2014 Pathways to Cures:
Clinical Translational Research Day at UCI

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Poster Session Abstracts

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55	Pain Management At Home In Children With Cancer: A Daily Diary Study	B	28
56	Evaluation Of Perirenal Adipose Tissue Volume As A Predictor Of Renal Cortical Neoplasm Histopathology	B	28
57	NRF2 Agonist Decreases Colonic Inflammation And Tight Junction Depletion In Rats With Chronic Kidney Disease	A	29
58	Working for the Weekend: The Effect of Cognitive Functioning, Social Support, and the Interdialytic Interval on Disease Self-Management Among Patients on Hemodialysis	A	29
59	Body Mass Index And Mortality In Kidney Transplant Recipients: A Systematic Review And Meta-Analysis	A	30
60	Peritumor Adipose Tissues Of PT3 Clear Cell And Chromophobe Renal Cell Carcinoma Exhibited Enhanced Wnt Activity, Leading To Increased Motility Of Human CCRCC Cell Line CAKI-2	A	30
61	A structure-function mechanism of rescuing oncogenic p53 mutants using a novel class of small molecules	B	31
62	Novel GABAmimetic activity of Withania somnifera on microtransplanted receptors	B	31
63	Creation Of A Personalized, Molecular-Based Approach To The Treatment Of Recurrent Or Refractory Pediatric And Adolescent Cancer	B	32
64	Characterization of an FTY720 analog with enhanced activity against BCR-ABL+ leukemias	B	32
65	Developing FTY720 Analogs To Starve Cancer Cells To Death	B	33
66	A comparison of standard and high sensitivity multiplexed cytokine/chemokine panels in plasma of cervical cancer survivors	B	33
67	Cranial transplantation of human neural stem cells ameliorates chemotherapy-induced cognitive impairment	B	34
68	Characterization And Assessment Of Transplanted Human Embryonic Stem Cell Derived Motor Neurons Into A Conus Medullaris/Cauda Equina Injury Model	B	34
69	Choroid Plexus Dysfunction in Alzheimer’s disease – Morphological Changes & Regeneration via Stem Cell Injections	B	35
70	True 32-Slice Intraoperative Computed Tomography In Conjunction With 3T MRI In The Treatment Of STN-Targeted Parkinson's Disease: Validation And A Potentially Paradigm-Changing Tool.	B	35
71	Assessment Of Adolescent Alcohol Usage Via Computerized Screening In The Emergency Department	A	36
72	Relationship Between Patients’ Degree Of Education And Readiness To Change Drinking Habits	A	36
73	Comparative Analysis Of Emergency Department Patients Lost To Follow-Up After Computerized Alcohol Screening And Brief Intervention	A	37
74	The Association of Alcohol-Use Disorders Identification Test and Readiness to Change Score in Alcohol-Related Emergency Department (ED) Visits	A	37
75	Efficacy of Baclofen in reducing symptoms of PTSD & Anxiety in Veterans with HCV & Alcohol use Disorders	A	38
76	Stellate Ganglion Block For Severe PTSD: Clinical Response And Psychophysiological Correlates	B	38
77	Burn Wound Exudate: Depth of Burn Predicts Cellular Recruitment	B	39
78	Telomere length measurements in post-mortem human brain in major depressive disorder	B	39
79	Use Of GDNF-Releasing Nerve Guidance Channels To Promote Motor Axon Regeneration Following Ventral Root Avulsion Injury In Rats	B	40
80	Imaging of the Adult Sinus Using a Low-Cost Optical Instrument	B	40
81	Ileostomy Reversal After Minimally Invasive Colorectal Surgery: Can it Still be Considered a Minor Procedure?	B	41
82	The Effect Of The Anti-Angiogenesis Agent Bevacizumab On The Hippocampal Volumes Of Patients Diagnosed With Recurrent, Treatment Resistant Malignant Gliomas	B	41
83	Repeated Streptococcus pyogenes infections induce an autoimmune Th17 cell phenotype and impair Blood Brain Barrier integrity in mice	B	42
84	Low-doses of cisplatin injure hippocampal synapses: A mechanism for ‘chemo’ brain?	B	42
85	SORAFENIB FOR THE TREATMENT OF HEPTOCELLULAR CARCINOMA: EXAMINING SURVIVAL BENEFIT OF VARYING SOEFENIB DOSAGES	B	43
86	Vertical Inhibition Of The PI3K Pathway Potently Sensitizes Diffuse Large B Cell Lymphoma To BCL-2 Antagonism	B	43
88	Marizomib (NPI-0052) Activity as a Single Agent in Malignant Glioma	B	44
89	Inhibition of mTOR Induces Chemo-Resistance in B-cell Acute Lymphoblastic Leukemia	B	44
90	Cortical connectivity is a marker of motor status after stroke	B	45
91	Laparoscopic Surgery For Gastric Malignancy: Outcomes Of A Minimally Invasive Oncologic Resection	A	45
92	Lipid-enriched diet rescues lethality and slows down progression in a murine model of VCP-associated disease	A	46
93	Outcome of Preoperative Weight Loss in Colorectal Surgery	A	46
95	Long-lasting reduction of blood pressure by electroacupuncture in patients with mild-moderate hypertension: Mechanism of action	A	47
96	Effect of 12 Weeks of Oral Betaine on Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) in Non-Diabetic Subjects with Mildly Elevated Fasting Blood Sugar	A	47
97	Rapamycin and Chloroquine: the in vitro and in vivo effects of autophagy-modifying drugs in valosin containing protein multisystem proteinopathy	B	48
98	Comparing Visual Analog Scale And Verbal Numeric Rating Scale In Patients With Chronic Pain	A	48
101	DNA Methylation is Altered in Human Skeletal Muscle in Response to Exercise Training	A	49
102	Actigraphy Use in a Patient with Inclusion Body Myopathy: a Case Report	A	49
103	Utility of the Timed Mile Run among Overweight Youth	A	50
104	California Statewide Prescription Drug Monitoring System And It’S Effect On Physician Prescribing Behavior Among Emergency Department Chronic Pain Patients	A	50

Poster Session: B - Poster #: 1

Is Porcine Islet Xenotransplantation Headed For Clinical Trials? - Prolonged Euglycemia Following Intraperitoneal Xenotransplantation Of Alginate Microencapsulated Young Porcine Islets Without Pharmacological Immunosuppression

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The primary hurdles facing human islet allotransplantation are a crippling scarcity of high-quality organ donors, inconsistent islet yields and the need for chronic immunosuppression. The aim of this study was to demonstrate that alginate encapsulated porcine islet xenografts can reverse diabetes in immune competent mice without the need for pharmacological immunosuppression. C57BL/6 mice (8 weeks old, n=20) were rendered diabetic using intravenous Streptozotocin (150 mg/kg). Diabetes was confirmed (3 days of hyperglycemia (BG > 350 mg/dL) after which, mice were maintained on subcutaneous insulin (Lantus, 1-2 u/day). Control, non-transplanted mice were maintained on insulin for a month. Pancreatic tissue from pre-weaned Landrace young pigs (22±0.5 days old) was cultured after partial enzymatic digestion for a 7 day period after which islets encapsulated in 3% UPLVM alginate were transplanted into the peritoneal cavity of diabetic C57Bl/6 mice. No immunosuppression was administered to any mice. Mean pre-transplant blood glucose levels were 505?43 in diabetic mice (mean?sem). All mice became euglycemic after transplantation. Non-encapsulated controls transplanted under the kidney capsule became hyperglycemic after 4 days of euglycemia. Encapsulated transplant groups demonstrated mean blood glucose levels of 141?24mg/dL at 30 days, 126?12 mg/dL at 60 days and122?8 mg/dL at 90 days post-transplant. Explanted encapsulated islets collected at the conclusion of the study (90 days) were viable (77±3% Newport Green/PI) and functional as demonstrated by GSIR, SI=2±0.4; (n=10) within the alginate capsules. The results of this study prove the translational potential of our bioencapsulated porcine islet xenografts in reversing hyperglycemia in immune competent recipients without the need for immunosuppression. Pivotal large animal studies are being planned in collaboration with the University of Minnesota following which we intend to carry forward with human clinical trials.

Keywords: Islet Transplantation; Xenotransplantation; Porcine xenograft; Encapsulation; Diabetes;

Poster Session: A - Poster #: 2

Automation Of Microcapsule Evaluation And Characterization For Use In Cell Transplantation

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Microencapsulated islet transplantation has demonstrated successful reversal of hyperglycemia without the need for immunosuppression in several small and large animal trials. However transplant outcomes are greatly influenced by microcapsule and islet morphology and encapsulation efficacy and characterization of a statistically acceptable sample size is painstakingly difficult and time consuming. We have developed an algorithm to automate microcapsule and microencapsulated islet analysis and characterization of size distribution, morphology, and encapsulation efficiency. Young porcine islets were encapsulated within 3% alginate microcapsules generated using an air-driven electrostatic encapsulator. A series of 10 images acquired using a standard inverted microscope were processed using an algorithm developed in our laboratory which provides specific data on microcapsule and islet morphology (size and shape) and encapsulation efficiency (% of blank capsules, % of unsatisfactory capsules with breakage/islet protrusion and distance between the islet center and capsule surface). This algorithm was compared against the conventional method where three independent observers used image analysis tools to calculate these parameters by hand. Using the conventional method, three independent observers required 12±6 minutes to measure 0 microcapsules, producing results with significant variants: 393±8µm, 390±13µm, 392±10µm. When using the algorithm, the same results were obtained within 37±3 seconds, and the measurement obtained was 391±11 µm (mean±SEM). Incorporation of our algorithm in post-encapsulation islet analysis will enable standardization of parameters for the translation of encapsulated-islet transplantation to clinical trials. Microcapsules can be rapidly and consistently characterized for pre-transplant assessment and quality analysis. This innovation will find wide applicability in the fields of islet and stem cell encapsulation and other microencapsulation proc

Keywords: Islet Transplantation; Biomaterials; Alginate Encapsulation; Diabetes; Automation;

Poster Session: B - Poster #: 4

Muscle Clips for Strabismus Surgery

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Strabismus refers to any misalignment of the eyes. Consequences of misalignment may be double vision in the adult, and loss of vision in children. Strabismus surgery involves detaching the eye muscle and repositioning it on the eyeball to create a change in eye alignment. The current art accomplishes this by sewing a suture onto the muscle terminus, detaching it from the globe and, using the needles attached to that suture, sew it directly to the eyeball. There is a risk of needle perforation of the eyeball when those needles are passed into the superficial layers of the eye, where the thickness varies from 0.3 to 1 mm. Perforation of the globe occurs in approximately 2% of cases and may cause a loss of vision due to internal bleeding and trauma to the retina. There are 3 pairs of muscles to each eye, for horizontal, vertical and rotational positioning, and each operation averages 2 muscles. We have conceived a device to obviate the need for passing needles through the eyeball and thereby eliminate the risk of vision loss in eye muscle surgery. The clip device creates an artificial extension of the muscle stump, such that after the muscle is detached, and suspended by a suture, it can be secured to the eye by passing the needles through the clip, and not through the actual eye wall. Substituting needle passage through a device and not through the eyeball will obviate risk of needle trauma to the eye. The device is conceived to be constructed of biodegradable polymers (lactic and glycolic acids) similar to Vicryl sutures, routinely employed in the current art. Since muscles reattach to the eye in as little as 2 weeks, maximal integrity of clip strength is only required for 30-60 days. A provisional patent application has been filed through the UCI Office of Technology Alliances. A model/prototype, developed in association with RapidTech, may be available. Clinical trials await prototype funding.

Keywords: Strabismus; Surgery; Muscle Clips; Biodegradable copolymers; Eye muscles;

Poster Session: A - Poster #: 5

Development Of A Novel iPad Based Laparoscopic Trainer And Comparison To A Standard Laparoscopic Trainer For Basic Laparoscopic Skills Testing

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OBJECTIVES: We developed the iTrainer (iT) as a portable laparoscopic trainer, which incorporates the iPad tablet. We then compared the iT to a standard pelvic trainer (SPT) to assess surgical skills as well as its image quality, resolution, brightness, comfort and overall performance. METHODS: We designed and constructed the iT to be compatible with the Apple iPad and standard laparoscopic instruments. Participants were assigned to perform the thread-the-loops task on both trainers and were prospectively randomized to start on either the iT or SPT. Each participant was allowed a 2-minute warm-up prior to the 2-minute testing period. We scored participants using the product of skill quality (0-4 scale) and quantity of loops threaded (0-10 scale). Participants then rated each trainer on image quality, resolution, brightness, comfort and overall performance on a five-point Likert scale. RESULTS: A total of 45 subjects including 10 undergraduates, 10 medical students, 10 residents, and 15 experts participated in this study. There was no significant difference between thread-the-loops task scores completed on the iT when compared to the SPT for all groups tested ($p>0.05$) with the exception of the medical student group, who performed better on the SPT ($p<0.05$). Upon evaluation of each trainer, participants rated the iT as having superior image quality and resolution when compared to the SPT ($p<0.05$), but rated the SPT higher in overall performance ($p<0.05$). Brightness and comfort were rated similarly for both trainers. DISCUSSION: We have demonstrated face and criterion validity for the thread-the-loops task on the iT. The iT rated superior in image quality and resolution but inferior in overall performance compared to the SPT. The iT provides trainees a unique advantage over SPT as an additional resource to laparoscopic training as it is inexpensive, portable and can be readily available for training. A 3D printed final model is currently being developed.

Keywords: Laparoscopic trainers; simulators; iPad tablet;

Poster Session: B - Poster #: 6

Vestibular Rehabilitation Using Wide-Angled Head Mounted Displays With Stereoscopic 3D

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OBJECTIVE The current standard of care for vestibular dysfunction is vestibular rehabilitation usually consisting of habituation, adaptation and exercises. Developing an appropriate virtual reality (VR) environment and using a wide-angled head mounted display (HMD), we believe that there would be an increased rate of improvement in symptoms and function through vestibulo-ocular reflex (VOR) recovery. METHODS The study will investigate the effects of the graded optokinetic stimulus on healthy subjects. The participants will be in a sitting position while using HMD due to concerns of safety and the real risk of imbalance and falls. Participants will be randomly divided into group D (dynamic) and group S (static). Each group will be in the same standard room and use the same settings while using the HMD. However, group D will be exposed to moving VR environments while group S will be exposed to static VR environments.Participants will be asked to complete the Situational Vertigo Questionnaire (SVQ) before being exposed to the VR environments. The SVQ is designed to assess the frequency of dizziness, giddiness, lightheadedness or unsteadiness induced by visually challenging stimuli such as walking through a maze or a supermarket aisle. The participants will be asked to again answer the SVQ throughout and after the study. Additionally, patients will be asked to complete the Dizziness Handicap Inventory (DHI), the Activities-specific Balance Confidence Scale (ABC), and the Dynamic Gait Index (DGI) to measure other outcomes. ANTICIPATED RESULTS Using a finely tuned virtual environment, we hope to investigate the primary effects of the virtual environment on health subject volunteers. SIGNIFICANCE OF IMPACT Adults suffering from vestibular dysfunction often experience dizziness and imbalance putting them at a higher risk for falls or discomfort. The result of our study might open new avenues of treatment for vestibular dysfunction.

Keywords: Vestibular Dysfunction; Virtual Reality; Head Mounted Displays; Imbalance; Dizziness;

Poster Session: A - Poster #: 8

Development And Initial Porcine And Cadaver Experience With Three-Dimensional Printing Of Endoscopic And Laparoscopic Equipment

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OBJECTIVES: Recent advances in three-dimensional printing technology have made it possible to print surgical devices. We report our initial experience with the printing and deployment of endoscopic and laparoscopic surgical equipment. METHODS: We created computer-aided designs for ureteral stents and laparoscopic trocars using SolidWorks. We developed three generations of stents, which were printed with an Objet500 Connex printer, and a fourth generation was printed with an EOSINT P395 printer. The trocars were printed with an Objet30 Pro printer. We deployed the printed stents and trocars in a female cadaver and in-vivo porcine model. We compared the printed trocars to two standard trocars for defect length and area. RESULTS: The first two-stent generations (7Fr and 9Fr) could not be printed with the lumen required to pass a guide-wire. The third generation 12Fr stent allowed passage of a 0.035 guide-wire. The 12Fr diameter limited its deployment, but it was introduced in a female cadaver through a ureteral access sheath. Fourth generation 9Fr stents were printed and deployed in a porcine model using standard Seldinger technique. The printed trocars were functional for the maintenance of pneumoperitoneum and instrument passage. The printed trocars had a larger superficial defect area ($p<0.001$) and length ($p=0.001$) compared to Karl Storz, and Ethicon trocars (29.41mm², 18.06mm², and 17.22mm², respectively and 14.29mm, 11.39mm, and 12.15mm, respectively). DISCUSSION: 3D printing of ureteral stents and trocars is feasible, and these devices can be deployed in porcine and cadaver models. 3D printing is rapidly advancing and may be clinically viable in the future.

Keywords: Rapid prototyping; ureteral stents; laparoscopic trocars; three-dimensional printing;

Poster Session: B - Poster #: 9

Educating Premedical Students About The Importance Of Cultural Competency

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With an ever-changing and progressively heterogeneous patient population, current healthcare systems require culturally competent physicians that are prepared to manage linguistic and social challenges. Through the UC Irvine School of Medicine, faculty, medical and undergraduate students established the annual Summer PreMed Program, a pioneering enrichment program designed to bolster the interest of a diverse body of premedical students in pursuing a healthcare career. The objective of our study was to investigate the effectiveness of the health disparities and cultural diversity module, a course where students learn how to interact and communicate with various patient populations as a physician. The workshop was based on a series of speaker presentations that included PowerPoint lectures, video passages and various collaborative activities. After the course, students were given an evaluation addressing the relevance and effectiveness of the module. Within a three-year period, feedback from a total of 311 students were collected and analyzed. Among the 311 evaluations, 258 (83%) of the students reported an overall increase in awareness and relevance in cultural competency and approximately 90% of the students noted an overall increase in their interest to pursue a career in healthcare. The main themes that were identified from the answers to the open-ended question, "How has this workshop helped you?", included a) better understanding of the relevance of cultural diversity in the healthcare profession, 2) better knowledge of various beliefs among different cultures, and 3) promoted interest towards healthcare careers. Additionally, using a scale from 1-5 (1= no relevance, 5 = extremely relevant), the average score for topic relevance obtained from all evaluations was 4.54. Overall, the health disparities and cultural diversity module proved to be a pivotal component of the Summer PreMed Program with regards to increasing cultural competency as a physician.

Keywords: cultural competency; pre-medical program; underrepresented minority; health disparities; cross-cultural interactions;

Poster Session: A - Poster #: 10

Application Of Continuous Incisional Infusion Of Local Anesthetic After Major Pediatric Urological Surgery

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Purpose: To determine the efficacy of the newly developed locally infused anesthetic, ON-Q® pain relief system (Kimberly-Clarke, GA USA), in improving postoperative pain, reducing narcotic requirement, and shortening recovery time after major pediatric urological surgery. Material and Methods: A case-control analysis comparing 20 patients undergoing major urological procedures who were treated postoperatively with the ON-Q system was compared to 20 patients treated with current hospital standard of care intravenous and oral analgesics. Pain was assessed in both groups by staff nurses using the Visual Analog Scale (VAS) or the Face, Legs, Activity, Cry, Consolability Scale (FLACC) depending on the child's age. Information regarding analgesic consumption along with recovery parameters such as temperature, start of oral nutrition, and length of hospitalization (LOH) were collected. Results: The ON-Q group experienced significantly lower ratings of maximal pain on the first postoperative day as compared to the control group (3 vs. 5.2, p=0.03) and a trend toward lower mean of maximal pain score on post operative day two (1.8 vs. 3.5, p=0.055). Systemic intravenous and oral analgesics were significantly lower on the day of surgery and the first postoperative day for the ON-Q group (p=0.014; and p=0.046 respectively). No differences in frequency of fever, start of oral nutrition and LOH were found between study groups. Conclusion: Continuous incisional infusion of local anesthetic with the ON-Q system is a viable option for postoperative pain management in children undergoing major urological surgeries. This technology significantly decreases the need for systemic analgesic consumption.

Keywords: Continuous Incisional Infusion of Local Anesthetic; ON-Q pain relief system; Post-operative pain;

Poster Session: A - Poster #: 11

Aerosol Transfer Of Bladder Urothelial And Smooth Muscle Cells Onto Demucosalized Colonic Segments For Bladder Augmentation: In Vivo, Long Term And Functional Results

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Objective:To determine the long-term durability & functional characteristics of demucosalized segments of colon repopulated with urothelial cells in the bladder of swine for use in augmentation cystoplasty. Methods: 9 swine were divided into 3 groups. The 1st group (control) underwent standard colocystoplasty; the 2nd group underwent colocystoplasty with colonic demucosalization and aerosol application of fibrin glue and urothelial cell mixture; in the 3rd group detrusor cells were added to the mixture described in group 2. The animals were then kept for 6 months. Absorptive function was assessed by examining absorption of water instilled in the bladder after ligation of the ureter. The secretory function was assessed by measuring the total urine sediment and protein content. Bladders were harvested for histological & immunohistochemical evaluation. Means & standard deviations were compared using Student T-Test. Results: All animals but 1 in the experimental groups showed confluent urothelial coverage of the colonic segment in the bladder without any evidence of fibrosis, inflammation or regrowth of colonic epithelial cells. Ten percent of the instilled water in the bladder was absorbed within an hour in the control group, but none in experimental groups ($p=0.02$). The total urine sediment and protein contents were higher in the control group compared to experimental groups ($p<0.05$). Conclusion: Aerosol transfer of bladder urothelial & detrusor cells onto a demucosalized intestinal segment for bladder augmentation is a viable technique that offers a histologically normal & confluent nonabsorptive or secretory urothelium, without colonic mucosa regrowth on long term evaluation.

Keywords: Aerosol; Bladder augmentation; Demucosalized colonic segment;

Poster Session: A - Poster #: 12

Predicting The Risk For Breakthrough Urinary Tract Infections In Children With Primary Vesicoureteral Reflux

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Objective: To construct a risk prediction instrument that stratifies patients with primary VUR into different risk groups according to their 2-year probability of having a breakthrough urinary tract infection(BTUTI) Methods: Information was collected on 252 retrospective patients with primary VUR and 56 prospective patients with primary VUR between June 2008-December 2010 retrospectively. All children were treated with antibiotic prophylaxis. VUR was corrected in cases where a BTUTI occurred. Bivariate analyses & binary logistic regression analyses were performed to identify factors associated with BTUTI. The final regression model was used to compute an estimation of the 2-year probability of BTUTI for each subject. The model was validated in a prospective cohort from January 2012-December 2012. Results: Bivariate analyses found that high-grade (IV-V) VUR (OR 9.4; 95%CI 3.8-23.5;$p<0.001$); initial presentation due to UTI (OR 5.3; 95%CI 1.1-24.7; $p=0.034$); & female gender (OR 2.6; 95%CI 0.097-, 7.11; $p<0.054$) were important risk factors for BTUTI. Subgroup analysis showed that bladder & bowel dysfunction was a significant risk factor for BTUTI & impact was more pronounced in low-grade VUR (I-III) (OR 2.8 for BBD, $p= 0.018$). In the retrospective sample the overall area under the receiver operating characteristic curve was 0.76 for the probability estimate model. Applied to a prospective validation sample, the model demonstrated predicted versus actual 2-year BTUTI rates of 19% versus 21% respectively & good performance as a discriminator of subsequent BTUTI (AUROC=0.80). Stratifying the patients into 3 distinct risk groups based on the parameters included in the risk model showed that the 2 years risk for BTUTI was 8.6%, 26.0% and 62.5% in the low, intermediate & high-risk groups respectively. Conclusion: 2-year incidence rate for BTUTI was significantly different between low, intermediate, & high risk groups. Instrument predicts an individuals 2-year risk of BTUTI

Keywords: Breakthrough urinary tract infections; pediatrics; primary vesicoureteral reflux; risk stratification; iReflux;

Poster Session: A - Poster #: 13

The Stubborn Calf: Can Restricting Blood Flow Induce Positive Musculoskeletal Change?

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Blood flow restriction (BFR) exercise is a technique that allows positive musculoskeletal changes. This integrates a low intensity exercise along with partial restriction of the targeted limb's blood flow. In previous studies, BFR training has yielded strength development that is similar to the results of traditional high intensity training. During exercise, it has been discovered that calf muscles are resistant from growing in size but quickly atrophy during periods of disuse. Therefore, this study aims to verify whether BFR training encourages changes in skeletal muscle hemodynamic, hypertrophy and strength by comparing the results of fatigue of calf muscle with either high or low intensity training. Over a five week training period, human subjects were observed by randomly assigning a leg with one of the three different training protocols: 1) Blood flow restriction-low intensity training (BFR-LIT), 2) high intensity (HIT), and 3) low intensity (LIT). Three different factors were then evaluated: body composition (fat and lean leg mass), hemodynamic values (deoxyhemoglobin, oxygen saturation, and oxyhemoglobin), and strength (isokinetic power and one repetition maximum). Each training protocol observed in an improvement in 1 RM ($p=0.004$) while BFR exhibited the most rapid increase. However, there were no significant changes. It is seen though that there is an improved isokinetic plantar flexion power across all velocities ($p < 0.001$) in LIT and HIT but it is not seen in BFR. In all protocols, there were no differences in lean mass, lower leg fat and preliminary analysis of hemodynamic changes. Within a short training time span, it seems that BFR, in comparison to HIT or LIT, does not gain positive benefit on variable relating to body composition, hemodynamic, and strength changes.

Keywords: Blood flow restriction; Low intensity training; High intensity training; Calf muscles; Skeletal muscles;

Poster Session: A - Poster #: 14

A Home-Based Telerehabilitation System For Patients With Stroke

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Evidence suggests that greater duration and intensity of rehabilitation therapy improves outcomes for patients with stroke. Delivery of care is often limited, however, e.g., due to systems of care delivery, cost, rural location, or difficulty traveling. The current study addressed this unmet need by examining the feasibility of a home-based telerehabilitation system. Entry criteria included age >18 yrs, 12-26 wk post stroke, and arm motor deficits (Fugl-Meyer (FM) score 22-55) that were stable. Each subject received 28 d of daily home-based telerehabilitation using a fixed system that we delivered/assembled. Each day consisted of 1 structured hour (testing, BP check, individualized exercises and games, and stroke prevention education) plus up to 1 hour of free play on dozens of games. Each week, subjects had a 1 videoconference with a licensed therapist and 1 with a research assistant; subjects could also phone the lab for technical support if needed. Enrollees were 54±17 yr (mean±SD), 6M/6F, with baseline FM=39±12 (range 23-55). Compliance was excellent, with subjects engaging in therapy 329 of 336 (97.9%) assigned days. Arm motor status improved (FM change 4.8±3.8 points from baseline to 1 mo post-therapy, $p=0.0015$). Although scores on tests of computer literacy declined with age ($r = -0.90$ to -0.92, $p<0.0001$), as expected, the arm motor gains derived from use of this system did not vary with age. The stroke education module was associated with significant gains in stroke prevention knowledge. BP was recorded by the patient, and results automatically transmitted to lab, on 97.9% of assigned days. Therapist videoconferences detected PHQ-2 scores consistent with depression in 3/12 patients. Therapists were able to review patient performances and upload revised therapy settings to the patient's home system without difficulty at any time of day. Results of this pilot study support the utility of a home-based system to effectively deliver telerehabilitation

Keywords: rehabilitation; stroke; therapist; home-based; subjects;

Poster Session: B - Poster #: 15

Automated Detection And Quantitative Analysis Of Sclerotic Lesions In The Spine On Computed Tomography Images

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OBJECTIVE: To develop computer-aided detection (CAD) software for detection of osteoblastic/sclerotic osseous metastasis in the spine, as an initial foray into a broader study of computational analysis of neoplastic and traumatic bone lesions. Aim: To design a computer algorithm for fully automated detection and quantitative characterization of sclerotic lesions of the thoracic and lumbar spine on computed tomography studies. METHODS: CT scans from 50 patients with studies demonstrating sclerotic metastatic disease to the spine were gathered. •Three general stages to process of CAD: Segmentation of anatomic structures of interest (spine) from "background structures": feature detection; classification • Segmentation of the spine was performed via thresholding and region growing • Watershed algorithm applied to detect lesion candidates (potential sclerotic bone metastasis) in each two dimensional (2-D) axial CT image • Candidate 2-D bone lesions identified on sequential axial CT images which demonstrate 2-D projectional overlap were merged to form 3-D candidate lesions or "blobs" • Set of features (lesion shape, density, location) was computed for each resulting 3-D candidate •A committee of SVMs (support vector machines) trained using these features and ground truth segmentation manually defined by experts was used to reduce false positive rate, resulting in final classification RESULTS: As described above, we developed a CAD system for detecting sclerotic metastatic bone lesions in the spine as visualized on CT. Unable to download pictures/images but will be in poster. DISCUSSION/IMPACT: CAD system will increase sensitivity for initial detection of sclerotic metastatic lesions in the spine. Future work could include software development for lesion detection in other skeleletal stuctures. Potential uses: initial lesion detection; lesion localization, characterization and classification; assessment of tumor burden; monitoring treatment efficacy.

Keywords: Computer-aided detection; CT; sclerotic lesions; bone metastasis; quantitative analysis;

Poster Session: A - Poster #: 16

Real Time Intraoperative Monitoring of Blood Loss with a Novel Tablet Application

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Introduction: Visual estimation and negotiation between the surgeon and anesthesiologist remain the standard of care in estimating intraoperative blood loss, yet they are demonstrably inaccurate. Real-time monitoring of blood loss intraoperatively is critical in fluid management and blood transfusion decisions given that hemodynamic signals and hemoglobin (Hb) measures are confounded by the body's compensation and the variability of intravascular hemodilution due to acute bleeding and fluid administration. The study goal was to assess the accuracy of a novel system for real time intraoperative monitoring of Hb loss on laparotomy sponges during joint arthroplasty where the incidence of both bleeding and transfusion is clinically significant. Methods: 51 patients in a consecutive series of joint arthroplasty and orthopedic trauma surgical cases were enrolled in this accuracy study. The novel system was used to measure Hb loss (g) and blood loss (mL) as sponges were removed from the surgical field intraoperatively. The novel system's measures were compared with a reference standard (mechanical rinsing and Hb assay) using linear regression and Bland Altman analysis. The new system's measures of blood loss were compared with the gravimetric method using regression, Bland-Altman analysis, and a paired t-test. Results: A strong positive linear correlation (r = 0.92 [95%CI 0.86 to 0.95) was observed between the novel system's measures and the reference standard. Bland-Altman analysis revealed a bias of 6.4 g [95% CI 4.7g to 8.2 g] Hb per patient and 95% narrow limits of agreement of -5.6 g to 18.5 g Hb per patient, compared to the reference method. Conclusion: The novel system demonstrated a significant accuracy improvement over current methods and may provide an easy and user-friendly objective metric for use in fluid management and surgical quality improvement in orthopaedic surgical procedures.

Keywords: blood loss; Joint Arthroplasty; Tablet application;

Poster Session: B - Poster #: 17

Hypothermic Pelvic Cooling Measured by Real Time MRI Imaging prior to Robot assisted Radical Prostatectomy (RARP); Feasibility and Implications.

