

9th Annual Translational Science Symposium
In Memory of David Seldin, MD, PhD
Race & Research: Old Challenges, New Approaches
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Poster Presentations



1. PREDICTED VITAMIN D STATUS AND INCIDENCE OF COLORECTAL CANCER IN THE BLACK WOMEN'S HEALTH STUDY

LAUREN BARBER,¹ HANNA GERLOVIN,² KIMBERLY A. BERTRAND,³ LAURA F. WHITE,⁴ HERMANT K. ROY,⁵ LUCILE L. ADAMS-CAMPBELL,⁶ LYNN ROSENBERG,³ JULIE R. PALMER,³

¹ Department of Epidemiology, Boston University School of Public Health, Boston, MA; ² U.S. Department of Veterans Affairs, Boston, MA; ³ Slone Epidemiology Center at Boston University, Boston, MA; ⁴ Department of Biostatistics, Boston University School of Public Health, Boston, MA; ⁵ Section of Gastroenterology, Boston Medical Center/Boston University School of Medicine, Boston, MA; ⁶ Georgetown Lombardi Comprehensive Cancer Center, Washington, DC

Introduction: Observational studies, mostly among white populations, suggest that low vitamin D levels increase risk of colorectal cancer. African Americans, who are disproportionately burdened by colorectal cancer, tend to have lower vitamin D levels compared to other populations. Observational studies, mostly among white populations, suggest that low vitamin D levels increase risk of colorectal cancer. African Americans, who are disproportionately burdened by colorectal cancer, tend to have lower vitamin D levels compared to other populations.

Methods: We assessed predicted vitamin D score in relation to colorectal cancer incidence among 49,534 participants in the Black Women's Health Study (BWHS), an ongoing prospective cohort study of African American women followed from 1995 to 2017 through biennial questionnaires. We used a previously validated prediction model, based on actual 25-hydroxyvitamin D values from a subset of participants, to derive predicted vitamin D scores at each questionnaire cycle for all BWHS participants. We calculated the cumulative average of predicted vitamin D score at every 2-year questionnaire cycle by averaging predicted scores up to and including the current timepoint. We used Cox proportional hazards regression to estimate hazard ratios (HR) and 95% confidence intervals (CI) for overall and site-specific colorectal cancer incidence according to quartiles of predicted vitamin D score, adjusting for colorectal cancer risk factors.

Results: During follow-up, 488 colorectal (370 colon; 105 rectal) cancer cases were confirmed. Women in the lowest quartile of predicted vitamin D score were estimated to have a 41% (HR=1.41, 95% CI 1.05-1.90) higher risk of colorectal cancer compared to those in the highest quartile. Comparable HRs were 1.44 (95% CI 1.02-2.01) for colon cancer and 1.34 (95% CI 0.70-2.56) for rectal cancer.

Conclusions: The results suggest that low vitamin D status may contribute to the disproportionately high incidence of colorectal cancer experienced by African Americans.



2. NOVEL COCRYSTALLIZATION OF APOLIPOPROTEIN A-I WITH BUTYRIC ACID

GRACE FERRI

Boston University School of Medicine

Introduction: Diseases of lipid metabolism, in particular cardiovascular atherosclerosis, remain the number one cause of morbidity and mortality in Western society. The well-documented anti-atherogenic role of high-density lipoprotein (HDL) is related to its involvement in reverse cholesterol transport (Fielding 211). When the transporter ABCA1 initiates cholesterol efflux from peripheral and hepatic cells, apolipoprotein A-I (apoA-I) binds the free cholesterol together with phospholipid to form discoidal nascent HDL (“good cholesterol”). The enzyme lecithin:cholesterol acyltransferase (LCAT) catalyzes the esterification of the cholesterol carried by HDL. ApoA-I activates LCAT for reverse cholesterol transport, wherein LCAT esterifies the cholesterol within the nascent HDL2 and facilitates maturation of HDL to a mature spherical form. After esterification, cholesterol can no longer diffuse back to the peripheral and hepatic cells. The esterified cholesterol, or cholesteryl ester, molecules form the hydrophobic core of the mature HDL particle and leave the circulation upon uptake by a hepatic scavenger receptor for excretion by the liver.

Methods: Research in Dr. Atkinson’s laboratory implicated the arginine 123 residue of apoA-I in the function of LCAT (Gorshokova 348). Based on the X-ray crystal structure, the Arg123 residues of each apoA-I monomer enclose a hydrophobic tunnel into which the lipid substrates of LCAT may be sequestered.

Results: ApoA-I has a closed conformation without lipid bound that transforms to a “double belt” encircling the nascent HDL disc (Segrest 31755; Mei 38570). When apoA-I activates LCAT, the tunnel should widen in order to present the substrates to LCAT for esterification (Gorshokova 348). However, the mechanism by which apoA-I interfaces with LCAT substrates remains unknown. CocrySTALLIZATION of apoA-I with the lipid component, butyric acid, will enable us to assess how the “double belt” of apoA-I opens in three-dimensional space.

Conclusions: Ultimately, research into the activation of LCAT by apoA-I should shed light on the atheroprotective mechanism of HDL and the prevention of cardiovascular disease (Xia 33143; Rosenson 1905; Gorshokova 348).



3. NOTCH ACTIVATION DURING MESODERM INDUCTION MODULATES EMERGENCE OF THE T/NK CELL LINEAGE FROM HUMAN IPSC

DAR HEINZE, SEONMI PARK, MNA HARATIANFAR, CARLOS VILLACORTA-MARTIN, ADITYA MITHAL, ANDREW MCCRACKEN, GUSTAVO MOSTOSLAVSKY

BUSM Center for Regenerative Medicine, Boston University School of Medicine

Introduction: A robust method of producing mature T cells from iPSCs is needed to realize their therapeutic potential.

Hypothesis: Notch 1 is known to be required for the production of definitive hematopoietic stem cells *in vivo*, leading us to hypothesize that activation of the Notch pathway would drive access to the T/NK cell lineage.

Methods: Using an optimized hematopoietic progenitor differentiation protocol followed by co-culture with OP9:hDLL4:hMHCII feeder cells, we found Notch activation from day 0-2 of differentiation yielded a robust increase in T/NK lineage cells.

Results: We confirmed T cell identity with surface markers, the upregulation of T cell genes, and robust proliferation of stimulated cultures. Our hematopoietic progenitors were also capable of differentiating into a natural-killer-like cell. The T/NK cell lineage decision was influenced by the plating density of hematopoietic progenitors into the co-culture system with low density favoring T cells. Single cell RNA sequencing during differentiation showed a clear developmental trajectory toward the T cell lineage. Day 42 T cells shared a highly similar transcriptional profile with human primary thymocytes. Sequencing of day 12 cultures showed that early Notch activation yielded a 6-fold increase in the putative HSPC population.

Conclusions: We conclude that Notch activation during early mesoderm induction yields an increased population of hematopoietic progenitors with robust access to the T/NK cell lineage.



4. QUANTIFICATION OF CORNEAL COLLAGEN CROSS-LINKING IN KERATOCONUS WITH INVERSE SPECTROSCOPIC OPTICAL COHERENCE TOMOGRAPHY

EUGENE HSU¹, WEIYE SONG², NATALIE SADLAK³, WANJIKU G. GITHERE³, STEVEN A. BAKER^{1,3}, ABIGAIL GOLDBERG³, NATALIE CHAVEZ³, MARISSA G. FIORELLO, BS³, JI YI^{1,2,4}, HYUNJOO J. LEE^{1,3}

¹ Boston University School of Medicine; ² Department of Medicine, Boston University School of Medicine ³ Department of Ophthalmology, Boston Medical Center; ⁴ Department of Ophthalmology and Bioengineering, Johns Hopkins University

Introduction: Optimization of corneal collagen cross-linking (CXL) is hindered by the inability to immediately measure treatment effects. Inverse spectroscopic optical coherence tomography (IS-OCT) is an emerging technique capable of non-invasively detecting nanoscale ultrastructural changes. The IS-OCT output measure D was previously found to increase with increased collagen cross-linking *in vitro*. We performed a pilot study to measure changes in keratoconus patient eyes before and after CXL by IS-OCT *in vivo*.

Methods: With IRB approval, keratoconus patients scheduled to undergo CXL were consented and enrolled. Standard epi-off CXL was performed in one eye (Glaukos, San Clemente, CA). Immediately preceding, and one month after unilateral CXL, both central corneas were imaged with dual channel visible and near-infrared light OCT. D was calculated and compared between eyes. A two-tailed paired Students t-test was used for statistical analysis.

