9th Annual
Medical Student Research Symposium

February 10, 2017
Johns Hopkins University School of Medicine
Armstrong Medical Education Building

Cover image courtesy of

Halley Darrach, MS2

"This summer I conducted research in the Department of Otolaryngology-Head and Neck Surgery studying how society perceives facial deformity. Though I've always enjoyed figure drawing, it's an art form often captured by solely the surface of the human body. After dissecting in lab and observing in the OR, I have a newfound appreciation for internal anatomy. Thus, I sketched this stylized radical neck dissection in an attempt to contrast the skin and what lies just beneath."

TABLE OF CONTENTS

Medical Student Research Symposium 2017

We are pleased to have you join us for the 9th 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.
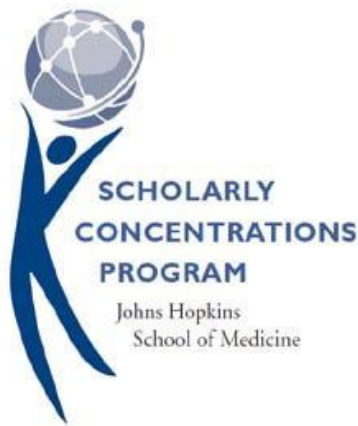
The Scholarly Concentration (SC) program is a faculty-mentored scholarly experience for medical students. This program provides the infrastructure and mentoring necessary for students to produce a scholarly project in an area of individual interest, and encourages the acquisition of attitudes and skills 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 and
Community Service** 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   **Coffee/Tea/Dessert**
AMEB 3rd Floor

3:40-4:45 PM   **Concurrent Oral Presentations**
RM 320, 326, 341, 342, 343, 344, 345, 370

4:50-5:30 PM   **Keynote speaker, *Dr. Khalil Ghanem***
MSRS Award Ceremony
AMEB 1st Floor Lecture Hall

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KEYNOTE SPEAKER

Khalil Ghanem, M.D., Ph.D.

Associate Professor of Medicine

Johns Hopkins University School of Medicine

Khalil Ghanem is an Associate Professor of Medicine in the Infectious Diseases Division at the Johns Hopkins University School of Medicine, the Deputy Director of Education for the Department of Medicine at Johns Hopkins Bayview Medical Center and has a joint appointment in Department of Population, Family, and Reproductive Health at the Johns Hopkins Bloomberg School of Public Health. Dr. Ghanem completed his medical training at Baylor College of Medicine in Houston, TX in 1996, and his residency there in Internal Medicine in 2000. He completed a Fellowship in Infectious Diseases at the Johns Hopkins Hospital in 2004. His research focuses on genitourinary infections, and in particular, on syphilis and the vaginal microbiome.

Faculty Judges

Alan Scott
Allan Gelber
Andrew Wolfe
Angela Guarda
Anne Murphy
Barry Nelkin
Barry Solomon
Bernard A. Cohen
Bhakti Hansoti
Brandi R. Page
Byoung Chol Oh
Carolyn Sufrin
Catherine Deangelis
Charlene Gamaldo
Cozumel Pruette
Craig Hendrix
Dagna Constenla
Daniel Ford
David Dowdy
David Hackam
Deidra Crews
Dolores Njoku
Dory Storms
Emily Boss
Eric B. Bass
Eric Balighian
Eric Jackson
Eric Kossoff

Lauren Osborne
Lee Peterlin
Lisa Ishii
Lode Swinnen
Lois Eldred
Lydia H. Pecker
Marco Grados
Margaret S. Chisolm
Mariana Brait
Mark Bicket
Marlis Gonzalez-Fernandez
Mary Carol Jennings
Mary Catherine Beach
Mary E. Fissell
Megan E. Collins
Meredith Atkinson
Michael Barone
Michael Crocetti
Michael Fingerhood
Michele Manahan
Mohammad O. Hoque
Myron L. Weisfeldt
Nara Lygia de Macena Sobreira
Noel T. Mueller
Paul Schaughency
Paul Sponseller
Paula Hurley
Randall Packard

Erin Michos

Feilim Mac Gabhann

Gabsang Lee

Gail Geller

Gerald Brandacher

Geraldine Seydoux

Graham Mooney

Helene Hedian

Ingo Ruczinski

Jacek L. Mostwin

Jacky Jennings

Jarushka Naidoo

Jean Kim

Joann Bodurtha

Jodi Segal

Joe Carrese

Joseph J. Gallo

Jun Luo

Kelly Dunn

Kelly Gebo

Kevin Psoter

Khalil Ghanem

Kunihiro Matsushita

Laura Hanyok

Raquel Greer

Richard L. Skolasky

Rosalyn Stewart

Rosemary Morgan

Roy Ziegelstein

S. Christy Sadreameli

Samuel M. Alaish

Sapna Kudchadkar

Sarah Wheelan

Sharon D. Solomon

Shawn Lupold

Shenandoah Robinnson

Somnath Saha

Srinivasan Yegnasubramanian

Stephen Broderick

Stephen Sozio

Subroto B.Chatterjee

Sudipto Ganguly

Suzanne Jan de Beur

Timothy F. Witham

Tina Tran

Tom Smith

Travis Rieder

Ya-Chi Ho

Schedule of Podium Presentations

12:20 PM   **Miriam Fox**   One Week Course of Trimethoprim-Sulfamethoxazole May Be as Effective as a Conventional One Week Course of Ciprofloxacin for the Treatment of Pyelonephritis in Women

12:32 PM   **Anna Goddu**   Words Matter: Using Stigmatizing Language in Patient Charts Negatively Impacts Physician Attitudes and Dosing of Pain Medication

12:44 PM   **Hasina Maredia**   Lung Allocation Score is Not Predictive of Post-Transplant Survival Among Pulmonary Hypertension Lung Transplant Recipients

12:56 PM   **Sophie Lin**   A Novel Risk Score to Predict New Atrial Fibrillation after Isolated Coronary Artery Bypass Grafting (CABG)

1:08 PM   **Marc Shi**   When treatment defines disease: The emergence and development of multidisciplinary pain clinics in the United States

1:20 PM   **Matthew Thimm**   Awareness and Interest in Pre-Exposure Prophylaxis (PrEP) Among Patients Using Public Sexually Transmitted Diseases (STD) Clinics

1:32 PM   **Victoria Huang**   New regulatory T cell targets in prostate cancer

1:44 PM   **Andrea Yonge**   Circumstances, locations, and outcomes of falls in patients with glaucoma

Schedule of Concurrent Oral Presentations

1. Basic Science: Room 320

3:40 PM	**Aishwarya Shukla**	Subcellular localization of the Lin28A miRNA biogenesis pathway under physiological conditions of learning
3:52 PM	**Amir Abdolrahim Poorheravi**	Tyrosine Phosphoproteome of the Cardiac Sarcomere
4:04 PM	**Leila Musavi**	Muscle-Derived Stem Cells Can Transform into Cells with Schwann Cell Phenotypes and Functional Myelination Properties in-vitro
4:16 PM	**Rupali Sood**	A Robust Methylated Gene Biomarker Assay to Distinguish Benign Breast Lesions from Malignant Breast Cancer
4:28 PM	**Madhavi Duvvuri**	Engineering a drug-eluting stent to treat laryngotracheal fibrosis

2. Basic Science and Clinical Science: Room 326

3:40 PM	**Amy Quan**	Characterizing the Effects of Growth Hormone on Ameliorating Chronic Denervation Injury and Improving Peripheral Nerve Regeneration and Muscle Function
3:52 PM	**Kingsley Asiedu**	89Zr-oxine complex positron emission tomography (PET) visualizes trafficking of bone marrow (BM) cells in a mouse transplant model
4:04 PM	**Cristina Viguera**	Assessment of Olfactory Dysfunction as a Potential Biomarker in Amyotrophic Lateral Sclerosis
4:16 PM	**Eric Xu**	High Initial CSF Protein Predicts the Need for Ventriculoperitoneal Shunting and Shunt Failure in Preterm Infants with Posthemorrhagic Hydrocephalus
4:28 PM	**Jaeyun Jane Wang**	Immune Checkpoint Markers in Melanoma: Expression in Brain Metastases Compared to Corresponding Extracranial Tumors

3. Clinical Science: Room 341

3:40 PM	**Margaret Sundel**	Perioperative neuroimaging with functional near-infrared spectroscopy (fNIRS) to evaluate post-operative delirium in elderly TAVR patients
3:52 PM	**Abia Abia**	ED-Based HIV Registry: A Method of Assessing ED and Hospital Resource Utilization by People living with HIV
4:04 PM	**Taylor Purvis**	Effect of Liberal Blood Transfusion on Clinical Outcomes and Cost in Spine Surgery Patients
4:16 PM	**Brendan Shi**	Biomechanical Strength of Rotator Cuff Repairs: A Systematic Review and Meta-Analysis of Cadaveric Studies
4:28 PM	**Abigail Lin**	The Impact of Complications during Ketogenic Diet Initiation on Seizure Outcomes in Children with Epilepsy

4. Clinical Science: Room 342

3:40 PM   **Carson Woodbury**   Sexual Well-being After Breast Cancer Surgery and Breast Reconstruction: A Systematic Review with Meta-Analysis

3:52 PM   **David Liao**   Graves' Ophthalmopathy Leads to Attentional Distraction: A 3-D Eye-tracking Study

4:04 PM   **Francisco Eguia**   Comparative volumetric analysis of the extent of resection of low grade gliomas and its role on survival

4:16 PM   **Hannah Carl**   Surgical Factors Associated with Prolonged Hospitalization after Reconstruction for Oncological Spine Surgery

5. Clinical Science: Room 343

3:40 PM   **Stephen Njau**   How complications, length of stay and
                                   hospital's region impact the cost of
                                   pancreaticoduodenectomy.

3:52 PM   **Julia Retzky**   The Subjective Shoulder Value Correlates
                                   Well with the American Shoulder and Elbow
                                   Surgeons Score in Patients Undergoing
                                   Rotator Cuff Repair, Total Shoulder
                                   Arthroplasty, and Reverse Total Shoulder
                                   Arthroplasty Pre- and Post-Operatively

4:04 PM   **Eric Weaver**   Teaching an Approach to Goals of Care
                                   Meetings in the Intensive Care Unit: Impact
                                   on Documentation

4:16 PM   **Marcelo Cerullo**   Physiologic Correlates of Intraoperative
                                   Blood Transfusion Among Patients
                                   Undergoing Major Gastrointestinal Surgery

4:28 PM   **Marcus Daniels**   The Flaw in Using Publication Number For
                                   Predicting Medical Student Academic Career
                                   Placement in Neurosurgery

6. Clinical Science: Room 344

3:40 PM	**Rebecca Glasser**	Intra-operative fluorescence of sciatic nerves improves visualization in initial and revision surgical procedures
3:52 PM	**Ridwan Alam**	Prospective Analysis of Active Surveillance for Small Renal Masses: Is It Safe?
4:04 PM	**Kathleen Chin**	Physical activity, Vitamin D, and Incident Atherosclerotic Cardiovascular Disease in the Atherosclerosis Risk in Communities (ARIC) study
4:16 PM	**Ross Pollack**	Impact of bystander AED use on survival and functional outcomes in shockable observed public cardiac arrest.
4:28 PM	**Zachary Janik**	White Coat Adherence in MTN-001

7. Clinical Science and Public Health: Room 345

3:40 PM	**Aldo Gonzalez**	Remission and Relapse of Type 2 Diabetes Mellitus after Bariatric Surgery: Vertical Sleeve Gastrectomy versus Roux-en-y Gastric Bypass
3:52 PM	**Elizabeth Uhlig**	Cost Effectiveness Analysis of Active Case Finding of Tuberculosis—Comparing Two Programs in India and Cambodia
4:04 PM	**Amy Huang**	Student adherence and satisfaction with eyeglass usage in the Baltimore Reading and Eye Disease Study (BREDS)
4:16 PM	**Moon Jeong Lee**	Accelerometer-assessed physical activity and its association with change in visual field loss in patients with glaucoma
4:28 PM	**Ruchi Doshi**	Factors Influencing Medical Student Preparedness and Skills to Provide Weight Management Services

8. Public Health, Ethics and the Art of Medicine, History of Medicine: Room 370

3:40 PM	**Mary Peeler**	Treatment of Opioid Use Disorder in Incarcerated Pregnant Women
3:52 PM	**Awa Sanneh**	Health Beliefs and Cervical, Breast and Colorectal Cancer Screening Rates in Baltimore's Muslim Women
4:04 PM	**Zach Reilly**	The TOP Study: Assessing Peri-operative Goals and Post-operative Satisfaction Among Transgender Men Undergoing Gender Affirming Chest Reconstruction Surgery
4:16 PM	**James Senter**	"Like Another Me": Reimagining Medicine and Identity in Healthcare
4:28 PM	**N. Jia Ahmad**	The Emergence of an Epidemic: NIDA, Heroin and the Birth of "Drug Abuse Epidemiology"

POSTER PRESENTERS

AMEB 2nd Floor

Listed Alphabetically (First Name) by Research Category

BASIC SCIENCE

#	Name	Title
1	**A. Karim Ahmed**	Establishment of Chordoma in a Rat Model
2	**Amy Quan**	Novel Peripheral Nerve Injury Animal Model Optimizes Measurement of Functional Recovery Following Chronic Denervation Injury
3	**Baltazar Zavala**	Hold that thought: Human subthalamic nucleus theta and beta oscillations are coherent with the lateral cortex during working memory inhibition.
4	**Bryce Small**	Validating the Block-and-Lock Strategy as a novel cure for HIV
5	**John Choi**	Treatment of Malignant Pediatric Brain Tumors via Suicide Transgene Expression Using PEGylated pPEG-3 PBAE Nanoparticles
6	**Maeva Nyandjo**	IL-33 critically modulates Treg responses in a mouse model of drug-induced hepatitis
7	**Michael Grzelak**	Designing an optimal rescue template to maximize CRIPSR-Cas editing efficiency in HEK cells
8	**Paul Michel**	Applying machine learning methods to predict the impact of common variants on gene regulation in type I diabetes
9	**Sarah Thompson**	Anti-CD123 scFv Expression in Non-Immune Cells for Targeting of Acute Myeloid Leukemia Cells for Synthetic Clearance
10	**Scott Shuldiner**	Development of a droplet digital methylation specific PCR assay to measure DNA methylation alterations as novel prostate cancer biomarkers

CLINICAL RESEARCH

#	Name	Title
11	**Abigail Lin**	Yttrium-90 radioembolization with adjuvant 90Y PET/CT-guided percutaneous ablation: Predicted dosimetric impact
12	**Adela Wu**	Pattern of HPA Axis Recovery after Successful Surgery for Cushing Disease
13	**Adela Wu**	Infantile Poor Vision in the Setting of Hypotonia and Oculomotor Apraxia
14	**Akachimere Uzosike**	Variability in growth kinetics of small renal masses on active surveillance
15	**Alan Shan**	Intraocular lens insertion during resident phacoemulsification cases: identification of intraoperative characteristics specific to lens choice
16	**Alex Jang**	Multiple Growth Periods Predict Unfavorable Pathology in Patients with Small Renal Masses Undergoing Active Surveillance
17	**Allison Wallingford**	Comparison of Functional Specificity between Conventional and Multichannel Electrode Montages for tDCS
18	**Anh Quynh Nguyen**	Willingness to Donate Organs Among Persons Living with HIV/AIDS
19	**Brendan Shi**	Pullout Strength in Augmented and Wide-suture Transosseous Rotator Cuff Repair: A Biomechanical Analysis
20	**Chengcheng Gui**	Characterization and predictive value of volume changes of extremity and pelvis soft-tissue sarcomas during radiotherapy prior to surgical resection
21	**Clarisa Diniz**	Comparison of biochemical recurrence free survival after radical prostatectomy among men in active surveillance following grade reclassification and men newly diagnosed with similar grade disease
22	**Damian Stobierski**	Brain Tumor Metastases from Primary Lung Cancers: Evaluating Risk Factors and Surgical Outcomes

23	**Daniel Kerekes**	Prevalence, Risk Factors, and Outcomes for Local and Distant Recurrence in Resected Sacral Chordomas: a Systematic Review
24	**Davis Rogers**	Influence of Fatigue on Motor Skill Learning
25	**Divya Rayapati**	Relationship between sleep quality components and depression in women with perinatal mood disorders
26	**Emily Boozalis**	Horizontal striae distensae of the lower back in teenage boys: an analysis of demographics and review of the literature
27	**Eric Xie**	Association of Ablation Parameters in Radiofrequency Rhizotomy for Trigeminal Neuralgia with Durability of Treatment
28	**Ethan Dyer**	The Johns Hopkins Corrie Smartphone Application
29	**Gloria Hong**	Ocular Involvement in Mucous Membrane Pemphigoid
30	**Halley Darrach**	The Other Race Effect: Caucasians display preferential attention towards racially congruent faces regardless of perceived attractiveness
31	**Hannah Carl**	Systematic Review of the Surgical Treatment of Extremity Lymphedema
32	**Hasina Maredia**	Second independent primary tumors among esophageal cancer survivors
33	**Hasina Maredia**	Is Lung Allocation Score Associated with Survival Among COPD Lung Transplant Registrants and Recipients?
34	**Hasina Maredia**	Age and Gender Disparities in Post-Lung Transplant Mortality
35	**Jared Hinkle**	Parkinson's Disease Psychosis is Independently Associated with Dyskinesia Severity
36	**Jenny Yan**	Single-Arm Phase II Study of Stereotactic Body Radiation Therapy (SBRT) Concurrent with Nelfinavir for Oligometastases
37	**John Ryan**	Stereotactic body radiation therapy for isolated local recurrence after surgical resection of pancreatic ductal adenocarcinoma appears to be safe and effective

38	**Jordan Tropf**	Inspiring Innovation: Introducing Biomedical Engineering Students to Orthopaedic Instruments and Procedures
39	**Joshua Yang**	A non-invasive urinary Common Rejection Module (uCRM) gene expression score enables accurate discrimination of acute rejection in kidney transplant patients
40	**Julia Retzky**	Epidemiological risk factors for ACL injury recurrence in NCAA athletes
41	**Luckmini Liyanage**	The optimal duration of helmet therapy after endoscopic craniectomy for infants with metopic craniosynostosis
42	**Marija Vasiljevic**	Making Time for Sleep in a Primary Care Clinic
43	**Matthew Woods**	MRI Analysis of Stent Fractures in COAST Trial
44	**Miguel Diaz**	Open sub-pectoral biceps tenodesis: A biomechanical comparison of interference screw and various fixation techniques
45	**Mohammed Alkhafaji**	Long Term Outcomes for Surgical Treatment of Superior Canal Dehiscence Syndrome
46	**Moustafa Abou Areda**	Even if Bracing Fails to Prevent Surgery, It May Benefit the Lumbar Spine in Adolescent Idiopathic Scoliosis
47	**Na Shin**	The Association of Minor and Major Depression with Health Problem-solving and Diabetes Self-care Activities in a Clinic-Based Population of Adults with Type 2 Diabetes Mellitus
48	**Naureen Huda**	Prevalences of depression and anxiety among pancreatic cancer patients and associations with survival
49	**Nicholas Mai**	Circulating Tumor DNA and the Risk of Recurrence in Triple Negative Breast Cancer Patients
50	**Niv Milbar**	Intravesical Gemcitabine and Docetaxel Is a Reasonable Alternative to Early Radical Cystectomy for Select Patients with High-grade Recurrent NMIBC
51	**Rachel Kim**	Posterior approaches for Symptomatic Metastatic Spinal Cord Compression
52	**Rachel Pedreira**	Pre-operative Radiation Predicts Hardware Failure in Patients with Spinal Metastases

53	**Rebecca DiBiase**	Exploring the Etiology of CAPD and Associated Risk Factors through Novel Diagnostic Tools
54	**Rebecca Glasser**	Sciatic nerves of Thy-1-YFP mice do not maintain fluorescence in the distal portion one week post-transection
55	**Rebecca Glasser**	The impact of conservative and surgical treatment on upper extremity specific disability and psychological state in patients with thumb osteoarthritis
56	**Russell Maxwel**	BRAF-V600 mutational status affects recurrence patterns of melanoma brain metastasis
57	**Samantha Roman**	Reasons for non-participation in a dietary intervention study among patients with multiple sclerosis.
58	**Sandeep Palepu**	Surgical Tricuspid Valve Detachment (TVD) in Perimembranous Ventricular Septal Defect (VSD) Repair Has Not Shown Significant Long Term Harm to Tricuspid Valve Function.
59	**Sanskriti Varma**	Weight Regain in Patients with Symptoms of Post-bariatric Surgery Hypoglycemia
60	**Shamsudini Hashi**	Management of Extranodal Lymphoma of the Spine: A Study of 30 Patients
61	**Sophia Chen**	Post-Discharge Complications after Esophagectomy Account for High Readmission Rates
62	**Taylor Purvis**	The Effect of Renal Dysfunction on Short-Term Outcomes after Lumbar Fusion
63	**Taylor Purvis**	Short-term outcomes after external fixation versus surgical fusion for cervical spine fractures without spinal cord injury in pediatric patients
64	**Taylor Purvis**	Impact of Smoking on Postoperative Complications after Anterior Cervical Discectomy and Fusion
65	**Taylor Purvis**	Crosswalking GAD-7 and PHQ-8 to the PROMIS Anxiety and Depression Health Domains among Patients Presenting for Spine Surgery
66	**Taylor Purvis**	Concurrent Validity and Responsiveness of PROMIS Health Domains Among Patients Presenting for Spine Surgery
67	**Trevor Davis**	Clinical Implications for High-Risk Surgical Patients with Infective Endocarditis

ETHICS and THE ART OF MEDICINE

#	Name	Title
68	**Amar Deshwar**	Understanding the Diagnostic Delay in Patients with Pancreatic Cancer
69	**Conisha Cooper**	Clinicians' Personal Experience of Trauma and its Impact on Screening Female Patients for Trauma
70	**Faisal Chaudhry**	Does Lecture Attendance Impact Undergraduate Medical Student Exam Performance?
71	**Jane Long**	An Observation
72	**Jennifer Plotkin**	Needs Assessment for First Year Medical Student Empathy Lab
73	**Jenny Wen**	Trauma Informed Care Needs Assessment of Internal Medicine Residents
74	**Kiley Hunkler**	Ethical Considerations of Military Physicians as Officers and Providers

HISTORY OF MEDICINE

#	Name	Title
75	**Jason Theis**	Bloodless Injuries: Emphasizing Combat Narratives Limits Military Veteran Access to Care for Posttraumatic Stress Disorder
76	**Nicole Lunardi**	The Pathogenesis of Youth: How Youth Became the Subject of Violence Prevention Programs

PUBLIC HEALTH and COMMUNITY SERVICE

#	Name	Title
80	**Christopher Counts**	Options for Restoring Competition in the Generic Drug Industry
81	**Eva Szymanski**	Variants in WFDC2 are associated with Woakes Syndrome
82	**James Ting**	Designing the algorithm for a low-cost, high-utility diagnostic tool for early ASD
83	**Jonathan Callan**	Improve Housing to Reduce Falls: Learning from the Baltimore Fall Reduction Initiative Engaging Neighborhoods and Data
84	**Kathryn Pearson**	Noninvasive Brain Stimulation in Parkinsonian Disorders: A Systematic Review
85	**Kendrick Wang**	Outcomes of Tyrosine Kinase Therapy for Brain Metastasis of Patients with Non-Small Cell Lung Carcinoma in Singapore
86	**Kingsley Asiedu**	The Role of Interdigitated Chemotherapy and Radiation in Managing High-Grade Soft -Tissue Sarcoma
87	**Lindsay Dickerson**	A pilot educational intervention and feasibility assessment of breast ultrasound in rural South Africa
80	**Melissa Lavoie**	Options for Restoring Competition in the Generic Drug Industry
88	**Michael Saheb Kashaf**	Shared Decision-Making and Outcomes in Type 2 Diabetes: A Systematic Review and Meta-Analysis
89	**Monica Tung**	A Systematic Review of the Determinants of Overuse of Radiologic Services in the Emergency Department
90	**Nisha Parikh**	Stress Reduction with Yoga among Low-Income Urban Minorities: A Scoping Review
91	**Stephanie Sweitzer**	Optimizing the HIV treatment cascade among men who have sex with men (MSM) in South Africa
92	**Thomas Brooke**	The Accuracy of Physicians' and Nurse Practitioners' Perceived Frailty in Transcatheter Aortic Valve Replacement Patients
93	**Zixiao Wang**	Merkel Cell Carcinoma in African Americans: a retrospective case-control study

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

Doug Hughes

Victor Raspa

John Steele

Mark Dodd

The Scholarly Concentrations Faculty

2017 MSRS Organizing Committee

Alexander Fischer

Joshua Prudent

Karim Ahmed

Victoria Huang

Megan May

Annie Wu

Judy Doong

Ali Ghasemzadeh

Carly Wasserman

Michele Massa

Dr. Mary Catherine Beach

Dr. Thomas Koenig

PODIUM PRESENTATION ABSTRACTS
Listed Alphabetically (First Name)

Andrea Yonge, MS 4

Mentor(s): Pradeep Ramulu, MD PhD
Glaucoma Center, Wilmer Eye Institute

Circumstances, locations, and outcomes of falls in patients with glaucoma

Authors: Andrea Yonge BS, Bonnielin Swenor PhD MPH, Rhonda Miller BA, Victoria Goldhammer MS OTR/L, Sheila West PhD PharmD, David Friedman MD PhD, Laura Gitlin PhD, Pradeep Ramulu MD PhD

Background: Glaucoma is associated with an increased risk for falls due to visual field (VF) loss and poor contrast sensitivity (CS). In this prospective, observational study, we characterize the circumstances, locations, and outcomes of falls in patients with glaucoma.

Methods: Patients aged 57 years or older receiving care for glaucoma filled out monthly calendars to report any falls. After each reported fall, a 30-item questionnaire was administered to the participant to determine the fall location, circumstances, and resulting injury (if any). Falls from September 2013 through May 2016 were included for analysis. Humphrey 24-2 VFs were obtained to calculate average integrated VF sensitivity, a measure of disease severity.

Results: One-hundred forty-two patients experienced a total of 330 falls. Mean baseline age was 71.3 years, and approximately half of participants were male (45.1%); patients fell an average of 2.3 times during the study period. Vision issues were cited as a direct cause in 15.9% of falls. Falls were slightly more common indoors (50.3%), and the most common location for indoor falls was the patient's home (117/166 falls, 70.5%). The stairs (29 falls, 24.8%) were the most common home area for falls. Among outdoor falls, 73 (44.5%) occurred within the vicinity of the home (e.g. driveway, yard). Overall, 143 of 330 total falls (43.3%) resulted in some injury, with 15 falls (4.5%) resulting in a fracture and 11 falls (3.3%) resulting in a hospital admission. Neither severity of VF nor CS loss predicted whether a fall would be injurious (p>0.56 for both).

Conclusion: Several participants fell multiple times during the study period, and severity of vision impairment did not predict whether a fall would be injurious. Interventions to prevent falls in this population should focus on the home environment and be directed toward all individuals who are at increased risk of falling, regardless of glaucoma severity.

Anna Goddu, MS 2

Mentor(s): Mary Catherine Beach, MD MPH
Department of Medicine

Words Matter: Using Stigmatizing Language in Patient Charts Negatively Impacts Physician Attitudes and Dosing of Pain Medication

Authors: Anna Goddu MSc, Katie O'Conor BS, Sophie Lanzkron MD MHS, Mustapha Saheed MD, Som Saha MD MPH, Monica Peek MD MPH, Carlton Haywood PhD MA, Mary Catherine Beach MD MPH

Background: Clinician bias contributes to healthcare disparities, and the language used to describe a patient may reflect that bias. Although medical records are a critical method of communicating about patients, no studies have evaluated patient charts as a means of transmitting bias from one provider to another. We hypothesized that stigmatizing language in a patient chart is associated with a subsequent clinician's attitudes towards the patient and management of the patient's pain.

Methods: Medical students and residents completed an online survey in which they were randomized to view one of two chart notes presenting medically-identical information about the same hypothetical patient, a 28-year-old man with sickle cell disease and vaso-occlusive crisis. One note employed stigmatizing language (abstracted from actual patient records); the other employed neutral language. We assessed attitudes towards the hypothetical patient using the previously-validated Positive Attitudes towards Sickle Cell Patients Scale (range 5-35) and pain management decisions (residents only) using two multiple-choice questions (composite range 1-7 representing intensity of pain treatment). We used t-tests and Wilcoxon rank-sum tests to calculate differences in attitudes and treatment based on study arm assignment.

Results: Respondents included 233 medical students and 180 residents (overall response rate 58%). Fifty-four percent identified as white, 55% as male and 56% were 25-29 years old. Exposure to the stigmatizing-language note was associated with more negative attitudes towards the patient (20.6 stigmatizing vs. 25.6 neutral, p<0.001). Furthermore, exposure to the stigmatizing-language note was associated with less aggressive pain management (5.56 stigmatizing vs. 6.22 neutral, p=0.003).

Conclusion: Stigmatizing language written by one provider in a patient's medical record negatively impacts subsequent providers' attitudes towards the patient and influences clinical decision-making. Future work should explore which dimensions of stigmatizing language are most harmful. Attention to the language used in medical records may promote patient-centered care and reduce healthcare disparities for stigmatized populations.

Hasina Maredia, MS 2

Mentor(s): Errol Bush, MD
Department of Surgery

Lung Allocation Score is Not Predictive of Post-Transplant Survival Among Pulmonary Hypertension Lung Transplant Recipients

Authors: Hasina Maredia BA, Mary Grace Bowring MPH, Allan Massie PhD, Shakirat Oyetunji MD, Christian Merlo MD PhD, Robert Higgins MD, Dorry Segev MD PhD, Errol Bush MD

Background: Pulmonary hypertension (PH) is a rapidly progressive and fatal disease often requiring lung transplant. Candidates are prioritized using the lung allocation score (LAS), which incorporates both predicted waitlist and post-transplant mortality. It currently not known whether LAS is actually associated with waitlist and post-transplant survival among PH patients, which we seek to address in this study.

Methods: Using the national Scientific Registry of Transplant Recipients database, we performed a retrospective observational study of 310 adult lung transplant candidates diagnosed with PH and listed for transplant between 5/1/2005-7/31/2015. Patients listed at multiple institutions were excluded. Cox regression was used to compare mortality based on time-varying LAS categories after adjusting for patient age, sex, race, and education level.

Results: Among all listed PH patients, 64% were transplanted. Among patients who were not transplanted, 62% died. LAS ranged 28-86. The median LAS at time of transplant was 35 (IQR 33-39).

In the adjusted model, PH patients on the waitlist have a 4.03 (95% CI: 2.11–7.72; p<0.001) times higher risk of death. There was a 5.55 (95% CI: 3.05–10.1) and 27.6 (95% CI: 11.8-64.4) times higher risk of death among LAS 36-46 and 47-100, respectively, in the waitlist group, but there was no difference in risk among transplanted patients by LAS category. There was a higher risk of death on waitlist compared to post-transplant in all LAS categories (p<0.001). The risk of death in 3.5 days on the waitlist was equivalent to the risk of death one-year post-transplant in LAS 47-100 (adjusted hazard ratio= 108.7; 95% CI: 6.49-1819.7; p<0.001).

Conclusion: Transplantation was associated with substantially lower risk of death in all LAS categories, but LAS was not associated with post-transplant mortality. As such, LAS may need to be adjusted in order to better reflect differences in post-transplant survival among PH patients.

Marc Shi, MS 2

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

When treatment defines disease: The emergence and development of multidisciplinary pain clinics in the United States

Authors: Marc Shi MSc, Jeremy Greene MD

Background: The treatment of chronic pain is one of the most intractable problems in medicine today, and there is little consensus regarding best practices for its management. Yet most contemporary practices in pain management originated from a single model: the multidisciplinary pain clinic, which first emerged in 1960 as an attempt to standardize pain treatment. This project explores the evolution of the chronic pain clinic to better understand how different implementations of this model have shaped the way that pain has been defined and managed.

Methods: This paper traces 5 early pain clinics in the 1960s and 1970s: those at Emory University, the University of Washington, Memorial Sloan Kettering Cancer Center, the Johns Hopkins University, and the New Hope Pain Center. Academic literature from each clinic was analyzed for language describing clinic structures, protocols and patients, and was supplemented where possible by interviews with clinicians associated with each clinic.

Results: While the sample clinics claimed to be drawing on the same model of treatment, there were differences in the structures of the clinics and the modalities of treatment that were utilized. In particular, clinics diverged on their uses of pharmaceutical treatments and conditioning-based behavioral therapy. Differences in treatment aligned with differing ideas about the mechanisms of pain, and were associated with differences in the way clinics described and approached patients' experiences of pain.

Conclusion: Divergent approaches to pain under the common banner of multidisciplinary clinics reflect the way in which clinical institutions are instrumental in defining the boundaries of an ambiguous clinical entity. As a standardized approach to pain becomes increasingly necessary, and multidisciplinary care gains popularity, multidisciplinary pain clinics provide a useful lesson on how a common framework can provide a shared language for approaching a clinical problem, while potentially obscuring the differences that define how treatment is delivered and experienced.

Matthew Thimm, MS 2

Mentor(s): Kathleen Page, MD
Medicine

Awareness and Interest in Pre-Exposure Prophylaxis (PrEP) Among Patients Using Public Sexually Transmitted Diseases (STD) Clinics

Authors: Matthew Thimm BS, Luke Johnsen DO, Kathleen Page MD

Background: Pre-Exposure Prophylaxis (PrEP) is a method of HIV prevention that involves a daily regimen of antiretroviral therapy, shown to be more than 90% effective at preventing new HIV infections. In 2016, the Baltimore City Health Department (BCHD) implemented a PrEP program at their sexually transmitted diseases (STD) clinics. This study aimed to assess awareness, interest, and sources of knowledge about PrEP among patients using these clinics, allowing BCHD to improve educational messages and PrEP enrollment.

Methods: We recruited 1,477 patients who attended BCHD STD clinics between 4/12/2016 and 8/15/2016. All patients were eligible to participate. Participants were provided a self-administered survey that assessed awareness, interest, and sources of knowledge about PrEP, as well as age, race, sex, and sexual preference. Univariate and multivariable logistic regression procedures examined predictors of awareness and interest.

Results: Mean age of participants was 32 (SD=11.9). 90.5% of participants were African American, 6.4% were white, and 3.1% were another race. 61.2% were male. 19.6% of the participants were aware of PrEP and 42.9% were interested in PrEP. <1% reported current PrEP use. Participants who were white (OR=2.23, p=0.002), race was other (OR=2.45, p=0.011), who reported a sexual preference for either sex (OR=2.21, p=0.011), or who reported a sexual preference for the same sex (OR=13.73, p<0.001) were more likely to be aware of PrEP. White participants (OR=0.61, p=0.036) were less likely to be interested in PrEP. Men who have sex with men (MSM) were significantly more likely to be aware (OR=17.31, p<0.001) and interested (OR=1.53, p=0.036) in PrEP. Sources of knowledge included healthcare providers (39.7%), friends (23.9%), and television (16.3%).

Conclusion: Awareness of PrEP among BCHD patients is comparable or higher than other studies, likely due to current education efforts in these clinics. While many patients are interested in PrEP, increasing PrEP enrollment will require careful education and recruitment strategies.

Miriam Fox, MS 2

Mentor(s): Pranita Tamma, MD, MHS
Pediatric Infectious Diseases

One Week Course of Trimethoprim-Sulfamethoxazole May Be as Effective as a Conventional One Week Course of Ciprofloxacin for the Treatment of Pyelonephritis in Women

Authors: Miriam Fox BS, Anna Conley BA, Michael Melia MD, Pranita Tamma MD MHS

Background: There are over 250,000 cases of pyelonephritis in the United States annually. The Infectious Diseases Society of America (IDSA) guidelines recommend either 14 days of oral trimethoprim-sulfamethoxazole (TMP-SMX) or 7 days of oral ciprofloxacin for the treatment of pyelonephritis. If a shorter course of TMP-SMX has similar efficacy to a 7-day course of ciprofloxacin, its use may reduce emergence of antibiotic resistance and healthcare costs. We compared the odds of a subsequent, symptomatic urinary tract infection (UTI) within 30 days for women with pyelonephritis receiving a 7-day course of TMP-SMX versus a 7-day course of ciprofloxacin.

Methods: Patient data were retrospectively collected via electronic medical record for women ages 16 and older with Escherichia coli pyelonephritis presenting to 5 healthcare facilities in greater Maryland between 2010 and 2016. Patients were excluded if they were pregnant or dialysis dependent, if their causative pathogen was not susceptible in vitro to the antibiotic treatment prescribed, or if they received greater than 72 hours of any antibiotic treatment other than TMP-SMX or ciprofloxacin.

Results: Of 264 women meeting eligibility criteria, 74 (28%) and 190 (72%) received 7 days of TMP-SMX and 7 days of ciprofloxacin, respectively. The likelihood of a recurrent E. coli UTI within 30 days for the TMP-SMX and ciprofloxacin groups was similar (OR: 1.45, 95% CI: 0.54-2.63). Subgroup analysis separately excluding bacteremic patients and patients requiring hospitalization also showed no statistically significant difference in the likelihood of recurrent UTI within 30 days.

Conclusion: Our findings suggest that 7 days of TMP-SMX therapy results in similar clinical outcomes compared with 7 days of ciprofloxacin for the treatment of pyelonephritis and warrants a randomized controlled trial of short course TMP-SMX therapy. Considering the high prevalence of pyelonephritis and rising antibiotic resistance levels, decreasing the length of antibiotic therapy can potentially impact a large number of women.

Sophie Lin, MS 2

Mentor(s): William Baumgartner, MD
Cardiac Surgery

A Novel Risk Score to Predict New Atrial Fibrillation after Isolated Coronary Artery Bypass Grafting (CABG)

Authors: Sophie Z Lin PhD, Todd C Crawford MD, Alejandro Suarez-Pierre MD, Michael V Carter, Duke E Cameron MD, William A Baumgartner MD, Kaushik Mandal MD

Background: Atrial Fibrillation (AF) is common after cardiac surgery and contributes to increased morbidity and mortality. Identifying risk factors for postoperative AF will improve risk stratification and facilitate preventative paradigms. Our objective was to derive and validate a risk score to predict AF after Coronary Artery Bypass Grafting (CABG) in patients without prior history of dysrhythmia.

Methods: This was a single center, retrospective study of patients who underwent isolated CABG at the Johns Hopkins Hospital from 2011-2015. Our outcome of interest was new onset AF during postoperative hospitalization. We excluded patients that did not have a preoperative measurement of left atrial diameter (LAdiam). The population was randomly divided into derivation (80%) and validation (20%) cohorts. We performed exploratory univariable logistic regression analysis in our derivation group. Variables associated with AF were then added manually forwards into a multivariable (MV) logistic regression model and the most parsimonious model was constructed. Significant risk factors from the MV model comprised the final risk score.

Results: 1307 patients underwent isolated CABG and 762 (58%) had preoperative LAdiam measured. 209/762 (27%) patients developed new onset AF including 165 (29%) in the derivation cohort. Four risk factors were independently associated with postoperative AF and included in our Predictors of Atrial Fibrillation After CABG (PAFAC) score. Adjusted odds ratios multiplied by a factor of 4 were used to assign points to each risk factor: age>60 years (5points), Caucasian race (5points), baseline GFR<90mL/min (4points) and LAdiam >4.5cm (4points). Scores ranged from 0-18. The PAFAC score was validated in the validation cohort and predicted incidence of AF strongly correlated with observed incidence (R=0.92).

Conclusion: This is the first AF risk calculator to incorporate left atrial diameter measurements in a model. In summary, the PAFAC score can be used to easily and reliably identify patients at high risk of developing AF after isolated CABG.

