Abstracts

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Housing screening and intervention among patients presenting to the Emergency Department

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ABSTRACT

Introduction: Individuals who experience unstable housing, a well-documented social determinant of health, experience increased morbidity and mortality compared to those stably housed. Patients who are unstably housed also utilize the emergency department (ED) more frequently due to limited access to primary care and preventative services. Therefore, the ED presents an opportune environment to assess and implement strategies to address the needs of vulnerable, unstably housed patients.

Purpose/Hypothesis: To identify and address the needs of unstably housed patients, we implemented a housing screening question protocol in the University of Iowa Healthcare's (UIHC) ED in February 2023. The screening question was written in collaboration with "Shelter House," a local community housing organization, and was an Epic prompt that stated, "Have you slept outside and/or received an eviction notice? Resources may be available." The purpose of this study was to 1) evaluate factors associated with the screening adherence, 2) factors associated with a positive screen, and 3) identify facilitators and barriers associated with utilization of this screening tool. We hypothesized that specific factors (e.g. lack of insurance, and non-Caucasian races) were associated with the decision to screen patients for housing status.

Methods: Using a mixed-methods convergent parallel study design, we captured quantitative data from hospital electronic medical records (EMR) and qualitative data from semi-structured interviews. Quantitative data included all patients who were seen by a provider in the UIHC ED between 02/24/2023 and 08/31/2024. Exposures included patient demographics (e.g., age, sex, race), temporality (e.g., season, time of day), and clinical characteristics (e.g., chief complaint). Outcomes in the quantitative arm were dichotomized as screened (yes, no) and screened positive (yes, no) among those screened. We interviewed UIHC ED nurses using an interview guide to discuss facilitators, barriers and areas of improvement for screening. Interviews were recorded, transcribed and independently coded to inductively identify key themes surrounding the implementation and utilization of the unstable housing screening protocol in the ED.

Findings/Results: Of the 77,299 ED encounters, 24,946 (32.27%) were screened for unstable housing, and 601 (2.41%) among those screened had a positive screen. Factors associated with decreased screening included patients older than 18, particularly those who are 18-29 (aOR: 0.38; 95%CI); patients presenting with a level 5 chief complaint acuity (aOR: 0.52; 95%CI); and those with a HEENT complaint (aOR: 0.67; 95%CI). Factors associated with increased positive screens among those screened included patients older than 18, particularly those who are 50-59 (aOR: 29.03; 95%CI); patients presenting with a level 5 chief complaint acuity (aOR: 7.99; 95%CI); and those presenting with a psychology complaint (aOR: 10.76; 95%CI). We identified the following key areas from interviews: Workflow Optimization and Design, Barriers to Effective Screening, Personalized Approaches to Screening, Staff Education, and Perceived Value and Utility of Screening.

Conclusion: We largely observed an inverse correlation for the evaluated exposures such that those who were most likely to screen positive were the least likely to be screened. In combination with feedback from the nursing staff, findings from this study will guide next steps including identifying strategies to address disparities in screening (e.g., reminders, education, evaluation), identifying short- and long-term outcomes associated with positive screens, and opportunities to improve the screening protocol and community health.

Title: Establishing the importance of Spur Cell Anemia (SCA) as a Prognostic Factor in Patients with Acute Alcohol-Associated Hepatitis

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Mentor: Kyle Brown

Background and aims

Acute alcoholic hepatitis (AAH) is a severe form of alcohol-related liver damage manifested by jaundice and coagulopathy that is associated with high mortality. Spur cell anemia (SCA) is an acquired form of non-autoimmune hemolytic anemia that occurs in chronic liver disease (CLD) due to various causes, most commonly alcohol-associated liver disease. SCA is characterized by acanthocytes (aka spur cells) on peripheral smear and evidence of hemolysis. The classical presentation of SCA is a severe hemolytic anemia unresponsive to transfusion and curable only by liver transplant. This form of SCA is rare, but recent studies suggest that there are milder forms of SCA, which are more common than is generally recognized. The frequency with which SCA complicates AAH has not been investigated, nor is it known whether SCA impacts outcomes of patients with AAH. The aims of this study were to address these questions.

Methods

Following IRB approval, a list of patients admitted to UIHC over 9 years with ICD codes corresponding to AAH were reviewed. The study group comprised 562 patients who met criteria for AAH (total bilirubin $\geq$ 3, AST:ALT $\geq$1.5, prothrombin time $\geq$12). Their records were reviewed to identify patients in whom acanthocytes were documented on morphology. Detailed chart reviews were performed on subjects with spur cells and in AAH patients without acanthocytes who were matched for age, sex and total bilirubin on admission. Information collected included comprehensive laboratory data, transfusion history, steroid treatment and response (where applicable), history of gastrointestinal bleeding during admission and results of endoscopy, other adverse events during hospitalization and outcome (alive or dead).

Results

Table 1: Statistically Significant Results

Parameter	Spur Cells + (n=71)	Spur Cells – (n=71)	P-value
Hemoglobin (g/dL)	8.60 +/- 2.51	10.77 +/- 1.84	<0.0001
Platelet Count (K/mm^3)	105.83 +/- 78.82	152.56 +/- 82.72	<0.0001
Creatinine (mg/dL)	1.68 +/- 1.28	1.11 +/- 1.09	0.0017
Peak PT	27.21 +/- 16.13	20.78 +/- 13.14	0.0128
Peak DF	87.11 +/- 77.73	58.03 +/- 64.49	0.0197
Length of Stay	13.99 +/- 16.09	9.61 +/- 9.98	0.006
Transfusion History	38 (53.5%)	12 (16.9%)	<0.00001
History of GI Bleed	35 (48.6%)	14 (19.4%)	0.00021
Outcome (deceased)	41 (57.7%)	30 (42.3%)	0.044

Discussion

Our data indicate that spur cells were present in a surprisingly high proportion of this group of patients hospitalized with AAH (71/562, 12.6%). Compared to matched controls with similar total bilirubin levels on admission, AAH patients with spur cells had more severe coagulopathy, more frequent GI bleeds, and required more transfusions. Renal dysfunction, a frequent comorbid condition in AAH, was more common in patients with spur cells as well. AAH patients with spur cells had significantly longer LOS and higher mortality. Notably, despite documentation of acanthocytes on morphology in the lab results, only 24% of these subjects had a complete hemolysis work-up during their inpatient stay. Because of the incomplete data, we cannot say for certain whether all these subjects had SCA. These findings add to prior studies showing that spur cells are relatively common in patients with CLD, and suggest that spur cells in patients with AAH may be an indicator a particularly poor prognosis. Increased attention to the presence of spur cells, including full hemolysis labs, should be considered in patients with AAH.

Establishing the effects of Hyperglycemic Induced Stress on Cyclin C levels in the Context of Mitochondrial Fission

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Abstract

The relationship between hyperglycemia, representative of the Western diet many Americans consume, and mitochondrial dynamics remains unclear. Mitochondria exist in equilibrium between fragmented and fused states, and under acute stress, lean towards fragmented states, resulting in increased cell damage over time. Cyclin C is a nuclear transcription cofactor within the Mediator complex which serves as a conduit between cell signaling events and RNA polymerase II-dependent gene expression. However, in response to acute stress such as ischemic injury, independent of Mediator complex, cyclin C translocates from the nucleus to the cytoplasm where it catalyzes mitochondrial fission (mitochondrial division) through Dynamin-related protein 1 (Drp1), which oligomerizes to constrict and sever the mitochondrial membrane.

We hypothesized that removing the cyclin C gene would reduce mitochondrial fission therefore reducing cellular damage in neonatal cardiomyocytes following metabolic stress. Additionally, we hypothesized that removing cyclin C in-vivo would confer beneficial metabolic effects in the form of improved glucose tolerance, healthier weight, reduced cardiomyocyte mitochondrial fission, and improved cardiac function.

To test our hypothesis, we performed in-vivo and in-vitro experiments in parallel. The in-vitro experiment involved culturing neonatal murine cardiomyocytes (NMCM) from cyclin C fl/fl mice for 96 hours. Half of the cells in culture received a virus containing cre recombinase, knocking out cyclin C NMCM 24 hours post-seeding. We then treated NMCMs acutely or chronically with low (5.5 mM), high (25 mM), or extreme glucose (50 mM) while also controlling for the effects of osmolarity using mannitol. The results of the in-vitro experiment are pending analysis for mitochondrial length, length-width ratio, and mitochondrial area.

The in-vivo experiment was in either wild type (WT) mice or cyclin C fl/fl mice with or without the cardiac inducible cre (mer-cre-mer). To identify cyclin C localization in the context of acute hyperglycemia, a glucose tolerance test (GTT) was done on 12-week-old, WT mice. Mice were sacrificed at different timepoints, and hearts were extracted and frozen for subsequent nuclear vs. cytoplasmic fractionation to determine cyclin C localization. Concurrently, cyclin C localization in the context of chronic hyperglycemia is being examined in WT mice through GTT, heart weight/body weight, western blotting to determine nuclear/cytoplasmic fractionation, and electron microscopy. Additional parallel studies are ongoing in the cyclin C cardiac knockout mice to determine the effect of cyclin C on mitochondria homeostasis in both acute and chronic hyperglycemia. Results are pending as these experiments are currently in progress.

The goal of this study is establishing the relationship between hyperglycemia and cyclin C localization, which activates and enhances Drp1 to induce mitochondrial fission in tissue in response to acute stress. By understanding this pathway, we aim to provide valuable insights into how cellular damage may be occurring in individuals with metabolic disorders. Additionally, this experiment will provide potential target pathways to act on or inhibit and therefore decrease the detrimental effects of type II diabetes, obesity, and hyperglycemia on the human body.

Understanding Patient Concerns About Postpartum Blood Pressure: A Qualitative Analysis of a Global Support Network

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Mentor: Donna Santillan

Introduction: Blood pressure changes in the postpartum period are particularly important for patients with preeclampsia. Although blood pressure typically decreases after delivery, many patients have persistent elevation for days to weeks, and new-onset hypertension or preeclampsia can develop up to six weeks postpartum. Postpartum hypertension - including new-onset preeclampsia - affects up to 2% of pregnancies in the United States. Because onset often occurs after hospital discharge, timely recognition depends on patient awareness of warning signs such as severe headache, visual changes, chest pain, epigastric pain, and blood pressure elevation. Additionally, blood pressure may remain elevated for weeks after birth, and patients with a history of preeclampsia have increased risks of persistent hypertension and later cardiovascular disease. A clear understanding of the expected recovery process can help patients differentiate between acceptable postpartum changes and symptoms requiring urgent care. Therefore, understanding patient knowledge gaps is critical to improving counseling and ultimately preventing adverse outcomes.

Methods: We conducted a qualitative analysis of member-generated questions in the *Preeclampsia, Eclampsia & HELLP Syndrome Survivors Global Support Network* Facebook group, which had over 55,300 members at the time of the study. Posts from 2022 and 2023 were searched using predetermined terms. Inclusion criteria required that posts be (1) from individuals in the postpartum period, (2) related to blood pressure, and (3) phrased as questions. Eligible posts were analyzed to identify the most frequent themes and commonly co-occurring topics.

Results: Across both years, the most frequent theme was alarm symptoms (24.51%), followed by future prognosis or subsequent pregnancies (22.77%), medication management (17.24%), and blood pressure monitoring (10.87%). Less than 10% of posts addressed each of trauma, diagnostic criteria, adverse effects, pathophysiology, lifestyle changes, or negative provider experiences. Common co-occurring themes included alarm symptoms with trauma, and alarm symptoms with future pregnancy prognosis or subsequent pregnancies.

Conclusion: This qualitative study identifies common gaps in postpartum hypertension education, with patient concerns most often centered on recognizing alarm symptoms, understanding long-term prognosis, and managing medications. The frequent overlap between alarm symptoms and trauma or future pregnancy questions highlights both the emotional and informational challenges patients face in the postpartum period. These findings point to the need for standardized, patient-centered educational interventions and targeted counseling in these specific areas. By focusing on the most common knowledge gaps, providers may be able to enhance postpartum care and patient outcomes.

The Utility of Renal Pyramidal Thickness as a Predictor of Vesicoureteral Reflux Outcomes

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Introduction

Vesicoureteral reflux (VUR) is a common pediatric urinary abnormality. Higher grades of VUR increase the risk of recurrent pyelonephritis and renal scarring while reducing the likelihood of spontaneous resolution. Unfortunately, grading of VUR is subjective and lacks objectivity and reliability. This study evaluated whether renal ultrasound (US) measurements could predict spontaneous VUR resolution and add to VUR grading. The hypothesis is that increased renal parenchymal (ParT) and renal medullary pyramidal thickness (PT) would be associated with increased chance of reflux resolution.

