic (CT) scans of patients subsequently survived to discharge will be compared with non-survivors in an effort to indicate prognostic signs to guide operative vs. expectant management.

**Efficacy and Feasibility of Combination Excimer Laser Therapy, Clobetasol Spray, and Calcitriol Ointment in the Treatment of Generalized Plaque Psoriasis**

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**Purpose:** To ascertain if a combination of the most powerful excimer laser, clobetasol spray, and calcitriol ointment is an effective and efficient treatment for generalized psoriasis.

**Methods:** This is a 12-week, on-going open-label, pilot trial evaluating the efficacy and safety of the combination of excimer laser therapy with clobetasol spray as the initial treatment of generalized psoriasis, followed by maintenance therapy with calcitriol ointment. All patients will receive excimer laser treatments twice weekly for the first 6 weeks. For the remaining 6 weeks, only patients who are less than or are concerned for falling below PASI 75 will continue twice weekly excimer laser treatments. In regards to topical therapies, the study will be conducted in three distinct periods (A, B, and C), each of 4 weeks duration. During Period A (weeks 1-4), patients will use clobetasol spray twice daily. During Period B (weeks 5-8), patients will use calcitriol ointment twice daily. During Period C (weeks 9-12), patients will use clobetasol spray twice daily and calcitriol ointment twice daily.
Results: Ten patients have been recruited so far. 6 out of 7 (86%) patients who completed the first 6 weeks achieved PASI 75. 4 out of 4 (100%) patients who completed all 12 weeks achieved PASI 75. More data will be available in the poster.

Conclusion: Preliminary data is promising. This proposed combination regimen for the treatment of generalized psoriasis has thus far demonstrated both outstanding efficacy and fast onset of action. Clobetasol spray may be an ideal partner to excimer laser therapy enhancing its efficacy and minimizing risk of phototoxic reaction from aggressive UVB irradiation involving many times the MED. Calcitriol ointment provides the required steroid holiday to prevent adrenal suppression. This approach may not be feasible for patients with generalized pustular, erythodermic, or guttate psoriasis. However, it may be feasible for a significant proportion of patients with generalized psoriasis with <20% body surface area involvement and reasonably confluent plaque configuration. Thus, an external approach with better efficacy than current treatment options and without any serious systemic risks may be within reach.

BREAST IMPLANTS AND MINIMALLY INVASIVE HEART SURGERY
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Keck School of Medicine of University of Southern California
Division of Plastic and Reconstructive Surgery, 1 Division of Cardiothoracic Surgery, 2 Department of Surgery
Los Angeles, California, USA

Introduction: The number of women affected by cardiac disease and the number of women with breast implants are both on the rise. Minimally invasive heart surgery offers several benefits including less blood loss, shorter hospital stay, faster recovery time, decreased pain, and improved cosmesis. Given that some cases of minimally invasive cardiac surgery require access to the third or fourth intercostal space of the anterior chest wall, the presence of breast implants could be problematic for cardiothoracic surgeons. We present five cases of women with long-standing breast implants who underwent minimally invasive cardiac valve surgery via an inframammary incision for access to the thoracic cavity.

Case Presentations: Our institution treated five women with breast implants undergoing minimally invasive valve surgeries. In our first case, a woman with mitral valve regurgitation and atrial fibrillation required her right subpectoral saline implant to be removed via an inframammary incision. Cardiothoracic surgeons performed minimally invasive mitral valve repair and Maze procedure through the third intercostal space, after which the same implant was replaced. Our second case presents an 84-year-old woman with severe mitral valve regurgitation and a complicated history of breast augmentation, including bilateral silicone injections that resulted in silicone granulomas and silicone implants that subsequently ruptured. Our plastic surgeon explanted both ruptured implants and silicone granulomas prior to her cardiothoracic surgeries. Given her age and the extent of her deformation, the patient was not offered immediate reconstruction and the implants were not replaced. Delayed reconstruction was discussed, but the patient declined further augmentation. Our third case was brought to us perioperatively, after
cardiothoracic surgeons encountered and removed the patient’s right saline breast implant while performing minimally invasive valve surgery. Our plastic surgeon sustained a rupture while handling the implant, so a new saline implant was placed. There were initial problems with asymmetry since only one side of the patient had been prepared for surgery, but after adjustments were made, symmetry was achieved. The final two cases were those of women who had their original right implants explanted prior to the minimally invasive cardiac surgery performed, after which a new implant was placed. The mean follow up time in our case series was 6.5 months, with a range of 2-10.25 months. There were no infections or complications other than the intraoperative rupture. All patients achieved symmetry and are satisfied with their appearance.

Conclusions: It is possible and safe to perform minimally invasive cardiac surgery on women with breast implants. It is important to recognize the potential dilemma breast implants pose to minimally invasive cardiac surgery and to be prepared to address these difficulties preoperatively when developing a surgical plan. It is recommended that a plastic surgeon be involved early on, so that patients can be informed about the necessary steps that may be needed with regards to their breast prosthesis. As this problem is more frequently encountered in the future, factors to take into consideration include the patient’s age, prior complications related to breast implants, the age of the implants, and the patient’s aesthetic desires. Our series demonstrates five patients with very different histories, who subsequently received individualized care. Multiple factors will determine how to optimally treat each case. As more women with breast implants undergo minimally invasive cardiac surgery, we will likely modify our consideration for and approach to these patients.

SONOPORATION ENHANCES CHEMOTHERAPEUTIC EFFICACY IN RETINAL PIGMENT EPITHELIAL CELLS IN VITRO

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2University of Southern California, Los Angeles, CA
3Children’s Hospital of Los Angeles, Los Angeles, CA
4Keck School of Medicine, University of Southern California, Los Angeles, CA

Purpose: To study the ability of ultrasound (US) and microbubbles (MB) to enhance entry of chemotherapeutic agents into retinal pigment epithelial (RPE) cells in vitro.

Methods: Enhanced cell permeability was studied by using confocal microscopy to quantify the intracellular fluorescence of cells exposed to doxorubicin (DOX) alone vs. doxorubicin with US + MB.

Results: Compared to treatment with doxorubicin alone, RPE cells showed increased permeability to doxorubicin with the addition of US + MB, with intracellular DOX localization increasing over 60 minutes.

Conclusions: US + MB facilitates the uptake of chemotherapy in RPE cells in vitro. Our experiment is the first attempt to combine chemotherapy with sonoporation in retinal cells. This technique may lead to more effective chemotherapy treatments for intraocular
tumors such as retinoblastoma, with less collateral damage to ocular tissues and systemic side effects.

Use of Octreotide for the Management of Chyle Leaks Following Neck Dissection

Objective

Nowlin Hudson, R.

Objective: Injury to the thoracic duct or lymphatic ducts in the base of the neck leading to chyle fistula is an uncommon, but known complication of neck dissection that has traditionally been difficult to treat. Historically chyle leaks have been treated with pressure dressings, no-fat diets, total parenteral nutrition, or injection with sclerosing agents. Prolonged chyle leaks can lead to metabolic imbalances, nutritional deficiencies, immunological complications, longer hospital stays, delayed healing, and necrosis of skin flaps. Octreotide is a synthetic analog of somatostatin that has been described for use in treating chylothorax, and may have utility in treating chyle fistula following neck dissection. The purpose of this study is to describe the use of octreotide in the treatment of chyle leak following neck dissection, and to determine if this leads to a more rapid resolution of chyle leak.

Methods: After obtaining IRB approval, we reviewed the charts of all patients who received octreotide in the last 3 years for treatment of chyle leak. The endpoints for this study include: 1) the amount of drainage from chyle leak per 24 hour period, 2) duration of treatment with octreotide, 3) time to resolution of chyle leak, 4) length of time treated with octreotide, 5) utilization of any dietary changes in treatment, 6) time to return to normal diet, and 7) length of hospitalization.

Results: We identified 4 patients with chyle leak following open neck surgery who were treated with octreotide. Chyle fistula was identified both clinically and by triglyceride levels in the drain fluid greater than 100. Maximum drain output was 290 cc in a 24 hour period. Once a chyle leak was identified, patients were started on octreotide 100 mcg subcutaneous 3 times daily. We noticed a precipitous drop in drain output after 2-3 days of octreotide treatment. Patient diet included nothing by mouth, medium chain fatty acid, and low fat diet prior to resuming a normal diet. Length of octreotide treatment ranged from 7-14 days. Hospital stays ranged from 2-10 days. 3 patients continued octreotide treatment at home for one week after resuming a normal diet. Side effects were minimal and included mild dizziness and flushing.

Conclusions: Octreotide is an effective means of treating chyle fistula following neck dissection. In all patients, treatment with octreotide led to resolution of chyle leak after several days of treatment. No patients required additional surgery. Diet management consisted of nothing by mouth, medium chain fatty acid diet, and resumption of normal diet in a short period of time. Side effects of octreotide were minimal. In conclusion, octreotide is effective in treating chyle leak following neck surgery and should be considered first line treatment in conjunction with dietary modification.
Hemangiopericytoma of the parotid: a case report

Nowlin Hudson, R.

**Objective:** Hemangiopericytomas were first described in by Stout and Murray as "vascular tumors arising from Zimmerman's pericytes." Pericytes are the spindle cells that surround capillaries to provide mechanical support and regulate the luminal diameter of capillaries. Hemangiopericytomas are rare neoplasms that can occur in any area of the body, and between 15 and 25% of hemangiopericytomas are known to occur in the head and neck region. However, primary presentation in the parotid gland as well as other salivary glands is exceedingly rare. A case of a 28-year-old female with a hemangiopericytoma of the right parotid region, and a review of the literature, is presented including the clinical, surgical, radiologic, and histologic features. Since these tumors are very rare and difficult to diagnose, their behavior has been notoriously difficult to predict. This case report aims to consider a rare case of a primary presentation of hemangiopericytoma in the parotid in order to examine the histopathological features that can be used to evaluate diagnostic criteria and prognosis as well as the treatment outcome for this disease.

**Methods:** The record of a 28 year old female presenting with a hemangiopericytoma of the parotid region was reviewed.

**Results:** A 28 year-old female presented with a non-tender growing parotid mass for one year following pregnancy. Examination demonstrated a 2.5 cm preauricular mass with no evidence of facial paralysis. Radiologic studies confirmed a lobulated 26 x 11 x 25mm preauricular mass at the level of the temporomandibular joint with no evidence of calcifications or bone involvement. FNA led to a preliminary diagnosis of low-grade spindle cell lesion was assigned with recommendation for surgical excision. A superficial parotidectomy was performed to resect the tumor with efforts were made to preserve the facial nerve with all appearing normally immediately post-operative except for palsy of the frontal branch. Histopathologic examination revealed a spindle cell lesion with 1 mitosis per 10 high power fields that was strongly positive for CD34, FLI-1, focally positive calponin, and CD68 while remaining negative for desmin, SMA, S-100, and keratin mix. The diagnosis of hemangiopericytoma was made at this time. At 3-month follow-up, all facial palsy was resolved and the patient received no adjunctive therapy. Currently, the patient is 18 months post-treatment with no evidence of recurrence at this time.

**Conclusions:** The clinical presentation of this case of hemangiopericytoma of the parotid was consistent with that described in the literature. Hemangiopericytoma is often a slow-growing, insidious tumor that is non-tender until late in the course of the disease when symptoms arise from pressure on adjacent structures. As a result, patients often wait years to seek treatment. Additionally, the immunohistochemical profile of hemangiopericytoma assisted with a diagnosis of this neoplasm by coinciding with the literature. Tumor cells typically stain positive for CD34 as was consistent with this case. Also, while normal pericytes stain positive for desmin and smooth muscle actin, hemangiopericytoma cells stain negative as was also demonstrated by this tumor. Surgical resection remains the standard treatment for hemangiopericytoma, while
adjunctive therapy continues to be evaluated, and this mode has shown to be successful thus far in this case.

EVALUATING THE ICCHOSE EDUCATIONAL CURRICULUM FOR ENHANCING SEXUAL KNOWLEDGE AND DECISION-MAKING IN AT-RISK ADOLESCENT GIRLS.

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**Goal:** Our goal is to create a framework for assessing current sexual knowledge and behaviors in order to improve decision-making in a local at-risk teenage female population. Adopting the iChoose educational curriculum and methodology used in last year’s pilot program at Roosevelt High School, we sought to revise and improve the program’s efficacy. At the conclusion of the iChoose workshop series, we expect to see an increase in awareness and healthy decision-making regarding sexual practice; this will be qualified by data analysis of pre- and post-workshop questionnaires.

**Methods:** Literature review was used to assess the status quo in the target population, and to evaluate current methods of health education and behavioral modification. These findings, in addition to survey evaluation of last year’s pilot program, guided redevelopment of the iChoose workshop curriculum. Literature review was also used to determine more effective means to measure knowledge, attitudes and behavior regarding sex. The pool of 35 potential participants is drawn from the Healthy Communities Initiative database, with selection for females at Roosevelt High School with a positive screen for risky sexual behavior in the last 2 years. iChoose workshops are being conducted in a series of four sessions, addressing topics such as decision-making, teen pregnancy and sexual health. Pre- and post-workshop responses will be compared to evaluate the effectiveness of the iChoose program.

**Results:** This study is still in progress, with workshops scheduled through February. We are working with Dr. Breck Nichols to analyze the data collected from pre- and post-workshop surveys. We hope to be involved in the continued development and evaluation of the iChoose program for the next several cycles, in which time we anticipate publishing the results.

**Conclusion:** Teen pregnancy represents a significant problem in California, with teen mothers less likely to earn a high school degree and more likely to experience birth and health complications. This study is essential in assessing sexual knowledge and behaviors in a local high-risk population, and in the development of an education/behavioral modification curriculum. From our results, we will gauge the value of a workshop series in creating significant change in the behaviors and attitudes of sexually active teen girls, and work to further develop iChoose as an effective educational tool.
Mapping of Myocardial ASL Perfusion and Perfusion Reserve Data

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INTRODUCTION:
Arterial spin labeling (ASL) is an emerging tool for the assessment of myocardial perfusion and perfusion reserve in humans. This technique uses radiofrequency excitation pulses to tag arterial blood itself. Images of the myocardium are obtained with (tagged) and without (control) the preparation pulse and a difference signal between the two images is calculated. However, this technique requires registration of multiple images and suffers from low signal-to-noise ratio (SNR) [1-4]. In this work, we present a novel approach for mapping perfusion and perfusion reserve based on ASL data. Unregistered spatial data is transformed into a polar coordinate frame and then simultaneously filtered and re-sampled onto a polar grid to boost SNR while generating useful visualizations [5]. This approach is tailored to the formation of quantitative maps from unregistered low-SNR data, and is not specific to ASL.

METHODS:
Mid-short-axis slices were imaged, and the left ventricle was manually segmented. All data were transformed to a polar coordinate frame based on the segmented contours, the center of mass, and the mid-interventricular septum (see Figure 1), leading to irregularly spaced data in the new frame. These data were then resampled at uniformly spaced intervals around the circumference of the left ventricle where each resampled data point was computed as a weighted average of sample values within its neighborhood, using a truncated Gaussian as the weights: \( W(\Delta \theta) = e^{-\frac{\Delta \theta^2}{2\sigma^2}} \cap (\Delta \theta/\theta_w) \). The standard deviation of the Gaussian, \( \sigma \), and the window width, \( \theta_w \), are free parameters. This approach allows for straightforward computation of noise power in the new coordinate frame. Myocardial blood flow (MBF), thermal noise, and physiological noise were then estimated from ASL signals as described in Ref. [1], and were plotted onto the polar coordinate frame.

RESULTS:
Data from twenty-nine patients were analyzed. Figure 2 shows data from a representative patient with a total occlusion of the left anterior descending (LAD) coronary artery, confirmed by X-ray angiography. When increasing the window size, \( \theta_w \), from \( \pi/6 \) to \( 2\pi \), the average thermal noise across all patients decreased from 0.060 to 0.020 ml/ml/min, while the average...
physiological noise decreased from 0.70 to 0.46 ml/ml/min. This indicates that physiological noise is spatially correlated. As shown in Figure 3, the use of broader filters reduces both thermal and physiological noise at the cost of decreased angular resolution, which hinders assessment of individual segments.