Results: The change in corneal D before and after CXL was $+1.78 \pm 0.36$ ($n = 3$), compared to -0.22 ± 0.34 ($n = 3$) in the contra-lateral non-CXL cornea ($p = 0.03$). Delta D in the anterior half of the cornea was $+1.83 \pm 0.12$ in CXL eyes vs. -0.21 ± 0.68 in non-CXL eyes ($p=0.047$). Delta D in the posterior half of the cornea was $+1.68 \pm 0.47$ in CXL eyes vs. -0.19 ± 0.37 in non-CXL eyes ($p=0.03$). The increase in D after CXL appeared more consistently higher in the anterior corneal stroma and diminished in the posterior-most region.

Conclusions: In this preliminary study, we found that IS-OCT can be used to image corneas quickly and non-invasively in patients. D was increased in corneas following CXL. IS-OCT could help quantitate CXL *in vivo*, but further study with additional patients and methods for improved data normalization are needed to validate these preliminary results.



5. RACIAL DISPARITIES IN LIFETIME ACCESS TO MEDICATIONS FOR OPIOID USE DISORDER AMONG HOSPITALIZED PERSONS WHO USE OPIOIDS

RAAGINI JAWA MD, MPH¹, ANDREA WANG MPH², MICHAEL D STEIN, MD³, BRADLEY ANDERSON PHD⁴, JANE M LIEBSCHUTZ MD, MPH⁵, CATHERINE STEWART³, KRISTINA T. PHILLIPS PHD⁶, JOSHUA A BAROCAS MD¹²

¹ Section of Infectious Diseases, Boston Medical Center, Boston, MA USA; ² Boston University School of Medicine, Boston, MA; ³ Boston University School of Public Health, Boston, MA; ⁴ Behavioral Medicine and Addictions Research, Butler Hospital, Providence, RI; ⁵ Division of General Internal Medicine, Center for Research on Health Care, University of Pittsburgh, Pittsburgh, PA; ⁶ Center for Integrated Health Care Research, Kaiser Permanente Hawaii

Introduction: Historically, receipt of medications for OUD (MOUD) has been influenced by a number of social factors, including structural racism within the healthcare system. Hospitalizations for opioid related complications have increased in the U.S. and can serve as an opportunity to decrease disparities to treatment access. We investigated the association between lifetime access to MOUD and race/ethnicity among a cohort of hospitalized persons.

Methods: We conducted a cross-sectional analysis of hospitalized patients who misuse opioids. The primary outcome was lifetime access to MOUD defined as ever prescribed buprenorphine or methadone. We assessed three race/ethnicity groups: 1) white, non-Latinx (white), 2) non-white, non-Latinx (non-white), and 3) Latinx. The non-white group comprised of 50 African-American, 7 mixed race, and 10 identifying as other. Individuals in the Latinx group were coded irrespective of racial identification. We used multivariable logistic regression to estimate the odds of lifetime receipt of MOUD, adjusting for age, gender, history of incarceration, homelessness, unemployment, and a standardized measure assessing trust in the medical profession.

Results: We included 252 participants: n=145 white, n= 67 non-white, n=40 Latinx. Non-white and Latinx individuals had lower proportions of lifetime access to MOUD than whites (59.7%, 70%, 77%, respectively). After adjusting for background characteristics and trust in the medical profession, the likelihood of prior MOUD treatment was significantly lower for non-white (adjusted odds ratio (aOR) = 0.15, 95%CI 0.06-0.35, p < 0.001) and Latinx participants (aOR = 0.40, 95%CI 0.16-0.98, p = 0.045) compared to white participants. Latinx participants had higher odds of ever receiving MOUD than non-white participants (aOR 2.71, 95%CI 1.05-7.01, p = 0.040).

Conclusions: Significant disparities exist among white, non-white and Latinx individuals regarding lifetime access to MOUD. Hospitalization may be an opportunity to address structural racism by referring racially/ethnically diverse patients to MOUD treatment.



6. COVID-19 ASSOCIATED WITH INCREASED IMMUNE CELL INFILTRATION IN THE PLACENTA

LILLIAN JUTTUKONDA, MD, PHD (1); ELISHA M. WACHMAN, MD (2); JEFFERY BOATENG (2); YOEL BENARROCH (3); ELIZABETH TAGLAUER, MD, PHD (2)

1 – Combined Residency Program in Pediatrics, Boston Medical Center and Children’s Hospital Boston
2 – Department of Pediatrics, Boston Medical Center
3 – Boston University School of Medicine

Introduction: Maternal COVID-19 infections are common in pregnancy, yet rates of infant SARS-CoV-2 transmission are low. As the interface between mother and fetus during pregnancy, the placenta may form a protective barrier against vertical transmission of COVID-19. Interestingly, the intrauterine immune response to maternal COVID-19 remains undefined. Major immune populations at the maternal-fetal interface include macrophages and natural killer (NK) cells which can mount cellular and inflammatory cytokine responses against viral infections. Understanding whether these cells respond to COVID-19 in the placenta may help understand intrauterine mechanisms preventing fetal transmission of SARS-CoV-2 in pregnancy.

Objective: Our objective was to examine the relative abundance of maternal CD14+ macrophages and CD56+ NK cells in human placental tissues in pregnancies affected by COVID-19 in comparison to contemporary controls.

Methods: Placental biopsies (including decidual tissue) were obtained from 8 SARS-CoV-2 positive pregnancies (COVID) and 5 contemporary SARS-CoV-2 negative pregnancies (Control) during a peak period of COVID-19 admissions at Boston Medical Center. Formalin-fixed cryosections were stained with primary antibodies (CD14 or CD56) and fluorescently labeled secondary antibodies. Immunofluorescence images of decidual tissue were obtained by automated acquisition and used to calculate a fluorescence ratio (FR) of corrected total cell fluorescence (CTCF) of target antigens over secondary-only negative background. FR of COVID and Control specimens were compared using independent t-tests.

Results: Using this methodology, we see an improvement in the stability and accuracy of network inference for each subtype individually – especially when the sample size is small – resulting in models that represent a broader and more accurate picture of the regulatory landscape.

Results: CD14+ macrophages and CD56+ NK cells were observed in all decidual tissues examined. Quantitative microscopy revealed significantly greater macrophage infiltrates in COVID samples compared to Control samples ($p < 0.01$, Figure 1). There were also significantly greater NK cell infiltrates in COVID samples compared to Controls ($p < 0.05$, Figure 2).

Conclusions: Our data demonstrate that NK cells and macrophages accumulate at the maternal-fetal interface in pregnancies complicated by COVID-19, suggesting these leukocyte populations may be important for preventing vertical transmission of SARS-CoV-2 during pregnancy.



7. CAROTID ARTERY ATHEROSCLEROSIS, CORONARY HEART DISEASE RISK, AND COGNITIVE IMPAIRMENT: THE FRAMINGHAM HEART STUDY

SONJA KYTÖMAA, MPH¹, PRAJAKTA JOSHI, BDS, MPH^{1,2}, JING YUAN, MD^{1,2,3}, YIJING LIN, BS^{1,2}, RHODA AU, PHD^{1,2,4,5}

1. Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, United States
2. Framingham Heart Study, Framingham, MA, United States
3. Department of Neurology, Peking Union Medical College Hospital, Beijing, China
4. Department of Neurology, Boston University School of Medicine, Boston, MA, United States
5. Department of Epidemiology, Boston University School of Public Health, Boston, MA, United States

Introduction: Several coronary heart disease (CHD) risk factors are associated with cognitive impairment. Addressing these risk factors may prevent cognitive impairment. However, the mechanism underlying the association is unclear.

Hypothesis: We hypothesized that the association between CHD risk and cognitive function is mediated by atherosclerosis.

Methods: We included 1924 participants (mean age=56.54±8.94) from the Framingham Offspring cohort who completed neuropsychological (NP) testing and ultrasound studies between 1999-2014. To estimate the proportion of the association between CHD risk and NP mediated by atherosclerosis, we used regression models relating CHD risk to NP and compared risk ratios adjusted and unadjusted for atherosclerosis. Models were also adjusted for education. We calculated CHD risk using a validated algorithm that combined age, gender, blood pressure, cholesterol, diabetes and smoking status. We aggregated domain-specific NP tests to derive executive function, memory and global cognition scores. Ultrasound measures of atherosclerosis included carotid artery stenosis, defined by peak-systolic velocity, and mean intimal-media thickness (IMT).

Results: CHD risk was inversely associated with memory (RR=0.49, p<0.001) executive function (RR=0.94, p<0.001), and global cognition (RR=0.40, p<0.001). Common carotid bulb IMT mediated 36% (p<0.001), 42% (p<0.001) and 36% (p<0.001) of the association between CHD risk and memory, executive function, and global cognition scores, respectively. Similar results were observed for internal carotid artery (ICA) IMT (estimated mediation for memory=25% p<0.001, executive function=23% p=0.002, global cognition=24% p<0.001) as well as left and right ICA stenosis (estimated mediation for memory=26% p<0.001, and 21% p<0.001, global cognition=23% p<0.001 and 21% p<0.001, respectively). Left and right ICA stenosis were not associated with executive function (p=0.46 and 0.08, respectively), thus did not mediate the association between CHD risk and executive function.