Victoria Huang, MS 2

Mentor(s): Charles Drake, MD PhD
Oncology

New regulatory T cell targets in prostate cancer

Authors: Victoria Huang BS, Yuki Muroyama MD, Charles Drake MD PhD

Background: Regulatory T cells (Tregs) play an important role in immune peripheral tolerance and thus help to control the balance between activating and inhibiting immune response. In the tumor microenvironment, Tregs suppress antitumor immunity. However, little is known about their mechanisms of action or regulation of function – key areas of understanding needed to maximize the benefits of tumor immunotherapy. Using RNAseq from prostate cancer patients, we have identified the genes that are highly expressed in human prostate tumor-infiltrating Tregs as compared to peripheral naïve CD4 T cells and peripheral CD4 Tregs (D1, D4, R1, and H1). In this study we aimed to develop an in vitro system to determine the role of these genes in Treg function.

Methods: We developed and optimized siRNA-based methods to knockdown target gene expression in human Tregs. Healthy human peripheral mononuclear cells (hPBMCs) were transfected via electroporation with siRNA against each target gene. The Treg cell population was then isolated using an immunomagnetic cell isolation kit. Flow cytometry was conducted to measure transfection efficiency and cell population purity. qRT-PCR was used to quantify the effect of siRNA on target gene expression. The Foxp3 gene was used as a control throughout the in vitro model.

Results: Transfection efficiency was optimized to about 85% with a 200nM siRNA concentration. qRT-PCR demonstrated up to 68% reduction in R1 mRNA expression, up to 70% reduction in H1 mRNA expression, and up to 89% reduction in Foxp3 mRNA expression in Tregs. However, D1 and D4 mRNA expression was not significantly affected with the tested siRNAs and more oligos will be trialed to increased knockdown efficiency.

Conclusion: The optimized transfection and sorting conditions will be used to manipulate Tregs for an in vitro suppression assay as a functional and quantitative measure of the effect of target gene knockdown on the suppressive activity of Tregs.

CONCURRENT
ORAL PRESENTATION
ABSTRACTS
Listed Alphabetically (First Name)

Abia Abia, MS 2

Mentor(s): Richard Rothman, MD/PhD
Department of Emergency Medicine

ED-Based HIV Registry: A Method of Assessing ED and Hospital Resource Utilization by People living with HIV

Authors: Abia Abia BS, Amir Mohareb MD, Anuj Patel MD, Yu-Hsiang Hsieh PhD, Richard Rothman MD/PhD

Background: The Emergency Department (ED) offers a novel venue to study health utilization and outcomes of PLWH who may lack proper linkage to routine HIV care. The purpose of our study was to create the first ever ED-based registry to investigate how PLWH utilize ED and hospital resources, and to identify qualities which may differ between HIV subgroups.

Methods: During the summer of 2016, a pilot ED registry was formed to include 100 PLWH seeking care in an urban ED. Enrolled patients completed a baseline survey and consented to review of their health-care utilization. Inclusion criteria were age (≥18) and seropositivity. Chart review included all health encounters within 2 years of index visit; resource utilization, viral suppression, and adequate retention-in-HIV-care (RHC) were abstracted. Adequate RHC was defined as ≥2 HIV-clinic visits in 12 months, scheduled ≥90 days apart. Statistical methods included student-t and chi-square tests.

Results: The majority of the 100 enrollees were male (57%), African-American (78%), and ≥50-years (61%). Enrolled patients visited the ED 3 (95%CI 2.7-3.8) times annually on average, which was significantly greater than the annual rate observed (1.2) in the general local adult population. Median ED length-of-stay for the cohort was 12.1 hours (IQR 8.1-19.9) which exceeded the general ED median of 7.6 hours (IQR 4.3-12.7). Overall, 62 of 100 reported receiving care in an HIV-clinic affiliated with the parent hospital. Of the 62, 51 (82%) had adequate RHC while 11 (18%) did not. ED visit and hospital admission rates did not differ significantly by RHC status; however, patients non-virally suppressed had higher odds of hospital admission than virally suppressed patients (OR 3.3, 95%CI 1.1-9.4).

Conclusion: ED HIV-positive patients have increased healthcare-demands than the general population and utilize more ED resources. Further, non-virally suppressed patients demonstrated a higher economic burden to the hospital with regard to inpatient admission rates.

Abigail Lin, MS 2

Mentor(s): Eric Kossoff, MD
Pediatric Neurology

The Impact of Complications during Ketogenic Diet Initiation on Seizure Outcomes in Children with Epilepsy

Authors: Abigail Lin BS, Zahava Turner RD, Sarah C. Doerrer CPNP, Anthony Stanfield BS, Eric H. Kossoff MD

Background: The high-fat, low-carbohydrate, adequate calorie ketogenic diet (KD) is widely used for refractory pediatric epilepsy. Most centers still admit children for several days to start the KD; the exact incidence of adverse effects during the admission, as well as their potential later impact on seizure reduction, has not been widely studied.

Methods: We performed a retrospective study of children with intractable epilepsy electively admitted for KD initiation at JHH from 2011-2016. Charts were reviewed for adverse effects (such as vomiting, lethargy, hypoglycemia) during the admission period and then examined for seizure reduction at 3 months. Chi-squared tests and two-tailed t-tests were done to identify whether specific complications or method of diet initiation affected outcomes. A rating scale (1-4) was created to categorize severity of adverse events.

Results: 158 children were admitted for KD initiation, mean age 4.6 years. Potentially attributable adverse effects of any kind occurred in 126 (80%), most commonly emesis, food refusal, and hypoglycemia. Seventy-three (46%) received some form of intervention by the medical team, most commonly juice (24%). Younger age was correlated with increased likelihood of moderate to severe adverse effects during admission, often repeated hypoglycemia (3.6 versus 4.9 years, p=0.04). Fasting at KD onset was more likely to result in lethargy and a single blood glucose in the 30-40 mg/dL range, but was not correlated with emesis, repeated hypoglycemia, or more severe adverse effect scores. There was no statistically significant correlation between the severity of immediate adverse effects and 3-month seizure reduction.

Conclusion: Increased severity of complications during hospital admission was not associated with worsened seizure outcomes at 3 months. Younger children were at greater risk for significant difficulties, and should be monitored closely. As fasting led to more lethargy and hypoglycemia, it may be prudent to avoid this in younger children.

Aishwarya Shukla, MS 2

Mentor(s): Mollie Meffert, MD, PhD
Biological Chemistry

Subcellular localization of the Lin28A miRNA biogenesis pathway under physiological conditions of learning

Authors: Aishwarya Shukla BA, Mollie Meffert MD, PhD

Background: Learning and memory require neurons to selectively alter their synaptic connections in response to various stimuli. This input specificity is maintained in part by local, transcription-independent regulatory mechanisms at synapses. MicroRNAs provide a regulatory mechanism for activity dependent translation of only a subset of neuronal mRNAs in response to extracellular stimuli such as BDNF (Brain-Derived Neurotrophic Factor). Previous work from our lab established that BDNF post-transcriptionally induces Lin28A, an RNA binding protein. Selective loss of Lin28A regulated miRNAs, most notably Let-7 miRNAs, relieves repression of neuronal pro-growth proteins such as GluA1 and CamKII that harbor Let-7 binding sites. In-vitro work has established differential local up-regulation of the Lin28A miRNA biogenesis pathway in response to BDNF stimulation, but the subcellular localization of Lin28A has not been studied in vivo. Environmental enrichment (EE) is an in vivo model for improved learning and memory in mice.

Methods: p60 adult wild type ICR mice are randomized to an EE or control group. EE mice are housed in an enriched cage containing play tubes, stringed beads, and nesting material for 2 hours, while control mice are housed in a standard home cage. Hippocampi are removed and isolated synapses (synaptosomes) are harvested by density gradient centrifugation. Whole hippocampus, cytosolic fraction, and synaptosome fraction lysates are analyzed via quantification of protein immunoblots for components of the Lin28A miRNA biogenesis pathway.

Results: At baseline, Lin28A levels were significantly higher in the synaptosome compared to the whole hippocampus and cytosol. With environmental enrichment, Lin28A levels increased significantly in the synaptosome but not in cytosol or whole hippocampus.

Conclusion: Under the physiologically relevant condition of environmental enrichment, the Lin28A microRNA biogenesis pathway is differentially up regulated at synapses. This provides a plausible mechanism for local regulation of synaptic plasticity-associated gene expression by the Lin28A pathway for learning and memory in vivo.

Aldo Gonzalez, MS 2

Mentor(s): Kimberley E. Steele, MD, PhD, FACS
Department of Surgery

Remission and Relapse of Type 2 Diabetes Mellitus after Bariatric Surgery: Vertical Sleeve Gastrectomy versus Roux-en-y Gastric Bypass

Authors: Aldo G. Gonzalez BA BS, Joseph K. Canner MHS, Hatim A. Alsulaim MD MPH, Kimberley E. Steele MD PhD FACS

Background: Bariatric surgery has been shown to be effective at inducing remission from type 2 diabetes mellitus (T2DM). Vertical sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are commonly performed and there is some evidence that RYGB may be more effective at inducing remission. However, there is no consensus if one procedure should be recommended over the other for patients with T2DM undergoing bariatric surgery.

Methods: Patient pharmacy claims information from 2010 through 2014 was compiled from the Truven Health Analytics Marketscan database of employer based health insurance claims data. The cohort included obese individuals 18 years old or older on antidiabetic medication with T2DM that underwent either VSG or RYGB. Those with cancer, ulcers, or less than 97% prescription or insurance coverage during follow-up time were excluded. Medication usage was as an indicator of T2DM status. Cox proportional hazard models that adjusted for age, gender, number of medications at surgery, hyperlipidemia (remission only), GERD (remission only), sleep apnea (relapse only), and length of stay in hospital after surgery (relapse only) were used to calculate hazard ratios for remission (cessation of antidiabetic medication usage after surgery) and relapse (commencement of antidiabetic medication after remission).

Results: The study population contained 2,746 patients with 65.4% females. During follow-up, 88.0% of patients achieved remission and of those, 22.5% relapsed. Patients that underwent RYGB had a 12% (HR 1.12, 95% CI ±0.11; p-value = 0.025) increased probability of achieving remission in comparison to VSG. Furthermore, patients that underwent RYGB had a 42% (HR 0.58, 95% CI ±0.11; p-value <0.001) decreased probability of relapsing compared to VSG.

Conclusion: The results suggest that while both procedures are initially effective at treating T2DM, RYGB may be better at producing lasting remission from T2DM. Clinicians may consider recommending RYGB over VSG for patients with T2DM undergoing bariatric surgery.

Amir Abdolrahim Poorheravi, MS 2

Mentor(s): Dr. Anne Murphy
Pediatric Cardiology

Tyrosine Phosphoproteome of the Cardiac Sarcomere

Authors: Amir Abdolrahim Poorheravi BS, Genaro Ramirez MD, Anne Murphy MD

The role of genetic mutation is well-established in heart disease, and genetic testing is frequently employed in hypertrophic patients; however, the potential effects of posttranslational modifications of cardiac sarcomere proteins are largely overlooked and have not yet impacted clinical care. The contractile force of the heart can be regulated by phosphorylation of the calcium handling proteins at specific, key sites. Advances in mass spectrometry have allowed accurate quantification of site-specific phosphorylation levels in human myocardial samples. Using these methods, human cardiac troponin I was shown to be phosphorylated at multiple serine and threonine residues, with physiological consequences. Tyrosine phosphoproteome of troponin I also varies between healthy and heart failure patients, but little is known about its role. We hypothesized that the sarcomere tyrosine phosphoproteome is regulated by pathways downstream of the ErbB2 tyrosine kinase receptor—antagonized by AG-825—and that it regulates cardiac function via site specific tyrosine phosphorylation of key sarcomere proteins. Mice with cardiac-specific ErbB2 overexpression develop cardiac hypertrophy. We hypothesized that inhibition of ErbB2 would protect against progressive cardiac disease and deleterious downstream signaling. We compared cardiac function, gross anatomical changes of the heart and histological sarcomere structure in four groups of mice: (1) ErbB2 overexpressing/saline treated, (2) non-transgenic littermate/saline treated, (3) ErbB2 overexpressing/AG-825 treated, and (4) non-transgenic littermate/AG-825 treated mice. We found a time-dependent decline in ejection fraction and fractional shortening of untreated ErbB2 overexpressing mice (P=0.04 and P=0.02). These measures did not decline in transgenic mice treated with AG-825 (P=0.91 and P=0.94), suggestive of its protective effect against hypertrophic cardiomyopathy in line with our hypothesis. In future, we plan to further characterize sarcomere protein tyrosine phosphorylation as a marker for functional status. Our research also emphasizes the potential of protein modifications as a new generation of biomarkers and biological targets for treatment of cardiac dysfunction.

Amy Huang, MS 2

Mentor(s): Megan Collins, MD
Pediatric Ophthalmology

Student adherence and satisfaction with eyeglass usage in the Baltimore Reading and Eye Disease Study (BREDS)

Authors: Lucy Mudie, MBBS MPH

Background: While school-based programs have become popular in identifying children with vision problems, few studies have examined the critical aspect of monitoring compliance after an initial intervention.[1] Poor adherence with glasses, a barrier to program efficacy, has been reported.[2] In our study, we examined student adherence and satisfaction with eyeglass usage in a school-based program.

Methods: Second and third graders attending twelve elementary schools received an in-school vision examination. Two pairs of eyeglasses were provided to children with refractive error (hyperopia ≥1D, myopia ≤0.5D, astigmatism ≥1D). Replacements were provided for lost or broken glasses. Children prescribed glasses had a follow-up vision exam and interview regarding their use and attitudes about eyeglasses.

Results: Of 320 students examined, 66.4% were prescribed eyeglasses based on study criteria. In follow-up assessments during the same academic year, 87.4% were wearing glasses. 89.4% reported being happy with their glasses and 86.4% believed their glasses looked good on them. 68.2% felt their glasses helped them see "a lot better" and 71.2% felt their glasses helped them read "a lot better." 20.2% reported being teased about wearing glasses.

Conclusion: In our school-based program, the majority of children were wearing glasses at follow-up. Most students were happy with glasses and the majority reported significant improvement in their ability to see and read. Adherence to eyeglass use was higher in our study than reported in previous studies.[3] This may be related to close monitoring and a robust replacement program. Social issues remain a barrier to compliance, as teasing was reported by one-fifth of students.

Amy Quan, MS 4

Mentor(s): Gerald Brandacher, MD
Plastic and Reconstructive Surgery

Characterizing the Effects of Growth Hormone on Ameliorating Chronic Denervation Injury and Improving Peripheral Nerve Regeneration and Muscle Function

Authors: Amy Quan MPH, Joseph Lopez MD MBA, Joshua Budihardjo BS, Sinan Xiang BS, Kiron Koshy MBBS, Howard Wang MD, Chris Cashman PhD, Ahmet Hoke MD PhD, Sami Tuffaha MD, WP Andrew Lee MD, Gerald Brandacher MD

Background: Recent studies suggest that growth hormone has the potential to augment axonal regeneration while simultaneously act on Schwann cells and muscle to minimize denervation atrophy prior to reinnervation. The purpose of this study was to assess the impact of growth hormone (GH) therapy on preventing the deleterious effects of chronic denervation injury on nerve regeneration and resulting muscle function.

Methods: We utilized a newly developed rat forelimb chronic denervation model to assess the effects of GH therapy on: a) improving nerve regeneration; and b) preventing muscle atrophy and augmenting muscle reinnervation and function. Four groups of rats were examined: (1) Group 1 (n = 8) underwent 8 weeks of median nerve denervation injury followed by repair; (2) Group 2 (experimental, n = 8) underwent 8 weeks of median nerve denervation with subsequent repair AND daily systemic GH treatment; (3) Group 3 (n = 8) underwent median nerve surgery without denervation injury and served as positive controls; (4) Group 4 (n = 8) were naïve controls. All animals underwent weekly muscle functional testing followed by median nerve and flexor muscle harvest for nerve histomorphometry, muscle atrophy, and reinnervation analysis.

Results: Median nerve regeneration was improved in growth hormone-treated animals when compared to untreated counterparts, indicated by increased axon density ($p<0.005$), axon diameter ($p<0.0001$), and myelin thickness ($p<0.0001$). Furthermore, growth hormone improved muscle reinnervation (38.0% vs. 27.9% neuromuscular junctions reinnervated; $p<0.02$) and prevented muscle atrophy, as indicated by increased cross-sectional area (1081±101.4 vs. 865±48.3 µM2; $p<0.02$). Finally, growth hormone-treated rats demonstrated greater functional muscle recovery as compared to untreated controls (forelimb grip strength: 1.8±0.3 vs. 1.0±0.1 N, $p=0.001$).

Conclusion: Growth hormone therapy significantly improves nerve regeneration and muscle reinnervation and function following chronic denervation injury. Future studies must examine growth hormone's clinical application in improving functional outcomes for patients with chronic denervation peripheral nerve injuries.

Awa Sanneh, MS 2

Mentor(s): David Celentano, ScD
Epidemiology

Health Beliefs and Cervical, Breast and Colorectal Cancer Screening Rates in Baltimore's Muslim Women

Authors: Awa Sanneh BS, David Celentano ScD

Background: Muslims are a growing minority in the United States and recent studies have shown that health disparities exist within Muslim communities in the U.S. There is a need for further study in this area as religion-related health beliefs and practices have been linked to care seeking behaviors of Muslims living in the US. This study explores breast, cervical and colorectal cancer screening rates in Baltimore's Muslim women and seeks to identify factors that may influence these screening behaviors.

Methods: We designed a survey consisting of 37 items, including questions about demographics, access to primary care, self-rated religiosity, history of cervical, breast and colorectal cancer screening and perceived barriers to screening. We used convenience sampling methods to survey Muslim women in the Baltimore area, ages 21+. Identical in-person self-administered surveys and online surveys were utilized for data collection from June to November 2016.

Results: We obtained 105 responses, with an age distribution that was nearly equal between the 21-29, 30-44 and 45+ age categories. The largest represented races were South Asians, African Americans, and Arabs, in descending order. Screening rates are consistently low for cervical (54%), breast (75%) and colorectal cancers (less than 50%) compared to national screening data. The second most cited reason for delayed screening was a lack of physician recommendation, after not feeling sick. Faith-based discrimination from healthcare workers was reported by 16% of participants. One-third (34%) of respondents delayed seeking care when there was no female provider available and an overwhelming majority preferred female providers to conduct their screenings.

Conclusion: The survey responses have identified trends that suggest ways to increase participation in cancer screening. Though not generalizable due to sampling methods, the low screening rates, delayed care-seeking behaviors and reports of discrimination suggest further exploration into a high-risk population that is subject to unique sociopolitical influences in current times.

Brendan Shi, MS 2

Mentor(s): Uma Srikumaran, MD
Orthopaedic Surgery

Biomechanical Strength of Rotator Cuff Repairs: A Systematic Review and Meta-Analysis of Cadaveric Studies

Authors: Brendan Shi BS, Miguel Diaz BS, Uma Srikumaran MD

Background: Biomechanical cadaveric studies have shown that transosseous equivalent (TOE) rotator cuff repairs (RCRs) achieve higher failure loads than other RCR types. However, these studies often fail to control for other potential predictors of construct integrity, such as number of sutures used. The goal of this meta-analysis was to account for confounding covariates and identify parameters that most reliably predict the biomechanical performance of RCR constructs.

Methods: A systematic search for biomechanical studies that measured RCR performance in cadaveric specimens was performed in PubMed and Embase. A meta-regression was performed on the pooled dataset with study outcomes (ultimate load, gap formation, mode of failure) as dependent variables and procedural parameters (construct type, suture number, etc.) as covariates. Stratification by covariates was performed.

Results: 46 eligible studies yielded 110 experimental groups for the meta-regression. Increased number of suture limbs correlated with higher ultimate load (B=40 N/limb, P<0.0005, 95% CI [28—52]) and reduced gap formation (B= -0.6 mm/limb, P<.006, 95% CI [-1 to -0.2]). Other positive predictors of ultimate load were number of sutures used, number of mattress stitches, and use of suture tape instead of No. 2 braided suture. When stratifying by suture limb number, no significant mean differences in ultimate load were found between TOE, double-row, single-row, and transosseous RCRs. However, use of TOE repair increased probability of catastrophic, or type 2, failure.

Conclusion: Our study indicates that the number of sutures, limbs, and mattress stitches in a repair construct are stronger predictors for overall strength than construct type. Further, use of TOE repair significantly increases the rate of catastrophic failure. More rigorous biomechanical studies are needed to quantify the trends delineated here and reevaluate the justification behind using TOE RCRs over other, less expensive constructs.

Carson Woodbury, MS 2

Mentor(s): Gedge Rosson, M.D.
Plastic & Reconstructive Surgery

Sexual Well-being After Breast Cancer Surgery and Breast Reconstruction: A Systematic Review with Meta-Analysis

Authors: Carson F. Woodbury, M.Phil., Charalampos Siotos, M.D., Eric L. Wan, B.S., Stella M. Seal, M.L.S., Carisa M. Cooney, M.P.H., Gedge D. Rosson, M.D.

Background: Sexual well-being may affect a woman's decision to have breast-conserving surgery or breast reconstruction after mastectomy. We conducted a systematic review to clarify sexual well-being outcomes after breast cancer surgery.

Methods: We searched Medline, Embase, Cochrane, Scopus, and Web of Science for studies about lumpectomy, mastectomy, and/or breast reconstruction in adult female breast cancer patients. Exclusion criteria included cosmetic procedures, non-cancer patients, <10 patients, and non-English language. Two authors independently screened titles and abstracts for eligibility. Data on sexual satisfaction, sexual function, and breast erogenous sensibility were extracted for a qualitative analysis of the literature. Meta-analysis was performed for validated questionnaires to quantitatively evaluate different surgical modalities.

Results: We identified 1193 studies after deduplication; 104 were eligible for data extraction. The most common study design was cross-sectional (51, 49%). Only 47 studies (45%) used validated patient-reported outcomes measures. Of 26 studies comparing mastectomy-only with mastectomy+reconstruction, 10 favored reconstruction (reconstruction patients had higher sexual satisfaction/function), 3 favored mastectomy-only, and 13 found no significant difference. 16 studies compared lumpectomy with mastectomy+reconstruction: 6 favored lumpectomy, 2 favored reconstruction, and 8 found no significant difference. Of 25 studies comparing lumpectomy with mastectomy-only, 11 favored lumpectomy, 1 favored mastectomy, and 13 found no significant difference. Meta-analysis of 3 studies using the Cancer Rehabilitation Evaluation System suggests lumpectomy is associated with higher sexual function than mastectomy-only although not at a statistically significant level (p=0.05). Meta-analysis of 2 studies using the Female Sexual Function Index indicates that patients with reconstruction had higher scores for sexual function compared to mastectomy-only patients (p<0.001).

Conclusion: Existing evidence tends to show better sexual satisfaction and function in lumpectomy and reconstruction patients compared to mastectomy-only patients, but analysis is hindered by the limited data comparable across studies. Patients and surgeons would likely benefit from additional, higher-evidence explorations of sexual well-being in breast cancer patients.

Cristina Viguera, MS 2

Mentor(s): Nicholas Maragakis, MD
Department of Neurology

Assessment of Olfactory Dysfunction as a Potential Biomarker in Amyotrophic Lateral Sclerosis

Authors: Cristina Viguera BS, Elizabeth Mosmiller, Aiana Rodriguez, Nicholas Maragakis MD

Background: Olfactory dysfunction (hyposmia) is a powerful biomarker for neurodegenerative disorders such as Parkinson's disease, preceding motor symptoms by several years and predicting future cognitive impairment. Olfactory dysfunction is an easy, inexpensive marker that could be tested with other biomarkers to aid in diagnosis and provide additional information about a particular patient's disease. This pilot study tests the prevalence of hyposmia amongst ALS patients.

Hypothesis: We anticipate that there will be a significant decrease in olfactory function in ALS patients as compared to normal controls.

Methods: Patients with familial or sporadic ALS were administered the University of Pennsylvania Smell Identification Test (UPSIT), the ALS Functional Rating Scale, ALS Cognitive Behavioral Screen, and forced vital capacity. Disease duration, site of ALS onset, genetic cause, and exposures to known causes of hyposmia were also recorded. Controls completed the UPSIT and the olfaction history survey.

Results: Of the 76 ALS participants enrolled to date, 54 had spinal onset, 19 had bulbar onset, and 3 had a different site of onset. The majority had a sporadic mutation (n=66). The mean UPSIT scores of ALS participants and controls (n=65) were 31.8 (SD=7.3) and 35.0 (SD=3.4) respectively. After adjusting for age, gender, and smoking history, ALS participants scored significantly lower on the UPSIT as compared to control participants (p=0.017).

Conclusion: Our preliminary data demonstrate that ALS participants scored significantly lower on the UPSIT, a validated measure of olfactory dysfunction. This method for assessing olfactory dysfunction can be performed quickly and without discomfort during an ALS clinic visit. With validation and further investigation, measures of olfactory dysfunction may become useful as a biomarker in predicting ALS subtype, disease severity, or disease progression.

David Liao, MS 2

Mentor(s): Lisa E. Ishii, MD
Department of Otolaryngology-Head and Neck Surgery

Graves' Ophthalmopathy Leads to Attentional Distraction: A 3-D Eye-tracking Study

Authors: David Liao BA, Masaru Ishii MD PhD, Halley M. Darrach BS, Andrew W. Joseph MD MPH, Shannon S. Joseph MD, Kristin L. Bater BA, Lisa E. Ishii MD MHS

Background: Graves' ophthalmopathy (GO) is an autoimmune disorder that can result in functional and cosmetic ocular impairments. Despite its impact on patients' quality of life, little is known about how these patients are perceived by society. Furthermore, previous social perception studies have primarily looked at the social penalty of facial lesions outside of the central triangle of the face (eyes, nose, mouth), whereas GO involves a distortion of organic structures within the triangle.

Methods: Blinded casual observers viewed three-dimensional images of four patient faces with severe Graves' ophthalmopathy and four controls. Faces were graded using the European Group on Graves' Orbitopathy classification system. Observers gazed freely upon frontal 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 predefined regions of interest, including the eyes, nose, and mouth, between severe GO and controls.

Results: 116 observers (mean age 26 years, 51% female) successfully completed the eye-tracking experiment. The majority of their attention was directed towards the central triangle (eyes, nose, mouth). On multivariate analysis, there were significant differences in the distribution of attention between control and severe faces within the central triangle (F=9.8314, p<0.0001). On planned post-hypothesis testing, observers attended significantly more to the eyes (in seconds) (p<0.0001, 95%CI[1.03,0.51]) and less to the nose (p<0.0001, 95%CI[0.23,0.62]) in severe GO patients. There was no significant difference in time spent on the mouth or the total time spent on the central triangle between the two groups.

Conclusion: Graves' ophthalmopathy preferentially redirects observer attention towards the eyes compared to control patients. These data lend insight into how altered observer perception of these patients' faces may potentially impact social interactions. Future studies should investigate how these changes in observer gaze patterns affect the social perception of GO patients.

Elizabeth Uhlig, MS 2

Mentor(s): David Dowdy, MD PhD
Epidemiology

Cost Effectiveness Analysis of Active Case Finding of Tuberculosis—Comparing Two Programs in India and Cambodia

Authors: Elizabeth Uhlig BA, Hojoon Sohn PhD, Karl Johnson, David Dowdy MD PhD

Background: Active case finding (ACF) plays an important role, particularly in remote communities with restricted access to health services, in identifying tuberculosis (TB) cases which otherwise would go undetected and contribute to TB transmission and the high burden of TB. Current evidence on cost-effectiveness of various ACF strategies is limited, so we assessed the impact and cost-effectiveness of two representative ACF models funded by the Stop TB Partnership's TB REACH initiatives in Cambodia and India from the health systems perspective.

Methods: Using decision analytic modelling (Treeage Pro 2016, Williamstown, MA USA), we compared the impact of two ACF programs to a baseline scenario of passive case finding (PCF), incorporating Markov cycles into a decision tree to analyze effects over time. The two ACF models were 1) a community TB screening with mobile diagnosis integrating GeneXpert and X-ray hosted at a local health center on a designated day and 2) house-to-house screening by community health workers (CHWs). We followed a hypothetical cohort of 100,000 patients suspected of active TB to generalize these scenarios in Cambodia and India, with the model's primary outcome comparing incremental cost (in 2015 USD) to additional cases found in the two respective ACF strategies. Data input sources include information gathered from the temporary programs in Cambodia and India, and published literature.

Results: In the ACF day model in Cambodia, 147 additional diagnoses were made compared to PCF, and the house-to-house program resulted in 225 additional diagnoses. The incremental cost per additional case detected was $14,781 and $8,209 in each program, respectively.

Conclusion: Deploying CHWs to residents' houses to screen for TB appeared to be both more cost-effective than the ACF Day strategy and also picked up a larger absolute number of cases. We will perform one- and multi-way, and probabilistic sensitivity analyses to assess the robustness of our model.

Eric Weaver, MS 2

Mentor(s): Janet Record, MD
Internal Medicine

Teaching an Approach to Goals of Care Meetings in the Intensive Care Unit: Impact on Documentation

Authors: Eric Weaver BA, Janet Record MD, Colleen Christmas MD

Background: Residents working in the medical intensive care unit (MICU) often report a disconnection between two essential goals: stabilizing critically ill patients, and learning about each patient's values and goals of care (GOC). We implemented a curriculum introducing an approach to GOC meetings and promoting documentation of key findings. We hypothesized that curriculum participants would document more family meeting notes (FMNs) and include more GOC information in transfer notes (TNs) and FMNs.

Methods: Residents and students rotating in the MICU during the intervention period (9/25/15-11/7/15) participated in 30-minute teaching sessions and received pocket cards outlining an approach to GOC meetings. We reviewed charts of 100 sequential MICU patient-stays during the pre-intervention (3/3/15-4/12/15) and intervention periods. TNs were included for patient-stays of 3 or more days. FMNs were reviewed for patient-stays of 3 or more days, or if the patient died in the MICU. All notes were coded for inclusion of GOC information taught in the curriculum.

Results: 49 pre-intervention and 57 intervention patient-stays were eligible for TN analysis; 67 and 71 patient-stays were eligible for FMN analysis. The rate of FMN documentation was similar between pre-intervention and intervention groups (n, %) (5, 7.5% vs. 10, 14.1%, p=0.277). The majority of TNs in both groups did not document medical teams' discussions of treatment goals with patients/families (41, 83.7% vs. 46, 80.7%). Post-intervention FMNs described patients' ability to participate in discussions more often than pre-intervention FMNs (6, 60% vs. 0, 0%, p=0.044). There was a nonsignificant trend toward more description of goal discussions in post-intervention FMNs, rather than a statement that "goals were discussed."

Conclusion: Patient's goals were documented infrequently in TNs and FMNs before and after a brief educational intervention on GOC meetings in the MICU. Future work should facilitate practice of GOC meetings and address barriers to documentation of key outcomes of these discussions.

Eric Xu, MS 2

Mentor(s): Edward Ahn, MD
Neurosurgery

High Initial CSF Protein Predicts the Need for Ventriculoperitoneal Shunting and Shunt Failure in Preterm Infants with Posthemorrhagic Hydrocephalus

Authors: Eric J. Xu BA, W. Lee Titsworth MD, Edward Ahn MD

Background: Neonatal intraventricular hemorrhage (IVH) with posthemorrhagic hydrocephalus (PHH) often requires temporary CSF diversion, but not all neonates require permanent shunting. We examined whether CSF collected at placement of these temporary devices can predict the need for permanent ventriculoperitoneal shunting (VPS).

Methods: Retrospective review of 98 preterm neonates with IVH and PHH who were temporized with either a ventricular reservoir or ventriculosubgaleal shunt. First ventricular CSF samples were collected at the time of insertion of the temporizing device. Primary outcomes were need for permanent VPS and VPS survival within the first year after placement. Multivariate logistic regression and stepwise elimination routine were used to determine permanent VPS outcomes. Shunt survival was determined by Cox proportional hazards regression and Kaplan-Meier survival analysis.

Results: CSF protein was significantly higher among neonates requiring a VPS than those who did not (217.0±132.2 vs. 168.6±59.0 mg/dL; p=0.02). Only high CSF protein (≥226 mg/dL) was predictive of an infant's need for subsequent permanent CSF diversion (OR=4.32 [1.09-17.07]; p=0.04). WBC, RBC, monocytes, polymorphonuclear cells, glucose, and medium and low protein (158-225 and <158 mg/dL) were not predictive of the need for shunting. Neonates with a medium protein class had 15.9% the risk of shunt failure compared to those with high protein (HR=6.28; p=0.01). At 100 days, only 5% and 18% of the medium and low protein class infants had suffered VPS failure, compared to nearly half of infants in the high protein class.

Conclusion: Among neonates, high CSF protein correlates with the need for VPS placement and lower VPS survival within the first year of life. These findings should be considered when selecting therapies and counselling families of infants with PHH. Furthermore, CSF protein should be considered in future studies that utilize the need for shunting or shunt survival in the neonatal period as an outcome.

Francisco Eguia , MS 2

Mentor(s): Alfredo Quinones-Hinojosa, MD
Neurosurgery

Comparative volumetric analysis of the extent of resection of low grade gliomas and its role on survival

Authors: Francisco Eguia BA, Chikezie Ikechukwu Eseonu MD, Karim ReFaey MD, Oscar Garcia MPH, Fausto J Rodriguez MD, Kaisorn Chaichana MD, Alfredo Quinones-Hinojosa MD

Background: Extent of tumor resection has been shown to improve prognosis for patients with low-grade gliomas (LGG); however, little is reported about the threshold of resection needed, while accounting for the genetic makeup of the LGGs, to improve patient outcome. The authors investigate the role of extent of resection (EOR) and genetic markers on patient outcome and survival for LGGs.

Methods: Retrospective cohort analysis of 109 LGG resection patients, of a single surgeon, between 2005-2015, was conducted. EOR was evaluated with volumetric computations of MRI, genetic markers (IDH1, 1p/19q co-deletion, and p53) were assessed, and their effects on survival and neurological outcome were evaluated.

Results: Median preoperative and postoperative tumor volumes were 29.7cm3 and 4.5cm3, respectively. Median EOR was 88.1%. Permanent postoperative neurological deficits were seen in 4.6% of patients. For EOR, estimated 5- and 8-year overall survival (OS) rates were 95% and 95% with EOR of 100%, 92% and 76% with EOR 90-99%, 82% and 54% with EOR 70-89%, and 76% and 54% for EOR <70%. There were 17 deaths (15.6%), and the median follow-up time was 5.2 years. EOR correlated significantly with OS (hazard ratio [HR]=0.979, 95% CI 0.961-0.980, p=0.029) and progression free survival (PFS) (HR=0.982, 95% CI 0.968-0.997, p=0.018). Malignant progression free survival (MPFS) was predicted by the 1p/19q co-deletion (HR = 0.148, 95% CI 0.019 - 1.148, p=0.048). Patients with EOR of 100% had significantly better OS than EOR < 90% (p=0.038). Patients with EOR ≥ 76% had better OS than EOR < 76% (p=0.025). Patients with EOR ≥ 71% had better PFS than EOR < 71% (p=0.030). Preoperative tumor volume had significant association with EOR (R2=0.049, p=0.031).

Conclusion: Increased EOR is associated with improved OS and PFS, while 1p/19q co-deletion provides improved MPFS. Understanding surgical resections and molecular markers of the tumor are important for management of LGG patients.

Hannah Carl, MS 2

Mentor(s): Justin Sacks, MD
Department of Plastic and Reconstructive Surgery

Surgical Factors Associated with Prolonged Hospitalization after Reconstruction for Oncological Spine Surgery

Authors: Hannah M Carl BS, Devin Coon MD MSE, Nicholas A Calotta BA, Rachel Pedreira BA, Justin M Sacks MD MBA

Background: Posterior trunk reconstruction following oncological resection is increasingly possible as a result of advances in spinal instrumentation, reconstructive approaches, and perioperative critical care. Extensive cases often require a muscle flap to obliterate dead space. Postsurgical wound complications and subsequent reoperations can lead to neural injury, higher hospital costs, and longer hospitalizations. We aim to identify risk factors that are associated with increased length of stay (LOS) for patients receiving flaps to close a spinal defect.

Methods: A single institution, retrospective cohort study was performed on all patients from 2002-2014 who received a muscle flap to close a spinal defect. Data extracted and analyzed included demographics, medical/surgical variables, and post-operative complications. Variables that were significantly associated with LOS ($p<0.05$) in univariate analysis were included in a stepwise regression model.

Results: A total of 288 cases were included in this study. Presence of instrumentation, pre-operative chemotherapy, wound dehiscence, cerebrospinal fluid (CSF) leak, partial/total flap loss, and medical morbidity occurrence were all independently associated with increased LOS in a combined multivariate model ($p \le 0.02$ for each of the six variables). Importantly, Kaplan-Meier analysis demonstrated that post-operative wound dehiscence increased length of stay by twelve days (median LOS 11 [95% CI: 9-14] without dehiscence versus 23 [95% CI: 14-28] with dehiscence, $p=0.02$).

Conclusion: Spinal tumor resections often create large cavitary defects that necessitate the use of muscle flaps for closure. Patients who receive chemotherapy, require instrumentation, or develop specific wound-related or medical complications, particularly deep venous thrombosis, are at an increased risk for prolonged hospitalization following spinal reconstruction. Thus, implementing measures to mitigate the occurrence of these adverse events will enhance the safety of the post-operative period and reduce the financial burden associated with unnecessarily long post-operative admissions.

Jaeyun Jane Wang, MS 2

Mentor(s): Michael Lim, MD
Neurosurgery

Immune Checkpoint Markers in Melanoma: Expression in Brain Metastases Compared to Corresponding Extracranial Tumors

Authors: Jaeyun Jane Wang BA, Peter Burger MD, Janis Taube MD, Michael Lim MD

Background: Immune responses to central nervous system tumors tend to be attenuated, so development of brain metastases may accelerate cancer progression both intra and extracranially due to an impaired anti-tumor immune response. Checkpoint molecules (PD-L1, PD-1, LAG-3, and TIM-3) have been linked to this diminished immune response, but immunohistochemistry staining to compare marker expression between brain and extracranial melanoma tumors has not been performed.

Methods: We identified 8 patients with extracranial melanoma tumors and matched brain metastases. Formalin fixed, paraffin embedded slides were stained for PD-L1, PD-1, LAG-3, and TIM-3 via immunohistochemistry. Qualitative analysis was performed to assess staining of the markers in tumor and lymphocyte cells.

Results: PD-1 and TIM-3 showed no variation in expression between tumor sites. PD-1 stained lymphocytes in 100% of extracranial and 100% of intracranial slides, while TIM-3 stained lymphocytes in 25% of extracranial and 25% of intracranial slides. Neither marker stained tumor cells. PD-L1 showed slight variation in staining between sites, with lymphocyte staining in 100% of extracranial and 87.5% of intracranial slides, and the same percentages per site for tumor cells. The greatest variability was observed in LAG-3 lymphocyte staining, with staining in 75% of extracranial and 25% of intracranial slides. No LAG-3 staining of tumor cells was noted. In addition, characteristic staining patterns were observed for PD-1 and PD-L1. PD-1 showed intense staining of lymphocytes infiltrating the tumor, while PD-L1 displayed membranous staining of tumor cells.

Conclusion: Preliminary analysis revealed few differences in PD-L1, PD-1, LAG-3, and TIM-3 expression intra and extracranially, which suggests that these markers are important in maintaining an immunosuppressive phenotype at both sites. Interestingly, LAG-3 staining of lymphocytes appeared more prominent in extracranial over intracranial tumors. Future studies should include more samples and also score the slides for staining intensity to provide a more sensitive measure of staining than positive versus negative.

