52nd

MEDICAL STUDENT

RESEARCH FORUM

February 4th, 2014

D1.502, 3-6 PM

Guest Speaker: George Buchanan, M.D.

Children's Cancer Fund Distinguished Chair in Pediatric Oncology and Hematology

University of Texas Southwestern Medical Center

52nd Medical Student Research Forum

Table of Contents

GENEROUSLY SPONSORED

BY

THE SOUTHWESTERN MEDICAL FOUNDATION

THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER AT DALLAS

FIFTY-SECOND ANNUAL MEDICAL STUDENT RESEARCH FORUM

TUESDAY, FEBRUARY 4th, 2014
3pm, D1.502

PROGRAM DIRECTOR: Rene Galindo, M.D., Ph.D.

52nd ANNUAL MEDICAL STUDENT RESEARCH FORUM

LIST OF ORAL PRESENTATIONS

Khrishen Cunnusamy
"Neuroantigen-specific CD8 T regulatory cells: a new member to the therapeutic toolkit against Multiple Sclerosis"

Brandon Jakubowski
"Generation of a novel *D. melanogaster* platform to elucidate oncogenic activity of common human p53 missense mutants"

Ernesto Llano
"Missense Mutation in Secretagogin as a Possible Cause of Ulcerative Colitis in Three Siblings**"**

Soa-Yih Sher
"Variations in melanoma histopathology reporting influences selection of sentinel lymph node biopsies in thin melanomas"

Cynthia Wei
"Contact lens-related microbial keratitis in a novel rabbit model."

James Ying
"Long Term Follow-up of prostate cancer patients who fail salvage radiation therapy and radical prostatectomy"

PRESENTATION OF GUEST SPEAKER

George Buchanan, M.D.

Children's Cancer Fund Distinguished Chair
in Pediatric Oncology and Hematology
Professor of Pediatrics and Internal Medicine

University of Texas Southwestern Medical Center

RECEPTION AND POSTER SESSION IMMEDIATELY FOLLOWING
A.W. HARRIS FACULTY CLUB

Special Recognition for Research

Dean's Research Scholar

Aaditya Nagarj
Mentor: Joachim Herz, M.D., Division of Molecular Genetics, Neurology & Neurotherapeutics, and Neuroscience

Niyatee Sumudra
Mentor: Carol Tamminga, M.D., Division of Psychiatry

Doris Duke Fellows

Soham Banerjee
Mentor: Ronald Peshock, M.D., Division of Radiology and Internal Medicine

Brian Benjamin
Mentor: Scott Grundy, M.D., Ph.D, Division of Internal Medicine and Clinical Nutrition

TABLE OF CONTENTS
Basic Research and Disease Models

KEY
Ω Oral Presenter - UT Southwestern Medical Student Research Forum
† NIDDK Medical Student Research Trainee
£ R25 NHLBI Research Trainee
Û UT Summer Research Program Participant
D Doris Duke Fellow

Proteomic discovery of functionally important pathways in myocardial ischemia-reperfusion injury

Kamran Ahmed
Mentors: Anthony Rosenzweig, MD, Hasmik Keshishian, PhD
Steven Carr, PhD- BIDMC Cardiovascular Institute

Background: Coronary heart disease, a source of myocardial ischemia-reperfusion injury (IRI), is the world's leading cause of death and disability. Insulin-like growth factor 1 (IGF1) transgenic (Tg) mouse hearts are protected from IRI, whereas Akt-Tg mouse hearts recover poorly from IRI. Surprisingly, Akt is a downstream component of IGF1 signaling. The Akt-Tg phenotype can be rescued by cardiac gene transfer of activated PI3-kinase (PI3K), another component of the IGF1 pathway, suggesting that PI3K-dependent but Akt-independent pathways are key determinants of IRI. To discern such pathways, we analyzed the proteomic and phosphoproteomic changes in wild-type (WT), IGF1-Tg, and Akt-Tg mouse hearts, identified 20 differentially regulated candidates as potential modifiers of IRI, and began testing their functional roles in an in vitro model. We hypothesize that the cardioprotection observed in IGF1 overexpression is a result of PI3K-dependent but Akt-independent signaling pathways.
Methods: WT hearts were collected at 4 time points of ex-vivo Langendorff IRI and analyzed with liquid chromatography-tandem mass spectrometry to determine protein expression and phosphorylation changes. IGF1-Tg and Akt-Tg hearts were analyzed at baseline. Protein network analysis was performed using Cytoscape software. The functional effects of candidates with expression or phosphorylation differences ≥2-fold were assessed in rat neonatal ventricular myocytes using in vitro redox-based viability assays and cell proliferation studies.
Results: In the WT IRI studies, 6403 proteins and 22833 phosphopeptides were quantified. During IRI, no proteins changed in expression, 45 phosphopeptides were upregulated, and 975 phosphopeptides were downregulated. In the IGF1-Tg and Akt-Tg hearts, 6700 proteins and 23000 phosphopeptides were quantified. In vitro knockdown of rho-associated protein kinase 2 (ROCK2) increased the viability signal by 17% in normoxia and 33% in simulated IRI ($p<0.05$) and increased EdU incorporation from 28.9% to 40.15% ($p<0.00001$). Network analysis of Akt-Tg hearts revealed significant downregulation of 23 out of 45 subunits of Complex I ($p<0.05$).
Conclusions: Dephosphorylation of the cardiac phosphoproteome is the dominant pattern in IRI, which may reflect phosphatase activation or reduced ATP levels inhibiting kinase activity. ROCK2 knockdown increased the viability signal by stimulating proliferation in vitro. Whether ROCK2 is involved in cardiomyogenesis in the adult heart will be addressed in future studies. Akt-Tg hearts may be susceptible to IRI due to a reduced ATP reserve caused by Complex I downregulation

Antigen-specific natural killer cell responses in chronic hepatitis C Infection

Kathryn Bowman
Mentors: Barbara Rehermann, MD, & Lauren E. Holz, PhD

Chronic hepatitis C virus (HCV) infection results in an inflammatory liver disease leading to fibrosis and cirrhosis. The progression of liver disease is thought to be immune-mediated because HCV itself is non-cytopathic. Given that HCV-specific T cells are diminished in number and functionally exhausted in chronic HCV infection, it remains unclear which cell population drives disease pathogenesis. Here, we investigated the function of natural killer (NK) cells, the major innate immune cell population in the liver. The NK cell population increases further in the setting of chronic hepatitis C infection and have multiple mechanisms of cytotoxicity. We investigated whether NK cells could respond to HCV in an antigen-specific manner.

PBMCs from 39 patients with chronic HCV infection (gt 1) not recently on medication (>2 years) were stimulated for 8 hours in a whole blood activation assay with pools of overlapping 18-mer peptides comprising HCV structural (E1, E2) and nonstructural (NS3) proteins. Cytokine production by NK cells and T cells was assessed by multicolor flow cytometry. The frequency of IFN-γ+ NK cells was 5 fold greater than the frequency of IFN-γ+ T cells. A minority of IFN-γ+ NK cells co-produced TNF-α. NK cell responses to HCV peptides varied between subjects, but did not correlate with T cell responses or viremia.

This study demonstrates that NK cells are activated in an antigen-specific manner in chronic HCV infection and respond to both structural and nonstructural HCV proteins. Natural killer cell cytokine and cytotoxic responses were larger than corresponding T cell responses. The mechanism of antigen-specific NK cell activation is currently under investigation.

.

Effects of age and diabetes on corneal epithelial nerve loss and the corneal epithelium in a Streptozotocin-induced Type-I diabetic mouse model

Daniel Cai
Mentors: Danielle Robertson, PhD, Meifang Zhu
Vindhya Koppaka, PhD, & Matthew Petroll, PhD

Alterations in corneal nerve morphology are increasingly being used as surrogate markers for disease severity and efficacy of therapeutic modalities in diabetes. In addition, the alterations themselves are associated with significant clinical sequelae. Despite the abundance of reports on corneal nerve morphology in recent years, information regarding the relationship between nerve loss and the pathobiology of diabetic corneal disease is limited. This study investigated systematic changes in corneal thickness and corneal nerve morphology using 3D imaging in vivo and in situ in a streptozotocin-induced diabetic mouse model. Streptozotocin-treated mice demonstrated elevated levels of serum glucose and growth retardation consistent with a severe diabetic state. A reduction in length of the subbasal nerve plexus (SBNP) was evident at disease durations of 6 and 12 weeks. Hyperglycemia-induced loss of the SBNP was associated with corneal epithelial thinning and alterations in basal cell density. Loss of the terminal epithelial nerves was associated with increased age in non-diabetic animals. This is the first rodent model of type 1 diabetes that exhibits corneal epithelial thinning associated with diabetic corneal neuropathy. These findings also indicate that the pathophysiological effects of age and diabetes differentially mediate nerve loss in the central cornea with corresponding effects on corneal epithelial homeostasis.

Sexually Dimorphic Role of G Protein-Coupled Estrogen Receptor (GPER) in Modulating Energy Homeostasis

Elizabeth Carstens
Mentors and Collaborators: Kathryn E. Davis, PhD, Boman G. Irani, Lana M. Gent, Lisa M. Hahner, & Deborah J. Clegg, PhD

The classical estrogen receptors, estrogen receptor -α- and estrogen receptor β, are well established in the regulation of body weight and energy homeostasis in both male and female mice, whereas, the role for a G protein-coupled estrogen receptor 1 (GPER) as a modulator of energy homeostasis remains controversial. This study sought to determine whether gene deletion of GPER (GPER KO) alters body weight, body adiposity, food intake, and energy homeostasis in both males and females. Male mice lacking GPER developed moderate obesity and larger adipocyte size beginning at 8 weeks of age, with significant reductions in energy expenditure, but not food intake or adipocyte number. Female GPER KO mice developed increased body weight relative to WT females a full 6 weeks later than the male GPER KO mice. Female GPER KO mice also had reductions in energy expenditure, but not significant increases in body fat content. Consistent with their decrease in energy expenditure, GPER KO males and females showed significant reductions in two brown fat thermogenic proteins. GPER KO females, prior to their divergence in body weight, were less sensitive than WT females to the feeding-inhibitory effects of leptin and CCK. Additionally, body weight was not modulated fully by ovariectomy or estradiol replacement in GPER KO mice. Estradiol treatment activated phosphorylated extracellular signal-regulated kinase (pERK) in WT but not GPER KO females. For the first time, GPER expression was found in the adipocyte but not the stromal fraction of adipose tissue. Together, these results provide new information elucidating a sexual dimorphism in GPER function in the development of postpubertal energy balance.

Novel insights into the molecular mechanisms underlying the dual targeting of CD54 and mTOR in human lymphoma cell lines

Felix Chang
Mentors: Ellen S. Vitetta, PhD, & Laurentiu Pop, MD

Background: There are more than 75,000 new cases of Non-Hodgkin lymphoma (NHL) and 12,000 NHL-related deaths reported annually in the U.S. Most patients are treated with combinations of chemotherapy and immunotherapy. While long term remissions can be induced, cures are rare. There is therefore a need for new combinatorial therapies that target several additional tumor markers and pathways in order to achieve synergic anti-tumor effects and to reduce side effects and the emergence of resistant tumor cells. In this study human lymphoma cells lines were treated with a combination of a small molecule inhibitor of the kinase, mTOR (rapamycin) and with an anti-human CD54 (ICAM-1) monoclonal antibody (UV3). Importantly, our previous work in mice showed that this combination has a synergistic effect on survival of human tumors in SCID mice.
Objective: To culture human lymphoma cells with rapamycin, anti-CD54 or the combination and investigate mechanisms underlying therapeutic responses.
Methods: Cultures of human B cell lymphoma cell lines (Namalwa, Raji, and DHL-4) were used. UV3 was purified from the supernatants of the hybridoma cell line. Flow cytometry was used to measure the binding of UV3 to the cell lines. Trypan blue exclusion was used to measure the effects of rapamycin and anti-CD54 on cell viability. Expression of key molecules was determined by western blot analysis. Enzyme-linked immunosorbent assays (ELISA) and intracellular staining were used to investigate alterations in the immune profile of the treated cells.
Results: Our *in vitro* observations suggest that the targeting of mTOR and CD54 have an impact on the upstream signals leading to stimulatory or inhibitory pathways that regulate cancer cell survival and pro- *vs.* anti-immune activity. Each cell line relied on different pathways for survival, as shown by their differential expression of several oncogenic, tumor suppressor, and apoptotic proteins. Most importantly, CD54 was upregulated after rapamycin treatment in all cell lines, most likely in an NF-κβ- dependent manner. Higher levels of CD54 made cells more susceptible to therapy with anti-CD54. Rapamycin abrogated or greatly reduced cytokine secretion in all the cell lines tested.
Conclusion: Our results demonstrate that NHL cell lines of the same histological tumor type are heterogeneous both with regard to the level of protein expression and the responsiveness to drugs that interfere with signaling pathways. This allows tumors to utilize multiple escape mechanisms to avoid the immune system. This study supports the evolving notion that therapies of individual patients should be guided by information acquired from the examination of activated genes and growth pathways in tumors from each patient.

Reference Values For Body Composition Determined By Dual Energy X-Ray Absorptiometry (DXA) In Europids

Stephanie Diaz
Mentor: Gloria Vega, PhD

This study aims to define reference range parameters of body composition in the non-obese population. Using a DXA machine, numerical results of Total Body Composition of patients with multiple visits were exported from GE version 14.10 onto Microsoft Excel. Results included Total Mass (kg), Fat Mass, Lean Mass, Bone Mineral Content (BMC), Trunk Total Mass, Lower Extremity Mass, and Visceral Adipose Tissue Mass (VAT). The weight change of 145 subjects that had multiple visits to the clinic needs to be considered. A percent change of their weight being either gained or lost from their initial visit to the most recent was determined. A percent change of Trunk Total Mass, Lower Extremity Mass, VAT Mass, and Fat and Lean Mass was also calculated. After obtaining a percent change of the particular region of interest, data was sub-grouped by gender and groups (Group A: (+) 0-10%, Group B: $\geq$10%, Group C: (+/-), Group D: (-) 0-10%, and Group E: (-) $\geq$10%). Bars graphs were designed that compared regions of interest to answer the question of what is being lost in terms of body composition when a subject loses or gains weight. A Fat versus Lean Mass percent change graph was formulated to show what is being lost or gained in terms of weight alteration. It is important to compare both Fat and Lean Mass because both total the Total Mass of a subject and when losing or gaining weight, we can observe which mass is being lost or gained first, or if it is being lost or gained proportionally [Total Mass (kg) = Fat Mass + Lean Mass + Bone Mineral Content]. Comparison of Trunk Total Mass, Lean Mass, and VAT Mass is just as important because fat distribution can be observed with weight shift. Next, comparison of blood chemistries such as triglyceride should be compared to VAT Mass. Thus, a relationship of body phenotype to metabolic phenotype is ideal because increased visceral fat and triglyceride levels are associated with insulin resistance. When comparing Total Fat and Lean Mass, Fat Mass is lost at a higher percentage than Lean mass. When comparing Trunk, Lower Extremities and VAT Mass, observations of VAT mass being lost and gained were apparent the most out of the three. Furthermore, whether gaining or losing weight, Trunk, Lower Extremities or VAT Mass is generally being gained or lost. In this study, individuals that conserved Visceral Adipose Tissue also gained weight. The inference is that when gaining weight, Trunk region or Lower Extremity region are first to be gained, then VAT Mass region is gained. Further analysis of triglyceride to VAT comparison is necessary. Overall, changes in body composition with weight loss reflect upon changes in metabolic risk.

Probing for New Rhabdomyosarcoma Pathogenesis Genes

Kathleen Evans
Mentor and Collaborators Rene Galindo, MD, PhD, Kathleen A. Galindo, PhD, & Xiangyi Li, PhD

Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma, the most aggressive form of which is caused by the PAX-FOXO1 fusion oncoprotein. How PAX-FOXO1 drives otherwise normal muscle lineage precursor cells to a neoplastic state remains unclear. To uncover new genes underlying RMS pathogenesis, the lab conducted an unbiased forward genetic screen in a *Drosophila* PAX-FOXO1 model, which revealed *Myocyte Enhancer Factor 2* (*MEF2*) as a PAX-FOXO1 gene target and effector. *Mef2* is a well-known nodal gene in myogenesis, but has not been interrogated for a role in RMS pathogenesis

To extend these studies from the *Drosophila* model to mammalian RMS pathobiology, we have turned to mouse myoblast (C2C12) cultured cells, and PAX-FOXO1 RMS cell lines. Of the four mammalian *MEF2* orthologs, preliminary data point towards *MEF2A* and *-C* as the orthologs active in RMS. My goal in the lab was to generate new C2C12 and RMS cell lines that conditionally silence or misexpress *MEF2A/C*. These new genetically modified cell lines are now actively being utilized by the lab to characterize how these *MEF2* orthologs influence normal myoblast differentiation, and the behavior of RMS cells.

B-Catenin and K-ras synergize to form Wilm's tumor with concurrent p53 pathway modulation

Austin Hembd
Mentors: Peter Clark, MD, & David DeGraff, PhD
Vanderbilt University

Humans can develop pediatric kidney tumors called Wilm's tumors. If one identifies the specific genes that cause Wilm's tumor, or that concomitantly change expression levels in the tumor tissue, then diagnosis and eventually drug targets for therapy are expedited. Characterizing genetic determinants in the mouse model can help actualize these future therapies. When the genes K-ras and β-Catenin are overexpressed in a mouse, it develops a renal tumor histologically identical to a human Wilm's tumor. Microarray analysis on mouse tumor tissue showed modulated expression levels of gene targets in the p53 tumor suppressor pathway. Immunohistochemistry stained mice tissue specifically for p53. In tissue with K-ras and β-catenin overexpression, p53 staining is positive surrounding the tumor. RT qPCR measured levels of gene expression of p53 pathway associated genes. Combination mutants β-Catenin and Kras were compared with controls. This PCR array analysis identified genes, such as c-Jun, Traf1, and Dapk1, that had significant expression changes in the combination mutant when compared to either mutant individually. The expression is modulated in a non-additive fashion in K-ras + β-catenin mutant tissues, which can explain the phenotype of Wilm's tumor in only double mutant mice. These genes individually represent targets for therapy in the future, and together represent an identifying fingerprint for diagnosis and prediction.

Generation of a novel *D. melanogaster* platform to elucidate oncogenic activity of common human p53 missense mutants

Brandon Jakubowski
Mentor and Collaborator: John Abrams, PhD, & Alejandro D'Brot

The tumor suppressor p53 prevents uncontrolled cell growth by three separate mechanisms: inducing apoptosis, initiating cell-cycle arrest, and activating DNA repair mechanisms in response to cell damage. Due to its central role in tumor eradication, it is unsurprising that p53 mutations are found in over half of human cancers. Unlike all other tumor suppressors however, 75% of these are missense mutations, with just six of them accounting for a third of all mutations found in the DNA binding domain of p53. Recent findings indicate that mutations in these "hotspot" locations may encode gain of function oncogenic activity to p53. Given their high prevalence, these mutations suggest a previously underappreciated selective advantage.

We sought to decode this novel oncogenic activity of human p53 mutations by exploiting the *Drosophila* model system. This organism shares a similar p53 regulatory network with humans, as well as many of the same DNA repair and pro-apoptotic target genes. We recently showed that human p53, despite millions of years of evolutionary distance, complements loss of function mutations in the native fly p53 gene. We used six humanized p53 Drosophila strains previously generated in the lab; these contain a human p53 gene insertion, each with one of the six most commonly found missense mutations in patients.

To study these mutations, we first profiled the expression patterns of wild type and mutant hp53 in the fly and their ability to rescue dp53 function. Expression levels of p53 were determined by immunofluorescence, while biological function was determined by the use of a GFP biosensor that specifically reports dp53 activity and acridine orange staining to identify dying cells in irradiated embryos.

Expression studies demonstrate that the reporter is activated within stem cells in region 1 of the germarium, while its activation was absent in p53 null mutants. This phenotype was recovered with a dp53 insertion rescue. Additionally, two separately generated hp53+ strains show unusually elevated levels of expression compared to the wild type strains, whereas all mutant strains show diminished reporter activation in the region 1 stem cells. Functional studies in the embryo and the wing disc demonstrate that both wild type flies and the dp53 rescue promote cell death after irradiation, while the p53 null mutant does not. The two hp53+ strains rescued the wild type phenotype in the embryo; however, one of the hp53+ strains, named B2, was unable to induce cell death in the wing disc. The missense mutant strains do not exhibit IR-induced apoptosis in the embryo, but preliminary imaging shows they may be able to in the wing disc. We also discovered that, unlike the six hotspot mutants, wild type human p53 localizes to unidentified subnuclear compartments. Importantly, this may allow us to stratify and characterize p53 mutations according to functional differences.

Inhibition of L-type and cyclic nucleotide-gated calcium channels demonstrates synergistic mechanisms for prolonging vascular contractions induced by a mimetic of thromboxane A_2

Joseph Kellum
Mentors and Collaborators: Paige L. Monnet, Maxwell R. Hinman, & James A. Orr
Department of Molecular Biosciences, University of Kansas

Previous experiments have demonstrated that the rates of relaxation of blood vessels treated with the thromboxane-A_2 mimetic, U-46619, are significantly lower when compared to vessels treated with other vasoactive agents (e.g. α-adrenergic agonists). As a means of investigating the molecular mechanisms responsible for this prolonged contraction, we examined the roles of two types of calcium channels. L-type Ca^{2+} channels have long been associated with the U-46619 contraction, while cyclic nucleotide-gated (CNG) Ca^{2+} channels have only recently been shown to be involved. We tested the hypothesis that functioning of both channels is necessary to prolong the U-46619 contraction. An isolated organ bath preparation was used to measure the rates of relaxation (g/min) in aortic vessel segments obtained from euthanized rabbits. Isolated vessels contracted with U-46619 were treated with either L-type channel inhibitor (nifedipine, 200 μM) or CNG channel inhibitor (L-cis-dilitiazem, 140 μM), or both inhibitors simultaneously. Mean rates of relaxation were obtained for the four treatment groups: nifedipine only ($7.95 \times 10^{-2} \pm 0.562 \times 10^{-2}$ g/min, n = 10), L-cis-diltiazem only ($6.36 \times 10^{-2} \pm 0.603 \times 10^{-2}$ g/min, n = 10), both inhibitors simultaneously ($6.93 \times 10^{-2} \pm 0.875 \times 10^{-2}$ g/min, n = 12), and a control with vehicle only ($3.94 \times 10^{-2} \pm 0.494 \times 10^{-2}$ g/min, n = 15). Statistical analysis of the data indicated that the mean relaxation rate for the vehicle-treated group differed significantly from the relaxation rates of the experimental groups ($P < 0.001$), which were deemed statistically synonymous ($P = 0.324$). These data indicate that inhibition of either calcium channel alone or both channels simultaneously leads to equivalent increases in the rate of relaxation. This demonstrates that optimal functioning of both channels is necessary for the prolonged contraction, characteristic of U-46619-treated vessels. These results may have implications for reversing the contractions in vessels during myocardial infarction or stroke.

Missense Mutation in Secretagogin as a Possible Cause of Ulcerative Colitis in Three Siblings

Ernesto Llano
Mentor: Ezra Burstein, MD, PhD
Collaborators: Lilliene Chan, MD, Steven M. Harrison, Haiying Li, PhD, Luis Sifuentes-Dominguez, MD, Jason Y. Park, MD, PhD, Jonathan C. Cohen, PhD, & Linda A. Baker, MD

Inflammatory bowel disease (IBD) consists of two disorders, Crohn's disease and ulcerative colitis (UC), which affect 1.4 million Americans. Genetic factors contribute to the development of these disorders but not all culprit genes have been identified. To further our understanding of the genetic causes of IBD, we examined a consanguinous family with a high incidence of childhood-onset UC. We performed exome sequencing of five siblings, three of which were diagnosed with severe UC before the age of 10. Given the parents' consanguinity, areas of homozygosity were examined using a SNP array. Two areas of homozygosity, in chromosomes 6 and 12, were shared by the three affected probands but not by their two unaffected siblings. Given the inheritance pattern in the pedigree, we speculated that a homozygous recessive mutation in a gene contained within these intervals should be responsible for the phenotype. Thus, a total of 140 potential genes were implicated. Variants found by exome sequencing were prioritized if they affected the three probands and not their unaffected siblings, and if they were rare in the general population according to their frequency in the 1000 genomes database. Afterwards, we cross-referenced the identified potential culprit variants found in the exome sequence analysis against the unique areas of homozygosity shared by the probands. The top candidate change was in *SCGN*, which had a coding variant (c. 433G>A/p.R77H) not previously found in the 1000 genomes database or in the dbSNP database. Sanger sequencing confirmed that both parents were carriers, the three probands were homozygous, and one sibling was a carrier while the other was wild-type. *SCGN* encodes a 276 amino acid, calcium-binding protein, secretagogin. The protein is expressed in tissues of neuroendocrine lineage, such as pancreatic β-cells and intestinal enteroendocrine cells. The coding change found in these patients is located in one of the calcium binding domains (EF hand 2). Immunohistochemical analyses of the patients' colon biopsies did not demonstrate a decrease of the presence of secretagogin when compared to controls, suggesting that the mutation does not affect expression, but may have a functional effect yet to be determined. We are building a molecular and cellular model of the R77H mutation to identify if this coding change alters the function of the protein. If a functional impairment of SCGN is confirmed, it could represent the first description of enteroendocrine dysfunction playing a role in IBD pathophysiology.

Isoflurane Preserves Viability of Highly Metabolic Renal Epithelial Cells Exposed to Anoxia

Vasudha Mantravadi
Mentors: Florian Hackl, MD, Joshua C. Vacanti, MD, Jessica Bauerle, MD, Koji Kojima, MD, PhD, Charles A. Vacanti, MD
Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Background: Cells subjected to ischemia, whether in the context of hypoxia, hypovolemia, or circulatory collapse, undergo damage and death as a result of oxygen deprivation. Previous studies have shown that general anesthetics can protect cells from ischemic injury by lowering their aerobic metabolism and decreasing production of toxic metabolites, among other mechanisms (1, 2, 3). This very preliminary study investigated the potential protective effect of isoflurane on the survival of cells that have a fairly high baseline metabolic rate, human renal proximal tubular epithelial cells (HK-2) and human microvascular endothelial cells (HMEC), in an anoxic environment.