Conclusions: The association between CHD risk and cognitive function is partially mediated by several atherosclerotic markers. These results provide insight into how CHD risk may increase risk of cognitive impairment.



8. PREGNANCY-RELATED CVD RISK MANAGEMENT IN THE FIRST POSTPARTUM YEAR

MARA MURRAY HORWITZ¹, MOLLY FISHER², CHRISTINE PRIFTI¹, KATHARINE WHITE³,
CHRISTINA YARRINGTON³, TRACY BATTAGLIA¹

Introduction: Several pregnancy complications are linked to future risk of cardiovascular disease (CVD) and can inform CVD prevention. However, most primary care internists have low levels of comfort and experience with pregnancy-related health. In addition, the Internal Medicine literature lacks comprehensive practical guidance for primary care clinicians (PCCs) regarding pregnancy-related CVD risk management.

Methods: We systematically searched 3 databases (PubMed, EMBASE, and CINAHL) and manually searched clinical websites (Guideline Central, ACOG, USPSTF, AAFP, ACP, SGIM, ADA, and AHA/ACC), Google, and Google Scholar for guidelines related to postpartum care in the United States from 2010 to 2020. Two authors independently conducted title and abstract screening followed by full text review for guidelines or society recommendations relevant to pregnancy-related CVD risk assessment or management by PCCs in the year after pregnancy. A third author resolved discrepancies.

Results: Of 972 unique publications, 12 met inclusion criteria, representing a range of clinical specialties. None was written specifically for Internal Medicine-trained PCCs. Several recommended comprehensive CVD risk assessment within 3 months postpartum for any patient with a “pregnancy-related CVD risk indicator,” followed by lifestyle counseling or pharmacotherapy and follow-up within 1 year postpartum. Additional screening and follow-up in the first postpartum year were recommended for patients with prior hypertensive disorders of pregnancy or gestational diabetes. Most recommendations were based on limited or inconsistent evidence, consensus or expert opinion, or were ungraded. Several areas of uncertainty for future research were identified, including CVD risk assessment that incorporates pregnancy complications, and the optimal timing and content of ongoing CVD risk assessments.

Conclusions: Clinical practice recommendations for the identification and management of pregnancy-related CVD risk by PCCs during the first postpartum year are scattered and generally based on unclear or weak evidence. Clear and comprehensive guidance is urgently needed to enable PCCs to address CVD risk after medically complicated pregnancies.



9. PATTERNS OF PREGNANCY-RELATED CVD RISK AND FOLLOW-UP AT BOSTON MEDICAL CENTER

MARA MURRAY HOWITZ¹, SAMANTHA PARKER², AYODELE AJAYI², CHRISTINA YARRINGTON³, TRACY BATTAGLIA³

¹Department of Medicine, Boston University School of Medicine, Boston, MA; ²Department of Epidemiology, Boston University School of Public Health, Boston, MA; ³Department of Obstetrics and Gynecology, Boston University School of Medicine, Boston, MA

Introduction: Pregnancy-related cardiovascular disease (CVD) risk indicators—complications associated with future CVD—warrant CVD prevention beginning within the first postpartum year. We sought to understand patterns of pregnancy-related CVD risk and follow-up at Boston Medical Center (BMC), in order to improve care delivery, equity, and long-term outcomes after medically complicated pregnancies.

Methods: We conducted a retrospective cohort study of patients with prenatal care and delivery at BMC between 2016 and 2018. Maternal demographic, obstetric, and health care encounter data were extracted from the medical record. Pregnancy-related CVD risk indicators were identified using ICD10 codes. We examined maternal sociodemographic and clinical characteristics, and timing of postpartum health care use, overall and between groups with and without a pregnancy-related CVD risk indicator.

Results: Of 3738 eligible patients, more than half identified as non-Hispanic Black and nearly one-fifth as Hispanic. Thirty percent had a primary language other than English. Over 70% were publicly insured. Nearly 40% (38.2%) had at least 1 pregnancy-related CVD risk indicator: hypertensive disorders of pregnancy (24.2%), preterm delivery (12.2%), low birth weight (11.5%), gestational diabetes (7.4%), or stillbirth (0.5%). Compared to those without any CVD risk indicator, only obesity (18.9% versus 28.6%) and caesarean delivery (34.6% versus 45.5%) were associated with having a pregnancy-related CVD risk indicator. Under two-thirds of patients had a health care encounter by 6 weeks postpartum, with higher rates after complicated pregnancies (67.0% vs 59.6%). At the end of 1 year postpartum, 20% of patients with a pregnancy-related CVD risk indicator still had no encounters for care.

Conclusions: Nearly 40% of patients delivering at BMC have a pregnancy-related CVD risk indicator, of whom at least 20% receive no care within the first postpartum year. Further research to understand facilitators and barriers to postpartum care, and interventions to support transitions to primary care after medically complicated pregnancies, are urgently needed.



10. IMPLEMENTATION AND IMPACT OF A SIMULATION-BASED MASS GATHERING MEDICINE TRAINING PROGRAM FOR BOSTON UNIVERSITY PREHOSPITAL PROVIDERS

E.G. PLAITANO^{1,3}, E.F. EVERETT¹, S.K. GOLDEN^{1,2}, K.M. RYAN^{1,2,3}

¹ Boston University EMS; ² Boston University School of Medicine; ³ Boston Medical Center, Department of Emergency Medicine

Introduction: Prehospital providers experience unique challenges during mass gathering events, but rarely receive specific training in mass gathering medicine. Event planning checklists have been published, but a gap exists between proposed medical preparation and actual implementation into clinical practice. To address this, existing guidelines were referenced to establish a novel lecture and simulation-based continuing education program for Boston University EMS providers. Small teams of students rotated through hands-on scenarios that utilized patient-actors and simulated comprehensive concert-venue emergencies. Scenarios were instructed by experienced large-venue emergency medical service (LVEMS) providers. This study aimed to describe the program and determine its impact in preparing providers for LVEMS coverage.

Methods: Optional, anonymous surveys were administered to students and instructors. Instructors assessed students pre/post-implementation using 5-point Likert scales (0-5) and impact was evaluated with two-sample *t*-tests. Students completed self-reported 4-point Likert scales (Unchanged=0, Large Improvement=3), and impact was evaluated through one-sample *t*-tests with a null hypothesis of no improvement. Mean Likert scores (95% CI) are reported.

Results: A total of 43/56 responses (response rate=76.8%) were received. Only 37.2% of providers felt prepared to work mass gatherings before the training and 60.5% stated that their previous education did not prepare them for LVEMS challenges. After simulated training, 97.4% of students reported increased preparation for large venue events. Students were 48.0% better at managing large-venue emergencies [3.08(2.574,3.593) vs. 2.08(1.520,2.647), $p<0.05$] and 32.4% more proficient at utilizing medical and extrication equipment [3.75(3.204,4.296) vs. 2.83(2.361,3.306), $p<0.05$]. Approximately 88.0% of responders self-reported increased triage skills [1.33(1.035,1.632), $p<0.0001$], 84.0% reported increased confidence providing LVEMS patient care [1.38(1.052,1.698), $p<0.0001$], and 92.0% reported better knowledge of LVEMS procedures [1.75(1.418,2.082), $p<0.0001$].

Conclusions: Analysis demonstrated that this novel training program increased LVEMS preparation and improved select large-venue emergency skills for prehospital providers, and may fill a gap in the education system regarding mass gathering medicine.



11. NARRATIVE REVIEW OF SMOKING CESSATION INTERVENTIONS FOR PEOPLE WITH HIV IN CHINA

SHANYIN YANG, HAO LIANG, LI YE, JIEGANG HUANG, JIANNAN LV, KARSTEN LUNZE, LISA M. QUINTILIANI

Boston University School of Medicine

Introduction: In China, there are an estimated 316 million smokers, accounting for 27.7% of the entire population. People with HIV (PWH) smoke at higher rates and are more vulnerable to tobacco's harms, causing worsened HIV-related symptoms, quality of life, and anti-retroviral therapy outcomes. There is a gap in knowledge about which strategies to incorporate into smoking cessation interventions, particularly those that can be delivered population-wide, for PWH in China to best target their unique needs.

Methods: We conducted a narrative literature review of strategies for smoking cessation among PWH in China, especially technology-assisted interventions due to their scalability potential, through Google Scholar and China CNKI databases in English and Chinese.

Results: We reviewed 21 descriptive studies, reports, and governmental documents which showed PWH in China made significantly more attempts to quit and are more interested in both in-person and technology-assisted interventions compared to non-PWH populations. Increasing perceived and actual social support facilitated cessation; internalized HIV stigma and psychological distress hindered cessation efforts. Furthermore, we reviewed an additional 25 studies reporting results of smoking cessation interventions in China. Almost half (n=11) of these 25 intervention studies incorporated technology-assisted approaches and showed increased quit rates for intervention compared to control groups. However, there were no technology-assisted smoking cessation interventions targeting the needs of PWH in China.

