11th annual

Medical Student Research Symposium

February 8, 2019 • Johns Hopkins University School of Medicine

Lucy Nam, MS2

Cardiac Organoids
(Photograph)

We created a two-color cardiac organoid system that enables in vitro modeling of cardiovascular development and disease. Here, we show organoids treated with various combinations of cytokines, allowing elucidation of biochemical mechanisms underlying heart development.

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Medical Student Research Symposium 2019

We are pleased to have you join us for the 11th annual Medical Student Research Symposium of the Johns Hopkins University School of Medicine. As clinicians in training, we are fortunate to work among faculty who conduct a broad range of investigation that yields advances in the knowledge of human health. For the past five years, we have been privileged to have an event that presents the extensive endeavors that students take to advance this mission at the school.

The mission of the Johns Hopkins University School of Medicine is to educate medical students, graduate students, and postdoctoral fellows in accordance with the highest professional standards; to prepare clinicians to practice patient-centered medicine of the highest standard; and to identify and answer fundamental questions in the mechanisms, prevention and treatment of disease, in health care delivery and in the basic sciences.

The Medical Student Research Symposium is a forum for medical students at Johns Hopkins to present their own research to the greater Hopkins community. It is an opportunity for students to participate in the exchange of intellectual ideas in a professional format and meet faculty who relish the pursuit of better science and more effective medicine. Our mission is for the Medical Student Research Symposium to foster the development of young researchers who will aid in the advancement of scientific medicine for years to come.

The Scholarly Concentrations (SC) program is a faculty-mentored scholarly experience for medical students. This program provides the infrastructure and mentoring necessary for students to produce a scholarly project in an area of individual interest, and encourages the acquisition of attitudes and skills for lifelong learning and scholarship.

The SC program offers the following five areas of study:

Basic Science
Sarah Wheelan,MD,PhD

Clinical Research
Kelly Gebo, MD, MPH
Jennifer Haythornthwaite, PhD
Steve Sozio, MD, MHS
Meredith Atkinson, MD

Ethics and the Art of Medicine
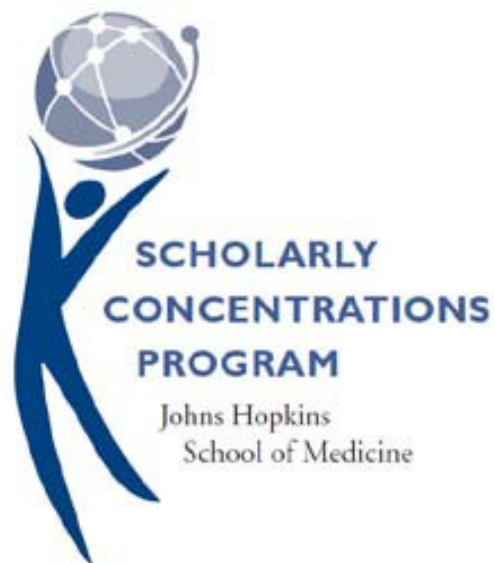Joe Carrese, MD, MPH
Gail Geller, ScD, MHS

History of Medicine
Randall Packard, PhD

Public Health Research
Eric Bass, MD, MPH
David Friedman, MD, PhD

The overall goals of the SC program are to promote intellectual curiosity, appreciation of scholarly inquiry, flexibility, passion for discovery, openness to new ideas, and the ability to work both independently and collaboratively.

Program Schedule

12:00 - 12:15 PM Registration/Lunch
AMEB main lobby

12:15 - 2:00 PM Podium Presentations
AMEB 1st floor lecture hall

2:00 - 3:30 PM Poster Session
AMEB 2nd floor atrium

3:30 PM Refreshments
AMEB 3rd floor

3:40 - 4:45 PM Concurrent Oral Presentations
AMEB 3rd floor presentation rooms

4:50 - 5:30 PM MSRS Award Ceremony
featuring
Keynote speaker,
Stephen Desiderio
M.D.,Ph.D.
AMEB 1st floor lecture hall

Keynote speaker

Stephen Desiderio M.D., Ph.D.
Professor Emeritus of Molecular Biology and Genetics
Professor Emeritus of Medicine
Johns Hopkins University School of Medicine

Stephen Desiderio studied molecular biology and Russian at Haverford College before pursuing medical and graduate studies at Johns Hopkins. As a postdoctoral fellow at the Massachusetts Institute of Technology and the Whitehead Institute, Dr. Desiderio began to study the role of genomic plasticity in the development of the immune system. Dr. Desiderio returned to Johns Hopkins in 1984 to join the Department of Molecular Biology and Genetics and the Howard Hughes Medical Institute (HHMI), rising to the rank of Professor and HHMI Investigator. For seven years he directed the Medical Scientist Training Program at Johns Hopkins. From 2003 to 2018 Dr. Desiderio served as Director of the Institute for Basic Biomedical Sciences (IBBS). As Director of the IBBS, Dr. Desiderio coordinated the activities of nine departments and five research centers, comprising nearly one-fifth of the extramurally funded research at the School of Medicine.

Dr. Desiderio belongs to a group of investigators who, beginning in the 1980s, helped establish the field of molecular immunology. Over the past 37 years Dr. Desiderio uncovered molecular mechanisms that determine how we distinguish "self" from "non-self"—specifically, how the body produces diverse sets of antibodies and defender cells to keep it safe from infection. His work not only has shown how this genomic plasticity is achieved in normal cells—by the shuffling of DNA during cell development—but has uncovered mechanisms that limit the potential damage associated with genomic plasticity, thereby protecting against cancer. Dr. Desiderio and his team also have helped define signals that instruct stem cells to become immune cells and trigger immune responses by foreign invaders. Dr. Desiderio's career illustrates the intimate relationship between basic discovery and medicine. His experiments on programmed DNA rearrangements have led to a deeper understanding of how cancers of the immune system arise, while his work on signaling has identified molecules that are now targets for the treatment of leukemia and lymphoma.

Dr. Desiderio is an associate editor of the Journal of Clinical Investigation and serves on the editorial board of the Journal of Molecular Medicine. He is a past member of the Maryland Life Sciences Advisory Board and the Board of the European Genetics Foundation. He has served on the NIH study section on Allergy and Immunology and as a scientific reviewer of NIH intramural programs. He has consulted for pharmaceutical and biotechnology firms and has served as a legal expert in the field of immunotherapeutics. Dr. Desiderio is an elected member of the Henry Kunkel Society, the American Society for Clinical Investigation and the Association of American Physicians.

Faculty Judges

Adam Kaplin
Alan Scott
Alejandro Garcia
Alena Savonenko
Alexandra Maertens
Alistair Kent
Amol Narang
Angie Boyce
Anne Murphy
Annelle Primm
Babak Behnam Azad
Balaji Krishnamachary
Bara Zuhaili
Barbara deLateur
Barry Nelkin
Ben Larman
Brandi Page
Brent Petty
Byoung Chol Oh
Caitlin Hicks
Carol Newill
Cesar Santa-Maria
Charles Steenbergen
Christine Ruggere
Christopher Fetsch
Christopher Heaphy
Christos Georgiades
Clint Cappiello
Cozumel Pruette
Daniel Ford
Daniel Rhee
Daria Gaykalova
David Hackam
Deborah Persaud
Debraj Mukherjee
Dionna Williams
Dmitri Artemov
Douglas Gladstone
Dylan Stewart
Ed Kraus
Eleni Tiniakou
Ellen Silbergeld
Eric Bass
Eric McCollum

Frances Northington
George Dover
Gerald Brandacher
Geraldine Seydoux
Gerard Gallucci
Gislin Dagnelie
Graham Mooney
Greg Pontone
Hanseok Ko
Heather McKay
Helen Hughes
Henry Jampel
Irina Burd
James Brasic
James Segars
Janet Crane
Jenell Coleman
Jeremy Greene
Jessica Rice
Jodi Segal
Johannes Thrul
John Huetsch
Juli Bollinger
Justin Mcarthur
Khalil Ghanem
Kristin Riekert
Kristin Voegtline
Liam Chen
Lloyd Miller
Lois Eldred
Luciane Kagohara
Maide Ozen
Marc Halushka
Marcelo Diaz-Bustamante
Mariana Brait
Mark Bicket
Mark E. Anderson
Marta Hanson
Martha Stevens
Mary Catherine Beach
Mary Fissell
Maxim Rosario
Megan Collins

Michael Blaha
Michael Erdek
Michele Manahan
Mikhail Pletnikov
Miroslaw Janowski
Mohan Krishnan
Monique Stins
Myron Weisfeldt
Nicole Shilkofski
Noton Dutta
Olga Charnaya
Pat Carroll
Paul Fuchs
Paul Nestadt
Paul Rosenberg
Paul Sponseller
Peiying Liu
Raquel Greer
Raul Chavez-Valdez
Richard Schaefer
Risa Wolf
Robert Anders
Robert Liddell
Robert Naclerio
Roy Ziegelstein
Russell Margolis
Samarjit Das
Sangeeta Ray
Sanjay Desai
Shanshan Jiang
Sheela N Magge
Sheng-fu Lo
Som Saha
Stefano Schena
Stephen Yang
Sudipto Ganguly
Tammy Brady
Tea Soon Park
Tina Tran
Tom Smith
Trinity Bivalacqua
Una McCann
Zhibin Wang

Schedule of Podium Presentations

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12:44 PM Hursuong Vongsachang — A Qualitative Approach to Understanding Reasons for Non-Participation and Barriers to Participation in School-Based Vision Programs

12:56 PM Lauren Claus — Parent experiences of their children's surgery: A narrative analysis of clinician-family perioperative communication and processes

1:08 PM Tae Kyung (Tony) Kim — Development and Visual Assessment of a Deep Learning System for Automated Tuberculosis Screening Using Chest Radiographs

1:20 PM Lochan Shah — How often is drug-free ketogenic diet therapy achieved and in whom?

1:32 PM Katharine Clark — A Phase I clinical trial testing topical artesunate as a treatment for cervical intraepithelial neoplasia 2/3 (CIN2/3)

1:44 PM Vanessa Peña — Targeting Mss51 as a therapeutic option for dystrophinopathy

Schedule of Concurrent Oral Presentations

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4:28 PM	Siddhartha Srivastava	The correlation between immune checkpoint markers in tumors with methylated and unmethylated MGMT promoters in glioblastoma

Room 341: *Clinical Science*

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3:52 PM Andy Ding — Repurposing the FDA-Approved Antiviral Drug Ribavirin as Targeted Therapy for Nasopharyngeal Carcinoma

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3:52 PM   Jane Long   Outcomes After Incompatible Living Donor Kidney Transplantation in Older Recipients

4:04 PM   Kyla Cordrey   Racial differences in cancer mortality for kidney transplant recipients

4:16 PM   Lucy Nam   A Novel Method for Generating Cardiac Organoids to Model Cardiovascular Development and Disease

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3:52 PM Michael Ou Outcomes following Eversion vs. Conventional Endarterectomy in the Vascular Quality Initiative Database

4:04 PM Mohamud Qadi The Decline In Live Kidney Donors In The United States

4:16 PM Nanki Hura Progression of Hearing Loss and Cochlear Implantation in Large Vestibular Aqueduct Syndrome

4:28 PM Nicholas Siegel Evaluating Lymph Node Involvement in Extremity Fungating Soft Tissue Sarcomas as a Sign of Early Metastasis

Room 344: *Clinical Science*

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4:04 PM	Sarah McAlister	Facilitating Adolescent Sexual Health Dialogues: Does Physician Gender Matter?
4:16 PM	Timothy Kim	Sacrificing the Superior Petrosal Vein during Microvascular Decompression Does Not Increase Vascular Complications: Experience from One Institution
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4	**Jason Lee**	Identification of novel candidate pancreatic beta cell-specific genes in type 1 diabetes
5	**Kori Porosnicu Rodriguez**	Modeling Breast Cancer Tumor Architecture In Vitro Using Mutant ESR1 Subclones
6	**Samuel Warner**	Skewing T cell phenotype for adoptive cell therapies
7	**Samuel Weinreb**	Phosphene Mapping for Intracortical Visual Prostheses
8	**Thomas Gracie**	The effect of pentose phosphate pathway knockdown on viability in metastatic PDAC over matched primary tumor cells

| 9 | **Yohannes Tsehay** | Membrane-localized Keratin-14 Promotes Tumor Invasion |
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Acknowledgements

The MSRS Organizing Committee would like to thank the following people for their support putting this event together. Without their help, this day would not have been possible.

Faculty Judges
The Office of Student Affairs
The Scholarly Concentrations Faculty

Mark Dodd
Doug Hughes
Victor Raspa
John Steele

PODIUM PRESENTATION ABSTRACTS
Listed in order of presentation

Grace Ma, MS 2

Mentor(s): Randall Packard
History of Medicine

A Cure for Epilepsy: History of Treatment at the Craig Colony

Authors: Grace Ma BS

Background: The Craig Colony was founded in Sonyea, New York in 1894, as one of the first institutions in the United States dedicated specifically for the care of epileptic patients. At this time, medical treatment of epilepsy was limited to a few agents that were often ineffective or harmful. At the Craig Colony, focus shifted to non-pharmacological treatment including the strict management of diet, hygiene and manual labor. This study examines how treatment at the Craig Colony was influenced by eugenics and associated with efforts to achieve the moral uplift of patients.

Methods: I examined Craig Colony Annual Reports between 1894 and 1951 to assess the views of institution management concerning the care and treatment of patients. I also examined news articles, publications from state associations, and writings by influential Craig Colony physicians. I used secondary sources on the history of epilepsy to understand the context in which the Colony was created and run.

Results: Craig Colony officials measured treatment success by patient adherence to a moral lifestyle as much as by a reduction in seizures. Patients' symptoms could be controlled, but this remission was dependent on their discipline to the lifestyle imposed by the Colony. Recurrence of seizures was attributed to a moral failing. These views were influenced by eugenics and the view that epilepsy was part of a patient's constitutional make-up. Moral treatment at the Colony functioned to regulate this make-up and keep symptoms in check.

Conclusion: The Craig Colony existed when treatment for epileptics was limited and technologies to accurately diagnose and monitor epilepsy were non-existent. At the same time, eugenic views were rising in popularity. These ideas influenced treatment at the Craig Colony, linking care with moral uplift. Although the colony was created for the benefit of epileptics, the connection of morality and cure led to their further stigmatization.

Sophie Z. Gu, MS 2

Mentor(s): David Friedman, MD
Wilmer Eye Institute, Department of Ophthalmology

The Handan Eye Study: Five-Year Incidence and Causes of Low Vision and Blindness in a Rural Chinese Adult Population

Authors: Sophie Z. Gu BA, David Friedman MD

Objective: To determine the five-year incidence and causes of low vision and blindness in a rural Chinese adult population.

Background: The global prevalence of visual impairment is projected to surge in the next few decades due to population growth and aging. This is of great consequence in China, which has one of the most rapidly aging populations in the world. Understanding the epidemiology of visual impairment is crucial for policy planning to meet growing eye care demands.

Methods: Residents of Handan in northern China were selected randomly and invited to participate in the Handan Eye Study. Participants underwent a comprehensive eye examination at baseline in 2007 and returned five years later. Following the World Health Organization (WHO) definitions, low vision was defined as visual acuity (VA) <20/60 but ≥20/400 and blindness as VA <20/400.

Results: Out of 6,830 baseline participants, 5,394 (79.0%) returned for follow-up. Mean age was 51 years and 55.4% were female. Based on presenting visual acuity (PVA), the five-year incidence rates of low vision and blindness were 7.4% (95% CI: 6.8%-8.1%) and 0.6% (0.5%-0.7%), respectively. Based on best-corrected visual acuity (BCVA), the corresponding figures were 1.5% (1.3%-1.8%) and 0.1% (0.1%-0.1%). Incidence of visual impairment was higher in women and increased with age (p<0.0001). Based on PVA, low vision was mainly due to cataract (46.5%) and refractive error (23.5%), while blindness was mainly due to cataract (51.5%). Cataract was also the leading cause of low vision and blindness based on BCVA (56.1% and 80%, respectively).

Conclusion: In a rural Chinese adult population in Handan, the five-year incidence of low vision and blindness is high and primarily due to unoperated cataract and uncorrected refractive error. These are largely preventable or treatable causes of visual impairment, reflecting the urgent need for improved eye care in this region.

Hursuong Vongsachang, MS 2

Mentor(s): Megan Collins, MD, MPH
Wilmer Eye Institute, Department of Ophthalmology

A Qualitative Approach to Understanding Reasons for Non-Participation and Barriers to Participation in School-Based Vision Programs

Authors: Hursuong Vongsachang BA, Amanda Inns PhD, Alyssa Kretz BA, Rani Mukherjee BA, David S. Friedman MD MPH PhD, Michael Repka MD MBA, Megan Collins MD MPH

Background: School-based vision programs have grown in popularity as a way to provide access to vision care. While prior work has focused on barriers to community follow-up and spectacle non-compliance in children, there is limited literature on parent and school staff perspectives regarding school-based vision programs. We examined reasons for non-participation and barriers to participation from parent and teacher perspectives.

Methods: We conducted 39 semi-structured focus groups, 18 with parents and 21 with teachers/staff across two cities, at schools offering school-based vision programs (screening, eye exams, and eyeglasses if needed). Focus groups ranged in size from 2-9 participants (median=5). Sessions were recorded, transcribed, and coded through an iterative process to develop themes using inductive analysis.

Results: Seventy-four parents and 117 teachers/staff participated. Participants most commonly reported having existing eye care, misunderstanding or confusion of the program, particularly in regards to cost and insurance, and skepticism of the program as reasons to decline participation. Beyond reasons why families elected not to participate, major barriers to participation included difficulty reaching parents and parents' lack of awareness of the program. Additionally, participants reported challenges with the consent form including obstacles receiving and returning signed forms and concerns with the complexity, literacy level, and language barriers of the form. Fear of sharing personal information and certain parental attitudes towards vision, such as not believing that their child needs glasses and low prioritization of eye care, contributed to both stated reasons for non-participation and barriers to participation.

Conclusion: To be successful, school-based vision programs must address reasons for non-participation and barriers to participation. This should include targeting services towards those without current access to eye care and building trust and parental understanding of the program. Effective strategies are needed to promote awareness about pediatric vision needs and school-based vision programs among parents and facilitate return of consent forms.

Lauren Claus, MS 2

Mentor(s): Emily Boss, MD
Department of Otolaryngology-Head and Neck Surgery

Parent experiences of their children's surgery: A narrative analysis of clinician-family perioperative communication and processes

Authors: Lauren Claus BA, Anne Links, MS, MHS, Janine Amos, DO, Heather DiCarlo, MD, Eric Jelin, MD, Mary Catherine Beach, MD, MPH, Emily Boss, MD, MPH

Background: Patient and family satisfaction, trust, and experience of care impact clinical treatment decision-making and outcomes. However, little is known about how parents experience communication about surgery for their child. We describe key aspects of the parental experience of care and communication in a pediatric surgical setting and identify opportunities for improvement.

Methods: We conducted a qualitative study involving semi-structured interviews between June and August 2018 with parents of children undergoing surgery at a major urban tertiary children's center. Interviews elicited narratives of parent values and preferences about communication and the surgeon/parent relationship. Interviews were transcribed and analyzed using narrative content analysis. Transcripts were coded by two independent raters, who compared coding and reached agreement.

Results: 20 parents of pediatric surgical patients participated. The pediatric patients aged 1-18 years and underwent a variety of elective surgical procedures in six subspecialties (ENT, plastic, urological, orthopedic, GI, and general pediatric surgery). Content analysis revealed 3 overarching themes and several subdomains of parental experience. The first theme of "clinician-parent communication" included interpersonal behaviors and technical skills of the surgeon. Parents valued surgeons incorporating multimodal information sharing techniques, surgeons recognizing their child's psychological needs, and surgeons including parents in decision-making. The second theme of "parental emotional experiences of communication" included domains of feeling worried, intimidated, offended, and overwhelmed. The third theme of "process improvement" included domains of anesthesia onset, emergence from anesthesia, and privacy. Parents provided suggestions for improvement related to communication and perioperative processes.

Conclusion: Parental experiences of surgical communication and processes focused on clinician communication behaviors, personal reactions to clinicians, and processes of surgical care. These narratives and identified themes may inform surgeon communication strategies and promote relationship- and family-centered surgical care for children.

Tae Kyung (Tony) Kim, MS 2

Mentor(s): Tony Lin, MD
Department of Radiology and Radiological Sciences

Development and Visual Assessment of a Deep Learning System for Automated Tuberculosis Screening Using Chest Radiographs

Authors: Tae Kyung Kim BA, Paul H Yi MD, Gregory D Hager PhD, Cheng Ting Lin MD

Background: Tuberculosis (TB) is a top cause of death worldwide, with high disease burden in developing countries. Screening efforts amongst TB patients have been limited due to barriers to healthcare access, which could be addressed via automated chest radiograph (CXR) screening methods utilizing deep learning. The purpose of this study was to develop and test the performance of a deep convolutional neural network (DCNN) for the automated detection of TB on CXRs.

Methods: We obtained 10,996 CXRs performed at the National Institutes of Health (NIH) via the NIH ChestX-Ray 14 database. A cardiothoracic radiologist reviewed and annotated each CXR for findings suggestive of TB or no findings suggestive of TB. We trained the ResNet-50 DCNN (pretrained on ImageNet) using this dataset and validated & tested the DCNN using 800 CXRs obtained for TB screening in Montgomery County, Maryland (USA) and Shenzhen, China. Receiver operating characteristic (ROC) curves with area under the curve (AUC) were generated to evaluate the DCNNs' performance. Visual validation of the algorithm was performed by creating heatmaps using Class Activation Mappings (CAM) (1).

Results: Our highest-performing DCNN achieved AUC of 0.91 for detection of TB in patients with clinical & pathologically-confirmed TB, with an optimal threshold value resulting in sensitivity of 92% and 70% specificity, compared to sensitivity and specificity of 78% and 51% reported in radiologists. Heatmaps revealed that the DCNN appropriately emphasized the same regions of interest as the human radiologist, such as cavitary and non-cavitary parenchymal nodules/masses and hilar lymphadenopathy.

Conclusion: We developed a DCNN with promising sensitivity and specificity as a TB screening algorithm. The DCNN was highly generalizable when tested against new CXRs performed in Chinese patients. The DCNN further emphasized similar regions as the human radiologist in its' decision-making, suggesting that DCNNs may serve as clinical tools for diagnosing TB; prospective clinical validation is warranted.

Lochan Shah, MS 3

Mentor(s): Eric Kossoff, MD
Department of Pediatric Neurology

How often is drug-free ketogenic diet therapy achieved and in whom?

Authors: Lochan Shah BA; Zahava Turner RD; Stacey Bessone RD; S. Parrish Winesett MD, Anthony Stanfield, Eric H. Kossoff MD

Background: Many parents of pediatric patients choose to start the ketogenic diet (KD) not only for seizure reduction, but also to potentially wean antiseizure drugs (ASD). Although there have been several publications regarding ASD reduction on the KD, it is unknown how often complete medication withdrawal occurs, how long this drug-free period lasts, or if there are characteristics describing patients who are more likely to be weaned off of all ASDs.

Methods: We reviewed the charts of all children started on the KD at JHH and JHACH from 1/11-4/18. Children were defined as achieving drug-free diet (DFD) status if they started the KD on at least 1 ASD and achieved at least 1 week where they were on the KD alone.

Results: 232 children were evaluated, with a mean of 2.4 ASD at onset (range 1-6). DFD status occurred in 43 (18.5%), of which 32 (13.8% of the full cohort) remained off ASDs for the remainder of their KD treatment course. DFD status was achieved at mean 7.5 months after KD onset, for a mean duration of 22.6 months. Eleven children restarted ASD after a mean of 7 months. Children achieving DFD therapy were more likely to be younger (3.8 vs. 4.9 years, p =0.02), have fewer ASDs at KD onset (1.7 vs 2.6, p <0.001), have Glut1 deficiency (12% vs 1%, p = 0.003) or epilepsy with myoclonic-atonic seizures (26% vs 37%, p < 0.001), but were less likely to have Lennox-Gastaut syndrome (5% vs 24%, p = 0.004) or gastrostromy tube (21% vs 42%, p=0.009).

Conclusion: Achieving complete ASD freedom while on the KD occurred in 1 in 5 children in our series, and for extended periods of time in 1 in 7. Younger children on fewer medications, with Glut1 deficiency and epilepsy with myoclonic-atonic seizures, were most likely to become drug-free.

Katharine Clark, MS2

Mentor(s): Cornelia L. Trimble, MD
Department of Gynecology and Obstetrics

A Phase I clinical trial testing topical artesunate as a treatment for cervical intraepithelial neoplasia 2/3 (CIN2/3)

Authors: Katharine T. Clark, Jie Fu, Maria Hom, Elizabeth Sauter, Mihaela Plesa, and Cornelia L. Trimble

Background: Current treatments for high grade cervical intraepithelial neoplasia (CIN2/3), the precursor to squamous cervical cancers, either resect or ablate tissue. These modalities carry a risk of life-altering sequelae, including either cervical incompetence or stenosis. A non-surgical treatment option for CIN2/3, and potentially for HPV lesions in other primary sites, would change the landscape of care, particularly in low-resource settings.

Methods: This phase I prospective study was designed to test safety, tolerability, and clinical efficacy of topical artesunate to treat CIN2/3. A total of 29 healthy women with biopsy-confirmed CIN2/3 received intravaginal artesunate in a dose-escalation design. Lesions were biopsied before and after treatment. Histologic regression was defined as CIN1 or less at wk15. Tissue-based studies to discern potential biomarkers predictive of response are ongoing.

Results: A total of 29 women were followed through 41 weeks. Study subjects had a median age of 32 [23-50] and a median BMI of 23.3 [18.62-40.21]. Half of the subjects [16/29 (55.2%)] were either previous or current smokers. Artesunate was well-tolerated. Reported adverse events were mild and resolved without intervention. Maturing clinical data suggest a dose-response effect of artesunate on CIN2/3. Regression rates observed in the first two dose groups have prompted a second protocol testing the use of artesunate suppositories to treat anal intra-epithelial lesions.

Conclusion: Based on its safety profile and ability to induce regression of CIN2/3, artesunate represents a novel beneficial therapy for women with pre-invasive papillomavirus lesions. As a topical treatment, artesunate has the potential to decrease adverse sequelae, in contrast to current treatment options.

Vanessa Peña, MS 2

Mentor(s): Kathryn Wagner, MD, PhD
Department of Neurology and Neuroscience

Targeting Mss51 as a therapeutic option for dystrophinopathy

Authors: Vanessa Peña BS, Yazmin Rovira Gonzalez BS, Kathryn Wagner, MD, PhD

Background: Duchenne muscular dystrophy is a rare and devastating disease that causes progressive muscle weakness and degeneration starting in early childhood. Mitochondrial dysfunction plays a key role in the pathophysiology of muscular dystrophies, and therefore, is a potential target for therapy. One such target is Mss51, a recently characterized mammalian muscle-specific protein that localized in mitochondria. Previous studies by our lab demonstrated that in vitro genetic disruption of Mss51 resulted in improved mitochondrial function, including ATP production, beta-oxidation, glycolysis, and oxidative phosphorylation.

Methods: Using a mouse model of Duchenne muscular dystrophy (mdx), we evaluated the effects of homozygous deletion of Mss51 using muscle function tests, histopathological analysis, mitochondrial function studies, and gene expression analysis.

Results: Mdx mice with deleted Mss51 (mdx-Mss51 KO) have improved muscle function as evidenced by endurance testing and fatigue testing, when compared to mdx controls. Using a cell-permeant fluorescent dye that marks healthy mitochondrial membrane potential, we found improved mitochondrial membrane stability with genetic ablation of Mss51. Muscle from mdx-Mss51 KO mice showed moderately enhanced transcription levels of antioxidant genes when compared to mdx controls.

Conclusion: Our data suggest that decreasing Mss51 expression may improve mitochondrial function, making this gene a viable target for the treatment of Duchenne muscular dystrophy. Further work will investigate the relationship between antioxidant production and mitochondrial membrane stability and evaluate Mss51 AAV-miRNA knockdown as a more realistic representation of therapeutic potential. We will also investigate the effectiveness of homozygous Mss51 deletion in the treatment of other forms of muscular dystrophy, such as limb-girdle muscular dystrophy.

CONCURRENT ORAL PRESENTATION ABSTRACTS
Listed alphabetically by first name of author

Alexandra Norton, MS 2

Mentor(s): Nicole Shilkofski, MD MEd
Department of Pediatrics

Midwives' Approaches to Family Planning with New Mothers in the Philippines' Mindanao Region

Authors: Alexandra Norton BA, Nicole Shilkofski MD MEd

Background: Access to and utilization of modern family planning methods has a significant impact on reducing both infant and maternal mortality. Recent legislation has sought to increase availability of modern methods to women in the Philippines, and numerous qualitative studies have examined patients' family planning opinions and practices. The purpose of this study was to explore family planning from the perspective of midwives, inquiring about factors impacting postpartum utilization among their patients.

Methods: This study was conducted utilizing a grounded theory approach. Semi-structured interviews were conducted with ten midwives representing three birthing clinics in urban and rural settings of the Philippines' Mindanao region. Patient encounters were observed in each location, for purposes of triangulation. The interviews were audio recorded and transcribed. The data was coded and analyzed for major themes.

Results: Four primary themes were identified. Patients often face challenging or prohibitive logistics in seeking to obtain their desired method, due to inventory fluctuations and differences in provider training at Barangay (neighborhood) Health Stations. There are superstitions, or 'hearsay,' associated with most modern methods, causing fear. Opinions held by 'neighbors' and 'banas' (partners) are also often cited as significant factors in family planning decisions. Finally, facts about benefits of birth spacing and return of fertility following pregnancy are common critical knowledge gaps that impact decisions.

Conclusion: This study illustrates the importance of the Filipino public health infrastructure, anchored in the Barangay Health Stations, operating consistently throughout the country. It also highlights the significance of cultural and social factors in decisions regarding family planning, and the importance of midwives being able to engage discussion and provide education within that context. Finally, it emphasizes the necessity of enhanced education regarding the fertility cycle, benefits of birth spacing, and importance of family planning. These conclusions parallel and support existing literature from qualitative studies of Filipina women's perspectives.

Alissa Rothman, MS 2

Mentor(s): Peter Calabresi, MD
Department of Neurology

Identifying clinically meaningful benchmarks of retinal atrophy in Multiple Sclerosis (MS)

Authors: Alissa Rothman BA, Kate Fitzgerald PhD, Elias Sotirchos MD, Ellen Mowry MD, Shiv Saidha MD, Peter Calabresi MD

Background: Optical coherence tomography (OCT) derived measures of retinal layer thicknesses have been shown to correlate with visual function, grey matter volume and disability scores in multiple sclerosis (MS). However, specific retinal thickness benchmarks associated with disability or socio-economic burden have not been reported. We sought to identify and validate retinal thickness benchmarks in patients living with MS.

Methods: We included MS patients who completed the Multiple Sclerosis Performance Test (MSPT) and had an OCT within 120 days. Neurological assessments included processing speed tests (PST), manual dexterity tests (MDT), and patient-reported disability status. We split patients randomly into training (n=479) and test sets (n=240). In the training set, we derived ganglion cell + inner plexiform layer (GCIP) benchmarks predicting use of a cane, or having PST or MDT scores <20th percentile using the minimum p-value from a set of sequential logistic regression models, dichotomizing GCIP thickness at candidate benchmarks. Candidate GCIP thickness benchmarks were then prospectively validated in the test set using logistic regression adjusting for age, sex and race.

Results: In the training set, we derived GCIP thickness benchmark of 64.43 μm. In the independent testing set, GCIP thicknesses ≤64.43 μm was associated with increased odds of cane use (Odds Ratio [OR]=4.06; 95% CI: 1.64-10.04; p<0.0001), increased odds of being below the 20th percentile on MDT (OR=3.08; 95% CI: 1.35-6.97; p<0.0001), and increased odds of being below the 20th percentile on PST (OR=5.66; 95% CI: 2.33-13.75; p<0.0001). GCIP thicknesses ≤64.43 μm demonstrated 3-fold increased odds of being unemployed or on disability (OR=3.28; 95% CI: 1.36-7.89; p=0.003).

Conclusion: We identified a clinically meaningful OCT benchmark of GCIP thickness ≤64.43 microns, which was correlated with both physical and cognitive disability, as well as measures of socio-economic burden. Larger longitudinal studies are needed to confirm the clinical utility of this proposed OCT benchmark.

Amira Collison, MS 2

Mentor(s): Chiadi Ndumele, MD PhD
Department of Cardiology

Socioeconomic Status and Incident Heart Failure Among Individuals with Diabetes, Obesity and Metabolic Syndrome: The Atherosclerosis Risk in Communities (ARIC) Study

Authors: Amira O Collison BS, Lena M Mathews MD; Lucia Kwak, Priya Palta PhD, Kunihiro Matsushita MD PhD, April P Carson PhD, Deidra C Crews MD ScM, Sherita H Golden MD MHS, Priya Vart MD, Lisa A Cooper MD MPH, Josef Coresh MD PhD, Gerardo Heiss MD PhD, Chiadi E Ndumele MD PhD

Background: Diabetes, metabolic syndrome (MS) and obesity are strong risk factors for incident heart failure (HF). Lower socioeconomic status (SES) is also linked to increased HF risk. Given the importance of lifestyle, self-management, and access to care in managing diabetes, MS and obesity, SES may confer greater risk among individuals with these conditions. We hypothesized that lower SES is associated with greater risk for incident HF among individuals with diabetes, MS or obesity than among those without these conditions.