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OBJECTIVE This study is an innovative application of Thermal MRI imaging as a feasibility method for maximization of improved clinical outcomes of Hypothermic Endorectal Balloon (ECB) in radical prostatectomy (RP). The effective depth and spread of hypothermic cooling was quantitatively mapped by thermo MRI to assess the dispersion and drop in temperature in pelvic tissue and to potentially reduce inflammatory cascade in potency neurovascular bundles (NVB) in men. METHODS Three subjects, prior to undergoing RARP, were cooled via an ECB, rendered MRI compatible by removing metal components for patient safety (HS2012-8392). Prior to cooling hypothermia, anatomic MR images identified the pelvic structures, and measured simultaneously at 3T scanner using 29, 3-mm thick axial slices matched to that of anatomical T2w but with 46-cm FOV and in 256x256 image matrix; the sequence is based on Philips' multishot EPI (echo planar imaging) with TR/TE=48/16 (ms), flip-angle at 20-degree and NSA=2 ('number of average'); the sequence was performed repeatedly during the cooling experiment with 76-sec temporal resolution while the phase data were collected using an integrated MR-HIFU workstation (Sonalleve, Philips) for processing temperature changes in real time. RESULTS A temperature drop of 20-25 degrees was achieved after an initial time delay of 10-15' for the ECB to cool. Anatomic images of the prostate and NVB and demonstrate cooling at this interface of 10-15 degrees, and that cooling extends into the prostate itself ~ 5 degrees, and disperses into the pelvic region as well. CONCLUSIONS Using a cooling balloon modified for MRI compatibility, we have demonstrated an effective method to measure the impact of a novel ECB balloon on NVB and surrounding structures and potentially useful to visualize the effectiveness of hypothermic saturation in other urologic tissue regions as well.

Keywords: radical prostatectomy; prostate cancer; MRI; hypothermia;

Poster Session: B - Poster #: 18

Designing a web-based cognitive behavior therapy program for treatment of patients with tinnitus

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OBJECTIVES/SPECIFIC AIMS: The aim of this project was to design and develop a cognitive behavioral therapy (CBT) program for tinnitus patients via a telemedicine approach. METHODS/STUDY POPULATION: A multidisciplinary group with otolaryngology, psychiatry, and software engineering formed in order to conduct this project between UC Irvine and Camp Pendleton. A thorough search of the literature on tinnitus and CBT was performed by team members using reference textbooks and PubMed and special keywords (tinnitus, CBT, web or internet based, software, application, meditation). The results were analyzed and the structure of the application was designed. HTML web page format was chosen for the platform as it can be accessed on any device and operating systems. RESULTS / ANTICIPATED RESULTS: This web based application is divided into eight modules that will take 8 weeks to be completed by the patient. Patients are given unique usernames and passwords. Once logged in, they should take surveys that screen them for anxiety, stress, PTSD (Post Traumatic Stress Disorder), and depression. This design enables care providers to manage or monitor patients remotely. Every week patients will go through the educational materials and do exercises. In addition, patients are given different meditation exercises each week. Separate modules for tinnitus education, feelings, thoughts, emotional processing, sleeping, physical activity, changing negative thoughts, thought restructuring, and reduction of worries and stress as well as body scan, mindful breathing and find your breath medication exercises exist in the program. DISCUSSION/SIGNIFICANCE OF IMPACT: CBT for tinnitus via a telemedicine approach enables care providers to better monitor their patients and may eventually lead to significant improvement in patient management. Clinical studies of this web-based CBT for tinnitus program are on the way.

Keywords: Tinnitus; Cognitive Behavior therapy; Telemedicine;

Poster Session: B - Poster #: 19

Testing of Methods to Promote Compliance in Self-Monitoring of Blood Glucose

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Self-monitoring of blood glucose (SMBG) provides data on how a diabetic patient's blood glucose levels fluctuate during the course of the day, allowing a healthcare provider to design an appropriate treatment regimen. Unfortunately, patients do not always follow the prescribed SMBG testing regimen. Noncompliance has been reported to be a particular issue among ethnic minorities and among those with limited English proficiency. Thus, we performed our study through the community health clinic at Share Our Selves (SOS), which is located near UC Irvine in the city of Costa Mesa and serves an uninsured population. We tested two approaches to improving patient compliance in SMBG. The first was the use of pain-free lancets to reduce the physical discomfort of the SMBG procedure. The second approach was a financial incentive of up to $50 for completing 2 glucose readings per day over a course of 31 days, while using standard lancets. A third group of subjects received standard lancets with no financial incentive and served as the control population. 60 subjects were enrolled in the study, with 20 subjects in each experimental cohort. Data was successfully collected from 50 subjects, while 10 subjects did not return their glucometers. Overall patient compliance was poor, with an overall average of only 32 ± 3 successful readings out of 62. No statistically significant difference was observed in patient compliance between the three experimental cohorts. On average, the group with the financial incentive did record the most readings, however the difference was only slightly greater than the control group, while the group with the pain-free lancets actually recorded the fewest readings. Again, in all cases, the differences were too small to be statistically significant. In conclusion, our limited study did not show that the use of pain-free lancets or financial incentive were able to achieve a significant improvement in patient compliance in an uninsured patient population.

Keywords: diabetes; glucose monitoring; patient compliance;

Poster Session: B - Poster #: 20

Implantable Continuous Lactate Sensor For Critical Care Medicine

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Objective: Increasing Lactate (or Lactic Acid) levels have been shown clinically to indicate early treatments associated with critical care including hemorrhagic shock, cyanide poisoning, hypoxia, and septic shock. However, frequent monitoring by current methods is not feasible in the field or critical care. Consequently frequent lactate measurements are not made, resulting in increased incidents of system-wide organ failure and death. The solution is "hand-free" continuous real-time monitoring of lactate with built in alarms to alert the clinical staff to changes in lactate levels. Methods: We have developed a small wireless Continuous Lactate Monitor (CLM) subdermal implant tested in rabbit models of cyanide poisoning. Sensors are fabricated using scalable processes amenable to roll-to-roll manufacturing. The wireless CLM is interrogated through the skin using light. In vivo CLM signals from cyanide poisoning/recovery and hemorrhage models in rabbits are related to blood lactate. Results: CLMs were fabricated, calibrated and implanted in rabbits. CLM values correlate strongly with blood lactate as levels rise following I.V. injection of cyanide. In cases where a rabbit recovers, CLM values precede falling blood lactate by as much as 20 minutes. Conclusions: We confirm the wireless capabilities of the CLM where the subdermal implant is interrogated through the skin using light. In vivo experiments validate the CLM as means to provide continuous measurements reflective of blood lactate levels with the additional benefit of preceding the blood during recovery. Our CLM technology will be instrumental during triage and critical care as an early warning/alarm of impending shock. We are currently designing clinical studies and pursuing translation to commercialization. Acknowledgements: Air Force Office of Research (FA9550-10-1-0538)

Keywords: Lactate; Biosensor; Optical; Critical Care;

Poster Session: B - Poster #: 21

Oxygen Permeability Characterization Of Clinical Uplvm Alginate Used For Islet Cell Encapsulation

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Objective: Encapsulated cells often have low viability, resulting from low oxygenation in the implant site, together with reduced oxygen diffusion arising from distance from the capsule surface to the cells inside, creating hypoxic and anoxic core.However, direct measurement of oxygen levels within encapsulated devices has not been reported, and it is yet unknown that hypoxia is the primary cause of cell death. Here, we are reporting a method of measuring oxygen within alginate capsules in vitro and in vivo non-invasively. Method: Oxygen-sensitive microparticles were fabricated comprising an oxygen-sensitive dye embedded within a polystyrene matrix. 3% UPLVM alginate (Novamatrix) beads containing oxygen sensors were made using encapsulator machine (Nisco), cross-linked by 120 mM CaCl2 (J.T Baker). We measured oxygen content of the beads by feeding different percentage of oxygen gas to multi-well plates containing the encapsulated probe in vitro. Encapsulated probes were then implanted subcutaneously in rat (Sprague-Dawley), exposed to different percentages of oxygen for breathing gas, and then partial pressure of oxygen within the capsules were measured at various times post implant. Results: In vitro results indicate that capsules are highly permeable to oxygen and are sensitive to oxygen levels throughout the clinical range. In vivo readings performed at various time-points post implantation show that the oxygen content within the implanted capsules changes as the implant site heals, and the dynamic delay between blood oxygen content and bead oxygen content also changes over time. Significance of impact We have developed a technique for measuring the oxygen concentration continuously inside an implanted capsules .This measurement could have implications for identifying designs that lead to either cell survival or cell death. By knowing the amount of oxygen within capsules, one may be able to correlate that level with critical points in the wound healing process.

Keywords: Oxygen probe; Hypoxia; Cell encapsulation; Oxygen concentration in vivo; angiogenesis;

Poster Session: B - Poster #: 22

Investigation Of Visceral Pain-Related Visceromotor Reflex And Urodynamic Changes In Mice With Bladder Tumor

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Objective: A UPII-mutant H-RAS transgenic mouse model of urothelial cancer has been used for preclinical testing for treatment of urinary bladder cancer. However, visceral pain and the urodynamic changes have not been investigated while the bladder tumor is developing. This study examined the visceral pain-related visceromotor reflex (VMR) and the changes of urodynamic recordings in both wild type and transgenic mice. Methods: 3 female wild type and 8 transgenic female (n=5) and male (n=3) mice were used. A PE-50 tubing was inserted into the bladder dome. Then a tubing was connected to a pressure sensor to obtain bladder pressure. Left external oblique muscle was exposed and embedded with wires to obtain VMR during voiding. In addition, the external urethral sphincter (EUS) activity was also obtained in female and male transgenic mice to investigate the sex differences on voiding function with bladder tumor. Results: In female transgenic mice, voiding frequency and peak bladder contraction had no significant change, but resting pressure and voiding threshold significantly increased compared to wild type mice. VMR amplitude and duration had significant increase in transgenic mice compared to wild type mice. Female transgenic mice had significantly stronger VMR amplitude and longer VMR duration whereas male transgenic mice showed larger EUS amplitude and shorter EUS duration during voiding. Discussion: Increase of resting pressure and voiding threshold in transgenic mice showed the bladder tumor resulted incomplete voiding. Increase of visceral pain-related VMR may indicate the transgenic mice suffer from visceral pain while the bladder tumor develops. Stronger EUS activity during voiding helps bladder emptying and amelioration of visceral pain. In summary, the UPII-mutant H-RAS mouse model is suitable to investigate the changes of urodynamic recording and the level of visceral pain during the formation of bladder tumor. Sex differences should be seriously considered.

Keywords: bladder; electromyography; external urethral sphincter; visceral pain;

Poster Session: B - Poster #: 25

Wireless-Based, Portable Low-Cost Screening For Oral Cancer By Basic Healthcare Personnel

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Background- Oral cancer causes >125,000 deaths annually. Treated early, 5-year survival =80%. However, approximately 75% of oral cancers are detected as advanced disease; typical 5-year survival rate is <20%. A critical need for early detection exists; there is no simple, low-cost, non-surgical means of screening for oral neoplasia, especially in remote regions. Purpose- To develop a low-cost, portable wireless networked device, usable by mobile healthcare workers in high-risk countries for early detection of oral cancer. Specifically to develop an inexpensive, small, robust portable diagnostic system for oral cancer based on Optical Coherence Tomography (OCT), set up the necessary infrastructure for wireless-networked use in India and identify its diagnostic efficacy. Methods- Existing OCT technology was completely re-engineered and a simple diagnostic algorithm indicating further diagnostic and treatment needs for each lesion developed. Ex vivo and in vivo imaging data were obtained and compared with conventional histopathology to determine diagnostic accuracy. Patients will be recruited and imaged in the field. Images are uploaded to a third party wireless system (Dropbox), which automatically synchronizes via Drobo system on both ends. Images are read at UCI or MSCC for clinicopathological follow-up. Results-A compact, inexpensive, robust, wireless-enabled OCT system was built. A support network with collaborators was developed addressing logistics, data acquisition and data transmission. Diagnostic-quality intra-oral images were successfully obtained. Algorithmic approaches were evaluated for their agreement with histopathology. A simple approach using reflectivity and thickness ratios of superficial anatomical structures provided excellent diagnostic sensitivity (.85%) and specificity (>82%). Conclusion- Using an innovative portable OCT-coupled wireless device and simple diagnostic algorithm, early detection of oral and mucosal epithelial cancers is possible.

Keywords: Cancer; Wireless; Health; OCT Imaging; India;

Poster Session: A - Poster #: 26

Rapid, single bacterial detection from blood using microencapsulated sensors

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The high mortality of blood stream infections is associated with the ineffectiveness and time-consuming process of bacterial detection and treatment. Unfortunately, blood culture, the gold standard for the detection of bacteremia, takes several days to obtain results. New molecular diagnosis methods, such as polymerase chain reaction (PCR), are often not sensitive enough to detect bacteria that occur at low concentrations in blood (1-100 colony-forming unit (CFU)/mL). Moreover, all these techniques are sophisticated and expensive, and therefore not well-suited for routine testing. Therefore, simple methods are urgently needed for rapid and sensitive identification of bacteria in blood, which has the potential to significantly reduce the mortality rate and the cost of medical care associated with blood stream infections. In this study, we have developed a system that detects bacteria in patient blood at single-cell sensitivity within a few hours. Our system integrates bacterium-detecting DNAzyme sensors, which are obtained by in vitro selection, with droplet microfluidics. Our central hypothesis was that the confinement of bacteria in droplets significantly increases the concentration of released target molecules that can be detected by the DNAzyme sensors in a rapid, real-time fashion. Specifically, infected patient blood was mixed with DNAzyme sensor solution, including bacteria lysis buffer, within the microfluidic channel, which was encapsulated in millions of individual picoliter droplets. Because bacteria exist at low numbers in blood, we anticipated each droplet will contain one or no bacteria. DNAzyme sensors fluoresced instantaneously in the droplets that contain bacterium. This rapid detection and early intervention will therefore significantly improve the chances of treating blood stream infections and reduce mortality.

Keywords: Microfluidic; droplet-based microfluidic; bacteria detection; single cell detection; Sepsis;

Poster Session: A - Poster #: 27

Cell type-specific analysis of epigenetic marks in human tissues.

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Objectives: The study of epigenetics involving solid organs has been hindered by the limitation of in vitro cultured cells or whole tissue. In this technology development proposal, we plan to isolate marker-specific cells from the epidermis through immunofluorescence sorting of cells from fixed tissues for Chromatin Immunopreciptiation (ChIP)-seq. We plan to develop the method to analyze histone modification signatures in mice and human skin from a chronic wound front. Methods: The newborn mice epidermal undifferentiated (K5+K10-LOR-), mid-differentiated (K5+K10+LOR- and K5-K10+LOR-) and terminal differentiated (K5-K10+LOR+) epidermal cell populations are sorted and used for ChIP-seq with H3K4me3 (active promoters mark) and H3K27me3 (repressive promoters mark) antibodies. Normal and wound front human skin will be processed by the same method. Results: We successfully sorted the 4 different epidermal populations from mice and are currently accumulating enough cells to perform multiple ChIP-seq experiments. In the mean time, we validated our method by H3K36Me3 ChIP-PCR, demonstrating that the K5+ population has higher fold enrichment in Itga6 gene body and lower fold enrichment in K10 gene body, whereas the ratio in K10+ population is reversed. In the future, we anticipate the H3K4Me3 and H3K27Me3 ChIP-seq will provide us a global view of epigenetic regulation of epidermal differentiation in diseased skin. Discussion: Since the chromatin is fixed immediately before tissue harvesting, the in vivo cell type-specific epigenetic state is preserved. Avoiding the need for transgenic markers, our approach uses endogenous intracellular markers. Our study in chronic wounds may suggest possible biomarkers and treatment targets, and the method may be applied to other skin diseases or tissues that are less tensile than skin. As clinical practice advances towards personalized medicine (PM), this in vivo ChIP technique may be directly applicable to the PM practice of the future.

Keywords: epigenetics; epidermis; wound;

Poster Session: A - Poster #: 28

Quantification Of Melanin In Vivo At Microscopic And Mesoscopic Spatial Scales

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Assessment of human skin in vivo at microscopic and mesoscopic spatial scales offers a way to characterize and understand its structure, function and health. We developed a quantitative approach based on nonlinear optical microscopy (NLOM) and quantitative spectroscopy for assessing the melanin content in human skin in vivo. The spectroscopic technique estimates melanin concentration across a wide field and in deep skin layers, while the NLOM technique provides information about the melanin distribution in the epidermal layers. The complementary abilities of these two optical technologies may be exploited to offer a better understanding of the relationship between melanin production as a response to UV exposure, melanin concentration and skin color. We have employed multi-photon microscopy (MPM) and spatially modulated quantitative spectroscopy (SMoQS) over the full range of Fitzpatrick skin types in vivo to determine melanin content and epidermal layer thickness at the microscopic and mesoscopic spatial scales, respectively. This study involved imaging healthy skin on 12 human subjects (5 males and 7 females) between the ages of 23 and 75 on a sun-exposed dorsal forearm and non-sun exposed volar arm. SMoQS is a quantitative spectroscopic technique that employs spatially-modulated light at multiple spatial frequencies to decouple absorption from scattering over the visible to near infrared range of wavelengths (400-1000nm). By exploiting the higher penetration depth in tissue at longer wavelengths, and by approximating human skin as a two-layer model, SMoQS is capable of determining epidermal thickness and layer-specific chromophore concentrations. Through two-photon excited fluorescence signal from melanin, the MPM was able to provide information about the distribution of melanin across the epidermal layers and also estimation of the melanin volume fraction in different skin types. Cross-sectional “histology-like” MPM images of skin were used to measure the epide

Keywords: melanin quantification; epidermal thickness; multi-photon microscopy; quantitative spectroscopy;

Poster Session: A - Poster #: 29

Imaging-Based Evaluation Of Stem Cell Therapy For Oral Mucositis

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Patients receiving cancer therapies such as chemotherapy, bone marrow transplantation and high-dose radiation therapy to the head and neck may be subjected to mucositis which has a debilitating effect on the alimentary tract (AT). The pathophysiology of mucositis is complex, and therapeutic treatment options remain an area requiring further study. Objective: This study explores the efficacy of Gingival Mesenchymal Stem Cell (GMSC) therapy in preventing and treating patients with chemotherapy-induced AT mucositis. MSC therapy may function in a twofold manner: an immunomodulator to suppress inflammation related tissue injury and a regenerative role to restore epithelial lining, providing a capability for reversing AT mucositis. Methods: In this controlled and randomized study, wild type C57BL/6 mice were administered intraperitoneal (IP) injections of 5-Flurouracil (5-FU), a chemotherapeutic agent, in order to induce mucositis. IP 5-FU was administered at 50 mg/kg/day at regular intervals until mucositis was sufficiently induced. Induction was assessed clinically and subsequently confirmed with the Non-Linear Optical Microscopy (NLOM). Confirmed cases were treated with Phosphate Buffered Saline (PBS) in the control group and with adherent or spheroidal GMSC in the test group. In vivo effects of the GMSCs were mapped using NLOM. Mice were humanely euthanized at day 1, 2, 3, 5, and 7 post treatment injection. The whole tongue was then removed for histological analysis. Results: All of the images illustrated that prior to 5-FU injections, the tongue papillae looked normal, however post 5-FU injections destruction of papillae and surface epithelial layer as well as altered vascularity were discernible. NLOM verified that stem cell treatment caused substantial regeneration of the surface epithelium and papillae, as well as restored vascular patterns, especially with the spheroidal GMSC. This offers a potential form of mitigation for patients undergoing cancer therapies.

Keywords: mucositis; Non-Linear Optical Microscopy; chemotherapy;

Poster Session: A - Poster #: 30

Development of a novel ChIP-based diagnostic assay for FSHD

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Although Facioscapulohumeral muscular dystrophy (FSHD) is reported to have a one in 20,000 incidence, there is great concern that the actual number of affected individuals is significantly higher due to undiagnosed cases (with a likely incidence of 1/7,000). Proper diagnosis depends initially on recognition of clinical signs and symptoms and differentiation of FSHD cases from other muscular dystrophies. Molecular studies have been used to reinforce the clinical impression. The primary approach has been through detection of 4qD4Z4 repeat contraction by pulsed-field gel electrophoresis (PFGE) following restriction digestion. However, this method cannot identify phenotypic FSHD (with no repeat contraction), and certain band patterns can prove difficult to interpret. More recently, DNA hypomethylation at the D4Z4 locus was also found to serve as a diagnostic marker. However, severe DNA hypomethylation was also found in the ICF syndrome cells, and thus is not FSHD-specific. We previously found a specific change in histone modification (histone H3 lysine 9 trimethylation (H3K9me3)) at the D4Z4 repeat sequences that is detected in both FSHD1 and FSHD2 patient cells by chromatin immunoprecipitation (ChIP). Importantly, this change is highly specific for FSHD, and is seen also in patient lymphoblasts from blood samples. Thus, we are testing the possibility that ChIP can be used to detect the loss of H3K9me3 in patient chromatin as a diagnostic method for FSHD in peripheral blood mononucleocytes (PBMCs) from patient blood samples. We believe that the project is highly translational and will provide an important immediate basis for the development of a novel diagnostic test for FSHD.

Keywords: FSHD; heterochromatin; H3K9me3; ChIP; diagnostics;

Poster Session: A - Poster #: 31

Analysis of Phenotype in a Large Cohort of Patients with Prader-Willi Syndrome: Differences between Gender, Molecular Type and Growth Hormone Use

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Prader-Willi syndrome (PWS) is a complex genetic disorder affecting 1 in 10,000 to 1 in 29,000 people of all ethnicities. We studied the differences in PWS phenotype, specifically behaviors and physical features, by gender, molecular type [paternal deletion or maternal UPD], and the influence of growth hormone treatment in a large patient cohort (N=330). Patients were recruited through the Rare Disease Clinical Research Network (RDCRN). There were 146 males (44%) and 181 females (56%). There were no significant differences in the mean age (13.4 y.), BMI (mean 25.4 kg/m2) or behavior problems between the sexes. There were 211 (64%) individuals with deletions and 119 (31%) with UPD. Mean age for those with deletion and UPD was 14.4 years and 11.6 years (p=0.032) respectively. Mean BMI for those with a deletion was 26.2 (SD=10.6) and for those with UPD was 24.0 (SD=9.2) (p=0.058). Statistically significant differences for physical features were found for: hypopigmented hair color (p<0.0005), almond shaped eyes (p=0.031), upslanting eyes (p=0.030), narrow nose bridge (p=0.020), and large thighs (p=0.001), including frequency of skin picking, and other aggressive behavior which were higher in deletions vs. UPD. Sixty-eight percent had received growth hormone treatment (N= 219) at a mean age of 4.6 years (SD=7.2). This study found that growth hormone treatment generally improved physical characteristic of PWS including BMI (p<0.0005). We found decreased frequency of flat occiput, round face, almond shaped eyes, hypotelorism, narrow nasal bridge, thin upper lip, downturned mouth and large thighs. In those treated with GH there was improvement in behaviors (p<0.0005) such as skin-picking, teacher reported attention and aggression in comparison to those who were not on GH treatment. These results expand the benefits of GH treatment and suggest that GH treatment should begin early upon diagnosis of PWS.

Keywords: Clinical Genetics; Genotype-Phenotype Correlations; Uniparental Disomy; Methylation; Dysmorphology;

Poster Session: A - Poster #: 32

The Autism Spectrum Disorders Stem Cell Resource at CHOC Children's: Implications for disease modeling and drug discovery.

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The autism spectrum disorders (ASDs) comprise a set of neurodevelopmental disorders that are, at best, poorly understood but are the fastest growing developmental disorder in the United States. As animal models of polygenic disorders such as the ASDs are difficult to validate, the derivation of induced pluripotent stem cells (iPSCs) by somatic cell reprogramming offers an alternative strategy for identifying the cellular mechanisms contributing to ASDs and development of new treatment options. Access to statistically relevant numbers of ASD patient cell lines, however, is still a limiting factor for the field. Here, we describe a new resource with over 200 cell lines (fibroblasts, iPSC clones, NSCs, glia) from unaffected volunteers and patients with a wide range of clinical ASD diagnoses, including Fragile X syndrome (FXS). We have shown that both normal and ASD-specific iPSCs can be differentiated toward a neural stem cell phenotype and terminally differentiated into action-potential firing neurons as well as glia. The ability to evaluate and compare data from a number of different cell lines will facilitate greater insight into the cause(s) and biology of the ASDs and will be extremely useful for uncovering new therapeutic, as well as diagnostic, targets. Importantly, some drug treatments have already shown promise in reversing the neurobiological abnormalities in iPSC-based models of ASD-associated diseases. The ASD STEM Cell Resource at CHOC will continue expanding its collection and make all lines available upon request with the goal of advancing the use of ASD patient cells as disease models by the scientific community.

Keywords: Autism Spectrum Disorder; iPSC; disease modeling; neuronal differentiation; electrophysiology;

Poster Session: A - Poster #: 33

Variable Clinical Features In 13 Patients With Pompe Disease

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Pompe disease is a lysosomal storage disorder caused by the deficiency of enzyme acid alpha-glucosidase (GAA) which results in accumulation of glycogen particularly in the skeletal, cardiac, and smooth muscles. The late-onset form with symptoms presenting in childhood through adulthood, is characterized by proximal muscle weakness, respiratory insufficiency, and unlike classic or infantile-onset form typically no cardiac involvement. We report our experience with one adolescent and 12 adult patients (3 F/10 M) with Pompe disease at one center. Patients ranged in ages from 18-69 y.(mean 51 y.) and were diagnosed at a range of 11-65 y (mean 37 y.) often after a history of progressive muscle disease of several years duration. Genetic sequencing revealed the common c.-32-13T>G mutation in 11/13 individuals including 3 siblings. Other mutations included: c.1655T>C, c.2238G>C c.2431delC, c.2655_2656delCG, c. 1951-1952delGGinsT, c.925G>A, c.1437+2T>C, c.1445C>G, c.525_526delTG, and c.1935C>A several of which are novel. Associated clinical features included scoliosis and cardiomyopathy in the adolescent, cardiomyopathy in an adult, BiPAP requirement in nine, tinnitus in four, and peripheral neuropathy in one, and one individual was born with partially developed hip and clubfoot. One individual developed an intracerebral aneurysm at the age of 43 y. which was successfully treated with surgery. All patients currently receive enzyme replacement therapy with alglucosidase alfa with different response rates on their muscle weakness, pulmonary function dynamometry, and functional studies. Only one individual developed an infusion reaction which has responded to medication. Our group of patients illustrate the variable range of clinical features and the importance of careful monitoring and early management of complications.

Keywords: Pompe; lysosomal storage disease; enzyme; mutation; muscle;

Poster Session: A - Poster #: 34

Comprehensive Clinical Evaluation In Patients With VCP Disease

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OBJECTIVES- We aim to establish the natural history of the VCP disease from a database of 39 individuals in 8 families harboring three missense mutations, R155H, R155C and R155P. METHODS- 21 affected, 7 presymptomatic carriers carrying VCP mutations and 11 unaffected members (Mean ages- 53.7, 42.5, 52.2 years; M10/F11, M1/F6, M5/F6) were evaluated at UCI. Clinical, laboratory and functional measurements were analyzed. RESULTS- 20 had myopathy, 8 had myopathy and Paget's disease and 1 had myopathy, Paget's and FTD. Average age of onset for myopathy and Paget's disease was 42.85 and 36.12 respectively. Creatinine kinase and alkaline phosphatase levels revealed higher levels in affected than in unaffected individuals and carriers. Affected individuals exhibited significantly lower IBMFRS and significantly higher scores in fatigue rating scale compared to controls ($p=0.001$ and $p=0.023$ respectively). There was a significant positive correlation between IBMFRS and MRC ($r2=0.890$) and a significant negative correlation between IBMFRS and Fatigue rating scale ($r2= -0.386$) ($p= 0.000$ and 0.047 respectively). Hand held dynamometry and biodex measurements revealed significant decrease in bulk or function of the muscles (knee extensors and flexors at 60 degrees; left knee flexors at 180 degrees) in affected individuals compared to traditional MRC scores. The average scores for 6MWT was significantly lower in affected individuals when compared to controls ($p= 0.013$). The mean scores for FVC best and FEV1 best were found out to be significantly lower in affected when compared to carriers ($p= 0.019$ and $p= 0.023$ respectively). Mean scores for PE Volume- Best was significantly lower in affected when compared to controls ($p= 0.002$). FVC best was positively linked to IBMFRS ($r =0.625$; $p<0.05$), MRC scores ($r2 = 0.792$; $p<0.01$). DISCUSSION- This study represents the most comprehensive evaluation of individuals with VCP disease to date which will help increase awareness of this disease.

Keywords: IBMPFD; VCP; Pagets disease of bone; Myopathy; frontotemporal dementia;

Poster Session: A - Poster #: 35

Exon Skipping Of The R155H VCP Mutation In Mice Partially Ameliorates The Pathogenesis Of Ibm

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Hereditary inclusion body myopathy, Paget's disease of bone and frontotemporal dementia (IBMPFD), is a rare, progressive and fatal disease caused by mutations in the VCP gene. The most common feature of this disease myopathy is present in 90% of individuals with an onset typically in the 30s. The progressive muscle weakness often progresses to respiratory failure or cardiac failure that can result in death at 40-60 years of age. Paget's disease of bone is observed in 50% of individuals with an onset in their 30-40s. Frontotemporal dementia is observed in 30% of patients with a later onset of 50s-60s. ALS is seen in 10-15 % of patients with a variety of VCP mutations. The Cre-LoxP system is an extremely powerful approach for generating novel mouse models to study the effect of the VCP disease mutation. The heterozygous knock-in mouse carrying the common VCP R155H/+ mutation in exon 5 with flanking Cre lox sites developed in our laboratory has many of the clinical features of the human disease. AIMS: The aim of the study was to try and ameliorate the disease by excising the mutated allele. METHODS: We crossed our knock-in VCP R155H/+ mutation mouse model with the ubiquitously expressing Tamoxifen (TM) -inducible R26CreER mouse model. Cre-mediated excision of the mutation carrying exon 5 was induced by treating the pregnant mice with Tamoxifen at 0.12 mg/g body weight by oral gavage at E.6.75 once. Pups were monitored on a weekly basis and weight measurements were taken. We characterized these animals by monitoring the progression of muscle pathology, strength, and biochemical assays up to the age of 15 months. RESULTS: There was improvement in muscle strength by grip strength testing in the Cre-Tamoxifen inducible VCP mutant mice. Quadriceps muscle from VCP R155H/+ treated mice showed improvement in histology and TDP-43, ubiquitin and autophagy pathology. DISCUSSION: This discovery provides the opportunity to develop a promising therapeutic strategy for patients.

Keywords: Cre-LoxP; exon skipping; myopathy; Paget; Dementia;

Poster Session: B - Poster #: 36

Penetrating Keratoplasty Performed With Femtosecond Laser Zig-Zag Incision: Suture-Pattern Comparison and Suture-Out Results

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Purpose: To report visual and astigmatism outcomes in patients who underwent zig-zag femtosecond laser enabled keratoplasty (FLEK) with subsequent full suture removal. To evaluate the effect of suture pattern on suture-out endpoints. Methods: Retrospective study at a referral academic practice evaluating uncorrected and corrected distance visual acuity (UDVA, CDVA) as well as manifest (Mrx cyl) and topographical (Topo cyl) astigmatism. 108 eyes underwent suture removal; data are presented for the 83 eyes estimated to have good visual potential (> 20/30). Suture patterns included: running (R) (N=58), interrupted (I) (N=19), combined (C) (N=7). Results: Full suture removal occurred on average 1.2 years [standard deviation 0.7] after FLEK. The pre vs post suture removal values were significant only for CDVA (showing improvement): UDVA from mean LogMar 0.74 [SD 0.45] to 0.68 [SD 0.45] (P=0.687), CDVA from 0.28 [SD 0.22] to 0.23 [SD 0.19] (P=0.024), Mrx cyl from 3.57 [SD 1.83] to 3.48 [SD 2.12] (P=0.906) and Topo cyl from 5.33 [SD 3.83] to 5.71 [SD 5.41] (P=0.547). No significant difference in outcomes were found between the different suture patterns in mean LogMar UDVA (R=0.72 [SD 0.47], I=0.82 [SD 0.41], C=0.66 [SD 0.48]), CDVA (R=0.24 [SD 0.18], I=0.41[SD 0.28], C=0.29 [SD 0.19]), Mrx cyl (R=3.15 [SD 1.76], I=4.58 [SD 1.47], C=4.04 [SD 2.39]) or Topo cyl (R=4.73 [SD 3.82], I=7.18 [SD 3.60], C=4.82 [SD 3.25]) (P>0.05 for all suture type comparisons). Conclusion: The zig-zag FLEK incision results in good vision and astigmatism after suture removal. Suture pattern did not statistically influence final suture out results although group sizes were asymmetric.