Materials and Methods

Medical records and imaging of children ≤2 years of age (median age [IQR] 0.37 [0.12–1.41] years) with primary VUR who underwent renal US within six months of initial voiding cystourethrogram (VCUG) and had ≥ 2 years of clinical follow up were reviewed. US measurements included renal length, PT, and ParT. Additional data included the age, sex, VUR grade, laterality, and UTI history. US parameters were compared using linear mixed models adjusted for age and sex. Logistic regression models assessed predictors of spontaneous resolution, including renal length, PT, and ParT in addition to age, gender, VUR grade, laterality, and UTI history.

Results

Of 202 patients, 78 (39%) achieved spontaneous resolution, 73 (36%) underwent operative intervention and 51 (25%) had persistent reflux. Lower grades of VUR were strongly associated with spontaneous resolution ($p = 0.002$ at 1 year; $p < 0.0001$ at 2 years). Higher grades of VUR correlated with lower mean PT and ParT ($p < 0.0001$). Compared to non-resolvers, patients with resolution had significantly smaller renal lengths ($p < 0.001$ at 1 year; $p = 0.015$ at 2 years), and larger PT ($p < 0.001$), and ParT ($p = 0.004$ at 1 year; $p = 0.019$ at 2 years)). Logistic regression demonstrated that pyramidal thickness was the strongest independent predictor of spontaneous resolution after VUR grade (AUC 0.702 at 1 year; 0.711 at 2 years). Combining PT with renal length improved predictive accuracy (AUC 0.73), and combining PT with VUR grade and renal length achieved the highest predictive accuracy (AUC up to 0.793 at 2 years).

Discussion

Increased PT and ParT and decreased renal length, were significantly associated with spontaneous VUR resolution, independent of grade. PT provided the strongest predictive value and enhanced discrimination beyond models with grade, age, gender, laterality and presenting symptoms. While reflux grade remains an important predictor of VUR outcomes, US measurements of renal length, PT, and ParT offer more objective and reproducible metrics that improve prediction models of spontaneous early VUR resolution.

Older Adults' Attitudes Towards Influenza, COVID-19, and Respiratory Syncytial Virus Vaccines. Y Alharithi, M1, A Scherer, PhD, MA Ward, MS, LA Herwaldt, MD

Background: Influenza (flu) virus, SARS-Co-V-2 (COVID-19), and respiratory syncytial virus (RSV) cause substantial morbidity and mortality among persons ≥ 60 years old. Vaccination significantly decreases the risk of severe disease, hospitalizations, and death caused by these viruses. These vaccines have become politicized and mis- and dis-information have led to decreased vaccination rates. In addition, many older adults are unaware that RSV can cause serious illness and that effective vaccines are recommended for their age group.

Purpose/Hypothesis: The purpose of this study was to understand older adults' (≥ 60 years old) perceptions, views, and sources of information on the flu, COVID-19, and RSV vaccines. We hypothesized that older adults' views on and acceptance of these 3 vaccines differ by vaccine.

Design: We recruited a nationally representative sample of the US population to answer an online survey assessing how older adults view flu, COVID-19, and RSV vaccines and whether their views and reported willingness to be vaccinated varied by vaccine and with demographic or other participant characteristics. We recruited a stratified random sample of US adults aged ≥ 60 years through Qualtrics Research Services.

Results: Most respondents (1,119; 72%) felt they weren't at high risk of a respiratory virus infection and 645 (41.59%) felt they weren't at high risk of serious illness if they were infected. Of the 1,551 respondents, 928 (59.8%) reported receiving the flu vaccine annually, 911 (58.7%) reported receiving a COVID-19 vaccine between 9/1/2023 and 8/31/2024, and 430 (27.7%) reported ever receiving an RSV vaccine. Older age ($p < 0.05$), more positive views on vaccines in general ($p < 0.0001$), and > 2 pre-existing health conditions ($p < 0.0001$) were significant predictors of vaccination rates for all 3 vaccines. Reasons for receiving the 3 vaccines were similar and were related to protecting oneself from serious illness/infection and following healthcare providers' recommendations. Reasons for not receiving the RSV vaccine and factors that could help "non-receivers" get vaccinated differed from those given for flu and COVID-19 vaccines. Significantly fewer "non-receivers" indicated they would never get the RSV vaccine (273/1,023; 26.7%) compared with flu (211/367; 57.5%) and COVID-19 (300/590; 50.9%) vaccines ($p < 0.05$; for both) and more "non-receivers" indicated that a healthcare provider's recommendation would help them receive the RSV vaccine (392/1,023; 38.3%) compared with the flu (23/367; 6.3%) or COVID-19 (73/590; 12.4%) vaccine ($p < 0.0001$). Of note, 145 of 1,023 (14.2%) respondents who had not received the RSV vaccine had "never heard of" the vaccine. Primary care providers (854/1,550; 55.1%), the CDC (647/1,550; 41.7%), and medical researchers or medical journal articles (503/1,550; 32.5%) were the most frequently selected trusted sources of information on COVID-19 vaccine, with news sources (11.3%) and social media (2.3%) among the least frequently selected sources.

Conclusions: Older adults' reasons for getting and for not getting respiratory virus vaccines varied by vaccine, the person's age, their underlying illnesses, and their views on vaccines in general. A substantial proportion of "non-receivers" might be willing to receive these vaccines if their primary care providers helped them understand their risk of serious infection, educated them about the vaccines, and recommended that they receive the vaccine.

Approaches to Clinical Uncertainty Among Physicians in Surgical versus Non-surgical Medical Specialties

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ABSTRACT

Introduction
Uncertainty is a ubiquitous entity in clinical practice that indiscriminately impacts all medical specialties. Physicians encounter this uncertainty when caring for every patient, every day. There appears to be relatively little published literature in this area, especially considering the permeative nature of uncertainty that infiltrates the medical field. There are even fewer papers published regarding the specific uncertainties that surgeons versus non-surgeons encounter and attempt to overcome in their daily practice.

Purpose
To our knowledge, this is the first initiative to assess, juxtapose, and rationalize the approaches to uncertainty in clinical judgment and medical decision-making among physicians in surgical versus non-surgical medical specialties.

Methods
A literature search was performed on PubMed using two iterations of Boolean operators: (1) "uncertainty" [ti] and "surg*" [ti]; (2) "uncertainty" [ti] and "decision making" [ti] and "physician". These PubMed searches with (1) "uncertainty" and any variant of "surgery, surgical, surgeon, etc." in the title and (2) "uncertainty" and "decision making" in the title with "physician" anywhere in the body of the article collected 185 candidate articles for review.

Results
Our findings suggest that surgeons are uniquely affected by uncertainty caused by the necessity of making rapid intraoperative decisions with little data, being unable to undo surgical actions after they have been committed, and having research that is typically lower on the classic "evidence pyramid" than non-surgeons. Surgeons overcome these uncertainties through operating "by feel," relying on teachings from their residency/fellowship training that gave them their "practice style," and utilizing instruments for novel purposes they were not originally designed for. Non-surgical uncertainty derives itself from the philosophical inability to ever truly and completely know anything, with prognostication being a prime example. Informed consent and shared-decision making are two of the most reliable strategies to overcome surgical and non-surgical uncertainty, which is aided by the ability to stop non-surgical interventions with few repercussions if medications are unsuccessful or intolerable.

Conclusions
Regardless of the clinical setting, uncertainty will be met. Medical education should venture to more readily and widely expose trainees to the uncertainty that awaits them so that they are more prepared to conquer it the best they can.

Refining Ocular Blood Flow Measurements in Age-Related Macular Degeneration with Structural Imaging and Perfusion Pressure

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Background: The hemodynamic theory of age-related macular degeneration (AMD) suggests that poor ocular perfusion is a risk factor for progression of the disease. It is therefore imperative that we are able to accurately measure blood flow to identify patients who are at risk for progression. Laser speckle flowgraphy (LSFG) can measure the rate of ocular blood flow, but measurements are highly variable in healthy eyes. These LSFG measurements are influenced appreciably by the presence of larger choroid vessels that can overshadow the true retina-perfusing flow in the capillaries and choriocapillaris. The thickness of this choroid layer is also highly variable and may contribute to the variability in LSFG measurements.

Purpose: Currently, the large intersubject variability in blood flow as determined by LSFG limits our ability to identify patients with poor perfusion that may be contributing to disease progression. The main aim of this project was therefore to determine a method for refining LSFG measurements to improve detection of abnormally low ocular blood flow in AMD patients. This was done by normalization to underlying choroid structure and calculation of resistance using LSFG measurements and ocular perfusion pressure.

Methods: We performed a multicenter prospective study with 80 patients enrolled from the University of Iowa and the Iowa City VA ophthalmology clinics. Patients with early, intermediate, and advanced non-exudative (dry) AMD were recruited along with age-matched controls. All subjects underwent non-invasive retinal imaging in both eyes when possible. Blood flow was measured in the three main vascular beds (choroid, optic nerve head, and retina) simultaneously using LSFG and was reported as mean blur rate (MBR). Intraocular pressure (IOP) and blood pressure were obtained for each patient prior to imaging. Subjects also underwent structural imaging using optical coherence tomography (OCT) to allow for measurement of thickness and vascularity of the retina and choroid. MBR values were obtained from the macula and optic nerve head LSFG scans for each patient. For the OCT images, we manually derived subfoveal choroid thickness (SFCT) measurements using built-in software. For statistical analysis, an ANOVA was initially done to determine differences in LSFG measured blood flow between controls and early, intermediate, and advanced AMD groups. A linear regression relating MBR from the macular LSFG image and SFCT measured from OCT was then conducted for all patients together and then separately for each group (control, early, intermediate, advanced). Additional regressions were performed relating MBR to ocular perfusion pressure (OPP) and SFCT + OPP. A second method for normalization was attempted by using OPP and MBR to calculate resistance (OPP/MBR) and an ANOVA was conducted on resistance values to determine if this varied by group.

Results: While average MBR was lower in patients with advanced AMD compared to controls and those with early and intermediate disease (6.40, 8.67, 8.68, and 7.93, respectively), there was no significant difference between groups as determined by the ANOVA test ($p=0.07$). Linear regression showed a loose correlation between MBR and SFCT ($p = 0.004$), between MBR and OPP ($p = 0.01$), and between MBR and SFCT + OPP ($p = 0.0009$) for all groups. Linear regressions relating MBR and SFCT were not significant for controls, early, and intermediate AMD. However, linear regression was significant for advanced AMD ($p = 0.004$). Further, an ANOVA test determined that resistance was significantly different by stage ($p = 0.008$). Resistance was highest with advanced AMD, followed by intermediate, early, and control groups.

Conclusion: Overall, the relatively loose correlations of both SFCT and OPP with MBR indicate that these values alone are not sufficient to account for the wide variability in LSFG-measured blood flow. We therefore decided not to do a normalization of MBR using SFCT or OPP. However, the significant finding that resistance to blood flow varies by stage and is highest in advanced AMD is interesting and could direct future study. This could be a potential way to correct for the high variability in LSFG measurements. Further, if bloodflow-modulating treatments are developed for AMD, resistance may be used to determine candidates who may benefit most from treatment. We will continue to follow subjects longitudinally and are interested in determining if resistance tends to increase as disease progresses. The finding of a significant correlation between SFCT and MBR in the advanced group is also interesting and could indicate that in the high resistance state of advanced AMD, bloodflow may be more influenced by choroid thickness. We are also interested in further studying how choroid structure may influence LSFG measurements. We are currently working with collaborators on automated segmentation of OCT scans to obtain an average choroid thickness over the entire retina, which will be more accurate than a single subfoveal measurement and may reveal a clearer correlation. Other anatomical structures may also be more important. For example, it may not be the thickness of the choroid, but the vascularity that is important. New OCT imaging modalities with higher vascular resolution like the DREAM OCT could make this a topic of interest for future studies.

Evaluating Post-Operative Outcomes of “On-track,” “Near-track,” and “Off-track” Shoulders via Pre-Operative Imaging of Latarjet Patients in the MOON Shoulder Instability Cohort

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BACKGROUND: Bony injury of the glenoid and the humeral head are important predictors of outcomes for anterior shoulder instability. The open Latarjet procedure has become a common treatment approach for significant bone loss of the anterior glenoid, combined bone loss, or recurrent dislocations after soft tissue procedures.

PURPOSE: The concept of the glenoid track (GT) and its relation to a Hills-Sachs lesion (HSL) has been validated regarding outcomes for soft tissue stabilization procedures. However, there remains a literature gap exploring the effect of the glenoid track and Latarjet outcomes. The purpose of this study was to analyze the impact of glenoid track on outcomes of Latarjet patients.