Methods: We studied 12,938 ARIC participants (mean age: 53 years, 26% black, 56% female) from the baseline visit (1987-1989) without CVD and with BMI ≥18.5 kg/m2. Income , education , and area deprivation index were evaluated as single measures of SES and in a combined SES score (high, medium, low). We constructed Cox regression models to estimate hazard ratios (HRs) for HF associated with SES (through 12/31/16), stratified by diabetes, MS and obesity status, separately, and with tests for interactions of SES with obesity, MS or diabetes.

Results: There were 2,551 HF events over a median 27 years. The lowest education level was more strongly associated with HF risk in the presence of diabetes (HR 3.17, 95% CI: 1.95-5.14), than in the absence of diabetes (HR 1.56, 95% CI: 1.31-1.86; p interaction <0.01)(Table). Significant interactions were also observed for diabetes and MS with most other SES measures. The combination of lowest education and diabetes was associated with an HR of 3.95 (3.21-4.87) for HF compared to the combination of highest education and no diabetes.

Conclusion: Low SES is associated with elevated HF risk, particularly among individuals with diabetes and metabolic syndrome. There is urgent need to understand the underlying mechanisms for this association, which may inform tailored interventions to address the marked HF risk in those with both low SES and diabetes/metabolic syndrome.

Andy Ding, MS 2

Mentor(s): Tyler, BA
Department of Neurosurgery

Repurposing the FDA-Approved Antiviral Drug Ribavirin as Targeted Therapy for Nasopharyngeal Carcinoma

Authors: Andy Ding BA, Sakibul Huq BS, Joshua Casaos BA, Manuel Morales BA, Tianna Zhao PhD, Noah Gorelick MD, Henry Brem MD, Betty Tyler BA, Nicolas Skuli PhD

Background: Nasopharyngeal carcinoma (NPC) is a squamous cell carcinoma that is often diagnosed at an advanced stage, leading to poor overall survival. Accumulating literature suggests that poor prognosis in NPC is correlated with elevated protein expression of EZH2, eIF4E, and IMPDH, which are modulated by the FDA-approved antiviral drug ribavirin. Based on this intersection of molecular signature and drug targets, we investigated the potential of repurposing ribavirin as a therapeutic agent for NPC.

Methods: Anti-neoplastic efficacy of ribavirin was assessed in vitro using cellular growth, scratch wound, and IMPDH activity assays on the NPC cell line CNE-2. Effects of ribavirin and/or radiotherapy (XRT) on tumor growth in vivo were assessed by measuring flank tumor volumes of CNE-2-implanted athymic nude mice. Finally, induction of apoptosis due to ribavirin was measured by quantifying cleaved caspase-3 positive cells in CNE-2 flank tumor sections.

Results: Ribavirin significantly decreased NPC proliferation and migratory capacity (Rib: 35.0% vs Ctrl: 50.9% wound closure, $p<0.001$). CNE-2 cells treated with ribavirin reported decreased activity of IMPDH (Rib: 0.192 IU/L vs. Ctrl: 0.328 IU/L, $p<0.05$), suggesting purine synthesis inhibition. Importantly, ribavirin reduced flank tumor growth (Rib: 1161 mm^3 vs Ctrl: 1556 mm^3, $p<0.05$) and is an effective treatment in combination with radiation therapy in human xenograft models of NPC (Rib+XRT: 697 mm3 vs Ctrl: 1556 mm^3, $p<0.001$).

Conclusion: Our work has shown that ribavirin effectively inhibits tumor growth, decreases tumor invasiveness, and induces tumor cell apoptosis. Ribavirin represents a safe and promising addition to current treatment regimens for NPC.

Angelica Ezeigwe, MS 2

Mentor(s): Erin Michos, MD
Department of Cardiology

The Novel Inflammatory Marker GlycA and the Prevalence and Progression of Valvular and Thoracic Aortic Calcification: The Multi-Ethnic Study of Atherosclerosis

Authors: Angelica Ezeigwe, BS, Oluwaseun E. Fashanu, MBBS, MPH, Di Zhao, PhD, Matthew J. Budoff, MD, James D. Otvos, PhD, Isac C. Thomas, MD, MPH, Samia Mora, MD, MHS, Martin Tibuakuu, MD, MPH, Erin D. Michos, MD, MHS

Background: GlycA is a novel composite biomarker of systemic inflammation reflecting posttranslational glycosylation of acute phase reactants. GlycA has been associated with coronary artery calcium, cardiovascular disease (CVD) events and all-cause mortality. Vascular calcifications outside of the coronary arteries have also been found to be risk markers of CVD and mortality. Whether GlycA is linked to Extra-Coronary Calcifications (ECC) is not well established.

Methods: We studied 6,462 MESA participants free of clinical CVD who had plasma GlycA measured at baseline. ECCs [calcification in the aortic valve (AVC), mitral annulus (MAC), ascending and descending thoracic aorta (ATAC, DTAC)] were ascertained at baseline and up to ~5-yrs later. Poisson regression models with robust variance estimation assessed associations of GlycA with prevalent and incident ECC. Linear mixed models assessed the cross-sectional and 5-yr change in ECC. Models adjusted for demographic and lifestyle factors.

Results: In cross-sectional analysis, GlycA (per SD increment) was positively associated with prevalent AVC, ATAC and DTAC with adjusted prevalence ratios (95% CI) of 1.08 (1.01-1.14), 1.18 (1.03-1.34) and 1.10 (1.06-1.14), respectively. There was also a significant association between GlycA and baseline extent of both ATAC and DTAC. Longitudinally, GlycA was positively associated with incident MAC and DTAC with adjusted incidence ratios of 1.18 (1.03-1.37) and 1.17 (1.07-1.28), respectively. GlycA was also associated with 5-yr change in MAC and DTAC extent.

Conclusion: In this diverse cohort free from clinical CVD, we found GlycA was positively associated with prevalent and incident ECC measures, in particular for progression of MAC and DTAC.

Barry Bryant, MS 2

Mentor(s): Paul Sponseller, MD, MBA
Department of Orthopedic Surgery

The Effect of Physician Trading Cards on Patient Satisfaction Scores for Pediatric Patients

Authors: Barry R. Bryant BS, Walter Klyce BA, Paul D. Sponseller MD, MBA

Background: Patient satisfaction is a major component of quality of care and an increasingly important determinant of hospital reimbursement metrics. This study examined the impact of a low-cost, child-centered intervention designed to better acquaint patients with their pediatric surgery team and improve patient satisfaction.

Methods: Customized, full-color "trading cards" were created for the pediatric orthopaedic surgery team at Johns Hopkins. Each card included the provider or trainee's full name, educational background, interests, picture, and a fun fact. A study team member distributed the cards to all hospitalized patients of a single attending surgeon over a 6-month period. The patients in the intervention arm were matched with a control group of patients who underwent the same surgeries during the corresponding 6-month period one year prior but did not receive trading cards. The primary outcome measure was the Child Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey, which we administered to both groups. These study-administered HCAHPS surveys were subsequently compared with the surgeon's official Press-Ganey-administered survey results.

Results: Fifty survey responses were collected (25 intervention and 25 control) with a response rate of 33 percent. Fifty-two percent of respondents were female. On the study-administered HCAHPS survey, the intervention group had a significantly higher overall rating of the hospital compared to the control group (9.7 ± 0.6 vs. 9.0 ± 1.2, $p = 0.026$), analyzed with a paired t-test. Increases were seen in the same domains in the Press-Ganey-administered HCAHPS survey for the same surgeon, totaling 9 control and 10 intervention patients.

Conclusion: The distribution of customized trading cards was associated with significant increases in the doctor-specific domains of the HCAHPS survey. This was confirmed by comparison with the hospital's official HCAHPS data for that surgeon. We believe that this type of intervention can increase physician-patient contact with minimal increases in cost or time.

Bernadette Wharton, MS 2

Mentor(s): Stacy Cooper, MD
Department of Pediatric Oncology

The initial communication of a pediatric oncology diagnosis by primary care and other pediatric providers

Authors: Bernadette Wharton BA, Dori Beeler PhD, Stacy Cooper MD

Background: Receiving a cancer diagnosis is a life-changing experience for patients and families. The importance of the initial discussion with an oncologist is well documented, but little is known about the communication of the initial diagnosis, often by a non-oncologist physician, and its impacts on transition to oncologic care. This study sought to understand the initial diagnosis experience from the patient, caregiver, and physician perspective.

Methods: Semi-structured interviews were conducted at a large academic medical center with recently diagnosed pediatric/adolescent oncology patients, caregivers, and their primary pediatricians or other non-oncologists involved in diagnosis. Interviews were transcribed, independently coded by two readers, and compared for agreement.

Results: Those involved in the initial cancer diagnosis of 29 patients were interviewed, encompassing 33 family caregivers, 12 patients, 12 primary pediatricians, and 14 other diagnosing physicians. Content analysis of interviews generated several major themes.
Patient-Caregiver:
-Urgency: Families often inferred a sense of urgency (regarding seeking referrals, tests, etc.) from physicians even when purpose of tests or diagnosis was unclear
-Language: 'Malignancy' and 'mass' were terms most often used by physicians during discussions, but these were often not understood as 'cancer' by families
-Role of PCP: PCP role viewed as limited before and particularly after diagnosis; families who saw a larger role primarily sought emotional support PCP or Diagnosing Physician:
-Communication influences: Factors including definitiveness of diagnosis, anticipated family reaction, and experience delivering cancer diagnoses impacted language used by physicians
-Role of PCP: Discordance among PCPs regarding scope of responsibility following diagnosis (maintaining support vs. stepping back)

Conclusion: There was wide variation in family experiences leading up to diagnosis, and physicians expressed a multitude of factors influencing how a diagnosis was communicated. Understanding these influences in conjunction with families' needs may allow physicians to better tailor messaging when delivering diagnoses and, in turn, improve patient transition to oncologic care.

Boateng Kubi, MS 2

Mentor(s): Fabian Johnston, MD
Department of Surgery

Surgical and Medical Oncology Inpatients' Preferences for Advance Care Planning

Authors: Boateng Kubi BS, Kimberley Lee MD, Lisa Cooper MD, Zachary Enumah MD, Fabian Johnston MD

Background: Despite its demonstrated benefits, opportunities for advance care planning (ACP) discussions continue to be missed, in part due to minimal understanding of patient preferences for, and experiences with ACP discussions. This study seeks to determine which practitioners oncology patients desire to have ACP discussions with, and the optimal timing which to do so. A secondary objective is to capture patient opinions and experiences regarding ACP.

Methods: Semi-structured bedside interview of 200 surgical and medical oncology patients in a tertiary academic hospital. A coding structure was used to analyze qualitative responses, and quantitative variables were assessed with chi-square tests for categorical variables and t-tests for continuous variables.

Results: Of the 200 subjects (124 surgical oncology, 76 medical oncology) only 24% reported having previously had ACP discussions with their physician despite 82.5% reporting a desire to do so. Patients felt that ACP discussions were a priority (to alleviate familial guilt, maintain control, and prevent others' values from guiding EOL), but reported that previous ACP discussions had been incomprehensive and ineffective. 43.5% of subjects preferred to have ACP discussions with their PCPs, compared with 7% and 5.5% for surgeons and oncologists respectively. Reasons cited included trust and familiarity with PCPs, lack of time invested by surgeons and oncologists, and patient belief that ACP fell outside scope of surgical practice. Most subjects (94%) preferred to have ACP discussions early, with 45% preferring to discuss while they were still healthy (before cancer diagnosis). Data also revealed that regardless of prognostic markers, most subjects preferred to have ACP discussions early in the course of cancer disease.

Conclusion: Despite the number of practitioners that they see, cancer patients prefer to have ACP discussions with their PCPs, and prefer to do so earlier rather than later. To improve uptake of ACP discussions, interventions must be better tailored to patient preferences.

Dana Goplerud, MS 2

Mentor(s): Sara B. Johnson, PhD, MPH
Department of Pediatrics

Maternal Subjective Social Status and Birth Outcomes

Authors: Dana Goplerud BS, Sara B. Johnson PhD MPH

Background: Low birth weight (LBW) is more prevalent among women with low socioeconomic status (SES). Few studies have examined the relationship of maternal subjective social status (SSS) with the health of their children. This study aims to explore the association of maternal SSS with neonatal health.

Methods: Pregnant women (n=112) were surveyed during pregnancy and 6 weeks postpartum. Participants ranked their SSS from 1 (low) to 10 (high) within their community (SSS-C) and American society (SSS-US). Multivariate analyses were performed to examine the relationship between SSS, maternal risk factors, and neonatal outcomes.

Results: Both SSS-US and SSS-C were positively correlated with maternal income, education, age, partner support, and self-rated health, and negatively correlated with financial stress and history of adverse childhood experiences (ACEs) (p<0.05). Additionally, SSS-C was negatively correlated with maternal BMI (p<0.05) and SSS-C scores were related to race (χ^2 (5, N = 91) = 13.61, p=0.034) and cigarette usage in pregnancy (χ^2 (3, N= 84) = 8.687, p=0.0130). Adjusting for income, education, and race in linear regression, SSS-US was associated with partner support (b=0.386, p=0.016) and SSS-C was associated with BMI (b=-1.078, p=0.029), financial stress (b=-0.572, p=0.036), and self-rated health (b=0.0972, p=0.030). SSS-C was associated with infant LBW in multivariate regression models accounting for age, BMI, and fetal sex (OR=0.424, p=0.046), or depression, isolation, and perceived stress (OR=0.445, p=0.040). However, this relationship was no longer significant when controlling for income, education, and race (OR 0.898, p = 0.803).

Conclusion: SSS can be a marker of socioeconomic and psychological wellbeing. Additionally, SSS-C can be used to understand risk for LBW pregnancy independent of psychological or biological risk factors. SSS may capture multiple aspects of objective SES using a single, non-stigmatizing screening tool. Screening for low SSS may be useful to identify women at higher risk for neonatal complications.

Daniel Weng, MS 2

Mentor(s): Seth Martin, MD, MHS
Department of Cardiology

Predictors of Elevated Heart Rate in Patients Recovering from Acute Myocardial Infarction - A Longitudinal Analysis of Apple Watch Heart Rate Recordings

Authors: Daniel Weng BA, Oluseye Ogunmoroti MD MPH, Matthias A Lee PhD, Ryan Demo BS, Seth Martin MD MPH

Background: Elevated resting heart rate (HR) at admission and discharge has been associated with higher mortality and morbidity during one-year and one-month follow-up among acute myocardial infarction (AMI) patients. However, most studies only examine snapshots of HR confined to the hospital setting. This study examines: 1) the longitudinal HR of patients recovering from AMI using the Apple Watch; 2) the predictors of elevated HR from admission to 30 days post-discharge.

Methods: Medical record data and Apple Watch HR recordings were obtained from patients enrolled in the MiCORE study. Descriptive statistics were analyzed, including the mean and time trends of HR. A mixed effects linear regression model was used to analyze patient admission characteristics, medical history, and demographics to obtain predictors of mean HR 30 days post-discharge. A mixed effects logistic regression model was used to calculate predictor coefficients associated with mean HR over 90 bpm.

Results: 1,245 HR recordings were obtained from 45 AMI patients. Mean HR was 73.33 bpm. A trend line comparing morning HRs over time showed a -0.206 bpm decrease per day. After adjusting for demographics and medications, dyslipidemia (+7.22 bpm, [95%CI]: 1.91 - 12.15), diabetes (+11.85 bpm, [95%CI]: 4.89 - 18.83), and left ventricular ejection fraction (LVEF) < 40% in patients over the age of 60 (+21.22 bpm, [95%CI]: 8.89 - 33.57) were significant predictors of elevated mean HR. The logistic model showed no significant predictors of HR over 90 bpm.

Conclusion: Patients recovering from AMI showed a small progressive decrease in mean HR over 30 days. Predictors of elevated HR 30 days post-discharge include dyslipidemia, diabetes, and LVEF < 40% in patients over the age of 60. No predictors were significantly associated with an increased odds ratio of a mean HR over 90 bpm.

David Mampre, MS 2

Mentor(s): Kaisorn Chaichana, MD
Department of Neurosurgery - Mayo Clinic, Jacksonville, Florida

Extending the resection beyond the contrast-enhancement for glioblastoma: feasibility, efficacy, and outcomes

Authors: David Mampre BS, Jeffrey Ehresman BS, Gabriel Pinilla-Monsalve MD, Maria Alejandra Gamboa Osorio MD, Alessandro Olivi MD, Alfredo Quinones-Hinojosa MD, Kaisorn Chaichana MD

Background: It is becoming well-established that increasing extent of resection with decreasing residual volume is associated with delayed recurrence and prolonged survival for patients with glioblastoma (GBM). These prior studies are based on evaluating the contrast-enhancing (CE) tumor and not the surrounding fluid attenuated inversion recovery (FLAIR) volume. It therefore remains unclear if resection beyond the CE portion of the tumor translates into improved outcomes for patients with GBM.

Methods: Adult patients who underwent resection of a primary glioblastoma at a tertiary care institution between January 1, 2007 and December 31, 2012 and underwent radiation and temozolomide chemotherapy were retrospectively reviewed. Pre and postoperative MRI images were measured for CE tumor and FLAIR volumes. Multivariate proportional hazards were used to assess associations with both time to recurrence and death after adjusting for age, performance status, and adjuvant therapy.

Results: 245 patients met the inclusion criteria. The median [IQR] preoperative CE and FLAIR tumor volumes were 31.9 [13.9–56.1] cm3 and 78.3 [44.7–115.6] cm3, respectively. Following surgery, the median [IQR] postoperative CE and FLAIR tumor volumes were 1.9 [0–7.1] cm3 and 59.7 [29.7–94.2] cm3, respect- ively. In multivariate analyses, the postoperative FLAIR volume was not associated with recurrence and/or survival (p>0.05). However, the postoperative CE tumor volume was significantly associated with both recurrence [HR (95%CI); 1.026 (1.005–1.048), p50.01] and survival [HR (95%CI); 1.027 (1.007–1.032), p50.001]. The postoperative FLAIR volume was also not associated with recurrence and/or survival among patients who underwent gross total resection of the CE portion of the tumor as well as those who underwent supratotal resection.

Conclusion: In this study, the volume of CE tumor remaining after resection is more important than FLAIR volume in regards to recurrence and survival for patients with GBM.

Derek Braverman, MS 2

Mentor(s): Matthew DeCamp, MD, PhD
Berman Institute of Bioethics

A Conceptual Analysis of "Clinical Significance" in Medical Care and Research

Authors: Derek Braverman BA

Background: The term "clinical significance" is frequently used in medical research and practice. However, ambiguity regarding the meaning of clinical significance can impair communication, for instance regarding the calculation of statistical power or the risks and benefits of interventions. The goal of this project was to conduct a clarifying conceptual analysis of clinical significance.

Methods: We conducted a narrative-style literature review to identify the range of settings in which clinical significance is used or defined. Then, we applied traditional philosophical methods to critically examine the assumptions, logic, and implications of these uses. From this process, we developed a novel conceptual analysis of clinical significance.

Results: Several types of definitions of clinical significance were identified, including ones tying the term to statistical significance as well as notions specific to clinical practice or medical research. Although these definitions are logically coherent and useful, they are highly contextual, creating a milieu in which different stakeholders employ the same term differently. However, these definitions of clinical significance cluster in two distinct categories, differing in their applications to either an individual patient or a population of patients. Importantly, it is this distinction that primarily underlies miscommunication about clinical significance. Based on this analysis, we argue that what is commonly called clinical significance should be understood as two separate concepts: individual-level clinical significance—understood as a difference in health status meaningful to an individual patient—and population-level clinical significance—understood as a difference in some outcome(s) large enough to alter medical practice.

Conclusion: As currently used, the term clinical significance is ambiguous. Clearly distinguishing the individual-level and population-level referents of clinical significance removes this ambiguity and has several implications for medical research and practice, not least of which include how power calculations are devised for much clinical research and the importance of statistical significance vis-à-vis patient care.

Garshasb Soroosh, MS 2

Mentor(s): Robert Siliciano, MD PhD
Department of Medicine

A potentially hypomorphic vif in an early treated patient with HIV: from bench to bedside and back

Authors: Garshasb Soroosh BS, Francesco Simonetti MD, Robert Siliciano MD PhD

Background: Background: The HIV-1 protein Vif evolved to counteract the human APOBEC3G (A3G), an antiviral enzyme that interferes with cDNA synthesis and leads to proviral G-to-A hypermutation. In spite of the established role of Vif in facilitating HIV-1 infection, there are few studies in vivo investigating whether HIV-1 infection with a deficient vif would impair disease progression.

Hypothesis: Patient 214, who had a low viral load and high CD4 count at diagnosis, has a hypomorphic vif. This results in a high frequency of hypermutated proviruses and decreased viral replicative capacity, consistent with the clinical presentation.

Methods: Methods: Single genome sequencing was performed on proviral DNA obtained from peripheral CD4+ T-cells and from viral culture ex vivo. Patient-derived vif mutants were tested for replicative fitness and frequency of A3G-induced hypermutation.

Results: Results: All vif sequences carry rare mutations (S116A and R132S) in the Cullin5 binding domain, a Vif region essential for A3G degradation. Consistent with this finding, a large fraction of proviruses from Patient 214 are hypermutated with a high frequency of G-to-A mutations. Quantitative viral outgrowth revealed delayed replication kinetics. These results led to the design of an assay to test the role of mutations in the Cullin5 binding domain of vif.

Conclusion: Conclusion: The study of a clinical isolate shows that mutations in the Cullin5 binding domain result in a hypomorphic Vif, and the corresponding loss of control of A3G generates the expected mutations in viruses that are produced. This may explain the partial control phenotype observed in Patient 214. Our results further elucidate the interplay between Vif and host proteins, and the contribution of innate mechanisms in controlling HIV-1 infection.

Hiroshi Aida, MS 2

Mentor(s): Uma Srikumaran, MD, MBA, MPH
Department of Orthopedic Surgery

The Effect of Implant Choice and Surgical Approach on Biceps Tenodesis Strength: A Systematic Review and Meta-Regression

Authors: Hiroshi Aida, BS, Brendan Shi, BS, and Uma Srikumaran, MD, MBA, MPH

Background: There has been a rise in the use of biceps tenodesis for the management of shoulder pain as well as known pathology in the long head of the biceps tendon (LHB). Despite its growing popularity, there remains a lack of consensus among clinical and biomechanical literature regarding both optimal implant choice (suture anchor vs. interference screw) and location of implant placement (suprapectoral vs. subpectoral). The goal of this meta-regression was to elucidate the effect of procedural parameters on the biomechanical performance of biceps tenodesis constructs.

Methods: We conducted a systematic search for biomechanical studies that measured the performance of biceps tenodesis repairs in human cadaveric specimens. Two independent reviewers extracted data from papers that met our inclusion criteria. A meta-regression was then performed on the pooled data set. Ultimate load and mode of failure were included as outcome variables and procedural parameters (fixation type, fixation site, implant size, number of implants and sutures used) were included as covariates.

Results: 25 biomechanical studies met our inclusion criteria, representing 494 total cadaveric specimens. Meta-regression revealed that using interference screws instead of suture anchors was associated with an 85 N increase in failure load (p=0.002). Furthermore, each additional suture used to attach the tendon to the implant was associated with a 53 N increase in failure load (p<0.001). While unadjusted analysis revealed that subpectoral repairs had a higher failure load than suprapectoral repairs (35 N, p=0.016), this relationship was not replicated in adjusted analysis.

Conclusion: These findings suggest that fixation with interference screws and increased suture number usage are significantly associated with biceps tenodesis strength. Although fixations using suture anchors show inferior failure load compared to those that use interference screws, incorporation of additional sutures may bolster their strength. Finally, we did not find a significant association between fixation site and repair strength.

Jane Long, MS 4

Mentor(s): Jacqueline Garonzik-Wang
Department of Surgery

Outcomes After Incompatible Living Donor Kidney Transplantation in Older Recipients

Authors: Jane Long BS, Kyle R. Jackson MD, Jennifer Motter MHS, Sunjae Bae KMD MPH, Allan Massie PhD, Madeleine Waldram BA, Karina Covarrubias BS, Jennifer Chen BA, Babak Orandi MD PhD, Niraj M. Desai MD, Dorry L. Segev MD PhD, Jacqueline Garonzik-Wang MD PhD

Background: Older individuals are the fastest-growing sub-group of transplant candidates and may increasingly consider incompatible living donor kidney transplantation (IKT). To inform appropriate risk counseling, we sought to quantify post-IKT outcomes in older recipients.

Methods: Methods: Using a 25-center SRTR-linked IKT cohort, we compared post-transplant outcomes of 222 older (age≥60) to 1136 younger (age<60) recipients. We analyzed mortality and death-censored graft survival (DCGS) using Cox regression, acute rejection (AR) and delayed graft function (DGF) using logistic regression, and length of stay (LOS) using negative binomial regression, adjusting for recipient characteristics. We also compared post-transplant outcomes of older IKT to compatible living donor kidney transplant (CLDKT) recipients.

Results: Results: Post-IKT, 1 and 5-year patient survival was lower (93.7% vs 96.2% and 58.11% vs 73.6%, p<0.001) and 1 and 5-year DCGS was higher (97.8% vs 94.5% and 85.6% vs 68.8%, p<0.001) in older recipients. After adjustment, older recipients had a 1.84x increased risk of mortality (adjusted Hazard Ratio [aHR]:1.351.842.51, p<0.001), were 2.33x less likely to develop death censored graft failure (DCGF) (aHR:0.25 0.43 0.80, p=0.007), and were 1.85 less likely to develop AR (adjusted Odds Ratio [aOR]:0.36 0.54 0.82, p=0.004), with no differences in DGF (aOR:0.47 1.09 2.56, p=0.8) or LOS (adjusted Incidence Rate Ratio [aIRR]:0.96 1.09 1.22, p=0.2). Compared to CLDKT recipients, older IKT recipients were 3.32x more likely to develop AR (aOR:1.58 3.32 6.96, p=0.001) and 1.53x more likely to have a longer LOS (aIRR:1.15 1.53 2.04, p=0.004), but had an equivalent risk of mortality, DCGF, and DGF.

Conclusion: Post-IKT, older recipients have worse survival, lower rates of DCGF and AR, and similar DGF and LOS compared to younger recipients. However, they have equivalent survival and DCGF to older CLDKT recipients and are more likely to develop AR and have longer LOS. These findings should be considered when counseling older recipients about IKT.

Jonlin Chen, MS 2

Mentor(s): Lisa Ishii, MD
Department of Otolaryngology

From Selfie to Surgery: Impacts of Self-Worth, Social Media, and Photo Editing on Cosmetic Surgery Attitudes

Authors: Jonlin Chen BA, Masaru Ishii MD, PhD, Lisa E. Ishii MD, MHS

Background: We are constantly surrounded by social media and the need to present our best, often digitally enhanced, self to the public. Photo manipulation tools including Snapchat filters are increasingly popular sources of inspiration for those seeking cosmetic surgery. Despite this, little research exists exploring social media as a motivator for cosmetic surgery. To address this gap, our study aimed to quantify how social media and photo editing alter attitudes toward cosmetic surgery.

Methods: We conducted a population-based survey study from July to September 2018.
Social media and photo editing usage was determined from the participant's self-reported time spent on social media, breadth of applications used, number of selfies uploaded, and time spent editing photos. The previously validated Acceptance of Cosmetic Surgery Scale rated each participant's attitudes toward surgery. Regression analysis and structural equation modeling established the effects of self-esteem, social media, and photo editing on surgical attitudes.

Results: 252 survey participants (mean age 24.7, 73% female) successfully completed the study. Participants with self-worth more contingent upon appearance had higher acceptance of cosmetic surgery (coefficient 0.36, 95% CI: 0.22, 0.50). Social media investment had a positive effect on consideration of surgery (coefficient 0.35, 95% CI: 0.04, 0.66). Planned hypothesis testing showed a higher acceptance of cosmetic surgery in Tinder (mean score 4.16 of 7, 95% CI: -1.23, -0.34), Snapchat (3.55, 95% CI: -0.70, -0.07), and/or Instagram filter users (3.40, 95% CI: -0.76, -0.01).

Conclusion: Our data suggests that higher investment in certain social media and photo editing platforms correlated with increased acceptance of surgery. This study can help guide future patient-physician discussions regarding cosmetic surgery outcomes, expectations, and patient candidacy.

Joseph Broderick, MS 2

Mentor(s): Koliastsos, MD
Department of Pathology

SARM1 knockout protection of the corticospinal tract and optic nerve

Authors: Joseph Broderick BA MA, Nikolaos Ziogas MD, Vassilis E. Koliatsos MD MBA

Background: Traumatic axonal injury (TAI) is an irreversible degenerative process of neuronal axons triggered by traumatic brain injury (TBI). TAI is the most frequently found pathology associated with TBI and inhibiting its progression could reduce damage to the brain. To this end, the SARM1 enzyme has been identified in in vitro assays as a pivotal enzyme in the TAI enzyme cascade. Inhibiting SARM1 could protect neuronal axons from degeneration following TBI.

Methods: We ablated SARM1 in 5 transgenic mice and administered a standardized concussive blow to induce TAI. We then used silver staining and stereography to identify degraded axons at 72 hours post injury in the cortical spinal and optic tracts. We compared these results to 5 wild type mice in a control group to determine the degree of protection.

Results: In wild type mice, 44% of axons in the corticospinal tract (CST) had degenerative changes after TAI while 11% of axons in the CST of the SARM1 mice showed such changes ($p < 0.0001$). No differences were seen in the optic tract of the two mouse strains.

Conclusion: Our data suggest that elimination of SARM1 confers protection from TAI in the CST, but not the optic tract. Further studies on the longevity of the protection should be performed, and the introduction of therapeutic agents inhibiting SARM1 should be tested. Finally, the potential difference in TAI mechanisms between the CST and optic tract warrants investigation.

Joshua Doyle, MS 2

Mentor(s): Alex Szalay, PhD
Department of Physics and Astronomy

Whole-slide registration for studying the immune tumor microenvironment

Authors: Joshua Doyle MS, Janis Taube MD MSc, Alex Szalay PhD

Background: Immunotherapies have revolutionized how we treat a number of cancer types. However, it is still not clear why only a fraction of patients and only some tumor types respond to therapy. Recent discoveries raise the possibility that the spatial organization of immune cells within the tumor microenvironment (TME) may be key in predicting patient outcomes. Promising technologies for studying spatial organization include microscopy, particularly immunolabeling. Emerging technologies for multispectral, multiplex immunofluorescence (MIF) are limited in that they can only highlight 6 immunoactive markers on a given slide, yet there are >25 immunoactive markers of interest that could potentially be targeted.

Methods: To overcome this limitation, chromogenic immunohistochemistry (IHC) can be performed on top of the MIF on the same slide, or multiple sequential slides can be stained and overlaid. This produces a set of images that, when registered, increases the number of antigens that can be targeted, imaged, and co-localized beyond the number possible with any one system independently. Precise registration and cell segmentation are critical when quantifying antigens at cell-to-cell interfaces and becomes challenging when unique antigens are imaged in sequential slides.

Results: Using mutual information as a registration criterion, we developed computational methods for registering 8-band MIF with bright-field immunohistochemical (IHC) stained images on the same slide and MIF with MIF on sequential slides.

Conclusion: In using this approach, multimodal whole-slide registration can increase information density and provide greater insight into cellular processes. This will be key in developing the next generation of biomarkers for immunotherapy.

Katie Tai, MS 2

Mentor(s): Adam Levin, MD
Department of Orthopedic Oncology

Renal cell carcinoma metastasized to bone responds differently than soft tissue metastases to receptor tyrosine kinase inhibitors (RTKIs) and immunotherapy (PD-1/PD-L1)

Authors: Katherine Tai BA, Jad El Abiad MD, Adam Levin MD

Background: Checkpoint inhibitors (PD-1/PD-L1 inhibitors) and targeted therapies (RTKIs) have drastically changed the standard of care in metastatic renal cell carcinoma (RCC). However, anecdotal evidence suggests these therapies are less effective for treating bone metastases than soft tissue metastases. This study aimed to evaluate the differential effect of treatment on bone versus soft tissue metastases from renal cell carcinoma.

Methods: The Cancer Registry database was queried for RCC patients treated at Johns Hopkins Hospital from 1997-2017 (n = 2453). 85 patients were identified who developed both bone and soft tissue metastatic disease and were treated with RTKIs or PD-1 inhibitors. The extent of metastasis was quantified at the time of therapy initiation, 3 months, 6 months, and 1 year time points. Changes in disease status from baseline were categorized as partial response (PR), complete response (CR), stable (S), or progressive disease (PD) based upon RECISTv1.1 and MDA criteria for soft tissue and bone metastases, respectively. Bone and soft tissue response to treatment were compared via Chi-squared tests. Paired t-tests and McNemar's tests are also planned.

Results: Chi-squared tests were completed on an initial subset of patients (n=40). A significantly lower proportion of osseous than soft tissue metastatic disease demonstrated progression at the 6 mo. (18% vs. 45%, $p = 0.02$), and 1 yr. time points (6% vs. 50%, $p = 0.01$). Additionally, a significantly higher proportion of osseous disease demonstrated stable disease at 3 mo. (75% vs. 47%, $p = 0.05$), 6 mo. (68% vs. 41%, $p = 0.04$), and 1 yr. time points (63% vs. 29%). No significant difference was shown in partial or complete response to therapy.