James Senter, MS 2

Mentor(s): Jacek Mostwin, MD
Urology

"Like Another Me": Reimagining Medicine and Identity in Healthcare

Authors: James Senter BS, Jacek Mostwin MD

Introduction: Medicine is a profession that relies on the stories of both patients and providers. However, communication of these stories is limited to standard methods of documentation that, while clinically useful, may omit some of the important themes that patients confront in dealing with illness. Previous qualitative studies have enumerated the themes of patient identity, transformation, and the patient-provider relationship as especially relevant in complex fields such as reconstructive surgery and oncology. However, discussion of these themes is limited and infrequent. Therefore, I pursued an alternative approach to document patient stories related to identity and transformation in order to showcase the narrative themes that are uncommonly addressed by traditional methods.

Process: I spent several months observing patients in two outpatient settings: a medical oncology clinic and a plastic and reconstructive surgery clinic. This served as the inspiration for a series of poems that I composed and a collection of photographs that I captured, edited, and then combined with the poetry.

Product: The final product is a presentation integrating poems and photographs to tell the stories of these patients and explore their identities with illness. The collection is preceded by a foreword discussing my inspiration and narrative themes. The poems draw on patient vignettes from clinic, while the photographs explore moments of vulnerability, examination, and change. A poetry reading and photographic presentation will be held in the medical school for students, faculty, and the patients who participated in the project.

Conclusion: Reorienting our traditional medical discourse with artistic forms such as photography and poetry may open a unique lens on the patient experience. The poetic verse and still imagery together may benefit and empower patients and similarly allow providers to reimagine illness, thus possibly strengthening the relationship between patient and provider.

Julia Retzky, MS 2

Mentor(s): Uma Srikumaran, MD
Orthopaedic Surgery - JHU

The Subjective Shoulder Value Correlates Well with the American Shoulder and Elbow Surgeons Score in Patients Undergoing Rotator Cuff Repair, Total Shoulder Arthroplasty, and Reverse Total Shoulder Arthroplasty Pre- and Post-Operatively

Authors: Julia Retzky BA, Casey Hannan BA, Eric Huish DO, Uma Srikumaran MD

Background: The American Shoulder and Elbow Surgeons Score (ASES) and the Subjective Shoulder Value (SSV) are questionnaires used to evaluate shoulder function. Relative to the ASES, the SSV is advantageous because it eliminates the need for an in-person visit and avoids the bias of inter-observer variability. This study aims to determine the correlation between ASES and SSV in patients undergoing rotator cuff repair (RCR), total shoulder arthroplasty (TSA), and reverse total shoulder arthroplasty (RSA) both pre- and 1-year post-operatively.

Methods: We performed a retrospective review of 224 consecutive patients undergoing RCR (n = 164), TSA (n = 40), or RSA (n = 20) at one institution from 2014-2015. Average scores for pain, SSV, and ASES were reported across the three groups pre- and post-operatively. Pearson correlation coefficients were calculated to determine the relationship between SSV and ASES scores pre- and post-operatively in RCR, TSA, and RSA patients.

Results: In the RCR group, there is a mildly positive correlation between SSV and ASES scores pre-operatively (r = 0.3882, p < 0.0001) and a strongly positive correlation post-operatively (r = 0.6817, p < 0.0001). In the RSA group, there is a strongly positive correlation pre-operatively (r = 0.6258, p = 0.5336) and post-operatively (r = 0.9444, p = 0.0156). In the TSA group, there is a strong correlation pre-operatively (r = 0.6258, p = 0.0011) and post-operatively (r = 0.8691, p = 0.0011).

Conclusion: SSV and ASES scores correlate well pre- and post-operatively in patients undergoing RCR, TSA, and RSA. The results of this study suggest that the SSV can be used in lieu of the ASES to evaluate shoulder function in these patient populations.

Kathleen Chin, MS 2

Mentor(s): Erin Michos, MD, MHS
Ciccarone Center for the Prevention of Heart Disease, Division of Cardiology

Physical activity, Vitamin D, and Incident Atherosclerotic Cardiovascular Disease in the Atherosclerosis Risk in Communities (ARIC) study

Authors: Kathleen Chin, BA, Di Zhao, PhD, Martin Tibuakuu, MD, MPH, Seth S. Martin, MD, MHS, Chiadi E. Ndumele, MD, MHS, Roberta Florido, MD, B. Gwen Windham, MD, MHS, Eliseo Guallar, MD, PhD, Pamela L. Lutsey, PhD, Erin D. Michos, MD, MHS

Background: Higher physical activity (PA) levels are associated with higher 25-hydroxyvitamin D [25(OH)D] levels, but it is unclear if a dose threshold exists. Individually, low PA and low 25(OH)D are associated with atherosclerotic cardiovascular disease (ASCVD), but their joint association with ASCVD risk is unknown. We examined the interrelation between PA and 25(OH)D, and potential effect modification of 25(OH)D on the association of PA with ASCVD.

Methods: We studied 10,342 ARIC participants free of ASCVD, with PA assessed by questionnaire at baseline (1987-1989), serum 25(OH)D measured at Visit 2 (1990-1992), and followed for ASCVD events from Visit 2 through 2013. PA was converted to minutes/week of moderate or vigorous exercise and categorized per American Heart Association (AHA) guidelines (recommended, intermediate, or poor). Multivariable-adjusted restricted cubic spline, Poisson and linear regression were used in a cross-sectional analysis of PA on 25(OH)D levels; Cox hazard models were used in a prospective analysis of PA on ASCVD outcomes, stratified by 25(OH)D status.

Results: Participants were on average 54±6 yrs, with 57% women, 21% black, 30% 25(OH)D-deficient (<20 ng/ml), and <40% meeting AHA-recommended PA. A nearly linear association was seen between PA and 25(OH)D levels in whites. Whites meeting recommended PA, compared to poor PA, were 37% less likely to have 25(OH)D deficiency [RR 0.63, (95% CI 0.56-0.71)]; there was no significant association in blacks. Over a mean follow-up of 19.3 years, 1,800 incident ASCVD events occurred. An interaction was present between 25(OH)D and PA on ASCVD risk (p=0.04). Recommended PA was associated with 29% reduced ASCVD risk [HR 0.71, (95% CI 0.56-0.90)] among participants with optimal 25(OH)D levels (≥30 ng/ml), but not among those in intermediate or deficient 25(OH)D groups.

Conclusion: PA is positively and linearly associated with higher 25(OH)D levels in whites, without dose threshold. 25(OH)D may have synergistic beneficial effects on ASCVD risk.

Kingsley Asiedu, MS 2

Mentor(s): Peter Choyke, MD and Noriko Sato, MD, Phd
National Cancer Institute

89Zr-oxine complex positron emission tomography (PET) visualizes trafficking of bone marrow (BM) cells in a mouse transplant model

Authors: Kingsley O. Asiedu, Medical Student BA; Sho Koyasu, Study Collaborators MD; Lawrence P. Szajek Study Collaborators MD; Peter Choyke, Research Mentor MD; Noriko Sato Research Mentor MD, PhD

Background: BM transplants are effective against myeloablative cancer therapies. However, there is no reliable method to monitor migration of donor cells and gauge the efficacy of their engraftment. We examined the ability of 89Zr-oxine complex, a long lived radio-conjugate, to label whole murine BM cells for imaging by PET.

Methods: BM cells were labeled with 89Zr-oxine and cultured with IL-15 or GM-CSF to examine the effect of labeling on their proliferation and differentiation. Labeled BM cells (107 cells/370 kBq) were transferred to mice (i.v.) for microPET/CT imaging. Some host mice received a 9.5 Gy whole body irradiation for BM ablation 24h prior to cell transfer. The effects of plerixafor (CXCR4 inhibitor, 5 mg/kg) and G-CSF (2.5 μg) on cell migration were observed. Furthermore, donor BM cell engraftment and differentiation in the hosts were determined 10 weeks after the transfer by analyzing the hosts BM and spleen by flow cytometry.

Results: 89Zr-oxine labeled BM cells proliferated and differentiated into mature natural killer (NK) and T cells when cultured with IL-15, and with GM-CSF, into dendritic cells (DCs). When transferred to mice, BM cells migrated to the BM quickly; plerixafor/G-CSF inhibited initial BM homing of the cells (0-2h, p≤0.05, n=4). After 4h, a majority of cells localized to the spleen, liver and BM (16.5%, 56.2%, 19.5% of whole-body activity, respectively). The migration pattern was similar between BM-ablated and non-ablated hosts within 5 days. Nevertheless, BM engraftment occurred only in the irradiated mice, in which the donor BM cells gave rise to mature peripheral immune cells, such as NK, T, and B cells and DCs.

Conclusion: 89Zr-oxine PET visualized CXCR4-dependent homing of BM cells to the BM. Initial BM migration occurred independent of BM ablation, however, cell engraftment required prior ablation. Importantly, 89Zr-oxine labeling did not impair differentiation function of BM cells and would, therefore, be useful for further studying these cells.

Leila Musavi, MS 2

Mentor(s): Anand Kumar, MD
Plastic and Reconstructive Surgery

Muscle-Derived Stem Cells Can Transform into Cells with Schwann Cell Phenotypes and Functional Myelination Properties in-vitro

Authors: Leila Musavi BA, Joseph Lopez MD MBA, Jose Escalante MD, Gerald Brandacher MD, Ahmet Hoke MD PhD, Anand Kumar MD

Background: Recently, there has been growing interest in the role of cellular therapy in providing a supportive glial environment for peripheral nerve regeneration. Muscle-derived stem cells (MDSCs) are a distinct population of immature progenitors cells with pronounced pluripotency, including osteogenic, vascular, and endothelial potential. However, few studies have explored the Schwann-cell differentiation potential of MDSCs in-vitro. The purpose of this study was to characterize the induction potential of MDSCs to differentiate into cells with Schwann-cell phenotypes using two neurogenic induction protocols.

Methods: MDSCs were isolated from 4-8 week old C57BL/6J mice using a previously described pre-plate technique. Two mesenchymal-stem cell (MSC) neurogenic induction protocols (P1 vs P2) composed of various glial growth factor combinations were used for Schwann cell differentiation of MDSCs. A Schwannoma cell line (S16) was used as a positive control for all experiments. Immunocytochemistry and flow cytometry were performed to assess expression of Schwann-cell markers including S-100 and p75 in Schwann-cell-induced MDSCs. In-vitro myelination assays were performed to assess the functional capabilities of these Schwann-cell-induced MDSCs.

Results: The two MSC induction protocols showed statistically significant differences in their Schwann cell induction potential ($p=0.004$). Schwann cell differentiation for 12 days using the P1 protocol led to an upregulation in the fraction of cells expressing S100 compared to the P2 protocol and the untreated MDSCs controls (CTCF 4.9 vs 0.5 vs 0.28, $p=0.002$). Flow cytometry revealed that Schwann cell differentiation using the P1 protocol led to an upregulation in the fraction of cells expressing p75 compared to untreated MDSCs controls ($21.0\pm1.6\%$ vs $6.63\pm2.4\%$, $p<0.001$). Furthermore, unstimulated MDSCs demonstrated no myelination capacity while P1-induced MDSCs showed myelination capabilities in-vitro.

Conclusion: MDSCs can be differentiated into cells with Schwann cell-like properties in-vitro. These findings suggest that MDSCs may have a potential application for cellular therapy in peripheral nerve regeneration.

Madhavi Duvvuri, MS 2

Mentor(s): Alexander Hillel, MD
Otolaryngology & Biomedical Engineering

Engineering a drug-eluting stent to treat laryngotracheal fibrosis

Authors: Madhavi Duvvuri M.Phil, Kevin Motz MD, Michael Murphy, MD, Alexander Hillel MD

Background: Laryngotracheal fibrosis occurs in 10% of patients who have been intubated. This fibrosis is thought to be due to an immune-mediated response, and scarring of the glottis, subglottis and the trachea can occur, resulting in dysphonia and aphonia, which requires subsequent surgeries to repair. Our goal was to develop a rapamycin-eluting stent that has a reliable drug-release profile and is mechanically durable so that it can be used to prevent fibrosis after initial intubation injury.

Methods: Biodegradable, biocompatible stents made of PLLA-PCL (70 % Poly-L-Lactide and 30% Polycaprolactone) and 50:50 PDLGA (Poly(DL-lactide-co-glycolide)) were fabricated using a glass mold. Rapamycin was incorporated into the polymer solutions before the stents dried in a vacuum. Stents were placed in a transwell culture dish in PBS at 37C to mimic biological conditions. Elution method and high performance liquid chromatography analysis (HPLC) was used to characterize rapamycin release profiles for each stent. Compression and tensile strength testing were completed using a rheometer to determine the stent's mechanical characteristics. Finally, a tracheal stent was fabricated to be placed into a mouse, using a sialendoscope.

Results: The PLLA-PCL stent exhibited greater mechanical strength compared to the PDLGA stent, whereas over 4 weeks, the PDLGA stent became brittle and disintegrated under simulated biological conditions. Moreover, the PLLA-PCL stent showed a reliable rapamycin release profile for 6 weeks. The PLLA-PCL stent was also placed successfully into the mouse - the first time a mouse model has been used to test a stent-based drug delivery system to the trachea.

Conclusion: We demonstrate that PLLA-PCL biodegradable stents showed superior mechanical strength and rapamycin release for 6 weeks compared to PDLGA stents. We also placed a drug-eluting stent in a mouse for the first time, creating a physiologically relevant model. The biodegradable rapamycin-eluting PLLA-PCL stent shows promise in being used to treat laryngotracheal fibrosis in future translational studies.

Marcelo Cerullo, MS 4

Mentor(s): Timothy M. Pawlik, MD MPH PhD
Department of Surgery

Physiologic Correlates of Intraoperative Blood Transfusion Among Patients Undergoing Major Gastrointestinal Surgery

Authors: Marcelo Cerullo MPH, Faiz Gani MBBS, Sophia Y. Chen BS, Joseph K. Canner MHS, William W. Yang BS, Steven M. Frank MD, Timothy M. Pawlik MD MPH PhD

Background: Guidelines for transfusion focus on nadir hemoglobin (Hb) levels. Hb triggers may not be helpful, however, in defining appropriate intraoperative use of packed red blood cells (PRBCs). We sought to define the use of intra-operative PRBCs relative to quantitative physiologic factors at the time of surgery.

Methods: Prospective intraoperative data on patients undergoing major gastrointestinal surgery between 2010 and 2014 were analyzed. Risk of intraoperative transfusion was assessed with multivariable extended Cox models using baseline clinical covariates and time-varying intraoperative covariates.

Results: Of 2,316 patients (a total of 1,095,169 measurements of heart rate or blood pressure), 357 (15.4%) received a transfusion intraoperatively. Mean pre-operative Hb was 12.6 g/dL (SD=2.0 g/dL), while the median estimated blood loss (EBL) was 200 mL (IQR: 100–55 mL). Receipt of transfusion was associated with a higher American Society of Anesthesiologists (ASA) class (ref: ASA class I-II; hazard ratio [HR]=1.39, 95%CI: 1.14–1.71, p=0.001) and a lower pre-operative Hb (per 1 g/dL increase; HR=0.70, 95%CI: 0.66–0.75, p<0.001). In addition, a heart rate increase of 10 beats/minute above the cumulative average at any measurement was associated with up to a 27% increased probability of transfusion (HR=1.27, 95%CI: 1.13–1.44, p<0.001); similarly, a decrease in mean arterial pressure (MAP) of 10 mm Hg was associated with a 7% increased likelihood of transfusion (HR=0.93, 95%CI: 87–0.99, p=0.026). In contrast, nadir Hb was not associated with the risk of receiving a transfusion (HR=1.10, 95%CI: 0.97–1.24, p=0.136). Among patients who received an intraoperative transfusion, 9.2% (n=33) never had a Hb nadir below 10 g/dL, nor an average MAP under 65 mmHg or a heart rate greater than 100 beats/min around the time of transfusion.

Conclusion: Intra-operative heart rate and MAP were strongly associated with odds of receiving a transfusion, though 10% of patients never had a physiological indicator for transfusion.

Marcus Daniels, MS 2

Mentor(s): Kaisorn Chaichana, MD
Neurosurgery

The Flaw in Using Publication Number For Predicting Medical Student Academic Career Placement in Neurosurgery

Authors: Marcus Daniels BA, Tomas Garzon-Muvdi MD, Kaisorn Chaichana MD

Background: The goal of neurosurgery residency programs is to train residents to become clinicians. A secondary goal of certain programs is training of academic surgeons. It is unclear if pre-residency and/or residency research work impacts academic neurosurgery placement post-residency. The goal of this study is to evaluate the impact that pre-residency and residency research publication has on attaining academic faculty positions. These factors may help residency programs identify applicants with a greater propensity to academic placement.

Methods: Alumni information was collected from 65 of the 108 (60%) neurosurgery residency websites. Graduates from these programs between 2005-2015 (N=949) were analyzed to determine factors associated with an academic career. Information on publications, citations, and H-index were obtained from Web of ScienceTM. Curriculum vitae and degrees determined if the physicians attained a research fellowship or PhD during medical school. Current position was designated as academic if the physician had a teaching position at a university hospital and private if the physician was not affiliated with a university hospital. Univariate and multivariate logistic regression models were used to identify factors associated with academic faculty positions post-residency.

Results: Of the 949 physicians included in the analysis, 339 (36%) were in academic positions, 518 (55%) in private practice, and 92 (10%) were still in training. 212 (22%) physicians performed a research fellowship (8.2%) or attained a PhD (14.1%) during medical school. Among those who had completed training, an academic career was associated with having two or more publications during residency [OR (95% CI): 3.87 (1.59-9.45); P< 0.003], H-index ≥ 2 during residency [OR (95% CI): 2.32 (1.40-1.69); P< 0.0001], and devoted research time before residency [OR (95% CI): 1.56 (1.10-2.22); P< 0.012]. Notably, publications before residency were not an independent indicator of academic placement.

Conclusion: These findings may help guide residency programs identify and/or cultivate neurosurgeons to become academic neurosurgeons.

Margaret Sundel, MS 2

Mentor(s): Karin Neufeld, MD MPH
Psychiatry and Behavioral Sciences

Perioperative neuroimaging with functional near-infrared spectroscopy (fNIRS) to evaluate post-operative delirium in elderly TAVR patients

Authors: Margaret Sundel BS, Carrie Goodson MD MHS, Wade Coomer, Esme Irvine BA, Nada Rendradjaja BA, Atsushi Yoshimura MD PhD, Zoë Tieges PhD, Alasdair MacLullich MD PhD, Rani Hasan MD, Atsushi Kamiya MD PhD, Karin Neufeld MD MPH

Background: Delirium, a clinically-defined syndrome of acute and fluctuating impairment in attention and awareness, is associated with long-term cognitive decline and increased mortality and occurs in 13-44% of patients after transcatheter aortic valve replacement (TAVR). Early detection is important for post-operative delirium management; however, there are currently no validated biomarkers of this syndrome. We sought to determine the feasibility and validity of functional near infrared spectroscopy (fNIRS), a noninvasive measure of cerebral blood flow (CBF), during attention testing to detect delirium in elderly patients undergoing TAVR. Patterns of CBF in delirious versus non-delirious patients may provide insight into the neuro-pathophysiology of post-operative delirium.

Methods: Elderly patients undergoing TAVR at Johns Hopkins Hospital completed baseline delirium and attention testing within one month before surgery and repeated these tests on post-operative day 1. Delirium was diagnosed using the Confusion Assessment Method (CAM) and severity of delirium was scored with the Delirium Rating Scale Revised-98 (DRS-R98). Attention was assessed with the Months of the Year Backwards (MOTYB) test and the Edinburgh Delirium Test Box (EDTB). Changes in CBF during attention testing were measured with fNIRS, and average change in CBF was compared between patients with versus without delirium.

Results: 44 patients completed testing, and post-operative delirium developed in 10 patients (22.7%). Average right temporal blood flow during baseline attention testing with the EDTB was significantly different (p=0.035) between patients who became delirious (-8.31 mMmm Oxy-Hb, SD=20.7) versus those who remained non-delirious (2.27, SD=7.74). Post-operatively, decreased blood flow during MOTYB in the right superior frontal gyrus correlated with higher delirium severity (r=-0.57, p=0.003), though this correlation was non-significant after false discovery rate correction.

Conclusion: Functional NIRS is a feasible technique to monitor changes in CBF during attention testing in elderly patients undergoing TAVR. Cerebral perfusion may be an important factor in the prediction and development of post-operative delirium.

Mary Peeler, MS 2

Mentor(s): Carolyn Sufrin, MD
Gynecology and Obstetrics

Treatment of Opioid Use Disorder in Incarcerated Pregnant Women

Authors: Mary Peeler BSPH, Carolyn Sufrin MD

Background: As rates of opioid use increase, treatment of incarcerated pregnant women with opioid use disorder (OUD) is a growing problem. Medication assisted treatment (MAT) with methadone or buprenorphine is the standard of care because abrupt discontinuation of opioids can cause preterm labor, fetal distress, or fetal demise. This study will fill the gaps in the existing literature by reporting correctional facilities' treatment of pregnant women with opioid use disorder.

Methods: The Pregnancy in Prisons Statistics (PIPS) study investigated pregnancy outcomes and comorbidities (including OUD) at a national sample of prisons, state departments of corrections, and select large jails in the U.S. Each facility completed a baseline survey of its pregnancy services, policies and accommodations and prospectively reported pregnancy rates and outcomes. Reporters varied by site and included medical directors and wardens.

Results: Twenty-four facilities completed the survey. Our results show that 20% of these facilities fail to provide on-going MAT throughout the pregnancy. Of those facilities that did provide MAT, 64% used methadone and 36% used buprenorphine. Of the 173 pregnant women admitted to the facilities in the first two months of data collection, 31 (17.9%) were reported to be opioid dependent at the time of admission. Of these, 14 were provided appropriate medication assisted treatment and 17 were detoxed from opiates with medications. There were no women who were reported to be detoxed from opioids 'cold-turkey.'

Conclusion: Opioid use is a significant problem for incarcerated pregnant women, with 17.9% reported to be dependent upon intake. A sizable minority (20%) of correctional facilities fail to provide medication assisted treatment—the current standard of care—to pregnant women with OUD. Information should be provided to correctional facilities to promote the use of MAT for opioid-dependent pregnant women to improve outcomes for incarcerated women and their babies.

Moon Jeong Lee, MS 2

Mentor(s): Pradeep Ramulu, MD
Department of Ophthalmology

Accelerometer-assessed physical activity and its association with change in visual field loss in patients with glaucoma

Authors: Moon Jeong Lee BS, Jiangxia Wang MS, David Friedman MD, PhD, Michael Boland MD, PhD, Carlos G. De Moraes MD, MPH, Pradeep Ramulu MD, PhD

Background: Cross-sectional studies have demonstrated lower levels of physical activity (PA) in persons with greater visual field (VF) loss, and that PA can protect against optic nerve damage in animal models of glaucoma. Here, we examined the association between PA levels and the rate of VF loss in a cohort of glaucoma patients under clinical care.

Methods: Study subjects were 141 adults with glaucoma and suspect glaucoma. Accelerometers were used to assess PA over 1 week with steps per day as the primary measure of activity. We analyzed 5 years of VF data prior to and following PA assessment to obtain point-wise sensitivities. Statistical analyses included linear mixed effects regression models accounting for correlation between eyes, hemifield and points within the same VF. The model incorporated several covariates and interactions given their established importance to disease progression.

Results: Mean age was 64.9 years at the time of activity assessment and 43% of subjects were male. In multivariate models, each increment of 1000 steps was associated with a 0.41 dB increase in overall sensitivity (p=0.048). Caucasian race and superior region were also associated with greater sensitivity (p<0.001). Overall, visual threshold sensitivities decreased by 0.24 dB/year (p=0.066). More steps was associated with a slower rate of sensitivity loss over time (+0.006 dB/year per 1000 steps, p<0.001). Factors associated with a faster rate of decline in sensitivity included glaucoma surgery, cataract surgery, age, non-Caucasian race and baseline severity (p<0.05 for all). There was no significant effect of hemifield region and intraocular pressure on the rate of progression (p>0.05 for all).

Conclusion: Increased PA was associated with a decreased rate of glaucoma-related VF loss. Future studies should prospectively investigate the effect of PA on VF loss in glaucoma to determine if lifestyle modifications (i.e. interventions to increase PA) can slow the rate of VF loss in glaucoma.

N. Jia Ahmad, MS 2

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

The Emergence of an Epidemic: NIDA, Heroin and the Birth of "Drug Abuse Epidemiology"

Authors: N. Jia Ahmad, BA

Background: In the 1970s, fears of a growing American opioid epidemic honed national attention on drug abuse. In response, the National Institute on Drug Abuse began monitoring emerging drug trends through the Community Epidemiology Work Group (CEWG), a network of researchers that convened biannually from 1976 to 2014. The CEWG played an instrumental role in defining the emerging field of drug abuse epidemiology; this project explores its methodologies and impact on contemporary discourses of addiction.

Methods: I conducted an analysis of reports published by the CEWG between 1976-2014, assessing changing definitions of drug abuse and methods for its epidemiological study. I examined the CEWG's impact by tracing its findings through NIDA, Congress, and news media.

Results: Early CEWG publications illustrate its members' struggles to define addicts, identify markers of drug use that could index addiction prevalence, and agree to the interpretation of chosen markers. Many of these indicators – notably criminal activity – were not chosen based on their proven relationships to drug use, but rather for convenience; they were codified because they appeared to confirm pre-existing suspicions about drug users. Ultimately CEWG findings were distributed to the public as scientific data, and in the distillation of their reports the epistemological reservations and implicit biases of the epidemiologists were obscured.

Conclusion: CEWG epidemiologists hoped to produce objective data about drug using populations, but their reliance on easily accessible police and hospital records reified social assumptions about the relationship between drug use, criminality, and mortality and diminished other ramifications of drug use. Similar indicators are prioritized by drug abuse epidemiologists to this day, demonstrating that methodologies of convenience have had a profound impact on our imagination of addiction. Now facing a new opioid epidemic, public health must take heed of these lessons by critically examining how researcher biases may become standardized within seemingly objective methodologies.

Rebecca Glasser, MS 2

Mentor(s): Jay Reidler, MD
Department of Orthopaedic Surgery

Intra-operative fluorescence of sciatic nerves improves visualization in initial and revision surgical procedures

Authors: Rebecca Glasser BA, Jay Reidler MD, Julia Retzky BA, Ryan Tomlinson PhD, Thomas Clemens PhD, Daniel Thorek PhD

Background: Iatrogenic nerve injury is an infrequent but serious complication of orthopedic surgeries that increases in prevalence in revision surgeries. Improved nerve visualization using selective intra-operative fluorescence has been proposed to avoid nerve damage. We assess the impact of fluorescence on nerve contrast with surrounding tissue compared to white light (WL) visualization in revision surgery and how this tool practically affects nerve identification in real-time.

Methods: Five adult Thy-1-YFP transgenic mice (N=10 legs) underwent initial sciatic nerve dissection surgery and revision at 3-6 weeks. Fluorescent (FL) and WL images were captured using fluorescent microscopy and Metamorph. We used ImageJ to calculate the signal:noise (SNR), or contrast, of the exposed nerve compared to background tissue. The time and number of attempts made to identify the sciatic nerve with and without fluorescence were recorded. Paired t-tests were performed to assess differences in contrast between WL and fluorescent visualization and between initial and revision surgeries.

Results: Fluorescent visualization of the sciatic nerve provided significantly higher contrast than non-fluorescent visualization during initial surgeries (Mean SNR WL 1.2 FL 4.4, p=0.0004) and revision surgeries (Mean SNR WL 1.5 FL 3.9, p=0.003). WL analysis revealed a slight but significantly increased contrast from initial to revision surgeries (p=0.019). There was no significant difference (p=0.25) in the time to nerve identification in revision surgery with fluorescence (Mean=5.5 min) and without (Mean=4 min). However, correct nerve identification on the first try was 100% with fluorescence and 70% without (N=10).

Conclusion: Fluorescent nerves significantly augment contrast in both initial and revision surgical contexts. Although nerve contrast in WL increased in revision surgery, the increase did not practically facilitate nerve identification. These data suggest surgical fluorescent nerve visualization can improve nerve identification and potentially avoid nerve damage. Future studies should explore human application, nerve-binding fluorescent compounds, and real-time fluorescent visualization during surgery.

Ridwan Alam, MS 4

Mentor(s): Phillip M. Pierorazio, MD
The James Buchanan Brady Urological Institute, Department of Urology

Prospective Analysis of Active Surveillance for Small Renal Masses: Is It Safe?

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Background: Active surveillance is an alternative to primary intervention aimed at reducing the overtreatment of small renal masses, defined as solid renal masses ≤4.0 cm (clinical stage T1a). No prospective studies to date have described intermediate-term outcomes for patients with small renal masses undergoing active surveillance.

Methods: Since 2009, the Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) registry prospectively enrolled 615 patients with small renal masses who chose to undergo primary intervention or active surveillance. Primary outcomes were cancer-specific survival and overall survival; secondary outcomes included progression-free survival. Progression was strictly defined as growth rate >0.5 cm/year, greatest tumor diameter >4.0 cm, metastatic disease, or elective crossover. Outcomes were evaluated using Kaplan-Meier survival analysis and comparisons were performed using the log-rank test.

Results: Of the 615 enrolled patients, 298 (48.5%) chose primary intervention and 317 (51.5%) chose active surveillance. From the active surveillance cohort, 45 (14.2%) patients underwent delayed intervention. Median follow-up time for the entire registry was 2.9 years, with 203 (33.0%) patients followed for 5 years or more. At baseline, patients who chose active surveillance were older (P < 0.001) and had more comorbidities (P < 0.001) than those who chose primary intervention. There was no difference in cancer-specific survival at 7 years between primary intervention and active surveillance (99.0% vs 100%, respectively, P = 0.3). However, overall survival was higher in patients with primary intervention when compared to active surveillance at 5 years (93.0% vs 80.2%, respectively) and 7 years (91.7% vs 65.9%, respectively, P = 0.002). The 5-year and 7-year progression-free survival in the active surveillance cohort was 83.9% and 71.4%, respectively.

Conclusion: In the intermediate-term, active surveillance appears to be as safe as and not inferior to primary intervention for carefully selected patients with small renal masses. As the registry matures, further studies will elucidate the effectiveness of active surveillance in the long-term.

Ross Pollack, MS 2

Mentor(s): Myron Weisfeldt, MD
Medicine

Impact of bystander AED use on survival and functional outcomes in shockable observed public cardiac arrest.

Authors: Ross Pollack BS, Siobhan P. Brown PhD, Tom Rea MD, Tom Aufderheide MD, Jason Buick EMT-P, Jim Christenson MD, Ahamed Idris MD, Jamie Jasti BS, Mike Kampp BS, Peter Kudenchuk MD, Susanne May PhD, Laurie Morrison MD, Marc Muhr EMT-P, Graham Nichol MD, Joseph P. Ornato MD, George Sopko MD, Christian Vaillancourt MD, Myron Weisfeldt MD

Background: Survival following out-of-hospital cardiac arrest with shockable rhythms can be significantly improved with rapid defibrillation. Although shockable cardiac arrest accounts for only one quarter of overall arrests, more than half of public cardiac arrests are shockable, indicating the potential importance of public-access-defibrillation. We sought to determine the benefit of public-access-defibrillation in survival and functional outcomes following public-witnessed cardiac arrest.

Methods: From 2011-2015 the Resuscitations Outcomes Consortium (ROC) prospectively collected cardiac arrest outcomes at 9 sites. Study participants were defined as individuals >18 years of age on whom resuscitation from non-traumatic cardiac arrest was attempted by EMS. The primary exposure was bystander-applied AED shock prior to EMS arrival compared to initial defibrillation by EMS. Survival to hospital discharge and discharge with favorable neurologic status were the primary outcome measures. Favorable neurologic status was defined as the patient having a modified-Rankin-score ≤2(2=Slight disability). Odds ratios were adjusted for age, sex, race, bystander-CPR, EMS response time, and study site.

Results: Out of 52,856 total cardiac arrest, 4115 witnessed and public cardiac arrests were analyzed of which 61% were shockable. A bystander-shock was applied in 19% of the shockable arrests. Patients shocked by a bystander were significantly more likely to survive to hospital discharge (67%vs43%) and to be discharged with favorable neurological outcome (57%vs33%) than patients shocked by EMS. The aOR associated with a bystander shock was 2.62(CI=2.07-3.31) for survival to hospital discharge and 2.73(CI=2.17-3.44) for discharge with favorable neurological outcome. The aOR of survival to discharge associated with bystander-shock improved with delayed EMS response.

Conclusion: At ROC sites the use of an AED by a bystander prior to EMS arrival in shockable witnessed public cardiac arrest significantly improves survival and functional outcomes particularly when EMS response is delayed. Continued emphasis on AED accessibility and utilization programs may further improve outcomes of shockable witnessed public cardiac arrest.

Ruchi Doshi, MS 4

Mentor(s): Kimberly Gudzune, MD MPH
School of Medicine

Factors Influencing Medical Student Preparedness and Skills to Provide Weight Management Services

Authors: Ruchi Doshi MPH, Kimberly Gudzune MD MPH, Michelle Van Ryn PhD, Sean Phelan PhD

Background: The obesity epidemic has prompted medical schools to increase obesity-related education. It is unclear how these curricula affect medical student self-efficacy to provide weight management services. Our objective was to identify aspects of educational training associated with high preparedness and skills in weight management services among U.S. medical students.

Methods: We conducted a national, cross-sectional, web-based survey study using a 2014 of fourth-year medical students collected as part of the Medical Student Cognitive Habits and Growth Evaluation Study (CHANGES) (68% response rate). Independent variables included: quality and quantity of interaction with peers and patients with obesity; communication and partnership skills training; physician role-modeling. Dependent variables included self-identified: preparedness in working with patients with obesity; skills in weight management counseling. We performed multilevel logistic regression adjusted for age, sex, race, BMI, intended medical specialty, attitudes towards patients with obesity, and social desirability.

Results: Most students were white, 50% were women, and 93% endorsed high preparedness and 51% endorsed high skills for weight management. Factors associated with preparedness included quantity of interaction with patients with obesity (OR 3.30, 95%CI 1.47-7.42) and hours of communication training (OR 1.20, 95%CI 1.02-1.43). Factors associated with skills included quantity (OR 1.46, 95%CI 1.16-1.83) and quality (OR 1.74, 95%CI 1.14-2.63) of interaction with peers with obesity and hours of partnership skills training (OR 1.18, 95%CI 1.08-1.29). Negative role modeling was not associated with weight management preparedness or skills.

Conclusion: Students perceived preparedness versus skills for weight management services differently. High amounts of interaction with patients with obesity and increased communication training increases perceived preparedness, while high quality and quantity of interaction with peers with obesity and increased partnership training increases perceived skills. Schools might consider increasing meaningful interactions with individuals with obesity or hours of interpersonal skills training to better prepare medical students to address obesity with their future patients.

Rupali Sood, MS 2

Mentor(s): Saraswati Sukumar, PhD
SKCCC Oncology- Breast Cancer Program

A Robust Methylated Gene Biomarker Assay to Distinguish Benign Breast Lesions from Malignant Breast Cancer

Authors: Rupali Sood BSc, Mary Jo Fackler PhD, Bradley Downs PhD, Danielle Meir Levi BA, Saraswati Sukumar PhD

Background: Although overall breast cancer (BC) incidence in the developing world is less than half the incidence in the developed world, population mortality rates are similar. This is primarily attributable to late diagnoses and limited access to timely treatment in low and middle-income countries (LMICs). We aim to develop an automated molecular assay for accurate diagnosis of benign breast lesions (usual ductal hyperplasia, papillomas, and fibroadenomas) versus malignant invasive ductal carcinoma (IDC) based on the differential methylation of genes known to be altered in BC.

Methods: Using archival benign breast disease and carcinoma samples, we screened 24 genes that were selected following global methylome analysis by quantitative multiplex-methylation specific polymerase chain reaction (PCR). This is a two-step nested PCR consisting first of gene-specific, and then methylation-specific amplification. Cumulative methylation index (CMI), a sum of % methylation in all genes assayed, was used to set a cut-off for the low level of gene methylation expected in benign tissue. Values above this level resulted in a "malignant" diagnosis.

Results: From an initial panel of 24 candidate genes, we used combinatorial testing and CMI to construct a panel of 6 genes to discriminate IDC from benign lesions with optimal sensitivity (95%), specificity (100%), and an accuracy of 98.5%. Adding or removing genes from this panel did not improve performance.

Conclusion: We derived a panel of 6 genes, some of which are novel, that showed low or no methylation in benign samples, but positive methylation in 95% of IDC. We are currently testing this panel in samples from Africa, China, and India. We have partnered with Cepheid Diagnostics to analyze this panel in an automated cartridge for quick diagnosis and ease of distribution in LMICs. Rapidly triaging and providing oral hormonal therapies on site could extend the lives of more than 70% of women with BC in LMICs.

Stephen Njau, MS 2

Mentor(s): Matthew Weiss, MD
Surgery and Oncology

How complications, length of stay and hospital's region impact the cost of pancreaticoduodenectomy.

Authors: Stephen Njau BS, Lauren Nicholas MD, Javed Ammar MD, Faiz Gani MD, Matthew Weiss MD.

Background: Pancreatic adenocarcinoma (PDAC) is a leading cause of cancer-related deaths in the US. Patients diagnosed with resectable PDAC undergo pancreaticoduodenectomy (the whipple procedure). The cost of pancreaticoduodenectomy varies greatly and there is no reliable cost prediction model. This study looked for association of various factors with the cost of pancreaticoduodenectomy.

Methods: Patients who had pancreaticoduodenectomy (1,995) between 2010-2014 were identified from the Truven Health MarketScan database. They were then matched to inpatient, outpatient, and drug prescription claims. The claims were mined for complications (12 most common), comorbidities, neoadjuvant/adjuvant therapy, length of hospital stay, cost of surgery, and demographic data. Comorbidities were coded using the Charlson Comorbidity Index (CCI). All these factors were analyzed against cost using the Kruskal-Wallis, chi-square, non-parametric correlation and linear regression tests. Dataset mining and analysis was done using the statistical software Stata. Maptile, spmap and US Census shapefiles were used for regional graphics.

Results: The median age of patients was 58 years, 51.4% were male, and the median cost of surgery $55,160. Age, sex, and CCI were found to have insignificant association to high cost ($p > 0.05$). Complications, neoadjuvant/adjuvant treatment, length of stay, and hospital's region were found to have statistically significant relationship to high cost ($p < 0.05$). Of the 12 complications, respiratory/renal failure, stroke, sepsis, and surgical site infection had a $p < 0.05$. Deep vein thrombosis, pneumonia, myocardial infarction, urinary tract infection, and cellulitis had a $p > 0.05$.

Conclusion: This study identified the subset of complications associated with high cost of pancreaticoduodenectomy and those that are not. However, it failed to identify new factors that would have contributed to the ongoing efforts to develop a cost prediction model. Such a model would help hospitals and insurance companies in anticipating, planning and setting costs of pancreaticoduodenectomy.

Taylor Purvis, MS 2

Mentor(s): Daniel M. Sciubba
Neurosurgery

Effect of Liberal Blood Transfusion on Clinical Outcomes and Cost in Spine Surgery Patients

Authors: Taylor E. Purvis, BA, C. Rory Goodwin, MD, PhD, Rafael De la Garza-Ramos, MD, A. Karim Ahmed, BS, Virginie Lafage, PhD, Brian J. Neuman, MD, Peter G. Passias, MD, Khaled M. Kebaish, MBBCh, MS, Steven M. Frank, MD, Daniel M. Sciubba, MD

Background: Blood transfusions in spine surgery are shown to be associated with increased patient morbidity. The association between transfusion performed using a liberal hemoglobin trigger—defined as an intraoperative hemoglobin level of ≥10 g/dL or a postoperative level of ≥8 g/dL—and perioperative morbidity and cost in spine surgery patients is unknown and thus was investigated in this study.