METHODS: Latarjet surgery patients within the MOON shoulder instability cohort, treated between December 2012 and August 2023, were analyzed. Patients that did not have 2-year follow-up were excluded, unless surgical failure occurred before 2 years post-op. Pre-operative magnetic resonance imaging and computed tomography scans were used to measure percentage glenoid bone loss, glenoid track width (GT) and Hills-Sachs interval (HSI) with subsequent calculation and classification into on-track (HSI<GT) or off-track (HSI>GT). On-track shoulders were further stratified into central-track (HSI/GT<75%) or peripheral-track (HSI/GT>75%). Distance-to-dislocation (DTD) was calculated for on-track shoulders and used to determine whether the shoulder is near-track (DTD<8mm). Stratified groups were analyzed in relation to a broad definition of surgical failure defined as recurrent subluxation, dislocation, or re-operation for instability, and 2-year patient-reported outcomes.

RESULTS: 164 subjects had suitable pre-operative imaging and 134 completed 2-year post-operative outcome surveys. 83 subjects were identified as having off-track lesions and 51 subjects were classified as on-track lesions. Of the on-track lesions, there were 27 central-track and 24 peripheral-track. DTD was used to classify 36 of the on-track as near-track. Recurrent subluxation, dislocation, and instability re-operation rates for the off-track versus on-track cohorts, respectively, were 30.1% vs 27.5% (p=0.74), 3.6% vs 2.0% (p=1.00), and 1.2% vs 0% (p=1.00). Overall, any type of failure was 32.5% vs 29.4% in off-track and on-track cohorts, respectively, for an odds ratio of 1.16 (95% CI=0.54-2.47, p=0.71). Within the on-track cohort, failure rates were 25.0% for near-track, 37.5% for peripheral-track, and 22.2% for central track (p=0.23).

CONCLUSION: This study found no significant differences in negative outcomes at 2 years for patients with either “on-track” or “off-track” shoulders undergoing the Latarjet procedure, affirming this as a suitable option for patients in either category. There were no significant differences seen between near-track, peripheral-track, or central-track within the on-track cohort as well.

Global Nitrogen Flux in Human Colorectal Cancer Cells

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Nitrogen distribution in cells and tissues impacts a multitude of metabolic processes vital to their survival. The kinetic and thermodynamic reactions controlling the flux of nitrogen are sensitive to many different triggers, like substrate concentration, that can alter the flux of nitrogen allowing it to relay through different metabolic pathways. Understanding this nitrogen relay is key to elucidating healthy physiology as well as disease mechanisms. One longstanding challenge, however, is that we cannot screen how nitrogen flows in an assortment of pathways simultaneously. Therefore, we devised a method to utilize metabolic profiling and isotope tracing to measure global nitrogen flux through several metabolites to further explore how nitrogen flux may act as switch in the metabolome.

We hypothesized that if cells are treated with different nitrogen feeding and stealing conditions, then we should observe differences in the global nitrogen flux between treatments. First, we cultured HCT 116s, a human colorectal cancer cell line, and treated them with nitrogen donors like glutamine and ammonium, and nitrogen sinks like alpha-ketoglutarate and dimethyl alpha-ketoglutarate (DMKG). We also used CB839 and DON, drugs that block nitrogen release from glutamine from different positions on the structure, and the vehicles that carried them: DMSO and DPBS. After 6 hours of treatment, we analyzed the cells metabolic profile using liquid chromatography mass spectrometry (LC-MS).

We determined that glutamine can add and DMKG can remove nitrogen from the metabolic environment, which alters the production of other amino acids upstream and downstream. For example, because DMKG can go through transamination, we saw an increase in glutamate synthesis in these cells. However, with glutamine, we see an increase in asparagine which is the reaction between aspartate and glutamine utilizing glutamine’s amide nitrogen as a source. These data shaped our isotope tracing experiment, where we treated the cells with the same nitrogen donors and sinks, as well as combinations of them, to uncover the relay of nitrogen in the metabolic system. Again, after 6 hours of treatment, we analyzed our cells with LC-MS but instead generated fractional heatmaps and isotopologue distributions to map nitrogen flux.

We found an interesting increase in SAICAr with cells treated with DMKG, glutamine, and both. There were differences between the groups in whether SAICAr had increase of one, 2, or 3 nitrogen isotopes. This compound is a key intermediate in purine metabolism and is associated with the disorder adenylosuccinate lyase deficiency. Discovery of the involvement of DMKG and glutamine in SAICAr metabolism highlights the power of that this method provides as a screening tool for nitrogen metabolism in cells and tissue. Next steps include deeper analysis of profiling and isotope datasets, expanding the isotope tracing method to cover more metabolites, and coupling this technique with proteome integral solubility alterations which will aid in identifying proteins involved with nitrogen regulation without the need for chemical modification.

The Consequences of Rurality on Body Mass Index and Surgical Outcomes in Patients Undergoing Total Joint Arthroplasty

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INTRODUCTION: Social determinants of health are an important contributing factor to outcomes for surgical patients. The prevalence of obesity, defined as a body mass index (BMI) of ≥30 kg/m2, has been increasing since the end of the 20th century in the United States. Obesity is heavily correlated with the risk of developing severe knee or hip osteoarthritis due to excessive and prolonged weight-bearing resulting in degeneration of hyaline cartilage in the joint. Rural populations are particularly vulnerable, with the prevalence of obesity being 6.2 times higher than for urban residents. Definitive treatment for severe osteoarthritis that has failed non-operative management is total joint arthroplasty (TJA).

HYPOTHESIS/PURPOSE: Our goal is to evaluate differences in demographics, body composition, and complication rates between rural and urban populations seeking primary total joint arthroplasty procedures. We hypothesized that rural patients receiving total hip and joint replacements have a higher average body mass index (BMI) and higher post-operative complication rates for periprosthetic joint infection and wound complications than urban patients.

METHODS: We performed a retrospective review of all patients who underwent TJA at the University of Iowa Hospitals and Clinics (UIHC) from 04/01/2014 to 04/01/2024. We analyzed their age, BMI, race, ethnicity, TJA procedure type and postoperative complications. Patients were designated as rural or urban by zip code, using the U.S. Census Bureau's definition of urbanity (area population density >5,000 or housing unit density >2,000). Only patients receiving primary total joint arthroplasty following a diagnosis of primary osteoarthritis were included in final analyses. Only the first qualifying procedure per patient within the study's time frame was included. Statistically significant differences between rural and urban patients were found using independent t-test and chi-square analysis. IRB approved conduction of the study.

FINDINGS/RESULTS: We identified 5,093 total patients, with 3,425 patients living in urban areas, and 1,668 in rural areas. Preliminary statistical analysis demonstrated significant differences in BMI, sex, and race between groups. Women and non-white patients were more likely to come from urban zip codes. The average BMI of urban patients (32.4 kg/m2, SD= 6.8) was significantly lower than that of rural patients (33.5 kg/m2, SD=6.6), with a p-value <0.0001. Patients with a BMI of less than 30 kg/m2 seeking TJA were more likely to be from urban areas, while patients with a BMI from 30-40 kg/m2 were more likely to be from rural areas, with a p-value <0.0001. Post-operative complications did not vary significantly by geographic location. Patients receiving both hip and knee arthroplasty followed these trends.

CONCLUSION/OVERALL SIGNIFICANCE: Based on the literature review, this is the first comparative study of BMI and postoperative complication rates among rural and urban patients undergoing total joint arthroplasty in Iowa. Our findings confirm the national trend of higher obesity prevalence in rural populations. The overrepresentation of urban patients in lower BMI quintiles (BMI <30 kg/m2) indicates the capacity for this population to seek earlier care. Similarities in complication rates for both urban and rural patients indicate. that despite higher BMI in rural areas, modern perioperative care and optimization programs are capable of leveling risk between the groups. Further inquiry is necessary to determine whether complication rates differ between BMI groups or when patients are stratified by risk factors. Limitations of this study include implementing a single-center design, as well as the use of BMI as a metric for obesity. This work addresses a critical barrier to optimizing surgical outcomes by clarifying how rural-urban differences in obesity contribute to complications after TJA. By defining these disparities, our study emphasizes the need to increase patient awareness in rural areas regarding the morbidity of obesity related to osteoarthritis.

Neurosurgeon attitudes and practice patterns regarding treatment of antiplatelet-associated traumatic intracranial hemorrhage

Chase Auman BS, Nick Mohr MD, MS, Brett Faine, PharmD, MS

Introduction and Purpose

Platelet transfusion and desmopressin (DDAVP) are commonly considered for antiplatelet reversal in traumatic intracranial hemorrhage (tICH), though their clinical benefit remains uncertain due to limited supporting data. The purpose of this study was to determine the opinions of academic neurosurgeons regarding the utility of available treatments to improve tICH outcomes.

Methods

Faculty neurosurgeons at 11 academic medical centers across the United States were surveyed in-person or virtually during faculty meetings to maintain a high response rate. Survey items were designed collaboratively by clinical and methodological experts, and responses were summarized using descriptive statistics.

Results

There were 66 responses from neurosurgeons, with a response rate of 62%. Of these respondents, 33% reported never administering platelets to tICH patients taking aspirin, while only 17% of respondents never administer platelets to tICH patients taking P2Y12 inhibitors. The majority (67% and 83%, respectively) at least sometimes administer platelets. Confidence in the ability of platelet transfusion to reduce hematoma expansion (mean 60 mm, SD 23 mm on 100-mm visual-analog scale [VAS]) and improve neurological outcomes (mean 41 mm, SD 25 mm on 100-mm VAS) was highly variable. Respondents also demonstrated wide variation in their agreement with national platelet transfusion guideline recommendations (mean 52 mm, SD 26 mm on 100-mm VAS). DDAVP was reported to be used less frequently, with 46% of respondents not using DDAVP for aspirin-associated tICH and 42% not using it to treat P2Y12 inhibitor-associated tICH. Compared to platelets, there is less confidence that DDAVP reduces hematoma expansion (mean 45 mm, SD 23 mm on 100-mm VAS) and improves neurological outcomes (mean 38 mm, SD 22 mm on 100-mm VAS). Across both antiplatelet agents, the most important factor influencing the decision to administer platelets or DDAVP was the perceived likelihood of a patient requiring a neurosurgical procedure (indicated by 91% and 88% of respondents, respectively). When asked if they would be willing to enroll patients in a no-intervention arm of a clinical trial, 89% of respondents responded “yes.”

Conclusions

Academic neurosurgeons reported variation in their utilization of platelet transfusion and DDAVP to treat antiplatelet-associated tICH. They also noted uncertainty in the effectiveness of these treatments, and a substantial portion disagreed with current practice guidelines. Their responses demonstrate a lack of agreement and underscore the need for a future clinical trial to evaluate the effectiveness of these interventions.

Association between differences in pediatric autism diagnoses by clinical team and sex, age, rurality, race, and socioeconomic status

Alexis Baker, Allan Andersen, and Ali McCue

Introduction/Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and interaction with repetitive patterns of behavior and interests. Evaluations include history, observation, and standardized tools such as the Autism Diagnostic Observation Schedule (ADOS-2). Clinicians use both tools and clinical judgement to provide a diagnosis. Preliminary data from the Center for Disabilities and Development showed that ASD diagnosis rates varied by day/provider team.

Aim/Hypothesis: This study was done to determine if differences in diagnosis rates could be attributed to differences in patient populations or to identify if there are areas of potential care disparity to address. We hypothesized that there is an association between differences in autism diagnosis rates by team and patient sex, age, rurality, race/ethnic background, and Medicaid status.

Methods: An Epic report was run to identify patients who were evaluated for autism from May 2024-May 2025 at the CDD based on the provider they saw. The report included clinician, age, sex/gender, race, county, insurance, and diagnoses. The patient charts were manually reviewed to confirm ASD diagnosis or not. Other diagnostic codes from the visit, such as ADHD, intellectual disability, and speech disorders were noted. These were found manually written in the note or coded in the encounter diagnosis section. Ten patients were excluded from analysis because they were to return for repeat evaluation, had no documentation, or had an access restriction. We used logistic regression analysis in R Studio to evaluate differences in diagnosis rate and the identified patient demographics.

Results: Differences in diagnosis rate by provider were significant after accounting for differences in age, race, rurality, insurance, and gender/sex. Child and adolescent psychiatrists and developmental and behavioral pediatricians were less likely to diagnose autism compared to psychologists. Non-white children were more likely to be diagnosed with autism than their white counterparts. Children over 12 were more likely than those less than 3 years old to be diagnosed. Children covered by private insurance were more likely to be diagnosed. There were no differences in rate when accounting for rurality or gender.

Discussion/Conclusion: Previous estimates from national data show a decreasing trend in gender diagnosis ratio, from 5:1 in the early 2000s to 3-4:1 in recent years. Our finding of no difference among the two could indicate a further improvement in the recognition/evaluation in girls or a change in rate. The results of lower rates among white children align with current literature findings, which shows an opposite trend from the early 2000s. Researchers suggest that previous racial disparities in receiving a diagnosis have decreased from increased access to care. Provider-specific differences is an underdeveloped area of research, but one study found that among pediatricians, there was more certainty when giving a child an ASD diagnosis and more disagreement when ruling ASD out, especially in the case of cooccurring developmental delays. With the rates varying depending on provider type even after adjusting for sociodemographic factors, there can be further investigation into why there is a disparity such as how confident the referring provider is that the child has ASD and breaking down the assessment tool scores. The results highlight disparities in diagnosis patterns across a variety of influences. Further research can look at what providers are giving additional/alternate diagnoses and if this correlates with educational background/provider type.