Keywords: Corneal Transplant; Astigmatism; Femtosecond Laser;

Poster Session: B - Poster #: 37

Visual Consequences Of iPad Use: A Pilot Study

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Background: With the increasing prevalence of electronic readers for vocational and professional use, it is important to discover if there are consequences in the consumption of these products. There are no studies in the literature quantifying the incidence or severity of eyestrain, nor the clinical characteristics that may predispose to these symptoms with electronic tablet use. Purpose: The primary objective of this pilot study is to assess the degree of eyestrain associated with iPad use compared to traditional paper format. The secondary outcomes of this study is to assess the rate of eyestrain associated with iPad use and identify any clinical characteristics which may be associated with the development of eyestrain. Methods: 41 students were randomly assigned to two groups (book/iPad). Participant posture, luminosity of the room and reading device were measured during a one hour reading session for both groups. At the end of the session, questionnaires were administered to determine symptoms. Results: Fisher's exact test statistical analysis found higher rates of eyestrain ($p=0.008$) and irritation ($p=0.011$) among the iPad group. There was no difference in rates of burning ($p=0.33$), dryness ($p=0.21$), eye pain ($p=0.23$), sensitivity to ambient lighting ($p=0.33$) and tired eyes ($p=0.70$) between the two groups. Conclusion: Reading on iPads may induce increased levels of irritation and eyestrain and further studies into predisposing factors and etiology are necessary.

Keywords: eyestrain; asthenopia; ocular complaints; computer vision syndrome; electronic readers and tablets;

Poster Session: B - Poster #: 38

Retinal progenitor cells for treatment of retinitis pigmentosa

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The clinical goal of this project is the transplantation of allogeneic retinal progenitor cells (RPCs) of human fetal origin to the vitreal cavity of patients with retinitis pigmentosa (RP), an incurable blinding disease. RP is genetic in nature. It is a photoreceptor degeneration with onset earlier and phenotype more severe than age-related macular degeneration (AMD). The initial loss of rods is a prelude to the subsequent loss of cones which culminates in total blindness since photoreceptors are CNS neurons and are not spontaneously regenerated. The therapeutic mechanism of action of RPCs involves trophic-mediated neuroprotection of host photoreceptors and reactivation of dysfunctional cones by the graft, resulting in improved vision. This has been demonstrated in dystrophic RCS rats at the anatomical, behavioral, and electrophysiological levels. Human donor tissue has been obtained under GTP conditions and maternal blood is routinely screened for adventitious agents. Human donor RPCs have undergone a wide range of tests including sterility, karyotype, marker expression, freeze-thaw viability, in vitro and in vivo tumorigenesis, biodistribution, and in vivo dose range. hRPCs have been grown and banked under GMP conditions using serum-free, xeno-free media. The product has been designated as an orphan drug by the FDA for treatment of RP. Ongoing work is directed towards the completion of all IND-enabling preclinical studies and the initiation of clinical trials in RP. There is much to recommend this approach, including simplicity, safety, and most of all the potential for a striking degree of stem cell-mediated efficacy in an untreatable blinding disease. Acknowledgements: The authors are grateful for funding from CIRM, the Lincy Foundation, Discovery Eye Foundation, the Polly and Michael Smith Foundation, and the Andrei Olenicoff Memorial Foundation. This work was conducted in partnership with NIH National Center for Advicing Translational Sciences.

Keywords: human retinal progenitor cells; retinitis pigmentosa; cell therapy; IND-enabling preclinical studies; orphan drug designation;

Poster Session: B - Poster #: 39

Home Pressure And Volume Measurement As A Screening Instrument To Identify Patients With Safe Intravesical Pressures: A Prospective Validation Study

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Purpose: We had clean intermittent catheterization (CIC) dependant patients use a simple ruler-based manometer to measure their intravesical home pressures prior to leakage or prior to scheduled drainage at home. These patients and their families generated a bladder pressure and volume diary (PVD). The aim of this study is to evaluate the ability of PVD to identify patients at low risk for having high bladder pressures measured during urodynamic study (UDS). Methods: We prospectively collected clinical, urodynamic, and home PVD data in children with spina bifida. Patients were asked to use a ruler to measure the height of the column of urine within the CIC catheter, with the zero centimeter mark at the urethral meatus in females and at the penoscrotal angle in males. Measurements were taken in the supine position with relaxed abdominal muscles. We defined abnormal intravesical pressures as Pdet pressures above 30cmH2O as measured by UDS. ROC Curves were plotted to correlate different PVD variables with abnormal intravesical pressures. Results: 30 children with spina bifida were included in the study. Mean age was 10 years (range 1-20 years). Home pressures measured at maximal CIC volume and mean PVD pressures were found to be the most reliable variables to predict UDS pressures above 30cmH2O [AUC 0.93(p=0.001) and AUC 0.87 (p=0.02) respectively]. Home pressure measured at maximal CIC volume below 20cmH2O was associated with normal bladder pressures (UDS pressures below 30cmH2O) with sensitivity of 100% and specificity of 80%. Conclusion: Home ruler pressure below 20 cmH2O provides a reliable measurement of safe bladder pressures. PVD is easy to perform, and is useful to monitor and screen bladder pressures of patients already performing CIC at home with no additional morbidity or cost. Patients with low pressures on PVD may be followed without multichannel UDS.

Keywords: Home pressure; Intravesical pressures; Screening instrument;

Poster Session: B - Poster #: 40

Endoscopic Correction Of Vesicoureteral Reflux Simulator Curriculum As An Effective Teaching Tool: Construct Validation Study

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Objective: Endoscopic bulking agent injection is a 1 to 2-minute, highly confined procedure with little room for adjustment, intra-operative correction, or revision. In this study we aim to demonstrate that this simulator curriculum of a porcine bladder simulator model for training and assessment of the surgical skills for the endoscopic correction of vesicoureteral reflux (VUR) is able to improve the performance of the surgeon carrying out the procedure. Methods: We developed a porcine bladder model placed in a training box. Dextranomer/Hyaluronic Acid (Dx/HA) syringes and needles were used. Lubricant gel was utilized to simulate Dx/HA consistency. After theoretical and hands-on demonstration of the surgical technique, trainees at different levels of expertise were asked to perform a cystoscopy, a submucosal injection, a subtrigonal injection, and a double-hit injection. Training was performed for two hours. Each trainee injected eight ureteral orifices. Each step of the first and last injection were evaluated by a single examiner (AK) using a detailed questionnaire. Paired T-Test was used to demonstrate significant performance improvement between the first and last injection of each part of the procedure. Results: 5 residents and 1 fellow participated in the study. Overall, the simulator curriculum demonstrated a significant improvement in performance between the first and last evaluation (56% to 92%; p=0.008). Specific parts of the procedure that showed significant improvement ($p<0.05$), were: ureteral orifice identification, ureteral orifice hydrodistention, 1st and 2nd injection, as well as location size and depth of the mound after injection. Conclusion: Dx/HA Endoscopic Injection Simulator is an effective teaching tool to improve the performance of the surgeon carrying out the procedure. This teaching curriculum may shorten the early learning curve and provide a greater understanding of the technical components of successful endoscopic VUR correction.

Keywords: training simulator; vesicoureteral reflux; endoscopic correction;

Poster Session: A - Poster #: 41

Success of Lumbar Puncture After Using Ultrasound to Find Landmarks

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A possible solution to address the setbacks of the traditional Lumbar Puncture(using the palpation method) is the incorporation of an ultrasound to help identify pertinent anatomical landmarks. The goal of the research study is to determine the efficiency and success of ultrasound guided lumbar punctures and compare this method to that of the traditional method of lumbar punctures guided by palpation. By using an ultrasound along the spinal vertebrae before the lumbar puncture, it is hypothesized that there will be a reduction in the number of reinsertions and redirections of the needle used to complete the procedure, a reduced procedure length, and a decrease in the red blood cell counts within the cerebrospinal fluid. Research associates will routinely screen for patients who exhibit the chief complaints of nausea, vomiting, fever, or headaches. These chief complaints are among the common symptoms felt by those diagnosed with meningitis and subarachnoid hemorrhages; therefore, patients exhibiting these symptoms have a chance of receiving a lumbar puncture (LP) procedure. Prior to the LP procedure, the physician and the research associate shall inform the patient of the purpose of the study and allow the patient to decide whether to participate or not. If the randomization of the two different methods fits with the physician's course of action when completing the spinal tap, the patient will be enrolled. The research associate will collect data on the length of the procedure, the number of reinsertions/redirections, as well as the RBC count of the patient. The results are currently still in progress. It is anticipated that ultrasound guided lumbar punctures will result in less reinsertions/redirections, decreased wait time, and less trauma done to the patient. The anticipated results would increase the accuracy of patient diagnoses and would also lead to an overall better quality of care for the patient by reducing the procedure length and discomfort.

Keywords: Lumbar Puncture; Spinal Tap; Ultrasound; Palpation;

Poster Session: A - Poster #: 42

Are Ultrasonographically Obtained Common Bile Dict Measurements In Emergency Department Patients With Symptomatic Gallstones Useful?

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The benefits of ultrasound are becoming clear to many physicians, having this diagnostic procedure become implemented as a standard of care for many hospitals. However, while current medical students may find themselves on an ultrasound rotation, current physicians have most likely missed this opportunity, having to learn how to utilize an ultrasound after their formal training. This can become an issue in implementing ultrasound as a standard of care because physicians may be less inclined to utilize ultrasounds due to inexperience and inability to dedicate time to become trained. However, one can promote the usage of ultrasound by making the procedure more simplified. This is exactly what our prospective study aims to achieve; we aim to effectively reduce the complexity associated with Right Upper Quadrant ultrasounds (RUQ) by determining whether or not the visualization, and measurement, of the common bile duct is necessary in patients with normal total bilirubin and alkaline phosphatase labs. We predict that the measurement of the common bile duct in patients with normal labs will be of limited clinical utility, allowing this parameter to be eliminated from future RUQ ultrasounds. Data was collected from adult patients who have a RUQ ultrasound ordered at the University of California, Irvine Medical Center emergency department. Data was collected from research associates who work in the emergency department every day from 8am-12am. At this time, we have analyzed a preliminary sample size of 23 patients, but have no statistically significant results regarding the correlation between the common bile duct diameter and final diagnosis for patients with normal lab values. However, additional data is currently being analyzed. If our hypothesis is supported, then the complexity of this procedure will dramatically decrease, enabling us to decrease the time it takes to learn and perform this exam, making ultrasound as a standard of care for this procedure more enticing.

Keywords: Ultrasound; Common Bile Duct; Procedure;

Poster Session: A - Poster #: 43

Emergency Department versus Radiology Department Pelvic Ultrasound and Effect on Patient Length of Stay: A Randomized Control Trial

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Intro: Although imaging studies are integral in diagnosing many patients presenting to the emergency department (ED), they often substantially extend patient length of stay (LOS). Bedside ultrasound performed by emergency physicians may yield many benefits including improved patient wait times and decreased overall LOS in the ED. We hypothesize there will be a significant decrease in the time to obtain an ultrasound image and an overall decreased LOS for patients who receive emergency department pelvic ultrasound (EDUS) compared to those that receive a radiology department pelvic ultrasound (RDUS). Methods: This is a prospective randomized clinical trial for 330 patients presenting to the ED requiring pelvic ultrasound imaging. Consented patients are randomized to EDUS on even days and RDUS on odd days. Time taken to obtain the ultrasound and total time spent in the ED are measured for each patient. Results: Fifty-four patients have been enrolled in the study from which 26 have been randomized to EDUS and 28 have been randomized to RDUS. The average time to perform pelvic ultrasound in the ED was 5.8 minutes while the average time to obtain pelvic ultrasound through radiology was significantly longer at 76.4 minutes ($p < 0.0001$). The average total time patients spent in the ED for EDUS was 219 minutes while the average total time patients spent in the ED for RDUS was significantly longer at 314 minutes ($p = 0.02$). Conclusions: Preliminary results show a statistically significant reduction in both time to obtain pelvic ultrasounds and total time spent in the emergency department for EDUS compared to RDUS. These initial results suggest that pelvic ultrasound performed at bedside by Emergency Physicians could positively impact patient care by reducing time to diagnosis, patient wait time and length of stay in the ED.

Keywords: ultrasound; pelvic; emergency; patient length of stay;

Poster Session: B - Poster #: 44

Diffuse optical spectroscopy probe for therapy monitoring in colorectal cancer

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Colorectal cancer (CRC) is the second most common cause of cancer death in the western world, with a high lifetime incidence of 6%. The optimization of surgical techniques, introduction of neoadjuvant therapies and recent developments in diagnostic imaging modalities, contributed to the significant decrease of the mortality by 20% in the last years. Diffuse Optical Spectroscopy (DOS) is a noninvasive technique that is commonly used to provide biochemical information on hemoglobin, bulk lipids and water concentration by measuring tissue absorption and reduced scattering coefficients in the Near-Infrared range (NIR) (650–1000 nm). DOS rapidly provides quantitative, functional information about tumor biochemical composition. In previous pilot studies on breast cancer chemotherapy monitoring, DOS has shown promising results in predicting tumor response before any neoadjuvant chemotherapy treatment and as early as one day after the start of therapy. However, DOS measurements require the use of a probe able to be in contact with the tissue under investigation to prevent light reflections at the air-tissue boundary. For measurements of tumors close to the outside skin (as in breast), probe size and geometry are relatively unrestricted. Measuring inside the rectum poses geometric and accessibility challenges. In this work we perform a feasibility study to the application of diffuse optical spectroscopy imaging (DOSI) in the rectum. We address the challenges with a design of a rectum probe that can be mounted on a standard 10 mm diameter laparoscope. We built a prototype probe and we were able to recover optical properties on both phantoms and colon tissue of Yorkshire pigs.

Keywords: colorectal; cancer; optics; spectroscopy; probe;

Poster Session: A - Poster #: 45

Laparoscopic Versus Open Ileostomy Reversal: Is There An Advantage To A Minimally Invasive Approach

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Purpose Ileostomy reversals are commonly performed procedures after colon and rectal operations. The aim of the study was to compare outcomes of laparoscopic and open ileostomy reversal. Methods 133 consecutive patients undergoing ileostomy reversal at our institution between June 2009 and August 2013 were analyzed using a retrospective database. The cohort was comprised of 79 laparoscopic and 54 open cases. The data was analyzed for operative characteristics, postoperative outcomes and 30-day morbidity and mortality. Statistical analysis was done using Chi square test, student t-test and Fischer's test where applicable. Results The two groups had comparable ASA scores, BMI and gender distribution. The laparoscopic group had a significantly longer duration of surgery (109 versus 93 minutes, p=0.03); however performed more lysis of adhesions (59% versus 26.5%, p=0.0001) and completed more hernia repairs (32.7% versus 7.6%, p=0.0002). The laparoscopic group included 43 (79.6%) extra-corporeal and 11 (20.4%) intra-corporeal anastomoses. The majority of wounds were closed by purse string in both open and laparoscopic cohorts (86% and 85% respectively). There was no significant difference in estimated blood loss (31 versus 39 ml) or median length of stay (4.0 versus 4.0 days). Post-operative outcomes studied included readmission rates, urinary retention, urinary tract infections, bleeding, ileus, sepsis, cardiac complications, surgical site infections (SSI) and overall mortality and morbidity. Superficial and deep SSI together were significantly higher in the open cohort (8.8% versus 0%, p=0.04). No significant difference was noted in any of the other variables, including organ space SSI, and no mortality was noted in either group. Conclusion Laparoscopy is safe and effective in ileostomy reversal, with potential benefits in terms of concomitant hernia repair, lysis of adhesions and lower wound infection rate. The possible drawback is a longer operating time.

Keywords: Ileostomy; Laparoscopy; Colorectal Surgery; Reversal; Lysis of Adhesions;

Poster Session: B - Poster #: 46

Managing Complications After Bariatric Surgery: Outcomes Of Laparoscopic Intervention

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Introduction: With obesity rates continuing to rise in the United States, the volume of bariatric operations has been exponentially increasing. A natural consequence of this has been a growing number of revisional surgeries being performed for the management of complications. The objective of this study was to analyze outcomes of laparoscopic intervention for the management of complications after bariatric surgery. Methods & Procedures: A retrospective review of data collected from an academic medical center between 2003 and 2013 was performed. All patients who underwent laparoscopic surgical intervention for the management of a complication after bariatric surgery were included. The efficacy of the intervention and its associated perioperative morbidity and mortality were analyzed. Minimal duration of follow-up was 30 days. Results: 91 consecutive patients who underwent laparoscopic surgery for obstruction (52.7%), bleeding (15.4%), abdominal pain (18.7%) and leak or band erosion (13.2%) were identified. Initial bariatric procedures included gastric bypass (58.2%), band (27.5%), sleeve (8.8%) and vertical banded gastroplasty (5.5%). There were no conversions to open laparotomy. Average estimate blood loss was 25 cc and two patients required a blood transfusion. Three patients (3%) were monitored in the Intensive Care Unit postoperatively. Mean overall duration of hospital stay was 4 days. The efficacy of the reoperation procedure was 100% for obstruction, bleeding, and abdominal pain. However, the efficacy of laparoscopic revision after leak was 80%, with 20% of patients developing a persistent leak requiring additional stent placement. Overall morbidity of laparoscopic intervention was 4.4%. Complications included stricture, abscess, obstruction and venous thromboembolism. There were no perioperative mortalities. Conclusion: The use of laparoscopic surgery to manage bariatric complications is feasible, safe and effective.

Keywords: Bariatric; laparoscopic; Obesity; obstruction; surgery;

Poster Session: B - Poster #: 47

A Nationwide Analysis of the Effects of Hypoalbuminemia on Outcomes of Colorectal Surgery Patients

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Objective There are limited data examining pre-operative hypoalbuminemia among patients undergoing colorectal resection. We sought to identify outcomes of such patients. Methods The NSQIP database was used to evaluate all patients who had preoperative hypoalbuminemia (serum albumin<3.5mg/dl) before colorectal resection from 2005 to 2012. Multivariate analysis using logistic regression was performed to quantify the association of hypoalbuminemia with postoperative complications. Results We sampled a total of 154,637 patients undergoing colorectal resection (total colectomy, partial colectomy, low anterior resection, abdominoperineal resection, and pelvic exenteration), of which 37,403 (24.2%) had preoperative hypoalbuminemia. The in-hospital mortality rate of patients who had hypoalbuminemia was significantly greater than patients without hypoalbuminemia (11.6% vs. 1.8%, Adjusted OR (AOR): 2.57, P<0.01). Postsurgical complications significantly associated (P<0.01) with hypoalbuminemia were as follows: hospitalization more than 30 days (AOR: 3), ventilator dependency more than 48 hours (AOR: 1.99), unplanned intubation (AOR: 1.86), pneumonia (AOR: 1.66), acute renal failure (AOR: 1.55), cardiac arrest (AOR: 1.54), wound disruption (AOR: 1.42), deep incisional surgical site infection (SSI) (AOR: 1.39), organ space SSI (AOR:1.30), urinary tract infection (AOR: 1.28), and superficial SSI (AOR:1.08). Discussion Hypoalbuminemia is a common preoperative condition in patients undergoing colorectal resection. Patients suffering from hypoalbuminemia were over two times more likely to die following colorectal resection. Postoperative pulmonary complications, especially ventilator dependency, and unplanned intubation also have strong associations with hypoalbuminemia. Large prospective trials should be planned to confirm these findings and to evaluate if intervention in patients with hypoalbuminemia is effective in decreasing postoperative complications.

Keywords: Hypoalbuminemia; Colorectal Surgery; Surgical Complications;

Poster Session: B - Poster #: 48

A Retrospective Study On The Association Between Audit Domain Scores And Demographic Factors, And Readiness To Change Scores In Emergency And Trauma Patients

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Objectives: The Alcohol Use Disorders Identification Test (AUDIT) result is a composite score of three domains of alcohol use: frequency, dependency, and harmful drinking patterns. Studies have analyzed these domains to validate AUDIT as a screening tool, but few have investigated their association with patient demographics. Methods: This retrospective study analyzed AUDIT domain scores in association with age, sex, language, education level, and readiness-to-change scores from adult emergency and trauma patients at a tertiary university hospital between January 2011 and December 2013. We analyzed data from 724 hazardous drinkers using one-way ANOVA testing, two-sample t-tests, and linear regression. Results: Age and sex were associated with drinking frequency: 18-20 year-olds and females scored significantly less than other groups. Individuals with less than high school education, those ages 40-49, and Spanish test-takers demonstrated significantly higher dependency scores than other groups. Ages 18-29 and 65+ were associated with significantly more harmful drinking patterns, and these individuals demonstrated greater willingness to change their drinking habits. “Preventing health problems” and “personal reasons” are associated with higher readiness to change score, even after controlling for education, age, sex, language and domain scores. Discussion: This study demonstrates that certain patient demographics are associated with each domain, and experiencing negative consequences of drinking results in higher readiness-to-change scores. Healthcare professionals can utilize individual domain scores along with these associated factors to create a more targeted approach in brief intervention.

Keywords: Alcohol; AUDIT; Domain Scores; Harmful Drinking; Demographics;

Poster Session: B - Poster #: 49

Comparison Of Institution-Specific Blood Order Schedule To Surgeon'S Recommendations

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Background Blood ordering practices have substantially changed since the introduction of the maximum surgical blood order schedule in 1974. A recent paper published by Frank et al.(2013) provides an algorithm to create an institution-specific blood order schedule in order to improve operating room efficiency and patient safety, as well as decrease costs, as they noted substantial over-ordering of blood products. This algorithm was used to create a blood order schedule for the University of California Irvine Medical Center, and the authors compared this schedule to the preoperative blood ordering practices of the institution's surgeons to determine whether current practices were consistent with blood usage and whether any room for improvement or cost savings might exist. Methods Blood utilization data from 34,214 patients who underwent one of 125 different procedure categories over a 37-month period (1/2011-1/ 2014) at UCI Medical Center were analyzed following the algorithm provided by Frank et al., creating an institution-specific blood order schedule. Current preoperative blood ordering practices were then solicited from 53 surgeons and were compared to this blood order schedule. A financial comparison was made between costs of blood orders for the 30,769 patients when following the blood order schedule and when following the surgeons' recommendations. Results Preliminary data analyzing 84 procedure categories indicates an under-ordering of blood products. This difference would equate to an increase in hospital charges of $791,857 per year when using the blood order schedule compared to the recommendations of the institution's surgeons. Conclusions Preliminary data suggests possible under-ordering preferences by the institution's surgeons, an unexpected finding when compared to those of Frank et al. While costs may increase using the blood order schedule, patient safety and timeliness of blood availability may be improved by implementation of this schedule.

Keywords: Preoperative management;

Poster Session: B - Poster #: 50

Research-Ready Clinical Brain Imaging Data

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Progress in our understanding of brain disorders increasingly relies on the collection of large imaging data sets. To date, our greatest resource, scanners across the US hospital system, has not been used effectively to aid in this endeavor. The use of standardized imaging protocols in the nation's hospital system and the ability to share images across institutions can provide a wealth of data relevant to patient care and research. The greater the standardization of collection, the greater the potential value and utility of the imaging data collected. The projects (1) collects brain imaging data with a standardized Short Imaging Protocol (SIP) for every patient who undergoes a clinical brain MRI scan in the radiology departments at the USC and UCI hospitals and to securely store and manage that imaging data at each institution, and (2) creates a federation across the two institutions to allow for cohort identification and retrieval of images based on subject characteristics. The standard short imaging protocol for this pilot study includes a high-resolution t1-weighted structural scan (~5 minutes), b1-weighted scans for intensity inhomogeneity corrections, and a Diffusion Tensor Imaging scan (~3.5 minutes). In addition, weekly phantom scans to track scanner stability will be performed. The imaging data is pushed from the scanners to virtual machines at each of the institutions that de-identify the imaging data. The de-identified images are stored on separate virtual machines at each of the institutions are used for data federation. An interface allows radiologists and researchers to query, view, and download de-identified images. This project reflects our commitment to creating a Southern California alliance of CTSI sites dedicated to image standardization and sharing.

Keywords: MRI; brain; imaging; translational; clinical;

Poster Session: B - Poster #: 51

Cancer-Tailored Intervention for Pain and Symptoms – A Pilot Study

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BACKGROUND: The majority of children undergoing cancer treatment experience pain and parents report many barriers to pain management. To address this issue, the goals of this two phase study were to: 1) Develop a mobile, tailored, pain management intervention for parents of children with cancer (C-TIPS) and 2) Conduct formative evaluation to assess the likeability and usability of this innovative program. METHODS: Phase I - Development of C-TIPS included collaboration with CalIT2 to create the software content of the application. Parental education material and tailoring questions were generated with a core team of nurses and oncologists. Phase II - Formative evaluation was conducted with 30 parents recruited from CHOC Children's Hospital. Parents participated in focus groups to evaluate C-TIPS using quantitative and qualitative methods. RESULTS: Phase I - C-TIPS is delivered on a computer tablet and includes 4 sections: an intake, training in diaphragmatic breathing, a stress management session using visual imagery and music paired with diaphragmatic breathing practice, and a pain management tutorial. Phase II – Single-sample t-tests confirmed that the ratings on the 0-10 C-TIPS helpfulness scale were significantly greater than the midpoint ("moderately helpful") of the scale (mean=9.33, $t(29)=17.96$, $p<.001$). Similarly, on the usefulness scale, mean ratings were significantly greater than the midpoint ("moderately useful") of the scale (mean=8.97, $t(29)=10.64$, $p<.001$). Parents responded positively to the program, reporting they had learned valuable information that would likely improve their child's pain experience. Parents also positively received the stress training tutorial and reported a significant decrease in stress levels ($t(29)=3.14$, $p = .004$). DISCUSSION: Overall parents found C-TIPS to be highly engaging and useful. A larger scale randomized control trial will need to be conducted in order to further determine efficacy in an outpatient cancer population.

Keywords: pain; pediatric; cancer; technology; mobile;

Poster Session: B - Poster #: 53

Effects of Ethnicity on Health Behaviors of Adolescent and Young Adult Childhood Cancer Survivors

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Objectives: The aim of this study was to compare the effects of ethnicity on health behaviors of AYA childhood cancer survivors. Methods: A cross-sectional cohort study design was utilized to assess the health behaviors of Hispanic (N=49) and non-Hispanic White (N=55) AYA childhood cancer survivors from a single cancer center. Participants completed the Child Health and Illness Profile, Adolescent Edition (CHIP-AE) to assess specific health behaviors: exercise, diet, alcohol and drug use, smoking, and sexual activity. Results: Participants (12-33 years old) reported similar demographic information, with the exception of household income and medical insurance status. Hispanic survivors reported lower household income and were less likely to be insured than their counterparts ($p=0.01$, $p=0.02$, respectively). In terms of health behaviors, Hispanic survivors were less likely to report eating salty foods (8.2%vs.23.6%, $p=0.03$), smoking cigarettes (8.2%vs.25.5%, $p=0.02$), wearing a bicycle helmet (61.9%vs.94.2%, $p<0.01$), and walking more than a mile within the past month (36.7%vs.60.0%, $p=0.02$). There were no group differences in sexual activity, age of first sexual encounter, and use of protection. Ethnicity was a significant predictor for cigarette smoking (OR 4.02, 95%CI 1.03-15.73), alcohol use (OR 3.41, 95%CI 1.32-8.77), wearing a bicycle helmet (OR 7.74, 95%CI 2.25-26.61), and walking more than one mile within the past month (OR 3.42, 95%CI 1.39-8.41), after controlling for insurance status and income. Discussion: Overall, AYA childhood cancer survivors report few adverse health behaviors although ethnic background may influence the development and practice of these behaviors. Hispanic AYA survivors were less likely to report alcohol and nicotine use, however they were also less likely to engage in safety behaviors and exercise, even after controlling for socioeconomic status. Future studies clarifying the mechanisms behind these differences are warranted.

Keywords: health behaviors; cancer survivors; adolescent and young adult (AYA);

Poster Session: B - Poster #: 55

Pain Management At Home In Children With Cancer: A Daily Diary Study

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Introduction: Due to the transition of care of pediatric cancer patients from the hospital to home setting, parents have become largely responsible for children's cancer pain management. Little empirical data exist on parental management of pediatric pain in cancer patients within the home setting; therefore the purpose of this study was to examine parental pain management of children undergoing treatment for cancer using a daily diary protocol. Methods: A total of 45 parent-child dyads were recruited from Children's Hospital of Orange County. Baseline demographic information was collected, including data regarding child quality of life, parent and child anxiety, child temperament, and parental attitudes towards analgesic use for children. Child-parent dyads then completed daily diaries of pain and analgesic administration for 14 consecutive days. Results: More than 50% of children were reported to experience chronic pain. Over the course of the 14-day study period, 40% of children received at least one dose of analgesic medication. Median dose frequency over the 14 days was 0 (IQR = 2.5). Parents who did not administer analgesics reported misconceptions regarding analgesic use for children ($p = 0.04$) and rated their children's quality of life higher compared to parents who did administer analgesics ($p = 0.01$). Children who received analgesics reported lower health-related ($p = 0.01$) and cancer-related ($p = 0.02$) quality of life, and were reported by their parents to be more social ($p = 0.002$) and less shy ($p = 0.01$) compared to children who received no medication. Conclusions: A significant proportion of children receiving outpatient cancer treatment were found to be experiencing chronic pain and receiving suboptimal pain management in the home setting. Improving pain management of cancer patients at home is vital in improving quality of life and decreasing the risk for long-term pain in children.

Keywords: daily diary; pain; pain at home; pain management; pediatric oncology;

Poster Session: B - Poster #: 56

Evaluation Of Perirenal Adipose Tissue Volume As A Predictor Of Renal Cortical Neoplasm Histopathology

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OBJECTIVES: Our previous evaluations of visceral and perirenal adipose tissue (PAT) have shown metabolic activity. Previously we have demonstrated that two-dimensional PAT measurements are associated with more aggressive renal cell carcinoma (RCC) subtypes. In this study, we evaluated total PAT volume as a predictor of renal tumor histopathology. METHODS: We retrospectively evaluated patients who underwent laparoscopic radical or partial nephrectomy for RCN. PAT volume was measured by post-processing of preoperative computed tomography images using Vitrea software (Vital Images, Inc., Minnetonka, MN). Total perirenal space volume was measured by manual contouring. Structures with densities greater than adipose tissue (e.g. kidney, adrenal gland, vessels) were subtracted out using organ segmentation, thereby yielding only a total PAT volume. Demographic, clinical and operative parameters, PAT volume, and their association with tumor histopathology were evaluated. RESULTS: In this pilot analysis, a total of 18 patients were included. There were 7 (39%) men and 11 (61%) women with a median body mass index (BMI) of 26 kg/m2. Median tumor size was 2.5 cm (1.3-6.0 cm), and the median PAT volume was 205.8 cm3. Mean PAT for RCC and benign histopathology was 345.50 cm3 and 92.67 cm3 respectively ($p=0.026$). DISCUSSION: In our preliminary analysis, increased PAT volume is a significant predictor of RCC histopathology over a benign RCN. With improvement in rapid 3D volumetric assessment of radiological data, PAT volume may be more accurate measurement of adipose tissue. Further analysis with more patients is in progress to confirm our initial findings.

