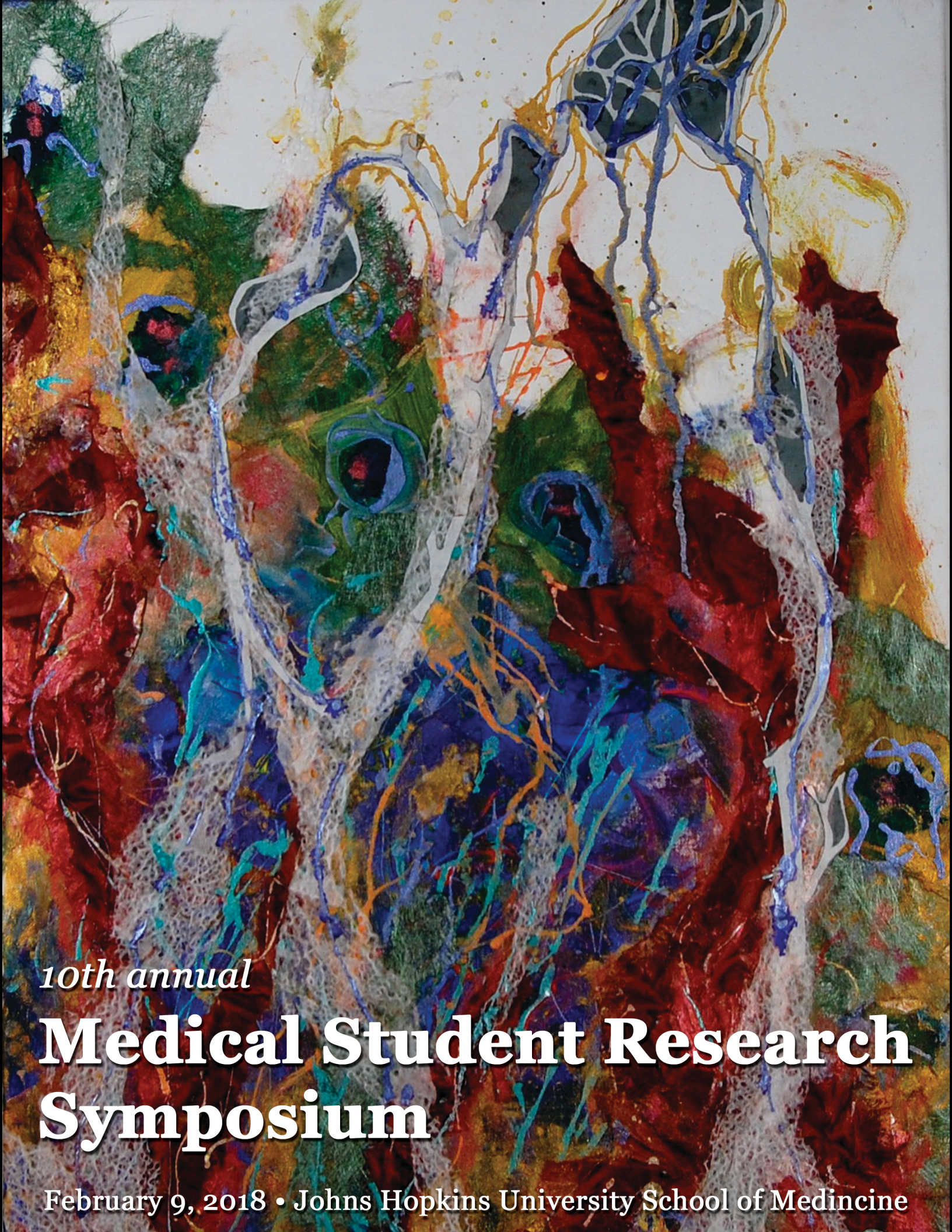

10th annual

Medical Student Research Symposium

February 9, 2018 • Johns Hopkins University School of Medincine

Cover image courtesy of

Sophia Diaz, MS2

H1N1

(Acrylic, Ink, and Paper on Canvas)

"H1N1" is an abstraction of a prototypical virus infecting a human cell. It was inspired by my immunology course, one of my first-ever biology courses, in college. Our professor had just lectured on Swine Flu, genetic drifts, shifts, and the importance of herd immunity--after which he arranged for volunteers to come in and vaccinate at least 100 students on their way out of the lecture hall ("You get a vaccine! And you get a vaccine!" he exclaimed, pointing at students in an Oprah Winfrey-like fashion). After studying Visual Arts at Brown University for two years, I was debating whether or not to continue my studies in the department, or to perhaps pursue a new path in Biotechnology & Physiology. This piece represents an important turning point for me. "H1N1" was the product of my doting on biology's dynamic prowess, ubiquity, and complete uncertainty, qualities that eventually brought me down a different path than the one I had originally begun.

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Medical Student Research Symposium 2018

We are pleased to have you join us for the 10th annual Medical Student Research Symposium of the Johns Hopkins University School of Medicine. As clinicians in training, we are fortunate to work among faculty who conduct a broad range of investigation that yields advances in the knowledge of human health. For the past five years, we have been privileged to have an event that presents the extensive endeavors that students take to advance this mission at the school.

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

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

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

The SC program offers the following five areas of study:

Basic Science
Sarah Wheelan,MD,PhD

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

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

History of Medicine
Randall Packard, PhD

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

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

Program Schedule

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AMEB main lobby

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

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

3:30 PM **Refreshments**
AMEB 3rd floor

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

4:50 - 5:30 PM **MSRS Award Ceremony**
featuring
Keynote speaker,
Dr. Andrew Cameron
AMEB 1st floor lecture hall

Keynote speaker

Andrew MacGregor Cameron, M.D., Ph.D.

Chief, Division of Transplantation
Johns Hopkins University School of Medicine

Andrew M. Cameron was born at the Johns Hopkins Hospital and raised in Baltimore. He attended Harvard College and the Johns Hopkins Medical School before completing his surgical training at the Mass General Hospital and UCLA. He returned to Hopkins in 2006 and now serves as an Associate Professor of Surgery, Director of the adult and pediatric Liver transplant programs, and Chief of the Division of Transplantation. Besides his clinical interests in Hepatitis C and liver cancer Dr. Cameron has an NIH funded basic science laboratory studying stem cells and the liver and is also active in efforts to increase organ donor registration using social media.

Faculty Judges

Aaron James
Abdel Hamad
Adam Kaplin
Alan Scott
Alejandro Garcia
Alexandra Maertens
Almamy Malick Kante
Amol Narang
Andrew Wolfe
Anthony D. So
Aruna Chandran
Barry Nelkin
Barry Solomon
Ben Larman
Bhakti Hansoti
Bruce Lawrence Klein
Carol Newill
Catherine Davis-Takacs
Cesar A. Santa-Maria
Chris Umbricht
Colleen Schreyer
Crystal C. Watkins
Dan Laheru
Daniel Safer
Daniela Cihakova
David Nauen
David Pickar
Dejan Budimirovic
Doris Lin
Durga Roy
Edward L. Bartlett, Jr.
Eniola Falomo
Farhad Vesuna
Genaro A. Ramirez Correa
Cerald Brandacher
Greg Pontone
Henry Jampel
James Brasic
James R. Ficke
Janet Crane
Jean Kim
Jeffrey John Meyer
Jeremiah Hinson
Jodi Segal
Kelly Metcalf Pate
Khalil Ghanem
Kimberley Steele
Kristen A. Marrone
Larissa Shimoda
Lloyd Miller
Lois Eldred
Marc Halushka
Mark Donowitz
Mark J. Brittle
Michael Fingerhood
Michele Manahan
Milan K. Joshi
Moise Ngwa
Morgan Katz
Nino Paichadze
Noton Dutta
Pamela Johnson
Peter Johnston
Phuoc Tran
Prasanna Santhanam
Rachel Damico
Rakhee Gawande
Richard Rothman
Robert David Stevens
Rosemary Morgan
Russell L. Margolis
Samuel M. Alaish
Saraswati Sukumar
Scott Lifchez
Seth Martin
Shizhong Han
Shuying Sun
Sophie Lanzkron
Sudipto Ganguly
Surojit Sur
Taekjip Ha
Una D. McCann
Venkataramana Sidhaye
Vinesh Vinayachandra

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Acknowledgements

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

Faculty Judges
The Office of Student Affairs
The Scholarly Concentrations Faculty

Mark Dodd
Doug Hughes
Victor Raspa
John Steele

PODIUM PRESENTATION ABSTRACTS

Listed alphabetically by first name of author

Ashlyn McRae, MS 2

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

Race to Residency: First Year Medical Students' Beliefs and Behaviors Related to the "Match"

Authors: Ashlyn McRae BS, Gail Geller ScD MHS, Joseph Carrese MD MPH, Douglas Hough PhD, Robert Shochet MD

Background: In recent years, the residency match process has become increasingly complex and competitive, with more pressure for medical students to perform well on USMLE Step 1 and engage in research. We explored the impact of the perceived competitiveness of residency match on first-year medical students at JHUSOM.

Methods: Using a mixed-methods design, we administered an end-of-year online survey to all first-year students. The survey included items about perceptions and behaviors related to the match and a validated personal growth scale. Chi-square analysis was used to identify associations between variables of interest. We also conducted four focus groups with a total of twenty-six first-year students. Standard content analysis was performed on focus group transcripts.

Results: The survey response rate was 74% (87/117). Respondents were representative of the class demographics. On average, students ranked USMLE Step 1 preparation, publishing and networking as more important for their success than excelling in classes. Eighty-nine percent felt they needed to work beyond the required curriculum to secure their desired residency position, with 59% reporting little to no trust that the curriculum would prepare them for match. Distrust in the formal curriculum was strongly associated with negative or no perceived personal growth during the first year of medical school ($p = 0.004$).

Major themes that emerged from the focus groups included shifting personal and professional goals, perceived negative climate in relation to resume building, and deteriorating peer relationships.

Major themes that emerged from the focus groups included shifting personal and professional goals, perceived negative climate in relation to resume building, and deteriorating peer relationships.

Conclusion: Uncertainties about securing a successful residency match appear to be influencing a shift in priorities and attitudes among first-year JHSOM students, adversely affecting peer interactions, the learning climate, and trust in the curriculum. Perhaps most concerning is an association of distrust with lack of perceived personal growth. Further research on this relationship is needed, as well as greater attention to how residency match stress impacts early medical students.

Daniel Borota, MS 2

Mentor(s): Paul Nestadt, MD
Department of Mental Health

Increasing Prevalence of Opioids in Maryland Suicides, by Objective Testing (2006-2017)

Authors: Daniel Borota BA, Ramin Mojtabai MD PhD MPH, David Fowler MD, Patrick Triplett MD, Paul S. Nestadt MD

Background: The rate of suicide and use of opioids are on the rise in the US. Prior studies have found increasing opioid involvement in suicides using national death certificate data. Using toxicology reports from the Maryland medical examiner, we evaluated trends in opioid use in suicide decedents in Maryland.

Methods: A retrospective analysis was performed on 5,876 suicides in Maryland from 2006 through 2017. The proportion of decedents who tested positive for opioids at autopsy was calculated for each year. Logistic regression was used to assess change in odds of being opioid positive, controlling for age, sex, and race. This analysis was repeated for cocaine and alcohol intoxication (BAL≥0.08%) to determine if changes in prevalence are unique to opioids.

Results: Prevalence of suicides testing positive for opioids increased significantly from 8.8% in 2006 to 17.7% in 2017. Taking all years into account, opioid prevalence increased with an odds ratio (OR) of 2.00 ($p<0.001$, 95%CI = 1.5-2.6). Cocaine prevalence decreased (OR = 0.33, $p<0.001$, 96%CI = 0.2-0.5), while there was no significant change for alcohol intoxication.

The largest increases in opioid prevalence were observed in 2014-17. The increase was most prominent in African-Americans (OR = 7.1, $p<0.001$, 95%CI = 2.9-17.3). Compared to non-opioid positive suicides, opioid-positive decedents were more likely to be female, white, and to have suicided by overdose (on opioids or other drugs). When we excluded overdose cases, the increase in opioid-use was even greater (OR=2.32).

Conclusion: Opioid use in suicide decedents more than doubled from 2006 to 2017. These results suggest that opioids are not only a concern for addiction and accidental overdose, but are also increasingly prevalent in completed suicides, even outside of overdoses. Consequently, suicide risk assessments should take opioid use into account. Furthermore, increased vigilance and awareness for suicidality is warranted among both opioid prescribers and users.

Jeremy Applebaum, MS 2

Mentor(s): Frank Lin, MD, PhD
Department of Otolaryngology - Head & Neck Surgery

Assessing long-term use of hearing aids and cochlear implants on loneliness in older adults with hearing loss

Authors: Jeremy Applebaum, BS, Matthew Hoyer, BS, Joshua Betz, MS, Adele Goman, PhD, Frank Lin, MD, PhD

Background: The impact of hearing loss treatment on long-term (>1 year post-treatment) outcomes such as communicative functioning have been well-established; however, the long-term impact of hearing loss treatment on distal outcomes, particularly loneliness, is limited.

Methods: In this five-year follow-up to the Studying Multiple Outcomes after Aural Rehabilitative Treatment (SMART) study, 81 participants who received a hearing aid (HA) or cochlear implant (CI) completed the University of California, Los Angeles (UCLA) loneliness scale at baseline, 6-months, 1-year, and 5-year time points. Generalized estimating equations were used to model the population average UCLA score over time.

Results: Loneliness scores were stable at all time points for HA users, while CI users showed significant reduced loneliness at 6-month and 1-year before returning to baseline at 5-years. Degree of loneliness was not associated with any measured demographic factor.

Conclusion: Our results demonstrate the short-term value of CI use in improving loneliness in adults with hearing loss. Future randomized control trials are needed to assess the contribution of normal aging on loneliness in older adults with hearing loss.

Nicholas Fung, MS 2

Mentor(s): Carole Fakhry, MD, MPH
Department of Otolaryngology - Head and Neck Surgery

Tumor-infiltrating lymphocyte expression predicts survival in human papillomavirus-positive oropharyngeal cancer

Authors: Nicholas Fung BS, Farhoud Faraji PhD, Munfarid Zaidi BS, Carole Fakhry MD MPH

Background: Human papillomavirus (HPV)-positive oropharyngeal squamous cell carcinoma (OPSCC) is associated with improved survival compared to HPV-negative OPSCC. Nonetheless, a subset of patients with HPV-positive OPSCC have poor prognosis. There is currently no biomarker available to identify this group of patients. However, expression of tumor-infiltrating lymphocytes (TIL) has previously been shown to be a potential prognostic indicator in HPV-positive OPSCC.

Objective: To evaluate the prognostic value of TIL abundance in resected HPV-positive OPSCC tumor specimens.

Methods: Hematoxylin and eosin stained tumor sections obtained from Johns Hopkins Hospital patients with HPV-positive OPSCC were quantified and sorted into three categories of TIL abundance (high, medium and low). Additional clinical and pathologic characteristics of the tumor were obtained through retrospective chart review. The prognostic effect of TIL abundance was evaluated with Kaplan-Meier, log-rank test, and Cox regression analyses considering recurrence free survival (RFS) as the primary outcome.

Results: This study included 141 patients with HPV-positive OPSCC. Patients with high/medium TIL quantity showed improved RFS (HR: 0.453, 95% CI: 0.222–0.927) compared to patients with low TIL abundance. Interestingly, improved RFS was also observed when comparing patients with a high TIL quantity with low TIL quantity patients (HR: 0.368, 95% CI: 0.150-0.900). In addition, the presence of extranodal extension (HR: 5.228, 95% CI: 1.635–16.716), lymphovascular invasion (HR: 2.860, 95% CI: 1.146–7.139) and perineural invasion (HR: 3.909, 95% CI: 1.572–9.721) were associated with a worse RFS.

Conclusion: Patients with the lowest tertile of TIL abundance were found to have significantly diminished RFS. This data suggests that the immune response plays a role in the improved survival seen in HPV-positive OPSCC and demonstrates that TIL abundance may enhance the prognostic evaluation in the context of AJCC 8th edition staging criteria for HPV-positive OPSCC.

Pauline Huynh, MS 2

Mentor(s): Lisa Ishii, MD MHA
Department of Otolaryngology-Head & Neck Surgery

Exploring Patient Motivations and the Impact of Asian Blepharoplasty

Authors: Pauline Huynh BA, Masaru Ishii MD PhD, Lisa E. Ishii MD MHA

Background: Asian blepharoplasty (AB) is a surgical procedure usually involving the creation of a supratarsal fold to produce a "double eyelid." Our study aims to characterize patient motivations for undergoing this surgery and its impact on quality of life domains.

Methods: We interviewed 19 individuals who desired or underwent AB to elicit their motivations for the procedure. Common themes were incorporated into a web-based exploratory survey, which was distributed through public access websites and to patients at a facial plastic surgery clinic in California. All participants quantified satisfaction with their eye shape before surgery and, if applicable, their motivations, post-surgical satisfaction, and changes in quality of life domains using 100-point visual analog scales. Paired T-tests, logistic regression, and factor analysis were used to explore motivations and changes in quality of life domains.

Results: 353 participants (mean age=25; 72.6% female) completed the survey. 204 participants expressed no desire for AB (control), 90 expressed some desire (Group 1), and 55 already underwent AB (Group 2). Baseline satisfaction scores (mean±SD) were 30.9±13.3, -0.99±22.3, and 4.8±31.4, respectively, and deemed significant after ANOVA testing ($p<0.0001$). Pairwise comparisons revealed that scores were lower in Groups 1 & 2 compared to the control group (both $p<0.0001$). Group 2's satisfaction scores increased to 30.7±20.6 after AB ($p<0.0001$). Factor analysis revealed an index describing the "looking-glass self" concept (comprised of media influence, low self-esteem, and negative stereotyping), which correlated with lower baseline satisfaction ($p<0.05$). A latent self-image index (comprised of happiness, self-esteem, and attractiveness) correlated with post-surgical satisfaction ($p<0.001$).

Conclusion: Respondents who desired or underwent AB reported lower satisfaction with eyelid shape, higher perception that their eyes limit social-professional opportunities, and appear to be motivated by the "looking-glass self" concept. AB was associated with improved satisfaction and self-image. The psychosocial implications of these associations require further study to improve screening for surgical candidacy.

Sakibul Huq, MS 2

Mentor(s): Betty Tyler, BA
Department of Neurosurgery

Ribavirin as an anti-tumor agent against adult glioblastoma and pediatric atypical teratoid rhabdoid tumor

Authors: Sakibul Huq BS, Joshua Casaos BS, Noah Gorelick MD, Henry Brem MD, Nicolas Skuli PhD, Betty Tyler BA

Ribavirin is an FDA-approved anti-viral drug that has recently been repurposed as an anti-tumor agent. Our laboratory previously demonstrated anti-tumor effects of ribavirin in cell and animal models of glioblastoma (GBM). However, the impact of these findings is limited by the blood-brain barrier, which reduces the effective dose of drugs achieved in the brain. In order to build upon our previous findings and optimize the delivery of ribavirin in GBM, we investigated the effects of ribavirin delivered locally via controlled release polymers placed at the site of tumor implantation. We demonstrated that ribavirin-loaded polymers are nontoxic and significantly improve survival of rats orthotopically implanted with GBM tumors. To expand upon these findings, we are currently evaluating the effects of locally delivered ribavirin on GBM in combination with radiation and temozolomide. Furthermore, to investigate whether ribavirin's anti-tumor effects also extend to pediatric brain tumors, we evaluated for the first time the potential of ribavirin as a therapeutic for atypical teratoid rhabdoid tumor (AT/RT), a highly aggressive pediatric brain tumor with no current standard of care. In mice orthotopically implanted with AT/RT, we found that ribavirin decreased tumor burden and extended lifespan in a cell-line dependent manner. To better understand the mechanism of action underlying these effects, we performed western blot experiments in three AT/RT cell lines. In all cell lines, ribavirin decreased expression of EZH2, a tumorigenic epigenetic modulator known to be overexpressed in AT/RT, in a dose-dependent manner. Other known oncogenic targets of ribavirin, including eIF4E and ERK, were also modulated in a cell-line dependent manner in AT/RT. Additional experiments are underway to evaluate the effects of ribavirin on AT/RT in combination with radiation and chemotherapy. Our findings offer increased translational potential of ribavirin in GBM as well as a possible new therapeutic option for children with AT/RT.

Seamus Hughes, MS 2

Mentor(s): David Dowdy, MD PhD
Department of Epidemiology

A Retrospective Study of TB Treatment in the Kisugu and Wabigalo Neighborhoods of Kampala, Uganda

Authors: Seamus B. Hughes BS, Katherine Robsky MPH, David W. Dowdy MD PhD

Background: Identifying obstacles that affect the outcome of patients undergoing tuberculosis (TB) treatment is important in providing efficacious, patient-centered care and limiting the development of drug resistance. The distance a patient resides from their treatment facility may be one such obstacle to achieving TB treatment success.

Methods: We performed a retrospective chart review of patients referred for TB diagnosis and/or treatment in two clinics serving low-income neighborhoods in Kampala, Uganda, between the years 2014 and 2016. We abstracted dates of evaluation, HIV status, age, gender, village/zone of residence, and treatment outcome. Our primary outcome was treatment success, defined as documented completion of at least six months of TB medications, and our primary exposure was distance between self-reported location of residence and the treating health facility. We evaluated the association between distance and treatment success using multivariable Poisson regression with robust estimates of variance, adjusting for HIV status, age, gender, and treatment facility.

Results: A total of 732 patient records were evaluated. Our patient population was 64% male, 41% HIV positive, and lived an average distance of 2.7 km away from the treating health facility. Distance of residence from treatment facility was not found to have a significant association with unfavorable treatment outcomes (adjusted risk ratio, aRR: 1.00, 95% confidence interval, CI: 0.99 - 1.00). Of the characteristics examined, only HIV-positive status was significantly associated with a higher risk of unfavorable treatment outcomes (aRR: 1.52, 95% CI: 1.06 – 2.19).

Conclusion: Distance between residence and clinic was not associated with worse treatment outcomes for TB in two low-income communities of Kampala, Uganda. HIV-positive patients may have higher probability of poor treatment outcomes. Future studies across a more diverse range of treatment facilities (including patients with substantially longer transit requirements) are warranted to more fully characterize the association between distance to clinic and poor treatment outcomes.

Won Kyu Choi, MS 2

Mentor(s): Clifford Weiss, MD
The Russell H. Morgan Department of Radiology and Radiological Science

A Comparison of the Micro Vascular Plug, Amplatzer Vascular Plug, and Coils in Pulmonary Arteriovenous Malformations Embolization

Authors: Won Kyu Choi BS, Christopher Bailey MD, Clifford Weiss MD

Background: Transcatheter embolization is a standard treatment option for pulmonary arteriovenous malformations (PAVMs). Conventionally, multiple coils have been used for PAVM embolization, but show significant recanalization rate. More recently, Amplatzer Vascular Plug (AVP) and Micro Vascular Plug System (MVP) have been used as alternatives. Our goal was to evaluate and compare clinical outcomes of these three embolic devices.

Methods: We retrospectively reviewed records of all PAVMs patients who were treated at Johns Hopkins Hospital with coils, AVP, or MVP using a single type of embolic device between October 2014 and July 2016. We defined technical success as an occlusion of the PAVM feeding artery with no evidence of flow post-procedurally. We collected procedural details, technical success rate, recanalization rate, and cost, where recanalization was determined using computer tomography angiography (CTA). We used multiple regression to evaluate the relationship with outcomes.

Results: A total of 68 patients with 102 PAVMs treatments were included in our study. All procedures with each type of embolic device achieved technical success. Procedure and fluoroscopy time and contrast amount were not different among the three devices. MVP demonstrated the lowest recanalization rates (0%), followed by AVP (7%) and coils (15%). Embolic device cost per procedure was the cheapest for AVP compared with both coils (95% CI [1.61, 2.51], $p < 0.0001$) and MVP (95% CI [0.24, 0.41], $p < 0.0001$), and MVP was cheaper than coils (95% CI [0.46, 0.48], $p = 0.0038$).

Conclusion: Vascular plugs demonstrated superior effectiveness and cost-efficiency compared with traditional coils in PAVMs embolization. Future studies should establish long-term results of AVP and MVP embolization with a larger patient data.

CONCURRENT ORAL PRESENTATION ABSTRACTS

Listed alphabetically by first name of author

Abigail Wang, MS 2

Mentor(s): Casey Humbyrd, MD
Department of Orthopaedic Surgery

Body Mass Index Cutoffs may Worsen Racial Disparities in Lower Extremity Joint Arthroplasty

Authors: Abigail Wang BS, Michelle Wong PhD, Casey Humbyrd MD

Background: Racial/ethnic and sex disparities in lower extremity joint arthroplasty (LEJA) are well-documented. Cost containment strategies, such as bundled payments, may limit access to LEJA for higher risk patients, such as those that are obese or diabetic. This may inadvertently exacerbate LEJA disparities. We examined how eligibility criteria based on body mass index (BMI) and hemoglobin A1c (HgbA1c) could affect disparities in access to LEJA. We hypothesized that cutoffs based on these criteria would significantly limit the eligibility of racial minorities vs. whites and females vs. males.

Methods: We pooled data from 43,792 adults aged 40 years from the 1999–2014 National Health and Nutrition Examination Survey (NHANES). Outcome variables were the following potential eligibility criteria: BMI ≤35, BMI ≤40, HgbA1c ≤8%. Predictors of interest were race/ethnicity, sex, educational level, and annual household income. Multivariable logistical regressions for each criterion included all predictors of interest, age, and survey year. Significance was assigned at $p < 0.05$.

Results: The BMI <35 criterion resulted in lower LEJA eligibility for blacks vs. whites (odds ratio [OR], 0.61; 95% confidence interval [CI], 0.56 to 0.67) and for females vs. males (OR, 0.62; 95% CI, 0.57 to 0.68). The HgbA1c <8% criterion resulted in less access for blacks (OR, 0.44; 95% CI, 0.37 to 0.52) and Hispanics (OR, 0.40; 95% CI, 0.33 to 0.49) vs. whites. For all ORs, $p < 0.01$.

Conclusion: Eligibility criteria based on BMI and HgbA1c may disproportionately affect racial/ethnic minorities and females. This effect is unsurprising since obesity and diabetes affects racial minorities more than whites, and obesity affects females more than males. Limitations of our study include use of self-reported data, and lack of data on other ethnicities, e.g. Asians, or ages above 80. In conclusion, disparities in LEJA access will likely worsen if eligibility for surgery is determined by BMI or HgbA1c.

Ahmed Eltahir, MS 2

Mentor(s): Betty Tyler, BA
Department of Neurosurgery

The efficacy of decoy nucleotide on tumor growth

Authors: Ahmed Eltahir, Betty Tyler

Background: Glioblastoma multiforme (GBM) is the most common type of brain cancer and has a poor prognosis with a median survival of 3 to 6 months. Alkylating agents such as Temozolomide (TMZ) are the first-line therapy to treat GBM. O6-methylguanine-DNA-methyltransferase (MGMT) is a DNA repair enzyme that has been shown to worsen prognosis. We used an in-vivo mouse study to see the effect of silencing MGMT using an oligonucleotide.

Methods: 30 nude mice were injected intracranially with 2x10^5 U87MG cells. They were then divided into five groups: control, control oligonucleotide, active oligonucleotide, TMZ, and active oligonucleotide plus TMZ. 10 mg/kg of TMZ were given orally on day 7 and day 25. 7 ug of oligonucleotides were infused directly into the tumor using convection enhanced therapy (CED) over the course of 5 minutes starting on day 7 and then every 4 days for 12 days and then 25 ug were infused every four days for 42 days. Kaplan meier survival curves were used to analyze the results.

Results: The control group had a median survival of 38 days, while the control oligonucleotide group and the active oligonucleotide group had a median survival of 40 and 42 days respectively. The TMZ group had a median survival of 50 days and the active oligonucleotide plus TMZ had a median survival of 51 days.

Conclusion: While the experimental groups survived longer than the control groups, there was no significant difference between the TMZ and the TMZ plus active oligonucleotide group. In addition, there was no significant difference between the control and active oligonucleotide. The data was inconclusive in determining whether the active oligo conferred any benefits. Future experiments will use different cell lines that might be better models in addition to increasing the dose of active oligonucleotide to achieve greater tumor suppressing effects.

Alexander Kim, MS 2

Mentor(s): David Friedman, MD, MPH, PhD
Wilmer Eye Institute

Outcomes from an Intraoperative Bleb Needling Procedure Augmented with Continuous Infusion

Authors: Alexander Kim MTM, Jayant Iyer MMed, David Friedman MD PhD MPH

Background: Although trabeculectomy is commonly used to lower intraocular pressure (IOP), only 60-75% are successful after four years due to scarring of the bleb. Bleb needling – to lyse scar tissue and allow better aqueous outflow – is one solution to reestablish the bleb in these patients. We previously reported that a modified intraoperative bleb needling technique maintains IOP at or below the target IOP in 64% of patients after 1 year and report longer follow-up in a larger sample of patients here.

Methods: In this retrospective study, we assessed consecutive patients undergoing intraoperative bleb needling at the Johns Hopkins Wilmer Eye Institute. In this technique, an infusion cannula is placed in the anterior chamber and fibrotic adhesions within the bleb are lysed with a 25-G needle transconjunctivally. The continuous infusion of balanced salt solution from the anterior chamber causes bleb elevation, guiding the endpoint of lysis for the procedure. A subconjunctival injection of 5-fluorouracil or mitomycin C is given after each case. Success was defined as achieving a previously determined target IOP.

Results: Needling was performed at an average of 4.5 years from the time of trabeculectomy (SD = 6.7). We observed a 73% success rate and a mean IOP lowering of 8.5 mmHg (95% CI, 5.8-11.3) at 1 year post-op, and 55% success and mean IOP lowering of 10.1 mmHg (95% CI, 6.1-14.0) at 2 years (N=98). 63.7% of patients did not require medications after 1 year, and 35.8% after 2 years. The average medication reduction was 0.9 at year 1 (95% CI, 0.5-1.2) and 0.2 at year 2 (95% CI, -0.3-0.8).

Conclusion: A modified bleb needling technique successfully lowers IOP for at least two years in the majority of patients, can be performed many years after trabeculectomy, and can be used to avoid more invasive procedures such as tube shunts or repeat trabeculectomy.

Alvaro Ibaseta, MS 2

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

Crossing the Cervicothoracic Junction in Cervical Spine Fusion Surgery Involves Higher Operative Risks, but Superior Long-term Outcomes

Authors: Alvaro Ibaseta MS, Richard L. Skolasky ScD, Rafa Rahman BS, Khaled M. Kebaish MD, Lee H. Riley III MD, Daniel M. Sciubba MD, David B. Cohen MD MPH, Brian J. Neuman MD

Background: Whether the cervicothoracic (CT) junction should be crossed in cervical fusion surgery remains up for debate. Keeping C7 as the distal end of the fusion risks adjacent segment disease (ASD) and can result in myelopathy or radiculopathy. Longer fusions are thought to increase operative risk and complexity, but result in lower rates of ASD. This study evaluates the risks and benefits of crossing the CT junction in cervical fusion surgery.

Methods: 187 patients were included and divided into a C7 end-of-fusion cohort (N_C7=68) and a CT-crossing cohort (N_T1=119). To evaluate operative risk, estimated blood loss (EBL), length of hospital stay and operative time were collected. Revision surgery data was also obtained. To evaluate patient-reported outcomes (PROs), Neck Disability Index (NDI) and SF-12 questionnaires (MCS12 and PCS12) were obtained both preoperatively and at follow-up. Changes in PRO scores () were analyzed. In terms of PROs, available data was limited (N_C7=5-10, N_T1=9-12).

Results: Multivariate regression analysis adjusting for age, gender and race showed that EBL (t=2.28, p=0.025, SE=66.03) and operative time (t=3.02, p=0.003, SE=20.37) are significantly increased in the T1 cohort. Length of hospital stay was not significantly different (t=1.02, p=0.31, SE=0.66). Mann-Whitney analysis of PROs showed no significant difference in ΔNDI (W=12, p=1), ΔMCS12 (W=20, p=0.24) and ΔPCS12 (W=47, p=0.13). Fisher analysis showed significantly higher revision rates in the C7 cohort (OR=5.61, CI=[0.97,58.33], p=0.028).

Conclusion: Increased surgical measures such as EBL and operative time show that crossing the CT junction results in a longer, riskier operation that may not be suitable for fragile patients. However, crossing the CT junction leads to lower revision rates, likely due to the avoidance of ASD, and comparable PROs (more PRO data is needed). Thus, the higher short-term risks of crossing the CT junction may be justified given it can help prevent complications without negatively affecting long-term patient-reported outcomes.

Aravind Krishnan, MS 2

Mentor(s): Errol Bush MD
Division of Thoracic Surgery

Double-negative αβ T cells are early responders to lung ischemic-reperfusion injury

Authors: Joshua Hsu ScM, Aravind Krishnan BA, Sul A Lee MD, Bo S. Kim MD, Hamid Rabb MD, Errol Bush MD

Background: Lung ischemia-reperfusion injury (IRI) remains one of the most common complications following lung transplantation and is often accompanied by renal insufficiency. Studies have shown that the ensuing inflammatory response damages lung epithelia during IRI. However, little is known about the cellular changes that occur in the lungs after IRI. Recent evidence has described a novel subset of αβ T cell receptor positive CD4-CD8- (double-negative; DN) T cells in the kidneys after IRI, which are hypothesized to possess anti-inflammatory capabilities. This study sought to characterize and investigate alterations in native DN T cell populations in the lungs and the role they may play in IRI.

Methods: An experimental murine lung IRI model was utilized in this study. Wild-type male, 8-week old C57BL/6 mice (n=4) weighing 23 to 25 g underwent lung ischemia-reperfusion injury, each paired with sham surgical controls (n=4). Ischemia was induced with left pulmonary artery (LPA) ligation for 30 minutes then reperfused for 3 hours. After exsanguination and systemic phosphate-buffered saline (PBS) perfusion, lung and kidney tissues were harvested for lymphocyte isolation. Individual leukocytes were sorted by flow cytometry, and subsets of T cell populations were quantified.