Ex-vivo characterization of intracranial atherosclerotic plaques: A correlation of vessel wall histology with HR-MRI using radiomics

Medical Student: Emily Baniewicz, BS
Mentors: Edgar A Samaniego, MD MS and Osorio Lopes Abath Neto, MD PhD
Collaborators: Andres Gudino, MD

Background
Few studies have correlated the histopathological features of intracranial plaques with imaging findings. Radiomics, or the extraction of quantitative data about shape, texture, and signal intensity from imaging, may provide further insight into identifying potentially vulnerable plaques.

Purpose
We aimed to identify which radiomic features (RFs) are associated with histopathological markers of high-risk intracranial atherosclerotic plaques using ex-vivo circle of Willis (CoW) specimens.

Methods
CoW specimens were collected and preserved in 10% buffered formalin. After clot removal using Polysorbate 20 dissolved in distilled water, specimens were embedded in 2% agarose and imaged on a 3T HR-MRI scanner. Following imaging, specimens were sent to histopathology, where they were analyzed using hematoxylin and eosin (H&E) for morphology, CD68 immunohistochemistry to evaluate for macrophage infiltration, and elastichrome staining to assess the integrity of the internal elastic lamina (IEL). MR images were matched with corresponding histological slides. Regions of interest from each plaque were segmented using 3D Slicer and RFs were extracted. The Mann-Whitney U test was used to assess differences in RFs between plaques with and without internal IEL disruption and presence of macrophage infiltration.

Results
Eight ICAD specimens and one control specimen from five patients were analyzed. Among the eight vessels with evidence of ICAD, 7/8 (87.5%) showed evidence of macrophages and 6/8 (75%) demonstrated IEL disruption. In specimens that were positive for macrophages, cluster tendency (OR:1.01 [95% CI: 1.00-1.03], p=0.02), correlation (OR:1.33 [95% CI: 1.10-1.63], p=0.003), difference entropy (OR:4.22 [95% CI: 1.40-12.74], p=0.01), joint entropy (OR:3.10 [95% CI: 1.20-7.98], p=0.01), and sum entropy (OR:3.63 [95% CI: 1.29-10.30), p=0.01] were significantly different from the control specimen. In specimens with IEL disruption, inverse variance (OR:1.05 [95% CI: 1.01-1.10], p=0.03), joint energy (OR:1.07 [95% CI: 1.02-1.13], p=0.006), maximum probability OR:1.07 [95% CI: 1.01-1.13], p=0.008), and small area low gray level emphasis (OR:1.05 (95% CI: 1.01-1.11), p=0.04) were significantly different from the control specimen.

Conclusion
Radiomic features were associated with IEL disruption and infiltration with macrophages on 3T HR-MRI.

Investigating the role of intercellular junctions on corneal endothelial cell mechano-transduction signaling in Fuchs endothelial corneal dystrophy

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Introduction: Corneal endothelial cells (CECs) perform critical barrier and ion pump functions resulting in the maintenance of corneal thickness and transparency. It is known that cell confluence, or the density and of cultured cells, affects junction formation cellular transcriptional processes involved in mechano-transduction signaling cascades that lead to morphological alterations. Specifically, in tissue explants, disruptive junctional changes result in nuclear translocation of transcription factors including YAP and TAZ, which mediate changes in other pathways indicating mechanical stress and regulated cell death via ferroptosis. In Fuchs endothelial corneal dystrophy (FECD), extracellular matrix deposits called "guttae" disrupt CEC confluence. However, the contributions of intermediate markers leading to changes in YAP/TAZ signaling are unclear and are further investigated here.

Hypothesis/Purpose: We hypothesize that the mechano-transduction pathway markers critical to cellular changes in CECs with different degrees of confluence will be expressed at different levels and in different locations within cells. Markers for tight junction formation, for example, should be expressed at higher levels with increasing degrees of confluence. Markers for YAP/TAZ, on the other hand, should be expressed at lower levels, in the cytoplasm, with increasing degrees of confluence. The expression changes in other markers investigated (involved in HIPPO, beta catenin, Wnt, and frizzled pathways) indicate which of them are likely to be the true mediators of the effects that occur between changes in tight junction markers and YAP/TAZ expression and localization.

Methods: Immortalized CEC lines (B4G12 cells) were grown in biological triplicates for 48 hours *in vitro* to different degrees of confluency based on different seeding densities (50k, 300k, and 750k cells per well). qPCR was performed in technical triplicates to assess expression changes across each level of confluency in markers of four different groupings: junction formation, intermediate signaling pathways, YAP/TAZ, and ferroptosis. Immunohistochemistry was performed for cells of different degrees of confluency to assess junction formation and YAP/TAZ localization.

Results: Based on qPCR, compared to wells seeded with 50k cells, wells seeded with 300k and 750k cells had increased expression of tight junction proteins (TJP1 showed a 0.63x fold-change for 300k cells and a 0.60x fold-change for 750k cells; CDH2 showed a 0.6018x fold-change for 300k cells and a 0.57x fold-change for 750k cells). Compared to wells seeded with 50k cells, wells seeded with 300k and 750k cells also showed lower expression levels of a beta catenin marker (CTNNB1), TAZ, and a ferroptosis marker (GPX4); they showed higher expression levels of pathway markers for Wnt (WNT5A, WNT5B), frizzled (FZD4), HIPPO (STK3), other ferroptosis markers (ASCL4, NCOA4), and YAP. In immunohistochemistry studies, tight junction proteins (TJP1 and CDH2) appeared to have increased expression at the cell membrane with increasing degrees of confluency. Expression of YAP and TAZ appeared relatively unchanged across the three groups.

Conclusions/Significance: As expected, tight junction proteins appeared to be expressed at higher levels in cells with increasing degrees of confluency based on qPCR and immunohistochemistry results, indicating that higher seeding densities of cells correspond to increased tight junction formation. qPCR results also suggested that higher seeding densities led to increased expression of YAP but decreased levels of TAZ; their potential functions as opposite mediators should be studied in greater detail. qPCR results also showed that the beta catenin pathway may be implicated as a mediator between tight junction proteins and YAP/TAZ nuclear localization, since its studied marker (CTNNB1) was expressed at a lower level in the groups of higher confluence. Ultimately, these studies will be repeated in primary cell lines from tissue explants to confirm findings and guide further studies using western blots and immunohistochemistry staining procedures.

Title of the presentation: ESKAPE Pathogen Transmission in an Anesthesia Work Area During Cesarean Delivery: A Quality Improvement Project

Your name, your mentor's name, and any other collaborators: Arnav Bhushan, BA; Franklin Dexter, MD, PhD ; Carmen Brindeiro, PhD; Randy W. Loftus, MD; Unyime Ituk, MD

Introduction with background/rationale: Surgical site infections following cesarean delivery pose significant risks to maternal health and increase healthcare costs. The University of Iowa's cesarean delivery SSI rate is approximately 2.7%, which is typical of national benchmarks, but stable rather than decreasing. Multiple earlier studies found that anesthesia work areas serve as reservoirs for *Staphylococcus aureus* and other ESKAPE pathogens (*Enterococcus faecium*, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter*), causing postoperative infections. However, pregnancy was an exclusion criterion.

Hypothesis/Purpose: We measured the frequency of ESKAPE pathogen transmission occurring within and between cesarean delivery cases at the University of Iowa's busiest obstetric operating room. A secondary objective was to quantify the percentage contribution of anesthesia machine contamination, which we expected to be less than at other inpatient surgical suites because cesarean deliveries rarely include general anesthesia. Measuring pathogen transmission informs targeted interventions, such as ultraviolet-C disinfection or enhanced hand hygiene.

Methods: This quality improvement project examined consecutive non-emergent cesarean deliveries in a single obstetric operating room (OR#2). Samples were collected from May 27, 2025, through August 29, 2025, on weekdays that had at least two cesarean deliveries. Research assistants were available for data collection on 54 of the 68 predetermined workdays. For each case, 11 swab sites and four hand samples collected with balanced electrolyte solution were sampled before and after surgery, including patient nares, axilla, groin, anesthesia attending and assistants' hands, anesthesia valve/dial, anesthesia's Omnicell and computer mouse, and intravenous access points. Samples were cultured at RDB Bioinformatics (Coralville) to detect *S. aureus* and other ESKAPE pathogens. Contamination was quantified in colony-forming units per surface area sampled (CFU). Anesthesia machine contamination was quantified in CFU. A threshold of ≥100 CFU was used to define significant contamination, consistent with previously established benchmarks. Wilcoxon-Mann-Whitney testing was applied to compare contamination levels between cases with and without observed transmission

Findings/Results: The study was conducted over a 12-week period (May 27–August 26), encompassing 76 cases across 47 distinct days, including 29 case pairs. The overall incidence of intraoperative ESKAPE pathogen transmission was 29% (23/76), comparable to the 20.48% benchmark reported in *Wall et al., J Clin Anesth 2022*, where ≥20% transmission was associated with surgical site infections ($p < 0.0001$). (The observed 29% will be greater, as pathology results for gram negatives are pending.) There were 3 between-case events, meaning a pathogen was transmitted from one patient to the next. By organism, methicillin-sensitive *S. aureus* accounted for 25% (19/76), methicillin-resistant *S. aureus* 7% (5/76), and vancomycin-resistant *Enterococcus* 4% (3/76). Transmission sources were traced to the hands of anesthesia providers in 18% (14/76), environmental reservoirs (mouse, Omnicell) in 11% (8/76), patient reservoirs in 5% (4/76), and the intravenous lumen in 1% (1/76). Contamination was measured across 15 reservoirs, with anesthesia machine valves/dials showing a median of 34 million CFU (25th percentile: 2.1 million; 75th percentile: 99 million). The lowest Wilcoxon-Mann-Whitney test P-value for the association of contamination and transmission was P=0.040 (mouse/Omnicell); however, after correction for multiple comparisons, no reservoir's contamination was statistically associated with transmission. Thus, matching our secondary hypothesis, unlike for non-obstetric cases, no reservoir had a significant association.

Conclusion/Overall significance/Broader perspective: ESKAPE pathogen transmission, including *Staphylococcus aureus*, were frequently observed in obstetric anesthesia work areas during cesarean delivery, with an incidence comparable to benchmarks linked to increased surgical site infections. Although anesthesia machine contamination demonstrated high colony counts, it did not correlate significantly with transmission. Future efforts will focus on hand hygiene (e.g., placement of hand sanitizer dispensers) and environmental decontamination.

Associations Between Early Childhood Anesthesia Exposure and Later Language and Executive Function Outcomes

Authors
Shalini Birari, BS; Amy L Conrad, PhD; Robert Block, PhD

Introduction/Background

Around 6 million children undergo general anesthesia each year in the United States alone, raising concerns about the potential for any long-term cognitive impacts. Past animal studies done in rodents and nonhuman primates have shown that commonly used anesthetic agents can result in lasting deficits in learning and memory. In humans, however, the evidence is mixed. While some studies have demonstrated that early exposure may have effects on language and executive function, others have shown no significant impact on neurocognitive outcomes. This uncertainty highlights the need for further research to clarify whether timing, duration, or frequency of early anesthesia exposure contributes to long-term differences in cognitive outcomes.

Hypothesis/Purpose

We hypothesized that earlier age of first exposure, longer total duration, and greater number of exposures before age 4 would predict poorer language and cognitive outcomes in later childhood.

Methods

Children with a history of anesthesia exposure before age 4 completed standardized assessments of language (Clinical Evaluation of Language Fundamentals, CELF) and executive function (NIH Toolbox). Regression models examined age at first exposure, total duration of exposure before age 4, and total number of exposures before age 4. Covariates included sex and age at testing. Surgery severity was included as a predictor to evaluate potential moderation of relationships between anesthesia and outcomes.

Findings/Results

A total of 360 adolescents completed testing (mean age = 13.71 (1.14)) and had information on at least one of the measures of anesthesia exposure. Across all models, age at testing was generally associated with higher performance across CELF and NIH Toolbox measures, despite use of age-corrected scores. However, older children scored lower on CELF sentence repetition tasks. In contrast to age, the anesthesia exposure variables, including age of first exposure, total duration, and number of exposures, were not consistently associated with worse outcomes. Earlier surgery and a greater number of exposures were unexpectedly associated with higher performance on language (Formulating Sentences) and working memory (NIH List Sorting), respectively. There were significant interactions with severity, where the relationship was stronger for less-severe procedures. These findings should be interpreted with caution given the number of analyses run and possibility of type I error[AC1] .