Conclusions: Promoting social support and decreasing HIV stigma through technology-assisted platforms are promising strategies for smoking cessation interventions for PWH in China. Rigorous qualitative research is needed to inform culturally appropriate cessation interventions. We are conducting qualitative interviews among PWH in China to develop a smoking cessation intervention including text messages through WeChat and telephone-based behavioral counseling. A pilot trial will then test its feasibility and preliminary efficacy. If effective, this approach has high potential to be delivered widely to the larger PWH population in China.



12. EVALUATING AND QUANTITATING AN INTRAPERATIVE FLURSCOPIC PROTOCOL TECHNIQUE FOR COMPONENT POSITION DURING ANTERIOR TOTAL HIP ARTHROPLASTY

SEHAR RESAD, RAHUL BHALE, RUIJIA NIU, MICHAEL KAIN

BMC Orthopedic Surgery, Boston University School of Medicine

Introduction: The outcome of total hip arthroplasty (THA) is highly dependent on the proper placement to the acetabular and femoral components to restore proper hip mechanics and equal leg lengths. Currently, many techniques such as robotics, navigation, custom implants, and intraoperative digital assessment programs have been shown to help ensure adequate component position. The goal of this study is to analyze the accuracy of implant position using basic preoperative planning templating and a standard intraoperative assessment protocol.

Methods: A retrospective review of THAs performed at an academic hospital from January 2018 to December 2019 via a direct anterior approach (DAA) were identified. Patient demographics such as sex, age at THA, BMI, laterality, and indication for THA were recorded. Postoperative standing radiographs at least 4 weeks after surgery were used to evaluate final implant position by measuring abduction angle, inclination, offset, and leg length discrepancy using the program TraumaCad.

Results: 77 THAs in 72 patients were included in this study. Postoperative measurements showed mean acetabular cup abduction of $24.5^{\circ} \pm 2.1$, acetabular cup inclination of $44.7^{\circ} \pm 2.1$, leg length discrepancy of 1.3 ± 7.1 mm and hip offset of 75.7 ± 5.9 mm with a mean difference in offset of 0.41 ± 2.8 mm compared to the contralateral side. Significant differences were seen in cup inclination in right hips compared to left hips and hip offset in obese patients compared to non-obese patients.

Conclusions: A single surgeon's technique using preoperative planning templating and an intraoperative assessment protocol without the use of external guidance programs or intra-operative technology achieved acceptable implant position.



13. BAYESIAN MULTIVARIATE NETWORK META-ANALYSIS MODEL FOR THE DIFFERENCE IN RESTRICTED MEAN SURVIVAL TIMES

XIAOYU TANG¹, LUDOVIC TRINQUART¹

¹ Boston University School of Public Health

Introduction: Network meta-analysis (NMA) is essential for decision-making in healthcare and policy. NMA enables inference for all pair-wise comparisons between interventions available for the same indication, by using both direct evidence and indirect evidence. In randomized trials with time-to event outcome data, such as lung cancer data, conventional NMA methods rely on the hazard ratio and the proportional hazards assumption, and ignore the varying follow-up durations across trials. To address these issues, we introduce a novel multivariate NMA model for the difference in restricted mean survival times (RMST).

Methods: Our model synthesizes all the available evidence from multiple time points simultaneously and borrows information across time points through within-study covariance and between-study covariance for the differences in RMST. We derived the within-study covariance and estimated the model under the Bayesian framework. We evaluated our model by conducting a simulation study and compared the results with conventional single-timepoint model. We illustrated the model on a network of 17 randomized trials of second-line treatments of advanced non-small-cell lung cancer.

Results: Our simulation study shows that multiple-timepoint model yields lower mean squared error over the conventional single-timepoint model at all time points, especially when the availability of evidence decreases. In our illustrative example, multiple-timepoint model yields increased precision and detects evidence of benefit at earlier timepoints as compared to the single-timepoint model. Our results suggest that nivolumab is superior to docetaxel and that docetaxel is superior to best supportive care in terms of RMST, but no other basic contrast gave significant differences in RMST.

Conclusions: Our novel model synthesizes the totality of the evidence available across multiple timepoints and has the advantage of providing a clinically interpretable measure of treatment effect, valid regardless of the proportional hazard assumption.



14. INVESTIGATING COPD GWAS IN IPSC-DERIVATED ALVEOLAR EPITHELIAL CELLS USING CRISPI

RHIANNON WERDER^{1,2}, MICHAEL CHO³, XIAOBO ZHOU⁴, DARRELL KOTTON^{1,2}, ANDREW WILSON^{1,2}

¹Center for Regenerative Medicine (CReM) of Boston University and Boston Medical Center; ²Pulmonary Center of Boston University School of Medicine, Boston, MA, USA; ³Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital; ⁴Department of Medicine, Brigham and Women's Hospital, Harvard Medical School

Introduction: The distal lung is lined by type 1 (AT1) and type 2 alveolar epithelial cells (AT2), with the latter important for producing surfactant and epithelial regeneration. Chronic obstructive pulmonary disease (COPD) is a debilitating disease affecting the lung epithelium. Poor lung function in adulthood precedes COPD diagnosis, and GWAS demonstrate overlapping risk variants with both COPD and low lung function. However, how these gene variants contribute mechanistically to lung function and/or epithelial dysfunction is poorly understood.

Hypothesis: In this study, we aim to assess how lung function genes affect epithelial cells and hypothesize that knock-down of genes of interest will modulate AT2 function.

Methods: We elected to use CRISPR interference (CRISPRi) to knock-down genes of interest. We engineered human induced pluripotent stem cell (iPSCs) to stably express an inducible, catalytically inactive Cas9 (dCas9) and used a lentiviral platform to deliver gRNAs targeted to the transcriptional start site of genes of interest.

Results: We used established lung directed differentiation protocols to produce iPSC-derived lung progenitors (expressing NKX2-1) then type 2 alveolar epithelial cells (iAT2s). Knock-down of many of the genes of interest commencing at the lung progenitor stage substantially affected differentiation of subsequent iAT2s. We also assessed the effect of knock-down in established iAT2s, including surfactant gene expression and proliferation. We found the absence of certain genes (e.g. HHIP, DSP or FAM13A) altered proliferation and/or increased surfactant gene expression (SFTPC, SFTPA1 and SFTPA2) expression in iAT2 cells.

Conclusions: In summary, we have developed a CRISPRi platform to knock-down genes of interest identified from COPD and lung function GWAS. We found that the majority of genes assessed affected at least one aspect of AT2 function (differentiation, proliferation or surfactant expression). Future studies will determine the molecular mechanisms by which these genes of interest control key functions of AT2 cells.



15. REMOTE DIAGNOSIS OF DEMENTIA USING AI METHODS ON CLOCK DRAWING IMAGES

SAMAD AMINI*, LIFU ZHANG, IOANNIS PASCHALIDIS, AMAN GUPTA

Center for Information & Systems Eng., Boston University

Introduction: Detection of any form of cognitive impairment is challenging and the subjects have to undergo numerous evaluations and clinical tests. Hence, it would be of great importance to design a reliable and accessible procedure by which patients may get diagnosed for dementia remotely. The capability of the Clock Drawing Test (CDT) as an effective cognitive assessment tool has motivated us to develop an online diagnostic tool by leveraging artificial intelligence techniques.

Methods: Digital pen recordings of 3; 263 normal subjects and 160 with dementia in the Framingham Heart Study (FHS) were collected, where all subjects have completed two analog clock drawings, one drawn on command and the other by copying. We first modified and trained a Convolutional Neural Network (CNN) pre-trained on the ImageNet dataset to extract high level features of the CDT images, which generated a score associated with the likelihood of dementia for each patient. The generated scores for both command and copy CDTs along with age were used to train a logistic regression model to more precisely classify individuals as demented or normal.

Results: We have evaluated the performance of the developed models by applying 5-fold cross validation on the FHS dataset. On the test dataset, the model (modified pre-trained CNN) based on command CDT images yielded an AUC of 0.813_{-0.043}. The logistic regression model using age and the generated scores of command and copy CDTs, yielded an average AUC and average F1 score of 0.906_{-0.014} and 0.946_{-0.005}, respectively.

Conclusions: Our method need not necessarily have access to digital biomarkers or clinical tests since the CDT can be completed using pen and paper, capturing the image using a smartphone. Hence, our method offers a cost-effective and accurate screening tool to diagnose dementia and related diseases remotely.



16. SUBCHONDRAL BONE LENGTH – A NOVEL IMAGING MARKER FOR KNEE OSTEOARTHRITIS

GARY HAN CHANG

Computational Biomedicine, Boston University School of Medicine

Introduction:

Objective: Develop a novel bone shape measure, subchondral bone length (SBL), that reflects the extent of cartilage loss and bone flattening in knee osteoarthritis (OA) and investigate how the distribution of SBL changes with the grade of OA.