Conclusion: Although further analysis is pending, initial results show that contrary to anecdotal evidence, osseous metastases may respond more favorably than soft tissue metastases to PD-1/PD-L1 and / or RTKI treatment.

Kyla Cordrey, MS 2

Mentor(s): Melissa Camp, MD & Jacqueline Garzonik Wang, MD
ERGOT Transplant Lab & Surgical Oncology

Racial differences in cancer mortality for kidney transplant recipients

Authors: Kyla Cordrey BA, Jennifer Motter BA MHS, Kyle Jackson MD, Amber Kernodle MD, Melissa Camp MD MPH, Tanjala Purnell PhD, Dorry Segev MD PhD, Jacqueline Garonzik Wang MD PhD

Background: Cancer is the second leading cause of post-transplant mortality. Since racial disparities have been reported in all aspects of transplant care, we sought to determine whether these disparities extend to post-transplant cancer mortality.

Methods: We studied 61, 398 kidney recipients transplanted between 1999 and 2016 using data from USRDS and SRTR. To determine cancer incidence, we used 528 ICD-9 codes for one of 21 cancer types. Patients were excluded if they had a previous history of cancer. We used multivariable Cox regression, treating cancer as a time-varying exposure to determine the association between race and post-transplant cancer mortality.

Results: Among 61,398 transplant recipients, 8,883 (14.5%) developed post-transplant cancer. The most common cancers were cervical (2.5%), kidney (2.3%), and prostate (2.2%) (Figure 1). Overall, transplant recipients with a post-transplant cancer had a 3.93-fold increased risk of mortality compared to transplant recipients who did not develop cancer (adjusted Hazard Ratio (aHR): $_{3.75}3.92_{4.10}$, p< 0.001); however, this relationship varied by race (Table 1). White recipients who developed cancer had a higher adjusted hazard ratio for mortality than all other racial/ethnic groups: Asian (aHR: $_{2.41}3.28_{4.43}$, p for interaction=0.03), Hispanic/Latino (aHR: $_{2.91}3.39_{3.94}$, p for interaction<0.001), and Black/African American (aHR: $_{2.64}2.89_{3.16}$, p for interaction<0.001).

Conclusion: While mortality was increased for recipients who developed post-transplant cancer, this risk was even greater for White recipients compared to other racial groups. Additional work is necessary to identify causes of these differences and how best to mitigate them.

Lucy Nam, MS 2

Mentor(s): Narutoshi Hibino MD PhD
Division of Cardiac Surgery

A Novel Method for Generating Cardiac Organoids to Model Cardiovascular Development and Disease

Authors: Lucy L. Nam BA, Matthew Miyamoto BA, Suraj Kannan BA, Narutoshi Hibino MD PhD, Chulan Kwon PhD, Peter Andersen PhD

Background: Several cardiac malformations are restricted to regions arising from two populations of cardiac progenitors known as the first or second heart field (FHF and SHF). The pathogenesis of these abnormalities is largely unexplored due to the inability to obtain pediatric tissue. Alternatively, pluripotent stem cell (PSC)-based cardiac organoids provide a platform to study heart development and present promising avenues to develop PSC-based therapeutics. We report a novel and reproducible method for generating precardiac organoids that recapitulate chamber-specific formation and facilitate high throughput analysis of heart development.

Methods: A dual-fluorescent reporter system was created to monitor heart field specification in vitro in PSC-derived cardiac progenitor cells. We generated precardiac organoids in 96 U-well plates and monitored the spatiotemporal formation of the FHF and SHF. Multi-well timelapse imaging and imaging analysis software were utilized to rapidly quantify FHF/SHF formation. Flow cytometry, qPCR and immunofluorescence were used to validate that our generated organoids recapitulated heart field formation.

Results: We developed a cardiac organoid system wherein the FHF is induced in the periphery and the SHF towards the center, demonstrating spatially organized heart field formation with minimal variability (coefficient of variation of 30% vs 50% in previous methods). Our approach enables rapid quantification by high-resolution live cell imaging, as confirmed by concurrent flow cytometry analysis. In an effort to selectively regulate chamber-specific development in the organoid system, we identified the small molecule CHIR99021 and the canonical Wnt agonist to effectively induce formation of SHF progenitors (CHIR RFP 16% vs 3% in control, Wnt RFP 77% vs 3% in control).

Conclusion: We developed a novel PSC-based cardiac organoid system to monitor heart field and chamber-specific development by live-imaging microscopy and flow cytometry analyses. This can be used to model disease biology in patient-derived PSCs and provide a molecular basis for development of improved targeted therapeutics in the clinic.

Lukas Mees, MS 2

Mentor(s): David Friedman, MD
Wilmer Eye Institute, Department of Ophthalmology

Validation of a head mounted virtual reality visual field screening device

Authors: Lukas Mees BA, Swati Upadhyaya MD, Pavan Kumar MD, Sandal Kotowala BS, Rengaraj Venkatesh MD, David Friedman MD

Glaucoma is the leading cause of irreversible blindness in the world. Visual field loss screening is a key part of detection and management of the condition. The current gold standard, the Humphrey visual field analyser (HFA), is large, expensive and can be uncomfortable for some patients. The current study investigated the C3 fields analyser (CFA), a virtual reality head mounted visual field analyzing device, as a possible replacement for glaucoma screening. The CFA was administered using a suprathreshold algorithm and compared to the 24-2 SITA HFA exam for 157 patients in the Pondicherry Aravind Eye Hospital. Patients were diagnosed as control or glaucoma by blinded researchers. The CFA was 38% sensitive and 91% specific for matching HFA results. The number of stimuli missed on the CFA correlated well with HFA mean deviation ($r = 0.62$, $P <0.001$), but less strongly with pattern standard deviation ($r = 0.36$, $P <0.001$). The area under the receiving operator characteristic curve (AROC) was 0.77 ± 0.06 for mild glaucoma (HFA mean deviation $\geq$ -6) and 0.86 ± 0.04 for moderate-advanced glaucoma (HFA mean deviation < -6). Each individual missed stimulus on the CFA had an average positive predictive value of 0.76 for identifying glaucoma. While it was not sensitive towards the gold standard (HFA), the CFA was still effective at identifying glaucoma subjects as shown by the robust AROC and positive predictive value. More studies are needed to improve sensitivity, to identify optimal stimulus intensity for screening and to develop a full threshold algorithm.

Megan Hunt, MS 2

Mentor(s): Dan Choi, MD
Division of Cardiac Surgery

Are We Feeding Extracorporeal Membrane Oxygenation (ECMO) Patients?: A Prospective Observational Study

Authors: Megan F Hunt, BS; Alejandro Suarez Pierre, MD; Xun Zhou, MD; Cecillia Lui, MD; Brian D. Lo, BS; Jessica Beattie, MPH, RD; Patricia M Brown, RD-AP; Ahmet Kilic, MD; Glenn J Whitman, MD; Chun W Choi, MD

Background: Approximately 6,000 patients are treated with extracorporeal membrane oxygenation (ECMO) annually worldwide. Despite this growing number, there is a paucity of data regarding their nutritional management.

Methods: We performed a prospective, observational study of ECMO and non-ECMO post-cardiotomy shock patients at our institution. Over a 3.5 year study period, we identified 58 ECMO patients and 257 non-ECMO patients. We further stratified ECMO patients for adequate nutrition ($\geq$ 50% caloric goal met, n=14) and inadequate (<50%, n=46). We identified type, amount, duration and disruption of nutritional delivery for each cohort and reported mortality, length of stay, discharge location, and adverse complications.

Results: ECMO patients met less of their caloric (31% vs. 42%, p=0.009) and protein goals (34% vs. 59%, p<0.001) compared to non-ECMO patients. Tube feeds were administered more slowly (28 vs 38ml/hr, p<0.001) and held for longer (7.8 vs. 4.6 hrs/day, p<0.001) in ECMO patients due to procedures (54.4% vs. 48.1%, p=0.061), high dose pressors (13.4% vs. 5.0%, p<0.001), and high residual (5.9% vs. 2.6%, p=0.010). Type of ECMO, veno-arterial (VA)(n= 40) vs. veno-venous (VV)(n=18), and ECMO cannulation, central (n=27) vs. peripheral (n=31), did not impact nutritional support. Gastric ulcers were more common in ECMO patients (10.3% vs 1.6%, p=0.003), but rates of ischemic bowel (1.7% vs. 3.2%) or diarrhea (29.3% vs 23.8%) were similar. Adequately fed ECMO patients had lower 30-day mortality (21.4% vs. 78.3%, p<0.001), were more likely to be discharged home (28.6% vs. 8.7%, p=0.003), were more likely to avoid readmission (50 vs. 13%, p=0.003), but were on ECMO longer (17.79 vs. 7.76 days, p<0.001).

Conclusion: ECMO patients received less nutrition support in protein and caloric intake compared to non-ECMO patients, because of decreased rate of tube feeds, procedure holds, and high pressors. Adequate nutrition improves outcomes in ECMO patients. Future research into optimal nutrition support and outcomes is needed.

Michael Ou, MS 2

Mentor(s): Mahmoud Malas, MD
Department of Vascular Surgery

Outcomes following Eversion vs. Conventional Endarterectomy in the Vascular Quality Initiative Database

Authors: Michael Tianhao Ou BS, Hanaa Dakour Aridi MD, Satinderjit Locham MD, Joseph Schneider MD, Mahmoud Malas MD

Background: Carotid endarterectomy is a surgical technique that reduces the risk of stroke by correcting carotid artery stenosis. However, there is no clear agreement on the optimal technique. The purpose of this study is to compare the postoperative outcomes and durability of conventional vs. eversion endarterectomy. Both of these surgeries may be performed with or without patch angioplasty, a technique that introduces a synthetic patch.

Methods: A retrospective review of the Vascular Quality Initiative (VQI) database between 2003 and 2018 was performed. Multivariable logistic and Cox-regression analysis were used to compare risk-adjusted 2-year outcomes (stroke, death, and high-grade restenosis) between conventional vs. eversion endarterectomy.

Results: A total of 95,726 patients were included, with a mean age of 71 years and 91% of Caucasian race. Conventional and eversion endarterectomy showed no significant differences in adjusted 2-year stroke/death (HR:0.94, 95%CI: 0.82-1.10) and 2-year high-grade restenosis (HR:0.92, 95%CI: 0.76-1.11), provided that conventional endarterectomy was performed with patch angioplasty. However, when comparing eversion endarterectomy to non-patched conventional endarterectomy, eversion endarterectomy was associated with lower hazard ratios of stroke/death (HR:0.78, 95%CI: 0.61-0.99) at 2 years of follow-up.

Conclusion: We found that conventional and eversion endarterectomy are similar in efficacy and safety at 2-years follow up, as long as conventional endarterectomy is performed with patch angioplasty. These findings suggest that surgeons may choose the technique they are most comfortable with, but should use patch angioplasty when possible if choosing to perform conventional endarterectomy.

Mohamud Qadi, MS 4

Mentor(s): Dr. Fawaz Al Ammary
Department of Medicine - Nephrology

The Decline In Live Kidney Donors In The United States

Authors: Mohamud A.Qadi, MPH (1), Fawaz Al Ammary, MD (1), Xun Luo MD, MPH (1), Abimereki D. Muzaale, MD, MPH (1), Allan B. Massie, PhD (1), Daniel C. Brennan, MD (1), Alexander C. Wiseman, MD (2), and Dorry L. Segev, MD, PhD (1)

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The number of live kidney donors has declined since 2005. This decline parallels the evolving knowledge of risk for biologically related, black, and younger donors. To responsibly promote donation, we sought to identify declining low-risk donor subgroups that might serve as targets for future interventions. We analyzed a national registry of 77,427 kidney donors and quantified the change in number of donors per 5-year increment from 2005-2017 using Poisson regression stratified by donor/recipient relationship and race/ethnicity. Among biologically related donors, there was a 3-29% decline in white donors of all ages, 12-31% decline in black donors of all ages, 15-18% decline in younger (<50 years) Hispanic donors, but a 10% increase in older ($\geq$50 years) Hispanic donors. Conversely, among unrelated donors, there was a 4-24% increase in white donors of all ages, 16-46% increase in Hispanic donors of all ages, 34% increase in older black donors, but no significant increase for younger black donors. Unlike unrelated donors, related donors were less likely to donate in recent years across race/ethnicity. While this decline might be understandable for related younger donors, it is less understandable for lower-risk related older donors. Biologically related older individuals are potential targets for interventions to promote donation.

Monica Meeks, MS 2

Mentor(s): John Sampson, MD
Department of Anesthesia and Critical Care Medicine

Sex-Based Differences in Patients Receiving Orthopedic Surgery at a Charitable Ambulatory Surgery Center in Honduras

Authors: Monica Meeks BA, Darren Eblovi MD, Merlin Antúnez MD, Kate Clitheroe MPH, John Sampson MD

Background: Sex-based disparities in surgical care in low-and-middle-income countries (LMICs) have not been well described. This study sought to examine gender differences in orthopedic surgery utilization at a charitable surgery center in Honduras. We hypothesized that women who receive orthopedic surgery present at a more advanced stage of disease.

Methods: A retrospective analysis was conducted for a sample of patients that received orthopedic surgery at the Holy Family Surgery Center (HFSC) in Honduras in 2017 (n = 343). Chi-squared tests were performed for descriptive statistics. Multivariate linear regressions were used to assess the effect of sex on preoperative disability (POD), as measured by World Health Organization Disability Assessment Schedule 2.0, and time spent with injury before surgery.

Results: Patients receiving orthopedic surgeries were more likely to be male (39.4% vs. 60.6%, $p < 0.001$). After adjusting for age, income, education level, and occupation, female orthopedic patients presented with a higher POD than males (ß= 0.11, $p < 0.001$). Additionally, females presented with higher POD for fracture repairs (ß = 0.153, $p = 0.041$), arthroscopy (ß = 0.157, $p = 0.013$), upper extremity procedures (ß = 0.214, $p = 0.003$), hand procedures (ß = 0.346, $p = 0.001$) and procedures indicated for trauma (ß = 0.11, $p = 0.008$). There was no overall significant difference in injury time, although females spent less time with injury before arthroplasty (ß = -70.6 months, $p = 0.014$), knee procedures (ß = -39.84 months, $p = 0.01$) and procedures for degenerative diseases (ß = -49.94 months, $p = 0.015$).

Conclusion: Female patients at HFSC received fewer orthopedic surgeries. Females receiving surgery reported more severe pre-operative disability than males for many types of procedures. More research is needed to understand cultural and biopsychosocial factors that may affect women's abilities to access orthopedic surgical care in LMICs such as Honduras.

Nanki Hura, MS 2

Mentor(s): Jonathan Walsh, MD
Department of Otolaryngology

Progression of Hearing Loss and Cochlear Implantation in Large Vestibular Aqueduct Syndrome

Authors: Nanki Hura BS, Matthew Stewart MD Ph.D, Jonathan Walsh MD

Background: Large vestibular aqueduct syndrome (LVAS) is a congenital inner ear malformation that commonly results in sensorineural hearing loss (SNHL) and cochlear implantation (CI). Though LVAS accounts for approximately 15% of pediatric SNHL, little is known regarding the rate and severity of SNHL progression in these patients. We sought to determine the relationship between patient age and the rate of decline in SNHL for LVAS patients receiving CI.

Methods: We performed a retrospective chart review of LVAS patients at our institution from 2015-2018 using ICD-10 "large vestibular aqueduct syndrome," and through identifying patients with CI who were diagnosed with LVAS between 2000-2014. For each patient, demographic information, surgical history, speech perception data, and audiometric data were collected. CI candidacy was approximated using a pure tone average (PTA) HL threshold of 70 decibels.

Results: Of the 112 patients with LVAS analyzed (55.4% female, average age 19, age range 2-62), there were 97 patients with bilateral LVAS, 7 with unilateral LVAS, and 8 unspecified in the chart. Forty-three patients had bilateral implants, 59 had unilateral implants, and 10 were not implanted/unspecified. The mean age at first implant was 8.52 years old [6.75, 10.29] and the mean age at second implant was 12.05 years old [8.21, 15.89], with the mean time between implants being 4.20 years [2.88, 5.52]. LVAS patients reached PTA HL threshold of 70 decibels at a mean age of 5.16 years old for the "worse ear," and at 9.86 years old for the "better ear."

Conclusion: On average, LVAS patients have a steep decline in hearing and approach CI candidacy within the first 5 to 10 years of life, but may experience delays in implantation. There is a moderate interval of time between bilateral CI. These data may assist with patient counseling and surgical anticipation in order to minimize delays in hearing rehabilitation.

Nathan Yueh, MS 2

Mentor(s): Robert Shochet, MD and Emily Frosch, MD
Humanities, Ethics, and Art

Saving Face: A Medical Student's Journey Through Depression

Authors: Nathan Yueh BA, Emily Frosch MD, Robert Shochet MD

Background: Worldwide, more than one quarter of medical students experience depressive symptoms, yet only a small fraction of those seek treatment. Many factors, such as stigma and fear of career repercussions, prevent students from seeking help. Asians are overrepresented in the medical school population compared to the general US population, yet, are also less likely to utilize mental health services compared to other ethnic groups. The goal of this project was to write a feature-length screenplay depicting the experience of a Chinese-American medical student battling depression.

Methods: To develop the story, the author studied the prevalence and causes of depression in medical school, and the perception of mental illness in Chinese communities. The author also read several firsthand accounts of young adults suffering from depression, from medical and non-medical, Chinese and non-Chinese individuals. Finally, the author drew on his own medical school experience and Chinese family background. Drafts of the screenplay were sent to three professional screenwriters for feedback. The author also consulted with two psychiatrists at Johns Hopkins to address medical accuracy and safety considerations. Several rounds of revision and feedback were undertaken over six months addressing both the medical and narrative perspectives.

Results: A 113-page screenplay was written about Amy Chan, a fictional first year medical student. Amy struggles to maintain her outer image of perfection despite her falling grades and depressive symptoms. Both the medical culture of "aequanimitas" and the Chinese concept of "saving face" prevent her from seeking help, until a suicide attempt forces her to confront her illness.

Conclusion: The author will pursue production of this screenplay, which has the potential to reach a wide audience, including non-medical viewers. The hope is that insights and lessons from this story may raise awareness about mental illness in medical students and inform the development of interventions to address this issue.

Neha Anand, MS 2

Mentor(s): David Bishai, MD, PhD
Population, Family, and Reproductive Health

Estimating the Effect of County Spending on Life Expectancy through Structural Equation Modeling

Authors: Neha Anand, BA, Carolina Cardona, MHS, Natalia Alfonso, MS, JP Leider, PhD, Mac MacCullough, PhD, MPH, Beth Resnick, DrPH, David Bishai, MD, PhD

Background: Studies have identified the impact of public health and social service spending on health outcomes in the US, suggesting that investments to improve health should not be limited to the health care sector. The following study analyzes county spending across several sectors to understand how county spending affects life expectancy.

Methods: We used 2007 annual spending data from the Census of Governments, a survey conducted every five years to collect tax, revenue, and expenditure data from every US county government. Through structural equation modeling, we classified counties' spending into "social," "infrastructure," or "law and order" indices. These metrics are based on actual 2007 quintiles of per capita county direct expenditure in 14 sectors. The goal of the structural equation model was to understand how each county's spending patterns in 2007 affected county projected life expectancy in 2010. To control for county economic status, we included a latent variable affecting life expectancy composed of poverty, unemployment, and total local government revenue.

Results: Constraining the effect of the "infrastructure" spending index to 1, a "social" spending index significantly increased life expectancy by 0.62 and a "law and order" spending index significantly decreased life expectancy by 0.26. This may suggest that counties that prioritize investments in infrastructure spending or social spending have a positive impact on their population's health that leads to higher life expectancy three years in the future compared to counties that focus on law and order spending.

Conclusion: The structural equation model found that counties with an "infrastructure" or "social spending" index in 2007 had significantly greater gains in life expectancy in 2010 than those with a "law and order" index in 2007. This may inform how county governments can redirect spending to benefit the health of constituents by investing more in infrastructure and social spending relative to law and order.

Nicholas Siegel, MS 2

Mentor(s): Adam Levin, MD
Department of Orthopedic Surgery

Evaluating Lymph Node Involvement in Extremity Fungating Soft Tissue Sarcomas as a Sign of Early Metastasis

Authors: Nicholas Siegel BS, Jad el Abiad MD, Adam Levin MD

Background: Soft-tissue sarcomas are rare malignancies and a small subset of these malignancies fungate through the overlying skin. Fungated tumors are inherently colonized with bacteria, potentially opening lymphatic channels to promote tumor propagation to lymph nodes. Many patients with fungation in the setting of soft tissue sarcomas have enlarged draining lymph nodes, though it is unclear whether these represent nodal metastasis versus an inflammatory nodal reaction. We sought to evaluate lymph nodes in the setting of fungated extremity soft tissue sarcomas.

Methods: From a Cancer Registry Database, we identified all soft tissue sarcomas between 1997-2017. We screened patients for fungating soft tissue sarcomas of the extremities. We then performed retrospective chart review of lymph node presentation, enlargement, and pathology. Patients were excluded if their lymph node pathology was not able to be determined either clinically or histologically.

Results: Fungating sarcomas of the extremities were found in 2.87% (30/1045) of patients screened. One patient was excluded from further study as their lymph node pathology could not be confirmed. Overall, 75.8% (22/29) were adjudicated to not have any lymph node metastasis. In addition, 10.3% (3/29) developed lymph node metastasis prior to tumor fungation, and 13.8% (4/29) developed lymph node metastasis following tumor fungation. Out of the eight patients who developed lymphadenopathy following tumor fungation, 50% (4/8) were confirmed to be nodal metastasis and 50% (4/8) were reactive inflammation.

Conclusion: Our findings indicate an equal likelihood of enlarged nodes in the setting of fungating sarcomas being reactive inflammation versus nodal metastasis. Additionally, the similar likelihood of developing nodal metastasis in pre or post fungating tumors indicates metastasis is most likely related to the underlying malignancy rather than tumor fungation. As such, our findings corroborate the difficult clinical decision physicians face in elucidating the pathology of enlarged draining nodes and deciding future treatment plans.

Pauline Huynh, MS 3

Mentor(s): Lisa Ishii, MD MHS; Masaru Ishii, MD PhD
Department of Otolaryngology-Head & Neck Surgery

Exploring Gaze Patterns of the Face in Profile View Before and After Rhytidectomy

Authors: Pauline P. Huynh, BA; Masaru Ishii, MD, PhD; Halley M. Darrach, BS; David Liao, BS; Michelle Juarez, BS; Nicholas Fung, BS; Kristin L. Bater, BA; Jason C. Nellis, MD; Patrick J. Byrne, MD, MBA; Kofi D.O. Boahene, MD; Lisa E. Ishii, MD, MHS

Background: While gaze patterns of the face in frontal view have been widely studied, whether there is a similar pattern when viewing faces in profile view has not been established. The effect of rhytidectomy on gaze patterns of the face in profile view is also unknown.

Methods: Blinded casual observers viewed images of 16 patient faces before and after rhytidectomy. Faces were graded using Facial Laxity Rating (FLR) Scale. To prevent a priming bias, observers viewed either a pre- or post-rhytidectomy photo of each patient, but not both. Observers gazed freely upon profile face images as an infrared eye-tracking monitor recorded their eye movements and fixations in real-time. Multivariate Hotelling's analysis followed by planned post-hypothesis testing was used to compare fixation durations for selected AOIs, including the eyes-nose-cheek (ENC) region, the lower face, and the neck, before and after rhytidectomy.

Results: 80 observers (mean age 24.8 years, 52.5% female) successfully completed the eye-tracking experiment. Most of their attention was directed towards the (in seconds [95% CI]) eyes (2.78 [2.62, 2.94]), nose (0.96 [0.86, 1.06]), cheek (0.73 [0.66, 0.81]), suggesting a presence of a different "central triangle." On multivariate analysis, there were significant differences in the distribution of attention between pre- and post-rhytidectomy faces ($T2=9.0232$, $F(3, 636)=2.9983$, $p<0.05$). On post-hypothesis testing, observers attended significantly less to the lower face ($p<0.05$). There was no significant difference in time spent on the neck or the total time spent on the ENC region between the two groups.

Conclusion: Gaze patterns of the face in profile view appear to differ from those of the face in frontal view, with more focus on the cheek rather than the mouth. Rhytidectomy reduces attention to the lower face, potentially validating patient concerns of attentional distraction.

Robert Chu, MS 2

Mentor(s): K. Ranh Voong, MD
Department of Radiation Oncology and Molecular Radiation Sciences

The Radiologic Response of Chemotherapy Alone versus Radiation and Chemotherapy in the Treatment of Thymic Epithelial Tumors

Authors: Robert F. Chu, B.A.; Amira Hussien, M.D.; Q. Kay Li, M.D., Ph.D.; Jiangxia Wang, M.S.; Adam Ferro, M.D.; Russell K. Hales, M.D.; Richard Battafarano M.D., Ph.D.; David Ettinger, M.D.; K. Ranh Voong, M.D., MPH

Background: When tumor cytoreduction is needed prior to resection in thymic epithelial tumors (TETs), it is unknown whether chemotherapy alone or a combination of radiation and chemotherapy (chemoRT) leads to better responses. We investigate radiological responses following chemotherapy as compared to chemoRT, as a proxy of tumor cytoreduction.

Methods: TETs treated at our institution between January 2007 and July 2018 were identified. Inclusion criteria included: (1) receipt of chemotherapy with or without radiation as initial cytoreductive therapy, (2) available pre- and post-treatment CT scans. Patient demographic information, tumor features, treatments, and outcomes were correlated. Groups were compared with Student's t and Wilcoxon rank-sum tests. Mixed-effects linear regression was used to compare changes in tumor size between the two treatment groups, adjusting for baseline tumor dimensions, patient age, and tumor histology. Survival was evaluated using Cox multivariate regression.

Results: 24 patients met inclusion criteria (chemotherapy: n=12, 50%; chemoRT: n=12, 50%). Median imaging follow-up time was 15 months (range: 0, 86). The median baseline tumor volume was 187.1 cc (range 28.7, 653.6); median diameter was 8.5 cm (range 4.5, 14.3). Multivariate regression showed improved radiologic response in patients treated with chemoRT as compared to chemotherapy alone, controlling for baseline tumor dimensions, patient age, and tumor histology: volume decreased by 47.0 cc more (p<0.001) and mean diameter decreased by 0.8 cm more (p=0.03). Patients who had already undergone chemotherapy demonstrated additional tumor shrinkage (median volume decrease=42.3%, p=0.03; median diameter decrease=13.0%, p=0.049) following subsequent radiation or chemoradiation. Surgical resection was associated with improved overall survival, controlling for age and tumor stage (hazard ratio=0.15, p=0.03). No significant association between presurgical treatment regimen and survival was found.

Conclusion: The combination of radiation and chemotherapy may be a viable alternative to chemotherapy alone in TETs requiring cytoreduction, especially in patients with poor response to initial chemotherapy.

Sam Erlinger, MS 3

Mentor(s): David Dowdy, MD PhD
Department of Epidemiology, Bloomberg School of Public Health

Tuberculosis patients with higher levels of poverty face equal or greater costs of illness

Authors: Sam Erlinger BA, N. Stracker, C. Hanrahan PhD, A. Nonyane PhD, L. Mmolawa, R. Tampi, A. Tucker, N. West, L. Lebina MBBS, N.A. Martinson MBBS, David Dowdy MD PhD

Background: Costs to patients suffering from tuberculosis (TB) can greatly affect patient wellbeing and impede access to care. These effects may be most strongly felt in patients with fewer resources, but such patients may also experience lower costs of care-seeking and treatment (for example, cheaper transportation taken, fewer care-seeking attempts before accessing public-sector clinics, fewer wages lost). Here we investigate how TB costs vary with poverty measured by a multidimensional poverty index and income.

Methods: We performed cross-sectional interviews of consecutive patients with TB across 56 public clinics in Limpopo Province, South Africa. Total TB episode costs were estimated from self-reported income, travel costs, and care-seeking time. Poverty was assessed using the South African Multidimensional Poverty Index (SAMPI) deprivation score, a 12-item household-level index, with higher scores indicating greater poverty. We used multivariable linear regression to evaluate this association between poverty and TB costs adjusting for age, sex, HIV status and travel time.

Results: Among 323 participants, 131 (42%) were deprived (deprivation score>0.33). For each 0.1-unit increase in deprivation score, total TB episode costs were 1.11 times greater (95% confidence interval, CI 0.97-1.26). TB episode costs were 1.19 times greater with each quintile of higher deprivation score (95% CI 1.00-1.40) but lower by a factor of 0.53 with each quintile of lower self-reported income (95% CI 0.46-0.62).

Conclusion: Individuals experiencing multidimensional poverty faced equal or higher costs of TB than non-impoverished patients – an association not captured through self-reported income. Targeted interventions are needed to identify these patients at the greatest financial risk and to provide social protections against catastrophic costs.

Sarah McAlister, MS 2

Mentor(s): Maria Trent, MD
Department of Pediatrics

Facilitating Adolescent Sexual Health Dialogues: Does Physician Gender Matter?

Authors: Sarah McAlister BS, R. Scott Strahlman MD, Maria Trent MD

Background: Sexual health dialogue between adolescents and physicians is an important component of adolescent sexual maturation and risk management counseling, but research shows it occurs too infrequently in healthcare settings. To better understand factors influencing sexual health dialogue, this study examines how physician gender affects patient comfort during such conversations.

Methods: One hundred and one adolescent patients from a pediatric primary care clinic in Columbia, Maryland completed a survey that included demographic measures (race, age, gender, gender of provider, sexual activity) and Likert-style survey items assessing comfort level during discussion of sexual health topics with a provider. A one-sample t-test determined if comfort-based physician gender preference was seen, and multiple linear regression models evaluated the effect of participant demographic variables on physician gender preference during sexual health conversations.

Results: Of the 101 participants, 45% were female and 55% were male, the mean age was 15.0 years (SD=2.2 years), and 42% of participants were white while 58% were nonwhite. A one-sample t-test revealed that participants showed physician gender preference during sexual health conversations (M=4.39, SD=3.55, null hypothesis of =0, p<0.001). A multiple linear regression model assessing the effect of demographic variables on comfort scores identified participant gender as the only demographic variable significantly affecting comfort scores (p<0.001, R2=0.62); male participants reported a 1.81-fold greater comfort with male providers than did female participants. A simple linear regression model assessing the effect of participant gender on magnitude of preference for a gender-concordant provider found a significant association (p=0.002, R2=0.08); female participants reported a 1.64-fold greater preference for gender-concordant physicians than did male participants.

Conclusion: Participant gender was highly associated with a preference for gender-concordant physician discussions about sexual health, with female participants more strongly preferring gender-concordant physicians than male participants. Additional research to determine the factors influencing this preference is warranted.

Siddhartha Srivastava, MS 2

Mentor(s): Michael Lim, MD
Department of Neurosurgery

The correlation between immune checkpoint markers in tumors with methylated and unmethylated MGMT promoters in glioblastoma

Authors: Siddhartha Srivastava BS, Timothy Kim BS, John Choi BS, Chris Jackson MD, Christina Jackson MD, Bartholomew White MD, Fausto Rodriguez MD, Michael Lim MD

Background: Glioblastoma (GBM) is a high-grade glioma and is considered the most aggressive primary brain tumor with a median overall survival of 11-15 months. Methylation of the promoter of the MGMT gene, which encodes a DNA repair protein, has been shown to be a good prognostic indicator for GBM survival. It is known that GBM has elevated expression of several immune checkpoint molecules that allow the tumor to evade anti-tumor immune response. Therefore, it is important to elucidate connections between prognostic factors like methylation status and immunologic markers in the tumor microenvironment (TME) that might lead to immunosuppression. Since patients with methylated MGMT promoters have a better clinical prognosis, we hypothesize that tumors with methylated MGMT promoters have less checkpoint expression in the tumor microenvironment.

Methods: Patients with resected GBM tumor samples were identified by pathology reports as having tumors with either methylated or unmethylated MGMT promoters, as shown by a methylation-specific PCR assay. Corresponding patient tumor biopsy samples were embedded in paraffin, sectioned, and then stained using specific antibodies for known immune checkpoint molecules: PD-1, PD-L1, LAG-3, TIM-3, CSF1R, and IDO-1.

Results: In our cohort of 34 patients, 17 had methylated MGMT promoter regions and 17 did not. Our hypothesis was refuted when we found no statistically significant difference between methylated and unmethylated MGMT promoter status for PD-1, PD-L1, LAG-3, TIM-3, CSF1R, or IDO-1 expression using Fisher exact test ($P > 0.05$). Also, the levels of immune checkpoint expression did not correlate to the patient's clinical prognosis, as indicated by their progression free survival.

Conclusion: Our study examined the relationship between immune checkpoint markers and methylation status of MGMT promoters in GBM. While there was no statistically significant difference between these two groups within the immunologic framework of this study, future studies are indicated to further profile immunologic markers in relation to GBM treatment prognosis.

Thomas Le, MS 2

Mentor(s): Marta Hanson, PhD
Department of The History of Medicine

Kampo Classifications: The Campaign into the ICD-11 from 2005-2018

Authors: Thomas Le, BS

Background: The WHO's International Classification of Diseases (ICD) is a classification standard for both epidemiological and health-management purposes. Work on the 11th ICD revision (ICD-11) began in 2007, which was released in June 2018. For the first time ever, the ICD incorporated a new chapter for traditional medicine classifications, with Chinese, Japanese, and Korean traditional medicines being initially included. This paper explores how Kampo, traditional Japanese medicine, was successfully incorporated into this new chapter.