Conclusion/Overall Significance

In this cohort, anesthesia exposure before the age of 4 was not associated with consistent long-term language or cognitive deficits. Instead, developmental age at testing explained most of the observed variability. These findings align with past studies indicating that early anesthesia exposure may not significantly impact cognitive development in children. However, given the overall mixed evidence regarding this topic, further investigation is warranted to better guide practices towards anesthesia exposure in children going forward.

Analysis of 3D ACL Reconstruction Tunnel Position Utilizing Weight Bearing CT

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INTRODUCTION: Accurate femoral and tibial tunnel placement during ACL reconstruction (ACLR) is critical in restoring normal knee biomechanics. Prior research suggests that deviations from the anatomic ACL footprint can alter rotational stability and compromise long-term outcomes.

PURPOSE: This study aims to quantify 3D femoral and tibial tunnel positions in ACLR patients and evaluate the reliability of these measurement methods.

METHODS: Using 48 weight-bearing CT (WBCT) scans from a previously collected cohort of 91 ACLR patients between 2023 and 2025, tibia and femur models were semi-automatically segmented. The tibia and femur were aligned to a standardized anatomical coordinate system based on a 2012 study by Dr. Austin Ramme and Dr. Brian Wolf. Cylinders representing the ACLR tunnel were fit to both the tibia and tunnel in the standardized coordinate system. Vector and position data were derived from the long axis of the aligned cylinders. Tunnel data was exported, and the anterior-posterior and medial-lateral tunnel angles were calculated for both femoral and tibial tunnels relative to the anatomical reference axes. These angles were used to assess tunnel position and their variability; with 10 ACLR patients randomly selected for inter- and intra-observer reliability assessment from two observers.

RESULTS: Compared to the findings in the 2012 study, 3D femoral and tibial tunnel positions from the WBCT scans in this study showed substantial differences on average in their deviations from the reference axes. Individual ACLR tunnels in this study also showed patient variability. Across the 10 randomly selected cases and six angle measures calculated for each case, intra-rater intraclass correlation coefficient (ICC) values were 0.88 or higher, while inter-rater ICC values were 0.75 or higher except for one angle. Mean differences were less than 3 degrees, independent of it was the same or different rater.

CONCLUSIONS: ACLR tunnel position has changed in the past decade, and substantial variation in tunnel placement still exists between individual cases. Using WBCT and a quantifiable 3D reference provides a reliable method for measuring 3D ACLR tunnel position and could be applied to future studies where tunnel position is an explorable variable.

Objective Assessment of Functional Recovery after Hip Preservation Surgery: Use of a novel cell-phone application to collect gait metrics

Aaron Blom, John C. Wheelwright, Yumeng Gao, Michael Willey

Background:

Objective assessment functional recovery after orthopaedic surgery can be challenging. Traditional methods rely on patient-reported outcome measures (PROMs) which are subject to recall bias, irregular collection, and limitations in capturing daily functional changes. Passively collected smart phone data may have the potential surpass these limitations and offer a more detailed, accurate, and descriptive picture of functional recovery after surgery. The Apple® Health App passively collects step count, walking speed, step length, double support percentage, and asymmetry percentage—providing a potentially innovative approach to objectively measure postoperative recovery. This study aimed to evaluate recovery across these gait metrics following hip preservation surgery and define timelines for return to baseline activity.

Methods:
Adolescents and young adults (aged 10-55 years old) that underwent hip preservation surgery (hip arthroscopy, periacetabular osteotomy (PAO), and/or femoral osteotomy) were enrolled in this study. Subjects were eligible if they had a personal smart phone capable of downloading applications and were familiar with using phone-based applications. Within the cohort, five gait metrics were analyzed: step count, walking speed, walking step length, double support percentage, and asymmetry percentage. Baseline values were defined as the median of data collected between 30 and 15 days prior to surgery. Postoperative values were summarized in 2-week intervals up to 6 months after surgery. Return to baseline was defined as the first time the postoperative median value was greater than or equal to baseline for step count, walking speed, and step length, or less than or equal to baseline for double support percentage and asymmetry percentage, where lower values indicate improvement. Recovery trajectories and the proportion of patients returning to baseline over time were evaluated for each metric. Data are presented as median (Q1 - Q3) for numeric variables due to skewed and/or non-normal distributions, and as count (%) for categorical variables. All statistical analyses were performed using R version 4.5.0.

Results:
60 participants were enrolled in the study. Overall, patients who had a PAO with or without hip arthroscopy returned to baseline more slowly than those who had arthroscopy only. For patients undergoing only hip arthroscopy (n=18), over 50% of patients had returned to baseline for step count by postoperative week 10. By postoperative week 14, over 50% of patients had returned to baseline for walking step length. Asymmetry percentage reached 50% return to baseline by postoperative week 16, while double support percentage and walking speed reached this threshold by postoperative week 18. By 6 months (week 26) postoperatively, all five metrics had reached their maximum observed rates of return to baseline: 88.9% for step count (week 24), 72.2% for walking step length (week 24), 64.7% for double support percentage (week 24), 76.5% for walking speed (week 24), and 64.7% for asymmetry (week 18). For patients undergoing PAO +/- hip arthroscopy (n=34), over 50% of patients had returned to baseline for walking step length by postoperative week 14. Step count reached 50% return to baseline at postoperative week 16, while walking speed and double support percentage reached this threshold by postoperative week 18. Walking asymmetry percentage did not reach 50% return to baseline during the 6-month period. By 6 months (week 26) postoperatively, four of the five metrics had reached their maximum observed rates of return to baseline: 57.6% for step count (week 20), 61.8% walking step length (week 20), 54.5% for walking speed (week 18), and 47.1% for walking asymmetry (week 18), while double support percentage reached a maximum rate of return to baseline of 57.7% at week 28. These findings suggest that most patients regained core walking function between weeks 14 and 18, with continued recovery through month 6.

Conclusion:
We found that recovery timelines vary across gait domains, but most patients can expect to reach baseline walking function for key metrics between 14 and 18 weeks after hip preservation surgery. Importantly, these objective measures provide a continuous, patient-specific recovery trajectory that may supplement traditional function-based PROMs and improve postoperative counseling. Integrating smartphone-based data collection with standard clinical follow-up could enhance precision rehabilitation strategies and shared decision-making in young, active patients undergoing hip preservation surgery. Future studies correlating these metrics with PROMIS and other validated outcome measures will further refine clinical utility.

Intraoperative phenylephrine use is not associated with acute kidney injury in patients undergoing burn surgery

Samuel Boes, BS
Mentors: Alexander Kurjatko, MD MPH; Colette Galet, PhD Collaborator: Sadaf Akbari, MD

Introduction. Burns are characterized by pathologic third-spacing of fluid leading to intravascular volume depletion, making hypotension a threat. Associations between intraoperative hypotension and acute kidney injury (AKI), cardiac complications, and mortality have been demonstrated in prior studies. Phenylephrine is a vasopressor commonly used to manage intraoperative hypotension. In a retrospective study, Khanna et al. demonstrated an independent association between intraoperative phenylephrine exposure and AKI in adults undergoing noncardiac surgery. However, the association between AKI and intraoperative phenylephrine exposure has not been explored in burn injured populations. Herein, we examined the association between intraoperative phenylephrine exposure and AKI and mortality among burn patients.

Hypothesis. We hypothesized that there would be an association between intraoperative exposure to phenylephrine and AKI. Additionally, we speculated that there would be no significant association of mode of administration and AKI and other outcomes among this population.

Methods. This was a retrospective cohort study. All adult burn patients admitted to our institution's burn treatment center from July 1, 2015 to June 30, 2024 who required at least one operation and had a postoperative serum creatinine value present within 7 days of their first surgery during the index admission were included in this study. Patients admitted for other traumatic injuries (e.g., frostbite) were excluded. Data were abstracted from our institution burn registry and electronic medical record. The primary exposure was intraoperative phenylephrine during the first burn-related surgery. Phenylephrine administration was further classified as bolus dosing, continuous infusion, or both. Outcomes were analyzed by mode of administration. Serum creatinine values from hospitalizations unrelated to the burn obtained within 90 days prior to burn presentation to our burn center were taken as baseline. If no such value existed, baseline creatinine was estimated by race and age per Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Primary outcomes were postoperative AKI and in-hospital mortality. Postoperative AKI was defined in accordance with KDIGO guidelines and based on serum creatinine. Secondary outcomes were hospital length of stay and discharge disposition. All analyses were performed using SPSS 28.0 (IBM, Chicago, IL), and $p < 0.05$ was considered significant. This study was approved by our university institutional review board.

Results. A total of 639 patients were included in this study; 393 received intraoperative phenylephrine. Of those 393, 247 received phenylephrine by bolus alone, 17 by infusion alone, and 129 by both modes. Patients in the phenylephrine group were significantly older (58 [42, 69] vs. 47 [33, 59] years, $p < 0.001$). No significance was observed in other demographics, comorbidities, and burn injury severity. The phenylephrine group was more likely to have a lower GCS on presentation (15 [14, 15] vs. 15 [15, 15], $p = 0.038$) and to receive intraoperative vasopressin (12.5% vs. 3.3%, $p < 0.001$) and ephedrine (17.8% vs. 8.1%, $p < 0.001$). There was no significant difference in postoperative AKI between the two groups (9.4% vs. 7.3%, $p = 0.358$) or in-hospital mortality (3.1% vs. 2.4%, $p = 0.648$). The phenylephrine group remained hospitalized longer (14 [9, 22] vs. 11 [7, 17] days, $p < 0.001$), received more burn related surgeries (1 [1, 2] vs. 1 [1, 2], $p = 0.017$), suffered preoperative AKI more often (27.8% vs. 18.3%, $p = 0.007$), and experienced postoperative hypotension more often (20.7% vs. 7.7%, $p < 0.001$) than the control group. Patients who received intraoperative phenylephrine were more likely to require higher level of care following discharge than the control group ($p = 0.025$). Patients who received phenylephrine infusion alone were more likely to suffer postoperative hypotension (infusion alone: 47.1% vs. bolus alone: 17.4% vs. both: 23.4%, $p = 0.009$), postoperative hyperglycemia (82.4% vs. 51.2% vs. 55.5%, $p = 0.041$), and die in the hospital (11.8% vs. 3.6% vs. 0.8%, $p = 0.032$) than those who received bolus alone or both bolus and infusion. Patients who received phenylephrine by bolus alone stayed in the hospital for less time than did those who received an infusion alone or in concert with boluses (18 [13, 31.5] vs. 12 [7, 20] vs. 18 [11, 28], $p < 0.001$).

Conclusion. Intraoperative phenylephrine use was not associated with increased risk of postoperative AKI or mortality in our burn cohort but was linked to postoperative hypotension and longer hospitalization. While these findings suggest phenylephrine may be safe from a renal perspective, prospective studies are needed to clarify whether alternative agents or dosing strategies can improve hemodynamic stability and outcomes in this vulnerable population.

Characterization of Retinal and Optic Nerve Changes in a Novel Mouse Model of Progressive Retinal Degeneration

Student: Architha Bommena
Mentor: Matthew Harper

Purpose: The purpose of this study was to characterize a new line of mice with progressive retinal degeneration using optical coherence tomography.

Methods: A single Jackson Diversity Outbred (JDO) mouse was observed with outer retina abnormalities. This mouse was used to generate progeny via breeding with C57BL6/J mice. The progeny were backbred to the founder mouse one (N1) or two (N2) times. The progeny were subsequently intercrossed. The structure of the retina was evaluated at different timepoints using optical coherence tomography (OCT), a non-invasive technique to image the retina. Manual retinal segmentation was performed to measure the following retinal thickness layers: the outer nuclear layer (ONL), retinal ganglion cell complex (RGCC), and total retinal thickness. Optic nerve cross-sectional area was quantified using the OCT images. ANOVA and linear regression analyses were conducted to determine associations between retinal thickness and optic nerve area.

Results: We observed significant degeneration and thinning in N1 and N2 mice compared to F1 mice. F1 mice maintained stable ONL and total retinal thickness until 30 weeks, consistent with normal age-related degeneration. In contrast, N1 and N2 generations exhibited significant thinning in ONL and RGCC as early as 10 weeks. Total retinal thickness loss was most pronounced in the N2 generation mice. While F1 optic nerve head (ONH) area remained consistent over time, later generations showed increased ONH area.

Conclusions: Overall, ONL and RGCC thinning parallel each other in N1 and N2 generation mice, indicating that both the photoreceptors and ganglion cells are impacted by this degenerative phenotype. N2 mice are consistently the most affected across all retinal metrics, supporting the idea that increased backcrossing to the founder amplified the phenotype and its severity. Additionally, backcrossing affects ONH morphology, although not necessarily in parallel with retinal thinning, suggesting additional underlying pathology. Genotyping of the founder mouse is currently underway, and future work will focus on longitudinal monitoring of these backcross generations as they age to further characterize disease progression and inheritance patterns.