Keywords: perirenal adipose tissue; renal cell carcinoma;

Poster Session: A - Poster #: 57

NRF2 Agonist Decreases Colonic Inflammation And Tight Junction Depletion In Rats With Chronic Kidney Disease

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Background: Gut inflammation is prevalent in chronic kidney disease (CKD) and contributes to systemic inflammation via disruption of the epithelial tight junction barrier with subsequent endotoxin translocation. Nrf2 (nuclear factor erythroid 2-related factor 2) is a key anti-inflammatory and anti-oxidative transcription factor that is deficient in CKD. Objectives: Examine effects of a potent Nrf2 activator RTA dh404 on inflammation and expression of tight junction proteins, in the colon of CKD rats. Methods: Sprague-Dawley rats were divided into 3 groups: 1) sham controls (n=5), 2) CKD (n=8), 3) CKD+Nrf2 treatment group (n=8). CKD was induced via 5/6 nephrectomy, and the CKD+Nrf2 group was given RTA dh404 (2 mg/kg/day) via oral gavage x10 weeks. Serum and plasma assays were done at termination of the study, and colon tissues were processed for Western blot, histology and immunostaining. Results: CKD induction resulted in elevated serum creatinine and plasma malondialdehyde (MDA, a marker of systemic oxidative stress). There was histological evidence of colitis with depletion of all 3 key components of the tight junction apparatus via Western blot and immunostaining (zona occludens-1, occludin and claudin-1). The Nrf2 suppressor protein Keap1 was inappropriately elevated in the colon of CKD rats. Treatment with RTA dh404 decreased Keap1 and significantly raised tissue Nrf2 levels, and decreased the inflammatory transcription factor NFkB. Colon from CKD+Nrf2 treated rats had decreased inflammatory and oxidative stress mediators (COX-2, MCP-1, iNOS), and lower plasma MDA levels. Additionally, Nrf2 agonist treatment restored expression of the tight junction proteins occludin and claudin-1 to levels equivalent with sham controls. Discussion: Treatment with a potent Nrf2 agonist decreased colonic inflammation and improved expression of tight junction proteins in CKD rats. There was concurrent decreased systemic oxidative stress.

Keywords: chronic kidney disease; gut inflammation; Nrf2 deficiency; oxidative stress; tight junction proteins;

Poster Session: A - Poster #: 58

Working for the Weekend: The Effect of Cognitive Functioning, Social Support, and the Interdialytic Interval on Disease Self-Management Among Patients on Hemodialysis

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Successful hemodialysis treatments depend largely on the end-stage renal disease (ESRD) patient's capacity for disease self-management. Patients who have greater social support may have more help with medication, fluid, and meals. However, cognitive problems are common among hemodialysis patients, which may decrease their treatment adherence. Cognitive dysfunction (CD) may increase as a function of time since last dialysis, such that patients may be increasingly compromised over the course of the interdialytic interval (IDI), making adherence to fluid and diet restrictions and medication regimens more difficult. Day 2 of the Weekend IDI may be particularly challenging for patients as compared to Weekday IDIs. The aim of the present study was to examine the relationship between social support, cognitive dysfunction, and IDI length. ESRD patients at UCI (N=18; 9=female; Mean Age=44.9 years) were administered a neuropsychological battery and engaged in one week of smartphone-based monitoring in which they reported on their activities, CD, and perceived support approximately 5 times/day. Preliminary results indicate that CD was minimal. It appears that time since dialysis influences both support and CD. Perceived support was slightly higher on IDIs (M=80.16, SD=24.11, Range 0-100) than dialysis days (M=75.04, SD=26.79, t=1.83, p=.069), but did not differ between Weekday and Weekend Day 2 IDIs. On Weekend Day 2, Ps reported CD in 13% of entries, compared to 30% of entries on Weekday IDIs, and CD was significantly lower on Weekend Day 2 than Weekday IDIs for all measures of CD, including reaction time (MDay2=.13, SD=.40; MWkday=.48, SD=.978; t=-3.14, p=.002), trouble thinking (MDay2=.02, SD=.149; MWkday=.31, SD=.65; t=-4.30, p<.0001), and confusion (MDay2=.02, SD=.15; MWkday=.17, SD=.47; t=-2.94, p=.004). These findings may explain differences in treatment adherence among hemodialysis patients and will be useful in developing patient-centered programs to improve dialysi

Keywords: ESRD; hemodialysis; disease self-management; cognitive function; social support;

Poster Session: A - Poster #: 59

Body Mass Index And Mortality In Kidney Transplant Recipients: A Systematic Review And Meta-Analysis

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Background: Higher body mass index (BMI) seems to be linked to survival advantage in maintenance hemodialysis patients. However, it is uncertain if this "obesity survival paradox" is also observed in kidney transplant recipients. Hence, we systematically reviewed the literature on the impact of pre-transplantation BMI on all-cause mortality in this population. Methods: We searched MEDLINE, EMBASE, Web of Science, CINAHL, and Cochrane CENTRAL for relevant studies up to July 2013. Two investigators independently selected the studies using predefined criteria, abstracted the data from the included studies, and independently assessed each study's quality using the Newcastle-Ottawa Quality Assessment Scale. In addition to the qualitative synthesis, we quantitatively pooled the results of the studies with clinical, methodological, and statistical homogeneity. Findings: We screened 7,123 records, from which we included 11 studies in this systematic review and 4 studies in the meta-analyses. In the only study that included children, obesity was linked to higher mortality in children of 6-12 years old. For adults, our meta-analyses indicated that compared to normal BMI, underweight [Hazard Ratio (HR): 1.09; 95% Confidence Interval (CI): 1.02-1.20], overweight (HR: 1.07; 95% CI: 1.04-1.12), and obese (HR: 1.20; 95% CI: 1.14-1.23) levels of BMI were associated with higher mortality. Interpretation: The presence of the obesity survival paradox is unlikely in kidney transplant recipients since both extremes of pre-transplantation BMI are linked to higher mortality in this population. However, multiple studies still suggest that kidney transplantation is beneficial relative to dialysis in each of these BMI subpopulations.

Keywords: Kidney transplantation; Mortality; Obesity; Body mass index; Reverse epidemiology;

Poster Session: A - Poster #: 60

Peritumor Adipose Tissues Of PT3 Clear Cell And Chromophobe Renal Cell Carcinoma Exhibited Enhanced Wnt Activity, Leading To Increased Motility Of Human CCRCC Cell Line CAKI-2

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OBJECTIVES: We evaluated secreted Wnt activity in peritumor adipose tissues (PAT) and a relationship between PAT and clear cell RCC (ccRRC) cells. METHODS: PAT was collected from 73 patients undergoing renal surgery and cultured for 24 hours to generate conditioned media (CM). The effect of PAT CM on the proliferation and migration of ccRCC cell line Caki-2 was measured by MTT assay and Boyden chamber cell migration assay, respectively. In addition, Wnt/ß-Catenin (ßC) activity in PAT CM was examined as induced levels of ßC. The proliferative and migratory responses are expressed as a stimulation index (SI) calculated by dividing the mean number of proliferative or migratory cells of PAT CM-stimulated wells by those of non-stimulated wells. Wnt activity is expressed as a ratio of the ßC level of PAT CM-stimulated cells divided by that of Wnt3a CM stimulated cells. RESULTS: The majority of PAT CMs from ccRCC patients exhibited strong Wnt activity as measured by induced levels of ßC. Compared to PAT CMs from pT1 and pT2, PAT CMs from pT3 ccRCC and chromophobe (ch) RCC resulted in enhanced Wnt activity (mean and SD: pT1, 0.73±0.58; pT2, 0.68±0.38; pT3, 1.12±0.37; chRCC, 1.52). PAT CMs from patients with benign pathology has no significant effect on proliferation and migration of Caki-2 cells. However, PAT CMs from pT3 and chRCC significantly increased the migration of Caki-2 (migratory SIs of pT3 and chRCC are 1.77±0.47 and 1.88 ± 0.96, respectively) with no effect on proliferation (mean SI, SD: pT3, 0.91 ± 0.19; ch, 1.02 ± 0.45). The increased migration of Caki-2 cells is associated with enhanced Wnt activity in PAT CMs. Fuhrman Grades were also associated with increased migration by PAT CMs. Increased tumor size was inversely associated with proliferative Sis. DISCUSSION: These results suggest a potential role of secreted Wnt factors for mediating the interaction between PAT and pT3 and chRCC toward increasing the migration capacity of ccRCC cells.

Keywords: clear cell renal cell carcinoma;

Poster Session: B - Poster #: 61

A structure-function mechanism of rescuing oncogenic p53 mutants using a novel class of small molecules

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The tumor suppressor p53 is an important cell-cycle regulating transcription factor that is mutated in 50% of human cancers. Most of these oncogenic p53 mutations create a single amino acid substitution in the DNA-binding domain (DBD), leading to continued expression of full-length but nonfunctional p53 protein. The most common of these p53 mutations, R175H [Arg at position 175 mutated to His], causes the DBD to become thermodynamically destabilized, losing its DNA-binding activity, and becoming nonfunctional at physiological temperatures. A pharmaceutical that can restore wild-type p53 function to R175H, or any of these single amino acid mutants, could have an enormous impact on our ability to treat cancers with p53 mutations. We identified a class of small molecules which are able to stabilize the R175H DBD and G245S DBD (another oncogenic mutation) in vitro and induce p53R175H- and p53G245S-dependent cell death in cancer cells, suggesting that these small molecules have the potential to target many oncogenic p53 mutants for reactivation. The objective is to understand the molecular mechanism that allows this class of small molecules to restore function to oncogenic p53 mutants, from atomic-level interactions with the p53 DBD to the changes in the biochemical functions of the p53 DBD. Our aims: 1) Understand the characteristics of small molecule binding and stabilization of oncogenic p53 DBD. 2) Determine interactions of the small molecules with oncogenic p53 DBD and structural effects upon binding. 3) Evaluate effects of the small molecules on the DNA-binding of oncogenic p53 DBD. 4) Evaluate effects of the small molecules on oncogenic p53 DBD protein-protein interactions.

Keywords: p53; drug design; cancer; tumor suppressor; apoptosis;

Poster Session: B - Poster #: 62

Novel GABAmimetic activity of Withania somnifera on microtransplanted receptors

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Withania somnifera (WS) is an herb used in traditional Ayurvedic medicine for its adaptogenic properties. It has been reported that WS has anti-convulsive, anti-anxiolytic and stress reducing effects. These pharmacological properties suggest that WS may function through reduction of excitatory signaling or by enhancing the inhibitory neurotransmission in the central nervous system (CNS). Yet the mechanisms by which WS acts at the cellular level remain unclear. The goal of this study was to test the hypothesis that WS has GABAmimetic action on GABAP and GABAA receptors, the main inhibitory receptors in the CNS. For this, we recorded the activity of native, rat brain GABAA ionotropic channels microtransplanted into Xenopus oocytes. Additionally, GABAP1 cRNA was microinjected into oocytes to generate functionally active homomeric receptors. 24-48 hours later, the effects of WS root powder preparations were tested on voltage-clamp recordings of oocytes. WS was prepared as a boiled decoction, a hot infusion and a dissolved solution; three commonly used preparations in traditional Ayurvedic medicine. Our results show that WS has GABAergic activity and its effect was larger when used as a hot infusion, eliciting an EC50 of 4.68 mg/mL ($p = 3.81$). In agreement with previous findings, WS generated inward currents in a dose dependent manner and elicited GABA-mimetic activity but at a lower efficacy compared to GABA. We also demonstrate the first reported activation of GABAP1 receptor by WS. WS application shows a concentration-dependent increase in inward current, with an EC50 value of 0.081 mg/mL ($p= 1.64$) and a high efficacy for GABAP1. Our results provide important evidence indicating that key constituents in WS may have an important role in the development of pharmacological treatments for neurological disorders associated with GABAergic signaling dysfunction such as general anxiety disorders, sleep disturbances, muscle spasms and seizures.

Keywords: Ashwagandha; GABA signaling; Pharmacology; Anxiety;

Poster Session: B - Poster #: 63

Creation Of A Personalized, Molecular-Based Approach To The Treatment Of Recurrent Or Refractory Pediatric And Adolescent Cancer

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The primary goals of our research program are to collect high-quality tumor and germline specimens from pediatric and adolescent patients with cancer, to perform whole genome sequencing (WGS) on both tumor and germline samples and mRNA sequencing on the tumor sample to obtain and characterize the molecular signature of the cancer, to better understand how disease may have circumvented therapy, and to identify ways in which it may be more effectively treated. The process begins with consent, followed by tissue procurement and extraction of DNA/RNA, and shipment of the specimens for sequencing. Returned data is analyzed in independent bioinformatics pipelines to maximize validity of results. Genomic variation is integrated with gene expression information to develop a molecular profile of each tumor. The process culminates with a multidisciplinary molecular profile tumor board meeting where results are interpreted and a clinical action plan (if appropriate) is developed for each patient. To date, 194 participants have been identified for study. Of those identified, 149 participants and/or families provided consent; 72 of whom had suspect recurrent or refractory disease and 77 of whom had a suspect new diagnosis. The most common reasons for not pursuing consent were administrative (e.g, potential patient was not scheduled for standard-of-care procedures; potential patient was identified too close to the scheduled procedure to obtain consent). WGS of the tumor and normal genomes has been undertaken for 38 patients, 25 of whom also had mRNA sequencing of their tumor. Of the patients with WGS data, seven cases are brain tumors, 14 cases are leukemias, seven cases are sarcomas, three cases are lymphomas and the remaining cases include one each of HLH, melanoma, mixed germ cell tumor, MDS, neuroblastoma, renal cell carcinoma, and Wilms tumor. Our experience has demonstrated the feasibility and effectiveness of clinical sequencing in pediatric and adolescent oncology.

Keywords: recurrent/refractory; pediatric; genomics; personalized medicine; oncology;

Poster Session: B - Poster #: 64

Characterization of an FTY720 analog with enhanced activity against BCR-ABL+ leukemias

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OBJECTIVE: To create analogs of the FDA-approved immunosuppressant FTY720 that retain its anti-cancer activity but lack its dose-limiting toxicity. Such analogs would down-regulate nutrient transporter proteins but would not activate sphingosine-1-phosphate receptors 1 and 3 (S1P1/3). METHODS: Activity at S1P1/3 was determined by lymphocyte sequestration and heart rate studies. The anti-cancer activity of the compounds was evaluated in leukemia cell lines, primary patient samples, and an in vivo mouse model. RESULTS: Our novel FTY720 analogs do not sequester lymphocytes (S1P1) or slow heart rate (S1P3) at the anti-leukemic dose. Because S1P1 and S1P3 effects are responsible for FTY720-induced bradycardia in humans, these analogs should lack FTY720's dose-limiting toxicity. Surprisingly, one compound (SH-RF-177) is much more active than its stereoisomers and FTY720, but only in BCR-ABL-driven leukemias. SH-RF-177 was also more active than its enantiomer against Ph+ patient-derived leukemias grown in stromal cell co-cultures. The enhanced activity of SH-RF-177 requires its phosphorylation by sphingosine kinase 2 (SK2) but appears to be independent of S1P receptors. Interestingly, SH-RF-177 does not efficiently down-regulate nutrient transporter proteins at the concentrations it kills cells, suggesting that it has an alternate mechanism of action. SIGNIFICANCE: SH-RF-177's in vivo activity, effectiveness against primary leukemias, and lack of S1P-dependent toxicities suggest that this compound could be therapeutically useful in BCR-Abl-driven leukemias.

Keywords: leukemia; BCR-ABL; FTY720;

Poster Session: B - Poster #: 65

Developing FTY720 Analogs To Starve Cancer Cells To Death

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Objective Cancer cells are susceptible to nutrient stress due to mutation-driven constitutive biosynthesis and suppression of autophagy, a catabolic recycling process. Sphingolipid-based drug FTY720 selectively kills cancer cells partly by inducing nutrient stress through down-regulation of surface nutrient transporters. Interestingly, FTY720 and FTY720-analogs induce cytoplasmic vacuolation in addition to nutrient transporter loss. Reducing the signaling lipid phosphatidylinositol-3,5-bisphosphate (PI(3,5)P2) by inhibiting PIKfyve, the kinase that generates PI(3,5)P2 from PI(3)P, vacuolates cells in a similar manner and also blocks autophagy. We hypothesize that FTY720 vacuolates cells by reducing PI(3,5)P2 levels thereby interfering with the protective autophagic response to FTY720-induced nutrient transporter loss. The aims of this study were to: 1) determine the mechanism by which FTY720 induces vacuolation and 2) investigate whether vacuolation contributes to its anti-neoplastic activity. Methods Phosphatidylinositol levels were measured by high-performance liquid chromatography. Confocal fluorescence microscopy was used to assess autophagic flux. Cell viability was measured by vital dye exclusion and flow cytometry. Results FTY720 reduced the fusion between autophagosomes and lysosomes which correlated with reduced PI(3,5)P2 levels shown in a preliminary measurement. Vacuolation induced by PIKfyve inhibition was not sufficient to kill cells but enhanced cell death when coupled to nutrient transporter loss. Reversal of vacuolation by over-expression of Vac14, a scaffold and regulatory protein for PIKfyve, conferred resistance to FTY720. Discussion FTY720-induced vacuolation reduced autophagic flux, exacerbating the nutrient stress induced by surface nutrient transporter loss. We believe vacuolation contributes to the anti-neoplastic activity of FTY720 and this activity should be retained by future FTY720 analogs developed for anti-cancer use.

Keywords: sphingolipid; autophagy; vacuolation; Phosphatidylinositol; cancer metabolism;

Poster Session: B - Poster #: 66

A comparison of standard and high sensitivity multiplexed cytokine/chemokine panels in plasma of cervical cancer survivors

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Objectives: The stress of cancer diagnosis and treatment can disrupt the psychoneuroimmunology axis, leading to changes in circulating cytokine levels. These levels may give valuable information as to how psychological stress affects the physiology of the immune system. Low concentrations of some cytokines in serum and plasma may require high sensitivity assays. High sensitivity and standard multiplex kits were compared for their ability to detect concentrations of 13 cytokines within the same set of patients using the Luminex MAGPIX®. Methods: Plasma samples from 12 cervical cancer survivors participating in a randomized biobehavioral clinical trial were tested for circulating cytokine levels with both a Milliplex® MAP high sensitivity or a standard human cytokine/chemokine magnetic bead kit (Millipore). All samples were run in duplicate. Each kit quantified 13 circulating cytokines/chemokines. The panels were run simultaneously, read on a Luminex MAGPIX® and analyzed with Milliplex Analyst 5.1 software. Test results were compared using the Wilcoxon matched-pairs signed rank test. Results: Significant differences were seen in the detection of 12 of 13 cytokines tested. Of these 12 were highly significant with a p value <0.0001. GM-CSF and TNFa were also significantly different with p values of 0.001 and 0.042, respectively. There was no significant difference in IL-8 detection between the kits (p=0.16). Means for the high sensitivity kit were all above the minimum detectable concentration. Means for GM-CSF and IL-13 were both below and means for IL-1ß and IL-2 were very close to this limit for the standard kit. Discussion: For determination of multiple circulating cytokines from human plasma, high sensitivity measures may be best. As the high sensitivity testing was able to identify cytokines present at concentrations below the minimum detectable level of the standard test, studies examining circulating cytokines may benefit from high sensitivity testing.

Keywords: cytokine; cancer; multiplex;

Poster Session: B - Poster #: 67

Cranial transplantation of human neural stem cells ameliorates chemotherapy-induced cognitive impairment

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Objective: The frequent use of chemotherapy to combat a range of malignancies can elicit severe cognitive dysfunction often referred to as "chemobrain" long after the cessation of treatment in as many as 75% of survivors. While cognitive health is a critical determinant of therapeutic outcome, chemobrain remains an unmet medical need that adversely impacts quality of life in pediatric and adult cancer survivors. To address this issue, we developed a rodent model of chemobrain to determine whether a stem cell based strategy could provide any neurocognitive benefits. Methods: Athymic nude rats were subjected to 4 treatments (1x/week, 100 mg/kg) of cyclophosphamide. 1 week following the last treatment, rats received bilateral intrahippocampal transplantation (4 sites/hippocampus, 100,000 cells/site, 800,000 cells/animal) of human neural stem cells. Animals were subjected to cognitive testing 1 month later, after which they were sacrificed for immmunohistochemistry and morphometric analysis of host neuronal structure. Results: Chronic cyclophosphamide treatment induced significant performance based decrements on hippocampal- and medial-prefrontal cortex-dependent behavioral tasks. Intrahippocampal transplantation of human neural stem cells resolved all cognitive impairments when animals were tested one month after the cessation of chemotherapy. In transplanted animals, improved cognition was associated with reduced neuroinflammation and a preservation of host neuronal structure. Neurons within the dentate gyrus and CA1 subfields of the hippocampus exhibited significant reductions in dendritic complexity and spine density following chemotherapy, effects that were ameliorated in the presence of surviving grafted cells. Significance: Data suggests that cranial transplantation of stem cells can reverse the adverse effects of chemobrain, in part, by attenuating neuroinflammation and preserving host neuronal architecture.

Keywords: chemobrain; transplantation; neural stem cells; dendritic complexity; neuroinflammation;

Poster Session: B - Poster #: 68

Characterization And Assessment Of Transplanted Human Embryonic Stem Cell Derived Motor Neurons Into A Conus Medullaris/Cauda Equina Injury Model

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Injuries that involve sacral spinal segments (conus medullaris - CM) and lumbosacral nerve roots (cauda equnia - CE) compose approximately 20% of all spinal cord injuries. CM/CE injuries result in degeneration and death of motor and autonomic neurons in the spinal cord and can lead to bladder, bowel, and sexual dysfunction. To model CM/CE injuries in a rodent animal model, L5-S2 ventral roots were unilaterally avulsed in adult female Sprague-Dawley rats. As a cell replacement therapy, human embryonic stem cells (hESCs) were differentiated in vitro towards a motor neuron phenotype by promoting the motor neuron Hb9 transcription factor and then transplanted into animals. hESC-derived motor and autonomic neurons and neuronal precursor cells (40k or 80k, 20k/µl) were transplanted into the L5/L6 lumbar region after a ventral root avulsion (VRA), a ventral root avulsion followed by implantation of L6 and S1 avulsed roots (VRI), or into naïve intact spinal cord (sham). Animals were sacrificed 2 or 4 weeks after transplantation, and tissue processed for immunohistochemical analysis for cell viability and characterization. In a subset of these animals immediately prior to sacrifice, bladder pressure and voided volumes were recorded during saline infusion into the bladder. Cell viability was quantitatively measured by immunoreacting sections with an antibody against Human Nuclear (HuNu) protein. At 2 weeks (n=6) 344.1 (s.d. 472.9) and at 10 weeks (n=1) 1536, average cells per section were calculated in VRA animals. In a separate set of pilot animals hESC-derived motor neurons were transplanted into VRA (n=2), VRI (n=2), or sham (n=2) animals followed by bi-monthly behavioral assessments. Metabolic cages were used to monitor spontaneous voiding behavior while Hargreaves Heat and Von Frey Hair Test assessed whether pain developed over time. If successful, our studies may result in a new treatment strategy to restore bladder function in subjects with CM/CE injury.

Keywords: spinal cord injury; hESC-derived motor neurons; cauda equina; urodynamics; voiding;

Poster Session: B - Poster #: 69

Choroid Plexus Dysfunction in Alzheimer's disease – Morphological Changes & Regeneration via Stem Cell Injections

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Background/Hypothesis: Alzheimer's disease (AD) is the 6th leading cause of death in the US, affects 5 million Americans & faces a treatment stalemate. Prior studies demonstrate that degeneration of choroid plexus (CP), a specialized tissue which filters Amyloid-Beta from the brain, is exacerbated by AD. We hypothesize that CP can be regenerated via inter-ventricular stem cell transplantation. First, we quantitatively assessed morphological alterations in the CP of human patients by post-mortem examination of CP from control and AD patients. Second, we demonstrate the viability of regenerating CP via dCPE (derived choroid plexus epithelial) stem cell injections. Methods: Sectioned slides of CP were imaged while blinded to patient diagnosis. Morphological changes were scored on a three-point scale. Goal 2: We established an aggregration-based neural induction method, applied BMP4 to ESC-derived neural precursors, selected for CPECs showing vesicular morphology that co-labeled for CPEC markers ZO1, Aqp1 & Ttr. ~200K RFP labelled cells were stereotaxically injected into lateral ventricles of CD1 mice. CP was dissected and fluoroscopically imaged. Results: Observations of age and disease afflicted CP were consistent with literature, but new morphological findings that haven't yet been documented were also observed. Goal 2: The cells successfully engraft into the host CP epithelium. Complete integration of dCPEC observed 48 and 72 hours post injection. This supports previous work showing that ESCs can be efficiently induced into a neural fate, and BMP4 sufficiency & dose-dependency for CPEC induction. Conclusion: CP changes with age, and deteriorates quicker in AD, potentially leading to reduced filtration of A-beta and likely exacerbating the pathophysiology of AD. Since the dCPECs show secretory activities in vitro and integrate into endogenous CP tissue, they are a likely viable therapeutic modality for the potential treatment of early stage AD.

Keywords: Alzheimers disease; Stem Cells; Regenerative Medicine; Tissue Transplantation; Choroid Plexus;

Poster Session: B - Poster #: 70

True 32-Slice Intraoperative Computed Tomography In Conjunction With 3T MRI In The Treatment Of STN-Targeted Parkinson's Disease: Validation And A Potentially Paradigm-Changing Tool.

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The STN is the most common target for motor-predominant PD. We are unaware of comparative studies on a cohort utilizing true intraoperative 32-slice CT, preoperative MR, macrostimulation, and microlectrode recordings in STN-targeted DBS implantation. This study initially was designed to describe the contribution of each to clinical outcome, arriving at the surprising conclusion below. The question of indirect versus direct-targeting has been investigated for quite some time, though the refinement in final lead position based on MER has been argued for by a number of investigators. Our work portends the exciting possibility of eliminating MER in this setting and thus decreasing operative time and potentially, complication rates. Clinical outcomes were quantified as shown in Figure 1. See Figure 2 for operative details. Figures 3 and 4 show the MER-influenced changes in final coordinates. Given a lead diameter of 1.27 mm and an electrode distance of 7.5 mm, this brought about the tantalizing question of whether or not we could use this system to directly target the STN. A blinded neuroradiologist in conjunction with neurosurgery staff/fellow selected an ideal target using our tri-planar fused CT/MR. Figure 5 shows projected/final lead coordinates. Figure 6 shows average range from target is 1.01 to 1.45 mm. Given robust clinical outcomes obtained with the ranges outlined above and the deviations listed in Figure 6, this study portends the exciting possibility of directly targeting the STN via high resolution CT/MRI and potentially eliminating the need for MER. Though we are conducting ongoing studies to verify this hypothesis, the use of our intraoperative scanner has resulted in nearly 90% of patients experiencing symptomatic relief. We encountered no hemorrhages, strokes, or infections and only 3 lead position change were undertaken, all intraoperatively. Thus this technique is an exciting improvement on current paradigms aside from targeting implications.

Keywords: deep brain stimulation; Parkinson's disease; intraoperative computed tomography,; microelectrode recording; direct targeting;

Poster Session: A - Poster #: 71

Assessment Of Adolescent Alcohol Usage Via Computerized Screening In The Emergency Department

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Excessive alcohol use is increasingly becoming a major public health problem that affects many patients who present to the emergency department (ED). The purpose of this research is to examine the effectiveness of Computerized Alcohol Screening and Brief Intervention in adolescent patients as compared to standard of care (no intervention). The overall goal is to identify at risk alcohol use and abuse in adolescents 12 to 17 years of age and provide intervention at an early stage. This is done by providing two screening tools - a shortened Alcohol Use and Disorders Identification Test (AUDIT-C) and a behavioral assessment called CRAFFT (car, relax, alone, friends and family, forget, trouble) that assess hazardous drinking habits. Those at-risk are followed up 3 months after the initial screening. Of the patients enrolled, a majority have decreased their level of alcohol consumption, indicating that CASI may be effective in reducing alcohol use among adolescent patients.

Keywords: translational research; adolescents; alcohol screening; intervention; health prevention;

Poster Session: A - Poster #: 72

Relationship Between Patients' Degree Of Education And Readiness To Change Drinking Habits

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Alcohol is currently the third leading cause of death nationally, causing approximately 100,000 deaths per year. Adults who dropped out of high school were seen to be approximately 6.34 times more likely to develop alcohol dependence than adults that attained a higher level of education. Since many of the patients who come to the Emergency Department (ED) lack access to primary health care, the ED provides many opportunities for alcohol screening and early intervention as patients are seen on a daily basis, 24 hours a day. Computerized screening via the Computerized Alcohol Screening and brief Intervention (CASI) tool has been shown to effectively reduce alcohol intake by 48-66%, while taking approximately 5-10 minutes to complete, cost-free for patients, and increases patient satisfaction and comfort by providing anonymity and simplicity. CASI identifies patients that are at risk for alcohol abuse via the Alcohol Use Disorders Identification Test (AUDIT) and provides them with a computerized intervention, educating them in making decisions beneficial to their health. There is no significant relationship between a patients' readiness to change and their level of education, change in AUDIT score at 3 months, or change in AUDIT score at 6 months. Results reported 12 of 14 patients (85.7%) decreased alcohol consumption after completing a follow-up survey three months after their initial screening and all 14 patients reported a drop in alcohol consumption after completing their six-month follow-up. CASI provides a computerized BNI that may hold long-term benefits in reducing alcohol consumption within patients presented at the ED.

Keywords: Education; Alcohol consumption; Emergency Department; CASI; Intervention;

Poster Session: A - Poster #: 73

Comparative Analysis Of Emergency Department Patients Lost To Follow-Up After Computerized Alcohol Screening And Brief Intervention

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Alcohol Screening, Brief Intervention and Referral to Treatment (SBIRT) has been widely implemented in medical facilities since 2010 when it became mandatory in all level 1 and 2 trauma centers. Many studies have evaluated the effectiveness of SBIRT by following up on patients screened to be at-risk drinkers. Most of these studies have reported a large loss to follow-up as their main limitation but few have tried to investigate the characteristics of those non-compliant to follow-up. This retrospective study analyzed demographic characteristics, Alcohol Use Disorder Identification Test (AUDIT) and readiness to change scores as well as reasons to change for 199 lost-to-follow-up and 221 completed follow-up patients who had undergone SBIRT at the UCI Emergency Department between June 2006 and May 2007. Independent sample t-tests, chi-square and linear regression models were used to analyze the data. Comparing baseline characteristics, 21-24 year-olds had higher percentage of completed follow-ups than older age groups (p=0.002, 95%CI 0.001-0.003). AUDIT scores showed those lost to follow-up had significantly more alcohol-related harmful behavior than those completed follow-up (2.04 vs.1.61 points). Those completed follow-up also reported more guilty feelings after drinking in the past year (p=0.004). Using linear regression, after adjusting for sex, language, ethnicity, readiness to change and individual AUDIT domain scores, having more hazardous alcohol-related behaviors were still associated with less follow-up compliance (OR= 0.89,95%CI 0.79-0.96). These results demonstrate differences between patients compliant to alcohol-related behavior modification with those lost to follow-up. At-risk drinkers are different in demographic characteristics as well as their alcohol drinking patterns, which suggest a need in more tailored approach to these patients. This can result in more effective motivational intervention and commitment to change for those lost to follow-up.