Methods: Cultured HK-2 and HMEC cells were incubated in a Forma Scientific® Anaerobic System at 37°C either in the absence (control) or presence (experimental) of 5% isoflurane for 0, 24, 48, 72, and 96 hours. Cell viability and metabolic activity were then assessed using live/dead fluorescence imaging and an MTT cell metabolism assay, respectively.

Results: In vitro exposure of cells to anoxia without isoflurane over a period 96 hours, resulted in a reduction of viability of HK-2 cells from a baseline of 98%, to approximately 8-9%. Over the same period of time, viability of cells exposed to isoflurane and anoxia decreased to 35%. This represented a fourfold increase in survival of HK-2 cells exposed to isoflurane at 96 hours. At earlier time points, both cell death in anoxia, and the protective effect of isoflurane were less dramatic. Exposure of the metabolically less active HMECs to anoxia resulted in very little cell death in either the controls (anoxia alone) or the experimentals (anoxia and isoflurane), with 98% of the cells surviving the exposure to anoxia in both cases. The net metabolic activity, as assessed by absorbance using the MTT assay, paralleled the cell viability in both cell types and groups.

Conclusion: In this preliminary study, continuous exposure of HK-2 cells to 5% isoflurane during anoxic incubation had a protective effect on both cell viability and total metabolic activity over a period of 96 hours. Whether this effect was also present in the less metabolically active HMECs, was not determined, as anoxia over the time period of the study had little effect on cell viability in either the experimental group or in the control group. The protective effect observed for HK-2 cells will likely vary with differences in metabolic requirements of different cell types, types and concentrations of anesthetic agents, and duration of anesthetic exposure. Anesthetic treatment may need to be tailored specifically to a cell type to confer the protective effects desired.

References:
1. Feng Y et al., Lab Medicine (2008), 39(6):356-360.
2. Popovic R et al., Anesthesiology (2000), 92(5):1343-9.
3. Samuta T et al., Anesth Analg (1993), 77:38-43.

Glutamatergic Signaling Abnormalities in the Anterior Cingulate Cortex and Hippocampus Across the Psychosis Dimension

Caitlin Meyer
Mentors: Wei Li, Kelly Gleason, Carol A. Tamminga, MD

Imaging studies in schizophrenia and acute psychosis routinely indicate reduced gray matter volume and reduced perfusion during task related activation in the ACC and hippocampus of schizophrenics compared with normal controls. Furthermore, post-mortem molecular findings suggest declarative memory impairments may be linked to alterations in glutamatergic transmission in both the hippocampus and ACC. In the hippocampus, a reduction in dentate gyrus (DG) glutamatergic output could simultaneously generate a change in homeostatic plasticity processes in cornu ammonis 3 (CA3) that result in increased activity in reaction to reduced afferent stimulation from the DG onto CA3 neurons (a process that could increase the pattern completion functions of CA3) and a decrease in glutamatergic signaling functions specific to the DG associated with pattern separation. In the anterior cingulate, decreased excitatory and/or increased inhibitory glutamatergic transmission could decrease error detection functionality. Cumulatively, the increase in pattern completion functionality caused by increased activity in the CA3 coupled with decreases in pattern separation functionality in the DG of the hippocampus along with decreased error detection signaling in the anterior cingulate could result in false associations that generate psychotic content while laying down new memories. To investigate this model we have collected hippocampal and anterior cingulate post-mortem tissue from a cohort (n=50) of 20 schizophrenics (10 off-drug, and 10 on-drug), 10 bipolar patients with psychosis and 20 matched normal controls. The hippocampus was dissected into 5 subunits (enterhinal cortex, subiculum, CA3, cornu ammonis 1, and DG) while the ACC was dissected into glutamatergic cortical layers I-III, and GABAergic layers Va-VI. We are currently measuring the protein levels of glutamate receptor subunits and postsynaptic scaffolding and signaling proteins using Western Blot analysis in the 5 subunits of the hippocampus and layers I-III, and Va-VI of the ACC. Our preliminary data demonstrates increased excitatory glutamatergic signaling activity in the CA3, as well as decreased excitatory glutamatergic signaling activity in the DG of schizophrenic hippocampi thus supporting our model. PSD95 is also increased in anterior cingulate cortex in layers 1-3 of schizophrenia tissue suggesting an increase in synaptic strength within this area, possibly due to increased afferent stimulation from the hippocampus. Results from this model could present novel pharmacological treatment targets for schizophrenia as well as guide reverse translational animal preparations for further research.

The Role of Arcuate AgRP Neurons in Ghrelin Food Reward Behavior

Christina Mosher
Mentor: Jeffrey Zigman, MD, PhD

Media coverage of the current obesity epidemic often ascribes stress as a major cause of excessive food intake in humans, with a particular increase in calorically dense 'comfort foods.' In the current study, the hormonal and neural link between stress and feeding behavior was further investigated using behavioral tests to monitor the rewarding effects of high fat diet in a novel transgenic mouse model. In particular, the octanoylated peptide hormone, ghrelin, plays a key role in appetite regulation as well as a behavioral role in the stress response. Synthesized and secreted by a small population of gastric epithelial cells, ghrelin is the only circulating hormone known to stimulate appetite. Importantly, ghrelin levels are significantly and persistently elevated in response to chronic stress. Also, ghrelin signaling enables the development of stress-induced conditioned place preference (CPP) for high fat diet, a reward-based eating behavior, and ghrelin minimizes stress-induced depressive-like behavior. The ghrelin receptor, known as the growth hormone secretagogue receptor (GHSR), is highly expressed in hypothalamic brain regions involved in homeostatic feeding, such as the arcuate nucleus (Arc). Preliminary studies in the lab indicate that acute ghrelin-induced feeding, which is not observed in GHSR-deficient (GHSR-null) mice, is partially restored in mice with GHSR expression only in Arc AgRP neurons. We now hypothesize that the GHSRs present on Arc AgRP neurons are sufficient to mediate the stress-induced development of food reward behavior in mice. To test this hypothesis, the lab has generated a novel, genetically engineered mouse line in which GHSR expression is limited only to Arc AgRP neurons. Such is possible due to a tamoxifen-inducible Cre recombinase, which in turn removes a loxP-flanked transcriptional blocking cassette from an altered GHSR gene, thus allowing tamoxifen-dependent, AgRP neuron-selective reactivation of GHSR expression. For these studies, littermates of 4 genotypes were used: wild-type mice, wild-type mice expressing Cre recombinase, GHSR-null mice, and mice with GHSRs expressed only in AgRP neurons, as described above. All mice were treated with tamoxifen for five days to activate Cre recombinase, allowed to recover for three weeks and monitored for ad-lib food intake for the last nine days of recovery. Mice were then subjected to a ten-day chronic social defeat stress (CSDS) protocol and afterward tested for depressive-like behavior using the social interaction (SI) test. Following the SI test, mice underwent a CPP for HFD protocol, which includes a pretest, twelve days of conditioning, and a test day. Data for an initial cohort of animals has been obtained and analyzed, and studies with additional cohorts are ongoing. The new mouse model with GHSRs expressed only in the Arc will assist in determining whether AgRP neurons in the Arc are sufficient to mediate ghrelin's effects on stress-induced food reward-behavior and stress-associated depressive-like behavior. Further work may include a similar tamoxifen-inducible, Cre-recombinase system expressing GHSRs only in the VTA or only in the hippocampus to narrow down where ghrelin has its food reward behavior effects.

Alterations in Neural Stem Cell Fate Following Transient Focal Ischemia

Derek Nguyen
Mentor and Collaborators: Robert Bachoo, MD, PhD, Vamsidhara Vemireddy, & James Battiste, MD

Introduction: The purpose of this experiment is to determine the differentiation identity of the neural stem cells (NSC) in the subventricular zone (SVZ) of adult mouse brain after a middle cerebral artery occlusion (MCAO). Injury to the brain causes a large number of changes including inflammation and apoptosis, but the reaction of NSC's has been more difficult to characterize because of the transient nature of their response. Previously, adult neural stem cells (NSC) in the SVZ have been observed to differentiate predominantly into cells with neuronal characteristics. This theory is questioned via a tamoxifen-inducible cre-recombinase (Cre-ER^{T2}) expression mouse model system.
Method: The Cre-ER^{T2} expression mouse model system is driven by the Cystatin-C promoter to label NSC's in a time specific manner and track their cell fate after MCAO. After the ischemia, these brain sections were stained with different immunohistochemicals at three separate time points. One set was co-labeled with GFAP, an astrocyte marker, and BrdU, a proliferation marker. Another set was co-labeled with DCX, a neuronal marker, and BrdU. This was used to differentiate between latent NSCs and proliferating NSCs by comparing the ipsilateral side (ischemic) with the contralateral side (control) of the brain.
Results: Compared to the contralateral, the ipsilateral side had a significant increase in GFAP/BrdU positive cells between day 3 and day 7 time points. The cell quantity dropped between day 7 to day 14 time points. Compared to the contralateral, the ipsilateral side had a decrease in DCX/BrdU positive cells between day 3 and day 7 time points. The cell quantity significantly increased between day 7 to day 14 time points, and the quantity at day 14 was about twice to that of the day 3 time point.
Discussion: This data demonstrated that after the MCAO, the stem cells are not just undergoing neurogenesis, but are for certain period of time, also differentiating into astrocytes that are migrating towards the site of injury. This phenomenon is only witnessed in the NSCs towards the day 7 time point. Afterwards and leading up to day 14, the NSCs seem to be changing their cell fate programming from the astrocyte pathway back to the intended neuronal pathway. Thus, the staining results verify that after an ischemia, NSCs within the SVZ regions of the brain undergo a constant change of programmed cell fate, alternating between immature neurons and astrocytes implicating future aims for "programmed" neurogenesis in the development of therapeutic strategies for the treatment of brain damage and disease.

Role of Complement Factor H Polymorphism and Diet in Neuroinflammation

Samuel Parnell, BS
Mentors and Collaborators: Rafael Ufret-Vincenty, MD, Adebimpe Kasumu, PhD, Bogale Aredo, PhD, & Xiao Chen, MD

Background: Multiple lines of evidence point towards an important role for complement factor H (Cfh) in neuroinflammation. Evidence of activated microglia and activated astrocytes has been found in the brains of both Parkinson's disease and Alzheimer's disease patients.[1] In addition, Cfh has been shown to be present in amyloid beta plaques in Alzheimer's disease.[2] Our laboratory has developed a mouse model of early AMD based on expressing variant Cfh molecules in mice.[3] The Cfh transgenic mice develop deposits under the retinal pigment epithelium, which resemble early changes seen on AMD. We believe these findings indicate that the variant Cfh molecules are less able to control chronic low grade inflammation at the tissue level.
Methods: Young (6m old) and aging (18m old) Cfh transgenic and control B6 mice were divided into groups and fed either a control diet or a high-fat diet for 5 months. Brains were collected after perfusion with 2% PFA/PBS and were post-fixed overnight in 4% PFA/PBS. Next, the brains were transferred to a 30% sucrose solution, weighed, and sectioned. Immunohistochemistry was then performed on 30 µm brain sections with antibodies specific for inflammatory, oxidative stress, and microglial markers. Stained images were visualized using a Leica fluorescence microscope with an objective lens of 10x. The microglia over the photographed field were counted and averaged in order to obtain a cells/field value for each mouse. Statistical analysis was then performed on the data.
Results: CfhTg brains weighed less than the corresponding B6 brains (0.447 vs. 0.482g; p=0.00024). Many of the tested antibodies, particularly those associated with oxidative stress, did not stain the sections, perhaps due to the fixation method. However, the anti-TREM2 and anti-Iba 1 antibodies stained well. There was no difference in the number of Iba-1+ microglia in the dentate gyrus of CfhTg vs. B6 mice (p=0.607). Younger mice seemed to have higher numbers of these cells compared to older mice (73.3 vs. 52.6 microglia/field; p=0.0352). In addition, the mice fed a high fat diet appeared to have less microglia per field compared to the mice fed a normal control diet (53.1 vs. 72.8 microglia/field; p=0.0469). TREM2 is considered to be a marker for microglial activation. Neither age (p=0.65), nor a high fat diet (p=0.435) appeared to affect the level of TREM2 expression. However, there was a trend towards higher numbers of TREM2+ cells in CfhTg mice compared to B6 mice (p=0.17), particularly in the old group of mice (p=0.12).
Conclusions: Reduced brain mass in CfhTg mice suggests increased CNS oxidative stress and tissue injury. There was no difference in the number of Iba-1+ microglial cells in CfhTg vs B6 mice. However, there was a trend towards increased microglial activation in Tg mice. More brains will be analyzed with alternative methods of tissue collection and additional antibodies to corroborate these findings.

Propionate increases Hyperpolarized H13CO3- Signal in Perfused Mouse Hearts

Colin Purmal
Mentors: Craig R. Malloy, MD, A. Dean Sherry, PhD, & Matthew E. Merritt, PhD

Background: As early as 2008, MR imaging of [1-^{13}C]pyruvate and its metabolites, including bicarbonate, in post-ischemic pig hearts was reported (1). Since the method does not use ionizing radiation, there is widespread interest in applications in other fields including oncology (2). In the heart, pyruvate is oxidized to acetyl-CoA and CO_2. Oxidation of hyperpolarized (HP) [1-^{13}C]pyruvate to HP [^{13}C]bicarbonate is reduced in injured myocardium, and the presence of preserved flux through pyruvate dehydrogenase (PDH) may identify viable myocardium (1). However, oxidation of alternative substrates normally present in the blood also reduces the appearance of HP [^{13}C]bicarbonate even in healthy myocardium (3). Propionate, a short-chain three-carbon fatty acid normally present in the blood, is known to activate PDH, and it is under study as a nutritional therapy for heart failure (4). The efficacy of propionate for restoring PDH flux in hearts supplied with high concentrations of glucose and fatty acids was studied using ^{13}C NMR isotopomer analysis paired with experiments using HP [1-^{13}C]pyruvate. ^{13}C NMR is a standard method for measuring fluxes in metabolic pathways.

Methods and Results: Hearts excised from fed C57/bl6 mice were perfused in Langendorff mode using a mixture of acetate (2 mM), glucose (8.25 mM), and with and without propionate (2 mM). O2 consumption was not changed for the two different perfusion conditions. Isotopomer analysis of extracts of the freeze-clamped hearts indicated that carboxylation of propionate was very active, as expected, and glucose oxidation was minimal. For HP experiments, the perfused heart was located inside a 10 mm cryogenically-cooled probe paired with a 14.1 Tesla nuclear magnetic resonance spectrometer. After addition of hyperpolarized pyruvate, NMR signals from lactate, alanine, bicarbonate, CO_2, aspartate, malate, acetyl-carnitine, and glutamate were detected in real time and in a highly reproducible manner. The presence of propionate increased appearance of HP [^{13}C]bicarbonate 37-fold. This is the first application of hyperpolarization with detection using a cryogenically-cooled probe.

Conclusion: In the presence of a high concentration of a competing substrate, propionate stimulates PDH flux in perfused mouse hearts as measured by the appearance of hyperpolarized [^{13}C]bicarbonate from metabolism of hyperpolarized [1-^{13}C]pyruvate.

References

1. Golman K, Petersson JS, Magnusson P, Johansson E, Akeson P, Chai CM, Hansson G, Månsson S. Cardiac metabolism measured noninvasively by hyperpolarized ^{13}C MRI. Magn Reson Med. 2008; 59: 1005-13. PMID: 18429038
2. Harrison CE, DeBerardinis RJ, Jindal AK, Yang C, Sherry AD, Malloy CR. Analysis of mitochondrial metabolism in cancer cells by combining hyperpolarization and isotopomer analysis. Proc Int Soc Magn Reson Med 2010;18:569.
3. Moreno KX, Sabelhaus SM, Merritt ME, Sherry AD, Malloy CR. Competition of Pyruvate with Physiological Substrates for Oxidation by the Heart: Implications for Studies with Hyperpolarized [1-^{13}C]Pyruvate. Am J Physiol Heart Circ Physiol. 2010; 298: H1556 - 64. PMID: 20207817
4. Lango R, Smoleski RT, Rogowski J, Siebert J, Wujtewicz M, S?omi?ska EM, Lysiak-Szyd?owska W, Yacoub MH. Propionyl-L-carnitine improves hemodynamics and metabolic markers of cardiac perfusion during coronary surgery in diabetic patients. Cardiovasc Drugs Ther. 2005; 19: 267-75. PMID: 16187006

Quality Assessment of Fiber Optic Pressure Sensors

Anna Rosenblatt
Mentors: Phillip D. Purdy, MD, & Kevin King, MD

Background: Since the functional features of an artery can correlate to the risk of cardiovascular events, intra-arterial pressures can be utilized as a tool to gain more information about the condition of a vessel or even downstream structural features in the vasculature. Pressure waveforms contain information regarding peak systolic and diastolic pressures, as well as the elasticity and possibly sites of reflection. Similarly, the pulse wave velocity can be indicative of the mechanical properties of the arterial system. Intravascular fiber optic pressure sensors are one tool that can be used to record continuous pressure readings.
Objective: In order to effectively maximize the capabilities of the RJC fiber optic pressure sensors, they must be tested to fully understand the magnitude of their capabilities. Specific tests were performed to analyze the behavior, precision, and accuracy in different scenarios.
Method: In vitro, four RJC fiber optic pressure sensors were immersed into known depths of water systematically. The pressures ranged from 0 mm H_2O to 500 mmH_2O. The pressure measurements included 6 measurements at low pressures (under 100 mmH_2O) and 1 measurement at 500 mmH_2O. Each pressure reading was approximately 10 seconds and the sensor recorded pressure measurements at a frequency of 1000 Hz. At each pressure reading, the variation and behavior of each individual sensor, the discrepancies between two sensors, as well as the accuracy compared to the theoretical pressure value were evaluated. In addition, the pressure receiver box and various methods of calibration were tested to ensure that there were not other factors causing a bias on the sensors' measurements.
Results: The sensors were found to have the capability of giving instantaneous pressure values with a precision of 0.03 mm Hg. The standard deviation of one pressure sensor at a constant pressure for 10 seconds was 0.15mmHg. The average difference between two sensors' pressure values that were calibrated simultaneously was 0.66 mmHg. Lastly, the accuracy of the sensors decreased at higher pressures. Specifically, at a pressure of 37 mmHg, the accuracy of the sensors was approximately 1.9%.
Conclusion: This data will be important for all future experiments and measurements that involve the RJC fiber optic pressure sensors. With a complete understanding of quantitatively how the sensors behave, it will be feasible to analyze results of future pressure measurements.

In vivo **Gene Expression Analysis of Brain Tumors in a Mouse Model of Glioblastoma**

Tyler Ellis Smith
Mentors: Tou Yia Vue, PhD, & Jane Johnson, PhD

Gliomas are the most common primary brain cancer, 90% of which are glioblastoma multiforme (GBM). GBMs are anaplastic, high grade (IV) tumors that have a poor prognosis and often kill patients within 14 months of diagnosis. Achaete-scute complex homolog 1 (Ascl1) is a basic-helix-loop-helix (bHLH) transcription factor necessary for the development of the central nervous system. Ascl1 is normally expressed in transit amplifying cells in the subgranular zone of the hippocampus and in the subventricular zone of the lateral ventricles, two areas associated with neurogenesis in the adult brain. In this study, using a mouse model of glioblastoma in which NF1 and p53 tumor suppressor genes were conditionally knocked-out (*NF1;p53*-CKO) in neural progenitors to reliably generate brain tumors, we examine the role of Ascl1 in glioma formation and/or progression. We show that Ascl1 is expressed in a subset of glioma tumor cells along with astrocyte (GFAP and NF1A) and oligodendrocyte (Olig2, PDGFRa, Sox10) lineage markers. Conditional deletion of *Ascl1* in the *NF1* and *p53* background (*Ascl1;NF1;p53*-CKO) reveals that although tumor formation persists in the absence of Ascl1, the survival rate of these mice significantly improves when compared to *NF1;p53*-CKO mice. Furthermore, the onset of symptoms in mice lacking *Ascl1* is delayed. Overall, these findings suggest that Ascl1 is a potential target to reduce tumor grade and mortality for patients with GBMs.

Effects of the Cox6a2 Protein on Mitochondrial Metabolism

Patrick Wedgeworth
Mentors: Beverly Rothermel, PhD, & Valentina Parra, PhD

Cox6a2 encodes a subunit of complex IV of the mitochondrial electron transport chain (ETC). Cox6a2 expression is specific to heart and skeletal muscle, whereas other tissues express a different isoform of this subunit, Cox6a1. Biochemical evidence suggests that electron transport through complexes containing Cox6a2 is more efficient than when only Cox6a1 is present. Cox6a2 KO mice are viable but display an elevation in whole body metabolism. To examine how loss of Cox6a2 impacts mitochondrial form and function in the heart, we used siRNA to deplete Cox6a2 from neonatal rat ventricular myocytes (NRVMs) in culture and transmission electron microscopy of the hearts from the Cox6a2 KO mice. Our results indicate that Cox6a2 levels increase in NRVMs in response to the hypertrophic agonist norepinephrine (NE). Depletion of Cox6a2 form NRVMz resulted in a reduction in the size of the individual mitochondria and a decrease in mitochondrial function, measured as oxygen consumption. In contrast, mitochondria in the hearts of the Cox6a2 KO mice were larger in area, more elongate, and appeared to have greater nugosity. We conclude that Cox6a2 impacts both mitochondrial morphology and function, however, further studies will be required to reconcile our *in vitro* and *in vivo* findings.

Contact Lens-Related Microbial Keratitis in a Novel Rabbit Model

Cynthia Wei
Mentors: Danielle M. Robertson, PhD, & Meifang Zhu

Background: Microbial keratitis (MK) is the most destructive complication associated with contact lens wear. *Pseudomonas aeruginosa* (PA) has been repeatedly identified as the primary causative agent in contact lens-related MK. Chronic hypoxia due to wear of low oxygen transmissible contact lenses has been shown to be a contributor to the pathobiology of infection. However, the annualized incidence of contact lens-related MK remains unchanged despite the widespread use of high oxygen transmissible silicone hydrogel lenses.
Objective: To establish a novel rabbit model of PA-mediated contact lens-related MK and characterize the time course and severity of infection following wear of high and non-oxygen transmissible contact lenses.
Methods: 12 female New Zealand white rabbits were used in these studies. All rabbits underwent a partial nictitating membranectomy to facilitate lens wear. Rabbit corneas were imaged at baseline, prior to lens wear, by *in vivo* confocal microscopy (IVCM). Rigid contact lenses were composed of polymethylmethacrylate (PMMA, non-oxygen transmissible) or Tisilfocon A (MZ, high oxygen transmissible). An inoculum of 10^8 CFU of an invasive corneal isolate of PA stably conjugated to GFP was delivered to the concave side of the lens and incubated overnight. To confirm PA adhesion to the different lens materials, additional contact lenses were prepared in parallel. Viable PA was removed by vortexing and plated for CFU analysis. Contact lenses were inserted onto the right eye and worn for a duration of 3 to 5 days. Following lens removal, corneas were graded, imaged by IVCM, and then removed for further analysis. Corneal tissue sections were stained with antibodies for myeloperoxidase to label infiltrated neutrophils and GFP to enhance visualization of PA, nuclei were counterstained with propidium iodide. Viable PA from the lens surface after wear and from ocular eye washes post infection were further assessed by standard colony counts.
Results: Ten out of 12 rabbits developed MK within 5 days of lens wear; 2 rabbits wearing PMMA lenses failed to infect within the 5 day period. In non-infected eyes, no PA was cultured from the worn lenses. In all cases of MK, rabbits wearing the high-oxygen transmissible MZ lens developed more severe infection. This was associated with greater adherence of PA to the lens surface prior to lens wear. Immunofluorescent staining of infected tissue confirmed the presence of GFP-PA and dense neutrophil infiltration.
Conclusion: This is the first rabbit model of contact lens-related MK. In this model, the fit of the rigid lens is similar to soft lens wear in the human eye and fails to provide adequate post lens tear exchange during blinking. Thus, increased PA adherence in the absence of adequate post lens tear exchange overrides the protective effects of oxygen on the corneal surface.

Leptin-mediated recovery of FGF21 expression in a fasted state mouse model

Tanner Wilson
Mentors: David Mangelsdorf, PhD, & Steven Kliewer, PhD

The fasted state protein hormone FGF21 has been shown in mice to stimulate adipocyte glucose uptake, increase energy expenditure, protect against diet-induced obesity, and lower blood glucose and triglycerides in diabetic models. Unpublished data from our lab suggests that while FGF21 is expressed in response to fasting and calorically restricted diets in females, it drops off after leptin has been depleted. Our objective was to replicate this in male mice and provide evidence that leptin is permissive to FGF21 expression in the liver.

First, we placed 20 mice on a 40% diet for 16 days, then delivered leptin or vehicle via osmotic mini-pump for 48 hours. No FGF21 was detectable in either group after 48 hours, yielding no definitive result.

Next, we fasted 14 mice for 48 hours with 6 fed controls, with each group divided into leptin and vehicle mini-pump treatment groups. In contradiction to our hypothesis, we observed higher FGF21 with vehicle than with leptin, corroborated by more FGF21 mRNA in the liver with vehicle. This paradox might be explained by the liver's attempt to make up for more energy being burned in other tissues due to leptin administration, a hypothesis supported by elevated G6Pc, IGFBP, and PGC1a mRNA in the liver under leptin conditions, as well as a faster decline in serum insulin and glucose with leptin than with vehicle.