**DISCUSSION:**
The proposed approach enables mapping of myocardial ASL perfusion and perfusion reserve in a polar space. Next steps include consideration of myocardial layers and optimization of imaging protocols, segmentation approaches, and polar space spatial filters to provide clinically valuable assessment of perfusion reserve.

**REFERENCES:**

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**Metal-Driven Operation of a Human K⁺ Channel (BK) Gating Ring Apparatus**

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**Goal:** High-conductance voltage- and Ca²⁺-activated K⁺ channels (BK) are potent regulators of vascular tone, neuronal activity and synaptic transmission. Its K⁺ conductance of ~250 pS is an order of magnitude larger than that observed in typical voltage-gated K⁺ selective channels, making the BK channel a powerful regulator of the cell membrane potential. BK sensitivity to intracellular ligands is conferred by a large C-terminal intracellular homo-tetrameric assembly known as the “gating ring”, the operation of which is currently unknown. The goal of this investigation is to shed light on the Ca²⁺ and Mg²⁺-driven operation of a purified human BK gating ring in solution.

**Methods:** Expression and purification of the wild-type (³²²IIEé ALK¹⁰⁰⁵) and Ca²⁺-bowl-neutralized (D894–898A) human BK C-terminus were performed from M15 [pREP4] cells. Protein identity was confirmed using mass spectrometry. Circular Dichroism spectra recorded between 190-260 nm were analyzed to estimate secondary structure composition. Size-exclusion chromatography was performed using a Superdex 200 10/300 column. The metal-sensing properties of the gating ring were probed using steady-state and time-resolved fluorescence experiments in combination with particle-scale Dynamic Light Scattering under physiologically-relevant conditions.
**Results:** Recombinant BK C-termini self-assemble into tetrameric gating rings in solution and undergo Ca\(^{2+}\)- and Mg\(^{2+}\)-dependent structural transitions. Increasing the free Ca\(^{2+}\) or Mg\(^{2+}\) accelerated the average Tryptophan fluorescence lifetime (\(\tau_{\text{avg}}\)) to \(~1.6\) ns (35 \(\mu\)M Ca\(^{2+}\) or 12 mM Mg\(^{2+}\)) from an initial \(~2.6\) ns (no ligand). The apparent Ca\(^{2+}\) affinity was estimated to be \(K_{1/2} \sim 0.29\) \(\epsilon\)M (\(n_1 \sim 3.4\)) and \(K_{2/1} \sim 3.5\) \(\epsilon\)M (\(n_2 \sim 2.1\)), suggesting at least two Ca\(^{2+}\) binding sites and cooperativity. The apparent Mg\(^{2+}\) affinity was estimated to be \(K_{1/2} \sim 154\) \(\epsilon\)M (\(n \sim 2.02\)).

A gating ring carrying the Ca\(^{2+}\)-bowl mutation was investigated to decrease its \(\tau_{\text{avg}}\) from \(~3.2\) ns (no Ca\(^{2+}\)) to \(\tau_{\text{avg}} \sim 2.7\) ns (35 \(\mu\)M). A Ca\(^{2+}\) affinity of \(K_{1/2} \sim 2.0\) \(\mu\)M (\(n \sim 2.4\)) was estimated. The Ca\(^{2+}\) bowl mutations abolished sensitivity for Mg\(^{2+}\) up to 12 mM. Ba\(^{2+}\) up to 12 mM did not alter the fluorescence properties of the gating ring.

**Conclusion:** We demonstrate Ca\(^{2+}\) and Mg\(^{2+}\)-induced structural transitions of the human BK gating ring. Importantly, these transitions occur in the range of concentration relevant to channel activation, suggesting that they represent molecular events that underlie ligand-dependent BK channel activation. Knowledge of BK channel operation may lead to therapeutic drugs to treat epilepsy, hypertension, or urinary incontinence.

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**TEN-YEAR EXPERIENCE WITH TOXIC EPIDERMAL NECROLYSIS**

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**Goal:** Toxic epidermal necrolysis (TEN) is a severe, exfoliating skin disease with a reported mortality rate of 25-50%. The purpose of this study is to describe presenting characteristics, management, and outcome of patients at LAC+USC Medical Center (LAC+USC) with the diagnosis of TEN and related conditions (Stevens-Johnson syndrome and erythema multiforme) to define factors that play a role in prognosis and optimal management.

**Methods:** We will conduct a retrospective review of charts of patients that have had such diagnoses within the past ten years at LAC+USC. Data will be recorded on a standardized data collection form. Data to be included are: patient demographics; etiologic agent; relevant past medical history (event that led to drugs being administered, premorbid allergies, medications, previous dermatologic conditions); comorbid conditions (e.g. malignancies); time from start of suspected drug to symptom development, presentation/admission, burn unit transfer, suspected drug discontinued; type of referring institution; presenting symptoms and physical condition (temperature, heart rate, description and distribution of lesions, extent of cutaneous involvement and
mucosal involvement); hematological parameters (white blood cell count and differential, platelet count, serum urea nitrogen, creatinine, glucose, bicarbonate, hemoglobin, sodium, potassium), frozen section/routine biopsy results, treatment (before and after referral), complications (number and type), outcome, cause of death (if applicable), and length of hospitalization. The SCORTEN value for each patient will be calculated and all data will be analyzed for prognostic factors. The data will be reported as percentages.

**Results:** This study is in the beginning of data collection. The background information has been researched, the methods and data collection tools created, and the study has gained IRB approval. A records search is currently being conducted by the medical records office of LAC+USC for charts from the past ten years containing the diagnosis codes of interest. Once the list has been compiled, chart review will begin for the specified data parameters. Once data collection is complete, the data will be analyzed and conclusions will be made. Ultimately, the results of this study will be submitted for publication. Ideally, our results will reveal parameters or management strategies important in decreasing the mortality rate of TEN and related conditions.

**Conclusion:** Since TEN is a highly fatal condition, the benefit of studying the experience of patients with TEN and related conditions will be to provide information regarding the most critical factors that influence prognosis, as well as to inform other institutions the optimal management strategies to decrease the mortality rate of TEN and related conditions.

**Using magnetic resonance imaging (MRI) to diagnose acute appendicitis in pediatric patients**

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**Goal:** The current protocol to diagnose acute appendicitis in pediatric patients calls for ultrasonography (US) to visualize the appendix. If the results from the US are not conclusive, then computed tomography (CT) must be done. The CT scans, however, expose children to radiation that has the potential to lead to health issues in adulthood. The goal of this study is to examine if magnetic resonance imaging (MRI) can be used instead of CT scans to diagnose acute appendicitis when the US is equivocal.

**Method:**
Inclusion criteria: All pediatric patients of ages 3-21 who present to the emergency room with symptoms of acute appendicitis and have an equivocal US.

MRI will only be available during these hours:
- Monday-Friday 6:30AM-10PM
- Saturday 8AM-5PM
- Unavailable on Sunday
Exclusion criteria: Need for moderate sedation for MRI due to inability to hold still
Failure to pass MRI metal screening
Critically ill patient

A data sheet is filled out for every patient that is included in the study. The questions on the data sheet include: History of abdominal pain, history of diarrhea, diarrhea in the ER, migration of pain to the right lower quadrant (RLQ), nausea, vomiting, anorexia, abdominal pain on exam, tenderness RLQ, rebound tenderness in the RLQ, cough/hopping/percussion tenderness in the RLQ, elevated temp, leukocytosis count, shift to left of neutrophils, CRP, electrolytes, ketones in urine, results of ultrasounds, CT and MRI.

Results: We are currently half-way done with patient recruitment, which is scheduled to run for a total of one year. At this time, I am recording the names of patients that present to the emergency room to rule out acute appendicitis. I check all charts to make sure the data on patients who fit the criteria is saved. Recently, we developed a data sheet that needs to be completed for every patient included in the study. I am currently working on filling out the data sheet on all patients that have already been enrolled. The data sheets will later be analyzed by biostatistics personal. We will evaluate the sensitivity and specificity of using MRI to diagnose acute appendicitis. We will also compare the sensitivity and specificity of MRI to CT results of the previous year. The gold standard for diagnosing acute appendicitis is surgical pathology.

Conclusion: Our goal is to show that MRI is an appropriate modality to diagnose acute appendicitis in pediatric patients. The benefit of the study includes sparing patients radiation exposure.

EVALUATING THE ICHOOSE EDUCATIONAL CURRICULUM FOR ENHANCING SEXUAL KNOWLEDGE AND DECISION-MAKING IN AT-RISK ADOLESCENT GIRLS.

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Year II medical students¹, KSOM, Univ. of So. California; LAC-USC Internal Medicine and Pediatrics²

Goal: Our goal is to create a framework for assessing sexual knowledge and behaviors, and to design a curriculum to improve sexual decision-making in local at-risk teenage females. Adopting the iChoose educational curriculum and methodology used in last year’s pilot program at Roosevelt High School, we sought to revise and improve the program’s efficacy and to increase the evaluative power of the survey. At the conclusion of the iChoose workshop series, we expect to see an increase in awareness and healthy decision-making regarding sexual practice; this will be quantified by data analysis of pre- and post-workshop questionnaires.

Methods: Literature review was used to assess the status quo in the target population, and to evaluate current methods of health education and behavioral modification. These
findings, in addition to survey evaluation of last year's pilot program, guided redevelopment of the iChoose workshop curriculum. Literature review was also used to determine more effective means to measure knowledge, attitudes and behavior regarding sex. The pool of 35 potential participants is drawn from the Healthy Communities Initiative database, with selection for females at Roosevelt High School with a positive screen for risky sexual behavior in the last 2 years. iChoose workshops are being conducted in a series of four sessions, addressing topics such as decision-making, teen pregnancy and sexual health. Pre- and post-workshop responses will be compared to evaluate the effectiveness of the iChoose program.

Results: This study is still in progress, with workshops scheduled through February. We are working with Dr. Breck Nichols to analyze the data collected from pre- and post-workshop surveys. We hope to be involved in the continued development and evaluation of the iChoose program for the next several cycles, in which time we anticipate publishing the results.

Conclusion: Teen pregnancy represents a significant problem in California, with teen mothers less likely to earn a high school degree and more likely to experience birth and health complications. This study is essential in assessing sexual knowledge and behaviors in a local high-risk population, and in the development of an education/behavioral modification curriculum. From our results, we will gauge the value of a workshop series in creating significant change in the behaviors and attitudes of sexually active teen girls, and work to further develop iChoose as an effective educational tool.

EVALUATING THE ICHOOSE EDUCATIONAL CURRICULUM FOR ENHANCING SEXUAL KNOWLEDGE AND DECISION-MAKING IN AT-RISK ADOLESCENT GIRLS.

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Goal: Our goal is to create a framework for assessing current sexual knowledge and behaviors in order to improve decision-making in a local at-risk teenage female population. Adopting the iChoose educational curriculum and methodology used in last year’s pilot program at Roosevelt High School, we sought to revise and improve the program’s efficacy. At the conclusion of the iChoose workshop series, we expect to see an increase in awareness and healthy decision-making regarding sexual practice; this will be qualified by data analysis of pre- and post-workshop questionnaires.

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**Purification of Vitronectin from human blood plasma for deriving induced pluripotent stem cells**

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**Goal:** Human blood plasma is a source of vitronectin (VTN), a commercially expensive extracellular matrix protein that promotes cell attachment to plastic for cell culture. Human VTN is essential for the attachment and spreading of successfully reprogrammed induced pluripotent stem (iPS) cells. The goal of this project is to purify VTN from human plasma as a cost effective alternative to commercially purchasing VTN. The plasma VTN will then be used to derive iPS cells from human dermal fibroblasts.

**Methods:** An IRB was written to obtain citrated human blood plasma from the LACoH Blood Bank that would otherwise be discarded. VTN was purified from treated human plasma via column chromatography. Purity was assessed by Western blot. The biological activity of plasma VTN was then compared to the control commercial VTN via both quantitative and qualitative cell-spreading assays.

**Results:** Purification of VTN was successful with a yield of 20mg from 1400ml of citrated human blood plasma. Cell spreading assays demonstrated biological activity of VTN in its ability to promote attachment, spreading and proliferation of human embryonic stem cells to an extent that is comparable to commercial VTN.

**Conclusion:** Purifying VTN from otherwise discarded human plasma is a viable and cost effective alternative to commercial VTN. This method will continue to be used by the Pera Lab to obtain VTN for derivation and characterization of iPS cells.
ASSOCIATION OF PHYSICAL ACTIVITY AND OBESITY IN CHILDREN AND ADOLESCENTS

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Goal: Perform literature searches to examine the longitudinal associations between physical activity and obesity in children and adolescents.

Methods: A series of literature searches was performed using the PubMed Advanced Search engine. Three search categories of interest were used: the independent variable (physical activity), the dependent variable (obesity), and the age range of the study population (ages 18 and younger). Key words for these categories included physical activity, exercise, obesity, body mass index (BMI), waist circumference, percent body fat, youth, children, and adolescents. Twenty-four total searches were performed, each using combinations of three key words (i.e., one key word from each of the three search categories). Retrieved article titles and abstracts were then read individually, and articles that specifically studied relationships between physical activity and obesity were downloaded. Only articles published after 2000 and with a study population aged 18 and younger were included. Intervention studies and randomized control trials were also excluded.

Results: The literature searches recovered 29 relevant articles. Of these, 22 were cross-sectional studies (i.e. subjects assessed for physical activity and obesity at one defined time), while 7 were longitudinal cohort studies (i.e. subjects being assessed multiple times over a defined period). There were marked similarities in the assessment methods used with every study measuring physical activity using recall questionnaires though differences in the methodologies of the questionnaires could be found, with approximately half of the studies focusing on moderate-to-vigorous physical activities versus overall activities of daily living. Moreover, about one third of the studies used self-reported weight and height to calculate BMI data rather than direct measurements. Two studies also utilized skinfold thickness in addition to BMI as an auxiliary measure of obesity. All of the studies concluded that there was a correlation between physical activity and obesity. In longitudinal studies, there was a statistically significant correlation between the decline in physical activity and increase in obesity during late adolescence and early adulthood.

Conclusion: Recall questionnaires and BMI were used universally to measure physical activity and obesity, respectively. While the uniformity in assessment methods allows for easier comparison of data, it may be useful to incorporate alternative measures of physical activity and obesity into future studies, including accelerometers, waist circumference, and skinfold thickness. Moreover, while cross-sectional studies comparing physical activity and obesity were common, there was a relative lack of cohort and longitudinal studies on the same subjects. This may be due to the added costs and time associated with studies that require follow-up. Encouraging additional longitudinal studies on these topics would provide additional insight into the relationship into how fluctuations in physical activity affect obesity in populations over time.
1600 Overdoses in Chile; Hospital Sótero del Río in Santiago, Chile; Retrospective Chart Review 2008-2010.

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**Goal:** While a nation-wide poison control registry exists in Chile, there is no mechanism by which individual hospitals monitor toxicity rates from controlled substances. The goal of this study is to establish to what extent the population served by Hospital Sótero del Río in Santiago, Chile abuses these products to the point of overdose.

**Methods:** This study is an explicit retrospective chart review at a single public hospital in Santiago de Chile: Hospital Sótero del Río. The records department at Sotero del Rio keeps a chart for every patient that has visited the ER in the last 5 years. These charts were searched for overdose presentations from July 2008 until June 2010 and information from the 1600 pharmaceutical overdose presentations found were documented on an excel sheet.

**Results:** Of all the intoxications, those by Benzodiazepines are the most numerous (almost 40%). However, they are responsible for a proportionally much smaller number of the resuscitations and deaths catalogued. Tricyclic acid anti-depressants, on the other hand, while responsible for fewer intoxications (10%), were involved in proportionally more poor outcomes. While the process of organizing the data gleaned from this chart review and analyzing it continues, other trends are also emerging, such as peaks in intoxications over the holidays and gender and age correlations consistent with previously published reports on this subject.