Keywords: SBIRT; AUDIT; Alcohol; Lost to follow-up; Completed follow-up;

Poster Session: A - Poster #: 74

The Association of Alcohol-Use Disorders Identification Test and Readiness to Change Score in Alcohol-Related Emergency Department (ED) Visits

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Objectives: From increased risk of major health issues to large economic costs, the negative consequences of alcohol abuse invade both macro and micro levels of societies. This study investigated various factors and characteristics associated with high Readiness-to-Change (RTC) scores. From the results, health professionals will be able to prioritize resources and more effectively provide brief intervention to patients who are most receptive to behavioral modification. Methods: The study was conducted at a tertiary care university hospital ED using Computerized Alcohol Screening and Brief Intervention (CASI). Adult patients who reported drinking more than the recommended National Institute of Alcohol Abuse and Alcoholism (NIAAA) guideline were included in the study. We excluded incarcerated, psychiatric, and patients who were unable to give consent. Multinomial logistic regression examined patient characteristics including age, Alcohol Use Disorder Identification Test (AUDIT) scores, trauma-relatedness visit, education, insurance status, language, cigarette and illicit drug usage. Results: From 1,285 electronic medical records, 512 indicated higher alcohol consumption than NIAAA recommendations. The 512 charts were categorized, with 55 alcohol related and 457 non-alcohol related ED visits. Using multinomial logistic regression, we predicted RTC scores. Patients of age group 50-64 had a 62% lower chance of reporting high RTC score than patients of age group 22-29. Additionally, patients of age group 22-29 had a higher probability of reporting high RTC than any other age group. Other patient characteristics did not predict either moderate or high RTC scores. Discussion: The ED allows for implementation of alcohol screening and prevention. Our study indicates resources should be targeted at younger patients in their twenties and thirties for successful changes in alcohol consumption behavior.

Keywords: Alcohol abuse; Screening; Brief intervention; Behavioral modification;

Poster Session: A - Poster #: 75

Efficacy of Baclofen in reducing symptoms of PTSD & Anxiety in Veterans with HCV & Alcohol use Disorders

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High rates of comorbid Post Traumatic Stress Disorder (PTSD) and alcohol use are common, particularly in military Veterans. The present study examined the relationship between changes in symptoms of PTSD and anxiety in relation to changes in self-reported drinking behavior. We hypothesized that Veterans reporting increases in PTSD and anxiety symptoms would also report increases in drinking behavior, and that changes in alcohol consumption would be predictive of changes in PTSD and anxiety symptoms. Data were utilized from a clinical trial of baclofen to reduce alcohol use in 180 Veterans with HCV. Participants were 99% Male, 66% White, 33% African American, 9% Hispanic and 7% of other ethnicities. All were HCV+, drinking more than 7 drinks per week or one heavy drinking day (4+ drinks) 2 weeks prior to study enrollment. Patients enrolled in the baclofen clinical trial completed the Timeline Followback (TLFB; measure of seven-day drinking totals), PTSD Checklist-Civilian (PCL-C), and Brief Symptom Inventory (BSI) anxiety subscale measures at baseline and at 12 weeks. Change scores were created for each variable by subtracting the 12 week score from the baseline score for both drinking level, BSI – Anxiety, and PTSD scores. Using a least squares regression, change in drinking was regressed onto change in PTSD symptoms however, the model was not-significant $F(1, 81) = 1.50$, $p = .2245$. A second regression showed that BSI-Anxiety subscores significantly changed with weekly drinking levels across 12 weeks, $F(1, 75) = 6.60$, $p = .01222$, and that the BSI-Anxiety change score was significantly predictive of change in weekly drinking levels ($t = 2.38$, $p = .022$; ß = .3339). Findings reveal that Veterans reporting decreases in drinking also report decreases in anxiety symptoms. Future analyses will be conducted testing Baclofen's effect on alcohol consumption, PTSD and anxiety symptoms. The unblinding process is currently in effect and results of Baclofen will be discussed.

Keywords: PTSD; Substance Abuse; Veterans; HCV;

Poster Session: B - Poster #: 76

Stellate Ganglion Block For Severe PTSD: Clinical Response And Psychophysiological Correlates

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Objective: To determine if stellate ganglion block (SGB) provides long-term symptomatic relief for those suffering from PTSD. Methods: 12 OIF/OEF veterans (1 female, 11 males; mean age 39 ± 11) with combat-related PTSD were enrolled. Subjects selected had severe PTSD symptoms with prominent hypervigilance. Subjects had a single right sided SGB using 2% lidocaine and 0.25% bupivicaine under fluoroscopic guidance. Outcome measures included the Clinician Administered PTSD scale (CAPS) and various psychophysiological measures collected at baseline and then at 1, 4, 12, and 24 weeks post block. Response was defined as a CAPS score of 45 or less. Results : Baseline CAPS score was 81 ± 14 (mean ± sd) indicating the subjects suffered from severe symptoms. CAPS scores declined by 38% to 50 ± 23 at one week post block, and further reduced to 45% of baseline (44 ± 27) at one month ($p < 0.01$) The effect faded at three months post block (59 ± 24, $p < 0.07$), and approached baseline at 6 months. 9 subjects met criteria as responders and exhibited a 59% reduction in CAPS to 32 ± 12 at 1 month. Subjective reports of overall anxiety levels paralleled the CAPS. Responders also evidenced reduced arousal levels as measured by Respiratory Sinus Arrhythmia (RSA). Significance of Impact: We confirm SGB is an efficacious, and rapid although temporary treatment for PTSD. We suggest its use for those at greatest risk is clearly warranted. Psychophysiological measures may be useful as biomarkers related to treatment outcome.

Keywords: PTSD; Stellate Ganglion Block; Respiratory Sinus Arrhythmia;

Poster Session: B - Poster #: 77

Burn Wound Exudate: Depth of Burn Predicts Cellular Recruitment

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Objectives: Previous research has demonstrated a correlation between burn injury and systemic cytokine response. Moreover, conflicting studies have identified burn wound fluid as being rich in either pro- or anti-inflammatory cytokines that may serve to modulate or retard the healing process. We aim to present the first data identifying the cellular makeup of burn wound exudate responsible for these cytokine levels and its correlation to the depth of burn insult. Methods: Four patients with less than 5% total body surface area burns admitted to the burn ICU were identified with fluid-containing burn blisters. Six to 12 hours after presentation, burn exudate was extracted under sterile technique using a large-bore syringe. Within 24 hours, each sample was passed through a 100 µm strainer and analyzed using flow cytometry. The cellular composition was characterized based on forward and side scatter and these measurements were compared to that of whole blood from a healthy patient previously stained for immunophenotyping. Results: Two patients suffered very superficial (VS) wounds. Exudate extracted from these wounds was relatively devoid of monocytes (0.1-3.2%) and granulocytes (0-11.2%), with the majority of the cell population comprised of lymphocytes (10.9–17.9%) and platelets. The remaining two patients sustained superficial partial thickness (SPT) wounds with exudate much more abundant in granulocytes (31.8–46.9%) and monocytes (8.4–14.6%). The lymphocyte population closely mirrored that in the VS burn group (9.4–14.8%). Discussion: Our preliminary data indicates a correlation between the cellular makeup of burn wound exudate and the depth of burn injury. Superficial wounds tend to heal with or without medical intervention, likely due to a lack of pro-inflammatory cells, whereas deeper burns usually require surgical debridement. It is possible that drainage rids these wounds of this pro-inflammatory milieu, thus facilitating the healing process.

Keywords: Burns; Burn wound exudate; Systemic inflammatory response syndrome; cellular recruitment; wound healing;

Poster Session: B - Poster #: 78

Telomere length measurements in post-mortem human brain in major depressive disorder

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Objectives: Telomeres, which are special sequences of DNA located at the end of chromosomes that preserve DNA integrity, naturally shrink with age and eventually can lead to cell death. Stress, a risk factor for psychiatric disorders, has been associated with telomere shortening in mood disorders and schizophrenia. To date the majority of investigations of telomere length in major depressive disorder (MDD) have been performed in blood cells, with only one study carried out using post mortem brain samples. However, in both cases no differences were found between MDDs and controls. The purpose of this study was to survey telomere length in the brain, by determining if differences in length could be observed between brain regions, and second to ascertain if telomere length shortening can be observed in MDD subjects. Methods: In this study we measured telomere length across five brain regions (dorsolateral prefrontal cortex, hippocampus, amygdala, nucleus accumbens, and substantia nigra) in 10 MDDs and 10 controls from brains obtained through the UCI Brain Bank. Telomere length was determined with qPCR using two genomic assays, one for a single copy gene and the other specific to the repetitive telomeric sequence. A ratio of the relative quantities was then used as a measure of telomere length. Results: Statistically significant differences were observed in telomere length between brain regions ($p<0.001$). Significantly lower telomere length was observed in MDDs compared to controls ($p=0.004$) within the hippocampus, while no significant differences were found in other brain regions. We also observed as expected, a negative correlation between age and telomere length, but the decreased telomere length remained significant even after controlling for age. Discussion: Our results revealed regional differences in telomere length in the human brain and a significant decrease of telomere length in the hippocampus of MDDs and provides further evidence linking stress to MDD.

Keywords: Major Depressive Disorder; Telomeres; Stress; Hippocampus;

Poster Session: B - Poster #: 79

Use Of GDNF-Releasing Nerve Guidance Channels To Promote Motor Axon Regeneration Following Ventral Root Avulsion Injury In Rats

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Trauma to the lower spine, as in cauda equina or conus medullaris injuries, can result in a wide array of neurological impairments including sensory and motor deficits and loss of autonomic function. These impairments arise from the acute injury causing motor and autonomic neuron retrograde degeneration. When spine trauma is extensive, grafting materials may be needed to bridge a tissue gap between the spinal cord and lesioned nerve roots. Here, we use a unilateral L5-S2 ventral root avulsion injury in rats, a model of cauda equina injury, to test a novel method to aid motor axon regeneration at the transition area between the central and peripheral nervous system. Nerve guidance channels (NGCs) composed of aligned protein-polymer composite fibers with human glial-cell derived neurotrophic factor (GDNF) or empty NGCs (control group) are implanted into the lateral L5/L4 spinal cord with the distal end of the channel tied off in order to assess whether spinal cord neurons may extend regenerating axons into the NGC releasing GDNF. The NGCs and spinal cord of rats in the experimental and control series are studied morphologically at 4 weeks post-operatively. Distal sections of NGCs are processed for electron microscopy and stained with toluidine blue for light microscopic assessment of motor axon growth through the channels. Spinal cord sections are stained with cresyl violet and motor neuron counts will determine whether any neuroprotection may be provided by the GDNF-releasing NGCs. Analysis is on going. We hypothesize that implanted GDNF NGCs will contain more axons than implanted empty channels and that more axotomized motoneurons survive in rats with GDNF NGCs. If successful, GDNF-releasing NGCs may provide an alternative to the use of peripheral nerve grafts for proximal nerve root repair of cauda equina injury in experimental models. Supported by: The Adelson Medical Research Foundation.

Keywords: nerve guidance channel; glial cell-derived neurotrophic factor; ventral root avulsion;

Poster Session: B - Poster #: 80

Imaging of the Adult Sinus Using a Low-Cost Optical Instrument

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Objectives: In the US, approximately one in seven people develop sinusitis (sinus infections) each year, and 20 million cases of acute bacterial sinusitis become chronic and require medical treatment. Over $3 billion/year is spent on all sinusitis-related cases. Chronic sinusitis generally evolves from a failure to accurately diagnose and treat acute cases. The purpose of this research is to develop a very low-cost optical imaging tool that will offer a quick and simple assessment of sinusitis suitable for use by both primary care doctors and physician extenders. Methods: Near infrared light (NIR), is well-known to penetrate deeply into tissues and is still detectable by conventional consumer-grade cameras. We have developed NIR imaging prototypes and imaged over 100 adult subjects in a medical clinic setting. All subjects provided written informed consent (HS# 2011-8295). The instrument consists of an array light-emitting diode (LED) light sources at 850 nm that are placed into the mouth. A modified digital camera takes a picture of the NIR light that travels through the face. Further, we have modeled the NIR light transport in the human head to gain understanding about how well the light samples the sinus cavity. Results: We have shown that using simple LED light sources and low resolution consumer-grade cameras can generate anatomical images of the adult maxillary sinus that compare well with the bulk findings of CT. Although the spatial resolution of the optical images was poor in relation to the CT, the general features of the maxillary sinus such as high versus low opacity were clearly distinguished. Simulations verified that even subtle changes in the mucosal lining may be detectable with this NIR imaging device. Significance: Ultimately, our device will help reduce health-care costs by optimizing and streamlining diagnosis and treatment. The sinus imager is currently a research device and is not intended to replace any medical procedures.

Keywords: Clinical Application; Medical Imaging; Near Infrared; Sinus disease;

Poster Session: B - Poster #: 81

Ileostomy Reversal After Minimally Invasive Colorectal Surgery: Can it Still be Considered a Minor Procedure?

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Introduction: To compare and contrast the morbidity and mortality of ileostomy reversal with the original minimally invasive colorectal surgical procedure requiring ileostomy creation. Methods and Procedures: 89 patients undergoing laparoscopic and robotic-assisted colorectal surgery followed by interval ileostomy reversal were selected. The cohort had 47 laparoscopic and 42 robotic cases, performed by 4 surgeons at a single institution. An internal comparison was done on the outcomes of the index procedure with respective ileostomy reversal for each patient. Postoperative outcomes and 30-day morbidity and mortality were analyzed. Statistical analysis was done using Chi square test, student t-test, analysis of variance and Fischer's test where applicable. GraphPad Software was used. Follow up was studied for a period of 30 days after the day of the procedure. Results: 42% of patients were female and the mean age was 58 years old. Cancer was a primary diagnosis in 57% of patients. The mean duration of the ileostomy prior to closure was 107 days. Median length of stay (LOS) was significantly longer for the index procedure compared to the ileostomy reversal (6.0 days vs. 4.0 days, p=0.0001). Mean estimated blood loss was higher (153 ml vs. 25 ml, p=0.0001) in the index procedure. A subset analysis of patients with a high BMI (>30, n=18), showed no statistically significant difference in LOS between the index procedure and the ileostomy reversal (5.0 vs. 4.0 days, p=0.4), while patients with a lower BMI (<30) had a significantly lower LOS (6.0 vs. 4.0, p=0.01) for the ileostomy reversal. Conclusion: In the setting of minimally invasive colorectal surgery, a subsequent ileostomy reversal has equivalent morbidity and mortality, but a shorter hospital stay and less blood loss. In patients with a higher BMI, however, ileostomy reversal was found to be equivalent to the initial colorectal resection in length of stay, blood loss, morbidity and mortality.

Keywords: Ileostomy; Robotic surgery; Minimally invasive surgery; Colorectal surgery; Reversal;

Poster Session: B - Poster #: 82

The Effect Of The Anti-Angiogenesis Agent Bevacizumab On The Hippocampal Volumes Of Patients Diagnosed With Recurrent, Treatment Resistant Malignant Gliomas

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Background: Malignant gliomas represent one of the most severe malignancies, with a two year survival rate of 20% for glioblastoma multiforme (GBM) patients. In an effort to improve the outcome, a significant number of patients receive multi-modal therapies such as surgery, radiation and chemotherapy, which tend to be associated with damage at multiple brain levels. Objective: To determine if the treatment with Bevacizumab induces regional alterations in hippocampal volume that correlate with cognitive impairment and poorer quality of life in patients with primary malignant brain tumors. Methods: This retrospective study was conducted at the Chao Family Comprehensive Cancer Center. For this, charts of past patients with known malignant glioma who presented for treatment during 2009-2012 were reviewed. Clinical data such as age, gender, WHO tumor grade, measurements of tumor, location of tumor, and time of survival since diagnosis were also collected. Bevacizumab therapy was correlated with MRI imaging obtained as well as with any neurocognitive and QoL testing that may have been done throughout the duration of therapy. Results: In all of the patients, as chemotherapy treatment progressed, there was a decrease in hippocampal volume that was offset from normal degradation of the hippocampal volume seen in people between the ages of 40-65. The average hippocampal volumes of the patients were much lower than those observed normally in their respective age groups. ($P < 0.0005$) The study is still being conducted; further finding and additional results will be available on the poster. Limitations: This is a retrospective study of a relatively small number of patients. Larger studies are needed to corroborate these findings. Conclusions: The findings demonstrate that there is a negative correlation between the progression of chemotherapy treatment and the hippocampal volume.

Keywords: glioma; bevacizumab; hippocampal volumes; magnetic resonance imaging;

Poster Session: B - Poster #: 83

Repeated Streptococcus pyogenes infections induce an autoimmune Th17 cell phenotype and impair Blood Brain Barrier integrity in mice

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Group A Streptococci (GAS, e.g. Streptococcus pyogenes) infections are associated with autoimmune diseases of the central nervous system (CNS) including movement disorders (Sydenham's chorea; SC) and neuropsychiatric syndromes (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus; PANDAS). GAS is known to induce autoreactive mimic antibodies against several CNS targets but how autoantibodies cross the blood-brain barrier (BBB) is unclear. Delivery of these antibodies into the mouse brain induces stereotyped behaviour and motor deficits similar to PANDAS symptoms, supporting an essential role of these antibodies in the disease. Intranasal GAS infection (i.n.) of mice initially induces a dominant antigen-specific Th17 response in the nasal-associated lymphoid tissue (NALT), an organ functionally analogous to human tonsils, and repeated infections drive those cells toward an IL-17+ IFN?+ phenotype implicated in many autoimmune diseases, including multiple sclerosis (MS). Using MHCII tetramers to track GAS-specific T cells, and tracer to evaluate BBB integrity, we demonstrate that GAS-specific Th17 cells enter the brain, disrupt the BBB and activate microglia, albeit bacteria are not detected in brains of inoculated mice. The phenotype and distribution of T cells suggests that they likely migrate from NALT into the olfactory bulb (OB), along the olfactory sensory axons and then disperse into other CNS regions. We identified degradation of the tight junctions between BBB endothelial cells and found circulating IgGs in brain sections of mice previously immunized by infection. These findings not only provide a novel breakthrough for understanding how recurrent GAS infections may impair brain function that lead to motor and neuropsychiatric disease, but also suggest a more general mechanism by which other infectious agents that induce Th17 immunity could exacerbate and contribute to neurovascular damage in other CNS autoimmune diseases.

Keywords: PANDAS; Streptococcus pyogenes; T cells; Blood Brain Barrier; autoantibodies;

Poster Session: B - Poster #: 84

Low-doses of cisplatin injure hippocampal synapses: A mechanism for 'chemo' brain?

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Objectives: Chemotherapy-related cognitive deficits are a major neurological problem. Cisplatin (CDDP) is a commonly used cancer drug which achieves high concentrations in the brain. We previously reported that CDDP causes neural stem/progenitor cells (NSCs) death. Since the disruption of dendritic spines is associated with cognitive impairments, we tested the hypothesis that CDDP also alters spine integrity in hippocampal neurons (HN) by a mitochondrial- mediated mechanism. Methods: Cultured rat HN and NSCs were treated with CDDP (0.1μM and 1μM). CDDP effects on dendritic spine integrity were studied by quantification of post-synaptic density protein (PSD95) puncta and GFP expressing neurons. BDNF mRNA levels were quantified by qRT-PCR. For in-vivo studies, rats were treated with 10mg/kg CDDP intraperitoneally daily for 2 days. Dendritic branching and spines were quantified by Golgi staining. TUNEL assay and Annexin V ICC was performed to detect apoptosis. Mitochondrial respiration was measured using a Clark electrode. Results: CDDP induced non-reversible damage to dendritic spines and branches in HN. Exposure to 1μM CDDP caused HN apoptosis, and severe mitochondrial deficits in the surviving HN. BDNF replacement using the CX456 ampakine partially reversed the CDDP damage. In-vivo treatment with CDDP caused a reduction of dendritic branches and decreased spine density in CA1 and CA3 HN. An acute increase in cell death was measured in these regions, as well as in NSCs located in the dentate gyrus. Discussion: At clinically relevant CDDP doses, dendritic damage and HN and NSCs death occur in-vivo. At doses lower than those found in chemotherapy patients, CDDP can potentially induce both severe synaptic damage and neuronal cell loss. This damage may be responsible for the cognitive impairment observed after chemotherapy treatment, and might be partially reversible using clinically available treatments (ampakines).

Keywords: Chemotherapy; Cisplatin; Hippocampal dendritic spines; Neural stem/precursor cells (NSCs); Neuronal apoptosis;

Poster Session: B - Poster #: 85

SORAFENIB FOR THE TREATMENT OF HEPTOCELLULAR CARCINOMA: EXAMINING SURVIVAL BENEFIT OF VARYING SOEFENIB DOSAGES

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Background: Sorafenib is the first chemotherapy agent to receive FDA approval for the treatment of hepatocellular carcinoma (HCC). The FDA granted approval based on results from an international, multicenter, randomized, double-blind, placebo-controlled trial using 400 mg twice daily dosage. In that trial, treatment with sorafenib was shown to prolong overall survival and delay time to radiographic progression. Unfortunately, many patients at this 400 mg twice-daily dosage experience significant side effects including diarrhea, weight loss, hand-foot syndrome, alopecia, anorexia, and hypertension. For some patients with prohibitively severe symptoms, their sorafenib dosage must be lowered or their treatment discontinued. Objectives: To better understand the affect of varying dosages of sorafenib treatment on overall survival benefit, time to progression of symptoms, time to radiographic progression, and toxicity profile. Methods: A retrospective analysis of all patients treated at a single institution between February 2007 and June 2013 who were prescribed sorafenib as part of their treatment regimen for inoperable hepatocellular carcinoma. Demographics, treatment, recurrence and survival data was retrieved from our prospectively-maintained database. Anticipated Results/Significance of Impact: Preliminary data analysis shows higher rates of major side effects like fatigue, hand-foot syndrome and diarrhea in the Asian population versus the non-Asian population. This study aims to identify the characteristics that may predispose patients to be intolerant of the standard sorafenib dosing. Sorafenib remains the drug of choice for inoperable HCC. This study may lead to a better understanding of the optimal sorafenib dosages for various populations and potentially to more individualized cancer treatment.

Keywords: hepatocellular carcinoma; sorafenib; nexavar; optimal dosage; hand-foot syndrome;

Poster Session: B - Poster #: 86

Vertical Inhibition Of The PI3K Pathway Potently Sensitizes Diffuse Large B Cell Lymphoma To BCL-2 Antagonism

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Current treatment for diffuse large B cell lymphoma (DLBCL), the most common form of adult lymphoma, has been only partially successful, with 40% of patients experiencing treatment failure or undergoing relapse. While significant progress has been made in the identification of risk factors contributing to relapse, few alternative therapies have emerged that effectively address them. One of these risk factors is over-expression of the anti-apoptotic protein, BCL-2, which is part of a family of proteins that collectively control the cell's sensitivity to apoptotic triggers (mitochondrial priming). Selective BCL-2 inhibitors (ABT-263 or ABT-199) can directly bind and antagonize BCL-2 and are sufficient to induce apoptosis. However, common oncogenic pathways, like the PI3K/AKT/mTOR pathway, modulate the balance of BCL-2 family proteins and may hinder the efficacy of BCL-2 antagonism. Therefore, in this study, we aimed to evaluate the utility of combining PI3K pathway inhibitors with BCL-2 inhibitors to maximize apoptosis in DLBCLs. We report that selective inhibition of key components in the PI3K pathway (PI3K, AKT, or mTOR) potently sensitized a panel of DLBCL cell lines to ABT-263-induced apoptosis. While the degree of sensitization was heavily dependent on which PI3K pathway component was targeted, dual inhibition of both PI3K and mTOR consistently elicited the most potent sensitization across several cell lines. Mechanistically, inhibition of the PI3K pathway led to a general increase in mitochondrial priming through multiple distinct effects on multiple BCL-2 family proteins. This project demonstrates the potential of combining inhibitors of the PI3K pathway and BCL-2 in the treatment of DLBCL.

Keywords: DLBCL; PI3K; AKT; mTOR; BCL-2;

Poster Session: B - Poster #: 88

Marizomib (NPI-0052) Activity as a Single Agent in Malignant Glioma

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OBJECTIVES: Pre-clinical studies have demonstrated that malignant cells are more susceptible to the cytotoxic effects of proteasome inhibition than normal cells, leading to the development of a powerful anti-cancer strategy by targeting proteasome. Marizomib (NPI-0052) is a second generation irreversible proteasome inhibitor, which has a more lipophilic structure and has a broader inhibition profile for the 20S proteasome compared to bortezomib and carfilzomib, two proteasome inhibitors approved by FDA. While bortezomib and carfilzomib have only modest activity as a treatment of malignant glioma (MG), marizomib might potentially be a novel therapeutic strategy for MG. METHODS: In this study, we investigated the activity of marizomib in primary cell cultures derived from a multitude of human brain tumors (high-grade and low-grade gliomas and meningiomas), normal neural stem/progenitor cells (NSCs) as well as established MG cell lines U-251 and D-54. The effect of marizomib on cell proliferation, motility, apoptosis and Reactive Oxygen Species (ROS) were evaluated in glioma cell lines. The inhibition of marizomib by ROS quenching agent N-acetyl cysteine (NAC) was also tested. RESULTS: The stem-like cells (GSCs) derived from MGs were the most severely affected, in contrast with the low-grade glioma, meningioma and NSC-derived cultures. Marizomib could inhibit proliferation, and significantly decreased migration and invasion of glioma cells. Marizomib treatment was associated with increased free radical production and apoptosis indicated by activation of Caspase-3 and cleavage of PARP. Those effects can be prohibited by exposure to the ROS quenching agent N-acetyl cysteine (NAC). DISCUSSION: These preclinical studies demonstrate a significant anti-tumor effect of marizomib in MG cells. More research into the use of marizomib as a potential treatment for MG was warranted.

Keywords: Malignant glioma; proteasome inhibition; marizomib; apoptosis; ROS;

Poster Session: B - Poster #: 89

Inhibition of mTOR Induces Chemo-Resistance in B-cell Acute Lymphoblastic Leukemia

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B-cell acute lymphoblastic leukemia (B-ALL) is the most common cancer in children. High-risk B-ALL patients often have activated oncogenic kinases like BCR-ABL, PDGFR and JAK. These kinases converge on the PI3K/AKT/mTOR pathway, which promotes cancer cell proliferation and survival. As a result, we tested combinations of various PI3K, AKT and mTOR inhibitors to block this survival pathway and sensitize B-ALL cells to standard chemotherapeutics. However, we found that mTOR inhibition in B-ALL cell lines induces apoptotic resistance to various agents used in standard chemotherapy, with the strongest protection against maintenance phase drugs methotrexate and 6-mercaptopurine. PI3K and AKT inhibitors can sensitize cells to certain drugs, but if they also reduce downstream mTOR activity, they protect against methotrexate and 6-mercaptopurine. Further work will be done to elucidate the mechanism of resistance. Thus far, we have found that mTOR inhibitors can reduce the amount of DNA damage caused by various DNA damaging chemotherapeutic agents. We also detect less ROS (reactive oxygen species) caused by chemotherapeutic agents when combined with mTOR inhibition. The most striking finding is that dasatinib either protects from or enhances methotrexate killing of Ph+ B-ALL cell lines, depending on whether dasatinib inhibits mTORC1 signaling. Thus, direct or indirect inhibitors of mTOR can inhibit the efficacy of maintenance phase chemotherapy drugs. Our findings affect not only the potential future use of PI3K pathway inhibitors in B-ALL but also the current use of dasatinib in high-risk patients.

Keywords: B-ALL; mTOR; PI3K; Dasatinib; Chemotherapy;

Poster Session: B - Poster #: 90

Cortical connectivity is a marker of motor status after stroke

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Neuroimaging markers of brain functional status that correlate with motor status could provide insight into the mechanisms underlying variance in therapeutic efficacy in patients with stroke. The current study evaluated performance of resting-state EEG connectivity as a neural marker of motor impairment in patients with chronic stroke enrolled in a study using home-based rehabilitation therapy. In a partial least squares regression model, connectivity with ipsilesional M1 was a robust marker of baseline impairment ($R2 = 0.78$), with ipsilesional M1 connectivity with ipsilesional frontal-premotor (PM) electrodes accounting for a significant amount of variance in baseline impairment scores ($R2 = 0.52$), even after controlling for corticospinal tract injury. Change in connectivity with ipsilesional M1 was also a good biomarker of motor improvement across therapy ($R2 = 0.61$), with individuals with greater increase in ipsilesional M1-PM connectivity demonstrating greater motor gains ($R2 = 0.34$). The results highlight connectivity to be a robust marker of cortical motor network status during motor recovery in chronic stroke.

Keywords: Telerehabilitation; EEG; connectivity; motor;

Poster Session: A - Poster #: 91

Laparoscopic Surgery For Gastric Malignancy: Outcomes Of A Minimally Invasive Oncologic Resection

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Introduction: Controversy remains over the safety and efficacy of laparoscopic gastric operations. The objective of this study was to evaluate the outcomes of patients who underwent laparoscopic gastrectomy and palliative bypass procedures. Methods: 86 patients who underwent laparoscopic intervention for gastric malignancy between January 2001 and August 2013 were reviewed. 94% of patients underwent laparoscopic gastrectomy, while 6% were found to be unresectable and required a palliative bypass. Main outcome measures included operative findings, conversion rate, hospital stay, morbidity, mortality and pathology. Results: Mean age was 68 years and 52% of patients were male. The majority of cases were performed for gastric adenocarcinoma (90%). Other indications included gastrointestinal stromal tumor (5.8%), dysplasia (1.2%), carcinoid (1.2%), and pancreatic cancer (1.2%). Eight patients (9.3%) underwent neoadjuvant therapy. Procedures performed included laparoscopic total gastrectomy (20%), subtotal gastrectomy (41%), distal gastrectomy (25%), proximal gastrectomy (5%), gastric wedge resection (3%) and palliative gastrojejunal bypass (6%). Eleven patients (13%) were monitored in the ICU postoperatively, with an overall mean ICU stay of 0.9 days. Median hospital stay was 4 days. There were no in-hospital or 30-day mortalities. Two intraoperative complications occurred in patients undergoing subtotal gastrectomy: ischemia of the Roux limb requiring resection and bleeding at the gastrojejunostomy anastomosis. The rate of major complications was 3.7% and minor complications was 9.9%. Anastomotic leak occurred in one patient following total gastrectomy (1.2%). Late complication rate was 11%, with stricture being the most common. Distribution of final pathology was: stage 0 (15%), stage I (47%), stage II (14%), stage III (10%) and stage IV (15%). Conclusion: Laparoscopic gastrectomy is safe and associated with low morbidity and mortality.