We performed another fast, but with 10 WT and 11 liver-specific LepR KO mice, with no fed controls and no mini-pumps. This genetic model gave support to our original hypothesis, as the LepR KO mice had significantly lower levels of FGF21 than did WT mice, particularly at around 18 hours into the fast. This suggests that leptin is permissive to FGF21 expression. Elevated liver G6Pc in LepR KO mice suggested liver compensation for perceived fasting, though expression of BMP8b and UCP1 in brown adipose tissue did not differ, suggesting that the basal metabolic rate may not have differed significantly.

Finally, we attempted to combine the pharmacologic and genetic models by repeating the previous experiment with leptin and vehicle mini-pump insertion. We saw lower FGF21 with leptin, as in the other pharmacologic experiments, and the vehicle control group directly contradicted the previous experiment. Many confounding variables, such as the stress of surgery and older mice, require further analysis.

While the genetic model agrees with our original hypothesis, we have yet to confirm this with a pharmacologic model. It is likely that secondary metabolic effects of pharmacologic leptin administration may be masking the leptin-induced recovery of FGF21 expression, and recovery of expression may be less pronounced in males.

TABLE OF CONTENTS
Research Design and Methods

KEY
Ω Oral Presenter - UT Southwestern Medical Student Research Forum
† NIDDK Medical Student Research Trainee
£ R25 NHLBI Research Trainee
Û UT Summer Research Program Participant
D Doris Duke Fellow

The Impact of Portable Electronic Devices on Attending Rounding Behaviors of Inpatient Internal Medicine Teams at an Academic Medical Center

Cameron Locke
Mentors and Collaborators: James Wagner, MD, Blake Barker, MD, Brett Moran, MD, & Adina Suss

Introduction: The advancement of mobile technologies is changing the way medicine is practiced. Portable devices give health care professionals access to electronic resources and patient health records without restricting them to stationary computers. However, little exists in the literature on how these devices impact the rounding behavior of health care teams at academic medical centers. There is general concern that the EHR will compel caregivers to spend less time with their patients; there is significant evidence in a prior unpublished study to support this unintended consequence. In this study the authors sought to identify whether the availability of tablet computers to inpatient internal medicine teams would combine the best of both previous rounding behaviors.
Methods: Research was conducted over a period of 28 days, consisting of observation of internal medicine teams randomized into intervention, who were provided with tablet computers, and control groups. Two observers recorded behaviors on a standardized checklist, which included domains of patient care, EHR use, and distractions.
Results: 323 patient encounters were recorded in the context of eighteen health care teams, fourteen control (160 encounters) and four intervention (163 encounters). General characteristics of each arm of the study are summarized below:

Variable	Control	Intervention	p-value
Tablet Used (y/n)	18.13%	50.31%	< 0.0001
Tablet Use Count	0.29	1.18	< 0.0001
Total Tech Use Count	2.01	2.00	0.3637
Tablet Distraction Count	0	0.26	< 0.0001
Total Distraction Count	1.84	2.60	0.0045
% Rounds on Wards	34.38%	71.17%	< 0.0001
Time per Patient (minutes)	12.37	10.62	0.0118
Time at Bedside (minutes)	3.28	3.71	0.6358

Discussion: Tablet possession is associated with increased ward rounding with the same level of access to EHR as would be offered by room rounding, shorter time spent discussing each patient, but increased time spent at the patient's bedside. This constellation of findings may suggest increased efficiency. Intervention teams experienced more distractions than control teams, as is expected due to the increased amount of ward rounding. However, the tablets themselves contributed to the number of distractions. These results can shed light on the role that tablet computers will play as we enter the electronic age of medicine.

Tablet Integration in the Internal Medicine Rounding model

Adina Suss
Mentors and Collaborators: James Wagner, MD, Blake Barker, MD, Brett Moran, MD, & Cameron Locke

Introduction: With the HI TECH Act offering incentives to all hospitals to implement electronic health record systems (EHR) by 2015, hospitals are likely to begin integrating this new technology. Now is a unique time to study the effects of integration of EHR systems in hospitals. Building on a prior pilot project studying of patterns of EHR use dynamics during rounds in internal medicine at a large public hospital at an academic medical center, our study looks at how altering the mobility and ease of use of the EHR affects rounding dynamics in rounds in internal medicine. A prior study had documented two patterns of rounding: on the wards (where patient interaction and distraction rates were higher) and in rounding rooms (where use of EHR was higher). The purpose of this study was to attempt to increase rates of ward rounding while maintaining use of EHR.

Methods: Seventeen internal medicine teams were randomized to receive electronic tablets (intervention) or not and followed on days when they were not on call. Behaviors were recorded on a standardized checklist which included sections assessing patient care, EHR use, teaching, and distractions for each patient encounter.

Results: 323 encounters observed were analyzed comparing the checklist items between intervention and control encounters as well as between encounters in which patient presentations occurred in the rounding room versus those which occurred on the wards. Data analysis is summarized in the following table:

Variable	Control	Intervention	p-value
Visited Patient(y/n)	70.63%	75.46%	0.3274
Exchanged info w pt. (y/n)	65.40%	74.86%	0.0291
Attending examined pt. (y/n)	47.94%	56.98%	0.0532
Plan of Care Discussed w pt. (y/n)	60.95%	70.95	0.0255
Total Time Rounding on pt. (s)	742	637	0.0118
Time in Direct Contact w pt. (s)	197	222	0.6358
Patient Related Teaching Time (s)	141	100	0.12
Non-pt. Related Teaching (s)	260	408	0.9415
Technical Distraction Count	0.06	0.43	< 0.0001
Total Distraction Count	1.84	2.60	0.0045
% Rounds on Wards	34.38%	71.17%	<0.0001
# pts. /day/team	8.67	9.13	0.29
Team Size	6.48	6.54	0.52

Discussion: The percentage of teams rounding on the wards was significantly higher for the intervention encounters. In keeping with the pilot study, ward presentation was associated with less time spent per patient encounter, but higher rates of interaction with the patient, including activities such as exchanging information with the patient and discussing the plan of care. There were also significantly more distractions in the intervention teams. This may be partially explained by the finding that distractions occur more frequently on the wards, but there were also many more technology-based distractions in the intervention team. Contrary to our hypothesis, there was not a significant difference in time spent teaching or time spent in contact with the patient.

New technological approaches to clinical trial recruitment : The efficacy of the Electronic Medical Records (EMR) database in enrolling patients in the GRADE Study.

Colleen Yard
Mentor: Philip Raskin, MD

The plethora of data that Electronic Medical Records (EMR) systems provide on patients makes these databases a great potential source of participants for clinical trials. However, it is crucial to find an efficient way to search through all of the data so that researchers can recruit patients that fit a study's inclusion criteria. With the NIH GRADE (Glycemia Reduction Approaches in Diabetes) study as a prototype, I will determine if an EMR database can be considered an effective recruitment tool for GRADE and other clinical trials in the future. To investigate if the EMR database could be a useful recruitment tool, a preliminary search of the EMR was performed, restricting the patient population to people that fit two of the major GRADE criteria: patients diagnosed with Type II Diabetes Mellitus only in the past 5 years, who were only on one diabetes medication: Metformin. Additionally, physicians listed as each patient's primary care provider were first contacted. This is standard procedure. If the physician responded and granted consent, the patient was then contacted via phone or e-mail.

The sheer number of people obtained from the EMR database made it seem like a great source of study participants; however, there was only a 1.7% success rate of enrolling patients from the EMR database. There are several reasons why the EMR database was not as effective as initially expected. First, identifying patients through the database requires that the primary care physician be contacted first, which provides an extra barrier to communication. With only about a 50% response rate of the physicians, we could not contact 30% of the qualifying patient population, or 157/517. The biggest problem with the EMR database was that 58% of the patients did not fit the original criteria we used to perform the search (diagnosed in the past 5 years and on Metformin). This was because our database search mistakenly included patients who were on Metformin *and* other diabetes medications, which is a disqualifying factor for the study.

In order for an EMR database to be a more effective recruitment tool, more specific medical search criteria should be used to find the correct patient population. Researchers should ensure that the members of the identified patient population each have a PCP, so that the contacted physician is someone informed about the patient's medical history. These improvements will make an EMR database an incredibly effective and low cost way to find patients for any clinical trial.

Evaluation Tool for Post-operative Cardiovascular Surgery Handoffs

Shi (Sherrie) Yu
Mentor: Philip Greilich, MD

Background: The burden of human error has proven to be reduced extensively by improving the quality and decreasing the variability of transfer-of-care, i.e. “handoff”, interactions, particularly in post-operative cardiovascular cases. During such high-risk clinical situations, patients are especially vulnerable to adverse events through poor communication or unnecessary delays. It has been shown that use of standardized handoff checklists can streamline the process. Our goal was to develop a reliable evaluation tool that would assess adherence to such a checklist in an effort to improve the quality of care provided to patients.
Methods: Both the handoff checklist and the evaluation tool were developed through collaboration with experts in the field, who identified the most crucial aspects that needed to be included in any post-operative handoff. Two observers each received five hours of training with the investigator, including observation of two ideal handoff simulations and a practical training period of 7 cases. To assess inter-rater reliability of each of the 8 items on the evaluation tool, percentage agreement and un-weighted kappa coefficients were calculated. Average kappa and percent agreement were then calculated by averaging these measures across all eight items. Kappa scores above 0.75 were considered excellent reliability.
Results: After the initial seven training cases, seventeen more handoffs were observed, for a total of twenty-four paired observation from June to October 2013. During the post-training cases, the handoff checklist was used 71% of the time. Percent agreement for each item ranged from 81% to 100%, with an average of 89% agreement. Kappa scores ranged from 0.66 to 1.0, with an average of 0.77.
Conclusion: In this study, the handoff evaluation tool tested was shown to have excellent inter-rater reliability and thus could be used in future studies by observers with a similar level of training. The development of this tool is essential for determining the effectiveness of a range of potential interventions intended to increase the efficacy of the handoff process following cardiac surgery.

TABLE OF CONTENTS
Clinical Research and Case Reports

KEY

Ω Oral Presenter Research Forum
† NIDDK Medical Student Research Trainee
£ R25 NHLBI Research Trainee
Û UT Summer Research Program Participant
D Doris Duke Fellow

Impaired cholesterol efflux capacity may help explain development of early coronary artery disease in subjects with very high HDL-C

Anandita Agarwala
Mentor: Daniel J. Rader, MD, University of Pennsylvania

Plasma levels of high-density lipoprotein cholesterol (HDL-C) are strongly inversely associated with coronary artery disease (CAD), and high HDL-C is generally associated with apparent 'protection' from CAD. A minority of individuals with very high HDL-C levels also develops CAD, a paradoxical phenotype. We hypothesize that such individuals may have HDL with altered structure and/ or function, and compared these individuals (cases) to individuals with very high HDL-C without CAD (controls).

We identified 55 subjects with HDL-C above the 90^{th} percentile, early CAD, and no major risk factors for coronary disease. We selected 120 controls without CAD, each matched for race, gender, and HDL-C level. Controls were selected to be the same age or no more than 10 years older than the cases. Studies to assess HDL composition and size distribution, cholesterol efflux capacity, and lecithin-cholesterol acyltransferase (LCAT) activity in cases and controls were conducted.

Comparison of HDL particle characteristics between cases and controls demonstrated a significant reduction in HDL phospholipid composition between cases and controls (92 ± 37 mg/dl vs. 109 ± 43 mg/dL, p value 0.0095). The mean plasma total cholesterol efflux capacity was significantly reduced in subjects with elevated HDL-C and CAD as compared to controls (1.96 ± 0.39 % efflux/ 2hr/ 1% plasma vs. 2.11 ± 0.43 % efflux/ 2hr/ 1% plasma, p value 0.040). The reduction became even more significant when looking at mean ABCA1- selective cholesterol efflux between cases and controls 0.60 ± 0.24 % efflux/ 2hr/ 1% plasma vs. 0.71 ± 0.32 % efflux/ 2hr/ 1% plasma, p value 0.033). Furthermore, there was a significant reduction in mean efflux per HDL particle in cases as compared to controls (0.023 ± 0.005 % efflux/ 2hr/ 1% plasma vs. 0.025 ± 0.006 % efflux/ 2hr/ 1% plasma, p value 0.029). No significant difference was observed between cases and controls in HDL particle size or plasma LCAT activity.

Reduced cholesterol efflux capacity in cases with elevated HDL-C and CAD may explain the development of early coronary artery disease. This finding reinforces the belief that cholesterol efflux capacity may in fact be a better predictor of the risk of coronary disease then HDL-C levels alone. Furthermore, the reduction in HDL phospholipid in the cases may help account for impaired cholesterol efflux.

Concurrent use of amylase and lipase for suspected pancreatitis is costly and unnecessary

Abdulhadi Akhtar
Mentor: Deepak Agrawal, MD, & Ravindra Sarode, MD

Background: Amylase and lipase are the 2 main enzymes used to make a diagnosis of acute pancreatitis. Prior studies have shown lipase is at least as sensitive and more specific than serum amylase in the diagnosis of AP. Based on current practice guidelines, lipase alone is sufficient and preferred.
Aims:
1. Determine the frequency of concurrent ordering of amylase and lipase
2. Determine the incremental benefit of ordering amylase along with lipase
3. Determine the cost savings if amylase is not ordered along with lipase
Methods: Data on all serum amylase and lipase orders at St Paul Hospital from January 2010 to August 2013 was collected and analyzed. For patients with amylase but not lipase elevated above the diagnostic threshold (3 times the upper limit of normal), medical charts were reviewed to determine how many of these patients had acute pancreatitis (defined as typical pancreatitis pain and cross sectional imaging consistent with acute pancreatitis). Cost data and reimbursement rates were obtained directly from laboratory personnel and the Medicare website.
Results: There were 26,254 orders (in 13,198 patients) to measure pancreatic enzymes. In 16,665 (63%) of these orders (in 9,938 patients), both amylase and lipase were ordered concurrently. Of these patients for whom both tests were ordered, 482 patients (4.8%) had either amylase or lipase elevated above the diagnostic threshold, i.e. 3 times the upper limit of normal. 63 of these patients had elevated serum amylase but not lipase. Chart review confirmed none of these patients had acute pancreatitis. Three patients were kept NPO for 1-3 days prolonging their hospital stay and 12 patients received unnecessary CT scans to rule out pancreatitis. Reimbursements for a serum amylase assay range from $8.91 for Medicare to upwards of $10-20 for private insurers. In 2011, Medicare Part B alone spent $5.12 million on 563,936 orders for serum amylase assays. The cost of performing a serum amylase test for a typical laboratory is around $4-6.
Conclusions:
1. Concurrent ordering of amylase and lipase happens 63% of the time
2. Adding amylase to lipase offers no incremental benefit and even results in additional unnecessary tests and treatment
3. Eliminating the use of serum amylase in suspected cases of acute pancreatitis would save the hospital $35,000 annually in direct costs

Barriers faced by an international NGO in establishing a rural health clinic in Andhra Pradesh, India

Benjamin Ammon
Mentor: Roger Bedimo, MD

Background: There are many challenges facing international NGOs that establish rural health clinics in developing countries. We set out to explore the challenges faced during the roll-out of such a clinic in India.
Methods: Qualitative information about a single clinic, the Mediciti Govind Shanthi Binjrajka Rural Health Training Center, and about the village, Aliabad (40km outside Hyderabad, India), was gathered through non-participatory observation. Qualitative information about the goals of the clinic and the ongoing process toward full functionality was obtained through personal interviews with the founder/chief executive of the clinic, the medical officer, and the staff.
Results: The following challenges were observed: (1) Community engagement: Efforts were made by the NGO to assess village residents views and attitudes towards health and establish partnerships with community stakeholders, and to concurrently gather biometric data of relevant health parameters, which allows the clinic to obtain the population buy in, and to measure its success. The timeliness of these efforts were hampered by the fact that few villagers visit the clinic since it just opened, so it will take a long time for the study to get a substantial sample size. (2) Clinic staff development: A recent medical school graduate was hired to be the primary care provider at the clinic. Additional staff hired included a pharmacist, security guard, kitchen and cleaning staff, and two nurses. Assessment of competency and optimal training of this staff was done by the clinic's founder and other members of the NGO. These efforts were hampered by a seasonal festival that preoccupied the entire village. Also, differences in norms of work ethic and professionalism constituted a serious barrier in this area. (3) Clinic facilities and supplies: Unreliability of electricity in this remote setting required the procurement of an electrical generator. Finding one and technicians to install and service it was a major challenge. This forecasts a serious problem for the reliability of supply systems for renewable supplies and medications when the clinic is fully functional.
Discussion: A first-hand observation of the rollout of a rural clinic by an NGO in rural India allowed us to observe some foreseeable and unforeseen obstacles that could seriously hamper such an operation. Poor community engagement could lead to poor acceptability and even suspicion of the clinic's activities. Guaranteeing a stable, trained, and motivated personnel is equally critical. Finally, the functionality of the facility is challenged by unreliable supply system. The clinic is in its first year of operation and will be under continued observation so that these barriers and attempted solutions to them can be characterized further.

Cardiovascular Risk Factors Predict the Spatial Distribution of White Matter Hyperintensities

Soham Banerjee
Mentor: Ron Peshock, MD, Kevin King, MD, Roderick McColl, PhD, & Anthony Whittemore, MD, PhD

Purpose: Increased volume of brain white matter hyperintensities (WMH) seen on MRI is associated with cardiovascular risk factors; however, WMH have also been attributed to normal aging. Recent studies have suggested that WMH in some brain regions are more strongly associated with specific risk factors. The purpose of this study was to create a map of every individual brain voxel that was significantly associated with risk factors (hypertension, diabetes, hyper-cholesterolemia) as compared to those without each risk factor. The aim of the study is to create a predictive model, which uses the WMH distribution to determine the associated underlying risk factor.
Methods: The MRI brain images used for analysis were obtained from 2066 participants in the Dallas Heart Study, a population based study. Each MRI brain was transformed onto a standard template that adjusts for participant variation in brain volume and shape, using the FSL SIENAX software. The participant's WMH distributions were then generated from their MRIs using an automated algorithm. For each risk factor, the subjects were divided into a case group and a control group. Each voxel of WMH was compared between the two groups using a two tailed nonparametric permutation test. A map of every voxel significantly associated with each risk factor was created.
Results: Of the total of 431891 voxels that comprise the distribution of WMH over the entire population, 26064 voxels (6%) were significantly associated with hypertension only. These hypertensive-associated voxels were prevalent anterior to the frontal horns of the lateral ventricles. Similarly, 22527 voxels (5%) were associated with diabetes only with a prevalence near the longitudinal cerebral fissure as well as lateral to the posterior horns of the lateral ventricles. 8088 voxels (2%) were associated with hyper-cholesterolemia only and were abundant posterior to the posterior horns of the lateral ventricles. 331588 voxels (77%) were not associated with a risk factor.
Conclusions: For hypertension, diabetes, and hyper-cholesterolemia, certain voxels were significantly associated with a risk factor, and maps of these voxels were created. Knowing the WMH distribution significantly associated with each risk factor will improve the specificity for evaluating patients for risk factor associated white matter injury. Importantly, this approach makes no a priori assumptions which divide the brain into functional regions or vascular territories.

Minor variations in contouring organs at risk results in significant impact on 2cc doses

Jennifer Barclay
Mentors: Kevin Albuquerque, MD, Arnold Pompoš, PhD,
& Xuejun Gu, PhD

Background: Per GEC-ESTRO guidelines for cervix HDR brachytherapy, the dose to the 2cc region receiving the most radiation (D_{2cc}) is used to correlate with toxicity. This region is derived from the contour created by the physician and is therefore subject to potential human error if the contour does not exactly delineate the organ boundary.
Objective: In this study, we assessed the effect that contouring errors of a few millimeters had on D_{2cc} of the bladder.
Methods: Brachytherapy treatment planning CT scans from ten cervical cancer patients were obtained for a total of forty-three CTs. On each CT, the axial pixel size was approximately 1mm by 1mm, and the distance between axial slices was 2mm. Twenty-six scans had contrast in the bladder, and seventeen did not. Bladders were manually delineated by the treating radiation oncologist on Varian's Eclipse v10 Brachyvision TPS. To assess the effect of contouring error on D_{2cc} of the bladder, we symmetrically shrank and expanded the margins of the clinical bladder contours by 1, 2, and 3 mm; and D_{2cc} was calculated for each new contour from the dose volume histogram.
Results: There was a significant change in the 2cc dose when the contour margins were altered ($P<0.001$). When the bladder contours were shrunk, mean percent change in the 2cc dose was -21%, -16%, and -13% for 3, 2, and 1 mm changes, respectively. Mean percent change was 15%, 19%, and 27% for 1, 2, and 3 mm expansions, respectively. On the three CTs where the bladder was closest to the cervix, there was a greater than 40% increase in the 2cc dose when the contour was expanded by 3 mm.
Conclusion: Contouring errors on the scale of millimeters could result in large under- or over-estimation of D_{2cc} of the bladder. Therefore, it is important to use great care when drawing bladder contours for radiation treatment planning since a 3 mm variation in contour could result in a 40% variation in D_{2cc} of the bladder.

Masking enhances accuracy of bladder deformation in multi-fraction adaptive brachytherapy as a first step toward composite dose estimation

Jennifer Barclay
Mentors: Kevin Albuquerque, MD, Arnold Pompoš, PhD,
& Xuejun Gu, PhD

Background: GEC-ESTRO guidelines for cervix HDR brachytherapy advocate measurement of the minimum dose to the 2cc volume of organs at risk (OAR) receiving the highest amount of radiation and summation across multiple treatment fractions to give a worst-case-scenario cumulative dose estimate. If the OAR from different fractions could be accurately co-registered using deformation, then a more accurate composite dose could be obtained.
Objective: As a first step toward composite dose estimation, we sought to assess and improve the quality of bladder deformation using a technique called masking, which involves resetting the pixel values within a contour.
Methods: CT scans from nine cervical cancer patients with bladders contoured by radiation oncologists were obtained, and the urethra near the bladder was contoured using the catheter as a fixed reference point. Three copies of each CT were made: the first was unaltered, the second had the bladder masked, and the third had the bladder masked at one pixel value and the rest of the body masked at a different pixel value. Using VelocityAI 2.8.1, the bladder was deformed onto the target (Fraction 1) planning CT from subsequent planning CTs in an attempt to match up the tissue from different fractions. To assess the accuracy of the deformation, several indices were used: the percent error of the deformed bladder volume from the expected volume, the conformality index, the Hausdorff distance, and the distance between the centers of the deformed urethra and the target urethra.
Results: Deformation quality improved with masking. The standard deviation of the percent error was reduced from 18.1% with no masking to 4.3% with masking. Mean conformality increased from 0.83 with no masking, to 0.91 with the bladder masked, to 0.93 with body and bladder masked ($P<0.001$). The mean Hausdorff distance decreased from 13.8mm without masking, to 9.1mm with the bladder masked, to 5.7mm with body and bladder masked ($P<0.001$). The mean error in the urethra deformation increased from 4.3mm without masking, to 5.2mm with the bladder masked, to 6.6mm with body and bladder masked ($P=0.08$).
Conclusion: The accuracy of bladder deformation can be significantly improved by masking. With masking, the volume and location of the deformed bladder more closely approached that of the target bladder than without masking. Thus masking has the potential to improve the accuracy of dose deformation and composite dose calculation in adaptive brachytherapy.

Ethnic Differences in Fatty Acid Oxidation

Brian Benjamin
Mentor and Collaborators: Scott M. Grundy, MD, PhD,
Gloria Vega, PhD, Magdalene Szuszkiewicz Garcia, MD,
& Yasuyo Wada, PhD

Introduction: Triglyceride levels of African Americans are significantly lower than those of Caucasians. This discrepancy complicates the recognition and diagnosis of metabolic disease in African Americans and represents a paradox in the metabolic health of African Americans. Many reasons for this difference have been explored including increased lipoprotein lipase activity, decreased hepatic lipase activity, and increased suppression of adipocyte lipolysis. Another possible explanation for this triglyceride discrepancy that has been sparsely explored is a difference in fatty acid oxidation between the two groups. The hypothesis of the present study is that the discrepancy in triglycerides can be explained, at least in part, by more efficient beta oxidation of fatty acids in the African American population.
Methods: A pilot study was initiated to examine whether a difference in beta oxidation of fatty acids between the two groups exists by examining the ratio of downstream metabolites of beta oxidation (beta hydroxybutyrate; BHB) to upstream metabolites (nonesterified fatty acids; NEFA). Healthy lean African American and Caucasian males were given a fat bolus (200 mg/kg Schepp's dairy heavy cream) hourly over a ten hour time period (fat tolerance test). BHB, NEFA, and plasma triglycerides were measured throughout the test. The data were plotted against time and area under the curve (AUC) was calculated for each plot using the trapezoid rule. The ratio of BHB to NEFA total AUC was calculated and compared between groups. One volunteer from the Caucasian group was excluded from analysis as an outlier based on fasting BHB levels (Grubb's test $p<0.01$). Groups were compared using 2 sample t-tests.
Results: Preliminary results (n=9 African Americans, n=8 Caucasians) demonstrate a trend, as predicted, for the ratio of BHB AUC to NEFA AUC to be higher in African Americans compared to Caucasians ($p<0.05$). Additionally, the BHB AUC is significantly higher in African Americans ($p<0.05$), further supporting the study hypothesis.
Conclusions: Initial results suggest that healthy lean African American men may be more efficient oxidizers of fatty acids when compared to healthy lean Caucasian men. This difference could be a contributing factor to the triglyceride difference observed in African Americans and Caucasians. The study is still ongoing and further recruitment and analysis remains to be done.