Methods: Data were obtained from inpatient surgical records at our institution from 2008 to 2015. Patients undergoing spinal fusion, tumor-related surgeries, and other identified spine surgeries were included. Variables analyzed included in-hospital morbidity, mortality, length of stay, and total costs associated with a liberal transfusion strategy.

Results: 6931 patients undergoing spine surgery were identified and stratified by procedure. Among patients with a whole hospital stay nadir hemoglobin between 8 to 10 g/dL, transfused patients demonstrated a longer in-hospital stay (median [IQR], 6 [5-9] vs. 4 [3-6] days; P<0.0001) and a higher perioperative morbidity (n=145, [11.5%] vs. n=74, [6.1%]; P<0.0001) than those not transfused. Even after adjusting for age, gender, race, ASA class, CCI score, estimated blood loss, baseline hemoglobin value, number of operated levels, and surgery type, logistic regression analysis revealed that patients with a nadir hemoglobin of 8-10 g/dL who were transfused had an independently higher risk of perioperative morbidity (odds ratio [OR] = 2.12; 95% confidence interval [CI], 1.24-3.64; P=0.006). Estimated additional costs associated with liberal trigger use ranged from $202,675 to $700,151 annually.

Conclusion: Transfusion using a liberal trigger is associated with increased morbidity, even after controlling for possible confounders. Our results suggest that modification of transfusion practice may be a potential area for improving patient outcomes and reducing costs.

Zach Reilly, MS 2

Mentor(s): Tonia Poteat PhD
Epidemiology

The TOP Study: Assessing Peri-operative Goals and Post-operative Satisfaction Among Transgender Men Undergoing Gender Affirming Chest Reconstruction Surgery

Authors: Zach Reilly BS, Mannat Malik MPH, Erin Cooney MSPH, Tonia Poteat PhD, Rachel Bluebond-Langner MD

Background: Currently, there is a dearth of research on the goals and experiences of transgender men (TM) (female-to-male) who have undergone or are seeking top surgery. This study aims to use qualitative research to (1) explore the pre-operative goals and priorities of TM seeking top surgery, and (2) understand factors influencing post-surgical satisfaction and quality of life among TM after top surgery

Methods: In-depth interviews were conducted with TM who have undergone top surgery (n=12), TM who plan to get top surgery (n = 12), and healthcare providers (HP) who have experience working with (n = 12) TM seeking top surgery. Participants were recruited through HP, local transgender organizations, and by word of mouth. Thematic analysis of interview transcripts was conducted using analysis software, Atlas.ti. A codebook was developed and modified iteratively based on interview guides and emergent themes.

Results: While TM participants reported satisfaction with top surgery and significant improvements in quality of life and mental health post-surgery, factors like scarcity of surgeons, finances, and difficulty navigating the surgical letter process hindered accessibility. Common goals were to be perceived as male, reduce gender dysphoria, and present shirtless in public. Post-operative TM consistently described how top surgery led to improvements in mental health through reduction in gender dysphoria. Scarring was a major concern for TM. Identity (race, gender, socioeconomic status, etc.) factors affected how patients experienced gender transition and the top surgery process. HP felt that empathy and culturally competent communication can improve healthcare experiences for TM seeking top surgery.

Conclusion: TM pursue top surgery for several reasons, many of which are related to gender affirmation. Efforts to improve the top surgery experience for TM should focus on strengthening knowledge of TM healthcare and enhancing healthcare accessibility. Further research is needed to quantify satisfaction and outcomes of top surgery.

Zachary Janik, MS 2

Mentor(s): Craig Hendrix, MD
Clinical Pharmacology

White Coat Adherence in MTN-001

Authors: Zachary Janik BS, Craig Hendrix MD

Background: HIV Pre-Exposure Prophylaxis (PrEP) efficacy depends on patient adherence, while interpreting trial results and applying interventions depends on accurate adherence estimations. White coat adherence (WCA) occurs when subjects dose only just prior to a clinic visit without previous consistent adherence. Tenofovir concentrations (TFV, $T_{1/2}$=17 hours) quantify recent dosing, but can falsely indicate consistent adherence if dosing only occurs near sampling. Tenofovir diphosphate measurements (TFV-DP, $T_{1/2}$=48 hours) are insusceptible to WCA bias. Quantifying WCA prevalence can inform whether simpler, cheaper methods alone (measuring TFV) or complicated, expensive approaches (measuring TFV-DP) are required to estimate adherence.

Methods: We defined WCA as dosing within 24 hours of a clinic visit without dosing for the prior week. In a test cohort of 45 subjects (HPTN 066), all doses were directly observed. Instances of an observed dose 24 hours prior to measurement without prior dosing served as the reference to determine thresholds for WCA TFV and TFV-DP concentrations that included 90% of the WCA reference group. These thresholds were then applied to test for WCA in MTN-001, a study with unobserved, prescribed daily dosing in 144 subjects at 7 sites.

Results: WCA thresholds were set as TFV>24.9 ng/mL, TFV-DP<10.3 fmol/10^6 cells (sensitivity = 90.91%, 95% CI: 62.26-98.38%). Thresholds applied to all HPTN 066 samples (1-7 doses/week), misidentified 3 non-WCA samples (false positive rate = 1.55%, 95% CI: 0.53-4.47%). Thresholds applied to MTN-001 demonstrated 14.03% prevalence of WCA (95% CI: 10.44-18.60%). 64% adherence using TFV alone differed significantly ($p<0.001$, Chi-squared test) from 51.80% adherence (95% CI: 45.94-57.61%) when TFV and TFV-DP were used to account for WCA. WCA prevalence at sites significantly differed ($p<0.001$, Chi-squared test), ranging from 0.00% to 39.13%.

Conclusion: WCA is sufficiently prevalent in MTN-001 such that TFV alone yields inflated adherence estimates. Combination with TFV-DP testing would ensure more accurate adherence measurement in some locations.

BASIC SCIENCE
POSTER ABSTRACTS
Listed Alphabetically (First Name)

A. Karim Ahmed, MS 2

Mentor(s): Daniel M. Sciubba, MD
Neurosurgery

Establishment of Chordoma in a Rat Model

Authors: A. Karim Ahmed BS, Rachel Sarabia-Estrada PhD, Alejandro Ruiz-Valls MD, Sagar R. Shah PhD, Alvaro Ordonez MD, Fausto Rodriguez MD, Hugo Guerrero-Cazares PhD, Ismael Jimenez-Estrada PhD, Esteban Velarde BS, Betty Tyler, Yuxin Li MD, Neil A. Phillips MS, C. Rory Goodwin MD PhD, Rory J. Petteys MD, Sanjay K. Jain MD, Gary L. Gallia MD PhD, Ziya L. Gokaslan MD, Alfredo Quinones-Hinojosa MD, Daniel M. Sciubba MD

Background: Chordoma (CHO) is a rare, slow-growing, malignant, locally aggressive cancer that is minimally responsive to conventional chemoradiation. Currently, there is no orthotopic animal model of spinal chordoma. The present study outlines creation and evaluation of the first orthotopic animal model of human chordoma in an immunocompromised rat.

Methods: U-CH 1 and JHC7 chordoma tumor tissue were subcutaneously implanted in the flanks of donor rats. Human sacral chordoma tumor tissue was excised from donor rats (U-CH 1 recurrent: n=11; JHC7 primary: n=11) and tumor pieces were engrafted in the lumbar spine of immunocompromised rats. A group of 6 sham rats and another with 6 intact rats were used as control groups. Nociceptive response was evaluated. Locomotion gait and open field test analysis were used to evaluate gait impairment. Rats were clinically observed for neurological impairment and pain response utilizing mechanical or thermal stimulation. Imaging of tumor-bearing rats was performing using microCT, MRI and NanoScan PET/CT to detect bone changes due tumor growth. Rats were euthanized 1.6 years after tumor implantation and the spines were harvested for immunhistochemistry.

Results: Tumor bearing portions of engrafted spines displayed typical CHO morphology and immunohistochemical staining. CT showed sclerotic lesions in the vertebral body of U-CH1 and JHC7 groups. Tumor growth was confirmed using MR imaging and contrast media. Locomotion gait analysis showed a disruption of the normal ambulatory pattern, with reduction in the step length and gait duration, in tumor-implanted animals—analogous to the human conditions. The distance traveled and speed was significantly reduced in the UCH-1 and JHC7 rats. Nociceptive response to a mechanical stimulus demonstrated a significant increase in mechanical hypo-algesia, in tumor-implanted rats.

Conclusion: This is the first orthotopic animal model of human CHO model in rats. This model reproduces cardinal clinical signs present in human patients such as ambulatory dysfunction and sensory deficits.

Amy Quan, MS 4

Mentor(s): Gerald Brandacher, MD
Plastic and Reconstructive Surgery

Novel Peripheral Nerve Injury Animal Model Optimizes Measurement of Functional Recovery Following Chronic Denervation Injury

Authors: Amy Quan MPH, Joseph Lopez MD MBA, Joshua Budihardjo BS, Sara Mermulla MBBS, Tariq Jawadi MBBS, Howard Wang MD, Ahmet Hoke MD PhD, Sami Tuffaha MD, WP Andrew Lee MD, Gerald Brandacher MD

Background: Chronic denervation causes significant damage to peripheral nerves and results in decreased regeneration potential after repair. Although the cellular and molecular effects of chronic denervation on peripheral nerve regeneration are well understood, previous studies have failed to reliably correlate these effects to functional outcomes. To address this problem, we have developed a novel upper extremity peripheral nerve injury animal model that optimizes measurement of functional return after chronic denervation injury.

Methods: We developed a forelimb chronic denervation rat model in which the median nerve was transected and left in discontinuity for 0, 8 or 12 weeks. After the period of denervation, the distal median nerve stump was co-apted to the proximal stump of a freshly cut ulnar nerve. Group 1 rats (n=8) underwent 0 weeks of denervation; Group 2 (n=8) underwent 8 weeks; and Group 3 (n=8) underwent 12 weeks. Functional recovery was tested weekly by measuring grip strength and recording compound muscle action potentials (CMAPs) in the operative limb.

Results: At fourteen weeks after ulnar-median neurorrhaphy, decreasing grip strength was recorded for rats who had sustained the greatest amount of denervation injury: Group 1 (2.26±0.29 Newtons) > Group 2 (0.97±0.14) > Group 3 (0.67±0.04), (p<0.0001). In addition, greater CMAP amplitude was detected in Group 1's operative limb (1.7±0.2 millivolts), as compared to Groups 2 and 3 (0.5±0.1, 0.5±0.2, respectively, p<0.001), and increasing CMAP latency was observed with increased periods of denervation: Group 1 (1.9±0.2 milliseconds) < Group 2 (2.4±0.4) < Group 3 (3.3±0.2), (p<0.001). Finally, decreasing flexor muscle weight corresponded with greater amount of denervation: Group 1 (0.8±0.03 grams) > Group 2 (0.5±0.02) > Group 3 (0.4±0.01), (p<0.05).

Conclusion: This novel forelimb chronic denervation model provides the first translatable animal model to optimize the measurement of functional recovery after different degrees of peripheral nerve chronic denervation injury.

Baltazar Zavala, MS 2

Mentor(s): Kareem Zaghloul, MD-PhD
National Institutes of Health Surgical Neurology Branch

Hold that thought: Human subthalamic nucleus theta and beta oscillations are coherent with the lateral cortex during working memory inhibition.

Authors: Baltazar Zavala PhD, Anthony Jang BA, Kareem Zaghloul MD-PhD

Background: The subthalamic nucleus (STN) is the most common target for therapeutic deep brain stimulation for Parkinson's disease. Though we are becoming increasingly aware of the role the STN plays in the inhibition of movement, there is growing evidence that the STN may also be critically involved in higher level non-motor cognition as well. Here we examine whether the coordinated activity between the cortex and the STN modulates the encoding of memory.

Methods: We simultaneously captured STN single-unit spiking, STN local field potentials, and cortical electrocorticography during DBS surgery as patients performed a novel working memory task. Subjects were sequentially shown 8 numbers and asked to either encode or ignore each number based on a simultaneously presented shape.

Results: During all correct trials, we observed a decrease in beta band (15-30 Hz) activity in the STN, the frontal cortex, and the lateral cortex. Crucially, this decrease was reversed to an increase in both the lateral cortex and the STN during the ignore trials. These two areas also showed increased beta band coherence during the ignore trials. Finally, the spiking of the STN neurons was also modulated during the task, with some neurons showing a trial type dependent change in firing rate.

Conclusion: In line with previously held notions that the STN acts as a gate that influences whether or not an action occurs, our results suggest that the same beta band gating mechanisms that inhibit movement in both motor control and pathological states such as Parkinson's disease may also play a role in inhibiting memory encoding. These findings help shed light on some of the non-motor deficits seen in Parkinson's disease as well as some of the side-affects associated with deep brain stimulation of the STN.

Bryce Small, MS 2

Mentor(s): Bob Siciliano, MD
Infectious Diseases

Validating the Block-and-Lock Strategy as a novel cure for HIV

Authors: Bryce Small BA, Ya-Chi Ho MD, MS, PhD, Bob Siciliano MD PhD, Janet Siciliano PhD

Background: While Human immunodeficiency virus type-1 (HIV-1) infection can be controlled by modern antiretroviral therapy (ART), any interruption in the treatment regimen can still lead to viral rebound. This rebound occurs primarily due to latent, integrated HIV-1 proviruses in resting CD4+ T cells, even in the presence of ART.

Methods: In our study, we explore whether HIV-1 transcription can be permanently silenced by cellular factors using a Block-and-Lock approach. The Block-and-Lock approach to HIV cure is aimed at permanent transcriptional inactivation of the HIV-1 gene in the latent reservoir, making patients functionally cured.
    We first refined and tested the lab's existing HIV-1 repression model in vitro. Then, molecular cloning, employing Gibson Assembly, was utilized to form lentiviral plasmids containing targeted gRNAs and an extended fusion protein of Cas, KRAB or DNMT3b, and BFP. Using a lentiviral transduction system, we introduced the above Cas plasmids into primary CD4+ T cells from HIV-infected patients. The goal being to direct these fusion proteins to gRNA-specific sites in the HIV 5' LTR. We hypothesize this will induce heterochromatin formation specifically over integrated HIV-1 genes, putting the viral gene into deep latency, where it cannot be activated. We will use bisulfite sequencing and nested qPCR to measure the HIV-1 copies with increased methylation, a surrogate for heterochromatin, and the amount of HIV-1 transcription after plasmid introduction.

Results: Due to the low transduction efficiency in patient cells, no conclusions could be drawn about the effects of KRAB and DNMT3b on HIV-1 expression and heterochromatin, in our first trial.

Conclusion: We suspect since the patient cells are from patients who have been on stable ART, their cells will be primed to resist HIV, and therefore lentiviral, infection. Since KRAB and DNMT3b are continually linked to HIV-1 transcriptional repression, we will repeat these experiments in healthy donor cells, increasing the transduction efficiency.

John Choi, MS 2

Mentor(s): Betty Tyler, BS
Neurosurgery

Treatment of Malignant Pediatric Brain Tumors via Suicide Transgene Expression Using PEGylated pPEG-3 PBAE Nanoparticles

Authors: John Choi MEd, Jordan Green MD, Martin Pomper MD, Henry Brem MD, Eric Jackson MD, Betty Tyler BS

Background: Medulloblastoma (MB) and atypical teratoid/rhabdoid tumors (AT/RT) are some of the most prevalent malignancies in pediatric populations. Current standard of care for pediatric tumors involves radiation therapy, which has high risks of developmental sequelae. In a previous study, gene therapy using non-viral Poly(beta-amino ester) (PBAE) nanoparticles carrying plasmids with the DNA suicide gene HSVtk was explored as an alternative treatment for CNS malignancies. Results showed promise in murine glioblastoma and gliosarcoma models with increased survival over controls ($p=0.0012$). However, when the same method was applied for pediatric brain tumors (MB and AT/RT), intolerable cytotoxicity and unspecified killing of normal gray matter along with tumor cells occurred.

Methods: Our lab took the polymeric approach used in prior studies and introduced two new additions to address the above cytotoxicity and specificity issues: (1) PEGylated tails to decrease the inherent cytotoxicity of the nanoparticles and (2) the use of a plasmid that includes a PEG-3 promoter specifically activated in cancer cells expressing transcription factors AP-1 and PEA-3 (i.e. MB and AT/RT cells). Experiments were first run in vitro using PEG-3 promoter eGFP and HSVtk plasmids for MB and AT/RT cell lines to test transfection efficacy, cytotoxicity and cell killing ability of the nanoparticles, with an immortalized fetal astrocyte cell line as a control to quantify the specificity of the nanoparticle for cancer cells.

Results: Promisingly, in in vitro studies, the PEGylated pPEG-3 nanoparticle treated group exhibited over 95% killing of cancer cells with less than 6% cytotoxicity vs controls without treatment.

Conclusion: These data suggest an alternative to higher risk treatments like radiation therapy and provide proof of principle for using gene therapy to treat malignancies in pediatric populations. Importantly, the profound nature of collaboration was appreciated in this interdisciplinary effort spanning multiple labs.

Maeva Nyandjo, MS 2

Mentor(s): Dolores Njoku, MD
Anesthesiology and Critical Care Medicine

IL-33 critically modulates Treg responses in a mouse model of drug-induced hepatitis

Authors: Maeva Nyandjo BS, Merylin Cottagiri MS, Dolores Njoku MD

Background: Drug-induced hepatitis is a rare, allergic and autoimmune complication of halogenated volatile anesthetic administration. Studies suggest that IL-4-mediated, Th2-polarized, immune reactions initiate drug-induced hepatitis. We modeled hepatitis in BALB/c mice by immunizing them with liver proteins covalently modified by trifluoroacetyl-chloride anesthetic metabolites (TFA-JHDN5). However, mechanisms that modulate severity of hepatitis remain elusive. IL-33 is a Th2 cytokine associated with severe allergic and autoimmune inflammation. IL-33 mediates inflammation through IL-4. We found that IL-33-/- mice developed drug-induced hepatitis, but when compared to BALB/c mice, had higher rates of death as well as diminished IL-10 protein and Foxp3+ regulatory T cell (Treg) RNA in their livers. A recent study showed that IL-33 promotes function of intestinal Tregs in a Th2 model of autoimmune colitis. We hypothesized that in drug-induced hepatitis, IL-33 modulates severity by promoting Treg maturation and function.

Methods: Treg numbers and CD4+T cell proliferation were assessed in BALB/c and IL-33-/- mice ± TFA-JHDN5 (100µg) subcutaneous immunization on days 0 and 7. CD45+(PerCP)CD4+(FITC) CD25+(PE)Foxp3+(APC) Tregs and proliferation were measured by flow cytometry. Proliferation (CD4+(APC)) was measured following CFSE labeling, stimulation with anti-CD3e/anti-CD28 (0.5ug/0.25ug, ThermoFisher) and co-culture ± Tregs, 1:100 (BALB/c, IL-33-/-) isolated using magnetic beads (Miltenyi) with and without IL-10 supplementation (0-10ng, ThermoFisher) in vitro. A p value< 0.05 was significant (Mann-WhitneyU)

Results: IL-33-/- mice produced fewer Tregs in the liver and spleen following immunizations (21.7% vs. 12.8%, p<0.05). CD4+T cell proliferation between IL-33-/- and BALB/c mice were similar, with or without immunizations. Tregs from BALB/c mice suppressed proliferation in IL-33-/- in both strains. Tregs from IL-33-/- mice increased proliferation in both strains. IL-10 supplementation did not modulate CD4+T cell proliferation or Treg numbers (32.0%, no supplementation vs. 35.0%, supplemented).

Conclusion: IL-33 is critically involved in the function and maturation of Tregs. Our findings have implications in morbidity and mortality in drug-induced hepatitis.

Michael Grzelak, MS 2

Mentor(s): Geraldine Seydoux, PhD
Molecular Biology and Genetics

Designing an optimal rescue template to maximize CRIPSR-Cas editing efficiency in HEK cells

Authors: Michael Grzelak BS, Andrew Folkmann PhD, Alexandre Paix PhD, Geraldine Seydoux PhD

Background: CRISPR-Cas is a popular genetic engineering method that has the potential to revolutionize the treatment of genetic human illnesses. The principle mechanism of CRISPR-based editing is the introduction of double stranded breaks (DSB) into the genome, and the specificity of CRISPR lies in its ability to introduce these breaks efficiently and accurately. The cell repairs the DSB either by Non-Homologous End Joining (NHEJ) which introduces knockout mutations, or by Homology Directed Repair (HDR) which uses an endogenous or exogenous DNA sequence as a rescue template to guide the repair of the break. This rescue template, often structured as a single-stranded oligodeoxynucleotide (ssODN), must share homology with the damaged DNA and can be designed to insert a new sequence into the genome. Although CRISPR-HDR is a potentially effective genetic engineering tool, several studies have reported low editing frequencies using this approach. We hypothesized that optimizing the design of the ssODN rescue template may increase editing efficiency.

Methods: We developed a standard GFP tagging protocol in HEK293 cells that allowed us to compare editing efficiencies across different ssODNs. We compared length of homology arms, polarity of the ssODN, and recoding of sequences around the edit.

Results: Our findings indicate that the optimal rescue template has homology arms that are 30nt in length, is sense stranded, and has silent mutations added to the region between the inserted sequence and the 3' homology arm. These results demonstrate that the structure of the rescue template plays a central role in CRISPR editing efficiency.

Conclusion: By using an optimal rescue template design, it is possible to maximize edit recovery and thus overcome one of the main limitations of the CRISPR-HDR technology.

Paul Michel, MS 2

Mentor(s): Michael Beer, PhD
Department of Biomedical Engineering

Applying machine learning methods to predict the impact of common variants on gene regulation in type I diabetes

Authors: Paul Michel, BA, Michael Beer, PhD

Background: Genome-wide association studies (GWAS) identify single nucleotide polymorphisms (SNPs) associated with disease traits. The SNPs identified in GWAS are rarely causative and usually fall in nontranscribed regions of the genome. This has motivated the hypothesis that many GWAS SNPs influence their disease phenotype by disrupting transcriptional regulation. Because GWAS SNPs are found on the same haplotype block as other SNPs, identifying causal variants and characterizing their regulatory impact remain challenging. Here, we applied machine learning methods to type I diabetes (T1D) associated SNPs to predict causal SNPs and quantify their impact on regulatory elements. We predicted that our machine learning classifier would produce a set of T1D associated SNPs that disrupt known gene regulatory motifs.

Methods: We selected 131 T1D GWAS SNPs to identify disease susceptibility loci. We then expanded the initial set to 9,842 SNPs by including other SNPs in linkage disequilibrium with the GWAS SNPs. Using DNAse I hypersensitivity data, we trained a support vector classifier (gkmSVM) to identify putative regulatory motifs in immune and pancreatic cells. This allowed us to score all possible 10-base pair sequences based on their similarity to these regulatory motifs. High scores indicate strong regulatory potential. We then calculated the induced change in score (deltaSVM) when any of our 9,842 SNPs were introduced to their native sequence. A SNP induces a large deltaSVM when it creates or obliterates a strong regulatory motif.

Results: Our methods produced a subset of 55 SNPs with large deltaSVM scores in regions corresponding to putative gene regulation. Most of these SNPs disrupt known transcription factor binding sites.

Conclusion: We generated a list of SNPs that are predicted to play a role in the pathogenesis of T1D because they disrupt regulatory motifs at T1D loci. Continuing work will focus on determining the gene targets for these motifs and their role in T1D.

Sarah Thompson, MS 3

Mentor(s): Takanari Inoue, PhD
Cell Biology

Anti-CD123 scFv Expression in Non-Immune Cells for Targeting of Acute Myeloid Leukemia Cells for Synthetic Clearance

Authors: Sarah Thompson, Kester Coutinho, Helen Wu, Takanari Inoue PhD

Background: As one of the most devastating adult and pediatric cancers, acute myeloid leukemia affects hundreds of thousands of patients and their families globally, with yearly mortality in the US exceeding 10,460. With such poor prognoses, there is a pressing need to develop effective therapies with minimal adverse effects. Traditional chemotherapy is frequently unsuccessful in eliminating leukemic stem cell populations, and emerging immune-based therapies like CAR-T leave patients vulnerable to potentially fatal cytokine storms.

Methods: Our novel technique utilizes Synthetic Clearance (SynC) of cancer cells, and has the potential to selectively target and clear leukemic cells without the generation of these side effects. The technique involves extracting a patient's own cells and engineering them to express receptors specific against cancer antigens. When reintroduced to patients, the engineered cells target cancer cells and behave as a high capacity sink, with the potential to inducibly trigger phagocytic machinery when bound to its target. In the case of AML, the marker CD123 (IL3-a) was selected.

Results: The objectives of this research were: 1) develop scFv against CD123, 2) subclone this nanobody into vectors containing fluorescent markers (mCh), a membrane targeting sequence (GPI and integrin), and machinery for rapamycin-inducible dimerization (FRB/FKBP), 3) express scFv on the membrane of non-immune cells (Cos7 and HeLa), 4) demonstrate AML cell binding in cells expressing anti-CD123 scFv.

Conclusion: These objectives were successfully accomplished using fluorescent cell microscopy to visualize nanobody expression and cell binding. This work provides proof of concept of the potential efficacy of SynC therapy in the treatment of AML. This research can contribute to future experiments evaluating phagocytosis of target AML cells and, hopefully, animal-based models of SynC therapy.

Scott Shuldiner, MS 2

Mentor(s): Vasan Yegnasubramanian
Oncology

Development of a droplet digital methylation specific PCR assay to measure DNA methylation alterations as novel prostate cancer biomarkers

Authors: Scott Shuldiner BS, Vasan Yegnasubramanian MD PhD

Early detection of aggressive prostate cancer, risk stratification and identification of patients likely to benefit from interventions, as well as monitoring methods to assess therapeutic response, remains problematic. Using genome-wide approaches, our group previously identified a panel of DNA methylation alterations that were associated with prostate cancer and its aggressiveness. Here, we report a DNA methylation based assay to non-invasively monitor tumor burden, as well as treatment effectiveness, in order to inform clinical decisions. This droplet digital methylation specific PCR (ddMSP) assay detects methylation status from small amounts of input DNA, such as those obtained from urine and cell-free plasma. With this method, we measured methylated GSTP1 promoter sequences, previously known to be methylated in >90% of prostate cancers but not in any normal prostate tissues. In initial experiments using prostate cancer cell line DNA, the assay demonstrated an assay sensitivity of detecting as few as 12-14 genome equivalents (lower limit of quantitation), with a >100-fold linear dynamic range of quantitation. The assay sensitivity, dynamic range, and specificity compared favorably with respect to a methylation sensitive restriction enzyme and droplet digital PCR (MSRE-ddPCR) based approach. Experiments to further assess the ddMSP assay performance, to develop a multiplexed internal standard for incorporation with the assay, and to extend the assay to allow measurement of multiple DNA methylation alterations, are currently ongoing. The translational nature of this work lays the groundwork for prospective clinical studies to assess the association between DNA methylation status and disease burden, therapeutic response and ultimately treatment outcomes. Ultimately, this will allow for the optimization of precision medicine based strategies for delivering individualized therapies for prostate cancer with the potential to greatly improve treatment outcomes.

CLINICAL SCIENCE POSTER ABSTRACTS
Listed Alphabetically (First Name)

Abigail Lin, MS 2

Mentor(s): Christos Georgiades, MD, PHD
Interventional Radiology

Yttrium-90 radioembolization with adjuvant 90Y PET/CT-guided percutaneous ablation: Predicted dosimetric impact

Authors: Abigail Lin, Alexander Pasciak, Yong C. Bradley MD, Christos Georgiades, MD, PhD

Background: 90Y PET/CT post-radioembolization imaging has demonstrated that the distribution of 90Y in the tumor is often non-uniform. As a potential tool for improving radioembolization therapy, we assessed the use of 90Y PET/CT as a guide for adjuvant percutaneous ablation of the portions of tumor receiving the lowest absorbed-dose.

Methods: 14 patients with primary or secondary liver cancer treated using 90Y radioembolization were included in this study. Each patient exhibited potentially under-treated areas of tumor following treatment (>30% of tumor receiving <100 Gy) based on quantitative 90Y PET/CT. 90Y PET/CT was used to guide electrode placement for simulated adjuvant radiofrequency ablation in areas of tumor receiving the lowest dose. The finite element method was used to solve Penne's bioheat transport equation, coupled with the Arrhenius thermal cell-death model to determine ablation zones in 3 dimensions. Tumor absorbed-dose metrics (average dose, D50, D70, D90, V100) were compared with and without adjuvant ablation. A paired-sample T-test was used to assess statistical significance. Correlation between tumor size and the effect of adjuvant ablation was evaluated using Spearman's rank and linear regression analysis.

Results: Compared to radioembolization alone, 90Y radioembolization with simulated adjuvant ablation was associated with increases in all tumor dose metrics evaluated. The mean average absorbed-dose increased by 11.2±6.9 Gy. Increases in D50, D70 and D90 were 11.0±6.9 Gy, 13.3±10.9 Gy and 11.8±10.8 Gy, respectively. The mean increase in V100 was 7.2±4.2%. All changes were statistically significant (P<0.01). A negative correlation between pre-ablation tumor volume and D50, average dose and V100 was identified (ρ<-0.5, P<0.05) suggesting that adjuvant percutaneous ablation may be less beneficial to patients with large tumor burdens.

Conclusion: 90Y radioembolization with adjuvant 90Y PET/CT-guided percutaneous ablation may be a valuable tool in the treatment of liver cancer. However, an additional prospective trial is needed to further evaluate this hybrid therapy.

Adela Wu, Student in Residence

Mentor(s): Roberto Salvatori, MD, Gary Gallia, MD
Endocrinology, Neurosurgery

Pattern of HPA Axis Recovery after Successful Surgery for Cushing Disease

Authors: Adela Wu ScB/AB, Anthony Asemota MD, Roberto Salvatori MD, Alfredo Quinones-Hinojosa MD, Gary Gallia MD

Background: Primary treatment of Cushing disease (CD) is surgical removal of the ACTH-secreting pituitary adenoma. Successfully treated patients develop postoperative adrenal insufficiency. An important aspect of long-term outcomes of CD treatment involves determining the length of glucocorticoid (GC) replacement therapy and hypothalamic-pituitary-adrenal (HPA) axis recovery following surgery.

Methods: We studied 62 CD cases who underwent surgery between 2005-2016, and became adrenal insufficient. We examined the correlation between the degree of hypercortisolism, assessed by 24-hour urinary free cortisol (UFC) and pre-operative ACTH values, and the timing of HPA axis recovery and CD recurrence.

Results: Within our cohort, the average age was 39 years. 52 patients had elevated UFC values. 40 patients had elevated pre-operative ACTH values. 47 patients recovered HPA axis function. The overall mean recovery period was 344 days. There was no significant correlation between the 24-hour UFC index or pre-operative ACTH value and time to HPA axis recovery. Of the 47 patients who recovered HPA-axis function, 6 had recurrent CD following discontinuation of GC therapy. The mean recovery period in patients who developed recurrent CD was [135.7 ± (SD 26) days] versus patients without recurrence [374.8 ± (SD 41) days], p=0.03. Most patients (9/14) who recovered HPA axis function within 6 months did not recur; however, 5/6 patients who recurred had GC therapy discontinued within 6 months after surgery.

Conclusion: Our data demonstrate that the degree of hypercortisolism does not correlate with recovery of HPA axis after surgery for CD. Patients who develop recurrent CD were more likely to have discontinued GC therapy within 6 months from initial surgery. Although the majority of patients who recovered adrenal function within 6 months post-operatively did not develop recurrence, it is recommended that closer follow-up for these patients may be necessary for possible early detection of recurrent CD.

Adela Wu, Student in Residence

Mentor(s): Megan Collins, MD
Neuro-Ophthalmology

Infantile Poor Vision in the Setting of Hypotonia and Oculomotor Apraxia

Authors: Adela Wu ScB/AB, Thomas Bosley MD, Megan Collins MD

Background: Afferent visual problems can be a manifestation of some genetic or developmental abnormalities. For infants with these problems, early visual assessments are essential for diagnosis and management. Infants with oculomotor apraxia (OMA), an inability to make adequate saccades, depend on compensatory head movements. Children with hypotonia and OMA do not demonstrate age-appropriate head support and therefore cannot perform head movements to fix or follow visual stimuli. Given these limitations, it can appear that children with hypotonia and OMA have afferent visual problems.

Methods: We performed a retrospective chart review on 6 pediatric patients with hypotonia and OMA who initially appeared to have poor vision. These patients were seen by two ophthalmologists at Johns Hopkins and King Khaled Eye Specialist Hospital. Serial ophthalmic and neurologic assessments were performed.

Results: Average age of patients at baseline was 15.2 months (5–36 months). Patients were followed for an average of 703.6 days (155–1905 days). All 6 patients demonstrated poor visual attention at baseline, as well as poor head control and delayed motor skills. At follow-up, all 6 patients demonstrated visual fixation improvement with use of compensatory head movements.

Conclusion: For 6 patients who demonstrated poor visual attention at baseline and raised concerns for afferent visual dysfunction, the improvement in vision, namely the ability to fix and follow objects, occurred in pacing with progressive improvement in hypotonia and the acquirement of head control and motor skills. Children with hypotonia and OMA may be incorrectly diagnosed with afferent visual problems. With improvement of head control and motor skills, their visual attention improves.

Akachimere Uzosike, Student in Residence

Mentor(s): Phillip Pierorazio, MD
Brady Urologic Institute

Variability in growth kinetics of small renal masses on active surveillance

Authors: Akachimere Uzosike BA, Michael H. Johnson MD, Hiten D. Patel MD, Mark Riffon MPH, Michael A. Gorin MD, Christian Pavlovich MD, Peter Chang MD, Andrew Wagner MD, James M. McKiernan MD, Bruce J. Trock MD, Mohamad E. Allaf MD, Phillip M. Pierorazio MD

Background: Active surveillance (AS) of small renal masses is emerging as a safe and effective strategy. To date, there is a paucity of robust, prospective data on growth rates of these masses as they pertain to clinical outcomes.

Methods: From 2009 – 2015, a prospective multi-institutional registry of patients with small renal masses (tumor diameter<4cm) was collected. Patients electing active surveillance received regularly scheduled imaging, with tumor characteristics collected throughout their enrollment in the registry.

Results: 518 patients were prospectively enrolled, of which 236 patients (45.6%) elected AS. 186 had follow-up imaging at time of this analysis, with a mean follow-up of 23.7 months. Overall mean growth rate was 0.29 ± 1.81 cm/year (median: 0.10 cm/year). Growth rate and variability decreased with time, with the mean growth rates at 6, 12, 24, and 48 months of 0.22 ± 0.57, 0.12 ± 0.38, 0.13 ± 0.27, and 0.09 ± 0.25 cm/year, respectively. Twenty-one patients (8.9%) crossed over to delayed intervention, with a mean growth rate of 0.56 ± 1.07cm/year (median: 0.39 cm/year). Progression-free survival (tumor size < 4cm and growth rate $\leq$ 0.5cm/year) was 94.9% and 80.1% at 2 and 4 years, respectively.

Conclusion: Growth kinetics of SRM is highly variable upon entrance into AS, with both growth rate and growth rate variability decreasing with time. Early in AS, worrisome growth rates may warrant re-assessment of risk stratification with additional imaging or consideration of biopsy prior to treatment. As patients progress on AS, GR may be an acceptable parameter for decision-making on intervention.

Alan Shan, MS 2

Mentor(s): Allen Eghrari, MD
Ophthalmology

Intraocular lens insertion during resident phacoemulsification cases: identification of intraoperative characteristics specific to lens choice

Authors: Alan Shan Sc.B, Guadalupe Villarreal M.D., Allen Eghrari M.D.

Background: Resident physicians training in ophthalmology utilize a variety of intraocular lenses across a minimum of 86 primary cases required for graduation. Supervising physicians would benefit from understanding the intraoperative characteristics of individual lenses, which would allow a precision approach to guidance for each.

Methods: To describe the duration and complications encountered during intraocular lens implantation of three models of intraocular lenses (Alcon MA50BM, SA60AT, SN60WF), 120 de-identified cataract surgery video recordings were obtained from a single surgeon and viewed using VLC media player 2.2.4. The "Jump to time (Previous frame) v2.1" VLC add-on was used to record the following time signatures: first incision, lens injector insertion, insertion/removal of tools, and procedure end-time. The type of lens used, the number of adjustments, and the occurrence of intraoperative complications were also recorded. Statistical methods used included one-way ANOVA and Poisson regression.

Results: Mean lens insertion duration was almost three times longer for the MA50BM (75.5s) versus the SA60AT (27.8s) or SN60WF (28.6s). These results were highly significant (p<0.001). However, mean post-insertion adjustment times for the SA60AT (25.0s) and SN60WF (25.1s) were longer than the MA50BM (15.7s), a trend that demonstrated marginal significance (p=0.053). No significant difference was appreciated in lens loading time, mean post-insertion adjustment tool use, or Sinskey hook use among intraocular lens types. Out of 117 completed cases, we noted three with lens ejection difficulties, and two with intraoperative capsule collapse and lens dislocation.

Conclusion: The MA50BM lens was associated with increased insertion time, while the SA60AT and SN60WF required a longer period for post-insertion adjustment, characteristics consistent with the MA50BM's larger lens and stiffer haptics. Despite slight differences in structure and cartridges used for insertion, the latter two lenses demonstrated similar intraoperative characteristics throughout the study.

Alex Jang, MS 2

Mentor(s): Phillip Pierorazio
Urology

Multiple Growth Periods Predict Unfavorable Pathology in Patients with Small Renal Masses Undergoing Active Surveillance

Authors: Alex Jang BA, Mark Riffon MPH, Alice Semerjian, MD, Michael H. Johnson MD, Michael A. Gorin MD, Mohamad E. Allaf MD, Phillip M. Pierorazio MD

Background: Previous retrospective studies have cited the overall growth rate of small renal masses (SRMs) as an indicator of malignancy. However, prospective studies of active surveillance (AS) have failed to show this correlation. The objective of this study was to characterize the growth of SRMs to determine potential biometric predictors of malignancy.

Methods: The Johns Hopkins Renal Mass Database and Delayed Intervention and Surveillance for Small Renal Masses Registry were queried, of which 1388 patients underwent surgical intervention for a SRM (clinical T1a). Of those patients, 124 with serial imaging (2 or more) prior to surgery were included. Patients were categorized based on their pathologic tumor grade and stage: favorable (benign, chromophobe, and low-grade pT1-2 RCC) vs. unfavorable (high-grade of any stage and low-grade pT3-4 RCC). A positive growth period was counted each time the difference in greatest tumor diameters between two images was positive.

Results: Of the 124 patients, 69.4% (86/124) had favorable pathology and 30.6% (38/124) had unfavorable pathology. Overall growth rate in cm/year was higher in the unfavorable group, but did not reach traditional levels of significance (mean[SD]=0.7[1.7] vs 1.6[2.8], p=0.07). A significant association between positive growth periods and unfavorable pathology was confirmed by the Cochran-Armitage trend test (p=0.02) and Somers' D (0.15, 95%CI [0.02, 0.29]). The ratio of favorable to unfavorable pathology was 1.8, 1.0, 0.66, 0.59 and 0 as the number of positive growth periods increased from 0 to 4 respectively.

Conclusion: Overall growth rate was not predictive of favorable or unfavorable pathology in this retrospective analysis. A positive association between number of positive growth periods and unfavorable pathology was seen. Future studies of larger sample size and ongoing prospective studies may elucidate the importance of the number of positive growth periods as an indicator of malignant potential in patients undergoing AS for SRMs.