**Conclusions:** As Chile works to modernize and improve its Health Ministry, information such as this can be very useful. This data and more that hopefully will continue to be collected can help the government target interventions where they are needed. In Chile many medications are much more readily available then they are in the United States, and knowing which ones are the worst offenders can inform new legislation to control this menace.

**Developing assays to evaluate hepatic pathology in Schistosoma japonicum infection**

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**Goal:** Schistosomiasis is considered second most important parasite disease by the World Health Organization. It affects more than 200 million people in developing countries every year. The mainstay tools for assessing hepatic pathology associated with Schistosoma infection have been CT scan and ultrasound, which are not readily available for many rural areas endemic for Schistosomiasis. Therefore there exists an increasing need to develop a reliable and cost-effective assay that helps assess the extent of hepatic pathology in patients with Schistosomiasis. Dr. Su's lab is currently working on identifying molecular markers whose levels correlate with both the degree of infection and the extent of cirrhosis in Schistosomiasis patients. Based on previous work on mice, two molecular markers 1) soluble
egg antigen (SEA) and 2) heat shock protein 60 (Hsp60) have shown promising results as potential candidates for a Schistosomiasis molecular assay.

**Methods:** We purchased New Zealand rabbits and obtained SEA and Hsp60 serum level prior to infection. For the treatment group, each rabbit was infected with 60 cercariae via abdominal contact. Both the control and treatment group were sacrificed 20 weeks post infection. Serum and liver samples were obtained. SEA and Hsp60 levels in serum samples were assessed using ELISA. To assess the level of hepatic pathology, we made 9 cross sections of each liver sample and calculated the average surface area of a total of 40 granulomas. Only granulomas with a visible centrally located egg are measured. In addition, we also planned to perform collagen I, III and alpha-smooth muscle actin immunohistochemical staining on the liver samples to further evaluate the severity of hepatic fibrosis.

**Results:** Preliminary results show there is a 1.5-fold difference in SEA level between infected and control groups. However, the difference in Hsp60 level is not as pronounced, indicating that Hsp60 may not be an ideal molecular marker with which we can clearly establish Schistosomiasis with high degree of certainty. Due to facility and time limitations of this project, liver samples were yet to be processed.

**Conclusion:** Soluble egg antigen (SEA) appears to be a very promising molecular marker to assess the level of infection. However, ELISA assay measuring SEA level can be expensive due to the high production cost to prepare anti-SEA IgG. In addition, assay correlating SEA level with liver pathology will only reflect the level of liver damage due to Schistosomiasis alone, as SEA is specific to Schistosomiasis. We wish to identify a marker whose level can reflect the overall hepatic pathology in a patient, i.e. from alcohol use and hepatitis etc. Such versatile marker will allow clinicians to better gauge the overall extent of hepatic condition and make the appropriate treatment recommendation. More work needs to be done to further elucidate the usefulness of SEA as a molecular marker for cost-effective Schistosomiasis clinical assay.

DEVELOPMENT OF A DISEASE-ORIENTED ELECTRONIC FOLDER FOR MULTIPLE SCLEROSIS PATIENTS

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**Background**

The management of multiple sclerosis (MS) patients is challenging and complex with regards to medical history review and tracking of MS disease progression in daily clinical treatment, longitudinal research studies, and clinical trials. Current medical record systems lack the ability to connect clinical data to radiological data, which is of utmost importance in MS care.

**Objectives**

To develop a disease-centric patient record system (eFolder system) which includes a graphical user interface (GUI); a comprehensive database that stores patient
demographics, clinical data, magnetic resonance imaging (MRI); and MS lesion computer-aided detection (CAD) including 3D lesion models.

Methods
The MS eFolder system database was created using MySQL (My Structured Query Language) and includes patient history, images, and CAD results along with anonymous patient demographic data. Detailed medical history, including environmental and genetic background is stored for each patient record. A web-based GUI created using PHP: Hypertext Preprocessor (PHP) scripting language communicates with the database and allows the user to view clinical data, perform data mining, input patient records, scroll MR images, and view a 3D lesion model based on CAD results.

Results
The MS eFolder system was successfully developed. Fifty anonymous patients have been entered into the database along with their imaging and CAD results data. Examples of using the eFolder system for tracking MS patients, clinical review, and data mining will be discussed and presented. Figures 1-4 are screenshots of the MS e-Folder system viewed in an internet browser window.

Figure 1. Main page as seen by an "administrator" level user viewing clinical data, MR images, a 3D lesion model, and query options.
Figure 2. An advanced query for relapse-remitting MS patients.

Figure 3. Query results page that displays 18 patient results after clicking "search" in "Advanced Query."
Conclusions
The MS eFolder system is a comprehensive informatics tool that melds clinical data, imaging, and CAD results in order to support clinicians and researchers. As a web-based tool, the eFolder system is accessible and implementable in any part of the world with internet access. The eFolder system has the potential to generate a personalized database that can prove useful in future clinical trials addressing the effect of targeted treatment to follow MS progression.

Curing Type 1 Diabetes with Stem Cell Therapy: A Literature Search Project

Louissaint, P.

Purpose
The purpose of my research project is to gain an understanding, through journal reading, of the various recent methods used to induce stem cell differentiation and coax the successfully differentiated cells into glucose responsive insulin producing cells for the treatment of Type 1 Diabetes. I will share my findings with the Chow lab in hopes that they will be able to use my research to better improve their laboratory methods for stem cell differentiation.

Methods
My methods for completing this research was entirely journal research and textbook based. Articles for review were obtained from Pub Med and all the background knowledge for diabetes was obtained from credible online resources and text books.

Results*
I have found that some of the research with the highest yields of functional differentiated stem cells comes from the groups that are not only most recently published, but from the
groups that simply tweak the work of previous researchers. For instance, one researcher noted that he could increase the yield of one step by 80% by just omitting a digestion that was once routinely common in the stem cell research field. Substantial research has been performed on mice, and other lab animals, that show that the major goal in this area of research, which is injection of differentiated stem cells in the portal venous system of these animals, is indeed possible. Studies showed that blood glucose levels were actually decreased in response to this injection. However, we are a long way away from human trials.

Summary
Although my literature search is not complete, I have learned of many more barriers to successfully creating glucose responsive insulin producing cells than I have found successes. It turns out that successful stem cell differentiation is very difficult and requires strict protocols and reproducibility by scientists in order to even come close to reproducing the physiology that is found in the endocrine pancreas. Many methods have been developed to create glucose responsive insulin producing cells. But, when other scientists, like the scientists working in the Chow lab for instance, try to recreate the conditions used by the publishing scientists their yields did not match; they were actually significantly less. Stem cell research in this area is barely ten years old and it is still very young. Therefore it is in my opinion that much energy and time be devoted to this new and integral area of research.

*It must be noted that since this is a literature research project, I am not myself discovering new methods to create stem cells. Rather I am compiling a list of recently published articles into one review and noting the differences between them.

Mixed Metal Implants

B. Loy¹, D. Acevedo², MD, J. Itamura³, MD

Year II medical student¹, KSOM, Univ. of So. California; LACoH-USC orthopedic resident², KSOM, Univ. of So. California; LACoH-USC orthopedic surgeon and associate professor²

Goal:
The purpose of this study is to evaluate all of the upper extremity fractures treated with open reduction and internal fixation with metallic implants that differed in metallic composition. We would like to determine the effects that mixing implants with different metals has on fracture healing, implant failure, and any other complications associated with the method of fixation.

Our hypothesis is that mixing metals in orthopaedic implants, particularly stainless steel and titanium, does not cause clinically significant non-unions to form.

Methods:
The study population would be limited to patients treated by Dr John Itamura. We will review the patients' radiographs and notes to determine the time until clinical and
radiographic union. The endpoint of this study is fracture union. Follow up will be reviewed until union. The dates will be from 1/1/99 until 9/31/09. We will include all of the patients with fractures of the upper extremity fixed with different metals. We will review the surgical schedules for the last 10 years for fractures fixed by Dr John Itamura. We will look through the op notes and select the patients who had different implants. We will then perform a chart review on these specific patients to look for complications and to see if they healed or not.

Results:
We are still reviewing patient files and gathering data, and my role (B. Loy) has been to access patient records and collect data. I have been meeting with the principle investigator, Dr John Itamura, and a resident working on the study, Dr. Daniel Acevedo throughout the data collecting process. When we finish the study we plan to publish the results in an orthopaedic journal.

Conclusion:
This study is viewed as being a first step in quantifying the differences in patient outcomes with two types of implants, either mixed metal (stainless steel and titanium plates), Dr. Itamura’s patients, or implants of one metal type, data in the literature. If we find that the mixed metal implants do not cause a delay in healing time or union this may encourage other practitioners to use mixed metal implants, which may lead to better patient care. This may also stimulate more research in the field of biomaterials and implantable devices. We believe it is important to quantify the efficacy of mixed metal implants.

The Facts about Human Papillomavirus in Surgical Smoke: what the literature really tells us

L. Manson¹, E. Damrose², MD

Year II Medical Student¹, Keck School Of Medicine, University of Southern California; Stanford School of Medicine²

Goal: There have been many articles published about the hazards of Human Papillomavirus (HPV) in laser-produced surgical smoke to operating room (OR) personnel. However, risk has been overstressed, and facts underemphasized. This review is aimed at identifying the true facts that have resulted from research on this topic, debunking the myths associated with infectivity of HPV in surgical smoke, and emphasizing the necessity of future work.

Methods: An in-depth PubMed literature search was performed on the topic of surgical smoke and HPV. Once all the articles were compiled, each one was thoroughly reviewed and the factual results were identified. A comprehensive depiction of what the literature proves to us about the infectivity of HPV in surgical smoke was determined from these facts. This analysis was then compared to the assumptions and projections made by each individual research paper regarding the topic as a whole. Conclusions were made regarding what the current research can prove, not what deductions can be made.
Results: The current literature on the topic proves the presence of HPV DNA in surgical smoke. However, no studies to date have shown HPV causing infection. Most studies on the topic assume that the presence of HPV DNA in surgical smoke proves its infectivity. Conclusion: There have been too many studies which assume smoke-derived HPV to be infectious without actual proof, and too few studies to determine that it’s harmless. Such a topic should be of paramount importance to anyone who steps foot in an OR because of the ubiquity of surgical devices that produce a smoke plume, and therefore more research needs to be done to obtain conclusive information.

EXERCISE-INDUCED NEURONAL ACTIVATION IN A MPTP MOUSE MODEL OF PARKINSON’S DISEASE

L. D.V. May 3, G. M. Petzinger 1,2, M. W. Jakowec 1,2, M. Vuckovic 1

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PURPOSE: Purpose of this study is to examine the molecular activation of neuronal populations in the indirect and direct pathways within the mouse striatum following exercise.

Synaptic plasticity, in the form of long-term depression (LTD) and long-term potentiation (LTP), is important for adaptive motor control and procedural memory. It has been suggested that its impairment could account for the onset and progression of motor symptoms of Parkinson’s disease. Using a mouse model of Parkinson’s disease, our lab has found that lesioned mice have a reduction in LTD, but that function can be rescued with exercise. Understanding this process would provide insight into the mechanism of disease and identify possible targets for future medical intervention.

Previous research has linked function to the AMPA receptor subunit composition, specifically Glutamate receptor 1 (GluR1) and Glutamate Receptor 2 (GluR2). In previous experiments the lab has shown that levels of GluR2 sharply dropped in dopamine depletion, resulting in the loss of LTD and maintenance of LTP. Exercise increased GluR2 subunit expression and normalized function in the synapse. Our lab is interested in possible long-term modulators of this effect, including mechanisms involved in trafficking, transcription, and translation.

Delta fos B (ΔfosB) is a transcription factor implicated in spine and synapse formation and in the regulation of glutamate receptor expression, especially the AMPA receptor subunits GluR1 and GluR2. Our lab hypothesized that exercise would restore function by activating ΔfosB, resulting in the upregulation of GluR1 and GluR2.
METHODS:
For this study, we used transgenic mice that had enhanced expression of green fluorescent protein (eGFP) under the control of the dopamine receptor D2 in medium spiny neurons (MSNs) of the indirect pathway. Mice were injected with 0.9% saline (control) or 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine (MPTP). MPTP has been shown to induce a loss of nigrostriatal neurons and decrease in striatal dopamine levels and is used in the mouse model of Parkinson’s disease. Treadmill exercise was initiated 5 days following saline or MPTP injections. Mice were run on a treadmill five days per week and the duration of exercise was incrementally increased (starting from one 30 min session per day to two) for 28 total days of exercise. In total, 12 mice were used for this study. There were four treatment groups: saline (n=2), saline + exercise (n=3), MPTP (n=3), MPTP + exercise (n=3). One animal was given kainic acid (20 mg/kg, subcutaneous) to serve as a positive control for $\Delta$fosB staining.

Brain tissue from all groups of mice was collected on the last day of exercise (42 days after saline or MPTP administration), fixed, frozen, and cut on a cryostat. Sections were stained for $\Delta$fosB and visualized with an Alexa Fluor (594) secondary antibody. They were co-stained with DAPI, a nuclear marker. To confirm the validity of this technique, $\Delta$fosB was also visualized with DAB, a method more commonly found in related literature. The dorsal striatum of every 6th section of striatal tissue between Bregma 1.18 and 0.26 was counted at 40x. Cells were either marked as $\Delta$fosB+/GFP+ or $\Delta$fosB+/GFP-.

RESULTS:
Although preliminary results showed increased numbers of $\Delta$fosB+ cells in both lesioned and unlesioned exercise groups, this effect was not statistically significant.

CONCLUSION:
While still preliminary, these results suggest that exercise modestly increases $\Delta$fosB in both the direct and the indirect pathways. A sample size calculation using current data indicated that increasing the sample size to 6 animals per group (double what was counted in the current experiment) would detect a statistically significant difference, if one is present. Therefore, the next step is to confirm our preliminary findings by using a larger sample size. Western blots will also be conducted to confirm elevations in $\Delta$fosB protein. Future studies will examine expression and protein levels of other transcription factors involved in synaptic plasticity, such as ERK.

These studies are important to our understanding of experience-dependent neuroplasticity and changes in synaptic strength that we believe are critical for providing benefit to motor behavior deficits that are found in both patients with Parkinson’s disease and the animal models we use in the lab.
Utility of routine labs used in medical clearance in pediatric patients presenting to the emergency department with a psychiatric diagnosis.

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Goals: In the majority of studies involving medical clearance of adult psychiatric patients, the use of routine laboratory testing has been shown to add little utility beyond history and physical. In children, urine toxicology screening has been shown not to alter disposition of psychiatric patients. The utility of other laboratories in the "medical screening" of psychiatric patients has not been well-studied. The objective of this study is to examine the significance of routine labs on altering management of those pediatric patients who present to the ED with psychiatric complaints.

Methods: We conducted a retrospective observational chart review of LAC+USC Emergency Department (ED) visits by pediatric patients for psychiatric reasons from April 2009 to November 2010. This is an interim analysis of preliminary data from the first 154 in a series of 1651 ED visits. Patient history, physical exam, laboratory results, management, and disposition data was obtained from the ED records.

Results: Of the 154 ED visits, labs were obtained in 114, with a total of 1134 resulted lab tests. Patients presenting for medication refills and those not placed on psychiatric holds were less likely to get laboratories sent. Six lab results ultimately affected management (5 UTI's requiring antibiotics, 1 microcytic anemia for which the patient was started on iron sulfate). An additional 107 lab values were abnormal, but did not alter management of the patients. No lab values obtained altered any patients' dispositions.

Conclusion: From our interim analysis, labs obtained on pediatric patients presenting to the ED for psychiatric reasons were rarely abnormal. They very rarely affected management, and the few significant abnormalities did not explain the psychiatric symptoms, and appeared to be unrelated findings. The findings of this study may be important in refining protocols for medical clearance in pediatric patients who present to the ED with a psychiatric diagnosis.