A simplified risk score for predicting the incidence of major complications after complex abdominal-pelvic resections

Adam Bennett
Mentor: John Mansour, MD

Background: The POSSUM system is used to predict risk of complications following general surgical procedures. This 17-factor instrument has been challenging to apply to most surgical oncology patient populations. Our aim is to develop a simplified scoring system which was highly correlated with the incidence of major complications.
Methods: We queried a single-institution IRB-approved prospective database from a surgical oncology population from January 2008 to December 2012. We identified patients undergoing complex abdominal or pelvic resections and factors associated with the development of major (Clavien >= 3) complications. Factors not included in the POSSUM system were incorporated into a new scoring system based on univariate correlation with complication rates (Chi-square). A composite scoring system (POSSUM-SO) was compared to standard POSSUM predictions using ROC analysis. Optimal binning generated an ideal cut-off value associated with major complications.
Results: We identified 831 patients undergoing pancreatic (23%), hepatic (23%), colorectal (22%), esophagogastric (16%), retroperitoneal (4%), combined (3%), or other type (10%) of resection. Major complications occurred in 17% of patients. Two original POSSUM factors were included in the new POSSUM-SO model (cardiac history and EBL). Four factors improved correlation with complication rate: gender (female/male-1/3 points); BMI (underweight or morbidly obese/others-4/1 points); operation type (retroperitoneal/ pancreatic or rectal/others-4/2/1 points); and cancer (no cancer/cancer-1/2 points). ROC analysis generated a greater AUC for the simplified 6-factor system than standard 17-factor POSSUM (AUC: 0.658 vs 0.631, See Figure 1). A model including the 5 preoperative factors generated a similar AUC compared to the original POSSUM (AUC: 0.622 vs. 0.631). Patients with POSSUM-SO >= 12 had a higher risk of major complications (22% vs 9%, p-value < 0.001).
Conclusions: A simplified composite scoring system is more closely associated with short term surgical outcomes than the POSSUM index. Validation in a large, independent dataset is necessary before the system can be widely applied.

A Review of Interval Appendectomy

Rachel C. Brady
Mentor and Collaborators: Adam C. Alder, MD, Lorrie S. Burkhalter, & Rachel I. Renkes

Background: Acute appendicitis has traditionally been treated with immediate appendectomy. Initial nonoperative treatment with antibiotics and abscess drainage has gained wide acceptance when patients present with a perforated appendix associated with periappendiceal abscess or phlegmon. Following successful nonoperative treatment, an interval appendectomy (IA) is routinely recommended to eliminate the risk of recurrent appendicitis. Surgeons have questioned the benefit of appendectomy after successful nonoperative management of complicated appendicitis.

Methods: A retrospective review of children managed nonoperatively for complicated appendicitis between June 2009 and December 2012 at Children's Medical Center was performed. Patients were assessed for the development of recurrent symptoms of appendicitis. Demographic data, presenting symptoms, imaging, treatment, clinical course and outcome were analyzed to identify potential associations with recurrent symptoms.

Results: A consecutive series of 100 children treated nonoperatively out of 3491 patients (2.8%) diagnosed with appendicitis during the study period were included. Eighteen patients (18%) experienced recurrent appendicitis prior to scheduled IA within a median of 16.1 days from diagnosis (range 6.9 - 73.7d). Seven patients did not recur during the study period, nor did they undergo an appendectomy.

There were no significant associations between gender, age, obesity status, race, or ethnicity and recurrent appendicitis symptoms. Similarly, the presence of a fecalith or well-defined abscess on imaging was not predictive of recurrence.

While the length of stay during the initial diagnostic admission was comparable, the cumulative length of stay including readmissions and appendectomy was significantly different between recurrent and non-recurrent groups (R median 239d, range 103-400d; NR median 166d, range 23-758d; P=0.01)

Conclusions: None of the clinical and demographic factors analyzed are associated with a risk of recurrent appendicitis. There is, not surprisingly, significantly longer total hospitalization associated with recurrent appendicitis. Additional study investigating the risk factors of recurrent symptoms in children managed non-operatively for complicated appendicitis may help predict which patients will benefit from IA.

Are More Randomized Controlled Trials Warranted To Evaluate the Safety of Erythropoietin in Cardiac Surgical Patients?

Lasya Challa

Mentor and Collaborators: Philip Greilich, MD**,** Tally Goldfarb, MD, Jing Liu, BS, Russell Roberson, MD, Michael Wait, MD, James Burner, MD, & Kenni Landgraf, RN, BSN

Introduction Preoperative anemia is a silent epidemic in cardiac surgery. It is associated with a two-fold increase in postoperative morbidity and mortality and leads to erythrocyte transfusions in 80% of these patients. Studies supporting the use of erythrocyte stimulating agent (ESA) in cardiac surgery are currently considered inadequate. We conducted a review of the literature to determine: 1) gaps in our current understanding of safe and effective use of ESA in this high-risk patient population and 2) if a randomized clinical trial comparing ESA to current clinical practice is warranted.

Methods We reviewed 130 papers and selected 7 articles that met the criteria for use of ESA in the preoperative period in patients with and without anemia undergoing open heart surgery.

Results Erythropoietin administration was found to increase perioperative hemoglobin levels and reduce the incidence of allogenic blood transfusion (ABT). ESAs appear to be more effective than administration of oral or intravenous iron alone. There is no convincing evidence that ESAs increase the incidence of adverse outcomes, including thromboembolic events. However, many of these trials were underpowered to detect complications. A number of limitations in these studies were noted and include: 1) treatment duration that was insufficient to increase red blood cell mass enough to avoid more than 1U of red blood cells 2) sub-optimal dosing regimen given ESA's pharmacodynamic characteristics; 3) methods for insuring transfusion triggers and safety concerns outlined in the package insert were observed and 4) optimal use of iron to support effective erythropoiesis in anemic patients.

Conclusion A randomized controlled pilot study designed to treat anemic patients with ESA and intravenous iron for 1-4 weeks prior to cardiac surgery is needed. Compliance with surveillance strategies for adhering to transfusion triggers and withholding doses of ESA, when indicated, should be measured. Endpoints such as percent of patients receiving no ABT and a composite measure of adverse outcome should be collected to perform sample size calculations for a larger multi-center trial in the future. Patient surveys and a method to assess the economic impact of ESA in cardiac surgery should also be included. We believe preoperative use of ESAs hold great potential for reducing ABT and improving outcomes in anemic patient scheduled for elective cardiac surgery. A protocol reflective of these objectives has been approved by the IRB and the study has initiated patient enrollment.

The Evaluation of Robotic Assisted Laparoscopic Resection of Rectal Cancer

Akshar Chauhan
Mentor: Glen C. Balch, MD

The surgical management of rectal cancers is evolving rapidly to incorporate minimally invasive surgical techniques as the preferred option compared to open laparotomy. The technical advantage that robotic surgery provides is the ability to perform a fine dissection in a narrow surgical field. The theoretical implications of this advantage include fewer conversions to an open procedure, fewer complications, and improved oncologic outcomes.

As part of an IRB-approved ongoing prospective database, we collected clinical and pathologic information for all rectal cancer patients undergoing robotic assisted proctectomy between April 2010 and October 2012. We then focused on the assessment of perioperative and short-term outcomes for these patients. Using the database, we identified 28 (18 males and 10 females) patients who underwent robotic assisted laparoscopic low anterior resection (LAR) or abdominoperineal resection (APR). Twenty-two patients had a LAR and six underwent APR. Of those in the LAR group, three underwent anterior pelvic exenteration. Median patient age was 60 years (range 40 to 87). Seventy-five percent of patients presented with clinical stage III disease, and seventy-nine percent of patients received preoperative chemotherapy and/or radiation therapy. Median OR time was 454 minutes (7.5 hours, range: 4.5 to 16.2 hours), and median length of stay was 6.5 days (range 3 to 28 days). Median blood loss was 150 mL (range: 100 to 750 mL). Twenty-five percent of patients experienced a major complication (Clavien grade IIIA or higher). One patient died of a pulmonary embolism at home 3 weeks postoperatively. All patients underwent a margin-negative resection of disease in the pelvis. Two procedures were converted to open laparotomy (7% conversion rate).

Robotic assisted laparoscopic proctectomy appears to be safe and feasible. The zero margin positive rate in this series is superior to the published rates of 1.2 to 27% in patients undergoing laparoscopic or open procedures. It remains to be seen whether the robotic assisted technique is superior to the conventional laparoscopic technique. Most likely, it is equivalent in rectal surgery of average complexity, and it provides yet another minimally invasive tool that may be preferable in more complicated rectal surgery. Further prospective clinical trials involving colorectal surgery patients are warranted to verify whether the benefits of this approach are clearly superior to that of open and laparoscopic-assisted rectal surgery and to elucidate the boundaries of patient selection and safety with this technique.

Is it safe to combine excisional procedures with liposuction in body contouring surgery?

Mo Chen
Mentor: Krista Hardy, BS, Kathryn Davis, PhD, Jingsheng Yan, PhD, Anoop Matthew, MPH, Jerzy Lysikowski, PhD, Gary Reed, MD, & Jeffrey M. Kenkel, MD, FACS

Background: Excisional procedures, including abdominoplasty, brachioplasty, thighplasty, and body lift are often combined with liposuction with the goals of minimizing cost and hospital stays while maximizing aesthetic results. The aim of this study is to evaluate postoperative complications in patients undergoing excisional surgery with or without liposuction. Risk factors for this type of combined body contouring surgery are also evaluated.
Methods: The electronic medical records of 413 patients undergoing body contouring surgery at UT Southwestern Medical Center were retrospectively reviewed. Three groups of patients were compared: liposuction only, excision only, and combined liposuction and excision surgeries. Some patients also received additional intra-abdominal, gynecologic, and breast procedures. Patient variables analyzed included age; body mass index (BMI); American Society of Anesthesiologists risk score (ASA score); Caprini score; operative time; co-morbidities (diabetes, hypertension, cardiovascular diseases, pulmonary diseases, and renal diseases); smoking status; prophylactic antibody use, and recent major surgery.
Results: No statistically significant differences in complication rates were found when comparing combined excision and liposuction surgeries to excision alone. Operative time was a significant risk factor for developing wound problems and overall complications. There was a trend for males and patients with higher BMI, older age (>45), and co-morbidities toward developing postoperative complications.
Conclusions: Combining excisional body contouring procedures with liposuction does not increase overall complication rates in this cohort of patients. Plastic surgeons should balance the number of combined procedures with estimated operative time in order to maximize patient safety.

Factors Associated with Contraceptive Choice in Chinese Women

CeCe Cheng
Mentor: Jeanne Sheffield, MD

Objective: The purpose of this study was to determine contraceptive choices in women in China and to assess the factors associated with their contraceptive choice.
Study Design: A prospective cohort trial from June 2013 to August 2013 was performed at Sun Yat-sen University in Guangzhou, China. Women were approached during either an inpatient or outpatient visit with an Obstetrics/Gynecology practitioner and asked to complete a survey in their native language (Mandarin Chinese). The survey included demographic and social data, socioeconomic status (SES), obstetric history, and contraceptive choice. Data were analyzed using Student's T-test and Chi-square test for continuous and categorical data, respectively. A $P<0.05$ was considered statistically significant.
Results: During the study period, a total of 128 women completed the survey. The mean age was 32.8 ± 9.6 years: 83.6% of the women were married. The majority of women were of Han ethnicity (95.9%), followed by Zhuang (1.6%), Dou (0.8%), Miao (0.8%), and Malian (0.8%) ethnic groups. 64.8% of the cohort were not religious, while 11.7% were Buddhists, 2.3% Christian, and 0.8% Muslim. Most women were non-smokers (75.8%). Women were grouped by socioeconomic class (SEC), with the majority of women having a monthly income between 2000 and 10,000 RMB each month. 9.4% were nulliparous, 50% had 1 pregnancy, and 39% had 2 or more pregnancies. A total of 65 elective abortions (EABs) were performed in 38 women. Contraception included condoms (60.3%), IUD (13.5%), OCP (1.6%), Plan B (3.2%), permanent sterilization (2.4%), abstinence (0.8%), NFP (0.8%) and none (17.5%). Most women chose to use condoms despite the one child policy in China. Women <21 and >35 years of age used some form of contraception compared with women in the 21-35 year old range who were more likely to not use contraception. Interestingly, women in the high (>10,000) SEC were more likely to not use any contraception compared with women in the low (<2,000) SEC ($P = 0.04$). When gravidity was compared to SEC, there was a clear distinction showing that women in the SEC extremes have more children (3 or more) than the middle SEC ($P=0.008$). Elective abortions were not associated with SEC ($P<0.3$).
Conclusion: Contraceptive use in China was clearly influenced by many factors, including age and SES. The high rate of condom use compared to longer, more sustainable methods of contraception and the high EAB rate highlight a need for better contraception education in China.

Cultural competency must be taken into consideration when implementing self-help groups, as alcoholism is an overlooked global issue.

Divya Kiran Chhabra
Mentor: Craig Katz, MD

Introduction: In 2004, there were 4.1 deaths from alcohol use disorders per 100,000 people in Saint Vincent and the Grenadines (SVG)- one of the highest rates in the world. There are no medical resources currently for patients with alcoholism. Thus, work was done to pilot self-help groups modeled on Alcoholic Anonymous (AA), in SVG in summer 2012. A follow-up team returned to SVG in summer 2013 to assess the success of those groups and to pilot more. This study looks at the piloted self-help groups in SVG and what specific factors were associated with their success.
Methods: Research entailed several focus groups in the communities including Barrouallie, Kingstown, Georgetown, Trumaca, Bequai, and Campden Park regarding community issues with alcoholism and local views about starting self-help groups. A convenience sample of local Kingstown inhabitants was also surveyed about their community's experience with alcohol and their knowledge of its effects. Finally, current and former self-help group members in Barrouallie, the only surviving group from 2012, were surveyed on their experiences with the group. Ultimately, five new self-help groups were piloted by the end of the 2013 summer.
Discussion: The only remaining self-help group after the 2012 pilot program was Barrouallie. This group had 9 participants attending since August 2013. Eight of them have stopped drinking completely, and the 9th member has been sober since July 2013. Eight members agreed that the group was "very helpful," and five of them joined the group through word of mouth. One participant noticed the "seriousness" of the group he saw at the park, so he decided to join. This openness was not apparent in the failed groups from 2012. When asked what could make their group more successful, about 2/3 of the subjects stated "encouraging more people to join the group." Of the former participants, 100% of them answered "yes" to whether the group helped them overcome their drinking problem. The former subjects stopped coming due to pregnancy or schedule conflicts. The current participants felt that forgoing anonymity would help to disseminate the group elsewhere in SVG. The group was then aired on local television to spread their message. Lastly, in the convenience sample from Kingstown, 75% of subjects claimed alcoholism is "not a disease," and the majority weren't aware of its specific organ effects.
Conclusion: Unlike the AA model, the group that succeeded in SVG from the summer 2012 explicitly shed its anonymity. This philosophy was used for establishing five new self-help groups whose viability is currently being assessed. The lack of alcohol education was apparent when the majority of locals surveyed didn't realize that it is a disease or how it affects the organs. The team initiated an educational campaign at camps and churches to promote prevention. The open culture of SVG allowed a unique group design to attain success. Cultural competency must be taken into consideration when implementing self-help groups, as alcoholism is an overlooked global issue.

Diagnostic Yield of Cervical Radiographs in Infants with Deformational Plagiocephaly

Min-Jeong Cho
Mentor: Alex Kane, MD

Background/Purpose: When evaluating infants with a diagnosis of deformational plagiocephaly, some providers routinely obtain infant cervical radiographs in order to rule out concomitant cervical bony anomalies. The purpose of this study was to determine the diagnostic yield of cervical radiographs in demonstrating cervical anomalies in a population of infants referred to a tertiary craniofacial center with deformational plagiocephaly (DF).
Methods/Description: After obtaining IRB approval, all patients with diagnosis of DP who underwent cervical radiographs between the years of 2011 to 2012 were reviewed. Cervical radiographic findings as determined by radiologists report, perinatal data, and physical exam findings were recorded, and descriptive statistics were generated.
Results: Electronic medical records of 462 patients with diagnosis of DP were reviewed. Abnormal findings were recorded in 6.49% of cervical radiograph reports (n+30/462). Of those with abnormal findings, 50% (n=15/30) demonstrated osseous abnormalities including: fracture (n=2), bony fusion (n=6), asymmetric clavicle (n=1), hypoplastic posterior elements of vertebrae (n=2), psuedosubluxation (n=1), increased vertebral distance (n=1), and rudimentary ribs (n=2). Those with non-osseous abnormalities (n=15/30) included head tilt (n=1), abnormal curvature (n=10), and hypertrophic tonsils (n=3). The other 97% of the study population were without osseous abnormalities.
Conclusions: There is a fairly low diagnostic year in ordering cervical radiographs in patients with deformational plagiocephaly. Considering the radiation exposure and cost associated with the practice of ordering routine cervical radiographs in all patients presenting with this DP, an inspection of its inclusion as a necessary step in the diagnosis algorithm is warranted.

Obesity & OSA in Children

Jonathan Choi
Mentor: Ron Mitchell, MD, & Travis Lewis, MD

Introduction: Childhood obesity is an increasingly health problem in the United States. It has been estimated that approximately 33% of American children are obese. Obesity puts one at risk of developing potentially serious health problems including obstructive sleep apnea (OSA). One of the most common treatments for OSA is Tonsillectomy and Adenoidectomy (T&A). However, there have been recent concerns that T&A leads to weight gain and negatively impacts obesity.
Objective: To investigate weight gain in children who have undergone T&A and compare them to a control population.
Methods: 150 children who have undergone T&A were followed for 18 months and compared to 150 controls seen for well child checks. Demographic information including height, weight and BMI was collected from EPIC Electronic Medical Records.
Results: All children had weight gain and increase in BMI over the study period. T&A resulted in greater weight gain and increase in BMI z-score that was not statistically significant. The difference was more pronounced in African American and Hispanic children. Age, sex and baseline weight had no impact on the results.
Discussion/Conclusion: T&A leads to weight gain in children that is not greater than that seen in the general population. African American and Hispanic children gained the most amount of weight in both groups during the 18 months they were followed. T&A should continue to be the first line treatment in children with OSA regardless of their baseline weight. Efforts should be directed at weight reduction in children to improve a variety of healthcare measures including OSA.

Disease Exacerbation of Multiple Sclerosis is Characterized by Loss of Terminally Differentiated Autoregulatory CD8+ T cells

Khrishen Cunnusamy
Mentors and Collaborators: Ethan J. Baughman, Jorge Franco, Sterling B. Ortega, Sushmita Sinha, Parul Chaudhary, Benjamin M. Greenberg, Elliot M. Frohman, & Nitin J. Karandikar

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system (CNS) that afflicts more than 400,000 people in the US. Although the etiology of the disease is unknown, pathogenic T cells are thought to underlie MS immune pathology. In contrast to the current paradigm, we recently showed that MS patients harbor CNS-specific CD8+ T regulatory cells (CD8 Tregs) that are deficient during disease relapse. In the current study, we demonstrate that the neuroantigen-specific CD8 Tregs were cytolytic and eliminated pathogenic CD4+ T cells. Sorting of CD8+ T cells using an array of surface cellular markers revealed that the CD8 Tregs were terminally differentiated (CD27-, CD45RO-). The CD8 Treg-mediated suppression was perforin, granzyme B, and interferon-γ-dependent. Interestingly, we found that MS patients with acute disease exacerbation displayed a significant loss (averaging 25%) in the terminally differentiated CD8+ T cells, with a concurrent loss in perforin and granzyme B expression. In order to restore the regulatory potential of impaired CD8 Tregs during exacerbation, we pre-treated exacerbation-derived bulk CD8+ T cells with the cytokine IL-12 and significantly increased the suppressive capability of the cells by ~48% through upregulation of granzyme B and perforin. Our studies uncover the immune suppressive mechanism of neuroantigen-specific CD8 Tregs, and may contribute to the design of clinically relevant immune therapies for MS patients.

Caregiving Understanding Assessment at the Comprehensive Epilepsy Center at Children's Medical Center

Shanup Dalal
Mentor and Collaborator: Susan Arnold, MD, & Christine Tran

Rationale: Electronic surveys are given to caregivers following a first visit to the Comprehensive Epilepsy Center at Children's Medical Center Dallas. The surveys assess caregivers' understanding of the diagnosis, impression on quality of care and recollection of specific education provided. Surveys were reviewed to determine if responses differed due to timing of survey and primary caregiver language.
Methods: From 2011 to 2013, 671 electronic surveys (Long Range Systems) were given to English and Spanish speaking caregivers of children seen at UT Southwestern Medical Center/Children's Medical Center, Dallas for evaluation of a first seizure or epilepsy. Caregivers were asked to choose preferred language; 118 Spanish and 553 English surveys were completed. 453 surveys were given at the end of the first visit, 218 surveys were given at the beginning of the second visit. 14 questions asked caregivers to rate care provided, explanation of diagnosis, medications prescribed, and seizure safety precautions. Information from both data sets were compared. A 4-point Likert Scale was used.
Results: 78% of caregivers in the first visit vs. 46% in the second visit thought the diagnosis was explained very well ($p \leq 0.01$). 80% in the first visit vs. 48% in the second visit believed they were involved in the decision making for their child's care at the most favorable level ($p \leq 0.01$). Overall care was given a more favorable rating at the first visit vs. the second visit (78% vs. 55%, $p \leq 0.01$). However, favorable ratings were similar between the two visits when the "good" and "very good" ratings were combined. Patient recollection of specific counseling measures was higher when measured at the first visit, including information about water safety ($p \leq 0.01$) and medication instructions ($p \leq 0.01$). Language affected favorable ratings. Although Spanish interpreters were available, 79% of Spanish speakers vs. 89% of English speakers stated the diagnosis was explained very well ($p \leq 0.01$). Spanish speakers felt less involved in decision making for their child's care (45% vs. 75%). Language related differences were less evident when asking about specific education provided.
Conclusion: For both general and specific questions, caregivers had more favorable impressions when asked at the first visit vs. the second visit. Spanish speakers tended to give fewer most favorable ratings for general questions vs. English speakers, but both rated specific information equally. Our findings suggest specific counseling measures about disease, medications, and safety should be reviewed at the second visit because patients may not recall previous information.

Intravenous to Oral Antibiotic Switch Therapy In South African Hospital

Kelly Davis
Mentors: Marc Mendelson, MD, PhD, & Tom Boyles, MD

Background and Objective: Switching from intravenous to oral antibiotic treatment can reduce the risk of site infections, shorten hospital stays and decrease cost of care. The objective of this study was to evaluate the current intravenous to oral antibiotic switch therapy at a large teaching hospital in South Africa that has recently implemented an antibiotic stewardship program and to highlight which patients could benefit from early switch therapy.
Methods: During a 1 month study, all patients receiving intravenous antibiotic therapy in the internal medicine wards were followed throughout the course of their intravenous therapy and were evaluated on their eligibility to switch to oral antibiotic therapy based on a list of criteria. Criteria included no indications for long- term IV use, availability of an oral alternative, patient is able to take oral medications and lacks indications of malabsorption, temperature less than 38°C for 24 hours and patient is improving or remaining stable. Data collected included the patient's duration of I.V. antibiotics, antibiotic regimen and dosage, indications for antibiotic therapy, reasoning for ending I.V. regimen and blood culture results.
Results: 55% (71/129) of patients receiving I.V. antibiotic therapy met all the criteria for switching to oral antibiotics and only 5.6% (4/71) of those were switched once the patient became eligible. Patients eligible for switching were continued on IV therapy for a mean of 3.1 (+/-1.6) days (median=3, IQR= 2-4 days) after meeting the criteria and the most common indications for therapy within this group were community-acquired pneumonia (58.2%), sepsis of unknown cause (13.4%) and urinary tract infection (11.9%). The most common IV antibiotics used in this group were Ceftriaxone 1g (77.6%) and Augmentin 1.2g (13.4%). 21.1% (15/71) of the patients meeting the criteria for switching did not have a blood culture sample taken prior to initiation of therapy.
Conclusions: The study highlighted the need for increased education on when to switch patients to oral antibiotics and highlighted problem areas such as patients being started on antibiotics without blood cultures being taken and continued I.V. therapy when patients are transferred from the emergency department.

TB Meningitis in an HIV-endemic Setting

Tianyi Du
Mentor: Kathleen Bateman, UCT Neurology

Introduction: Tuberculous meningitis (TBM) is a clinical challenge because early treatment is essential yet early diagnosis is difficult. Furthermore, TBM is often associated with HIV co-infection. This diagnostic study had three main objectives: **1)** To test the performance of existing diagnostic rules in an HIV-endemic setting; **2)** To determine which admissions variables are most predictive of TBM; **3)** To compare the clinical presentation of TBM in HIV-positive vs. HIV-negative patients.
Methods: This prospective, observational cohort consists of 96 patients from Tygerberg Hospital in Stellenbosch, South Africa. Criteria for entry were age > 15 years, clinical features of meningitis, and an abnormal lumbar puncture (high CSF protein or CSF pleocytosis). Data include the standard clinical and laboratory values: age, gender, duration of symptoms, neurological exam findings, CSF values, blood, microscopy, culture, imaging, etc. **1)** Two diagnostic algorithms described by Thwaites (*Lancet*, 2002) are tested: LRM (logistic regression) and CART (classification tree). We determine each patient's TBM status according to Thwaites' criteria, and then calculate the sensitivities and specificities of LRM and CART. **2)** Distributions are compared between Definite TBM and Not TBM groups, first in HIV-positive and then in HIV-negative patients, using the appropriate tests for continuous and categorical variables. **3)** The same methods are used to compare distributions between HIV-positive and HIV-negative patients with Definite TBM.
Results: In HIV-negative patients, LRM had a sensitivity of 100% and a specificity of 37.5%, while CART had a sensitivity of 91% and a specificity of 50%. In HIV-positive patients, this fell to sensitivity = 100%, specificity = 12.5% for LRM, and sensitivity = 94%, specificity = 12.5% for CART. In HIV-negative patients, factors including CSF white cell count, WBC count, blood sodium, age, duration of symptoms, and presence of systemic symptoms were statistically significant ($p < 0.05$). In HIV-positive patients, only two variables were statistically significant: CSF glucose and positive chest x-ray. In patients with Definite TBM, clinical presentation was generally similar, regardless of HIV status- with the exceptions of age and WBC count.
Conclusion: The data suggest that in HIV-positive patients, there is considerable overlap in presentation between TBM and other forms of meningitis, making a challenging diagnostic problem even harder. Current algorithms are in urgent need of revision, especially in HIV-positive patients.