Allison Wallingford, MS 2

Mentor(s): Pablo Celnik, MD
Physical Medicine and Rehabilitation

Comparison of Functional Specificity between Conventional and Multichannel Electrode Montages for tDCS

Authors: Allison Wallingford BA, Claudia Ammann MS, Pablo Celnik MD

Background: Transcranial Direct Current Stimulation (tDCS) is a form of non-invasive brain stimulation capable of modulating brain excitability. To better understand and improve the effects of tDCS, our objective is to compare neuromodulatory effects and spatial specificity of the traditional bipolar tDCS and a multichannel tDCS electrode montage applied to the primary motor cortex (M1).

Methods: Thirteen healthy subjects each received tDCS (Neuroelectrics, Spain) targeting the first dorsal interosseous (FDI) representation of M1 with traditional bipolar stimulation (two saline soaked sponges as electrodes), multichannel stimulation, and sham stimulation in three separate sessions. Using transcranial magnetic stimulation (TMS), we assessed the excitability of M1 along the motor strip targeting FDI, buccinator, anterior deltoid, and tibialis anterior at two time points before tDCS and three after tDCS. EMG was recorded and peak-to-peak motor-evoked-potential (MEP) amplitude was quantified.
For each session, we calculated average MEP amplitude at each time point for each muscle and normalized post-tDCS averages as percent increases from pre-tDCS averages. We analyzed the data using polynomial nested repeated measures ANOVA.

Results: Group averages suggest that bipolar stimulation resulted in larger increases in FDI MEP amplitudes and deltoid MEP amplitudes compared to the multichannel montage. The buccinator and TA muscles showed little change in MEPs pre- and post-tDCS. However, one-way ANOVAs performed for each muscle under each tDCS condition did not show statistically significant variation of MEP average with time point. Two-way ANOVAs performed for each tDCS condition did not show significant variation with muscle or time point.

Conclusion: Group averages suggest bipolar tDCS induced a larger and broader effect on brain excitability. ANOVA did not show a significant effect of tDCS on normalized MEP amplitude, likely due to high variation between subjects' baseline responses to TMS. We will continue testing subjects to better understand effects of different tDCS conditions.

Anh Quynh Nguyen, MS 2

Mentor(s): Christine Durand, MD
Department of Medicine/Division of Infectious Diseases

Willingness to Donate Organs Among Persons Living with HIV/AIDS

Authors: Anh Q. Nguyen BA, Samantha Halpern BS, Komal Kumar MPH, Saad Anjum BS, Sarah Rasmussen BS, Allan Massie PhD, Aaron A.R. Tobian MD PhD, Dorry L. Segev MD PhD, Jeremy Sugarman MD MPH, Christine M. Durand MD

Background: HIV-to-HIV organ transplantation is now permissible under research protocols pursuant to the HIV Organ Policy Equity (HOPE) Act. Implementation of the HOPE Act depends on willingness to donate organs among persons living with HIV/AIDS (PLWH), which is currently unknown in the U.S.

Methods: We conducted a cross-sectional survey on willingness to donate organs among HIV-infected patients at Johns Hopkins Hospital using convenience sampling. Fisher's exact and chi-squared tests were used to examine differences in willingness to donate.

Results: Among 115 participants, median age was 55, median length of HIV diagnosis was 20 years, 51.8% were male, 91.3% were African American, and 52.2% were co-infected with Hepatitis C. The majority (80.0%) were willing to be deceased donors; 61.75% were willing to be living donors. Most (81.7%) knew of the current organ shortage; however, only 23.9% were aware of the HOPE Act and 22% were registered organ donors. Compared to those who were unwilling to be deceased donors, willing participants were more likely to trust the medical system ($p<0.001$) and to believe HIV would not affect organ function in transplant recipients ($p=0.001$). Participants who were willing to be living donors were less likely than those unwilling to be living donors to be concerned about going through surgery ($p<0.01$), or to believe that donation would worsen their health ($p<0.001$), change their HIV treatment ($p<0.01$), or cause poor health due to HIV ($p<0.001$). There were no significant associations between participants' knowledge of the organ shortage, the HOPE Act, or past medical history with willingness to donate organs.

Conclusion: At our center, the majority of PLWH expressed willingness to donate organs though most were not registered donors. These findings support the HOPE Act's potential to expand the donor pool and mitigate the organ shortage crisis while highlighting the need for donor registration outreach among PLWH.

Brendan Shi, MS 2

Mentor(s): Uma Srikumaran, MD
Orthopaedic Surgery

Pullout Strength in Augmented and Wide-suture Transosseous Rotator Cuff Repair: A Biomechanical Analysis

Authors: Brendan Shi BS, Miguel Diaz BS, Stephen Belkoff PhD, Uma Srikumaran MD

Background: The goal of this study was to evaluate two new methods of improving transosseous rotator cuff repair pull-out strength in osteopenic bone. We analyzed the effect of a) augmenting the lateral tunnel and b) using wide-dimension suture instead of No. 2 suture.

Methods: 12 pairs of osteopenic, cadaveric upper extremities were identified by DEXA screening. Six pairs were randomized to be repaired with No. 2 Ultrabraid suture, while the other six were repaired with 2-mm Ultratape suture. Within each suture type, one side of each pair was randomly assigned to undergo lateral tunnel cement augmentation while the contralateral side underwent standard repair. One bone tunnel and one suture were placed in the head of all 24 humeri. Specimens were mounted at 20° to the horizontal and tested to failure with an MTS system. Generalized linear latent and mixed models analysis (GLLAMM) was used to assess differences in pullout strength, with potential confounding factors (age, sex, bone density T-score) included as covariates.

Results: Specimens repaired with wide dimension suture demonstrated a significant improvement in pullout strength (B=51 N, $p<0.048$, 95% CI [0.35—103]) over specimens repaired with standard No. 2 suture. Augmentation of the lateral tunnel demonstrated no significant improvement of pullout strength (95% CI [-52—44]). Age, sex, and bone density T-score had no significant effect on pullout strength.

Conclusion: Our study showed that using 2-mm wide dimension suture significantly improves the pullout strength of transosseous rotator cuff repairs in osteopenic bone. This simple change improves the feasibility of using transosseous repairs in older patients.

Chengcheng Gui, MS 2

Mentor(s): Stephanie Terezakis, MD
Radiation Oncology and Molecular Radiation Sciences

Characterization and predictive value of volume changes of extremity and pelvis soft-tissue sarcomas during radiotherapy prior to surgical resection

Authors: Chengcheng Gui BSE, Carol D Morris MD MS, Christian F Meyer MD MS PhD, Adam S Levin MD, Deborah A Frassica MD, Curtiland Deville MD, Stephanie A Terezakis MD

Background: In treating extremity soft tissue sarcomas with radiotherapy (RT) preceding surgical resection, pre-treatment tumor volume predicts survival and recurrence. However, changes in tumor volume during RT are not well-characterized, and their relationship to outcomes is unknown.

Methods: Patients with extremity or pelvis soft tissue sarcomas treated at our institution from 2013-2016 with RT prior to resection were identified retrospectively. Tumor volumes were measured using cone-beam CT images taken daily throughout RT. Linear regression evaluated the linearity of volume changes. Kruskal-Wallis tests, Mann-Whitney U tests, and linear regression evaluated patient and treatment characteristics as predictors of volume change. Logistic and Cox regression evaluated volume change as a predictor of resection margin status, local recurrence, and distant recurrence.

Results: Of 31 cases, median age was 52 years (range, 9-87 years). Twenty-four cases (77%) involved lower extremities or pelvises; 7 (23%) involved upper extremities. Twenty-seven (87%) were high-grade, and 27 (87%) were primary tumors. At the start of RT, median tumor volume was 199mL (range, 7.1-4885mL). Linear regression showed significant volume changes during RT in 16 tumors (52%) (p<0.05), including all 14 (45%) in which volume change exceeded 5%. Of these, 4 (13%) increased and 12 (39%) decreased in volume. Myxoid liposarcoma (5 cases, 16%) predicted decreasing volume (p=0.0005). Sequential chemoradiation (4 cases, 13%) predicted increasing volume (p=0.006) and corresponded to longer times from diagnosis to RT (p=0.02). Four cases (13%) involved positive resection margins. Two (6%) involved local recurrence and 5 (16%) involved distant recurrence, at median 3.9 and 6.9 months post-resection, respectively. Volume changes did not predict margin status (OR=1.009[0.970,1.080]), local recurrence (HR=1.036[0.941,1.141]), or distant recurrence (HR=1.012[0.973,1.053]).

Conclusion: Volume changes of pelvis and extremity soft tissue sarcomas followed linear trends during RT. Volume changes reflected histological subtype and treatment characteristics but did not predict margin status or recurrence after resection.

Clarisa Diniz, MS 3

Mentor(s): Dr. Ballentine Carter
Urology

Comparison of biochemical recurrence free survival after radical prostatectomy among men in active surveillance following grade reclassification and men newly diagnosed with similar grade disease

Authors: Clarissa P. Diniz, H. Ballentine Carter, Jonathan I. Epstein, Mufaddal Mamawala

Background: Prostate cancer diagnosed with prostate-specific antigen (PSA)–based screening often has a protracted natural history posing minimal threat during a lifetime. Thus, active surveillance (AS) has evolved as a strategy for reducing over treatment of indolent PCa identified through screening.

While AS is being increasingly adopted world-wide, exits from AS in the absence of a progression in disease (reclassification) are common. Stakeholders in a Patient-Centered Outcomes Research grant questioned the clinical implications of biopsy grade reclassification while on AS.

Methods: We conducted a retrospective analysis of men undergoing RP from 1995-2015 and identified 2 groups; 122 men in AS who underwent RP following GR (7(3+4) or greater, grade group 2 and above) and 4433 men who underwent immediate RP (IRP) following a diagnosis of grade group 2 and above. bRFS was assessed using Kaplan Meir and multivariate Cox regression analyses.

Results: Of 122 men in AS, 13 (10.7%) had biochemical recurrence (BCR) as compared to 777 of 4,433 (17.5%) men that underwent IRP (p =0.007). As compared to the IRP group, men on AS were significantly older (p <0.001), had a higher proportion of low volume cancers (p <0.001), a lower PSA density (p =0.001), and a lower rate of GS upgrade at surgery (p <0.001). bRFS was higher for men in the AS cohort compared to IRP group (p = 0.046, Fig 1). After adjustment for confounders, the difference in bRFS between groups was no longer significant (HR = 0.77; 95% CI, 0.41 to 1.46).

Conclusion: AS patients that are reclassified to grade group 2 and above have a higher bRFS after surgery as compared to those undergoing IRP with similar grade disease. These differences are likely due to selection criteria for AS. Our findings help inform patient decisions regarding the risk of entering an AS program.

Damian Stobierski, MS 2

Mentor(s): Kaisorn Chaichana, MD
Neurosurgery

Brain Tumor Metastases from Primary Lung Cancers: Evaluating Risk Factors and Surgical Outcomes

Authors: Damian Stobierski MS, Chikezie Eseonu MD, Kaisorn Chaichana MD

Background: Surgical resection is one treatment option for patients with metastatic lung cancer to the brain. However, there is currently a lack of data to help determine which patients are good candidates for surgery vs other treatment options such as radiation therapy. We attempt to identify the pre-surgical disease factors associated with more favorable outcomes to better identify good surgical candidates.

Methods: All patients who underwent surgical resection for metastatic lung cancer to the brain at our institution from 2008 through 2015 were identified and their medical records retrospectively analyzed. Data was collected on comorbid conditions, pre-operative functional status, tumor characteristics via pathology and radiology, pre-surgical management, post-surgical complications, disease progression, and death. Primary outcome analyzed was length of survival; secondary outcomes were length of hospital stay, readmission, and recurrence of tumor. Kaplan-Meier survival analysis was used to estimate mortality trends, and logistic regression was used to identify factors associated with worse outcomes.

Results: Analysis is not yet complete.

Conclusion: We hope to identify novel risk factors for worse outcomes and strengthen the evidence behind others. Such information may help surgeons better determine who is a good surgical candidate. It may also help surgeons discuss treatment options with their patients with more rigor.

Daniel Kerekes, MS 2

Mentor(s): Dan Sciubba, MD
Neurosurgery

Prevalence, Risk Factors, and Outcomes for Local and Distant Recurrence in Resected Sacral Chordomas: a Systematic Review

Authors: Daniel Kerekes BS, Rory Goodwin MD/PhD, Ali Ahmed BS, Dan Sciubba MD

Background: Sacral chordomas are extremely rare, primary bone tumors of the spine, and are treated with en bloc resection. Despite the current literature consensus that local recurrence is the most important determinant of long-term survival for patients with this disease, large studies investigating recurrence in sacral chordomas are generally lacking.

Methods: We performed a systematic review of five online databases to find articles published since 1980 that report survival, recurrence outcomes, and/or prognostic factors for the resected sacral chordoma patient population. Characteristics and clinical outcomes of the pooled published cohort are reported. Fisher exact tests and unpaired t-tests were used to investigate patient- and treatment-associated prognostic factors for local and distant recurrence. Survival analyses were performed for time to local recurrence and time to death in patients with local recurrence vs. without recurrence.

Results: 57 studies consisting of 1,232 unique patients were included in this review. This pooled population of resected sacral chordoma patients had a mean presenting age of 56 and a male:female ratio of 1.6:1. Local and distant recurrence occurred in 42.7% and 22.4% of patients, respectively. Kaplan-Meier median survival times for patients with and without recurrence were 98 and 209 months after surgery, respectively. Mean times to local and distant recurrence were 40 and 60 months, respectively. Wide surgical margin and posterior surgical approach were associated with lower rates of local recurrence, and wide surgical margin, female sex, and patient age ≥65 were associated with lower rates of distant recurrence.

Conclusion: While surgical margin remains the most significant prognostic factor for both local and distant recurrence, surgical approach may also be associated with local recurrence – a novel finding. Both sex and age may be associated with distant recurrence. This study endorses a wide surgical margin as the most essential goal of management, and compels regular and long-term follow-up for this disease.

Davis Rogers, MS 2

Mentor(s): Meret Branscheidt, MD
The Human Brain Physiology and Stimulation Laboratory, Department of Physical Medicine &
Rehabilitation, Johns Hopkins Medical Institute

Influence of Fatigue on Motor Skill Learning

Authors: Davis Rogers BA, Panagiotis Kassavetis Ph. D, Meret Branscheidt MD, Pablo Celnik MD

Background: It is unknown how performance under fatigue affects motor learning. This study aims to assess the effects of fatigue on motor learning, focusing on acquisition and retention of motor skills.

Methods: 78 healthy subjects (55% male, 42% non-white, age 22-32) were recruited. Experiment 1: 38 subjects were randomly assigned to a no-fatigue (NoFTG) or fatigue (FTG) group. Over 2 days, participants learned a motor skill task consisting of isometric contractions of the index finger and thumb. Only on Day 1, fatigue was induced in FTG by sustaining maximum isometric contraction using a hand-held force transducer prior to training. Experiment 2: 40 subjects followed the same protocol, but were randomly divided to receive repetitive transcranial magnetic stimulation (rTMS) over either the primary motor cortex (FTGdepo) or sham location (FTGsham) at the end of Day 1. RmANOVA was used to determine the effects of group and time on skill measure (speed and accuracy). Post-hoc comparisons used student t-tests with Bonferroni correction. Online learning gains were explored by linear regression models and pairwise permutation tests.

Results: Experiment 1: Learning rates of FTG were significantly worse than NoFTG on Day 1 ($p=0.01$) as well as Day 2 ($p=0.05$). Experiment 2: The effect of prolonged impaired performance after learning under fatigue was replicated. Importantly, on Day 2, FTGdepo improved in skill measure, showing no significant difference from NoFTG ($p=0.02$), while FTGsham still performed significantly worse ($p=0.08$).

Conclusion: Our results suggest that fatigue not only affects skill acquisition, but also impacts consecutive performance even in the absence of fatigue. These findings have implications for motor learning in athletics and rehabilitation. Interestingly, by interfering with motor memory consolidation using rTMS, we could attenuate the detrimental effect of fatigue on subsequent training days. Future studies should uncover why training under fatigue on initial exposure elicits prolonged effects on motor learning.

Divya Rayapati, MS 2

Mentor(s): Lauren Osborne, MD
Reproductive Psychiatry

Relationship between sleep quality components and depression in women with perinatal mood disorders

Authors: Divya Rayapati BA, Katie Washington-Cole BA, Katherine McEvoy MD, Lauren Osborne MD

Background: Depression in pregnancy and postpartum is common (up to 20% of women) and debilitating. There is emerging evidence that poor sleep quality is a risk factor for perinatal depression. Studies have examined the relationship between sleep quality and perinatal mood symptoms in subjects without pre-existing mood disorders. Since women with pre-existing illness are at the highest risk for worsening symptoms in the perinatal period, it is vital to consider risk factors in this highly vulnerable group. Our objective was to examine the association of sleep efficiency, day time dysfunction and sleep latency with the development of depressive symptoms. We hypothesize that these components would be associated with depression in late, but not early, postpartum.

Methods: We included 62 mood-disordered pregnant women in a previous prospective cohort study with available data from at least one pregnancy and one postpartum visit (one and three months). The Pittsburgh Sleep Quality Index (PSQI) measured sleep quality, and the Inventory of Depressive Symptomology (IDS) assessed depressive symptom severity. Bivariate and multivariate linear regression models examined the association between IDS and subscale and global PSQI scores adjusted for confounders.

Results: Higher IDS scores at three months postpartum were associated with higher overall sleep quality, sleep latency, sleep efficiency, daytime dysfunction, and global PSQI scores at one month postpartum; higher PSQI scores reflect worse sleep outcomes. Using sleep medications in the third trimester was associated with depression at 3 months postpartum, not 1 month. Concurrent sleep problems (notably sleep quality, latency, daytime dysfunction) correlated with depression at third trimester, 1 month, and 3 months postpartum.

Conclusion: Considering this cohort of pregnant women at risk for postpartum mood disorder, the association between third trimester sleep quality and perinatal depressive symptoms may provide the basis for clinical interventions aimed at improving sleep and monitoring efficacy, which could in turn improve symptoms postpartum.

Emily Boozalis, MS 2

Mentor(s): Bernard Cohen, MD
Pediatric Dermatology

Horizontal striae distensae of the lower back in teenage boys: an analysis of demographics and review of the literature

Authors: Emily Boozalis BA, Candrice Heath MD, Katherine Puttgen MD, Anna Grossberg MD, Bernard A Cohen MD

Background: The purpose of this study is to examine the clinical characteristics and demographics of teenage boys with horizontal striae distensae (SD) of the lower back in an outpatient setting, and to investigate potential risk factors for this condition.

Methods: Retrospective medical chart reviews and telephone survey studies were completed on an outpatient cohort of 12 teenage boys 0–18 years old with a diagnosis of transverse SD of the lower back at a single-center, university-based pediatric dermatology practice. We evaluated clinical features of the striae, patient demographics, and past medical history. A review of the literature concerning risk factors associated with this type of striae was undertaken using Pubmed.

Results: Of the 14 patients that we contacted, 12 participated in our study. The average age of onset was 14.3 years old. All boys were above the 50th percentile in height at the time of onset. Eight patients (66.7%) reported a significant growth spurt prior to the appearance of the stretch marks. Most striae were asymptomatic. None of the children with horizontal SD of the lower back had a history of unmonitored exogenous steroid use or bacterial infection with either Bartonella henselae or Borrelia burgdorferi. Only one (8.3%) had a chronic medical condition. Almost all of the patients (91.7%) had at least one first-degree relative with stretch marks.

Conclusion: Our results indicate that horizontal SD of the lower back in adolescent boys is associated with a rapid growth spurt, tall stature, and a family history of stretch marks. There is no association between this clinical finding and any underlying chronic medical conditions, exogenous steroid use, or infection with either Bartonella henselae or Borrelia burgdorferi. Thus, a careful review of systems and counseling without further medical testing is a reasonable approach in managing adolescent boys with horizontal striae of the lower back.

Eric Xie, MS 2

Mentor(s): Chetan Bettegowda, MD PhD
Neurosurgery

Association of Ablation Parameters in Radiofrequency Rhizotomy for Trigeminal Neuralgia with Durability of Treatment

Authors: Eric Xie BA, Tomas Garzon-Muvdi MD, Chetan Bettegowda MD PhD

Background: Radiofrequency ablation (RF) rhizotomy is a surgical therapy for treatment of trigeminal neuralgia (TN) in patients who fail medical therapy. Though RF has been commonplace for 40 years, there is limited literature on the effects of RF parameters (temperature and duration) on the surgical outcome or the use of higher-intensity treatment in repeat rhizotomies. We investigated the association between RF parameters and treatment efficacy, represented as time until subsequent procedure (TSP).

Methods: This retrospective study was performed among TN RF patients at Johns Hopkins Hospital from 1990 through August 2016. We included 476 RF procedures with temperature and duration data, effective pain relief, and subsequent follow-up procedure. Temperature and duration were obtained from surgeon's notes, pain relief from patient reporting, and TSP from the medical record. To account for pairing of temperature and duration, we created index (Inx) as a product of temperature and duration in each procedure. Kendall's tau and partial correlation analysis (rho) assessed the relationship of temperature, duration, and Inx with TSP adjusting for traditional risk factors (age, gender, race).

Results: At time of procedure, participants were aged 65 ± 14 yrs, 38% male, and 73% white, 18% African American, 9% other. Higher temperature, higher duration, and higher Inx were associated with shorter TSP (respectively: rho = -0.22, $p < 0.0001$; rho = -0.09, $p = 0.032$; rho = -0.14, $p = 0.002$).
To control for intensified treatment in repeat procedures, we also binned the variables by procedure count. Inx did not correlate with TSP at the first or second procedure but higher Inx correlated with shorter TSP in >3 procedure (rho = -0.17, $p = 0.035$).

Conclusion: Higher temperature and duration of treatment in TN RF may correlate with decreased treatment efficacy as indicated by less time until subsequent procedures. Higher intensity treatment may not be more effective as procedure count increases.

Ethan Dyer, MS 2

Mentor(s): Martin, MD
Cardiology

The Johns Hopkins Corrie Smartphone Application

Authors: Ethan Dyer MD, Francoise Marvel MD, Seth Martin MD

Background: The Johns Hopkins Corrie Smartphone Application supplements the recovery process for cardiac patients early in the hospitalization course to improve their health engagement. The Johns Hopkins Myocardial infarction, COmbined device, Recovery Enhancement (MiCORE) study aims to assess the feasibility and usability of the Corrie App.

Methods: An iOS alpha version of the Corrie App was developed using Apple's CareKit framework through a collaboration between Johns Hopkins Medicine, Johns Hopkins Computer Science, the Whiting School of Engineering, and the Carey Business School. The multidisciplinary research team worked directly with Apple to improve usability and integrate the companion devices (e.g., Apple Watch). A starter kit and script were created to help providers guide patients through the app.

The MiCORE study began September 15th, 2016 in the cardiology inpatient units at Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center, where patients have been offered the Corrie Application and Apple Watch. The research team collaborate with inpatient care teams to assist patients with downloading the app. Observational data on patient satisfaction and engagement, medication adherence for 30 days following discharge, and 30-day readmission will be collected.

Results: Functionally, the Corrie App builds patients' medication self-management skills, helps coordinate follow-up appointments, educates patients about heart health, facilitates pharmacy interaction to access medication, and connects patients with health resources. Using an easy-to-follow starter kit, healthcare workers can assist in installing the app on a patient's mobile device early in the hospitalization process so that the patient can familiarize him or herself with it and ask nurses and doctors questions.

Conclusion: This study will continue to drive development of a mobile application that not only improves overall patient outcomes, but bridges disparities faced by our most vulnerable patients. The study has recruited 5 patients so far.

Gloria Hong, MS 2

Mentor(s): Jennifer Thorne, MD
Ophthalmology

Ocular Involvement in Mucous Membrane Pemphigoid

Authors: Gloria H. Hong BA, Jennifer E. Thorne MD

Background: Mucous membrane pemphigoid (MMP) is a potentially life threatening, autoimmune disease affecting mucosal surfaces. Ocular MMP can lead to blindness if untreated. We characterized demographic and clinical features of MMP patients with and without ocular disease. We also calculated the risk of developing ocular MMP or a secondary extra-ocular area of active MMP and identified risk factors for new-onset disease.

Methods: We performed a retrospective chart review of 162 biopsy-proven MMP patients. Wilcoxon rank-sum test and chi-square test, Kaplan-Meier curves, and Cox regression models were used for statistical analyses.

Results: At presentation, 109 of 162 MMP patients (67.3%) had ocular involvement. The median [IQR] age was higher for ocular MMP patients than those without ocular disease (68 [59,78] years vs. 61 [49,69] years, p=0.004). Ninety-eight (89.9%) ocular MMP patients were Caucasian; 55 (50.5%) were female. Patients with ocular involvement were more likely to be male (49.5% vs. 30.2%, p=0.02). A history of trichiasis was more common among patients with ocular MMP (60.6% vs. 5.7%, p<0.001). At presentation, 78 (71.6%) ocular MMP patients also had extra-ocular involvement, with the oropharynx (89.7%) most commonly involved. Over a median follow-up time of 6.1 years (mean=7.5 years, range=1 month to 22 years), the risk of developing ocular MMP was 0.014 per eye-year (EY) (95% CI=0.005/EY, 0.034/EY). The risk of developing a new location of extra-ocular MMP was 0.020/EY (95% CI=0.007, 0.043). Smoking was a risk factor for developing an additional extra-ocular MMP location (HR=4.09, p=0.05).

Conclusion: MMP patients with ocular involvement were more likely to be older, male, and have a history of trichiasis than those without ocular involvement. Patients presenting with only extra-ocular MMP are at risk for developing ocular MMP, and all MMP patients are at risk for developing secondary extra-ocular MMP, although these risks are low. Long-term follow-up is necessary to detect new-onset disease.

Halley Darrach, MS 2

Mentor(s): Lisa Ishii, MD MHS
Otolaryngology

The Other Race Effect: Caucasians display preferential attention towards racially congruent faces regardless of perceived attractiveness

Authors: Halley Darrach BS, Masaru Ishii MD PhD, David Liao BA, Jason C Nellis MD, Roxana Cobo MD, Kristin L Bater BA, Lisa E Ishii MD MHS

Background: Race and deformity impact how casual observers view individuals. While the attentional distraction incurred by deformity and the alterations in scan-path when presented with different-race individuals have been well-documented, the effect of both race and perceived attractiveness on visual fixation time has not been investigated.

Methods: Naïve participants recruited on the Johns Hopkins Medical Campus were randomly presented with 32 paired facial images of Caucasian and Latino patients – taken pre and post-rhinoplasty for correction of nasal deformity – while measuring visual scan-paths using infrared eye-tracking technology. Paired images were displayed for 400ms and participants were instructed to casually gaze upon the faces. A web-based survey containing the images of the same 32 patients was distributed, and independent observers graded each patient on perceived attractiveness using a sliding 0-100 scale. Planned hypothesis testing was conducted using a three-way ANOVA to compare patient race, observer race, and attractiveness with respect to visual fixation time.

Results: 134 participants (mean age 26, 50.75% female) successfully completed the eye-tracking experiment. 51 participants identified as Caucasian and 13 as Latino. 125 Caucasian observers completed our web-based survey (mean age 30, 63.48% female). ANOVA analysis of Caucasian scan paths (in milliseconds) displayed a gaze preference for Caucasian faces and a penalty for Latino faces ($p < 0.00001$, 95%CI[-29.95,-10.99]). When controlling for attractiveness, Caucasian observers demonstrated no association between gaze preference and perceived attractiveness ($p = 0.179$, 95%CI[-0.771,0.143]). No gaze preference was seen amongst Latino participants ($p > 0.05$).

Conclusion: When presented with two faces, Caucasian observers demonstrated a significant gaze preference for Caucasian faces compared to Latino faces. Similar to prior studies, these data suggest a same-race facial preference. This pilot study serves as a starting point for future studies – incorporating larger and more diverse cohorts – to investigate the effect of race on observer gaze preferences and social perceptions.

Hannah Carl, MS 2

Mentor(s): Justin Sacks, MD
Department of Plastic and Reconstructive Surgery

Systematic Review of the Surgical Treatment of Extremity Lymphedema

Authors: Hannah Carl BS, Gurjot Walia BS, Ricardo Bello MD, Emily Clarke-Pearson MD, Aladdin Hassanein MD, Brian Cho MD, Rachel Pedreira BA, Justin Sacks MD MBA

Background: While conservative management of extremity lymphedema remains the first-line approach, surgery is effective in select patients. The purpose of this study was to review the literature and develop a treatment algorithm based on the highest quality lymphedema research.

Methods: A systematic literature review was performed to examine the surgical treatments for lymphedema. Studies were categorized into five groups describing excision, liposuction, lymphovenous anastomosis (LVA), vascularized lymph node transfer (VLNT), and combined/multiple approaches. Studies were scored for methodological quality using the Methodological Index for Non-Randomized Studies (MINORS) scoring system. High quality articles were reviewed and the following data was extracted: number of patients, stage of lymphedema, surgical procedure, length of follow-up, volume or circumference reduction, measurement technique, reported complications, and additional interventions.

Results: Sixty-nine articles met inclusion criteria and were assigned MINORS scores with a maximum score of 16 or 24 for non-comparative or comparative studies, respectively. The average MINORS scores using non-comparative criteria were 12.1 for excision, 13.2 for liposuction, 12.6 for LVA, 13.1 for VLNT, and 13.5 for combined/multiple approaches. Thirty-nine studies scoring >12/16 or >19/24 were considered high quality and valid for use in creating a management algorithm. In studies measuring excess volume reduction, the mean reduction was 96.6% (95% CI: 86.2-107%) for liposuction, 33.1% (95% CI: 14.4-51.9%) for LVA, and 26.4% (95% CI: -7.98-60.8%) for VLNT.

Conclusion: Although the overall quality of lymphedema literature is fair, the MINORS scoring system is an effective method to isolate high quality studies. These studies were used to develop an evidence-based algorithm to guide clinical practice and identify patients who may benefit from surgical management. With ongoing compression treatment, both reductive and physiologic approaches can safely and effectively treat lymphedema. Furthermore, future studies with a particular focus on patient follow-up and quality of life will improve the validity of lymphedema surgery research.

Hasina Maredia, MS 2

Mentor(s): Stephen Yang, MD
Department of Surgery

Second independent primary tumors among esophageal cancer survivors

Authors: Hasina Maredia BA, Craig Hooker PhD, Trevor A Davis BS, Stephen C Yang, MD

Background: With improved therapy leading to better survival of esophageal cancer patients, there is more time for development of second primary cancers. Several gaps exist in understanding the development of second cancers such as time frame and risk factors, including risk from esophageal cancer treatment (chemotherapy, surgery, radiation). We seek to characterize second tumors occurring among esophageal cancer survivors in order to inform patient management.

Methods: We conducted a retrospective chart review of 637 esophageal cancer patients diagnosed between 2003-2015 at Johns Hopkins Hospital. Cases were defined as esophageal cancer survivors developing a second, independent primary tumor, and case-controls were matched by age, histology, and time of follow up. We compared clinical characteristics and treatment methods between cases and controls.

Results: Among 637 esophageal cancer survivors, 21 (3.3%) patients developed a subsequent tumor. The median (IQR) time to second primary after the esophageal cancer was 2.2 years (0.7–3.4). The secondary tumors were GI (28%), prostate (19%), bladder (14%), lung (14%), hematological (9.5%), kidney (9.5%), and skin (4.7%). Third subsequent primary cancers occurred in 29% of cases. There was no significant difference in smoking prevalence, race, and esophageal cancer treatment type, including radiation exposure and dose, between cases and controls ($p > 0.05$). Furthermore, 17 additional patients had synchronous tumors, diagnosed within two months of the esophageal tumor.

Conclusion: Despite a relatively low prevalence of secondary tumors among esophageal cancer survivors, a high percentage of patients who developed secondary tumors also developed tertiary tumors. Our current findings will inform follow-up and screening guidelines for esophageal cancers survivors which are currently lacking. Given radiation exposure and smoking prevalence were not associated with risk of secondary tumors and because there was a high prevalence of synchronous tumors, investigation into biological risk factors such as immunogenetics that predispose patients to multiple tumors will be explored.

Hasina Maredia, MS 2

Mentor(s): Errol Bush, MD
Department of Surgery

Is Lung Allocation Score Associated with Survival Among COPD Lung Transplant Registrants and Recipients?

Authors: Hasina Maredia BA, Mary Grace Bowring MPH, Allan Massie PhD, Shakirat Oyetunji MD, Christian Merlo MD PhD, Robert Higgins MD, Dorry Segev MD PhD, Errol Bush MD

Background: COPD is one of the most common indications for transplantation, but a relatively stable disease. It is currently not known whether the lung allocation score (LAS) is associated with of waitlist and post-transplant mortality among COPD patients, which we seek to address in this study.

Methods: Using the Scientific Registry of Transplant Recipients national database, we performed a retrospective observational study of 3,699 adult lung transplant candidates diagnosed with COPD and listed for transplant between 5/1/2005-7/31/2015. Patients listed at multiple institutions were excluded. Kaplan Meier curves and Cox regression were used to compare mortality based on time-varying LAS by categories (<31, 31-35, 36-46, 47-60, 61-100), after adjusting for patient age, sex, race, and education level.

Results: Among all listed, 91% were transplanted. Among those who were not transplanted, 45% died, representing 4% of the COPD patients listed. The median (IQR) LAS at time of transplant was 34 (32-35). Among those transplanted, the median (IQR) time on waitlist was 98 days (30.5-289).

In the adjusted model, COPD patients on the waitlist have a 2.77 (95% CI: 2.18-3.53) times higher risk of death compared to transplanted patients (p<0.001). The risk of death was significantly higher among waitlist candidates in LAS categories > 36, but the risk of death post-transplant was significantly higher only among LAS 61-100. For all LAS categories, the risk of waitlist mortality was higher than transplant mortality. In LAS 61-100, the risk of death on the waitlist in 13 days was equivalent to the risk of death post-transplant in one year.

Conclusion: While transplantation was associated with lower mortality compared to waitlist only at all LAS categories, LAS was associated with elevated post-transplant mortality only at high scores of 61-100. LAS may need to be revised in order to truly reflect post-transplant survival among COPD patients across all scores.

Hasina Maredia, MS 2

Mentor(s): Errol Bush, MD
Department of Surgery

Age and Gender Disparities in Post-Lung Transplant Mortality

Authors: Hasina Maredia BA, Mary Grace Bowring MPH, Allan Massie PhD, Shakirat Oyetunji MD, Christian Merlo MD PhD, Robert Higgins MD, Dorry Segev MD PhD, Errol Bush MD

Background: The lung allocation score (LAS) was established in May 2005 to prioritize transplant candidates based on predicted waitlist and post-transplant mortality. We examine whether there are disparities in post-lung transplant mortality by gender, age, and sex following the implementation of LAS. Identifying characteristics associated with mortality can allow for closer monitoring and prognostication for patients at higher risk.

Methods: Using the Scientific Registry of Transplant Recipients national database, we performed a retrospective observational study of adult lung transplant recipients from 5/1/2005-7/31/2015. Kaplan Meier curves and Cox regression were used to compare risk by race (African American; AA and non-African American; non-AA), sex, and age (18-30, 31-40, 41-60 and 61-80) after adjusting for donor and recipient characteristics, as well as transplant procedure type (unilateral or bilateral) and LAS.

Results: Differences in risk of post-transplant mortality by gender and age categories were significant ($p<0.001$), while there was no significant difference in mortality between AA and non-AA recipients ($p=0.2$). In the adjusted model, relative to recipients aged 41-60, recipients aged 18-30 and 61-81 years had 25% (95% CI: 9%–44%; $p<0.001$) and 36% (95% CI: 28%–45%; $p<0.001$) higher risk of mortality, respectively, while recipients aged 31-40 had 18% (95% CI: 5%-22%; $p<0.01$) lower risk. Relative to comparable male recipients, female recipients had 9% (95% CI: 4-14%) lower risk of death ($p=0.02$), while there was no significant difference between AA and non-AA recipients ($p=0.8$).

Conclusion: For a given LAS, women had lower risk of death and recipients aged 18-30 and 61-81 had higher risk of death relative to 41-60 year old recipients. Unlike liver and heart transplants, there was no significant difference by race in lung transplant outcomes. LAS, which takes into account age, may not be reflecting post-transplant outcomes accurately and may require adjustment. Further investigation into potential biological mechanisms for these disparities is warranted.

Jared Hinkle, MS 2

Mentor(s): Gregory Pontone, MD
Psychiatry and Behavioral Sciences

Parkinson's Disease Psychosis is Independently Associated with Dyskinesia Severity

Authors: Jared Hinkle BS, Kate Perepezko BA/MSPH, Catherine C. Bakker MS, Ted M. Dawson, MD/PhD, Vanessa Johnson BS, Zoltan Mari MD, Cherie L. Marvel PhD, Kelly A. Mills MD, Alexander Pantelyat MD, Olga Pletnikova MD Liana S. Rosenthal MD, Melissa D. Shepard MD, Daniel A. Stevens BS, Juan C. Troncoso MD, Jiangxia Wang MS, Gregory M. Pontone MD

Background: Psychosis and dyskinesias have each been linked to aberrant serotonergic modulation of striatal and cortical circuits in Parkinson's disease (PD). Our objective was to determine whether psychosis in PD is clinically associated with increased dyskinesia severity.

Methods: We analyzed data from 116 patients enrolled in the Morris K. Udall Parkinson's Disease Research Center of Excellence Longitudinal Study at Johns Hopkins University. Psychiatric diagnoses were established by psychiatrist interview per DSM-IV criteria. Dyskinesias were measured using items 32-35 of part IV of the Unified Parkinson's Disease Rating Scale (UPDRS-IV). We used a generalized estimated equation (GEE) approach in logistic regression to test for an association between dyskinesia severity and a psychosis diagnosis while controlling for known psychosis risk factors.

Results: Twenty patients in our sample (17.2%) were diagnosed with psychosis at baseline and the cumulative prevalence of psychosis in the study was 43.1% (50 patients). In univariate analyses of patients at baseline, dyskinesia duration, associated pain, and related disability were each significantly associated with psychosis ($p < 0.05$), as was disease duration ($p < 0.001$). In multivariate regression analysis with GEE evaluating dyskinesia measures simultaneously, the disability caused by dyskinesias was associated with psychosis (odds ratio: 1.46; 95% CI: 1.02-2.10; $p = 0.041$). Use of anticholinergic medications (odds ratio: 3.20; 95% CI: 1.53-6.71; $p = 0.002$), DSM-IV diagnosed dementia (odds ratio: 5.62; 95% CI: 2.81-11.26; $p < 0.001$), and levodopa equivalent dose (odds ratio: 1.42; 95% CI: 1.09-1.84; $p = 0.009$) were also significantly associated with psychosis. Psychosis was not associated with other motor complications of therapy assessed by the UPDRS-IV.

Conclusion: Dyskinesia-related disability correlates with the presence of psychosis in PD patients. Given the evidence for shared underlying serotonergic dysregulation in these PD complications, pharmacotherapy targeting serotonin receptors may prove dually useful in their management.

Jenny Yan, MS 2

Mentor(s): Stephanie Terezakis
Radiation Oncology

Single-Arm Phase II Study of Stereotactic Body Radiation Therapy (SBRT) Concurrent with Nelfinavir for Oligometastases

Authors: Jenny Yan MS, Riley McIntyre BA, Stephanie Terezakis MD

Background: Patients with oligometastatic disease have poor rates of disease progression and no currently standardized therapy. The objective of this phase II prospective study was to determine the lesion response to stereotactic body radiation therapy (SBRT) with concurrent Nelfinavir oral therapy, an HIV protease inhibitor, in patients with oligometastatic disease in the lung, liver, lymph node, and/or bone with various primary tumors.