Results: αβ TCR+CD4-CD8- DN T cells significantly increased in the ischemic-injured lung following LPA ligation when compared to sham subjects (Figure 1). Flow cytometric analysis revealed a 2.5-fold change of DN T cells between the injured and control lung ($p<0.001$) as well as a 2-fold increase of DN T cells in the kidneys following LPA ligation ($p<0.005$).

Conclusion: We demonstrated early DN T cell expansion following lung IRI. In addition, the alteration of DN T cells in the kidneys after lung IRI may suggest communication between the two organs. Prior studies have characterized DN T cells as having anti-inflammatory properties, which may suggest a protective role in lung IRI.

Arun Chandra, MS 2

Mentor(s): Hiroshi Ashikaga, MD
Department of Cardiology

Deep Learning Algorithm to Predict Sudden Cardiac Death

Authors: Hiroshi Ashikaga, MD, PhD, Arun Chandra BSE, Robert G. Weiss, MD, Michael Stillabower MD, Gary Gerstenblith, MD, Gordon F. Tomaselli, MD, Katherine C. Wu, MD

Abstract: Although implantable cardioverter-defibrillators (ICD) save lives of high-risk patients for primary prevention of sudden cardiac death, only a minority of ICD recipients experience appropriate firings. We hypothesized that an image-based supervised deep learning algorithm predicts appropriate firings. We prospectively performed gadolinium-enhanced cardiac magnetic resonance (CMR) prior to ICD implantation in 335 primary prevention ICD candidates with ischemic (n=176; 53%) and nonischemic cardiomyopathy (n=159; 47%). During the median follow-up of 5.2 years, 66 patients (20%) developed appropriate firings due to ventricular tachycardia or fibrillation. We rescaled the short-axis CMR to a 3-D matrix of 299 voxels x 299 voxels x 11 slices with normalized signal intensity between -1 and 1. The in-plane resolution was rescaled to 0.75 mm x 0.75 mm, with a region of interest of 224 mm x 224 mm including the entire heart. We randomly split the patients into the training (80%) and the validation set (20%), and trained a deep convolutional neural network to adjudicate if the patient developed appropriate firings or not based on CMR voxel intensities. We used a modified Xception architecture with depth-wise separable convolutions proposed by Chollet. The model weights were modified for each CMR using backpropagation. We reshuffled the training and the validation set with each training epoch. To avoid overfitting, we used data augmentation, including random rotation, shift and shear, to increase the data set to 2,000 cases with equally distributed clinical outcomes. The validation accuracy of the algorithm reached 93% after 10 epochs to predict appropriate ICD firings based on pre-implantation CMR. We conclude that a CMR-based deep learning algorithm can predict appropriate ICD firings with 93% accuracy in primary prevention ICD candidates. Further investigation is warranted to determine if it improves risk stratification compared with the current standard of care.

Christine Gummerson, MS 2

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

Protecting Health through Pollution Control: Medicine, Politics, and London's Great Smog of 1952

Author: Christine Gummerson BA

Background: Ambient air pollution exposure causes approximately 3 million deaths per year worldwide. It is associated with myriad medical conditions, including respiratory disease, cardiovascular disease, neonatal anomalies, and cancer. The inefficacy of existing law in mitigating these harms has profound implications for public health; severe smogs continue to engulf populous cities as climate change threatens only to worsen these episodes. This study explores the relationship between pollution research and legislative progress through the lens of London's Great Smog of 1952, a catastrophic event that caused thousands of deaths. It examines how medical professionals understood the health impact of the Great Smog, and how this perspective informed Britain's Clean Air Act of 1956—the first example of national clean air policy in a major industrialized country.

Methods: Primary sources at the UK National Archives, Wellcome Library, London Metropolitan Archives and London School of Economics were collated and analyzed. Published materials and secondary literature contextualize the study.

Results: Clinical researchers, government medical officers, and major health organizations broadly agreed that poor air quality, especially that of the Great Smog, negatively impacted the health of London's residents. However, methodological limitations in epidemiological practice coupled with insufficient data compromised their ability to offer Parliament strong evidence for specific legislative actions. Existing records reveal that, ultimately, it was not scientific certainty about smog's health effects but rather a strong public desire for pollution control measures that ushered globally-pioneering clean air policy into British law.

Conclusion: This history suggests that clinicians might impact environmental health policy more meaningfully were they to emphasize the preventative health benefits of aggressive pollution control. While current research regarding the precise role of different atmospheric exposures in disease pathophysiology is important, the methodological complexity and limited generalizability of these studies may serve to perpetuate political inaction as much as they further scientific understanding.

Derick Ansah, MS 2

Mentor(s): Sheila West, PhD
Wilmer Eye Institute

A Cross-Sectional Study of Antibiotic Resistance Associated with Pharmacy and Healthcare Practices in Tanzania

Authors: Derick Ansah BS, Jerusha Weaver MPH, Beatriz Munoz MS, Evan Bloch MD, Chris Coles PhD, Thomas Lietman MD, Shiela West PhD

Background: Mass drug administration (MDA) of azithromycin is integral to the control of trachoma. A study in Tanzania found a high prevalence of azithromycin resistance (14.3%) among Streptococcus pneumoniae isolated from children born after MDA cessation. We sought to determine whether availability of azithromycin and prescribing practices for the treatment of pneumonia contribute to azithromycin resistance after MDA cessation.

Methods: A cross sectional survey was conducted in 644 randomly selected communities in Kilosa district, Tanzania. Each community was geospatially mapped and surveyed for the presence of a pharmacy and the availability of azithromycin and erythromycin. In thirty randomly selected communities, a random sample of 60 children under 5 years of age were evaluated for resistance testing. A questionnaire was administered to heads of households (n = 1285) to determine how children with symptoms of pneumonia were treated.

Results: Azithromycin and erythromycin were available in 28.1% and 88.9% of pharmacies, respectively. Availability of azithromycin in a community did not correlate with the presence of resistant isolates of Streptococcus pneumoniae ($p = 0.37$) and Escherichia coli ($p = 0.64$). Neither azithromycin availability ($p = 0.58$) nor azithromycin resistance (i.e. to Streptococcus pneumoniae [$p = 0.69$] or Escherichia coli [$p = 0.38$]) were correlated with proximity to main roads. All households surveyed communicated that they would take their child with symptoms of pneumonia to a hospital and ensure completion of an antibiotic course; 96% of households reported that they would not request a particular drug and all households stated that they would follow a pharmacist's recommendation for medication.

Conclusion: The findings suggest that availability of azithromycin and healthcare practices of community members are not the major factors in the development of azithromycin resistance. Erythromycin cross-resistance, antimicrobial stewardship at the pharmacy/hospital level and antibiotic use in food animals have the potential to develop resistance and merit further investigation.

Diana Bongiorno, MS 2

Mentor(s): Roland Faigle, MD PhD
Department of Neurology

Comorbid Psychiatric Disease is Associated with Lower Rates of Thrombolysis in Ischemic Stroke

Authors: Diana M. Bongiorno BA BS, Gail L. Daumit MD MHS, Rebecca F. Gottesman MD PhD, Roland Faigle MD PhD

Background: Intravenous thrombolysis (IVT) improves outcomes after acute ischemic strokes (AIS) but is underutilized in vulnerable patients such as racial minorities, women, and those with low income. Patients with mental illness are another vulnerable patient population. Mental illness affects approximately 18% of U.S. adults, and these individuals experience inequities in treatment for a range of medical conditions, and are more likely to die within a year after a stroke. We aimed to determine if comorbid psychiatric disease is associated with differences in IVT use in AIS.

Methods: We studied AIS admissions, identified by ICD9-CM codes, from 2007-2011 in the Nationwide Inpatient Sample. Psychiatric disease was defined by ICD9-CM codes for secondary diagnoses of schizophrenia or other psychoses, bipolar disorder, depression, or anxiety. We used logistic regression to test the association between IVT and psychiatric disease, controlling for demographic, clinical, and hospital characteristics.

Results: Of the 335,923 AIS cases that met inclusion criteria, 12.8% had any of the specified psychiatric comorbidities. IVT was used in 3.6% of those with, and 4.5% of those without, psychiatric disease ($p<0.001$). In multivariable logistic regression, having any psychiatric disease was associated with 20% lower odds of IVT (OR 0.80, 95% CI 0.76-0.85). When each psychiatric diagnosis was analyzed separately, schizophrenia and other psychoses were associated with nearly 40% lower odds of IVT (OR 0.61, 95% CI 0.50-0.74). Lower odds of IVT were found in those with depression (OR 0.85, 95% CI 0.79-0.91) or anxiety (OR 0.88, 95% CI 0.79-0.97), compared to those without psychiatric disease. The association between bipolar disorder and IVT did not reach statistical significance (OR 0.86, 95% CI 0.71-1.05).

Conclusion: AIS patients with comorbid psychiatric disease have significantly lower odds of receiving IVT. Understanding barriers to IVT use in such patients may help in developing interventions to improve outcomes and increase access to evidence-based stroke care.

Esther Hsiang, Student in Residence

Mentor(s): Eugene Semenov, MD
Department of Dermatology

Psoriatic Arthritis and Hearing Loss: Data from the National Health and Nutrition Examination Survey

Authors: Yevgeniy R. Semenov MD MA, Esther Y. Hsiang BA, Amy Huang, BA, Xuan Hui, MD ScM, Shawn G. Kwatra, MD, Bernard Cohen, MD, Milan Anadkat, MD

Abstract: Few studies have examined the impact of psoriatic arthritis on hearing impairment. Our aim is to investigate this association in a nationally-representative sample of the U.S. population. Given the known association of hearing impairment and psychiatric comorbidities, a secondary aim is to investigate the impact of psoriatic arthritis on mental well-being. We used data from the National Health and Nutrition Examination Surveys for adults aged ≥ 20 years (n=10,746). Association of psoriatic arthritis with above outcomes was modeled using multivariable generalized linear and ordinal logistic regression models, adjusted for demographics and medical comorbidities. Structural equation models (SEM) were developed to explore the extent to which hearing impairment mediates the effect of psoriatic arthritis on mental health. Psoriatic arthritis was present in 1.1% of the study population. Individuals with psoriatic arthritis were more likely to report hearing difficulties (OR 1.74, p = 0.005), seeing a mental health provider (OR 1.94, p = 0.019), have an average of 2.37 more days of poor mental health over last month (p = 0.002), and were more likely to be depressed (OR 2.66, p = 0.001), than normal controls. SEM analysis revealed that hearing impairment mediated 7.0%, 8.6%, and 6.4% of the effect of psoriatic arthritis on days of poor mental health, seeing a mental health provider, and depression, respectively. This study suggests that psoriatic arthritis is independently associated with a significantly increased risk of hearing impairment, which, in turn, partially mediates an association with poorer psychiatric outcomes. As such, the results of this study call for an increased awareness of these comorbidities when treating patients with psoriatic arthritis.

Eve Bishop, MS 2

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

Cardiac Amyloidosis: Causes and Consequences of a Delayed Diagnosis

Authors: Eve Bishop BA, Marc Halushka MD PhD

Background: On-time diagnosis of cardiac amyloidosis (CA) is correlated with better response to therapy, yet there are reports of patients with long delays in diagnosis. Our objectives were to identify predictors of delayed diagnosis and to evaluate the impact of delayed diagnosis on CA severity.

Methods: Retrospective chart review was performed to determine time from patient-reported symptom onset to diagnosis in all patients diagnosed with CA between May 2014-April 2017 at a single center. Diagnosis was made by endomyocardial biopsy (EMB) and amyloid type was determined using mass spectrometry (MS). Histopathologic CA severity was characterized by amyloid deposition seen on EMB and scored on a 4-tiered scale. Linear and logistical regression models were utilized to 1) determine the baseline characteristics associated with delayed diagnosis, and 2) evaluate the impact of delayed diagnosis on CA severity.

Results: Eighty-two patients with CA were identified. Fifty-two patients had transthyretin (ATTR) amyloid and thirty patients had light-chain (AL) amyloid. The cohort was 27% female, 30% African American, and mean (SD) age at diagnosis was 70.6(9.8) years. Median (IQR) diagnostic delay was 21.7(11.3-55.4) months. Delayed diagnosis was significantly associated with ATTR amyloid type (risk ratio (rr)=2.17, 95% CI [1.31,3.59],p=0.003), carpal tunnel surgery (rr=2.13[1.49,3.03],p<0.001), pacemaker use (rr=1.90[1.55,2.31],p<0.001), age at first symptom (rr=1.85[1.30,2.60],p=0.001), neuropathy as first symptom (rr=1.72 [1.24,2.40],p=0.001), having COPD (rr=1.24[1.03,1.50],p=0.021), and having chronic kidney disease (rr=1.23[1.02,1.49], p=0.027). Delayed diagnosis of greater than two years was significantly associated with histopathologic CA severity (odds ratio=4.81[1.66,13.95],p=0.004), Troponin I (rr=2.48[1.25,4.93],p=0.009), and NT proBNP (rr=2.11[1.35,3.30],p=0.001) at time of diagnosis.

Conclusion: Seven clinical characteristics were identified as significantly associated with delayed diagnosis, and this delay was significantly associated with CA severity. Patients presenting with these characteristics in the setting of cardiac symptoms should be evaluated for CA to ensure a prompt diagnosis and better prognosis.

Helen Xun, MS 2

Mentor(s): Joseph Lopez, M.D. M.B.A.; WP Andrew Lee, M.D.
Division of Plastic and Reconstructive Surgery

Schwann Cell-like Cells (iMDSC) Differentiated from Muscle-Derived Stem Cells (MDSC) Improve Neuromuscular Re-innervation and Functional Outcomes After Rodent Upper Extremity Peripheral Nerve Trauma

Authors: Helen Xun, B.S.; Joseph Lopez, M.D. M.B.A.; Pooja Yesantharao, M.S.; Leila Musavi, B.S.; Kim X. Sinan, B.S.; Howard D. Wang, M.D., Amy Quan, M.D.; Markus Tammia, Ph.D.; Aysel Cetinkaya-Fisgin Ph.D.; Ahmet Hoke M.D. Ph.D.; Gerald Brandacher M.D.; WP Andrew Lee, M.D.; Anand Kumar, M.D.

Background: Peripheral nerve injuries are common, and have debilitating effects on nerve and muscle function. A major challenge in peripheral nerve regeneration is the atrophy or loss of Schwann cells (SC). Recent interest has focused on using stem-cell derived SC for cellular replacement therapy. Mesenchymal stem cells have been proposed to be a good source of SC, but candidates thus far investigated were unsuccessful: bone marrow biopsies are invasive, and adipose-derived stem cells rapidly dedifferentiate without stimulating media. Consequently, there is a pressing need to identify alternative mesenchymal stem cell sources for SC cellular replacement therapy to improve peripheral nerve regeneration.

Methods: Our lab derived SC-like cells from GFP+ muscle-derived stem cells (GFP+ MDSCs) to investigate the potential of SC replacement therapy in the promotion of peripheral nerve regeneration. To assess the in-vivo effects of GFP+ MDSC-derived SC-like cells (GFP+ iMDSC), we used a median nerve injury model developed in our laboratory. Four groups (n=5 per group) of rats with median nerve injuries were examined: (1) animals treated with PBS after nerve trauma; (2) naive controls; (3) animals treated with GFP+ MDSCs; (4) animals treated with GFP+ iMDSCs. All animals underwent weekly upper extremity functional testing. Five weeks post-treatment, the median nerve and extrinsic finger flexor muscles were harvested for analysis of GFP+ MDSC engraftment and proliferation, muscle weight and atrophy, nerve histomorphometry and myelination, and neuromuscular re-innervation.

Results: Five weeks post-injection, GFP+ iMDSC remain stably transformed in-vivo (S100+), are proliferative (Ki-67+), and localize in the endoneurium of the median nerve. iMDSC therapy improved muscle re-innervation ($p = 0.033$), decreased muscle atrophy ($p = 0.0143$), and demonstrated greater functional muscle recovery ($p < 0.0001$).

Conclusion: In rodents with upper extremity nerve trauma, therapy with Schwann-Cell like cells from muscle-derived stem cells (iMDSCs) decreases denervation and muscle atrophy, improves neuromuscular re-innervation, and improves functional outcomes.

Ilan Caplan, MS 3

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

Unclaimed Cadavers at U.S. Medical Schools: Disclosure and Discomfort Among Anatomy Course Leaders

Authors: Ilan Caplan BA, Matthew DeCamp MD PhD

Background: Use of unclaimed bodies (UBs) in U.S. anatomy labs, legalized in the 1800s, has declined since the rise of willed body donation programs. However, some schools still use UBs, which has generated controversy when students were unaware of or troubled by the practice. Whether or how to inform students has not been studied. We collected data on the use of, education around, and attitudes toward UB use at U.S. medical schools.

Methods: We surveyed anatomy course leaders at 146 U.S. AAMC schools with pre-clinical programs. Participants were asked structured and open-ended questions about UB use; disclosure of UB use to students; personal comfort with UB use; and the importance of informing students.

Results: Participants responded from 89 schools (61%). 12% reported using or possibly using UBs, and 7% did not know whether UBs were used. Overall 54% were uncomfortable with UB use; respondents from schools that use UBs were more likely to be comfortable with that use. Reasons for not using UBs included ethical considerations (eg, questions about consent) and safety concerns (eg, risk of unknown infection). 64% of respondents believed it important to inform students when UBs are used. Among schools using UBs, about 1/3 informed students, 1/3 did not, and 1/3 did sometimes. Reasons for informing students included the value of transparency and fostering students' professional development (eg, their understanding of respect for patients or social justice), but some respondents felt unprepared to inform students.

Conclusion: Few medical schools currently use unclaimed bodies, but most anatomy course leaders believe students should be informed about their use. Educating medical students about the history and current practice of UB use could promote their professional development, but novel educational interventions may be needed to support anatomy course leaders in teaching the ethical dimensions of UB use.

Jake Awtry, MS 2

Mentor(s): Elena MacFarlane, PhD
McKusick-Nathans Institute of Genetic Medicine

Investigating epigenetic contributions to pathologic angiotensin II type I receptor expression in Loeys-Dietz syndrome

Authors: Jake Awtry BA MA, Rustam Bagirzadeh, Elena MacFarlane PhD

Loeys-Dietz Syndrome (LDS) is a congenital disorder caused by heterozygous loss-of-function mutations in positive effectors of the TGF-β signaling pathway. In addition to symptoms involving the skeletal and immune systems, LDS patients develop aortic root aneurysm. Current understanding maintains that paracrine signaling between vascular smooth muscle cells (VSMCs) from the embryologically-distinct anterior heart field (AHF) and cardiac neural crest (CNC) cell populations is critical to aneurysm pathogenesis and driven by idiopathic angiotensin II type I receptor (Agtr1a) overexpression in AHF VSMCs. We hypothesize that Agtr1a overexpression in LDS-AHF VSMCs is epigenetically determined during development. To identify epigenetic regulators of Agtr1a we treated murine model primary VSMCs of each lineage and genotype with inhibitors of epigenetic modifiers and quantified Agtr1a expression via RT-qPCR. Inhibiting class I histone deacetylases (HDACs), but not classes II, III, or IV, induced Agtr1a expression in WT-AHF and WT-CNC VSMCs to levels similar to those observed in LDS-AHF VSMCs. However, inhibitors of histone acetyltransferases, BET bromodomains, methylation, and CREBBP/EP300 failed to significantly reduce Agtr1a expression in mutant AHF VSMCs, suggesting that these factors do not significantly regulate Agtr1a. We additionally investigated the epigenetic regulation of Agtr1a by assessing chromatin accessibility using ATACseq. Libraries for WT-AHF, WT-CNC, LDS-AHF, and LDS-CNC VSMCs were sequenced, with full analysis forthcoming. Finally, we attempted to alter the epigenetic state of the Agtr1a locus by identifying putative regulatory enhancers using ChIPseq data from ENCODE and cloning sgRNA-containing plasmids targeting these regions. Ongoing work leverages these plasmids with a dCas9-KRAB fusion protein to promote closed chromatin and reduce Agtr1a expression. Our work demonstrates class I HDAC regulation of Agtr1a expression, provides data on genome-wide chromatin accessibility in LDS and WT VSMCs, and initiates a strategy to epigenetically silence Agtr1a. Future work will seek to exploit epigenetic regulatory mechanisms to therapeutically decrease Agtr1a expression.

Jennifer Qin, MS 2

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

Pharmacy-level Barriers to Implementing Expedited Partner Therapy in Baltimore, Maryland

Authors: Jennifer Z. QIN, BA, Clarissa P. Diniz, BA, Jenell S. Coleman, MD

Background: Addressing record high rates of Chlamydia trachomatis (Ct) incidence in the United States requires utilizing effective strategies, such as expedited partner therapy (EPT), to reduce reinfection and further transmission. EPT, given as a prescription or medication, treats the sexual partners of index patients diagnosed with a sexually transmitted infection (STI) without prior medical evaluation of the partners. We sought to identify pharmacy-level barriers to implementing prescription-EPT for Ct treatment.

Methods: We used spatial analysis and ArcGIS, a geographic information system, to map and assess geospatial access to pharmacies within Baltimore, Maryland. We also surveyed all retail pharmacies in neighborhoods with the highest rates of Ct (1180.25-4255.31 per 100,000 persons).

Results: Census tracts with the highest Ct incidence rates had lower median pharmacy density than other census tracts (26.9 per 100,000 v. 31.4 per 100,000, P<.001). We identified 25 pharmacy deserts. Areas defined as pharmacy deserts had larger proportions of Black and Hispanic/Latino populations compared to non-Hispanic whites (93.1% v. 6.3%, P<.001) and trended toward higher median Ct incidence rates (1170.0 per 100,000 v. 1094.5 per 100,000, P=.110) than non-pharmacy desert areas. Of the 52 pharmacies identified, 96% (50/52) responded to our survey. Less than a fifth of pharmacists (18%, 9/50) were aware of EPT for Ct. Most pharmacists (59%, 27/46) confirmed they would fill an EPT prescription. The cost of a single dose of azithromycin (1 gram) ranged from 5-39.99 USD (median, 30 USD).

Conclusion: Limited geographic access to pharmacies, lack of pharmacist awareness of EPT, and wide variation in medication cost are potential barriers to implementing prescription-EPT. Most pharmacists were generally receptive to learning about and filling EPT prescriptions, suggesting the need for wide dissemination of educational material targeted to pharmacists. In areas with limited pharmacy access, EPT strategies that do not depend on partners physically accessing a pharmacy merit consideration.

Katherine Culbreath, MS 4

Mentor(s): Daniel Rhee, MD
Department of Surgery, Division of Pediatric Surgery

Risk Factors for Adverse Outcomes in Children Undergoing Resection of Primary Liver Tumors

Authors: Katherine Culbreath BS, Alejandro Garcia MD, Ira Leeds MD, Todd Crawford MD, Emily Boss MD, Daniel Rhee MD

Background: For children with primary malignant hepatic tumors, complete tumor resection offers the best chance of long-term disease-free survival. Unfortunately, these patients often present with anemia and, in advanced disease, with failure to thrive which may affect surgical outcomes. The goal of this study is to determine the effect of preoperative anemia and need for nutritional support (NS) on surgical outcomes in children undergoing a major resection for malignant tumors of the liver.

Methods: This is a retrospective cohort study of children undergoing a major liver resection for primary malignant hepatic tumors. Data was collected using the National Surgical Quality Improvement Program Pediatric database from 2012-2015. Demographics, comorbidities, and 30-day outcomes were compared by anemia (defined by age-specific clinical practice guidelines) and preoperative NS (defined as requiring parenteral or enteral feeds) using Fishers exact test. Outcomes include postoperative complications and hospital readmissions. Propensity score matching was performed to control for significant confounders.

Results: 110 children were included in the study with 76 (69.1%) anemic patients and 36 (32.7%) receiving NS. Children with NS were more likely to have cardiac ($p=0.01$), respiratory ($p<0.01$), neurologic ($p<0.01$), and hematologic comorbidities ($p=0.02$). There were 22 (20.0%) postoperative complications and 6 (5.5%) hospital readmissions. After propensity score matching, there was no significant difference in complications between anemic and non-anemic patients (20.6% vs 35.3%, $p=0.28$). Patients receiving NS had an increased rate of complications compared to those not (33.3% vs 11.1%, $p=0.04$). Neither anemia ($p=0.61$) nor NS use ($p=0.05$) had a significant association with readmissions.

Conclusion: Anemia and NS are common in children undergoing resection of malignant liver tumors. NS was associated with several comorbidities and an increased risk of complications after surgery. Thus, the need for nutritional support preoperatively may warrant special attention as a marker of overall conditioning and nutritional status that may result in worse surgical outcomes.

Kevin Xin, MS 2

Mentor(s): Gerald Brandacher
Division of Plastic Surgery

Poly-caprolactone Nanofiber Nerve Wrap Improves Nerve Regeneration and Rodent Functional Outcomes after Delayed Nerve Repair

Authors: Kevin Xin, Joseph Lopez, Amy Quan, Angelo A. Leto Barone, Joshua Budihardjo, Kim X. Sinan, Russell Martin, Zuhaib Ibrahim, Hai-Quan Mao, WP Andrew Lee, Gerald Brandacher

Background: Proper nerve repair plays a critical role in facilitating a neuron's ability to regenerate. Unfortunately, nerve repairs can be compromised by scar proliferation, which has a deleterious impact on patient recovery. Hence, there has been a long-standing clinical interest in developing neuroprotective agents that can reduce scar burden and improve peripheral nerve regeneration after nerve transection. The purpose of this study was to evaluate the efficacy of electrospun poly-caprolactone (PCL) nerve-conduits in improving rat median nerve regeneration.

Methods: Rats had their median nerve severed and repair was delayed for 8-weeks to simulate chronic denervation. Afterwards, transected median nerves were repaired either with nerve-conduit (experimental group) or without nerve-conduit (negative control). Rats were given 14 weeks to recover before the flexor muscles and median nerve were dissected for analysis. A Student t-test was used to evaluate for statistical significance.

Results: Results demonstrated a significantly higher nerve axon count (nerve-conduit = 1769 ± 672 axons, without nerve-conduit = 1072 ± 123.80 axons, $p = 0.0468$) and flexor muscle mass (nerve-conduit = 0.629 ± 0.054 g, without nerve-conduit = 0.511 ± 0.07 g, $p = 0.0175$) in the nerve-conduit group. With regard to functional recovery, at 14 weeks post-repair, rats treated with nerve-conduits had regained 34.9 % of naïve baseline hand grip strength. In comparison, rats treated with ulnar grafts regained only 25.4% of baseline hand grip strength. The difference in grip strength was statistically significant (nerve-conduit = 1.67 ± 0.04 N, without nerve-conduit = 0.97 ± 0.39 N, $p = 0.036$). Sirius red staining revealed less collagen deposition at the nerve co-aptation site of rats treated with nerve-conduits ($p < 0.05$).

Conclusion: Biodegradable, PCL nanofiber nerve-conduits can improve nerve regeneration and subsequent physiological extremity function in the setting of delayed nerve repair by decreasing the scar burden at nerve co-aptation sites.

Li-Kuang Chen, MS 2

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

Submuscular Plates Versus Flexible Nails in Preadolescent Femur Shaft Fractures

Authors: Li-Kuang Chen BA, Brian T Sullivan BS, Paul D Sponseller MD, MBA

Background: Femur shaft fractures are the most common fracture requiring inpatient treatment in children. Surgery is indicated in children over age five, but research comparing the characteristics and outcomes of two surgical methods, submuscular plating (SMP) and flexible nailing (FN), is lacking. We compared patient characteristics, operative time, estimated blood loss (EBL), postoperative length of stay, and incidence of complications after insertion and removal of SMP versus FN in children with femur shaft fractures.

Methods: We reviewed clinical and radiographic records of 58 children with femur shaft fractures who underwent treatment with SMP (N=30) or FN (N=28) by 1 surgeon from 2005 to 2017. Children with pathologic fractures or musculoskeletal comorbidities were excluded. Primary outcomes were operative time and EBL; secondary outcomes were postoperative length of stay and complications. Fisher exact, Pearson chi-squared, Mann-Whitney tests, and linear regression were used as appropriate.

Results: Mean age was 7.7±2.0 years; median follow-up length was 6.8 (interquartile range:28) months. Insertion of FN was associated with significantly shorter operative time (ß=−24min, P<0.001), lower EBL (ß=−38mL, P<0.001), and shorter hospital stay (ß=−0.2d, P=0.032) compared with insertion of SMP, given the same fracture morphology and time from beginning of study period. Removal of FN was also associated with significantly shorter operative time (ß=−15min, P<0.001), while the difference in EBL was not significant (P=0.080). Four SMP and 3 FN patients developed surgical site infections. Two SMP and 7 FN patients experienced implant irritation that resolved with removal. No other complications occurred, and incidence of complications was not significantly different.

Conclusion: Compared to FN, SMP was associated with significantly longer operative times, greater EBL during insertion, and longer post-insertion hospital stay in children with femur shaft fractures independent of fracture morphology. Although SMP is more stable in length and rotation, these disadvantages should be considered when scheduling surgery.

Luke W. Bonham, MS 2

Mentor(s): Pradeep Y Ramulu MD PhD
Wilmer Eye Institute

Retinal Imaging as a Predictor of Functional Outcomes in Glaucoma

Authors: Luke W Bonham BS, Aleksandra Mihailovic MS, Sheila West PhD, David Friedman MD PhD, Pradeep Y Ramulu MD PhD

Background: OCT estimates of parapapillary retinal nerve fiber layer (RNFL) thickness and macular ganglion cell/inner plexiform layer (GCIPL) thickness have recently been associated with quality of life (QoL) in glaucoma. Here, we examine whether these OCT metrics are associated with disability measures beyond QoL, and whether they predict disability independent of visual field (VF) damage.

Methods: One hundred fifty-six adult glaucoma patients received OCT scans to measure RNFL and GCIPL thicknesses. Disability was assessed using a battery of tests including: glaucoma-related QoL, fear of falling, reading speed, and steps per day. Multivariable regression models adjusting for age, race, gender, and other relevant covariates were used to test whether better-eye RNFL or GCIPL thickness was associated with each disability measure, and whether these OCT measures could predict disability independent of VF mean deviation (MD).

Results: Greater VF damage was associated with more severe disability in all measures ($p<0.05$). In the full study population, lower RNFL and GCIPL thicknesses were associated with lower QoL scores. Neither RNFL nor GCIPL thicknesses predicted disability in other measures or QoL scores independent of VF MD ($p>0.05$ for all). To avoid floor and ceiling effects, additional analyses were run in patients whose OCT measures fell between the thicknesses generally associated with normal VFs (55-75µm). In these restricted analyses, RNFL thickness was associated with 2 disability measures (QoL scores, $p=0.047$; fear of falling, $p=0.04$) independent of VF MD, though no such association was observed for GCIPL thickness ($p>0.17$).

Conclusion: After adjusting for floor and ceiling effects, RNFL, but not GCIPL, thickness predicts disability measures independent of VF damage severity, suggesting that RNFL thickness may provide patient-relevant information beyond what is captured by VF testing. Total RNFL thickness may capture information relevant to patient disability by virtue of its ability to gather information outside the region evaluated by standard central VF testing.

Maisa Nimer, MS 2

Mentor(s): Phyllis Sharps, PhD
Johns Hopkins School of Nursing

Exploring the pattern of multiple partners among abused pregnant women

Authors: Maisa Nimer BS, Linda Bullock PhD, Phyllis Sharps PhD

Background: Intimate partner violence (IPV) during pregnancy is an important public health concern, but little is known about the role multiple partners play. The Domestic Violence Enhanced Home Visitation Program (DOVE) examined the effectiveness of nurse home visitation for reducing IPV against pregnant women longitudinally. In this study, we explored the effects of multiple partners on women's mental health and relationships.

Methods: A cross sectional analysis was performed on 239 women (147 rural, 92 urban) in the DOVE randomized control trial. Data was collected on the women's demographics, number of abusers, frequency of abuse, type of abuse, housing of participants, depression scores, support scores, and self-esteem scores.

Results: We found three patterns of partner relationships: single partner (1 partner; partner was abusive), mixed partners (2 or more partners; at least 1 partner was abusive), and multiple partners (2 or more partners; at least 2 or more partners were abusive). The urban and rural sites had different distributions of each category with 55% of urban women reporting mixed partners and 45% of rural women reporting multiple partners. In the urban sample, women in the multiple partner category had the highest rates of abuse over time (75% positive after 12 months), whereas in the rural sample, single partner women had the highest (81% positive after 12 months). For both urban and rural, women in multiple partners had the highest simultaneous physical, psychological, and sexual abuse (38% urban and 17% rural women after 12 months) and the highest depression scale scores.

Conclusion: Screening for IPV during pregnancy is routine, yet women are rarely asked about multiple partners. Our study showed that not only do many women have multiple partners, but also these abusive partners can have a negative impact on their mental health. There is a need for screening to be expanded to include multiple partners.

Marina Horiates, MS 2

Mentor(s): Madeline Leong, MD
Department of Internal Medicine and Palliative Care

Metastasis: a theatrical exploration of cancer invading the boundary between physician and patient.

Authors: Marina Horiates BA, Gail Geller ScD MHS, Joseph Carrese MD MPH, Kyle Yoder BA

Background: Theater has often been used to portray the difficult topic of what it means to be a cancer patient, and further a physician-cancer-patient. As a cancer survivor and medical student, I was interested in exploring the interplay between these two unique populations of cancer patients through the literary genre of drama.

Methods: I selected a play as the vehicle for exploring this topic because I felt that dialogue could best demonstrate the impact patients and physicians-as-patients can have on one another. I prepared for writing this play by conducting interviews with select cancer survivors, journaling about my own perspectives as a survivor of childhood leukemia, and reading both prose and plays about the experiences of other cancer patients, including Malignant: medical ethicists confront cancer and Wit. The first draft of the play was workshopped with the Lyra Theater company in New York City; revisions were based in part on feedback gained at this workshop.

Results: This is a one-act play entitled "Metastasis: a changing," depicting a diverse range of cancer patient experiences. Each scene centers on one character telling his or her story to Skylar Rana, a medical student who reflects on her own experiences as a cancer survivor and future physician. The scenes explore various themes including physician communication, cancer stereotypes, the role of caregiving, mortality, and the art of resilience.

Conclusion: The act of writing this play yielded personal insights for me as a medical student and cancer survivor, highlighting the role of the creative arts as a vehicle for reflection. The play invites audience members, particularly healthcare providers, to explore the impact of cancer and other illnesses on their lives. A limitation of this piece is a lack of socioeconomic and ethnic diversity among the play's characters, which may be an opportunity for expanding the project in the future.