Assessing Complications of Epiphysiodesis for Leg Length Discrepancy

Samuel Dunn and Tyler Terrill
Mentors: John Birch, MD, & Marina Makarov, MD

Introduction: Leg length discrepancy in children and adolescents is a serious orthopedic problem that can cause leg and back problems due to abnormal gait. This condition may be congenital or caused by disease or trauma. One method to correct leg length discrepancies in children is to perform an epiphysiodesis. This surgical procedure removes one or more growth plates from the femur, tibia, or fibula. This operation slows down the growth of the long leg to allow the shorter leg to catch up, or at least prevent the discrepancy from increasing. As there has been no large study of epiphysiodesis patients in the literature, the rates for surgical complications and errors associated with this surgery are not well known. These complications may include infections, nerve damage, and incomplete epiphysiodesis, which often results in an angular deformity. Because of the lack of understanding for rate of complications and characteristics associated with these, we studied a large patient population to gain insight into these aspects of the procedure.
Methods: The patient population at Texas Scottish Rite Hospital for Children undergoing epiphysiodesis for the treatment of leg length discrepancy from 1980 to 2008 was examined by a retrospective review of both charts and radiographs, with a total of 755 patients included in the study. The information recorded in the study included the extent of leg length discrepancy, angular measurements of the joints, method of epiphysiodesis, postoperative development of angular deformities, underlying etiology, length correction prediction, and other clinical features.
Results: Of the 755 patients examined, 38 had surgical complications, (5%). Of these patients, 27 had incomplete epiphysiodesis, 6 had neurological problems, 3 had overcorrection of the leg length discrepancy, and 2 had other complications not specific to this procedure. Patients incurring complications had statistically significant risk factors that include greater leg length discrepancies at the time of epiphysiodesis, congenital defects instead of acquired ones, and younger age. There were also trends towards open curettage method, epiphysiodesis involving the femoral growth plate, and male gender as risk factors, though these did not achieve statistical significance.
Discussion: It is important that surgeons understand which populations of patients are at greater risk for complications during this procedure, so that extra caution may be taken to prevent harm. Also, parents should be aware that there is a 5% risk of surgical complication, so that they may be fully informed before committing to the procedure.

A Prospective Study Comparing Vancomycin and Clindamycin in the Treatment Of Soft Tissue Infections in An ED Observation Unit

Nick Faulconer & David Pacheco
Mentor: Lynn Roppolo, MD

Introduction: Many patients who present to the emergency department (ED) with soft tissue infections (cellulitis) are thought to be due to a resistant strain of *Staphylococcus aureus* known as "community acquired MRSA", and is only responsive to a few antibiotics such as vancomycin and clindamycin. There has been growing resistance to the commonly used clindamycin for patients resulting in more clinicians choosing vancomycin to treat these infections. However, it is not known whether one of these treatments is more effective in treating these infections in patients admitted to ED observation units where the patients typically receive more than one dose of an IV antibiotic. For this reason, our study sought to evaluate characteristics of patients receiving vancomycin over clindamycin and to compare the effectiveness of each.

Methods: Patients admitted to the Parkland Observation Unit from the ED with a soft tissue infection thought to be due to MRSA and were recruited and consented if they were given vancomycin or clindamycin at the discretion of the ED physicians. The largest diameter of the infected area was measured. Pertinent clinical information and antibiotics given were recorded. Follow-up phone calls were made 1 to 2 weeks after discharge to determine if the patient's infection had resolved.

Results: A total of 35 patients were enrolled over a 16-week period. An additional 15 patients were consented but were lost to phone follow-up and were not enrolled. The average age was 45 years (range 18 to 73), 55% were females. 74.3% (n=26) received clindamycin, 25.7% (n=9) received vancomycin. 22% (2/9) of patients receiving vancomycin had at least one prior skin infection while only 8% (2/26) of patients receiving clindamycin had a prior skin infection. 66% (6/9) of patients with areas of cellulitis > 10cm received vancomycin versus 38% (10/26) who received clindamycin. 55% of patients who received vancomycin were diabetic versus 27% (7/26) of patients who received clindamycin. 44% (4/9) of patients who received vancomycin were back to their baseline versus 65% (17/26) who received clindamycin.

Conclusion: This pilot investigation did demonstrate that clinicians are reserving vancomycin for higher risk patients such as those who have diabetes, prior skin infections or larger areas of cellulitis. However, a larger percentage of patients who received clindamycin were at their baseline at follow-up. One possibility could be that the vancomycin patients were transitioned to a much less effective oral antibiotic on discharge and that patients who are at higher risk and are given vancomycin, should be not be admitted to ED observation units.

Interventions to increase colorectal cancer screening among underserved populations: A systemic review

Zhou Geng
Mentor: Samir Gupta, MD

Background: Colorectal Cancer (CRC) screening saves lives, but screening rates remain low among the underserved. We conducted a systematic review of studies that tested interventions for increasing screening among the underserved.
Methods: We searched PubMed for studies published 1/1979-3/2013 and included English-language, randomized controlled trials of interventions for increasing screening among underserved populations that reported on our primary outcome of interest: screening participation. The underserved were defined as any group with screening rates lower than the national average, including individuals who were uninsured, minorities, immigrants, poor, low literacy, and/or living in rural or inner-city areas. For each study we categorized whether interventions used primarily an outreach vs. inreach approach. We denied outreach as interventions that were initiated outside the context of a clinic visit, in contrast to inreach, as interventions that were initiated by a clinic visit.
Results: We included 47 studies, of which 26 were outreach and 21 were inreach studies. Among outreach studies, 12 evaluated community-outreach interventions, such as use of lay health educators to educate churchgoers; 14 tested safety-net facilityoutreach, such as offering fecal occult blood test for screening. Among inreach studies, 16 tested patient-level interventions, such as in-clinic patient education; and 5 tested provider/system-level interventions, such as offering providers feedback on patient panel screening rates. Of 26 outreach studies, 69% reported interventions were effective, including 50% for community outreach, and 86% for safety-net facility-outreach; of 21 inreach studies, 71% reported increased screening rates, including 69% of patient-level interventions, and 80% of provider/system-level interventions. Range of intervention effectiveness over control arms varied markedly: 5% to 66% for outreach, and 8% to 42% for inreach interventions. Among outreach studies, community outreach- delivered, culturally-tailored, language-concordant education interventions appeared to be most effective. Among inreach studies, language-concordant in-clinic patient education showed particular promise.
Conclusions: A number of outreach and inreach interventions have been proven effective for increasing screening among underserved populations. Culturally tailored, language concordant interventions including patient education appeared particularly effective. Future work should focus on comparing intervention strategies.

A Longitudinal Study of the Impact of Morphea on Quality of Life Over Time

Simer Grewal
Mentor: Heidi Jacobe, MD

Background: Morphea is an inflammatory disorder that has subsequent clinical manifestations of sclerosis and atrophy of the dermis and underlying tissue. Resulting cosmetic disfigurement or functional impairments are likely to persist even after the transition to inactive disease. The impact of Morphea on a patient's self-reported health-related quality of life (HRQOL) is not well described in medical literature.
Objective: To determine the impact of specific clinical, treatment, and demographic variables on self-reported QoL over time of the Morphea in adults and children (MAC) cohort. As a secondary objective, to correlate physician measures to patient reported QoL measures in order to determine which aspects of morphea are important to patients that might not be addressed in physician based outcomes.
Methods: Adult patients of the MAC cohort with ≥ 2 visits with a recorded HRQOL measure were studied. Self-reported HRQOL was examined via three previously validated questionnaires. Each included patient had at least 2 Dermatology Life Quality Indexes (DLQI). In addition, the Skindex-29+3 with an added morphea specific subscale and the Short Form 36 were included when available. In order to capture physician assessment of disease, Physician Global Assessment of disease (PGA), *Modified Rodnan Skin Score* (*MRSS*) and Localized Scleroderma Skin Severity Index (LOSSI) with its damage correlate LOSDI were employed.
Results: A total of 110 adult patients with 307 visits were included in these analyses. The QoL for patients with morphea is shown to be worse than the general population, with mean scores below 50 for SF-36 PCS and MCS scores. Though there was a marked decrease in activity, as measured by a 68 percent change in both PGA-A and LOSSI, QoL measures only had slight improvement with an 11.34 percent change over the same course of time. The damage measures (PGA-D, LOSDI) had an average 6.66 percent improvement.
Limitations: All patients were seen at one referral center, which resulted in a skew towards more severe forms of morphea. The sample size, though larger than anything to date, limits complexity of statistical analysis.
Conclusion: A decrease in disease severity does not mean an improvement in QoL. Lesions often don't disappear even as they transition to inactivity but rather leave frequent permanent sequalae. This indicates a need for further studies examining treatment of residual cosmetic and functional sequalae.

Sterilization and re-use of single use medical devices in India as a safe and acceptable method of cost reduction

Carolina Gutierrez
Mentor: Hari Raja, MD

Background: The sterilization and reuse of medical equipment marked by the manufacturers for single use only is a common practice in many hospitals in India. This practice becomes a concern when patient safety is compromised. The adverse reactions a patient may experience that may be tied to the reuse of SUDs include fever, hypertension, hypotension, sudoresis, chills, bleeding, nausea and vomiting (1). There is no national licensing regulatory authority in India (2). Hospitals follow an in-house protocol to determine safe standards of sterilization and reuse. This raises the question of whether protocols used in India are enough to prevent adverse reactions.
Objective: The objective of this study is to analyze the outcomes of Percutaneous Transluminal Coronary Angioplasty (PTCA) patients at different hospitals in India in order to determine the correlation between reuse of single use devices and adverse reactions.
Methods: The study took place in two hospitals in India with different economic resources, Medanta Medicity (high income) and Bangalore Baptist Hospital (low income). A retrospective chart review was done for PTCA patients at each hospital to determine whether there were any correlations between the number of reused SUDs used in a procedure and adverse outcomes. Forty PTCA patient charts were analyzed in Medanta and 42 in BBH. Reasons for hospitalization were similar at both hospitals. Data regarding the SUDs used during the procedure, and information regarding serious and non-serious adverse reactions following procedures was collected. Serious adverse reactions were considered death, pyrogen reactions and extended hospital stays. Non-serious complications included formation of a hematoma, discoloration, oozing, swelling, or bleeding at the entry site. P values<0.05 were considered significant.
Results: An independent T-test indicated a significant ($p<.001$) increase in the mean percentage in the number of reused SUDs at BBH. There was no difference in the number of complications that developed after surgery between the hospitals, despite the significant difference in the number of SUDs per procedure. When analyzing length of stay, the results showed significant ($p<.001$) increase in the average mean stay for patients in BBH which may be attributed to the initial health status of patients. No significant differences were found between hospitals in the severity of complications was analyzed (serious vs. non-serious).
Conclusion: There was no significant correlation between the reuse of single use medical devices and adverse outcomes for PTCA at either of the two hospitals in which the study took place.

Demographics and Quality of Life in Emergent Dialysis Patients

Andrew Hogan
Mentor: Robert Sutor, DO

Introduction*:* Patients with End Stage Renal Disease (ESRD) must undergo hemodialysis several times per week for renal dysfunction. Chronic dialysis drastically affects the lifestyles of ESRD patients, as it is time-consuming and uncomfortable. A high number of unfunded ESRD patients present to the Emergency Department (ED) at Parkland Hospital for dialysis. These patients accounted for over 7300 ED visits in 2009. Providing emergent dialysis via the ED has been shown to be more costly than providing scheduled dialysis. To date, all psychometric analyses of demographics and quality of life in chronic dialysis patients focus on insured patients in traditional dialysis centers. This study attempts to acquire and analyze such data on the emergent dialysis population at Parkland Hospital. Data will ultimately be compared to control patients from the Parkland system.
Methods*:* A demographic survey developed at UT Southwestern and the established "Kidney Disease Quality Of Life (KDQOL(TM)) Instrument" were presented to ESRD patients seeking dialysis in the Parkland ED. A comprehensive list of 165 suitable patients was obtained from Parkland Nephrology. With a goal of 80% recruitment of those identified, patients were recruited upon presentation 24 hours a day, 7 days a week for a 4-week period beginning on July 8, 2013. In total, 55 data points from each patient were aggregated.
Results*:* Of 101 chronic dialysis patients approached during the initial 4 weeks, 88 completed the survey. Although 39% of listed patients were not surveyed by the end of the 4 weeks, raw data collection has recently been completed. Demographic data reveal a predominantly male, Hispanic, middle-aged, undocumented, and uninsured ESRD patient population seeking dialysis in the Parkland ED. The KDQOL data indicate a majority of surveyed patients rate their current health negatively, while only 9% do so positively. Additional data quantifying the impact of chronic dialysis on patient lifestyles await analysis.
Discussion*:* The demographic data reveal that 68% of the chronic dialysis patients thus surveyed have lived in the USA for more than 5 years, yet only 15% received a diagnosis requiring dialysis over 5 years ago. This finding seems to contradict the currently accepted idea that the need for dialysis is the primary motivating factor bringing most of these patients to the USA. Quality of life data remains to be compared between the unfunded emergent population and the Nephrology clinic population. Descriptors for the emergent patients are expected to be more negative, or at best equivalent to those for the scheduled patients. Considering the higher cost of emergent dialysis, the results of this comparison are expected to support an argument for providing scheduled dialysis for unfunded ESRD patients.

DAB2IP Pathway Protein Status in High-risk Prostate Cancer Correlates With Outcomes for Patients Following Radiation Therapy

Corbin Jacobs
Mentor: D. Nathan Kim, PhD

Introduction: Decreased expression of DAB2IP tumor suppressor in prostate cancer (PCa) has been associated with worse prognosis and radiation resistance. EZH2, an upstream protein shown to down regulate DAB2IP, has also been associated with aggressive PCa. We investigated the role of DAB2IP and/or EZH2 as prognostic biomarkers following radiation therapy (RT) in high-risk PCa patients.
Methods: Immunohistochemistry was performed and scored by an expert genitourinary pathologist. Freedom from biochemical failure (FFBF) was determined using the Phoenix definition. Castration resistance-free survival (CRFS) was determined when ≥2 episodes of rising prostate-specific antigen (PSA) occurred while on standard hormone therapy. Distant metastasis-free survival (DMFS) was determined from clinical data review. Log-rank test and Cox regression were used to determine significance of biomarker with clinical outcome.
Results: 54 patients with high-risk PCa (stage ≥ T3a, or Gleason score ≥ 8, or PSA ≥ 20) treated with RT from 2005-2012 at UT Southwestern were evaluated. 28% (13/46) of patients revealed DAB2IP-reduction while 72% (33/46) retained DAB2IP. For EZH2, the intensity level was grade (G) 0 in 1 (2%), G1 in 9 (19%), G2 in 29 (60%), and G3 in 9 (19%) patients. Median follow up was 34.0 months (m) (range 6.7-76.1) for DAB2IP-reduced patients, 29.9 m (6.1-84.6) for DAB2IP-retained patients, and 32.6 m (range 2.8-84.6) for the EZH2 study. Patients with reduced DAB2IP demonstrated worse outcome compared to patients retaining DAB2IP, including FFBF (4-year = 37% vs. 89%; $p = 0.04$), DMFS (4-year = 36% vs. 97%; $p = 0.05$), and CRFS (4-year = 50% vs. 90%; $p = 0.02$). Intensity of EZH2 expression trended toward significance for worse FFBF and CRFS ($p = 0.07$). Patients with reduced DAB2IP or EZH2 G3 expression exhibited worse FFBF (4-year = 32% vs. 95%; $p = 0.02$), CRFS (4-year = 28% vs. 100%; $p < 0.01$), and DMFS (4-year = 39% vs. 100%; $p = 0.04$) compared to patients with retained DAB2IP and EZH2 G0-G2. Also, 6 of the 7 patients that developed castration resistance had reduced DAB2IP or EZH2 G3.
Conclusion: This study suggests that DAB2IP reduction is a potent biomarker that portends worse outcome despite definitive RT for patients with high-risk PCa. EZH2 is expressed in most high-risk PCa tumors evaluated and is a less potent discriminator of outcome in this study. Increased sample size and longer follow up may show that EZH2 is also predictive of outcome. DAB2IP status in combination with degree of EZH2 expression may be useful for determining patients with worst outcome within the high-risk PCa population.

Association of Demographic Factors and Outcomes in Necrotizing Enterocolitis Patients

Nistha J. Jajal
Mentors: Rachel I. Renkes, & Diana L. Diesen, MD

Background: Necrotizing enterocolitis (NEC) is characterized by inflammation and ischemia of the intestines in neonates. NEC is the most common cause of emergency abdominal surgery in this population with a mortality rate of 15-50%. Prior studies have identified patient, hospital, and treatment factors that affect mortality, morbidity, and length of stay (LOS) in patients with NEC. Insurance status and race are two patient demographics associated with NEC outcomes disparities. Our study examined the relationship between insurance status and race on outcomes in NEC patients.
Methods: After IRB approval, we conducted a retrospective chart review of infants diagnosed with NEC in the NICU Database from 2000-2010. Eligible study cohort included neonates between 22 0/7^{ths} and 39 6/7^{ths} week gestation. Morbidity was defined as presence of (i) intraventricular hemorrhage (IVH), (ii) acquired pneumonia (AP), (iii) bronchopulmonary dysplasia (BPD), (iv) sepsis, or (v) surgery intervention; surgery was further categorized into NEC-related surgical procedures and GI surgical procedures unrelated to NEC. In all calculations, we adjusted for the effects of estimated gestational age (EGA), birth weight (BW), multiple births, and patent ductus arteriosus (PDA) on outcomes. Statistical analyses, including Chi-square and General Linear Model, were used to determine the relationship between race and insurance status on outcomes including mortality, morbidity, and LOS.
Results: We identified 168 patients with a racial breakdown of: Hispanic (61.3%), African American (29.8%), Caucasian (6.5%), and Other (2.4%). There was no statistically significant correlation between race and mortality, morbidity, or LOS. Insurance was grouped as: None (48%), State/Federal (44%), and Private (8%). There was no statistically significant correlation between insurance status and mortality, morbidity, or LOS. Morbidity was common in this population: 66 (39.3%) IVH, 23 (13.7%) AP, 52 (31%) BPD, and 165 (98.2%) sepsis. Mortality was 29.8% for the entire group with a significant correlation between NEC surgery and mortality ($p=0.0001$). There was a trend between lack of insurance and NEC requiring surgical intervention ($p=0.098$).
Conclusion: Variation in NEC outcomes are influenced by patient, hospital, and treatment factors. In our population, there was no association between insurance status and mortality, morbidity, or LOS, once stratified by EGA, BW, multiple births, or PDA. Race was also not a predictor of mortality, morbidity, or LOS once adjusted for EGA, BW, multiple births, or PDA. Larger studies are needed to improve our prevention and treatment of NEC.

Application of the Caprini Risk Assessment Model in Evaluation of Non-VTE Complications in Plastic and Reconstructive Surgery Patients

Sam Jeong
Mentor: Kathryn Davis, MD

Goals/Purpose: The Caprini Risk Assessment Model (RAM) is an ordinal scoring tool used to quantify and categorize a patient's risk for venous thromboembolism in the post-surgery setting. However, there has been no similar exploration into predictive associations of this score with the other potential complications of surgical procedures. This is surprising because the full list of variables that comprise an individual Caprini score involve a host of systemic factors that involve multiple organ systems. This study investigates whether Caprini scores can be applied to non-VTE complications.
Methods/Technique: Authors undertook a retrospective chart review of 1598 encounters for a series of complex reconstructive and body-contouring operations at an academic medical institution. Input variables included Caprini score components, patient co-morbidities, and prophylactic use. Output variables were postoperative complications. Tests for proportions were performed on percentile data. Non-percentile data was treated with comparison of means (t-test). Odds ratios for complications were calculated for stratified risk groups and compared.
Results/Complications: The overall complication rate was 28.03%. DVT incidence was 1.50%. In comparing complication vs. complication-free patients, age, BMI, operation time, hypertension, diabetes, renal disease, and cancer were statistically significant. For DVT versus DVT-free patients, sex, BMI, operation time, smoking status, diabetes, hypertension, and prior DVT were significant. Increasing Caprini scores are associated with increasing odds ratios (OR) for dehiscence (1.73, $p = 0.028$), infection (2.04, $p = 0.0003$), seroma (1.52, $p = .045$), hematoma (2.12, $p = 0.050$), and necrosis (2.83, $p = 0.0004$) with a corresponding overall OR increase of 1.69 ($p < 0.0001$). These odds ratios parallel similar increases in the baseline occurrence rates for the noted complications.
Conclusions: The data demonstrates that Caprini scores can be applied preoperatively to categorize a patient's risk of developing multiple non-VTE complications. Patients in the higher risk categories will be at an increased risk of suffering from wound dehiscence, infection, seroma, hematoma, and necrosis. Considering these potential complications as a single group, a high-risk patient has a 69% increased odds of suffering at least one problem compared with low-risk individuals. Unfortunately, few preoperative steps can be taken to directly address the complications that the Caprini model is predictive for. However, these results can help physicians better understand which complications to keep watch for most rigorously during postoperative monitoring. In addition, the data can guide conservations with patients during initial preoperative consultations.

Knowledge, Attitudes and Practice (KAP) of hand washing and effect of interactive hand washing curriculum among school children in rural Kathmandu, Nepal

Ramu Kharel
Mentor: Kavita Bhavan, MD, & Pankaj Bhattarai

Introduction: Communicable diseases one of the major leading causes of death among children in South Asia. Respiratory and intestinal, or "diarrheal", infections are associated with the greatest morbidity and mortality among children and adolescents. Numerous studies have previously demonstrated the importance of hand washing to reduce the transmission of infectious diseases. Our study evaluated the (KAP) of hygiene among school children in rural Kathmandu, orphan children in urban Kathmandu, and HIV positive orphan children in urban Hyderabad, India. We measured the effectiveness of a new hand hygiene curriculum in improving hand-washing behavior among children in our study population.

Methods: This is a longitudinal study with ongoing data collection over a two year period. Our study population is comprised of 75 students (5^{th}-8^{th} grade) from a rural school and 14 students enrolled from an urban orphanage in Nepal, in addition to 35 HIV positive children from Hyderabad, India. Students received education on hand hygiene through a standardized curriculum developed for level of literacy and age group through a series of interactive sessions. The study group was then given surveys (along with re-teaching the curriculum) every two months. Leaders were designated among study population to engage in covert hand washing observation. Survey data consisted of hand washing practice, knowledge about indications and technique of hand washing, and attitude towards hand washing. Covert observation included different indications for hand washing and allows the observer to record if hands hygiene technique was adequate per designated guidelines, inadequate, or if hand washing did not occur at all after each indication.

Discussion and Conclusion: Preliminary study findings emphasize the need for hand washing education. There is evidence in the literature supporting adequate hand washing as a means to lower the infection rate of numerous communicable diseases in the pediatric population. Sustained implementation of the hand hygiene curriculum will likely result in better hand washing behavior compared to one time implementation.

Health Related Quality Of Life In Morphea

Natasha K.Klimas
Mentor: Heidi Jacobe, MD

Objective: Little is known about the health-related quality of life (HRQOL) of patients with morphea, and previous studies have yielded conflicting results. We sought to evaluate the impact of morphea on HRQOL and determine which demographic and clinical variables are associated with impact on HRQOL.

Methods: Cross sectional survey Morphea in Adults and Children (MAC) cohort.

Results: Patients with morphea a have worse skin-specific HRQOL than those with other skin diseases, including non-melanoma skin cancer, vitiligo, and alopecia (lowest P <.0001). The morphea population was found to have significantly worse global HRQOL scores than the general U.S. population for all subscales with the exception of bodily pain (all P ≤.004). Comorbidity (r =.35-.51, P ≤ .0029 -.0001) and symptoms of pruritus (r =.38 -.64, P ≤.001-.0001) and pain (r =.46-.74, P <.0001) were associated with impairment in multiple domains of skin-specific and global HRQOL. Physician-based measures of disease severity correlated with patient-reported HRQOL.

Conclusion: Patients with morphea have negative impact on HRQOL particularly if symptoms are present. Providers should be aware of this when evaluating and treating patients.

Factors that predict poor outcomes after treatment of un-ruptured anterior communicating artery aneurysms

Govind Krishnan
Mentor: Jonathan White, MD

Introduction: Management of un-ruptured anterior communicating artery (ACOM) aneurysm is variable. The objective of this study was to identify demographic information, presentation indices, and clinical information that could help predict pattern outcomes after undergoing treatment for an un-ruptured ACOM aneurysm.
Methods: The study was a retrospective review of 139 patients with un-ruptured ACOM aneurysms from 2007 to 2012, who underwent either microsurgical clipping or endovascular coiling to treat the aneurysm. Demographics, medical history, presenting condition and patient outcomes were analyzed. The outcome of the treatment was quantified using the Glasgow Outcomes Score. A score of 3 or greater at discharge was considered favorable. Multivariate regression analysis was used to identify significant predictors of poor outcomes.
Results: A favorable outcome at discharge was achieved in 116 of the 139 total patients (83.45%). Multivariate analysis identified patient age grated than 70 ($p<0.005$), history of prior brain injury or surgery ($p<0.005$), current but not precious smoking ($p<0.05$), aneurysms of size greater than 20 mm ($p<0.05$), duration of temporary occlusions greater than 20 minutes ($p<0.001$), and the use of microsurgical clipping ($p<0.005$) as significant predictors of poor outcome.
Conclusion: Age over 70, prior history of brain injury, current smoking, and an aneurysm size greater than 20 mm, along with the use of clipping and a duration of temporary occlusion greater than 20 minutes are the strongest predictors of poor outcome from treatment of un-ruptured ACOM aneurysms. This would indicate that treatment should be reconsidered in patients with any of the above risk factors and coiling should be attempted whenever possible.