Methods: A fast region-based convolutional neural network was trained to locate the region of interest from sagittal dual-echo steady state MRI sequences of knee images obtained from the Osteoarthritis Initiative. Publicly available annotations of the cartilage and menisci were used as references to annotate the tibia and the femur in 61 knees. A separate deep neural network (U-Net) was developed to learn these annotations. Model predictions were compared with radiologist-driven annotations on an independent test set (n=27 knees). The U-Net was applied to automatically extract bone shapes and define SBL, which characterizes the extent of overlying cartilage and bone flattening (n=9,434 knees). We evaluated if SBL differentiated knees with radiographic joint space narrowing (JSN) from knees without it.

Results: Our analysis showed statistically significant differences in SBL when comparing MRI cross-sections at similar location (medial vs lateral) of knees with no JSN to knees of only medial JSN or knees of only lateral JSN. When we further examined the mean values of SBL that were different in knees with JSN > 0 versus those with JSN=0 and how they differed, we found that knees with JSN>0 had higher mean SBL values than knees with JSN=0, especially in the central-most regions of the knee.

Conclusions: SBL appears to be a promising imaging biomarker of knee OA. More studies are needed to fully evaluate its potential to associate with various radiographic features of OA severity. In the absence of availability of gender identity data in administrative databases, findings from this study suggest promising strategies for identifying transgender individuals in large datasets.



17. VIDEO AND TV WATCHING IMPEDES DEVELOPMENT OF COMPLEX LANGUAGE COMPREHENSION IN YOUNG CHILDREN WITH AUTISM

LIZA FRIDBERG

CAS Neuroscience – Undergrad, Boston University College of Arts and Sciences

Introduction: The effect of video and TV watching duration on 2 to 5-year-old children with autism was investigated in the largest and the longest observational study to-date.

Methods: Parents assessed development of 3,227 children quarterly for three years.

Results: Longer video and TV watching were associated with better development of expressive language but significantly impeded development of complex language comprehension. On the annualized basis, low-TV users (< 40 min TV per day) improved their language comprehension 1.4 times faster than high-TV users (> 2 hours TV per day). This difference was statistically significant ($p=0.01$). At the same time, high-TV users improved their expressive language 1.3 times faster than low-TV users. This difference was not statistically significant ($p=0.07$).

Conclusions: No effect of video and TV watching duration on sociability, cognition, or health was detected.



18. TRANSLATION OF POLICY INTO CLINICAL PRACTICE: THE IMPACT OF CHAMPS ON MATERNAL CHILD HEALTH AND RACIAL DISPARITIES IN MISSISSIPPI HOSPITALS

MAETAL HAAS-KOGAN¹, LAURA BURNHAM, MPH¹; REBECCA KNAPP, MPH, RN, IBCLC¹;
KIMARIE BUGG, DNP, MPH, IBCLC, CLC²; NATHAN NICKEL, PHD, MPH³; PAIGE BELIVEAU, MA¹;
LORI FELDMAN-WINTER, MD, MPH, FAAP, FABM⁴; ANNE MEREWOOD, PHD, MPH¹

¹Division of General Pediatrics, Boston Medical Center, Boston, MA; ²Reaching Our Sisters Everywhere, Inc., Lithonia, GA; ³Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ⁴Department of Pediatrics, The Children's Regional Hospital at Cooper - Cooper Medical School of Rowan University, Camden, NJ

Introduction: Low breastfeeding rates, which predominantly affect underserved and minority populations in the US, are a risk factor for poor infant health. The WHO Baby-Friendly Hospital Initiative (BFHI) offers a set of guidelines (the Ten Steps to Successful Breastfeeding) that aim to increase breastfeeding rates and improve maternal child health practice. The Center for Health Equity, Education, and Research (CHEER) created the Communities and Hospitals Advancing Maternity Practices (CHAMPS) program to help hospitals translate the Ten Steps guidance into policy, with the goal of gaining Baby-Friendly designation. In 2014, CHAMPS launched in Mississippi, which had no Baby-Friendly hospitals and the lowest breastfeeding rates in the US.

Hypothesis: We hypothesized that implementation of the Ten Steps in Mississippi would translate into increased breastfeeding initiation and exclusivity rates, and decreased racial disparities.

Methods: From 2014-2019 Mississippi hospitals enrolled into CHAMPS, which provided intensive support and training to help implement the Ten Steps. We tracked and analyzed monthly aggregate hospital data stratified by race on breastfeeding, skin-to-skin care, and rooming-in practices. Changes were analyzed by t-tests using SPSS.

Results: All 39 hospitals that enrolled into CHAMPS worked on implementation of the Ten Steps, and 22 gained Baby-Friendly designation, from zero designated hospitals at baseline; this accounted for >50% of Mississippi births. Breastfeeding initiation in CHAMPS hospitals increased from 56% to 66% ($p < .05$) and exclusivity from 26% to 37% ($p < .05$). The disparity between Black and White dyads decreased by 17%. Skin-to-skin and rooming-in rates increased significantly for all dyads. Skin-to-skin increased from 31% to 91% ($p < .01$) after vaginal birth and from 20% to 86% ($p < .01$) after cesarean birth. Rooming-in increased from 19% to 86% ($p < .01$).

Conclusions: Translation of the Ten Steps into policy and practice significantly increased breastfeeding initiation and exclusivity, and decreased racial disparities in breastfeeding rates in Mississippi. We proposed a novel approach to include family history, as is often available from medical charts, and showed improved power to detect genetic association with rare variants in large cohorts or biobanks.



19. ENHANCING MRI DRIVEN AD CLASSIFICATION USING GENERATIVE ADVERSARIAL LEARNING

PRAJAKTA JOSHI

Boston University School of Medicine

Introduction: Rapid improvements in neuroimaging techniques such as magnetic resonance imaging (MRI) have brought us closer to having a validated method of identifying Alzheimer's disease (AD). Longitudinal assessment is essential for both diagnosing AD and understanding its mechanisms; however, the acquisition of images at different time points with a different MRI technologies poses inherent technical bias. Accurate detection of AD is contingent on the signal-to-noise ratio (SNR) of the imaging data, which is directly connected to instrument-related parameters such as magnetic field strength. As such, scanner improvements can lead to increased sensitivity to detect subtle biological changes. We need an approach that can be used to develop extended longitudinal sequences of images without being biased by technological imaging standard. A potential way to address part of the problem can be using generative adversarial learning (GAN), which is capable of converting image from one domain to another domain. As such, scanner improvements can lead to increased sensitivity to detect subtle biological changes. GAN can generate images of improved quality but their ability to augment image-based classification tasks is not fully explored. We evaluated if a modified GAN can learn from MRI scans of multiple magnetic field strength to enhance AD classification performance.

Methods: T1-weighted brain MRI scans from 151 participants of the Alzheimer's Disease Neuroimaging Initiative (ADNI), who underwent both 1.5 Tesla (1.5T) and 3 Tesla imaging at the same time were selected to construct a GAN model. This model was trained along with a three-dimensional fully convolutional network (FCN) using the generated images (1.5T*) as inputs to predict AD status. Quality of the generated images was evaluated using signal to noise ratio (SNR), Blind/Referenceless Image Spatial Quality Evaluator (BRISQUE) and Natural Image Quality Evaluator (NIQE). Data from the Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL, n=107), and the National Alzheimer's Coordinating Center (NACC, n=565) was used for model validation.

Results: The mean quality of the generated (1.5T*) images was consistently higher than the 1.5T images, as measured using SNR, BRISQUE and NIQE on the validation datasets. The 1.5T*-based FCN classifier performed better than the FCN model trained using the 1.5T scans. Specifically, the mean area under curve increased from 0.907 to 0.932, from 0.934 to 0.940 and from 0.870 to 0.907 on the ADNI test, AIBL and NACC datasets, respectively.

Conclusions: This study demonstrates that GAN frameworks can be constructed to simultaneously improve image quality and augment AD classification performance.



20. FULFILLING AN UNMET NEED: INTEGRATING FAMILY PLANNING SERVICES INTO OFFICE BASED ADDICTION THERAPY

EUNG-MI LEE (PGY-4), SARAH O'CONNOR, MD (PGY-3); RUSHINA PANCHOLI, MPH, MBA;
ELISABETH WOODHAMS, MD, MSC; ELIZABETH PATTON, MD, MPHIL, MSC

Department of Obstetrics & Gynecology, Boston Medical Center, Boston University School of Medicine

Introduction: Women with opioid use disorder (OUD) have unique concerns related to reproductive health. Previous studies have found that women with OUD reported unintended pregnancies at two to three times the rate of the general population, suggesting unmet reproductive healthcare needs. Given the structure of office-based addiction treatment (OBAT) programs in which patients present at frequent intervals to a health care provider, there is an opportunity to address these disparities. This qualitative study aims to investigate the feasibility of and barriers to integrating family planning (FP) services into OBAT from the perspective of clinicians specializing in treatment of OUD.