Michael Bell, MS 2

Mentor(s): Trinity Bivalacqua, MD, PhD
The James Buchanan Brady Urological Institute

Novel preclinical models to investigate gene transfer therapy in the bladder

Authors: Michael Bell M.S., Gregory A. Joice M.D., Justin La Favor Ph.D., Nikolai A. Sopko M.D. Ph.D., Trinity J. Bivalacqua M.D. Ph.D.

Background: Gene therapy is a promising area of investigation for treating malignant and benign bladder pathologies. In-vivo gene transfection is resource intensive thus not ideal for screening new therapeutic technologies. The RhoA pathway is involved in smooth muscle contraction and cancer processes. Its inhibitor RhoGDI is a therapeutic target of interest. We validated a novel ex-vivo bladder model to facilitate a high throughput investigation of methods and targets in the treatment pipeline for bladder pathologies.

Methods: NCBI BLAST was used to compare rat and human RhoGDI coding sequences. Human RhoGDI was cloned into a eCMV-based expression vector. NBTII rat bladder cancer cell lines were transfected using FuGENE (Promega, USA) and human protein expression and interaction with endogenous RhoA were tested using flow cytometry, immunofluorescence, and RNA expression analysis. Bladders were harvested from female Lewis Rats (~250g), sectioned sagittally, cultured for 72-hours following transfection with RhoGDI, and analyzed as described above. Non-transfected cultured bladder segments were analyzed using myography for viability and intact smooth muscle physiology in response to 120 mM KCl and 30uM carbachol.

Results: Human and rodent RhoGDI protein homology is 96%. Human RhoGDI was successfully transfected into NBTII and ex-vivo cultured bladder segments. qPCR analysis demonstrated rodent ROCK1 and ROCK2 were significantly decreased by 23.6% ($p=0.034$) and 40.0% ($p=0.015$), respectively following human RhoGDI transfection as compared to transfection control NBTII cells. Non-transfected ex-vivo cultured bladder strips successfully contracted to KCl (mean 0.88+/-0.48 mN/mg tissue) and carbachol (1.82+/-0.97 mN/mg tissue) stimulation. Similar to NBTII cells, qPCR analysis demonstrated rodent ROCK1 and ROCK2 were significantly decreased by 15.0% ($p=0.035$) and 22.4% ($p=0.010$), respectively following human RhoGDI transfection as compared to transfection control bladder strips.

Conclusion: Ex-vivo bladder culture, transfection, and physiological assessment are feasible and may provide a high-throughput method to test novel gene transfer technologies before in-vivo testing.

Michael Fliotsos, MS 2

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

Associations of Body Mass Index from Early-, Mid-, and Older- Adulthood with Incident Heart Failure and Cardiovascular Disease: The Multi-Ethnic Study of Atherosclerosis (MESA)

Authors: Michael Fliotsos, BS, Di Zhao, PhD, Chiadi E. Ndumele, MD, MHS (a,b), Eliseo Guallar, MD, PhD, Gregory L. Burke, MD, Dhananjay Vaidya, PhD, MB BS, Vishal Rao, MD, MPH, Joseph (Chris) A. Delaney, PhD,, Erin D. Michos, MD, MHS

Background: Obesity contributes significantly to increased risk of cardiovascular disease (CVD) and particularly heart failure (HF). However, an elevated body mass index (BMI) in older adults might not fully reflect the additional risk associated with excess weight at a younger age. We determined the prognostic value of self-reported weights from early- and mid-adulthood, after accounting for current weight, with incident HF and CVD.

Methods: We studied 6,437 MESA participants (aged 45-84 years) with self-reported weights at ages 20 and 40 (by questionnaire) and measured weight at the baseline exam (2000-2002). BMI was calculated using measured height at baseline. Cox hazard models assessed relationships between BMI at each age with HF and CVD.

Results: Participant mean age was 62±10 years and 53% were women. Over a median follow-up of 13 years, 290 HF and 828 CVD events occurred. Elevated BMI at each age point (age 20, age 40, and MESA baseline) was independently associated with HF, and to lesser extent with CVD. After adjustment for demographics, CVD risk factors, and baseline BMI, higher self-reported BMIs at ages 20 and 40 years were independently associated with increased risk of incident HF with hazard ratios (HR) 1.18 (95% CI 1.05-1.32) and 1.30 (1.15-1.46), respectively, per 1 SD higher BMI. Participants with self-reported obesity (BMI≥30) at age 20 [HR 3.20 (1.93-5.32)] and age 40 [HR 1.92 (1.31-2.83)] had greater HF risk, even after accounting for current BMI. For incident CVD, only higher self-reported BMI at age 20 (per 1 SD) was associated after accounting for current BMI [HR 1.09 (1.01-1.17)].

Conclusion: Assessment of self-reported lifetime weights is a simple tool easily utilized in any clinical encounter. Although subject to recall bias, self-reported weights provide prognostic information about future HF risk, incremental to current BMI, in a multi-ethnic cohort of middle-aged to older adults.

Michael Harper, MS 2

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

The Association Of Hearing Loss With Loneliness And Social Isolation: A Systematic Review

Authors: Michael Harper MM, Jeremy Applebaum, Matthew Hoyer, Nicholas Reed AuD, Frank Lin MD

Background: Age-related hearing loss is highly prevalent and is independently associated with accelerated cognitive decline. One proposed mechanism behind this association stems from decreased social engagement. Hearing loss directly impairs communication and may contribute to both perceived loneliness and objective social isolation. Importantly, this may represent a modifiable pathway and offer a significant opportunity for intervention. The objective of this study was to review literature examining the association of hearing loss with loneliness and social isolation among adults with age-related hearing loss.

Methods: We performed a structured literature search of five databases (PubMed, Embase, CINAHL, PsychINFO, and Cochrane). Retrieved studies were reviewed in two stages: a two-person title/abstract review followed by a single-author full-text review. Inclusion criteria for studies were: (1) original, peer-reviewed research article; (2) enrolled subjects with age-related hearing loss (measured or self-reported); (3) utilized validated measures of loneliness and/or social isolation; and (4) in English. Included studies were assessed for risk of bias using a modified NIH Quality Assessment Tool.

Results: Our search yielded 2,048 citations for review. From these we identified 9 papers describing the relationship between hearing loss and loneliness and 3 describing the relationship between hearing loss and social isolation. Due to the heterogeneity of study instruments, quantitative meta-analyses could not be performed. However, 8 of 9 loneliness studies and all 3 social isolation studies presented significant associations with hearing loss. Additionally, two of these studies presented longitudinal data suggesting a possible causal relationship between hearing loss and loneliness.

Conclusion: This review suggests a relationship exists between hearing loss and both loneliness and social isolation, but further research is needed. While future studies using pure-tone audiometry are needed to quantitatively assess the effects of hearing loss as a continuous variable, in clinical practice self-report questionnaires may better identify patients at the greatest risk of loneliness and social isolation.

Michael McColl, MS 2

Mentor(s): Gedge Rosson, MD
Department of Plastic and Reconstructive Surgery

Optimal Post-Operative Antibiotic Prophylaxis After Breast Surgery: A Meta-Analysis

Authors: Charalampos Siotos, MD, Michael McColl, BS, Mohamad E. Sebai, MBBS, Stella M. Seal, MLS, Michele A. Manahan, MD, Mehran Habibi, MD, Carisa M. Cooney, MPH, Gedge D. Rosson, MD

Background: Current clinical guidelines dictate the use of prophylactic antibiotics antibiotic after breast surgery for the prevention of surgical site infections (SSI). However, there is no agreement among physicians on whether post-operative prophylaxis after clean surgeries, like breast surgery is necessary nor is there agreement on the duration of the prophylaxis. We sought to systematically evaluate the current literature regarding the optimal use and duration of post-operative antibiotic prophylaxis in plastic breast surgery.

Methods: We systematically searched the PubMed, Embase, Cochrane and Web of Science databases for relevant articles published until January 2017. We performed meta-analysis employing Random Effects Model and the RevMan software.

Results: Our search revealed 727 articles, which were screened based on their title and abstract. Of them 56 were screened based on the full text. Following the screening process, 10 studies (one randomized trial, one observational prospective and eight retrospective) met our criteria. Overall, 4,354 patients were included who underwent mastectomy, breast reconstruction, breast reduction or breast augmentation. Meta-analysis of 6 studies showed that pre-operative only use of antibiotics was associated with higher risk for SSI, although not at a statistically significant level (2,902 patients, OR=1.54, 95%CI [0.87-2.74], p=0.31, I2=64%). The results of our second meta-analysis indicates that short duration (≤24 hours) of post-operative antibiotics was statistically significantly associated with higher odds of SSI (5 studies, 2,843 patients, OR=1.59, 95%CI [1.02-2.46], p=0.04, I2=28%).

Conclusion: Our results support a benefit of postoperative antibiotic use and suggest a prolonged (>24 hours) course of antibiotics for clean breast surgeries, especially for those performed on cancer patients. There is a need for further study that weighs the protective effect of postoperative prophylactic antibiotic use against the challenges of patient complications, microbial resistance, and cost in this unique setting of cancer related breast surgery in order to accurately delineate a best practice.

Michelle Juarez , MS 2

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

Thyroidectomy neck scars lead to attentional distraction: an objective measurement of social attention using eye-tracking

Authors: Michelle C. Juarez BS, Masaru Ishii, MD, PhD, Jason Nellis, MD, Kristin Bater, BA, Lisa Ishii, MD

Background: Thyroidectomy is a common medical procedure used to treat various thyroid disorders. New and innovative technologies have allowed for minimally invasive approaches to reduce neck scar visibility, yet little is known about the social perception of neck scars. This study seeks to understand how thyroidectomy neck scars impact how observers direct visual attention.

Methods: Blinded casual observers viewed images of 8 patients with thyroidectomy neck scars, 8 controls with no scars, and 2 patients that underwent trans-oral thyroidectomy surgery. Observers gazed freely upon frontal face images as an infrared eye tracking monitor recorded their eye movements. One-way ANOVA testing was used to compare fixation durations for predefined areas of interest including the eyes, nose, mouth, central triangle, peripheral face, and neck between scar patients and controls.

Results: 130 participants successfully completed the eye-tracking experiment. Observers gazing on both control and scar patients directed most of their attention to the central triangle. We found no significant differences in fixation times for the nose, eyes, mouth and central triangle between controls and scar patients. Fixation times for the neck and peripheral face regions were significantly different between the two groups, however. Observers paid more attention to the neck area (245 ms, $p < .0001$, 95% CI [127.7, 362.4]ms) and less attention to the peripheral face (-283.9 ms, $p < .04$, 95% CI[-555.5, -12.35]ms) in patients with neck scars than in controls. In other words, observers preferentially redirected their attention towards the neck in scar patients.

Conclusion: Casual observers directed attention in a measurably different way when gazing on patients with thyroidectomy scars as compared to control patients. Thyroidectomy scars preferentially redirect observer attention towards the neck compared to control patients. These findings shed light onto the altered observer perceptions of patients with thyroidectomy scars and can be used to direct our reconstructive efforts.

Michelle Recto, MS 2

Mentor(s): Anne Murphy, MD
Department of Pediatrics

A novel alpha-tropomyosin mutation (D55N) is associated with familial dilated cardiomyopathy

Authors: Michelle A. Recto BA, Brittney Murray MS, Anne M. Murphy MD

Background: Dilated cardiomyopathy (DCM) is the most common form of cardiomyopathy and is associated with significant morbidity and mortality. Familial forms constitute the single most common etiology of DCM, and many genes and mutations have been implicated in DCM, most of which code for structural components of the sarcomere, costamere, or nuclear membrane. Identifying pathogenic mutations is critical in determining pathophysiology and possible therapeutic interventions. We report familial DCM spanning four generations in a family of Greek descent associated with a novel α-tropomyosin (TPM1) mutation, D55N. TPM1 mutations have previously been reported in both hypertrophic and dilated cardiomyopathy.

Methods: A retrospective analysis of the pedigree was conducted. The proband and each participating family member (n=8) underwent a history, physical exam, electrocardiogram, echocardiogram, and genetic testing for the D55N mutation. Individuals were considered to have clinical DCM if they met either of the following criteria: i) fractional shortening below 25% or left ventricular ejection fraction below 45%, or ii) left ventricular end diastolic dimension greater than 117% of the normal value adjusted for body surface area and age.

Results: The age of diagnosis of clinical DCM in the genotyped participants ranged from the fourth to the seventh decade of life. However, family members that were presumed affected but not genotyped spanned in age from six months to eighty-six years old, including two individuals who underwent orthotopic heart transplant in the first and second decades of life. The pattern of inheritance of DCM in this family was found to be autosomal dominant with a 71% penetrance.

Conclusion: The association of the D55N mutation in the TPM1 gene with DCM serves as additional support for TPM1 being a disease gene for DCM. Further investigation is ongoing to determine the functional impact of the mutant in order to better understand the pathophysiology of DCM.

Munfarid Zaidi, MS 2

Mentor(s): Carole Fakhry, MD
Department of Otolaryngology - Head and Neck Surgery

Increasing Age of HPV-Positive and HPV-Negative Oropharyngeal Cancer Patients Over Time: Analysis of the National Cancer Database

Authors: Munfarid Zaidi BS, Eleni Rettig MD, Farhoud Faraji PhD, Margueritta El Asmer MD, Nicholas Fung BS, Carole Fakhry MD

Background: A subset of oropharynx cancers (OPC) are associated with human papillomavirus (HPV) infection. Among patients under the age of 55, OPC is more commonly HPV-associated. A recent analysis described increases in OPC incidence among individuals older than 65 years, but it is unknown whether HPV is responsible for this trend. HPV-related OPC is associated with improved survival compared with non-HPV OPC. To inform future clinical trial design, our objective was to determine whether HPV-positive status confers prognostic advantage to older individuals.

Methods: This was a retrospective cohort study performed in 29,504 patients in the National Cancer Database (NCDB). Tumors which tested positive for HPV of high-risk or unknown type were "HPV-positive", tumors which tested negative for high-risk HPV were "HPV-negative", and tumors without testing were "unknown". Age was categorized into four groups: ages 18-49, 50-59, 60-69, and 70-90. Prevalence trends by age were calculated by nonparametric test of trends. The effect of tumor HPV status on survival was evaluated with Kaplan-Meier and Cox proportional hazards regression methods.

Results: The prevalence of HPV-positive tumors increased significantly from 2010-2014 in all age groups ($p_{trend}<0.001$ for all). The increase was more dramatic in patients 70+ year old (from 45% to 60%) than in the younger age groups (60% to 69% for 60-69 year olds, and 65% to 71% for 50-59 year olds). Among patients 70+ years old, HPV-positive tumor status was associated with improved survival (HR 0.60, $P<0.001$), however this was significantly attenuated when compared with younger age groups (HRs of 0.40-0.46 for younger age groups, $P<0.001$ for all).

Conclusion: An HPV-attributable increase in OPC prevalence was observed in all age groups from 2010 to 2014. HPV-positive status confers an attenuated reduction in risk for mortality in 70+ year olds, warranting inclusion of this cohort in future clinical trials.

Pranjal Gupta, MS 2

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

Gender differences in MYL4 mosaic pattern of protein expression in cardiomyocytes

Authors: Pranjal B. Gupta, B.E., Vince DeMario, B.S., Raj Amin, M.D., Robert S. Sterling, M.D., Harpal S. Khanujah, M.D., William W. Yang, B.S., Paul M. Ness, M.D., Steven M. Frank, M.D.

Background: Recent studies support giving less blood to patients, and have also demonstrated adverse outcomes and significant costs associated with unnecessary transfusions. We recently implemented a comprehensive, system-wide, blood management program aimed at reducing overall blood utilization. This study examined transfusion practice and clinical outcomes in all 2,951 orthopedic surgery patients at Johns Hopkins Bayview Medical Center between January 2013 and June 2016.

Methods: In January 2015 we initiated provider education, use of tranexamic acid (an antifibrinolytic), a new surgical blood order schedule, electronic best practice advisories, a "Why Give 2 When 1 Will Do?" campaign advocating single unit RBC transfusions, and audits with provider feedback for guideline compliance. Patients were divided into pre- or post-blood management cohorts based on surgical date, and compared using in-hospital databases.

Results: Aggregate patient complexity measured by casemix index and age was slightly but significantly higher in the post-blood management group. The mean hemoglobin transfusion trigger and target decreased by 0.88 g/dL and 0.65 g/dL respectively ($P<0.0001$) in the post-blood management cohort. There was a 37% decrease in the proportion of patients transfused ($P<0.0001$), and a 24% decrease in mean RBC units per patient ($P=0.036$). Median length of stay decreased by 1 day ($P<0.0001$), and the morbid event rate decreased from 1.4% to 0.5% ($P=0.01$). Mortality rate was unchanged and 30-day readmission rate significantly decreased from 8.8% to 6.0% ($P=0.007$).

Conclusion: Our results demonstrate that implementation of a comprehensive patient blood management program reduced overall blood utilization in orthopedic surgery, and is associated with shortened length of stay and fewer readmissions, with a decrease or no change in adverse outcomes.

Rahul Sachdev, MS 2

Mentor(s): Rita Kalyani, MD
Department of Endocrinology

Preoperative Factors Associated with Insulin-Free Survival after Total Pancreatectomy with Islet Auto Transplantation

Authors: Rahul Sachdev B.S., Parichoy Choudhur PhD, Rita Kalyani MD

Background: Total pancreatectomy with Islet Autotransplantation (TPIAT) is a surgical intervention used to prevent post-surgical diabetes amongst patients undergoing pancreatectomy. Currently, islet yield is the only consistent predictor of insulin independence post-TPIAT. However, islet yield can only be measured postoperatively, eliminating its use in both patient selection and counseling, suggesting other preoperative factors are needed.

Methods: In this prospective cohort study, we gathered preoperative imaging and demographic data from participants without underlying diabetes who underwent TPIAT at Johns Hopkins Hospital between 2011 and 2016. All patients underwent T1 MRI and dual phase contrast enhanced CT. CT was used to collect data regarding pancreatic volume, pancreatic duct dilation, presence of abnormal side branches, and the presence of calcification. MRI was used to collect data regarding abnormal side branches and calcification. Both CT and MRI were used to determine Cambridge Classification preoperatively.

After imaging data was collected, t-test, logistic regression, and ROC analysis was used to determine the association between imaging variables and insulin status 1-year post-TPIAT.

Results: 34 participants were recruited for the study. At one year, 10 participants were insulin independent and the 24 were insulin dependent. The presence of abnormal side branches, as found using CT scans, was higher in the insulin dependent group as opposed to the insulin independent group (29% vs. 0%, p-value 0.034). Similarly, MRI also showed a positive correlation between the presence of abnormal side branches and insulin dependence (54% vs. 11%, p-value: .047).

Conclusion: Imaging, in the form of both CT and MRI, can be used as a valuable predictor of insulin independence post-TPIAT. In particular, we found that the presence of abnormal side branches was associated with negative outcomes, in the form of higher rates of insulin dependence post-TPIAT. This finding the conclusion that CT and MRI can serve as valuable tools to predict insulin outcomes post-TPIAT.

Rakesh Goli, MS 2

Mentor(s): John W. McEvoy, M.B.B.Ch., M.E.H.P., M.H.S.
Division of Cardiology

Dose Dependent Effects of Intravenous Fentanyl Administration on Ticagrelor Absorption and Platelet Inhibition in Patients Receiving Percutaneous Coronary Intervention: A Sub-Analysis of the PACIFY Randomized Clinical Trial

Authors: Rakesh R. Goli B.A., Khalil Ibrahim M.D., Thomas S. Kickler M.D., William A. Clarke Ph.D., Steven P. Schulman M.D., John W. McEvoy M.B.B.Ch., M.E.H.P., M.H.S.

Background: Rapid and intense platelet inhibition is essential in the treatment of patients undergoing percutaneous coronary intervention (PCI). We recently demonstrated that patients randomized to fentanyl, an intravenous opiate commonly administered during PCI, have delayed gastrointestinal absorption of oral P2Y12 inhibitors and attenuated platelet inhibition. In this secondary-analysis of the PACIFY trial, we studied whether the dose of fentanyl administered has implications for platelet inhibition outcomes.

Methods: We enrolled 212 patients requiring clinically indicated coronary angiography into a single-center blinded trial, randomized to undergo the procedure either with or without intravenous fentanyl in a 1:1 fashion. Of these, 70 required 180 mg ticagrelor loading for PCI; 35 patients received fentanyl (with the dose provided at the discretion of the treating cardiologist) and 35 received no fentanyl. Platelet function was measured at 2 hours after ticagrelor administration using VerifyNow (Platelet Reactivity Units, PRU) and using impedance aggregometry (measuring ADP-induced platelet aggregation).

Results: The mean (SD) total fentanyl dose administered for PCI among the 35 PACIFY patients randomized to fentanyl was 100mcg (±53mcg). Comparison of patients receiving above or below the mean fentanyl dose revealed borderline lower ADP-induced platelet aggregation among those who received less fentanyl (30% with fentanyl <100mcg vs. 40% with fentanyl ≥100mcg, p=0.059). In linear regression analyses, for every unit increase in cumulative procedural fentanyl dose, there was a 37-unit increase in PRU (p=0.03) and an 11% increase in ADP-induced platelet aggregation (p=0.01).

Conclusion: We have previously shown that patients randomized to fentanyl have slower absorption of oral ticagrelor, attenuating its effect on platelet inhibition. This secondary analysis now demonstrates that the mechanism of this effect appears to be dose-dependent. The results of this study should motivate interventional cardiologists to consider whether fentanyl is needed and, if it is, to minimize the dose when rapid platelet inhibition is desired.

Ravi Medikonda, MS 2

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

Glutamate Modulation Synergizes with anti-PD-1 Immunotherapy in Glioblastoma Treatment

Authors: Ravi Medikonda BA, Zineb Belcaid MD, Michael Lim MD

Background: Glioblastoma (GBM) is a highly invasive brain cancer with a median survival of 14 months. Recently, advances in cancer immunotherapy (modulating the tumor microenvironment to enhance the immune system's ability to eliminate tumor cells) such as anti-PD-1 treatment have shown to improve survival in several tumors. It is known that GBM increases glutamate in the tumor microenvironment causing excitotoxicity and neuronal death. We hypothesize that this increase in glutamate inhibits the anti-tumor immune response. Thus, we are currently studying BHV (a drug that decreases glutamate in the tumor microenvironment) and its potential to synergize with immunotherapy.

Methods: We conducted a survival study in which mice were injected with murine GL261 glioma cells and treated with either anti-PD-1 only, BHV only, or anti-PD-1 and BHV. Then, we performed a depletion study in which mice with GL261 tumors received anti-CD4 or anti-CD8 to deplete the respective T-lymphocyte subtype. These mice were treated with BHV only or anti-PD-1 and BHV.

Results: In the survival study, we found a statistically significant survival benefit for the anti-PD1 and BHV combination treatment compared to either BHV only or anti-PD1 only ($p < 0.05$). The depletion study showed a rapid decline in survival for the treatment arms depleted of CD4 T-lymphocytes compared to the control and CD8-depleted treatment arms ($p < 0.05$).

Conclusion: Our in vivo results suggest that BHV and anti-PD-1 have a synergistic benefit to survival. Furthermore, it appears that CD4 depletion affects survival to a greater extent than CD8 depletion and both anti-PD1 and BHV are more effective when CD4 T-lymphocytes are present. To further elucidate the relationship between BHV treatment and immune cell activity, we plan to treat mice with BHV and perform immunohistochemistry staining in brain tissue for immune cell markers to assess immune cell migration to the tumor site.

Regina de Luna, MS 4

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

Poor balance, visual field damage and falls in glaucoma

Authors: Regina A. de Luna, BS, Aleksandra Mihailovic, ScM, Angeline M. Nguyen, MD, David S. Friedman, MD, PhD, Sheila K. West, PhD, Laura N. Gitlin, PhD, Pradeep Y. Ramulu, MD, PhD

Background: Falls are the leading cause of death in patients over 65 years old in the US and result in economic losses of over $37 billion. Vision and balance have independently been identified as major risk factors for falls in small study populations. Prior work has shown that visually impaired patients are twice as likely to fall compared to their normal sighted counterparts, and balance deficits among geriatric populations predict recurrent fall risk. What is less understood is whether poor balance can explain the increased rate of falls in populations suffering from vision loss. The purpose of this study is to evaluate the relationship between balance and falls among glaucoma patients, and to determine if balance accounts for the association between visual field (VF) damage from glaucoma and falls.

Methods: Balance data were collected on 233 patients with glaucoma using sensors that measured root mean squared (RMS) sway (RMS of the acceleration vector length) with the patient standing on a foam surface with eyes opened. Negative binomial regression was used to determine: (1) if balance predicted fall rates in a population of glaucoma patients, (2) if the impact of balance on fall rates increased when patients had worse VF damage, and (3) if balance mediated the relationship between VF damage and falls in glaucoma.

Results: Average patient age was 70.5 years (range 57-93). Worse balance, as judged by RMS sway was associated with greater fall rates per step taken ($p<0.001$). When both balance and IVF sensitivity were incorporated into the same regression model, both were found to independently predict falls per step (VF loss: $p=0.01$; RMS sway: $p=0.001$). However, balance was not noted to impact fall rates more strongly when patients had greater VF loss ($p=0.32$).

Conclusion: VF damage and balance are independent contributors to falls, however the association between VF damage and falls does not appear to be mediated by poor balance. These results suggest that variables other than balance, such as gait or hazard perception, may instead account for an increased rate of falls in glaucoma patients.

Ross Liao, MS 2

Mentor(s): Phillip Pierorazio, MD
The James Buchanan Brady Urological Institute

Incidence of Lower Pathologic Stage in Patients Treated with Neoadjuvant Chemotherapy for High-Risk Upper Tract Urothelial Carcinoma

Authors: Ross S. Liao BA, Mohit Gupta MD, Zeyad R. Schwen MD, Hiten D. Patel MD, Max Kates MD, Michael H. Johnson MD PhD, Noah M. Hahn MD, David McConkey PhD, Trinity J. Bivalacqua MD PhD, Phillip M. Pierorazio MD

Background: High-risk upper tract urothelial carcinoma has been associated with poor survival outcomes. Limited retrospective data supports the use of neoadjuvant chemotherapy prior to radical nephroureterectomy. We evaluated the change in pathologic stage distribution in patients with high-risk upper tract urothelial carcinoma who underwent neoadjuvant chemotherapy followed by radical nephroureterectomy to validate prior findings.

Methods: We performed a retrospective analysis of 240 patients at The Johns Hopkins Hospital from 2003-2017 with upper tract urothelial carcinoma. Patients with biopsy-proven high-grade disease with a visible lesion on cross-sectional imaging were offered neoadjuvant chemotherapy prior to radical nephroureterectomy. A control group comprised of a time-matched cohort of patients with biopsy-proven high-grade disease underwent extirpative surgery alone. Chi-square and Fisher exact tests were used to evaluate clinical and pathologic variables between cohorts.

Results: There were 32 patients in the study group and 208 patients in the control group. A significantly lower pathologic stage was noted in the study group compared to the control group ($P<0.001$). The incidence of patients with pT2 disease or higher was significantly lower in patients treated with neoadjuvant chemotherapy (37.5% vs. 59.6%; $p=0.02$). There was a 46.5% reduction in the incidence of pT3 disease or higher in study group patients without clinically-node positive or low-volume metastatic disease (25.9% vs. 48.4%; $p=0.04$). A 9.4% complete remission rate was observed in patients undergoing neoadjuvant chemotherapy.

Conclusion: Patients with high-risk upper tract urothelial carcinoma treated with neoadjuvant chemotherapy are noted to have lower pathologic stage distribution compared to those treated with radical nephroureterectomy alone.

Sina Famenini, MS 2

Mentor(s): Trinity J. Bivalacqua, MD, PhD
The James Buchanan Brady Urological Institute

BCG Retreatment in BCG Relapsing/Unresponsive patients: A Reexamination of the AUA NMIBC Guidelines

Authors: Sina Famenini BS, Max Kates, MD, Hiten D. Patel, MD, MPH, Trinity Jude Bivalacqua, MD, PhD.

Background: Transurethral resection of bladder tumor (TURBT) followed by Bacillus Calmette-Guèrin (BCG) immunotherapy is the first-line, and recommended second-line treatment for patients with non-muscle invasive bladder cancer (NMIBC). However, little evidence exists for the efficacy of repeat BCG compared to alternative treatments. We aimed to address whether non-BCG modalities as sequential intravesical chemotherapy are superior alternatives to repeat BCG.

Methods: We performed a retrospective review of 143 patients who received an induction course of BCG as first-line intravesical treatment for NMIBC at JHH (2005-16). Demographics and outcomes [response rate, bladder-intact rate, and Recurrence-free survival (RFS)] were analyzed using chi-squared, paired t-test, Kaplan-Meier, and Cox proportional hazard models.

Results: 143 patients were included of which 84% were male and 80% Caucasian. 113 did not respond to first-line BCG with 101 receiving second-line intravesical therapy (77 BCG+Interferon (IFN) and 24 non-BCG treatments). Response rate for BCG+/-IFN was 45.5% vs. 20.8% for non-BCG modalities (p=0.03). The RFS after second-line therapy was 2.3 years for BCG+/-IFN vs. 1.30 years for non-BCG modalities (p=0.05). Those treated with second-line BCG+IFN had similar likelihood for recurrence as those treated with BCG alone (hazard ratio (HR)=1.044, 95% CI 0.57-1.9, p=0.89). Patients receiving non-BCG treatment were twice as likely to recur (HR=1.96 95% CI 1.14-3.35, p=0.015) than those treated with BCG+/-IFN. In total, 24 patients with NMIBC refractory to intravesical treatment underwent cystectomy, 7 after first-line and 17 after second-line treatment. Those treated with BCG+/-IFN had a non-significantly 24.2% lower bladder-intact rate when compared to those who received non-BCG second-line therapies (67.5% vs. 91.7% p=0.074).

Conclusion: The addition of Interferon to second-line BCG does not improve response rate and RFS. Bladder-intact rate is non-significantly higher for BCG+/-IFN compared to other modalities. BCG+/-IFN second-line intravesical therapy correlates with longer RFS compared to non-BCG modalities. BCG-based therapy appears superior based on currently available data.

Sophia Diaz, MS 2

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

Over the Counter DNA: The Rise of Genomic Alternative Medicine since the Human Genome Project

Authors: Sophia Diaz BSc, Nathaniel Comfort PhD

Background: DNA-based skin creams, supplements, and fitness regimens now comprise Americans' $30.2 billion expenditure on alternative medicine. They became a trend thanks to scientific discoveries prompted by the Human Genome Project (HGP), legislation like the Genomics and Personalized Medicine Act, and the rise of big data. Originally touting humanity's shared genetic foundation, the HGP instead led to a new DNA essentialism based on the self. This project analyzes how entrepreneurs have harnessed this shift in health and beauty industries.

Methods: Online research was conducted to identify health and beauty brands that utilize DNA sequencing, DNA/DNA repair enzymes, and DNA-related symbolism as part of their branding strategy. Three were selected as case studies: a bespoke dietary supplement based on gene sequencing, skin creams utilizing DNA repair enzymes, and DNA-supporting supplements. Oral history interviews were conducted with the companies' CEOs, founders, Marketing VPs, scientists, and an unaffiliated Johns Hopkins geneticist.

Results: There were three major findings. First, scientific authority, such as Nobel-prize-winning technology, distinguished company founder(s), and clinical studies attract customers, making it integral to DNA-related product marketing. Second, DNA-related products promote the idea of obtaining control over one's health. Not only do consumers feel empowered with knowledge of their genetic predilections, but they also become the makers of their own regimens by combining products of their choice. Third, the use of these DNA-based methods appeals to the demand of personalizing healthcare.

Conclusion: The post-HGP landscape along with discontent in the U.S. healthcare system create desire in the patient-consumer for high-tech, alternative products that offer control over their health. This research disputes where true control lies: with the consumer, or with the companies mining and interpreting their genetic data. By analyzing these products' evolution, this study explores Americans' socio-cultural perception of DNA, the future of healthcare, and health ownership..

Suganya Sridharma, MS 2

Mentor(s): Hadi Kharrazi, MD, PhD
Division of Health Sciences Informatics

Prevalence and Risk Factors of Pediatric Falls in Maryland

Authors: Suganya Sridharma SB, Amyna Husain MD, Hadi Kharrazi MD PhD

Background: Falls are the leading cause of hospitalization and emergency department (ED) injury-related visits among children under 15 years. Annually, 3.5 million children visit hospitals for fall injuries in the United States. In this study, we define the prevalence of and identify risk factors for pediatric fall injuries in Maryland (MD).

Methods: We obtained MD hospital inpatient, outpatient, and ED visit records of 764,257 MD patients 19 years and younger for 2013-2015 from the MD Health Services Cost Review Commission. We calculated prevalence of fall injury stratified by age group (0-12 months and 1-4, 5-9, 10-14, 15-19 years), race, ethnicity, type of insurance, and area of residence. We generated a logistic regression model to predict the risk of fall injury from 27 clinical variables. Finally, we categorized fall mechanisms and examined incidence across age groups.

Results: From 2013-2015, 84,892 children visited MD hospitals for fall injuries, representing 11.1% of all children seen. Of all pediatric visits to the ED, 7.44% were due to fall injuries. Mapping displayed a high rate of fall injury near the Northwest border of Washington D.C. and a variety of rates among block groups within Baltimore City. Of all children who experienced falls, 52.3% had public insurance. Falls were most likely in males aged 5-9 years, and in whites and those of non-Hispanic origin. Predictive modeling identified increased risk of fall injury associated with attention deficit disorder and asthma, and decreased risk associated with depression. Seizure disorder was associated with decreased risk in those younger than 9, but increased risk in those over 15. Among children ages 1-4, the most common fall mechanism was from furniture.

Conclusion: We identified specific demographic, environmental, and medical risk factors for falls in MD children. Our findings can be used to target environmental interventions and anticipatory guidance to high-risk locations and populations.