Engraftment of tumorgrafts predicts for development of metastasis in patients with localized renal cell carcinoma

Xiaoyue Li & Felix Thomas
Mentor: James Brugarolas, MD, PhD

Purpose: This retrospective study compares tumorgraft engraftment with development of metastatic renal cell carcinoma (RCC) in patients after the resection of localized tumor in order to determine the potential clinical applications of tumorgraft models.
Materials and Methods: We analyzed tumorgraft lines derived from primary tumor samples of 180 patients. Odds ratios and Kaplan-Meier analyses were used to determine the correlation between tumor engraftment and patient outcome.
Results: There were primary tumor samples from a total of 22 patients who had metastatic disease at the time of surgery. These tumors engrafted at a higher frequency than those of patients who did not have metastatic disease at the time of surgery (OR=3.39, p=0.0099). Of the 158 patients who had localized RCC at the time of surgery, patients whose tumors engrafted developed metastasis at a higher frequency (OR=3.53, p=0.01174) than those whose tumors did not engraft. Patients with engrafted tumors also had a marked decrease in progression-free survival and RCC-specific progression-free survival, but not overall survival.
Conclusions: Engraftment of tumors in mice may be an independent predictor of patient outcome and thus has the potential to become a powerful clinical tool. It also may provide an experimental system to dissect determinants of metastases. Finally, selecting tissue from patients with metastatic RCC at the time of surgery can be used to increase the efficiency of engraftment in RCC tumorgraft models.

Prognostic value of surgical margins during endoscopic resection of paranasal sinus malignancy

Lakshman Manjunath
Mentor and Collaborator: Pete S. Batra, MD, FACS,
& Taylor Derousseau

Background: Complete tumor resection with intraoperative frozen section control remains a central tenet of head and neck surgical oncology. The purpose of the present study was evaluate the significance of margins in predicting local recurrence and disease status following endoscopic resection of sinonasal cancer.
Methods: This single-institution observational cohort study was performed on 68 patients over a 5-year period that underwent curative minimally invasive endoscopic resection (MIER) for sinonasal malignancies.
Results: The mean age was 58.8 years and 69.1% were male. The mean follow-up after definitive MIER was 15.9 months. A mean of 10.8 margins were taken per surgery (range 2 – 27). False negative frozen section analysis was 22.1% for the entire cohort, being slightly higher at 25.0% for T3 or T4 malignancies. At the last follow-up, no evidence of disease (NED) status was noted in 60.0% of those with positive margins versus 83.0% in those with negative margins, respectively ($p = 0.0795$). Regional or distant recurrences were observed in 39.9% of patients with positive margins and 13.2% of those with negative margins, respectively. Disease free survival (DFS) was 9.7 months for patients with positive margins, whereas those with negative margins had a DFS of 15.9 months.
Conclusion: Statistical significance could not be achieved regarding the prognostic value of margin status on patient outcome. However, NED status as a function of residual microscopic disease proved to be marginally significant. These results suggest that complete resection with clear margins may reduce mortality in patients undergoing MIER for cancers of the paranasal sinuses.

Is breast cancer a risk factor for glaucoma?

Nathan Markel
Mentor: Karanjit Kooner, MD

Purpose: In 2012, we reported that women with primary open angle glaucoma (POAG) had a twofold increase in the prevalence of breast cancer (BC). To determine which factors may predispose women with BC to POAG, we analyzed the UT Southwestern Cancer Data Warehouse (CDW).
Methods: An IRB approved retrospective chart study was performed utilizing the CDW. To ensure accurate POAG diagnosis, only patients with BC who visited university eye clinics were included. Males were excluded. Patients were categorized as having POAG (Group A) or having no POAG (Group B), and were also age matched. Data was collected on the following POAG factors: family history, cup/disc ratio, intraocular pressure, visual field defects, and medications. Data was also collected on the following BC factors: family history, risk factors, stage, grade, markers, surgery, radiation therapy, hormonal therapy, chemotherapy, and corticosteroid use. Groups were compared using Fisher's Exact and Wilcoxon Rank sum tests for categorical and continuous variables, respectively.
Results: There were 20 patients in Group A and 95 patients in Group B. Both groups had a similar age at BC diagnosis (yrs.; 67.0±12.5 vs 66.8±9.7) and duration of follow up (median 2.7 vs 2.2 yrs., p=0.9). Both groups received radiation therapy at similar rates (65.0% vs 58.4%, p=0.6), but Group A patients received less chemotherapy (25.0% vs 43.4%, p=0.05). All other variables yielded no significant findings.
Discussion: BC treatment is usually based on markers and severity, but we found no differences in the stage, grade, or markers of either group. A lower rate of chemotherapy in Group A may suggest that POAG patients suffered from less aggressive BC overall. Another explanation is that Group A patients experienced less responsive BC, wherein chemotherapy would have provided no therapeutic or palliative benefit. Limitations of our analysis were a small number of women with POAG and a need for a longer duration of follow-up. We cannot rule out medical surveillance bias.
Conclusions: No variables adequately explained why women with BC may have higher prevalence of POAG. Confirmation that POAG is connected with BC could have important clinical implications for history taking and screening in both POAG and BC. A prospective study with longer follow-up could more accurately examine the connection between these diseases.

References

1. Barte, F.M., et al. Systemic illnesses in glaucoma: a possible link between glaucoma and breast cancer? *ARVO Meeting Abstracts*, 2012. 53(6): p. 6386.

The Orthopaedic Burden of Firearm Injuries in Cape Town, South Africa

Case Martin
Mentor: Sithombo Maqungo, M.D.

Background: Firearm injuries present an immense financial burden on the South African state. In 2005, up to 127,000 firearm-injured victims sought state health care assistance per annum while firearms claimed another 15,000 lives. Patients presenting with firearm-related injuries requiring orthopedic treatment represent a sizeable percentage of all gunshot wound patients, and because many of these patients require expensive, artificial implants, the cost per patient is higher than costs calculated in 2005 for abdominal wounds.
Objective: Our study sought to calculate the average cost of treating gunshot wound victims requiring orthopedic interventions in a South African government tertiary level hospital.
Methods: This retrospective study reviewed all orthopedic trauma inpatients at Groote Schuur Hospital (GSH) over a 12-month period in 2012. The study surveyed more than 1,500 orthopedic admissions and identified those presenting with gunshot wounds. A subsequent folder review yielded data used for a cost analysis using operating theatre time, implant cost, duration of hospital and high-care unit stay, and diagnostic-imaging studies performed.
Results: A total of 116 patients were admitted to the orthopedic wards for gunshot wound injuries that caused 142 fractures. The majority of injuries occurred in the lower limbs with 35% of all fractures in femurs, 15% in tibias, and 11% in fibulas. Ninety-five patients received surgical treatment for a total of 128 orthopedic procedures, 15 concurrent general surgery procedures, and a cumulative operative time of 197 hours 42 minutes. Each patient was hit by an average of 1.69 bullets. Ninety-three of the patients received an implant during surgery. The hospital took 1,227 x-rays on these patients, who in total spent 321 days in the Trauma Ward, 28 days in the ICU, and 720 days on the orthopedic wards. Statistical analysis of the total cost per patient is still pending as we await the collection of the specific costs of diagnostic imaging tests from the GSH Radiology Department and each plate, nail, and screw from various orthopedic implant companies.
Conclusion: This study will contribute to the literature of assessing costs associated with firearm injuries in South Africa. The average cost per patient can then be extrapolated to assess the total cost of firearm-related injuries in orthopedics across South Africa. With these figures, trauma care providers can lobby for more orthopedic funding and training opportunities while also supporting the redirection of financial resources to primary prevention initiatives.

A Ready Reference for Estimating Dose to Pelvic Node Metastases from Brachytherapy in Cervical Cancer

Matthew McKeever
Mentor and Collaborators: Kevin Albuquerque, MD, Lindsay Hwang, & Jennifer Barclay

Introduction: Metastasis to lymph nodes is one of the best predictive indicators of recurrence and death for cervical cancer patients. A dose of greater than 55 Gy is recommended for nodes 2 cm or less for durable control. It is expected that nodes closer to the radiation source will receive a higher dose. In this study we explored the relationship between lymph node location and the Point A dose as a means of assisting the radiation oncologist to determine the required boost dose.
Methods: This retrospective study from 2009 through 2013 included 29 cervical cancer patients receiving high dose rate brachytherapy and had a total of 60 metastases to pelvic lymph nodes. The lymph nodes were mapped and contoured in the treatment planning system.. The external beam and brachytherapy doses and percentage of brachytherapy point A dose received by each lymph node were calculated.
Results: The median doses from brachytherapy and external beam radiation to the lymph nodes were 5.5 Gy (range, 1.4-12.4 Gy) and 49.6 Gy (range, 42.5-62.9 Gy), respectively. The median total dose for all lymph nodes was 56.5 Gy (range, 46.5-66.3 Gy). The dose from brachytherapy accounted for 9.97% of the total dose to the lymph node. The location of the lymph node affected the dose received. The common iliac nodes, which were furthest from the uterus, received 3.18 Gy (11.09 % of point A); the internal iliac nodes received 4.29 Gy (16.43% of point A); and the external iliac nodes, which were closest to the uterus, received 6.05 Gy (21.75% of point A). As expected, nodes closer to the uterus received higher doses of brachytherapy radiation.
Discussion and Conclusion: The common iliac nodes received the smallest fraction of the brachytherapy dose and thus need the greatest external boost dose. Also the internal iliac lymph nodes above the sacroiliac joint, the external iliac lymph nodes anterior to the acetabular line, and the external iliac nodes lateral to the external iliac artery received a smaller amount of the brachytherapy dose than the rest of the nodes in their group. This will require them to have a higher boost dose from external beam compared to other nodes in their group. The results of this study provide radiation oncologists a reference for determining which nodes require an external beam boost dose and the optimal boost dose for those nodes. Improved optimization of the boost dose should lead to better local control and outcomes for patients.

Assessment of Drinking Water Fluoride Contamination In Rural Rajasthan, India

Kajal Mehta
Mentor: Pranavi Sreeramoju, MD

Introduction: Skeletal and dental fluorosis are crippling diseases associated with consumption of water with excess fluoride. The diseases manifest with symptoms such as severe staining, pitting, enamel damage and cracking of teeth in dental fluorosis to stiffness, joint pain, crippling, kyphosis, invalidism, and GI complications in skeletal fluorosis. Fluorosis is an endemic public health issue in many developing regions around the world, including areas of India. A study conducted in Rajasthan, India shows the prevalence of dental fluorosis to be 70.6-100% in village children and 68-100% in village adults. Prevalence of skeletal fluorosis was 5.2% among children and ranged from 7.4% to 37.7% in adults. The present study hopes to address the underlying problem of fluorosis in Rajasthan, India by analyzing water quality in the region.
Methods: This study is a retrospective observational study based on water data collected over a ten month period by the Jal Bhagirathi Foundation (JBF) in Jodhpur, India for a European Union funded water monitoring project. The water data are from the nearby Jalore, Barmer and Jaisalmer Districts, with water samples from all drinking water sources including handpumps, deep bore wells, tube wells, government run pipelines, ponds, lakes, and reverse osmosis water purification systems. The water samples were collected by trained JBF staff in sterile 1L containers, and the water quality testing was carried out by the on-site chemistry lab manager. Fluoride levels were tested within 24 hours of water sampling using a benchtop multiparameter meter and a fluoride electrode in 100 mL water. Additional tests for color, odor, turbidity, pH, alkalinity, total dissolved solutes, and presence of fecal bacteria were performed on each sample.
Results/Outcomes: The data were analyzed for frequency of fluoride levels above the recommended level of 1 parts per million (ppm). Of the water samples tested for fluoride concentration, 57 of 156 samples (36.5%) showed concentrations above 1ppm. The mean fluoride concentration of all tested water samples was .81ppm, with a standard deviation of .73ppm.
Conclusion: The results demonstrate over one-third of the sampled drinking water is potentially toxic to the health of its consumers. This incidence is particularly alarming in the arid conditions of Rajasthan where rural inhabitants have limited water resources, leading them to rely heavily on these harmful supplies. These results provide an impetus to approach the problem by increasing community education of unsafe drinking water sources and methods of purification, including home systems and community-wide solutions like reserve osmosis plants.

Standard calcium supplementation may increase kidney stone risk: a study in women with postmenopausal osteoporosis.

Colleen Menegaz
Mentors and Collaborators: Beverly Adams-Huet, MS, Xilong Li, & Craig Rubin, MD

Introduction: The US prevalence of kidney stones has increased from 2.6% in 1972 to 8.4% in 2010.The majority of stones contain calcium (Ca) with hypercalciuria (hCa) highly associated with stone formation. Postmenopausal osteoporosis (pmo) is a common problem affecting 30% of postmenopausal women in the US. Supplementation with Ca and vitamin D (D) is recommended for most older women.
Purpose: To determine the percentage of patients (pts) who become hypercalciuric while receiving Ca and D supplementation for pmo and to identify biochemical predictors for higher risk of developing hCa.
Methods: 84 ambulatory women aged ≥55 yrs in a RT comparing alendronate (ALN) and sustained-release sodium fluoride (SRF) for the tx of pmo received standard Ca and D supplements. 24-hr urinary Ca (uCa) and deoxypyridinoline and serum D, PTH and bone-specific alk. phos. were measured at 0 and 12 mos. We determined the percentage of pts who became hypercalciuric (uCa >250 mg/24h) during tx. to identify predictors of hCa. Changes in biochemical variables were assessed with mixed model repeated measures analysis. Logistic regression analysis was used to assess predictors of elevated uCa and construct receiver operating characteristic (ROC) curves.
Results: 42 pts were randomized to ALN and 42 to SRF. 67 pts completed ≥ one yr. 90% (27/30) of the ALN group and 92% (33/36) of the SRF group had normal uCa excretion at baseline. Patients with normal uCa at baseline experienced significant increases in uCa in the first year (ALN $p=0.01$, SRF $p<0.0001$). However, baseline hypercalciurics experienced no significant increase in uCa from baseline after Ca and D supplementation. In all, 13% (4/30) of ALN pts became hypercalciuric ($p= 0.41$) vs. 28% (10/36) in the SRF group ($p=0.002$). The best-fit multi-variable model determined baseline uCa ($p=0.02$) and D ($p=0.03$) were strong predictors of hCa at 12 mo. and produced a favorable ROC curve (0.90). Baseline uCa was a consistently strong predictor of hCa and a simple logistic regression analysis generated a ROC curve (0.84) which determined that 180 mg/d uCa at baseline was a strong predictive cut-point for detection of pts at higher risk of hCa with treatment.
Conclusion: 21% of patients became hypercalciuric on recommended doses of Ca and D. Current Ca and D supplementation practice may have significant public health consequences by contributing to the growing incidence of nephrolithiasis. Practice guidelines should consider assessing baseline 24-hr uCa in all pts and 12 mo. 24-hr uCa in pts with baseline uCa ≥of 180 mg/24h.

Application of the "Hybrid Approach" to Chronic Total Occlusions in a Contemporary Multicenter US Registry

Rohan Menon
Mentor: Emmanouil Brilakis, MD

Background: The "hybrid" approach to coronary chronic total occlusion (CTO) crossing was developed to optimize procedural efficacy, efficiency, and safety. Current strategies of crossing CTOs include antegrade wire escalation, antegrade dissection re-entry, and the retrograde approach. The "hybrid" approach is an algorithm that, based on angiographic characteristics of the lesion, streamlines the selection of the optimal technique for crossing the CTO. The goal of this study was to analyze the impact of the "hybrid" approach to CTO percutaneous coronary intervention on procedural workflow and outcomes at five high-volume US centers.
Methods: We examined the procedural techniques and outcomes of 489 consecutive CTO cases performed using the "hybrid" approach between 2012 and 2013 at 5 US centers from cities including Appleton WI, Atlanta GA, Bellingham WA, Kansas City MO, and Dallas TX.
Results: Mean age was 63.8 ± 9.8 years and 86.9% of the patients were men, with high prevalence of diabetes mellitus (41.7%) and prior coronary artery bypass graft surgery (35.7%). Most target CTOs were located in the right coronary artery (61.5%), followed by the left anterior descending artery (20.9%) and left circumflex (16.8%). Dual injection was used in 73.3%. Overall, antegrade wire escalation was used in 62.8%, antegrade dissection re-entry in 38.9% and retrograde in 44.2%. Among successful cases, the final successful crossing technique was antegrade wire escalation in 40.6%, antegrade dissection and re-entry in 27.5%, and retrograde in 31.9%. The initial crossing strategy was successful in 62.0% of the patients, whereas 35.8% required an additional 1 to 4 crossing strategies. Technical success was achieved in 91.6% and major procedural complications occurred in 1.6%. Mean contrast volume, fluoroscopy time, and air kerma radiation exposure were 297.6 ± 154.7 ml, 48.9 ± 31.4 min, 4.4 ± 3.8 Gray, respectively.
Conclusion: Application of the "hybrid" approach to CTO crossing resulted in high success and low complication rates among a varied operator group and hospital structure, further supporting the value of the "hybrid" approach in crossing these challenging coronary lesions.

The Effects of Extracellular Volume Status on Ambulatory Blood Pressure in Patients with Intradialytic Hypertention

Christopher Molina
Mentor: Peter Van Buren, MD

Background: lntradialytic hypertension (HTN), defined as an increase in systolic blood pressure (BP) >10 mmHg from pre to post-hemodialysis (HD),occurs regularly in approximately 15o/o of HD patients. Previous studieshave shown patients with intradialytic HTN display higher overall ambulatory BP and have higher mortality rates when compared to HD controls. As extracellular volume overload contributes to HTN in HD patients, it has been proposed that intradialytic HTN patients have increased extracellular volume. Still, atypical ambulatory BP patterns seen in intradialytic HTN patients suggest extracellular volume may not be a primary determinant of BP in this population. Thus, we hypothesize extracellular fluid volume will be similar in patients with intradialytic HTN and HD controls when adjusting for total body water.
Methods: ln a case control study we recruited hypertensive HD patients with pre HD systolic BP >140 mmHg or post HD systolic BP >130 mmHg. Case subjects with intradialytic HTN were defined as having systolic BP increases >10 mmHg from pre to post-HD. Control subjects were defined as having systolic BP decreases >10 mmHg from pre to post- HD. We obtained measurements of total body water, extracellular water, and intracellular water before and after HD in all subjects using multifrequency bioimpedance spectroscopy. We compared the ratio of extracellular water to total body water between groups using t-tests for pre and post dialysis measurements.
Results: Case subjects (n=4) had an average ambulatory systolic BP of 140 mmHg (20) and controls (n=4) had an average of 1a0 (9.8). Before dialysis, case subjects had a ratio of 0.49 (.03) vs. 0.a6 (.02) in controls (p=0.2). After dialysis, the ratio was 0.45 (0.03) in cases and .44 (0.01) in controls (p=0.4).
Discussion: The ratio of extracellular water to total body water was similar in subjects with intradialytic HTN both before and after HD compared to HD controls. While a larger sample size will be required to establish whether extracellular volume status is different in this patient population, the results of this study suggest increased extracellular volume is not a distinguishing feature of intradialytic HTN. Further etiologies for increased BP including excessive vascular resistance should be explored to explain the phenomenon of intradialytic hypertension.

Factors influencing low birth weight in Bangalore, India

Sabha Momin
Mentor: Hari Raja, MD

Background: Low birth weight is defined as less than 2.5 kg. This can lead to many problems for the child such as impaired growth and mental development, risk of chronic disease, and increased mortality and morbidity rate. The incidence of low birth weight in India is nearly 7.5 million annually (nearly 25% of newborns annually), which is the highest of any country. In contrast, the US has a low birth weight rate of 8% annually.
Objective/Motivation: The objective of this study is to explore the maternal factors associated with low birth weight including mode of delivery, age of mother, gestational period, presence of anemia, and maternal nutritional factors.
Methods/Approach/Materials: This was an observational study involving mothers with newborns of low birth weight over a 4-week period at Bangalore Baptist Hospital in Bangalore, India. After identifying cases of low birth weight and talking to the patient's mother, information regarding the delivery was collected from the patient's medical records. Collected data included findings such as the age and weight of the mother (used to represent nutritional level of mother), baby's birth weight, mode of delivery, gestational age, and hemoglobin levels before and after delivery. This study highlights a representative case that illustrates the common maternal factors associated with low birth weight infants in India.
Results/Outcome: In this particular case, the mother was 24 years old and weighed 110 lbs. before pregnancy. Her baby weighed 2.2 lbs., and her hemoglobin levels before and after the delivery were 9.6g/dL and 9.1g/dL respectively (threshold for anemia 11g/dL in pregnant women). It was also noted that she had not come to the hospital for any prenatal checkups. As this case presents, this women's child is of low birth weight, and factors that increased the risk of low birth weight included nutritional status of the mother, as well as the presence of anemia.
Conclusion: Low birth weight in India is most likely due to the nutritional status of the mother, and the presence of anemia. In comparison, the primary factors in the U.S influencing low birth weight are: genetics, age, nutrition, prenatal care, and smoking. Proper prenatal care and other measures such as proper education of nutritional health should be implemented to increase awareness and decrease risk of low birth weight amongst women in India.

Gamification of Exercise and Its Application for Fall Prevention Among Patients with Diabetes and Peripheral Neuropathy

Elizabeth Monier
Mentors and Collaborators: Bijan Najafi, Gurtej Grewal, Jackie Lee-Eng, Robert Menzies, Talal K. Talal, & David G. Armstrong

Background: Individuals with diabetic peripheral neuropathy (DPN) often experience concomitant impaired proprioception and postural instability. Diminished peripheral sensory input, as found in DPN, has been associated with an increased risk of falling in elderly diabetics. Conventional balance training often consisting of Tai Chi, physiotherapy, and strength training has demonstrated an improvement in effective balance control for DPN patients, but these conditioning regimens do not provide visual feedback to help compensate for impaired proprioception.
Methods: In a randomized trial study, the efficacy of an innovative game-based balance and proprioception training program for patients with DPN was assessed through direct evaluation of changes in body sway before and after the exercise protocol using body worn sensor technology. Participants were randomized to either intervention or sham groupings. All participants' baseline gait and balance were assessed at the initial visit and again after four weeks. Twice weekly, the intervention group participated in a training regimen based on virtual simulation for a total of four weeks. Postural sway was assessed before and after each training session. The gaming exercise consisted of a series of ankle point-to-point reaching tasks as well as crossing a series of virtual obstacles of varying heights. During exercise training, the body-mounted sensors connected to the created program to produce real-time animation of lower extremity joint position for the participant to view on a computer monitor.
Results: Forty-one eligible subjects have been recruited to date; however, the results of 15 participants (Age: 56.3 ± 4.9, BMI: 30 ± 15 kg/m^2) who completed the four-week exercise program have been reported. The preliminary results suggest that the active group reduced ankle sway by 76% (2.82 ± 2.8° to 0.66 ± 0.47°), hip sway by 81% (7.96 ± 9° to 1.48 ± 1.2°) and center of mass (COM) sway by 76% (0.69 ± 0.7° to 0.16 ± 0.11°) during eyes open balance assessment. Similar reductions during eyes closed assessments were observed with reductions of 50%, 24% and 45% for ankle, hip and COM sway, respectively.
Conclusion: This research implemented a novel balance rehabilitation strategy for patients with diabetic peripheral neuropathy based on virtual reality technology that helps compensate for impaired joint proprioception. The method employed body sensors to generate an interactive user interface for real-time visual feedback based on ankle-joint motion, similar to a video game. The study provides evidence that visual illustration of extremity position in an interactive setting coupled with motor control tasks may be an effective rehabilitation method for postural instability in patients with diabetic peripheral neuropathy.

Needs assessment of adolescent sexual health topics in Yantalo, San Martinas

Shivani Murarka
Mentors: Luis Vasquez, MD, & Theresa Barton, MD

Background: Yantaló, San Martín is a village located in the jungle region of Peru. Due to a high national adolescent pregnancy rate of approximately 13%, the Yantaló Foundation, a non-profit organization, enlists foreign volunteers to conduct school-based sex education. This project aimed conduct a baseline needs assessment regarding adolescent sexual health topics as well as to gain the community's input and opinions about improving adolescent sexual health.
Methods: The project was three-pronged. First, a survey of 218 high school students, aged 11-19 and from Yantaló and Los Ángeles, was conducted. Questions included religious preference, after-school jobs, social factors (drinking, smoking, movies), family relationships, how they currently receive information regarding sexual health, how they would prefer to receive information regarding sexual health, their opinion of the school's current curriculum regarding sexual health, and 3 true/false questions to determine their baseline understanding of sexual health. Second, 19 community members from Yantaló and Los Ángeles were interviewed using a semi-structured questionnaire. They were asked their opinion of adolescent sexual health in the region, what they believed was the largest concern, and how they thought it could be improved. Community members included policemen, physicians, obstetricians, medical technicians, teachers, local government officials, and mothers. Third, a Sexual Health Education Curriculum Assessment Tool was used to assess the school's proposed curriculum.
Results: Student surveys revealed that 78% believed they needed more sexual education in school, and less than 50% of the students chose the correct answers on the knowledge-based questions. Students indicated they preferred to receive information from parents and doctors, a change from the norm of receiving information from teachers. Qualitative assessment of community interviews revealed that community members suggested a committee of representatives from the municipality, police, clinic, high school and the Foundation work together to enhance classes and provide extracurricular talks and personal guidance to the youth of Yantaló on sexual health topics. The proposed curriculum lacked in the areas of providing local resources, discussing contraceptive methods, family planning and STDs, and fostering communication with a trusted adult.
Conclusions: The data from this study were presented to potential representatives, and they were receptive to forming a committee. It was also recommended that they conduct a baseline assessment of the students' knowledge at the start of the next school year.