Methods: After obtaining IRB approval, we conducted semi-structured interviews with clinicians to better understand the unique strengths and barriers of providing FP services within OBAT clinics. Interviews were recorded, transcribed, and analyzed using a codebook based on the Promoting Action on Research Implementation (PARIHS) and Ottawa Decision Support frameworks.

Results: Participant interviews (n=19) highlighted several key themes: 1) high relevance of FP counseling to the holistic care offered in OBAT clinics; 2) tension felt by patients and clinicians when considering outcomes of an unplanned pregnancy on recovery: concern about the destabilizing influence of an unplanned pregnancy versus the potentially motivating effect of parenthood; 3) complexity of including nuanced FP counseling into OBAT visits including need for additional education to provide effective patient-centered contraceptive counseling; 4) logistics of providing timely access to contraception requiring procedures; 5) conflicting priorities between ensuring patients have a contraceptive plan and concern for potential reproductive coercion.

Conclusions: OBAT programs involve regular visits with consistent and trusted clinical teams, making them an optimal setting to provide high-quality FP care to women with OUD. Implementation will require thoughtful planning and incorporate clinical education, logistics, and broad engagement of clinical teams to effectively meet the reproductive health needs of patients with OUD.



21. COMPUTER MODELING FOR OPTIMIZATION OF ENDOUROLOGICAL ROBOTIC DEVICES

DANIEL C. LESLIE¹, LIZ B. WANG¹, MAX MCCANDLESS², HARIN LEE², SHEILA RUSSO², DAVID S. WANG¹, AND SHAUN E. WASON¹

¹Boston University School of Medicine, Boston, MA, ²Boston University, Boston, MA

Introduction: Soft robotics uses deformable materials to create minimally-invasive surgical devices, where gentle manipulation of tissue is crucial. We propose a novel soft robotic anti-retropulsion device to prevent stone migration during ureteroscopy. The ideal device must be thin enough to slide past a ureteral stone, yet be able to expand over 10-mm in diameter to prevent proximal stone fragment migration. To reduce in-person laboratory work during the COVID-19 pandemic, we design and test our device using software.

Methods: Prototype soft robotic anti-retropulsion devices and actuators were tested in the finite element modeling (FEM) software, Abaqus. Material properties were programmed from previously published, experimentally-validated modeling. We used Ecoflex silicone given its superior expansion under pressure for balloon actuation. Simulated pressure was applied to the inner surface of balloon actuators of varying dimensions, and final geometry (deformation) after expansion under pressure was modeled.

Results: Configurations of soft robotic actuators were iteratively designed and tested in Abaqus software. The initial device design was a cylindrical, 1-mm-diameter balloon tested at 0.1mm and 0.05mm thickness of Ecoflex silicone. Simulated pressure of 30kPa and 20kPa resulted in deformation diameters of 4.5mm and 7.3mm, respectively, below our ideal 10mm diameter. Final device design was 1mm thick and planar, resulting in deformations greater than 12mm at 10kPa, large enough to prevent stone migration proximally in a dilated ureter. Our device conforms to the irregular geometry of the ureter upon deployment with low pressure actuation. This minimizes the potential tissue trauma when compared with current high pressure, low compliance balloons (861 kPa) or metal devices.

Conclusions: Computer modeling tools enable rapid prototyping of soft robotic endourological surgical devices. We optimize balloon deformation under pressure for a novel soft robotic anti-retropulsion device. Our final design slides by ureteral stones then gently actuates over 12mm at low pressure to minimize trauma.



22. DEEP LEARNING DRIVEN ASSESSMENT OF INFLAMMATORY REGIONS IN DIGITIZED KIDNEY BIOPSIES

CHRISTOPHER LIN, CHARITHA VADLAMUDI, DIVYA VEERAPANENI, QING ZHAO, SAEMI JUNG, BOXI HUANG, JIAMING ZHANG, HUI CHEN, HELMUT RENNKE, SUSHRUT S. WAIKAR, JOEL M. HENDERSON, VIPUL C. CHITALIA, VIJAYA B. KOLACHALAMA

Section of Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, MA, USA – 02118

Introduction: Nephritis produces injury by disrupting the renal structure with inflammatory cell proliferation. Pathologists visually estimate and compartmentalize nephritis into glomerular or interstitial regions. Computational approaches can assist with a more detailed characterization of this manifestation.

Methods: We developed a deep learning framework to classify nephritis on digitized renal biopsies. A patch-based deep neural network (pDNN) model was constructed using whole slide images obtained from chronic kidney disease patients admitted to Boston Medical Center (n=96). The pathologist-driven categorization of nephritis was used as the output label to train the pDNN model. Grad-CAM based visualization was then used to automatically identify regions of predicted cell proliferation. Performance of the models was evaluated using a subset of data that was not used for training and the regions of interest identified by the visualization method were confirmed by a team of pathologists.

Results: The pDNN model accurately predicted the type of nephritis on test data (Accuracy: 82%; Sensitivity: 83%; Precision: 85%). The visualization technique showed high correspondence with pathologist annotated regions of hypercellularity. Our results indicate that deep learning frameworks have the capability to emulate the expert pathologist classification and can segment the regions of cell proliferation which in turn provides a rationale by which the overall prediction is inferred on the type of nephritis.

Conclusions: Deep learning can provide a rational framework for accurate assessment of nephritis and may assist clinicopathologic diagnosis by identifying regions of cell proliferation.



23. IMPACT OF A SYSTEMWIDE INCIDENTAL ADRENAL MASS QUALITY IMPROVEMENT INITIATIVE: A PROSPECTIVE STUDY

ALISON PEASE WOODS, MD^{1,2,7}, TIMOTHY FEENEY, MD, MSC, MPH^{1,3}, AVNEESH GUPTA, MD⁴, PHILIP E. KNAPP, MD, MS⁵, DAVID MCANENY, MD¹, F. THURSTON DRAKE, MD, MPH¹

¹Department of Surgery, Boston University School of Medicine and Boston Medical Center, Boston, MA

²Division of Surgical Oncology, Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD

³Now in the Department of Epidemiology, University of North Carolina, Chapel Hill, NC

⁴Department of Radiology, Boston University School of Medicine and Boston Medical Center, Boston, MA

⁵Department of Medicine, Boston University School of Medicine and Boston Medical Center, Boston, MA

Introduction: Appropriate follow-up after discovery of incidental adrenal masses (IAMS) is infrequent. We hypothesized that a quality improvement (QI) program could improve the management of IAMS.

Methods: This systemwide initiative targeted primary care providers (PCPs) after IAM detection. It incorporated (1) chart-based messages and emails to PCPs, (2) an evidence-based algorithm for IAM workup, and (3) standardized recommendations in radiology reports. Data were prospectively collected in 2019 (the “QI cohort”) and compared to a historical, pre-intervention cohort diagnosed with IAMS in 2016. The primary outcome was the initiation of an IAM workup by the PCP, defined as relevant clinical history-taking, laboratory screening, follow-up imaging, or specialist referral. Outcomes were assessed using Fisher’s exact test, multivariable logistic regression, and 2-sample t test of log-transformed time data.

Results: The QI cohort included 206 patients, versus 225 in the historical cohort. Patients who died during admission or had severe life-limiting conditions were excluded. All patients had ≥ 6 months of follow-up. In the overall QI cohort, 37.4% (77/206) met the primary endpoint for PCP-initiated workup, compared to 25.8% (58/225) in the historical cohort ($p=0.013$). Implementation of the standardized radiology template was not universal. Among those whose radiology reports included standardized IAM recommendations, 55.8% (29/52) received IAM follow-up. After adjusting for insurance status and initial imaging setting (e.g., inpatient, outpatient, emergency department), patients in the QI cohort had 1.84 times higher odds (95%CI 1.12-3.03) of PCP-initiated IAM workup. Median time to initial PCP follow-up visit was shorter in the QI cohort compared to the historical cohort (24.5 days vs. 42 days, $p=0.022$).

Conclusions: This intervention was associated with increased IAM evaluation and decreased time to follow-up. A majority (55.8%) of patients receiving all 3 QI initiative components underwent IAM evaluation, suggesting that simple, moderately time-intensive initiatives can successfully increase appropriate follow-up after IAM detection.



24. MECHANICAL TEMPORAL SUMMATION IS ASSOCIATED WITH GREATER MUSCLE CO-CONTRACTION DURING WALKING IN KNEE OSTEOARTHRITIS

SOYOUNG LEE, MS¹, TUHINA NEOGI, MD², PHD; SAMANTHA EIGENBROT, MS¹; JOSHUA J. STEFANIK, PT³, PHD; KERRY E. COSTELLO, PHD^{1,2}; DEEPAK KUMAR, PT, PHD^{1,2}

¹Boston University; Boston University School of Medicine²; Northeastern University³

Introduction: People with knee osteoarthritis (OA) walk with excessive muscular co-contraction known to worsen the disease. Central pain sensitization seen in chronic pain could be associated with muscle activation during walking.