Keywords: None

Poster Session: A - Poster #: 92

Lipid-enriched diet rescues lethality and slows down progression in a murine model of VCP-associated disease

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Despite intense investigations, the discovery of effective novel advancements/therapies and the disease mechanisms underlying Valosin containing protein (VCP)-associated myopathies and neurodegenerative disorders remain elusive. VCP diseases, caused by mutations in the VCP gene, are a clinically and genetically heterogeneous group of disorders with manifestations varying from hereditary inclusion body myopathy, Paget's disease of bone, frontotemporal dementia (IBMPFD), amyotrophic lateral sclerosis (ALS), and other neurodegenerative changes. Affected individuals exhibit scapular winging and progressive muscle weakness and die from cardiac and respiratory failure. Histologically, patients display rimmed vacuoles and TAR DNA Binding Protein-43 (TDP-43)-positive ubiquitinated inclusion bodies in muscles. Currently, there are no effective treatments for patients with VCP-related myopathies. VCP mouse models carrying the common R155H mutation include several of the clinical features typical of human diseases. Here, we examined the effects of varying dietary lipid percentages on VCPR155H/+, VCPR155H/R155H and wild type (WT) mice from birth till 9 months of age. Disease progression was monitored and analyzed using survival curves, pathological and immunohistochemical methods. The 9% LED regimen improved survival, motor activity, muscle pathology and autophagy cascade. A targeted lipidomic analysis of skeletal muscle and liver revealed improvements in tissue levels of non-esterified palmitic acid and ceramide (d18:1/16:0), two lipotoxic substances, elevations of which were found in in the untreated homozygous mice. The ability to reverse lethality, increase survival, and ameliorate myopathy and lipids deficits in homozygous animals suggests that lipid supplementation may be a promising therapeutic strategy for patients with VCP-associated neurodegenerative diseases. Interestingly VCP mice fed increased lipid diet concentrations of 12%, 15%, 30%, and 48% showed no improvemen

Keywords: IBMPFD; Myopathy; neurodegenerative; Lipid-enriched diet; ceramide;

Poster Session: A - Poster #: 93

Outcome of Preoperative Weight Loss in Colorectal Surgery

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Objectives: There are limited data regarding the outcomes of patients with preoperative weight loss in colorectal surgery. We sought to identify complications associated with weight loss in colorectal surgery. Methods: The NSQIP database was used to examine the clinical data of patients undergoing colorectal resection from 2005-2011 who had preoperative weight loss (more than 10% in six months). Multivariate regression analysis was performed to identify complications associated with weight loss. Results We sampled a total of 80,503 patients who were admitted non-emergently for colorectal resection, without history of preoperative chemotherapy in last 30 days before operation and without disseminated cancer. The incidence of preoperative weight loss was 4.9%. The in-hospital mortality rate of patients who had preoperative weight loss was more than two times greater than patients without preoperative weight loss (3.74% vs. 1.50%, adjusted OR (AOR): 1.53, $P<0.01$). There are statically significant correlations ($P<0.05$) between preoperative weight loss and preoperative hypoalbuminemia (serum albumin level < 3.5mg/dl) (AOR: 3.17), and preoperative anemia (hematocrit < 33) (AOR: 2.24). Postsurgical complications associated with preoperative weight loss include ($P<0.05$): unplanned intubation (AOR: 1.61), ventilator dependency more than 48hours (AOR: 1.38), and pneumonia (AOR: 1.49). Discussion Preoperative weight loss has a prevalence of 4.9% in colorectal resections. Patients suffering from preoperative weight loss are more likely to die. Patients with preoperative weight loss are more likely to have preoperative hypoalbuminemia, and anemia. In the presence of preoperative weight loss, risk of postoperative complications increases, especially respiratory complications.

Keywords: Weight loss; Colorectal Surgery; Outcomes;

Poster Session: A - Poster #: 95

Long-lasting reduction of blood pressure by electroacupuncture in patients with mild-moderate hypertension: Mechanism of action

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Acupuncture and electroacupuncture (EA) increasingly are being used as complementary medical therapies for a number of diseases including hypertension (HTN). EA is associated with a lower incidence of side effects than pharmacological therapy and therefore increasingly is sought by patients. However, reluctance of physicians to use EA to treat HTN remains strong because its mechanisms of action are largely unknown and because of the many weaknesses in previous acupuncture research. The present study identified the acupoints and parameters of EA stimulation that most effectively reduce systolic blood pressure (SBP) and diastolic blood pressure (DBP) in patients with mild to moderate HTN (BP: >140<180 / >90<110 mmHg). Thirty six hypertensive patients without medication were assessed with 24 hr ambulatory BP monitoring, and EA at P5-6 and S36-37 given once weekly for 30 min for eight weeks. The 8-week treatment decreased peak (19 mmHg) and average (5 mmHg) SBP/24hrs in 25 patients (69%). The peak and average DBP/24hrs decreased respectively by 6 and 5 mmHg. Heart rate was unchanged. After termination of EA treatment, SBP remained reduced for an additional four weeks but over the next four weeks returned to near pretreatment levels. Eleven patients (31%) did not respond to the EA treatment. Both SBP and DBP/24hrs were not reduced in 28 other patients treated with control acupoints (Li6-7+G37-39). These data suggest that EA at select acupoints, performed once weekly for 8 weeks, significantly reduced BP. This beneficial effect was slow in onset but persisted for a prolonged period of time. In subgroups of patients we measured plasma catecholamines (n=25), renin (n=22) and aldosterone (n=18). After eight weeks of EA, plasma concentrations of nor-epinephrine, renin and aldosterone decreased significantly (P<0.05) in the EA-responders in contrast to non-responders. Thus, the renal sympathetic function and renin-aldosterone system were related to EA inhibition o

Keywords: hypertension; electroacupuncture; responders and non-responders; plasma catecholamine; renbin-aldosterone;

Poster Session: A - Poster #: 96

Effect of 12 Weeks of Oral Betaine on Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) in Non-Diabetic Subjects with Mildly Elevated Fasting Blood Sugar

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Introduction: The primary aim of this multiple ascending dose study was to assess the efficacy of betaine in reducing HOMA-IR, a validated surrogate for the ‘gold standard’ euglycemic glucose clamp, in non-diabetic, insulin resistant subjects. Secondary outcomes included safety, and the effect of betaine on liver injury (AST, ALT), inflammatory markers (hs-CRP, uric acid), lipids, and HA1c. Methods: This study was a prospective, unblinded, multiple ascending dose study of oral betaine in subjects with fasting blood sugar between 100 and 125 mg/dL and HOMA-IR>3.0. Exclusions included diabetes, >2 drinks of alcohol/day, liver disease other than NAFLD, HIV, or severe co-morbidities. Patients were given placebo twice daily for 4 weeks, after which subjects were given oral betaine at 2, 4, and 6 grams twice daily for 4 weeks/dose. Fasting insulin, glucose, glycosylated hemoglobin, liver function tests, uric acid, and hs-CRP were measured at each visit during this time frame. Data was analyzed using 2-sided, paired t-test. Results: A total of 40 patients were screened with 19 male patients mean age 63 enrolled. One patient dropped out at Week 8 for non-adverse events. HOMA-IR scores did not improve significantly at week 12 of treatment. Similarly, neither uric acid, hs-CRP, AST, nor ALT improved significantly with betaine treatment. Analysis of secondary outcomes found that almost all values at baseline were within the normal range. Although the numbers were small, all patients with elevated ALT, uric acid or hs-CRP at baseline had improvement at the end of betaine treatment. There were no serious adverse events related to betaine treatment. Conclusions: Betaine treatment for 12 weeks did not improve HOMA-IR in this population. Betaine did not improve ALT, hs-CRP, uric acid or HA1c. However, betaine did improve ALT and inflammatory markers in select patients. Betaine may also have raised total, LDL and HDL cholesterol in a dose dependent fashion.

Keywords: fatty liver; betaine; nafld; tmg; steatohepatitis;

Poster Session: B - Poster #: 97

Rapamycin and Chloroquine: the in vitro and in vivo effects of autophagy-modifying drugs in valosin containing protein multisystem proteinopathy

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Mutations in the valosin containing protein (VCP) gene cause hereditary Inclusion body myopathy (hIBM) associated with Paget disease of bone (PDB), frontotemporal dementia (FTD), more recently termed multisystem proteinopathy (MSP). Affected individuals exhibit scapular winging and die from progressive muscle weakness, and cardiac and respiratory failure, typically in their 40s to 50s. Histologically, patients show the presence of rimmed vacuoles and TAR DNA-binding protein 43 (TDP-43)-positive large ubiquitinated inclusion bodies in the muscles. We have generated a VCPR155H/+ knock-in mouse model which recapitulates the disease phenotype and impaired autophagy typically observed in patients with VCP disease. Autophagy-modifying agents such as rapamycin and chloroquine at pharmacological doses have previously shown to alter the autophagic flux and autophagic signaling intermediates. Herein, we report administration of rapamycin, a specific inhibitor of the mechanistic target of rapamycin (mTOR) signaling pathway, to 19-month old VCPR155H/+ mice. Rapamycin-treated mice demonstrated significant improvement in muscle performance, quadriceps histological analysis, and rescue of defective autophagy by decreasing the protein expression levels of TDP-43, p62/SQSTM1, optineurin, ubiquitin, and LC3-I/II and inhibiting the mTORC1 pathway substrates. Conversely, chloroquine-treated 19-month old VCPR155H/+ mice revealed progressive muscle weakness, cytoplasmic accumulation of TDP-43, ubiquitin-positive inclusion bodies and increased LC3-I/II, p62/SQSTM1, and optineurin expression levels. These findings may have implications for further development of interventions targeting the mTOR pathway and restoring autophagic flux and for future potential systemic therapies in a broad range of VCP-related neurodegenerative multisystem proteinopathies.

Keywords: Valosin Containing Protein; IBMPFD; ALS; Rapamycin;

Poster Session: A - Poster #: 98

Comparing Visual Analog Scale And Verbal Numeric Rating Scale In Patients With Chronic Pain

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Pain is an unfortunate sequela to a wide spectrum of illnesses and disease states among patients. Pain scales are widely used by physicians to gauge the level of a patient's pain experience and to appropriately prescribe pharmacological or interventional treatments for pain management. Previous studies have compared multiple pain scales in Trauma and Emergency Units. However, pain scale comparisons have not been assisted in patients with recurrent chronic pain. Here, we compared the Visual Analog Scale (VAS) and Verbal Numerical Rating Scale (VNRS) in patients with recurring chronic pain. This research utilizes a sample of 43 patients seen in the Pain Clinic at the Gottschalk Medical Plaza since February of Winter Quarter 2014. We found that upon admission, the linear regression (R2) between the scales is 0.806 and 0.852 upon discharge. Additionally, through Hospital Anxiety and Depression Scale self-reporting, 55.8% and 60.5% of patients did not report (score of <8) anxiety and depression and 44.2% and 39.5% of patients report having mild to severe (score of >7) anxiety or depression, respectively. Additionally, the quality of life (5D-EQ) self-reporting average health outcome score for women and men is 60% and 50%, respectively. Our study suggest that further research must be conducted to identify the efficacy of a specific pain scale in determining the pain experienced in patients with recurring chronic pain.

Keywords: VAS; VNRS; Chronic Pain; HADS; Quality of Life;

Poster Session: A - Poster #: 101

DNA Methylation is Altered in Human Skeletal Muscle in Response to Exercise Training

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DNA methylation is an epigenetic modification, which is influenced by environmental stimuli (e.g., exercise), and can play an important role in the adaptive process involving altered gene expression. Currently, little is known on DNA methylation status in muscle undergoing remodeling in response to exercise training. PURPOSE: To determine if exercise training would induce alteration in DNA methylation in human skeletal muscle. METHODS: Thirty three subjects, 20-26 y/o, were assigned to one of two 5-week exercise protocols: a) Resistance Exercise (RE), 2 days a week, or b) Combined Aerobic and RE (AE+RE), 5 days a week: DNA was extracted from the vastus lateralis muscle, treated with sodium bisulfite, and analyzed for methylation using the Infinium HumanMethylation450 BeadChip (Illumina). Statistical analysis was done using Partek Genomics Suite. RESULTS: Both exercise protocols altered the methylation status in the vastus lateralis muscle, however the AE+RE protocol had a greater effect (6976 CpG sites compared to 970 CpG sites in the RE only ($P<0.0005$). These altered CpG sites correspond to 3323 and 692 genes respectively. Of these, only 197 genes were common in both paradigms. In the AE+RE group we identified Kegg pathways that were enriched with genes with altered methylation; e.g., insulin signaling, focal adhesion, phosphatidylinositol, MAPK, and Notch signaling (EASE<0.05). CONCLUSION: Two different exercise protocols generated differential response in DNA methylation. The altered genes are part of important signaling and structural pathways that are involved in muscle plasticity. This is the first study demonstrating that only five weeks of training can alter DNA methylation in human skeletal muscle. This information can enhance our understanding of complex molecular mechanisms leading to muscle plasticity in response to exercise stimulus.

Keywords: Epigenetics; Infinium HumanMethylation450 BeadChip; Aerobic Exercise; Resistance Exercise; Kegg Pathways;

Poster Session: A - Poster #: 102

Actigraphy Use in a Patient with Inclusion Body Myopathy: a Case Report

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Inclusion Body Myopathy (IBM) associated with VCP mutations is a rare genetic disorder characterized by progressive muscle weakness, reduced physical activity (PA), pain, and abnormal sleep. PURPOSE: To monitor PA and sleep pattern in a wheelchair bound patient with IBM over 15 months. We hypothesized that PA would progressively decrease and sleep would become less efficient. METHODS: An Actigraph worn on the wrist was used to collect 24h motion data. Data was collected for a total of 268 days, and was grouped into 11 blocks. For daytime, data from 11am to 7pm was used. One way ANOVA was applied to detect PA differences among the 11 blocks. Linear regression was used to detect significant changes in daily PA over time. Sleep patterns were analyzed using Actilife built-in Sleep Analyses. RESULTS: Actigraph data corresponded well to activity log report. The patient reported progressive decline in hand strength during the study and had to adjust movement to compensate and complete tasks of daily life. Despite a 30% decline in hand grip force ($P<.05$), there was no significant change in Actigraph daily PA over the 15 months, as demonstrated by a flat regression line. Sleep efficiency ranged from 75 to 82% in the first 10 blocks and was significantly below normal ($p<.01$). However, it was normalized during the last block. Interestingly, the patient associated the improved sleep with using melatonin & acetaminophen. CONCLUSION: There can be a significant decline in muscle strength that remains undetected with wrist actigraphy. The patient compensated for progressive weakness by finding alternate muscle use paradigms to complete specific tasks. Improved methods to characterize daily PA in people with neuromuscular disease might prove useful in identifying how patients compensate for progressive weakness. Currently wrist actigraphy and activity log are both needed for this evaluation. Finally, wrist actigraphy can be effectively used to monitor sleep pattern.

Keywords: accelerometer; Myopathy; Physical Activity; Sleep Efficiency

Poster Session: A - Poster #: 103

Utility of the Timed Mile Run among Overweight Youth

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Purpose: The Mile Run/Walk test (MRW) is commonly used to assess students' cardiovascular fitness as a component of the FITNESSGRAM. This study examines the utility of the MRW among overweight youth. Methods: Students in a school-based physical activity study (N = 59; mean age = 11.05 +/- .34 years; 50% Hispanic; 50% Male; 41% overweight) completed a MRW and a standardized test of cardiovascular fitness, and wore an Actigraph activity monitor for one week to assess moderate-to-vigorous activity (MVPA). Results: The correlation between predicted VO2max (based on MRW and BMI) and measured VO2max (from the graded exercise test) was strong ($r = .78$, $p < .001$) for both overweight and normal weight youth. All students identified by the MRW as being in the "needs improvement" zone of the FTNESSGRAM were at or above the 85th percentile for BMI. MVPA was associated with measured VO2max ($r = .33$, $p < .01$), but not with predicted VO2max. Conclusions: The MRW offers a valid estimate of VO2max among both normal weight and overweight youth. In terms of yielding behavioral recommendations, however, BMI and objective monitoring of activity may be more useful.

Keywords: School; Fitness; Assessment; Obesity;

Poster Session: A - Poster #: 104

California Statewide Prescription Drug Monitoring System And It'S Effect On Physician Prescribing Behavior Among Emergency Department Chronic Pain Patients

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The number of overdose deaths due to prescription opioid analgesics is greater than the number of deaths due to heroin and cocaine abuse combined, and is increasing at an alarming rate. An attempt to curtail this problem may stem from providing prescribing physicians with additional patient information obtained from the Prescription Drug Monitoring Program (PDMP). We have observed alterations in prescription behavior patterns after utilization of a PDMP by emergency physicians on patients who present to the emergency department for chronic pain. We prospectively collected data on 168 chronic pain patient encounters in the ED from September 2012 to December 2013. Thirty-four physicians were monitored in their prescribing behavior. Physicians evaluated chronic pain patients in the ED and were approached by research associates to determine the number, strength, and type of analgesics being prescribed. Subsequently, physicians accessed the PDMP for that encounter and were asked if there was a change in their prescribing patterns after viewing the PDMP. Binomial confidence intervals were calculated for the data. The prescribing physicians changed the prescription after accessing PDMP in 79 (47%) cases (95% CI 39.3%-54.9%). 16 (20%) of these were changes (increase and decrease) to the number of pills prescribed (95% CI 12.4%-31.1%), while 63 (80%) were changes to the type of drug prescribed (95% CI 69.2%-87.9%). Of the 168 cases, 46 (27%) were prescription changes that decreased the strength of narcotic analgesic, the number of pills, or the dosage of the medication (95% CI 20.8%-34.8%). 26 (15%) were prescription changes that increased the strength of the narcotic analgesic, the number of pills, or the dosage of the medication (95% CI 10.4%-21.8%). In our study, physician prescribing patterns were changed 47% of the time after accessing PDMP in the ED. The results suggest PDMP is a useful modality in identifying patients presenting in the ED for chronic pain. Futur

Keywords: Prescription Drug Monitoring Program;

Poster Session: A - Poster #: 105

The Inter-Rater Reliability And Validation Of Psystart Mental Health Triage Instrument In Adult Trauma Patients

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The purpose of this prospective pilot study is to assess both the inter-rater agreement between emergency medicine attending and resident physicians, as well as to validate the effectiveness and accuracy of the PsySTART Rapid Mental Health Triage and Incident Management System within UCI Medical Center's Emergency Department. This two-fold study involves physician observation and patient interview via completion of three identical PsySTART tag forms that list 13 mental health risk factors concerning the patient's well-being and their trauma experience. In a consecutive sample of 112 English-speaking, physically-stable adult trauma patients, 18 years of age and older, that took place from November 2013 to March 2014, 95 patients (84.8%) had PsySTART tag forms completed by the two physicians. Among those 95, 48 of the patients were interviewed. The unweighted Cohen's kappa of the risk factors ranged from 0.0951 to 0.4934 ($p < 0.05$), indicating slight to moderate inter-rater agreement. Amongst the attending physicians, the sensitivity ranged from 0-0.379, the specificity ranged from 0.3-0.923, the PPV ranged from 0-0.846, and the NPV ranged from 0.441-0.977. For resident physicians, the sensitivity ranged from 0-0.345, the specificity ranged from 0.667-1, the PPV ranged from 0-1, and the NPV ranged from 0.474-0.978. The data provide no evidence that suggest the rating physicians agree strongly beyond pure chance in regards to assessing a patient's PsySTART risk factors. In addition, the high specificity alludes to the strong agreement of the absence of a risk factor, while the low sensitivity suggests the weaker likelihood that the physician observed the presence of a risk factor among trauma patients enrolled.

Keywords: None

Poster Session: A - Poster #: 106

Comparative Effectiveness Of Patient Participation Training Vs Diabetes Education In Low Socioeconomic Status Patients With Type 2 Diabetes: A Pragmatic Randomized Trial Of Coached Care

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OBJECTIVES: We compared the impact on glycemic control of two community health worker (CHW) interventions: Coached Care, where the CHW teaches patients skills to participate more actively in their care, versus Diabetes Education, where the CHW presents information about diabetes but no training on participation skills. METHODS/STUDY POPULATION: An ethnically diverse, low-income sample of type 2 diabetes patients with HbA1c >7.5% was recruited. Participants (N=545) were randomized to either Coached Care or Diabetes Education. In both arms, the CHW met the patients at the clinic before every diabetes-related medical visit during the study period to conduct a 20-minute session. Change in HbA1c from baseline to one-year follow-up was estimated using a linear mixed model adjusting for age, sex, race and education. RESULTS: Reduction in HbA1c was greater in patients randomized to Coached Care (-0.43% 95%CI -0.59, -0.26; $p<0.0001$) versus Diabetes Education (-0.10% 95%CI: -0.28, 0.08; $p=0.27$), in spite of similar intensity of medication therapy. DISCUSSION: CHW's teaching patient participation skills improved glycemic control in this diverse, low-income sample.

Keywords: diabetes; patient participation; disparities;

Poster Session: A - Poster #: 107

Beyond the numbers: Addressing challenging life circumstances during the medical visit for low-income patients with type 2 diabetes

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Objectives: The study examined how patients with type 2 diabetes and physicians discuss challenging life circumstances during the medical visit and create a plan of care that accounts for them. Methods/Study population: The sample of patients (N=387) consisted of low-income non-Hispanic White, Latino and Vietnamese American patients treated for type 2 diabetes who consented to the Reducing Racial Disparities in Diabetes Coached Care study (R2D2C2) at UC Irvine outpatient clinics between 2007-2013. First, medical records were examined to identify patients with "red flags", such as uncontrolled glucose, cholesterol or blood pressure, that would indicate to the physician that the patient may be struggling to manage their diabetes. For those patients with at least one red flag in their record, audio recordings of the medical visit were analyzed using a validated coding method. Each recording was coded to indicate whether (1) a hidden "contextual factor", such as financial problems or a lack of social support, was discussed as a possible contributor to their poor outcomes and (2) whether the contextual factor was addressed by the doctor with a "contextualized plan of care", in which treatment would be modified or new resources introduced to help the patient address the contextual factor. Results: Preliminary results indicate that approximately 62% of the 387 patients had at least one red flag raised. An array of contextual factors thought to contribute to these red flags were revealed in the audio recordings, but often times were not addressed in the plan of care. Discussion: Patients facing challenging life circumstances, even individuals with access to medical care, fail to realize the full benefit of existing therapies, largely because their treatment regimens are not tailored to meet their needs. This study illuminates the importance of promoting more effective doctor-patient communication to tailor regimens to a patient's life context to improve outcomes.

Keywords: Diabetes Type 2; Disparities; Doctor-patient communication; Tailored treatments; Contextual Factors;

Poster Session: A - Poster #: 108

Mobile health applications in older Hispanic patients and their family caregivers to improve self-care and adherence to warfarin therapy

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BACKGROUND: Older Hispanic adults are at substantial risk for cardiovascular and cerebrovascular disorders that require oral anticoagulation treatment. Tremendous progress has been made in the use of anticoagulants but the treatment effectiveness is largely dependent on a patient's ability to follow the regimen. Older Hispanics report it is difficult to do this and risk reduced therapeutic benefit and adverse outcomes. Mobile health (mHealth) tools can assist older adults to manage anticoagulation but such tools have not been tailored for older Hispanics. OBJECTIVES: The goal of the study is to design and test an mHealth intervention, composed of several culturally appropriate and age-sensitive components. METHODS: We recruited Spanish-speaking participants on oral anticoagulation therapy and their family caregivers. Topics included medication self-management strategies and use of health technology. Participants reviewed commercial health apps. The group discussions were audio-taped and transcribed. The data have been analyzed to draw common themes. RESULTS: Nine patients and 5 caregivers participated in four group sessions. Majority of patients reported they do not use health technology due to the expense. However, they commented that medication reminders or Vitamin K apps would be helpful with family support. Caregivers expressed health apps would be helpful to provide care for parents with chronic diseases. DISCUSSION/IMPACT: Older Hispanics and caregivers are open to learn and use mhealth technology. We have used the data in developing mHealth-based intervention for older Hispanics to improve self-care and adherence.

Keywords: Mobile Health; Anticoagulation Treatment; Older adults; Chronic diseases; Adherence;

Poster Session: A - Poster #: 109

The Economic Impact Of A Community-Based Home Visitation Program On Birth Outcomes: Moms Orange County

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Academic partner: University of California Irvine, Program in Nursing Science Community partner: MOMS Orange County

Purpose: The purpose of this research was to provide preliminary evidence about the economic impact of the MOMS Orange County maternal-child health coordination model on birth outcomes. Methods: This study included an academic and community partnership approach. MOMS provided a de-identified dataset. MOMS and UCI's Program in Nursing discussed and generated the analysis plan. UCI's Program in Nursing Science was responsible for conducting relevant analyses of the MOMS data. The Orange County (OC), California (CA) State and U.S. birth outcomes were obtained from the literature and were used to compare with MOMS' birth data. In 2010, 1,103 pregnant women who participated in the MOMS program delivered babies. The study calculated the cost savings of the MOMS program in reducing negative birth outcomes in 2010. Results: Women in the MOMS program were found to have lower preterm births and low birth weight births than the county, state and national averages 2010 (MOMS: 5.9% vs. OC: 9.1% vs. CA:10% vs. U.S.: 12%). If 1,103 births were randomly selected at the county, state and national levels, it is found that MOMS has 31 fewer preterm births than in OC, 41 fewer than in CA State, and 63 fewer than in the U.S. According to an Institute of Medicine report, the estimated cost per infant born preterm in the U.S. is $51,600. Using 1,103 births from 2010 from MOMS participants, we estimate that MOMS generates $1.6 million in savings in OC, $2.1 million in CA state and $3.2 million in the U.S. in reducing preterm births. The same estimate was applied to very low birth weight births ($280,000 per VLBW birth). We estimate that MOMS generates $560,000 savings in OC, $1.1 million in CA state and $2.2 million in the U.S. through reducing VLBW deliveries. Implications: The evidence suggests that MOMS Orange County has the potential to save significant healthcare costs by increasing the rates of positive birth outcomes.

Keywords: home visitation; cost saving; health disparity;

Poster Session: A - Poster #: 110

Developing Ergonomic Injury Prevention Programs for Vietnamese Supermarket Workers

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With the small funding provided by the ICTS, the project team has managed to make multiple accomplishments, which included: a) a new understanding of the injury prevention needs in the targeted community, b) new program directions, and c) an expanded partnership with more community and academic institutions for future research funding. A needs assessment survey with the workers and managers indicated that: 90% of the workers were Vietnamese and 10% were Latino. Preferred languages of the injury prevention training were: Vietnamese, Spanish and English. A set of injury prevention posters in Vietnamese, Spanish and English have been developed. The future directions of this project are: a) identifying innovative ways to conduct and evaluate the training program, and b) identifying different channels to outreach more supermarkets. This project has also led to a new partnership between the UCI and the UCLA Labor and Occupational Safety and Health to implement an injury prevention training program for Asian and Latino Americans in Orange County. In addition, this partnership project has led to development of new research areas and identification of funding for future research.

Keywords: Community research; Vietnamese Americans; Injury prevention;

Poster Session: A - Poster #: 111

YKL-40 As A Marker Of Endothelial Dysfunction And Hypertension In Obstructive Sleep Apnea

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Purpose: Obstructive sleep apnea (OSA) is a common chronic disorder affecting 15-24% of the adults and is associated with increased morbidity and mortality. Majority of patients with OSA are subjected to intermittent hypoxemia during sleep which leads to an oxidative and inflammatory state. The exact mechanism (s) underlying the increased risk for cardiovascular disease is not entirely clear. YKL-40 is an inflammatory marker with participation in extracellular matrix remodeling and with an established role in angiogenesis. Substantial evidence indicates that YKL-40 might participate in processes during early stages of atherosclerosis. We sought to determine the role of YKL-40 in endothelial dysfunction and hypertension in OSA. Methods: We studies 93 subjects in four groups according to OSA and hypertension status. Endothelial-dependent vasodilation was assessed using flow-mediated vasodilation (FMD). YKL-40, vascular endothelial growth factor (VEGF) and soluble form of VEGF receptor-1or sFlt-1, antagonistic to VEGF, were measured in plasma using ELISA method. Results: FMD was markedly impaired in hypertensive OSA (8.0%±0.5) compared to normotensive OSA (13.5%±0.5, P<0.0001) and non-OSA with (10.5%±0.8, P<0.01) and without hypertension (16.1%±1.0, P<0.0001). YKL-40 was significantly elevated in hypertensive OSA compared to other three groups and had a negative correlation with FMD (r=-0.37, P=0.0008). VEGF levels were significantly elevated in both OSA groups compared with non-OSA subjects and showed a positive correlation with apnea-hypopnea index (r=0.36, P=0.0009). sFlt-1 was elevated in only OSA groups. sFlt-1/VEGF ratio, a measure of anti-VEGF activity, had a significant positive correlation with YKL-40 (r=0.38, P=0.01). Conclusion: Elevated circulating levels of YKL-40 are associated with endothelial dysfunction and hypertension in OSA patients. Patients with similarly severe OSA but without endothelial dysfunction or hypertension have YKL-40 levels comparable to control subjects. The mechanism for YKL-40 expression appears to be related, in part, to suppression of VEGF by sFlt-1. This specificity suggests YKL-40 could be a potential biomarker for endothelial dysfunction in OSA.

Keywords: sleep apnea; YKL-40; cardiovascular; hypertension; endothelial function;

Poster Session: A - Poster #: 112

Activation of peripheral mu-receptors suppresses ischemic mediator-induced cardiac excitatory reflex responses

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Myocardial ischemia evokes cardiac sympathoexcitatory reflex responses through stimulation of cardiac spinal afferents. We have demonstrated that a P2X2/3 agonist stimulates ischemia-sensitive, but not ischemia-insensitive cardiac sympathetic afferents, while blockade of peripheral opioid receptors with naloxone enhances the responses of these afferents to P2 receptor activation with ATP. In the present study we tested the hypothesis that opioids, through stimulation of peripheral μ-opioid receptors, inhibit excitatory reflex responses induced by ATP. Hemodynamic parameters were recorded in six anesthetized rats after bilateral vagotomy. Injection of the P2X2/3 receptor agonist a,ß-meATP (125-250 nmol), into pericardial sack increased mean blood pressure (BP) from 85±6 to 115±7 mmHg, a response that was reduced by 19% following activation of peripheral opioid μ-receptors with intrapericardial DAMGO, a selective μ-receptor agonist. In contrast, blockade of opioid μ-receptors with intrapericardial CTOP, selective μ-receptor antagonist, exaggerated the a,ß-meATP-induced BP response by 22% in five other rats. Single-unit cardiac afferent recordings showed that epicardial CTOP enhanced the responses of 5 ischemia-sensitive cardiac spinal afferents to a,ß-meATP by 51%. Together, these data suggest that peripheral μ-opioid receptor stimulation suppresses P2X2/3 receptor evoked cardiac excitatory reflex responses through inhibition of ischemia-sensitive cardiac sympathetic afferents. (Supported by NIH Grant HL66217)

Keywords: Cardiac sympathetic afferent; pressor reflex; Myocardial ischemia; opioid receptors; angina pectoris;

Poster Session: A - Poster #: 113

An elPBN-rVLM excitatory pathway participates in cardiac-sympathoexcitatory responses

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We have demonstrated that the external lateral parabrachial nucleus (elPBN) within the pons and rostral ventrolateral medulla (rVLM) are involved in central processing of excitatory cardiovascular reflexes during stimulation of cardiac sympathetic afferents. Direct projections from the elPBN to the rVLM exist. Moreover, glutamatergic neurons in the elPBN are activated by inputs from cardiac sympathetic afferents. However, there is no information on involvement of elPBN-rVLM excitatory pathways in regulation of cardiovascular responses following stimulation of cardiac sympathetic nerves. Thus, in the present study we evaluated the possibility that excitatory glutamatergic pathways from the elPBN to the rVLM participate in processing sympathoexcitatory responses evoked by stimulation of cardiac sympathetic afferents. First, in three rats, retrograde fluorescent microspheres were microinjected into the rVLM followed by epicardial stimulation with a, ß–meATP. We frequently noted elPBN neurons triple-labeled with the retrograde tracer, vesicular glutamate transporter 3 and c-Fos, but rarely in two controls, suggesting that elPBN glutamatergic neurons activated by the cardiac stimulation directly project to the rVLM. Second, we found that electrical stimulation of the cardiac sympathetic nerves evoked activity in three elPBN neurons. Finally, in twelve separate cats, we recorded pre-sympathetic rVLM activity evoked by cardiac sympathetic nerve stimulation following activation or inhibition of the elPBN. We observed that stimulation of the elPBN by microinjecting dl-homocysteic acid (4 nM, 50 nl) increased rVLM activity and evoked rVLM responses to cardiac nerve stimulation ($P<0.05$; n=5). Blockade of the elPBN with kynurenic acid (25 mM, 50 nl) reduced cardiac-evoked rVLM activity ($P<0.05$; n=4). These data suggest that an excitatory glutmatergic pathway from the elPBN to the rVLM contributes to cardiac-sympathoexcitatory responses.