Methods: Through interviews with various ICD-11 and Kampo stakeholders, I examined the factors that advanced Kampo's inclusion into the ICD-11. This analysis was complemented by a critical review of WHO notes, news articles, and field study at the Center for Kampo Medicine at Keio University in Tokyo, Japan.

Results: The "official" reason why the WHO decided to include Kampo categories into the ICD-11 was for demographic statistical purposes. However, underneath this objective reason was an elaborate campaign by Kampo physicians to advocate for Kampo medicine into the ICD-11. One factor that helped Kampo physicians in their campaign was the fact that all Kampo physicians are required to have a medical degree. This requirement does not exist for Chinese or Korean traditional medicine physicians. Kampo practitioners thus exhibited "medical bilingualism." This unique "medical bilingualism" helped bridge the divide between Western and Eastern medicine philosophies, in order to reach a common ground of compromise between them.

Conclusion: Traditional medicines are being increasingly examined for their therapeutic value and their cost-efficiency. Their future role in Western healthcare is uncertain, in part because of the incommensurable philosophies in Western and traditional medicine. Kampo physicians were able to incorporate themselves into the once-exclusive ICD-11 because they utilized their ability to bridge these differences. In this way, traditional medicines in the ICD-11 represents a future direction of medicine, with further collaborations between Western and traditional medicine.

Timothy Kim, MS 2

Mentor(s): Michael Lim, MD
Department of Neurosurgery

Sacrificing the Superior Petrosal Vein during Microvascular Decompression Does Not Increase Vascular Complications: Experience from One Institution

Authors: Timothy Kim, BS; Yuanxuan Xia, BA; Leila Mashouf, BS; Kisha Patel; Risheng Xu, MD, PhD; Joshua Casaos, BS; Eileen Kim, MA; Alice Hung, BA; Adela Wu, BS; Tomas Garzon-Muvdi, MD; Matthew Bender, MD; Christopher Jackson, MD; Chetan Bettegowda, MD, PhD; Michael Lim, MD

Background: Microvascular decompression (MVD) is an established procedure for treating conditions such as trigeminal neuralgia and hemifacial spasm. However, during a standard retrosigmoid approach, the decision to sacrifice the superior petrosal vein (SPV) is controversial due to reports of complications including life-threatening brainstem infarction and cerebellar edema. This study analyzes the potential for vascular complications when the SPV is sacrificed during an MVD.

Methods: Retrospective chart review was performed to identify all MVDs from 2007-2018 by the two senior authors. Cases with ≥1 month of follow-up were included and sacrifice of the SPV or its branches was noted. The primary outcome was complications related to SPV sacrifice including sinus thrombosis, cerebellar edema, and midbrain or pontine infarction. Imaging was used to confirm all potential vascular complications noted in medical records. Fisher's exact test and unpaired t-tests were used to compare between groups.

Results: 732 MVD cases were identified and 592 met inclusion criteria with an average follow-up of 11.8 ± 16.4 months and a male-to-female ratio of 1:2.2. 146 patients (24.7%) had previous interventions and 10 patients had previous ipsilateral MVDs. The SPV was sacrificed in 217 cases and retained in 375 cases. At final follow-up, 152 patients (70.0%) were pain-free in the sacrificed group and 251 patients (66.9%) were pain-free in the non-sacrificed group ($p = 0.465$). No SPV-related vascular complications were found in this study. Two unrelated cases of vascular complications were identified and both were in the non-sacrificed group. One case involved cerebellar bleeding while the other was an ipsilateral transverse sinus thrombosis.

Conclusion: In MVDs, there is no difference in rate of vascular complications when the SPV is sacrificed compared to preserved. If cranial nerve visualization during standard retrosigmoid approach is impaired by the SPV, our data suggest that experienced surgeons should strongly consider SPV resection to optimize safe decompression.

Youkyung Sophie Roh, MS 2

Mentor(s): Ellen Mowry, MD
Department of Neurology

Initiation of higher-efficacy disease-modifying therapy and depressive symptom evolution in patients with multiple sclerosis

Authors: Youkyung Sophie Roh BA, Kathryn Fitzgerald ScD, Ellen Mowry MD

Background: Depression, common in people with multiple sclerosis (MS), is associated with excess morbidity and mortality in MS. MS disease-modifying therapies (DMTs) themselves may have favorable or unfavorable effects on depression etiology and symptomatology. Lower-efficacy DMTs (DMT-L) like interferons may increase depression risk, whereas higher-efficacy DMTs (DMT-H) may exert antidepressive properties, possibly mediated by their strong anti-inflammatory effects.

Methods: Using data from MS PATHS (Multiple Sclerosis Partners Advancing Technology and Health Solutions), an ongoing, 10-site longitudinal study, we used multivariable-adjusted mixed effects regression models to compare rates of change in depressive symptom severity, as measured by the Quality of Life in Neurological Disorders (Neuro-QoL) depression subscale, for MS patients 6- and 12 months after initiating different DMTs. DMT-L included interferons, glatiramer acetate, fingolimod, dimethyl fumarate; DMT-H included natalizumab, rituximab, ocrelizumab and alemtuzumab. We restricted our study population to patients who have relapsing-remitting MS, are new initiators of DMTs, and completed Neuro-QoL depression scales. Secondary analyses excluded interferons from the DMT-L category. Other analyses stratified by sex, race, disability status, and antidepressant use.

Results: In interim analyses, 1436 participants (average age: 45.1 ± 12.3y; 1090 [76%] female; average follow-up: 0.80 ± 0.40y) initiated a new therapy and had follow-up Neuro-QoL depression scores; 747 participants initiated DMT-L while 462 participants initiated DMT-H. Relative to initiation of DMT-L, initiation of DMT-H was potentially associated with -0.47 point/year reduction in NeuroQoL depression scores, though results did not attain statistical significance (95%CI: -1.00, 0.06; p=0.09). Results were consistent in analyses excluding interferons from DMT-L (annual reduction in depression scores: -0.57; 95%CI: -1.20, 0.06; p=0.08). We did not observe potential effect modification in stratified analyses.

Conclusion: Initiation of higher-efficacy MS therapies may have favorable effects on depressive symptoms in MS patients; future analyses incorporating additional follow-up from this cohort are planned.

Zach Murphy, MS 2

Mentor(s): Michael Boland, MD PhD
Wilmer Eye Institute, Department of Ophthalmology

Hospital quality and safety outcomes associated with meaningful use of electronic health records 2014 to 2016

Authors: Zach Murphy MA, Michael Boland MD PhD

Background: The HITECH act created "Meaningful Use" (MU) incentives for hospitals to implement Electronic Health Records (EHRs) with the goal of improving the quality and safety of healthcare. This study examined whether differences in MU performance metrics were associated with differences in hospital quality and safety measures.

Methods: We identified a cross-sectional sample of acute-care hospitals in the US using public data from CMS and similar national datasets in the timeframe 2014-2016. We used multinomial logistic regression models to assess the relationships between 7 MU performance measures and tertiles of Hospital Value-Based Purchasing (HVBP) program domain scores (clinical care, safety, experience of care, and efficiency) while controlling for hospital characteristics. Note higher scores are better for each HVBP domain. We included pairwise interaction terms between each performance measure and use of the four most prevalent ("top") EHR vendors.

Results: The total sample size was 2299. Among hospitals not using any top EHRs, each 10% increase in medication reconciliation was associated with increased risk of being in the upper versus lower tertile for efficiency (RRR = 1.40, p < 0.000). Similar results were found for medication orders placed through the EHR and experience of care (RRR = 1.48, p = 0.004). The top EHRs were associated with mixed interaction effects modulating the effects of EHR performance on outcomes. The most negative interaction was Epic with medication reconciliation on experience of care (RRR = 0.5696, p = 0.0169) and the most positive was Cerner with record access by patients on experience of care (RRR = 1.9387, p = 0.001).

Conclusion: These findings suggest that the impact of changes in EHR performance measures on hospital safety and quality is in some cases dependent on the EHR vendor used. Further investigation into the vendor-specific solutions that underlie these modulating factors is necessary, which may guide future EHR development.

Zane Frazer, MS 2

Mentor(s): Lauren Jansson, MD
Center for Addiction and Pregnancy

Treatment for Substance Use Disorders in Pregnant Women- Motivators and Barriers

Authors: Zane Frazer BS, Krystle McConnell MPH, Lauren Jansson MD

Background: Recently there has been a rise in opioid prescription rates and use by pregnant women, resulting in increased rates of Neonatal Abstinence Syndrome (NAS). Multidisciplinary treatment at a comprehensive care facility is the standard of care for pregnant women with substance use disorder (SUD), which not all women in this population receive . There is little existing qualitative research exploring motivators and barriers regarding access to necessary treatment.

Methods: This qualitative study used interviews to explore factors that motivated pregnant women with SUD to seek comprehensive care, as well as common hesitations/ barriers to treatment. The study included n=20 women in treatment at the Center for Addiction and Pregnancy—a comprehensive care facility at Johns Hopkins Bayview Medical Center-- between July and October 2018. Participants were compensated for participation in 30-question interviews, which were recorded and transcribed using Trint software and evaluated using NVivo qualitative analysis software.

Results: Subjects were primarily Caucasian, multigravida, with an average age of 29 years. Opioids were the primary drug of choice. Major motivators to seek treatment included readiness to stop using, concern for the health of the baby (including NAS), custody of the child(ren) and homelessness. Barriers to treatment included fear of attention from Child Protective Services, not wanting to be away from children/partner, lack of affordable childcare and transportation and low capacity on the housing unit.

Conclusion: Interviews highlighted significant barriers to treatment for this population, whether patients' hesitations to pursue treatment or logistical obstacles that interfered with consistent treatment. Identifying these themes creates an opportunity to reduce barriers and reinforce motivators, thereby increasing access to care. This is one approach to addressing the opioid crisis in the US and its effects on the high-risk and vulnerable population of pregnant women and their children.

POSTER ABSTRACTS: BASIC SCIENCE
Listed alphabetically by first name of author

1. Adam D'Sa, MS 2

Mentor(s): Sarah Wheelan, MD
Department of Oncology

Allele-Specific Gene Expression in Patients with First Episode Psychosis

Authors: Adam D'Sa BA, Jonathan Pevsner PhD, Sarah Wheelan MD PhD

Background: Patients with first episode psychosis (FEP) reliably progress to schizophrenia, bipolar disorder, or major depression. FEP is a purely clinical diagnosis with no prognostic value for a patient's course of illness. The phenomenon of allele-specific expression is a manner of genetic variation in which one allele is expressed at a significantly higher level than the other at a heterozygous locus. We hypothesize that, at the time of their initial diagnosis, patients with FEP are preferentially expressing one allele over the other at a variety of genetic positions, and that this allelic imbalance may be either functionally important or reflect downstream effects of a larger epigenetic mechanism.

Methods: The Genome Analysis Toolkit (GATK) was used to analyze paired DNA and mRNA sequencing data from patients with FEP for allele-specific expression. Gene set analysis using RTopper was performed to gauge whether affected genes preferentially clustered into functional groups.

Results: Among the FEP patients, several thousand candidate genes were identified, whose allelic expression levels were significantly altered from the expected 1:1 ratio. Gene set analysis suggests that metabolic pathways, particularly metabolite transport, are more likely to be affected; immune pathways are also overrepresented.

Conclusion: Multiple genes showed significant allelic imbalance in these samples; while none were recurrent across a large number of samples, several pathways, mostly membrane transport, are involved in the majority of the samples. Further followup is needed, particularly in characterizing control subjects. Ongoing metabolomics studies will be helpful in determining whether this imbalance in expression has any functional consequences. Other followup analyses will include examination of genomic regions adjacent to these genes, as the epigenetic mechanisms causing biased expression are likely to affect other nearby genes as well.

2. Ambrose Rice, MS 2

Mentor(s): Christine Pratilis
Department of Oncology

Determination of the adaptive signaling response to HRAS inhibition in models of malignant peripheral nerve sheath tumor (MPNST) characterized by loss of NF1.

Authors: Ambrose Rice BS, Ava Wang PhD, Christine Pratilis MD

Malignant peripheral nerve sheath tumors (MPNST) are rare, aggressive soft tissue sarcomas that most often arise from or within a pre-existing benign nerve sheath tumor (neurofibroma or plexiform neurofibroma) and are thought to be derived from Schwann cell origin. MPNST are difficult to treat due to their aggressive nature, limited response to chemotherapy and radiation, and limitations in other therapeutic methods. MPNST occur most often in patients who have germline loss of the NF1 gene, however they also occur sporadically. The NF1 gene is a tumor suppressor gene that encodes neurofibromin, a RAS GTPase-activating protein, that regulates downstream pathways of RAS such as MAPK/ERK or PI3K. Loss of NF1 can lead to enhanced RAS activity and therefore hyperactivity of its downstream pathways. In this study, we explore whether MPNST have preferential signaling through one of the three RAS isoforms (HRAS, NRAS, KRAS) in the setting of loss of NF1; this has important functional consequences as the isoforms are not entirely interchangeable. Only HRAS can be delocalized from the cell membrane and inactivated through farnesyl transferase inhibitors (FTI). NRAS and KRAS cannot be disrupted through this method as both possess a secondary mechanism of prenylation through geranylgeranyl transferases. We tested inhibition of HRAS by disrupting its membrane association using FTI tipifarnib in MPNST cell lines and performed immunoblot analysis to characterize changes in signaling responses of downstream of active RAS. We have found that inhibition of farnesyl transferase alone is ineffective for inhibition of downstream RAS signaling in MPNST models. We will expand our investigation of MPNST using immunoprecipitation assays specific for each isoform of RAS.

3. Eilrayna Gelyana, MS 2

Mentor(s): Jeffrey Rubens, MD
Department of Oncology

Treatment with PAC-1 to extend survival in AT/RT

Authors: Eilrayna Gelyana BA, Jeffrey Rubens MD

Background: Atypical Teratoid/Rhabdoid Tumors (AT/RT) are highly resistant to cytotoxic chemotherapies, leading to frequent treatment failure and poor survival. Resistance to cell death is achieved by mutations in key regulatory points along the apoptotic signaling pathway. We hypothesize that activation of caspase-3, an "executioner" caspase, by PAC-1 will circumvent upstream protective abnormalities in AT/RT's apoptotic signaling pathway to induce high rates of apoptosis and inhibit tumor cell proliferation.

Methods: We treated three AT/RT tumor cell lines with PAC-1 and measured expression of apoptotic markers, cell proliferation, and cell death by Western blot, cell viability assays, and immunohistochemical staining.

Results: AT/RT cell lines showed increased caspase-3 activation, increased cell death, and decreased cell proliferation with increasing doses of PAC-1.

Conclusion: Our data suggest that PAC-1 may be effective in circumventing therapeutic resistance in AT/RT cells by activating caspase-3 and inducing cell death. We will expand our investigation of AT/RT treatment with PAC-1 in future studies with combinatorial treatments that may act through complementary mechanisms to further augment the activation of caspase-3 and the induction of apoptosis in AT/RT cells.

4. Jason Lee, MS 2

Mentor(s): John Todd, PhD

JDRF/Wellcome Trust Diabetes and Inflammation Laboratory, Wellcome Trust Centre for Human Genetics, University of Oxford

Identification of novel candidate pancreatic beta cell-specific genes in type 1 diabetes

Authors: Jason T.C. Lee MSc, M. Irina Stefana PhD, John A. Todd PhD

Background: Traditional genome wide association studies identifying causal genes in type 1 diabetes prioritized those that influence immune cell function. However, recent studies have identified subsets of genes that influence both type 1 and type 2 diabetes pathogenesis, suggesting beta cell specific effects. In this study, we aim to identify new candidate genes near type 1 diabetes risk loci that contribute to pathogenesis in a beta cell specific manner.

Methods: A candidate SNP library was generated by expanding our index SNP list (57 positions from ImmunoBase) to include all SNPs in linkage disequilibrium to their respective indices. The expanded SNPs were then overlapped with pancreatic endocrine transcription factor ChIP-seq data to identify loci of interest in beta cells. One candidate gene, MAPT, was further interrogated in murine beta cells via single cell RNAseq of islet cells containing a full length human MAPT locus on a murine Mapt deficient background.

Results: Expansion of the 57 index SNPs linked to type 1 diabetes yielded 5689 SNPs for analysis. Overlap with transcription factor (PDX1, MAFB, NKX2.2, NKX6.1, FOXA2) binding sites derived from ChIP-seq data yielded between 5-36 SNPs per transcription factor for follow-up. Interestingly, candidate loci were enriched for the binding of multiple transcription factors. Many novel candidate genes were found to be near risk loci. SNPs found in anti-oxidant response elements identified by NRF2 ChIP-seq found heavy enrichment in the MAPT region encoding for protein Tau. Single cell RNAseq of murine pancreatic islet cells expressing human Tau found ectopic expression of hormones (GCG, SST, PPY) in pancreatic beta cells unique to other endocrine cell lineages as compared to their knockout counterparts.

Conclusion: We have demonstrated a new approach to the identification of candidate genes in pancreatic beta cells that contribute to type 1 diabetes pathogenesis.

5. Kori Porosnicu Rodriguez, MS 2

Mentor(s): Ben Park, MD, PhD
Department of Oncology

Modeling Breast Cancer Tumor Architecture In Vitro Using Mutant ESR1 Subclones

Authors: Kori Porosnicu Rodriguez BA, Dong Ho, Swathi Karthikeyan, Ian Waters, Lauren Dennison, David Chu PhD, Eric Christenson MD, Natasha Hunter MD, Joshua Donaldson MD-PhD, Ben Park MD-PhD

Background: Studies have revealed that breast cancer tumors can be made up of genetically distinct subclonal populations which cooperate together to promote tumor maintenance, growth, and survival. Around 70% of breast cancers express estrogen receptor alpha, which is particularly enriched in metastatic therapy-resistant cancers. Resistance to available endocrine therapies often occurs due to mutations in the ESR1 gene encoding this receptor. This study explores the effects of the two most common ESR1 mutations, Y537S and D538G, on cell proliferation and resistance to endocrine therapy when grown in co-cultures.

Methods: ESR1 Y537S and D538G knock-in cell lines were derived from MCF7 breast cancer cell lines using an adeno-associated virus. ESR1 Y537S and D538G mutant cells were tagged with either GFP or tdTomato (RFP) respectively using lentiviral infection. Additionally, two populations of wild-type (WT) MCF7 cells were tagged with GFP or RFP. The ESR1 mutant cell populations were single cell seeded to produce genetically identical subclonal colonies and those with the strongest GFP or RFP expression were selected for future co-culture experiments. Co-cultures were established with: (1) ESR1 Y537S clones and WT cells, (2) ESR1 D538G and WT cells, and (3) ESR1 Y537S and D538G under conditions (A) without estradiol, (B) with estradiol, and (C) with estradiol and fulvestrant.

Results: Tagged cell lines of the two subclonal populations were established with intact mutations and original MCF7 growth phenotype. It is too early to draw conclusions regarding tumor architecture and cell proliferation from our co-cultures since they are not yet confluent.

Conclusion: We will continue to maintain our co-cultures until they reach confluency, at which point we will image them and use droplet-digital PCR to compare clonal proliferation in vitro. This will provide insight into subclonal interactions within heterogenous breast cancer tumors in the hopes that this will provide targetable vulnerabilities for future therapies.

6. Samuel Warner, MS 2

Mentor(s): Jonathan Schneck
Institute of Cellular Engineering

Skewing T cell phenotype for adoptive cell therapies

Authors: Samuel Warner, Ariel Isser, Jonathan Schneck

Adoptive T cell therapy is an emerging treatment strategy for a variety of cancers. There is evidence that central memory T cells – a phenotypic subset of memory CD8+ T cells localized in the spleen and lymph nodes – exhibit superior long-term anti-tumor activity in comparison to the effector memory T cell counterparts that remain in circulation. We hypothesized that a population of antigen-specific CD8+ T cells could be skewed toward either an effector or central memory phenotype by modulating stimulatory signals during T cell activation. T cell activation requires two independent signals at the cell surface, both of which are necessary for activation. The first signal originates at the T cell receptor complex (signal 1), while the second signal comes from an assortment of co-stimulatory receptors (signal 2). Signal 2 stimulation was modulated experimentally in two different ways. First, we utilized two different signal 2 stimulatory ligands, CD28 and 4-1BB, alone or in combination with each other. Second, signal 2 was applied either at the same time (concurrent group) as signal 1 or one hour after (1-hour-delayed group). The 1-hour-delayed application of 4-1BB alone led to significantly larger percentages of central memory antigen-specific T cells when compared to the concurrent application of CD28 alone. Conversely, the concurrent application of CD28 alone led to significantly higher percentages of effector memory antigen-specific T cells relative to the 1-hour-delayed application of 4-1BB alone. While the functional ramifications of these phenotypic shifts have not been characterized, future adoptive T cell therapy experiments using murine models of melanoma may provide insights into the anti-tumor functionality of each subset.

7. Samuel Weinreb, MS 2

Mentor(s): Gislin Dagnelie, MS, PhD

Wilmer Eye Institute, Department of Ophthalmology

Phosphene Mapping for Intracortical Visual Prostheses

Authors: Samuel Weinreb BS, Liancheng Yang MS, Roksana Sadeghi MSc, Gislin Dagnelie MS PhD

Background: Intracortical visual prostheses (ICVPs) are a novel class of devices that transmit visual stimuli from an external camera to an electrode array implanted in the visual cortex, thereby eliciting visual percepts (phosphenes) and restoring limited functional vision to the blind. The visual world must be encoded into patterns of electrode stimulation that produce intelligible images, requiring knowledge of where in the visual field each electrode produces a phosphene. This project aims to develop a multi-modality phosphene mapping method for calibration of ICVPs.

Methods: We simulated the perceptual experience of electrode stimulation in an ICVP recipient by displaying phosphenes (points of light) to sighted subjects using a virtual reality headset. Subjects indicated the position of each phosphene within their visual field by making a saccade or pointing a finger towards the perceived target, and these movements were measured with infrared sensors. A set of known points was presented in order to determine calibration parameters for each subject, which were used to apply linear adjustments to the measurements to reconstruct the initial set of points.

Results: Average R-squared between presented and reconstructed coordinates were 0.97 for eye tracking and 0.95 for finger tracking. By applying linear adjustments, a set of calibration points was recreated with an average root-mean-square error (RMSE) of 0.131 normalized units. Similar methods applied to finger tracking produced maps with average RMSE of 0.226.

Conclusion: Phosphene maps reconstructed by tracking saccades had less random error and systemic distortion than those produced by tracking finger position. Eye tracking thus appears more promising as a primary method for ICVP calibration, whereas finger tracking may be useful as an adjunct or as a standalone phosphene mapping method in individuals without intact eye movements. Next steps include applying nonlinear adjustments to the measurements and integrating data from both modalities with relative mapping of adjacent phosphene pairs.

8. Thomas Gracie, MS 2

Mentor(s): Andrew Feinberg, MD MPH
Department of Molecular Biology and Genetics

The effect of pentose phosphate pathway knockdown on viability in metastatic PDAC over matched primary tumor cells.

Authors: Thomas Gracie BA, Veronica Rodriguez PhD, Andrew Feinberg MD MPH

Background: Metastatic PDAC cells have demonstrated widespread differences in histone methylation relative to matched primary tumor cells, a process associated with the increased heterochromatin loss in these cells relative to matched primary tumor cells. Recent findings suggest histone methylation is sensitive to flux through the pentose phosphate pathway (PPP). It follows that targeting of the PPP with antimetabolites could potentially reverse epigenetic changes in metastatic PDAC cells, resulting in cytotoxicity.

Methods: To investigate this possibility, A13B (primary tumor PDAC) cells and A13D (patient-matched distant metastatic) cells were plated at varying densities and dosed with increasing concentrations of 6AN, a drug which inhibits G6PDH. Cell survival was then assessed with CellTiterGlo, a luminescence assay for ATP. IC50 curves were then generated for 6AN in A13B versus A13D cells.

Results: At a density of 2K cells per well, IC50 values in micromoles/L were 33.1 for A13B and 39.0 for A13D. At 5K cells/well, IC50 values were 86.4 (trial 1) and 62.7 (trial 2) for A13B; for A13D the IC50 values were 25.4 (trial 1) and 53.0 (trial 2). Lastly, at 10K cells/well, A13B IC50 values were 204.6 (trial 1) and 37.4 (trial 2) and A13D values were 91.9 (trial 1) and 57.5 (trial 2).

Conclusion: For nearly every trial, IC50 values for A13B and A13D fell within the same order of magnitude, failing to support the hypothesis that 6AN is more cytotoxic to A13D cells than A13B cells. Given that similar studies have found a significant difference here, it is likely that confounding variables affected the data. One potential confounder may have been insufficient removal of intercellular adhesions; microscopy of wells seeded with A13B showed that the cells generally plated in groups rather than as colony forming units (CFU). To avoid this possibility, future studies should lengthen trypsin exposure and incorporate filtration to facilitate precise seeding.

9. Yohannes Tsehay, MS 2

Mentor(s): Joel Bader
Department of Biomedical Engineering

Membrane-localized Keratin-14 Promotes Tumor Invasion

Authors: Yohannes Tsehay BA, Andrei Kucharavy PhD, Hildur Knutsdottir PhD, Veena Padmanaban M.S, Joel Bader PhD

Background: Metastasis is the main predictor of outcome for patients with cancer, yet the molecular mechanism driving invasive phenotypes is not well understood, hindering development of assays and therapeutics for this stage of cancer progression. In this study, we characterize a molecular biomarker for invasion in greater detail, using an automated computer model. The model quantifies the invasive potential of tumors, allowing for quantification of even minor contributions to an invasive phenotype from individual genes, and can potentially be used to establish interactions among genes. Keratin 14 (K14) is a known molecular biomarker that is correlated with poor outcomes in breast cancer patients. We apply our automated computer model, which was built in Python, to test the hypothesis that K14 is directly correlated with automatically generated invasion scores, independent of tumor size.

Methods: We used two different transgenic mice as our breast cancer tumor models. Organoids were generated from these mice, and each organoid had a corresponding differential interference contrast image, K14 image, and a boundary around the organoid drawn manually which was used to generate an invasion score for the organoid using our automated system. The parameters assessed include the following: entire K14 expression, peripheral K14 expression (edges of the organoid), central K14 expression (center of the organoid), and organoid size.

Results: Peripheral K14 expression showed the strongest correlation with invasion scores for both types of transgenic mice. However, this relationship was more prominent in one mouse model than the other (average r-squared values of 0.308 for the first mouse model and 0.113 for the second).

Conclusion: The results suggest that K14 expression in cells located in the periphery may be an important marker of invasion, and since the strength of this relationship depended on the mouse model used, additional factors play a role in invasion and dissemination.

10. Zoe Cosner, MS 2

Mentor(s): Fred Bunz MD. PhD.

Department of Radiation Oncology and Molecular Radiation Sciences

Assessing the role of ARF in the human innate antiviral response

Authors: Zoe Cosner BS., Fred Bunz MD. PhD.

Background: The tumor suppressor ARF, an upstream regulator of p53, has a unique gene structure, sharing an exon with cell cycle regulator p16. Interestingly, these proteins are encoded in different reading frames and share no structural homology. ARF expression increases in response to viral infection, suggesting an antiviral role for ARF, which could explain the utility for this unusual gene structure.

Methods: To investigate the roles of ARF and p16 in host antiviral response, we performed qRT-PCR in lung cancer H1299 cells and non-cancer immortalized RPE cells infected with wild type and E1a-mutant adenovirus. Additionally we have generated CRISPR knockouts of ARF and the entire ARF/p16 locus in H1299 cells, and are in the process of creating RPE knockouts. These cell lines can be used to investigate viral response in the absence of these genes.

Results: The qRT-PCR analysis indicates that during wild type adenovirus infection, H1299 cells up-regulate both ARF and p16, while RPE cells down-regulate both proteins. However, infection with E1a mutant adenovirus does not alter ARF or p16 expression in either cell line.

Conclusion: We demonstrated that cancer and immortalized cells altered expression of p16 and ARF coordinately in response to adenovirus, suggesting that the overlapping nature of the locus prevents independent regulation. This regulation of p16/ARF expression is done in an E1a-dependent manner. Additionally, the difference in response of cancerous and immortalized cells may reflect cancer-based alterations in innate immune response. To further investigate the relationship between these proteins, and the difference between cancerous and non-cancerous cellular response, we will quantify protein expression in response to viral infection in both cell lines. Understanding the mechanism of p16/ARF induction in response to viral infection and how that reflects innate immune differences between cancerous and non-cancerous cells may provide greater knowledge of the ARF-p53 regulatory pathway, providing possibilities for future therapies.

POSTER ABSTRACTS: CLINICAL SCIENCE
Listed alphabetically by first name of author

11. Aarti Purohit, MS 2

Mentor(s): Mahmoud Malas, MD

Department of Vascular Surgery - Bayview Medical Center

Outcomes of Autogenous Fistulas and Prosthetic Grafts for Hemodialysis Access in Diabetic and Non-Diabetic Patients

Authors: Aarti Purohit BA, Isibor J. Arhuidese MD MPH, Satinderjit Locham MD,Mahmoud Malas MD

Background: Diabetes mellitus is one of the primary etiologies of end stage renal disease (ESRD), and the management of diabetic ESRD patients remains problematic as they are particularly vulnerable to poor outcomes following the creation of vascular access. This study examines the impact of diabetes on the outcomes of autogenous fistulas and prosthetic grafts for hemodialysis access in a large population-based cohort of patients.

Methods: A retrospective analysis of all patients in the United State Renal Data System (USRDS) who initiated hemodialysis between January 1, 2007 and December 31, 2011 was performed. Chi-square, T-tests, Kaplan-Meier, log-rank tests, multivariable logistic and Cox regression analyses were employed to evaluate time to maturation, interventions, patency, access infection and mortality.

Results: The study evaluated outcomes following placement of 180681 (78.5%) autogenous fistulas and 49423 (21.5%) prosthetic grafts in 126806 (55.1%) diabetic and 103298 (44.9%) non-diabetic patients. There was no difference in maturation time for diabetics compared to non-diabetics who received autogenous fistulas (aHR: 0.99; 95%CI: 0.96-1.04, P=0.962) and prosthetic grafts (aHR: 1.00; 95%CI: 0.94-1.07, P=0.91). Risk adjusted analyses showed marginally higher primary (aHR: 1.05; 95%CI: 1.04-1.06; p<0.001), primary assisted (aHR: 1.03; 95%CI: 1.01-1.04; p<0.001) and secondary (aHR: 1.02; 95%CI: 1.01-1.03; p<0.001) patency for non-diabetics relative to diabetics who received autogenous fistulas. These groups showed no difference in patency among prosthetic graft recipients and no difference in severe infection following either prosthetic graft or autogenous fistula (aHR: 0.99; 95%CI: 0.92-1.08; P=0.90). Diabetic patients did show an increased risk of mortality with both fistula and graft use.

Conclusion: These findings demonstrate higher risk of mortality with both fistulas and prosthetic grafts for patients with diabetes mellitus as well as negative access-related outcomes such as patency and access infection. These outcomes are important considerations for both physicians and patients for deciding the choice of treatment options for hemodialysis.

12. Alejandro Chara, MS 2

Mentor(s): Nicholas Theodore, MD
Department of Neurosurgery

Effects of the Renin-angiotensin System Inhibitors on Spinal Cord Dysfunction and Imaging Features of Spinal Cord Compression: Retrospective Analysis of a Cohort of Symptomatic Cervical Spondylosis Patients

Authors: Alejandro Chara BS, Alexander Perdomo-Pantoja MD, Samuel Kalb MD, Corinna Zygourakis MD, Karim Ahmed BA, Zachary Pennington BA, Timothy Witham MD, Nicholas Theodore MD

Background: Cervical spondylosis involves the progressive collapse of intervertebral discs resulting in narrowing of the spinal canal, spinal cord compression and cervical myelopathy. Potentially beneficial effects of renin-angiotensin system (RAS) blockers in the central nervous system have been reported. Our objective was to determine if RAS blockers and other antihypertensive drugs correlate with preoperative clinical status and radiological markers of spinal cord compression in cervical spondylotic disease.

Methods: Demographic data, comorbidities, antihypertensive medications, and functional status (including modified Japanese Orthopedic Association (mJOA) and Nurick grading scales) of symptomatic spondylotic patients were retrospectively collected. We evaluated percent canal and cord compromise, surface area of T2 signal cord change, and pixel intensity of signal cord change compared to normal cord.

Results: 121 patients met the inclusion criteria, including 43 (35.5%) females and 78 (64.5%) males, with a median age of 57.7 years. 70 (57.9%) patients had hypertension. 68 (97.1%) hypertensive patients were taking antihypertensive drugs (21 ARBs, 22 ACEIs, and 25 other). Sagittal T2-weighted MRIs showed maximum canal compromise (MCC) was positively correlated with maximum spinal cord compression (MSCC) (r=0.806, p<0.001). MSCC was negatively correlated with the signal intensity ratio (SIR) (r=-0.546, p<0.001). Higher SIR correlates with a lower signal intensity in the compressed spinal cord. Patients treated with RAS blockers, ARBs, and diuretics displayed higher SIR compared to untreated individuals (p=0.03, 0.04, and 0.03, respectively). ACEIs and diuretics were associated with lower preoperative mJOA scores (p=0.003, 0.01, and 0.01, respectively). Likewise, therapy with calcium antagonists and diuretics was related to higher Nurick scores (p=0.01, 0.02, 0.01, respectively).