Bone-Anchored Hearing Aid versus Surgical Repair for Children with Congenital Aural Atresia
A Comparison Study of Outcomes

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Background: Congenital aural atresia is a rare condition in children affecting 1 in 10,000 to 20,000 annually. Operative management through the bone-anchored hearing aid
(BAHA) or atresia repair can restore hearing to facilitate normal development. In this study, the aim was to compare both interventions regarding audiologic outcomes, surgical complications, and quality of life.

**Methods:** Participants were identified by type of surgical intervention and identified with a diagnosis of congenital aural atresia. All charts were reviewed for complications and audiometric data. A quality of life questionnaire was administered to a subset of patients.

**Results:** Eighty nine children were studied with 63 having undergone atresia repair and 26 BAHA implantations. Children were younger in the BAHA group (mean, 15 y) compared to reconstruction (mean, 21 y). Data was analyzed with Statistical Analysis Software (SAS). Audiometric data showed improved hearing, with a narrowing in the air-bone gap (ABG) for both BAHA as well as reconstruction but with greater improvement in both the short (p = 0.0127) and long term (p = 0.0010). Overall complications were less in frequency for the BAHA patients and the number of revision surgeries were fewer (p = 0.0458). Quality of life assessment for all children demonstrated no statistical significant between both groups.

**Conclusion:** While the quality of life between the two groups was not significant, BAHA implantation appears to provide more reliable audiologic improvement and fewer complications relative to traditional atresia repair and may be a preferable surgical option for pediatric patients with congenital aural atresia.

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**10 YEARS OF MECHANICAL COMPLICATIONS WITH CENTRAL VENOUS CATHETERIZATION IN TRAUMA PATIENTS AT A LEVEL I TRAUMA CENTER**

Division of Trauma and Surgical Critical Care, LAC+USC Medical Center

Moe D, MS; Ives C, MS; Inaba K, MD; Branco B.C, MD; Talving P, MD; Lam L, MD; Demetriades D, MD, PhD.

**BACKGROUND:** Central venous catheterization has been associated with both infectious and mechanical complications. Although catheter related blood stream infections are tracked, little is known about mechanical complications. A 10 year experience with mechanical complications of central venous catheterization and the corresponding impact on management was reviewed.

**METHODS:** Retrospective review of central venous catheter related complications from trauma morbidity and mortality records from 1999-2009.

**RESULTS:** There were 5115 central lines placed in 2838 ICU patients for a total of 25521 ICU line days. There was a total of 143 complications, 65 infectious, 78 mechanical (65% pneumothorax, 9% cannulation of the artery, 8% thrombosis, 4% accidental line removal, 4% vessel injury, 2% air embolism, 2% arrhythmia, 5% other). Total incidence of CVC complications was 3.6 per 1000 ICU line days (infectious=2.5 per 1000 line days, mechanical=2.4 per 1000 line days). Rate of mechanical complications by location was: 1.3% subclavian vs 0.5% IJ vs 0.43% femoral (p <0.001). 37.2% of complications resulted in a change in management (93% chest tube insertion). After adjusting for age, ISS, BMI, and number of lines, ICU length of stay for patients
with mechanical CVC complications was longer than for those without (31.25 ± 35.2 days vs 15.6 ± 17.3 days, \( p < 0.001 \)). There was no difference in mortality.

**CONCLUSION:** Mechanical complications were as common as infectious complications and resulted in a change in management in over 1/3 of cases. Interventions to decrease the rate of mechanical complications warrant further study.

**Retinoic acid activates lymphangiogenesis and enhances lymphatic regeneration**

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(4 These authors equally contributed to this study)

**Goal:** Lymphadenectomy, a surgical dissection of lymph node, is an essential clinical procedure to make both diagnosis and prognosis for cancer patients. However, lymphatic obstruction due to removal of lymph nodes results in lymphedema and presents the most common post-surgical complication for breast cancer survivors. As the survival rates for breast cancer continue to increase each year, nearly one quarter of survivors suffer from this painful and disfiguring arm swelling without adequate treatment available. To this aim, the Plastic Surgery Research Department has teamed with Dr. Young Hong, an expert in lymphangiogenesis, to test a novel solution to this surgical problem. The role of the plastics department was to provide a reproducible animal model of lymphedema.

**Methods:** In order to predictably and reproducibly induce lymphedema in a mouse tail model, I used a surgical microscope to measure 1 cm distal to the joining of the tail to the body and excise a 2mm long circumferential strip of mouse tail, epidermis, and dermis. Methylene blue was then injected into the distal portion of the mouse tail, and the lymph vessels lining the two major arteries were visualized. Under the microscope, these lymphatic vessels were carefully removed, preserving the delicate blood supply to the tail. As blood went to the tip of the tail, but lymph could not return, the tail distal to the incision developed lymphedema. After reproducibly inducing lymphedema by microsurgical ablation of tail lymphatics, Dr. Hong's lab applied their novel solution to look for an increase in lymphangiogenesis.

**Results:** Here, we report that retinoic acids (RA), especially 9-cis RA, activate lymphangiogenesis by promoting proliferation and migration of lymphatic endothelial cells through FGF signaling. After finding that 9-cis RA represses the expression of the cell cycle progression inhibitors, p27 and p57, by downregulating Prox1 and that Prox1 downregulation is required for 9-cis RA-mediated repression of p27 and p57, we showed that 9-cis RA activates lymphangiogenesis in vivo based on mouse trachea, matrigel plug
and cornea pocket assays. Subsequently, we defined a therapeutic potency of 9-cis RA using experimental mouse tail lymphedema model.

**Conclusion:** As it stands, no adequate solutions exist for the treatment of Lymphedema, but with the increased availability of surgical models to represent the disease, the possibilities to test novel treatments allows researchers to get closer to an adequate solution. Surgical excision of circumferential skin of a mouse tail with ablation of underlying lymph vessels is adequate to create a reproducible lymphedema model. Together, our in vitro and animal study demonstrates that retinoic acid effectively induces lymphangiogenesis and presents a possible therapeutic modality to treat postsurgical lymphedema of cancer patients.

**Selective Chest Radiography in Blunt Trauma**

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**Goal:** Chest x-ray (CXR) is routinely used in the work-up of emergency department (ED) patients with blunt trauma, however, this imaging is of little diagnostic value in the majority of cases. The non-selective use of radiography in blunt trauma wastes time, money, and resources within the ED, and exposes patients to unnecessary radiation. The purpose of this study was to validate a set of clinical criteria that could be used to safely exclude patients at risk for significant intra-thoracic injury and therefore safely forego CXR.

**Methods:** Resident ED Physicians were asked to answer the following questions after ordering CXR of blunt trauma patients in their care⁶ Do they have altered mental status? Are they Intoxicated? Do they have any distracting injuries? Was the mechanism of injury rapid deceleration? Are they older than sixty-five? Are they complaining of chest pain? Do they have chest wall tenderness? The answers to these clinical criteria were subsequently compared with CXR radiology reports that evaluated the presence of significant intra-thoracic injury.

**Results:** Although the study is ongoing, the current data suggests that in those patients who meet none of the mentioned clinical criteria, significant intra-thoracic injury can be excluded with almost 100% negative predictive value.

**Conclusion:** By incorporating these clinical criteria into a decision making instrument, clinicians can safely forego unneeded CXR for a large number of blunt trauma patients.
Survey of Guatemalan Peoples Attitudes Towards and Access to Healthcare in Guatemala

O. Myint and J. Rielly MD

Goal: Over 50 percent of people in the city of Los Angeles identify as Latino. Many of the Latino population in Los Angeles have recently immigrated from Guatemala. By having a better understanding of how cultural and social background can influence health seeking behavior, we will be better able to provide more effective healthcare. The goal of this study is two folds: Firstly, to better understand the nuances of Latino attitudes towards healthcare, using the population in Quetzaltenango, Guatemala as an example. Secondly, this study looks at the access to healthcare, and the relationship people had with their healthcare professional in both subject and objective manner to better understand the main barriers limiting access to healthcare in a developing nation such as Guatemala.

Method: A survey 38 questionnaire was used to obtain data. The survey was broken into the following categories: demographic, access to healthcare, relationship with the healthcare system and attitudes towards healthcare professionals. The surveys were done at local clinics and hospitals in Quetzaltenango. Willing subjects over eighteen were consented orally and given the survey orally. The interviews took on average about 20 minutes. All interviews were conducted by me (O.Myint). The questionnaire was changed throughout the study to make it more fitting for the population being surveyed. The survey was mostly short answer questions or yes or no questions. SPSS statistical methods are used to analysis the data. The data was collected over a period of 5 weeks.

Results: Overall there were 48 participants. The demographic data showed that the study population is not a good representation of the Guatemalan population since most of the interviewed were from people from the second largest city in Guatemala. The healthcare system was divided into a private sector and public sector. Monetary issues are the main barriers to health services, and those who could not pay used public clinics. Those who used the public healthcare services had a longer wait time to be seen by a physician but reported to be equally satisfied by the treatment they received. The study also showed that most subjects had a positive attitude towards the healthcare system and their healthcare providers.

Conclusion: This study help me understand better the system of medical care in Guatemala and the kind of barriers that prevent people from receiving better healthcare. It also help me better understand the influences Latino culture has on shaping the attitudes and perceptions people have of their illness. Lastly this experience taught me how to better design a research questionnaire.
Identification of early markers in venous ischemia of microvascular free flaps


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Purpose: Trauma, congenital malformations, and post tumor removal often present reconstructive challenges necessitating free tissue or flap transfer. Free flap viability relies on adequate blood perfusion through microvascular anastomoses of the donor artery and vein to those of the recipient site. Venous ischemia can irreversibly damage a flap, necessitating surgical revision if not resulting in total flap loss, an event occurring in up to 10% of free flap procedures. Flap failure by venous ischemia is likely accompanied by changes in genetic expression. The aims of this study are to characterize a model by determining the critical duration of ischemia to lead to irreversible damage and to identify key cellular markers of venous ischemia at this time point.

Methods: A lower abdominal flap measuring 2 x 2 cm and supplied by the superficial inferior epigasteric (SIE) vessels was elevated on male Sprague Dawley rats. The vessels were separated and the vein was clamped with a surgical microclip. To determine the time point of irreversible damage, the vein was congested for various time points (n=20) along with control, after which the clamp was removed to allow for reperfusion. Digital images were captured at this point as well as every other day and processed with ImageJ to determine area of flap survival. In another experiment, experimental (n=5) and control flaps (n=5) were harvested immediately after congestion for histological analysis, RNA isolation, and gene expression using microarray.

Results: Flap survival significantly declined when undergoing 4 hours of venous ischemia as compared to 3.5 hr or any shorter duration (17.3%, p=0.04). Microarray analysis revealed 2,327 genes with a greater than two-fold difference in expression compared to control, among them: Proline rich, lacrimal 1 (100.4, p=0.001), Variable coding sequence A1 (33.5, p=0.001), Mucin 1, cell surface associated (6.9, p<0.001), Interlukin 1β (-14.5, p<0.001), and Ficolin B (-42.3, p<0.001). Histological analysis demonstrated venous congestion, but no other perceivable differences compared to control.

Conclusion: This study confirms that changes in genetic expression levels do accompany venous ischemia, and that the mentioned genes can be further investigated as potential targets to minimize the deleterious effects of venous compromise in free flaps.

Predictors of Perforation in Cases of Appendicitis in Children

Nosanov, L.

Introduction: Although numerous studies on appendicitis cite young age as a predictor for perforation, none has specifically examined perforation rates by age. We hypothesized that there may be a threshold age where the likelihood of perforation...
decreases. In this study, we examined the relationship of age and other accepted predictors of perforation.

**Methods:** Following IRB approval, we performed a single-institution retrospective analysis of all children diagnosed with appendicitis from 2004-2010. Patient demographics, pre-operative history and physical, labs, imaging, and intra-operative diagnosis were recorded. Perforation rates by age were compared. Chi-square analysis was used to confirm the threshold separating older and younger children. A multivariate logistic regression analysis was used to identify the independent pre-operative predictors of perforation, using binomial age stratified by our identified threshold.

**Results:** 1,386 consecutive patients were identified with appendicitis. There was non-linear variation in perforation rates by age (Figure). The threshold in perforation rates occurred between the ages of 4 and 5 years. Children under 5 had a significantly higher perforation rate than children 5 and over (p = 0.0001). There was no difference in perforation rate between children ages 5-10 years and children ages 10-15 years (p=0.529). Multivariate analysis identified age, days of symptoms, vomiting, and tenderness on palpation as predictors of perforation. Individual perforation rate curves showed trimodal peaks, even when corrected for delay in administering antibiotics and operation, white count, and CRP.

**Discussion:** The data demonstrate that a threshold age exists that is associated with a higher likelihood of perforation from appendicitis. This is the first study analyzing perforation rates by year of age utilizing an appropriate, rather than an arbitrary threshold, as in previous studies. By utilizing our threshold we can appropriately take age into account when developing protocols used to determine which children should receive CT scans as well as which children should receive non-operative treatment. Our trimodal distribution of perforation by days of symptoms and age differs from a smaller previous report that identified a linear relationship. We suggest that the mechanisms involved in the development of early perforated appendicitis are likely different than those seen in later perforations.

**The Impact of Endoscopic Ultrasound (EUS) in a Safety Net Health Care System**

Papademetriou, M.

**Background and Aim:** Endoscopic ultrasound (EUS) has emerged as a premiere technique to evaluate and sample lesions of the foregut, pancreas, and posterior mediastinum. However, this technology has primarily been used at major tertiary referral centers. Our aim was to assess the impact of endoscopic ultrasound on the management of primarily underprivileged patients in a large safety net health care network hospital.

**Methods:** Sixty-three consecutive EUS cases at the Los Angeles County Hospital (LAC), which provides care for a diverse population of underprivileged patients, were reviewed.

The performance of EUS in this setting was compared to 63 consecutive cases performed during the same time period by the same endosonographer at the University Southern
California University Hospital/Norris Cancer Center (USC/NCC), a large tertiary referral center.

**Results:** The median age of patients at USC/NCC was 60 years, 52% were non-Hispanic whites, 33% were Hispanic, and 11% were African or Asian American. At LAC the median age was 60 years, 7% were non Hispanic whites, 67% were Hispanic, and 17% were African or Asian American.

Among the EUS cases performed at USC/NCC, 46% were accompanied by fine needle aspiration (FNA) compared to 65% at LAC. The final diagnosis was confirmed to be a malignancy in 41% of patients seen at LAC with the most common lesions being pancreas adenocarcinoma, gastric cancer, and non-pancreatic biliary neoplasms. At USC/NCC 29% were eventually found to have malignancy with pancreas adenocarcinoma and metastatic cancer of unknown primary being the most common lesions.

In both groups the most common benign diagnosis was chronic pancreatitis, though 10% of patients at LAC had duplication or choledochal cysts.

A definitive answer requiring no further diagnostic tests or tissue sampling was achieved in 84% of patients at LAC which was not significantly different from the results at USC/NCC, 88%. Problems with patient sedation, indeterminate cytology results, and inability to completely characterize or access lesions were reasons for requiring additional evaluation. More patients had LAC subsequently underwent chemotherapy and/or surgery 43% than at USC/NCC, 25%.

**Conclusion:** There was no significant difference in the ability of EUS to obtain definite answers to inform patient care at a large safety net hospital compared to a tertiary referral center. Patients at the safety net hospital were more likely to have malignancy and require chemotherapy and/or surgery than those at the referral center. These results suggest that an EUS program may have an equivalent and perhaps even greater impact on the care of patients in a safety net hospital as compared to a tertiary referral center.