Keywords: parabrachial nucleus; rostral ventrolateral medulla; cardiovascular reflexes; cardial stimulation;

Poster Session: A - Poster #: 114

Screening of Young Athletes for Hypertrophic Cardiomyopathy using Echocardiography

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Background: Hypertrophic cardiomyopathy is the leading cause of sudden cardiac death in young athletes. Screening with electrocardiogram identifies many false positive cases. Objective: To screen for and determine the prevalence of abnormalities of the heart, specifically hypertrophic cardiomyopathy, in a population of young athletes using echocardiogram. Methods: University of California, Irvine medical students were recruited and trained to obtain cardiac ultrasound images to detect hypertrophic cardiomyopathy (HCM) in local high school athletes. Ten Orange County, California high schools or colleges hosted the ultrasound cardiac screening team of 5-15 medical students and 1-2 supervising physicians as part of student athlete physical events. An average of 120 student athletes were scanned during each 4-hour screening. For each athlete, a medical student obtained 2-second video-clips of parasternal long (PSL) and parasternal short (PSS) cardiac views. From the parasternal short view, the muscular ventricular septum and the left ventricular wall were monitored in motion mode (m-mode) and were measured in systole and diastole on a still m-mode image. The recorded ultrasound videos and images were reviewed by a pediatric cardiologist after the screening and rated as good, acceptable, or poor, as well as evaluated for HCM. Results: Cardiac ultrasound data was collected for 1283 young athletes in Orange County, CA over a four month period. The cardiologist analyzing the scans rated 87% of PSL & PSS videos and 95% of m-mode images as good or acceptable. Caliper measurements on the m-mode image were correct or close 84% of the time. Four student athletes were identified as having HCM, and 56 additional students were found to have borderline HCM. Conclusion: Screening student athletes for HCM using ultrasound performed by trained medical students identifies HCM cases near the currently reported rate of 1 in 500.

Keywords: Cardiac; Ultrasound; Student; Athlete; Cardiomyopathy

Poster Session: A - Poster #: 115

Persistence Of Eeg Activity In The Right Visual Cortex After Cardiac Arrest In A Rodent Model

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Introduction: Scientists and theologians have long been fascinated by the phenomenon of near-death experiences (NDE), reported as extremely vivid imagery when humans survive a near-fatal encounter. Recent quantitative electroencephalogram (EEG) studies suggest that the brain transiently becomes active during cardiac arrest (CA). Additionally, the occipital lobes, harboring the visual cortices, are thought to facilitate NDE. Hypothesis: We examined whether EEG activity remains resilient during and after cardiac arrest, and whether the visual cortex harbors the highest activity. Methods: EEG leads (L/R frontal lobes and L/R occipital lobes) were implanted in 15 adult Wistar Rats. One week later, rats underwent 7-minute asphyxial CA while undergoing EEG. EEG sub-band analysis was done using Information Quantity (IQ), an entropy based nonlinear calculation of the variability and content of EEG. Results: During CA induction, we find that EEG IQ in the R occipital lobe is significantly resistant to suppression at the EEG alpha sub-bands (8-12Hz; slope of EEG decrement = -0.0086 IQ/min ±0.0028 [Std Dev]) and slow gamma sub-bands (30-50Hz; -0.0085±0.0027 IQ/min) in comparison to either L frontal lobe (-0.0203±0.0040 [alpha], -0.0261±0.0044 [slow gamma]), R frontal lobe (-0.0193±0.0043 [alpha], -0.0236±0.0054[slow gamma]) or the L occipital lobe (-0.0198±0.0045 [alpha], -0.0227±0.0055 [slow gamma]). All p-values<0.001. Conclusions: These data show that, in a rodent model of CA, the R visual cortex has profound resistance to loss of EEG entropy, most robustly in the alpha and slow gamma EEG sub-bands. In humans, gamma range EEG is associated with waking consciousness and deep mentation. While the importance of the R visual cortex in imagery is known, our data is the first to demonstrate resilience of the R visual cortex during death. Upon further validation in humans, these data may better elucidate mechanisms of NDE-related imagery.

Keywords: coma; cardiac arrest; EEG; visual cortex; near-death experience;

Poster Session: A - Poster #: 116

4D-Flow Echocardiography

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Objective: To quantify cardiovascular flow fields in 3D and time using echocardiography. Methods: We developed 4D-Flow Echocardiography (4D-Flow Echo) that is a novel method to quantify the cardiovascular flow fields in 3D and time. 4D-Flow Echo utilizes modern matrix array 3D ultrasound probe and scans the heart in a unique way, which results in faster scanning of one heartbeat, with higher resolution in each frame. 4D-Flow Echo applies a multi-planar velocity reconstruction approach that characterizes 3D incompressible flows based on reconstruction of 2D velocity fields. We validated the method in computer-generated exemplary 3D flows. Also, we experimentally reconstructed 3D flow inside a model of the heart's Right Ventricle (RV) in a heart-flow-simulator. We also applied the method to an in-vivo echocardiography data of the left ventricle. Results: The results for 3D flow inside the RV model suggested the metamorphosis of the original vortex ring, which forms downstream of the tricuspid valve in the early systole, into a streamline-single-leg vortex extending toward the outlet. This supports the observation made by another group. The reconstructed 3D flow for in-vivo data depicted the incoming transmitral jet filling the LV. The results for both in-vitro and in-vivo experiments illustrate the feasibility of this method. Discussion/Significance of Impact: Understanding blood flow is critical as it is the fingerprint of cardiac performance. Each heart disease has unique blood flow characteristics and any variation in the blood flow pattern may indicate a change in cardiac performance. Quantifying 3D cardiac flow pattern has remained a challenging fluid dynamics problem and modern velocimetry techniques cannot yet acquire data with sufficient spatial and temporal resolution to improve clinical diagnosis. 4D-Flow Echo, presents an economical, portable, and a more convenient way compared to other modalities such as flow-sensitive magnetic resonance imaging.

Keywords: 4D-Flow; Echocardiography; Cardiac flows; Medical Imaging;

Poster Session: A - Poster #: 117

Differential cardiovascular responses elicited by point specific acupuncture during phenylbiguanide-induced reflex stimulation

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Stimulation of cardiopulmonary receptors with phenylbiguanide (PBG) consequent to vagal activation decreases blood pressure (BP) and heart rate (HR) mediated by the nucleus ambiguus (NA) and nucleus tractus solitarii (NTS). EA at P5-6 reverses PBG-induced reflex bradycardia through modulatory actions in the NA. The current study examined effects of EA at P5-6 (median nerves), ST36-37 (deep peroneal nerve), LI4-L7 (branches of median and superficial radial nerves) and G37-39 (superficial peroneal nerve) acupoints on the PBG reflexes in the NTS. We hypothesized that point specific EA modulation of PBG-induced vasodepression and bradycardia is related to differential levels of EA-related somatic and cutaneous afferent evoked activity in cardiovascular and EA-sensitive NTS neurons. NTS activity and HR and BP responses were recorded every 10 min during either repeated stimulation of the cervical vagus or iv PBG in cats. After two consistent responses, 30 min EA was applied bilaterally at P5-6, ST36-37, LI4-L7 or G37-39. NTS neurons displayed cardiac rhythmicity, convergence from vagal and baroreceptor afferents, and nerves located under acupoints. Kainic acid into the medial NTS decreased bradycardia from -40±10 to -18±2 b/m and depressor from -32±6 to -20±2 mmHg. EA at P5-6 reduced for over 60 min the depressor by 67% and bradycardia by 60%. Unlike LI4-L7 and G37-39, EA at ST36-37 reduced the depressor by 56% and the bradycardia by 60%. Brief activation of median and deep peroneal nerves showed much greater NTS evoked activity, compared to cutaneous nerves. Unlike LI4-L7 and G37-39, EA at P5-6 and ST 36-37 reduced vagal evoked NTS activity from 12±2.0 to 2±0.8 and 11.5±1.3 to 2±1.2 spikes/30stim, respectively. Thus at the different acupoints, brief stimulation differentially activates cardiovascular NTS neurons and following 30 min EA elicits point specific responses to PBG stimulation. These data support point specific EA responses that reverse cardiovascul

Keywords: bradycardia; depressor; specific acupoints; nucleus tractus solitarius; parasympathetic;

Poster Session: B - Poster #: 118

Individual Variability In Endothelial-Dependent Vasodilation In Response To Obstructive Sleep Apnea And Hypoxia: Implications For Cardiovascular Risk Stratification

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Background: Obstructive sleep apnea (OSA) has been shown to increase population burden of cardiovascular diseases including hypertension. However, these epidemiologic studies do not identify individuals at risk. The relative risks for development of incident coronary artery events, stroke or hypertension are in the order of less than 3-fold. Endothelial dysfunction is considered the underlying initial and maintaining mechanism for atherosclerosis. We hypothesized that there are individual variabilities in endothelial function and susceptibility to hypertension in response to OSA and hypoxia indices (ODI,oxygen desaturation index; T<90, time asleep with SaO2<90%). Methods: 63 patients (50 men and 13 women) with apnea-hypopnea index of >20/hr on polysomnography and CPAP naïve underwent flow-mediated vasodilation (FMD) as a measure of endothelial-dependent vasodilatory capacity. Existing hypertension was considered as an adverse cardiovascular outcome. Results: Age, yr BMI, kg/m2 AHI/hr ODI/hr T<90,min FMD, % Normotensive, n=27 47.9±2.2 36.3±1.5 41±5 32±5 34±8 13.5±0.5 Hypertensive, n=36 56.1±1.4 37.5±1.2 48±4 36±4 40±9 8.2±0.5* The two groups were comparable for BMI, AHI and hypoxia exposure. However, hypertensive group was older by ~8 years. There was no gender difference in AHI or FMD. There was no correlation between AHI, arousal index, ODI, T<90 and FMD. The Pearson coefficient of determination, r2, for age was 0.096, P=0.01. However, in a logistic regression analysis, only hypertension correlated with FMD (parameter estimate, -3.39, P=0.0007) and not other variables including age and diabetes. Data as means±SE; *P<0.0001; unpaired t-test. Conclusion: Patients with OSA without hypertension but with similar OSA severity and hypoxia exposure have relatively preserved endothelial-dependent vasodilatory capacity suggesting divergent vascular responses to OSA. FMD can potentially be used for cardiovascular risk assessment and therapeutic decisions in this population. A prospective longitudinal study is needed to determine FMD as a biomarker of adverse outcome in patients with OSA.

Keywords: sleep apnea; flow mediated vasodilation; cardiovascular; hypoxia;

Poster Session: A - Poster #: 119

DIAGNOSTIC YIELD OF AMBULATORY ECG PATCH MONITORING IN CHILDREN FROM A NATIONAL REGISTRY i

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INTRODUCTION: The diagnostic yield of continuous ECG monitoring in children for periods longer than a typical Holter monitor is unclear. We aimed to characterize the diagnostic yield, arrhythmia type and time to first arrhythmia using a clinical repository of national ambulatory ECG data in children. METHODS: We performed a cross-sectional study of 2116 consecutive children receiving their first Zio patch for clinical indications from January 2011 to December 2013. De-identified data was extracted from a clinical registry for analysis and provided by the service provider. RESULTS: There were 2116 children in this analysis cohort (57% females, age 12.7 ± 4 years, range 1d-17 years). Mean monitoring duration was 7.9 +/- 4.3 days. The top five indications for monitoring included palpitations (n=705, 33%), syncope (n=314, 15%), tachycardia (n=170, 8%), chest pain (n=154, 7.3%), and arrhythmia (n=102, 5%). Arrhythmias were detected in 10.4% patients with palpitations, 8.0% of patients with syncope, 11.8% of patients with tachycardia, 5.8% of patients with chest pain and 15.7% of patients with arrhythmias. Of the arrhythmias, SVT > 4 beats was detected most commonly (n=78, 30.5 %). Asymptomatic arrhythmias were detected de novo in 176 patients (8.3%) by continuous recording. The mean time to first arrhythmia was 2.6 +/- 3.1 days. 55% of first detected arrhythmias occurred beyond 48 hours from the start of monitoring. CONCLUSIONS: The diagnostic yield of continuous ECG patch monitoring in children was high beyond 48 hours from the start of monitoring and should be considered in children who are candidates for longer-term ECG monitoring.

Keywords: Ambulatory ECG monitoring; Cardiac arrhythmias; External loop recorder; Palpitations; Syncope;

Poster Session: B - Poster #: 120

INTRAVENOUS (IV) IRON INTENSIFIES OXIDATIVE STRESS AND ACCELERATES CKD PROGRESSION IN EXPERIMENTAL ANIMALS

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Background: Excessive use of intravenous (IV) iron preparations for the management of anemia increases the risk of iron overload in the dialysis population. Catalytically active iron intensifies oxidative stress and causes tissue damage. Oxidative stress is a major mediator of progression of chronic kidney disease (CKD) and its adverse consequences. Residual renal function is highly valuable for the well being of end-stage renal disease patients. Objectives: This study tested the hypothesis that due to the prevailing oxidative stress and inflammation, CKD animals are more susceptible to the damaging effects of IV iron than healthy animals. Methods: CKD was induced in male Sprague-Dawley rats via 5/6 nephrectomy and observed for 6 weeks. CKD rats and healthy controls (CTL) were treated with 2 weekly doses of iron sucrose (10 mg/kg body weight) via tail-vein injection and euthanized 1 week later. The 4 treatment groups were: 1 = CTL non-treated, 2 = CTL+iron, 3 = CKD non-treated, 4 = CKD+iron. Results: CKD animals had proteinuria, elevated plasma creatinine (Cr) and reduced plasma iron levels. IV iron therapy intensified oxidative stress, increased labile plasma iron (LPI) and caused further rise in plasma Cr and proteinuria. This was associated with iron deposition in the remnant kidney, and worsening of glomerulosclerosis and interstitial fibrosis in IV iron-treated compared to non-treated CKD rats. None of these biochemical or histological effects were seen in the IV iron-treated CTL animals. Discussion: IV iron therapy aggravated oxidative stress and renal dysfunction in CKD rats but was well tolerated in healthy rats. Our study suggests that judicious use of iron therapy is warranted to avoid loss of residual kidney function in patients with CKD.

Keywords: intravenous iron therapy; chronic kidney disease; oxidative stress; proteinuria;

Poster Session: A - Poster #: 121

Advances In Surgical Education: Using The iPad And iTunes U To Deliver A Mobile Digital Curriculum

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Objective: The 80-hour workweek has necessitated a shift in surgical training toward better utilization of time outside the operating room. Tablets provide immense potential to complement the surgical trainee's experience by providing just-in-time access to clinical resources. A digital curriculum can assist in all aspects of education, particularly in learning laparoscopic and endoscopic procedures. We hypothesize that by providing iPads to surgical residents with an organized digital curriculum, their access to quality references will improve, resulting in increased clinical efficiency, higher American Board of Surgery In-Training Exam (ABSITE) Scores and better patient education. Description of Methods: iPad tablets were distributed to all residents and fellows in our general surgery program. Specifically tailored iTunes U courses were constructed for each surgical rotation. Once enrolled in the courses, each resident was given access to a digital course curriculum. These course curriculums include goals and objectives tailored toward each Post Graduate Year level, academic materials chosen by attending faculty, key published articles, and links to recommended Surgical Council on Resident Education (SCORE) modules. Courses pertaining to laparoscopic and endoscopic surgery include technical videos that are high quality and have been selected by minimally invasive surgeons. Rather than utilizing unreliable resources, our residents and fellows now have easy access to credible media that can be viewed instantaneously on a tablet. Preliminary Results: A survey was handed out to all residents prior to iPad distribution. Of 31 completed surveys, 100% stated they used a smartphone and 90% stated they used their smartphone for clinical applications. 68% of residents agreed or strongly agreed that an iPad would add significant value to their current workflow. 71% stated that they currently use applications on their smartphone

Keywords: Ipad; Surgical Education; Digital Curriculum;

Poster Session: B - Poster #: 122

A Community Based Initiative: Peer Mentoring To Teach Healthy Habits

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Purpose of Study: Education about healthy habits through peer mentorship has not been explored in the literature. The objective of the Healthy Habit Initiative at UC Irvine School of Medicine was to determine whether an interactive session using a cascading mentorship is effective in teaching elementary students about healthy habits. Methods Used: Under the direction of one faculty, undergraduate and high school students designed a curriculum to teach elementary students about the food pyramid and the importance of exercise. The program required the active participation of the elementary schools students. A survey was distributed after each session to evaluate the effectiveness of the program. Summary of Results: One faculty, two undergraduate students, and nine high school students conducted the sessions at six different elementary schools. 304 elementary school students participated in the program. A comparison of responses by elementary students before and after the sessions is shown below. The workshops increased the knowledge of elementary students about healthy eating and importance of exercise. The college and high school student mentors expressed that their interest in life-long civic engagement and confidence increased as a result of this project. Conclusions: The Healthy Habit Initiative based on peer mentorship was very effective in teaching very young students about the food pyramid and the importance of exercise. The program also inspired a sense of life-long civic engagement in the high school and college student mentors. Comparison of the Responses Pre and Post Sessions: Pre test (N=304, % answered correctly): Q1: 66%, Q2:10%, Q3:79%, Q4:54% Post test (N=196, % answered correctly): Q1: 96%, Q2:58%, Q3:82%, Q4:84%

Keywords: Healthy Habits; Peer Mentorship;

Poster Session: B - Poster #: 123

Peer Relationships and Status in Children with Attention-Deficit/Hyperactivity Disorder

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The core symptomatic behavioral problems (i.e., inattention, hyperactivity, and impulsivity) associated with attention-deficit/hyperactive disorder (ADHD) often negatively interfere with social interactions, and children with ADHD, particularly those with comorbid Oppositional Defiance Disorder (ODD), are at increased risk for peer rejection. Few studies have investigated immediate impressions of peer acceptance and rejection strictly among a sample of children with ADHD. Using multi-informant reports, the present study examined individual child factors (social competence, ADHD symptom type and severity, and comorbid ODD) and parent factors (personality traits and parenting stress) in relation to social status among children with ADHD. Participants included 82 children (71% boys) with ADHD (46.3% comorbid ODD) ages 7-9 years (M = 7.73, SD = .80) and their parents (89% mothers) as part of a social skills intervention. Children's social competence, problematic externalizing and internalizing behaviors, and ADHD and ODD symptom severity were rated by parents and community teachers. Parent self-report of personality traits and parenting stress were also collected. Children's social status was assessed with a measure of peer-reported acceptance and rejection as well as likability. Findings from bivariate correlations examining links among children's social competence, behavioral functioning, and social status will be presented along with analyses of mediating factors (parenting stress, parental personality, comorbidity) in these associations. The findings from this project will further inform research on whether social dysfunction is uniformly experienced among a group children with ADHD, and identifying key child and parent factors that may differentially impact children's social status may help enhance tailored social skills and behavioral interventions for families of children with ADHD.

Keywords: ADHD

Poster Session: A - Poster #: 124

Exhaled Breath As A Non-Invasive Assay For Rapid Diagnosis And Real-Time Monitoring Of Serious Infectious Diseases And Systemic Inflammation In Humans

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The overall objective of this study is to investigate the utility of carbon monoxide (CO) concentration in exhaled breath as a tool for the rapid diagnosis and monitoring of infectious disease in humans. We have previously collected and measured the contents of the breath of mice with systemic bacterial infection or following injection with lipopolysaccharide (endotoxin). The animal studies indicated that an increase in the exhaled CO that was normalized to CO2 concentration correlated with bacterial burden, endotoxin dose, and the blood concentration of heme oxygenase-1 enzyme, the main source of endogenous CO. This suggests that infections which increase heme oxygenase-1 activity should subsequently increase the CO in exhaled breath, which could be measured and used for diagnostic and monitoring purposes. These results prompted the investigation of CO/CO2 in exhaled human breath. A pilot study was conducted in which samples were collected from seven healthy individuals daily over the course of a week. This study was used to determine the inter- and intra-subject CO and CO2 concentration variations in healthy adults. Exhaled breath samples were collected in stainless steel canisters fitted with a Swagelok T and Teflon tubing. The evacuated canisters were opened as the subject simultaneously exhaled into the Teflon tube, filling the canister. Samples were also collected from the room to account for background concentrations. CO and CO2 were then measured using gas chromatography. The results demonstrated that while the inter-subject CO concentrations varied, the concentrations for each subject remained relatively constant over time. However, this pilot study was conducted on a small scale and a larger more comprehensive study is needed to determine the overall range of CO in exhaled breath and explore the factors that affect it. Future studies include collection and analysis of hospitalized patients to compare infected and healthy breath on a larger scale.

Keywords: Exhaled breath; Infectious Disease; Carbon Monoxide; Diagnosis;

Poster Session: B - Poster #: 125

The Impact of Ironman Triathlon on Innate Immune Cell Numbers and Function

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Prolonged, high-intensity endurance exercise activities such as the Ironman Triathlon (lasting 10-12 hours) profoundly perturb homeostasis in a variety of physiological systems, and would likely impact key cellular components of innate immunity (e.g., natural killer cells and monocytes), a "first responder" to stress and infection. The effect of such exercise on numbers and functional indexes of circulating innate immune cells is poorly understood. PURPOSE: To study the impact of the Ironman Triathlon on innate immune cell number and function. We hypothesized that there would be immediate effects on measures of number of cells and cellular activation in NK cells (KIR, killer cell immunoglobulin-like receptors) and in monocytes (toll-like receptors, TLR) which would continue throughout the recovery period. METHODS: 10 elite male triathletes, 32-64 y/o volunteered. Blood was drawn between 2-3 days before the triathlon (baseline), and during recovery at 1-, 24-, and 48-h after completion. CBC and standard flow cytometry methods were used to determine monocyte and NK cell (CD3- CD56+) count, NK dim and bright subpopulation (CD56dim and CD56bright), and cell function (NK, KIR2DL2; and monocyte, TLR4). Repeated Measure ANOVA was applied ($p<0.05$). RESULTS: NK cell number did not change from baseline at 1- or 24-h recovery, but declined significantly at 48-h due to a decrease in the number of the NK dim population. Total monocyte count increased at 1-h and remained elevated at 24-h. The expression of KIR2DL2 on NK cells was elevated at 24-h. CONCLUSION: The Ironman Triathlon impacted circulating numbers of key innate immune cells, NK and monocytes. NK cells appear to leave the circulatory compartment by 48-h. Moreover, NK cell activation was inhibited at 24-h into recovery. In contrast, monocytes were increased over baseline for at least 24-h but without change in their activation.

Keywords: Innate Immune Cells; Leukocytes; Flow Cytometry; NK Cells; Extreme Exercise

Poster Session: B - Poster #: 126

Targeting Neuroinflammation With The TNF-Alpha Inhibitor, "Etanercept'

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The primary therapeutic goal for treating Alzheimer's disease has been the reduction of ß-amyloid (Aß), however, reducing neuroinflammation may act as a supplemental therapy. Our study was conducted to determine whether the anti-inflammatory medication, Etanercept (Embrel), could be an effective therapeutic to target the pro-infllammatory actions elicited by TNF-alpha with in the brain. We treated non-transgenic mice systemically with LPS (0.5mg/kg) followed by either 10mg/kg, or 50mg/kg of Etanercept; twice weekly for two weeks. After the two week treatment, the mice were sacrificed to observe the neuroinflammatory response within the hippocampus. Our results reveal that despite Etanercept inability to pass the blood brain barrier, we observed a reduction in reactive microglia, which suggests an attenuation in inflammation. These results suggest that Etanercept can reduce neuroinflammation and warrants further study as a potential AD therapeutic.

Keywords: Neuroinflammation; Alzheimer's Disease; TNF-alpha;

Poster Session: A - Poster #: 127

Microvascular Dysfunction and Air Pollution Exposures in a Repeated Measures Cohort Study

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Objectives: To investigate the effects of short-term exposures to TRAP on microvascular function and biomarkers related to oxidative stress and inflammation. Methods: This is a cohort panel study with repeated measurement in 46 non-smoking elderly subjects aged 65 to 95 years living in the Los Angeles air basin, who were monitored with =12 weekly clinic follow-ups July 2012-February 2013. Hourly ambient exposures included particulate matter <2.5 μm in diameter (PM2.5), black carbon (BC), carbon monoxide (CO), nitrogen oxides(NOX), and ozone(O3). Seven-day average personal exposures to NOX preceding clinic follow-ups were measured. Microvascular function was measured with forearm blood flow dilatation response to brachial artery occlusion using a noninvasive plethysmograph (EndoPAT 2000) yielding the reactive hyperemia index (RHI). Biomarkers of systemic oxidative stress(oxLDL) and inflammation (IL-6) were analyzed using peripheral blood plasma samples. A linear mixed-effects model was used to analyze relations of air pollutants to RHI and biomarkers, adjusting for heat index and other potential confounders. Results: We found that 3-day and/or 5-day average ambient TRAP (BC, CO, NO2 and NOX), but not PM2.5 or O3, were significantly associated with decreased RHI, indicating impaired microvascular function. To a similar degree, RHI was inversely associated with 7-day average personal NOX. OxLDL and IL-6 were significantly increased in relation to elevations in 3-day and 1-day average BC, respectively. Discussion: Impaired microvascular function was found after short-term ambient and personal exposures to TRAP. Elevated systemic oxidative stress and inflammation were found with exposures to BC, indicating a potential role of systemic oxidative stress and inflammation in relations between exposures and microvascular dysfunction. Outcomes studied may be biological pathways by which TRAP exposures affect pathogenesis of atherosclerosis and acute cardiovascular events.

Keywords: microvascular function; longitudinal studay; oxidative stress; air pollution; epidemiology;

Poster Session: A - Poster #: 128

Analysis of Exhaled Volatile Organic Compounds (VOC) in Intubated Preterm Infants

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Human exhaled breath contains numerous volatile gases. Once successfully identified, it is conceivable that these gas biomarkers will allow early detection of disease with minimal risk to the preterm infants on a ventilator. We hypothesize that exhaled breath from preterm infants in ventilator might generate specific volatile gases, which could reflect underlying physiological alterations. The goal of the study is to measure exhaled VOC in intubated preterm infants and to correlate the results with their underlying lung disease. The study was conducted at UCI Medical center. Preterm infants (n=5, <37 weeks gestational age) who required intubation and conventional ventilatory support were enrolled. Two of them were intubated for respiratory distress syndrome (RDS), one had respiratory failure (RF), and two were intubated for surgery without any signs of lung problems (Control). Breath samples were obtained from the expiratory limb of the ventilator circuit. Each sample was subjected to a multi-column multi-detector gas chromatography system that is capable of identifying and quantifying gases in trace concentrations in ranges from parts per million (ppm) to parts per quadrillion (ppq). Exhaled breath samples showed evidence of increased CO2 confirming the validity of our technique. The mean (SD) concentration of CO2 was 4804 (1489) ppm from intubated preterm infants and 616 (71) ppm from ambient room samples. A total of 75 VOCs were obtained; and 16 were identified “interesting” with possible trends among RDS, RF, and control samples. As an example, chloroform levels were 46 (4.5) ppt, 14.7 ppt, and 16 (0.2) ppt in the breath samples of RDS, RF, and controls, respectively. The ambient room levels of chloroform were 39 (11.3) ppt. Our study demonstrates 1) for the first time the ability to detect exhaled breath gases from intubated preterm infants and 2) several VOCs (i.e., chloroform) show potential to be used as gas biomarkers for RDS.

Keywords: Exhaled breath gas; VOC; preterm infants; ventilated

Poster Session: A - Poster #: 129

A Novel Approach to Asthma Inhaler Compliance using Breath Measurement of Aerosol

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RATIONALE: Asthma inhalers are the first line of asthma treatment. However, one of the most vexing problems facing clinicians and researchers has been the lack of technologies to measure treatment compliance. We hypothesized that hydrofluoroalkane 134a(the most commonly used aerosol propellant in the metered dose inhaler) can be measured in the exhaled human breath and can be used for monitoring asthma inhaler compliance. METHODS: six healthy controls, 25-48 yr old males and females, participated in the study. They were randomly assigned to inhaled corticosteroid (Flovent HFA, n=3) or short acting bronchodilator (Proventil HFA, n=3). After obtaining informed consent, baseline exhaled breath sampling and standard lung function test (PFT) were performed prior to the medication dispersion. Then, the subjects were asked to take two puffs of either Flovent HFA (GlaxoSmith Kline) or Proventil HFA (Merck & CO., INC) with a spacer (AeroChamber Plus Flow-Vu, Monaghan). Breath sampling and lung function test were performed immediately after inhalation, then at 2, 4, 6, 8, 24, and 48 hours post administration. HFA concentration in the breath samples were quantified using mass spectrometer. Nonlinear weighted least-square technique were applied to fit the bi-exponential model to breath HFA elimination data for each subject. Results: At baseline, mean (SD) levels of HFA in the breath were 259 (171) ppt. Right after inhalation, HFA breath levels went up to hundreds of ppm and were still well above ambient levels 24 hrs post administration. After a typical single inhalation, breath HFA elimination followed a bi-exponential decaying pattern for at least 48 hours, a useful interval in the clinical setting. Discussion/Summary: This study demonstrates that HFA can be measured in the exhaled breath of healthy participants, and breath HFA concentration is still detectable at 24 to 48 hours post typical asthma inhaler administration.

Keywords: asthma inhaler; compliance; HFA-134a; non-invasive breath measurement; HFA elimination;

Poster Session: A - Poster #: 130

Linking Genetic Potential and Active Metabolism in Cystic Fibrosis (CF) Microbial Communities to Find Biomarkers of Disease State

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OBJECTIVE: Disease progression and response to treatment are both difficult to predict in the dynamic and persistent microbial infections unique to the airways of each Cystic Fibrosis patient. Combining metabolites found in the breath and sputum of CF patients with microbial metagenomes and clinical data may enable detection of active microbial metabolism specific to a particular microbial community and disease state. METHODS: A cross-sectional study of seven CF patients and five healthy controls was conducted, along with a longitudinal study of a CF patient over the course of 6 months and through two periods of increased inflammation and symptoms known as an exacerbation. Induced sputum and breath samples were collected to simultaneously probe: breath gas metabolites, sputum metabolites with both GC-MS and LC-MS, metagenomic sequence of unamplified microbial DNA from intact cells, 16S rDNA amplified microbial DNA, along with model culture pH, redox state, and 16S taxonomic profile. Breath gases were analyzed using GC-MS analysis methods established in the Rowland-Blake lab at UCI. RESULTS: Using Random Forests to search for the metabolites that best separate sputum samples collected during an exacerbation from stable samples, we found indicators of exacerbation including: fermentation products including 2,3-butanediol and citric acid, products of amino acid metabolism such as putrescine and aminovaleric acid, and nucleic acids including uracil and hypoxanthine. SIGNIFICANCE: Molecules detected in the breath and sputum of patients with lung infections including CF may enable taxonomic identification of the microbes driving the infection, and also probe the local conditions and interactions leading to their production. Synergism between bacteria is mediated by metabolites produced in the biogeochemical circumstances unique to local conditions in an individual lung. This may enable earlier and more specific diagnosis and treatment of CF pulmonary exacerbations.