Conclusion: In symptomatic spondylotic patients, RAS inhibitors were associated with higher SIR than in untreated hypertensive patients. Those hypertensive patients treated with ACEIs/diuretics/calcium antagonists displayed worse preoperative functional status compared to non-hypertensive patients. Further studies are needed to confirm an effect of RAS inhibitors in spinal cord damage.

13. Antonio Salas, MS 2

Mentor(s): Arturo Casadevall, MD-PhD
Bloomberg School of Public Health

Cryptococcus neoformans impact on inflammatory pathways mediated through mitochondria

Authors: Antonio Salas BS, Carolina Coelho PhD, Arturo Casadevall MD-PhD

Background: Cryptococcus neoformans (Cn) is an opportunistic pathogenic fungus that requires a robust macrophage and T-cell response to prevent disease. Interferon gamma (IFNγ), via JAK/STAT pathways, is critical for protection from Cn infection due to its ability to activate macrophage antifungal programs. Mitochondria have been shown to support macrophage activation after infection and synthesize antimicrobial molecules including itaconate, in particular after IFNγ stimulation. To link JAK/STAT-dependent IFNγ signaling and macrophage mitochondrial modulation, we investigated expression of STAT1-6 and Irg1 (gene coding for the mitochondrial enzyme that produces itaconate) upon Cn infection. In addition, we tested itaconate's impact on Cn growth to elucidate its antifungal capacity.

Methods: Macrophages (J774.16 cell line and bone-marrow-derived macrophages – BMDM) were infected with Cn in the presence of IFNγ for 2 and 24 hours. Gene expression of Stat1-6 and Irg1 were evaluated by RT-qPCR. Protein expression of STAT1-6 and the phosphorylation status of STAT1 and STAT3 were measured by western blot. Cn growth in liquid media was measured by visual inspection. Ratio paired t-test was used for statistical analysis.

Results: Our results show upregulation of STAT1-3 gene levels dependent on IFNγ, while Cn infection does not modulate these genes. Similar results were observed for protein and phosphorylation levels of STAT1 and STAT3. Irg1 gene expression was upregulated during Cn infection in J774.16 cells (3.87±1.01-fold; p=0.0173) and BMDM (12.2±1.65-fold; p=0.0027) and during IFNγ treatment alone (41.1±23.77-fold; p=0.006). Cn growth in liquid media was reduced in the presence of itaconate.

Conclusion: In our conditions, IFNγ efficiently activates the STAT1-3 pathways while Cn infection had little effect on STAT expression. Cn's ability to minimally stimulate the STAT1-6 pathways may contribute to the pathogen's evasion of macrophage killing. Itaconate production during infection, which is greatly potentiated by IFNγ, may explain IFNγ-dependent anticryptococcal activity.

14. Austin Burns, MS 2

Mentor(s): Dr. Glenn Whitman
Division of Cardiac Surgery

Reduction of postoperative red blood cell transfusions through weekly data presentations

Authors: Austin Burns BS, Megan Hunt BS, Brian Lo BS, Cecillia Lui MD, Alejandro Suarez Pierre MD, Xun Zhou MD, Kenton Zehr MD, Glenn Whitman MD

Background: Due to potential morbidity and mortality, national guidelines recommend limiting postoperative blood transfusions. However, the Johns Hopkins Division of Cardiac Surgery transfuses significantly more frequently than comparable institutions nationally. We sought to examine whether an evidence-based, systems approach limiting elective transfusions to postoperative patients with a hemoglobin level (Hb trigger) < 8g/dL, would lead to improved performance regarding the rate of patients transfused postoperatively.

Methods: All postoperative blood transfusion from adult patients who underwent a cardiac surgery procedure between 3/20/2018 and 9/21/2018 and received 0-4 postoperative blood transfusions were included. During a run-up period between 3/20/2018 and 6/20/2018, data regarding Hb triggers preceding each transfusion order were collected, publicly presented on 6/21/2018 to attending cardiac surgeons and residents, and served as a baseline. Subsequently, Hb triggers were collected on all patients meeting inclusion criteria and presented weekly until 9/21/2018 (display period). Using a univariate chi-square analysis, we examined the display period to see if there was a) a decrease in the proportion of postoperative transfusions given at a Hb trigger of >8g/dL, and b) an increase in the proportion of patients receiving no transfusions.

Results: Data from 497 patients were analyzed. There were 245 postoperative transfusions from 3/20/2018–6/20/2018 and 194 postoperative transfusions from 6/21/2018–9/21/2018. The total proportion of blood transfusions with a Hb trigger >8g/dL decreased significantly from 27.3% to 18.0%, (p=0.022). There was no significant difference in the proportion of transfusions given per patient between the run-up and display periods (p=0.787).

Conclusion: While weekly presentations were not associated with a significant decrease in the proportion of postoperative transfusions given per patient, they were associated with decreasing the proportion of transfusions given for a Hb trigger >8g/dL. While further analysis is required to elucidate if a causal relationship exists, these results indicate that such presentations may be effective.

15. Barbara Dietrick, MS 2

Mentor(s): Allen Everett, MD
Department of Pediatrics

Biomarkers in Neonatal Brain Injury

Authors: Barbara Dietrick MS, Eleanor Molloy MB PhD, Jie Zhu BS, David Graham MS PhD, Aurelie Roux PhD, Robert Harlan MS, Gregory Ellis PhD, Allen Everett MD

Background: Hypoxic ischemic encephalopathy (HIE) is a common cause of neurological disability and death in neonates. However, current clinical methods are insufficient to identify risk, discriminate severity, and monitor therapeutic efficacy. Therefore, we aimed to investigate the use of a multi-marker biomarker panel (ELISA) and metabolomics to identify molecules in serum associated with neurodevelopmental outcome and provide insights into mechanisms.

Methods: A retrospective cohort study of serum from neonates with HIE (N=45, day of life 0-1) and healthy term neonates (N=30, ≥36 weeks gestation) born in Ireland from 2011 to 2018 were analyzed. Using ELISAs we measured neuronal and inflammatory proteins. We determined metabolite levels using a targeted panel of 225 metabolites by mass spectrometry. Protein and metabolite concentrations were correlated with clinical severity defined as Sarnat scores of encephalopathy. Analysis by Mann Whitney U test, Kruskal-Wallis test, Spearman correlations, and one-way ANOVA with a significance level of P≤0.05.

Results: CNS necrosis markers GFAP, NRGN, and Tau were increased in patients (p=0.039, p=0.011, p=0.001), whereas VEGF and BDNF were lower in patients compared to controls (p=0.0002, p=0.05). Inflammation is a secondary injury mechanism and IL-6, IL-8, and IL-10 were higher in patients compared to controls (p=0.0001, p=0.002, p<0.0001). Tau was higher in patients with moderate-to-severe compared to mild encephalopathy (p=0.026). VEGF was lower in patients with moderate-to-severe compared to mild encephalopathy (p=0.035). In serum, 57 metabolites were quantifiable. Lysine, pipecolic acid, and 2,3-Diaminoproprionic acid were correlated with encephalopathy severity (p=0.0003, p=0.000097, p=0.0002).

Conclusion: All 8 biomarkers representing CNS necrosis and inflammation had different concentrations in neonates with HIE compared to controls. Additionally, decreased BDNF, a necessary neuronal survival factor, could serve as a therapeutic target. Our metabolomics discovery revealed excitotoxicity as a predominant mechanism of injury. Therefore, these biomarkers may be useful for triaging, providing prognoses, monitoring therapies, and illuminating new adjunct treatment strategies.

16. Breanne McCarthy, MS3

Mentor(s): Rani Hasan, MD
Division of Interventional Cardiology

Inflammation, Cognitive Changes, and Clinical Outcomes in Frail and Non-Frail Older Adults undergoing Cardiopulmonary Bypass Surgery

Authors: Dr Matthew Czarny, Nada Sie, Khala Marshall-Watkins, Francis Kirkland, Christine McLeod, Dr Rhondalyn McLean, Dr Gary Gerstenblith

Background: Advanced age is associated with a rise in inflammatory mediators that may predispose the elderly to worse outcomes, particularly following a major stressor. Cardiopulmonary bypass (CPB) surgery itself induces a complex inflammatory response. Our objective was to examine the relationship between frailty, inflammation, and clinical outcomes in patients undergoing CPB surgery to generate preliminary data for future planned interventional studies designed to modify perioperative inflammation.

Methods: We included adults aged 70 years or older undergoing CPB surgery at Johns Hopkins Hospital from April 2012 to September 2013. Serum inflammatory mediators (tumor necrosis factor-α (TNF-α), high-sensitivity C-reactive protein (hsCRP), angiotensin, and interleukins) were measured: preoperatively, perioperatively, and postoperative day 1, day 4, and 1 month. Change in inflammatory markers over time was analyzed using a Kruskal-Wallis test. Frailty was assessed using grip strength, walking distance, weight change, and self-reported fatigue. Participants were then stratified as either "frail" or "non-frail." Clinical outcomes of interest included a composite of death, myocardial infarction (MI), transient ischemic attack (TIA); and a composite of respiratory failure/renal failure/bleeding/infection. Another outcome of interest included discharge disposition, based on hospital/ICU/rehabilitation lengths of stay, discharge location, and readmission rates. Postoperative cognitive changes were assessed using the mini-mental status exam (MMSE). Comorbidities were accounted for using the Charlson Comorbidity Index. Multiple linear and logistic regression analyses were used to examine the association between the exposures of interest and clinical outcomes, with significance set at $P<0.05$.

Results: A total of 48 participants were enrolled. 13 participants completed pre- and post-operative MMSE. Blood specimens were obtained for 45 participants. 21 participants had tissue specimens. Data analysis is ongoing.

Conclusion: Analysis is ongoing. We hypothesize that increased preoperative inflammation is associated with increased risk for poor outcomes, worse discharge disposition, and greater cognitive decline in both frail and non-frail older adults following CPB surgery.

17. Brian Lo, MS 2

Mentor(s): Dr. Ahmet Kilic, MD
Division of Cardiac Surgery

Matchmaking Just Got Easier: Impact of Phenotypic Donor-Recipient Likeness in Heart Transplantation

Authors: Brian D. Lo BS, Alejandro Suarez-Pierre MD, Xun Zhou MD, Cecillia Lui MD, Megan F. Hunt BS, Glenn J. Whitman MD, Chun W. Choi MD, Ahmet Kilic MD

Background: Heart transplantation is the gold standard in the treatment of end-stage heart failure. Unfortunately, the number of patients requiring transplantation constantly exceeds the number of donor hearts available. This has guided significant research on ways to optimize the heart allocation process, with a particular emphasis on determining the relative importance of physiological and phenotypic characteristics when matching donors and recipients. Previous studies on phenotypic matching have only analyzed the impact of matching individual variables such as gender and age. This study examines the potential benefit of phenotypic matching of multiple factors simultaneously.

Methods: Adult patients undergoing heart transplantation between 2006 and 2016 were identified from the Organ Procurement and Transplantation Network database. Phenotypic matching was defined based on six factors: body mass index difference >30%, age difference >30%, height difference >7%, non-identical ABO blood grouping, ethnicity, and gender. 0-1 mismatched characteristics were considered phenotypically-like matching, while 2-6 mismatches were considered phenotypically-unlike matching. The primary study endpoint was one-year survival. Risk-adjusted mortality was examined with multivariable Cox regression models.

Results: During the study period, 20,052 adult patients underwent heart transplantation, of which 9,595 (47.9%) were phenotypically-like matched and 10,457 (52.1%) were phenotypically-unlike matched. No differences in 1-year survival were seen between like and unlike matched patients (risk-adjusted OR 1.05, 95% CI 0.96-1.15, p=0.305) after controlling for clinically relevant covariates. Subgroup analyses demonstrated no survival differences after stratification based on hospital volume and initial waitlist status. Phenotypically-like matched patients had longer waitlist times compared to unlike matched patients (225 days versus 192 days, p<0.001.)

Conclusion: Waiting for a phenotypically matched heart provides no survival benefit, and may be causing more harm to patients, as evidenced by their prolonged waitlist times. This challenges the belief that a perfect donor heart exists. We should encourage ourselves to accept organs sooner for patients waiting for a heart transplant.

18. Bridgette McCormick, MS 2

Mentor(s): Dr. Angie Jelin, MD
Department of Gynecology and Obstetrics

Outcomes of both complex and isolated cases of infants with large stomach on fetal ultrasound

Authors: B. McCormick, K. Blakemore, E. Jelin, C. Johnson, J. Bishop, A. Jelin

Background: A sonographically large fetal stomach (LS) has resulted in gastrointestinal obstruction, per case reports, and is often followed with serial ultrasounds. However, predictive value of this has never been quantified. We hypothesize that a small percent of large stomach cases will result in a diagnosis of GI obstruction.

Methods: We performed a retrospective cohort study of all prenatal cases with a LS visualized between Jan 02-June16 with a LS on US at Johns Hopkins Hospital based on a stomach size normogram. Inclusion criteria required a liveborn delivery within the Johns Hopkins health system, excluding pregnancy loss/termination cases and cases delivered outside JHHS. We defined a LS as an increased measurement in 2 or greater dimensions based on a normogram. Cases were classified as isolated or complex based on additional US findings at initial LS presentation. We collected demographics, sonographic findings, and postnatal outcomes.

Results: We identified 340 fetuses with LS. 233 met inclusion criteria, including 160 isolated and 73 complex. Of the 160 isolated cases, none evolved into a GI obstruction or anomaly. Those with isolated findings were significantly less likely to deliver preterm (n=24, 15.0% vs n=31, 42.5%, p<0.001). Isolated cases were less likely to be complicated by polyhydramnios (n=13, 8.1% vs. n=18, 24.7%, p<0.001), NICU admittance (n=30, 18.8% vs n=70, 95.9%, P<0.001) or neonatal procedure (n=1, 0.63% vs. n=60, 82.2, p<0.001). The single isolated surgery was an esophagogastrodupodenoscopy performed for G-tube placement for respiratory distress while eating. The stomach and duodenum were noted to appear normal during this procedure.

Conclusion: While a sonographically large fetal stomach has been reported to result in gastrointestinal obstruction, the rate may be lower than previously hypothesized. We found that <1% of large fetal stomachs resulted in obstruction. When isolated, a large stomach is not a sole indication for ultrasounds and postnatal imaging.

19. Chau D. Vo, MS 3

Mentor(s): Alexander Coon, MD
Department of Neurosurgery

Safety and Efficacy of Flow Diversion for Middle Cerebral Artery Aneurysms

Authors: Chau D. Vo BA, Jessica K. Campos MD, Matthew T. Bender MD, Bowen Jiang MD, David A. Zarrin BS, Arun Chandra MD, Justin M. Caplan MD, Judy Huang MD, Rafael J Tamargo MD, Li-Mei Lin MD, Geoffrey P. Colby MD PhD, Alexander L. Coon

Background: The Pipeline Embolization Device has demonstrated safety and efficacy in some off-label applications, with limited reports of its use for aneurysms along the middle cerebral artery.

Methods: Patients with MCA aneurysms treated with flow diversion were identified. Follow-up angiography was performed at 6 and 12 months. Occlusion was graded as complete, trace filling, entry remnant, or aneurysm filling. Clopidogrel was discontinued at 6 months; aspirin was reduced to 81mg from 325mg daily at 12 months.

Results: There were 40 cases of flow diversion for 41 MCA aneurysms, with 93% (38/40) successful rate. Twenty-nine patients(76%) were female. Average age was 53±15years, average size 5.4±4.7mm, neck size 2.7±1.1mm. Ten aneurysms arose from M1(26%), 22 MCA bifurcation(58%), 5 M2(13%) and 1 distal MCA(3%). Average size of MCA bifurcation aneurysms was 5.2mm(1.8-15mm), neck size 3mm(1.5- 5.5mm). Thirteen cases(34%) had previous treatment, and 14(37%) had subarachnoid hemorrhage. Morphology was 89%saccular, 8%fusiform and 1%dissecting. Balloon remodeling was performed in 2 cases(5%), adjunctive coiling in 4 cases(11%). There were 2 in-situ thromboses(5%). One occurrence resolved following abciximab administration with no clinical significance. The other, an irregular right MCA bifurcation aneurysm treated with PED and coiling, was complicated by intra-procedural in-stent platelet accumulation and resolved with abciximab administration, however, the patient suffered left lower extremity paresis at last follow-up. This was the only major complication(1/38;2.6%), and no mortalities. Minor complications(3/38;8%) included one minor stroke, one asymptomatic ICA dissection, and one post-operative cranial nerve III palsy without evidence for carotid cavernous fistula.
Follow-up angiography was available for 34/38(89%) cases at average 12.4 months. Complete occlusion was achieved in 66%(n=25), and 74% (n=28), at 6-, and 12-months, respectively. Of 14/19 MCA bifurcation aneurysms with available follow-up, 74% were completely occluded at average 11 months.

Conclusion: Treatment of MCA aneurysms with PED offers a favorable occlusion rate(74%) with acceptable major complication rate(2.6%).

20. Christa LiBrizzi, MS 3

Mentor(s): Rushyuan Jay Lee
Department of Orthopedic Surgery

Girls Play Tough, Too: The Role of Gender in Pediatric Supracondylar Humerus Fractures

Authors: Christa L. LiBrizzi BS, Walter Klyce BS, Alvaro Ibaseta Fidalgo BS MS, Claire Shannon MD, Rushyuan J. Lee MD

Background: Supracondylar humerus fractures (SCHFx) are a common pediatric injury which are historically associated with falls on an extended, non-dominant arm in adolescent boys. Past literature reports boys are approximately 1.5 to 2 times more likely than girls to sustain SCHFx but little research exists characterizing sex differences of fracture patterns and complications. This study sought to characterize the difference in incidence, mechanism of injury, associated nerve deficits, fracture subtype and treatment in girls compared to boys. We hypothesized the incidence of SCHFx in girls would increase over the study period and the fracture characteristics would resemble that of boys.

Methods: A retrospective review was conducted of all patients with SCHFx treated at a single institution from 2008 to 2017, primarily looking at sex distribution for SCHFx fractures over time, both overall and by Gartland type. Secondarily we also noted neurologic injuries, mechanism of injury, and nonoperative versus operative treatment.

Results: A total of 1253 SCHFx were identified during the study period. In the 10-year period, girls sustained more SCHFx overall (653/1253) than boys (600/1253), but was not statistically significant by two-tailed binomial test (p=0.14). The year-to-year percentage of girls with SCHFx ranged from 45.6%-61.8%. Girls were significantly younger than boys at time of fracture (5.5 ± 2.5 years vs. 6.1 ± 2.5 years p=0.0002). Both sexes most commonly sustained SCHFx after falling from monkey bars. Of the 118 (9.4%) nerve injuries, neurologic injury had a significant association with boys (p=0.009). There was no sex associated difference in proportion of Type 3 fractures (p=0.12) or operative treatment (p=0.40).

Conclusion: This study did not observe sex predilection for supracondylar humerus fractures or Gartland type. While this finding may not affect practice, it does serve to contradict literature and persisting stereotypes about the typical sex of patients with supracondylar humerus fractures and subsequent complications.

21. Colleen Hanlon, MS 2

Mentor(s): Tammy Brady, MD PhD
Department of Pediatric Nephrology

The Role of Obstructive Sleep Apnea in Left Ventricular Hypertrophy of Obese and Overweight Children

Authors: Colleen Hanlon BS, Laura Sterni MD, Edem Binka MD, Jeffrey Garofano PhD, Tammy Brady MD PhD

Background: Obesity is associated with structural and functional cardiac changes, including left ventricular hypertrophy. LVH in children can track into adulthood, leading to arrhythmias and cardiac events. We sought to determine the association of obstructive sleep apnea (OSA) with LVH among obese youth with elevated blood pressure.

Methods: A cross-sectional analysis of the baseline visits of 61 patients in a pediatric hypertension clinic between 1/2015 and 1/2018. Patients were obese individuals with elevated blood pressure, ages 5-21 years old. LVH was defined as: LVMI ≥38.6 g/m2.7, LVMI ≥95th percentile, or LVMI ≥51 g/m2.7. OSA was defined using a sleep study when available, or using the Pediatric Sleep Questionnaire. Children with and without OSA were compared using Fisher's exact tests, Student's t-tests, and Wilcoxon Rank Sum. Multivariable logistic regression was used to evaluate the association between OSA and LVH.

Results: Children with OSA were more likely to have LVMI ≥38.6 g/m2.7 (85.7% vs. 59.4%, p=0.047). OSA was associated with 4.11 times greater odds of LVMI ≥38.6 g/m2.7 (95% CI 1.15, 14.65; p=0.030). This association remained significant after adjustment for age, sex, race, and BMI z-score. A severe obstructive apnea hypopnea index (AHI >10) was associated with 14.00 times greater odds of LVMI ≥38.6 g/m2.7 (95% CI 1.14, 172.64, p=0.039), 14.00 times greater odds of LVMI ≥95th percentile (95% CI 1.14, 172.64, p=0.039), and 13.33 times greater odds of LVMI ≥51 g/m2.7 (95% CI 1.07, 166.37, p=0.044).

Conclusion: OSA was associated with LVH among obese youth with elevated blood pressure. OSA was significantly associated with LVMI ≥38.6 g/m2.7, even after adjustment for age, sex, race, and BMI z-score. The association between OSA and LVH was stronger when LVH was defined as LVMI ≥38.6 g/m2.7 as compared to LVMI ≥51 g/m2.7; the former value may be a more sensitive marker for end-organ damage in the pediatric population.

22. David Liao, Student in Residence

Mentor(s): Lisa Ishii, MD, MHS; Masaru Ishii, MD, PhD
Department of Otolaryngology - Head and Neck Surgery

Willingness to Pay for Increased Attractiveness and Perceived Success through Hair Transplant

Authors: David Liao, BA; Masaru Ishii, MD, PhD; Kristin L. Bater, BA; Lisa E. Ishii, MD, MHS

Background: According to the International Society of Hair Restoration 2017 Practice Census Report, over 130,000 hair restoration procedures were done in the United States in 2016. The study objective is to determine the monetary value of changes in age, attractiveness, and success through hair transplant in men as perceived by society.

Methods: A web-based survey was used to recruit a random sample of casual observers. The survey included pre- and post-procedural photos of six patients who underwent hair transplant and 4 controls who did not undergo any procedure. Participants were asked to quantitatively rate (1) the change in perceived age, attractiveness, and success as well as (2) the monetary value in US dollars they would associate with these changes using 100-point visual analog scales (centered at 0 from -50 to +50). Multilevel mixed-effects linear regression was used to determine the association between willingness to pay for hair transplant and changes in perceived age, attractiveness, and success.

Results: 152 respondents successfully completed the survey. Hair transplant had a positive and statistically significant effect on attractiveness and perceived success. Our regression model showed that the value of hair transplant without any change in age, attractiveness, or perceived success was $672.75 (95% CI $468.93—964.81, p<0.001). On average, those after hair transplant were rated to appear 3.76 years younger, and responders said they would pay an additional $102.12 (95% CI $80.94—90.36, p=0.012) for this result. Meanwhile, participants were willing to pay an additional $1,539.39 (95% CI $1,021.09—2,207.11, p<0.001) for a one standard deviation increase in attractiveness and an additional $924.18 (95% CI $338.78—1,638.67, p<0.001) for a one standard deviation increase in perceived success.

Conclusion: There is a significant association between change in attractiveness and perceived success from a hair transplant and its monetary value as rated by society.

23. Dylan Hardenbergh, MS 2

Mentor(s): Amy DeZern, MD
Division of Hematologic Malignancies

PNH Clones and Clinical Outcomes in Aplastic Anemia Patients

Authors: Dylan Hardenbergh BA, Amanda Blackford ScM, Amy DeZern MD

Background: Aplastic anemia (AA) is a rare bone marrow failure (BMF) disorder that consumes extensive healthcare resources and confers significant morbidity and mortality. Treatments include immunosuppressive therapy (IST) and bone marrow transplantation. Paroxysmal nocturnal hemoglobinuria (PNH) is a related BMF disease. Approximately 70% of AA patients have clonal populations of PNH cells at diagnosis, and the presence of a PNH clone is hypothesized to be associated with improved outcomes. Here we seek to explore the utility of PNH clone size as a predictor of response to IST.

Methods: This retrospective study examines patients assessed for PNH clones at a single center from 1/2003 to 6/2018 through review of a computerized medical records database. AA diagnosis was made by standard criteria. The presence of a PNH clone was detected by fluorescein-labeled proaerolysin. IST was defined as high-dose cyclophosphamide or anti-thymocyte globulin, and response to IST was reported per published methods. Statistical analysis for comparison included Wilcoxon rank sum, t-tests, and Fisher's exact tests.

Results: The cohort of 285 patients had a mean age at diagnosis of 40.5 years. 53.7% were female, and 112 were AA patients treated with IST. At 6 months following treatment, 33% showed no response (NR), 48.2% showed partial response (PR), 13.4% showed complete response (CR), and 5.4% were unknown. Forty-seven of these patients had a PNH clone documented prior to treatment. Among this group, CR patients had a larger median granulocytes clone (7.5%) compared to PR (1.2%) or NR (1.0%) patients. CR patients had a smaller median PNH clone size in monocytes (0.06%) compared to PR (0.5%) or NR (1.0%) patients.

Conclusion: The combined PR/CR rate of 62% is consistent with reported IST response rates. Larger PNH granulocyte clone size appears to be associated with increased response to IST. PNH clone size should be incorporated into therapeutic decisions for AA patients.

24. Erica Stern, MS 2

Mentor(s): Lindsay Borden, PhD

Department of Rheumatology, Department of Psychiatry

Disparity between Patient and Parent Perceptions of Psychological and Functional Status in Pediatric Lupus

Authors: Erica Stern BS, Lindsay Borden PhD, Sangeeta Sule MD

Background: Children with lupus report problems with physical functioning, while 50-60% also display neuropsychiatric dysfunction. The objective of this study was to compare patient and parent assessments of psychological and physical manifestations in lupus.

Methods: Survey data from lupus patients under the age of 18 and their parents at the Johns Hopkins Pediatric Rheumatology Multidisciplinary Clinic was retrospectively reviewed. Patients and their parents independently completed the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric/Parent Proxy Profile 25, assessing problems in social/emotional (i.e. depression, anxiety, peer relationships) and physical (i.e. fatigue, pain, mobility) functioning. Child and parent reported scores were correlated using Pearson's R on SPSS Statistics 24 software.

Results: Nine patients (89% female, 11% male; 78% African American, 11% Asian, 11% Hispanic) with mean age 12.99 years (SD=3.95) and mean 23.87 months since diagnosis (SD=29.50) were included.
No child reported measures were significantly correlated to their parent's report, including depression, anxiety and pain scores. Only physical mobility approached statistical significance as correlated between child and parent reports (r=0.757, p=0.051, N=7). Child reported anxiety and parent reported pain measures were significantly correlated (r=0.769, p=0.043, N=7). A trend was seen between parent reported depression and pain (r=0.731, p=0.062, N=7), but not child reported depression and pain. Children reporting higher depression scores reported more social/emotional problems but not physical problems (r=0.903, p=0.002, N=8; r=0.294, p=0.480, N=8), while parents reporting greater child depression reported both more social/emotional problems and physical problems (r=0.892, p=0.007, N=7; r=0.800, p=0.031, N=7).

Conclusion: Children and their parents do not interpret their lupus symptoms similarly. There was poor agreement between child and parent reports of psychological functioning in particular. This should be looked at in a larger cohort of children with lupus, while providers should be aware of these disparities in perceptions when assessing treatment progress and overall functioning of pediatric patients.

25. Feras Shamoun, MS 2

Mentor(s): Timothy Witham, MD
Department of Neurosurgery

Effects of Renin-Angiotensin System Inhibitors on Spinal Fusion: Retrospective Analysis of a Cohort of ACDF Patients.

Authors: Feras Shamoun B.Sc*, Alexander Perdomo-Pantoja MD*, Christina Holmes PHD, Wataru Ishida MD, Nicholas Theodore MD, Sheng-Fu Larry Lo M.D, Timothy F Witham MD

Background: Although instrumentation and bone graft alternatives has enhanced spinal fusion rates, pseudarthrosis remains a common problem. Recent evidence suggests an association between Renin-angiotensin system (RAS) blockers and bone healing, particularly in the context of osteoporotic bone fractures. Therefore, in this study we investigate the relationship between the use of antihypertensive medication and outcomes in anterior cervical discectomy and fusion (ACDF) surgery.

Methods: We performed a retrospective chart review of degenerative disc disease patients who underwent ACDF in 2015-2017 at Johns Hopkins Hospital, with 1-year minimum follow-up. Information on demographics, comorbidities, antihypertensive medication, neurological examination, and fusion status were collected. Spinal fusion was evaluated via plain cervical x-ray, resorting to dynamic radiographs in cases of uncertainty. Chi square and multivariable analyses were performed to determine the significance of the correlations.

Results: 200 patient met the inclusion criteria (86 females and 114 males, median age of 53.7 years). 82 hypertensive patients were identified, of which 77 (92.7%) were taking antihypertensive drugs. 36.4% of patients received angiotensin II receptor blockers [ARBs], while 35.1% received angiotensin-converting enzyme inhibitors [ACEIs]. Patients treated with ARBs exhibited a higher fusion rate compared to those untreated (p= 0.04) while patients on ACEIs exhibited lower fusion rates compared to untreated patients (p= 0.02). In the neurological examination analysis, ACEIs, hypertension status, and older age displayed lower modified Japanese Orthopedic Association (mJOA) recovery rate (p=0.001, <0.001, and <0.001, respectively) in the bivariate analysis

Conclusion: Our study shows that treatment of ACDF patients with ARBs was associated with higher fusion rates than untreated patients while patients treated with ACEIs demonstrate lower fusion rates. Further studies are required to confirm beneficial effects of ARB treatment on spinal fusion. This can provide an insight into how hypertension should be managed in spinal fusion patients

26. Francisco Eguia, MS 4

Mentor(s): Paul Sponseller, MD
Department of Pediatric Orthopedics

Can We Predict Choice of Academic Career in Orthopaedic Surgery?

Authors: Francisco Eguia BA, Caleb Gottlich, BS,MS, Gilberto Lobaton, BS, Kareem Kebaish BS, Marcus Daniels BS, Paul D. Sponseller MD

Background: Many students and residents pursuing orthopaedic surgery partake in academic activity including publication of research. It is unclear what factors, particularly academic activity as measured by pre-residency and residency publications, are associated with choosing a career in academic orthopaedics.

Methods: Orthopaedic residency alumni information was collected from 68 random residency websites. Graduates from 2011-2016 (n=1,183) were analyzed to determine factors associated with choosing an academic career. Scopus was used to collect information on publications, citations, and H-index. Current position was collected from a Google search and was classified as academic if the physician had an academic title signifying inclusion in a teaching department. Medical school ranking was determined from the research list of U.S. News & World Report 2019.Univariate analysis was used to determine whether academic activity or demographic variables were associated with academic career choice.

Results: Of the 1,183 physicians analyzed, 252 (21%) were in academic positions and 932 (79%) were nonacademic. The majority held an MD (90%), and 23 (2%) held an MD,PhD. Women made up 14% of the sample. Demographic variables significantly associated with a choice of academic career included having a PhD ($p<0.001$), and attending a top 20 or top 10 medical school ($p<0.001$, $p=0.005$, respectively). Sex was not associated with an academic career choice ($p=0.094$). Academic surgeons had an average of 1.7 and 5.4 publications before and during residency, respectively. Both of these rates were significantly higher than figures in those with nonacademic careers (0.8 and 2.3, respectively, $p<0.0001$).

Conclusion: 21% of orthopaedic residency graduates chose an academic career. They were more likely to graduate from a top tier medical school, have a PhD, and publish before and during residency than their nonacademic peers. We acknowledge limitations in classifying "academic" and that affiliations may change later. However, these findings may help identify and develop future academic orthopaedic surgeons.

27. Gregory Toci, MS 2

Mentor(s): Adam Levin, MD
Department of Orthopaedic Surgery

Mirels Score Effectiveness in Predicting Pathologic Fracture in Multiple Myeloma Lesions: A Retrospective Cohort Study

Authors: Gregory Toci BS, Jarred Bressner MD, Adam Levin MD

Background: Prophylactic fixation is favored over treatment of completed fractures in bone lesions from multiple myeloma (MM). Mirels score is used to predict fracture risk by considering lesion characteristics, location, size, and pain. Mirels was generated from many neoplasm types but has not been verified for MM.

Methods: Radiograph reports of MM patients (2003-2017) were reviewed for long bone lesions (inclusion criteria: >1-year follow-up or a skeletal-related event). Mirels performance was evaluated, and multinomial logistic regression identified trends between fracture and nonfracture groups for creation of a scoring system. Receiver operating characteristic curves compared scoring systems. Scoring systems were validated using 100 additional lesions not previously characterized.