Surekha Mullangi, MS 2

Mentor(s): Tariq Shafi, MBBS, MHS
Department of Medicine

HEMO Study Results Suggest that Clinical Parameters and Novel Solutes Explain Less than 9% of Variability in Uremic Symptoms

Authors: Surekha Mullangi BA, Eugene P. Rhee MD, Eliseo Guallar MD, Tammy L. Sirich MD, Timothy W. Meyer MD, Thomas H. Hostetter MD, Natalie S. Plummer, Seungyoung Hwang MS MSE, Noori Kim MD, Neil R. Powe MD MPH MBA, Tariq Shafi MBBS MHS

Background: Uremic symptoms are common in dialysis patients and contribute to poor quality of life. However, the specific toxins causing uremic symptoms are unknown. The goal of our study was to determine if novel uremic solutes were associated with uremic symptoms and to determine the association of uremic symptoms with long-term outcomes.

Methods: We measured nine uremic solutes (p-cresol sulfate, indoxyl sulfate, hippurate, phenylacetylglutamine, choline, betaine, trimethylamine-N-oxide, asymmetric and symmetric dimethylarginine, and methylguanidine) in 1,259 participants of the Hemodialysis (HEMO) Study. Uremic symptoms, including fatigue, pruritus, anorexia, nausea, excessive daytime sleep, difficulty concentrating, and pain, were assessed using a standardized questionnaire (SF-36) and converted to a numeric score for each symptom (range 0-100). We also calculated a uremic symptom score (average score of symptoms) for each patient. We determined if the levels of measured solutes were associated with symptom scores or other clinical and laboratory data. We also analyzed the association of uremic symptoms with death, cardiovascular events, and infectious hospitalizations, using Cox proportional hazard models.

Results: Mean age was 58 years, 64% were black and 44% male. Symptoms were frequent at baseline (fatigue: 70%, anorexia: 48%, pruritus: 73%, nausea: 47%, daytime sleep: 63%, difficulty concentrating: 55%, and pain: 74%) and highly persistent at Year 1 of follow-up (range: 48% to 75%). Of the novel solutes, only P-cresol sulfate was associated with pruritus at baseline and year 1 ($p<0.01$). There were no other consistent associations (multivariable model R2 range: 1% to 9%). Presence of symptoms was significantly associated with death (hazard ratio 1.10; 95% confidence interval, 1.03-1.17), cardiovascular events (1.17, 1.09-1.25), and infection-related hospitalizations (1.12, 1.05-1.20). Worsening of symptoms during follow-up was also associated with worse outcomes.

Conclusion: Uremic symptoms are common, persistent, and identify patients at high risk of complications, but are not explained by novel uremic solutes or routine dialysis parameters.

Teresa Oszkinis, MS 2

Mentor(s): Janet Record, MD
Department of Medicine

Caring for the Seriously Ill Curriculum: Teaching Medical Trainees How to Engage in Patient-Centered Communication in the ICU Setting

Authors: Teresa Oszkinis BA, Colleen Christmas MD, Janet Record MD

Background: Goals of care (GOC) conversations with patients and their families are essential in the ICU to align care with the patient's values and priorities. Yet, residents often feel unprepared to engage in these discussions in the setting of a critical illness. The purpose of our study was to teach residents how to lead and document GOC discussions with ICU patients and their families.

Methods: Internal medicine residents rotating in the ICU participated in bi-weekly interactive teaching sessions and received pocket cards outlining an approach to GOC meetings. We then conducted a pre-post analysis of 186 pre-intervention and 192 post-intervention ICU patient-stays. We coded transfer notes (TNs) and family meeting notes (FMNs) from before and after the intervention for the presence of GOC domains taught in the curriculum. Our primary outcome measure was the rate of GOC documentation for ICU patient-stays (pre vs. post-intervention). Our secondary outcome measure was the number of notes functioning as FMNs, and of those, the number of notes specifically labeled as FMNs (pre vs. post-intervention).

Results: The rate of documentation of a patient's typical day increased after the intervention (2.69% vs. 8.33%, p=0.023). All other GOC domains exhibited no change between the pre- and post-intervention periods. Dedicated FMN documentation increased from 2 (1.08% of patient-stays) to 10 (5.21% of patient-stays) (p=0.036). Nonetheless, the number of patient-stays with at least one note functioning as a FMN was similar between the pre-intervention (N, %) (12, 6.45%) and post-intervention (16, 8.33%) periods (p=0.558).

Conclusion: We found that patients' GOC were documented infrequently, regardless of our educational intervention. While the number of dedicated FMNs increased after the intervention, FMNs remained rare among ICU patient-stays. Future work should focus on identifying best methods to teach the skills necessary to lead GOC meetings as well as barriers to documentation of key outcomes of these discussions.

POSTER ABSTRACTS: BASIC SCIENCE

Listed alphabetically by first name of author

1. Ashlie Sewdass, MS 3

Mentor(s): James Segars, MD
Department of Gynecology and Obstetrics

FSH Signaling is Augmented by AKAP13

Authors: Ashlie Sewdass BA, Paul Driggers PhD, Kamaria Cayton Vaught MD, James Segars, MD

Background: AKAP13 (A Kinase Anchoring Protein 13) is a Protein Kinase A anchoring protein expressed in granulosa cells and oocytes. During follicle maturation, granulosa cells respond to follicle stimulating hormone (FSH) leading to an increase in cAMP and differentiate from the preantral to preovulatory state. We hypothesize that AKAP13 plays a crucial role in coordinating a PKA-mediated phosphorylation signaling cascade which enables folliculogenesis to occur. To test this, we reconstituted FSH signaling using an in vitro model with COS-7 cells.

Methods: COS-7 cells were grown to 50% confluency and transfected with 1.0µg of CRE-Luciferase plasmid and 0.2 µg expression plasmid of FSH-Receptor for 24 hours. Twenty-four hours post-transfection, cells were treated with vehicle control (0.9% sodium chloride), 0.01 I.U. FSH/mL, 0.1 I.U. FSH/mL, 1.0 I.U. FSH/mL. Eight hours post-FSH treatment, cells were lysed and assayed for CRE-luciferase activity and normalized to protein concentration using Precision Red. To determine the effect of AKAP13 FSH-induced CREB activation, COS-7 cells were transfected with CRE-luc, AKAP13 (0.5 µg) and FSH-R expression plasmid, treated with vehicle control versus FSH and assayed for CRE-luciferase activity, as noted above.

Results: With FSH stimulation, Cos-7 cells transfected with FSH-R and Cre-Luc demonstrated FSH-dependent activation of CRE-luciferase in a dose-responsive manner. Addition of 1.0 I.U. FSH/mL showed a 3-fold higher induction of CREB activation compared to vehicle control. Co-expression of AKAP13 and FSH-R resulted in an increase in CRE-Luc activity compared to cells expressing FSH-R alone after stimulation with FSH. Treatment with the highest dose, 2.0 IU FSH/ml, resulted in a 6.4-fold increase in CRE-luciferase activity compared to empty expression vector.

Conclusion: Coexpression of AKAP13 augmented FSH-induced CRE-luciferase activity. This study supports a role of AKAP13 in folliculogenesis in granulosa cells.

2. Blake Johnson, MS 2

Mentor(s): David Hackam, MD PhD
Department of Surgery

A novel platform for determining the effects of the enteric nervous system on the intestinal epithelium in the pathogenesis of gut disease

Authors: Blake Johnson, Mitchell R. Ladd, Carolyn Gosztyla, Cait Costello, Adam Werts, Laura Martin, Emilyn Banfield, Hongpeng Jia, Peng Lu, William Fulton, Sanxia Wang, Thomas Prindle, Yukihiro Yamaguchi, Jungeun Sung, Chhinder Sodhi, John March, David J. Hackam

Background: The enteric nervous system (ENS) serves integral functions in the intestine such as maintenance of intestinal barrier function and coordination of peristalsis and is impaired in Hirschprung's disease and short bowel syndrome. Recent advances in the development of an artificial intestine have been limited by failure to achieve peristalsis, in part due to inadequate techniques to study the ENS. We have now isolated enteric neurospheres from the intestine and sought to develop an ex vivo platform for the study of the effects of ENS on proliferation and differentiation of intestinal stem cells (enteroids). Additionally, we evaluated the ability of enteric and neural cells to populate poly(glycerol sebacate) (PGS) synthetic bioscaffolds.

Methods: Intestinal stem cell crypts and myenteric plexus ENS cells were isolated from murine small intestine and differentiated into enteroids and neurospheres; these were then combined in physiologically relevant ratios for 48 hours and analyzed for growth and differentiation. Enteroids and neurospheres were then seeded and co-cultured on biological PGS intestinal scaffolds and assessed for coverage over time via confocal microscopy.

Results: The presence of neurospheres induced increased intestinal stem cell proliferation as revealed by upregulation of Ki-67 and decreased differentiation as revealed by reduced secretory (mucin 2, lysozyme) and absorptive (sucrase-isomaltase) markers. Strikingly, enteroids and neurospheres demonstrated ability to co-populate synthetic intestinal scaffold with neural projections extending between enteroids on neighboring villi, indicative of functional potential.

Conclusion: We have developed a novel platform for the study of neural interactions with enteroids in vitro and determined that neurospheres maintain enteroids in a more stem-like, less differentiated state, which would be expected to enhance in vivo intestinal regenerative capacity, benefitting the management of diseases like short bowel syndrome and Hirschprung's disease and the development of an artificial intestine.

3. Brad Isaacs, MS 2

Mentor(s): Patrick Cahan, PhD
Department of Biomedical Engineering

Evaluating cancer cell lines as models using CellNet and RNA-seq

Authors: Brad Isaacs BS, Patrick Cahan PhD

Abstract: Cell lines derived from tumors are used extensively in research of tumorigenesis, cancer biology, and preclinical drug development. Recent studies have demonstrated that some derived cell lines do not fully recapitulate the molecular pathways and genomic signatures of their original tumor tissues. These findings have implications for fields of inquiry that require reproducible and valid in vitro cancer models, leading to misleading or contradictory results and contributing inefficiencies to the research process. In order to determine the reliability of cancer cell lines, we extended the computational platform CellNet. CellNet uses RNA-sequencing to reconstruct Gene Regulatory Networks (GRNs): interconnected pathways of transcription factors that determine the steady-state expression levels of particular cells. The GRNs primarily active in a cell form a signature that can offer insight into the function, role, and identity of an individual cell type. In this study, we developed Cancer CellNet (CCN), which contains processed data from The Cancer Genome Atlas relevant to 1761 human tumors, representing 29 tumor types and subtypes. We then analyze 608 sequences from The Cancer Cell Line Encyclopedia (CCLE), a genomic database cataloguing frequently researched cancer cell lines, with CCN to compute how well these cell lines model individual tumor types. Further work will include developing a scorecard of frequently published cancer cell lines. This scorecard will offer researchers the ability to choose CCN's most accurate models for their experiments, facilitating more reproducible and precise studies. As a proof of concept, we will use CCN to iteratively identify candidate regulators of pathways in order to experimentally perturb and improve the tumor type fidelity of several cell lines, as assessed by increased expression of tumor specific markers.

4. Dan Soffer, MS 2

Mentor(s): Tao Wang, MD
McKusick-Nathans Institute of Genetic Medicine

Investigating a mechanism behind dopamine transporter regulation as a contributing factor to psychiatric disease

Authors: Dan Soffer B.S., Tao Wang MD

Screens for genes that cause intellectual disability when mutated are essential to better understand the molecular basis of intellectual function and disability in humans. DHHC-15, which encodes a neuronally enriched protein palmitoyltransferase (PAT), has been implicated in intellectual disability. Palmitoylation is a reversible and dynamic process, analogous to phosphorylation/dephosphorylation, which alters responsiveness of target proteins to regulatory signals. Palmitoylation controls multiple functions of integral membrane proteins, including catalytic activity, trafficking, subcellular targeting, and turnover. Interestingly, DHHC15 knockout (KO) mouse models showed no significant cognitive impairment, but did possess a specific reduction of dopamine in the striatum and a distinct behavioral profile including hyperactivity and increased sensitivity to the psychostimulant amphetamine. This phenotype, though milder, is similar to that of the well characterized dopamine transporter (DAT) KO mouse. The DAT is the primary protein controlling the concentration and duration of dopamine (DA) in the synapse. The DAT is a major target for both abused and therapeutic drugs and is regulated via acute and chronic mechanisms during momentary physiological demands, long-term disease, and drug addiction states. Identifying regulators of the DAT is important for the discovery of new treatments for the vast range of diseases in which the DAT is implicated. We hypothesize that abnormalities in the DHHC15 KO phenotype may be mediated by the DAT, which has reduced transport capacity and an increased rate of degradation in its depalmitoylated state. In this study, we tested this hypothesis via cotransfection of HEK293 cells with mouse DAT (mDAT) and DHHC15 and measuring DAT palmitoylation with and without DHHC15 using the acyl-biotin exchange assay. Once complete, we will be able to confirm whether DHHC15 is indeed capable of regulating the DAT.

5. Joshua Prudent, MS 4

Mentor(s): Patrick Brown, MD
Division of Pediatric Oncology

Combination of Tyrosine Kinase Inhibitors and Histone Deacetylase Inhibitors in Treatment of TKI-Resistant Pediatric Philadelphia-Positive Acute Lymphoblastic Leukemia

Authors: Joshua Prudent BD, Gordon Cohen MD, Patrick Brown MD

Background: Overall survival against pediatric Philadelphia chromosome-positive ALL (p-Ph+ ALL) remains below other pediatric ALLs, with TKI-resistance (TR) necessitating new treatments. The most common cause of adult TR, ABL1 mutations, is a minority in pediatric TR, and dysregulated BCL6 activity is hypothesized to be an alternative resistance mechanism in wild-type ABL1 (wt) disease. Histone deacetylase inhibitors (HDACi's) target the BCL6 complex and reduce its activity, possibly returning TKI sensitivity. This combination of HDACis and TKIs has not been explored in resistant disease.

Methods: To study this combination, a murine cohort was engrafted with a TR-wt p-Ph+ ALL (NALM1), and split into TKI (imatinib), HDACi (panobinostat), combination, and control arms, with peripheral engraftment and survival trended. BCL6 expression in vitro was also quantified by qPCR with aforementioned treatment arms in NALM1. In addition, a TR-wt cell line was produced from TKI-sensitive p-Ph+ ALL (SupB15) through serial exposure in vitro. Viability studies with these treatment arms were performed in the TR-wt SupB15, to determine synergy.

Results: The viability studies produced combination indexes ranging from a high of 0.767 and a low of 0.226. The qPCR also showed increased BCL6 expression, peaking at 36 hours in the imatinib (2x control), panobinostat (3x) and combination (7x) treatment arms. In the murine model, combination treatment slowed engraftment initially, but without survival benefit- median survivals in days of 52 (panobinostat), 68 (combination), 80 (control), and 87 (imatinib).

Conclusion: The viability studies showed pronounced synergy in vitro. However, the toxicity of panobinostat likely shadowed any survival benefit with combination treatment. A change in treatment regimen may reveal a survival benefit in a repeat study. The qPCR results imply that BCL6 expression is impacted by this combination. We will need Western studies to fully ascertain BCL6 protein activation levels. These experiments drive us closer to implementation of this combination in patient therapies.

6. Kevin Pineault, MS 2

Mentor(s): Brian Ladle, MD PhD
Pediatric Oncology

Augmenting Immunotherapy for Anti-PD1 Blockade Resistant Sarcomas

Authors: Kevin Pineault BS, Maggie Phillips BS, Himavanth Gatla PhD, Brian Ladle MD PhD

Background: Soft tissue sarcomas (STS), a rare collection of cancers originating from connective tissues, have proven difficult to treat with immune-based therapies, due both to immunologic tolerance and lack of tumor antigens expressed. Epigenetic modifiers, such as histone deacetylase inhibitors (HDACi) and DNA methyltransferase inhibitors (DNMTi), show potential to induce STS tumor antigen expression. Additionally, stimulator of interferon genes (STING) agonists have been shown to induce inflammatory responses that eliminate tumors resistant to PD-1 blockade.

We hypothesize that (i) treatment of STS-bearing mice with Panobinostat, a HDACi, in combination with 5-azacytidine (5AZA), a DNMTi, will induce expression of tumor antigens, and (ii) intratumoral delivery of STING agonist will cause immune cell activation against Panobinostat-induced tumor antigens.

Methods: We treated STS cells with Panobinostat and/or 5AZA and measured genetic and epigenetic alterations. To assess STING agonist immune stimulatory properties in vitro, we treated splenocytes with STING agonist, and measured interferon-β gene expression.

Results: Treatment of STS cells in vitro with Panobinostat caused significant histone acetylation, DNA demethylation, and increased expression of tumor antigens, and addition of 5AZA enhanced these effects. Excitingly, treatment of tumors derived from STS cell lines in vivo resulted in increased expression of tumor antigens. Preliminary experiments with STING agonists triggered robust expression of interferon-β with a clear dose response.

Conclusion: Epigenetic modification initiated significant expression of silenced tumor antigens, which may improve immune detection of these resistant sarcomas. The combination of epigenetic modification and STING agonist shows promise to make STS responsive to anti-PD1 immunotherapy.

Future steps: Tumors will be harvested and processed after combining Panobinostat, STING agonist, and PD1 antibodies to assess degree of immune infiltration, checkpoint expression, and functionality against expressed antigens.

7. Sarah DiNapoli, MS 2

Mentor(s): Cynthia Sears, MD
Department of Medicine - Oncology

Influence of Gut Microbiome on Tumor Growth and Immune Response to Tumor

Authors: Sarah DiNapoli BA, Joell Gills PhD, Franck Housseau PhD, Drew Pardoll MD, PhD, Cynthia Sears MD

Background: Despite recent advances in checkpoint blockade immunotherapy, improving patient response rates remains a major challenge in cancer treatment. Variation in patients' gut microbiomes may play a role in how effectively the immune system responds to tumor growth and anti-PD1 or anti-CTLA4 immunotherapy.

Methods: To develop an in vivo system for assessing the effects of the gut microbiome on immunologic responses to cancer, we examined the influence of stool from a healthy patient on the colonic immune system, tumor growth and immunologic response to tumor in germ-free mice. Germ-free C57BL/6 mice received patient stool via oral lavage one or five weeks prior to subcutaneous flank inoculation with B16F10 melanoma cells.

Results: Colonic T cell and myeloid cell populations changed in response to tumor inoculation with similar changes in phenotype across stool-colonized and germ-free groups. Comparison of the two stool-colonized mouse groups with germ-free controls at 17 days post-inoculation indicated no significant difference in tumor growth across groups with variable tumor growth within groups. Flow cytometric analysis of tumor-infiltrating lymphocytes (TILs) showed decreased TILs in tumors from mice who received stool lavage 1 week prior to tumor inoculation compared to the 5-week stool group and germ-free controls.

Conclusion: Overall, mice that received stool lavage did not have significantly different colonic immune cell phenotypes or tumor growth compared to germ-free mice, though timing of tumor inoculation post-stool lavage influenced TIL counts. This germ-free syngeneic mouse model, when optimized, will provide a unique in vivo method for assessing how differences in patient gut microbiome can influence tumor growth, the systemic immune system and, ultimately, response to immunotherapy. Further work, including examining alternative syngeneic tumor cell lines and adding checkpoint blockade agents, will be required to elicit the impact of gut colonization on the immune response to cancer.

8. Sonal Chaudhari, MS 2

Mentor(s): Richard Jones, MD
Department of Medicine - Hematology

Role of cytochrome P450 enzymes in the maintenance of breast cancer metastatic to bone

Authors: Sonal Chaudhari BS, Yu-Ting Chang MS, Christopher Esteb BS, Richard Jones MD

Background: Metastasis of cancer cells causes most cancer-related deaths, prompting interest in understanding the cellular and molecular mechanisms of metastasis. Cancer homeostasis largely depends on the tumor microenvironment. Interactions between malignant cells and their surrounding stroma contribute to many processes in cancer biology, including carcinogenesis and resistance to therapy. For example, multiple myeloma and leukemia cells can be protected from systemic chemotherapy by stromal cytochrome P450 enzymes (CYPs) that are found in the bone marrow (BM). We hypothesized that stromal CYPs protect solid tumors metastases in the BM.

Methods: We used a conditioned media model to mimic tumor microenvironment, asking whether a human BM mesenchymal stroma cell line (FSTRO) can affect growth of a breast adenocarcinoma metastatic cell line (MCF7).

Results: We first established the IC50 of Doxorubicin of MCF7 cells to be 50nM, a concentration which also preserved substantial growth of seeded stromal cells. We found that the stromal conditioned media protected MCF7 cells from treatment with Doxorubicin, while it had no such effect in stroma-free conditions. Preliminary results also show that the concomitant treatment of Doxorubicin and Clarithromycin (a CYP3A4 inhibitor) reduces the protection of MCF7 cells in stromal conditioned media, while it had no rescue effect in stroma-free cultures.

Conclusion: Our results suggest that breast carcinoma cells are relatively resistant to Doxorubicin in the presence of BM stroma and that this resistance can be overcome by Clarithromycin. Together, these in vitro data suggest that like its role in hematological malignancies, stroma in the BM microenvironment creates biochemical niches in the BM that protect metastatic disease from systemic chemotherapy. Future studies will aim to understand the mechanisms of protection of solid tumor metastases in the BM microenvironment.

9. Tejus Pradeep, MS 2

Mentor(s): Paul Kim, MD PhD
Department of Psychiatry

Bryostatin-1 Treatment Remyelinates the Corpus Callosum in a Lysolecithin-Induced Demyelination Model of Multiple Sclerosis

Authors: Tejus Pradeep BA, Michael Kornberg MD PhD, Hasti Atashi BA, Paul Kim MD PhD

Multiple sclerosis (MS) is an autoimmune, demyelinating disease of the CNS. Bryostatin-1, a naturally occurring macrolide lactone produced by the bryozoan species, showed promising results in earlier studies in an experimental autoimmune encephalitis (EAE) model, which is frequently used to screen candidate MS drugs despite being purely a T cell-mediated, immunological system. As demyelination is the key central pathology of MS, a lysolecithin-induced focal demyelination model has been receiving recent attention. We sought to assess the efficacy of bryostatin-1 in the more physiologically relevant demyelination model. Established mouse brain coordinates and protocols were followed for stereotactic injection of lysolecithin into the genu of the corpus callosum. After inducing successful demyelination, bryostatin-1 was injected intraperitoneally and established to show remyelination of the affected site. Further experiments were done at different time points to confirm that bryostatin-1 was remyelinating the damaged corpus callosum, rather than exerting a solely neuroprotective effect by preventing demyelination. This establishes bryostatin-1 as the only compound to show efficacy in the EAE and lysolecithin models of MS, suggesting that it has both immunomodulatory and pro-remyelinative effects. Further research is being done to confirm bryostatin-1 in an even more rigorous cuprizone model of demyelination. Additional research will elucidate the mechanism of action of bryostatin-1, so that insights into its molecular pathways will allow us to design drugs that may successfully harness its uniquely dual immunological and remyelinative impacts. Ultimately, this will improve our understanding of the multi-faceted pathology of MS and improve patient outcomes in the future.

10. Tony Wang, MS 2

Mentor(s): Marc Halushka, MD PhD
Cardiovascular Pathology

Mosaic patterns of protein expression exist in the heart and associate with gender

Authors: Tony Y. Wang BS, Dan E. Arking MD, Karen Fox-Talbot BA, Joseph J. Maleszewski MD, Renu Virmani MD, Marc K. Halushka MD PhD

Background: Skeletal muscle myocytes can be segregated into fast-twitch and slow-twitch fibers, based on their mosaic pattern of protein expression as noted by immunohistochemical staining. We hypothesized that an analogous muscle fiber differentiation may exist in the heart and sought to test whether this mosaicism was related to cardiac phenotypes.

Methods: We used HPASubC to analyze 52,737 immunohistochemically-stained heart images for 12,814 proteins from the Human Protein Atlas (HPA). We performed immunohistochemistry on four proteins: MYL3, MYL4, MYOM1 and PAM. We further evaluated MYL4 staining across four cardiac tissue microarrays (TMAs) taken from subjects with sudden cardiac death, hypertrophic cardiomyopathy, dilated cardiomyopathy, ischemic cardiomyopathy, and controls. Samples were selected from autopsy and heart transplant patients, with disease phenotype assessed from gross analysis and patient history. We developed an algorithm using CellProfiler software to semi-automatically quantify the percentage of myocytes that stained positively for MYL4, defined as "mosaicism." We utilized a linear mixed model to account for confounding factors such as age, race, BMI, and disease states in determining the relationship of MYL4 to disease and gender.

Results: We identified 143 (1.1%) proteins that showed staining mosaicism in the heart HPA images, 60 of which belonging to a single interactome. We further investigated MYL4 across 737 cores of heart tissue from four TMAs. Our CellProfiler data demonstrated that male hearts (16.8±13.6%) showed a significantly higher percentage of mosaicism than female hearts (10.1±9.9%; $p<1x10-8$). Patients with HCM (26.6±16.2%) showed higher mosaicism in MYL4 compared to control (14.5±13.5%) when measured at the left ventricular free wall ($p<0.002$), but failed to show significant difference in mosaicism at the septum.

Conclusion: We report the first broad discovery of cardiomyocyte fiber protein expression mosaicism, resulting in distinct phenotypes of myocytes. We describe novel changes in cardiac expression of MYL4 that may underlie sex- and disease-related differences in cardiac contractility.

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POSTER ABSTRACTS: CLINICAL SCIENCE

Listed alphabetically by first name of author

11. Alvaro Ibaseta, MS 2

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

SRS Scores Can Predict PROMIS Scores in Adult Spinal Deformity Patients

Authors: Alvaro Ibaseta MS, Richard L. Skolasky ScD, Rafa Rahman BS, Khaled M. Kebaish MD, Lee H. Riley III MD, Daniel M. Sciubba MD, David B. Cohen MD MPH, Brian J. Neuman MD

Background: The NIH encourages the use of PROMIS to assess health related quality of life (HRQL). However, in patients with ASD, providers have traditionally relied on the SRS outcomes questionnaire. This instrument assesses patients on pain, physical function, self-image, mental health and satisfaction, domains covered broadly by PROMIS. To encourage comparisons, existing data needs to be translated to the PROMIS domain scores. This study establishes and validates a method by which existing SRS scores can be accurately translated to PROMIS measures.

Methods: Complete PROMIS and SRS questionnaires were obtained for 174 ASD surgery patients. These were divided into a preoperative, derivation cohort(N=81), and a postoperative, validation cohort(N=93). Using the derivation cohort, each PROMIS domain was modeled as a function of existing SRS scores using linear regression. For example: $PROMIS\_Pain=\alpha\_Pain+\beta\_Pain\cdot SRS\_Pain+\beta\_Function\cdot SRS\_Function$. Using the validation cohort, the regression equations were used to estimate PROMIS scores from existing SRS scores. Finally, PROMIS estimates obtained were correlated to actual PROMIS scores in the validation cohort, to examine adequate translation.

Results: Linear regression showed that PROMIS_Pain is significantly dependent on SRS_pain (b_pain=-4.21,SE=0.80,p<0.001) and physical function (b_function=-6.50,SE=1.21,p<0.001). PROMIS_Physical_Function is dependent on SRS_pain (b_pain=3.28,SE=1.14,p<0.001), physical function (b function=4.50,SE=1.90,p=0.019), and self-image (b_image=3.08,SE=1.27,p=0.018). PROMIS_Anxiety is dependent on SRS_mental_health (b_mental=-7.96,SE=0.93,p<0.001). Depression is dependent on SRS_mental_health (b_mental= -9.75, SE=0.82, p<0.001). Finally, PROMIS_Satisfaction_with_Participation_in_Social_Roles is dependent on SRS_pain (bpain=6.34, SE=0.91,p<0.001). Pearson correlation coefficients demonstrated moderate to strong correlation between estimated and actual PROMIS domain scores in the postoperative, validation cohort: Pain, r=0.79, CI=[0.70, 0.86], p<0.001; Physical Function, r=0.66,CI=[0.53, 0.76],p<0.001; Anxiety,r=0.64,CI=[0.49, 0.76],p<0.001; Depression, r=0.57,CI=[0.41, 0.69],p<0.001; and Satisfaction with Participation in Social Roles, r=0.59,CI=[0.43, 0.71],p<0.001.

Conclusion: PROMIS domain scores estimated from existing SRS scores through our proposed linear regression model correlate moderately to actual PROMIS scores. Thus, SRS scores can be directly translated to PROMIS scores in all the evaluated health domains (Pain, Physical Function, Anxiety, Depression and Satisfaction with Participation in Social Roles) for ASD patients.

12. Aanika Balaji, MS 2

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

Immune-related adverse events requiring inpatient management: spectrum of toxicity, treatment, and outcomes

Authors: Aanika Balaji BS, Jiajia Zhang MD, Kristen Marrone MD, Hany Elmariah MD, Mark Yarchoan MD, Matthias Holdhoff MD, Jacquelyn W. Zimmerman MD PhD, Khalid Hajjir MD, Deborah Kay Armstrong MD, Daniel A. Laheru MD, Ranee Mehra MD, Won Jin Ho MD, Joshua E. Reuss MD, Joseph Heng MD, Paz Vellanki MD PhD, Jarushka Naidoo MD

Background: Immune checkpoint inhibitors (ICIs) are anti-cancer agents now in routine clinical practice, and may cause immune-related adverse events (irAEs). The proportion of inpatient admissions for irAEs, spectrum of toxicities, management and outcomes are not well described.

Methods: Patients with solid tumors admitted to inpatient oncology service at JHH over 3 months were identified. Patient demographics, treatment details, ICIs, irAE management data were recorded in an IRB-approved database. IrAE diagnoses were confirmed by the treating physician and oncologist. Associations between clinical details and irAEs were evaluated using Fisher's exact test.

Results: Of 240 inpatient oncology patients: 53 (22.1%) received ICIs and 25% (13/53) were irAE admissions. Most irAEs admissions were high grade (CTCAE grade 1-2: 6/13, 46%; grade 3+: 7/13, 54%) and included: colitis (31%), pneumonitis (23%), skin rash (8%), fever (8%), pancreatitis (8%), fatigue (8%), and renal transplant rejection (8%). Treatment for irAEs included: ICI withhold (2/13, 15%), oral/IV corticosteroids (10/13, 76%), and infliximab (1/13, 8%); with 85% of patients requiring subspecialty consultations. IrAE admissions had shorter median lengths of stay vs. other inpatients (5 vs. 6 days). Most irAEs resolved/improved (11/13, 85%), 15% worsened (1/13), or died (1/13). There was a numerically higher risk of any/grade 3+ irAEs for those: treated with combination vs. monotherapy (33% vs 23%; 100% vs 40%), age > 65 vs < 65 (33% vs 15%; 56% vs 50%), and former/current vs. never smokers (31% vs 19%; 63% vs 40%), however, differences were not statistically significant.

Conclusion: Patients with irAEs constitute a notable minority of inpatient oncology admissions, with a higher incidence than reported in clinical trials. Initial data suggest patients treated with combination ICIs, aged > 65, and former/current smokers may be more likely to be admitted for irAEs. Most irAE admissions require subspecialty consultations, signifying a growing need for multidisciplinary irAE management.

13. Allison Haley, MS 2

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

Post-Operative Protocol for Autologous Free Flap Breast Reconstruction Optimizing Resources and Patient Safety

Authors: Allison Haley BS, Tobias Bos BSc, Brian Cho MD, Deepa Bhat MD, Hannah Carl BS, Benjamin Ostrander BS, Michele Manahan MD, Gedge Rosson MD, Justin M. Sacks MD, MBA, FACS

Background: Patients who receive autologous free flap breast reconstruction are commonly admitted to the intensive care unit (ICU) postoperatively for close monitoring of flap viability. With the advent of devices that enable continuous tissue-oximetry monitoring, it may no longer be necessary for these patients to go to the ICU post-operatively. We evaluated whether our three-day post-operative protocol not only maintained excellent clinical outcomes, but also was more cost and resource effective than protocols with longer length of stay (LOS) or overutilization of the ICU.

Methods: We retrospectively reviewed charts of all patients admitted to our institution from January 2013-August 2014 for autologous free flap breast reconstruction. We abstracted demographics, LOS and short-term complications and compared those to the literature. Costs were collected from the Department of Plastic and Reconstructive Surgery.

Results: We reviewed 153 consecutive patients with a total of 239 free flaps using our post-operative protocol. The mean age was 50 years (SD=10.2) and mean body mass index (BMI) was 29.4 (SD=5.2). Our institution's rate of flap failure was not significantly different from the published national rate ($p=0.367$). Unplanned reoperation was significantly lower than the published national rate ($p<0.001$). Patients were cared for immediately on the general surgical floor, which cost median $1827/day compared to the national average for monitoring a non-mechanically ventilated patient in the ICU of $6667/day. We used one tissue oximetry probe per free flap, which cost $713 each. 71% of patients were discharged on or before POD 3. Abstracted reasons for discharge after POD 5 were due to complications, including PE, infection, and DVT.

Conclusion: The autologous breast reconstruction post-operative protocol initiated by our institution is more cost and resource effective than protocols utilizing the ICU. Our protocol serves as a streamlined approach that allows reallocation of valuable resources and minimizes healthcare costs without compromising patient safety.

14. Breanne McCarthy, MS 2

Mentor(s): Rani Hasan, MD
Department of Medicine - Cardiology

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

Authors: Breanne McCarthy BS, Matthew Czarny MD, Nada Sie BA, Khala Marshall-Watkins, Frances Kirkland RN, Christine McLeod RN, Rhondalyn McLean MD, Gary Gerstenblith MD, Rani Hasan MD

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

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

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

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

15. Chau Vo, MS 2

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

Cervical and Cavernous Internal Carotid Artery Tortuosity Does Not Predict Complexity or Outcome in Mechanical Thrombectomy for Acute Ischemic Stroke

Authors: Chau D Vo BA, Jessica K Campos MD, David A Zarrin BS, Matthew T Bender MD, Bowen Jiang MD, Justin M Caplan MD, Li-Mei Lin MD, Elisabeth B Marsh MD, Steven Zeiler MD PhD, Geoffrey P Colby MD PhD, Rafael H Llinas MD, Alexander L Coon MD

Background: Given the robust tri-axial catheter setups required, tortuosity of the cervical and cavernous internal carotid artery has been shown to be a predictor of procedural success, complexity, and complications for intracranial embolization. We sought to investigate its role in mechanical thrombectomy for ischemic stroke.