**Application of MR perfusion and permeability parameters to distinguish pseudoprogression from recurrent disease in patients with high-grade gliomas**

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**Hypothesis:** Patients with pseudoprogression will demonstrate low relative cerebral blood volume (rCBV) and mildly elevated permeability (Ktrans), whereas those patients with true disease progression will display increased rCBV (>1.75) and markedly increased permeability (Ktrans), consistent with neovascularity.
**Background:** The current standard of care for patients with high-grade gliomas is maximal safe resection chemotherapy using temozolomide, and radiation therapy. Following multimodal therapy, the current measure of therapeutic response has been largely based on the MacDonald response criteria, which relies on changes in contrast-enhancing regions on MRI. However, reliance on this method is problematic because contrast-enhancing regions of true disease progression and treatment related necrosis (i.e. pseudoprogression) could appear similar because both of the aforementioned conditions result in a breakdown of the blood brain barrier (Bobek-Billewicz 2008). Increasing contrast-enhancement noted on surveillance MR imaging, usually within 12 weeks of radiation, poses a diagnostic dilemma to clinicians: either switch the patient to a different therapy or continue the existing regimen with close observation.

MR perfusion and permeability metrics may predict which patients will go on to develop progressive disease versus those who will stabilize or improve. MR perfusion and permeability imaging proposes to measure the degree of tumor angiogenesis and capillary permeability, both of which are important biological indicators of malignancy in neoplasms (Cha 2005). The relative cerebral blood volume (rCBV) is measured using a region of interest drawn within the tumor and compared against a region of normal white matter, usually in the contralateral (and presumably unaffected) hemisphere (Clarke 2009).

Elevated levels of rCBV correlate with active tumor, while normal or reduced rCBV often indicates effective treatment. A recent study by Law et al. showed that the rCBV values in perfusion MR imaging can be used to predict median time to progression in patients with gliomas, independent of pathologic findings (Law 2008). Pathologically, radiation necrosis is an occlusive vasculopathy while in high-grade gliomas, there is neoangiogenesis without occlusion of the vascular lumen. Therefore, while both lesions will enhance, radiation necrosis will demonstrate mildly elevated permeability, while high-glioma will demonstrate markedly elevated permeability. This information would prove vital to physicians in charge of patient care.

**Methods:** MR perfusion and permeability metrics of 20 high-grade glioma patients with MRI findings of increased enhanced enhancement after the completion of radiation therapy were evaluated. Relative cerebral blood volume (rCBV) and vascular permeability (Ktrans) were determined in the abnormally enhancing regions. Patients were classified as having pseudoprogression or true early progression based on subsequent imaging and pathology data at re-operation (if available).

**Results:** rCBV and Ktrans of those with true early progression was significantly increased compared with those classified as having pseudoprogression. In patients for whom pretreatment perfusion and permeability metrics were available, there appeared to be a trend toward increasing rCBV and Ktrans relative to baseline in those with true early progression while in those with pseudoprogression, they appeared to decrease. My role in this project has been to collect relevant clinical data in patients diagnosed with high-grade gliomas at LAC-USC County, assess rCBV and KTrans values from patients at the LAC-USC County, and burn selected imaging scans on to CD for further analysis at the University Hospital. I meet with Jesse Jones, Dr. Mark Shiroishi, and Dr. Meng Law on a regular basis. The results of this abstract have been submitted to the 2011 ASNR meeting and ultimately we expect to publish the results of this study.
Conclusion
MR perfusion and permeability appear to show promise in distinguishing pseudoprogression from true early progression. An ongoing prospective trial is underway to enroll more patients to further validate these preliminary findings.

Targeted Integration, Zinc Finger Nucleases and Lymphocyte Progenitor Selective Expansion in Post Bone Marrow/Hematopoietic Stem Cell Transplant Recipients.

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Introduction: There are many complications that may arise in post bone marrow transplant patients, since the transplanted stem cells require several months to re-establish white cell counts sufficient to battle infections. And although antibiotics are a standard prophylaxis, patients can succumb to serious infections. Neutrophils and phagocytic cells recover in about 1 month, but it takes 6-12 months for T cells and 12-24 months for B cell recovery. In collaboration with the lab of Dr. Gay Crooks at UCLA, we are investigating ways to selectively increase the rate of lymphocyte recovery by inserting the F36VMpl gene, which can increase the rate of proliferation when expressed and activated, into the genome of lymphocyte progenitor cells with the use of zinc finger nuclease (ZFN) technology.

F36VMpl is a fusion protein where the F36V domain has been engineered to selectively bind to a chemical inducer of dimerization (CID), AP20187, and is fused to the Mpl signaling domain. In its native form, Mpl signals megakaryocyte proliferation when dimerized by Tpo binding. When expressed in a cell, F36VMpl is therefore a CID inducible inducer of proliferation. ZFNs are a genome engineering tool that can be used to promote site-specific integration of F36VMpl at a unique site in the human genome, in this case the adeno-associated virus integration site 1 (AAVS1), if the F36VMpl gene is expressed from a cassette containing flanking regions of homology to AAVS1.

Methods: Two initial plasmids, AAVS1 PGK-F36VMpl, with AAVS1 homology arms, and a control plasmid without homology arms, were constructed using molecular cloning techniques. The plasmids were co-transfected with AAVS1 ZFNs into peripheral blood mononuclear cells (PBMCs). The action of the ZFNs will allow integration of the F36VMpl cassette from only the plasmid with the AAVS1 homology arms. The plasmid without homology arms is used as a control to demonstrate the specificity of integration. Integration, indicated by stable production of the F36Mpl protein can be analyzed by Western blotting and FACS.

Results: Plasmids expressing PGK-F36VMPL, with and without AAVS1 homology, were constructed and verified by check digest, PCR analysis and sequencing. Both plasmids where transfected into PBMCs and analyzed for expression by FACS. However, the FACS results were inconclusive in these initial experiments and will need to be repeated.
Conclusion: Selective expansion of defined sets of hematopoietic precursors may be useful as a way to speed post-transplant recovery of the lymphocyte population. It may also be used in other settings. We are also investigating the possibility of simultaneously knocking out the CCR5 gene and selecting for such engineered cells through F36VMpl as a way to provide HIV infected individuals with T cells that are resistant to infection.

Congenital Coronary Conundrums: Identifying and Addressing Anomalies of the Coronary Arteries

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Goal: Congenital coronary artery anomalies often present on routine cardiac CT. However, identifying these anomalies accurately and determining the risk to the patient can be challenging. The goal of this study was to emphasize the importance of recognizing these coronary artery anomalies and of understanding their potential pathophysiological manifestations. We also investigated the management of these anomalies and their importance in pre-surgical or percutaneous planning.

Methods: We amassed cases of coronary artery anomalies found in previous patients at LACoH and UH. This was done by looking at patient records and various cases noted by the Radiology Department. Literature searches were done regarding the congenital coronary artery variants to understand potential clinical implications and treatment options. Data was assembled into an educational exhibit for presentation to other radiologists at the RSNA (Radiological Society of North America) 2010 annual assembly.

Results: Data from patients was amassed but did not give statistically interpretable results. A literature search was done to differentiate clinically significant congenital coronary artery anomalies from anomalies which are usually asymptomatic. Images, typical presentations, results of literature searches, and discussions were compiled into a didactic presentation for other radiologists. A wide array of variants which may affect the coronary arteries was discussed, including common and uncommon entities as well as variations of normal anatomy. Additionally, coronary artery anomalies which could result in clinical symptoms and/or procedural complications were reviewed with an emphasis on these features.

Conclusion: Congenital coronary artery anomalies have varying clinical presentations and prognoses. Because cardiac CT is emerging as the study of choice in the evaluation of coronary artery anomalies, radiologists must be comfortable with the identification and management of these anomalies, as they are being identified with increasing frequency on CT. The benefit of this study is to educate other radiologists about the challenges in diagnosing congenital coronary artery anomalies and the implications that they can have on the health and future management of patients.
Trends in emergency bedside ultrasound for the detection of hydronephrosis in a population with computed tomography-proven stones

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Objectives. Non-contrast computed tomography (CT) is widely regarded as the gold standard for diagnosis of urolithiasis in emergency department (ED) patients. However, it is costly, time-consuming and exposes patients to significant doses of ionizing radiation. Hydronephrosis on bedside ultrasound is a sign of a ureteral stone, and has a reported sensitivity of 72-83% for identification of unilateral hydronephrosis when compared to CT. The purpose of this study was to evaluate trends in sensitivity related to stone size and number; as well as determine if the previously reported sensitivity would be observed in a minority/uninsured population.

Methods. This was a structured, explicit, retrospective chart review based at an urban academic ED with an annual census of approximately 160,000 patient visits. Previously published criteria for improving the value of medical record reviews were followed closely. Two investigators, each blinded to the study hypothesis, used a standard data abstraction form to independently review charts. All adult patients (>18 years) from July 1, 2009 to January 31, 2010 with a final diagnosis of renal colic were queried. Of these charts, those with CT evidence of renal calculus by attending radiologist read were examined for results of bedside ultrasound performed by an emergency physician. Only those patient encounters with both CT proven renal calculi and documented bedside ultrasound results were included. STATA 10 software (College Station, TX) was used to analyze data. Ordinal logistic regression analysis was performed to evaluate trends in stone size and number.

Results. Of the 125 patients who met inclusion criteria, 92% were non-white and 95.2% were uninsured. The overall sensitivity of ultrasound for detection of hydronephrosis was 78.4% [95% Confidence Interval (CI) = 70.2-85.3%]. Stones were visualized on ultrasound among 8.8% [95%CI: 3.8%, 13.8%] of subjects. The overall sensitivity of a positive ultrasound finding of either hydronephrosis or visualized stones was 82.4% [95%CI: 75.6%, 89.2%]. Based on a prior assumption that ultrasound would detect hydronephrosis more often in patients with larger stones, we found a statistically significant (p = 0.016) difference in detecting hydronephrosis in patients with a stone ≥6mm (sensitivity = 90% [95% CI = 82-98%]) compared to a stone <6mm (sensitivity = 75% [95% CI = 65-86%]). For those with three or more stones, sensitivity was 100% [95% CI = 63-100%]. Sensitivity in patients with two stones was 94% [95% CI = 82-100%] and 75% [95% CI = 65-83%] with a single stone. There were no patients with a stone size greater than 5mm that had both a negative ultrasound and lack of hematuria.
Conclusion. In our uninsured and underinsured minority population with CT-proven urolithiasis, ED bedside ultrasonography showed similar overall sensitivity for detecting hydronephrosis compared with other populations. ED bedside ultrasonography sensitivity significantly improved in patients with stones greater than 6 mm compared to those with smaller stones. Medical expulsive treatment could be obviated by a rational clinical evaluation and use of urinalysis and bedside ultrasound.

Investigation of DNA Methyltransferase Isoforms in Chronic Myelogenous Leukemia

Robertson, Edward:

Background:

DNA methylation is a chemical modification of DNA that can be inherited without changing the original sequence of DNA. DNA methylation involves the addition of a methyl group to DNA that occurs in a CpG dinucleotide. DNA methyltransferase (DNMT) is the enzyme responsible for catalyzing the transfer of a methyl group to DNA. Within the enzyme class of DNMTs there are three known enzymes: DNMT1, the most abundant DNMT in mammalian cells, that functions to methylate hemimethylated CpG dinucleotides, DNMT2, which actually methylates RNA and not DNA, and DNMT3, that could methylate both hemimethylated and unmethylated CpG dinucleotides. DNMT3 has 3 conserved forms, DNMT3A, 3B, and 3L. Each DNMT enzyme has multiple DNMT isoforms identified.

DNA methylation plays a critical role in disease processes, such as cancer, where the gene promoter CpG islands can acquire abnormal hypermethylation, which associated with transcriptional silencing. Consequently, gene silencing frequently takes place in tumor suppressor genes that function to protect against and regulate the effects of cancer. Therefore, it is of importance to note that hypermethylation of promoter regions is a frequent epigenetic change that occurs in tumors. In comparison to normal patients, the DNA patterns of patients with chronic myelogenous leukemia (CML) show a marked presence of DNMT3 variants, in particular, ΔDNMT 3A and 3B. In turn, these variant forms of DNA methyltransferase may be responsible for the deviant methylation patterns and cancer phenotype.

We hypothesize that DNA hypermethylation that is commonly found in CML is due to aberrant expression of specific DNA methyltransferase isoforms.

Methods:

White blood cells (WBC) from patients with CML and patients without leukemia were collected. From these WBC samples, RNA was extracted, reverse transcription was performed, and primers were then designed to detect specific DNMT isoforms.

Results:

We have developed a method to determine DNMT isoform expression using Multiplex reverse transcriptase-PCR. We have validated this assay using cancer cell lines. Our study of the specific DNMT isoforms in CML patients is ongoing.
Conclusion:
Chronic myelogenous leukemia is a disease involving changes in DNA methylation. Moreover, CML is a disease, in which, different DNMT isoforms are expressed. Comparison of DNA methylation via DNMT isoform expression is ongoing.

DETERMINING THE DIFFERENCE IN BACTERIAL CULTURES IN CESAREAN SECTIONS WITH CHLORAPREP vs. BETADINE AS PRE-OP SURGICAL SCRUBS.

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Goal: Cesarean deliveries are on the rise and are associated with an increased incidence of postoperative infection; this overall increased risk varies with the use of different preoperative antimicrobial preps. Studies have shown that controversy exists over which antiseptic skin preparation - 2% chlorhexidine- gluconate, 70% isopropyl alcohol (Chloraprep) or povidone-iodine 10% (Betadine) - is most effective for preventing postoperative surgical wound infections. In an attempt to improve the current standard of care, this prospective randomized control trial compares the difference in postoperative wound complications with the use of Chloraprep vs Betaine as preoperative antiseptics in cesarean sections.

Methods: Pregnant women greater than 36 weeks gestation admitted for scheduled primary or repeat c-sections at LAC+USC were considered for inclusion in this study. After informed consent was obtained, all patients received a complete physical exam and were randomly selected to be pre-operatively prepped with either Chloraprep or Betadine; a swab from the incision site was immediately sent to pathology after the prep. The patients were reassessed multiple times over the next 18 days post-op.

Results: The study is ongoing, and once we have >66 patients, we will compile the final data to compare the difference in bacteria cultures. In addition, we will compare the difference in postoperative wound infections measured by the presence of purulent drainage, temperature greater than 100.4 F, and induration at the incision site. Lastly, we will compare the difference in incidence of wound seroma and infection.

Conclusion: The standard of care at Los Angeles County Hospital for preoperative skin antiseptic in cesarean sections is Betadine. However, many other hospitals have made the transition to using Chloraprep. Since my hypothesis is that Chloraprep is in fact better, I aim to alert the Department of Ob/Gyn of the potential benefits of switching pre-op scrubs.
Evaluation of the Efficacy and Safety of a Levonorgestrel-Releasing Intrauterine Contraceptive System

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Goal: There is currently no intrauterine contraceptive device with FDA approval for nulliparous women. The study sponsor is studying the efficacy and safety of a new levonorgestrel releasing intrauterine device with a shorter vertical arm. This study will also include women with a wider age range and wider BMI range than women included in safety and efficacy testing for Mirena.

Methods: This is a phase 3, multicenter, randomized study. Subjects 16-35 years old will be divided into two groups. One group will receive the experimental IUS and the other will receive Mirena, and the safety and efficacy will be compared. Also, a group of women 36-45 will receive the experimental IUS as a non-randomized cohort. Subjects will be followed and evaluated for five years.

Results: The initial expulsion rate of the experimental IUS was higher than expected so the study has been temporarily halted to redesign the inserter.

Summary/Conclusion: Interim analysis revealed a higher than expected expulsion rate with the experimental intrauterine system. The study sponsor is redesigning the inserter to reduce the difficulties experienced with insertion that is believed be causing the higher than expected expulsion rate.