Results: 357 lesions from 165 patients (49% male; mean±standard error, 61±1 years) resulted in 25 pathologic fractures (7%) and nine prophylactic fixations (3%). Significant differences between fracture/nonfracture groups in regression were: Mirels score, width fraction, latency (diagnosis to lesion identification), area (cm2), radiation treatment, and pain (mild, moderate, functional). Mirels sensitivity was 32% and specificity was 93% (area under curve (AUC), 0.70). The novel score, incorporating latency, area, radiation, and pain, sensitivity was 76% and specificity was 81% (AUC, 0.80). 8 of 31 (26%) fractured when Mirels suggested fixation, and 17 of 317 (5%) fractured when not suggested. 19 of 81 (23%) fractured when our score suggested fixation, and 6 of 261 (2%) fractured when not suggested. Both Mirels and our score suggested fixation in five (56%) of the prophylactic fixations. Validation using 100 lesions (4 fractures) resulted in novel score sensitivity of 100% and specificity of 99% (Mirels: sensitivity 75%, specificity 91%).

Conclusion: Mirels score is limited in identifying at-risk lesions in MM. A novel scoring system was created using the largest cohort evaluating lesions in MM literature to date. Further research should be performed to evaluate the efficacy of the newly proposed scoring system.

28. Ingharan Siddarthan, MS 2

Mentor(s): Eugene Shenderov, MD, DPhil
Department of Oncology

Deep Learning Algorithm for Detection of Acute Promyelocytic Leukemia from Peripheral Blood

Authors: Ingharan J Siddarthan, BA, Bo Shiun Lai, PhD, John-William Sidhom, MSE, Adam Luo, Thomas Kickler, MD, Alex Baras, MD, PhD, Mark Levis MD, Eugene Shenderov, MD, DPhil

Background: Acute promyelocytic leukemia (APL) is a treatable cancer, is considered a medical emergency at presentation, and its outcomes depend on early detection and initiation of appropriate therapy. Diagnosis of APL is limited by availability of resources and complicated by heterogeneity of presentation. Deep Learning is a series of computational methods that allow an algorithm to program itself through large-volume data analysis. We present a Deep Learning algorithm with the potential to detect APL through analysis of peripheral blood smears (PBS).

Methods: 203 patients of Johns Hopkins Hospital from 1989-2018 were selected based on confirmed t(15;17) or PML-RAR mutation status, and their demographic, molecular, and clinical characteristics and PBS were collected. Additionally, PBS of clinically normal and acute myelogenous leukemia (AML) patients were collected. A Cellavision and pathologist-verified subset of each cell type was utilized to train the algorithm to differentiate between normal/AML/APL. We assessed the predictive performance of the algorithm via Receiver-Operating-Characteristic (ROC) curves.

Results: Median (range) age was 49 (4-90) with approximately equal males/females, WBC (*1000/uL) was 3.01 (0.2-172.53) and platelets (*1000/uL) was 35 (3-386). Easy bruising/bleeding and fatigue were the most common presentation complications. Hemorrhage and infection were the most common causes of early death. ROC curves show an AUC for APL, AML, normal respectively as 0.7757, 0.8707, and 0.9317.

Conclusion: We present the largest single-institution Western cohort of APL patients to date. We show the first use case for Deep Learning in hematologic malignancy diagnosis and as a promising tool to emergently diagnose APL. These results support further prospective validation of this technology. Global health implications include aiding rapid diagnosis of APL in low-resource settings without access to extensive molecular/clinical studies or without experts to rapidly analyze PBS at presentation.

29. Jason Liew, MS 2

Mentor(s): Judy Huang, MD
Department of Neurosurgery

Embolization in High-Grade Arteriovenous Malformations

Authors: Jason Liew BA, Wuyang Yang MD MS, Risheng Xu MD PhD, Yuxi Chen, James Feghali MD, Justin Caplan MD, Rafael J Tamargo MD, Judy Huang MD

Background: The effectiveness of embolization for intervention of high-grade arteriovenous malformations(AVMs) has yet to be demonstrated. It is unclear whether embolization of these lesions may be associated with adverse events or functional outcome at last follow-up. We aim to elucidate the functional outcome and rates of hemorrhage in patients receiving only endovascular intervention of their high-grade AVMs when compared to untreated patients.

Methods: We retrospectively reviewed all grade IV and V AVM patients seen at our institution from 1990-2017. Patients were divided into two groups, those who received embolization and those who were conservatively managed. The primary outcome was mRS improvement at last follow-up. Secondary outcomes included obliteration and hemorrhage rates as well as mRS and clinical features at last follow-up.

Results: A total of 54 patients were included, 16.7%(n=9) of these patients were embolized. The mean age of embolized patients was 33.4 years compared with 37.6 years in the untreated group(p=0.535). 11.1%(n=1) of the patients in the embolized group presented with a ruptured AVM as opposed to 24.4%(n=11) in the untreated group. Improvement in mRS at last follow-up was slightly more prevalent in treated patients (50%(n=6) vs. 22.5%(n=9), though the difference was not significant (p=0.065). None of the embolized patients experienced hemorrhage during follow-up compared with 7 patients(15.6%) from the untreated group(p=0.586). The follow-up duration for treated patients was 7.71 years compared with 8.95 for untreated patients (p=0.741).

Conclusion: Treatment of high-grade AVMs with embolization is controversial and the functional outcome of patients following embolization are not well defined. Our data suggests that embolization is not associated with worse functional outcomes however, no patients in our study achieved obliteration and therefore embolization does not preclude them from future hemorrhage.

30. Jeffrey Elsner, MS 2

Mentor(s): Thuy Ngo
Johns Hopkins School of Medicine

A Bibliometric Analysis of the Integrated Plastic Surgery Match

Authors: Jeffrey Elsner BA, Mallory Toci, Scott Lifchez MD, Thuy Ngo DO M.Ed

Background: Successfully matched applicants to plastic surgery listed an average of 14.2 "abstracts, presentations and publications" on the Electronic Residency Application Service in 2018. This study quantifies the peer-reviewed publications of successful applicants, and examines whether productivity of matched students differs between residency programs.

Methods: The complete cohort of 159 students matched in 2017 was identified using program websites. Resident names were queried in Scopus and their bibliometric variables captured. Residency programs were divided into quintiles by Doximity research rank. All variables were non-normally distributed and quintiles compared by Wilcoxon or Kruskal-Wallis tests.

Results: Matched applicants had a median(IQR) of 2(0-4) total publications, 1(0-4) original research (excluding reviews/case reports) publications, 0(0-1) total first-authorships, 0(0-1) original first-authorships, and 1(0-2) total h-index. Compared to the second quintile, applicants matched to the first quintile of programs had significantly higher total publications (p=0.02), original publications (p=0.04), total first-authorships (p=0.01), and original first-authorships (p=0.03). No significant differences were found within second through fifth quintiles. Compared to other quintiles, published persons matched to the first quintile were significantly more likely to have published in a surgical journal (p=0.02) and plastic surgery journal (p<0.01).

Conclusion: Despite reporting many presentations, abstracts and publications, successfully matched applicants typically have authorship on few peer-reviewed publications, with first-authorships rare. Students matched to the first quintile residency programs were significantly higher by most bibliometric variables. These findings provide additional resources for advising students interested in matching plastic surgery.

31. Jenice Cheah, MS 2

Mentor(s): Marc Halushka, MD PhD
Department of Pathology

Subproteome of Cardiac Myocyte T-Tubules

Authors: Jenice Cheah BS, Tim Nieuwenhuis, Marc Haushka MD PhD

Background: Transverse tubules (t-tubules) are important structural elements, derived from sarcolemma, found on all striated myocytes. These specialized organelles create a scaffold for many proteins crucial to the effective propagation of signal in cardiac excitation-contraction coupling. The full protein composition of this region is unknown.

Methods: We characterized the t-tubule subproteome using 52,033 immunohistochemical images covering 13,203 proteins from the Human Protein Atlas (HPA) cardiac tissue microarrays. We used HPASubC, a suite of Python tools, to rapidly review and classify each image for a specific t-tubule staining pattern. The tools Gene Cards, String 10.5, and Gene Ontology (GO) Consortium as well as literature searches were used to understand pathways and relationships between the proteins.

Results: There were 96 likely t-tubule proteins by HPASubC. Of these, 12 were matrisome proteins and 3 were mitochondrial proteins. A literature search identified 54 t-tubule proteins. A comparison of those lists revealed only 17 proteins in common, including 8 of the matrisome proteins. For the 81 HPASubC t-tubule proteins, a query for biological process, the top GO terms were "caveola assembly", "receptor-mediated endocytosis of a virus by host cell" and "protein localization to a membrane raft." String10.5 revealed that 37 of the 80 proteins generated a single interconnected network.

Conclusion: We identified 78 novel, putative t-tubule proteins and validated 17, expanding and improving our knowledge of this important subcellular structure of the cardiac myocyte using HPASubC and the HPA. This information can be used to identify new structural targets involved in excitation-contraction coupling that may be altered in disease.

32. Jennifer Chen, MS 2

Mentor(s): Jacqueline Garonzik Wang, MD
Department of Surgery

Deceased Donor Kidney Transplantation Rates for Highly Sensitized Patients Under the New Kidney Allocation System

Authors: Jennifer Chen BA, Kyle R. Jackson MD, Karina Covarrubias BS, Courtenay Holscher MD, Xun Luo MD MPH, Allan Massie PhD, Niraj Desai MD, Dorry L. Segev MD PhD, Jacqueline Garonzik-Wang MD PhD

Background: Deceased donor kidney transplantation (DDKT) rates for highly sensitized (HS) candidates, defined as candidates with calculated panel reactive antibody (cPRA) > 80%, increased early after implementation of the Kidney Allocation System (KAS) in 2014. However, this may represent a bolus effect and a granular investigation of the current state of DDKT for HS candidates remains necessary.

Methods: We analyzed data from the Scientific Registry of Transplant Recipients (SRTR), which includes information on all donor, waitlisted, and transplant candidates in the United States. We identified 270,722 adult (age ≥ 18 years) kidney-only waitlist candidates and DDKT recipients. Of these, 30,031 were transplanted from 12/4/2011-12/3/2014 (pre-KAS) and 35,172 were transplanted 12/4/2014-12/3/2017 (post-KAS). DDKT rates for HS candidates before and after KAS were analyzed using adjusted negative binomial regression and cumulative incidence of DDKT was measured using a competing-risk framework.

Results: Post-KAS, candidates with the highest levels of sensitization had an increased DDKT rate compared to pre-KAS (cPRA 98% adjusted incidence rate ratio [aIRR]: 1.77 (1.27-2.46), $p=0.001$, cPRA 99% aIRR: 4.36 (3.18-5.98), $p<0.001$, cPRA 99.5-99.9% aIRR: 24.29 (16.91-34.89), $p<0.001$, and cPRA 99.9+% aIRR: 11.58 (8.79-15.26), $p<0.001$). To determine whether these changes produced more equitable access to DDKT, we compared DDKT rates of HS to non-HS candidates (cPRA 0-79%). Post-KAS, cPRA 98% candidates had equivalent transplant rates to non-HS candidates (aIRR: 0.94 (0.65-1.36), $p=0.8$). cPRA 99.5-99.9% candidates had increased DDKT rates compared to non-HS candidates (aIRR: 3.50 (2.46-4.98), $p<0.001$) but cPRA 99.9+% candidates had significantly lower DDKT rates (aIRR: 0.40 (0.29-0.56), $p<0.001$). The range of likelihood of DDKT at 3-years for a given cPRA category narrowed substantially post-KAS (20.2-48.4%) versus pre-KAS (4.2-44.4%).

Conclusion: KAS has produced sustained increases in DDKT rates for the most HS candidates (cPRA 98+%). Although heterogeneity exists among cPRA 99.5+% candidates, KAS has resulted in more balanced access to DDKT across cPRA groups.

33. Jerry Tsai, MS 2

Mentor(s): Luis Garza, MD, PhD
Department of Dermatology

Disruption and rebound of the skin microbiota after systemic antibiotic treatment of acne

Authors: Jerry Tsai BA, Anna L. Chien MD, Sherry Leung BA, Emmanuel F. Mongodin PhD, Amanda M. Nelson PhD, Sewon Kang MD, Luis A. Garza MD, PhD

Background: Acne vulgaris is a disease of the pilosebaceous unit associated with colonization by Cutibacterium acnes. Given the widespread use of systemic antibiotics for treatment of moderate to severe acne, it is important to understand their impact on not only C. acnes, but also the complete bacterial community of the skin.

Methods: Four female adult participants with facial acne were prescribed minocycline (100mg PO BID) for 4 weeks. We sampled skin from the forehead, cheek, and chin for 16S rRNA gene sequencing at 4 timepoints – baseline, 4 weeks after starting minocycline, then 1 week and 8 weeks after discontinuation of minocycline. We used the QIIME bioinformatics software to identify bacterial taxa and compute within-sample bacterial diversity (alpha diversity) and inter-sample bacterial diversity (beta-diversity). Comparisons of alpha diversity and relative abundance of bacteria between samples were performed with t-tests with Monte Carlo permutations, while comparisons of beta diversity were performed with the analysis of similarity (ANOSIM).

Results: Across all four participants, antibiotic treatment resulted in a 1.4-fold reduction of C. acnes (P=0.04) with recovery following cessation of treatment. We also identified distinct patterns of change in multiple bacterial genera, including a transient 5.6-fold increase in Pseudomonas spp. (P<0.001) immediately following antibiotic treatment, as well as a persistent 1.7-fold increase in Streptococcus spp. (P=0.04) and 4.7-fold decrease in Lactobacillus spp. (P=0.02) at 8 weeks following antibiotic withdrawal. On average, bacterial diversity decreased from baseline with antibiotic administration, followed by its recovery. Principal coordinates analysis demonstrated clustering of samples by subject and by timepoint among individual subjects (ANOSIM, P=0.001).

Conclusion: Antibiotic treatment affects the composition and diversity of the skin microbiota, with variable rates of recovery across individuals and parallel changes in specific bacterial populations. Understanding the impact of antibiotics on the skin microbiota may help clinicians decrease the likelihood of skin comorbidities related to microbial dysbiosis.

34. John Morkos, MS 2

Mentor(s): Russell Hales

Department of Radiation Oncology and Molecular Radiation Sciences

Single Pulmonary Nodule Project

Authors: John Morkos BS, Adam Ferro MD, Russell Hales MD

Background: Solitary pulmonary nodules (SPNs) are a common finding in patients who have a high risk for lung cancer. However, most nodules are benign though surgical biopsies that carry significant risk are still necessary for determining with absolute certainty whether a nodule is malignant or not. Nomograms have been created to predict the likelihood that a pulmonary nodule represents primary lung cancer based on images and clinical features. However, the extensive use of metabolic imaging has not been incorporated into the most commonly used predictive nomograms. In this study, we incorporate PET variables (max SUV, mean SUV, and standard2 dev SUV) with clinical and CT variables to create a more accurate, probabilistic model for predicting the malignancy status of solitary pulmonary nodules.

Methods: 436 patients with unbiopsied pulmonary nodules were taken for resection at Johns Hopkins Hospital between 2007 and 2016. Of the 436 patients, 163 patients met all of the following features: solitary nodule, PET imaging prior to resection and nodule volume<25cc. After accounting for clinical and CT variables, PET variables in benign and malignant nodules were compared to assess their significance in predicting the malignancy of SPN.

Results: 113 patients had malignant nodules and 50 had benign nodules. Metabolic imaging features associated with malignancy included SUV max (4.55 versus 3.42, malignant versus benign, $p=0.05$), standard deviation SUV (0.74 versus 0.52, $p=0.03$) and a trend in Peak SUV BW (3.31 versus 2.55, $p=0.07$).

Conclusion: Patients with solitary pulmonary nodules were demonstrated to show metabolic features on pre-treatment imaging that correlated with an increased likelihood of malignancy. The next steps of this project will layer clinical and non-metabolic imaging features with metabolic imaging to create a more robust nomogram for lung cancer prediction in patients with pulmonary nodules

35. Julia Gips, MS 2

Mentor(s): Carolyn Sufrin, M.D., Ph.D.
Department of Gynecology and Obstetrics

Does Distance Decrease Healthcare Options for Pregnant, Incarcerated Women? Mapping the Distance between Abortion Providers and Prisons

Authors: Julia Gips BS, Lauren Beal, Carolyn Sufrin M.D., Ph.D.

Background: Pregnant, incarcerated people retain the constitutional right to abortion, but available evidence suggests that many cannot access abortion while in custody. State and federal prisons are often located in remote areas. There is a known shortage of abortion providers across the U.S., especially in remote areas. This study seeks to map the proximity of prisons to abortion clinics in order to better understand whether access to abortion care providers might contribute to the difficulties incarcerated pregnant people face when seeking an abortion.

Methods: We used publicly available information to record the locations of all abortion clinics in the United States, as well as any state or federal prisons that house at least 10 women. We then used these geographic data points to map the prisons and abortion clinics and record the distances between them using an interactive, Google mapping tool. Distance data were analyzed in each state to determine mileage to nearest abortion clinic, and according to state abortion laws.

Results: We mapped 643 abortion clinics, 75 state prisons and 20 federal prisons. The largest minimum distance between a state prison and abortion clinic was 383.45 miles, the shortest was 2.23 miles. The largest minimum distance between a federal prison and abortion clinic was 117.54 miles, the shortest was 0.485 miles. There were 4 states in which the minimum distance between any type of prison and an abortion clinic was above 100 miles.

Conclusion: Abortion clinics are located far away from both state and federal prisons. This may contribute to the numerous barriers pregnant incarcerated people face when searching for abortion care.

36. Julie Kim, MS 2

Mentor(s): Frank Lin, MD PhD
Department of Otolaryngology

Retinal Signs and Hearing Loss in the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS)

Authors: Julie Kim BS, Nicholas Reed AuD, Alison Abraham PhD, Moon Jeong Lee BS, A. Richey Sharrett MD DrPH, Frank Lin MD PhD, Jennifer A. Deal, PhD

Background: Age-related hearing loss is highly prevalent and treatable. Given its relationship with adverse health outcomes, understanding its etiology may have implications for disease prevention. Microvascular disease may contribute to hearing loss through a reduced cochlear blood supply, but few epidemiologic studies have examined this relationship. Using retinal signs as a proxy for microvascular disease, we quantified the association between microvascular retinal signs and hearing in ARIC-NCS.

Methods: Participants were a subset of the ARIC cohort (US prospective cohort study, baseline visit in 1987-89) who underwent retinal fundus photography in 2011-13 and a hearing assessment in 2016-17 with complete covariate data. Hearing was measured using the better-hearing ear pure tone average (PTA) of air conduction speech thresholds (0.5, 1, 2, and 4kHz). Retinal signs included retinopathy, arteriovenous (AV) nicking, and generalized arteriolar narrowing, measured using the central retinal arteriolar equivalent (CRAE). Multivariable-adjusted linear regression was used to estimate the association between retinal signs and hearing.

Results: After full adjustment in the analytic cohort (N=1458, 67-90 years, 57% female, 20% black), the difference in PTA per 10 decibel hearing level (dB HL) comparing persons with and without retinopathy was 2.21 (95% CI:[-0.22, 4.63]), suggesting that retinopathy is associated with poorer hearing, although this finding was not statistically significant (p=0.074). The association was stronger in participants without diabetes; difference in PTA per 10 dB HL comparing participants with and without retinopathy (N=42) was 4.14 (p=0.045). In analyses quantifying mean differences in hearing thresholds at individual frequencies by retinopathy status, estimates trended towards retinopathy being associated with better high-frequency hearing (8kHz, -4.24 (95% CI:[-7.39, -1.09]).

Conclusion: In this population-based study, retinopathy was associated with later poorer hearing in the speech frequencies in a small number of participants without diabetes, pointing to the need for further epidemiologic studies to elucidate the degree of microvascular contributions to hearing loss.

37. Katerina Lin, MS 2

Mentor(s): Sapna Kudchadkar, MD, PhD
Department of Anesthesia

Delirium in Critically Ill Children

Authors: Katerina Lin and Sapna Kudchadkar, MD, PhD

Background: Delirium in the PICU is a serious medical concern for pediatric patients suffering from critical illness. We investigated patient characteristics associated with early assessment at a tertiary level PICU. We examined whether children with risk factors for delirium, including younger age, mechanical ventilation, and use of physical restraints, received early evaluation.

Methods: We conducted a retrospective analysis of 100 pediatric patients presenting to the PICU following implementation of an interdisciplinary quality improvement program called PICU Up! (details described in prior research). Delirium was measured using the Pediatric Confusion Assessment Method for the ICU. Patients were admitted for at least 3 days. We evaluated patients at PICU day 2 (early evaluation) versus PICU day 3 (later evaluation). Univariate analysis and logistic regression of patient characteristics were performed.

Results: Forty patients reported with delirium assessment. Patients with this documentation were more likely to have normal baseline motor function (p=.07) and supplemental consultation through pediatric pain services (p=.02). Twenty-four patients had early evaluation; in univariate analysis, these patients were more likely to have higher maximum pain scores (p=0.05) compared to those with later evaluation. Other characteristics, including age, physical restraints, PRISM, intellectual disability, and use of antipsychotics were not major factors. In the logistic regression, the odds of early delirium screening for every one point increase in pain score was 1.25 (95% CI: 1.01-1.56, p=0.04).

Conclusion: Delirium evaluation is underreported in the PICU. Patients with higher maximum pain scores tended to have earlier delirium screening, suggesting that hyperactive patients are receiving earlier evaluations. This study contributes to our understanding of patient characteristics leading to delayed assessment and may inform future initiatives targeting delirium in critically ill children. Further prospective studies are necessary to determine barriers to delirium screening in the critical care unit.

38. Katherine Fomchenko, MS 2

Mentor(s): Marc Halushka, M.D., Ph.D.
Department of Pathology

Mosaic expression of over 2,000 proteins indicate wide diversity between fast and slow-twitch skeletal muscle fibers

Authors: Katherine M. Fomchenko B.S., Marc K. Halushka M.D., Ph.D.

Methods: Using HPASubC, 50,351 skeletal muscle images from HPA were obtained. We assigned each image a score, validated by a board-certified pathologist, based on the level of confidence that the image displayed mosaic protein expression. These scores were used to characterize the proteins reflected in each image into confidence categories of "real," "likely," and "unknown," reflecting the strength of mosaicism. Stratified by this characterization, the proteins discovered were analyzed using Gene Ontology (GO) and String webtools, as well as compared to previously published skeletal muscle proteomic databases.

Results: In total, 2,143 proteins were differentially expressed in skeletal muscle, with 367 proteins in "real," 1,223 in "likely," and 553 in "unknown" categories respectively. A significant number or our proteins were newly described with only 745 proteins (34.3%) and 578 proteins (27.0%) overlapping the mass-spectrometry based Human Skeletal Muscle Proteome and the Mann laboratory single fiber proteome.1 Some of the novel "real" mosaic proteins identified include GLRX2, TMEM161A, CLDND1, CCDC80, and SYDE1. GO terms with the highest enrichment across all mosaic proteins were "fructose 1,6-bisphosphate metabolic process" and "muscle filament sliding," while the "real" confidence category had the highest enrichment for "transition between fast and slow fiber" and "muscle filament sliding."

Conclusion: Our careful evaluation of >50,000 images using HPASubC yielded a number of proteins mosaic in skeletal muscle that had not been previously described. Many of these proteins had interesting functional classifications. This data could be used to further understand the role of skeletal muscle in disease and aging.

39. Katherine Whang, MS 2

Mentor(s): Shawn Kwatra, MD
Department of Dermatology

Atopic Dermatitis is associated with increased risk of multiple ocular comorbidities

Authors: Katherine Whang BS, Kishan Govind MD, Raveena Khanna BA, Adrienne W. Scott MD, Shawn G. Kwatra MD

Background: We are testing the use of artesunate, which is a WHO-approved front-line treatment of acute malaria, as a topical treatment for CIN2/3. Although it is incompletely understood how artesunate mediates cell death, one possible mechanism of action is via its interaction with intracellular iron, generating reactive oxygen species (ROS).

Methods: We collected retrospective data on demographics and comorbidities of patients age 18 years and older seen at the Johns Hopkins Hospital System (JHHS) from 2013-2018 using the Slicer Dicer feature of electronic medical record system EPIC. We determined the prevalence of dry eye syndrome, ophthalmic herpes simplex, cataracts, glaucoma, retinal detachment, iritis, uveitis, keratoconjunctivitis, keratoconus, conjunctivitis, and blepharitis in patients with a concomitant diagnosis of atopic dermatitis (n=8992) compared to control subjects within the general patient population 18 years and older (n=4764955).

Results: Of the ocular conditions studied, the following ocular surface diseases had the greatest association with AD: blepharitis (OR 10.99 [10.08-11.98], p<0.001) conjunctivitis (OR 12.88 [12.00-13.82], p<0.001), keratoconjunctivitis (OR 8.21 [6.91-9.73], p<0.001), and dry eye (OR 6.72 [5.88-7.69], p<0.001). Additionally, patients with AD also had a higher incidence as compared to the general population of the following conditions: keratoconus(OR 5.40 [3.61-7.78], p<0.001), uveitis(OR 5.43 [4.33-6.73], p<0.001), retinal detachment(OR 3.22 [2.39-4.26], p<0.001), glaucoma(OR 4.13 [3.68-4.63], p<0.001), cataracts(OR 4.89 [4.55-5.25], p<0.001), and ophthalmic herpes simplex(OR 4.90 [2.23-9.34], p<0.001).

Conclusion: We found that patients with atopic dermatitis are significantly more likely to experience a variety of ocular complications as compared to the general population. These findings highlight the need for a collaborative effort by dermatology and ophthalmology in ensuring early diagnosis of ophthalmic involvement in patients with atopic dermatitis for early intervention to prevent vision threatening complications.

40. Kathryn Pearson; Taylor Purvis, MS 4

Mentor(s): Steven Frank, MD
Department of Anesthesiology and Critical Care Medicine

Greater Anemia Tolerance in Females Compared to Males for Inpatient Mortality

Authors: Mereze Visagie, Kathryn Pearson, Taylor E. Purvis, Eric A. Gehrie, Steven M. Frank

Background: Although women have a lower baseline hemoglobin (Hb) compared to men, it is unknown whether women have a greater tolerance for anemia when hospitalized. As a result, we tested the hypothesis that women can tolerate a lower absolute Hb than men without an increase in inpatient mortality.

Methods: After receiving IRB approval, we conducted a retrospective cohort study using a database with all adult patients admitted to Johns Hopkins Hospital from January, 2009 to June, 2016. The relationship between nadir Hb during the hospitalization and inpatient mortality was assessed for non-transfused males and females. The percentage change in Hb (delta Hb) was also assessed in relation to mortality. A multivariable logistic regression was used to determine risk-adjusted differences between men and women for the likelihood of inpatient mortality at Hb thresholds of 5, 6, and 7 g/dL.

Results: Among 190,549 non-transfused patients, males with a nadir Hb level of ≤ 6.0 g/dL had a greater incidence of in-hospital mortality, whereas females did not show this difference. Inpatient mortality increased significantly in both men and women when the Hb decrease was > 50% from baseline (Figure B). The risk-adjusted odds for inpatient mortality was significantly greater for men compared to women at a nadir Hb of 6 g/dL, but this sex-related difference was not significant at 5 and 7 g/dL (Table).

Conclusion: Our findings demonstrate that overall, women tolerate a lower nadir Hb, but a similar delta Hb compared to men, when inpatient mortality is the primary outcome. The findings suggest that a nadir Hb of 6 g/dL may be safe in women, but not for men.

41. Kendrick Wang, MS 4

Mentor(s): Albert Jun, MD

Wilmer Eye Institute, Department of Ophthalmology

Intraocular Lens Power Prediction for Cataract Surgery in Eyes with Abnormal Corneal Topography

Authors: Kendrick Wang BS, John Ladas MD, Divya Srikumaran MD, Aazim Siddiqui MD, Albert Jun MD.

Background: Cataract is the leading cause of vision loss. An important factor to patient outcomes after cataract extraction and intraocular lens (IOL) implantation is the calculation of IOL power. There are several mathematical formulas that estimate the IOL power for implantation based on "normal" eyes with regular corneal topography. This project examines the outcomes of cataract surgery and the accuracy of IOL power prediction in individuals with corneal ectasia, resulting in abnormal corneal topography.

Methods: This study analyzed a cohort of 46 eyes with corneal ectasia which underwent cataract surgery at Johns Hopkins. Pre- and post-operative data were gathered through retrospective chart review. The IOL power selected and refractive outcome predicted by various formulas were determined and compared.

Results: Out of 46 eyes, four eyes had best corrected visual acuity (BCVA) of worse than 20/40. The most common BCVA was 20/25. Hoffer Q, SRK/T, Holladay I, SRK/II, Barrett, and Ladas Super Formula (LSF) were applied to all patients except one without recorded biometry information. The first three formulas predicted an implant lens power for every eye. The Barrett and LSF formulas both failed to predict an IOL power in four eyes due to values outside the accepted range for these formulas. The theoretical predicted postoperative spherical equivalent (SE) by these six formulas were not statistically equal ($p<0.001$). The mean absolute difference of SE predicted by the Hoffer Q, SRK/T, Holladay I, SRK/II, Barrett, and LSF formulas compared to actual postoperative SE were 0.915(95%CI: 0.629 – 1.201), 1.083(95%CI: 0.730 – 1.436), 0.812(95%CI: 0.551 – 1.073), 1.693(95%CI: 0.882 – 2.504), 0.791(95%CI: 0.511 – 1.071), and 0.912(95%CI: 0.626 – 1.198) respectively.

Conclusion: Current formulas fail to accurately predict IOL power for eyes with abnormal corneal topography. All formulas had visually significant (>0.5D) absolute error compared to postoperative SE. Postoperative vision could improve with refinement of IOL formulas for eyes with abnormal corneal topography.

42. Kevin Pineault, MS 3

Mentor(s): Yuri Agrawal
Department of Otolaryngology-Head and Neck Surgery

Bilateral vestibular loss is associated with decreased cognitive performance

Authors: Kevin Pineault BS, Deryck Pearson BA, Eric Wei BA, Rebecca Kamil MD, Yuri Agrawal MD

Background: Recent studies into how the vestibular system impacts function have revealed key roles in maintaining balance and posture and in higher order cognitive processes. Despite evidence demonstrating vestibular functional impairment impacting cognitive performance (i.e. executive function and visuospatial ability), it is unknown if the cognitive deficiency in these vestibular patients is different than the cognitive performance in matched healthy aging adults.

Methods: We recruited 54 patients with a diagnosed vestibular disorder (14 with normal vestibular function, 4 with unilateral vestibular loss and 22 and bilateral vestibular loss) from the Johns Hopkins Neurotology Clinic. Vestibular function was measured with cervical vestibular-evoked myogenic potential (cVEMP) responses, and multiple cognitive tests were administered to assess cognitive performance among participants. 152 matched control participants were recruited from the Baltimore Longitudinal Study of Aging (BLSA).

Results: Using multivariate linear regression analyses, patients with bilateral vestibular loss had significant decreases in performance on two cognitive tests, the Trail Making Test (TMT) (β 26.5, 95% CI 2.3, 50.8) and the Benton Visual Retention Test (β 4.4, 95% CI 1.3, 7.5). In our case control analysis, patients presenting to the Neurotology clinic had significantly decreased performance on the TMT compared to matched BLSA controls (OR 1.01, 95% CI 1.004, 1.03).

Conclusion: This study determined that bilateral vestibular impairment significantly affects cognitive performance. Additionally, cognitive performance deficits determined by one of the cognitive tests used in our battery was determined to be significantly different from matched healthy aging adults. Further investigation into the differences in cognitive performance among vestibular patients and matched healthy individuals may encourage the use of cognitive tests to guide rehabilitation and physical therapy for those with diagnosed vestibular disorders.

43. Lena Chen, MS 2

Mentor(s): Jonathon Russell, MD
Department of Otolaryngology - Head and Neck Surgery

Comparison of postoperative scar cosmesis outcomes in transoral versus transcervical thyroidectomy/parathyroidectomy recipients using the Scar Cosmesis Assessment and Rating (SCAR) Scale

Authors: Lena W. Chen BA; Christopher R. Razavi MD; Hanna Hong; Akeweh Fondong; Rohit Ranganath MD; Ralph P. Tufano MD MBA; Jonathon O. Russell MD

Background: The transcervical approach to the central neck has been used to safely perform thyroid and parathyroid surgery for over 100 years, but some studies have demonstrated that the residual scar can negatively impact patient quality of life. The transoral endoscopic approach to the central neck eliminates this morbidity. It has been demonstrated to be safe and effective in performing thyroidectomy, parathyroidectomy, and central neck dissection. Given the primary benefit of the technique is cosmetic, there is a need for an objective study comparing cosmetic outcomes between the open and transoral techniques. Here we present such a study.

Methods: Standardized photographs of postoperative thyroidectomy and parathyroidectomy patients completed via the transcervical and transoral techniques were reviewed. Images were scored by three endocrine surgeons using the validated Scar Cosmesis Assessment and Rating (SCAR) Scale. SCAR scores between techniques were compared using a Mann-Whitney U test. Inter-rater reliability (IRR) was determined using an intraclass correlation coefficient (ICC) for consistency, with 2-way mixed-effects model.

Results: Forty-eight patients were included for analysis, with 30 (63%) and 18 (37%) being performed via the transcervical and transoral techniques respectively. The mean age was 48.8 (st. dev. 15.1), and 36/48 (75%) were female. Median postoperative follow-up time was 3.1 (range 1-34) weeks. The transcervical group had a median SCAR score of 5 (range 0-13) compared to 0 (range 0-10) for the transoral group ($p < 0.001$). IRR was excellent (ICC of 0.90; 95% CI: 0.83-0.95).