Untangling copathology: tau and TDP-43 in human brain tissue from dementia patients

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Introduction: Dementia poses a major burden to individuals and society, and this is expected to rise with an aging population. Protein aggregation, including modifications such as hyperphosphorylation, is a hallmark of neurodegenerative diseases. Tau and TDP-43 are both commonly implicated in dementias, typically associated with different diseases but shown to colocalize in certain cases. Because most patients present with mixed pathology, studying copathologies is important for understanding disease progression, diagnosis, and treatment. The Aldridge Lab previously observed tau and TDP-43 staining in the same cells of the brainstem locus coeruleus (LC) in adjacent thin sections. Since this copathology is not well established in the literature, the question arose whether the costaining was genuine or an artifact.

Purpose: To determine whether tau and TDP-43 costaining in human brain tissue represents true colocalization or results from artifacts such as autofluorescence or nonspecific binding.

Method: Human brain tissue from the LC and anterior cingulate cortex (ACC) was obtained from the Iowa Neuropathology Research Laboratory. Sections were paraffin-embedded, mounted, antigen-retrieved with a low-pH buffer, and photobleached with blue light for 24 hours to reduce autofluorescence. Slides were incubated with a primary antibody mixture (anti-sheep TH, phosphorylated tau [AT8], and phosphorylated TDP-43) in normal donkey serum at 4°C for 12–16 hours in a humidified chamber box. The following day, sections were incubated at room temperature with secondary antibodies (Alexa Fluor 488, 568, and 647). Slides were counterstained with DAPI, cover-slipped, and imaged with a slide-scanning microscope (10x) and a confocal microscope (60x).

Results: Confocal imaging revealed distinct patterns of tau and TDP-43 overlap in the LC. There was a high degree of overlap in cells stained for tau and TDP-43 in the LC: 8/9 TDP-43 positive neurons were also positive for tau, and 8/11 tau positive neurons were also positive for TDP-43. The staining of TDP-43 showed different patterns, where there was hazy staining of neuromelanin, nuclear staining, or staining in the cytoplasm consisting of bright dots. Next, ACC sections were imaged to examine differences between brain regions. The staining patterns of tau and TDP-43 overlap in the ACC were very similar to that in the LC with some slight differences. In the ACC, 18/22 TDP-43 positive neurons were also positive for tau, and 18/25 tau positive neurons were also positive for TDP-43. This was still a high degree of overlap, but less so than in the LC. Similar TDP-43 staining patterns arose, where there were some bright dots and places with a faint haze. Although, the ACC does not have neuromelanin like the LC so there was no staining of neuromelanin.

Conclusion: These findings support true colocalization of tau and TDP-43 in both the LC and ACC. To enable consistent quantification, qualitative criteria were developed: bright dots of TDP-43 staining was counted as positive, while hazy and/or strictly nuclear staining was counted as negative. Because staining often exists along a continuum, consistent criteria are essential. Future directions include higher-resolution confocal imaging on the ACC sections to determine whether tau and TDP-43 signals are superimposed or distinct, DAB immunohistochemistry for greater sensitivity, and incorporation of positive and negative controls. With evidence supporting true costaining, future studies can investigate the biological significance of tau/TDP-43 copathologies in dementias.

The Impact of Maternal Depression and Its Treatment on Offspring Cardiac Outcomes

Student: Brynn Bowers

Mentor: Sarah E. Haskell, DO

Collaborators: Dilara Mat, Adrianne Rahde Bischoff, Donna Santillan, Scott Stuart, Patrick J. McNamara, Tarah T. Colaizy, Benjamin E. Reinking

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Background: Approximately 20% of pregnant women experience depressive symptoms during the perinatal period. The most common treatment for depression is selective serotonin reuptake inhibitors (SSRIs), currently prescribed to 10-15% of all pregnant women. Our prior research suggests smaller left ventricular dimensions with SSRI exposure in animal models and a pilot human study, but there is a paucity of data on the cardiovascular outcomes of infants born to depressed mothers. We hypothesized that in utero SSRI exposure will lead to reduced left ventricular size and cardiac function.

Purpose: Determine the impact of maternal depression and its treatment on offspring ventricular size and cardiac function.

Methods: Pregnant women, ages 18-45, with or without depression were prospectively enrolled in our study. Data included in this study analysis is from the first 100 enrolled subjects and their offspring. A Structured Clinical Interview for DSM-V Axis I Disorders (SCID) was performed to confirm the diagnosis of major depressive disorder (MDD). Validated surveys were performed to assess maternal depression throughout pregnancy. Surveys and medical charts were reviewed to assess depression treatment. Term infants underwent targeted neonatal echocardiography at 24-48 hours.

Results: In total, 87 pregnant women and 83 infants were included in our analysis. Pregnant women were classified into 4 groups: never-depressed, past MDD, current MDD on SSRIs, and current MDD receiving psychotherapy. Differences were noted in maternal marital status, education level, and employment ($p<0.05$). Maternal depression scores demonstrate the absence or remission of depression in all 4 groups. No differences were observed in newborn demographics, though premature infants were noted only in groups with current depression. Significant differences were observed between groups in mitral valve annulus, left ventricular area in diastole, relative wall thickness, left ventricle (LV) stroke volume, LV ejection fraction, and PDA presence ($p<0.05$). When specifically evaluated for depression exposure, our findings suggest smaller LV dimensions in infants of mothers on current SSRI therapy but not in infants of mothers with current or prior depression.

Conclusions: The study is ongoing but our interim analysis suggests an SSRI-induced small LV phenotype consistent with our prior animal studies. We anticipate this study at the time of completion will be beneficial in evaluating the role of maternal depression and effects of treatment on infant cardiovascular outcomes.

Impact of a reduction of indications for mandatory newborn umbilical testing for illicit substance exposure

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Background:
Substance use during pregnancy is an ongoing public health issue and a major preventable cause of maternal mortality. Stigma and fear of legal reporting leads many patients to avoid care or disclosure, ultimately causing increased negative outcomes. While the American Medical Association (AMA) and American College of Obstetricians and Gynecologists (ACOG) support a treatment-focused approach, the inconsistent policy landscape across the U.S. allows for a criminal justice dominated system to persist. Given the significant legal and social repercussions of substance use in pregnancy, testing processes must be designed in a socially conscious and ethically informed manner. UI Healthcare uses risk based criteria to determine if umbilical cord testing for substances is indicated. This criteria has been the subject of much debate on a local and statewide level. In February 2023, a narrowed list of risk indications was instituted by the Department of Pediatrics to minimize biased and unindicated testing. This study evaluates the impact of the policy change on testing results.

Methods:
A retrospective chart review of medical records was completed for a cohort of 356 babies and their birthing parent whose umbilical cords underwent substance testing following delivery from February 12th, 2023, to October 15th, 2024. Patient demographics, obstetrical history, indications for umbilical cord testing and the results were collected. Data from previous review at UI Healthcare on umbilical cord testing prior to reduced indications served as a control. Open Epi 3.02 was used for statistical comparisons with t-test, chi square and fisher exact tests as indicated.

Results:
Demographics: 356 individual dyads were reviewed. The majority of subjects with umbilical cord tests identified as white (243, 68.3%), with 57 subjects reported as Black (16.0%). The majority had public insurance (212, 59.6%).
Umbilical cord drug screening results: 87 (24.4%) of umbilical tests returned positive for substances and 63 (72.4%) showed non-prescribed substances. The most common substance found was marijuana (THC) (55, 85.9%). Additionally, 12 (18.8%) showed stimulants, 4 (6.3%) opiates, and 1 (1.6%) benzodiazepines. When comparing data before and after narrowed indications, there was no statistically significant difference in the percent of umbilical cord tests that yielded a positive result for illicit substances. There was a significant reduction in testing ordered for subjects with public insurance (64.9% vs 59,6%, p=0.0391).
Inappropriate Tests: On review, it was found that the majority (236, 66.3%) of ordered umbilical tests did not meet the narrowed criteria for testing and the documented indications required to order testing were inaccurate. 82 (34.7%) of inappropriate tests marked “active alcohol use” on the cord order but had reported tobacco use and no record of alcohol use was found. The indication of “active alcohol use” was checked significantly more after the reduction of indications (28.2% vs 45.5%, p<0.000001), likely due to the use of this indication to test persons with tobacco use, an indication that was removed from the testing policy. In fact, significantly less subjects in this cohort reported alcohol use in pregnancy than prior to the policy change (5.3% vs 1.7%, p=0.0374). 52 (22.0%) of tests marked “active non-medical drug use” on the cord order, but notes state a history of substance use was the indication, which had been removed as an accepted indication. 24 (10.2%) of inappropriate tests marked “no prenatal care” on the cord order, but patients had engaged in late or less than recommended number of visits. 11 tests (4.7%) marked “no” for all indications on the cord order, but testing was sent. Of the 236 umbilical test that were not ordered based on the narrowed policy of risk factors, only 20 (8.5%) were positive for an illicit substance. 15 (75.0%) of these were positive for THC only, 3 (15.0%) were positive for stimulants, and 2 (10.0%) were positive for opiates. 100% of positive cord tests that were unindicated resulted in a formal CPS report.

Conclusions:
Two-thirds of umbilical cord tests ordered during the study period were unindicated according to the new narrowed criteria. Concrete patterns of discrepancies were identified between the charted indication in a patient’s medical record and the indications checked on the umbilical cord drug testing order form. After the reduction of indications was implemented, there was no statistically significant changes in the proportion of tests positive for an illicit substance. This lack of statistical significance may be attributed to the relatively high proportion of drug tests in the study that did not follow the new policy. Of the unindicated tests ordered, only 8.5 % were positive and <3% percent resulted from an illicit substance other than THC, which was removed from the umbilical cord drug panel in October 2024. These results indicate a disconnect between the updated policy and the enduring culture surrounding neonate umbilical cord testing. Education and advocacy across departments and institutions is required to put change into practice. Unconscious bias training may be helpful to reduce the number of unindicated tests and allow for testing of the intended patient population.

Are Artificial Sweeteners a Useful Tool For Intentional Weight-loss?: Systematic Review and Meta-analysis

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Introduction: Artificial sweeteners (AS) provide sweet taste without adding calories as part of reduced-calorie diets for the management of obesity. However, the literature on artificial sweetener consumption and bodyweight is unclear due to conflicting outcomes between observational studies and randomized-controlled trials (RCTs) and the heterogeneity of RCT study designs.

Purpose: Assess via meta-analysis of human randomized-controlled clinical trials the effect of artificial sweetener consumption on body weight management in the context of intentional weight-loss and weight-loss maintenance protocols.

Methods: Pubmed, SCOPUS, and Cochrane databases were systematically searched, from inception to November, 2024, for RCTs comparing the efficacy of weight-loss protocols that included AS consumption with controls which did not. Statistical analysis was performed in R software 4.4.1., a DerSimonian and Laird random-effects model was employed to compute mean differences (MD) and Standard mean differences (SMD) with 95% confidence intervals (CI), and a p-value of < 0.05 was considered statistically significant. Heterogeneity was examined with the Cochran Q test, prediction interval, and I^2 statistics. The results were reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guideline. The protocol was prospectively registered in PROSPERO under CRD42025634280.

Results: There were 7 studies (n=1,479) that met the inclusion criteria for active weight-loss outcomes, and 4 studies (n=656) for a separate analysis of weight-loss maintenance outcomes. After a mean active weight-loss period of 18 weeks, there were no statistically significant differences for the primary outcome of body weight (MD: 0.0373 Kg, 95% CI: [−1.0179; 1.0924], P = 0.945, I^2 = 78.4%) nor for the secondary outcomes of waist circumference and systolic blood pressure. There were small but statistically significant differences favoring control for the secondary outcomes of diastolic blood pressure (MD: 1.7672 mmHg, 95% CI: [0.1106; 3.4237], P = 0.037, I^2 = 0.0%) and body mass index (MD: 0.4547 Kg/cm^2, 95% CI: [0.1091; 0.8004], P = 0.010, I^2 =0.0%). Data for weight-loss maintenance was similar for body weight (SMD: −1.8364, 95% CI: [−4.8750; 1.2021], P = 0.236, I^2 = 91.4%), waist circumference, and systolic blood pressure. Qualitatively, all AS groups achieved statistically significant decreases in body weight during active weight-loss, and subjects in the AS groups in 3 of the maintenance studies maintained all weight-loss, with those in the fourth study maintaining the majority.

Conclusion: Subjects in both AS and control groups achieved significant weight-loss and weight-loss maintenance in RCTs with no clinically significant differences. AS consumption may be useful for aiding in weight-loss and weight-loss maintenance depending on individual dietary preferences and craving responses during weight management protocols.