DUCTAL CARCINOMA IN SITU: A Systematic Review of Key Clinical Questions

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Purpose: With the advent of screening mammography, diagnosis of Ductal Carcinoma in Situ (DCIS) has increased dramatically, and to date no definitive consensus for optimal management of these patients exists. This review attempts to answer seven crucial treatment questions in order to help guide decision making of health care providers. These questions are: 1. Is DCIS an obligate precursor of invasive carcinoma? 2. How often does DCIS identified by screening fail to progress to invasive disease? 3. What is the role of MRI in imaging patients with DCIS? 4. When is mastectomy necessary for DCIS? 5. What margin width is adequate for excision? 6. When is radiation therapy necessary after breast-conserving excision? 7. What is the role of sentinel lymphadenectomy in axillary staging for DCIS?

Methods: Published studies were found searching the MEDLINE database and reviewing evidence presented in the 2009 State of the Science Conference on Ductal Carcinoma in Situ (DCIS). Over 400 papers were published in the last six years on the topic. Results were narrowed by reviewing each article and selecting based on journal impact, strength
of design, references used and applicability towards the questions of interest. These papers were then cross referenced and relevant citations were retrieved and included.

**Results:** First, DCIS is not an obligate precursor lesion. However, in 30% of cases, if left untreated, DCIS represents a transitional step between normal breast tissue and invasive carcinoma, with potentially deadly consequences. Second, screen detected DCIS that fails to progress to invasive disease if left untreated represents a minority of cases, ranging from 5-30%, with this population representing overdiagnosis and overtreatment of DCIS. Furthermore, MRI utilization is an especially complicated issue, with the evidence to date supporting its utility only in addition to current protocols and imaging techniques such as mammography; not as a screening tool. Even so, no study to date has shown an improvement in outcome through the use of MRI in DCIS diagnosis and management. The answer to the question, which DCIS patients should receive mastectomy, broke down into four subsets of women with. These were, women who had a recurrence of DCIS or invasive carcinoma, women with multicentric disease, women with BRCA mutations, and women for whom breast conserving surgery (BCS) would not achieve adequate cosmesis and would benefit from mastectomy combined with breast reconstruction. For patients who receive mastectomy or BCS plus radiotherapy it appears that a margin of 2 mm is adequate, while those treated by excision alone, show an incremental benefit for larger clear margin status, up to 10 mm. The decision to include radiotherapy in the management of women with DCIS was supported by all prospective studies done to date. There is retrospective evidence that identifies subsets of women who would not benefit from radiation, using tumor associated factors such as size, grade, histology, etc. to stratify DCIS lesions into different treatment courses. And finally, the current recommendation is to not perform sentinel lymph node biopsy (SNLB) in DCIS cases as pure DCIS has low potential for lymph node metastases.

**Conclusion:** While the management of DCIS is clearly complex, the evidence presented in this study, along with provider judgment, begin to answer some of the most crucial treatment questions surrounding DCIS. DCIS is not an obligate precursor of invasive disease, but has the potential to progress. While some contend DCIS is over treated, to date the evidence supports overdiagnosis and treatment representing a minority of DCIS cases. MRI has a role in the evaluation of DCIS patients, not as a screening tool, but as a way to potentially improve sensitivity and detect contralateral disease. Mastectomy is the treatment of choice for those with recurrent disease, multicentric disease, BRCA carriers and ultimately all patients who choose this option, as the choice is ultimately theirs. Depending on the treatment, a margin status of either 2 mm or 10 mm confers the lowest likelihood of recurrence, for those receiving BCS plus radiotherapy vs. excision alone respectively. And as of now, radiotherapy decreases the risk of recurrence across all groups of women with DCIS and should be strongly considered in all DCIS cases treated with BCS. Lastly, SNLB should not be used routinely for patients diagnosed with DCIS because of the low potential for lymph node metastases in cases of pure DCIS.
Has The Cloud Lifted? A FEASIBILITY STUDY OF SECOND HAND SMOKE IN MUMBAI RESTAURANTS 20 MONTHS AFTER ANTI-SMOKING LEGISLATION IN INDIA

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Objectives: We performed a study to monitor indoor second-hand smoke (SHS) exposure in Mumbai, India following the Government of India’s recent legislature banning smoking in all public places. Using a diverse group of restaurants, we assessed indoor PM$_{2.5}$ levels as indicators of the ban enforcement according to restaurant type, socioeconomic status, and education status of patrons. We aimed to assess the feasibility of using PM$_{2.5}$ monitoring and passive air nicotine methods in obtaining accurate readings in an urban Indian center.

Methods: Twenty restaurants within Mumbai were selected by convenience sampling. The sample included many different types of restaurants, covering a broad range of socioeconomic class patronage. The owner or manager on duty completed an interviewer-administered questionnaire describing basic characteristics of the restaurant and the estimated education level of patrons. PM$_{2.5}$ monitoring was performed for 30 minutes inside each location in addition to a total of ten minutes outside for the purpose of ascertaining the baseline air quality. PM$_{2.5}$ data are presented as the difference between indoor and outdoor readings.

Results: In this study, 62.5% of restaurant owners approached agreed to participate. We found that the median indoor PM 2.5 level was [median (high, low)] 0.012 (-0.04, 1.43) mg/m$^3$. Seven out of the 20 restaurants had PM$_{2.5}$ readings that were below the corresponding outdoor measurement, pointing to the high level of environmental PM$_{2.5}$ pollution present in Mumbai.

Conclusion: This study suggests that presently the enforcement of the smoking ban is inadequate. Further research is needed to identify the locations that present the greatest risk for SHS exposure in Mumbai and in other regions in India. This study demonstrates that while it is feasible to perform the PM$_{2.5}$ monitoring in an urban Indian center like Mumbai, the environmental PM$_{2.5}$ pollution presents difficulty for interpreting the results. Using this methodology, we are not able to discern PM$_{2.5}$ elevations as being nicotine-specific or environmentally derived, which is a complication for monitoring in high density, high pollution settings.
Penile Cancer at Los Angeles County Medical Center and Norris Cancer Center: Outcomes, Molecular markers, and the Potential for Targeted Therapy

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Objectives: Squamous Cell Carcinoma of the Penis (SCCP) carries a high morbidity and mortality rate which is compounded by the potentially disfiguring consequences. While it is a rare entity in developed nations, it represents up to 20% of male cancers in the developing world and shares a higher incidence in specific US minority communities. Globally, the worldwide variation in penile cancer incidence is postulated to correlate with differences in socio-economic, hygienic, and religious factors; in addition, human papilloma virus (HPV) infection is strongly associated with 59-69% of cases testing positive for the viral DNA. Current research is centered on understanding the factors involved in the molecular oncogenesis associated with SCCP. While, near-universal EGFR over-expression has been documented, little is known about its clinical implications. The potential role of other common oncogenic including KRAS mutations, ERCC1 and TS expression remain to be fully explored and could yield vital information for response to therapy, as ERCC1 and TS expression are associated with response to platinum and 5FU chemotherapy in other tumors. This is particularly important considering that the individuals with SCCP are often from a population that is recalcitrant to health care and having the ability to accurately predict an individual’s response to chemotherapy based on the molecular signature of their tumor could expedite choosing an effective treatment.

Methods: After IRB approval, a retrospective case review of patients with penile cancer tumor specimens at LAC-USC Medical Center and Norris Comprehensive Cancer Center was completed. 52 patients were identified from 1995-2010. Follow up data was obtained via clinic records and the LAC tumor registry. ERCC1, EGFR and TS expression were evaluated by RT-PCR; additionally ERCC1 and EGFR were evaluated by Immunohistochemistry Staining (IHC).

Results: The median age is 52 (range: 36-80) and the racial breakdown is 72% Hispanic, 15% (Non-Hispanic) White, 6.5% Asian, and 6.5% African American. Clinically, 6 were diagnosed with stage Tis, 10 had T1, 23 had T2, and 12 had T3. 19 of the patients had pathologic documentation of lymph node involvement. The median follow up time was 1.8 years (longest 16.3 years). EGFR over-expression was common, verified by both by RNA amplification and immunohistochemistry staining (RNA median expression: 5.09; IHC: 7/22 with 2+). EGFR expression significantly with more advanced T stage (> T2) and Grade [poor differentiation] (p=0.01 and 0.034 by Fisher’s exact test, respectively). It did not correlate with survival or lymph node involvement in multivariate analysis. Lower expression of EGFR corresponded to a higher likelihood of response to chemotherapy [RR] (67% RR in EGFR<7 vs. 33% in EGFR>=7, p=0.31). ERCC1 expression was less common and TS expression was intermediate (RNA median expression: 0.65, IHC: 4/22 with 2+; RNA median expression: 1.88, respectively).
Neither ERCC1 or TS expression were not associated with grade, stage or survival. There were no KRAS mutations identified.

**Conclusions:** Identifying an algorithm for intervention according to risk could not only prove to be life saving for penile cancer patients, but also spare lower-risk individuals the side effects of extensive surgery which include psychosexual morbidity as well as lymphedema, local wound infections and necrosis. Tumor molecular expression pattern could be exploited to predict the possibility of response to chemotherapy. EGFR over-expression correlates to tumor grade and showed an inverse trend with chemotherapy response. EGFR status may serve as a potential target for risk stratification of penile cancer patients and also serve as a novel target for therapy. Furthermore, the lack of KRAS mutation may predict a good likelihood of response to EGFR-targeted therapy.

**POSITRON EMISSION TOMOGRAPHY FOR PREDICTING METASTATIC DISEASE IN BLADDER CARCINOMA IN PATIENTS UNDERGOING RADICAL CYSTECTOMY WITH EXTENDED LYMPHADENECTOMY.**

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**Purpose:** Novel imaging modalities are needed to detect occult metastatic disease in bladder carcinoma. Knowledge of regional lymphatic spread could be used to target therapies towards metastatic disease and to spare the morbidity of cystectomy in patients with distant metastases. Furthermore, these modalities if proven effective could direct the use of neo-adjuvant therapy in higher stage disease. We investigate the role of positron emission tomography/computed tomography (PET/CT) with [18F]fluorodeoxyglucose (FDG) in predicting lymph node metastatic disease in patients undergoing radical cystectomy for all stages of carcinoma of the bladder.

**Materials and Methods:** Review of the USC Institute of Urology patient database over the past eight years revealed 28 patients who underwent both a radical cystectomy with complete lymphadenectomy and a FDG-PET/CT preoperatively. Comparing the FDG-PET/CT reports with the post-cystectomy pathology of the lymph nodes yielded the ability of FDG-PET/CT to detect metastatic disease.

**Results:** Of the 28 patients, six had a positive FDG-PET/CT prior to cystectomy. Of these, three had positive nodes on extended node dissection. Of the 3 false positives, 1 patient had a history of lymphoma and another had a history of other malignancy. Of the 22 patients who had negative PET scans, two had positive pelvic lymph nodes. FDG-PET/CT demonstrated a positive predictive value of 50% (three of six), a negative predictive value of 91% (20 of 22), a sensitivity of 60% (three of five), and a specificity of 87% (20 of 23).

**Conclusions:** FDG-PET/CT correctly detected metastatic disease in three of 28 patients. While the negative predictive value and specificity are high at 91% and 87%, respectively, the low positive predictive value and the occurrence of documented false positive results puts into question its role in making decisions regarding treatment.
PET/CT may have value as a confirmatory test, but caution should be taken when using it for exclusionary purposes. Furthermore, its high costs should be weighed against the low efficacy of FDG-PET/CT imaging in predicting metastatic bladder carcinoma.

**Incidental Pulmonary Nodules Detected on Cardiac CTA in the Setting of Non-acute Suspected or Known CAD: Projected Number, Cost, and Increased Radiation Dose**

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**PURPOSE:** The aim of this study was to determine the prevalence of incidental pulmonary nodules detected during cardiac CTA in a consecutive cohort of patients with suspected coronary artery disease and to project the test burden based on existing guidelines.

**METHOD AND MATERIALS:** We included 2,989 consecutive patients referred to cardiac CTA from 2005-2007. Patients with incidental pulmonary nodules were identified through review of clinical CT reports. Patients with definitively benign or previously known nodules were excluded. The number of recommended follow up chest CT scans was projected based upon the Fleischner guidelines after review of data sets by radiologists. Cost of the subsequent CT exams was calculated using Medicare rates. Published estimates of radiation dose for standard chest CT (9.1 mSv) were used to calculate cumulative radiation exposure.

**RESULTS:** Overall, incidental pulmonary nodules were detected in 693 patients (23.2%, 63.8% male, 61±13 years-old). Average size of the largest nodule was 4.8±3.1 mm (range 2-26 mm). Follow-up recommendations for chest CT per Fleischner guidelines were: no follow-up in 195 patients (28.1%), one CT scan in 280 patients (40.4%), two CT scans in 130 (18.8%) patients, three CT scans in 59 (8.5%) patients, and further evaluation with FDG-PET or tissue sampling in 29 (4.2%) patients. With a total of 717 subsequent chest CT scans, the projected overall cost was $1,296,000 and projected increased radiation exposure was 6.5 Sieverts. If all highly suspicious nodules were biopsied rather than evaluated with FDG-PET, total cost would increase by $28,130. During follow-up 4 pathology-confirmed lung cancers were detected.

**CONCLUSION:** Pulmonary nodules are found in more than 20% of patients with suspected CAD referred for cardiac CTA. The application of the Fleischner guidelines for follow-up of these nodules results in substantial additional cost and radiation exposure. Formal cost effectiveness and quality of life analysis may need to be performed in order to define specific reporting guidelines in this setting.
Aortic Distensibility and its Relationship to the Presence and Morphology of Coronary Atherosclerosis using MDCT

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Purpose: Aortic distensibility (AD) is a measure of vessel wall elasticity and is inversely proportional to disease severity and presence of cardiovascular risk factors. We sought to determine the degree of AD and its relation to the presence and coronary plaque type using MDCT.

Methods: In 293 patients (53±12 years, 63% male), retrospectively-gated MDCT were performed. We measured areas of the ascending and descending aorta across 10 phases of the cardiac cycle (multiphase reformation 10% increments). Ascending and descending AD was calculated as maximum change in area/(minimum area x pulse pressure). Presence and type of coronary plaque morphology was evaluated based on the 17-segment model.

Results: As shown in Figure 1, with the exception of non-calcified plaque, the presence of plaque resulted in lower AD. In multivariable models adjusted for traditional cardiac risk factors, glomerular filtration rate, and local aortic plaque, for every 1 mmHg⁻¹10⁻³ increase in AD, there was a 20-27% reduction in risk of having any plaque (ascending AD: odds ratio [OR]=0.80, 95% confidence interval [CI]0.66-0.95, p=0.01; descending AD: OR=0.73, 95% CI:0.58-0.91, p=0.005), and an 18-29% reduction for calcified plaque (ascending AD: OR=0.82 95% CI: 0.68-0.99, p=0.04; descending AD: OR=0.71, 95% CI:0.56-0.90, p=0.004). For mixed plaque, a 21% risk reduction was seen for every 1 mmHg⁻¹10⁻³ increase in ascending AD (OR=0.79, 95% CI:0.64-0.98, p=0.03) but not for descending AD. After adding age to the models, these associations were no longer significant (all p>0.39). AD was not associated with noncalcified plaque (all p=NS).

Conclusion: Coronary atherosclerosis is associated with less distensible aorta. Given the relationship of AD with calcified and mixed, but not non-calcified plaque, the factors leading to reduced AD may be similar to that of coronary disease progression and is driven by advancing age.
Mammographic findings after Intraoperative Radiotherapy of the Breast Compared to Traditional External Beam Radiation

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Goal: The TARGIT Trial is an ongoing randomized clinical trial at Norris Comprehensive Cancer Center evaluating intraoperative radiotherapy (IORT) given as a single treatment during surgery in comparison to the standard 1-month course of post-operative radiotherapy (EBRT) in women undergoing a lumpectomy for breast cancer. The recent 4-year follow up results of the international clinical trial show the two treatments to be equally efficacious in terms of reducing the risk of cancer recurrence within the breast after lumpectomy. The intraoperative radiotherapy has been shown to have additional benefits to the patient, including fewer severe wound-healing problems, and less compliance issues stemming from the inconvenience of daily therapy of conventional radiation therapy. However, no studies have compared the radiologic changes in breast tissue post lumpectomy and radiation therapy in the two treatment groups. The goal of this study is to identify, quantify, and compare the mammographic findings of patients who received IORT and EBRT in a prospective, randomized, controlled clinical trial.