Conclusion: Patients undergoing transoral approaches to the central neck had significantly improved postoperative cosmesis as compared to those undergoing transcervical procedures. The excellent IRR for the SCAR scale in our series suggests that it is a reliable tool to evaluate scar cosmesis from postoperative thyroid- and parathyroidectomy photographs.

44. Luke Glover, MS 2

Mentor(s): Stephanie Terezakis, MD

Department of Radiation Oncology and Molecular Radiation Sciences

Palliative Radiation Therapy for Children in Two Unique Health Systems

Authors: Avani Rao MD, Maria Figueiredo MD, Nikhil Yegya-Raman, Shuchi Sehgal, Qinyu Chen MHS, Sara Alcorn MD, MPH, Michael Chen MD, Matthew Ladra MD, Rosangela Villar MD, Luke Glover BS, Stephanie Terezakis MD

Background: The integration and outcomes of pediatric palliative radiation therapy (RT) vary across healthcare systems. This study describes the practice and clinical outcomes of palliative RT in the US and Brazil.

Methods: The indication for treatment, RT technique, and toxicity of palliative RT of pediatric oncology patients (<21 years-old) from 2010-2016 in two Brazil-based and one US-based academic centers were reviewed in this study. Each center independently gathered clinical data from their electronic medical records. Response to symptoms was evaluated on patients with available follow-up data.

Results: 88 pediatric patients were treated with palliative RT totaling 131 cases of palliative radiation therapy. 49 patients from the US cohort comprised 84 cases; 39 patients from the Brazil cohort comprised 46 cases. The most common indication for palliative RT was pain (55% overall. 63% US; 39% Brazil). Prophylactic prevention of impending symptoms occurred in both cohorts (10% US; 2% Brazil). 67% of patients experienced a complete (CR) or partial response (PR) to palliative RT for their palliative indication, 12% reported stable symptoms (SS), and 22% reported progressive symptoms (PS). When pain indicated palliative RT, 83% of patients experienced CR/PR, facilitating reduction or discontinuation of opiate use in 46% of these patients.

Conclusion: While implementation may vary across health systems, palliative RT is a useful, safe, and effective tool for pediatric oncology patients. These data provide a snapshot of the clinical practices and results using palliative RT for pediatric patients treated in two unique healthcare environments demonstrating its success across systems.

45. Marcus Daniels, MS 4

Mentor(s): Max Kates, MD
Department of Urology

Contemporary Oncologic Outcomes of Second Induction Course BCG in Patients with Non-Muscle Invasive Bladder Cancer

Authors: Marcus Daniels BA, Emily Barry BS, Mark Schoenberg MD, Trinity Bivalacqua MD/PhD, Alex Sankin MD, Max Kates MD

Background: The 2016 AUA Guidelines for non-muscle-invasive bladder cancer (NMIBC) advocate 2nd intravesical induction course of Bacillus Calmette-Guérin (BCG) for patients with persistent/recurrent Ta or CIS after 1st BCG induction course. Evidence for a 2nd course is limited. We sought to investigate contemporary oncologic outcomes of a 2nd induction course of BCG in a multi-institutional cohort.

Methods: Three hundred fifty-three patients who received induction BCG ± interferon for NMIBC since 2001 at 2 institutions were identified. Patients were categorized as receiving primary 6-week induction therapy (BCG1) or subsequent 2nd 6-week induction therapy (BCG2) for patients who recurred. Baseline demographic and tumor characteristics were compared, and Kaplan-Meier curves were constructed to assess for high-grade recurrence-free survival (HgRFS) among both groups. Logistic regression determined factors associated with recurrence after BCG2.

Results: A total of 353 patients received BCG1 and 116 patients received BCG2. Maintenance therapy was given to 33.1% of patients after BCG1 and 37.1% of patients after BCG2. Median follow-up time was 26.3 months. Demographics were similar between cohorts. BCG1 patients had more T1 (40.8% vs 25%, p= 0.002) and less CIS (13.9% vs 33.6%, p= <0.001). BCG2 patients had higher 1-year (64.3% vs 76.7%, p= 0.013) and 3-year (54.7% vs 65.6%, p= 0.040) HgRFS. Progression to MIBC was identified in 1.4% of BCG1 patients vs 3.4% in BCG2 patients (p=0.17). Stage at recurrence was similar for each group. No factors were associated with recurrence after BCG2.

Conclusion: In well selected patients, a 2nd course of BCG is efficacious with a durable HgRFS. These results validate the 2016 AUA guidelines of a 2nd course of intravesical BCG after initial tumor recurrence.

46. Mark Ren, MS 2

Mentor(s): Christopher Abularrage, MD
Department of Surgery

Bibliometric Analysis of Academic Vascular Surgery Training Programs and Faculty

Authors: Mark Ren BS, Benjamin Bigelow BS, Christopher Abularrage MD

Background: Scientific research a core value of academic medicine and one of the most important factors for promotion in academic careers. Exposure to the research process and opportunities to conduct and publish scholarly work is therefore integral part of an academic vascular surgery residency program. However, there is no published evaluation of research productivity for academic vascular surgery departments and faculty.

Methods: A list of academic vascular programs was obtained from the Accreditation Council for Graduate Medical Education (ACGME). Faculty were identified from departmental websites, and demographic information (academic rank, sex) were recorded when available. A database of published research for each faculty member was created using Scopus, the largest database of peer reviewed literature. Publication statistics from our database were then used to create bibliometric profiles, including h-index, hc-index, and m-quotient, for each faculty member. Sum and mean of faculty h-indices were calculated for each program according to their listed faculty members.

Results: A total of 906 vascular surgeons from 113 training programs were analyzed. The mean h-index (± SEM) for all surgeons was 13.8 ± 0.44. The cohort included 744 male and 162 female vascular surgeons. Mean h-indices were higher for each consecutive academic rank: 28.7 ± 0.98 (n=209) for professors, 13.8 ± 0.68 (n=170) for associate professors, and 6.72 ± 0.35 (n=297) for assistant professors. The average sum of faculty h-indices for each program was 111 ± 6.48.

Conclusion: This is the most detailed summary to date of the research productivity of academic vascular surgeons and training programs. The information provided can serve as a mechanism to further evaluate research trends in academic vascular surgery.

47. Michelle Recto, MS 3

Mentor(s): Maria Trent, MD
Department of Pediatrics

Please Be Careful with Me: Discrepancies between Adolescent Expectations and Clinician Perspectives on the Management of Pelvic Inflammatory Disease

Authors: Maria Trent MD MPH, Michelle Recto BA, Qiang Qian MS, Arlene Butz BSN ScD, Kevin D. Frick PhD, Jonathan M. Ellen MD, Harold Lehmann MD PhD

Study Objective: To clarify clinician perspectives in the context of consumer expectations for better application of national guidelines for the treatment of pelvic inflammatory disease (PID).
Design: Cross-sectional study.
Setting: Urban academic pediatric and adolescent medicine practices and school-based health clinics in a large urban community with a high prevalence of sexually transmitted infections (STI).
Participants: Female patients aged 12-19, parents raising an adolescent over the age of 12 in the urban community, and clinicians who serve adolescents collected from regional and national listservs.
Interventions: None.

Main Outcome Measures: Visual analog scale (VAS) scores on a scale of 0 to 10 corresponding to preferences on patient disposition in 17 clinical scenarios for a hypothetical patient with PID.

Results: Compared to adolescents, clinicians were significantly more likely to endorse hospitalizations when patients presented with severe or complicated illness (0.9, SE 0.22, p<0.001), possible surgical emergency (0.83, SE 0.2, p<0.001), concurrent pregnancy (0.59, SE 0.3, p=0.046), failure of outpatient treatment (0.58, SE 0.29, p=0.045). Compared to clinicians, adolescents were significantly more likely to endorse hospitalizations when patients presented at a young age (1.36, SE 0.38, p<0.001), were homeless (0.88, SE 0.32, p=0.007), were afraid to inform a partner (1.66, SE 0.40, p<0.001), or had unaware parents (2.86, SE 0.39, p<0.001).

Conclusion: Clinicians were more likely to recommend hospitalization when doing so adhered to national guidelines on PID treatment. Adolescents opted for hospitalization more often than clinicians in scenarios where patients exhibited social vulnerability. Clinicians should engage with adolescents in shared disposition planning and use a more nuanced approach to PID management for adolescents who may not be able to tolerate an outpatient regimen.

48. Rafa Rahman, MS 3

Mentor(s): Brian J Neuman, MD
Department of Orthopaedic Surgery

Determining Clinically Meaningful PROMIS Severity Ranges for Lumbar Degenerative Patients

Authors: Rafa Rahman BS, Alvaro Ibaseta MS, Jay S Reidler MD, Richard L Skolasky Sc.D., David B Cohen MD MPH, Daniel M. Sciubba MD, Khaled M. Kebaish MD MBBCh MS, Brian J Neuman MD

Background: PROMIS provides severity ranges in many domains. These ranges are determined based on the general population, using a normalized mean score of 50 and standard deviation of 10. Lumbar degenerative (LD) patients have worse scores compared to the general population, making these ranges clinically meaningless in the care of LD patients. Our objective was to determine PROMIS severity ranges specific to LD patients.

Methods: Preoperative PROMIS scores in Pain Interference, Physical Function, Fatigue, Anxiety, Depression, Sleep Disturbance, and Satisfaction with Social Roles were retrospectively analyzed for LD patients. To create LD-specific severity ranges, the average and standard deviation (SD) for each PROMIS domain were calculated for the cohort. Scores 1.0-2.0 SD worse than the mean were considered "moderately worse" than the LD average, scores 2.0 or more SD worse than the mean were "severely worse," and scores 1.0 or more SD better were "moderately better."

Results: For 407 LD patients (avg. age 57.2 years; 51.8% male; 78.7% White, 12.4% AA, 8.9% other), average PROMIS score and severity ranges were determined: Pain Interference average: 64.5, moderately better: <57.1, moderately worse: 71.8-79.2, severely worse: >79.2; Physical Function average: 35.3, moderately better: >43.2, moderately worse: 19.6-27.5, severely worse: <19.6; Fatigue average: 57.6, moderately better: <47.9, moderately worse: 67.2-76.9, severely worse: >76.9; Anxiety average: 53.8, moderately better: <44.3, moderately worse: 63.2-72.7, severely worse: >72.7; Depression average: 49.6, moderately better: <40.0, moderately worse: 59.3-68.9, severely worse: >68.9; Sleep Disturbance average: 56.0, moderately better: <46.7, moderately worse: 65.2-74.4; severely worse: >74.4; Satisfaction with Participation in Social Roles average: 40.4, moderately better: >49.0; moderately worse: 23.3-31.8; severely worse: <23.3.

Conclusion: While PROMIS provides severity ranges useful for the general population, lumbar degenerative patients on average have worse scores. We provide clinically meaningful PROMIS severity ranges for these patients, to allow surgeons to better assess severity and aid in point-of-care decision-making.

49. Rohan Bajaj, MS 3

Mentor(s): Gislin Dagnelie

Wilmer Eye Institute, Department of Opthamology

Surveillance Technology in the Bionic Eye: Efficacy of a Thermal Camera in the ARGUS II Retinal Prosthesis System

Authors: Rohan Bajaj, Roksana Sadeghi, Paul Gibson, Avi Caspi, Arup Roy, Gislin Dagnelie

Background: The ARGUS II retinal prosthesis restores the ability to perceive images and movements in patients with end-stage photoreceptor degeneration. The system uses a processor to transform images from a camera into data that are wirelessly transmitted to a retinal implant. A trial was performed to compare the efficacy of a thermal-camera to the standard camera.

Methods: Four patients with ARGUS were selected at Wilmer Institute. 4 tasks were performed: (1) Mobility Task- human target stood at 1/4 locations. The participant would walk to the target. (2) Bowls Task- up to 4 white bowls filled with hot water were placed in front of the subject. The subject would indicate if a specific bowl was missing. (3) Cups Task- two white cups filled with hot water on a table; the subject would indicate the closer cup. (4) Distant Person Task- human target stood in front of the subject and the subject would indicate the distance to the target. 20-60 trials were completed for each task with each camera. Chi-squared and Wilcoxon-signed-rank-test were used to assess accuracy and response times variance between the two cameras. Accuracy was defined as successful task completion on first attempt.

Results: Of the participants, 3 were male and average age was 74. In each task, the thermal camera increased the subject's accuracy as compared to the standard camera: 98.7%vs57.5% ($\chi2=37.84, p<0.001$) in (1), 71.3%vs52.1% ($\chi2=22.65, p<0.001$) in (2), 80.8%vs63.9% ($\chi2=9.30, p=0.002$) in (3), and 73.3%vs34.2% ($\chi2=74.05, p<0.001$) in (4). Wilcoxon-signed-rank comparison of medians revealed no significant differences in response time between either camera for successfully completed tasks ($p>0.05$).

Conclusion: In this study, the thermal camera outperformed the standard camera in all tasks. This suggests that a thermal-vision camera may be of benefit in environments with distinct heat profiles. These findings have the potential to further improve the accessibility of hundreds of patients with ARGUS.

50. Sasicha Manupipatpong, MS 2

Mentor(s): Clifford Weiss, MD
Department of Interventional Radiology

Y-90 endovascular radiosurgery for the treatment of glioblastoma multiforme: A pilot study in a canine model

Authors: Sasicha Manupipatpong BS, Alexander S Pasciak PhD, Ferdinand K Hui MD, Rebecca A Krimins DVM, Dara L Kraitchman VMD, Clifford R Weiss MD

Background: Glioblastoma multiforme (GBM) is the most common and aggressive cancer of the central nervous system. Cancer cell infiltration beyond imaged tumor boundaries and neurotoxicity, respectively, curtail the ability of surgical resection and radiation therapy to effectively prolong survival. We propose Y-90 endovascular radiosurgery (ER) as an alternative approach to treatment, due to its ability to minimize off-target radiation and inherent localization to hypervascular tumors.

Methods: To demonstrate the safety and feasibility of Y-90 ER in the brain, three healthy research-bred dogs (hound mix, 23.0-28.6kg) received Y-90 injections, each in a different vessel (in order: left posterior cerebral artery, left middle cerebral artery, right internal carotid artery) accessed under fluoroscopic guidance via posterior circulation. Post-radioembolization PET/CT was performed to confirm bead distribution. Subjects were survived 4 weeks, with neurological exams and bloodwork completed as clinically indicated. Pre- and post-procedure MRI were performed to identify necrosis, inflammation, or infarction. Upon sacrifice, the brain was extracted for microCT scanning and pathology.

Results: All three dogs tolerated the procedure well: only the latter two showed neurological symptoms consistent with effects on the treated hemisphere, which resolved within a week. PET/CT and microCT confirmed bead deposition in treated vessel territories. 43.6%, 26.1%, and 5.2% of treated vessel territories in the first, second, and third dogs, respectively, received over 70Gy of radiation, which is the threshold for neuronal necrosis in fractionated external beam radiation therapy. Pathology showed perivascular inflammation more pronounced in the treated hemisphere and bead-associated infarctions in the first two dogs, as well as bilateral granulomas likely from prior disease in the first dog.

Conclusion: Our results show that Y-90 ER in the canine brain is feasible and doesn't result in permanent neurological deficits. To determine the viability of Y-90 ER as a treatment for GBM, client-owned dogs with hypervascular axial brain tumors will next be treated.

51. Ved Tanavde, MS 2

Mentor(s): Stephen Yang, MD
Division of Thoracic Surgery-Dept. of Surgery

Inpatient Opioid Consumption Following Esophagectomy: A Retrospective Cohort Study

Authors: Ved Tanavde BA, Trevor Davis MD, Lillian Tsai MD, Richard Battafarano MD, Christopher Wolfgang MD, Stephen Yang MD

Background: Esophagectomy is a complex surgical procedure for esophageal cancer in which all or part of the esophagus is removed and rebuilt from the stomach. Although the procedure is associated with significant morbidity and postoperative pain, there is no published data on opioid consumption in esophagectomy patients. This study aims to determine factors associated with increased opioid consumption following esophagectomy.

Methods: We retrospectively reviewed inpatient records of patients who underwent esophagectomy at our Institution from 2016-18. Data was collected on all opioid administrations, including patient-controlled analgesia, intravenous infusion, oral, and all other modalities. We used simple and multivariable linear regression as well as unpaired t tests to assess factors associated with increased opioid consumption.

Results: There were 102 patients (83 males, median age 65) in our cohort. Multivariable regression analysis determined younger age and preoperative psychiatric history as significantly predictive of increased total opioid consumption, controlling for BMI, gender, length of stay, and history of outpatient opioid use ($F_{(6,95)} = 11.353$, $p<0.0001$, $R = 0.65$). Forty-nine patients had preoperative mental health diagnoses with past year receipt of benzodiazepines, antidepressants, or antipsychotics, and 53 patients had no mental health diagnosis or psychiatric treatment (mean ages 61.2 and 63.4). Unpaired t-tests showed significant differences in daily and cumulative opioid consumption between the two groups, with mean use of 89.26 milligram morphine equivalents (MMEs) per day and 1244 MMEs total in the psychiatric history group, and 54.47 MMEs per day and 695.9 MMEs total in the no psychiatric history group (difference of means 34.79 ± 8.841 and 547.8 ± 129.9, 95% CIs 17.25 to 52.34 and 290.2 to 805.5; $p= 0.0002$ and $p<0.0001$).

Conclusion: Our results suggest that younger patients or patients with preoperative psychiatric history have increased opioid requirements following esophagectomy. These findings may help in the design of guidelines for pain management in this population.

POSTER ABSTRACTS: ETHICS AND THE ART OF MEDICINE

Listed alphabetically by first name of author

52. Benjamin Miller, MS 2

Mentor(s): Sara Keller, MD, MPH, MSPH
Department of Infectious Disease

Statements about Antibiotic Side-Effects and Patient Desire for Unnecessary Antibiotics

Authors: Benjamin Miller BS, Sujay Pathak MD, Sara Keller MD MPH MSPH

Background: Antibiotic resistance is a global health emergency fueled in part by unindicated use of antibiotics. Current public education campaigns primarily focus on the risks of global antibiotic resistance or society-wide adverse impacts of antibiotic misuse. There has been little research into whether highlighting adverse side-effects on an individual patient, or on people close to the individual, may be more impactful in reducing patient requests for unindicated antibiotics than statements about resistance or the societal impact of antibiotic misuse.

Methods: We administered a survey at a primary care clinic. Participants rated 18 statements about adverse impacts of antibiotics on how that statement changed their likelihood to request antibiotics for an upper respiratory tract infection (URI). This included 8 statements about how antibiotics may harm the individual taking the antibiotic, 4 statements about harm to people close to the individual, and 6 statements about negative impacts on society. Before and after the survey, participants rated how likely they were to request antibiotics for a URI.

Results: Of 1,150 adult patients in clinic over the six days of the survey, 250 completed the survey. Statements about individual harm decreased participants' desire for antibiotics more (mean score 2.70) than statements about harm to people close to the individual (mean 2.82), more than statements about resistance (mean 3.01), and more than statements related to societal impacts (mean 3.20). All statements decreased patient scores; and likelihood to request antibiotics decreased from 5.3 at the beginning of the survey to 3.1 at the end (P Value <.001).

Conclusion: Statements about how antibiotics harm the individual had a greater impact than statements about harm to others close to an individual, or resistance or societal impacts. Our results suggest that when dissuading patients from unindicated antibiotics, providers and public health campaigns focus on the harm of antibiotics to the individual.

53. Cecilia Vichier-Guerre, MS 2

Mentor(s): Rachel Thornton, MD PhD
Department of Health, Behavior, and Society, Johns Hopkins Bloomberg School of Public Health

Students' Perspectives on Health Equity Curricula in U.S. Medical Schools

Authors: Cecilia Vichier-Guerre BA, Gail Geller ScD, Joseph Carrese MD, Rachel Thornton MD

Background: White Coats for Black Lives published its inaugural Racial Justice Report Card ("Report Card") in 2018, rating a subset of U.S. medical schools based on whether and how the curriculum addresses racial justice. We sought to understand if medical schools with higher grades on the Report Card are more likely to discuss race as a social construct, and attribute health disparities to structural barriers.

Methods: We conducted a multi-institutional survey of 2,664 medical students at 5 of the 10 schools selected for the Report Card. Medical schools were selected using cluster sampling based on Report Card grades. The survey included basic demographics, 22-Likert scale questions and 3 short-answer questions. Likert responses were analyzed using standard univariate and bivariate statistics. Content-analysis was used to identify major themes from the open-ended responses.

Results: A total of 390/2,664 students (11 to 20% depending on the school) completed the electronic survey. Most participants (82%) have at some point felt uncomfortable by faculty comments regarding marginalized groups, yet, most (65%) think they have a voice to change their curriculum. Overall, medical students reported race is discussed more as a social construct than a biological concept and health disparities are attributed more to structural barriers than individual choice, but variation exists among schools corresponding to Report Card grade. Similarly, medical students' perception of faculty behaviors, including use of person-centered language and portrayal of primary care, varied among schools corresponding to Report Card grade. Content-analysis revealed common themes among schools, including specific comments regarding marginalized groups, confusion about the discussion of race, and suggestions to improve health equity curricula.

Conclusion: Although race is more often portrayed as a social construct than a biological concept, variation among schools remains. Future research should explore how specific school policies, such as anti-racism training, could be influencing differences in curriculum and faculty behaviors.

54. Joshua Prudent, MS 4

Mentor(s): Joseph Cofrancesco, MD; Barry Solomon, MD
Institute of Educational Excellence

A Student-Created Clinical Teaching Honor Society- the Distinguished Teaching Society of Johns Hopkins

Authors: Joshua Prudent BA, Pranjal Gupta BS, Joseph Cofrancesco MD, Barry Solomon MD

Background: The Johns Hopkins School of Medicine's medical students founded a clinical teaching honor society in 2015, to help promote educational excellence on the Wards. Membership to the Distinguished Teaching Society (DTS) of JHUSOM is available to any physician who teaches Johns Hopkins medical students, and thus includes housestaff and faculty from throughout our institution. Our process for development and judging the award can be utilized by other institutions, to recognize great clinical teachers.
Hypothesis/Aims: To describe the development and structure of a student-led clinical teaching honor society for potential replication

Methods/Results:
FOUNDING: A volunteer team of students began a literature search and stakeholder assessment, merging clinical education research with input from institutional leaders in medical education. The list of characteristics were ranked by the student body, which was used to create a judging rubric with three categories- feedback, role modeling, and teaching process.
JUDGING: In the nominations, students are asked to "describe why you are nominating this individual". All nominees are then asked to share their teaching activities, and opinions on what characteristics "exemplify clinical teaching excellence". The nomination and nominee's responses are de-identified and assessed by trained student judges, utilizing the rubric. The top scoring nominees are re-identified, shared for comment by the student body and clinical leadership, and finally selected for induction.
INDUCTION: At the Induction Ceremony, inductees receive a DTS whitecoat pin and lanyard, along with a certificate signed by the medical student body president and the Dean of Education. They also are featured in an online profile on our web portal- dts.johnshopkins.edu .

Conclusion: The Distinguished Teaching Society has a thorough and evidence-based approach to assessing education excellence on the Wards, which can be easily replicated at other Schools of Medicine. Further study is needed to assess its impact on learner/teacher satisfaction and the overall learning environment.

55. Ruoxi Yu, MS 2

Mentor(s): Kathleen Page, MD
Department of Infectious Disease

Waiting for Doctor: An Ethnographic Study of Patients Waiting for Appointments

Authors: Ruoxi Yu BA, Kathleen Page MD

Background: Studies of waiting rooms have shown that increased wait times for appointments have correlated with decreased patient satisfaction. While ethnographies of waiting in social welfare settings have explored people's experiences of waiting, there has been a relative lack of understanding about what patients in the clinic experience when waiting for appointments. This study investigated patients' waiting and explored how waiting is conceptualized and embodied by patients.

Methods: This was a qualitative study involving direct observation in the waiting area at the Bartlett Specialty Clinic at Johns Hopkins Hospital and semi-structured interviews of patients who attended that clinic. Field notes of observations and transcripts of interviews were analyzed using standard content analysis.

Results: A total of n=10 interviews (5 female- and 5 male-identifying patients) were conducted A total of 25 hours of observation was performed. Analysis of the interview transcripts and observation field notes identified the following themes: 1) waiting is not a passive act, 2) waiting is both a collective and individual experience and 3) waiting is a learned experience. Overall, patients do not just sit while waiting and do use the time productively. Collective waiting provides a community of support in which patients can build social capital while individual waiting is framed by individual lived experience. Given this, the specific experience of waiting in the clinic is an experience learned from repeated interactions with the healthcare system.

Conclusion: Understanding how patients experience waiting can reveal areas of intervention to improve the clinic experience. This study found that waiting can be an active and productive experience that reflects the environment of the clinic. A limitation of this study is that it only involved one clinic so the findings may not apply to other settings. More work in a variety of settings is needed to provide a holistic understanding of waiting in the clinic.

56. Sonal Chaudhari, MS 3

Mentor(s): Silka Patel, MD MPH
Department of Gynecology and Obstetrics

Medical Students Encounter Values Conflicts Frequently During Clinical Clerkships: the Need of Values Clarification Curricula In Medical Education

Authors: Sonal Chaudhari BS, Stephanie Zuo MD, Jennifer Robinson MD MPH, Silka Patel MD MPH

Background: Few models of clinical curricula for medical students emphasize values clarification (VC) education. VC is a psychotherapy technique that can help individuals increase awareness of personal values that shape everyday decisions and actions. It can provide individuals with an opportunity to reflect on personal moral dilemmas and allows values to be analyzed and more clearly communicated to others. Since values incongruence is associated with increased risk of burnout, VC methods may be valuable because medical students often encounter values conflicts during clinical clerkships.

Methods: We assessed students' feedback after they participated in a VC session, facilitated by trained physicians and focused on the topic of abortion, during their Women's Health (WH) clerkship at Johns Hopkins University School of Medicine.

Results: 67% of medical students responded to the survey (n=133). Approximately 80% of students agreed or somewhat agreed that a session dedicated to VC regarding difficult patient scenarios would be beneficial during their clinical rotations. 63% of students reported encountering conflicts in which their values were different from their patients' in multiple clerkships. Of significance, students encountered values conflicts more frequently in WH clerkship compared to Medicine (n=89, p=0.052), Surgery (n=87, p=0.002) and Neurology (n=49, p=0.0003). After participation in the VC session, 89% of students agreed or somewhat agreed that they gained increased awareness of personal values, 92% recognized values conflicts, 90% grew more aware of the effects of their values on patients, 81% could better engage with patients with differing values, 75% noticed increased empathy for patients, and 79% were better able to process values conflicts.

Conclusion: Given that a session dedicated to clarifying students' values can yield positive outcomes, offering values clarification education is essential. We encourage medical schools to endorse VC education in core clinical medical curricula of any clinical clerkship to encourage student self-reflection and to enrich students' clinical experiences.

POSTER ABSTRACTS: HISTORY OF MEDICINE

Listed alphabetically by first name of author

57. Abby Fahnestock, MS 2

Mentor(s): Nathaniel Comfort, PhD
Institute of the History of Medicine

From Defect to Diagnosis: Changing Language of Disability in Medical Education

Authors: Abby Fahnestock BA, Nathaniel Comfort PhD

Background: People with intellectual disabilities suffer from higher mortality rates, increased rates of undiagnosed and mismanaged conditions, and shorter life expectancy. Alongside this disparity is the in utero elimination of many children suspected to receive the diagnosis of "disabled". To what extent is this disparity in care the product of how physicians have been taught to think about disability? This paper explores the history of how intellectual disability has been dealt with in medical education in the United States and how this may contribute to the disparities in care.

Methods: Attending to language, I critically examined the Johns Hopkins University School of Medicine's course catalogs (1894-2004) and major medical textbooks of the 20th century, Osler's Medical Textbook (1903-1910) and Goldman-Cecil Medical Textbook (1927-2004). In order to detail surrounding scientific thought I investigated archival collections of prominent physician lecturers at Hopkins. Secondary historical literature on disability, eugenics, and medical education contextualize this investigation.

Results: This investigation reveals a reduction of language quality and quantity in the medical curriculum surrounding intellectual disability throughout the 20th century, offering itself as an explanation for the noted reduction of care and research. Language of intellectual disability first appears in the 1920's with the term "mental defect." The language shifts as different societal, political, and scientific forces urge medicine to think critically about the language it uses. The shifts consist of: mental defect to mental deficiency, which is further specified to classifications of feeble-minded, idiot, or imbecile, to mental retardation, to intellectual disability.

Conclusion: Through this investigation I trace the shifts in language surrounding intellectual disability in medical education, noting the correlation between language used and care given. Thus, this investigation asks physicians and educators to attend more closely to the language they use, especially when their language results in profound disparity and the elimination of certain groups of people.

58. Benjamin Bigelow, MS 2

Mentor(s): Graham Mooney, PhD
Institute of the History of Medicine

The AMA Responds to Gun Violence: A History of Physicians and Firearm Policy in the USA

Authors: Ben Bigelow BS, Graham Mooney PhD

Background: In 2016, there was 38,658 firearm-related deaths in the United States. Firearm policies including gun rights, control, and violence are among the most debated issues in the US. The American Medical Association (AMA) often features in these debates. Yet, the AMA did not take a substantial position on firearms until 1987 whereas other organizations first released position statements from the late 1960s. This project examines the history of the AMA's decisions to adopt policy positions on firearms.

Methods: The AMA's firearm proposals were analyzed to assess policy changes. Arguments by physicians expressed in committee reports, during annual meetings, and in medical journals were examined. The positions of other organizations (e.g., the Presbyterian Church) were studied for comparison.

Results: In 2018, the AMA released a policy calling for the ban of firearms sales to those under 21, heralded as a "sweeping" and "unprecedented" move, a major shift from AMA's position decades earlier. The AMA refused to take a stance on firearms in the 1970s, other than to state they "abhorred" their use in crimes and supported harsher punishments. A policy on control was not adopted until after a report on firearms by the AMA's scientific affairs committee in 1987. Over the next six years the AMA called for further regulatory policies and supported the 1993 Brady Bill, which mandated background checks for firearms purchases.

Conclusion: The shift in policy of the AMA from an organization that took no stance on firearm policies to one which actively supported firearm control took two decades. The process included debate amongst members at annual meetings and in journals across the country. Contrary to the belief that these policies were short-sighted emotional reactions to firearm violence, the AMA policies were founded on research and were developed cautiously over time.

59. Sandra Ahn, MS 2

Mentor(s): Jeremy Greene, MD
Institute of the History of Medicine

Negotiating Mania: Patient Experiences in 20th Century America

Authors: Sandra Ahn MA

Background: Manic depressive illness, a condition characterized by episodes of extreme elation and depression, is the source of constant investigation in the medical literature. Presently, bipolar disease is the most common cause of suicide. Since the mid-20th century, psychiatry has adopted a more patient-centered paradigm of care. Adolf Meyer, the first director of the Phipps Psychiatric Clinic at the Johns Hopkins Hospital (1913-1941), advocated the centrality of the patient and the patient's life story for guiding treatment. This study explores how Meyer's patients negotiated their illness across three "domains" of care, emphasizing patients' lived experiences outside the clinic.

Methods: I traced the experiences of seven patients spanning decades by examining Meyer's publications and papers from the Adolf Meyer Collection at the Chesney Medical Archives. I focused on private patient correspondences, including letters from relatives, friends, and superintendents from other mental hospitals, medical records, staff conferences, and Meyer's working notes.

Results: Three domains of patient care emerged: first, the relationship with Meyer, who influenced all aspects of patient care; second, the patients' social network of relatives and friends; and third, a network of mental hospitals in which patients sometimes found themselves. Because of these layers of care, conflict emerged from diverging perspectives on manic depression and the extent to which patient behavior should be constrained. Meyer believed that a consensus of opinions and experiences acted as a buffer against the chaos of the manic impulse. Patients, on the other hand, argued that the very declaration of their "insanity" excluded them from that consensus and, therefore, society.

Conclusion: Patients experienced their illnesses in relation to a network of care beyond the clinic itself. The study revealed that patients are active participants in conceptualizing and negotiating their illness. Understanding this perspective can advance a patient-centered paradigm for the care of the mentally ill in the present day.

POSTER ABSTRACTS: PUBLIC HEALTH RESEARCH
Listed alphabetically by first name of author

60. Alexandra Berges, MS 2

Mentor(s): Kunal Parikh, PhD
Center for Bioengineering Innovation & Design

What are the optimal instrument holding techniques to streamline small incision cataract surgical training?

Authors: Alexandra Berges BS, David Friedman MD, Shameema Sikder MD, Kunal Parikh PhD

Background: Determining optimal instrument holding technique is difficult for trainees, yet it can significantly affect surgical difficulty and outcomes.This is particularly true in ocular surgery when attention is often focused on the microscope view during surgery. The goal of this study was to determine major successful instrument holding archetypes used in small incision cataract surgery (SICS), a low-cost small-incision form of extracapsular cataract extraction that is primarily performed in the developing world.

Methods: Experienced surgeons (n=5), senior fellows and junior consultants (n=5), and trainees (n=5) at Aravind Eye Care System Hospital, Madurai, India were interviewed regarding their instrument holding techniques and complications associated with different positions. Experienced surgeons performed 5 steps during SICS (scleral incision, scleral tunnel, sideport, corneal tunnel, and capsulorhexis) on an ex vivo eye, and photos/videos depicting each hand position technique were compared to identify common archetypes in holding technique and to develop a nomenclature for different positions. Interview transcriptions were used to synthesize common technical considerations for each surgical step.