Reproducibility and Inter-Rater Agreement of Human Readers in Nystagmus Waveform Classification

Student: Anthony Chen **Mentor:** Alina Dumitrescu

Collaborators: Kristin Davis, Joel Vandelune, Veronica Peotta-Jacobsen, Fangfang Jiang, Gideon Zamba, Arlene Drack

Background: Nystagmus is a clinical symptom that manifests as abnormal, repetitive, and involuntary eye movements. Nystagmoid eye movements are characterized by their direction, amplitude, frequency, and foveation time (time spent on target). An understudied area of diagnostic testing for nystagmus is waveform analysis, which describes eye recordings of nystagmus based on the types of movement patterns exhibited. There is some preliminary evidence that suggests that clinical characteristics of nystagmus movements may indicate the underlying etiology; however, this remains unproven. A significant limitation of using eye movement descriptions as a diagnostic tool is the subjectivity of eye movement evaluation by clinicians. Video recording of eye movements and analysis of the tracings of recordings are intended to improve the reliability of the analysis.

Purpose: This prospective study aims to analyze the reproducibility between human interpreters of eye movement recordings by measuring inter-rater agreement.

Methods: This prospective cohort study recruited patients who presented to the University of Iowa Ophthalmology Department with nystagmus. Patients underwent a comprehensive workup to diagnose the cause of nystagmus, followed by a video recording of their eye movements. Patients were recorded under 20 different conditions, including various directions of gaze and illumination. Two independent raters assigned waveform classifications to each recording based on waveform morphology while blinded to each other's assignments. Raters selected from a total of 13 waveform classifications, distinguished based on the patterns of saccades, foveation, and slow-phase movement. Assigned classes were compared and labeled as matches, non-matches, or unmatched. Inter-rater agreement was analyzed using percent agreement, unweighted Cohen's Kappa and Brier score. Cohen's Kappa measures agreement after taking into account agreement by chance, and Brier score measures the accuracy of the raters' classifications.

Results: 44 patients have been enrolled and assigned waveform classes, which produced a total of 943 comparisons. A high number of conditions were marked as "no nystagmus" due to the absence of any nystagmoid movement in certain lighting conditions or gaze directions. A separate "exclusion group" was analyzed that excluded all "no nystagmus" classifications to not inflate inter-rater agreement.

The percent agreement is 67.0% for all comparisons and 53.0% in the exclusion group. These groups have a Kappa value of 0.569 (95% CI, 0.530–0.609) and 0.464 (95% CI, 0.413–0.514) respectively, which both correspond to *"moderate"* agreement. The Brier scores are 0.0645 and 0.0383 respectively, indicating higher accuracy.

Further analysis grouped the 13 classes into 6 broader categories based on shared characteristics, which improved inter-rater agreement compared to the standard analysis. Percent agreement is 73.4%, Kappa value is 0.633 (95% CI, 0.594–0.671) and Brier score is 0.0849 in the group with all comparisons and is 65.7%, 0.531 (95% CI, 0.474-0.588) and 0.0611 respectively in the exclusion group.

Conclusions: This study demonstrates that automated recordings of nystagmus and subsequent waveform classification are possible. The subjectivity and lower reliability of human readers in describing/analyzing the tracing of nystagmus are demonstrated. While some specific waveform classes can be reliably classified, others suffer from significant inter-rater disagreement. Using broader categories helps reduce inter-rater disagreement and is an avenue of further study. A more reliable and objective method using machine learning should be established to classify nystagmus more accurately.

Assessment of prognostic value of baseline hematologic profile in cutaneous T-cell lymphoma

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Background: Cutaneous T-cell lymphomas (CTCL) pose a unique challenge to diagnosis and management due to their protean clinical manifestations, variety of pathologic findings, and lack of reliably effective and durable treatments. Occupying the intersection between oncology and dermatology, CTCL encompasses both primarily skin disease as represented by mycosis fungoides (MF) and leukemic disease, as represented by Sezary syndrome (SS). Optimal management of CTCL requires accurate staging, and currently the NCCN (National Cancer Consortium Network) recommends Tumor-Node-Metastases-Blood (TNMB) integration. With respect to the blood category in staging for CTCL, stratification is based upon peripheral blood flow cytometry (PBFC), which measures absolute counts of either $CD4^+CD7^-$ or $CD4^+CD26^-$ cells and stratifies them into B0 [<250 μL cells], B1 [>250/μL to <1000/μL cells], and B2 [>1000/μL cells]. Although PBFC currently serves as the gold standard for measuring blood involvement in CTCL staging, other blood parameters which may also reflect hematological tumor burden and therefore inform staging and predict prognosis in CTCL patients deserve exploration. In 2020, a retrospective study following MF patients over a period of 17 years found that elevated lactate dehydrogenase (LDH) at the time of diagnosis was correlated with advanced disease stage. Conversely, in a more recent study investigating survival and prognostic factors in patients with CTCL, a univariate analysis of patients with MF/SS revealed no significant prognostic value with elevated serum LDH. Given this question of the true prognostic import of LDH as well as other blood parameters of the complete blood count, additional study is warranted.

Purpose: This study assessed the baseline complete blood count parameters and lactate dehydrogenase values for association with staging and prognosis of patients with cutaneous T-cell lymphoma.

Methods: Following institutional IRB approval for the study, wea retrospective analysis of the University of Iowa multidisciplinary Cutaneous Lymphoma Program registry for all MF/Sezary patients was conducted. All patient charts were manually reviewed to ensure they met the inclusion criteria of new diagnosis MF in adults (>18 years old), and a profile of clinical, laboratory, and pathologic information was collected. CBC and LDH data were collected for patients at diagnosis. The association between hematologic profiles at diagnosis and initial B stage (determined by PBFC), initial overall stage, max B stage (determined by PBFC), max overall stage was evaluated via the Kruskal-Wallis test. The effect of hematologic profiles at diagnosis on five-year overall survival was assessed using Cox regression.

Results: This study included a total of 109 CTCL patients (33 female, 76 male) with an average age at diagnosis of 59.0 (range 14-94). Based on univariate analysis, higher initial overall stage ($p=0.02$, $p=0.01$), max B-stage ($p=0.01$, $p=0.01$), and max overall stage ($p=0.02$, $p<0.01$) were all associated with significant increase in WBC count and LDH. A higher initial B-stage ($p=0.04$) was also associated with a significant increase in WBC count alone. Additionally, WBC count and LDH were positively associated with a higher risk of death within five years of diagnosis, with hazard ratios of 1.08 ($p<0.01$, Units=1) and 1.05 ($p<0.01$, Units=10), respectively, on univariate analysis. In multivariate analysis based on forward selection, the two most important characteristics associated with five-year overall survival were age at diagnosis (Adjusted HR 1.04, $p<0.01$, Units=1) and WBC count (Adjusted HR 1.08, $p<0.01$, Units=1)

Conclusion: This study revealed that higher WBC count and LDH measurements at the time of CTCL diagnosis were associated with not only higher initial overall staging of the disease at diagnosis, but also higher max B-staging and max overall staging evaluated throughout the course of the disease. These results support the potential utility of initial WBC count and LDH as adjunctive tools in evaluating initial disease severity and predictors for max disease progression/Furthermore, results showed, on average, a 1-year increase in age at diagnosis is associated with a 4% increase in risk of death within five years and a 1-unit increase in WBC count at diagnosis is associated with an 8% increase in risk of death within five years. These results provide further insight into the characteristics that could help inform prognosis and overall survival in CTCL patients.

Deep Learning Quantification of Intraretinal Fluid Correlates with Visual Outcomes in Diabetic Macular Edema

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Funding: Fraternal Order of Eagles Diabetes Research Center

Introduction:

Diabetic retinopathy (DR) is an ocular complication of diabetes mellitus (DM) and is the leading cause of vision loss in the working-age population. This is primarily due to diabetic macular edema (DME), characterized by swelling and thickening of the macula caused by intraretinal (IRF) and subretinal fluid (SRF) accumulation, readily detectable using non-invasive optical coherence tomography (OCT) imaging of the retina. Despite gold standard treatment with intravitreal anti-vascular endothelial growth-factor (anti-VEGF) injections, 30-50% of patients show an incomplete response to treatment. We hypothesized that OCT-derived fluid indices and key clinical features are most correlated with BCVA. To identify patients who do not respond well to treatment, we aimed to identify AI-derived OCT fluid biomarkers and clinical features that correlate most with best corrected visual acuity (VA) to predict treatment outcomes.

Methods:

We completed a retrospective analysis of a dataset of 101 eyes of 76 patients with non-proliferative diabetic retinopathy (NPDR) and DME who received anti-VEGF and/or steroid injections in the UIHC retina injection clinic from 2010-2024. We obtained clinical data and 1486 Heidelberg or Cirrus spectral domain OCT images for automated analysis. Our backbone image segmentation model was a U-net convolutional neural network trained on patients from the University of Iowa with age-related macular degeneration (AMD) and RETOUCH public datasets. The model was optimized using DME data graded by an expert to calculate en face measurements of IRF, SRF and pigment epithelial detachment (PED). In addition, intracystic hyperreflective material (ICHM), defined as hyperreflectivity exceeding that of the outer nuclear layer (ONL) within cystic lesions, was annotated and incorporated into the training process to enable the model to learn this feature. Individual fluid correlations with BCVA were then calculated for each feature. To determine the correlation of both clinical and OCT features with BCVA, we first conducted multivariate linear regression. To account for complex feature interaction and weighting of features, we used an XGBoost regressor to model features most predictive of BCVA, which uses native categorical handling and built-in support for missing values. Performance was evaluated using the correlation coefficient (R). The model was interpreted using XGBoost's gain-based feature importance, extracted after training on each fold.

Results:

The Dice coefficients of the backbone AMD model for fluid segmentation were 90.2 (IRF), 83.1 (SRF), and 80.9 (PED). After optimization for OCTs with DME, the Dice coefficient for intraretinal fluid (IRF) segmentation was 70.3. Using fluid segmentation optimized with DME tracings, IRF volume, largest component of IRF enface area, IRF horizontal extent, and ICHM enface area fluid indices were significantly correlated with BCVA ($p < 0.05$). Multivariate linear regression between clinical and OCT features with BCVA showed significant but weak correlation ($R = 0.239$). Using the XGBoost regressor model, the correlation was much more robust ($R = 0.763$). The top 10 OCT and clinical features most important for BCVA were low VA, cancer, refractive error, smoking history, DR severity, HbA1c, anti-VEGF or steroid group, IRF horizontal extent, drug type, and glaucoma.

Conclusion:

This study validates a promising model for automated fluid segmentation in DME. We showed that there are significant correlations between OCT fluid indices and BCVA, showing that fluid measurements may serve as indicators for functional vision impairment. We also demonstrated that our regressor model using both clinical and imaging features is valid for determining which features are most important for BCVA. This research is an important first step in developing a method to predict treatment response in DME.

Does CAG repeat length in the HTT gene confer a developmental benefit for those not at risk for Huntington's disease?

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Introduction/Hypothesis: Huntington's Disease (HD) is a fatal, degenerative brain disorder caused by an abnormal expansion of a DNA sequence (CAG repeats) within the Huntingtin (HTT) gene. While all humans carry the HTT gene and its CAG repeats, the disease develops when the number of repeats exceeds 40. One theory of disease etiology is that HTT drives the development of a superior brain early in life that makes it vulnerable to later degeneration. An approach to better understand how HTT influences brain development is to examine its effects in individuals whose CAG repeat length falls below the disease threshold. An earlier study in our lab suggests that among subjects with 10–35 repeats, higher repeat counts were associated with larger brain volumes. Building on that work, this follow-up study investigates how CAG repeat length affects brain function—rather than structure—using MRI to assess resting state functional connectivity (rsFC). Given that rsFC changes over time with brain development, we hypothesized that the CAG repeat effects may have an effect on the maturation of these networks.

Methods: We acquired anatomical and resting-state neuroimaging from participants of ages 6-22 who had a parent or grandparent with HD (Gene-non expanded; GNE; n=205) and those with no HD family history (Controls; n = 179). Resting state MRI scans were analyzed to determine average rsFC within seven canonical cortical networks and the striatum, which is primarily affected in patients with extended CAG repeats. Mixed-effects linear regression models were used to determine the association between CAG repeat length and region-of-interest (ROI) rsFC. To visualize how CAG repeat length impacts the age effect on ROI rsFC, we compared the association between age and ROI rsFC between patients in the upper and lower CAG repeat quartiles.

Results: We found significant negative correlations between CAG repeat length and in rsFC within bilateral putamen rsFC (BI_PUT: $p<0.001$), left visual network ($p<0.005$), and right limbic network ($p<0.005$), with the left putamen showing the strongest association. Within these regions, higher CAG length was associated with lower connectivity. Age also correlated with significant decreases in rsFC in all ROIs, except for the visual cortex. In the putamen, we were able to visualize that subjects with the highest CAG had steeper slopes of the aging effect, suggesting that higher Cag repeats resulted in faster maturation ($p>0.05$).