Objective: The purpose of this study was to investigate the association of pain sensitization with knee muscle co-contraction during walking in people with knee OA.

Methods: In participants with symptomatic knee OA, central sensitization was assessed as mechanical temporal summation (TS) at the patella of the painful knee. TS was considered present if there was an increase in pain rating during or after a train of 10 mechanical stimuli applied via Von Frey monofilaments compared with pain rating after a single stimulus. Vastus lateralis (VL) and medialis (VM), lateral hamstrings (LH) and gastrocnemius (LG), and medial hamstrings (MH) and gastrocnemius (MG) muscle activity was recorded using surface electromyography (EMG) while walking at self-selected and fast paces. Muscle co-contraction index (CCI) was calculated using published methods for medial and lateral muscle pairs during pre-activation, loading response, and midstance phases of gait. Independent sample t-tests were used to compare CCIs between people with and without mechanical TS.

Results: Of 42 participants in this study, 57% had mechanical TS at the affected knee. Compared to those without TS, during pre-activation, people with TS had 41.3% and 39.3% greater VL-LH CCI at a self-selected pace fast pace, respectively, as well as 41.9% greater VM-MH CCI at a fast pace. During loading response, TS group showed 64.2% and 73.1% greater VM-MH CCI at self-selected pace and fast pace, respectively. TS group had 80.3% greater VL-LG CCI during midstance at a self-selected pace.

Conclusions: Central sensitization may be associated with altered motor function during daily activities like walking. These results indicate that strategies to reduce pain sensitization may also assist with normalization of motor patterns in people with knee OA.



25. ASSOCIATION OF PAIN INTENSITY AND PATTERNS WITH RESPONSE TO EXERCISE IN KNEE OSTEOARTHRITIS

SOYOUNG LEE, MS¹, TUHINA NEOGI, MD², PHD; DEEPAK KUMAR, PT, PHD^{1,2}

Boston University¹; Boston University School of Medicine²

Introduction: While exercise is recommended as the first-line intervention for people with knee osteoarthritis (OA), many do not respond to exercise interventions. Immediate response to exercise can be assessed as a reduction in pain threshold, a phenomenon known as impaired exercise-induced hypoalgesia (EIH). EIH can be impaired in people with chronic pain. Understanding clinical characteristics associated with impaired EIH could guide personalized interventions.

Objective: The objective of this study was to determine the relation of knee pain intensity and pattern with the presence of impaired EIH in people with knee OA.

Methods: Pain intensity was assessed using a numeric pain rating scale (0-10 NRS) in individuals with symptomatic knee OA (n=26). The Intermittent and Constant OA pain (ICOAP) questionnaire was used to determine pattern of knee pain, i.e. intermittent or constant pain. Response to a bout of knee exercises was assessed the change in pressure pain threshold (PPT) after exercise at the knee and wrist. Impaired EIH was defined as no change or reduction in PPT. We use separate logistic regression models to assess the association of NRS, ICOAP subscales with presence of impaired EIH, adjusting for age, sex, and BMI.

Results: In this cohort, 36% and 46% had impaired EIH at the knee and wrist, respectively. One-unit higher NRS was associated with 57% and 63% greater odds of impaired EIH at knee (n=25) and wrist (n=26), respectively. One-unit higher intermittent ICOAP score was associated with 53% greater odds of impaired EIH at the knee. Total and constant ICOAP scores were not associated with impaired EIH.

Conclusions: Our results suggest that a substantial proportion of people with knee OA have an impaired EIH response. We also observed that greater knee pain intensity and intermittent pain patterns may interfere with the ability to participate in exercise, limiting the EIH response.



26. THE SIX STAGES OF ENGAGEMENT IN ADHD TREATMENT: RESULTS FROM A QUALITATIVE STUDY WITH DIVERSE, URBAN PARENTS

SIKOV, JENNIFER, BA^{1,2}; LOUBEAU, J. KRISTEL, MS¹; ZOLLI, NICOLE, MA³; BAUL, TITHI, MPH¹; RABIN, MEGAN¹; HASAN, SYEDA, BA¹; ROSEN, KATHERINE, BA¹; BUONOCORE, OLIVIA, BS¹; LEJEUNE, JULIA¹; DAYAL, ROHAN¹; FORTUNA, LISA, MD, MPH, MDIV⁴; BORBA, CHRISTINA, PHD, MPH³; SILVERSTEIN, MICHAEL, MD, MPH^{1,3}, SPENCER, ANDREA, MD^{1,3}

¹Boston Medical Center, 1 Boston Medical Center Pl. Boston, MA 02118

²Boston University, Department of Psychological & Brain Sciences, 64 Cummington Mall, Boston, MA 02215

³Boston University School of Medicine, 72 E. Concord St. Boston, MA 02118

⁴University of California, San Francisco, CA

Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common and morbid pediatric behavioral health conditions. While there are many effective treatments for ADHD, treatment utilization and adherence remain extremely poor, especially among socioeconomically disadvantaged and underrepresented minority families. The goal of this study is to examine the process by which families become engaged in ADHD treatment and the barriers and facilitators encountered that could serve as targets for an intervention to improve engagement in care.

Methods: We conducted in-depth, semi-structured qualitative interviews with 41 primary caregivers of diverse youth aged 3-17 years old in treatment for ADHD at an urban safety-net hospital. Interview topics included ADHD diagnostic and treatment experiences, community attitudes and stigma, intervention preferences, and other factors influencing treatment access and decision making. Interview transcripts were independently coded by 3 research investigators on common themes using grounded theory and thematic analysis.

Results: Caregivers described six stages in the process of obtaining and engaging in care for their child's ADHD: 1) Normalization & Hesitation; 2) Fear & Stigmatization; 3) Caregiver Advocacy; 4) Communication & Navigation; 5) Care & Validation; and 6) Preparation & Transition. Stages were described both as barriers as well as necessary and important milestones in the process of engagement in care. Successful completion of each stage facilitated progression through subsequent stages, while difficulty resolving any particular stage interfered with completion of subsequent stages and treatment engagement. Caregivers reported internal and external barriers and facilitators attributed to the success of navigating each stage.

Conclusions: This framework could be used to develop new strategies to measure engagement, as well as plan and deliver interventions to improve engagement in ADHD treatment. This research merits further development of strategies to support families across the continuum of decisions faced while managing ADHD.



27. MINIATURIZATION AND MULTIPLEXING OF LIPID SAMPLE PREPARATION FOR GC-MS ANALYSIS

JOSHUA G. SINGH¹, MATTHEW B. AU²; LINGYI L. DENG²

¹Boston University, Department of Biomedical Engineering, Boston, MA.

²Boston Medical Center, Department of Medicine, Boston, MA

Introduction: Although there have been many advances in lipid characterization methods, lipid extraction continues to be conducted using the traditional Folch method which is both toxic and low-throughput. We evaluated the feasibility of a novel preparation methodology which reduces sample volume, decreases solvent toxicity and increases throughput. Our hypothesis was that the lipid extraction procedure can be miniaturized and multiplexed to make it compatible with modern sample preparation devices.

Methods: A solvent extraction and phase partition system was used to extract lipids from human serum samples. The extracted lipids were then chemically derivatized and analyzed by GC-MS. Different containers and solvents were tested to optimize the extraction process. The optimal container and solvent pair was evaluated based on two criteria: its lipid yield and its ability to minimize plastic contamination. The miniaturization potential of the system was tested by analyzing the differences in lipid yield from four different human serum sample volumes. Plastic contamination was quantified in a separate experiment by assessing the presence of phenols, hydrocarbons and other plastic markers.

Results: A 96 well-plate with glass inserts was chosen for the container as it is solvent resistant, compatible with laboratory devices and can increase throughput by 32-96x. Iso-octane rather than chloroform was chosen as the solvent to decrease toxicity. Also, a device that can serve as a “keeper” for chemical treatments and extraction processes was identified. Finally, fatty acid analysis for four different sample volumes (15 ul, 30 ul, 50 ul and 100 ul) showed that the system can decrease the amount of sample needed by 50-75% depending on the application.

Conclusions: The developed methodology can be paired with laboratory devices to automate the lipid extraction procedure. This could greatly enhance the ability of labs to conduct clinical lipid analysis studies by increasing process throughput by up to 96x.