Methods: Patients with oligometastatic disease at 5 or fewer sites at the Sidney Kimmel Comprehensive Cancer Center were enrolled and given 1250 mg of Nelfinavir twice daily for 7 days prior to a single dose of 15 Gy SBRT per lesion. Patients repeated the same Nelfinavir therapy after radiation and were followed up at 6 months for tumor lesion response. CT and/or MRI scans were obtained and lesions were measured using metric notation with a ruler from electronic medical record scans. Responses were categorized based on Response Evaluation Criteria in Solid Tumors (RECIST 1.1) as: complete response (no lesion present), partial response (>30% decrease), progressive disease (>20% increase), and stable response, based on changes in the longest dimension.

Results: 34 patients and 61 lesions were evaluated for lesion response and patient response at the primary endpoint. There was an 83.6% lesion response (CI:6.83%-26.0%, p=0.00001) of either complete, partial, or stable lesion size and 72.1% (CI:16.3%-39.4%), p=0.0003) for patient response. No significant differences in lesion or patient response for type of primary, metastatic site, or number of metastases were found using the Fisher-Exact test (p>0.05).

Conclusion: SBRT can be delivered safely with Nelfinavir, with promising clinical outcomes and high tumor control for oligometastatic patients. This information provides insight into future research in the concurrent use of radiosensitizers with SBRT and may provide curative effects for oligometastatic patients.

John Ryan, MS 2

Mentor(s): Joseph Herman, MD, MSc
Department of Radiation Oncology and Molecular Radiation Sciences

Stereotactic body radiation therapy for isolated local recurrence after surgical resection of pancreatic ductal adenocarcinoma appears to be safe and effective

Authors: John F. Ryan, BS, Vincent P. Groot, BS, Lauren M. Rosati, BS, Amy Hacker-Prietz MS, PA-C, Lei Zheng MD, Daniel A Laheru MD, Jin He MD, PhD, Timothy M. Pawlik, MD, MPH, PhD, Matthew J. Weiss MD, Christopher L. Wolfgang MD, PhD, Joseph M. Herman, MD, MSc

Background: A standardized treatment regimen for isolated local recurrence (ILR) of pancreatic ductal adenocarcinoma after surgical resection has not been established. We evaluated the outcomes of patients with ILR treated with stereotactic body radiation therapy (SBRT).

Methods: We retrospectively reviewed the records of patients with ILR treated with SBRT at our institution between 2010 and 2016. Palliation of pre-SBRT symptoms was assessed at 3-month follow-up. Treatment-related toxicity was evaluated using NCI-CTCAE, version 4.0. Associations between patient or treatment characteristics and overall survival (OS), progression-free survival (PFS), and local progression-free survival (LPFS) were assessed with the log-rank test and Cox univariate and multivariate proportional hazards models.

Results: Fifty-one patients who received SBRT for ILR were identified. Twenty-five (49%) received neoadjuvant or adjuvant radiation therapy prior to recurrence. Twenty-six (51%) were radiation-naïve. Median OS was 36 months from the date of histologic diagnosis. From the first day of SBRT, median OS, PFS, and LPFS were 16, 7, and 10 months, respectively. Patients with a recurrence-free interval ≥9 months after surgery had superior OS (P=0.02). Maintenance chemotherapy after SBRT was associated with superior OS (P<0.001) and LPFS (P=0.03). On multivariate analysis, poorly differentiated tumor grade (HR=11.27, 95% CI [2.83, 44.90]), positive surgical margins (HR=0.13, [0.03, 0.47]), and receiving maintenance chemotherapy (HR=0.14, [0.05, 0.40]) were independently associated with OS. Positive surgical margins (HR=0.26, [0.07, 0.92]) and receiving maintenance chemotherapy (HR=0.30, [0.10, 0.87]) were associated with LPFS. Ten of 16 patients (63%) experienced abdominal pain relief after SBRT. Rates of acute and late grade 3 gastrointestinal toxicity were 2% and 8%, respectively. No grade 4 or 5 gastrointestinal toxicity was observed.

Conclusion: SBRT safely provides local control and symptom palliation for patients with ILR. SBRT may be most beneficial to patients with a recurrence-free interval ≥9 months who can tolerate maintenance chemotherapy.

Jordan Tropf, MS 3

Mentor(s): Jay Reidler, MD
Orthopaedic Surgery

Inspiring Innovation: Introducing Biomedical Engineering Students to Orthopaedic Instruments and Procedures

Authors: Jordan Tropf BS, Jay Reidler MD, Brian Neuman MD, James Ficke MD, Dawn Laporte MD.

Background: Most biomedical engineering (BME) curricula expose students to surgical procedures through passive shadowing. In this study, we examined the impact of a hands-on cadaveric surgical procedure on inspiring orthopaedic innovation amongst BME students.

Methods: BME students participated in fixating a cadaveric ankle or wrist fracture with drills, plates, and screws loaned through an education grant from an orthopaedic supply company. Post procedural surveys were gathered from 14 JHU biomedical engineering students to assess the pertinence and impact of a case based surgical orthopaedic procedure that was guided by JHU faculty and resident orthopaedic surgeons. Quantitative variables were assessed on a 5-point Likert scale to evaluate the perceived impact of the study. Qualitative feedback gave open ended information pertaining to the usefulness of the study.

Results: The participation rate in the survey was 70%. All 14 participating BME students reported an increased interest in engineering orthopaedic devices. On a 5 point Likert scale, BME students rated the overall usefulness of the cadaveric procedure in the scope of their bioengineering curriculum an average of 4.4. They also rated the usefulness of future hands on operations an average of 4.4. 57% of students reported that they learned new bioengineering principles during the procedure and 64% reported applying already learned principles. 86% of students conveyed that the hands on experience gave new insights or perspectives related to biomedical engineering and 64% reported specific new ideas that they developed during or as a result of the experience.

Conclusion: Having BME students participate in cadaveric surgical procedures is a unique approach that is not part of the standard curriculum. Through this novel approach, BME students gain hands-on exposure to surgical procedures that inspires orthopaedic-specific innovation through a foundational education in orthopaedics. BME students find the activity useful, intellectually stimulating, and idea-generating.

Joshua Yang, MS 1

Mentor(s): Minnie Sarwal, MD, PhD
Surgery

A non-invasive urinary Common Rejection Module (uCRM) gene expression score enables accurate discrimination of acute rejection in kidney transplant patients

Authors: Joshua Yang MTM; Tara Sigdel PhD; Oriol Bestard MD, PhD; Yolanda Ng MD; Szu-Chuan Hsieh; Nicole Dvorak; Silke Roedder PharmD, PhD; Izabella Damm; Juliane Liberto, Sharvin Nandoe, Tim Tran; Minnie Sarwal MD, PhD

Background: Kidney transplantation is the preferred modality for treatment of end-stage renal disease (ESRD) by any cause. While this therapeutic approach has become a routine practice worldwide, long-term kidney allograft outcomes have not improved as expected despite a better understanding of the immunology of allograft rejection and the advent of novel and more potent immunosuppressive agents. The most plausible explanation for this unmet achievement relies on the rather poor immune-risk assessment of transplant patients in current clinical practice.

Methods: A common rejection module (CRM) consisting of 11 genes expressed on allograft biopsies was recently shown to be highly accurate to discriminate patients undergoing acute rejection (AR), correlate with the extent of graft injury, and predict future allograft damage. Cell pellet from 117 urine samples were evaluated for expression values of all 11 using qPCR. ROC analysis was performed to assess clinical utility of these CRM genes. Symbolic regression was used to create a urinary CRM (uCRM) score from a subset of these genes.

Results: The 5-gene uCRM score calculated from gene expression in the urine cell pellet was significantly higher in AR than in stable (STA) and in BK viral nephropathy (BKVN) (9.705 ± 1.018 vs. 0.4567 ± 0.1213 and 1.45 ± 0.3917 respectively, $p<0.0001$) and significantly discriminated AR from STA and BKVN patients with high accuracy (AUC=0.9723; 95% CI = 0.9426 – 1.0000, $p<0.0001$). In a validation set, a threshold of 1.896 showed 100% sensitivity and 85.7% specificity to discriminate high-risk from low-risk patients for AR.

Conclusion: By using a previously published gene list, we investigated the role of this panel as a surrogate biomarker panel. The 5-gene uCRM score in urine samples is able to non-invasively detect kidney transplant patients at high risk of AR and could provide a tool for AR risk assessment for kidney transplant patients.

Julia Retzky, MS 2

Mentor(s): Miho J Tanaka, MD
Orthopaedic Surgery - JHU

Epidemiological risk factors for ACL injury recurrence in NCAA athletes

Authors: Julia Retzky BA, Lynne Jones PhD, Miho J Tanaka MD

Background: ACL injuries are common, tending to affect female more than male athletes. Re-injury to the ACL is reported to be 1-9% after primary surgery. We hypothesize that female athletes, compared to male athletes within the same sport, will have higher rates of ACL re-injury.

Methods: NCAA Injury Surveillance Program ACL injury data was provided by the Datalys Center for Sports Injury Research and Prevention. Data was analyzed using STATA. Chi-square tests were used to compare rates of ACL re-injury by gender, sport, season, event type, injury mechanism, history of previous surgery, and injury outcome. Logistic regression was used to compare the frequency of ACL recurrence by gender and sport and to identify risk factors for ACL recurrence.

Results: Significant associations were noted between ACL recurrence and gender ($p = 0.047$), sport ($p = 0.017$), season ($p = 0.004$), event type ($p = 0.006$), injury mechanism ($p < 0.001$), history of previous surgery ($p < 0.001$), and injury outcome ($p < 0.001$). Females are 1.47 times more likely to experience ACL recurrence than males ($p = 0.048$). ACL recurrence is more likely to occur for both genders during preseason compared to other seasons ($p = 0.0029$), 1.7 times more likely to occur during practice compared to a game ($p = 0.007$), 2.4 times more likely to occur if the athlete did not have surgery on their primary tear ($p < 0.001$), and 1.5 times more likely to occur via non-contact compared to contact mechanisms ($p = 0.035$).

Conclusion: Risk factors for ACL recurrence were identified including gender, timing in the season, event type, history of previous surgery, and mechanism of injury. These findings support targeted injury prevention. Further discussion is encouraged regarding modification of current return-to-play guidelines based on these identified risk factors.

Luckmini Liyanage, MS 2

Mentor(s): Edward Ahn, MD
Neurosurgery

The optimal duration of helmet therapy after endoscopic craniectomy for infants with metopic craniosynostosis

Authors: Luckmini Liyanage BA, Xiaobu Ye MD, Edward Ahn MD

Background: Endoscopic craniectomy followed by helmeting is an effective surgical treatment for craniosynostosis in young infants. The optimal duration of helmet therapy remains unknown, but important to determine for cost and quality of life considerations. The purpose of this study was to use objective anthropometric indices to determine timecourse of response and optimal post-operative helmet duration.

Methods: We retrospectively analyzed laser images 13 metopic synostosis patients at Johns Hopkins Hospital treated with endoscopic craniectomy followed by helmeting. We analyzed the metopic index (MI) (midfrontozygomatic diameter / biparietal diameter) to determine timecourse of response to metopic craniosynostosis respectively. Statistical tests include Student's T-test for means and Pearson's correlation.

Results: The mean age at surgery was 2.3 months with a mean time of helmeting of 8.04 months. Mean MI was 0.44+0.05 preoperatively increased to 0.54+0.04 at maximum attained at a mean of 4.4 months. There was a statistically significant retraction of the MI from its peak to the time of helmet removal (mean= -0.03+ 0.02, 95%CI -0.04 to -0.02). After helmet discontinuation, the MI increased by 3% from an average MI of 0.51+0.05 to 0.52+0.04 at last follow up, but this was non-significant. The MI at the last follow up was significantly correlated with the peak MI (p=0.006). There was also a positive correlation between pre-op MI and peak MI.

Conclusion: Our findings demonstrate that with metopic craniosynostosis the maximum correction is reached around 4 months, with a significant retraction during further helmeting. Helmeting after peak correction did not correlate with final improved final outcome.

Marija Vasiljevic, MS 2

Mentor(s): Rachel Salas, MD
Neurology

Making Time for Sleep in a Primary Care Clinic

Authors: Marija Vasiljevic BA, Sharon Dlhosh MD, Charlene E. Gamaldo MD, Alyssa Gamaldo PhD, Peter Dziedzic MS, Rachel E. Salas MD

Background: There are approximately 6,200 board-certified sleep experts in the U.S. despite an estimated 70 million Americans who suffer from disrupted sleep. This calls for greater efforts to identify and manage patients with poor sleep at the primary care level. Therefore, the aim of this study is to evaluate the utility of MySleepScript, an iPad clinical tool for assessing sleep disturbance, in a primary care setting.

Methods: An experimental cohort of patients (n=21; 16W) at a Johns Hopkins Community Physicians practice were surveyed for potential sleep disturbances. Patients completed a battery of validated sleep questionnaires using a mobile Health platform, MySleepScript, during a regular clinic visit. Additionally, medical records were reviewed for clinical information to explore any provider evaluation or management of sleep disturbance in these patients. We then compared the medical records, with regards to sleep, of a cohort of control patients (n=60; 42W) to those of patients who completed MySleepScript.

Results: 67% of patients (n=14) who completed MySleepScript demonstrated a Pittsburgh Sleep Quality Index score of >5, falling in the "poor sleeper" range. One patient (5%) in the group that completed the tool was referred to a sleep specialist, while MySleepScript recommended a sleep specialist referral for 10 patients (48%), who identified with symptoms and risk factors worrisome for a potential sleep disorder.

Conclusion: Poor sleep quality was reported in the majority of patients using MySleepScript, supporting the importance of identifying these patients in a primary care setting. MySleepScript identified a concern for sleep disturbance(s) warranting sleep specialist referral in patients who were not identified by physician alone, suggesting this tool could capture more patients with sleep care needs in a primary care setting.

Matthew Woods, MS 2

Mentor(s): Lasya Gaur, MD
Pediatric Cardiology

MRI Analysis of Stent Fractures in COAST Trial

Authors: Matthew Woods BIS, B. Ambale-Venkatesh PhD, R. Ringel MD, J. Lima MD, L. Gaur MD

Background: Stent therapy for Coarctation of the aorta (CoA) is effective for CoA relief as shown by the prospective multicenter Coarctation of the Aorta Stent Trial (COAST). However, these stents can be susceptible to fracture and aortic stiffness may predict this complication. Aortic stiffness measures, pulse wave velocity (PWV) and aortic distensibility (AD), measured by cardiac MRI were compared in COAST participants who developed stent fractures versus those who did not.

Methods: 104 participants underwent implantation of the bare-metal Cheatham Platinum stent for CoA in COAST. 94 subjects underwent cardiac MRIs at 12 and/or 24 months following stent implantation as part of the COAST I trial. PWV and AD were analyzed using validated semi-automated aorta analysis software (ARTFUN) on phase contrast images at the level of the ascending and descending aorta. All measurements were performed blinded and only cases with adequate images were included. Comparison between groups was performed by Students t-test (for parametric variables) and the Mann-Whitney U test (for non-parametric variables). Covariate analysis was performed by the analysis of covariance (ANCOVA).

Results: Of 94 CMR studies, 57 (61%) were adequate for preliminary analysis at 12 or 24-month follow up. Mean age of participants without stent fractures (N=43) and those with (N=14) was 14.7±5.6 years vs. 19.6±10.7 years (p=0.1). PWV was not significantly different. When adjusted for age, PWV was higher in those with stent fractures (4.2±0.22 vs. 3.2±0.38; p=0.03). AD in the ascending and descending aorta is comparable.

Conclusion: Vascular profiling in CoA stent implantation may be valuable. Adjusting for age, subjects with stent fractures had evidence of increased PWV, indicative of increased wall stiffness. Additional prospective CMR studies with more subjects, uniform MRI protocols, and pre-implantation data are needed to determine whether aortic biomechanics are predictive of stent fractures and whether there are changes from baseline values prior to stent implantation.

Miguel Diaz, MS 2

Mentor(s): Uma Srikumaran
Orthopedics

Open sub-pectoral biceps tenodesis: A biomechanical comparison of interference screw and various fixation techniques

Authors: Miguel Diaz BS, Matthew Baker MD, Stephen Belkoff PhD, Uma Srikumaran MD

Background: The long head of the biceps tendon (LHB) has been implicated in multiple pathologic processes about the shoulder including: instability, SLAP tears, rotator cuff tears, and inflammation. Surgical treatment directed towards addressing LHB pathology consists of tenodesis utilizing various fixation methods. The purpose of this study was to biomechanically compare six biceps tenodesis techniques to evaluate the potential difference of anchor size, type, and configuration.

Methods: 42 fresh-frozen cadaver shoulders (mean age, 72 years [range 54 to 89 years; SD, 9.8 years]; 71% male specimens) were dissected leaving the proximal humerus, proximal biceps tendon, and pectoralis major insertion. Specimens were randomized to 1 of 6 groups and a sub-pectoral biceps tenodesis was performed. The six techniques were interference screw (IS), Endobutton (EB), double-loaded 2.9mm PEEK anchor (DL-2.9), double-loaded 1.9mm all-suture anchor (DL-1.9), single-loaded 1.7mm all-suture anchor (SL-1.7), and soft tissue tenodesis (ST). The specimens underwent load to failure axial traction on a materials testing machine. A generalized linear and latent mixed model with a random effects term was utilized to account for donor specimen pairing during analysis.

Results: The mean failure loads [95% CI] were as follows: IS group 78.6 N [58.1-99.1], ST group 100.3 N [77.7-122.9], DL-1.9 group 120.6 N [101.3-139.8], EB group 136.7 N [104.5-168.9], DL-2.9 group 141.0 N [111.3-170.7], and SL-1.7 group 142.0 N [107.9-176.1]. Failure occurred at the tendon in almost all specimens, however 5 specimens sustained anchor failure during mechanical loading.

Conclusion: The load to failure testing of the interference screw group demonstrated statistically significant lower results than the endobutton and anchor techniques (p = .04). These results may be taken into consideration when the orthopedic surgeon selects the appropriate fixation technique, while recognizing that tendon failure is likely to occur before failure of the surgical construct.

Mohammed Alkhafaji, MS 2

Mentor(s): John Carey, MD
Otolaryngology-Head and Neck Surgery

Long Term Outcomes for Surgical Treatment of Superior Canal Dehiscence Syndrome

Authors: Mohammed Alkhafaji BS, Seth E. Pross MD, Sanskriti Varma BS, Jeffrey D. Sharon MD, John P. Carey MD

Background: Superior Canal Dehiscence Syndrome (SCDS) is characterized by dizziness, imbalance, oscillopsia, autophony, and pulsatile tinnitus, along with the radiographic finding of thinning or dehiscence of the temporal bone overlying the superior canal. SCDS is treated surgically with plugging of the superior canal via middle cranial fossa approach or transmastoid approach. We set out to evaluate the long term impact of surgical treatment on the clinical manifestations of SCDS in patients treated surgically at a single tertiary referral center.

Methods: We studied the patient-reported outcomes of surgery using a 55-item web-based survey instrument distributed to adults who have undergone surgery for SCDS with at least one year of follow-up. The main outcome measure was resolution of characteristic SCDS symptoms: dizziness, imbalance, oscillopsia, tinnitus, etc., and patient-reported quality of life.

Results: 95 (43%) of 219 eligible patients completed the survey (60% female, mean (SD) age 55 (10) years). Surgery was performed predominantly by middle fossa craniotomy (91%). The mean (SD) follow-up time was 5.3 (3.65) years (range 1-20 years). Pre-operatively, the most commonly bothersome symptoms were imbalance (44%), autophony (40%), and sensitivity to loud sounds (39%). The majority of patients reported improvement in overall symptoms (95%), and quality of life (90%), while a minority reported worse symptoms (3.2%) and quality of life (8.6%). The symptoms with greatest mean improvement on a ten-point scale were autophony (6.5), pulsatile tinnitus (6.1), and sensitivity to loud sounds (5.2), while those with the least improvement were imbalance (2.4), dizziness (3.3), and headache (2.0).

Conclusion: This study represents the largest long-term follow up assessment of SCDS symptoms after surgical repair. Our results indicate a sustained benefit one year or more after the procedure for the majority of patients, with auditory symptoms showing the most significant improvement.

Moustafa Abou Areda, MS 2

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

Even if Bracing Fails to Prevent Surgery, It May Benefit the Lumbar Spine in Adolescent Idiopathic Scoliosis

Authors: Moustafa Abou Areda BA, Adam Margalit BS, Paul Sponseller MD, MBA

Background: Bracing decreases curve progression in adolescent idiopathic scoliosis (AIS). Surgeons use the Lenke-classification-system to aid in surgical decision-making by classifying curves by type (1-6), lumbar modification (A,B,C), and sagittal profile. If bracing allows fusion of fewer lumbar vertebrae, patients would have improved quality of life by retaining greater ranges of motion. We hypothesized that even if curves progressed to surgical range, braced-patients would have decreased lumbar curve magnitudes and fewer lumbar fusion levels. Our purpose was to compare the distribution of Lenke types between braced and unbraced-patients, specifically examining bracing's effects on lumbar curvature.

Methods: This is a retrospective review of surgical AIS patients seen by one surgeon from 2005-2015. Patients were identified as braced or unbraced according to Scoliosis Research Society criteria. Both groups were subdivided based on Lenke classification (Lenke 3 and 6 representing greater lumbar curve severity than Lenke 1) to compare the distribution. Lumbar modifier distributions (A,B,C: representing increasing lumbar curve severity) were examined between groups in Lenke types 1,2,3. Additionally, braced-patients were matched for age and preoperative thoracic Cobb angle, with unbraced-patients to determine differences in lumbar curve magnitude. Chi-squared and student-independent-t-tests were performed.

Results: 432 patients were studied; (n=357) unbraced vs. (n=75) braced. A significantly higher proportion of Lenke 1 patients were in the braced-group and a higher proportion of Lenke 3 and 6 patients in the unbraced-group.

After matching, unbraced-patients had a 10° (95%CI:6°-14°) larger lumbar curve compared to braced-patients (44°vs.34, p<0.001) pre-surgery. Comparing modifiers in Lenke 1 patients yielded significant differences in the proportion of Lenke 1A (81%vs.39%, p<0.001) and 1B (14%vs.39%, p=0.002) patients between the braced and unbraced-groups, respectively. Finally, unbraced-patients had 2.3 (95%CI:1.2-4.5, p=0.02) times higher odds of having fusion distal to the L1 vertebra.

Conclusion: We demonstrate an unrecognized benefit in bracing the lumbar spine that extends beyond its traditional preventative purpose.

Na Shin, MS 2

Mentor(s): Sherita Hill Golden, MD
Department of Endocrinology

The Association of Minor and Major Depression with Health Problem-solving and Diabetes Self-care Activities in a Clinic-Based Population of Adults with Type 2 Diabetes Mellitus

Authors: Na Shin, BA, Felicia Hill-Briggs, PhD, Susan Langan, MS, MPH, Jennifer L. Payne, MD, Constantine Lyketsos, MD, MHS, Sherita Hill Golden, MD, MHS

Background: Major depressive disorder (MDD) may lead to poor control of type 2 diabetes (T2DM) via impaired problem-solving and self-care behaviors; however, these associations have not been examined in minor depressive disorder (MinDD). We examined whether problem-solving and diabetes self-management behaviors differ by depression diagnosis in adults with T2DM.

Methods: We screened a clinical sample of 702 adults with T2DM for depressive symptoms and performed a structured diagnostic psychiatric interview on 52 screen positive and a convenience sample of 51 screen negative individuals. Depression diagnoses were made using Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) Text Revised criteria and categorized as MinDD (n=17), MDD (n=24), or no depression (n=62). Participants completed the Health Problem-Solving Scale (HPSS) questionnaire and the Summary of Diabetes Self-Care Activities (SDSCA) questionnaire to determine their problem-solving and T2DM self-management skills, respectively. Linear regression was used to compare the mean total and sub-category HPSS and SDSCA scores by depression diagnosis, adjusting for age, sex, race, and diabetes duration.

Results: Total HPSS scores for those with MDD (=-4.38; p<0.001) and MinDD (=-2.77; p<0.01) were lower than for those with no depression, following multivariable adjustment. Total SDSCA score for those with MDD (=-10.1; p<0.01) was lower compared to those with no depression. This association became non-significant with adjustment for total HPSS. While there was a trend toward lower SDSCA score in those with MinD (=-5.66) compared to no depression, the association was not significant in unadjusted or adjusted models.

Conclusion: Individuals with T2DM and both MinDD and MDD have impaired health problem-solving ability. Those with MDD have impaired diabetes self-management behaviors, partially explained by impaired health problem solving. Future studies should determine whether problem-solving therapy to treat MinDD patients may improve depression outcomes and whether integrated problem-solving for depression and diabetes self-management may be beneficial in those with T2DM and MDD.

Naureen Huda, MS 2

Mentor(s): Joseph Herman, MD
Radiation Oncology

Prevalences of depression and anxiety among pancreatic cancer patients and associations with survival

Authors: Naureen Huda BS, Lauren Rosati BS, Joseph Herman MD

Background: Pancreatic cancer is associated with one of the highest rates of depression among all cancers. The prevalences of depression and anxiety and their effects on survival in pancreatic cancer patients have been examined previously with varying results. Additional studies are needed to clarify the relationships between cancer and psychiatric comorbidities.

Methods: The aim of this study was to determine the prevalences of depression and anxiety among pancreatic ductal adenocarcinoma (PDAC) patients seen at Johns Hopkins Pancreas Multidisciplinary Cancer (PMDC) clinic and whether these disorders are associated with worse survival after diagnosis.

Medical records of 100 consecutive PDAC patients seen at PMDC clinic from 2006 to 2008 were retrospectively reviewed. Patients were considered to have depression or anxiety if there was record of pre-/co-existing depression or anxiety and/or depression or anxiety medications in their chart notes. Gender, race, marital status, performance status, and survival from diagnosis were recorded. Univariate analyses were performed for relevant relationships.

Results: 51 patients were male, 49 female. 88% of patients were white, 72% married, and 47% surgically resectable. 14% had evidence of depression and 16% had evidence of anxiety. Anxiety was associated with worse median overall survival from time of diagnosis (11.5 months vs. 19.7 months without anxiety, p=0.027), while depression was not (14.9 months vs. 18.0 months without depression, p=0.316).

Conclusion: The prevalences of depression and anxiety among pancreatic cancer patients observed here were lower than in other studies. It is possible that depression and anxiety are underdiagnosed in this population and/or under-recorded in patients' charts. This study presents evidence that anxiety may negatively impact pancreatic cancer patients' survival post-diagnosis. Psychiatric comorbidities should be more routinely screened for and recorded in patients' charts so that associations between such disorders and cancer can be more accurately understood and patients' care appropriately tailored. Future study will incorporate larger sample size.

Nicholas Mai, MS 2

Mentor(s): Ben Ho Park, MD PhD
Oncology

Circulating Tumor DNA and the Risk of Recurrence in Triple Negative Breast Cancer Patients

Authors: Nicholas Mai BS, Lavina Bharwani MD, Ben Ho Park MD, PhD

Background: Although adjuvant chemotherapy for breast cancer can reduce the risk of recurrence, the majority of patients (~70%) are cured with surgery alone. With the addition of adjuvant chemotherapy, this cure rates are further improved by an additional 10% to 15%. However, in this paradigm, oncologists treat virtually all breast cancer patients after surgery with chemotherapy, since there is no method for distinguishing those with minimal microscopic residual disease from those who are already cured. Therefore, circulating plasma tumor DNA should be a viable biomarker for minimal residual disease, specifically in the context of triple negative breast cancer (ER-, ER-, HER2-, a breast cancer subtype with a five year recurrence window after treatment).

Methods: In this prospective cohort study, we analyzed a collection of FFPE (Formalin-Fixed Parafin-Embedded) tumor tissue with associated blood plasma samples from 40 Singaporean patients with triple negative breast cancer (ER-, PR-, HER2-) and sequenced the tumor samples via next-gen sequencing to find trackable tumor mutations. Plasma DNA was extracted from blood plasma samples, and the plasma DNA was assessed for mutations found in the tumor using ddPCR.

Results: Of our original 40 FFPE tumor samples, 10 were deemed too degraded or low quality for analytical use. From the remaining, we've fully sequenced and tracked three patients so far (1 positive, 2 negative/equivocal for circulating tumor DNA in plasma). None of the three patients have yet recurred and are still within the 5-year window for recurrence.

Conclusion: In this prospective study, we conclude that tracking disease using a blood based assay after surgery and systemic therapies will be feasible. The ability to determine whether the presence or absence of plasma tumor DNA after standard of care therapy can predict for disease recurrence or cure, respectively, will require long term follow up of this cohort and expansion of the study

Niv Milbar, MS 2

Mentor(s): Trinity J. Bivalacqua, M.D., Ph.D.
The James Buchanan Brady Urological Institute

Intravesical Gemcitabine and Docetaxel Is a Reasonable Alternative to Early Radical Cystectomy for Select Patients with High-grade Recurrent NMIBC

Authors: Niv Milbar B.A., Max Kates M.D., Meera R. Chappidi M.P.H., Mark P. Schoenberg M.D., Trinity J. Bivalacqua M.D., Ph.D.

Background: Bacillus Calmette-Guerin (BCG) unresponsive patients with Non-Muscle Invasive Bladder Cancer (NMIBC) who prefer bladder preservation over Radical Cystectomy (RC) or are poor surgical candidates may be offered intravesical therapies. 2nd line intravesical Gemcitabine (GEM) combined with Docetaxel (DOCE) has been offered at Johns Hopkins Hospital (JHH) since 2011. Our objective was to evaluate JHH experience with GEM/DOCE, and specifically to address whether considering low-grade (LG) vs high-grade (HG) recurrence endpoints influenced our outcomes.

Methods: 33 patients who received full induction courses of GEM/DOCE since 2011 were identified in the IRB-approved JHH NMIBC database. Multivariable logistic regression determined factors associated with LG and HG recurrence. Univariable and multivariable cox proportional hazard models evaluated risk factors for all-grade recurrence-free survival (AG-RFS) and HG recurrence-free survival (HG-RFS).

Results: Median AG-RFS was 7.6 months with 42% 1-year and 27% 2-year AG-RFS. Median HG-RFS was 17.5 months with 57% 1-year and 44% 2- year HG-RFS. There were 5 LG recurrences, 11 HG recurrences, and 3 progressions. Of these, 7 patients eventually had RCs. Within initial LGTa presentation, 80% (4/5) had LG and 20% (1/5) had HG recurrence. Within initial HG-NMIBC presentation, 46% (13/28) had HG recurrence. Only in univariable cox models, LGTa presentation showed increased risk of AG-RFS (HR 3.18, 95% CI 1.08-9.40, p=0.036), but comparable HG-RFS (HR 0.32, 95% CI 0.04-2.47, p=0.275).

Conclusion: GEM/DOCE is a well-tolerated alternative to immediate RC for highly selected patients with HG-NMIBC. As anticipated, including LG recurrence as an endpoint for RFS made GEM/DOCE appear less efficacious. However, since standard of care for LG recurrence is further intravesical therapy, it may not be an appropriate endpoint, as its recurrence often does not result in RC or worse cancer outcomes. Future studies of 2nd line therapies for NMIBC should identify HG endpoints based on clinically meaningful outcomes of interest.

Rachel Kim, MS 2

Mentor(s): Daniel Sciubba, MD
Department of Neurosurgery

Posterior approaches for Symptomatic Metastatic Spinal Cord Compression

Authors: Rachel C. Kim BS, C. Rory Goodwin MD PhD, Camilo Molina MD, Benjamin D. Elder MD PhD, Nancy Abu-Bonsrah BS, Daniel M. Sciubba MD

Background: Today, surgical approaches for epidural spinal neoplasms are mostly chosen by their practicality in relation to the region of the affected spine. There are a variety of posterior approaches for spinal metastases, including laminectomy with or without instrumentation for stabilization, transpedicular corpectomy, and costotransversectomy. The goal of this review is to critically evaluate each posterior approach, considering the clinical context for which it is intended with regards to metastatic spine disease.

Methods: A systematic review of literature was performed employing PUBMED and a review of bibliographies of reviewed articles. The search query was broad and formulated to combine a number of subheadings and keywords that included the interventions and pathology of interest. The full text articles were then screened according to a rigorous inclusion and exclusion criteria.

Results: 35 total studies were evaluated as eligible and included in this review. The most common clinical outcomes reported for each surgical approach were percentage of patients with neurological improvement (NI) and proportion of patients with the ability to walk post operatively (WPO). Of the studies on posterior laminectomy, transpedicular corpectomy, and costotransvertectomy, the median NI was 71.75%, 80%, and 100%, respectively. The median WPO for each procedure was 83.5%, 81%, and 88.35%, respectively. Pain relief, surgical complication, and survival were other clinical outcomes reported on and analyzed in this review.

Conclusion: In conclusion, our recommendations are the following. Laminectomy with stabilization is recommended for improvement in neurological outcome and reduction of pain in selected patients. It is recommended that the use of laminectomy alone be carefully considered. Both transpedicular corpectomy and costotransversectomy are recommended with the expectations to improve neurological outcomes and reduce pain in properly selected patients with spinal metastases. It should be noted, however, that there was a limited number of studies available on costotransversectomy. This should be an area of future study.

Rachel Pedreira, MS 2

Mentor(s): Justin Sacks, MD
Plastic Surgery

Pre-operative Radiation Predicts Hardware Failure in Patients with Spinal Metastases

Authors: Rachel Pedreira BA, Rory Goodwin MD, Daniel Sciubba MD, Justin Sacks MD

Background: Metastatic cancer to the spine is highly morbid and associated with a poor prognosis. The spinal column is the most common site of skeletal metastases, affecting approximately 30% of individuals with cancer. Spinal tumor resection carries risk for significant morbidity and instability as a result of construct hardware failure. Our objective was to identify risk factors for hardware failure in patients undergoing resection of metastatic spinal tumors and subsequent spinal column reconstruction.

Methods: A retrospective cohort study was conducted with 159 patients status-post surgery for metastatic tumor removal in the spine. Data on demographics, tumor etiology, and peri-operative treatment was analyzed. Frequencies were compared with chi-squared testing and means were compared with one-way analysis of variance. A multivariate Cox proportional hazards model was use to elicit independent factors associated with hardware failure; factors with a p-value <0.200 on univariate analysis were in included in this model.

Results: 3 out of 159 patients (1.9%) experienced hardware failure. 37.8% of patients in the non-hardware failure group sustained pre-operative radiation therapy while 100% of the patients in the hardware failure group were pre-operatively radiated making pre-operative radiation a statistically significant predictor of hardware failure in this patient population (p=0.029). We also observed a trend for patients with longer life expectancies to experience hardware failure with a mean survival of 16.7 (± 22.6) months in failure cohort vs. 33 (± 30) months in the non-failure group (p=0.450). Finally, among the patients that experienced hardware failure, underlying primary tumor etiology was either breast (66.7%) or prostate (33.3%).

Conclusion: Pre-operative radiation may impede construct healing and increase the risk for hardware failure re-operation in patients with spinal reconstruction following tumor removal. Longer survival time along with breast and prostate cancer may also be associated with an increased risk of hardware failure in patients with metastatic disease to the spine.

Rebecca DiBiase , MS 3

Mentor(s): Alexander Hoon, MD
Neurodevelopmental Medicine

Exploring the Etiology of CAPD and Associated Risk Factors through Novel Diagnostic Tools

Authors: Rebecca DiBiase BA, Alexander Hoon MD, Joseph Pillion Ph.D, Elaine Stashinko Ph.D

Background: Central auditory processing disorders (CAPD) are characterized by clinically diagnosed hearing deficits distinct from peripheral loss. The Listening in Spatialized Noise – Sentences (LiSN-S) Test has emerged as a new diagnostic tool. It assesses speech reception threshold by creating a three-dimensional environment for the listener, whose task is to distinguish the primary sentence among competing noises. The test is divided into 5 subcategories, and we hypothesized that patients' subcategory scores vary with risk factors and comorbidities. We hope that identifying patterns between subcategory results and risk factors will elucidate the etiology of CAPD and advance comorbidity screening.

Methods: Participants were taken from a pool of children aged 7 to 17 previously diagnosed with CAPD at the Kennedy Krieger Institute in Baltimore, MD. Results on the LiSN-S subcategories were recorded, as well as a number of other demographic and clinical variables. Data were subsequently compiled and analyzed.

Results: In examining LiSN-S scores, the most notable findings were identified in the Total Advantage subcategory results. When stratified by risk factor, the mean scores in this category were significantly different between children with ADHD, ASD, academic failure, and history of encephalopathy, and their counterparts without these comorbidities. In the other test subcategories, children with comorbidities tended to have similar scores to those without them.

Conclusion: The results suggest that there is a high rate of comorbid academic failure, ADHD, ASD, and history of encephalopathy in children with CAPD. Children with these risk factors tend to score significantly lower on the Total Advantage subcategory of the LiSN-S test. This novel finding implies that the etiology of CAPD in these children may be different from other patients without these risk factors. Clinically, this can help audiologists identify children who may benefit from evaluation for other conditions that perhaps augment the social and cognitive difficulties they experience alongside their CAPD.

Rebecca Glasser, MS 2

Mentor(s): Jay Reidler, MD
Department of Orthopaedic Surgery

Sciatic nerves of Thy-1-YFP mice do not maintain fluorescence in the distal portion one week post-transection

Authors: Rebecca Glasser BA, Jay Reidler MD, Julia Retzky BA, Ryan Tomlinson PhD, Thomas Clemens PhD, Daniel Thorek PhD

Background: Transgenic Thy-1-YFP mice have fluorescently-labeled sensory nerves and are used to examine axonal development and regeneration after damage. We tested the novel application of this model to facilitate nerve identification and visualize nerve injury prevalent in surgery. This study characterizes the fluorescent behavior of these injured nerves not previously reported.

Methods: Six adult Thy-1-YFP mice underwent bilateral sciatic nerve dissection with initial data from N=7 legs. Sciatic nerves were transected. Revision dissections occurred at 1 (N=2), 2 (N=4), and 6 weeks (N=5). Fluorescent and white light (WL) images were obtained using fluorescent microscopy and Metamorph. We calculated the signal:noise (SNR), or fluorescent intensity, of proximal and distal nerve ends using ImageJ. SNR of WL images were controls. Paired t-tests were used to determine the significance of differences between nerve ends at each time point.

Results: Comparing fluorescent proximal and distal sciatic nerve ends, SNR was not significantly different during initial surgery (Mean SNR=proximal 3.6, distal 3.7, p=0.2) or 1 week revision (Mean SNR=5.3, 2.6, p=0.2). Distal nerve end fluorescence significantly dropped compared to the fluorescent proximal end during revision at 2 weeks (Mean SNR=3.8, 1.0, p=0.004) and 6 weeks (Mean SNR=3.2, 0.92, p=0.002). At 2 and 6-weeks, the fluorescent distal nerve end was not significantly distinguishable from the same nerve in WL (p=0.4, p=0.3). The SNR was not significantly different between non-fluorescent proximal and distal ends in WL (Mean SNR=1.1, 1.1, p=0.8).

Conclusion: Fluorescence of the distal end of a transected sciatic nerve decreases to control level after 2 weeks, while the proximal end persistently fluoresces. This suggests that Thy-1-YFP mice are suboptimal models to facilitate nerve identification and repair in revision cases of severed nerves, unless revision occurs within 2 weeks of the initial surgery. Future studies should analyze fluorescent properties of partially torn nerves and explore maintaining fluorescence in severed nerves.

Rebecca Glasser, MS 2

Mentor(s): Dawn LaPorte, MD
Department of Orthopaedic Surgery

The impact of conservative and surgical treatment on upper extremity specific disability and psychological state in patients with osteoarthritis

Authors: Rebecca Glasser BA, Michal McDowell BA, Lynne Jones MS PhD, Dawn LaPorte MD

Background: Trapeziometacarpal osteoarthritis (TMC OA) is nearly universal in human aging. Symptoms can be debilitating, reduce daily functionality and social participation, and are highly modulated by psychological state. TMC OA is managed by surgical and non-surgical methods, though there is currently no consensus which is preferred despite its prevalence.