Intravascular Ultrasonography Analysis of the AngiographiC Evaluation of the Everolimus-Eluting Stent in Chronic Total Occlusions (ACE-CTO trial)

Rachita Navara, BS
Mentor: Emmanouil Brilakis, MD, PhD

Purpose: Chronic total coronary occlusions (CTOs) are challenging to treat in part due to high rates of restenosis after stenting. Drug-eluting stents improve outcomes compared to bare metal stents. The goal of the present study was to evaluate the angiographic, intravascular ultrasonography (IVUS) and clinical outcomes after implantation of the Everolimus-Eluting Stent (EES) in CTOs.
Methods: One hundred consecutive CTO patients who were successfully treated using EES at the Dallas VAMC between 2009-2012 were enrolled in the AngiographiC Evaluation of the Everolimus-Eluting Stent in Chronic Total Occlusions (ACE-CTO trial: NCT01012869). Patients underwent follow-up angiography and IVUS imaging at 8 months and clinical follow-up at 12 months. The primary endpoint of this study, binary angiographic restenosis, was defined as >50% minimum lumen diameter stenosis at 8-month follow-up quantitative coronary angiography. The primary endpoint of the IVUS analysis was 8-month in-stent neointimal hyperplasia (NIH) volume (stent volume-lumen volume).
Results: Patients had high prevalence of hypertension (91%), hyperlipidemia (90%), diabetes (47%), prior MI (51%), and prior PCI (21%). Of the 89 patients who underwent follow-up angiography, binary in-stent angiographic restenosis occurred in 41 patients (46%), and IVUS analysis was performed in 61 patients. IVUS was not performed in 24 patients (8 of whom had occlusive in-stent restenosis), and suboptimal image quality precluded analysis in 4 patients. Mean and median neointimal hyperplasia volume were 68 ±100 and 26 (0, 91) mm^3, respectively. This corresponded to a mean and median percent volume obstruction of 12% ± 15% and 5% (0%, 24%), respectively. No NIH could be detected in 33% of patients.
Conclusions: EES implantation in CTO patients is associated with high rates of angiographic restenosis as well as revascularization, yet most patients derived significant symptomatic improvement despite focal NIH formation.

Impact of National Cancer Institute (NCI)-mandated scientific review on cancer clinical trial protocol development

Ning Ning
Mentors: Jingsheng Yan, Xian-Jin Xie,PhD, & David E. Gerber, MD

Background: The National Cancer Institute (NCI) requirement that all clinical trials involving cancer patients at NCI-designated cancer centers undergo a scientific protocol review before Institutional Review Board (IRB) review is unique among all medical specialties. Little is known about the impact of scientific review on protocol development. Given heightened interest in the quality and timeliness of oncology clinical trials, we evaluated the scientific review process at an NCI designated center.
Methods: We collected data on all oncology clinical trials that underwent full board review by the UT Southwestern Harold C. Simmons Cancer Center Protocol Review and Monitoring Committee (PRMC) from January 1, 2009, through June 30, 2013. The following data were collected: trial characteristics, PRMC decisions, protocol clarifications and changes requested by PRMC, and subsequent protocol modifications. We analyzed the association between trial characteristics and PRMC protocol modifications using Chi-square testing, Fisher's exact testing, and logistic regression.
Result: A total of 226 trials were included in our analysis. Of these studies, 23% were institutional (investigator-initiated) trials. Initial PRMC initial decisions were: approved (40%), approved pending response (52%), defer (7%), and disapprove (1%). Across the 226 trials, the PRMC requested 270 changes; total number of requested changes per protocol ranged from 0 (66% of trials) to 17. The number of requested changes per protocol was significantly associated with trial type (mean 0.7 for industry-sponsored versus 3.0 for investigator-initiated; $P<0.001$) and study year (mean 0.7 in 2009 versus 2.4 in 2013; $P=0.03$). Forty-nine percent of requested changes applied directly to trial protocols, with the remainder related to consent form (13%) or other documentation (38%). Protocol-related requested changes were as follows: design (53%), intervention (24%), evidence-background-rationale (14%), and population (11%). Compared to those for industry-sponsored trials, PRMC requested changes for investigator-initiated trials were more likely to be implemented (91% versus 83%; $P=0.08$). A pronounced difference was noted for requested changes related to trial design: among 154 industry-sponsored trials, 28 changes to study design were requested (average 0.2 per trial), and 8 changes (29% of requests) were implemented; among 52 investigator-initiated trials, 39 changes to study design were requested (average 0.8 per trial), and 35 changes (90% of requests) were implemented.
Conclusion: To our knowledge, this is the first study to evaluate the impact of NCI-mandated scientific protocol review in cancer clinical trial development. While this process appears to have a substantial impact on investigator-initiated trial protocols, effect on industry-sponsored trials is less clear.

Increasing Immunization Rate Among Children Experiencing Homelessness

Jeffrey Okonye
Mentor: Nora Gimpel, MD

Introduction Children experiencing temporary homelessness are at higher risk for encountering communicable diseases that can be prevented by vaccines. Even if a child is homeless he/she is still required to have the appropriate vaccines to enroll in school. In 2010 a study performed at the Center of Hope Clinic for women and children discovered that only 23% of the children present were current on required immunizations. The goal of this project was to increase the vaccine coverage rate among homeless youth (under the age of 18) by improving the existing vaccination protocol and implementing a caregiver education program.
Method Children participating in this study were sheltered at the Union Gospel Mission Center of Hope (UGM). Families are allowed to stay up to 90 days. The first month of the study involved observing the current vaccine protocols in place to determine what areas needed improvement or if any additions were necessary. Interviews with the shelter staff were scheduled to better understand the admission process for the women and children. This allowed for an assessment of the areas both the shelter and clinic inside the shelter needed to improve on in order to properly educate the families and efficiently immunize unvaccinated children. During the second month, a consistent set of protocols addressing vaccine records and administration were developed and implemented for both the shelter and the clinic. Also, a packet including a created pamphlet and educational handouts from the CDC were given to caregivers.
Results At the end of the study a vaccination program that fostered communication between the clinic and the Center of Hope staff was created, and a process was started to include vaccination records as a requirement for entry into the shelter. Caregivers are now made aware of the need to vaccinate their children upon entry to the shelter and are encouraged to visit the clinic in a timely fashion. Protocols were established to help maintain better vaccine records for both child patients and others in the shelter. The foundation for a reoccurring vaccination administration event was created in order to capture the children that do not visit the clinic or only have a brief stay in the shelter. In total, 71 children had their vaccination records assessed. The immunization rate amongst those children in the shelter improved from a baseline of 35.71% to 52.38% at the end of month two. Also, medical students were educated on the proper ways to administer vaccines, their importance in disease prevention in children and Immtrac, the Texas Immunization Registry.

Burden of glaucoma adjunct eye disease

Kisan Parikh, BS
Mentor: Karanjit Kooner, MD

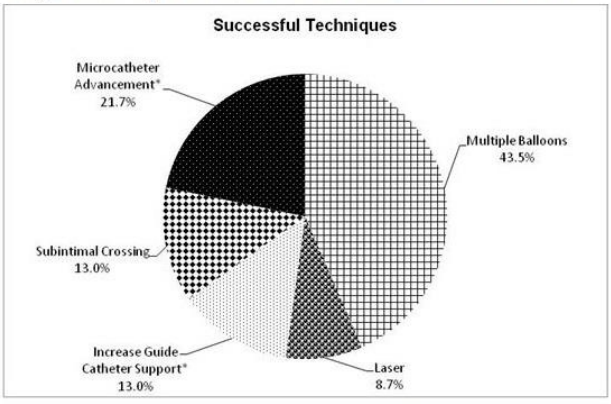
Purpose: The purpose of this study was to better understand the broad impact of primary open-angle glaucoma (POAG) by identifying eye conditions commonly associated with this multifactorial disease.
Methods: An IRB-approved retrospective chart study was conducted at a major academic institution. A total of 713 ethnically diverse patients met the inclusion criteria: 411 were diagnosed with POAG and 302 were controls with no glaucoma diagnosis. Information was collected on: demographics, refractive errors, and ocular ailments. Cochran-Mantel-Haenszel tests were used to compare eye disease prevalence between the two groups.
Results: The POAG group (mean age: 64.3, SD=13.3) was 44% female and the control group (mean age: 64.8, SD=12.3) was 47% female. The POAG group showed a higher prevalence of astigmatism (80% vs 60%,$p<0.0001$), myopia (66% vs 54%,$p=0.0004$), legal blindness (4.6% vs 1%,$p= 0.004$), pseudophakia (43% vs 35%,$p=0.01$), blepharitis (18% vs 12%,$p=0.006$), retinal detachment (4.1% vs 1.3%, $p=0.03$), central retinal vein occlusion (CRVO) (3.4% vs 0%,$p=0.001$), ptosis (12% v 4%,$p=0.0001$), and uveitis (2.4% vs 0.3%,$p=0.02$).
Discussion: The POAG group had an increased prevalence of astigmatism, myopia, legal blindness, pseudophakia, blepharitis, retinal detachment, CRVO, ptosis, and uveitis. Some of these results are explainable and expected. Glaucoma is the second leading cause of legal blindness in the United States. In addition, myopes have an increased risk of POAG and retinal detachment compared to emmetropes. The increased prevalence of blepharitis is likely due to side-effects of glaucoma medications. Another side effect is an increased risk of cataracts, which may explain the increased prevalence of pseudophakia. Lastly, glaucoma is a known risk factor for CRVO. The results involving uveitis and ptosis are more difficult to explain.
Conclusions: This study has shown that patients with POAG have a host of other ocular diseases that may affect their quality of life. Awareness of these associations and their causes would be invaluable to clinicians as they screen for and treat ocular diseases. Future work to replicate the findings of this study and the elucidation of potential mechanisms underlying these associations are indicated.

Prevalence and Treatment of "Balloon Uncrossable" Coronary Chronic Total Occlusions

Siddarth Patel
Mentor: Emmanouil S. Brilakis, MD

Background: The frequency and outcomes of “balloon uncrossable” coronary chronic total occlusions (CTOs) has received limited study.
Methods: We retrospectively examined 373 CTO percutaneous coronary interventions (PCI) performed at our institution between 2005 and 2013 to determine the frequency and treatment of “balloon uncrossable” CTOs.
Results: The mean age of patients was 63.7 ± 8.3 years, and 98.9% were male. Twenty four patients (6.4%) were found to have a "balloon uncrossable" CTO. Compared to other CTO PCI patients, those with "balloon uncrossable" CTOs had similar clinical and angiographic characteristics. Patients with “balloon uncrossable” CTOs had longer procedure time (184.5 ± 77.9 vs. 134.0 ± 69.0 min, p<0.01), fluoroscopy time (55.2 ± 24.9 vs. 37.9 ± 20.8 min, p<0.01), and received high contrast volume (404.4 ± 137.9 vs. 351.7 ± 138.5 ml, p=0.085), but had similar incidence of major complications (8.3% vs. 3.2%, p=0.25) compared to patients without “balloon uncrossable” CTOs. Successful crossing of the "balloon uncrossable" CTO was achieved in 22 of 24 patients (91.7%) using a variety of techniques (Figure).
Conclusions: "Ballon uncrossable" CTOs are encountered in 6.4% of contemporary CTO PCIs and can be successfully treated in most patients using a variety of techniques.

Figure: Techniques for Treatment of "Balloon Uncrossable" CTOs



*Increased Guide Catheter support encompasses the following techniques: distal anchoring, side-branch anchoring, and use of a guide catheter extension. Microcatheter advancement was performed with Tornus, Corsair, Gopher, FineCross, Progreat, and QuickCross microcatheters.

The effectiveness and cultural practicality of ceramic water filters in the Kiwcha community of Ecuador

Diana Pham
Mentor: Nora Gimpel, MD

Introduction: Does the ceramic water filters reduce the number of people with water borne parasites, reduce the incidence of diarrhea and improve water drinking habits compared to a community without water filters?
Qualitative Data- I went to two different communities, Pukara Quinche (with water filters) and Huashig (without water filters) and collected their fecal samples to analyze any presence of parasites. I compared each community to see if the percentage of people with one or more parasites in their feces was less in Pukara Quinche than Hua Shig. I also compared whether the water filters have maintained its effectiveness since its implementation in 2011 by comparing previous years' data.
Quantitative Data: For 2013, I interviewed the two communities about their opinions of the water filters (but if they have no water filters, how they clean their water), the frequency of using water filters, their drinking water practices and any abdominal-related illnesses in the past year. There are several important variables that I failed to take into account.
Results: In general, the results show that water filters have a positive impact on creating awareness for clean water, but more should be done to improve overall hygienic habits as well as maintain the sustainability of the use of water filters. Although the results show that the effects of water filters is culturally specific for the Kichwa community, the issue of sustainability and improvement in overall hygienic habits (in addition to the implementation of water filters) can be universally applied to many other low-income and low health literacy people with no access to clean water because it is easy to use and easy to store. While the water filters were shown to lower the incidence of health problems, however, it seemed to not significantly reduce the overall percentage of people with parasites. This discrepancy further shows that while the water filters provide a good temporary point of source clean water, but it should not be a permanent solution on delivering accessible clean water to the entire communities. It neglects the fact that the government will have less incentive to improve the water system to the poor community, if they feel the water filters is sufficient enough to deliver free water.

Long-Term Outcomes with First vs Second Generation Drug-Eluting Stents in Saphenous Vein Graft Lesions

Nagendra Pokala
Mentor: Emmanouil Brilakis, MD

Background: Compared to bare metal stents, first-generation drug-eluting stents (DES) significantly improved post-procedural outcomes in aortocoronary saphenous vein graft (SVG) lesions, but there is limited information on outcomes after use of second-generation DES.
Methods: We compared the outcomes of patients who received first-generation DES (n=82) with those who received second-generation DES (n=166) in SVG lesions at our institution between 2006 and 2013. Major adverse cardiac events (MACE) were defined as the composite of all-cause death, myocardial infarction, and target vessel revascularization.
Results: Mean age was 66.0 years and 97.6% of the patients were men. Mean SVG age was 11.1 ± 0.4 years. First-generation DES were sirolimus-eluting (n=17) and paclitaxel-eluting (n=65) stents. Second-generation DES were everolimus-eluting (n=115) and zotarolimus-eluting (n=51) stents. Median follow-up was 41 months. At 2 years post-procedure, patients with first- and second-generation DES had similar rates of death (20.00% vs. 20.91%, p=0.881), target lesion revascularization (16.13% vs. 20.00%, p=0.541), target vessel revascularization (20.63% vs. 23.16%, p=0.709), myocardial infarction (25.76% vs. 23.00%, p=0.684), and MACE (40.04% vs. 40.87%, p=0.764), respectively.
Conclusions: Outcomes with first and second generation DES in SVGs are similar. Novel stent designs are needed to further improve the clinical outcomes in this challenging lesion subgroup.

Stone Recurrence of First-Time Kidney Stone Formers after Ureteroscopy

Shreeya Popat
Mentor: Yair Lotan, MD, Jodi Antonelli, MD, & Margaret Pearle

First-time kidney stone formers who did not receive medical treatment for their stones were historically reported to have recurrence rates as high as 50% within ten years of their initial diagnosis.[1-2,4-5] These reports, however, relied on self-reported data and/or older imaging modalities such as plain radiograph and ultrasound. These types of imaging are not sensitive or specific for small stones that oftentimes later become symptomatic and mistakenly present as a recurrence of disease instead of, more accurately, a progression of their initial stone burden.

The modern era of CT reduces the possibility of such small stones being missed during primary presentation and mistakenly identified as a stone recurrence upon symptom manifestation. Therefore, a contemporary study of stone formation will provide a more accurate determination of true stone recurrence rate. To accomplish this goal, we planned a retrospective study examining all patients who underwent ureteroscopy at UT Southwestern and Parkland from 2009 to present: a total of 350 patients. For these patients, I collected data regarding their demographics, past medical and surgical history, family history, and stone formation history. Out of these patients, 110 presented to our facilities as first-time stone formers (the remaining 240 had a past history of stones). For this subpopulation of patients, we gathered data regarding their recent urologic procedures, radiologic studies, laboratory data (including serum and urine analysis), and medical management (if any).

We hope that this information will lead to several insights. First, it will provide a more accurate stone recurrence rate that is not confounded by progressions of stone disease. Second, it will contribute to guidelines about metabolic evaluation and medical management of first time stone formers. Historically, up to 80% of first-time stone formers have been found to have a metabolic abnormality of comparable severity to those of recurrent stone formers.[3] Still, while recurrent stone formers typically receive both drug and dietary regimens, most first-time stone formers do not for reasons such as cost, side effects of medications, and the burden of life-long treatment. Hopefully, this work will ascertain the consequences of such conservative management and provide a wider array of information that will prove instrumental in the treatment of kidney stone patients.

References

1. Ahlstrand, C, Tiselius HG. “Recurrences during a 10-year follow-up after first renal stone episode.” *Urological research*. 1990;18(6):397-399.
2. Ljunghall S, Danielson BG. “A prospective study of renal stone recurrences.” *British journal of urology.* Apr 1984; 56(2): 122-124.
3. Pak CY, Resnick MI. “Medical therapy and new approaches to the management of urolithiasis.” *The urologic clinics of North America*. May 1982;127(5):855-858.
4. Sutherland JW, Parks JH, Coe FL. “Recurrence after a single renal stone in a community practice.” *Mineral and electrolyte metabolism*. 1985; 11(4): 267-269.
5. Trinchieri A, Ostini F, Nespoli R, Rovera F, Montanari E, Zanetti G. “A prospective study of recurrence rate and risk factors for recurrence after a first renal stone.” *The journal of urology*. Jul 1999: 162(1):27-30.

A Prospective Study Evaluating QT Intervals After Antiemetics and Antihistamines in Unfunded Emergent Dialysis with Baseline QT Prolongation

Nashid Shinthia & Peter Ye
Mentors and Collaborators: Lynn Roppolo, MD, Walt Green, MD, Scott Burdette, & Jessica Nelson

Introduction: QT corrected (QTc) prolongation increases the risk of sudden cardiac death (SCD) by 60% in adult patients. Some patients with end stage renal disease (ESRD) have QTc prolongation. Medications such as anti-emetics and anti-histamines can cause QTc prolongation and are typically avoided in patients with pre-existing QTc prolongation. However, these medications are routinely used in the Parkland Emergency Department (ED) to treat uremic symptoms in ESRD patients who do not have funding for routinely scheduled hemodialysis (HD). The purpose of this project was to determine the effects of these medications on the QTc interval in these patients.
Methods: Unfunded ESRD patients who presented to the Parkland ED for emergent HD were identified through the electronic medical record called EPIC. Patients who had a prolonged QTc interval on their baseline EKG on presentation to the ED, defined as above 450 in males and 470 msec in females, were recruited and consent was obtained. Approximately two hours after the patient received any antiemetic or antihistamine medication for their uremic symptoms, a second EKG was ordered and the QTc interval was measured. The medical records of recruited patients were reviewed a week after the ED visit to determine if they were admitted for any arrhythmias.
Results: 29% (44/152) of the ESRD patients in the Parkland ED during the study 4-week study period had QT prolongation and were consented to participate in the study. These 44 patients had 107 Parkland ED visits during the study period. The mean age was 43, with 77% men and 23% women. All were Hispanic. The mean number of years on HD was 3.8. The mean frequency of HD was every 3.8 days. The mean QTc on the most recent *prior* EKG was 482.1 msec. The mean QTc was 483.7 msec on presentation to the ED. Mean electrolyte levels were 5.6 K+, 8.5 Ca^{2+}, 2.7 Mg^{2+}, and 7.2 Ph^{3-}. The frequency and dose of medications given during each ED visit were as follows: promethazine 56.1% (24.7/44) with a mean total dose of 24.7mg; ondansetron 50% (22/44) with a mean total dose of 4.9mg; diphenhydramine 52.3% (23/44) with a mean dose of 31.3 mg; hydroxyzine 11.4% (5/44) with a mean dose of 22mg; and prochlorperazine 13.6% (6/44) with a mean dose of 9.2mg. The mean QTc interval measured 2 hours after these medications were given was 483.8msec. 100% of patients were followed up 1 week later. None of the patients were admitted for life-threatening arrhythmias.
Conclusion: This investigation demonstrates that these medications known to cause QTc prolongation are safe to use in therapeutic doses in ESRD patients with pre-existing QT prolongation.

Identification of drivers of tumor lymphangiogenesis in non-small cell lung cancer (NSCLC)

Robert Carson Sibley
Mentor: Rolf Brekken, PhD, & Michael Dellinger, PhD

Background: Non-small Cell Lung Carcinomas (NSCLCs) frequently spread to regional lymph nodes before they colonize other regions of the body, and the status of regional lymph nodes is an important prognostic factor for predicting the outcome of patients with lung cancer. It has recently been demonstrated that lymphangiogenesis, the sprouting of new lymphatic vessels from pre-existing vessels, facilitates the lymphogenous dissemination of NSCLC. However, the molecular mechanisms driving lymphangiogenesis in NSCLC are poorly understood.
Objective: Our aim was to identify novel lymphangiogenic genes by identifying lymphangiogenic lung tumor cell lines, and then to use microarray data to generate a "lymphangiogenic" gene signature.
Methods: Tumors from 13 lung tumor cell lines were stained with antibodies against LYVE-1 and Podoplanin. Lymphatic vessels were counted in 5 representative 20X fields per tumor. Average lymphatic vessel densities were then calculated. Cell lines were grouped into lymphangiogenic, non-lymphangiogenic, and intermediate categories. Microarray data from the two extreme groups were then compared to generate a "lymphangiogenic" signature.
Results: Four cell lines, (Calu-1, H1993, HCC461, and HCC827) displayed high intratumoral lymphatic density, and five cell lines (Calu-3, H1155, H1395, H1975, and H2073) displayed no intratumoral lymphatic vessels. The "lymphangiogenic" signature obtained from the microarray data from these groups contained 146 genes, including the lymphatic growth factor VEGF-C.
Conclusions: Our preliminary findings suggest that VEGF-C is an important driver of tumor lymphangiogenesis in NSCLC. The other 145 genes in the signature may also serve novel functions in regulating tumor lymphangiogenesis. Together, the results from this project provide mechanistic insight into the process of tumor lymphangiogenesis and metastasis. We believe that this information will lead to the development of new prognostic or predictive markers and therapeutic strategies to improve the outcome of patients with lung cancer.

Coronary artery disease: Case studies demonstrating risk factor variability in South Asian populations

Leonora Slatnick
Mentor: Hari Raja, MD

Background: Coronary artery disease (CAD) is the leading cause of death both in India and the United States, causing about 600,000 deaths per year in the U.S. and about 1.46 million deaths per year in India (CDC). Major risk factors for developing CAD include smoking, hypertension, hypercholesterolemia, diabetes, advanced age, family history, male sex, and obesity. Minor risk factors include stress and biological markers. Although the prevalence of cardiovascular risk factors varies in different populations, the end results of myocardial infarction and stroke are similar.
Objective: CAD in South Asia has followed a similar epidemiological trend as the U.S. over the past ten years, with an increased incidence correlating with increased industrialization. The purpose of the study was to elucidate risk factors for the increased incidence and identify any epidemiological differences between South Asia and the US.
Methods: Two representative patients were chosen as case studies over a four-week period at two different hospitals in India. The first patient was from Medanta Medicity, a private hospital of high socioeconomic class in an urban area in the northern part of India (Gurgaon, India). The second patient was from the southern part of India (Bangalore Baptist Hospital in Bangalore, India), a community-based hospital with a more rural population. The case studies were analyzed to determine epidemiological trends of cardiovascular risk factors in different Indian populations (north vs. south, urban vs. rural).
Results: The key factors that differentiated the two South Asian patients included income and dietary habits, smoking, and access to effective healthcare. However, the differences between the two Indian patients were not significant. In contrast, there were more striking differences between Indian and U.S. patients. Although the risk factors are similar, Indian patients present much earlier in life than US patients with CAD. Indian patients have a body habitus with disproportionately higher truncal adiposity, which predisposes to CAD at a lower BMI than typical American patients. The higher truncal adiposity in South Asians also correlates with increased incidence of metabolic syndrome in the South Asian population and a likely higher risk of CAD [1]. In addition the risk increases at a BMI> 23 kg/m^2, which is less than the standard of 25 kg/m^2 used in the US.
Conclusion: This study illustrates the significant epidemiological differences between South Asian and US patients with CAD. Risk stratification cannot remain a “one size fits all” scheme and requires an individualized approach to improve care for the South Asian population abroad and in the U.S.

The Impact of Medical Therapy on Short- and Long-Term Outcomes of Surgical Therapy for Culture-Positive Infective Endocarditis

John Squiers & David Xu
Mentor: J. Michael DiMaio, MD

Background: Valve surgery is recommended for a limited number of patients with infective endocarditis (IE) meeting complicated, often anecdotal, criteria. Up to half of patients receiving medical therapy for culture-positive IE are prescribed inappropriate antibiotics for the etiologic microorganism. The impact of medical therapy on surgical outcomes is not well defined by existing literature.
Design and Setting: Retrospective, observational cohort study conducted from 1990 to 2013. Data were collected from patient charts. Antibiotic therapy was graded as appropriate or inappropriate according to the most recent guidelines of the American Heart Association.
Participants: 286 consecutive patients with culture-positive IE by the Duke Modified Criteria undergoing therapeutic valve surgery. 177 (62%) received appropriate antibiotic therapy and 93 (33%) received inappropriate antibiotic therapy. Antibiotic regimens of the 16 (5%) remaining patients could not be assessed.
Results: Kaplan-Meier survival analysis showed no statistical difference in survival between the appropriate and inappropriate therapy groups (p=0.795). Intraoperative deaths occurred in 3.4% of the appropriate therapy group and 3.2% of the inappropriate therapy group. All-cause mortality within 30 days of operation was 15% (95%CI: 10,20) in the appropriate group and 12% (5,20) in the inappropriate group. Two-year and five-year survival rates were 62% (55,70) and 48% (40,58) in the appropriate group and 63% (54,75) and 52% (42,65) in the inappropriate group. Contingency analysis of potentially confounding variables revealed the two cohorts had few statistically significant differences in frequencies of etiologic microorganism and comorbidities. There were no statistically significant differences between the groups in their gender composition, racial composition, mean age, or frequencies of affected valves.
Conclusion: Although appropriate antibiotics are clearly superior for patients receiving medical therapy alone to treat IE, it appears that short-term and long-term survival of patients undergoing valve surgery are not affected by the appropriateness of prior medical therapy. This suggests that among the many variables physicians must weigh when considering surgical therapy for IE, the patients' antibiotic therapy regimen may not be an important factor. Further analysis may reveal other variables predictive of short or long-term mortality in these patients.