Results: For each SICS step we identified 1-2 major archetypes and key modifying variables utilized in the observed instrument handling techniques. Key differences included thumb placement and number of fingers supporting the instrument (quadripod vs. tripod). Modifying variables included index finger curvature and amount of flexion. Complications associated with altered hand positions included capsulorhexis stability, scleral tunnel, and IOL placement. For several steps, positions were correlated to glove size and pen holding positions.

Conclusion: Our findings show that there are multiple successful instrument holding techniques that were demonstrated by expert ophthalmologists, which were impacted by factors such as glove size and pen holding method. The developed SICS hand position nomenclature will enable trainees to pick optimal hand positions in an informed manner, influence surgical instrument design, and ultimately improve global cataract surgery outcomes.

61. Allison Peng, MS 2

Mentor(s): Michael Blaha, MD MPH
Department of Medicine - Cardiology

Long-term All-cause and Cause-specific Mortality in Asymptomatic Patients with Coronary Artery Calcium ≥ 1000

Authors: Allison W Peng BS, Mohammadhassan Mirbolouk MD, Zeina A Dardari MS, Olusola A Orimoloye MBBS MPH, Albert D Osei MD MPH, Michael J Blaha MD MPH

Background: Coronary artery calcium (CAC) is commonly used to quantify cardiovascular risk. Current guidelines classify CAC>300 or 400 as the highest risk group, yet little is known about the potentially unique imaging characteristics and mortality risk in individuals with CAC≥1000. We thoroughly explored the demographic and imaging characteristics, as well as all-cause and cause-specific mortality of CAC≥1000 patients in the largest dataset of this population to date.

Methods: We included 66,636 asymptomatic adults from the CAC Consortium, a large retrospective multicenter clinical cohort. Mean patient follow-up was 12.3 ± 3.9 years for CVD, CHD, cancer, and all-cause mortality. Using multivariable Cox proportional hazards regression models adjusted for age, sex, and traditional risk factors, we assessed the relative mortality hazard of individuals with CAC≥1000 compared first against a reference of CAC=0, and then against CAC 400-999.

Results: There were 2,869 patients with CAC≥1000 (86.3% male, mean age 66.3 ± 9.7 years). Most CAC ≥ 1000 patients had 4-vessel CAC (mean 3.5 ± 0.6 vessels), and had greater total CAC area, higher mean CAC density, and more extra-coronary calcium (79% with TAC, 46% with AVC, 21% with MVC) compared to CAC 400-999. After full adjustment, those with CAC ≥ 1000 had 5.04 (3.92-6.48), 6.79 (4.74-9.73), 1.55 (1.23-1.95), and 2.89-fold (2.53-3.31) risk of CVD, CHD, cancer, and all-cause mortality, respectively, compared to those with CAC=0. The CAC≥1000 group had a 1.71- (1.41-2.08), 1.84- (1.43-2.36), 1.36- (1.07-1.73), and 1.51-fold (1.33-1.70) increased CVD, CHD, cancer, and all-cause mortality compared to CAC 400-999. Graphical analysis of CAC≥1000 revealed no upper threshold of risk with CAC.

Conclusion: Patients with extensive CAC (CAC≥1000) represent a unique, very high-risk phenotype with mortality (0.80%/yr) commensurate with high-risk secondary prevention patients (0.77%/yr from the FOURIER trial). Future guidelines should consider CAC≥1000 a distinct risk group which may benefit from the most aggressive preventive therapy.

62. Bairavi Shankar, MS 2

Mentor(s): Josephine Feliciano, MD; Jarushka Naidoo, MD
Department of Oncology

Patterns of Electronic Medical Record Use in Lung Cancer Patients: Prevalence and Association with Patient-Reported Anxiety

Authors: Bairavi Shankar BA, Jiajia Zhang MD MPH, Patrick M. Forde MBBS, Kristen A. Marrone MD, Ronan J. Kelly MD MBA, David S. Ettinger MD, Christine L. Hann MD PhD, Julie R. Brahmer MD, Jarushka Naidoo MBBS, Josephine L. Feliciano MD

Background: Use of the Electronic Medical Record (EMR) is complex for patients and healthcare providers, and its impacts may vary by patient population. This IRB-approved questionnaire evaluated the prevalence of use of the EMR and patient-reported anxiety in lung cancer (LC) patients.

Methods: Patients with LC at a tertiary center between 06/2018-12/2018 participated in the survey. Patients were included if they were above 18 years of age and were willing and able to complete the questionnaire. EMR use was defined as viewing lab results or radiology reports on a patient EMR portal. Patient demographics, EMR use, tumor and treatment data, and self-assessment of anxiety (PROMIS-Anxiety metric) were collected. Associations between patient features and EMR use as well as anxiety score were examined.

Results: 100 LC patients (stage I/II: 12, III/IV:80, unknown: 8) completed surveys. 90% (90/100) reported preference to receive information in person from healthcare providers. 54(54%) patients used the EMR, of which 100% and 83% (45/54) used it to view lab results or radiology reports, respectively. Never smokers and stage IV patients were more likely to use the EMR vs. current/former smokers or stage I-III patients (both $p<0.05$). However, in the entire cohort, there was no significant difference in anxiety scores between EMR users and non-EMR users in univariate and multivariate analysis (both $p>0.1$).

Conclusion: 90% of all surveyed prefer to receive healthcare information in person from their provider, but the majority uses the EMR to access personal healthcare data. EMR use is more common amongst never smokers and patients with stage IV disease. There were no observed differences in patient-reported anxiety after receiving healthcare information for EMR users vs. non-EMR users. Further evaluation of the impacts of the EMR on cancer patients is warranted, and counseling and guidance in EMR use may be necessary for patients.

63. Brittany Tsou, MS 2

Mentor(s): Corinne Keet, MD
Division of Pediatric Allergy and Immunology

Clinical features of an FPIES cohort

Authors: Brittany C. Tsou BS, Robert A. Wood MD, Jennifer A. Dantzer MD, Corinne Keet MD MS PhD

Background: This case series characterizes clinical features of food protein-induced enterocolitis syndrome (FPIES), a non-IgE-mediated food allergy that is often under-recognized.

Methods: Retrospective chart review of patients of the Johns Hopkins Pediatric Allergy clinic from 5/1/13-5/1/18 with a physician diagnosis of FPIES before age 5 years.

Results: Of 1994 patients with food allergy aged < 5 years, 74 (4%) were diagnosed with FPIES, with or without other food allergy (20 individual foods and 223 reactions) with a median follow-up to age of 3.2 years (25-75%: 1.3- 5.4). 44 (60%) were male; the median age of reaction was 6 months (25-75%: 5-8). 35 (47%) had FPIES to multiple foods (median: 2, range: 2-6). Common triggers included oat (37%), rice (28%), sweet potato (16%), milk (15%), and soy (14%). Of 11 with milk FPIES, 2 (18%) had FPIES to soy. Of 27 with oat FPIES, 14 (52%) reacted to rice. 47 (21%) reactions from 32 (43%) patients resulted in emergency department visits. 12 (16%) had positive IgE tests to at least one of the foods causing FPIES and 36 (49%) were sensitized to other foods with sensitization to a median of 5 foods (25-75%: 2-10). 41 (32%) follow-up oral food challenges occurred in 30 patients, and 22 (54%) were negative.

Conclusion: In this cohort of patients with FPIES, oat and rice were the most common triggers, and about half reacted to multiple foods. Food sensitization was common, but more often to foods other than those causing FPIES.

64. Caroline Plott, MS 2

Mentor(s): Sara Johnson, MPH PhD
Department of General Pediatric and Adolescent Medicine

Pediatric Exposure to Elevated Indoor Classroom Temperatures is Associated with More Asthma Related Healthcare Visits

Authors: Caroline Plott; Paul Spin PhD; Sara Johnson MPH PhD

Background: Exposure to both high and low outdoor temperature extremes has been shown by previous studies to trigger asthma symptoms. However, the association between small indoor temperature variations and asthmatic symptoms in children has not been well described. This study examines the relationship between indoor school temperature exposure and asthma related school health center utilization in a cohort of elementary and middle school students in Baltimore, MD.

Methods: School-measured classroom temperature data were available for two years. Asthma-related visits to the school nurse (SN) or the onsite pediatrician/advanced practice nurse (PNP) were used as a proxy for asthma exacerbations. The relationship between classroom temperature exposure and a subsequent asthma-related health visit was modeled using a logistic regression adjusting for sex, grade level, outdoor temperature, and whether the student had a non-asthma related appointment. We calculated the probability of an asthma visit after exposure to varying temperatures, and fitted this to a restricted cubic spline model with three knots. Since asthma symptoms may present days after exposure to extreme temperatures, we took into account the time-delayed effect of temperature exposure on asthma symptoms by considering whether a student had an asthma related visit within a defined time range after the initial indoor temperature exposure (from one to thirty days).

Results: For both PNP and SN visits, we found that exposure to temperatures above approximately 78˚F were correlated with an increased risk of an asthma visit within ten calendar days of the exposure. Conversely, there was not a significant increase in risk of asthma related visits for students exposed to indoor temperatures below 78˚F. We did not see a significant correlation between non-asthma healthcare visits and indoor temperature exposure.

Conclusion: Our results indicate that improving the control of indoor classroom temperature, particularly avoiding temperatures over 78˚F, may lower the risk of pediatric asthma exacerbation.

65. Catalina Garzon, MS 2

Mentor(s): David Friedman, M.D., M.P.H., Ph.D.
Wilmer Eye Institute, Department of Ophthalmology

Retrospective Outcomes Review of Implementing Intraocular Pressure Assessments in Young Adults

Authors: Catalina Garzon BA, Annamalai Odayappan, MD, David Friedman M.D., M.P.H., Ph.D.

Background: Screening for glaucoma in young adults is challenging as the disease is uncommon in this population. However, many young people visit an eye doctor, and this is an opportunity to identify those with or at risk for developing glaucoma. The Aravind Eye Hospitals, India recently started routinely measuring intraocular pressure (IOP) in adults who receive a routine examination in order to improve detection rates of ocular hypertension (OHT) and glaucoma.

Methods: A retrospective chart review of adults (18-40 years) who were screened for IOP elevation from November 2017 - June 15th, 2018 in Pondicherry, India. Additional patients were referred based on optic nerve appearance. Analyses include detection of glaucoma/OHT and calculation of the yield of this screening paradigm.

Results: 28,369 patients were examined in the general units and 296 were referred to the glaucoma unit (1.05%). 84 had IOP > 21 (OHT) and 208 were referred for reasons other than IOP elevation. The hypertensive group had a mean IOP of 29.3 ±8.4 mmHg with a range of 22-56 mmHg, and the following diagnoses: 46 (55%) patients with OHT, glaucoma or angle closure (true positives), 16 (19%) patients were healthy (false positives), and 22 (26%) patients required further examination. In contrast, the normotensive group was characterized by a mean IOP of 16±2.5 with a range of 10-20 mmHg, and the following diagnoses: 13 (6%) patients with OHT or glaucoma (true positives), 125 (61%) patients were healthy (false positives), and 69 (33%) patients required further examination.

Conclusion: One out of every 600 patients between 18 and 40 years of age examined in the general units was found to have IOP about 21 mmHg and ultimately was diagnosed as having angle closure, OHT, or glaucoma. Given the young age of individuals identified and the potential to treat and prevent disease, the benefits seem to outweigh the low cost of screening in this fashion.

66. Jake Ruddy, MS 2

Mentor(s): Geetanjali Chander, MD
Department of Medicine

Is concurrent cocaine and alcohol use associated with poorer HIV outcomes in persons living with HIV?

Authors: Jake Ruddy BS, Geetanjali Chander MD

Background: Hazardous alcohol and cocaine use have both been associated with HIV disease progression independently of antiretroviral therapy and secondarily to decreased antiretroviral therapy. Alcohol and cocaine use frequently co-occur, but are often examined separately in persons living with HIV. This study characterized how varying levels of concurrent alcohol and cocaine use are associated with ART use, ART adherence score, and HIV-1 RNA.

Methods: In an alcohol reduction clinical trial in persons living with HIV in Baltimore, Maryland, we conducted a cross-sectional study of 215 participants from the trial's baseline. Data was obtained from an Audio Computer-Assisted Self Interview and laboratory testing. The outcomes assessed were ART adherence (≥90% on visual analogue scale), HIV-1 RNA (<50 copies/ml used as undetectable), and ART use (yes or no). Cocaine use was assessed by urine cocaine and past 30 days self-reported use. Alcohol use assessed by AUDIT score. Covariates of interest included total drug use, hospitalizations, as well as symptoms of depression and anxiety. We used multivariable logistic regression to examine the variables.

Results: Out of 215 participants, 62.4% reported no cocaine use in the past 30 days, 21.9% reported 1-6 days use, and 15.7% reported 7-30 days use. Within AUDIT scoring, 15.2% scored in the low risk drinking group, 31.3% in medium risk, 12.4% in high risk, and 41.2% in addiction likely. In the group reporting 7-30 days of cocaine use, a lower AUDIT score was associated with higher ART adherence (OR 0.381, CI 0.167-0.868). On the other side, in the AUDIT high risk and addiction likely groups, lower cocaine use was associated with higher ART adherence (OR 0.56, CI 0.320-0.990).

Conclusion: In patients using both cocaine and alcohol, increased ART adherence may be able to be achieved by helping patients decrease use of one substance, even if use of the other substance remains the same.

67. Jill Sorcher, MS 2

Mentor(s): Jordan Duval-Arnould, DrPH, MPH; Oluwakemi Badaki-Makun, MD
Department of Anesthesiology & Critical Care Medicine

End-tidal carbon dioxide use during pediatric cardiac arrests in a large academic children's hospital, 2013-2018

Authors: Jill L. Sorcher BA, Elizabeth A. Hunt MD, MPH, PhD, Donald H. Shaffner MD, Justin Jeffers MD, Heather Newton BS, RN, Oluwakemi Badaki-Makun MD, Jordan Duval-Arnould DrPH, MPH

Background: End-tidal carbon dioxide (ETCO2), the partial pressure of carbon dioxide (CO_2) at the completion of an exhaled breath, has been show to correlate well with pulmonary blood flow and coronary perfusion pressure. Expert consensus states that ETCO2 > 20 mmHg should be targeted as a marker of quality of cardiopulmonary resuscitation (CPR) based on evidence from adult clinical populations and pediatric animal models. The American Heart Association Pediatric Basic Life Support Guidelines states that ETCO2 may considered to evaluate quality of chest compressions, but specific values have not been established.

Methods: This was a prospective observational study of ETCO2, CPR quality and return of spontaneous circulation. The study population included any pediatric patient who received chest compressions from January 1, 2013 through July 10, 2018 in the Johns Hopkins Children's Center. During this time, 458 arrest events requiring chest compressions occurred. Of these 458 events, 275 events utilized ETCO2 in some capacity and 199 of these events recorded ETCO2 on a Zoll R Series® defibrillator. Data files from 146 of these events were successfully obtained and contained 3001 minutes of total data. 2200 of these minutes included ETCO2 data and 2156 minutes contained both chest compression and ETCO2 data; values are reported as median (IQR).

Results: ETCO2 obtained for all 3001 minutes of data was 14 mmHg (0-29) and excluding minutes prior to the first detected use of ETCO2 was 16 mmHg (4-31). When comparing patients who survived to those who did not, we observed a significant difference in ETCO2 between those who survived and those who did not (ROSC: 25 [15-30] vs. NO ROSC: 15 [9-22]; $p<0.001$).

Conclusion: This sample represents the largest collection of ETCO2 and compression data in pediatric patients. Our findings suggest that achieving larger ETCO2 values than is currently recommended is significantly associated with ROSC in pediatric patients.

68. Jonathan Callan, Student in Residence

Mentor(s): Megan Collins, MD MPH
Wilmer Eye Institute, Department of Opthamology

Program Building Considerations for School-Based Delivery of Eye Care

Authors: Jonathan Callan BS, Megan Collins MD MPH

Introduction: In the United States, it is estimated that 20-25% of school-age children have vision problems, with uncorrected refractive error identified as the most common reason for visual impairment [1]. Though many children are successfully identified to have visual impairment through vision screenings, there is marked variation in accessing recommended follow-up care. To address access issues, there has been a shift towards school-based models for delivery of routine vision care and eyeglasses [2]. Many different school-based vision programs have been constructed across the U.S., but few have examined the challenges to program building and sustainability. Based on experience working in Baltimore and a review of relevant literature, our group created a framework for considerations when building a school-based vision program.

Considerations: Before creating a program, it is important to build strategic partnerships, conduct a thorough needs assessment, and consider communication strategies that will allow for maximum reach. They must also have appropriate personnel and funding in place to be able to grow out of the pilot phase. Once live, specific eligibility criteria for eye exams, components of the eye exam, prescribing guidelines, and mechanisms to refer children with non-refractive pathology to community eye care providers must be determined. For programmatic sustainability, programs need to develop mechanisms to ensure children are wearing glasses and to replace lost/broken glasses. Financially, they must consider the role of philanthropic support, federal and state funding, and options to bill Medicaid or private insurers.

Conclusions: Although recognizing vision problems among children is essential, it is only the first step in effective delivery of eye care. Further challenges prevent follow-up for evaluation and treatment, even after vision problems have been identified. Understanding and navigating these challenges will be essential to solving this public health issue.

69. Kevin MacKrell, MS 2

Mentor(s): Paul Nestadt, MD
Department of Psychiatry and Behavioral Sciences

Assessing the Outcomes of Positive Suicide Ideation Screening in Inpatient non-Psychiatric Settings

Authors: Kevin MacKrell BS, Oscar Bienvenu MD, PhD, Ted Avi Gerstenblith MD, Elizabeth Prince DO, Paul Nestadt, MD

Background: The Joint Commission released Sentinel Alert 56 recommending universally screening all patients for suicidal ideation (SI) in all patient care settings. However, the absolute risk in non-psychiatric patients of suicide completion in one year after expressing suicide ideation is 0.23% and current widely used suicide screeners poorly predict suicide mortality. The purpose of our study was to determine how well different SI screeners predict the need for psychiatric intervention for a patient.

Methods: We conducted a retrospective chart review over a one-year period of 14,000 non-psychiatric inpatients at Johns Hopkins Hospital who had been screened for SI. We determined and used Chi-Square tests to evaluate what proportion of patients screen positive for SI, how many of these patients received a psychiatric consult, and what proportion receive a psychiatric intervention. A Fisher Exact Test was used to evaluate the proportion of psychiatric interventions used. We determined the sensitivity, specificity, positive predictive value, and number needed to treat for a positive suicidality screen leading to a psychiatric intervention.

Results: The median age was x, y% were women, and a% of patients screened positive for suicide. b% of positive screens received a psychiatric consult, and c% received a psychiatric intervention, with d being the most likely intervention (e%, p=f). A positive SI screen had a g sensitivity, h specificity , and i positive predictive value for predicting the implementation of psychiatric intervention. To identify one patient who would need a psychiatric intervention, j patients would need to be screened.

Conclusion: Limitations of this study included only psychiatric admissions to Johns Hopkins Hospital were tracked. Psychiatric consultants may disagree on the need for intervention in a given patient. Finally, there will be variations in documentation of suicide screening across departments and some information may not be documented.

70. Laurence Hou, MS 2

Mentor(s): David Friedman, MD
Wilmer Eye Institute, Department of Opthamology

Increasing Physical Activity in Chinese Glaucoma Patients with a Social Media Support Group: A Randomized Control Trial Using WeChat Mobile Phone Application

Authors: Laurence Hou BA, Xiafei Pan MD, Kai Xu MD, Jingjing Zuo MD, Cha Lou MD, Yuanbo Liang MD, David Friedman MD

Background: Exercise is known to decrease intraocular pressure and improve blood flow to the optic nerve which may delay the progression of glaucoma. Our study sought to utilize WeChat, the most used social media platform in China, to promote behavior change. Our objective was to assess the efficacy of using WeChat Groups as an intervention to increase physical activity in Chinese glaucoma patients.

Methods: Two-armed randomized control trial. Eligible subjects from the Eye Hospital of Wenzhou Medical University were enrolled in the study (June to December 2018). Participants were instructed to wear an accelerometer for 1-week to establish baseline step count and then randomized to either a WeChat intervention group or control group for 1-month. Both groups were advised to move briskly for at least 30-minutes/day and to achieve 10,000 average daily steps (20% increase in average daily steps if baseline was ≥10,000 steps). Participants in both groups received a handout with their step count, goals, and exercise tips. All participants in the intervention cohort were also added to a WeChat Group where they could interact, receive reminders, and health education materials.

Results: Preliminary results: 90 patients were enrolled and 57 were included in our analysis (control, n=34; intervention, n=23). The intervention group showed a statistically significant increase in average daily steps; (p=0.014; at 7-days, 6821±2467; at 30 days, 8896±3019). A 1-unit increase in Age was associated with a decrease of 124 average daily steps at 30 days (p=0.131, β=-124, CI=-200 to -48). The control group demonstrated a statistically significant increase in average daily steps [p=0.041; at 7-days, 7711 (2409, 11396); at 30 days, 9098 (2772, 16331).

Conclusion: Compared to the control group, the WeChat intervention group was not more effective at increasing average daily steps in Chinese glaucoma patients.

71. Lydia Adnane, MS 2

Mentor(s): Casey Humbyrd
Department of Orthopedics

Limb Reconstruction vs. Amputation: Creation of a Shared Decision-making Aid

Authors: Lydia Adnane BA, Casey Humbyrd MD

Background: Shared decision-making aids have been shown to help patients in understanding and weighing their treatment options appropriately. For emotionally vulnerable patients deciding between limb reconstruction and amputation due to severe lower extremity trauma, it is especially important that they have access to easily-digestible education materials. The purpose of this study is two-fold: 1) to establish the need for a shared-decision making tool for this patient population via literature review 2) to create that decision-making tool.

Methods: A thorough literature review was conducted prior to creation of the decision aid to demonstrate the need for the creation of a tool. PubMed, Scopus, CINAHL Plus, and Embase searches were conducted for the concepts of patient education, decision making, amputation or limb reconstruction, and lower extremity with controlled vocabulary and keywords. There were no limits made for language or date range. Of the 214 database results, 109 were contained the included search terms, but none included creation of a decision-making tool. A prototype was created, using outcomes research largely gathered from the LEAP study. The LEAP study obtained data based on the outcomes of 545 patients who'd decided between amputation and lower extremity reconstruction. The prototype has been modified to be similar to a tool developed for parents considering adenotonsillectomy for their children. The model was selected for its accessibility, feasibility, and comprehension.

Results: In future studies, we hope to pilot the aid. We hope that a shared-decision making tool would increase patient knowledge and competency.

Conclusion: In the case of high-energy trauma causing limb-threatening injury, it is essential that patients understand and can make informed decisions. The consequences of inappropriate treatment can have life-long implications for both the health of the limb and the psychological and sociological well-being of the patient. A shared decision-making tool providing adequate educational materials could be of help to patients making this complex decision.

72. Neel Koyawala, MS 2

Mentor(s): Brendan Saloner, PhD

Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health

Changes in outpatient services and medication use following a non-fatal opioid overdose in the West Virginia Medicaid program

Authors: Neel Koyawala BA BS, Rachel Landis MPP, Colleen L. Barry PhD MPP, Bradley D. Stein MD PhD, Brendan Saloner PhD

Background: Patients infrequently receive medications for opioid use disorder (MOUD) after a nonfatal overdose, despite protective effects against future deaths. Psychiatric comorbidities are common among people who overdose and increase risk of overdose. We examine changes in receipt of MOUD and treatment for mental health conditions following a nonfatal overdose among Medicaid enrollees in West Virginia.

Methods: We obtained West Virginia Medicaid claims data for individuals enrolled under the Affordable Care Act expansion from 2014 to 2016. The sample was restricted to 301 people continuously Medicaid-enrolled for 6 months prior to and 12 months following an overdose. Paired t-tests were used to compare individual receipt of services and medications in months 1-3 prior to overdose versus other 3-month segments post-overdose. Monthly trends were graphically displayed.

Results: The sample was 60% male and 91% non-Hispanic White with mean age of 34.5 years; 54% of people had a diagnosis of depression, anxiety disorder, bipolar disorder, or schizophrenia. By twelve months post-overdose, individuals were more likely to receive buprenorphine (4.7% versus 8.3%, P=.02) and less likely to receive opioid analgesics (35.9% versus 23.6%, P<.001), or benzodiazepines (15.9% versus 11.6%, P=.03), compared to the three months prior to overdose. They were also less likely to receive mental health counseling (23.3% versus 15.3%, P=<.01). Differences were not significant for OUD office visits and receipt of naltrexone, antidepressants, antipsychotics, antianxiety, or antimania drugs.

Conclusion: Focusing on the state with the highest overdose rate, we find that overall treatment for OUD post-overdose remained very low. Less than 10% of people every month post-overdose received MOUD or mental health counseling. Rates of mental health counseling declined post-overdose. Our study is the first to investigate changes in treatment for psychiatric comorbidities following a non-fatal overdose. Nonfatal overdoses are opportunities to facilitate treatment of OUD and co-occurring psychiatric comorbidities.

73. Nur Cardakli, MS 2

Mentor(s): Harry Quigley, MD

Glaucoma Center of Excellence, Wilmer Eye Institute, Department of Opthamology

Long-term functional outcomes of trabeculectomy revision surgery

Authors: Nur Cardakli BS, Samuel Weinreb BS, Joan Jefferys ScM, Harry Quigley MD

Background: While trabeculectomy is often highly successful at attaining long-term reductions in IOP in glaucoma patients, potential complications include hypotony, bleb leak, dysesthesia, and IOP above target. Surgical revision of trabeculectomy has been reported to have variable outcomes. Various techniques for revision, specific complications, and duration may be important determinants of revision success.

Methods: Retrospective case series of 310 eyes (310 individuals) who underwent revision of trabeculectomy at the Wilmer Eye Institute between 2007-2015. Successful revision was defined as maintenance of long-term IOP control at or below target, no further glaucoma-related reoperations, no major complications during revision surgery, and no dysfunctional hypotony.

Results: Mean time between original surgery and revision was 3.1±4.0 years; mean follow-up from revision to last exam was 4.4±2.9 years. The overall success rate was 57.7% (179/310) at last follow-up. Success rates by indication for revision are: dysesthesia (64%, 18/28), hypotony (62%, 86/138), bleb leak (56%, 68/121), and uncontrolled IOP (37%, 7/19). Success at 1, 2, 5, and 8 years after revision were 76%, 68%, 57%, and 50% (Kaplan-Meier); success was similar among revision indications (p=0.43). Further surgery after revision was needed in 30% of cases during follow-up: about half were additional IOP-lowering procedures and half were further revisions. Duration of symptoms prior to revision was not consistently associated with loss of VA between original surgery and last follow-up. Eyes that lost the most VA prior to revision for hypotony tended to be the same eyes that regained the most vision after revision; eyes that underwent revision for hypotony with shorter duration of symptoms showed greater improvement of VA between revision surgery and last follow-up (p=0.01).

Conclusion: Revision of trabeculectomy was successful in a majority of eyes for at least 5 years. Some loss of VA occurred after years of follow-up, due either to the complication or other causes.

74. Priyal Gandhi, MS 2

Mentor(s): Yuri Agrawal, MD
Department of Otolaryngology-Head & Neck Surgery

Self-Reported Sense of Direction and Vestibular Function in the Baltimore Longitudinal Study of Aging (BLSA)

Authors: Priyal Gandhi BA, Yuri Agrawal MD

Background: Age-related vestibular loss has been linked to impaired spatial cognition. While several studies have shown that vestibular input is necessary for accurate spatial cognition, they do not account for individual differences in intrinsic navigational ability. Numeric scales of self-reported sense of direction have been found to correlate well with objective measures of navigational ability. In this study, we evaluated age-related variation in self-reported sense of direction. We will also determine how vestibular function in aging adults is associated with sense of direction. We hypothesize that vestibular function will be related to self-reported sense of direction in healthy older adults.

Methods: Participants for this cross-sectional study were recruited from the Baltimore Longitudinal Study of Aging. In a modified version of the Santa Barbara Sense-of-Direction Scale, participants rated statements about spatial and navigational abilities from a scale of 1 to 7. A lower average score indicated lower self-reported sense of direction. Vestibular function testing consisted of the cervical vestibular-evoked myogenic potential (cVEMP) to assess saccular function, the ocular VEMP to assess utricular function, and the video head-impulse test to assess semicircular canal function based on vestibular ocular reflex. Multivariate linear regression will be used to investigate the relationship between vestibular function and self-reported sense of direction.

Results: The study sample included 41 participants with mean($\pm$SD) age of 75.4($\pm$16.6) years and mean($\pm$SD) Sense-of-Direction Scale score of 3.7($\pm$0.72). Linear regression demonstrated a 0.01 decrease in Sense-of-Direction Scale score with a 1 year increase in age (p=0.117); this association was not statistically significant.

Conclusion: We observed a downward trend in self-reported sense of direction with increasing age that is consistent with previous work on age-related variation in sense of direction. We will continue to explore associations between self-reported sense of direction and measures of vestibular function with a larger study sample.

75. Robert Young, MS 2

Mentor(s): Alexander Coon, MD; Matthew Bender, MD
Department of Neurosurgery

Twisting: Prevalence and Risk Factors of an Under-Reported Intra-Procedural Complication Associated with Pipeline Flow Diversion of Cerebral Aneurysms

Authors: Robert W.C. Young BS, Matthew T. Bender MD, Jessica K. Campos MD, Bowen Jiang MD, David A. Zarrin BS, Chau D. Vo BS, Justin M. Caplan MD, Judy Huang MD, Rafael J. Tamargo MD, Li-Mei Lin MD, Geoffrey P. Colby MD PhD, Alexander L. Coon MD

Background: Pipeline Embolization Device "twisting" manifests with appearance of a "figure 8" in perpendicular planes on DSA.

Methods: Case images were reviewed for instances of twisting from a prospectively-maintained, IRB-approved database of patients undergoing flow diversion for cerebral aneurysm.

Results: From August 2011 to December 2017, 999 Pipeline Embolization Device flow diverting stents were attempted in 782 cases in 653 patients. 24 PED twists were observed in 20 patients (2.40%, 24/999). Multivariate analysis revealed predictors of twisting to be: Large and giant aneurysms (OR=9.6, p=0.006; OR=26.2, p=0.001), increased PED length (OR=1.1, p=0.002), advanced patient age (OR=1.1, p=0.003), and a cavernous ICA tortuosity grade of III or IV (OR=2.8, p=0.051). Of the 20 cases that encountered PED twisting, the twisted stent was able to be remediated in 75% (15/20) of cases. In 15% of cases (3/20), the twisted stent was removed and a new PED was placed successfully without twisting; and in 10% of cases (2/20) the twisted stents were removed and the procedure was aborted. Overall procedural success was obtained in 90% of cases (18/20). Major and minor complications were observed in 10% and 5% of cases in which a twist was observed and twisting was not a predictor of major complication on multivariate analysis. The rate of complete occlusion for PED cases in which there was a twist was low (42% of those with DSA at 6 months and 40% at 12 months), but did not achieve statistical significance in multivariate analysis.

Conclusion: Twisting is a rare event during PED deployment, more likely to occur while treating large aneurysms with long devices in the setting of significant tortuosity. While twisting did not predict major complications in this series, remediation is challenging and demonstrates a trend towards inferior occlusion outcomes.

76. Shanaz Daneshdoost, MS 2

Mentor(s): Adam Levin, MD
Department of Orthopaedic Surgery

Bisphosphonate therapy for treating osteonecrosis in pediatric leukemia patients: A systematic review

Authors: Shanaz Daneshdoost BA, Jad El Abiad MD, Carrie Price MLS, Adam Levin MD

Background: Despite improving outcomes in pediatric leukemia patients, complications such as osteonecrosis are still common. Treatments include conservative management, bisphosphonate therapy, core decompression, and joint arthroplasty, although there is limited data on the use of bisphosphonates. We conducted a systematic review to investigate the potential role of bisphosphonates in reducing pain, improving function, and stabilizing lesions in pediatric leukemia patients.

Methods: We performed a literature search using PubMed, Embase, Cochrane, Web of Science, Scopus, CINAHL, and ClinicalTrials.gov. Of the 221 articles retrieved, we included five (retrospective, observational, and non-randomized interventional) studies that assessed the use of bisphosphonates for treating osteonecrosis in pediatric leukemia. Case reports, letters to the editor, conference notes, and abstracts without accompanying manuscripts were excluded. All eligible studies were critically appraised using the MINORS criteria.

Results: Bisphosphonates, especially when combined with conservative therapies, were associated with improved pain and mobility in 63.0% and 47.4% of patients, respectively. Compared to those treated with conservative therapy alone, patients treated with bisphosphonates demonstrated better pain outcomes, with a higher proportion of patients reporting mild/moderate pain or no pain at all ($p<0.005$). 63.6% of patients treated with bisphosphonates achieved improved or full mobility, compared to 27.3% of those treated with conservative therapy alone ($p<0.05$). However, 50% of patients demonstrated progressive joint destruction despite bisphosphonate therapy. No adverse events were reported, with the exception of acute phase reactions seen in one study.

Conclusion: Our findings suggest that bisphosphonates, when combined with conservative therapy, may be a useful tool for managing pain and improving mobility in pediatric leukemia patients with osteonecrosis, but may be less effective in preventing further joint destruction and collapse. The current data is unable to fully appreciate the potential implications of treatment with bisphosphonates when combined with other modalities such as core decompression.

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