Methods: We identified patients with TMC OA ICD-10 code M 18. from Johns Hopkins Department of Orthopedic Surgery from 2014-16. Through in-person (100% response) and mail recruitment (55% response), 28 participants were grouped based on receiving non-surgical or surgical TMC OA treatment. Each completed PROMIS short form questionnaires on upper extremity function (UEF), depression, and pain interference (PI). Linear regression evaluated the relationship of UEF with surgical versus non-surgical treatment, depression, PI, and radiographic severity.

Results: Mean ages of non-surgical (n=6) and surgical groups (n=22) were 69.8 years and 68.2 years, respectively, with more females in both groups (67% and 73%). Radiographic severity did not significantly impact UEF in either group (non-surgical $p=0.3$, surgical $p=0.8$). Linear regression showed no significant relationship of UEF with age, sex, race, hand affected, other hand surgery, or other hand problems. UEF significantly decreased in the non-surgical group, but not in the surgical group, as time from diagnosis ($p=0.04$, $p=0.06$) and last treatment to survey increased ($p=0.02$, $p=0.2$). Depression did not significantly impact UEF significant in both groups. However, PI significantly negatively impacted UEF ($p=0.04$, $p=0.005$). PI was not significantly modulated by the variables assessed. Despite stratifying by non-surgical versus surgical treatment, management option did not significantly influence UEF ($p=0.6$).

Conclusion: This study substantiates the ambiguity surrounding TMC OA treatment and suggests that PI most strongly correlates with UEF post-treatment, regardless of conservative management or surgery. Future prospective studies should assess changes in psychological state from TMC OA diagnosis through treatment and evaluate optimal patient candidacy for surgical treatment.

Russell Maxwel, MS 4

Mentor(s): Michael Lim, MD
Neurosurgery

BRAF-V600 mutational status affects recurrence patterns of melanoma brain metastasis

Authors: Russell Maxwell BS, Tomas Garzon-Muvdi MD, Evan J. Lipson MD, William H. Sharfman, Chetan Bettegowda, Kristin J. Redmond, Lawrence R. Kleinberg, Xiaobu Ye MD, Michael Lim MD

Brain metastasis is common and carries a poor prognosis in melanoma. A single institution, retrospective cohort of 225 melanoma patients was analyzed to determine if BRAF-V600 mutational status was associated with brain metastasis. Eighty-three of the 225 patients (37%) had BRAF-V600 mutations. At initial diagnosis, BRAF-V600 mutations were associated with younger age ($P \leq 0.001$), higher proportion of females ($P = 0.0037$), higher AJCC stage ($P = 0.030$), regional lymph node involvement ($P = 0.047$), and family history of cancer ($P = 0.044$). Compared to BRAF-WT, BRAF-V600 patients had an increased risk of brain metastasis in multivariate analysis (OR = 2.24; 95% CL = 1.10-4.58; $P = 0.027$). However, BRAF-V600 patients treated with a selective BRAF inhibitor (BRAFi) had a similar risk of brain metastasis compared to BRAF-WT patients (OR = 1.00; 95% CL = 0.37-2.65; $P = 0.98$). Moreover, treatment with BRAFi significantly prolonged the time from initial diagnosis to brain metastasis diagnosis (HR = 0.30; 95% CL = 0.11-0.79; $P = 0.015$). Compared to other tissues, the brain was the most frequent site of metastasis in BRAF-V600 patients without BRAFi (42±7%). The frequency of brain metastasis was lower in BRAF-WT and BRAF-V600 patients with BRAFi (25±4% and 25±8%, respectively). The proportion of patients with brain metastasis as the only site was 40%, 60%, and 0% in the BRAF-WT, BRAF-V600 without BRAFi, and BRAF-V600 with BRAFi groups, respectively. This study provides clinical evidence on the importance of BRAF-V600 mutations and BRAF inhibition in the progression to melanoma brain metastasis. We are currently utilizing a preclinical model to interrogate molecular mechanisms by which aberrant BRAF signaling mediates this increased brain metastasis risk.

Samantha Roman, Student in Residence

Mentor(s): Ellen Mowry, MD MCR
Neurology

Reasons for non-participation in a dietary intervention study among patients with multiple sclerosis.

Authors: Samantha Roman BS, Kathryn Fitzgerald PhD, Diane Steinbach RN, Lauren Ryan BSN RN, Ellen Mowry MD MCR

Background: Obesity and alterations in gut microbiota have been identified as risk factors for multiple sclerosis (MS), and comorbidity with metabolic syndrome diseases is associated with greater levels of MS disability, suggesting diet may play a role in MS risk and prognosis. MS patients often cite an eagerness to improve outcomes through diet modification; however, in clinical practice few patients make dietary changes, and recruitment into dietary studies is a challenge. The reasons MS patients do not participate in such studies remains largely unknown. This study evaluated the reasons why patients with MS declined participation in a dietary intervention study, and whether those who participated differed systematically from those who did not.

Methods: Patients with MS receiving monthly natalizumab infusions in the Johns Hopkins MS Center were offered participation in a 6-month trial of calorie restriction or altered calorie timing, depending on body mass index (BMI) and other eligibility criteria. Rates of and reasons for refusal to participate were documented.

Results: Of 112 eligible patients approached to date, 58 (51.8%) declined participation. There were no significant differences between those who enrolled versus declined with respect to race, sex, age, or BMI (all P>0.30). 57 patients provided a primary reason for declining participation in the study, including: being uninterested/unwilling to make diet changes (35.1%), being too busy (26.3%), wanting time to consider/maybe at next visit (17.5%), having a specific protocol/health concern (12.3%), and changing infusion center/stopping infusions during the study period (12.3%). All patients who initially said "maybe" ultimately declined participation.

Conclusion: People with MS declined participation in this dietary intervention study for many reasons. There were no notable demographic differences between patients who enrolled and those who declined participation. Considering diet may influence MS prognosis, future research should investigate strategies to improve patient recruitment and retention for dietary modification studies.

Sandeep Palepu, MS 2

Mentor(s): Dr. Narutoshi Hibino
Cardiothoracic Surgery

Surgical Tricuspid Valve Detachment (TVD) in Perimembranous Ventricular Septal Defect (VSD) Repair Has Not Shown Significant Long Term Harm to Tricuspid Valve Function.

Authors: Sandeep Palepu BA, Dr. Narutoshi Hibino MD

Background: Despite the widespread use of Tricuspid Valve Detachment (TVD) in Ventricular Septal Defect (VSD) repair for improved visualization of and access to the defect, there have been few studies that evaluate the long term effects of TVD on tricuspid valve function and residual VSD. Our objective was to determine if TVD in perimembranous VSD repair is associated with long term tricuspid regurgitation and residual VSD.

Methods: 272 patients less than 18 years of age with perimembranous VSD who underwent surgical repair at Hopkins between 1995 and 2013 were included in this analysis. 86 (31.6%) patients underwent TVD at the surgeon's discretion. Both groups had follow up echocardiography analyzed for degree of tricuspid valve regurgitation (defined as trivial, mild, moderate, and severe, assigned as 1-4, respectively, using the 2003 Journal of the American Society of Echocardiography recommendations). Intergroup differences in categorical variables (including degree of tricuspid regurgitation) were evaluated via the Fisher exact test while differences in continuous variables (such as age and weight) were evaluated with the Mann-Whitney U test.

Results: 57% of subjects were male, with a mean (SD) age of 743 (1101) days at the time of surgery. There was no significant difference in age between TVD and non-TVD. Mean (SD) follow-up time to echocardiography was 7.5 (5.2) years post-operation. There was no significant difference in degree of tricuspid regurgitation in subjects with and without TVD with the mean degree of tricuspid regurgitation of both groups falling within the trivial to mild range ($p = 0.54$). 12.7% of TVD subjects and 16.8% of non-TVD subjects have a residual VSD post-operatively, a nonsignificant difference across groups ($p = 0.64$).

Conclusion: Those who underwent TVD have demonstrated no significant limitations to tricuspid valve function with no significant difference in residual VSD, suggesting that TVD is a safe and efficacious technique for VSD repair in the long term. However, this is observational and a prospective trial would be required to definitively demonstrate the safety and efficacy of the detachment approach.

Sanskriti Varma, MS 2

Mentor(s): Clare Lee, MD
Department of Endocrinology

Weight Regain in Patients with Symptoms of Post-bariatric Surgery Hypoglycemia

Authors: Sanskriti Varma, Jeanne M. Clark, Thomas Magnuson, Michael Schweitzer, Kimberly Steele, Todd T Brown, Clare J. Lee

Background: Weight regain and symptoms of postprandial hypoglycemia have been observed in a subset of post-bariatric surgery (PBS) patients. Hypoglycemic symptoms may be an important driver of increased caloric intake in PBS patients, thus contributing to weight regain (WR). This study aims to determine whether PBS patients with hypoglycemic symptoms are at increased risk for WR.

Methods: Patients who underwent Roux-en-Y gastric bypass (RYGB) or vertical sleeve gastrectomy (VSG) at the Johns Hopkins Center for Bariatric Surgery from Aug2008-Aug2012 were mailed a survey, from which weight and hypoglycemic symptoms were assessed. Percent WR was calculated and compared between dates of survey completion and postoperative year 1. Multivariable logistic regression was used.

Results: Of 1119 patients, 428 (38.2%) respondents were eligible for analysis. WR was observed in 79.2% (N=339), while 20.8% (N=89) had no WR or weight loss at a mean of 29 ± 14 months. Those who had WR showed median (IQR) WR of 10.8% (5.6,19.4). Compared to those who did not regain, patients with WR over 5.6% were more likely to report PBS hypoglycemic symptoms (OR=1.73, 1.05-2.86), less likely to maintain nutritional adherence (OR= 0.43, 0.28-0.68), reported longer time since postop year 1 (OR=1.06, 1.05-1.08). Age, gender, race, surgery type, pre-existing diabetes, preoperative BMI, and weight loss were not significantly associated with WR. Among those who always/very often maintained nutritional adherence the interaction between WR and hypoglycemic symptoms remained strong (OR = 2.50; 95% CI: 1.18-5.28). When including patients who never/rarely/sometimes maintained nutritional adherence, the association between WR and hypoglycemic symptoms was no longer significant (OR = 1.35; 95% CI: 0.68-2.70).

Conclusion: Weight regain was common in PBS patients with hypoglycemic symptoms and in those who with longer time since surgery and lower nutritional adherence. Further studies are warranted to elucidate the role of hypoglycemia among other risk factors in PBS weight regain.

Shamsudini Hashi, MS 2

Mentor(s): Daniel Sciubba, MD
Neurological Surgery

Management of Extranodal Lymphoma of the Spine: A Study of 30 Patients

Authors: Shamsudini Hashi, BS, C. Rory Goodwin, MD, PhD, A. Karim Ahmed, BS, Daniel M. Sciubba, MD

Background: Patients with lymphoma involving the spinal column (5.8% and 6.5% in Hodgkin and Non-Hodgkin, respectively) may present with pain, neurological compromise, or loss of spinal integrity. We aim to compare the clinical presentation, treatment, and outcomes of patients who underwent either nonsurgical or surgical intervention.

Methods: The medical records of 30 patients with spinal lymphoma from 03/2006 to 08/2015 were retrospectively reviewed for demographic information, presenting characteristics, treatment, ambulatory status, neurological function, pain medication use, and survival. Patients with any duration of follow-up having sufficient information were included in this study.

Results: This study cohort was comprised of mostly male individuals in their 6th-7th decade of life. Non-Hodgkin lymphoma accounted for 93% of cases with these lesions having a propensity for the thoracolumbar spine. Eleven patients (37%) were managed nonsurgically, and 19 (63%) underwent surgery (84% had an unknown diagnosis at time of surgery). The median length of follow-up was 16 and 3 months for the nonsurgical and surgical groups, respectively. The surgical group had a lower baseline Karnofsky performance score (p=0.024), but the presenting characteristics were similar among the two groups. All non-ambulatory patients underwent surgery in an attempt to restore ambulation. In both groups, all ambulatory patients remained ambulatory at their last known follow-up. All living patients saw an improvement or a preservation of neurological function at one year, regardless of treatment. Narcotic use was prevalent in both groups at all measured time points. The overall mean survival was 87.6 months with no significant difference between treatment groups (p=0.256).

Conclusion: Although, no statistically significant difference was found in terms of presentation, pain medication use, preservation of neurological function, or survival between the two groups, this likely reflects the small cohort of patients in this study. Future multi-center prospective studies on patients with clear surgical indications are needed to provide further information.

Sophia Chen, Student in Residence

Mentor(s): Daniela Molena, MD
Surgery

Post-Discharge Complications after Esophagectomy Account for High Readmission Rates

Authors: Sophia Y. Chen, BS, Daniela Molena, MD, Miloslawa Stem, MS, Benedetto Mungo, MD, Anne O. Lidor, MD, MPH

Background: Little is known about post-discharge complications (PDC) after esophagectomy. We sought to identify the rates of PDC, associated risk factors, and their influence on early hospital outcomes.

Methods: We used the 2005-2013 American College of Surgeons National Surgical Quality Improvement Program database to identify patients ≥ 18 years of age who underwent an esophagectomy. The primary outcome was PDC, and secondary outcomes were hospital readmission and reoperation. A modified Poisson regression analysis was used to identify risk factors associated with developing PDC, and risk ratios were estimated.

Results: 4,483 total patients were identified, with 8.9% developing PDC within 30-days after esophagectomy. Patients who experienced complications post-discharge had a median initial length of hospital stay of 9 days; however, PDC occurred on average 14 days following surgery.   Patients with PDC had greater rates of wound infection (41.0% vs. 19.3, $p<0.001$), venous thromboembolism (16.3% vs. 8.9%, $p<0.001$), and organ space surgical site infection (17.1% vs. 11.0%, $p=0.001$) than patients with pre-discharge complication. The overall readmission rate was 19.1%. PDC patients were overwhelmingly more likely to have a reoperation (39.5% vs. 22.4%, $p<0.001$) and readmission (66.9% vs. 6.6%, $p<0.001$). BMI 25-29.9 and BMI ≥ 30 were associated with increased risk of PDC compared to normal BMI (18.5-25), while prolonged length of stay and pre-discharge complication were associated with decreased risk of PDC.

Conclusion: PDC after esophagectomy account for a significant number of reoperations and readmissions. Adopting best practices to reduce common PDC like venous thromboembolism and infection, and performing interventions for higher-risk individuals such as those with higher BMI, should be considered. Because longer hospital lengths of stay may decrease the risk of developing PDC in esophagectomy patients, efforts that emphasize shorter hospital lengths of stay should be reevaluated, with more energy directed towards optimizing patient health prior to discharge instead.

Taylor Purvis, MS 2

Mentor(s): Daniel M. Sciubba
Neurosurgery

The Effect of Renal Dysfunction on Short-Term Outcomes after Lumbar Fusion

Authors: Taylor E. Purvis, BA, Remi A. Kessler, Christine Boone, BS, Benjamin D. Elder, MD/PhD, C. Rory Goodwin, MD/PhD, Daniel M. Sciubba, MD

Background: Chronic kidney disease, indicated by preoperative HD use or low GFR, is associated with poor clinical outcomes following spine surgery. It is unknown whether this holds true for lumbar fusion patients nationwide or if similar trends are observed using creatinine as a marker of renal dysfunction.

Methods: Baseline and outcome data were obtained from the 2005-2014 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database for patients under the age of 18 who underwent non-emergent lumbar fusion surgery. Preoperative HD status and GFR and creatinine levels were extracted. Variables analyzed included development of at least one complication, development of a major complication, in-hospital mortality, and length of stay.

Results: A total of 29,136 patients were identified; 55 (0.19%) with preoperative HD, and 29,081 (99.81%) without. Preoperative HD was not significantly associated with development of any one complication (OR, 1.900; 95% CI, 0.880-4.103; P=0.102) or major complication (OR, 2.019; 95% CI, 0.710-5.737; P=0.187). Among patients without HD, those with severe preoperative kidney dysfunction as estimated by GFR were more likely to develop a complication (GFR=15-30 ml/min/1.73m2; OR, 3.82; 95% CI, 2.061-7.082; P=<0.0001 and GFR=30-45 ml/min/1.73m2; OR, 2.124; 95% CI, 1.506-2.996; P<0.0001). Compared to patients with normal preoperative creatinine levels (0.75-1.0 mg/dL), patients with elevated creatinine were more likely to develop at least one complication.

Conclusion: Patients using HD preoperatively did not have higher odds of developing complications than non-HD users. Among non-HD users, those with low estimated GFR and elevated creatinine levels were more likely to have perioperative complications.

Taylor Purvis, MS 2

Mentor(s): Daniel M. Sciubba
Neurosurgery

Short-term outcomes after external fixation versus surgical fusion for cervical spine fractures without spinal cord injury in pediatric patients

Authors: Taylor E. Purvis BA, Rafael De la Garza-Ramos MD, Nancy Abu-Bonsrah BS, C. Rory Goodwin MD, PhD, Mari L. Groves MD, Michael C. Ain MD, Daniel M. Sciubba MD

Background: Pediatric cervical spine injuries without spinal cord injury can be treated using either surgical fusion or halo vest immobilization. Despite widespread use of these two treatment options, no studies within the pediatric population have compared outcomes by injury location or addressed this issue using national data. We used the Nationwide Inpatient Sample (NIS) to compare in-hospital complication rates following either surgical fusion or external fixation in pediatric patients with atlantoaxial and subaxial injuries.

Methods: Baseline and outcome data were obtained from the 2002-2011 NIS for patients under the age of 18 with a diagnosis of cervical spine fracture without spinal cord injury or cervical spine subluxation. Patients who underwent halo immobilization or internal fixation were included for analysis. Variables analyzed included length of stay, in-hospital mortality, discharge disposition, total hospital charges, and development of at least one in-hospital complication.

Results: A total of 2,878 pediatric patients with cervical spine injury were identified; 1,462 patients (50.8%) with atlantoaxial (C1-2) injury and 1,416 (49.2%) with subaxial (C3-7) injury. Among atlantoaxial injury patients, halo fixation was associated with lower total charges ($73,786 vs. $98,158, p=0.040) and a lower likelihood of developing at least one complication (1.9% vs. 6.8%, p=0.029) compared to surgical fusion, and was a more common treatment for subluxation alone (16.4% vs. 2.6%, p<0.001). Among subaxial injury patients, there were no significant differences in total charges (p=0.142), complication occurrence (p=0.334), or length of stay (p=0.196). Subaxial subluxation injuries alone were treated more often with surgical fusion (2.2% vs. 1.2%, p<0.001).

Conclusion: Pediatric patients with atlantoaxial injury may warrant initial consideration of external fixation due to lower overall complication rates and decreased cost. Future studies are necessary to examine whether similar outcomes are found in pediatric patients with simultaneous spinal cord injury.

Taylor Purvis, MS 2

Mentor(s): Daniel M. Sciubba
Neurosurgery

Impact of Smoking on Postoperative Complications after Anterior Cervical Discectomy and Fusion

Authors: Taylor E. Purvis, BA; Haroldo J. Rodriguez; A. Karim Ahmed, BS; Christine Boone, BS; Rafael De la Garza-Ramos, MD; Benjamin D. Elder, MD, PhD; C. Rory Goodwin, MD, PhD; Daniel M. Sciubba, MD

Background: The relationship between smoking and the risk of postoperative complications among anterior cervical discectomy and fusion (ACDF) patients remains uncertain.

Methods: Baseline and outcome data were obtained from the 2005-2014 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database for patients under the age of 18 who underwent non-emergent ACDF surgery. Information on current smoking and ever-smoking status was extracted. Outcomes included development of at least one complication, development of a major complication, in-hospital mortality, and length of stay.

Results: ACDF patients were either current smokers (7,847, 30.3%) or not current smokers (18,022, 69.7%); 33.0% of all patients (n=8542) had ever smoked. Current smoking status was not associated with increased odds of any one complication (P=0.584) or any major complication (P=0.138). In addition, using the number of pack-years as the primary independent variable, multivariate logistic regression analysis revealed that the number of pack-years was not significantly associated with greater odds of developing any one complication (P=0.276) or any major complication (P=0.334). However, ever-smoker status did present significantly higher odds of any major complication (OR, 1.333; 95% CI 1.007-1.764; P=0.044) than for non-smokers.

Conclusion: Current smoking status is not associated with postoperative complications among ACDF patients, and there is no relationship between the number of pack-years and the odds of developing any one complication or any major complication. These results suggest that any patient with a prior smoking history should be considered a higher risk surgical candidate when attempting ACDF.

Taylor Purvis, MS 2

Mentor(s): Dr. Richard Skolasky, ScD
Orthopaedics

Crosswalking GAD-7 and PHQ-8 to the PROMIS Anxiety and Depression Health Domains among Patients Presenting for Spine Surgery

Authors: Taylor E. Purvis, BA, Brian J. Neuman, MD, Lee H. Riley, III, MD, and Richard L. Skolasky, ScD

Background: Psychological distress is a risk factor for poor spine surgery outcomes. It is unknown whether the PROMIS instrument is a reliable alternative to the Generalized Anxiety Disorder 7-item scale (GAD-7) and Patient Health Questionnaire 8-item depression scale (PHQ-8) questionnaires for assessing anxiety and depression in patients before spine surgery.

Methods: Adults undergoing spine surgery at one institution from 2015 to 2016 completed the GAD-7 questionnaire, PHQ-8 questionnaire, and PROMIS anxiety and depression domain computer adaptive tests preoperatively. Published crosswalk tables were used to estimate PROMIS scores on the basis of GAD-7 and PHQ-8 scores. Statistical significance was accepted as $P<0.05$.

Results: Included in the study were 399 cervical and lumbar spine surgery patients. Correlation calculations were moderately strong between PROMIS anxiety and GAD-7 crosswalked scores ($r = 0.73$; $P < 0.0001$; intraclass correlation coefficient = 0.69) and between PROMIS depression and PHQ-8 crosswalked scores ($r = 0.72$; $P < 0.0001$; intraclass correlation coefficient = 0.73). The intraclass correlation coefficient of 0.69 suggests low consistency between scores. For the GAD-7 and PHQ-8, 86% of patients (for both) were classified in identical dichotomous symptom severity categories by the directly derived and crosswalked PROMIS scores. Bland-Altman plots show that for GAD-7 versus crosswalked PROMIS anxiety scores, the mean bias was −1.15 and the 95% limits of agreement were −15.4 and 13.1. For PHQ-8 versus crosswalked PROMIS depression scores, the mean bias was −2.55 and the 95% limits of agreement were −16.7 and 11.6.

Conclusion: PROMIS effectively screens for depression and anxiety in patients undergoing spine surgery. Traditional GAD-7 and PHQ-8 scores can be effectively translated to PROMIS scores.

Taylor Purvis, MS 2

Mentor(s): Dr. Richard L. Skolasky, ScD
Orthopaedics

Concurrent Validity and Responsiveness of PROMIS Health Domains Among Patients Presenting for Spine Surgery

Authors: Taylor E. Purvis, BA, Shalini Selverajah, MD, Elena Andreou, Brian J. Neuman, MD, Lee H. Riley, III, MD, and Richard L. Skolasky, ScD

Background: Patient-Reported Outcomes Measurement Information System (PROMIS) health domains (anxiety, depression, fatigue, pain, physical function, satisfaction with participation in social roles, and sleep disturbance) may measure quality of care and determine minimal important differences (MIDs) after spine surgery. We examined the concurrent validity of PROMIS domains before and the responsiveness and PROMIS domain MIDs after surgery.

Methods: We included 368 adults undergoing surgery for degenerative spine conditions at 1 academic spine center from February 2015 through June 2016. Concurrent validity was determined by correlations of PROMIS domains with legacy measures assessed preoperatively. Responsiveness of PROMIS domains was determined using distributional-based, cross-sectional anchor-based, and longitudinal anchor-based criteria (preoperative to postoperative change, within 6 months) anchored to the North American Spine Society Patient Satisfaction Index criteria. Statistical significance was accepted as $p < 0.05$.

Results: All PROMIS domains showed moderate to strong correlations with Neck Disability Index, Oswestry Disability Index, Medical Outcome Study Short Form-12 mental health component, and Brief Pain Inventory pain interference; and weak correlations with intensity of back/leg pain and neck/arm pain (except between PROMIS pain and neck pain [$r = 0.53$, $p < 0.05$]). PROMIS domains were well-correlated with Generalized Anxiety Disorder-7 and Patient Health Questionnaire-8 except physical function and satisfaction with social roles, which showed weak correlations. The PROMIS pain domain showed strong responsiveness ($r = -0.95$); satisfaction with social roles ($r = 0.76$), physical function ($r = 0.57$), anxiety ($r = -0.54$), sleep disturbance ($r = -0.59$), and fatigue ($r = -0.60$) showed moderate responsiveness. Depression ($r = -0.37$) had weak responsiveness. PROMIS domain MIDs were 5–6 points.

Conclusion: PROMIS domains are a valid assessment of health in this population and were responsive to postoperative improvements in symptoms and quality of life.

Trevor Davis, MS 3

Mentor(s): Mohammad A. Bashir, MD
Division of Cardiothoracic Surgery, Department of Surgery, University of Iowa Hospitals and Clinics

Clinical Implications for High-Risk Surgical Patients with Infective Endocarditis

Authors: Trevor A. Davis BS, Kalpaj R. Parekh MD, Jay K. Bhama MD, Domenico Calcaterra MD PhD, Mohammad A. Bashir MD

Background: Infective endocarditis (IE) is associated with high morbidity and mortality. We aimed to determine the utility of the Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAPS) II in predicting patients at risk for all-cause 30-day mortality.

Methods: A hospital-based nested case-control study was performed, which included 92 surgically treated IE patients (SIEP) and 79 medically treated IE patients (MIEP) from a prospectively maintained database of patients who had clinically confirmed IE according to the modified Duke criteria between 2010-2014. APACHE II and SAPS II were calculated for patients admitted to the ICU at time of initial hospital presentation. Logistic regression was used to analyze factors associated with APACHE II, SAPS II, and all-cause mortality.

Results: High APACHE II score was associated with increased 30-day mortality (p=0.008). For a score of ≥12 (70 patients), mortality was 53.2%. For each 5-point increase in APACHE II, an 18.9% (95% CI 7.7-31.1; p=0.0007) increase in discharge creatinine was found. For SIEP, an APACHE II ≥12 was associated with longer cardiopulmonary bypass time (178.5 minutes versus 130.5 minutes; p=0.008) and longer aortic cross-clamp time (132 minutes versus 103 minutes; p=0.022). Focusing solely on SIEP, no statistically significant association was found between APACHE II and 30-day mortality. For all patients, higher SAPS II score was associated with greater mortality (p= <0.0001). In addition, higher SAPS II was associated with longer duration of inotropic support (p=0.039), longer duration of intubation (p=0.044), longer ICU stay (p=0.0006), and higher creatinine level at discharge (p=0.0004). A SAPS II ≥18 for SIEP was associated with greater mortality compared to scores ≤18 (37% [23/62] versus 17% [5/30]; p=0.046).

Conclusion: APACHE II and SAPS II scores have the ability to predict 30-day all-cause mortality. SAPS II is a predictor of operative mortality and should be emphasized is assessing surgical risk.

ETHICS AND THE ART OF MEDICINE POSTER ABSTRACTS

Listed Alphabetically (First Name)

Amar Deshwar, MS 2

Mentor(s): Daniel Laheru, MD
 Skip Viragh Center for Pancreas Cancer

Understanding the Diagnostic Delay in Patients with Pancreatic Cancer

Authors: Amar Deshwar BSc, Deirdre Torto MHA, Daniel Laheru MD

Background: Pancreatic cancer (PC) is estimated to become the second leading cause of cancer death in the US by 2020. While surgery is the only curative option, only 20% of PC is resectable at diagnosis due to local extension or metastasis. Therefore, early detection is thought to be an important determinant of survival. We sought to understand the time and resources expended in diagnosing PC, and determine whether these could be correlated with receiving surgical resection.

Methods: A retrospective EMR analysis of patients seen for pancreatic adenocarcinoma at Johns Hopkins in 2014 was conducted. Patients were divided into two categories: initial treatment of surgery (S) or non-surgical treatment with chemotherapy or radiation (NS). "Time to diagnosis" was the time in days from first medical presentation until diagnosis of PC. "Diagnostic tests" included all forms of imaging, biopsies, and surgeries that took place from the first medical presentation till the day treatment began.

Results: Of 120 patients, 41 were in the S cohort, while 79 were in the NS group. The mean time to diagnosis was 30.4 days for S and 64.5 days for NS ($p < .05$). There was no significant difference in mean time from diagnosis to start of treatment: 26.8 days (S) and 32.9 days (NS). The mean number of diagnostic tests was 8.5 (S) and 10.7 (NS) ($p < .05$).

Conclusion: On average, PC patients treated surgically had a shorter time to diagnosis and underwent fewer diagnostic tests than those patients who were treated with either chemotherapy or radiation. These data, which may suggest that diagnostic delay of PC leads to worse outcomes, could help inform which diagnostic routes are most efficient. Further analysis on the diagnostic tests performed may provide insight into how to improve time to diagnosis and ultimately reduce mortality of this devastating disease.

Conisha Cooper, MS 2

Mentor(s): Jenell Coleman, MD, MPH
Obstetrics and Gynecology

Clinicians' Personal Experience of Trauma and its Impact on Screening Female Patients for Trauma

Authors: Conisha Cooper, BA, Denis Antoine, MD, Amy S. D. Lee, DNP, ARNP, WHNP-BC, Nathan Irvin, MD, Jenell Coleman, MD, MPH

Background: Physical and sexual trauma can impact the health of patients, yet screening rates are low. Factors associated with screening behavior are not well understood. We sought to determine whether clinicians' personal experience of physical or sexual trauma was associated with screening their female patients for trauma.

Methods: We conducted an online survey of 1648 physicians and nurses at a single academic institution. Self-reported screening of female patients was assessed using a 5-point Likert scale from 1 (never) to 5 (always). Separate validated tools were used to assess physical and sexual trauma. Descriptive and univariate statistics were performed.

Results: Among 212 survey respondents, 78% were female and the median was age 40.8 ([interquartile range] 32-48). The majority were white (74.5%) and were nurses (42%). Respondents were from the following disciplines: Ob/Gyn (30.2%), Emergency Medicine (34.0%), Psychiatry (23.6%) and Primary Care (12.3%). The median screening score was 3.9 (3.4-4.3). Overall, 71.7% of clinicians reported a personal history of sexual and/or physical trauma. There were no significant differences in screening scores between those with a personal history of trauma (3.9, [3.5-4.3]) vs no history of trauma (3.8 [3.3-4.3], p=.76). Greater number of years in practice was associated with higher screening scores (p=.02), as was having a departmental screening policy (p<.001). Scores were significantly higher in Ob/Gyn (4.2 [3.9-4.4]) vs Emergency Medicine (3.66 [3.3-3.9], p<.001) and Primary Care (3.7 [3.1-4.1] p=.007). There were no differences between nurses and physicians (p=.25).

Conclusion: The prevalence of personal history of trauma was high among our clinician cohort but this history of trauma was not associated with clinician screening behavior. Future research should explore why screening scores were higher in Ob/Gyn, and successful strategies should be disseminated and implemented within other disciplines. Additionally, all departments may want to implement a screening policy to standardize practice.

Faisal Chaudhry, MS 2

Mentor(s): Teresa Johnson, PhD
Health Sciences Informatics

Does Lecture Attendance Impact Undergraduate Medical Student Exam Performance?

Authors: Faisal Chaudhry BA, Harry Goldberg PhD, Teresa Johnson, PhD

Background: The impact of in-person lecture attendance on exam scores in undergraduate medical education is not well understood. The goal of this study was to determine whether and why there was a difference in test performance between undergraduate medical students who attend optional lectures live versus those who watch recorded lectures online.

Methods: We tracked the live attendance, recorded lecture viewership, and exam scores of 115 first year medical students at JHUSOM over 10 weeks during their Neurosciences (NSS) and Psychiatry (BMB) courses. In addition, a survey assessing students' compliance with study methods and reasons affecting their lecture attendance habits was collected. Finally, pre-tests for both courses were administered to control for students' prior knowledge in the course material.

Results: While recorded lecture viewership statistics have not yet been delivered to the study team, preliminary results indicate little correlation between live lecture attendance and corresponding exam scores during that course (for NSS $r=0.18$, $p=0.05$; for BMB $r=0.12$, $p=0.20$). There was a clear temporal trend, with fewer students attending live lectures as the courses progressed. Contrary to prior research, significant gender differences did not exist either in the correlation between exam scores and live attendance or in the reasons why students chose to attend lectures.
The survey indicated only 2 students believed their exam scores would increase as a result of attending live lectures. The most commonly cited reason students chose to attend live lectures was "to keep on a structured schedule" (55%), while the most common reason not to attend live lectures was to "save time watching lecture recordings at a faster speed" (69%).

Conclusion: We conclude there is little to no relationship between in-person lecture attendance and exam scores in these two courses. Future studies should be performed longitudinally to investigate if this holds true over the entire medical school curriculum.

Jane Long, MS 2

Mentor(s): Dr. Margaret Chisolm
Psychiatry and Behavioral Sciences

An Observation

Authors: Jane Long MFA, Margaret Chisolm MD

Background: The medical gaze constitutes a physician's ability to identify signs of a disease process. The signs a physician uses to make a diagnosis depend on a physician's subjectivity, including their own sensations, perceptions, and experiences. The idea that subjective perceptions can inform an ultimately objective determination generates an interesting tension. This project aimed to explore how disease is diagnosed, presented, and understood through experimental film.

Methods: Twenty people from various backgrounds were interviewed about their experiences of being a patient, either presently or in the past. Participants were recruited from various cities in the United States via posters, social media, and online listings. Anyone who was 18 years or older, had the capacity to consent, and had been or is currently a patient was eligible to participate. The interviews were conducted and documented via video, audio, and or written responses.

Eight additional interviews were conducted with professionals from various fields related to medicine and the history of medicine. These professionals included artists, writers, and physicians.

Archival materials on the history of how illness and patients were presented, depicted, and diagnosed were viewed at the Mutter Museum, the Cushing Center at Yale, the Morbid Anatomy Museum, and the Countway Library of Medicine. Materials included objects, records, correspondences, drawings, etc.

Results: Most of the film's audio and visuals, which included staging of scenes, 3D models, photographs, animations, and a score, drew inspiration from the interviews and archival materials. For some parts of the film, the archival material and interviews were directly incorporated and presented.

Conclusion: A non-linear exploration of ideas about how patients, diseases, and illnesses are diagnosed, presented, and understood, revealed the priorities and foci of the medical gaze and observation. By presenting what is seen, a story of what the medical gaze and observation fails to see was revealed.

Jennifer Plotkin, MS 2

Mentor(s): Robert Shochet, MD
School of Medicine

Needs Assessment for First Year Medical Student Empathy Lab

Authors: Jennifer Plotkin BS, Robert Shochet MD

Background: Teaching empathic communication is an important medical education goal. At JHUSOM, first year students learn this skill through the Clinical Foundations of Medicine (CFM) course. The purpose of this study was to conduct a needs assessment to inform the development of a 60-90 minute empathy lab curriculum for year one students during CFM to support the development of empathic communication skills.

Methods: The needs assessment consisted of two parts: four focus groups with course stakeholders and a review of student performance data in interpersonal communication. The focus groups consisted of two groups of first year medical students who completed the CFM course (total n = 13), one group of 7 standardized patients and one group of 7 volunteer outpatients. Focus group transcripts were independently coded and iteratively reviewed to identify major themes. For the quantitative data, we analyzed aggregate CFM student performance data on SP-scored interpersonal scales (IPS) for two different CFM clinical examinations from 2013-2015.

Results: Themes derived from the student focus groups were categorized into learning challenges, growth during the course, and communication strategies. Students struggled with being vulnerable and anxious while interviewing. Strategies and circumstances that lowered anxiety resulted in successful patient interactions and improvement. Students' perspective on empathy became more consistent with their learning group. Patients described what they value in empathic interactions including displaying vulnerability and communicating empathy nonverbally as "leaning in". Students emphasized verbal content while patients prioritized nonverbal communication. Preliminary quantitative data analysis did not reveal a statistically significant improvement in CFM scores on empathy-related questions between October and December.

Conclusion: Students' major challenges stemmed from showing vulnerability and interviewing anxiety. Patients valued nonverbal student cues. Training in empathic communication for early medical students should address both students' sense of vulnerability and anxiety and cultivate powerful nonverbal expression.

Jenny Wen, MS 2

Mentor(s): Anika Alvanzo, MD
General Internal Medicine

Trauma Informed Care Needs Assessment of Internal Medicine Residents

Authors: Jenny Wen BA, Colleen Christmas MD, Anika Alvanzo MD

Background: In the US, 60-90% of adults have experienced trauma, defined as an event or series of events (such as abuse, loss, or chronic stressors) that negatively affect health. Trauma exposure is strongly associated with proportional increases in chronic diseases, behavioral health disorders, and risky behaviors. We aimed to examine the knowledge, attitudes, and perceived skills of Internal Medicine residents regarding managing patients with histories of trauma, as well as residents' desires for additional training in Trauma Informed Care (TIC).

Methods: We conducted an online survey of residents enrolled in 4 Internal Medicine programs in Baltimore, Maryland to assess the following behaviors: recognizing, screening, managing, and referring patients with trauma histories. Items addressed residents' knowledge, attitudes, self-assessed preparedness, and close personal experiences with trauma. Nonparametric tests (Kruskal-Wallis, Fisher's exact, and Wilcoxon rank sum) were used for analysis.

Results: 168 residents responded to the survey (54%), of whom 44% were female, 55% White, 28% Asian, 4% Black and 13.2% unknown/other. Knowledge and preparedness were very limited. 83% percent of respondents underestimated trauma prevalence; 31.7% felt inadequately prepared to appropriately respond to positive disclosures; and 91.8% wished for additional training on trauma and trauma informed care. Factors significantly associated with higher frequency of screening patients include greater perceived preparedness to identify, respond to, and refer patients (p =.0001 –.012); familiarity with referral resources (p=.005); comfort in discussing trauma with patients (p =.003); and perceived faculty (p =.001) and workplace support (p =.038). Differences among genders, years in training, and program sites were minimal.

Conclusion: Internal Medicine residents in Baltimore feel unprepared in identifying, responding to, managing, and referring patients with histories of trauma. Knowledge about prevalence and risks for comorbidities was very limited. Our results support the need for integration of trauma and Trauma Informed Care training into graduate medical education for Internal Medicine residents.

Kiley Hunkler, MS 2

Mentor(s): Gail Geller, ScD, MHS
Berman Institute of Bioethics

Ethical Considerations of Military Physicians as Officers and Providers

Authors: Kiley Hunkler, BS, MSc, MSt; Gail Geller, ScD, MHS

Background: Military physicians face unique challenges arising from dual roles as officers and clinicians. A 2015 review by the Assistant Secretary of Defense for Health Affairs found that the Department of Defense "would benefit from a common baseline education and training requirement in medical ethics". This project serves as a needs assessment for creating standardized ethical training for military physicians.

Methods: We conducted an online survey of all medical students attending Basic Officer Leader Course (N=250) to assess their knowledge of and attitudes toward military medical guidelines, and their opinions about relevant hypothetical ethical scenarios for which no guidelines exist. Standard statistical methods were used for analysis.

Results: 54 military medical students completed the survey (22%). 35% correctly responded to at least 4 out of 5 ethical vignettes according to current military regulations. Most respondents were knowledgeable about medical discretion principles (80%), triage guidelines (70%), and physicians' duty to provide care despite personal reservations concerning the conflict (83%). 56% of respondents were aware of tight restrictions on military physicians' involvement in interrogations (prior military ethical training significantly improved knowledge, p=0.04), and 41% understood nuances of commander's authority in hunger strikes. Respondents' attitudes toward current regulations were generally favorable, but 63% disagreed with prioritizing medical necessity over combatant or national status during triage. Regarding ethical scenarios without guidelines, most respondents emphasized detainees' right to health care and American Soldiers' autonomy in refusing certain vaccines.