Methods: Thirty-one patients undergoing breast conserving therapy for early stage invasive breast cancer between July 2005 and December 2009 at Norris Comprehensive Cancer Center were included in this study. The IORT and EBRT treatment groups were compared with regard to the 1, 2, and 4-year incidence of six (6) post-operative mammographic findings: architectural distortion, skin thickening, skin retraction, calcifications, fat necrosis, and mass density. The analysis of mammographic findings was performed by an independent, blinded breast radiologist.

Results: The blinded review of 93 sets of mammograms of 15 IORT and 16 EBRT patients demonstrated no statistically significant difference on univariate analysis in the incidence of each outcome measure (architectural distortion, skin thickening, skin retraction, calcifications, fat necrosis, and mass density) at years 1, 2, and 4 post-operatively.

Conclusion: The subacute and chronic mammographic findings of patients treated with single fraction IORT were indistinguishable from the mammographic findings of patients who received conventional external breast radiotherapy. Compared to EBRT, there was no indication that IORT impaired mammographic surveillance for breast cancer recurrence. These findings have implications that could effect the standard of care in women undergoing breast conserving surgery for early stage invasive breast cancer.
Metronomic Chemotherapy and Combination Chemotherapy with Green Tea Extract in Ovarian Cancer Treatment

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Background: Metronomic dosing of chemotherapeutic agents, defined as a more frequent low dosing regimen without break periods, has shown efficacy in the treatment of cancers commensurate with traditional maximal tolerated dosing (MTD). One mechanism in which metronomic dosing has been hypothesized to elicit its antitumor effects is via inhibition of angiogenesis. However, since metronomic therapy has not been proven to result in complete elimination of angiogenesis, other mechanisms for cancer progression are likely involved. The chemopreventive molecule, epigallocatechin-3-gallate (EGCG), a natural polyphenol in green tea, has been shown to prolong survival among ovarian cancer patients, and may do so by inhibiting the cell’s metabolic activity, abrogating endoplasmic reticulum (ER) stress, and decreasing vascular endothelial growth factor (VEGF) expression. I hypothesize that combination treatment with EGCG and metronomic docetaxel in ovarian cancer cell lines will have greater effects in decreasing ER-stress, decreasing angiogenesis, and increasing tumor cell kill, compared to either treatment alone.

Methods: This study aims to examine the effects of EGCG and metronomic docetaxel on human ovarian cancer cell lines, as well as the effects of combination therapy with EGCG. Platinum-sensitive (A2780) and platinum-resistant (A2780-Cp70) human ovarian carcinoma cells will be treated with combinations of metronomically dosed docetaxel, MTD docetaxel and EGCG, and evaluated for ER stress factors by Western blotting. Cytotoxicity experiments will be conducted on cells treated with docetaxel or EGCG using MTT assay to determine the cytotoxicity of the following regimens: 1) docetaxel dosed in an MTD manner, 2) MTD docetaxel combined with EGCG, 3) metronomic docetaxel, and 4) metronomic docetaxel combined with EGCG. Secondly, The effects of MTD and metronomic dosing of docetaxel on ER stress in human ovarian cancer cells in vitro will be determined by Western blot analysis. Human ovarian cancer cells will be treated according to the IC₅₀ dose as determined from MTT assays, whole tumor cell lysate will be collected, and the amount of protein will be quantified. Western blot analysis of the cell lysate at different time points (e.g., 6h, 8h, 12h, etc.) will be conducted to compare the expression levels of ER stress factors (GRP78, GRP94, CHOP, Xbp-1s, PERK, ATF4 and eIF2α) in each single and combination treatment, for both the chemosensitive and the chemoresistant cell lines. Given that EGCG can mitigate ER stress, the time at which EGCG is administered will be varied in order to determine whether or not pre-treatment, concurrent with treatment, or post-treatment relief of ER stress potentiates cytotoxic chemotherapies.
**Expected Results:** While many of the cytotoxic effects of metronomic docetaxel are known, I propose investigating whether or not these effects may be mediated in part by ER stress and the proteins associated with ER stress. First, I propose EGCG monotherapy and combination EGCG-metronomic docetaxel will elicit cytotoxic effects on both chemosensitive and chemoresistant human ovarian cancer cell lines *in vitro*, with combination therapy eliciting a greater cytotoxic effect compared to EGCG alone. Also, combined treatment with metronomic docetaxel and EGCG will result in lower levels of mediators of ER stress. Lastly, because EGCG can abrogate ER stress in cancer cells, I hypothesize that pre-treatment of human ovarian cancer cells will increase the tumor cell’s sensitivity to metronomic docetaxel, which will result in increased cytotoxicity in ovarian cancer cell lines in vitro.

**Conclusion:** Despite current treatments, management of patients with ovarian cancer remains a challenge due to high risk of recurrence and the development of chemoresistance. Understanding the mechanisms behind cancer cell proliferation and apoptosis, as well as the mechanisms for developing chemoresistance can present novel therapeutic strategies to treat ovarian cancer. Investigation and development of alternative dosing regimens of chemotherapeutic agents coupled with "natural" chemopreventive agents that maximize tumor cell kill with minimal untoward effects on normal cells provide a unique therapeutic option for patients with recurrent ovarian cancer.

**Menopausal Hormones and Skin Cancer Risk in Postmenopausal Women: the Women’s Health Initiative Hormone Therapy Trials.**

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**PURPOSE:** Case-control studies have reported a higher risk of non-melanoma skin cancers (NMSC) with oral contraceptive use. The associations of menopausal hormone therapy (HT) with NMSC and melanoma were evaluated in randomized controlled trials of combined estrogen plus progestin (E+P) and estrogen only (E-alone) HT.

**METHODS:** Postmenopausal women aged 50-79 years were randomly assigned to conjugated equine estrogen (CEE, 0.625 mg/d) plus medroxyprogesterone acetate (2.5 mg/d) or placebo if they had an intact uterus (N=16,608) or to the CEE alone or placebo if they had a prior hysterectomy (N=10,739) for a mean follow-up of 5.6 years and 7.1 years, respectively. NMSC (N= in E+P trial, N= in E-only trial; Total N=1800) and
melanoma (N=, N=, respectively; Total N=95) skin cancers were ascertained by annual self-report; melanoma underwent physician adjudication.

RESULTS: Both incident NMSC and melanoma rates were similar between active hormone and placebo groups in the combined HT trials (hazard ratio, HR: 0.98; 95% confidence interval, CI: 0.89, 1.07 and HR: 0.92; 95% CI: 0.61, 1.37, respectively). Results were similar for the E+P and E-alone trials, when analyzed individually. HT did not affect NMSC or melanoma outcomes within any of pre-specified subgroups, e.g. age, BMI, UV exposure, history of cancer, or NSAID use.

CONCLUSION: Menopausal hormone therapy did not affect overall incidence of NMSC or melanoma. These findings do not support a role of menopausal estrogen or progestin in the development of skin cancer in women.

Retrospective Chart Review of Multimodality Therapy for High Grade Sarcomas

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Goal: Determining the most effective treatment protocol for high grade sarcomas is important to ensure optimal outcomes for patients suffering from these illnesses. Previous literature has shown that a multimodal approach to treating sarcomas through the use of neoadjuvant and adjuvant chemotherapy and radiation, in addition to surgery, increases the chance of survival of a high grade sarcoma to 60% from 20-30%. This treatment plan also reduces the rate of local occurrence in addition to metastases. The USC University Hospital Orthopaedic Oncology Center has gathered follow-up data on a large population of patients who have undergone surgery at University Hospital as a part of their multimodal therapy to treat their sarcomas. This goal of this retrospective study is examine the different outcomes in patients who have undergone surgery to remove their sarcomas, and see how the rates of survival, local recurrence and metastases are affected by adjuvant therapies being administered in conjunction with surgery.

Methods: This is a retrospective chart review of the database maintained by the University Hospital Orthopaedic Oncology service for patients treated for high grade soft-tissue sarcomas with surgical resection, as well as neoadjuvant/adjuvant chemotherapy and/or radiation therapy. Patients will not be contacted. A waiver of HIPAA authorization will be requested from IRB. Each patient's medical records will be reviewed by the investigator for demographics, past surgical/therapy history and course of disease. Information will be collected on individual data collection sheets and stored in a password-protected excel spread sheet. A code will be used to protect patient confidentiality. The key to the code will be kept separate from the data. At the completion of the data analysis the key to the code will be destroyed. All patients will be staged according to the American Joint Committee on Cancer (AJCC) system. Microscopically, the tumor will be classified as high-grade based on established criteria including the degree of nuclear pleomorphism, degree of differentiation, and number of

1, 12
mitoses per high power field. \textsuperscript{1,12} A clear margin will be defined as a minimum of 10 mm between the surgical margin and evidence of tumor. \textsuperscript{1,12}

**Eligibility Criteria:**
- Histologically confirmed high grade soft-tissue sarcoma
- Treated with surgical resection and neoadjuvant/adjuvant therapies
- Treated at USC University Hospital with at least 6 months of clinical follow-up
- No subject will be excluded from the study on the basis of gender, racial or ethnic origin.

**Results:** This study has been ongoing since June 2010 and my role (N. Taheri) has been to access patient records and collecting data about each patient's treatment in order to create a spreadsheet for later analysis, and ultimately to publish/present the results of the updated study on multimodality treatment. Currently all the sarcoma patient records in the Orthopedic Oncology Service database have been collected and are being prepared for statistical analysis.

**Conclusion:** The benefit of this study will be to provide an updated evaluation of multimodality therapy in the treatment of high grade sarcomas. The last study that evaluated the role of neoadjuvant and adjuvant therapies such as chemotherapy and radiation was published in 1991, so this study will determine the benefit of administering chemotherapy/radiation before and after surgical treatment of high grade sarcomas by determining the rate of recurrence/metastases and overall patient outcome in relation to adjuvant therapy. At this point the data needs to be analyzed before any trends or conclusions can be made.

**THE EFFECT OF MATERNAL STRESS ON BIRTH WEIGHT AND NEURODEVELOPMENT IS MEDIATED VIA EPIGENETIC MODIFICATIONS**

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**Goal:** Neurodevelopment and cognitive function are vital in the modern knowledge based economies. The effects of malnutrition and toxicants have been extensively studied, but little is known about the role of social stress (e.g., poverty, violence, poor social supports, and negative life events). It is well known that stress adversely affects health and neurodevelopment, but it is not clear exactly how it does so. We hypothesize that stress modifies that response to nutritional deficiencies (iron deficiency) and environmental toxicants (lead poisoning), and that it may do so via epigenetic modifications.

**Methods:** We recruited a cohort of 1000 Mexican mothers and their newborn children. We collected data on socioeconomic status, stress, self esteem, exposure to violence, ferritin, and complete blood count for the mothers every few months pre and post-partum. At birth, we measured lead concentration in the cord blood, fetal birth weight, and gestational age. Every few months, we would assess growth (height, weight, head
circumference), and neurodevelopment with the Bayley Scales of Infant Development, which measures cognitive, language, motor, social-emotional, and adaptive behavior. From the blood samples, we analyzed the infant’s CBC, ferritin, lead levels. We also assessed the infant’s methylation at LINE-1, ALU, 11-beta-hydroxylase, glucocorticoid receptor NR3, H19, and insulin-like growth factor. We analyzed the effects of stress and lead on neurodevelopment, growth, and epigenetics with linear and mixed models in R 2.9.

**Results:** We found a significant positive relationship between LINE-1 methylation and maternal stress as measured by the Perceived Stress Scale (t = 0.6, df = 165, p < 0.01) and the Edinburgh Postnatal Depression Scale (t = 0.49, df = 165, p < 0.01). Maternal self esteem (measured by the Coopersmith survey) was negatively associated with LINE-1 methylation (t = -2.19, df = 166, p = 0.03). Methylation at 11-beta-hydroxylase was marginally negatively associated with maternal lead levels as measured by patella lead (t = -1.84, p = 0.069) and third trimester blood lead (t = -1.82, p = 0.071). Birth weight was positively associated with LINE-1 methylation (t = 2.68, p = 0.009). There were no significant relationships between Bayley scores and maternal stress or methylation.

**Conclusion:** Stress decreases LINE-1 methylation, and LINE-1 methylation is positively associated with fetal birth weight, so this could account for the negative relationship between stress and birth weight. Our study is still a work in progress, but these preliminary results support our hypothesis that environmental exposures and maternal stress affect DNA methylation in the developing fetus, which in turn affects its birth weight.

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**Hemodynamic Support during High Risk PCI: A Comparison of In-Hospital events between Intra-Aortic Balloon Pump, Tandem Heart and Impella**

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**Objectives:** The goal of this study is to examine the hospital outcomes of high risk percutaneous coronary interventions (PCI) performed with hemodynamic support by Intra-Aortic Balloon Pump (IABP), Tandem Heart (TH) or Impella (IMP).

**Methods:** In our single center retrospective study, we identified 75 patients who underwent high risk PCI with hemodynamic support from March 2007 to January 2010. Number of patients per group: IABP=48, TH=12 and IMP=15. The primary end point was major in-hospital adverse cardiac events (MACE) consisting of re-infarction, repeat revascularization and death. The secondary endpoint was in-hospital vascular complications defined as need for transfusion, vascular repair or CVA.

**Results:** Patients in the IMP group were older compared to IABP and TH (p=0.003). Gender, BMI, history of diabetes, CVA, peripheral vascular disease and renal insufficiency were equivalent between groups. The primary endpoint of MACE was not
significantly different between IMP, TH and IABP groups (p=0.36). The secondary endpoint of in-hospital vascular complications was higher in the TH group compared to IABP and IMP (p=0.043). Patients in the IABP group were more likely to receive protamine (p<0.001) and have the device removed immediately after the procedure (p<0.0001) compared to TH and IMP groups. There were no significant outcome differences between IABP and IMP groups.

Conclusion: In our study, there was no difference in hospital MACE between Intra-Aortic Balloon Pump, Tandem Heart or Impella supported high risk PCI patients. In-hospital vascular complications were increased in the Tandem Heart group. Patient outcomes in the Intra-Aortic Balloon Pump and Impella groups were equivalent.

Translational Link Between Obesity and Ovarian Carcinoma Provides Justification for Community-Based Obesity Interventions

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Goal: Despite advances in surgical technique and chemotherapeutics, ovarian cancer remains the most deadly gynecologic malignancy due in part to advanced stage at presentation and poor screening tools. Increasing data show that obesity is associated with cancer progression and treatment resistance, and this effect may be modified by endoplasmic reticulum (ER)-stress seen in obese patients. Therefore, validated community outreach programs may provide further benefit by reducing obesity-related prognostic factors that may contribute to advanced ovarian carcinoma. Taken together, the clinical, translational, and interventional information generated from this study will provide novel translatable markers for ER-stress and cancer progression in the setting of obesity, and further justify implementation of approved obesity interventions.

Methods: The clinicopathologic and translational aim is to determine the expression of GRP78, a marker of ER-stress, among patients from a cancer registry for use as a potential prognostic and therapeutic marker for cancer progression and treatment. In total, 122 patients who underwent cytoreductive surgery for epithelial ovarian, fallopian tube and primary peritoneal cancer were identified from a cancer registry at LAC+USC after IRB approval. Clinicopathologic, demographic, and survival information was obtained from medical records for 62 patients. Assays for GRP78 were analyzed using a semi-quantitative metric comprised of intensity and distribution of expression within tumors by immunohistochemical analysis of formalin-fixed, paraffin-embedded tumor from surgery. Data was analyzed by uni- and multivariate analysis, and is ongoing for the remaining identified patients.