Methods: A prospectively-collected, IRB-approved database was analyzed for all patients who underwent mechanical thrombectomy for anterior circulation large vessel occlusion from 2012-2017. Cervical ICA tortuosity was defined as pharyngeal loop or hairpin turn. Cavernous tortuosity was defined as type III or IV cavernous ICA with a posterior or superior deflection at the posterior genu.

Results: There were 20 patients with cervical tortuosity and 40 without. There were 19 patients with high-grade cavernous anatomy, 40 low-grade anatomy, and one missing data. Patients were similar in age, gender, NIHSS and CT ASPECTS scores. Cervical tortuosity: Last-normal time to groin puncture was similar for patients without and with cervical tortuosity(mean 379 minutes vs 266,p=0.19). There was no difference in procedural time(57 vs. 65 minutes,p=0.44). Recanalization success rates were similar(83% vs. 80%,p=0.99). 30-day mortality was 33% for patients without tortuosity and 30%(p=0.79) for patients with tortuosity. There was a trend toward improved outcomes in patients without tortuosity, 28% of whom achieved mRS0-2 as compared with 15% of patients with tortuosity(p=0.35), but this was not statistically significant. Cavernous ICA: Low-grade and high-grade cavernous ICA tortuosity groups were comparable for last-normal time to groin puncture(344 vs. 345 minutes,p=0.99). No significant differences in procedural time(61 vs. 59 minutes,p=0.90) or recanalization rates(78% vs. 89%,p=0.48) were observed. There was a trend toward higher mortality in patients with low cavernous grade(35% vs. 21%,p=0.25), and a greater percentage of high-grade cavernous patients achieved good functional outcomes(mRS0-2 18% vs. 37%,p=0.12).

Conclusion: Vascular tortuosity is not a predictor of procedural complexity or outcome in MT.

16. Christa LiBrizzi, MS 2

Mentor(s): Edward McFarland, MD
Department of Orthopaedics

Is it Necessary to Locate the Axillary Nerve in the Surgical Exposure during Anatomical or Reverse Total Shoulder Arthroplasty?

Authors: Christa LiBrizzi BS, Edward McFarland, MD

Background: During shoulder arthroplasty, it has been suggested by many that to prevent injury to the axillary nerve the surgeon should either palpate the axillary nerve, directly visualize the nerve or use the "tug test."
The hypothesis of this study is that neither direct palpation of the axillary nerve, direct visualization of the nerve nor use of the "tug test" are necessary for prevention of axillary nerve injury primary TSA or RTSA.

Methods: In all patients undergoing primary TSA and RTSA performed by one surgeon between 2003 and 2017, none had direct visualization, palpation or use of a tug test to protect the axillary nerve. The primary outcome was the presence of an isolated clinically evident axillary nerve injury within 3 months of the arthroplasty date. Patients with axillary nerve injuries had a minimum follow-up of 12 months after the diagnosis of the injury.

Results: 882 primary shoulder arthroplasties (342 TSA and 530 RTSA) were performed during the study period. 3 patients with less than 3 months of follow were excluded. There were 6 patients with an isolated axillary nerve injury with an incidence of 0.7%, with a rate in TSA of 0.3% and in RTSA a rate of 0.9%. All the patients with axillary nerve injury experienced complete neurologic recovery at last follow-up.

Conclusion: This study suggests that direct visualization, direct palpation or use of the "tug test" for finding the axillary nerve is not necessary when performing primary TSA or RTSA.

17. Christina Kwon, MS 2

Mentor(s): Bernard Cohen, MD
Department of Dermatology

Risk of Systemic Complications and Multiple Infantile Hemangiomas

Authors: Christina Kwon BA, Jacqueline Selph MD, Bernard Cohen MD

Background: Infantile hemangiomas are the most common soft tumors in infancy. When there are multiple lesions, they can be associated with visceral hemangiomatosis, particularly, the involvement of the liver or gastrointestinal tract. Historically, work-up for visceral involvement is recommended when there are more than five hemangiomas present, even though the relationship between number of hemangiomas and systemic complications is not known.

Methods: We conducted a retrospective cross-sectional study of all patients at Johns Hopkins Hospital seen from 2003-2017 for multiple infantile hemangiomas. Information was abstracted from the electronic health record or paper medical records. This included: number, size and location of the hemangiomas, the presence of any secondary features such as ulceration, progress at each follow-up visit if applicable, whether ultrasound was conducted, and medications prescribed.

Results: We evaluated 45 patients; the average age at presentation was 4.8 months. There were 35 females, 10 males and of these patients, 37 were Caucasian, 3 were African American, 4 were Hispanic/Latino, and 1 was Asian/Pacific Islander. The mean(±SD) number of hemangiomas was 8(±3.425). Visceral involvement was suspected in 17 patients, and an ultrasound was performed in 18. Of the 45 patients with greater than 5 hemangiomas, the number with systemic involvement was 0. It should be noted that some patients had complications from premature birth and were imaged for reasons other than suspected visceral involvement due to hemangiomas.

Conclusion: For patients with more than five multiple infantile hemangiomas, there was no clear relationship between the number of hemangiomas and systemic involvement. This refutes current guidelines for visceral involvement of hemangiomas, and needs further multi-center investigation.

18. Eric Wei, MS 2

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

Vestibular Loss Predicts Poorer Spatial Cognition in Patients with Alzheimer's Disease

Authors: Eric X. Wei BA, Esther S. Oh MD PhD, Aisha Harun MD, Matthew Ehrenburg BA, Yuri Agrawal MD MPH

Background: The vestibular system is an important contributor to balance control, spatial orientation, and falls risk. Recent evidence has shown that Alzheimer's disease (AD) patients have a higher prevalence of vestibular impairment relative to healthy controls. We sought to evaluate whether vestibular loss is specifically associated with poor spatial cognitive skills among patients with mild cognitive impairment (MCI) and AD.

Methods: We recruited 50 patients (22 MCI and 28 AD) and measured vestibular physiologic function. Spatial cognitive function was assessed using the Money Road Map Test (MRMT). General cognitive function was assessed with the Mini Mental Status Examination (MMSE). We evaluated the association between vestibular loss and performance on the MRMT. MMSE score was added to the regression model to assess whether vestibular loss is associated with visuospatial impairment independent of a general decline in cognition.

Results: In multivariable linear regression analyses adjusted for age, gender, and education, MCI and AD patients with vestibular loss made significantly more errors on the MRMT relative to patients with normal vestibular function (unilateral vestibular loss β 7.7, 95% CI 2.9, 12.4; bilateral vestibular loss β 6.9, 95% CI 2.5, 11.2). The addition of MMSE in the model did not substantially impact the coefficients for vestibular loss (unilateral vestibular loss β=7.3, 95% CI 2.4, 12.1; bilateral vestibular loss β=6.4, 95% CI 1.9, 10.9). We further stratified AD patients into "spatially normal" and "spatially impaired" groups based on MRMT performance, and found that the prevalence of vestibular loss was significantly higher in the spatially impaired AD group relative to the spatially normal AD group according to Fischer's exact test ($p = 0.002$).

Conclusion: These findings support the hypothesis that vestibular loss contributes specifically to a decline in spatial cognitive ability in MCI and AD patients, independently of general cognitive decline, and may predict a "spatially impaired" subtype of AD.

19. Eva Luderowski, MS 2

Mentor(s): Jennifer Haythornthwaite, MD, PhD
Department of Psychiatry and Behavioral Sciences

A New, MRI-Based Classification System for Tibial Spine Fractures in Pediatric Patients

Authors: Eva Luderowski BA, Maria Tuca MD, Elizabeth Gausden MD, Christine Goodbody MD, Gabrielle Konin MD, Daniel Green MD

Background: Tibial spine fractures (TSFs) are commonly graded according to the Meyers and McKeever (MM) classification system, which is based on a qualitative evaluation of x-rays. However, although MRI images can provide important clinical information about these fractures and the surrounding tissue, there is no MRI-based classification system. This study aims to (1) establish the intra- and inter-rater reliability of the MM system for use with x-rays, (2) propose a quantitative, MRI-based system, and (3) assess how often using the MRI-based system changes the classification and recommended treatment plan as previously determined using MM.

Methods: We designed an MRI-based system for classifying TSFs. The new system has three grades based on quantitative displacement patterns of the fractured fragment and tissue entrapment. Four raters from a tertiary care center evaluated 20 fractures according to the MM and MRI-based systems. Observers graded the same images at two time points at least one week apart, after which we compared the intra- and inter-rater reliability of each system (using Fleiss' kappa and weighted kappa, respectively) and assessed how often using the MRI-based system changed the MM-derived fracture grade.

Results: Both the MM and MRI-based systems exhibit fair to moderate intra- and inter-rater reliability (average kappa values ranged from 0.38-0.66). Use of the MRI-based system changed the fracture grade and as a result modified the treatment recommendations in 33% of cases. Of grades that were changed, 20% were previously unnoticed fractures, 40% underwent a raise in grade, and 40% were graded as lower than before.

Conclusion: The MRI-based system is as reliable as MM, provides quantitative criteria for classifying fractures, and potentially clarifies treatment indications for TSFs.

20. George Zhang, MS 2

Mentor(s): Charles Della Santina, MD PhD
Department of Otolaryngology - Head and Neck Surgery

Improved method for clinical assessment of dynamic visual acuity

Authors: George Zhang BS, Desi Schoo MD, Grace Tan MD, Dale Roberts MS, Charles Della Santina MD PhD

Background: Balance disorders involving the vestibular system are prevalent and can be devastating. In those with vestibular dysfunction, impaired stimulation of the semicircular canals can lead to dysfunction of the vestibulo-ocular reflex (VOR), resulting in a decrease in visual acuity during motion in comparison to static measurement. Dynamic visual acuity (DVA) is a method of assessing VOR that is both simple and non-invasive.

Methods: Using MATLAB and Arduino C, we developed a computerized system testing DVA that flashes an 8-direction optotype (Landolt C) when a user-set critical head thrust (HT) velocity is reached. Similar to a traditional Snellen chart, the letter decreases by logMAR 0.1 after five trials on each line. In order to ensure timely display of the optotype, HT-to-optotype latency testing was conducted using a photodiode and oscilloscope setup. The system will be evaluated on healthy individuals recruited from the general community. Subject VA was determined at the level at which they could no longer reliably identify the letter orientation.

Results: Subjects will be collected broadly across gender, ethnicity, age, and degree of visual correction (myopia or hyperopia). In our preliminary assessments, the device produced DVA values in all canal planes (yaw, LARP, RALP) similar to those generated by previously used DVA devices in the lab. Additionally, HT-to-optotype display latency was determined to be approximately 0.20ms, ensuring that the subject is viewing the optotype appropriately (i.e., immediately following critical velocity).

Conclusion: Currently, we have a working proof-of-concept model for a multi-channel measuring tool for DVA. Compared to previous models, we have found that the device is advantageous in that it is simple, displays with low HT-to-optotype latency (~.20ms) and is able to determine logMAR using less head thrusts via an adaptive mechanism. Given these attributes, we believe that our device is an attractive option for usage as a universal DVA measurement tool.

21. Ha Vi Nguyen , MS 2

Mentor(s): Katherine Puttgen, MD
Department of Pediatric Dermatology

Burn Pediatric SCAAR FX Study

Authors: Ha Vi Nguyen BS., Sagar Patel BS., BA, Katherine Puttgen MD

Background: Ablative fractional carbon dioxide laser therapy has been shown to improve the texture, thickness and appearance of hypertrophic burn scars by creating microscopic wounds on the surface of the skin to catalyze the healing process. Current literature lacks studies exploring outcomes in a pediatric burn population receiving ablative carbon dioxide laser therapy.

Methods: A retrospective chart review analysis of pediatrics patients seen at the Johns Hopkins Pediatric Burn Center receiving SCAAR FX ablative fractional carbon dioxide laser therapy (n= 35). The Modified Seattle Scar Scale was used to grade the pictures of the scars based on scar surface appearance, scar height, and color mismatch on a 4-point scale (1= close to uninjured skin in appearance, 4= most abnormal in appearance to uninjured skin). Two trained researchers graded the photos independently and the final score is an average of the two researchers. A kappa coefficient will be calculated to determine the interrater reliability.

Results: Preliminary analysis indicates significant difference in scar surface appearance, scar height, and color mismatch with treatment. The interrater reliability kappa coefficeint is still pending analysis.

Conclusion: Empirically, ablative fractional carbon dioxide laser therapy shows improvement in patients' outcomes based on the scar surface appearance, scar height, and color mismatch.

22. Jeff Ehresman, MS 2

Mentor(s): Kaisorn Chaichana, MD
Department of Neurosurgery

The relevance of Simpson grade resections in the modern neurosurgical treatment of World Health Organization Grade 1, 2, and 3 meningiomas

Authors: Jeff Ehresman, BS, Tomas Garzon-Muvdi, MD, Davis Rogers, BA, Michael Lim, MD, Gary L. Gallia, MD, PhD.; Jon Weingart, MD, Henry Brem, MD, Chetan Bettegowda, MD, PhD, Kaisorn L. Chaichana, MD

Background: The Simpson grading system has played an important role in classifying the extent of surgical resections of meningiomas. This study set out to determine if this grading system predicts meningioma recurrence in a modern cohort of patients with tumors of all World Health Organization (WHO) grades.

Methods: Medical records for all adult patients who underwent primary, non-biopsy resection of a meningioma at a tertiary care institution between 2007 and 2015 were retrospectively reviewed. Of the 852 patients who underwent surgery during the reviewed period, 280 were excluded based on exclusion criteria. The clinical, operative, and hospital records of the remaining 572 patients were retrospectively reviewed. Stepwise multivariate proportional hazard analyses were used to identify associations with recurrence following resection. Log-rank analyses were used to compare Kaplan-Meier plots for time to recurrence between each Simpson grade.

Results: Of the 572 patients who met the inclusion criteria, 72 (12.6%) presented with recurrence. The factors associated with recurrence after gross-total resection (Simpson I-III: N=414) were non-WHO grade 1 (HR [95 % CI] 6.215 [2.864-12.419], p < .0001) and preoperative neurological deficits (HR [95 % CI] 2.862 [1.512-5.499], p = 0.001). Factors associated with recurrence after subtotal resections (Simpson IV: N=158) were African-American patients (HR [95 % CI] 2.776 [1.232-5.890], p = 0.02) and parafalcine location (HR [95 % CI] 3.956 [1.624-8.775], p = 0.004). Notably, the Simpson grading scale was not an independent risk factor for recurrence.

Conclusion: The identification and consideration of the factors associated with recurrence after gross-total or subtotal resections may help guide treatment strategies for patients with meningiomas. Patients who possess these factors may be predisposed to recurrence and therefore may warrant closer surveillance imaging and/or adjuvant therapies.

23. Jose Reyes, MS 2

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

Symptomatology and Clinical Demographics of Patients Presenting with Oral Non-Group A Streptococcus

Authors: Jose Reyes BS, Karen Carroll MD, Mustapha Saheed MD, and Richard Rothman MD PhD

Background: Non-group A Streptococcus (non-GAS); Group B (GBS), C (GCS), and G (GGS) Streptococci; are causes of invasive disease, largely in patients with underlying co-morbidities. Non-GAS organisms are collected orally in patients with pharyngitis at rates similar to GAS, but antibiotic treatment of oral non-GAS is debated. The aim of this study was to describe the characteristics of patients with non-GAS positive throat culture and to compare differences in patients with GAS positive throat cultures.

Methods: In this retrospective cohort study, we evaluated all patients seen at the Johns Hopkins Hospital Adult and Pediatric Emergency Departments from 06-2012 to 08-2016 who presented with a positive throat culture for GAS or non-GAS. The symptoms, clinical demographics, and treatment were recorded, and differences were evaluated using multinomial logistic regressions.

Results: A total of 568 throat cultures returned positive for GAS (n=210), GBS (n=230), GCS (n=44), GCS/GGS coinfection (n=64), or GGS (n=20). GBS was 34% and 56% less likely to present with fever and lymphadenopathy, while it was 50% and 71% more likely to present with cough and rhinorrhea compared to GAS (p=<0.05). The remaining non-GAS presented with these symptoms at rates similar to GAS. GAS had the highest rate of antibiotic treatment (67.1%), while GBS, GCS/GGS, and GGS were 68%, 49%, and 73% less likely to be treated than GAS, respectively (p=<0.05). The relative risk of having a GBS positive throat culture was 288% (p=0.004) in patients with diabetes mellitus and 139% (p=0.45) in patients with immunologic diseases.

Conclusion: Patients with positive GBS cultures were more likely to present with symptoms indicative of viral pharyngitis. Although this suggests symptom presentation in most GBS positive patients was viral in origin, the presence of colonizing GBS orally serves as a potential portal of entry for invasive disease in at-risk populations such as diabetic or immunocompromised patients.

24. Julia Wainger, MS 2

Mentor(s): Kristin, Voegtline, Ph.D.
Department of Pediatrics and General Adolescent Medicine

Right-Hand 2D:4D Ratio Predicts Hyperactivity-Inattention and Conduct Problems in Early Childhood

Authors: Julia Wainger BA, Kristin Voegtline Ph.D.

Background: Prenatal testosterone exposure has been increasingly recognized as an important mediator of brain organization, yet fetal levels are difficult to assess noninvasively. The second digit to fourth digit ratio (2D:4D) is a biomarker for fetal hormone exposure that has linked prenatal testosterone to a variety of adult behavioral phenotypes. However, these associations have not been frequently investigated in children.

Methods: Participants were selected from the Prenatal Indicators of Child Self-Regulation Study, which examined maternal, infant, and early childhood testosterone levels and early childhood behavioral outcomes. The analysis included 87 maternal-child pairs with 2D:4D ratios and behavioral data measured at age 5. Student's t-tests, Pearson's correlation and linear regression models were used to assess the relationships between 2D:4D ratio and emotional problems, conduct, hyperactivity, peer problems, and prosocial ability as measured by teachers through the Strengths and Difficulties Questionnaire.

Results: Right-hand 2D:4D significantly predicted ratings of conduct problems, (β = -19.7, $t(66)$ = -2.26, $p < 0.05$). Additionally, right-hand 2D:4D significantly predicted ratings of hyperactivity-inattention, (β = -41.11, $t(67)$ = -3.34, $p < 0.01$). Sex (β = -34.97, $t(67)$ = -2.40, $p < 0.05$), the interaction between sex and right-hand 2D:4D (β = 35.04, $t(67)$ = -2.29, $p < 0.05$), and maternal age (β = -0.158, $t(67)$ = -2.54, $p < 0.05$) also predicted teacher ratings of hyperactivity-inattention. Left-hand ratio was not associated with any behavioral outcomes as assessed by teachers.

Conclusion: This study demonstrates that right-hand 2D:4D ratio has the potential to serve as a non-invasive biomarker for hyperactivity-inattention and conduct problems in early childhood. These results also suggest that increased prenatal testosterone exposure may predispose children to these behavioral outcomes, especially for male children.

25. Leah Mische, MS 4

Mentor(s): Pavan Bhargava, MD, MBBS
Department of Neurology

A phase 1/2 trial of Tauroursodeoxycholic acid supplementation in progressive MS patients

Authors: Leah Mische BS, Sandra Cassard ScD, Ellen Mowry MD, Peter Calabresi MD, Pavan Bhargava MD, MBBS

Background: Progressive Multiple Sclerosis (MS) is an autoimmune neurodegenerative disorder which leads to significant disability. In our preliminary studies using untargeted metabolomics, we identified aberrant primary and secondary bile acid metabolism in MS patients. In other neurodegenerative disorders, bile acids reduced neuroinflammation and were neuroprotective. This study aims to determine safety, tolerability and the anti-inflammatory effect of the bile acid tauroursodeoxycholic acid (TUDCA).

Methods: This will be a randomized (1:1), double-blind, parallel group, placebo controlled trial of TUDCA 1 gram versus placebo twice daily for 16 weeks in patients with progressive MS. Participants will have bile acid levels below the 25th percentile for healthy controls as determined by a targeted metabolomics assay using banked plasma samples. The other major inclusion criteria include maintenance on MS therapy for six months and no recent relapses. Major exclusion criteria include a history of cholecystectomy, recent steroid use or a diagnosis of another neuroinflammatory disorder. We will obtain plasma, peripheral blood mononuclear cells, stool samples and clinical measures at baseline, mid-study and at the end of the study.

The primary outcome of the trial will be safety and tolerability of TUDCA while secondary outcomes will include change in plasma bile acid levels, alteration in gut microbiota and in peripheral immune cell function. To achieve a power of 85% to detect a 50-70% change in bile acid levels, a sample size of 60 was chosen.

Results: The trial is in set to start in early January 2018 and does not yet have results.

Conclusion: This trial will help demonstrate the safety and tolerability of TUDCA in progressive MS in addition to examining the effect of this intervention on multiple exploratory end-points. This trial has the potential to demonstrate a novel therapeutic option for progressive MS.

26. Lisa Zhang, MS 2

Mentor(s): John P. Carey, MD
Department of Otolaryngology-Head and Neck Surgery

A Case-Control Study of Hearing Outcomes between Middle Fossa Craniotomy and Transmastoid Approach for Surgical Repair of Superior Semicircular Canal Dehiscence Syndrome

Authors: Lisa Zhang BS, Francis X Creighton Jr. MD, Bryan Ward MD, Steve Bowditch AuD CCC-A, John P Carey MD

Background:
Objective: To compare postoperative hearing outcomes for transmastoid (TM) approach to middle cranial fossa (MCF) approach for surgical repair of superior semicircular canal dehiscence syndrome (SCDS).
Study Design: Historical case-control study
Setting: Tertiary referral center
Patients: 13 consecutive SCDS cases who underwent TM plugging of the superior canal; "controls" were 15 audiogram-matched patients who underwent MCF plugging and resurfacing.
Main Outcome Measures: Differences between preoperative, 7-day postoperative, and long-term (>6 weeks) postoperative air and bone conduction, speech discrimination scores (SDS), and pure tone averages (PTA) in TM cases vs MCF controls.

Methods: MCF controls were selected by matching preoperative BC thresholds from the TM cases within 10-dBs in ≥80% of recorded frequencies. Wilcoxon signed-rank tests were performed to compare main measurement outcomes between matches.

Results:
No statistically significant differences were found in long-term postoperative AC and BC thresholds at any frequency. Similarily, there were no differences in long-term SDS or PTA ($p=0.43$ and $p=0.38$, respectively). However, at 7-days postoperative, patients who underwent TM repair had significantly lower SDS than those who underwent MCF repair ($p<0.05$). This may reflect greater incidence of middle ear/mastoid effusions 7 days following the TM approach.

Define Professional Practice Gap and Education Needs: Understanding effects on hearing outcomes from different surgical approaches for SCDS.

Desired Result: A better understanding of hearing outcomes from different surgical techniques could better inform management of SCDS.

27. Lochan Shah, MS 2

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

A novel smartphone and wearable intervention improving recovery from acute myocardial infarction: Insights on uptake and feature usage patterns

Authors: Lochan Shah BA, Francoise A. Marvel MD, Erin Spaulding RN, William Yang MD, Helen Xun BS, Farhan Merali MD MBA, Matthias Lee PhD, Oluwaseun E. Fashanu MBBS MPH, Seth S. Martin MD MHS FACC FAHA

Background: Despite strong interest in mobile health (mHealth) interventions, there is little research on the feasibility and effectiveness of utilizing wearables and smartphone apps in non-healthy patients. Our team built the 1st cardiology CareKit application ("Corrie") to empower patient self-management following acute myocardial infarction (AMI), improve the hospital discharge process, and improve patient outcomes. Here, we sought to quantify the uptake and feature-usage patterns of Corrie.

Methods: This prospective observational study enrolled AMI patients at JH Bayview and JHH. All patients used the Corrie iPhone app and Apple Watch. EMR and app-usage data were assessed. Corrie features were classified into four categories: vital-signs tracking, medication adherence, education, and follow-up appointment coordination.

Results: Corrie patients were 69.9% men, 14.5% Black, 44.6% older than 60, and 27.7% Medicare/Medicaid. 30-day readmission rates in Corrie-enrolled patients (3%, N=77) were significantly lower than the Johns Hopkins historical control (19%, N=200, $p<0.001$). Available app-usage data (N=24) from recently deployed backend data tracking found that the app was used for a mean of 10 days. Patients spent most time on the education feature, followed by the medication and vitals features (median 26.6, 10.6, and 3.3 minutes respectively). They visited the medication feature most often (mean 30% of days). 31.1% of patients completed 1+ educational materials. Similar proportions of older (60+) and younger (≤60) patients completed >50% educational materials (14.3% vs 16.9%). 17% of patients recorded ≥2/3 follow-up visits.

Conclusion: Significantly lower readmission rates in the Corrie population suggest the potential for mHealth to improve outcomes for AMI patients. App engagement across different ages, races, genders, and insurance-status groups suggests a place for mHealth across a broad demographic spectrum. However, incompletion of any one feature suggests room for improvement. Our next step is exploring factors influencing feature engagement.

28. Matt Hoyer, MS 2

Mentor(s): Frank Lin, MD, PhD
Department of Otolaryngology - Head & Neck Surgery

Long-term depression and mental health functioning after hearing intervention in older adults with hearing loss

Authors: Matthew Hoyer BS, Jeremy Applebaum BS, Adele Goman PhD, Joshua Betz MS, Frank Lin MD, PhD

Background: Previous studies have identified an association between hearing aid (HA) or cochlear implant (CI) use in older adults with hearing loss and decreased rates of depression over one year. This study aims to examine this association long-term (4-6 years).

Methods: A cross-sectional analysis was conducted of 145 patients who presented for HA or CI and were enrolled in the Studying Multiple Outcomes after Aural Rehabilitative Treatment (SMART) study from 2011 to 2013. Participants were re-contacted in 2017, with 81 patients completing the follow-up assessment. The 36-Item Medical Outcomes Study Short-Form (SF-36) was self-administered to assess patients for mental health functioning and depressive symptoms.

Results: Previous studies show improvement in SF-36 mental health score at 6 months and 1 year, among both HA and CI users. Exploratory analysis reveals that, at 4-6 years, mental health scores are improved compared to baseline, albeit by a smaller margin than those seen at 6 months and 1 year. More in-depth analysis is currently in progress.

Conclusion: Hearing intervention with either HA or CI appears to be associated with an improvement in mental health functioning and depressive symptoms 4-6 years from the time of intervention.

29. Matthew Hadad, MS 2

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

Surgically-Relevant Patterns in Triplane Fractures: A Mapping Study

Authors: Matthew Hadad BS, Brian Sullivan BS, Paul Sponseller MD

Background: The triplane ankle fracture is characterized by an axial-plane fracture through the physis, a sagittal-plane fracture through the epiphysis, and a coronal-plane fracture through the metaphysis of the distal tibia. These fractures often require surgical management. Axial fracture lines determine optimal screw trajectories for surgical fixation. The purpose of our study was to identify fracture patterns in triplane fractures by illustrating the fracture lines in the axial planes of the distal tibial metaphysis and epiphysis.

Methods: We retrospectively reviewed records of children presenting with ankle fractures at one center from January 2007 through June 2017. Thirty-three cases of triplane fractures with available computed tomography (CT) scans were identified. Fractures in the axial plane of the metaphysis were identified 10 mm above the physis, and fractures in the epiphysis were identified midway between the physis and inferior tibial articular surface. Fracture lines were drawn and superimposed on the unfractured bone templates to generate fracture maps, and heat maps were then created to show areas of high and low fracture density.

Results: In the metaphysis, a medial-lateral fracture line in the posterior metaphysis was seen in 30 cases. There were clear zones of rare fracture involvement in the anterior and anterolateral metaphysis. In the epiphysis, all cases demonstrated fracture into the anterior epiphysis. An anterior-posterior fracture line in the anterior epiphysis was a common feature in 29 cases. Clear zones were seen in the anteromedial, anterolateral, and posterolateral epiphysis.

Conclusion: Fracture mapping of triplane fractures suggests conserved axial fracture patterns in the metaphysis and anterior epiphysis with additional class-dependent patterns in the posterior epiphysis. The clear zones presented herein are good candidates for the entry and exit points of screws used for fixation because they are likely areas of good screw purchase.

30. Matthew Wood, MS 2

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

Capturing the Burden of Experience: Hearing from AIS Patients and Parents after Posterior Spinal Arthrodesis

Authors: Matthew Wood BS, Derek Nhan BS, Brian Sullivan BS, and Paul Sponseller MD MBA

Background: The burden of corrective spinal surgery for adolescent idiopathic scoliosis (AIS) and associated recovery on patients and their parents is largely unknown. Previous studies have shown a discrepancy between parent/patient scores regarding self-image and overall satisfaction with surgery. However, no previous study has evaluated self-reported difficulty enduring the post-operative course. The purpose of our study was to capture and associate the reported experiences of patients and parents following posterior spinal arthrodesis.

Methods: All patients who underwent initial posterior spinal arthrodesis for AIS in 2015-2016 by a single surgeon at a tertiary care center were reviewed. Of the 40 patient/parent pairs successfully contacted, 18 patient/parent pairs, 1 individual patient, and 10 individual parents completed a telephone survey developed by the research team (59% response rate). Survey domains included appearance, activity level, recovery timetable, and impact of experience in Likert scale and open response format. Sub-group analysis included dividing respondents into two groups: post-operative time less than 1-year (n=20) and greater than 1-year (n=27). Statistical analyses included T-tests for continuous and Chi-square tests for categorical data.

Results: Patients and parents in both sub-groups reported similar scores regarding the difficulty of their surgical experience; however, the group with less post-operative time reported significantly greater impact on their life (p=0.005). No other differences between these groups were noted. After thematic analysis of all responses, the most frequently reported best aspect of arthrodesis was improvement in posture/appearance with no difference between patients/parents (patients:11/19, parents:16/28, p=0.959). The most frequently reported difficulty was physical pain (patients:9/19, parents:15/28, p=0.676).

Conclusion: Our results indicate that the burden of arthrodesis for AIS is typically a painful but short-term experience with decreased impact after the first post-operative year, resulting in improved posture/appearance. This has implications in improving perioperative care for posterior spinal arthrodesis, emphasizing adequate pain management and providing an expected timeline for patients/parents.

31. Michael Bell, MS 2

Mentor(s): Heather Di Carlo, MD
The James Buchanan Brady Urological Institute

30-day perioperative outcomes and characteristics of pediatric patients undergoing pyeloplasty in a contemporary national cohort

Authors: Michael Bell M.S., Greg Joice M.D., Nikolai Sopko M.D. Ph.D., Kara Choate M.D., Hiten Patel M.D. M.P.H., Matt Kasprenski M.D., John Gearhart M.D., Heather Di Carlo M.D.

Background: Pyeloplasty remains the gold standard for surgical correction of ureteropelvic junction obstruction in symptomatic patients. This procedure can be done via robotic, open, or laparoscopic approach. There are limited data on the 30-day perioperative outcome of children undergoing pyeloplasty. We sought to characterize patients undergoing pediatric pyeloplasty and explored the overall rates of complications and readmission specifically to determine if there were differences in outcomes following a minimally invasive surgical approach.

Methods: Hematoxylin and eosin stained tumor sections obtained from Johns Hopkins Hospital patients with HPV-positive OPSCC were quantified and sorted into three categories of TIL abundance (high, medium and low). Additional clinical and pathologic characteristics of the tumor were obtained through retrospective chart review. The prognostic effect of TIL abundance was evaluated with Kaplan-Meier, log-rank test, and Cox regression analyses considering recurrence free survival (RFS) as the primary outcome.

Results: This study included 141 patients with HPV-positive OPSCC. Patients with high/medium TIL quantity showed improved RFS (HR: 0.453, 95% CI: 0.222–0.927) compared to patients with low TIL abundance. Interestingly, improved RFS was also observed when comparing patients with a high TIL quantity with low TIL quantity patients (HR: 0.368, 95% CI: 0.150-0.900). In addition, the presence of extranodal extension (HR: 5.228, 95% CI: 1.635–16.716), lymphovascular invasion (HR: 2.860, 95% CI: 1.146–7.139) and perineural invasion (HR: 3.909, 95% CI: 1.572–9.721) were associated with a worse RFS.

Conclusion: Patients with the lowest tertile of TIL abundance were found to have significantly diminished RFS. This data suggests that the immune response plays a role in the improved survival seen in HPV-positive OPSCC and demonstrates that TIL abundance may enhance the prognostic evaluation in the context of AJCC 8th edition staging criteria for HPV-positive OPSCC.

32. Mitchell Huang, MS 2

Mentor(s): H. Ballentine Carter
The James Buchanan Brady Urological Institute

Apparent diffusion coefficient predicts risk of grade reclassification in men on active surveillance for prostate cancer

Authors: Mitchell Huang BA, Mufaddal Mamawala MBBS, MPH, Katarzyna J. Macura MD, PhD, Patricia Landis BA, Jonathan Epstein MD, H. Ballentine Carter MD

Background: Improving risk prediction tools may increase retention and limit unnecessary biopsies in prostate cancer active surveillance (AS) programs. We investigated if apparent diffusion coefficient (ADC) on baseline MRI (bMRI) predicts grade reclassification while in AS.

Methods: We retrospectively examined 259 patients in the Johns Hopkins AS program (2010 – 2017) who had bMRI showing a prostate lesion with ADC score and a later surveillance biopsy. The median follow-up before bMRI was 17 months (IQR: 7 mos. – 52 mos.) and median ADC on bMRI was 900x10-6 mm2/s (IQR 700 - 1070). Using the lowest quartile ADC of 700 as a cut-off, we conducted survival analysis on the association between ADC and upgrading to grade group (GG)≥2 and the more aggressive GG≥3 cancer.

Results: Out of 259 men, 74 (29%) and 24 (9%) upgraded to GG≥2 and GG≥3, respectively. Compared to non-upgraders, upgraders had higher PSA density (PSAD) (median, 0.10 vs. 0.08, p = 0.001), higher proportion of low-risk cancer (54% vs. 35%, p = 0.005), and lower ADC on bMRI (median, 805 vs. 930, p = 0.01). There was no difference in median follow-up before bMRI (13 mos. vs. 19 mos., p = 0.72). Controlling for PSAD and risk-status, men with ADC<700 had elevated risk of upgrading to GG≥2 (HR = 1.9, 95% CI: 1.1 - 3.1) and GG≥3 (HR = 2.5, 95% CI: 1.1 - 5.8). 5-year survival without upgrading was lower for men with ADC<700 compared to men with ADC≥700 for both GG≥2 (42% vs. 57%) as well as GG≥3 (68% vs. 85%), both p<0.05.