Conclusion: Ethical training for future and current military physicians (even those with prior military service) is necessary and should focus on triage complexities and knowledge gaps among military medical students, such as interrogation limits and commander's authority. Significant differences between those with and without prior ethics exposure suggest that standardized ethical training will improve knowledge. Future research should explore what drives agreement with regulations and address issues of soldier-patient autonomy.

HISTORY OF MEDICINE
POSTER ABSTRACTS
Listed Alphabetically (First Name)

Jason Theis, MS 2

Mentor(s): Randall Packard
Department of the History of Medicine

Bloodless Injuries: Emphasizing Combat Narratives Limits Military Veteran Access to Care for Posttraumatic Stress Disorder

Authors: Jason Theis

Background: Posttraumatic stress disorder (PTSD) is a hallmark injury of the ongoing Global War on Terrorism (GWoT) despite its low incidence compared to previous conflicts, yet 30 percent of veterans who meet the diagnostic criteria for PTSD go untreated. This paper argues that the inability of veterans to access care is in part the result of patient advocate groups constructing the narrative of PTSD as a combat-centric disorder. This narrative consequently reduces attention to non-combat stressors, which account for a fifth of all reported PTSD cases among veterans in the Millennium Cohort Study. This paper explores the history of these patient advocate efforts and how they have contributed to the underappreciation and lack of care for PTSD precipitated by non-combat stressors.

Methods: A systematic review of ad campaigns sponsored by veteran service organizations and the VA, and congressional transcripts from 1970 to 2016 were used to identify the major themes that appeared in lobby efforts on behalf of veterans with PTSD.

Results: Combat exposure is the major narrative used to promote the patient experience of veterans with PTSD from the Vietnam Era to present. Little emphasis has been placed on traumatic experiences such as sexual assault and non-combat stressors despite their historical prevalence in military settings. Care providers have expressed concerns regarding PTSD over-reporting, and have historically questioned the validity of non-combat stressors as malingering or symptom misrepresentation by the veteran for personal benefit.

Conclusion: The link between combat exposure and PTSD is well supported. However, the primary narrative suggesting that all cases of PTSD result from combat exposure overshadows other non-combat traumatic exposures that occur in a military setting. The emphasis on combat exposure by patient advocates creates a restricted frame that can act as a barrier to care, and lead to implicit biases in peers, unit leaders, and health care providers.

Nicole Lunardi, MS 2

Mentor(s): Graham Mooney
History of Medicine

The Pathogenesis of Youth: How Youth Became the Subject of Violence Prevention Programs

Authors: Nicole Lunardi, MSPH

Background: Nationally, homicide remains a leading cause of death among people 15-34 years of age. Baltimore City's homicide rate has consistently ranked highly among large American cities. The history of violence prevention programs in Baltimore City provides an important example of how a biopsychosocial problem is addressed in order to save lives. This project aims to understand how violence prevention initiatives came to target minority youth between 1970 and 1995.

Methods: This project analyzed local news media, the Baltimore Sun and the Afro, and the Mayor's Papers from the Baltimore City Archives to identify city-level violence prevention initiatives.

Results: Between 1970 and 1995, crime, drugs and violence garnered local and national attention. Minority neighborhoods in Baltimore City, subject to long-standing institutional racism, had more structural barriers for abating violence than wealthier, non-minority areas. Violence became synonymous with minority Baltimore City neighborhoods. Furthermore, the construction of the vicious criminal and innocent victim social narrative resulted in a political context, which generally favored punishment and enforcement over prevention. Prevention initiatives focusing on at-risk youth and families, however, were a notable exception to this trend. As such, youth became the face of prevention initiatives, while at-risk adults and individuals of any age with a history of violence were deemed less worthy of social investment.

Conclusion: Violence, a major contributor to morbidity and mortality, is a result of complex biopsychosocial factors that reflect generations of institutional racism. Societal and political values have strongly influenced which programs and populations are worth attention and funding. The prevailing notion that those with a history of violence, particularly adults, were beyond redemption limited the scope of prevention initiatives to youth. This investigation demonstrates the importance of understanding how politics and media create social narratives that permeate across disciplines and ultimately influence resource allocation.

PUBLIC HEALTH
and COMMUNITY SERVICE
POSTER ABSTRACTS
Listed Alphabetically (First Name)

(Annie) Yingyao Song, MS 3

Mentor(s): Deidra C. Crews, MD
Johns Hopkins Department of Nephrology

Socio-demographic and Clinical Correlates of Micronutrient Intakes among Urban African American Females with Uncontrolled Hypertension

Authors: Annie Y. Song, MS and Deidra C. Crews, MD, ScM; Patti Ephraim, MPH; Yang Liu, MPH, BSN; Lisa A. Cooper, MD, MPH; L. Ebony Boulware MD, MPH

Background: Dietary factors, influenced by social and cultural settings, may contribute to poor health outcomes in urban African Americans (AAs), including kidney disease. It has been previously shown that females are more deficient in renal protective micronutrients than males.

Methods: In a randomized trial of 117 AA females in Baltimore with uncontrolled hypertension, we used the Block Fruit-Vegetable-Fiber Screener to estimate baseline daily micronutrient intakes. To determine the association between sociodemographic factors and micronutrient intakes, we used multivariable and logistic regressions. We then determined the association between micronutrient intakes and reduced kidney function [estimated glomerular filtration rate <60 ml/min per 1.73m2 (eGFR<60) and albumin-to-creatinine ratio of 30 mg/mmol or more (ACR>30)] using logistic regressions. All analyses were adjusted for age and BMI.

Results: Median intakes for magnesium, potassium and dietary fiber were lower than Institute of Medicine recommendations. Sociodemographic factors statistically significantly associated with intakes of vitamin C, magnesium, dietary fiber and potassium (adjusted β coefficient [95% confidence interval]) were age ≥60 years (-21.82[-37.22,-6.42]; -54.91[-82.15,-27.66]; -4371[-6156,-2587]; -488.31[-757.15,-219.48]), and lower-than-median health numeracy scores (-22.97[-37.51,-8.44]; -40.31[-65.86,-14.77]; -2590[-4254,-925]; -399.18[-651.96,-146.39]). Income, education, literacy, exercise, food insecurity, tobacco use were not significantly associated with micronutrient intakes.

Lower (less than median) intakes of vitamin C (Odds Ratio (OR)=3.32 [1.46, 7.50]), magnesium (3.76 [1.62,8.74]), dietary fiber (2.96 [1.32,6.64]), and potassium (3.63 [1.58,8.32]) were statistically significantly associated with ACR>30, but not with eGFR<60.

Conclusion: AA females with uncontrolled hypertension who are older or with low health numeracy lack the recommended micronutrients that could favorably influence their renal function, suggesting a need for targeted interventions for these populations.

Anvesh Annadanam, MS 2

Mentor(s): David S. Friedman, MD, MPH, PhD
Wilmer Eye Institute

Self-refraction using a simple device reliably predicts manifest refraction

Authors: Anvesh Annadanam BS, Varshini Varadaraj MBBS MS MPH, Lucy Mudie MBBS MPH, Alice Liu, William G. Plum BS, J. Kevin White BS MA, Megan E. Collins MD, David S. Friedman MD MPH PhD

Background: Uncorrected refractive error (RE) is the most common cause of preventable visual impairment globally. The need for highly trained personnel to carry out refractions increases the cost of spectacles and limits outreach in poorer regions. Newer technologies allowing for self-refraction (SR) may be a cost-effective alternative. The USee device contains a self-adjustable refraction bar that allows users to determine their own spherical RE. We report on the accuracy and usability of USee compared to conventional methods in measuring RE.

Methods: Sixty adults with uncorrected visual acuity (VA) < 20/30 and spherical equivalent (SE) RE between −6.00 and +6.00 diopters (D) completed manifest refraction (MR) by an optometrist, SR with USee, and VA testing using a logMAR chart.

Results: Subjects, recruited from Wilmer eye clinics at Johns Hopkins, were a mean (±SD) 53.1 (±18.6) years old, and 27 (45.0%) were male. Mean (±SD) SE measured by MR [−0.90 D (±2.53)] differed from that measured by SR [−1.22 D (±2.42)], $p < 0.002$]. The proportion of subjects correctable to ≥ 20/30 was higher for MR (96.7%) than SR (83.3%, $p < 0.006$). Failure to achieve VA ≥ 20/30 with SR was associated with increasing age (per year, OR: 1.05; 95% CI: 1.00 – 1.10) and higher cylindrical power (per D, OR: 7.26; 95% CI: 1.88 – 28.1). Subjectively, 95% thought USee was easy to use, 85% thought SR correction was better than being uncorrected, 57% thought SR correction compared to their current corrective lenses, and 53% rated their vision as "very good" or "excellent" with SR correction.

Conclusion: USee provides acceptable RE and VA correction in adults. Although the device cannot correct astigmatism, many subjects found it easy to use and better than wearing no corrective lenses. Programs using USee could provide glasses on the spot and satisfaction could be determined immediately with pop-in lenses.

Brian Lentz, MS 2

Mentor(s): Bhakti Hansoti, MBChB, MPH
Emergency Medicine

Validity of Emergency Department Triage Tools: Addressing Heterogeneous Definitions of Over-Triage and Under-Triage

Authors: Brian A. Lentz MS, BS; Alexander Jenson MD, MPH; Jeremiah S. Hinson MD, PhD; Scott Levin PhD; Stephanie Cabral; Kevin George; Edbert B. Hsu MD, MPH; Gabor Kelen MD; Bhakti Hansoti MBChB, MPH

Background: Triage aims to allocate resources as effectively as possible based on patient acuity. The effectiveness of triage is commonly measured as reliability and validity, often reported as over-/under-triage. In theory, triage tool validation research allows for informed decision making prior to implementation. This is limited, however, given the heterogeneous definitions of over-/under-triage that exist in the literature. In this study, we sought to characterize the variation in over-/under-triage definition and propose a uniform standard to guide future research.

Methods: A systematic review of the peer-reviewed published literature for emergency department triage tool validation studies was conducted by searching Pubmed, EMBASE, Web of Science, and Scopus. This was supplemented by administering a survey to 65 triage experts. The survey was embedded with a summary of the systematic review results and sought to elicit opinions on uniform standards for over-/under-triage metrics.

Results: A total of 5,174 studies were identified by the search of which 34 were included in the final review. Most definitions of over-/under-triage (76%) were based on true acuity as determined by a panel of experts. A smaller proportion (18%) were based on patient outcome markers (i.e. admission or discharge). The majority of survey respondents (58%), however, ranked outcome-based methodologies superior to expert-based methodologies.

Conclusion: Current heterogeneity hinders analysis of triage tool validity and limits triage tool research. We present a set of novel uniform standards to calculate over-/under-triage metrics that if universally adopted would facilitate the comparison of triage tool research across study sites and aid informed implementation.

Christopher Counts, MS 2

Mentor(s): Gerard Anderson, PhD
Bloomberg School of Public Health, Department of Health Policy and Management

Options for Restoring Competition in the Generic Drug Industry

Authors: Melissa Lavoie BS, Christopher Counts MSc, Elizabeth Fracica MPH, Mariana Socal MD, Gerard Anderson PhD

Background: Recently, decreased competition in the generics industry has contributed to high-profile price spikes and shortages. When Martin Shkreli became the sole producer of pyrimethamine in 2015, its price soared by 5500%. Between 2010 and 2015, 300 drugs experienced a price spike of 100% or more. In 2015, 417 shortages were reported. In response, researchers and policymakers have explored ways to reinvigorate competition. This study aims to identify policy proposals for preventing generic drug price increases and shortages, and to select those measures most likely to promote market entry and competition.

Methods: We reviewed the PubMed and EBSCO Legal Periodicals Full Text databases to identify US-focused policy proposals aiming to address generic drug shortages and/or price spikes. We excluded articles published before 1984, the year the Hatch-Waxman Act was passed. The search strategy used index terms and title and abstract keywords. Two researchers independently screened the abstracts and selected articles for full-text review based on relevance. We then assessed each policy's ability to promote market entry for drugs with one generic manufacturer and increase competition in consolidated markets.

Results: The search retrieved 3,698 articles, of which 190 were potentially relevant after reviewing abstracts. Full-text review yielded 34 articles presenting 56 unique policy proposals. The proposals fell into four categories: finding alternative sources, adjusting regulations, changing prescribing and purchasing patterns, and incentivizing manufacturers to enter the market. Four types of policies were most likely to encourage companies to enter the market while also preventing price increases and shortages: creating options (such as importation) that deter price increases, providing financial incentives to manufacturers to enter and remain in the market, reducing the backlog of generic drug applications, and taking enforcement action against anticompetitive behavior.

Conclusion: Policymakers should implement policies in the four above areas to prevent generic drug price spikes and shortages.

Eva Szymanski, MS 2

Mentor(s): Garry Cutting, MD
McKusick-Nathans Institute of Genetic Medicine

Variants in WFDC2 are associated with Woakes Syndrome

Authors: Eva Szymanski BS, Briana Vecchio-Pagàn PhD, Garry Cutting MD

Background: Woakes Syndrome is a rare condition characterized by severe recurrent nasal polyposis in childhood with broadening of the nose, frontal sinus aplasia, dyscrinia, and bronchiectasis. The syndrome appears to be hereditary, but genetic etiology is unknown. Our group previously reported two sisters with presumed Woakes Syndrome, both with recurrent, destructive nasal polyposis resistant to standard medical and surgical therapies. The presence of Woakes Syndrome in two siblings and absence in both parents suggested an autosomal recessive genetic etiology. Evaluations for recessive disorders known to cause nasal polyposis were negative. Our objective was to assess the two siblings for previously unknown genetic contributions to their disease.

Methods: The family was consented (IRB NA_00045758), and whole exome sequencing was performed (Illumina HiSeq 2500). PCR amplification was performed on nasal polyp tissue from the proband, unaffected nasal tissue, and cell lines. Immunohistochemistry was performed on nasal polyp tissue from the proband's affected sister, unaffected sinus tissue, and control tissue types.

Results: Compound heterozygous mutations in WFDC2 were found in both affected sisters and were predicted to cause loss of expression and function of the WFDC2 protein. Consistent with the prediction, the WFDC2 gene did not amplify from nasal polyp biopsy RNA in the proband, and preliminary immunohistochemistry studies show the WFDC2 protein is not expressed in nasal polyp tissue in the proband's affected sister.

Conclusion: WFDC2 is normally expressed in several tissues, including the nasopharynx, and is known to have aberrant expression in cancers and in cystic fibrosis lungs. Its exact function is unknown, though it is predicted to be a component of the innate immune response in the lung and naso-oropharynx. Further studies are warranted to confirm our findings and explain the mechanism for disease. However, our study indicates that loss of expression of WFDC2 contributes to the pathogenesis of Woakes Syndrome.

James Ting, MS 2

Mentor(s): Robert Gilman, MD
School of Public Health, International Health

Designing the algorithm for a low-cost, high-utility diagnostic tool for early ASD

Authors: James Ting BA, Natalia Vargas Cuentas PhD, Avid Roman-Gonzalez PhD, Mirko Zimic PhD, Robert Gilman MD

Background: Autism spectrum disorder (ASD) currently affects nearly 1 in 160 children worldwide, causing 111 DALYs lost per 100,000 people. Even in high-resource settings in the US, the current gold standard diagnostic tools (ADOS, ADI-R, eye-tracking) are rarely used (< 5%); and in over two-thirds of evaluations, no validated diagnostics are used due to the associated length of testing and need for extensive training. Cheap, portable, and easy-to-administer diagnostic technique for ASD screening in low resource settings are still severely lacking.

Methods: In this study, we designed a diagnostic tool that operates as an executable on a portable tablet with a webcam. A child is seated in the lap of the mother throughout the diagnostic test. A video is displayed on the tablet to the child, while the webcam records the child's eye movements. The visual preference algorithm then calculates the child's preference for a dynamic social or dynamic object scene. We then recruited 50 control subjects without a prior history of ASD to demonstrate the validity of the algorithm in calculating the visual preference of the individuals.

Results: The study results have not been fully analyzed, and so it cannot be determined yet whether the algorithm correctly differentiates visual preference of the child for either the dynamic social or object scenes of the diagnostic video, as compared to a designated gold standard.

Conclusion: A new diagnostic tool has been proposed for appropriate utilization in mobile, low-resource settings. The validity of the approach is currently being studied. Future testing of the sensitivity and specificity of such a diagnostic tool with different design parameters (specific introductory scenes, dynamic social scenes, dynamic object scene, and GUI layout) can be studied to determine the specific efficacy of such a diagnostic tool.

Jonathan Callan, MS 2

Mentor(s): Joshua Sharfstein, MDD
JHSPH

Improve Housing to Reduce Falls: Learning from the Baltimore Fall Reduction Initiative Engaging Neighborhoods and Data

Authors: Jonathan Callan BS, Joshua Sharfstein MD

Background: The Baltimore Fall Reduction Initiative Engaging Neighborhoods and Data (B'FRIEND) is a project run by the Baltimore City Health Department. The project will attempt to use near real-time surveillance of falls to catalyze innovative programs to prevent falls.

Before fall data is collected and disseminated, it was deemed important to understand what is currently being done in Baltimore to combat falls in the elderly particularly with regards to housing and environmental fall risk reduction. This past summer, housing repair organizations and initiatives that make up the current fall reduction landscape in Baltimore City were examined to deduce the gaps in Baltimore's housing landscape.

Methods: In order to better understand the fall reduction landscape, a literature review was completed of housing and situational fall risk. Also community partners who work in the area of home repair (CHAI, Civic Works, and Banner Neighborhoods) were interviewed. Most of these interviews were coupled with a shadowing experience where I would follow a social worker or contractor from the organization on their house visits to elderly Baltimoreans' homes. After these interactions I used my notes to compile advantages and gaps of these services.

Results: During interviews all of the organizations were found to be understaffed and underfunded. In order to serve their communities need additional funding. It was found that these organizations also do not communicate with each other to a large extent and they operate under many different guidelines and conditions.

Conclusion: Based on interviews with partner organizations, the key barriers to filling the gaps in fall reduction services are funding and staffing. Many organizations exist in Baltimore City to reduce the fall risk of older adult residents but these organizations are frequently unable to provide the resources they intend to provide in a timescale that is actually helpful.

Kathryn Pearson, MS 2

Mentor(s): Alexander Pantelyat, MD
Department of Neurology

Noninvasive Brain Stimulation in Parkinsonian Disorders: A Systematic Review

Authors: Kathryn Pearson BA, Zoltan Mari MD, Alexander Pantelyat MD

Background: Noninvasive brain stimulation (NIBS) has emerged as a promising method of modulating cortical activity, and has been utilized to treat numerous neurological and psychiatric disorders. Recently, NIBS has been explored as an intervention to ameliorate motor deficits in Parkinson disease (PD) and other parkinsonian disorders.

Methods: We conducted a systematic search of PubMed, Web of Science, and Embase. Our search criteria returned results for therapeutic NIBS in PD, corticobasal syndrome (CBS), progressive supranuclear palsy (PSP), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), and secondary parkinsonism patients. Eligible studies were randomized, controlled trials with at least ten enrolled participants assessing semiquantitative (MDS-UPDRS) or quantitative measures of motor function as a primary or secondary endpoint. Fifty-four articles were selected for inclusion. Due to a small number of results on atypical parkinsonian disorders, we reviewed all relevant articles regardless of randomization and sample size.

Results: The majority of included studies employed transcranial magnetic stimulation (TMS). The strongest evidence supported the efficacy of rTMS stimulation over the motor cortex in improving bradykinesia and freezing of gait. Among transcranial direct current stimulation (tDCS) studies, we found evidence for the improvement of global bradykinesia after anodal tDCS over M1 or the prefrontal cortex. Studies involving atypical parkinsonian disorders were underpowered and insufficiently unified in their procedures to identify strong patterns. Only 18 studies measured subjective patient-reported outcomes following stimulation, with mixed results.

Conclusion: Results for TMS and tDCS show promise for the alleviation of bradykinesia in PD patients, although larger studies with longitudinal follow-up are needed. Conclusions on NIBS for atypical parkinsonian disorders are limited by the disparate methodologies across studies, small sample sizes and lack of proper controlling. Because NIBS is not yet an approved treatment for PD patients, greater emphasis should be placed on subjective patient outcomes and minimal clinically important differences in future studies.

Kendrick Wang, MS 2

Mentor(s): Alex Yuang-Chi Chang, MD
Oncology

Outcomes of Tyrosine Kinase Therapy for Brain Metastasis of Patients with Non-Small Cell Lung Carcinoma in Singapore

Authors: Kendrick Wang BA, Alex Yuang-Chi Chang MD

Background: Lung cancer has a high incidence of brain metastasis. Current management of brain metastasis in non-small cell lung carcinoma (NSCLC) patients has a low survival time of only 6-10mo. Thus, targeted therapies, like tyrosine kinase inhibitors (TKIs), against driver mutations warrant exploration. This study investigates TKI therapy for NSCLC patients with brain metastasis seen at Johns Hopkins Singapore (JHS).

Methods: Patients with primary NSCLC and brain metastasis seen at JHS from 2006-2016 were divided based on whether they had identified driver mutations in their primary tumor and whether they had undergone treatment with TKIs after the diagnosis of brain metastasis. Kaplan-Meier survival curves were generated and log-rank tests and cox proportional hazard tests were performed.

Results: Out of a total of 65 identified cases of NSCLC patients with brain metastasis, 10 had no known driver mutations, 24 had at least one driver mutation, and 31 did not have genetic testing performed. The median survival of patients without mutations and without TKIs was 5.8mo, of patients with mutations and with TKIs was 19.6mo, of patients without genetic testing and without TKIs was 8.4mo, and of patients without genetic testing and with TKIs was 18.1mo.
Survival curves of these four groups displayed increased survival in patients with mutations who had TKIs. Log-rank testing between individuals with mutations and TKI treatment versus individuals without TKIs indicated a p-value of 0.07, and a cox proportional hazard ratio of -0.71 was obtained.

Conclusion: TKI use in mutation positive patients increased survival, observed in survival time and Kaplan-Meier curves. The cox proportional hazard ratio signifies a decreased death rate with TKI therapy. However, the log-ranked p-value, borders on statistical significance. Nonetheless, our results seem to suggest a trend of improved survival with TKI use in patients with mutations, and we suggest further research of TKI therapy for brain metastasis.

Kingsley Asiedu, MS 2

Mentor(s): Stephanie Terezakis & Carol Morris
Radiation Oncology and Molecular Radiation Sciences & Orthopaedic Surgery-Oncology

The Role of Interdigitated Chemotherapy and Radiation in Managing High-Grade Soft-Tissue Sarcoma

Authors: Kingsley Asiedu, Chengcheng Gui, Carol Morris, Stephanie Terezakis

Background: Soft tissue sarcomas account for 1% of all cancers. Management has been challenging for clinicians owing to the various histological subtypes of the disease. Therefore, prognosis for patients with high-grade soft-tissue sarcoma (STS) remains poor. The goal of this study was to review treatment outcomes of patients with high-grade STS treated with interdigitated neoadjuvant chemotherapy (CT) and radiation and compare them to those of patients who received sequential CT and radiation. Additionally, we reviewed the wound outcomes of patients following the interventions.

Methods: Patients with high-grade STS (1997 to 2016) were planned for treatment with 3 cycles of neoadjuvant CT, interdigitated or sequential preoperative radiation therapy (44 or 50 Gy, respectively, administered in split courses with a potential 16 Gy postoperative boost), and 3 cycles of postoperative CT. Cancer control outcomes in addition to wound outcomes were analyzed.

Results: 49 patients with high-grade STS were evaluated. Median age was 51 years and the median longest tumor diameter was 10.9 cm. All 49 patients received either 2 or 3 cycles of neoadjuvant CT and all patients completed neoadjuvant RT. The estimated 3-year rate for overall survival was 73% for patients treated with interdigitated therapy and 58% for patients treated with sequential CT and radiation. Disease free survival was 62% with interdigitated therapy and 46% with sequential therapy. Wound complications rates was not significantly different between the two interventions.

Conclusion: Patients with high-grade STS treated with interdigitated neoadjuvant CT and radiation before surgical resection had excellent rates of disease-free survival and overall survival in comparison to patients who received sequential therapy. The differences in the two interventions did not significantly alter wound complication rates. In conclusion, interdigitated CT and RT approach will continue to play an important role in the management of patients with high-grade STS.

Lindsay Dickerson, MS 2

Mentor(s): Susan Harvey, MD
Department of Radiology and Radiological Science

A pilot educational intervention and feasibility assessment of breast ultrasound in rural South Africa

Authors: Lindsay K. Dickerson BA, Anne F. Rositch PhD, MSPH, Susan Lucas MD, Susan C. Harvey MD

Background: Breast cancer is the leading cause of cancer death in women worldwide, with strikingly high mortality in low- and middle-income countries (LMICs) due to scarcity of detection, diagnosis, and treatment. With mammography unavailable, ultrasound (US) offers a viable alternative. The literature reports successful US training in various domains, but a curriculum focused on breast is novel. We hypothesized feasibility (knowledge acquisition, perceived utility, and self-efficacy) of a breast US training program for detection of breast cancer by non-physician providers.

Methods: Training was implemented for 12 providers at Hlokomela clinic in Hoedspruit, South Africa over three weeks. Didactic presentations and example cases were followed by a pre-survey and test (n=12). All providers received hands-on training with nurses as models; five providers trained with patients. A post-test (n=12) assessed overall knowledge retention and acquisition, and a post-survey (n=10) gauged program acceptance and provider self-efficacy with breast US.

Results: The pre- to post- test averages improved by 68% total and in four competencies (foundational knowledge, descriptive categories, benign vs. malignant, and lesion identification). On the post-survey, providers expressed that US could significantly impact breast cancer detection (9.1/10), treatment (7.9/10), and survival (8.7/10) in their community and endorsed moderate confidence in their scanning (6.3/10) and image-interpreting abilities (5.6/10).

Conclusion: Our research supports feasibility of breast US training as part of a breast education program in LMICs. Pre/post-test results and observed proficiency indicate that training non-physician providers is achievable. Post-survey responses indicate program acceptance, provider self-efficacy with US, and community-based ownership of a breast cancer screening and awareness initiative. Limitations include the narrow timeframe of training and associated lack of pathology seen, but we are currently moving forward with plans for long-term follow-up and quality control. Future work may show that breast US is viable for early detection where mammography is unavailable.

Melissa Lavoie, MS 2

Mentor(s): Gerard Anderson, PhD
Health Policy and Management, School of Public Health

Options for Restoring Competition in the Generic Drug Industry

Authors: Melissa Lavoie BS, Christopher Counts BS (ML and CC are joint first authors), Elizabeth Fracica BA, Mariana Socal MD, Gerard Anderson PhD

Background: Recently, decreased competition in the generics industry has contributed to high-profile price spikes and shortages. For instance, when Martin Shkreli became the sole producer of pyrimethamine in 2015, its price soared by 5500%. Between 2010 and 2015, 300 drugs experienced a price spike of 100% or more. 417 shortages were reported in 2015. In response, researchers and policymakers have explored ways to reinvigorate competition. This study aims to identify policy proposals for preventing generic drug price increases and shortages, and to select those measures most likely to promote market entry and competition.

Methods: We reviewed the PubMed and EBSCO Legal Periodicals Full Text databases to identify US-focused policy proposals aiming to address generic drug shortages and/or price spikes. We excluded articles published before 1984, the year the Hatch-Waxman Act was passed. The search strategy used index terms and title and abstract keywords. Two researchers independently screened the abstracts and selected articles for full-text review based on relevance. We then assessed each policy's ability to promote market entry for drugs with one generic manufacturer and increase competition in consolidated markets.

Results: The search retrieved 3,698 articles, of which 190 were potentially relevant after reviewing abstracts. Full-text review yielded 34 articles presenting 56 unique policy proposals. The proposals fell into four categories: finding alternative sources, adjusting regulations, changing prescribing and purchasing patterns, and incentivizing manufacturers to enter the market. Four types of policies were most likely to encourage companies to enter the market while also preventing price increases and shortages: creating options (such as importation) that deter price increases, providing financial incentives to manufacturers to enter and remain in the market, reducing the backlog of generic drug applications, and taking enforcement action against anticompetitive behavior.

Conclusion: Policymakers should implement policies in the four above areas to prevent generic drug price spikes and shortages.

Michael Saheb Kashaf, MS 2

Mentor(s): Dr. Zackary Berger
General Internal Medicine

Shared Decision-Making and Outcomes in Type 2 Diabetes: A Systematic Review and Meta-Analysis

Authors: Michael Saheb Kashaf MSc, Elizabeth McGill MSc, Zackary Berger MD/PhD

Background: Type II diabetes (T2DM) is a chronic disease which requires lifelong management and a therapeutic alliance between patient and provider. Shared decision-making (SDM) is an approach to clinical decision-making in which patients and practitioners jointly consider outcome probabilities and patient preferences in order to arrive at a decision based on mutual agreement. Decision-making is an important dimension of diabetes management and SDM is therefore expected to impact disease outcomes. This review systematically examines the association between SDM and outcomes in T2DM.

Methods: We searched bibliographic databases and gray literature sources without date restrictions. Sources included the Cochrane Database, Embase, MEDLINE, PsycINFO, CINAHL, PsycEXTRA, Open Grey, Grey Literature Report, RAND, NICE, Institute of Medicine, and Google. Eligible studies used longitudinal designs to examine the association between patient participation in adult T2DM management decision-making and process of care and/or clinical outcomes. We subjected all included studies to dual data extraction and quality assessment for methodological rigor. We synthesized outcomes using meta-analyses where reporting was sufficiently homogenous or alternatively synthesized in narrative fashion.

Results: The search retrieved 4,592 records, which we screened by title, abstract, and full-text to identify relevant studies. The review included 16 studies. We found evidence of an association between SDM and improved decision quality, patient knowledge and risk perception. We found little evidence of an association with glycemic control, patient satisfaction, quality of life, medication adherence or trust in physician. The strength of evidence was greatest for outcomes amenable to meta-analysis – decision quality and glycemic control.

Conclusion: The investigation was limited by literature variability in the operationalization of SDM, which may affect both search sensitivity and finding generalizability. This work elucidates the potential clinical utility of SDM in the management of T2DM and informs future research on the topic. Accumulating empirical evidence of clinical utility provides impetus for broader uptake of SDM.

Monica Tung, MS 1

Mentor(s): Jodi Segal, MD, MPH
Medicine - General Internal Medicine

A Systematic Review of the Determinants of Overuse of Radiologic Services in the Emergency Department

Authors: Monica Tung, BA, Ritu Sharma, BS, Stephanie Nothelle, MD, Jean Pannikotu, BS, Jodi Segal, MD, MPH

Background: Introduction. Overuse of radiologic services, where imaging tests are provided under circumstances where the propensity for harm exceeds the propensity for benefit, comprises a risk to patient safety and a burden on health systems. However, the patient, physician, and systemic level determinants that drive these unnecessary scans are poorly defined.
Objective. We aimed to identify determinants of overused imaging in the Emergency Department (ED).

Methods: Methods. Paired reviewers systematically searched for relevant published literature in PubMed and Embase from January 1996 to October 2016. One reviewer extracted key data and a second verified the accuracy. The determinants of overuse were qualitatively synthesized.

Results: Results. Twenty-one articles were included. Fifteen evaluated computerized tomography (CT) scans in patents presenting to a regional ED who were transferred to a level 1 trauma center. Nine investigated reasons for duplicate scanning; incomplete transfer of data and poor image quality were most frequently reported. Factors significantly associated with unnecessary pre-transfer scanning or repeated scanning after transfer, in multiple studies, included older patient age, higher injury severity score (ISS) and greater distance between hospitals. Six additional studies analyzed patient, physician and systemic determinants of overuse in ED imaging workup for varied conditions.
Limitations. This review is limited to the published, English literature from the United States. The included studies mostly had moderate risks of bias with poor reporting of participant characteristics and little attention to confounding.

Conclusion: Conclusions. This was a heterogeneous body of literature. Older patient age and higher ISS were the most consistently cited significant determinants of ED imaging overuse. Scan duplication, in transferred trauma patients, was the most described type of overuse. Technological deficits in the transferred data was frequently cited and is actionable.

Nisha Parikh, MS 2

Mentor(s): Kimberly Gudzune, MD
Welch Center For Prevention, Epidemiology, and Clinical Research

Stress Reduction with Yoga among Low-Income Urban Minorities: A Scoping Review

Authors: Nisha Parikh MD, Kimberly Gudzune, MD

Background: Yoga focuses on calming the mind and body through a combination of physical postures, breathing exercises, and/or meditation. Yoga might reduce stress among low-income urban minorities; however, the feasibility and effectiveness of such interventions in this population are unclear. We conducted a scoping review to examine how yoga influences these outcomes among racial/ethnic minorities that are low-income and/or urban.

Methods: We searched MEDLINE and PsychInfo from inception to August 2016 for randomized controlled trials, case series, cohort studies, cross-sectional studies, and qualitative studies involving movement or postural-based yoga practices that were published in English. Our search criteria included at least one of the following: inner city or urban, low-income, or low socioeconomic status. One reviewer abstracted information on study design, population characteristics, and relevant outcomes, which was synthesized qualitatively.

Results: Of the 4,523 citations identified, 28 studies met our eligibility criteria and 4 reported stress-related outcomes. All 4 of these studies occurred in school settings where children's age ranged from 10 to 17 years. Three studies occurred predominantly among African-American children, and the other among Hispanics. Involuntary coping assessed via the Response to Stress Questionnaire showed a statistically significant stress reduction benefit among elementary school children (between-group difference 0.30; $p<0.001$) in one study, but not among high school students in another. Measures to evaluate stress outcomes differed across studies making synthesis challenging, and validated measures were not always used.

Conclusion: Overall, we found few studies that have examined the feasibility or effectiveness of yoga among low-income urban minorities. To date, yoga among children in school settings shows some early promising benefits among younger students, but no studies have examined stress reduction benefits among adults in our population. Additional research is needed among low-income urban minorities to document long-term results of yoga interventions using previously validated measures of stress.

Stephanie Sweitzer, MS 2

Mentor(s): Stefan Baral, MD MPH MBA
Department of Epidemiology

Optimizing the HIV treatment cascade among men who have sex with men (MSM) in South Africa

Authors: Stephanie Sweitzer MSPH, Nancy Phaswana-Mafuya PhD, Travis Sanchez DVM MPH, Rachel Valencia MPH, Stefan Baral MD MPH MBA

Background: In South Africa, HIV prevalence is approximately 17.9% in the general population, and men who have sex with men (MSM) are estimated to have an even greater burden of infection. Optimizing the HIV treatment cascade is a crucial component of comprehensive HIV prevention and treatment programs, but to date little research has been done to determine the most effective ways to engage and retain MSM in care in this setting. The present study is aimed at investigating the acceptability and effectiveness of a package of innovative interventions to promote linkage and retention in care among HIV-positive MSM in South Africa.

Methods: MSM were recruited in Cape Town (CT) and Port Elizabeth (PE) using respondent driven sampling, peer referral, and time and location sampling. At both sites, participants completed a short survey covering demographics, sexual behavior, and healthcare utilization; received HIV testing and counseling; and were referred to sensitized clinics for HIV care. In addition, MSM enrolled at the CT site received point-of-care CD4 and creatinine testing for antiretroviral therapy eligibility, onsite treatment initiation (if eligible), peer navigator support, and appointment reminders.

Results: The PE site enrolled 64 HIV-positive MSM, with 35 eligible for ART. Recruitment is still ongoing in CT, with 26 HIV-positive MSM enrolled to date, and 13 eligible for ART. Enrollment of HIV-positive MSM has proven especially challenging in CT as a result of relatively high prior engagement in care among this population.

Conclusion: Differential success in enrollment points to differences in access to care between these cities, and an unmet need for HIV programming among PE MSM. Further analysis of study data as it becomes available will be used to ascertain barriers to care in this population, assess the utility of this package of interventions by comparing healthcare utilization between sites, and explore healthcare policy implications of this project.

Thomas Brooke, MS 2

Mentor(s): Rani Hasan, MD
Department of Cardiology

The Accuracy of Physicians' and Nurse Practitioners' Perceived Frailty in Transcatheter Aortic Valve Replacement Patients

Authors: Thomas Brooke BS, Nada Rendradjaja BS, Esme Irvine BS, Rani Hasan MD

Background: Frailty is defined as a medical syndrome characterized by a loss of physiologic reserve that increases vulnerability to acute stressors. Frailty is associated with increased mortality in patients undergoing several cardiac procedures, including transcatheter aortic valve replacement (TAVR). Frailty has been implicated to enhance the predictive capacity of current surgical risk scoring tools, such as the Society of Thoracic Surgeons risk score. Though physicians supplement such tools with a subjective assessment of frailty, little research has focused on the accuracy of these assessments. The limited data on this subject demonstrates poor provider accuracy, ranging from 40 to 70% correct.

Methods: Surgeons, cardiologists and nurse practitioners evaluating patients for TAVR at the Johns Hopkins Hospital were asked to anonymously evaluate the frailty of their patients. Patients' objective frailty was then measured according to the Fried frailty scale as a part of a prospective cohort study of Hopkins TAVR patients.

Results: The providers completed 54 surveys on 17 patients. The mean patient age was 84 years old and 47% were male. Four cardiologists completed 20 surveys, 2 surgeons completed 17 surveys and 2 nurse practitioners completed 17 surveys. Fourteen of the patients were frail and 3 were intermediately frail. Providers correctly assessed frailty between 58% and 65% of the time. Using clustered logistic regression, only increasing patient age was significantly associated with accurate provider estimations (p=0.038).

Conclusion: As seen with other studies, nurse practitioners, cardiothoracic surgeons and interventional cardiologists are all similarly mediocre at estimating frailty. Increasing patient age was the only characteristic that improved providers' estimation accuracy, not provider specialty nor other patient demographics. Given physicians poor ability to estimate frailty, TAVR teams may benefit from incorporating objective frailty assessments into their routine assessments. In addition, the high prevalence of frailty in the TAVR population may necessitate an adjusted threshold for frailty.

Zixiao Wang, MS 2

Mentor(s): Ginette Okoye, MD
Dermatology

Merkel Cell Carcinoma in African Americans: a retrospective case-control study

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Background: Merkel cell carcinoma (MCC) is an aggressive skin cancer associated with early spread, recurrence, and high mortality. Risk factors for developing MCC include age, male-sex, UV irradiation, immunosuppression, and Merkel cell polyomavirus (MCPyV) infection. To date, the vast majority of literature on MCC pertains to the cancer in Caucasian and East-Asian patients; the natural history and prognosis of MCC are unclear in populations of African descent.

Methods: We conducted a single-institution, case-controlled retrospective study of patients treated for MCC at JHH and JHBMC. Candidates were identified through the dermatopathology database and only patients treated at JHMI, and for whom complete records are available, were included. Relevant information was abstracted from EMR and characteristics of the two populations were compared through Mann-Whitney and Fisher's exact tests.

Results: Review of the JH dermatopathology database for MCC cases yielded 10 black patients and 30 white patients (matched for date of diagnosis) suitable for this study. Our study identified no significant differences between black and white MCC patients. Clinical characteristics such as age at diagnosis, sex, presence of identifiable primary tumour, size and location of primary tumour, clinical stage at diagnosis, and access to dermatologist evaluation were comparable between the two patient populations.

Conclusion: This study found no significant differences in the age of diagnosis or tumour characteristics between black and white MCC patients. Although this is the largest cohort of black MCC patients studied to date, it is nevertheless a small sample size and limits the power of our study.