28. E-CIGARETTES AND THEIR IMPACT ON PERIODONTAL HEALTH: A SYSTEMATIC REVIEW

JYOTI SONKAR¹, REBECCA CAMERON², MELANIE MELGAREJO², MOHAMED ELSALHY³

- 1 - Clinical Assistant Professor, Boston University, Goldman School of Dental Medicine, Boston, MA
- 2 - Predoctoral dental students, University of New England College of Dental Medicine, Portland, ME
- 3 - Assistant Clinical Professor, University of New England College of Dental Medicine, Portland, ME

Introduction: As of June 2020, numerous states in United States have passed law supporting unrestricted use of electronic cigarettes indoors thus increasing sales by 300% in past 4 years. This has led to unhindered and unrestricted consumption amongst young adults leading to development of unhealthy habits impacting general and oral health. The objective of this systematic review is to explore the evidence related to the relationship between electronic cigarettes (EC) and periodontal health.

Methods: PubMed, Scopus, Google-Scholar, Cochrane Library, Embase, and Ovid MEDLINE were searched using various combinations of the keywords. Twelve studies were included. Six studies were clinical, and six studies were performed in-vitro.

Results: In 2 studies, EC smokers had 0.4-1mm increased probing depths compared to non-smokers. In other 2 studies, when the subjects switched from combustible tobacco to vaping thus decreasing their nicotine content, they found increase in bleeding sites but less plaque accumulation. In one study, bone levels, probing depths, levels of salivary IL6, IL2 and cotinine levels were similar between EC users and non-smokers. However, the invitro studies reported increase proinflammatory cytokine release, DNA damage in human gingival fibroblasts. When the cells were exposed to nicotine levels for over 48 hours, altered cellular activity, inhibition of type 1 collagen release, decreased cellular migration and increased lactose dehydrogenase activity were noted. An interesting finding derived from this study is association between certain flavors and their effects on the fibroblasts. While flavors such as hazelnut and lime did not exert any negatives effects, menthol severely affected cell vitality and proliferation.

Conclusions: E cigarettes are less harmful alternative to tobacco smoking however, they do exert a negative impact on the periodontal health. There is a need for more standardized randomized controlled clinical trials and/or prospective cohort studies that assesses the impact of exclusive e-cigarette users on their periodontium.



29. SOCIAL DETERMINANTS OF HEALTH AND THEIR EFFECTIONS ON PREDICTING MISSED BREAST IMAGING APPOINTMENTS

SHAHABEDDIN SOTUDIAN^{*1}, AARON AFRAN², CHRISTINA A LEBEDIS², ANNA F RIVES², IOANNIS CH. PASCHALIDIS^{1,3}, MICHAEL D.C. FISHMAN²

¹Department of Electrical and Computer Engineering, Division of Systems Engineering, Boston University, Boston, MA, United States

²Department of Radiology, Boston Medical Center, Boston University School of Medicine, Boston, MA, United States

³Department of Biomedical Engineering, Boston University, Boston, MA, United States

Introduction: Predictive models utilizing social determinants of health (SDH), demographic data, and local weather data were trained to predict missed imaging appointments (MIA) among breast imaging patients at Boston Medical Center. We compared MIA incidence among patients described in terms of many different variables, including social needs, demographics, imaging utilization, appointment features, and weather conditions at the date of the appointment.

Methods: This HIPAA compliant retrospective study was IRB approved. Informed consent was waived. After data preprocessing steps, the dataset contained 9,970 patients and 36,606 appointments from 1/1/2015 to 12/31/2019. We identified 51 potentially impactful variables used in the initial prediction model and assessed each patient for MIA. We then developed a parsimonious model via statistical feature selection, which isolated the 28 most predictive variables. We utilized linear and non-linear models including support vector machines (SVM), logistic regression (LR), and random forest (RF) to predict MIA and compared their performance.

Results: The highest-performing full model (using all 51 features) is the nonlinear RF that achieved an AUC of 71% and an F1 score of 77%. Linear and easier to interpret models achieved comparable AUC and F1 scores using just 28 variables. The most impactful variables on missed appointments were appointment-specific; weather features, SDH, and demographics had less predictive power. Inadequate access to transportation (OR=1.10) and difficulty paying utility bills (OR=1.09) both came close to statistical association with more missed appointments.

Conclusions: High accuracy prediction of MIA is not practical due to the complex and multifactorial etiologies of MIA. However, the algorithms presented achieved acceptable performance and demonstrated that appointment timing and department of order origin were useful predictors of MIA. In contrast with non-modifiable demographic factors, we can address SDH to decrease the incidence of MIA. For instance, identifying transportation as an impactful SDH would justify providing ride-share vouchers to selected patients.



30. CO-SEGMENTATION OF GLOMERULI ON HISTOLOGICAL IMAGES FROM MULTIPLE STAINS USING DEEP LEARNING

DIVYA VEERAPANENI¹, YICHI ZHANG¹, ESHAN NIRODY¹, MINCAN YANG¹, SAEMI JUNG¹, YASH BENGALI¹, MARINKA ZITNIK², VIPUL C. CHITALIA³, CLARISSA A. CASSOL⁴, VIJAYA B. KOLACHALAMA^{1,5*}

¹Section of Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, MA, USA – 02118

²Department of Biomedical Informatics, Harvard University, Boston, MA, USA – 02215

³Renal Section, Department of Medicine, Boston University School of Medicine, Boston, MA, USA – 02118

⁴Arkana Laboratories, Little Rock, AR, USA - 72211

⁵Department of Computer Science & Faculty of Computing & Data Sciences, Boston University, Boston, MA, USA -02115

Introduction: Pathologists rely on multiple histological stains as part of routine renal biopsy workup in patients with kidney disease.

Objective: We evaluated if a deep learning framework can facilitate assessment of glomeruli from digitized images derived from four different histological stains.

Methods: We developed a computational pipeline to identify and segment the glomeruli from whole slide images (WSIs) of Periodic Acid-Schiff (PAS), Hematoxylin and Eosin (H&E), Jones Methenamine Silver (Jones), and Trichrome stains obtained from kidney biopsies of 60 patients at Ohio State University Wexner Medical Center. Image registration was performed on all four WSIs obtained per patient biopsy and a sliding window operation was defined to crop each histological image to smaller patches. Each image patch was then assigned one of the following labels: no glomerulus, normal or partially sclerosed (NPS) glomerulus, or globally sclerosed (GS) glomerulus, based on whether the patch contained the pathologist-driven annotation of a glomerulus. Four independent patch-level convolutional neural network (CNN) models were trained with stain-specific image patches as inputs and corresponding labels as output. Using these models, an image processing algorithm was developed to process the test WSIs and map the identified glomeruli across different stains. A report identifying glomeruli across different stains and percentage of glomerulosclerosis was generated.

Results: Performance on test data for PAS images is as follows: Accuracy = $97.7 \pm 0.98\%$, Kappa = 0.667 ± 0.13 .

Conclusions: Through deep learning, our work has the potential to directly assist pathologists to examine human kidney biopsies.



31. NOVEL PREFRONTAL SYNTHESIS INTERVENTION IMPROVES LANGUAGE IN CHILDREN WITH AUTISM

ANDREY VYSHEDSKIY^{1,2}, EDWARD KHOKHLOVICH, RITA DUNN², ALEXANDER FAISMAN, JONAH ELGART², LISA LOKSHINA², YURIY GANKIN, SIMONE OSTROVSKY², LAUREN DETORRES², STEPHEN M EDELSON³, PETR O ILYINSKII

¹Boston University, Boston, USA

²Imagination LLC, Boston, MMA, USA

³Autism Research Institute, San Diego, CA, USA

Introduction: Prefrontal synthesis (PFS) is defined as the ability to juxtapose mental visuospatial objects at will. Paralysis of PFS may be responsible for the lack of comprehension of spatial prepositions, semantically-reversible sentences, and recursive sentences observed in 30 to 40% of individuals with autism spectrum disorder (ASD). We hypothesized that PFS-targeting intervention can improve language ability in children with ASD.

Methods: In this report we present data from a three-year-long clinical trial of 6,454 ASD children age 2 to 12 years, which were administered a PFS-targeting intervention. The test group included participants who completed more than one thousand exercises and made no more than one error per exercise. The control group was selected from the rest of participants by a matching procedure. Each test group participant was matched to the control group participant by age, gender, expressive language, receptive language, sociability, cognitive awareness, and health score at 1st evaluation using propensity score analysis. The test group showed 2.2-fold improvement in receptive language score vs. control group ($p < 0.0001$) and 1.4-fold improvement in expressive language ($p = 0.0144$). No statistically significant change was detected in other subscales not targeted by the exercises.

Results: Performance on test data for PAS images is as follows: Accuracy = $97.7 \pm 0.98\%$, Kappa = 0.667 ± 0.13 .

Conclusions: 1) PFS is an essential component of full language and exercises training PFS are an indispensable component of language therapy. 2) MITA instructional framework is well-suited for language therapy, in terms of how stimulus is adapted automatically to a child's performance and how performance improves over trials. 3) Intensive MITA exercises can lead to significant long-term gains in both receptive and expressive language.