Conclusion: For AS patients, lower ADC scores correlate with increased risk of cancer upgrading and could be a useful variable for risk prediction. Greater acceptance of MRI evaluation with ADC may diminish the role of contrast-enhancement MRI, thereby reducing cost, invasiveness, and time spent under a magnetic field.

33. Nicholas Andrade, MS 2

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

FRAX Does Not Significantly Predict Development of Pseudoarthrosis After Spinal Fusion Surgery

Authors: Nicholas Andrade BS, Brian Neuman MD

Background: Pseudarthrosis is a complication of spinal fusion. The Fracture Risk Assessment Tool (FRAX) is used to assess bone quality and risk of hip fracture, and has been found to predict proximal junctional kyphosis (PJK). In this study, we evaluate the ability of FRAX to predict pseudarthrosis.

Methods: 188 spinal fusion patients were retrospectively reviewed. Records were obtained through Johns Hopkins Hospital's EPR service. Adjusted odds ratio analysis was conducted to assess the FRAX tool's utility in predicting pseudarthrosis. FRAX was calculated including bone mineral density (BMD) when available ("FRAX with BMD," n = 62), and without it when unavailable ("FRAX no BMD," n = 126). BMD alone as a predictor was evaluated as well through similar analysis.

Results: 53 (28%) patients were of male sex. The mean age was 63.0 yrs (range 39.9-87.6 yrs). 36 (19%) patients required revision surgery for pseudarthrosis. 12 (19.4%) of the FRAX with BMD group and 24 (19.0%) of the FRAX no BMD group developed pseudarthrosis. FRAX was not found to significantly predict need for pseudarthrosis revision surgery in any group (FRAX with BMD, FRAX no BMD, or All FRAX [combined data]). The only significant predictor of pseudarthrosis was a BMD T-score of ≤-3.65, representing the bottom 0.01% of individuals.

Conclusion: Although FRAX is a useful tool to assess bone quality and predict PJK, FRAX was found not to be predictive of the development of pseudarthrosis in this population. Only BMD was found to significantly predict pseudarthrosis, but at a threshold that has little clinical utility.

34. Nicholas Fung, MS 2

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

Parkinson's Disease Anxiety is associated with Lewy bodies in the Anterior Cingulate Cortex

Authors: Nicholas Fung BS, Masaru Ishii MD PhD, Lisa Ishii MD MHS

Background: Patients seeking stretched earlobe reconstruction often cite social perception as a primary reason. To date, there have been no studies attempting to measure the impact of stretched earlobe piercings on casual observer perceptions.

Methods: 30 nude mice were injected intracranially with 2x10^5 U87MG cells. They were then divided into five groups: control, control oligonucleotide, active oligonucleotide, TMZ, and active oligonucleotide plus TMZ. 10 mg/kg of TMZ were given orally on day 7 and day 25. 7 ug of oligonucleotides were infused directly into the tumor using convection enhanced therapy (CED) over the course of 5 minutes starting on day 7 and then every 4 days for 12 days and then 25 ug were infused every four days for 42 days. Kaplan meier survival curves were used to analyze the results.

Results: The control group had a median survival of 38 days, while the control oligonucleotide group and the active oligonucleotide group had a median survival of 40 and 42 days respectively. The TMZ group had a median survival of 50 days and the active oligonucleotide plus TMZ had a median survival of 51 days.

Conclusion: While the experimental groups survived longer than the control groups, there was no significant difference between the TMZ and the TMZ plus active oligonucleotide group. In addition, there was no significant difference between the control and active oligonucleotide. The data was inconclusive in determining whether the active oligo conferred any benefits. Future experiments will use different cell lines that might be better models in addition to increasing the dose of active oligonucleotide to achieve greater tumor suppressing effects.

35. Nicole Fischer, MS 2

Mentor(s): Gregory Pontone, MD MHS
Department of Psychiatry

Parkinson's Disease Anxiety is associated with Lewy bodies in the Anterior Cingulate Cortex

Authors: Nicole Mercado Fischer BA, Kate Perepezko BA MSPH, Jared Hinkle BS, Catherine Bakker MD, Martinus P.G. Broen MD PhD, Ankur Butala MD, Ted Dawson MD PhD, Albert Leentjans MD PhD, Zoltan Mari MD, Cherie Marvel PhD, Kelly Mills MD, Emile Moukheiber MD, Alexander Pantelyat MD, Olga Pletnikova MD, Liana Rosenthal MD, Melissa Shepard MD, Juan Troncoso MD, Jiangxia Wang MD, Gregory Pontone MD MHS

Background: The pathological basis of anxiety in Parkinson's disease (PD) is poorly understood. The goal of this study is to determine if there is an association between anxiety and the presence and regional distribution of Lewy bodies in brains from PD participants.

Methods: The brains of eighty-one participants with pathologically confirmed PD were assessed for the severity of Lewy body pathology in the frontal, temporal, and parietal lobes, anterior cingulate cortex, transentorhinal cortex, nucleus basalis of Meynert, cranial nerves IX-X, substantia nigra, locus coeruleus, and amygdala. Anxiety was assessed at baseline and every two years through self-report questionnaire and review of medical records. Participants were divided into two cohorts, anxious and non-anxious. Associations between history of anxiety and regional Lewy body severity were assessed with Chi-square and Fisher's exact tests.

Results: Of 81 patients with pathology-confirmed PD, 50 (62%) were identified as "anxious". Anxious and non-anxious PD cohorts had similar Hoehn and Yahr stage and overall Braak pathology score. Compared to the non-anxious PD participants, the anxious cohort had significantly higher Lewy body scores in the anterior cingulate cortex ($p=0.016$).

Conclusion: This clinicopathological investigation found a higher Lewy body frequency in the anterior cingulate cortex to be associated with the presence of anxiety in patients with PD. These results provide further insight into the neuropathological basis of anxiety in PD which could inform the development of new treatments.

36. Niv Milbar, MS 3

Mentor(s): Trinity J. Bivalacqua, MD PhD
The James Buchanan Brady Urological Institute

Impact of Intravesical Therapy for Non-Muscle Invasive Bladder Cancer on the Accuracy of Urinary Cytology

Authors: Niv Milbar BA, Mohit Gupta MD, Filippo Pederzoli MD, Meera R. Chappidi MD, Max Kates MD, David J. McConkey MD, Trinity J. Bivalacqua MD, PhD

Background: Urine cytology remains an essential diagnostic tool in the surveillance of patients with non-muscle invasive bladder cancer (NMIBC). The sensitivity of cytology for high-grade (HG) tumors has been reported to be between 37%-60% in recently published reports. The correlation of urine cytology with biopsy specimens to determine its accuracy following induction intravesical therapy, however, has not previously been performed.

Methods: A retrospective review was performed of patients who underwent intravesical therapy for biopsy-proven NMIBC between 2009-2016 at our institution. Patients underwent cytology and bladder biopsies in the operating room within 12 weeks after completing intravesical therapy. Only patients with complete information regarding urine cytologies and pathologic biopsy results were included in the analysis. The accuracy of urinary cytology in predicting HG disease recurrence following intravesical induction was evaluated and confirmed by biopsy.

Results: 203 cytology samples were analyzed from patients who met inclusion criteria. 128 (63.1%) samples were from patients who underwent induction Bacillus Calmette-Guerin (BCG) therapy; the remainder were treated with alternative therapies. Cytology was positive for HG disease in 22/128 patients (sensitivity, 30%; 95% CI 19%-43%). Cytology had a specificity 94% (95% CI, 86%-98%), PPV 82% (95% CI 60%-95%), and NPV 60% (95% CI 50%-70%). If the cytology interpretation was broadened to include HG and "suspicious for HG" findings, the sensitivity increased to 42% (95% CI 29%-55%) and specificity decreased to 87% (95% CI 77%-94%). For patients treated with BCG for HG disease (including Ta, T1, and CIS), cytology was positive for HG in 22/114 patients (sensitivity, 32%; 95% CI 20%-46%; specificity, 93%; 95% CI 83%-98%).

Conclusion: While urinary cytology maintains a high specificity following intravesical therapy, it also demonstrates a low sensitivity for potentially aggressive HG urothelial carcinoma. Further evaluation of more effective, clinic-based enhanced cystoscopy techniques is warranted to better identify patients at risk of disease recurrence following BCG therapy.

37. Oluseye Oduyale, MS 2

Mentor(s): Fasika Woreta MD, PhD
Wilmer Eye Institute

Clinical Characteristics and Outcomes in Patients Undergoing Enucleation after Ocular Trauma

Authors: Oluseye Oduyale, Fasika Woreta MD MPH

Background: Ocular emergencies and injury represent a significant burden to the EDs, causing long-term sequelae, reduced quality of life and financial cost. This study investigates the clinical characteristics and outcomes of patients undergoing primary versus enucleation/evisceration procedures after presenting to the ED at Johns Hopkins Wilmer. We hope the results of this study will provide insight to decision-making in EDs and characterize patients that are more likely to benefit from primary enucleations.

Methods: We performed a retrospective chart review of 78 patients enucleated after presenting with ocular trauma from 2010 to 2016. Patient data was obtained from EPIC Hyperspace.

Results: Demographics – 65% men, 35% women. 40% White, 37% Black, 8% Hispanic. Assault was the most common cause of traumas, 27, eye infections, 12, falls, 11, were also common. 58 were diagnosed with an open globe and 10 with endophthalmitis. The average of patients at presentation was 45 years. Patients waited an average of 213 days between presentation and enucleation, requiring an average of 1.42 procedures before or along with enucleation, the most common being open globe repair and eyelid/brow repair. Patients had an average of 0.45 systemic comorbidities at the time of enucleation. Patients experienced an average of 1.67 complications after presenting to the ED.

The 36 patients that were primarily enucleated were an average of 40.3 years, while patients with secondary enucleations were an average of 50.4 years. 19% of primary enucleations were due to endophthalmitis, compared to 12% of secondaries. 86% of primary enucleations patients presented with were perceived no light, compared to 52% of secondaries. Patients that underwent primary enucleations had an average of 0.56 systemic comorbidities compared to 0.35 in patients with secondaries. Primary enucleated patients experienced an average of 0.25 complications after presentation compared to 1.95 in patients with secondaries.

Conclusion: Patients undergoing primary enucleations tend to be older with more systemic comorbidities, presenting with more severe vision less. Additionally, these patients experience less complication rates.

38. Pooja Yesantharao, MS 2

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

Characterizing long-term pneumonectomy outcomes through risk factor and survival analyses

Authors: Pooja Yesantharao MS, Trevor Davis BS, Stephen Yang MD

Background: Parenchymal-sparing procedures have been increasingly favored over pneumonectomy. However, pneumonectomy is still thought to be required to manage centrally-located and locally advanced tumors. Although perioperative and early postoperative pneumonectomy outcomes have been characterized, only a few studies have examined 5-year mortality in pneumonectomy patients. This study characterizes the long-term outcomes and survival of pneumonectomy patients. This study also identifies prognostic factors for long-term survival after pneumonectomy and risk factors for associated morbidity and mortality.

Methods: From January 2000 to June 2016, 41 non-small cell lung cancer (NSCLC) patients were selected for pneumonectomy. Survival analyses were completed using the Kaplan-Meier method, and multivariate Cox proportional hazards modeling was used to estimate predictors of long-term morbidity and mortality. Risk factors for pneumonectomy-related morbidity were identified through univariate analyses followed by stepwise inclusion in a multivariate regression. Prognostic factors predicting long-term survival were also identified via univariate and multivariate analysis.

Results: The mean age of the patient cohort at the time of surgery was 60 years (standard deviation = 11). Thirty seven of the 41 patients were current or past smokers. No patient had a history of prior cardiothoracic surgery. Thirty six patients had lesions classified as either grade II or III. Post-operative complications included atrial fibrillation (n = 7), anemia (n= 2), infection (n= 2), and respiratory distress (n= 2). The median survival was 19 months, with a 5-year survival of 24%, and a 10-year survival of 7%. A right-sided lesion, no tobacco use, a tumor grade lower than II, and squamous cell carcinoma (SCC) histology type were associated with improved survival upon univariate analyses, though only tobacco use and SCC histology type were associated with improved survival upon multivariate analyses.

Conclusion: This study characterizes the long-term outcomes post-pneumonectomy in NSCLC patients, and identifies risk factors associated with morbidity and mortality in this patient cohort.

39. Rafa Rahman, MS 2

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

Depression and Anxiety Progression Correlates with Spine Surgery Outcomes

Authors: Rafa Rahman BS, Richard L. Skolasky MA Sc.D, Alvaro Ibaseta MS, Lee H. Riley III MD, David B. Cohen MD, Daniel M. Sciubba MD, Khaled M. Kebaish MBBCh MS, Brian J. Neuman MD

Background: Studies demonstrate that patients endorse psychiatric symptoms preoperatively and that psychiatric distress negatively impacts postoperative outcomes. Little is known about how depression or anxiety progression affects outcomes. We differentiate depression and anxiety progression patterns among spine surgery patients, and compare surgical outcomes.

Methods: PROMIS Computer Adaptive Testing scores for Depression, Anxiety, Pain Interference, Physical Function, Sleep Disturbance, and Satisfaction with Social Role were collected for spine surgery patients preoperatively and 3 months postoperatively. Patients were stratified based on perioperative progression of depression and anxiety scores: 1) Persistent, 2) Postoperatively Improved, 3) Postoperatively Developed, and 4) No Psychiatric Distress. Multiple linear regression compared change in outcomes, adjusting for potential confounders.

Results: Of 240 patients (average age: 58.4 years; 45% male) 26.5% had preoperative depression and 44.2% had preoperative anxiety. Compared to No Depression subgroup, Persistently Depressed patients had significantly less improvement in pain interference by 6.2 PROMIS points, physical function (6.7), sleep disturbance (8.9), and satisfaction with social role (7.6). Patients with Postoperatively Developed Depression had significantly less improvement in pain interference (5.8), sleep disturbance (6.1), and satisfaction with social role (5.8). Compared to No Anxiety subgroup, Postoperatively Developed Anxiety patients had significantly less improvement in pain interference (6.3), sleep disturbance (7.4), and satisfaction with social role (6.3). There is no difference in preoperative depression scores between those with persistent versus postoperatively improved depression. The same is true for anxiety.

Conclusion: Many patients present with preoperative depression or anxiety. Surgical outcomes are worse in those with persistent or postoperatively developed depression, and postoperatively developed anxiety. Presence of postoperative depression or anxiety may have more effect on surgical outcomes than preoperative depression or anxiety. Appropriate management should be provided for patients with symptoms of psychiatric distress.

40. Rohan Bajaj, MS 2

Mentor(s): David S. Friedman, MD, MPH, PhD
Wilmer Eye Institute

Outcomes of Modified Trabeculectomy Closure Technique

Authors: Rohan P. Bajaj BSc, Moon J. Lee BSc, Henry D. Jampel MD, Jayant V. Iyer MD, David S. Friedman MD

Background: Most surgeons perform trabeculectomies using a fornix-based approach disinserting the conjunctiva at the limbus and reapproximating it with a variety of approaches. A modified trabeculectomy technique has been developed in which the conjunctiva is incised 3 mm posterior to the limbus and is reapproximated using two nylon sutures, burying the posterior conjunctiva under an anterior lip of conjunctiva at the limbus. We examined the outcomes of this modified closure technique.

Methods: A retrospective review was completed on trabeculectomies performed by two glaucoma surgeons at the Wilmer Eye Institute. The main outcome measures were mean reduction in postoperative intraocular pressure (IOP) and number of medications at 12 months, and total number of complications during follow up. Need for bleb needling was included as a secondary measure.

Results: We analyzed 64 eyes that underwent standard trabeculectomy closure and 45 eyes that underwent the modified closure. Demographics for the modified cohort: 60% male (53.1% in standard), 31.1% African American (46.8% in standard), and average age of 66.4 ± 12.0 years (67.3 ± 12.1 years in standard). There was no difference in reduction of mean IOP pre- and postoperatively at 12 months; 12.3 ± 8.5 mm Hg for the standard technique vs. 9.7 ± 8.5 mm Hg for the modified technique, ($p>0.05$). There were similar rates of post-operative complications. Compared to the standard technique, the modified technique had 0% (vs. 1.6%) hypotony, 11.1% (vs. 3.1%) bleb leaks, 6.7% (vs. 0%) choroidal effusion, and 4.4% (vs. 1.6%) subconjunctival hemorrhage ($p>0.05$ for all). Furthermore, bleb needling was performed at similar rates (15.6% vs 6.3%; modified vs standard respectively, $p>0.05$).

Conclusion: The modified closure technique provided similar results to standard closure for trabeculectomy. The closure is subjectively easier to perform and reduces surgical time. Additional prospective studies are needed to determine the likelihood of early wound leaks with this approach.

41. Rui Han Liu, MS 2

Mentor(s): Thomas Reifsnyder, MD
Department of Surgery

Revascularization of Failed Lower Extremity Bypass Grafts using Autologous Vein Conduit is Effective for Limb Salvaging

Authors: Rui Han Liu BA, Charles D. Fraser III MD, Xun Zhou MD, Robert J. Beaulieu MD, Thomas Reifsnyder MD

Background: Management of threatened limbs following repeated lower extremity bypass graft failures remain a subject of debate. The purpose of this study is to review the utility of lower extremity bypass revision following graft failure in achieving limb salvage and freedom from amputation.

Methods: All patients who underwent revision of previous infrainguinal arterial bypass grafts from 2006 to 2016 by a single surgeon were retrospectively reviewed. Bypasses were categorized into three major groups: femoral-popliteal, femoral-distal, and popliteal-distal arterial bypasses. Freedom from above or below knee amputation (FFA) was defined as number of days from operative date to subsequent amputation or most recent follow up if no subsequent amputation was required. FFA was determined using the Kaplan-Meier method.

Results: From 2006 to 2016, 101 patients underwent revisions of their infrainguinal bypasses (40.6% female; 59.4% male). 23 patients had femoral-popliteal artery bypass, 71 had femoral-distal artery bypass, and 7 had popliteal-distal artery bypass. 57.4% (n = 58) of patients underwent one previous bypass while 42.6% (n = 43) underwent more than one previous bypass. Of the patients with two or more prior bypasses, 20.9% (n=9) required subsequent amputation, while only 1.7% (n=1) of patients with one prior bypass required amputation. FFA was 757 days for patients with one previous bypass and 263 days for patients with two or more previous bypasses. No patients with femoral-popliteal bypasses required amputation while 11.3% (n=8) of the femoral-distal and 28.6% (n=2) of the popliteal-distal bypasses required subsequent amputations.

Conclusion: A significant FFA rate can be achieved with revascularization following graft failure, although more distal bypass revisions resulted in higher incidences of subsequent lower extremity amputation. This suggests that aggressive surgical revision for failing lower extremity bypass grafts is effective in preserving threatened extremities.

42. Sagar Patel, MS 2

Mentor(s): Katherine Puttgen, MD
Department of Pediatric Dermatology

Laser Settings in the Management of Pediatric Burn Scars with Fractional CO2 Laser Therapy

Authors: Sagar Patel BA BS, Ha Vi Nguyen BS, Melissa Fannon MSN, F. Dylan Stewart MD, Katherine B. Puttgen MD

Background: Ablative fractionated carbon dioxide (AFCO2) laser therapy can improve function, appearance, and symptoms of hypertrophic scars. However, limited guidelines for AFCO2 on pediatric burn scars exist due to inadequate literature. This study aims to describe our center's experience with pediatric AFCO2 to evaluate the AFCO2 therapy settings.

Methods: Injury characteristics, demographics, and laser settings were recorded through retrospective chart review of 37 pediatric burn patients treated with AFCO2 at Johns Hopkins Hospital from December 2016 to August 2017. Scars were rated using the Matching Assessment of Photographs and Scars (MAPS) scale which evaluates scar surface, height, and color. Patients were classified by Fitzpatrick Skin Phototype and burn severity. ANOVA and student's t-tests were used to analyze variations in laser settings and outcomes among patient groups.

Results: Eighteen subjects (48.6%) were male with mean age 4.26±4.4 years. Seventy percent identified as non-white and 70% were classified as a Type IV, V, or VI on the Fitzpatrick Scale. Full thickness burns were sustained by 75% of patients, and 25% suffered partial thickness burns. Improvements were noted in scar texture, height, and pigmentation. The mean AFCO2 energy in the SCAAR FX setting was 97.56mJ±28.8. Facial scars received lower SCAAR FX energy (M=85.97mJ±28.1, $p<.01$) than trunk(M=95.29mJ±28.3) or limbs(M=102.2mJ±28.3), but DEEP FX energy levels did not differ significantly across body regions ($p=.08$). MAPS analysis revealed no scar improvement.

Conclusion: AFCO2 can manage hypertrophic pediatric burn scars from partial and full thickness burns, especially in patients with darker skin tones. Our center experienced no adverse events. SCAAR FX energy levels are adjusted significantly for different body regions suggesting different treatment paradigms for different regions. The MAPS scale was not effective in evaluating AFCO2 benefits. This data can inform clinical decisions as additional centers adopt AFCO2 for pediatric burn scars.

43. Shagnik Ray, MS 2

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

Variations in Maxillary Labial Frenum Morphology of Healthy Newborns

Authors: Shagnik Ray BA, Christopher Golden MD, David Tunkel MD, Emily Boss MD, Margaret Skinner MD, Suzanne Rubin PNP, Patricia Smouse PNP, Jonathan Walsh MD

Background: The variation in length, thickness, and attachment characteristics of the maxillary labial frenum in newborns has had limited objective studies. However, there is increasing discussion of the labial frenum's contribution to breastfeeding difficulty, as well as the role of labial frenotomy. Additionally, there is no classification for upper lip frenum morphology in infants, based on such objective measurements. The objectives of this study were to measure the anatomic variations of the maxillary labial frenum and to propose a classification system based upon anatomic measurements, appearance, and morphology.

Methods: A prospective cross-sectional study of the maxillary labial frena of healthy newborns without craniofacial anomalies born at an academic medical center was performed. High definition digital photographs using a standard protocol were obtained of the maxillary frenum. Standardized measurements of frenum alveolar and lip attachment, frenum thickness, and frenum length were made with ImageJ software. LATCH scores, birth weight, and demographic data were collected and analyzed.

Results: 124 participants were enrolled. The mean±standard deviations for frenum parameters are as follows: alveolar edge to frenum(1.51mm±0.81),frenum length(5.16mm±1.66),frenum to vermilion border(6.12mm±2.01),frenum gingival thickness(0.89mm±0.37),frenum labial thickness(2.86mm±1.34),frenum to alveolus length ratio(0.25±0.13), and frenum to lip length ratio(0.90±0.09). An anatomic based classification system is proposed using the frenum parameters.

Conclusion: This study presents the variation in maxillary labial frenum morphology of healthy newborns and proposes an anatomic classification system. Further studies are warranted to investigate frenum morphological types and their effects on breastfeeding.

44. Smirnov Exilus, MS 2

Mentor(s): Uma Srikumaran, MD
Department of Orthopeadic Surgery

Comparison of lateralized reverse shoulder arthroplasty outcome in acute fracture and cuff arthropathy indications

Authors: Smirnov Exilus BA, Uma Srikumaran MD

Background: Originally indicated for pseudoparalsysis and degenerative shoulders with massive rotator cuff deficiency, reverse shoulder arthroplasty (RSA) is now given significant consideration in acute fractures of the proximal humerus with comminuted tuberosities. We assess for differences in functional outcome when RSA is performed for acute fracture and cuff arthropathy indications.

Methods: We performed a retrospective cohort study of all patients who underwent RSA by a single surgeon at the Johns Hopkins Hospital. Excluded in this study were RSA performed in fracture sequelae and revision indications. A minimum follow-up of 12 months was required for inclusion. The t test was used to evaluate for differences in mean post-operative subjective shoulder value (SSV), forward flexion (FF), abduction (AB), and external rotation angles between cohorts. A p value of 0.5 was considered statistically significant.

Results: Between March 2012 and October 2016, 82 elderly patients underwent reverse shoulder arthroplasty by a single surgeon at our institution. There were a total 32 acute fractures, 49 cuff arthropathy cases and one revision surgery. A total of 38 patients were lost to follow-up and did not have post-operative data at the one year mark. Of the remaining 44 cases, there 16 in the fracture cohort (F) and 28 in the arthropathy group (A). No statistically significant differences were observed in SSV (F 70% vs A 76%, p = 0.48), FF (F 127.5˚ vs A 134.8˚, p = 0.38) and AB (F 85.6 ˚ vs A 87.8˚). A statistically significant difference was observed in external rotation with the arm at the side (F 20.8˚ vs A 41.6˚, p = 0.02).

Conclusion: Though originally indicated for cuff arthropathy, RSA demonstrates similar improvements in some range of motion parameters in a subset of acute fracture patients but not in external rotation at the side. Further investigation in a larger sample of patients with a minimum of two-year follow-up is needed to confirm this finding.

45. Surekha Mullangi, MS 2

Mentor(s): Tariq Shafi, MBBS, MHS
Department of Medicine

Integrative Point-of-Care Ultrasound Curriculum Imparts Diagnostic Skills Relevant to Nephrology

Authors: Surekha Mullangi BA, Stephen Sozio MD MHS, Steven Menez MD, Carol Martire RDCS, Tariq Shafi MBBS MHS

Background: The utility of point-of-care ultrasound (POCUS) has been expanding as a multipurpose diagnostic tool to enhance physical examination. However, a clear, nephrology-specific, curriculum has not been established. We developed and implemented a POCUS curriculum that teaches focused skills to nephrology fellows. The goal of our study is to describe our initial experience with this innovative program.

Methods: The Johns Hopkins Renal Fellowship POCUS curriculum is a two-week elective that provides focused training to assess the following: heart (ejection fraction, pericardial effusion, chamber size), lungs (pulmonary edema, effusion, pneumothorax), inferior vena cava (diameter, collapsibility), kidney (size, echogenicity, hydronephrosis), bladder (volume), and dialysis fistula (depth, diameter). We teach these skills using a combination of didactic lectures, guided scanning, and independent scanning. We grade image interpretation skills using a Qualtrics-based test and image acquisition skills using a POCUS-Objective Structured Clinical Examination (OSCE). Pre-tests and post-tests are administrated prior to and after completion of the program. Comfort with skills is gauged using a 5-point Likert scale.

Results: Over the past year,12 fellows have participated in the course; 4 have completed all modules and the remaining are continuing training. Of the 12, 67% of fellows reported using POCUS for diagnostic purposes, but none were formally trained in use and 75% did not have formal education on ultrasound principles. The fellows that completed the course reported significant improvement ($p < 0.05$) in assessing all educational domains. Comparing pre-test to post-test scores, fellows felt significantly more confident identifying and assessing pathology across all domains following the course (0.27 (0.46) to 4.53 (0.74)). At the end of the course, 100% of fellows agreed that POCUS was easy to obtain, improved assessment of patients, should be a part of the fellowship, and that other nephrology faculty should be trained.

Conclusion: A 2-week nephrology-specific POCUS curriculum is feasible and enhances fellows' learning experience.

46. Tai-Kyung Hairston, MS 2

Mentor(s): Emily Boss, MD
Department of Pediatric Otolaryngology

The Tonsillectomy Tweet: A Social Media Perspective of Parent Concerns and Priorities in Pediatric Tonsillectomy

Authors: Tai Kyung Hairston BS, Anne R. Links MS MHS, Vandra Harris MD, Jonathan Walsh MD, Mary Catherine Beach MD MPH, Emily F. Boss MD MPH

Background: Despite the frequency of pediatric tonsillectomy, little is known regarding parental experience, priorities, or concerns about this common surgery. In this study, we systematically evaluate posts in a well-known social media site to gauge parent per-spectives of tonsillectomy in children that may not otherwise be revealed in a routine clinical encounter.

Methods: In this mixed methods analysis, we searched Twitter© for terms related to tonsillectomy posted by parents between 2008-2017. We applied modified grounded theory to de-velop a coding taxonomy in which to classify tweets. Three reviewers reviewed tweets for thematic synthesis and classification. We calculated frequencies for each theme, which were not mutually-exclusive.

Results: Of 5801 tweets retrieved, 786 matched search criteria. Tweets related to overarching themes of procedural concerns (N=664, 84.5%) and attitudes/experiences (N=634, 80.7%). Common tweets related to procedural concern regarded surgical indication ("sick for months"; N=85,10.8%), recovery [N=316, 40.2%; including pain ("poor baby suffering"; N=88, 11.2%) nutrition ("won't eat"; N=97, 12.3%)], and parental ("harder on the parents than the kid"; (N=77,9.8%)). Common tweets regarding attitudes/experiences include tenor of overall care ("not prepared for this"; N=225, 28.6%), and fears/apprehensions ("frankly, I'm terrified"; N=209, 26.6%). Parents also tweeted regarding the surgeon (N=40, 5.1%), costs ("tonsillectomy cost $2,400"; N=49, 6.2%), and health systems (N=11,1.4%).

Conclusion: This analysis provides insight into parent perspectives on pediatric tonsillectomy. Parents commonly tweet concerns about tonsillectomy which may be underestimated in routine surgeon-parent dialogue. Findings may be used to guide clinicians in educating and counseling parents, and engage parents and children in shared decision-making for tonsillectomy.

47. William Tobolowsky, MS 2

Mentor(s): Joseph Lopez, MD
Department of Plastic and Reconstructive Surgery

Rigid External Distraction followed by Secondary Bone Grafting For Large Maxillary Advancements in Cleft Lip and Palate Patients

Authors: William Tobolowsky BS, Pranjal Gupta BE, Regina Cho MSE, Joseph Lopez MD, Anthony Tufaro MD.

Background: Maxillary hypoplasia after cleft lip and palate repair can result in significant functional and aesthetic impairments. Distraction osteogenesis is currently used to correct severe midface retrusion, but patients continue to suffer from a high relapse rate. The purpose of this study was to describe preliminary surgical outcomes utilizing a two-stage technique that may optimize skeletal stability in patients with severe maxillary hypoplasia.

Methods: A retrospective review of all cleft lip and palate patients with severe maxillary hypoplasia evaluated by a single surgeon at a tertiary care center from 2003-2014 was performed. 12 subjects were identified and underwent maxillary advancement via a two-stage technique: (1) Le Fort I external rigid distraction, followed by (2) Le Fort I re-osteotomy, autologous iliac crest bone graft application, and plate-fixation. Post-operative cephalograms were taken on average 1 year following surgery.

Results: A distraction rate of 1 mm/day was achieved with an average of 14 mm of maxillary advancement. Average increase in SNA was +9.03˚, with an increase from 71.84˚ to 80.88˚ (normal=82.0˚, p-value < 0.0001), no significant change in SNB, and a +9.63˚ change in ANB from -7.76˚ to 1.88˚ (normal=1.6˚, p-value < 0.0001).

Conclusion: Distraction osteogenesis alone is associated with a significant degree of relapse post-operatively. The described two-step procedure had similar cephalometric improvements as compared to conventional DO. Successive bone grafting as a second procedure may help ameliorate this risk, and optimize correction of maxillary hypoplasia in susceptible populations.

48. Yi Shao, MS 2

Mentor(s): Marilyn Albert, PhD
Department of Neurology

Lifestyle activity engagement as a predictor of cognitive decline

Authors: Yi Shao BS, Corinne Pettigrew PhD, Anja Soldan PhD, Marilyn Albert PhD

Background: Studies suggest approximately 35% of dementia cases are attributable to modifiable factors, underlying the importance of targeting risk factors that may delay or prevent dementia-related cognitive decline. Although participation in physical, cognitively stimulating, and social activities may be protective, it is unknown if the effects of activity engagement are independent of other factors that affect dementia risk, and whether the protective effects of activity engagement differ for individuals who have remained cognitively normal (CN) over time versus those who progress to mild cognitive impairment (MCI). Our objective was to examine the relationship between current activity engagement and prior cognitive trajectories and whether these associations are modified by APOE-4 genetic status, age, or cognitive reserve.

Methods: Our subjects from the BIOCARD study were CN at baseline with annual clinical and cognitive assessments for up to 20 years. Starting in 2015, participants self-reported their engagement in various lifestyle activities on the CHAMPS (Community Healthy Activities Model Program for Seniors) activity questionnaire, which surveys frequency and duration per week of 40 different activities. A cognitive reserve score was constructed based on baseline measures of reading, vocabulary, and education. Our data was analyzed using linear mixed effects regression models.

Results Among subjects who progressed to MCI (N=27, mean age at CHAMPS visit = 75 y, 52% female), greater engagement across all lifestyle activities was associated with less decline in prior cognitive performance over time. However, among individuals who remained CN (N=162, mean age at CHAMPS visit = 70 y, 62% female), engagement in lifestyle activities was not correlated with prior cognitive trajectories. Additionally, these interactions were determined to be independent of APOE-4 genetic status, age, and level of cognitive reserve.

Conclusion: Our results suggest that greater engagement in all activities may modify the trajectory of cognitive decline among older adults who develop symptoms of MCI.

49. Yuanxuan Xia, Student in Residence

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

Role of Adjuvant Therapy in Patients Who Present with a Presumed Hemorrhagic Melanoma Brain Metastasis that is Negative on Pathology

Authors: Yuanxuan Xia BA, Leila Mashouf, Evan Lipson MD, William Sharfman MD, Chetan Bettegowda MD PhD, Kristin Redmond MD MPH, Lawrence Kleinberg MD, Michael Lim MD

Background: Melanoma brain metastases can present with intracranial hemorrhage. However, when surgical resections are performed on such lesions, pathology reports can return with no tumor. Physicians must then decide on the role of adjuvant radiotherapy to the surgical site. The decision-making process is challenging because bloody lesions could make it difficult to obtain a specimen with malignant cells, even if they are present. Here, we report on the outcomes of a series of melanoma patients with "negative pathology" hemorrhagic brain lesions.

Methods: All patients at a single institution with melanoma who underwent craniotomy for a hemorrhagic brain lesion in the setting of known metastatic melanoma since 2008 were identified through retrospective chart review. The primary outcome was recurrence at the former site of hemorrhage and resection.