Keywords: Cystic Fibrosis; Metabolomics; Microbiome;

Poster Session: A - Poster #: 131

T1rho Mapping Of Femoral Cartilage At 3T: Regional Analyses Based On Full-Thickness And Deep/Superficial Layers

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Objectives: T1rho-mapping via MRI has shown to be sensitive to proteoglycan content, a promising biomarker in quantitative assessment of early osteoarthritic cartilage damage. This study investigates the normal range of T1rho values from different cartilage compartments in healthy volunteers. Methods: Twenty knees with equal number of left/right knees (mean: 28.9; range: 19-38 yr) were investigated in this study. T1rho images were acquired at a 3T scanner and were processed off-line using a custom processing tool prepared in Matlab: image-realignment prior to a monoexponential fitting for T1rho mapping. For regional assessment of T1rho values in femoral cartilage, a manual cartilage segmentation was carried out across the entire knee and ROI-averaged T1rho values from the segmented cartilage were obtained from 3 separate compartments: trochlea and lateral/medial condyles. Each compartment was assessed using 3 separate slices representing medial, central, and lateral locations from each region and utilizing the full thickness of cartilage layer as well as dividing the layer into 2 halves: deep and superficial layer. Results: Fig. 1 shows representative color-coded 3d-constructed T1rho maps of the full-thickness layer of femoral cartilage. ROI-averaged T1rho values from 3 different locations (M: medial; C: central; L: lateral) in each compartment are summarized in the table. The difference in T1rho values between the deep and superficial layers were also analyzed using a paired student's t-test. Discussion: The results demonstrate that the 3 different compartments of femoral cartilage studied here exhibited a similar T1rho value when the entire cartilage was averaged over. Except for trochlea at central and lateral positions, the superficial layer demonstrated a higher T1rho value in comparison to that of deep layer from the same cartilage and their differences were statistically significant in all compartments/locations investigated here.

Keywords: MRI; knee; cartilage; T1rho; osteoarthritis;

Poster Session: A - Poster #: 132

Assessment Of Inter-Operator Agreement In Articular Cartilage Segmentation Based On 3D Profiles Of T2 And T1Rho Values

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Objectives: Assessment of inter-operator agreement in manual image segmentation of femoral cartilage by two operators based on resulting 3-dimensional T2/T1rho profiles. Methods: 20 knees with equal number of left/right knees (mean 28.9 yr. of age; range: 19-38) of healthy volunteers were scanned on a 3T MR-scanner for T2/T1rho-mapping in 31 sagittal slices with FOV/slice-thickness/image-matrix (140/3-mm/512x512). Two operators carried out a manual-tracing of cartilage boundary independently and separately for T2 and T1rho dataset using a custom program prepared in Matlab. Upon completion of cartilage segmentation in each slice, the program also performed automatically the placement of an arch-center and subsequent angular segmentations in step of 4-degree along the manually extracted cartilage boundary. Using anatomical landmarks, each subject's knee was normalized into a 24-slice template prior to group analyses of T2/T1rho profile from each operator. The agreement between the operators was then assessed based on group mean and standard deviation over the overlapping angular range on each of the 24-slice template. Anticipated Results: The group-mean values of T2/T1rho obtained from the 2 operators will be compared with each other and will be assessed to be in good agreement (i.e., interchangeable) should they be well within the respective group standard-deviation derived from each operator's. Any angular segments/slices exhibiting less than good agreement will be compensated by taking the averages of the group-mean values from the 2 operators before constructing a 3D spatial distribution of T2 and T1rho values/ranges that are considered to be that of normal cartilage. Significance of Impact: T2/T1rho-mapping promises to be a valuable tool in quantitative assessment of cartilage degeneration. Such assessment, however, requires an understanding of what is considered as normal values/ranges, which is further complicated with multi-operator based assessment.

Keywords: MRI; knee; cartilage; T2; T1rho;

Poster Session: A - Poster #: 133

Estrogen Replacement Therapy Significantly Upregulates the Hydrogen Sulfide Biosynthesis System in the Uterine Artery of Ovariectomized Ewes.

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INTRODUCTION: Estrogens potently dilate blood vessels throughout the body with the greatest response in the uterus that is largely mediated by enhanced production of uterine artery (UA) nitric oxide (NO); however, additional mechanisms are involved since NO inhibition only blocks ~65% of the estrogen-induced response. Hydrogen sulfide (H2S) has been described as a novel vasodilator, which is primarily synthesized from L-cysteine by cystathionine ß-synthase (CBS) and cystathionine ?-lyase (CSE). Hypothesis: Estrogens stimulate UA H2S biosynthesis. METHODS: Ovariectomized nonpregnant ewes (n=5/group) were treated with vehicle (OVX/Veh) or estrogen replacement therapy (OVX/ERT, 1 µg estrodiol-17ß/kg body weight, 5-6 days). Intact UA and denuded UA (UASM) samples were obtained and analyzed for: 1) CBS/CSE mRNA by qRT-PCR; 2) CBS/CSE protein by immunoblotting and their cellular specific (endothelium vs. smooth muscle) localization/expression by immunofluorescence microscopy; and 3) H2S production by the Methylene Blue assay. RESULTS: ERT significantly ($P<0.01$) stimulated CBS mRNA and protein without altering CSE mRNA and protein expressions in UA and UASM of OVX ewes. Levels of UA and UASM CBS mRNA were 5.03 (± 1.00 SD) and 5.60 (± 0.93)-fold greater, and levels of CBS UA and UASM protein were 3.51 (±0.51) and 4.67 (±0.09)-fold greater in OVX/ERT than that of OVX/Veh ewes, respectively. Immunofluorescence microscopic analyses confirmed the CBS and CSE protein expression patterns. ERT also stimulated H2S production in UA protein lysates compared to controls, which was blocked by incubation with specific inhibitors of CBS and CSE. CONCLUSIONS: Exogenous estrogens upregulate UA H2S biosynthesis in OVX sheep, suggesting that H2S contributes to estrogen-induced uterine vasodilatation.

Keywords: Hydrogen Sulfide; Estrogen; Uterine Artery;

Poster Session: A - Poster #: 134

Preeclampsia-upregulated Angiogenesis-associated MicroRNA-20b Inhibit Trophoblast Syncytialization and Migration

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Introduction: Cytotrophoblast (CTB) differentiation is important in spiral artery remodeling during placentation. In normal human placentation, mononucleated cytotrophoblast functions as placental “stem cells” that differentiate into multinucleated syncytiotrophoblast (STB) via the villous pathway and invasive extravillous trophoblast (EVT) via the extravillous pathway. Shallow EVT invasion and incomplete spiral artery remodeling are primary correlates of preeclampsia (PE). MicroRNAs (miRNAs) are a class of noncoding 21-25 nucleotide RNAs that negatively regulate gene expression post-transcriptionally. We have shown that angiogenesis-associated miRNA-20b is upregulated in PE placentas compared to controls. Hypothesis: MiRNA-20b inhibits CTB syncytialization via the villous pathway and inhibits EVT migration and invasion via the extravillous pathway. Methods: The precursor of miR-20b was amplified and cloned into the lentiviral pGIPZ vector. The miR-20b lentiviral vector was packaged and tittered in 293T cells and then used for overexpressing miR-20b in both human EVT derived HTR-8/SVneo cells and human placenta choriocarcinoma trophoblast derived BeWo cells. BeWo cells were used as the cell model to study CTB syncytialization. Cell fusion was determined by counting the percentage of multinucleated STB-like cells that BeWo cells formed after culture for 2-3 days. Cell migration and invasion of HTR-8/SVneo cells were assessed by transwell migration and matrigel invasion assays. Results: Overexpression of miR-20b suppressed the formation of fusion cells along with down-regulation of EFNB2 expression compared with the negative control transfected BeWo cells. Overexpression of miR-20b in HTR-8/SVneo cells significantly inhibited cell migration and invasion compared with the control cells. Conclusion: PE-upregulated angiogenesis-associated miRNA-20b inhibits CTB syncytialization via the villous pathway and EVT migration and invasion via the extravillous pathway.

Keywords: microRNA; trophoblast; migration; differentiation; placenta;

Poster Session: B - Poster #: 135

Normal T2 Map Profile Of Entire Femoral Cartilage At 3-Tesla MRI

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Objectives: T2 mapping is currently available as a clinical MR protocol for quantitative evaluation of early cartilage degeneration. However there is no current publication data of the normal T2 map profiles of the entire healthy knee, focusing on topographic variation and inter-rater reliability . The purpose of this study was to determine standard T2 map profiles from the entire femoral cartilage of normal volunteers. Methods: Twenty knees (mean age 28.9; range 19-38) were evaluated with a sagittal T2 map sequence at a clinical 3T MRI. Manual cartilage segmentation was performed by an orthopedic surgeon (R1) and a radiologist (R2) independently. ROI-averaged T2 values from the segmented cartilage were obtained across the entire knee. Prior to analyses, we defined 3 separate slices representing the center of trochlea and medial/lateral condyles in each subject with reference to axial and coronal reconstructed images. The difference in T2 values between the deep and the superficial layers in each component as well as entire cartilage were analyzed using a paired student's t-test. Inter-rater reliability was assessed using interclass correlation coefficient (ICC). Results: Reliability was excellent (ICC=0.84). The superficial layer demonstrated significantly higher T2 values than the deep layer at each medial condyle ($P < 0.05$), trochlea, lateral condyle and entire cartilage (each $P < 0.0001$). The superficial layer showed higher T2 values than those of the deep layer around the direction of main magnetic field (B0), in other words, area of weight bearing. Magic angle effect was seen as bimodal peaks of T2 value at approximately ±55° with respect to B0. Discussion: The results demonstrate that T2 values of femoral cartilage exhibited dependency to both orientation and thickness of the cartilage in the magnetic field. These data will serve as a foundation for subsequent analyses of early and advanced osteoarthritis.

Keywords: T2 map profile; MRI; knee cartilage; magic angle effect;

Poster Session: B - Poster #: 136

Normal T1Rho Profiles Based On Cartilage Segmentation By Two Operators

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OBJECTIVES: Osteoarthritis (OA) is associated with degeneration of articular cartilage. We could quantify the cartilage damage before appearing morphological change by using biochemical MRI techniques, such as T1rho and T2 mapping. However it is not well understood what can be considered as a normal range of T1rho values, and factors affecting T1rho mapping such as imaging protocol and operator-dependent manual cartilage segmentation. The purpose of this study is to assess the potential factors could affect the reproducibility, and make normalized T1rho mapping of healthy knee cartilage. MATERIALS AND METHODS: 20 healthy volunteers (mean: 28.9 y.o., range: 19-38) were enrolled in this study. All MR studies were performed on a 3.0-T unit utilizing an 8-channel knee coil and 31 sagittal slices (140/3mm). Two T1rho images of each subject were acquired on the pulse sequence of balanced steady state free precession (b-FFE) and spoiled gradient echo (SPGR). Cartilage segmentation was performed by a radiologist (R1) and a orthopaedic surgeon (R2) independently by using a custom processing tool prepared in Matlab. Inter-observer reliability and the variability between two imaging protocols were calculated. We also calculated the average T1rho values on normalized knee cartilage, and made 3D-graph. RESULTS: Average T1rho value of whole knee cartilage extracted by R1 is 56.77±2.97 on SPGR sequence, 58.68±3.12 on b-FFE sequence, and that by R2 is 56.96±2.07, 59.33±1.88 on each pulse sequence. Pearson's correlation coefficient is 0.84 between R1 and R2 on SPGR, and 0.80 on b-FFE sequence. CONCLUSIONS: Interobserver-reliability of measurement on T1rho profiles is excellent on T1rho SPGR sequence, and good on b-FFE sequence. T1rho value could tend to be calculated higher on b-FFE sequence than SPGR sequence. We must pay attention to exist affecting factors which causes variability, and need standardization and validation before clinical application.

Keywords: T1rho profile; biochemical MRI; knee cartilage; osteoarthritis; inter-observer reliability;

Poster Session: B - Poster #: 137

Topical Application of Tranexamic Acid Does not Affect Electrophysiological and Neurovascular markers in an Animal Model

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Abstract Objective Tranexamic acid (TXA) is a safe and effective anti-fibrinolytic agent that has been used systemically and topically in total knee arthroplasty (TKA) and total hip arthroplasty (THA) to reduce blood loss and transfusion rate. As the hip joint does not have a defined capsule like the knee joint, the topical application of tranexamic acid entirely envelops the sciatic nerve. As the accidental application of TXA in spinal cord has been shown to produces seizures, we sought to investigate if the effect of topical application of TXA on the sciatic nerve has a deleterious effect. Methods We used an animal model that closely simulates the sciatic nerve exposure in total hip arthroplasty to determine the effects of TXA on neural form and function by evaluating electrodiagnostic changes (EDX), histological signs of nerve injury, macrophage recruitment, and changes in blood nerve barrier (BNB) both at an early and late time point after application of subtherapeutic, therapeutic, and supratherapeutic concentrations of TXA. Results At both the early and late time points, there were no persistent and statistically significant differences in EDX, macrophage recruitment, and changes in BNB between control and TXA treated nerve. Discussion In our animal model that simulated the topical application of tranexamic acid in total hip arthroplasty, tranexamic acid does not appear to have any short or long lasting effect on the sciatic nerve.

Keywords: total joint replacement; tranexamic acid; sciatic nerve; topical application;

Poster Session: B - Poster #: 138

Assessment Of Inter-Operator Agreement In Manual Image-Segmentation Of Femoral Cartilage

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Objectives: Quantification of inter-operator agreement in manual image segmentation of femoral cartilage by two operators. Methods: 20 knees with equal number of left/right knees (mean 28.9 yr. of age; range: 19-38) of healthy volunteers were scanned on a 3T MR-scanner for T2-mapping in 31 sagittal slices with FOV/slice-thickness/image-matrix (140/3-mm/512x512). Two operators carried out a manual-tracing of cartilage boundary independently using a custom program prepared in Matlab on the same set of images. Upon completion of cartilage segmentation in each slice, the program also performed automatically the placement of an arch-center and subsequent angular segmentations in step of 4-degree along the manually extracted cartilage boundary. The agreement between the operators was then assessed based on 3 geometrical aspects resulting from the final angular segmentation: radial distances to the arch-center and center of each angular segment from the upper left corner of image and size of each angular segment (number of pixels). Each of the 3 geometrical aspects was investigated using Bland-Altman method as well as correlation analysis. Results: The mean differences in radial distance to the arch-center and center of each angular segment were -0.799 and -0.280 (mm), respectively, with the negative sign indicating that the values from operator-1 were smaller than that of operator-2; the correlation coefficients for these quantities were 0.969 and 0.998, respectively. The mean difference and correlation coefficient in size of angular segment was 7.338 and 0.798, respectively. Discussion: Despite its time-consuming nature, manual ROI-tracing (region-of-interest) is still considered as the gold-standard in segmentation of femoral cartilage for subsequent image-based analyses. Hence, it is important to first assess the level of agreement between the operators before such task in manual segmentation can be divided up among different operators without undue bias.

Keywords: MRI; knee; cartilage; inter-operator agreement; segmentation;

Poster Session: A - Poster #: 139

Human Placental Expression Of Corin: Effects Of Gestational Age And Differential Phenotypes Of Preeclampsia

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Introduction: Impaired spiral artery remodeling is a major pathology of the human pregnancy-specific hypertensive disorder preeclampsia (PE). Corin is a cardiac protease important for regulating blood pressure. Placental corin deficiency perturbs mouse spiral artery remodeling, resulting in hypertension during pregnancy. However, whether placental corin expression is developmentally regulated and affected by preeclampsia during human pregnancy is not well-understood. Hypothesis: Human placental corin expression is developmentally regulated and downregulated in preeclampsia. Methods: Normal placentas were collected from the first (5-11 wks, n=9) and second (14 - 17 wks, n=8) trimester pregnancies of elective terminations and the third trimester at delivery (38 - 39 wks, n=7). Placentas were also collected from C-sections of term severe preeclampsia with small for gestational age (PE-SGA, n=3) or appropriate gestational age (PE-AGA, n=6), severe preeclampsia with gestational diabetes mellitus (PE-GDM, n=4) and GDM (n=5) controls, as well as early-onset (prior to 34 wks) PE with SGA (pre-SGA, n=3), AGA (n=6), and gestational age matched preterm controls (n=7). Total RNA samples were extracted for measuring corin mRNA expression by real-time quantitative PCR (RT-qPCR) and quantified by ?CT algorithm using L-19 as the reference. Results: Placental levels of corin mRNA increases with gestational age and are significantly greater in the third compared to the first and second trimesters ($p<0.01$). Placental corin mRNA levels in pre-PE-SGA did not differ from that of pre-AGA. However, the levels are significantly lower in the PE-SGA and PE-GDM compared to normotensive controls ($p<0.05$). No difference was found between the GDM and normotensive placentas. Conclusions: Human placental corin mRNA expression increases during pregnancy and is downregulated in preeclampsia, suggesting a role of corin in placental development and the pathogenesis of the disease.

Keywords: preeclampsia; corin; pregnancy; trophoblast;

Poster Session: A - Poster #: 140

Initial investigation of combined single-photon emission computed tomography (SPECT) and magnetic resonance (MR) imaging of a human ovarian tumor xenograft using 123I-bevacizumab

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Objectives: To determine the feasibility of detecting 123I-labeled bevacizumab by nuclear SPECT and anatomic MRI in an ovarian cancer mouse model as a predictive model for clinical bevacizumab (Avastin) response. Methods: SKOV3ip1 cells were injected by intraperitoneal route into female NCr nude mice (1.5 x 106 million cells/200 uL). 7T-MRI was performed weekly under ketamine anesthesia until measurable tumors (5 to10 mm) were detected. One mg of bevacizumab per 2 mCi of sodium 123I in solution was mixed over iodination beads. Mice were then injected with 1 mCi of 123I-bevacizumab. Combined SPECT, employing a nuclear radiation detector consisting of 50.8×50.8×5 mm of cadmium-zinc-telluride (CZT) crystal with electronic readout, and MR imaging was performed at 12, 24, 36, and 48 hours after injection. Results: Measurable tumors were detected at 5-6 weeks post-injection, and all animals developed ascites. MR images were optimal when acquired using a 2D fat-suppressed spin-echo pulse sequence with the following parameters: repetition time (TR) = 3.5 s, echo time (TE) = 30 ms, FOV = 40×40 mm, matrix = 256×256, slice thickness = 1 mm, number of averages = 2. 123I-bevacizumab localized to measurable peritoneal tumors in the 3 mice that were imaged (Figure 1). The optimal uptake time was 24 hours post injection. Fifteen mice died following either administration of ketamine or injection of 123I-bevacizumab. All had ascites and intravascular volume depletion determined by tail vein collapse, and all had extensive miliary carcinomatosis at necroscopy. Conclusions: Detection of radiolabeled bevacizumab was feasible by SPECT imaging. This specific animal model was suboptimal for pre-clinical development secondary to miliary distribution of non-measurable tumors and moribund condition of animals when tumors were measurable. We are now employing a larger animal (RNU rat) and larger tumors (HeyA8) for further development.

Keywords: anti-angiogenesis; functional onco-imaging; advanced diagnostics; ovarian cancer;

Poster Session: B - Poster #: 141

Clinic in the Park: Developing a Model for Community-Based Outreach Programs

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BACKGROUND: Clinic in the Park, a community-based model of health promotion formed by a collaborative of nonprofit, academic, public and private entities to provide one-stop-shop-for health at a Farmers Market on a Sunday. METHODS: Tools to evaluate include passports tracking services rendered; counts of visitors (total per service station); and visitor and collaborator satisfaction/needs surveys. Measurable outcomes include: 1) number of families connected to health care and other services; 2) number of safety net screenings (e.g. vision, hearing, dental, BMI/dietitian consults, proper child safety seat); 3) health promotion tools provided (including booster seats, bicycle helmet fittings, developmental activities); 4) visitor and collaborator satisfaction. RESULTS: In the first 18 months, 12,279 visitors (all ages) received 20,843 discrete services, which included many who only wanted to "chat" with our health professionals. Examples of services/screenings included 2,890 connection to health insurance and other income eligible services; 656 dental services (0-17 years); 424 hearing screenings; 1,723 health eating chats/BMI; 2,321 early literacy/books; 3,305 child safety tools/strategies. Visitors are 35% Hispanic and 55% from underserved communities. Many came to chat with health professionals. Fresh produce was provided to visitors from local farmers. CONCLUSIONS: A community public venue for health serves as a model for improving population health by connecting to services, safety net screening, and providing promotion strategies and tools not offered in the traditional medical office. The next phase is a study of impact on a cohort of low-income family visitors and a determination of enhancing outreach strategies to low income families.

Keywords: public health; community based; collaboration;

Poster Session: B - Poster #: 142

Clinic in the Park: Promoting Health

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Clinic in the Park, located in OC Great Park farmers market, focuses on connecting families to health services. One service provided is health chats with a Registered Dietician (RD) at a Healthy Eating ,Healthy Weight Station (HEHWS). The goals of HEHWS are to decrease risk of overweight/obesity by increasing nutrition knowledge and promoting healthy behaviors. Body Mass Index (BMI) are calculated from height and weight. They are interpreted as underweight, normal weight, overweight or obese using Center for Disease Control's (CDC) BMI classification. Visitors are asked to complete a survey on fruit/vegetable consumption and physical activity. Responses are compared to the 2010 Dietary Guidelines recommended intake of fruits/vegetable and CDC's recommended amount of physical activity. The RD reviews the BMI and/or survey with the visitor and provides a health chat to reinforce nutrition knowledge and health behavior. Nutrition focused educational materials are provided. Between September 2013 and March 2014, 588 individuals visited the HEHWS. 181 BMI measurements and 65 surveys were completed. 49% of visitors were at healthy weight while 15% were underweight, 21% overweight and 14% obese. Survey results revealed 29% of visitors reported consuming the recommended minimum 5 servings of fruits/vegetables a day while 40% did not know the recommended intake. 75% of adults performed physical activity less than the recommended 150 minutes/week while over half of children (56%) reported physical activity less than the recommended 60 minutes/day. Education and promotion of healthy behaviors need to continue at the HEHWS. Goals include promoting increased fruit/vegetable consumption and physical activity, as at least half of visitors reported not meeting recommendations. Methods include providing a tour of the Great Park's farm for visitors to learn about and sample produce and incorporate "Let's Move" campaign to promote physical activity.

Keywords: None

Poster Session: B - Poster #: 143

Can neighborhood associations partner with schools to promoter after hour health programming? A pilot program in Santa Ana, California

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OBJECTIVES/SPECIFIC AIMS The Madison Park Neighborhood Association (MPNA) is located in the City of Santa Ana, CA. The population of Santa Ana is 80% Latino and 50% foreign born. Central Santa Ana is older and more dense, it lacks sufficient safe open park space. The 92701 zip code of Santa Ana, one of the most densely populated places in the state and 92% Latino, has only 3 acres of park for 61,000 residents. Using a community-based participatory re¬search (CBPR) approach, MPNA using a Joint use Land Agreement with a neighborhood school, launched project GREEN (Getting Residents Engaged in Exercise & Nutrition) in 2012. This initiative provides 8 weeks of programming cycles four times a year. Project GREEN programming offers chronic disease prevention and nutrition education workshops and engaging physical activities for both youth and adults. The aim of this study was to explored how Hispanic mothers and key community stakeholders viewed perspectives on barriers to healthy eating and physical activity, using an after school program setting. METHODS/STUDY POPULATION: The 2012- 2013 8-week programming was offered to 596 individuals mostly low income Latino residents. In Fall 2013 we recruited Hispanic women who participating in the zumba classes offered three-times per week, 27 Hispanic women made up the GREEN evaluation group. In addition to the 1 hour zumba class,our participants engaged in interview/focus groups, and completed a pre/post surveys, including questionnaires regarding community safety, physical activity and evaluated the 20 minute interactive diabetes education curriculum (Para tu Salud, American Diabetes Association). RESULTS/ANTICIPATED RESULTS: Of the 27recruited participants, 20 finished 8 weeks of the educational curriculum. Participants described ecological and psychoso¬cial barriers in neighborhoods (e.g. 75% of identified a lack of safety in parks/neighborhoods, 65% acknowledged easy accessibility to fast food), at home (e.g., 50% use

Keywords: CBPR; built environment; physical activity;

Poster Session: B - Poster #: 144

Fitness, Fatness and Obesity

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Background/Specific Aim: Fitness and fatness are clearly related but incorrectly interchanged. We wondered if a simple cardiorespiratory fitness test could improve the identification of obese children who are unfit and at even greater risk of cardiovascular disease. Our center recently demonstrated a high correlation between delta Work Rate/delta Heart Rate (?WR/?HR - the slope of the HR-WR relationship) determined from cycle ergometry and lean body mass (LBM), determined by DXA in normal weight children; ?WR/?HR was also highly correlated with peak VO2. Thus, our study aimed to identify if ?WR/?HR could be used to estimate LBM in obese children and provide insight into fitness. Methods: We examined the relationship between ?WR/?HR and body size indices (LBM, percent fat and Body Mass Index (BMI)) in 56 obese (BMI>95th percentile) children, 8-18 years [female 58%]. ?WR/?HR was determined by linear regression. Relationships between ?WR/?HR and body size indices were assessed using Pearson correlation (r). Results: ?WR/?HR was highly correlated with LBM [r=0.90] and moderately correlated with BMI [r=0.61]. ?WR/?HR also remained highly correlated with peak VO2 [r=0.86]. Discussion: A variable derived from a submaximal exercise test reflected LBM in obese children. Limited correlation between ?WR/?HR and BMI in obese subjects highlights the dissociation between fitness and fatness in child obesity. Asking already fit but obese children to increase exercise based solely on an estimate of body fat (e.g., BMI) may have limited value in reducing their obesity. ?WR/?HR may prove useful in the evaluation and management of the obese child. Funding: NIH PO1 HD048721 and ULI TR000153

Keywords: fitness; obesity; adiposity; body mass index; lean muscle mass;

Poster Session: B - Poster #: 145

Asthma Burden In Underserved Vietnamese Children

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Objectives: Vietnamese constitutes one of the fastest growing minority groups in America, with the largest concentration in Orange County, California. Yet, there are limited data on the prevalence of asthma in Vietnamese children. Our study evaluated the burden of asthma, including its prevalence, prior diagnosis, and asthma severity in addition to key contributing factors. Methods: Five elementary schools in Orange County that were predominantly Vietnamese with low socioeconomic status were selected for participation. Validated surveys were distributed to all students ages 3-12 in these schools with materials available in English, Vietnamese, and Spanish. Surveys included questions to identify the burden of asthma and related key factors. Surveys were answered by parents and returned to schools. Results: There were 1530 participants eligible for analysis. Asthma prevalence risk was 30.4%, and of these, 77.4% had a prior diagnosis and 43.5% had persistent severity. Those who answered in Vietnamese, compared to English, were more likely to have a higher prevalence (p=.004). Key risk factors included living in the United States for 10 or more years (p=.019) and smoker in the household (p=.015). Discussion: Asthma prevalence in low socioeconomic status Vietnamese children was found to be higher than commonly recognized. Given the limited information in this population, our current findings could affect health care policies that allow appropriate funding for programs dedicated to asthma care in this growing population.

Keywords: health needs assessment; Vietnamese children; asthma; prevalence; Asians;

Poster Session: A - Poster #: 146

Measuring The Effectiveness Of A Chronic Disease Self-Management Program Among Latino Adults

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Background/Aims: Latinos are disproportionately at risk for chronic health conditions and experience barriers to care. Culturally tailored and low-cost self-management programs are a cost-effective way to decrease the gap in chronic disease treatment and management disparities in the Latino community. The study aims to evaluate the addition of a coping strategies session to the culturally tailored Tomando Control de Su Salud self-management curriculum (Lorig, Ritter, & Gonzalez, 2003) on health status, symptoms, and self-efficacy among Spanish-speaking Latinos with chronic illnesses. Method: Twenty Latino adults with chronic illnesses were enrolled in a 7-week self-management program, led by two licensed Tomando Control de Su Salud facilitators. Pre-assessments were collected through closed-ended questionnaires. Post-assessments were collected through closed-ended questionnaires and ethnographic interviews. Results: Most participants were females (n=19; 95%). All participants were foreign-born, with the majority born in Mexico (n= 18). All participants have a diagnosed chronic illness; many have been diagnosed with high blood pressure (50%), rheumatoid arthritis (45%), and diabetes (35%). Most stated they needed medical attention in the past 12 months, but did not obtain medical care (60%), citing high cost as the largest barrier (55%). 7-week outcomes indicate an improvement in self-efficacy scores for six out of eight disease-related self-efficacy dimensions. Four coping strategies were identified: medication-use, motivation for self and family, exercise, and stoicism. Conclusion/Discussion: There is a need to offer financially accessible health services to foreign-born Latinos with chronic health conditions. Future research directions include measuring one-year impact of the self-management session on health status, symptoms, and self-efficacy. These findings may have implications on disseminating cost-effective and culturally tailored program sessions.

Keywords: Latino; chronic disease; self-management;

Poster Session: B - Poster #: 147

Age and Severity of Externalizing and Internalizing Symptoms in a Population of Children in a Behavioral Health Day Treatment Program

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Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are neurodevelopmental disorders that affect the functioning of school-aged children in both academic and social settings. Furthermore, children with ADHD or ASD have been found to exhibit internalizing and externalizing symptoms (Kessler et al 2006; Mahan & Matson 2011). Internalizing and externalizing symptoms in the classification of mental disorders are distinguished by whether symptoms are focused inwards towards the self (e.g., inattentive, anxious, depressed) or focused outward towards others or outside the self (e.g., aggression, hyperactivity) (Conner et al., 2003; Harris et al., 2014). Research has demonstrated there is a relatively significant decline in the severity of hyperactive and impulsive externalizing symptoms as age increases but that inattentive, internalizing symptoms remain relatively stable (Biederman et al., 2000; Riddle et al., 2013; Turgay et al., 2012). The present descriptive cross-sectional study aims to characterize the population of children enrolled at the University of California, Irvine Health Child Development School (UCI CDS) between 1983 and 1993 and to examine the age-related differences in their prevalence of internalizing and externalizing symptoms at enrollment. Correlational analysis found that father-reported externalizing symptoms of Oppositional Defiant Disorder and Conduct Disorder increase with age, while other symptoms such as hyperactivity and internalizing symptoms are not related to change in age at enrollment.

Keywords: ADHD; ASD; Internalizing; Externalizing; Age; Clinical; Behavior Intervention

Poster Session: B - Poster #: 148

An Effective Summer Enrichment Program to Garner the Interest of a Diverse Population of Youth towards health careers

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Purpose of Study: The need for enrichment programs that expose a diverse population of youth to health careers is urgent. In this report, we describe the effectiveness of a unique and highly interactive enrichment program in garnering the interest of a diverse population of high school students towards a career in health care. Methods Used: To give youth a glimpse of life in medical school, we designed a very structured summer enrichment program that mimics the medical school's interactive curriculum. The workshops included but were not limited to cadaver lab, bedside ultrasound, suturing, robotics, patient interviews, and splinting. The students were accepted through an application process. We encouraged participation of those underrepresented in medicine (URIM) by providing scholarships. A feedback survey was distributed at the end of the program to measure the effectiveness of the program in helping them with their future goals and professional development as well as the effectiveness of the workshops. A 5-point scale was used, 1 = least effective or 5 most effective). Summary of Results: During the summers of 2012 and 2013, 280 high school students participated in the program and 22% were URIM. Of 280, 257 (92%) complete evaluations were collected. The average rating of the workshops ranged from 3.4 to 5.0, with cadaver lab and patient interview each having the highest rating of 4.76. As a result of this program, students gave an average rating of 4.7 out of 5 regarding their motivation to pursue a career in medicine, rating of 4.59 for understanding evidence based medicine, a rating of 4.45 for comfort in interviewing patients, and a rating of 4.43 for interest in mentoring in the future. Conclusions: The Summer Premed Program at UC Irvine School of Medicine was very successful in promoting the interest of a diverse population of youth towards a career in medicine. Long-term follow-up of the participants' career choices is needed.

Keywords: Youth; Health; Careers; Summer; Interactive;