Acknowledgment: Supported in part by an Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship

Combined Ultrasound and Fluoroscopic Guidance for Radiofrequency Ablation of the Obturator Never for Intractable Cancer associated with Hip Pain

Jonathan Stone
Mentor: Gerald Matchett

Management of pain from skeletal metastases is notoriously difficult. Case reports and case series have described radiofrequency ablation of the obturator never branches to the femoral head for treatment of intractable hip pain. Ablation of the obturator branches to the femoral head is technically difficult because of the bony and vascular anatomy, including close proximity of the femoral vessels. Here, we present the case of a 79-year-old woman with intractable right hip pain and inability to ambulate secondary metastatic non-small cell lung cancer in the femoral head and acetabulum, treated with thermal radiofrequency ablation of the obturator and femoral nerve branched to the femoral head. Ablation of the obturator nerve was done via anterior placement of the radiofrequency needle under combined ultrasound and fluoroscopic guidance, passing the radiofrequency needle between the femoral artery and femoral vein. Real-time ultrasound guidance was used to avoid vascular puncture. Thermal radiofrequency ablation resulted in sustained pain relief and resumption in the ability of the patient to ambulate. From this case, we suggest that anterior approach to the obturator nerve branches to the femoral head may be technically feasible using combined ultrasound and fluoroscopic guidance to avoid vascular puncture.

Development, Implementation, and Evaluation of Interventions to Improve Hygiene in Orphanages in South India

Sindhu Sudanagunta
Mentor: Dr. Naylor, Dr. Sreeramoju
Collaborators: Ramu Kharel, Ben Ammon, Chukwuemika Aroh

India has over 400 million children and adolescents, the most of any country worldwide. Also, more than 1/3 of its population is made up of children under the age of 15. As UNICEF notes, "Hand washing with soap, particularly after contact with excreta, can reduce diarrheal diseases by over 40% and respiratory infections by 30%. Diarrhea and respiratory infections are the number one cause for child deaths in India." This population is the future of India and good health needs to be maintained for longevity and productivity. This project aimed to bring hygiene awareness and education to Sphoorti Foundation, an orphanage in Hyderabad, India which serves over 200 children ranging from 5-15 years. For the intervention, a basic hygiene curriculum was created which attempted to be simple yet interactive, meet the needs of the orphanage, and accommodate the resources available. The curriculum addressed proper methods and situations for hand washing, importance of and techniques in bathing, and oral hygiene. Once on site, the curriculum was taught to 10 student volunteers (ages 14-15). The students learned the curriculum, made posters and signs as teaching aids, and choreographed and recorded two dance videos to supplement their instruction. Of the 200 children at Sphoorti Foundation, 50 were randomly selected to be screened for pre-intervention prevalence rates of URI, diarrhea, dental issues, etc. This screening showed that, in the past month, 42% suffered from a cough, 34% from a cold, 36% reported pruritus, and 58% claimed they had head lice. A month long intervention was led by the student volunteers under the direction of Sindhu Sudanagunta and consisted of class room teaching, presentations, dances, posters and signs around the orphanage, and competitions in proper hand washing before meals. Another health screening of 50 randomly chosen children was performed a week after the hygiene intervention and showed that, in the past month 22% suffered from cough, 30% from cold, 10% reported pruritus, and 48% with head lice. The initial data supports the already known fact that hand hygiene and other basic hygiene practices such as proper oral care and regular bathing improve health outcomes. The future of this project would be to further promote these practices such that they become daily habits of the children and a culture of proper hygiene is integrated into Sphoorti. This will ensure that new children taken into Sphoorti will learn the same habits by watching and learning from their older counterparts.

Efficacy of Acupuncture use for management and relief of pain

John Tang
Mentor: Dr. Ruan, Dept of Acupuncture, SYSU First Affiliated Hospital

Traditional Chinese medicine (TCM) has been practiced since antiquity, but there is still a relative dearth of modern scientific research on the efficacy and mechanism of action of many TCM techniques. I wanted to investigate both the demographics of use, attitudes towards traditional medicine, and self-reported improvement of symptoms after use of TCM in the acupuncture department of a modern Chinese hospital. In order to conduct this experiment, I created a survey asking demographical information including age, gender, reason and area of pain, duration of pain; perceptional questions including attitude towards acupuncture, other treatments previously tried (Western or alternative medicine therapies), reason for choosing acupuncture (previous use with symptom relief, recommendation from friends or family, all other treatments attempted had not provided relief, etc); and pain symptoms before and after a five-session treatment course with acupuncture, rated on a 10 scale. Of the twenty-three subjects interviewed, fourteen reported pain relief of greater than 2 units on the pain scale, two subjects reported no change, and no subjects reported an increase of symptoms. After standardizing pain relief as a percentage of initial pain symptoms, eighteen subjects reported a greater than 30% decrease in pain after treatment, with nine subjects reporting a greater than 60% decrease in symptoms. While these results seem promising, this is only a preliminary study with a small sample size and a lack of a control group for comparison. A more robust future study should control for placebo by using a sham acupuncture comparison group as well as a no treatment group and could look at more patients with a wider range of attitudes and experiences with traditional medicine. Since these patients were selected from the acupuncture department instead of the general public, there is inherent selection bias in the patient population, and thus the demographic and perceptional information obtained did not have an adequate variation for meaningful analysis. Acupuncture seems to have potential for certain illnesses and symptoms, but more careful and wide-scale analysis is necessary to clarify

Initial Evaluation by Primary Care Providers Referring Children to a Pediatric Epilepsy Center

Christine Tran
Mentor: Susan Arnold, MD

Background: Practice guidelines for the evaluation of a first seizure or new-onset epilepsy include evaluation with EEG and counseling regarding seizure precautions. The Comprehensive Epilepsy Center and Children's Medical Center Dallas require primary care providers (PCPs) to send medical records with each referral of a child for evaluation of new onset seizures or epilepsy. PCP notes were analyzed to determine the frequency with which diagnostic testing was ordered, whether safety counseling was provided and completeness of the history recorded.
Hypothesis: Primary care providers' notes referring pediatric patients to the Pediatric Epilepsy Center are more complete when using electronic medical records compared to written medical records.
Methods: 226 PCP notes documenting seizures or epilepsy as a reason for referral to the UT Southwestern Medical Center were reviewed. The notes were analyzed for 5 items related to completeness (including seizures in history, a medication list, a review of systems, a neurological exam and plan to refer to neurology). In addition, we evaluated whether additional diagnostic testing was ordered, whether safety teaching was provided and patient insurance status.
Results: 35% of PCPs documented a plan to order EEG as part of the initial seizure evaluation, but only 17% included seizure safety teaching in their notes. Electronic medical records tended to be more complete than written notes, with 75% of electronic notes including at least 4 or 5 items, compared to 47% of written notes ($p \leq .01$). However, electronic PCP notes were more likely than written PCP notes to incorrectly indicate "no seizures" in the review of systems (12% vs. 0%, $p \leq .01$). There were no significant differences between electronic and written PCP notes in tests ordered, safety counseling, medications listed and inclusion of detailed descriptions of seizures.
Conclusion: Pediatricians are doing a better job at ordering testing than providing safety counseling to patients with new onset seizures. Although private insurance did not impact effectiveness of patient care, it did impact utilization of electronic medical records. PCPs that used electronic records tended to have more complete notes, but sometimes sacrificed accuracy in review of systems and HPI. Electronic PCP notes were not more likely to have useful information. Our results suggest that PCPs might benefit from better access to resources for seizure safety education, perhaps incorporated into the electronic medical record.

Who reports sling and mesh complications to the Utilization of the Manufacturer and User Facility Device Experience (MAUDE) Database?

Kristina R. Tzartzeva

Mentors and Collaborators: Syed X. Hussain, Emily X. Rosenfeld, Chasta Bascu, Jack Hou, MD, Alana Christie, & Philippe E. Zimmern, MD

Introduction: The Manufacturer and User Facility Device Experience (MAUDE) database was created in 1991 for the reporting of medical device complications[1]. Mandatory reporting is expected from the industry to allow for fast discovery of medical device malfunctions. Physicians should report as well, either directly or via their industrial partners. In the wake of escalating number of reports prompting 2 recent FDA notifications, we searched for who is reporting information into the system.

Methods: For the period 2008 – 2012, reports on vaginal mesh and sling complications submitted to the MAUDE database were extracted and analyzed for the reporter occupation. In addition, the submission process was studied by recording the time required to submit a short series of 11 recent complication referrals.

Results: From a total of 15,452 mesh or sling submitted reports (SR), little change was noted in the number of submissions between 2008-2011 (Average 936 SR/year). In 2012, the SR numbers increased exponentially, reaching 11,710. The majority of reports where a reporter occupation was provided were submitted by either lawyers or physicians (ratio 3:1) in 2012. After going through the online submission orientation, our average submission time for each report was 16:32 minutes, ranging from 11:40 min to 20:31 min.

Conclusions: Physicians are increasingly reporting device complications but less so than lawyers. The ethical responsibility to report device complications is hampered by a rather time-consuming process and the lack of a complication classification system.

1.*FDA U.S. Food and Drug Administration*. 05.02.2013 06.09.2013]; Available from: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/ucm127891.htm.

Using a Minimally Invasive, Transurethral Endoscopic Holmium Laser Approach for the Treatment of Urethral Erosion

Kristina R. Tzartzeva

Mentors and Collaborators: Emily C. Rosenfeld, Syed A. Hussain, Chasta D. Bascu, Jack C. Hou, MD, & Philippe E. Zimmern, MD

Introduction and Objectives: To evaluate the use of a Holmium laser in the treatment of urethral erosion. Urethral erosion is traditionally treated with open, transvaginal surgical procedures. The transurethral endoscopic excision with a Holmium laser (TEEH) is a new, minimally invasive alternative to the traditional operation.

Methods: Following Institutional Review Board (IRB) approval, charts of 9 women treated for urethral erosion using TEEH were reviewed. The number of TEEH treatments required to achieve complete removal of eroded mesh as demonstrated with a follow up cystoscopy was determined. The duration of each treatment, stricture complications, and amount of mesh removed with each procedure, or debulking, were also examined.

Results Obtained:: On average each TEEH treatment lasted 42 minutes (15-80min). Complete removal of erosion was achieved in 7/9 cases. Of those, 1 case required 3 TEEH treatment, 2 cases required 2 treatments, and 4 cases required 1 treatment. In the cases where complete resolution was not achieved, debulking of the eroded material was accomplished. No stricture complications were observed.

Conclusion: TEEH is a safe, minimally-invasive, time-sparing procedure that is easier to perform than the traditional open surgery, since it does not require urethrotomy with subsequent urethral reconstruction. TEEH decreases stricture complications and can be used as a debulking method in cases of severe erosion that would require follow-up open surgery.

What Do Parents Want for Their Overweight Children When Visiting the Pediatrician

Carla Upperman
Mentors: Christy Turer, MD, & Glenn Flores, MD

Objective: To determine whether parental preferences regarding primary-care weight-management strategies and perception of child overweight (OW) differ by child age, gender, race/ethnicity (R/E), or weight status, and whether preferences differ when a parent agrees that their child is OW.
Methods: Cross-sectional surveys were administered to a consecutive series of parents of 2-18 year-old (yo) OW (BMI ≥85th percentile [%]) children at a primary-care clinic serving predominately Latino and African-American (AA) children. The 20-question survey assessed preferences regarding primary-care weight-management strategies and perception of child OW. Multivariable analyses examined factors associated with presence of the child during weight discussions being helpful (vs. neutral/harmful), agreement with the child's OW assessment, and prescribing weight-loss diets.
Results: For parents (N=217), the mean age was 34 years, mean BMI, 33 kg/m^2, and 53% had a high-school degree or less. Of the children, 34% were 2-5 yo, 38% 6-11 yo, 28% 12-18 yo, 43% female, 61% Latino, 33% AA, 36% OW, 42% obese, and 22% severely obese (SO). Of parents, 83% stated that child presence during weight discussions would be helpful, 69% agreed that their child was OW, and 74% agreed that pediatricians should prescribe weight-loss diets. In the multivariable analyses, parents of older (compared with 2-5 yo, 6-11 yo: OR, 4.6, 95% CI, 1.3-16; 12-18 yo: OR, 23, 95% CI, 4-136) and male (OR, 5.0; 95% CI, 1.7-10) children had greater odds of stating that child presence during weight discussions would be helpful. Compared with parents of OW children, those of obese (OR, 3.8; 95% CI, 1.7-8.7) and SO (OR, 13.6; 95% CI, 4.0-46.6) children had greater odds of agreeing that their child was OW. Latinos (OR, 5.0; 95% CI, 2-10) and parents who agreed that their child was OW (OR, 2.4; 95% CI, 1.03-5.8) had greater odds of stating that pediatricians should prescribe weight-loss diets.
Conclusion: Most parents, particularly those of older and male children, view child presence during weight discussions as helpful. Parents of OW children may need assistance with recognizing that their child is OW, and Latinos and those who agree that their child is OW may be most receptive to weight-loss diets. The findings suggest that weight-management strategies tailored to child age, gender, recognition of child OW, and R/E may be important in improving child weight status

Does a positive family history of glaucoma foretell severity?

Khiem VU
Mentors and Collaborators: Nathan L. Markel, Kisan Parikh, Karanjit S. Kooner, MD, Beverley Adams-Huet, MS, Xilong Li

Purpose/Relevance: There is a threefold increase in the risk of primary open-angle glaucoma (POAG) in individuals with positive family history. We wished to see if the family history also led to a more severe form of the disease.
Methods: In an IRB-approved retrospective chart study at a university-affiliated medical center, data was collected from 224 patients diagnosed with glaucoma. Positive family history was defined by first, second, or third degree relatives affected (FHx-pos). Patients with negative family history were referred to as controls. Patients with unknown family history were excluded. Age, gender, race, BMI, cup/disk ratio (C/D), visual field defects, intraocular pressure (IOP), central corneal thickness (CCT), and current glaucoma medications were recorded. FHx-pos and control groups were compared using Fisher's Exact and Wilcoxon Rank sum tests for categorical and continuous variables, respectively.
Results: Among patients with glaucoma, there were 82, 120, and 22 patients with positive, negative, and unknown family history, respectively. The FHx-pos group was 47.6% white, 39% black, and 13.4% Hispanic, while the control group was 40.8% white, 40.8% black, and 18.4% Hispanic; no clinically significant differences were noted. Both groups were similar in age (63.3±14.8 vs. 64.9±11.8 years, p=0.5) and CCT (539 vs. 540 μm, p=0.8). The FHx-pos group was predominantly female (70.7% vs. 45%, p<0.001), had elevated IOPs (16.9±4.0 vs. 15.7±4.2 mm Hg, p=0.040), and were prescribed more glaucoma medications (98.9 vs. 92.5%, p=0.05). The mean C/D for both groups was approximately 0.73 (p=0.86) with the FHx-pos group having slightly more optic cupping (29.6 vs. 26.1% of patients, defined as C/D > 0.9; p=0.6).
Discussion: The results suggest that glaucoma patients with affected relatives tend to be female. Sex-specific genetic factors or expression may contribute to disease progression, but a full mechanism has yet to be completely delineated. The FHx-pos group also had higher IOP, required more medications, and experienced slightly more optic nerve cupping, all of which indicate a more severe form of the disease.
Conclusion: The results of this study corroborate the importance of taking a family history of glaucoma. This is especially important for females, for whom aggressive treatment may be necessary. The gender finding merits further study into the possible heritability of predisposing factors in the pathogenesis of POAG in female populations.
References:
Fingert JH. Primary open-angle glaucoma genes. Eye. 2011; 25, 587–595

Long Term Follow-up of Prostate Cancer Patients Who Fail Salvage Radiation Therapy and Radical Prostatectomy

James Ying
Mentor: D. Nathan Kim, MD, PhD

Purpose/Objectives: Salvage radiation therapy (SRT) is an effective treatment for prostate cancer (PCa) that has recurred after radical prostatectomy. Long term follow up in men who developed biochemical recurrence (BCR) after SRT is less well described in literature. This study follows the natural history of patients treated with SRT > 13 years ago.
Materials/Methods: 61 patients with PCa treated with SRT during 1992-2000 at UT Southwestern were identified. Survival was calculated using the Kaplan-Meier method. Log-rank test and Cox regression were used to determine significance of clinical parameters with outcome.
Results: Median follow-up for the 61 patients was 126 months (3-238). Median age at SRT was 62 (46-83), 15% of patients had pathologic Gleason score (pGS) 8-10 disease, 14% had pre-surgical PSA > 20, 63% had pT3+ disease, 59% had positive margin at time of surgery. Of 61 patients, 34 (56%) had treatment failure after SRT. 5 y and 10 y freedom from PSA failure (FFPF) were 51% and 33% respectively. pGS significantly correlated with FFPF (p=.0042) and overall survival (OS) (p=.0022). Seminal vesicle invasion (p=.0357, HR 2.07, 1.0-4.2), lymphovascular invasion (p=.035, HR 5.28, 0.9-32.2), and pre-SRT PSA (p=.015, HR 2.27, 1.14-4.5) were associated with decreased FFPF. For the 34 patients who had BCR, median follow-up was 157.5 months (13-238). Median time to BCR following SRT was 30 months (3-138). 19 (56%) received androgen deprivation therapy (ADT). Median time from BCR to initiating ADT was 48 months (0-151). Outcome after BCR is as follows. OS at 5 and 10 y were 79% and 59% (median 13.6 y). PCa-specific survival (PCSS) at 5 and 10 y were 89% and 73%. Distant metastasis free survival at 5 and 10 y were 75%. Castration resistant free survival at 5 and 10 y were 81% and 70%. Time to BCR after SRT < 1 year (p=.0005, HR 3.92, 2.7-33.6) and < 2 years (p=.021, HR 2.52, 1.2-9.2) significantly correlated with decreased OS, compared to < 3 years (p=.054) and < 5 years (p=.073).
Conclusions: Clinical parameters predictive of treatment failure after SRT are presented. Unfortunately, 25% of patients who fail SRT developed distant metastases within 5 yrs of failure. 56% of those who failed eventually also required ADT. Such events could have significant emotional impact, affect quality of life, and lead to morbidity related to salvage therapy. However, while up to 27% of patients died from PCa after BCR at 10 years, only patients who failed SRT in less than 2 years had a significantly worse OS. Overall, patients who fail SRT treatment can have a prolonged median overall survival of 13.6 years.

From Free Clinic to Medical Home: A Longitudinal Study of Low-Income Dallas Residents Accessing Primary Care

Andrew Yu

Mentor and Collaborators: Nora Gimpel, MD, Patti Pagels, PA-C, Mary Beth Westerman, Jessica Ballou, Shaam Mahasneh, Rosemary Peterson

Objectives: To understand what factors are associated with successful referral of uninsured Dallas County residents from a free clinic to a patient-centered medical home operated by the publicly funded Parkland Health and Hospital System.

Methods: In this longitudinal study, we approached Dallas County residents age ≥18 presenting at a free clinic who have never applied for or received Parkland Health Plus (PH+), the healthcare assistance program for uninsured adults in Dallas County. Patients were educated about and referred to PH+ based on standardized scripts detailing enrollment requirements, benefits, and costs of PH+. Enrollment in this study was offered after education and referral. Informed consent and demographic information were collected at enrollment. Follow-up calls were made at regular intervals to check enrollment status. After 10 months, our records were cross-checked with Parkland electronic medical records to verify last known status. Final enrollment status was documented as: applied for PH+ (y/n), approved for PH+ (y/n), or approved for PH+ and clinic appointment made (y/n). For those patients who were not approved for PH+, we determined the reason based on a combination of follow-up call data and electronic medical records.

Results: 137 persons were educated and referred to PH+. 84 participants enrolled in our study, 29 were ineligible, and 24 were not interested. 54 patients (64%) did not apply for PH+ coverage and 30 patients (36%) did apply. 17 were approved for PH+, 11 were no-shows at their eligibility appointment, 1 qualified for alternative medical coverage (Medicaid), and 1 was ineligible (income limit exceeded). Of the 17 approved for PH+, 14 had clinic appointments at last check. 3 patients who did not apply for PH+ nonetheless received PH+ coverage after presenting at the Parkland ER. The only demographic factor associated with PH+ approval was the presence of a chronic disease diagnosis (χ^2=4.25, p=0.039).

Conclusions: The majority of participants did not receive PH+, with the largest drop-off occurring during the initial step of applying for PH+. 18 of 19 patients who went to their eligibility appointment received some sort of coverage, suggesting that appropriate patients are being referred. 14 of 17 PH+ approved patients had clinic appointments at the conclusion of the study, suggesting that primary care is accessible in Dallas. Patients with chronic disease may have been more motivated to seek PH+ coverage. Further study is needed to understand what interventions may improve successful referral of uninsured patients to medical homes.

A comparison of patient and physician perceptions for invasive cardiac procedures

Michael C. Yu
Mentor: Dharam J. Kumbhani, MD, SM

Introduction: A patient's understanding of the risks and benefits of a medical procedure is a necessary component of a patient's informed decision. Yet studies show that patients often overestimate the potential benefits of a treatment. We hypothesize that patients overestimate the benefit of cardiac catheterization for stable angina.
Objective: To compare patient and cardiologist perceptions of the benefit of cardiac catheterization for stable angina.
Design: Survey.
Setting: Academic center.
Participants: 10 elderly patients who underwent cardiac catheterization for stable angina; their 9 referring cardiologists.
Measurements: Patients' and cardiologists' demographics and pre-procedural perception of the risk and benefit of cardiac catheterization in the treatment of stable angina.
Results: Mean patient age was 68.4 years (40% female; 80% Caucasian, non-Hispanic). Seven out of nine cardiologists and 5/10 patients believed that cardiac catheterization would reduce angina symptoms. Only 1/9 cardiologists, but 8/10 patients believed cardiac catheterization would reduce the patient's risk of myocardial infarction (MI) and 0/9 cardiologists, but 6/10 patients believed cardiac catheterization would reduce the patient's risk of a fatal MI. Patients were more likely to report a ≥ 25% risk of repeat intervention within 2 years than their referring cardiologist (5/10, 2/9, respectively). Perceptions regarding periprocedural complication rates were fairly concordant, although patients tended to underestimate them compared with their cardiologists (median 1.0% vs. 1.5%).
Conclusion: While patients and their referring cardiologists generally agree on the likelihood of angina reduction from cardiac catheterization, patients overestimate the reduction of MI risk and the need for repeat procedures following cardiac catheterization.

Funding: American Federation of Aging Research (AFAR) through the Medical Student Training in Aging Research (MSTAR) Program.

Patient Satisfaction with Different Treatment Modalities for Vitiligo

Vivian Zhu
Mentor: Amit Pandya, MD

Introduction: A wide variety of treatment modalities are currently used for vitiligo. Previous studies' outcome measures typically focus on the repigmentation rate based on clinician evaluation. Recently it has been emphasized that patient satisfaction with treatment is an important outcome measure, which is lacking in the great majority of vitiligo treatment studies.
Objective: The purpose of this study was to determine patient satisfaction with the most commonly used treatments for vitiligo: Topical corticosteroids, topical tacrolimus ointment and NBUVB phototherapy.
Methods: 58 patients with generalized and segmental vitiligo enrolled in the Dallas Vitiligo Registry. Each were asked to assess their overall satisfaction with the treatments they had received; taking into account the treatment regimen, amount of repigmentation achieved, and any associated side effects. All responses were recorded using a visual analog scale completed by the patient.
Results: Demographics:

- 37 females, 21 males
- Median age 43 years
- Median disease duration 9.5 years (6 months- 51 years)

Type of vitiligo: Generalized: 55 patients Segmental: 3 patients. There was a significant difference ($P<0.05$, ANOVA analysis) in overall patient satisfaction between the different therapies used. Patients rated NBUVB phototherapy as the most satisfactory treatment, followed by topical steroids and finally, tacrolimus. Sub-analysis comparing treatment satisfaction to 1) disease duration and 2) Fitzpatrick types (I-III vs. IV-VI) respectively, revealed no statistical differences.
Discussion/Conclusion: A recent literature review of vitiligo studies over the past 40 years demonstrated that only 7% of studies measure patient satisfaction with treatment. Gauging overall satisfaction with treatment has important implications on the physician-patient relationship, compliance with therapy, and development of novel treatment modalities, all of which in turn has an impact on patient quality of life. This study, although small, suggests there is a difference in patient satisfaction between commonly used treatments for vitiligo.

Changes in Free Flap Reconstructions over a 10 year Period: Analysis of Clinical Outcomes

Vivian Zhu
Mentor: Larry Myers, MD, FACS

Objectives: To compare free flap reconstructive cases of the biennium's, 2000-01 (early group) and 2010-11 (later group), with respect to patient demographics, perioperative variables, complications and outcomes; and to discuss the evolution in free flap reconstruction by a single surgeon at a single institution during these time periods.
Study Design: Retrospective, case controlled, cohort study.
Methods: Consecutive free flap reconstructions from the biennum, 2000-01 and 2010-11 were collected into two cohorts. Retrospective chart review was performed to extract patient demographics, perioperative variables, and outcomes. Cohorts were compared with respect to extracted data with statistical significance set at $P < .05$.
Results: There were 24 free flap reconstructions performed in 2000-01 (early group) and 49 performed in 2010-11 (later group). There were 3 flap failures in both groups. The patients in the early group had a smaller flap area (82.5 cm2 ± 60.5) than the later group (156.9 cm ± 115.9), p=0.0006. The harvest time, ischemia time, estimated blood loss and intraoperative fluid administration were all statistically significantly higher in the early group compared to the later group, $p<0.005$. The ICU stay was slightly decreased for the early group (4.02 days ± 4.3) compared to the later group (4.33 ± 4.1), p=0.773. Although the total hospital stay was shorter for the later group (12.8 days ± 5.6), it was not statistically significant from the early group (16.1 days ± 12.15).
Conclusions: Patients are undergoing larger, more complex free flap reconstructions compared to a decade ago. Despite these clinical challenges, increased efficiency stemming from accumulated institutional experience have led to decreased operative times, total length of stay, and complication rates and increased overall success rates.

NOTES