Results: We identified 9 patients with a median post-operative follow-up time of 8.3 months. The median number of brain lesions at the time of craniotomy was 3 (1-25). Seven of these 9 patients who presented with a hemorrhagic lesion had prior history of melanoma brain metastases of which 2 had prior craniotomies and 7 had prior radiation to the lesion of interest. Eight of the 9 patients had prior immunotherapy. Post-operatively, 1 patient received stereotactic radiosurgery (SRS) to the operative bed, whereas the other 8 were observed with close interval scans. No patients in the (+)SRS group developed a melanoma metastasis at the site of interest whereas only one patient in the (–)SRS group did.

Conclusion: Patients with a history of known melanoma presenting with a suspected hemorrhagic brain metastasis that instead has negative pathology may benefit from close observation.

50. Zach Pennington, MS 2

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

Minimally Invasive Versus Conventional Spine Surgery for Vertebral Metastases: A Systematic Review of the Evidence

Authors: Zach Pennington, A. Karim Ahmed, Camilo A. Molina, Ilya Laufer, Daniel M. Sciubba

Background: One of the major determinants of surgical candidacy in patients with symptomatic spinal metastases is the ability of the patient to tolerate the procedure-associated morbidity. In other pathologies, minimally invasive (MIS) procedures have been suggested to have lower intra-operative morbidity while providing similar outcomes.

Methods: We conducted a systematic review of the PubMed library searching for articles that directly compared the operative and post-operative outcomes of patients treated for symptomatic spinal metastases. Inclusion criteria were articles reporting 2 or more cases of patients > 18y.o. treated with MIS or open approaches for spinal metastases. Studies reporting results in spinal metastases patients that could not be disentangled from other pathologies were excluded. A meta-analysis was performed for each outcome with greater than 20 total patients per treatment group.

Results: Our search returned 1594 articles, of which 9 articles met the criteria for inclusion. All articles were level III evidence. Of these, 6 articles reported mean estimated blood loss, 6 reported mean operative time, 3 reported length of hospital stay, 4 reported pain relief on VAS scale, 9 reported neurological improvement greater than 1 ASIA grade, and 9 studies reported complication rates. Meta-analysis demonstrated MIS procedures to have lower blood loss (-608.3mL; $p < 0.00001$), shorter operative time (-69.6min; $p < 0.00001$), shorter length of stay (-0.55 days; $p < 0.0001$), and lower complication rates (OR = 0.58; $p = 0.05$). Neurological improvement ($p = 0.94$) and pain relief ($p = 0.66$) did not differ between the two groups.

Conclusion: Recent advances in minimally invasive techniques may reduce surgical morbidity while providing similar symptomatic improvement in patients treated for spinal metastases. As a result, MIS techniques may expand the pool of patients with spinal metastases who are candidates for operative management.

POSTER ABSTRACTS: ETHICS AND THE ART OF MEDICINE

Listed alphabetically by first name of author

51. Anna Weimer, MS 2

Mentor(s): Evan Bloch, MD
Department of Pathology

Blood Transfusion Safety in Sub-Saharan Africa: A Literature Review of the Latest Changes and Challenges in the 21st Century

Authors: Anna Weimer BA, CT Tagny MD, Jean Baptiste Tapko MD, Christa Gouws MD, Aaron Andrew Ross Tobian MD, PhD , Evan Bloch MD

Background: Blood transfusion is an essential therapy for a range of clinical indications in Sub-Saharan Africa (SSA). Transfusion is needed to manage trauma, obstetric hemorrhage, and malaria-associated anemia. Nonetheless, access to a safe and adequate blood supply has proven challenging in SSA. Systemic deficiencies in policy, collections, testing, and post-transfusion surveillance have prompted strategic intervention by the WHO and other foreign bodies. In the early 2000s, funding gained momentum in large part due to influx from PEPFAR under the umbrella of HIV mitigation. Despite infusion of funds, inadequacies persist. In light of continued challenges, we sought to evaluate what is known about the current status of regional blood transfusion safety in SSA.

Methods: We conducted a literature review of the PubMed database using but not restricted to the following search terms: “blood safety”, “transfusion guidelines”, “Sub-Saharan Africa”; we included “grey literature” containing governing bodies websites (e.g. WHO). Articles published in English from 2009 to the present were reviewed.

Results: Of 705 articles identified, 107 were reviewed. External funding is linked to operational gains, including recruitment of voluntary donors and expanded testing for the major transfusion transmissible infections. Funding has declined for transfusion safety over the past five years. Risk to transfusion recipients remains largely uncharacterized. Positive developments include new education and training initiatives in the region, and a robust accreditation process that has been implemented successfully by the African Society of Blood Transfusion.

Conclusion: The decline in funding for transfusion safety has strained the ability to maintain or improve related services. The broader ramifications of funding –specifically regarding sustainability- are not fully understood raising questions about responsibility of external aid. Continued areas of need include data collection and dissemination, epidemiological surveillance for transfusion transmissible infections, donor recruitment, quality assurance and oversight of laboratory testing, and hemovigilance. Collectively, these impact planning for the future.

52. Patrick Meyers, MS 2

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

Failure to Document Psychosocial Risk Factors is Associated with Increased Complications from Cancer Surgery

Authors: Patrick M Meyers BA, Ira L Leeds MD, Elliott R Haut MD, Jonathan E Efron MD, Fabian M Johnston MD

Background: Certain behavioral traits and inadequate social support may be risk factors for complications following cancer surgery. While psychosocial risk factors are often discussed in the context of cancer care, it is unclear if conventional patient evaluation is capturing them.

Methods: Adult patients at a tertiary academic medical center were surveyed prior to curative abdominal cancer surgery to assess six psychosocial risk factors including resilience, resourcefulness, substance use, and depression. These risk factors were also assessed by restrospective chart review before surgery and compared to survey results. Concordance was calculated using positive and negative agreement and Cohen's Kappa. Patients positive by the study's questionnaire but not the medical record were categorized as "clinically undocumented." Thirty-day postoperative complications were abstracted by chart review. Complication rates for those with and without undocumented risk factors were compared using Fisher's exact test.

Results: We identified 107 eligible patients (60% male, median age of 65, IQR 55-71). Among those, 77% were identified as having one or more psychosocial risk factors by study questionnaire compared to 45% by chart review. Comparisons between chart review and patient survey revealed poor positive agreement (0-14%) and moderate-to-strong negative agreement (51-90%) among all risk factors. Additionally, Kappa analysis demonstrated poor-to-fair agreement among all risk factors (κ = 0.142 to 0.423). The overall complication rate was 43%. The complication rate for patients with at least one clinically undocumented risk factor was 49.9% versus 38.7% in those without (p=0.294), while five risk factors demonstrated a consistent trend of higher complication rates when undocumented.

Conclusion: This study suggests a high level of discordance between formal screening and clinician documentation for psychosocial risk factors. There is a nonsignificant association between undocumented risk factors and worse postoperative outcomes. Further work should demonstrate whether structured screening of psychosocial risk factors may improve preoperative risk stratification to allow for early intervention.

POSTER ABSTRACTS: HISTORY OF MEDICINE

Listed alphabetically by first name of author

53. Tiffany Brocke, MS 2

Mentor(s): Mary Fissell PhD; Graham Mooney PhD
Department of the History of Medicine

Race and Reputation: The Influence of the Johns Hopkins Hospital on Abortion Access in Baltimore, 1945-1973.

Authors: Tiffany Brocke BS, Graham Mooney PhD, Mary Fissell PhD

Abstract: Abortion is politically and culturally contested in America. The Supreme Court's 1973 Roe v. Wade decision was a dramatic shift in abortion policymaking; historical work on the context of this decision has focused on feminist activism and racial disparities in abortion outcomes prior to legalization. However, prior to the emergence of second-wave feminism, physicians had worked for over a decade to change abortion care. Furthermore, no study exists on the impact of one hospital on city, state, and national abortion landscapes. The Johns Hopkins Hospital in Baltimore presents an enlightening case study of how physicians capitalized on shifting public attitudes toward abortion to achieve reform that laid groundwork for Roe, and the limitations of that physician-led reform.

To this end, I reviewed archival collections of Johns Hopkins doctors and other Baltimore stakeholders, and Baltimore newspapers. Secondary literature provided historical and scholarly context for the project.

Before Roe, abortion politics in Maryland were largely physician-driven. Motivated by the evolving perceptions of illegal abortion as a public health issue, and legal abortion as a therapy for social ills, Hopkins doctors liberalized abortion policies within their institution and statewide. Although they advocated for a groundbreaking Maryland reform law in 1968, their ability to meet the needs of their patients was hampered by two factors. First, healthcare access in Baltimore was profoundly shaped by race, and the 1968 legislation failed to solve the complex problems of disparities in abortion access between Black and white women, so that Black women benefited least from these changes. Second, the desire to protect the reputation of the Johns Hopkins Hospital led physicians to tightly control the availability of abortions. Thus, Johns Hopkins abortion policies were shaped by racial dynamics in Baltimore, and as a result contributed to the perpetuation of racial divides in citywide abortion access.

POSTER ABSTRACTS: PUBLIC HEALTH RESEARCH

Listed alphabetically by first name of author

54. Alice Zhou, MS 2

Mentor(s): David Yousem, MD
Department of Radiology

Cost-effectiveness Analysis in Radiology: Methodological Variation and its Impact on Interpretation

Authors: Alice Zhou BS, Matthew D. Alvin MD MBA MS MA, David M. Yousem MD MBA

Background: Cost-effectiveness research has become a prominent focus in radiology. However, the lack of a standardized CEA methodology may lead to conflicting conclusions on the cost-effectiveness of an imaging modality and hinder CEA applications toward policy. This study reviews existing CEAs in radiology to identify areas of methodological variation, explore their impact on interpretation, and discuss optimal strategies to address key problems observed.

Methods: We performed a systematic review of cost-effectiveness literature in radiology over the past 5 years to determine cost and quality of life methodology. Studies were identified by querying MEDLINE, EconLit, and the Tufts Medical Center CEA registry.

Results: 30 cost-effectiveness studies met our inclusion criteria. Nineteen were conducted from the payer perspective (63.3%), six from the societal perspective (20%), and five from the hospital perspective (16.7%). Only 23 explicitly stated their perspective (76.7%). Cost inclusion varied greatly between studies; adverse effects of imaging (16.7%) and future complications (40%) were the least frequently included direct costs. Sixteen (53.3%) studies adjusted costs for inflation, and 18 of 24 studies with long follow-up periods discounted costs and outcomes (75%). Twenty-nine studies used incremental cost-effectiveness ratios (ICER). Twenty-two of them (75.9%) compared ICERs to a willingness-to-pay threshold, and 10 used cost-effectiveness acceptability curves (34.5%).

Conclusion: We observed significant methodological variation within the 30 studies reviewed, at times compounded by unclear reporting of methods. Based on key problem areas observed, we make four recommendations to optimize the performance of CEAs in the future: proper choice of perspective and outcomes measures, inclusion of a cost inventory table, and comparison of results to a range of willingness-to-pay thresholds. These recommendations are not comprehensive. Further work is required to create and disseminate a standardized, accurate means of performing CEAs and to ensure comparability and transparency for policymakers seeking to apply cost-effectiveness results.

55. Aneesha Cheedalla, MS 2

Mentor(s): Kathleen Page, MD
Department of Medicine

Hepatitis C Linkage to Care and Treatment Outcomes at the Baltimore City Health Department

Authors: Aneesha Cheedalla BA, Amanda Rosecrans MD MHS, Kathleen Page MD

Abstract: The introduction of Direct Acting Antivirals (DAAs) for the treatment of Hepatitis C virus (HCV) allows patients to be cured, but several barriers exist to completing treatment. In 2014, the Baltimore City Health Department (BCHD) began an HCV treatment program at its Sexually Transmitted Diseases (STD) Clinics. Among patients diagnosed with chronic Hepatitis C (HCV RNA+) between December 2015 and March 2017 (n = 401), 67% of patients were linked to care at the STD Clinic and 20% achieved SVR during the follow up period. Among those who initiated HCV therapy (n= 130), 60% completed therapy and achieved SVR, 10% did not complete therapy, and 30% are currently on therapy. From patients with available insurance information (n=347), the proportion of patients linked to care was associated with type of insurance (Medicaid 73.6%, Medicare 78.1%, and private insurance 95.8%; p = 0.033). Medicaid recipients were less likely to achieve SVR (Medicaid 18.9%, Medicare 28.1%, and private insurance 37.5%; p = 0.005). Patients who injected drugs (IDU) in the last 12 months (n = 41/222) had lower treatment initiation rates (26.8% vs 45.9%; p = 0.043), but no difference in achieving a cure (17.1% vs 23.2%; p = 0.294). The integration of HCV treatment at the BCHD STD Clinics serves as an example for expanding access to DAAs in low-income populations. Systemic factors such as insurance approval (Medicaid requires Metavir score ≥ F2 for treatment) and recent IDU still play a large role in determining HCV treatment and cure rates.

56. Anna Marie Young, MS 2

Mentor(s): Rachel Seay, MD
Department of Gynecology and Obstetrics

Differences in access to Spanish Speaking Providers, Birth Outcomes and Patient Satisfaction in Hispanic Women Enrolled in Group Prenatal Care vs Individual Prenatal Care.

Authors: Anna Marie Pacheco Young BS, Rachel Chan Seay MD, Carla Bossano MD

Abstract: Immigration from Latin America to Baltimore has resulted in an influx of Spanish speaking patients needing obstetric care at Johns Hopkins Bayview. Women from this community face significant barriers in seeking prenatal care including limited English proficiency and lack of social support. To address these barriers, we sought to implement an innovative form of prenatal care known as CenteringPregnancy. CenteringPregnancy is a group prenatal care model which includes health assessments, education, and social networks. It has been shown to improve rates of preterm delivery, breastfeeding, patient satisfaction, and postpartum depression. Starting in February of 2017, CenteringPregnancy was offered at Bayview with the following goals: to increase the number of appointments with Spanish speaking providers, to improve birth outcomes, and to provide a more supportive and culturally sensitive environment for Hispanic mothers. All low risk, Spanish speaking mothers at Bayview were offered participation in the program. To date, 87 women have completed the program. Preliminary data shows that 23% of Centering participants delivered by C-section and 22% delivered preterm. Number of appointments with a Spanish speaking provider were compared from February 2016/7 to August 2016/7. In 2016, 7% of appointments were done with a Spanish speaking provider. After implementing Centering, this number was increased to 13%. Overall, women who participated in Centering reported in their anonymous post program surveys feeling comfortable in sharing their experiences when surrounded by women of their community and felt they received better care and attention as a result. Given the data shown and the reported satisfaction, CenteringPregnancy has allowed for more appointments with a Spanish speaking provider and a more supportive environment for Hispanic mothers. More data on obstetric outcomes is necessary and currently being gathered for comparison.

57. Borna Kassiri, MS 2

Mentor(s): Karen Sfanos, PhD
The James Buchanan Brady Urological Institute

Profiling the Urinary and Gastrointestinal Microbiota in Children Presenting to Urology with or without Antibiotic Exposure

Authors: Borna Kassiri BS, Matthew Kasprenski MD, Eva Shrestha BA, Leslie Mangold MS, Ming Hsien-Wang MD, Karen Sfanos PhD

Background: New technologies have led to a paradigm shift in our understanding of the complexity of microbial communities associated with the human body. Thus, the clinical dogma that urine is sterile has been challenged. Urine in adults contains microbiota that are representative of a distinct microbiome in the urinary tract. However, the urinary microbiome has yet to be characterized in children. We hypothesized that the urinary microbiota likely begin colonizing the urinary tract in the childhood. We aimed to 1) establish a biorepository of urine and stool from a pediatric population and 2) compare the urinary and gastrointestinal (GI) microbiome in children with or without prior antibiotic exposure.

Methods: We collected urine via transurethral catheterization and fecal samples via rectal swab from 20 pediatric males presenting to urology at Johns Hopkins (ages 3 months to 8 years). We extracted DNA out of 10 urine and 20 fecal samples from these patients. The sample consists of 10 fecal and 5 urine samples from 10 patients without antibiotic exposure and from 10 age-matched patients with antibiotic exposure. The two groups underwent 16S ribosomal DNA Illumina amplicon sequencing to explicate their GI and urinary microbiota.

Results: We found evidence of a urinary microbiome in pediatric males, with a similar species composition to that previously described in adult men, although in differing proportions. Urine bacterial load was similar to levels found in adult men, and was unexpectedly higher in patients with previous antibiotic exposure. In addition, we found alterations in both the GI and urinary microbiome in patients that had undergone antibiotic prophylaxis for congenital genitourinary malformations compared to children presenting to urology for other reasons.

Conclusion: While we have discovered the existence of the urinary microbiome in pediatric males, future studies are warranted to further elucidate the pediatric GI and urinary microbiome, and to establish the long-term effects of antibiotic prophylaxis.

58. Erinola Araoye, MS 2

Mentor(s): Khara Simpson, MD
Department of Gynecology and Obstetrics

Education to Reduce Anxiety in Patients Undergoing Surgery

Authors: Erinola Araoye BA

Background: Anxiety is common in patients undergoing surgery and preoperative health literacy is a factor known to affect anxiety. This systematic review sought to identify educational interventions that can reduce preoperative anxiety and the tools used to quantify preoperative anxiety.

Methods: The literature search used PubMed to identify relevant English language studies conducted in adults in the last 10 years, using the term combination "anxiety"[Mesh] and “surgery” [tiab] or "preoperative Period"[Mesh] and “patient education” [tiab]. A similar search used CINAL Plus. Abstracts that did not indicate preoperative anxiety as the primary outcome or had pediatric population were excluded. Fully reviewed articles were excluded if focus was on a postoperative outcome or there was an additional intervention other than education.

Results: Ten studies were eligible for review. Size varied from 10 participants to 400. Five studies concluded that preoperative anxiety can be reduced by an educational intervention, 3 found no effect, 1 found an increase and 1 found no difference between formats of education when keeping content constant. Educational interventions used include text, audiovisual, telephone calls, interviewing and Knowledge Test Feedback. Intervention, size and measurements varied across studies, thus meta-analysis is not feasible. Two of the 3 studies that found no effect educated on anesthetic only; the study that found increased anxiety was in dental surgery. Studies that included information on illness, preoperative and postoperative care were more likely to see reduction in anxiety than studies that limited information to anesthesia. The State Trait Anxiety Inventory (STAI) is most frequently used to quantify anxiety due to ease of use, validity and reliability in anxiety measurement.

Conclusion: Preoperative anxiety can be reduced through educational intervention depending on surgical field and information content. Interventions seeking to reduce anxiety should include preoperative, surgical and postoperative information. The State Trait Anxiety Inventory is the preferred tool for measuring anxiety.

59. Jeremy Miller, MS 2

Mentor(s): Jennifer Reesman, PhD
Kennedy Krieger Institute

Needs Assessment of Parenting Stress and Sensitive Discipline in Families with Deaf Children at Kennedy Krieger Institute

Authors: Jeremy Miller BS, Jennifer Reesman PhD

Background: Parenting stress is associated with increased internalizing and externalizing behavior problems of children, negative and coercive interactions of parents with children, and authoritarian and power-assertive discipline strategies. Unique stressors for parents of deaf children include communication difficulties, medical and audiological care, and educational challenges. We sought to conduct a needs assessment of families of deaf children to identify specific requirements for adapting an evidence-based parenting intervention to promote sensitive caregiving, positive social-emotional child outcomes, and reduce parenting stress.

Methods: Our needs assessment involved direct observation and coding of child and parent behavior at Kennedy Krieger Institute during intake appointments, neuropsychiatric testing of deaf children, and follow-up appointments with parents about results and strategies. The needs assessment also relied on semi-structured interviews with key stakeholders: parents of deaf children, deaf adults, social workers and neuropsychologists who specialize in work with deaf families, American Sign Language (ASL) interpreters, and certified Teachers of the Deaf (TOD).

Results: Key findings include: (1) Hearing parents frequently experience stress about having to teach their child language. (2) Regular contact with professionals who are fluent in ASL or routinely work with deaf children had a positive influence on parental stress and child's behavior reported by parent. (3) Parents vary widely in stress experienced during activities specific to caring for their deaf child (e.g. audiological care, education).

Conclusion: We concluded that regular contact with professionals who are fluent in ASL and who routinely work with deaf children will likely positively contribute to efficacy of a parenting intervention. Finally, based on the diversity of our particular sample, we recommend that parenting interventions should be adapted for use with families with deaf children to accommodate various methods of home communication as well as additional disabilities.

60. Kathryn Clark, MS 2

Mentor(s): Bhakti Hansoti, MBChB, MPH PhD
Department of Emergency Medicine

Defining the Burden of Disease in the South African Emergency Department

Authors: Kathryn Clark BA, Aditi Rao BS, Bhakti Hansoti MBChB, MPH PhD

Background: Emergency medicine is an emerging specialty in many low and middle income countries that provides a large proportion of medical care. Although much is known about patients utilizing these services in the United States, this has been identified as an unmet need in Sub-Saharan Africa. Better understanding of the burden of disease will help to guide training and resource allocation priorities, however lack of electronic medical records and standardized data collection systems has made it hard to obtain this information. This prospective study sought to collect information on the burden of disease to better understand the landscape of South Africa.

Methods: A cross-sectional observational study was performed in the context of the point prevalence HIV testing study conducted in two large tertiary care centers and one regional hospital in the Eastern Cape region of South Africa. All patients presenting to the emergency department during the eight-week study period who met inclusion criteria were approached by study staff and consented for Point of Care (POC) HIV testing and collection of demographic information. Simple descriptive statistics were used to analyze data.

Results: During the study period data was collected on 2357 patients who utilized the Frere Hospital and 622 patients at the Nelson Mandela Academic Hospital. Patients were young (41.2 % and 32.6% respectively between ages 18-30 years), male (57.8% and 60.2%), and presented with traumatic injuries (70.4% and 41.5%). The most frequent presenting complaints were stab/ gunshot wounds at 18.3% and 20.2% respectively. We also collected data on 1258 patients utilizing the district level hospital, Mthatha Regional, finding that 40.1% were between 18-30 years, presenting with mostly traumatic injuries (27.3%), but were comprised of more females (57.1%). Stab wounds/ gunshot injuries were the second most common complaint (7.2%), just behind lower respiratory tract infections (8.7%).

Conclusion: A large burden of care delivered in the emergency departments in the Eastern Cape region of South Africa is for traumatic injuries. Local clinical capacitation efforts must focus on trauma training.

61. Lauren Sutherland, MS 2

Mentor(s): Wendy Bennett, MD
General Internal Medicine and The Welch Center for Prevention, Epidemiology, and Clinical Research

Risk perception for future chronic disease and health behaviors among women with gestational diabetes and pre-eclampsia: A cohort study

Authors: Lauren Sutherland BS, Donna Neale MD, Janice Henderson MD, Wendy L. Bennett MD

Background: Women diagnosed with gestational diabetes (GDM) or pre-eclampsia (PE) are at a greater risk of developing type 2 diabetes and cardiovascular disease (CVD). Greater perception of chronic disease risk is associated with health behavior changes in pregnant women. Women with GDM were found to have low risk perception despite their complication. Little research has examined whether women with pre-eclampsia perceive risk of future CVD. Our objectives were to assess associations between pregnancy complication (GDM or PE) and receipt of health advice, risk perception, and prenatal health behaviors.

Methods: We recruited 137 women with pre-eclampsia (n=54), GDM (n=75), or both (n=8) immediately following delivery. Of the 137 participants, 79 completed baseline and 3-month interviews (57.7% response rate). We used descriptive statistics and logistic regression models to assess the association between pregnancy complications and risk perception, health behaviors, and receipt of health advice, after adjusting for demographic and socioeconomic factors.

Results: Compared to women with GDM, women with pre-eclampsia were significantly younger, more likely to have Medicaid, and more likely to be nulliparous prior to this pregnancy. Both groups had low levels of risk perception with no significant difference in risk perception scores. Women with pre-eclampsia were less likely to receive health advice from their provider compared to women with GDM. Women with higher risk perception were more likely to change their physical activity level during pregnancy. There was no significant association between risk perception and diet or receipt of health advice.

Conclusion: Pregnancy and the postpartum period are critical, but often missed, opportunities for providing health advice and engaging women in chronic disease prevention. However, the relationship between health advice and risk perception is still uncertain. Future interventions focusing on health risk communication in the postpartum period could enhance women's motivation to make positive and sustainable health behavioral changes.

62. Leah Weston, MS 2

Mentor(s): Roni Neff, PhD
Center for a Livable Future, Bloomberg School of Public Health

Trends and health implications of rising meat consumption in low- and middle-income countries: How concerned should we be?

Authors: Leah Weston BA, Rebecca Ramsing MPH RD, Roni Neff PhD

Background: Global meat consumption is rising. This study summarizes the trends and drivers underlying the current rise in meat consumption in low- and middle-income countries (LMICs) in order to better understand how the health consequences related to meat intake may evolve as global meat intake continues climbing.

Methods: Semi-systematic review of published literature and publicly-available databases using nine culturally, economically, and geographically distinct LMICs as illustrations of global trends.

Results: In LMICs, meat consumption rises with income (GDP), socioeconomic status, and physical access (through urbanization and trade), and is modified by cultural and sociodemographic factors such as gender and age. Changes in meat consumption over the last 50 years varied highly by country. China experienced the greatest increase (11-fold; average consumption 265g/capita/day), India, the smallest increase (1.8-fold; average consumption 24g/capita/day), and Kenya experienced a small decrease (0.1-fold; average consumption 51g/capita/day). According to the trend line fit to the past 10 years, per capita meat consumption in Brazil, China, and Vietnam may reach current US levels in the next 10-15 years. In the East Asian countries studied, rising red meat consumption was driven by increased pork intake. In Middle Eastern and American countries, poultry has become the predominant meat consumed, driving down the proportion of red meats in their diet.

Conclusion: Recent changes in the quantity and type of meat consumed vary widely between countries and geographical regions. Although meat consumption in LMICs lags behind high income countries (HICs), its rapid rise in some middle-income countries is particularly concerning. If reported discrepancies in the meat-related NCD burden in HICs vs. LMICs can be attributed to differences in absolute consumption, we might expect high meat consumption to become a more relevant factor in NCD burden in the coming years. Rising consumption and meat-related NCDs should be monitored closely, particularly in countries with rising red meat consumption.

63. Maria Molinaro, MS 2

Mentor(s): Deanna Saylor, MD
Department of Neurology

The International HIV Dementia Scale as a screening tool for HAND in Uganda

Authors: Maria Molinaro, Deanna Saylor, Gertrude Nakigozi, Noelline Nakasujja, Kevin Robertson, Ronald H. Gray, Maria J. Wawer, Ned Sacktor

Background: HIV-associated neurocognitive disorder (HAND) is common but often under-diagnosed. The International HIV Dementia Scale (IHDS) is a screening tool for HIV-associated dementia (HAD), but has not been studied in rural Sub-Saharan Africa or for less severe HAND stages. We assessed the IHDS utility in detecting HAND in rural Rakai, Uganda in antiretroviral (ART)-naïve and experienced adults.

Methods: 400 HIV+ ART-naïve participants underwent neurological, functional status, and neuropsychological assessments including the IHDS. 313 participants were re-evaluated after two years. HAND stages (asymptomatic neurocognitive impairment [ANI], minor neurocognitive disorder [MND], HAD) were determined based on the Frascati criteria using normative data from 400 HIV- adults from Rakai. IHDS sensitivity, specificity, and area under the ROC curve (AUC) were determined for both visits.

Results: At baseline, participants' mean age was 35 years (SD 8), 53% were male, and 54% had ≤4th grade education. All were ART-naïve, 50% had CD4<200, and 50% had CD4 350-500. At follow-up, 93% were on ART with mean CD4 411. At baseline, sensitivity, specificity and AUC were: For any HAND stage [ANI, MND, HAD], IHDS ≤9:63%, 63%, 0.628; ≤10: 81%, 36%, 0.585. For symptomatic HAND (MND, HAD), ≤9: 65%, 62%, 0.63; ≤10: 83%, 36%, 0.50. For detecting HAD, ≤9: 82%, 53%, 0.67; ≤10: 92%, 29%, 0.60. At the two year follow-up, sensitivity, specificity, and AUC were: For any HAND stage, IHDS ≤9: 48%, 79%, 0.63; ≤10: 69%, 58%, 0.63. For detecting symptomatic HAND, ≤9: 50%, 78%, 0.63; ≤10: 76%, 54%, 0.65. For detecting HAD, ≤9: 71%, 68%, 0.69; ≤10: 94%, 45%, AUC 0.70.

Conclusion: The IHDS is a potentially useful screening tool for neurocognitive impairment in rural Uganda for both ART-naïve and ART-experienced adults. However, it demonstrates higher sensitivity for detecting more severe HAND stages and is more sensitive in ART-naïve patients.

64. Megan Hadley, MS 2

Mentor(s): Susan Harvey, MD
The Russell H. Morgan Department of Radiology and Radiological Science

Assessment and Improvement Strategies for a Breast Cancer Early Detection Program in Rural South Africa

Authors: Megan E. Hadley BS, Lisa Mullen MD, Eniola Falomo MD, Anne F. Rositch MSPH PhD, Susan C. Harvey MD

Background: Breast cancer screening programs initiated in resource-limited settings require continued support and evaluation. We assess the challenges of an ultrasound-based breast cancer screening program in rural South Africa one year after project implementation and develop potential solutions.

Methods: A WHO-endorsed RAD-AID Radiology Readiness Assessment was used in conjunction with a five-week period of daily observation to assess existing documentation methods. Based on stakeholders' input and the Breast Imaging Reporting and Data System (BI-RADSTM), we developed a new documentation system. Staff training incorporated demonstration, peer teaching, and supervised clinical use, followed by a confidential, post-implementation survey assessing feasibility, attitudes, and clinical impact. The survey included 16 scaled and 3 open-ended questions.

Results: Resource limitations included lack of computer workstations, unpredictable electrical power supply, and inconsistent internet access. The assessment revealed incomplete documentation of clinical exam findings and history, inconsistent documentation of lesions, limited communication between providers, and no documentation of follow up. Findings led to the development of three tools: a history and risk assessment paper form, a clinical assessment paper form, and a computerized patient-tracking database compliant with BI-RADS. The entire team completed a post-implementation survey. 71% (5/7) indicated positive or very positive general attitudes, 100% of respondents agreed or strongly agreed to the following statements: the documentation system is useful, is easy to use, improves overall quality of care, improves follow-up, improves decision making, improves access to clinical information, improves communication between clinicians and patients. We assessed the burden caused by the new tools and 5 of 7 providers reported that the system increased visit time, yet 3 out of those 5 felt the process was valuable.

Conclusion: Implementing breast cancer screening in resource-limited regions is challenging. Continued support and assessment of evolving needs are essential. Documentation, communication, and follow-up are critical components of a successful screening program.

65. Natalie Ullman, MS 4

Mentor(s): Daniel Hanley, MD and Wendy Ziai, MD
Department of Neurology

Third Ventricle Obstruction by Thalamic Intracerebral Hemorrhage Predicts Poor Functional Outcome Among Patients Treated with Alteplase in the CLEAR III Trial

Authors: Natalie L Ullman MPH, Pouya Tahsili Fahadan MD, Carol B Thompson MS MBA, Wendy C Ziai MD MPH, Daniel F Hanley MD

Background: The Clot Lysis: Evaluating Accelerated Resolution of IVH (CLEAR III) trial examined whether irrigating the ventricular system with Alteplase improved functional outcomes in patients with small intracerebral hemorrhage (ICH) and large intraventricular hemorrhage (IVH). Thalamic ICH location was common and was associated with poor outcome. One possible explanation is thalamic ICH-associated mass effect obstructing the 3rd ventricle. We hypothesized that patients with thalamic ICH obstructing the 3rd ventricle would have worse functional outcomes compared to patients without obstructing lesions.

Methods: ICH obstruction of 3rd ventricle was defined as 3rd ventricle compression on 1 or more axial computed tomography slices visually impeding cerebral spinal fluid flow. If the 3rd ventricle was casted with IVH it was scored as such. Multivariable logistic regression analyses were used to determine whether obstruction of the 3rd ventricle predicts poor functional outcomes defined as modified Rankin score (mRS) 4-6, higher mRS, and mortality at 180 days. Models were adjusted for thalamic ICH location, ICH volume, IVH volume, age, hydrocephalus, baseline Glasgow coma scale, and percentage of low cerebral perfusion pressures during treatment.

Results: Among saline-treated patients obstruction of the 3rd ventricle by IVH was a significant predictor of higher mRS at 180 days (OR = 1.87, CI: 1.01-3.47), and mortality at 180 days (OR = 2.73, CI: 1.27-5.87) while obstruction by ICH was not. In contrast, among Alteplase-treated patients, obstruction by ICH was a significant predictor of mRS 4-6 (OR = 3.20, CI: 1.30-7.88) and higher mRS at 180 days (OR = 2.33, CI: 1.24-4.35), while obstruction by IVH was not.

Conclusion: Poor outcomes were associated with mass-related obstruction of the 3rd ventricle from thalamic ICH in Alteplase-treated patients, and from IVH in saline-treated patients. Once the ventricular system is cleared with Alteplase, obstruction of cerebral spinal fluid flow from thalamic ICH might become important in functional recovery.

66. Noore-Sabah Khan, MS 2

Mentor(s): Jessica Colburn, MD
Department of Geriatric Medicine

The Effectiveness of a Quality Improvement Project for Advance Care Planning among Older Adults

Authors: Noore-Sabah Khan BA, Jacqueline Massare BS, Naaz A. Hussain MD, Maura J. McGuire MD, Jane Marks RN, MS, Danelle Cayea MD, Jessica Colburn MD

Background: Advance Care Planning (ACP) documentation has been shown to increase compliance with patient preferences, improve quality of end-of-life care for the patient and family, and reduce costs of end-of-life care without increasing mortality. However, studies on barriers to ACP note a need to routinely incorporate ACP in the clinic, with a particular emphasis on interventions that integrate ACP into time pressured clinic workflows. The purpose of this study is to determine the ability of a Quality Improvement (QI) project focused on clinic workflow to increase rates of: (1) ACP documentation by ≥ 60% among patients 65 years or older, and (2) correct placement of the advance directive in the electronic medical record.