The second aim involved direct obesity intervention in a Boyle Heights community center by 1) improving knowledge of and reducing barriers to healthy lifestyle choices through sustainability of an health-conscious workshop series entitled Una Vida
determining the impact of a clinically-validated IRB-approved obesity intervention called BodyWorks® (Office of Women’s Health), a 10-week, 10-15 hour course in this same group. The pre- and post intervention study outcome variables include both anthropometric (BMI, abdominal circumference) as well as qualitative measurements of knowledge of healthy eating habits and exercise by validated survey.

**Results:** The mean BMI of the cohort was 26.9 (±6.9 SD). GRP78 was highly expressed in 83.9% of tumors, and significantly correlated with body mass index (BMI) in the cohort (p=0.038). Additionally, GRP78 was associated with likelihood of gross residual disease after maximal cytoreductive effort (p=0.022) and histological subtype (p<0.001). On multivariate analysis, a trend towards diminished overall survival was evident among patients with increased GRP78 expression (p=0.08), and is expected to reach statistical significance for decreased survival and diminished progression-free survival after inclusion of the remaining 60 patients.

Una Vida Saludable workshops from March 2010-January 2011 on healthy substitutions, at-home fitness, yoga/mindfulness, and nutritional labels were given at the early education center to over 50 participants. Participants expressed high-degree of interest in the community intervention study, and an expedited IRB was filed to implement BodyWorks curriculum following successful receipt of the Krieger Foundation Grant. As a result, 9 first and second year medical students were trained on administration and implementation of BodyWorks to prepare for initiation of the course. Biometric data collection, consent, and courses will commence March 2011 following final IRB review.

**Conclusion:** Expression of GRP78 in ovarian tumors, its association with increased BMI, and trend towards poor survival further justify translational studies to understand the link between obesity and cancer prognosis as a means to provide targeted therapeutic interventions and markers for disease recurrence. Additionally, these results provide justification for community validated interventions aimed at obesity prevention, which may reduce risk of ovarian carcinoma in addition to chronic disease burden.

**Future Directions:** The last aim of the project is to determine whether adipocytes confer a malignant phenotype to ovarian carcinoma cells measured by increased invasion, and migration, as well as decreased anchorage-dependent growth. Using an institutional material transfer agreement (MTA), we acquired commercially available well-established human ovarian cancer cell lines from the American Type Culture Collection (ATCC). Human mesenchymal stem cells are currently being differentiated into adipocytes, and well-characterized human ovarian cancer cell lines, SKOV-3, A2780, OVCAR-8 and differentiated adipocytes will be co-cultured. Assays for migration/anchorage dependent growth and ER-stress will be conducted in co-cultured ovarian carcinoma cells and carcinoma cells not exposed to (i.e., co-cultured with) adipocytes. Additionally, initiation of BodyWorks will commence in March 2011 and continue through July 2011. Outcomes discussed will be characterized to elucidate the impact of the intervention.
Refractory Reflux after the Duodenal Switch: what to do?

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Gastroesophageal reflux disease (GERD), already prevalent in obese patients, may be induced or exacerbated by the duodenal switch (DS) because of failure to recognize a hiatal hernia, creating an excessively narrow gastric pouch at the incisura or encroaching on the LES by the most proximal stapler. We report our experience of near-total gastrectomy for truly refractory GERD. In 15 DS patients with pH proven refractory GERD, near total gastrectomy leaving a typical 5cm lesser curve pouch was performed 6.5 years (2-10) after DS. Small bowel anastomoses were untouched except in one patient with malnutrition. Median BMI was 48 (22-62) kg/m2 prior to DS and 34 (29-41) prior to gastrectomy. Median hospital stay was 5 days (4-61). Major complications included leaks in two patients in whom DS had been a revisional procedure: both underwent reoperation with drainage and stenting, and in one further patient a leak was suspected but not visualized. There were no deaths: the above three patients had a prolonged course requiring multiple endoscopies and wound dressings, and three patients had early endoscopic dilation and two others required common channel lengthening. At 0.9 years (0.05, 2.71) post-gastrectomy, only two patients require long term PPIs. 14 patients could be contacted, all of whom reported improvement in GERD symptoms. BMI at latest follow up was 29.5 (19-35). Near-total gastrectomy is effective in abolition of GERD but carries a risk of major complications especially if the DS was not the first bariatric procedure. Dumping is not an issue and malnutrition is rare.

Does the degree of ST segment elevation correlate with the rise in markers of myocardial infarction in ST-elevation MI?

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\textbf{Purpose:} The goal of my summer project was to see whether the degree of ST segment elevation in ST-elevation myocardial infarction (STEMI) correlates with the severity of infarction, as measured by the elevation in serum Troponin. If such a correlation were shown to exist, the ECG of a patient presenting with STEMI could be a quick, inexpensive, and non-invasive tool to assess the status of the patient, and potentially useful in predicting outcome or in choosing the aggressiveness of therapy.

\textbf{Methods:} The study's subjects were patients from the database of the cardiology department at Ichilov Hospital (Tel-Aviv), who had been documented by ECG as having had an STEMI upon presentation to the emergency room. This research was conducted under the direction of Drs. Dan Justo (Geriatrics) and Shmuel Banai (Cardiology). Over
400 patients were included in this study. Patients displaying pathologies on their ECGs such as bundle branch blocks or atrial fibrillation were excluded from the analysis. I measured the ST segment elevation in all 12 leads, at 3 different points: at the J point, at 1 mm to the right of the J Point, or at 2 mm to the right of the J Point, studies having shown that there is a significant amount of variability in the point above baseline at which physicians and researchers choose to measure ST segment elevation.

**Results:** The study is ongoing. For greater scientific validity, all of the ECG strips that I read are to be independently read by an experienced physician. Then the data may be averaged and results obtained in the following way: the value of the ST elevations at the J point will be summed across all 12 leads and the final value will be correlated with the increase in Troponin levels and possibly with other relevant data from the patient’s chart. We also planned to sum the values across all 12 leads for each of the other 2 points and perform the same analysis. This would allow us to see if the results that we obtain when measuring ST segment elevation at the J point change when the ST elevation is measured at other points.

**Conclusions:** ECG is a non-invasive procedure, with results obtained immediately upon patient admission. The goal of this study is to see whether the degree of ST elevation in STEMI patients as seen on ECG can be a simple and reliable measure of the severity of the MI. Thus, ECG could potentially be used independently of serum Troponin levels to assess a patient’s condition. As the study is ongoing and the data necessary for analysis is in the process of being collected, no conclusions can yet be drawn from the study. Participation in this study created a foundation for me to learn about the interpretation of ECGs.

**A PHASE II STUDY OF A MODIFIED PEGYLATED LIPOSOMAL DOXORUBICIN (PLD), BORTEZOMIB AND DEXAMETHASON REGIMEN FOR PATIENTS WITH PREVIOUSLY UNTREATED MULTIPLE MYELOMA (MM)**

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**Background:**
PLD and bortezomib (BORT) are FDA-approved for MM patients who have received one prior therapy. We have previously demonstrated in laboratory studies that lower doses of PLD administered more frequently are better tolerated than higher doses given less often.
The combination of BORT and dexamethasone (DEX) is effective for previously untreated MM patients. Prior studies by our group have shown that intravenous administration of DEX 40 mg, BORT 1.0 mg/m$^2$ and PLD 5 mg/m$^2$ (DVD) on days 1, 4, 8, and 11 of a 28-day cycle is effective for relapsed/refractory MM patients and well tolerated.

**Methods:**
We conducted a single-arm multi-center phase II study for previously untreated MM patients to evaluate the DVD regimen. Patients were treated to a maximum response plus two additional cycles or completed a maximum of eight cycles of therapy without disease progression.

**Results:**
Thirty-five patients were enrolled with a median age of 65 years (range, 42-82 years). All patients are currently evaluable for response and toxicity, respectively. Thirty (86%) patients have shown objective responses to the DVD regimen, including 7 (20%) complete responses, 2 (6%) very good partial responses, 16 (46%) partial responses, and 5 (14%) minimal responses. Among the other 5 patients, 3 (13%) had stable disease and 2 experienced progression of their disease. The median time to first response was 1 month (range 1-12), and the median time to best response was 3 months (range 1-12).

To date, 7 patients have shown progressive disease: four progressions occurred while on DVD (two of these patients responded initially but then went on to progress during the course of treatment), and 3 occurred while off DVD. The median number of cycles completed was 7 (1-8).

Hematologic toxicity was rare in our study. We recorded 0 grade 2 anemias and 2 grade 3 (5.7%). Thrombocytopenia occurred in only 2 of our patients (5.7%). Only 3 (8.6%) of our patients suffered neutropenia, including 2 grade 3 and 1 grade 2. Peripheral neuropathy was also relatively rare, occurring in 11 patients (31.4%) overall: this included two grade 3, three grade 2 and the remainder grade 1. Hand-foot syndrome occurred in only 2 of our patients (5.7%), and both instances were grade 1. Notably, there have been no cases of stomatitis.

**Conclusions:**
Thus, these results suggest that the DVD regimen using this modified schedule and doses of these drugs is well tolerated and produces high response rates for previously untreated MM patients.
Runx2 Transcriptome of Prostate Cancer Cells: Insights into Invasiveness and Bone Metastasis

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Goal: Prostate cancer (PCa) cells preferentially metastasize to bone at least in part by acquiring osteomimetic properties. Runx2, an osteoblast master transcription factor, is aberrantly expressed in PCa cells, and promotes their metastatic phenotype. The transcriptional programs regulated by Runx2 have been extensively studied during osteoblastogenesis, where it activates or represses target genes in a context-dependent manner. However, little is known about the gene regulatory networks influenced by Runx2 in PCa cells.

Methods: We therefore investigated genome wide expression changes in PCa cells in response to Runx2. We engineered a C4-2B PCa sub-line called C4-2B/Rx2^dox, which conditionally expresses Runx2 upon Doxycycline (Dox) treatment.

Results: Transcriptome profiling using whole genome expression array followed by in silico analysis indicated that Runx2 upregulated a multitude of genes with prominent cancer associated functions. They included secreted factors (CSF2, SDF-1), proteolytic enzymes (MMP9, CST7), cytoskeleton modulators (SDC2, Twinfilin, SH3PXD2A), intracellular signaling molecules (DUSP1, SPHK1, RASD1) and transcription factors (Sox9, SNAI2, SMAD3) functioning in epithelium to mesenchyme transition (EMT), tissue invasion, as well as homing and attachment to bone. Consistent with the gene expression data, induction of Runx2 in C4-2B cells enhanced their invasiveness. It also promoted cellular quiescence by blocking the G1/S phase transition during cell cycle progression. Furthermore, the cell cycle block was reversed as Runx2 levels declined after Dox withdrawal.

Conclusion: The Runx2 transcriptome in PCa cells highlights plausible mechanisms underlying their metastatic phenotype, including tissue invasion, homing to bone and promotion of high bone turnover. Runx2 is therefore an attractive target for the development of novel diagnostic, prognostic and therapeutic approaches to PCa management. Targeting Runx2 may prove more effective than focusing on its individual downstream genes and pathways.

Keywords: Runx2, Prostate Cancer, Metastasis, Bone, Osteoblast
Role of Class A Scavenger Receptor in Host Immune Response in *S. japonicum* infection

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**Goal:** Schistosomiasis is a disease caused by parasitic trematodes belonging to the *Schistosoma* genus. In China, approximately 725,000 people are infected and infections are caused primarily by the *Schistosoma japonicum* species. The pathophysiology of schistosomiasis is strongly influenced by host immune response. Schistoma eggs secrete soluble egg antigen (SEA). Antigen presenting cells recognize SEA and form granulomas. Over time, these granulomas can lead to liver fibrosis, hepatosplenomegaly, liver portal hypertension, and ascites. Recent evidence has shown a role of Class A Scavenger receptors (SR-A) in schistosoma infection. We suspect that SR-A recognizes SEA and subsequently induces the host immune response that is the underlying cause of granulomas in chronic schistosoma infection. The goal of this study will be to survey the relationship between SR-A and SEA by comparing IgG (bound to SEA) levels in SR-A KO mice and in wildtype mice infected with *S. japonicum*.

**Methods:** SR-A knockout mice were obtained. We compared the immune response to SEA in *Schistosoma japonicum* infected WT mice with *Schistosoma japonicum* infected SR-A KO mice. An indirect ELISA was used to measure IgG1 and total IgG bound to SEA in uninfected WT, uninfected SR-A KO, infected WT, and infected SR-A KO mice. Uninfected WT and uninfected SR-A KO mice served as negative controls. SEA was harvested from the liver of 5 week post-infected mice and plated in the wells. Blood serum obtained from the four groups of mice was allowed to bind the SEA antigen. Enzyme-linked anti-mouse IgG and antimouse IgG1 was added to detect the amount of total IgG and IgG1 bound to SEA, respectively. The plates were read at 450nm.

**Results:** In the wildtype controls, the infected mice showed a greater increase in both total IgG and IgG1 bound to SEA compared to uninfected mice. The increase in SR-A KO infected mice was even greater than the increase observed in WT infected mice. Thus the presence of SR-A receptors in infected mice seems to suppress IgG immune response.

**Conclusion:** The experiment is a first step in understanding the relationship between SR-A and host immune response in *Schistosoma japonicum* infection. The results indicate that SR-A on macrophages have an inverse relationship with IgG levels. The next step is to derive the mechanism by which SR-A influences TLR-4 and IgG expression. Ultimately we hope to find the relationship between SR-A and granuloma size and formation in chronic schistosomiasis infection.
Rapid Reversal of Warfarin Induced Hemorrhage in the Emergency Room

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Warfarin, an oral vitamin K antagonist, is used to prevent arterial and venous thromboembolism in patients suffering from a multitude of diseases. In 2004, 31 million warfarin prescriptions were dispensed in the United States.¹ Warfarin inhibits the activation of the vitamin K dependent clotting factors (factors II, VII, IX, X) and regulatory proteins (proteins C, S, and Z). It is one of the leading drugs implicated in emergency room visits for adverse drug reactions.² Annually the frequency of bleeding complications associated with overanticoagulation is 15 to 20 percent; with fatal bleeds as high as 1 to 3 percent. The most effective method of warfarin reversal is the use of Four Factor Prothrombin Complex Concentrate which is widely used throughout Europe but is unavailable in the United States. The current therapies available to emergency room physicians in the US are Fresh Frozen Plasma, recombinant Factor VIIa, Factor Eight Inhibitory Bypassing Activity or Three Factor Prothrombin Complex Concentrate concomitantly administered with vitamin K. We review advantages and disadvantages of these and recommend Three Factor PCC with small doses of rFVIIa, with vitamin K in life threatening situations if Four Factor PCC is unavailable.

Cathepsin S as a biomarker in the tears of patients with Sjogren’s Syndrome and other autoimmune diseases

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Goal: Sjögren's syndrome (SjS) is a chronic autoimmune disease characterized by inflammation and destruction of the lacrimal and salivary glands, leading to dry mucosal membranes. Preliminary studies indicate that biomarkers such as cathepsin S (CATS) are significantly elevated in the tears of patients with SjS and other autoimmune diseases. This study seeks to understand how CATS levels in human tears may correlate with the presence or progression of autoimmune diseases, specifically SjS.

Methods: Tear samples are collected using a Schirmer's Test performed on patients with various autoimmune disorders who volunteered at USC University Hospital's rheumatology clinic. The tear samples are analyzed for CATS activity and total protein concentration in Dr. Hamm-Alvarez's lab.

Results: Results obtained from 64 patient samples do not show a strong correlation between CATS activity level and autoimmune disease diagnosis. However, the early data does show a positive association between time since first diagnosis and CATS activity (Figure 1). More samples will be obtained and analyzed pending approval of an updated IRB.
**Conclusion:** It appears that elevated CATS activity is not specific for SjS in populations already being treated for SjS. However, the data suggests that CATS may have potential value as a biomarker for tracking the progression of autoimmune disease.

Figure 1. CATS activity in patients with chronic rheumatoid diseases.