Methods: We conducted a cross-sectional chart review with a pre-post analysis of 500 randomly selected charts, with 250 each before and after implementation of the QI project in a primary care practice.

Results: Overall, ACP documentation (including Living Will, Health Care Agent/Power of Attorney, and/or 5 Wishes) increased from 11.6% before implementation of the QI project to 27.2% after implementation, representing a greater than 60% increase. MOLST documentation increased from 3.6% to 44% after the QI project, representing one of the largest improvements. Although overall, the percentage of charts with incorrectly placed documentation or documentation without dates was small, we did not find a decrease in these factors compared to charts from the pre-implementation period.

Conclusion: Therefore, the QI project effectively increased rates of ACP documentation and most documents (>90%) were entered correctly as outlined by the clinic workflow, but improvement may still be made to decrease the percentage of missing or incorrectly placed documents. This data presents encouraging results supporting implementation of the clinic workflow outlined by the QI project to other primary care sites in order to address barriers to ACP documentation.

67. Omar Najjar, MS 2

Mentor(s): Tom Donner, MD
Johns Hopkins Diabetes Center

Diabetic foot complications in a tertiary care center in Lebanon: retrospective study identifying burden and gaps in management

Authors: Omar Najjar BS, Lamia Jouhar MD, Rola Jaafar PhD, Omar Itani BS, Jamal Hoballah MD

Background: Diabetic foot ulcers (DFUs) are one of the most common complications of diabetes mellitus (DM), with a lifetime incidence risk as high as 25%. DM is estimated to affect 13% of the Lebanese population aged 25+, and poor DM management and foot examination rates have been reported among most diabetics. DFUs are expected to be a significant source of morbidity among Lebanese, but little data exists regarding their burden in Lebanon.

Methods: The study is a retrospective analysis of 278 patients admitted with DFUs at the American University of Beirut Medical Center (AUBMC) between January 2008 and June 2017, with a total of 384 admissions.

Results: The average patient age was 66.6 ± 12.3 years with a male predominance (194 patients, 69.8%). Most patients had a duration of diabetes of 10 years or greater (171 patients, 61.5%), poor diabetes control (mean HbA1c of 8.8 ± 2.3%), and a high rate of comorbidities. Nearly half the admissions involved gangrenous DFUs of Wagner grade 4 or 5 (177, 46.1%). 276 cases (71.9%) were managed surgically via debridement, angioplasty, bypass surgery, or amputations. There were 31 (8.1%) major amputations and 16 (5.8%) in-hospital mortalities. Comparison of Lebanese nationals based on financial coverage showed that uninsured patients had a higher mean HbA1c than insured patients ($p=0.034$), lower surgery rates ($p=0.026$), and greater loss to follow-up ($p<0.001$). Comparison of Lebanese and international patients (109 admissions, 28.6%) showed that internationals were more likely to have grade 4 or 5 DFUs ($p=0.002$) and be managed surgically ($p<0.001$) but had lower in-hospital mortality ($p=0.045$).

Conclusion: Patients with DFUs at AUBMC are generally elderly with poor glycemic control and multiple comorbidities. Major amputation and mortality rates were comparable to those in other middle-income countries. Disparities based on financial coverage were noted in the management of DM and DFUs.

68. Orit Abrahim, MS 2

Mentor(s): Larry Chang, MD
Department of Medicine

Evaluation of a Rapid Diagnostic Test for Sepsis in Cancer Patients and other Critically Ill Patients in Uganda

Authors: Orit Abrahim MPH, Dr. Henry Kajumbula MBChB, MD, Fatuma Nalubega BA, Meklit Workneh MD, MPH

Background: In Uganda, severe sepsis results in high mortality that is attributable in part to high rates of antimicrobial resistance. The FilmArray multiplex PCR with Blood Culture Identification Panel (BCID) is a rapid diagnostic test (RDT) that may improve antimicrobial stewardship and patient outcomes compared to blood culture which has lengthy turnaround times and requires largely unavailable resources. Our study sought to compare the performance of the BCID to standard blood culture in the identification of organisms and antibiotic susceptibility in Kampala, Uganda.

Methods: The study was conducted at the Mulago Hospital Intensive Care Unit (ICU) and the Uganda Cancer Institute (UCI) in Kampala, Uganda. Adult inpatients 18 years or older with 2 or more features of sepsis (SIRS criteria) and/or confirmed or suspected source of infection were eligible for the study. A total of 16ml of blood was collected from 2 venipuncture sites and isolates identified using Gram-stain and routine biochemical tests.

Results: 87 patient samples were collected between July and December 2017. 7 cultures were ruled to be contaminants and the true positive rate (12/87) was 13.8% by blood culture and 11.5% by BCID. 83.3% (10/12) of true positives by blood culture were gram negative organisms. The major etiologic agents of sepsis were Acinetobacter species, Klebsiella pneumoniae, Escherichia coli, and Pseudomonas aeruginosa. The antimicrobial resistance genes included in the BCID were not sufficient for the organisms in this setting.

Conclusion: There is a preponderance of Gram-negative organisms in this setting in contrast to multicenter evaluations in the U.S. where the majority of isolates are Gram positive organisms. Organisms that are relatively common in this setting such as Salmonella Typhi are only identified to the family level by BCID. Preliminary evaluation finds that BCID identifies more polymicrobial organisms than blood culture but may miss non-Klebsiella carbapenameses that are more common in this setting.

69. Reba Watsky, MS 2

Mentor(s): Frederick Barrett, PhD
Department of Psychiatry and Behavioral Sciences

Scientific and Legal Standing of Psychedelics for Therapeutic Use

Authors: Rebecca E Watsky BA, Frederick Barrett PhD

Background: Current treatments for mood, anxiety, and other psychiatric disorders fail to adequately control symptoms for many patients. Mid-20th-century research suggested that psychedelics including ayahuasca, psilocybin, and lysergic acid diethylamide (LSD) may have therapeutic effects. Recent clinical trials addressed the anxiolytic, antidepressive, and antiaddictive potential of psychedelics. Despite the possible utility of psychedelics for some psychiatric diseases, their safety and efficacy remain in question, and their use is limited by their status as Schedule 1 controlled substances under the Controlled Substances Act (CSA).

Methods: We performed a systematic review of clinical trials since 1990 using psilocybin, LSD, or ayahuasca for the treatment of anxiety disorders, depression, or substance dependence. We assessed the safety of psychedelics using these trials and earlier data.

To understand legal hurdles for psychedelics, we determined the Food and Drug Administration (FDA) and Drug Enforcement Agency requirements for making drugs medically available. Using the example of dronabinol, a synthetic marijuana derivative that changed CSA classifications, we examined the theoretical legal trajectory of psilocybin.

Results: All clinical trials reviewed showed statistically significant, often sustained decreases in symptoms of interest with psychedelic administration. No physiological or psychological side effects were noted to last beyond one day. In large mid-century trials, prolonged adverse psychological effects were extremely rare.
Approval for medical use through the FDA can lead to CSA reclassification. The existing data on psilocybin is comparable to the data used to support dronabinol rescheduling, save for insufficiently large trials for psilocybin.

Conclusion: We found that psychedelics can be used safely with antidepressive, anxiolytic, and antiaddictive effects. Larger clinical trials may lead to FDA approval for medical use, followed by rescheduling under the CSA. Our work was limited by small sample sizes, heterogeneous studies, and an inexact comparison between dronabinol and psilocybin. Further research will be possible as larger psychedelic trials are completed.

70. Sara Jones, MS 2

Mentor(s): Jordan Duval-Arnould, MPH DrPH
Department of Anesthesiology and Critical Care Medicine

Closing the Gap: Optimizing Performance to Reduce Interruptions in CPR

Authors: Sara I. Jones BA, Elizabeth A. Hunt MD, MPH, Ph.D., Justin M. Jeffers MD, Andrew Stella MS, MA, Jordan M. Duval-Arnould MPH, Dr.PH

Background: An important measure of high performance resuscitation is minimizing interruptions in chest compressions. The AHA recommends avoiding pauses and targeting a chest compression fraction (CCF) > 80%. We hypothesize that interruption times are excessively long and negatively impact CCF.

Methods: A retrospective study using video review of a convenience sample of in-situ simulated cardiopulmonary arrests in the Johns Hopkins Children's Center between September 2013 and June 2017 was conducted. These simulations were clinically realistic in terms of environment, team composition, and patient traits. A framework was developed to characterize interruptions and two new metrics were defined: ITE (the difference between actual and guideline-indicated allowable duration), and $CCFP$ (chest compression fraction with all ITE excluded). Interruption start and stop time was measured and used to generate ITE values. Descriptive statistics were generated for interruption-level and event-level variables and reported as median (IQR). Differences between median CCF and CCFP were assessed using Wilcoxon rank sum. Comparisons of interruption proportion before and after the first five minutes were assessed using the X2 test statistic.

Results: 766 interruptions occurred over 22 events. Event duration was 463s (398-553), with 34.8 interruptions per event. Interruption duration was 3s (2-4) and ITE duration was 1s (0-2). CCF was 75.97% (67.71-80.73) and $CCFP$ was 83.38% (80.35-87.35). Comparing CCF to CCFP found an absolute percent difference of 7.4% (CCF:75.97% vs. CCFp: 83.38%; p< 0.001). A significant difference proportion of interruption by initiation category in the first 5 minutes was discovered (Directed:80.0% vs, Autonomous: 50.7%; p=0.004).

Conclusion: This lays the groundwork for studying inefficiency during CPR associated with chest compression interruptions. The framework we created allows for the determination of significant avoidable interruption time. By further elucidating the nature of interruptions, we can design and implement targeted interventions to improve patient outcomes.

71. Theresa Aguilar, MS 2

Mentor(s): William Checkley, MD
Johns Hopkins University School of Medicine

Sleep disordered breathing and cardiopulmonary disease in Peruvian highlanders

Authors: Theresa Aguilar BS, Alan Schwartz MD, Luu Pham MD, William Checkley MD, Dina Goodman MSPH

Background: Sleep disordered breathing (SDB) is a highly prevalent disease that is associated with systemic inflammation, metabolic stress, hypertension, and cardiopulmonary disease. At high altitude, hypoxia amplifies sleep-related ventilatory disturbances and amplifies SDB. In Puno, Peru (3825 m above sea level), our group has documented 80% prevalence of SDB, which was associated with chronic mountain sickness and hemoglobin A1c elevations. Affordable therapeutic options are limited in these settings. Sleeping on an incline can improve upper airway collapsibility and ventilation/perfusion mismatch, and may therefore mitigate SDB. Our objective is to pilot postural therapy for SDB in Peruvian highlanders. We hypothesize that, compared to sleeping flat, sleeping at a 15-degree incline improves SDB severity, measured by mean nocturnal oxyhemoglobin saturation and apneic event frequency.

Methods: Participants aged >40 years and with BMI ≥ 25 kg/m2 were enrolled in a randomized-cross over trial of sleeping on a 15˚ wedge mattress compared to 0° in their own mattress, while undergoing home sleep study (WatchPat, Itamar Ltd.). We compared mean oxyhemoglobin saturation (SPO2) and apnea hypopnea index (AHI) in each posture with paired t-tests. We assessed the tolerability of inclined sleep by comparing sleep time between nights.

Results: 11 subjects (8 female, age 62±8.7, and BMI 30.5±4.1) completed both nights. Compared to sleeping flat, sleeping on an incline significantly increased mean nocturnal SPO2 from an average of 82.7% to 84.0% (p=0.01). Postural therapy did not significantly change AHI (32.0 vs. 33.7, p=0.74) or total sleep time (357.9 minutes vs 387.5, p=0.41).

Conclusion: Sleeping on a 15-degree incline is well-tolerated and improves nocturnal hypoxemia. Postural therapy represents a cost-effective strategy to mitigate SDB in low resource settings. Additional studies are necessary to determine the effects of postural therapy on SBD-related cardiometabolic sequelae.

72. Xiangyun John Duan, MS 2

Mentor(s): Harry A Quigley, MD
Department of Ophthalmology

Evaluation of Automated Algorithm for Depth of the Lamina Cribrosa of the Optic Nerve Head in Optical Coherence Tomography Images

Authors: Xiangyun John Duan BS, Joan L Jefferys MS, Christopher Lee BS, Harry A Quigley MD

Background: Current investigation of the optic nerve head (ONH) using optical coherence tomography (OCT) imaging requires manual marking of anatomical features of interest, a process that is time-intensive and impedes expanded research in this area. The purpose of this study was to compare the accuracy and precision of an image grading algorithm to that of human graders in identifying the anterior lamina cribrosa depth (ALD), Bruch's Membrane opening (BMO), and the choroid-sclera interface (CSI) on OCT images of the ONH.

Methods: Adult patients of the Wilmer Glaucoma Center of Excellence were imaged using the Heidelberg Spectralis OCT instruments. Human graders marked the BMO, CSI, and ALD. The same data was generated by the image grading algorithm. Concordance in markings of those features were made between successive gradings of the same image by one human, successive gradings of the same eye by the algorithm, gradings of the same image by different humans, and gradings of the same image by a human and by the algorithm.

Results: Adult patients of the Wilmer Glaucoma Center of Excellence were imaged using the Heidelberg Spectralis OCT instruments. Human graders marked the BMO, CSI, and ALD. The same data was generated by the image grading algorithm. Concordance in markings of those features were made between successive gradings of the same image by one human, successive gradings of the same eye by the algorithm, gradings of the same image by different humans, and gradings of the same image by a human and by the algorithm.

Conclusion: Mean human inter-observer variation of ALD was 6.11µm ($p<0.0001$), mean variation of BMO was 12.13µm ($p<0.0001$), and mean difference in CSI width was 0.652µm ($p=0.88$). These values will be compared with analogous values for human intra-observer variation, algorithm intra-observer variation, and human-algorithm variation. Results from those analyses are pending.

73. Zhuo (Tony) Su, MS 2

Mentor(s): Jodi Segal, MD MPH
Department of Internal Medicine

National trends in the pharmacological management of sickle cell disease by office-based physicians in the United States, 2012–2015

Authors: Zhuo Su BS, Foluso Joy Ogunsile MD, Jodi Beth Segal MD MPH

Background: Sickle cell disease (SCD) is a serious inherited blood disorder. Previous research reported underutilization of hydroxyurea, the only approved drug therapy for SCD until 2017. However, little is known about whether treatment patterns for SCD have changed over time. This study aimed to identify the temporal trends in SCD treatment patterns in the United States (US).

Methods: We used nationally representative audit data from the QuintilesIMS National Disease and Therapeutic Index to examine medications prescribed between 2012 and 2015 to patients with SCD during visits to office-based physicians in the continental US. We used descriptive statistics to evaluate the counts of visits and medication prescriptions. We calculated 95% confidence intervals (CIs) for our estimates using tables of relative standard errors provided by QuintilesIMS.

Results: Visits by patients with SCD to office-based physicians in the US increased steadily from 279 thousand (K) [95% CI: 271K–288K] in 2012 to 433K [420K–447K] in 2015. The most frequently prescribed medications were opioids (prescribed in 33% of visits in 2012 to 55% in 2015), folic acid (29% to 38%), hydroxyurea (14% to 36%), antibiotics (13% to 30%), and iron-chelating agents (5% to 12%). Visits with opioid prescriptions increased from 93K [90K–96K] in 2012 to 239K [232K–247K] in 2015. Visits with hydroxyurea prescriptions increased from 39K [37K–41K] to 154K [149K–159K].

Conclusion: Although hydroxyurea use in SCD appeared to have increased from 2012 to 2015, still only about a third of visits resulted in a hydroxyurea prescription in 2015. Opioids were the most frequently prescribed medication throughout the analysis period, and their use also appeared to have increased. Limitations of this study included possible sampling errors and inability to assess clinical appropriateness of individual medication prescriptions from aggregate data. Future research is needed to identify factors driving the observed trends in SCD treatment patterns.

ABSTRACT APPENDIX: ADDITIONAL ABSTRACTS

Listed alphabetically by first name of author

The following abstracts represent additional projects of Johns Hopkins medical students that are not being presented in the Medical Student Research Symposium due to a limit on the number of presentations allowed per student.

Alvaro Ibaseta, MS 2

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

Crossing the Cervicothoracic Junction in Cervical Spine Fusion Surgery Involves Higher Operative Risks, but Superior Long-term Outcomes

Authors: Alvaro Ibaseta MS, Richard L. Skolasky ScD, Rafa Rahman BS, Khaled M. Kebaish MD, Lee H. Riley III MD, Daniel M. Sciubba MD, David B. Cohen MD MPH, Brian J. Neuman MD

Background: Whether the cervicothoracic (CT) junction should be crossed in cervical fusion surgery remains up for debate. Keeping C7 as the distal end of the fusion risks adjacent segment disease (ASD) and can result in myelopathy or radiculopathy. Longer fusions are thought to increase operative risk and complexity, but result in lower rates of ASD. This study evaluates the risks and benefits of crossing the CT junction in cervical fusion surgery.

Methods: 187 patients were included and divided into a C7 end-of-fusion cohort (C7, N=68) and a CT-crossing cohort (T1, N=119). To evaluate operative risk, estimated blood loss (EBL), length of hospital stay and operative time were collected. Revision surgery data was also obtained. To evaluate patient-reported outcomes (PROs), Neck Disability Index (NDI) and SF-12 questionnaires (MCS12 and PCS12) were obtained both preoperatively and at follow-up. Changes in PRO scores () were analyzed, but available data was limited (N=8).

Results: Multivariate regression analysis adjusting for age, gender and race showed that EBL (t=2.28, p=0.025, SE=66.03) and operative time (t=3.02, p=0.003, SE=20.37) are significantly increased in the T1 cohort. Length of hospital stay was not significantly different (t=1.02, p=0.31, SE=0.66). Mann-Whitney analysis of PROs showed no significant difference in NDI (W=12, p=1), MCS12 (W=20, p=0.24) and PCS12 (W=47, p=0.13). Fisher analysis showed significantly higher revision rates in the C7 cohort (OR=5.61, CI=[0.97, 58.33], p=0.028).

Conclusion: Increased surgical measures such as EBL and operative time show that crossing the CT junction results in a longer, riskier operation that may not be suitable for fragile patients. However, crossing the CT junction leads to lower revision rates, likely due to the avoidance of ASD, and comparable PROs (more PRO data is needed). Thus, the higher short-term risks of crossing the CT junction may be justified given it can help prevent complications without negatively affecting long-term patient-reported outcomes.

Chau Vo, MS 2

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

Pipeline embolization for salvage treatment of previously-stented residual and recurrent cerebral aneurysm

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

Background: This study assesses the safety and effectiveness of the Pipeline Embolization Device (PED) as a treatment for persistent and recurrent aneurysms previously treated with either vascular reconstruction device(VRD) or flow diverter(FD).

Methods: A prospective, IRB-approved database was analyzed for patients treated with PED for aneurysms previously treated with a stent.

Results: There were 20 procedures performed on 18 patients, including 11 with prior FD, 7 with VRD, and 2 previously treated with both. Overall, 15 aneurysms were saccular(75%) and size was 13.5±7.6mm. Location was ICA in 14 cases(70%) and posterior circulation in 6 cases(30%). Average prior treatments were 1.7(range1-4). Previously-FD cases were re-treated at average 18.1 months for aneurysm persistence, including 2 cases of device foreshortening. Each case used 1 device, 82% with distal coverage and 82% with proximal coverage of prior stent. Balloon remodeling was performed in 3 cases(27%) and no in-stent thrombosis was observed. Previously-VRD stent-coiled cases were re-treated at an average of 87.5 months for recurrence. These cases used average 1.9 devices, 89% with distal and 100% proximal coverage. Adjunctive coiling was performed in 1 case(11%), balloon remodeling in 5 cases(56%), and 2 cases(28%) developed intra-procedural thrombosis resolved with abciximab. Re-VRD cases involved longer procedure time(59.1 vs 33.7 min,p=0.02) and higher radiation exposure(3812 vs 2132mGy,p=0.03). Angiographic follow-up was available for 16 cases(80%). Complete occlusion was 56% at 17.1 months in re-FD, and 57% at 8.1 months in re-VRD. Two complications occurred. One patient with a mid-basilar aneurysm previously treated with a FD, experienced brain stem stroke leading to death 4 years after PED re-treatment. One patient who underwent PED for recurrence after stent-coiling of an ophthalmic-ICA aneurysm had asymptomatic proximal ICA occlusion on follow-up angiography.

Conclusion: Salvage flow diversion for previously-stented aneurysms is technically challenging but offers good prospects of aneurysm obliteration with acceptable complication rates.

Eric Sung, MS 2

Mentor(s): Hiroshi Ashikaga, MD
Department of Cardiac Electrophysiology

Distinguishing Scroll Wave Dynamics using Network Theory Metrics

Authors: Eric Sung BA, Hiroshi Ashikaga MD

Abstract: Ventricular fibrillation is the leading cause of sudden cardiac death, yet the electrophysiological mechanisms underpinning its dynamics are still under investigation. One of the leading hypotheses revolves around a phenomenon known as scroll wave break-up. Scroll waves in cardiac tissue are waves of depolarization that rotate about a one-dimensional axis called the filament and geometrically resemble the shape of a scroll. Scroll waves are believed to be the underlying mechanism of re-entrant ventricular tachycardia. Break-up of these scroll waves gives rise to multiple smaller ensembles of aberrant depolarization and subsequently ventricular fibrillation (i.e. conversion from VT to VF). However, not all scroll waves will necessarily persist and undergo break-up; some scroll waves terminate on their own (ex: a ventricular tachycardia that resolves spontaneously). Therefore, discerning between scroll waves that terminate versus those that persist has clinical consequences.

To better understand when scroll waves persist or terminate, we simulated scroll waves using custom written code in MATLAB 2017a. We induced scroll waves in silico in a 2 mm x 2 mm x 1 mm piece of isotropic heart tissue using a random stimulation protocol. From each simulated scroll wave, we identified and extracted the associated filament. Because a filament is one-dimensional as opposed to a three-dimensional scroll wave, we used the filament as the surrogate for further analyses. To facilitate these analyses, we proceeded to convert each filament into a network to be able to utilize network theory metrics. Lastly, we identified metrics from each filament network to be able to discern whether or not it would persist or self-terminate. We found that by using the graph Laplacian of the filament network, we could adequately predict whether a filament was more likely to persist or self-terminate.

Eric Wei, MS 2

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

Vestibular Loss in Alzheimer's Disease is Associated with Driving Difficulty

Authors: Eric X. Wei BA, Esther S. Oh MD PhD, Aisha Harun MD, Matthew Ehrenburg BA, Yuri Agrawal MD MPH

Background: Patients with Alzheimer's disease (AD) experience increased rates of vestibular loss. Recent studies suggest that vestibular loss in AD patients is associated with impaired spatial cognitive function, as measured by tests performed in the clinical setting. However, the impact of vestibular loss on everyday behaviors that rely on spatial cognitive function is unknown. In this study, we evaluated the association between vestibular function and real-world impairments – driving difficulty, falls, and losing objects – in patients with cognitive impairment.

Methods: We recruited 60 patients (21 MCI, 39 AD) from an interdisciplinary Memory Clinic. Vestibular physiologic function was measured, and a visuospatial questionnaire was administered to assess whether participants experienced impairments in driving difficulty, losing objects, falls, and fear of falling. Additionally, spatial cognitive function was assessed using the Money Road Map Test (MRMT). We evaluated the association between vestibular loss and each item in the visuospatial questionnaire. Additionally, we adjusted for performance on MRMT to assess whether the association between vestibular loss and driving difficulty was mediated by spatial cognition.

Results: In multiple logistic regression analyses adjusting for age, sex and education, MCI and AD patients with bilateral vestibular loss had a significant, greater than 12-fold odds of driving difficulty (OR 12.1, 95% CI 1.2, 117.7) compared to MCI and AD patients with normal vestibular function. We did not observe any significant difference in the odds of losing objects, falling, or fear of falling by level of vestibular function. Additionally, the association between bilateral vestibular loss and driving difficulty was substantially attenuated after adjusting for performance on MRMT, a measure of spatial cognition (OR 4.0, 95% CI 0.3, 48.2).

Conclusion: This study suggests a novel link between vestibular loss and driving difficulty in MCI and AD patients, and demonstrates that driving difficulty may be a real-world manifestation of impaired spatial cognition associated with vestibular loss.

Joshua Yang, MS 2

Mentor(s): Taekjip Ha, PhD
Department of Bioengineering

Superhelicase-Dependent Isothermal DNA Amplification

Authors: Joshua Yang MTM, Taekjip Ha PhD

Background: Isothermal DNA amplification methods have significant utility in applications such as diagnostics in low resource settings. While helicase-dependent amplification (HDA) has previously been described as one such method, existing implementations are limited by the lack of helicase processivity. We show that an engineered superhelicase can be used in concert with DNA polymerases to amplify DNA under isothermal conditions, enabling point-of-care diagnostic capabilities without the need for thermocyclers.

Methods: The Rep-X and PcrA-X superhelicases were generated from mutations of the E. coli Rep and the B. stearothermophilus PcrA helicases. Isothermal amplification reactions were performed by combining helicases, polymerases, SSB, template DNA, primers, and buffer into a microtube and allowed to incubate for 90 minutes. Amplification products were analyzed using real-time fluorescence monitoring or purified using a QIAquick purification kit and subject to gel electrophoresis.

Results: As a requirement for DNA amplification, blunt-ended DNA must first be separated. While wild-type helicases have been reported to lack this ability, both Rep-X and PcrA-X were able to unwind blunt-end DNA. Using yeast DNA as a template, a region of 196 base pairs was amplified in a manner dependent on the presence of superhelicase, polymerase, SSB, and ATP and could be done isothermally at both 37C and 57C within 90 minutes of incubation. Measurement of fluorescence during amplification showed that the reaction reached saturation by 30 minutes and that the kinetics of doubling were between 1.37 and 1.45 minutes per cycle, speeds that rival those of PCR and are faster than the 3 minutes reported by commercial HDA kits.

Conclusion: We present proof-of-concept of an isothermal DNA amplification method without thermocycling. Because the reaction can be run at 37C, this approach is amenable for use in low-resource and point-of-care settings where inexpensive, quick diagnostic screening tools can make a significant impact on healthcare outcomes.

Kevin Xin, MS 2

Mentor(s): Gerald Brandacher
Division of Plastic and Reconstructive Surgery

Poly-caprolactone Nanofiber Nerve Wrap Improves Nerve Regeneration and Rodent Functional Outcomes after Delayed Nerve Repair

Authors: Kevin Xin, Joseph Lopez, Amy Quan, Angelo A. Leto Barone, Joshua Budihardjo, Kim X. Sinan, Russell Martin, Zuhaib Ibrahim, Hai-Quan Mao, WP Andrew Lee, Gerald Brandacher

Background: Proper nerve repair plays a critical role in facilitating a neuron's ability to regenerate. Unfortunately, nerve repairs can be compromised by scar proliferation, which has a deleterious impact on patient recovery. Hence, there has been a long-standing clinical interest in developing neuroprotective agents that can reduce scar burden and improve peripheral nerve regeneration after nerve transection. The purpose of this study was to evaluate the efficacy of electrospun poly-caprolactone (PCL) nerve-conduits in improving rat median nerve regeneration.

Methods: Rats had their median nerve severed and repair was delayed for 8-weeks to simulate chronic denervation. Afterwards, transected median nerves were repaired either with nerve-conduit (experimental group) or without nerve-conduit (negative control). Rats were given 14 weeks to recover before the flexor muscles and median nerve were dissected for analysis. A Student t-test was used to evaluate for statistical significance.

Results: Results demonstrated a significantly higher nerve axon count (nerve-conduit = 1769 ± 672 axons, without nerve-conduit = 1072 ± 123.80 axons, $p = 0.0468$) and flexor muscle mass (nerve-conduit = 0.629 ± 0.054 g, without nerve-conduit = 0.511 ± 0.07 g, $p = 0.0175$) in the nerve-conduit group. With regard to functional recovery, at 14 weeks post-repair, rats treated with nerve-conduits had regained 34.9 % of naïve baseline hand grip strength. In comparison, rats treated without nerve-conduits regained only 25.4% of baseline hand grip strength. The difference in grip strength was statistically significant (nerve-conduit = 1.67 ± 0.04 N, without nerve-conduit = 0.97 ± 0.39 N, $p = 0.036$). Sirius red staining revealed less collagen deposition at the nerve co-aptation site of rats treated with nerve-conduits ($p < 0.05$).

Conclusion: Biodegradable, PCL nanofiber nerve-conduits can improve nerve regeneration and subsequent physiological extremity function in the setting of delayed nerve repair by decreasing the scar burden at nerve co-aptation sites.

Rakesh Goli, MS 2

Mentor(s): William R. Thompson, MD
Division of Pediatric Cardiology

Electronic Cardiac Auscultation as a Method to Detect Pathologic Murmurs in Pediatric Hypertrophic Cardiomyopathy

Authors: Rakesh R. Goli BA, William R. Thompson MD

Background: Hypertrophic cardiomyopathy (HCM) is a genetic disorder highly implicated as a major cause of sudden death in pediatric patients, particularly in young athletes. As of now, echocardiogram is the current gold standard for diagnosis, yet remains ineffective as a screening tool. The goal of this study is to determine the utility of electronic cardiac auscultation with automated signal analysis as a possible screening method for patients with hypertrophic cardiomyopathy.

Methods: Several 20-second recordings at the apex or left mid sternal border were taken with a 3M Littmann Model 3200 Electronic Stethoscope while patients simultaneously received either a transthoracic echocardiogram (TTE) or an exercise stress echocardiogram (ESE). Recordings were analyzed by the eMurmur app created by CSD labs based on an algorithm to detect the presence and differentiate between innocent and pathologic murmurs.

Results: The goal of this study is to perform a feasibility analysis based on the automated signal analysis. 3 females and 3 males of age range 12-17 were initially recorded during ESE and TTE to finalize an auscultation protocol. 5 females and 4 males (age range 2-18; 6 with murmur/3 with no murmur; 4 ESE/5 TTE; 47 recordings) were recorded with a finalized protocol and the recordings have been sent to CSD labs for signal analysis.

Conclusion: Electronic cardiac auscultation has improved tremendously with technological advances furthered by automated signal analysis algorithms. The study demonstrates that this technology has the ability to identify potential high-risk patients with pathologic HCM murmurs, providing a much-needed effective and efficient screening tool in the pediatric setting.

Zach Pennington, MS 2

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Department of Neurosurgery

Construct Length and Patient Age As Predictors of Discharge Disposition, Ability to Drive, and Return to Work in Patients Undergoing Occipitocervical and Occipitothoracic Fusion

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Background: Occipitocervical (OC) and occipitocervicothoracic (OCT) fusions are surgical interventions commonly used to address craniocervical instability. These procedures have been shown to produce significant improvement of pain and neurological symptoms, however few reports exist that describe changes in functional status of patients undergoing these procedures.

Methods: We retrospectively reviewed all patients who underwent OC or OCT fusions at Johns Hopkins Hospital between August 2005 and October 2014. Patients were evaluated regarding baseline demographics – age, gender, race, and body mass index (BMI) – smoking history, presenting symptoms, medical comorbidities, NPDI and KPS. We also recorded the surgical approach (i.e. anterior/posterior, or posterior alone), peri-operative and post-operative outcomes, and status at last follow-up. Successful fusion and time to fusion were established by routine radiographic evaluation.

Results: We included 131 patients in the study, of whom 77% underwent OCT fusion and 23% underwent OC fusion. Of these, 27 completed the EQ-5D and 26 completed the NPDI. Increasing age was associated with a decreased likelihood of being discharged home ($p < 0.05$) and delayed return to work after surgery ($r = 0.47$, $p < 0.05$). There was no significant difference in post-operative complications between patients, but patients with longer constructs were less likely to retain the ability to drive post-surgically ($r=0.39$, $p=0.049$).

Conclusion: Our results showed that compared to older patients, younger patients were more likely to be discharged home and less likely to resume work activities after OC or OCT fusion. Additionally, patients with longer constructs were less likely to be able to drive, with no patients having constructs greater than 10 levels being able to drive post-operatively.

Zach Pennington, MS 2

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Visceral Fat Volume on Standard CT is an Independent Predictor of Survival in Patients Treated Surgically for Spinal Metastases

Authors: Zach Pennington BS, A. Karim Ahmed BS, Nancy Abu-Bonsrah MD, Eric Sankey MD, C. Rory Goodwin MD, J.J. Verlaan MD, Daniel M. Sciubba MD

Background: Life expectancy is a strong determinant of surgical candidacy in patients with spinal metastases. In this study, we seek to demonstrate whether pre-operative body fat and muscle volumes are independent predictors of post-operative survival in patients surgically treated for spinal metastases.

Methods: All patients treated at Johns Hopkins between 8/1/2004–7/1/2013 with pre-operative abdominal CT scans acquired within 3 months of surgery were reviewed. Pre-operative and post-operative treatment, pre-operative neurological status and body composition, Charlson Comorbidity Index, primary tumor type, extent of progression, and Tomita and Tokuhashi scores were collected. Multivariable logistic regressions were used to determine independent predictors of 3mo, 6mo, and 12mo survival and the models were assessed with receiver-operating characteristic (ROC) curves.

Results: We examined 99 patients (median age 59, 59.6% male). The most common primary lesions were lung (16.2%) and prostate (14.1%). Independent predictors of 3mo survival were visceral fat area (VFA) (95% CI: 1.00-1.18 per 1000mm2; p = 0.04), post-operative chemotherapy ([1.01-3.41]; p = 0.04), and a Tomita score < 3 ([1.17-19.93]; p = 0.03). The only independent predictor of 6mo survival was VFA ([1.01-1.21] per 1000mm2; p = 0.04). Independent predictors of 12mo survival were subcutaneous fat area ([1.00-1.07] per 1000mm2; p = 0.05), breast primary tumor type ([1.17-18.81]; p = 0.03), the absence of visceral metastases ([1.25-4.36]; p = 0.008), and being ambulatory pre-operatively ([1.07-4.95]; p = 0.03). The ROC curve AUC values for the 3mo, 6mo, and 12mo models were 0.8196, 0.7795, and 0.8027, respectively.

Conclusion: Visceral fat mass is a positive independent predictor of post-operative survival in patients treated surgically for spinal metastases. As a result, the accuracy of current prognostic tools could be potentially improved via incorporation of visceral fat volume as a risk factor.

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