Conclusions: For participants below disease threshold, both age and CAG repeat length predict lower functional connectivity in the putamen, limbic, and visual networks, suggesting that CAG repeat may contribute to accelerated aging in these brain networks.

The Effect of Operative Techniques on Delayed Wound Healing in Direct Anterior Approach Total Hip Arthroplasty

Cole Rich, Yumeng Gao, MS, Dallas Vanorny MD, PhD

Introduction: A common complication of the direct anterior approach for total hip arthroplasty (DAA THA) is superficial wound dehiscence and delayed wound healing. While certain preoperative factors such as body mass index (BMI) are associated with higher rates of delayed wound healing, there remains limited information on the role of incision length, operative time, and superficial closure technique. This study aimed to identify both preoperative and intraoperative predictors of delayed wound healing in DAA THA.

Methods: This retrospective cohort study included patients who underwent primary DAA THA for osteoarthritis at a single institution between August 2024 and March 2025. Several preoperative labs, medications, and demographic variables were recorded. Intraoperative variables included procedure time, estimated blood loss, incision length, use of Wound VAC, and superficial closure with either Dermabond or staples. Delayed wound healing was qualified based on clinical documentation and images up to 6 weeks postoperatively.

Results: A total of 95 patients were included in the study, of whom 14 experienced delayed wound healing. The median age was 65.0 years, and 55.8% were female. Based on BMI, nearly half of patients were classified as obese (BMI $\geq$ 30 kg/m^2). In the delayed wound healing cohort, BMI was significantly higher compared to the normal healing cohort (median: 37.2 vs. 29.1 kg/m^2, $p = 0.003$). No significant association was found between incision length and delayed wound healing status ($p = 0.28$). Delayed wound healing occurred in 7.8% of those not obese, 17.1% of those with Class I and II obesity, and 100% of those with Class III obesity. These differences were statistically significant ($p = 0.001$). Pairwise comparisons showed the Class III obesity group had significantly higher wound complication rates than both non-obese and Class I and II obesity groups ($p < 0.02$). No significant differences were found between Class I and II obesity patients and non-obese patients ($p = 0.21$).

Conclusion: This study highlights BMI as a strong predictor of delayed wound healing following DAA THA. Because of this, those with higher BMI may be indicated for an alternative approach or alternative closure technique. Future studies should explore closure methods and other intraoperative variables in high-BMI patients undergoing DAA THA.

Association Between LET Anchor Placement and Risk of Subsequent Arthroscopy Following Primary ACL Reconstruction

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Background: Lateral extra-articular tenodesis (LET) is more commonly added to primary anterior cruciate ligament reconstructions (ACLR) in high-risk patients in attempts to reduce re-rupture rates and improve anterolateral rotary laxity. The procedure involves using a portion of the iliotibial band, leaving it attached distally at Gerdy's tubercle, and passing it under the lateral collateral ligament before anchoring it proximally near the lateral epicondyle of the femur. Currently, there are no surgical guidelines specifying the exact anchor placement for the LET.

Objective: Femoral attachment has been postulated to relate to graft tensioning and loss of extension during recovery. This study aimed to examine the relationship between LET femoral anchor placement and return to the OR for cyclops debridement or loss of extension.

Methods: We conducted a matched case–control study of patients who underwent primary ACLR with patellar or quadriceps tendon autografts and LET between January 2018 and December 2024. Nine patients were identified who required subsequent arthroscopy due to a lack of extension, arthrofibrosis, or cyclops debridement. Controls were identified as patients who did not experience extension limitations or return to the OR. Each case was matched 1:2 to controls by age, sex, and graft tendon type. LET anchor placement was measured by two raters and quantified as the distance anterior/posterior to the posterior femoral cortex line (PFCL), and the distance distal/proximal to a line perpendicular to the PFCL at the posterior condylar flare (PCF). Additional variables evaluated included BMI, meniscal treatment, preoperative activity level, and whether the anchor was placed within a previously identified isometric zone. Univariable conditional logistic regression was used to assess associations with subsequent arthroscopy, accounting for the matched design.

Results: A total of 27 patients (9 requiring repeat arthroscopy, 18 matched controls) were included. The median age was 18.0 years (17.0 - 20.0), and 56% were female. Anchor placement in the anterior/posterior dimension was 18.3 mm (12.4 - 21.9) in repeat arthroscopy cases and 13.4 mm (8.2 - 17.9) in controls ($p = 0.17$). Placement in the distal/proximal dimension was -9.9 mm (-11.7 to -3.5) in repeat arthroscopy cases and -8.6 mm (-14.3 to -1.5) in controls ($p = 0.57$). LET anchors were placed outside the previously identified isometric zone in 89% of both groups. None of the investigated variables were significantly associated with subsequent arthroscopy (all $p > 0.05$).

Clinical Significance: No significant difference in the risk of subsequent arthroscopy was seen for primary ACLR based on LET anchor placement or other variables of interest; however, the limited sample size may have reduced our ability to detect meaningful associations. As LET procedures become increasingly common, further studies should investigate long-term outcomes after ACLR with LET, including graft failure rates, return-to-sport timing, and patient-reported outcomes. Determining whether precise LET fixation during ACLR impacts post-surgical outcomes will inform future surgical practice.

The Efficacy of Regional Anesthesia in Reducing Post-Autograft Opioid Consumption in Burn Patients

Drew Danner, Dr. Nada Sadek, Dr. Lucy Wibbenmeyer, Dr. Franklin Dexter, Eric Vallin

Introduction:

Burn patients are subject to extreme pain from both their original injuries and from the subsequent series of procedures needed to treat the burns. Autografting, one of the most common treatments for burns, is also considered to be one of the most painful due to the creation of large open wounds where the skin was harvested. Due to the severity and duration of the pain associated with burns and autografting, providing adequate analgesia is often heavily reliant on opioids. Opioid medications are efficient analgesics, however, they have many negative side effects and patients rapidly develop physiological tolerance, so minimizing opioid use has become a major area of interest. One alternate method of pain control is the use of regional anesthesia for the autograft donor site, such as fascia iliaca blocks and lumbar epidurals; however, there is currently limited literature of their application and efficacy in the burn population. The purpose of this study was to assess the efficacy of blocks for regional anesthesia of thigh donor sites in reducing post-operative opioid consumption, patient reported pain scores, and opioid-induced adverse effects.

Methods:

Patients admitted to the burn center from January 1, 2011, to May 15, 2025, who underwent autografting of their burn injuries with donor site harvest from their lower extremities were included in the study. Data collected from the Burn Registry and the electronic medical records included demographics (age, sex, BMI, substance use history), burn history (mechanism, total burn area), hospital course (pain scores, opioid consumption, ondansetron received, operative day, area grafted, time to discharge) and regional anesthesia variables (type of catheter or single shot, medication administered, and length of time given). Descriptive statistics were used to determine differences between the block and non-block groups. Additional analysis was performed on the type of block, indwelling catheter versus single shot. Significance was established at a standard difference > 0.35 or < -0.35.

Results:

The study population consisted of 526 patients, of which 165 (31.3%) had donor site blocks and 361 (68.6%) did not. The study population was predominately male (394, 74.9% male) with an average burn size of 8.5%, (range 0.4-72.5%). Overall preoperative pain was 3.8 ± 2.5 and post operative pain at 24, 48 and 72 hours was (5.4± 2.0, 4.6 ± 2.1, 4.5± 2.1, respectively). Post operative pain did not return to preoperative pain levels during the study. The highest OME equivalents occurred during the first 24 hours, doubling from the pre-operative period (54.2 ± 56.9 vs 99.8 ± 76.4). The groups were well-matched in their demographic, burn injury data and hospital variables. While the overall differences between the experimental and control groups was non-significant, when looking specifically at block type, indwelling catheter block patients (77, 46.6%) had more opioids (71.4 vs 34.94, standard difference 0.68) and higher pain scores (4.2 vs 3.4, standard difference 0.31) in the 24 hours before the OR than those patients who received single shots (87, 52.7%). The amount and type of anesthetic administered differed within block type. In patients who received indwelling catheters, groin catheters (20, 12.4%) remained in place for 42.2 ± 15.2 hours, and epidurals (50, 31%) remained in place for 47.8± 24.2 hours, with peripheral catheters having significantly higher OME consumption and reported pain across multiple time periods compared to epidurals.

Conclusions:

This single center, retrospective study shows no significant difference in pain control or opioid consumption with regional anesthesia blocks for donor sites. However, limitations such as small study sample, inconsistent documentation, the absence of uniform analgesia protocols across years and attending physicians, and the inability to control for confounding variables limit findings. The study does, however, illustrate the variability in the practice and documentation of regional blocks and highlights the opportunity for standardization. In order to determine the efficacy of donor site blocks, a prospective multicenter study with a minimum of 524 patients is required for the findings to detect a clinically meaningful difference. The findings of this study highlight the difficulties in assessing subjective values such as pain and support other related literature in the need for more formal prospective studies in burn-related pain control methods.

Evaluation of hydrocortisone use in suspected critical illness related corticosteroid insufficiency (CIRCI) in hypotensive burn patients during their first week of hospitalization

Riley Dean, MS 2
Dr. Lucy Wibbenmeyer, Clinical Professor of Surgery
Junlin Liao, PhD, Assistant Research Scientist/Engineer, Associate Mentor

Introduction: Critical illness-related corticosteroid insufficiency (CIRCI) is a syndrome in which critically ill patients exhibit relative adrenal insufficiency and tissue resistance to corticosteroids, resulting in vasogenic shock that is refractory to vasopressors. Current guidelines support the use of hydrocortisone to treat refractory shock in burn patients, but research on efficacy and long-term sequela remains inconsistent and limited. In line with the literature, we hypothesized that patients with increasing age, more severe burns in terms of percentage total body surface area (TBSA) burned, and inhalation injury will have higher association with the development of CIRCI. Additionally, we hypothesized that corticosteroid need would associate with decreased vasopressor treatment time but would also be associated with an increased risk of mortality and long-term complications secondary to patient acuity.
Methods: Burn patients admitted from January 2015 to December 2025 who required vasopressors during the first week constituted our study group. Both the Burn Registry and the electronic medical record were queried for the following variables: demographics, burn data, hospital course, and treatments. Outcome variables included length of stay (LOS), infections, antibiotics days, glucose>200 days, units of insulin used, mortality, and days of vasopressors. Complications included infections and graft loss. The specific steroid, length of treatment, and average daily amount were recorded. Vasopressor type and length of treatment was recorded. Outcome variables included LOS, infections, antibiotics days, glucose>200 days, units of insulin used, mortality, and days of vasopressors. Patients were divided into two groups dependent on the diagnosis of CIRCI or no CIRCI. Students t-test and chi square were used respectively to compare the groups. A multivariant analysis including significant and related variables was performed to determine independent predictors of CIRCI. Significance was determined at $P<0.05$ level.
Results: The study group consisted of 87 patients, 47 of whom received steroids for a diagnosis of CIRCI and 40 who did not. All patients in the study group received vasopressors. Of patients who received a serum cortisol level, three fourths had a level under 18 ug/dL (75.86%), and 37.9% had a serum cortisol level under 10 ug/dL. Patients who received hydrocortisone were more likely to have a higher percentage TBSA (38.62 ± 25.66 v 25.60± 24.02). They were also likely to require more resuscitation (16.06± 10.5L v 8.86± 9.12L), have longer LOS (52.24± 55.5v 28.22± 31.83), longer duration of vasopressor treatment (6.01± 3.99 v 4.11± 3.15), and more days spent on a ventilator (20.88± 33.12 v 8.07± 9.55), all $p<0.05$. There was no difference in mortality of other complications. Age and fluid received during the first resuscitation independently predicted CIRCI.
Conclusion: Overall, we found that over 50% of patients in vasodilatory shock during their first week of burn were diagnosed with CIRCI and received steroids. This group appeared more critically ill and had more intensive critical care needs, but their treatment was not associated with increased sequela that is commonly associated with steroid use. Older age and more fluid received during resuscitation predicted the use of steroids. We would recommend a multicenter study due to the small number of patients at a given hospital with CIRCI after burn injury.

The Influence of Cytokine Priming on the Efferocytosis of MSCs

Daniela Del Bosque Siller, James Ankrum, PhD

Background: Mesenchymal stromal cells (MSCs) exert therapeutic immunomodulatory effects when injected intravenously but their mechanism of action has been debated. Recently, MSC clearance from monocytes through a process called efferocytosis has been identified as a potential mechanism of MSC therapy. Recent work suggests that the viability of MSCs prior to efferocytosis does not impact the efficiency of uptake by monocytes, but does impact the ability of monocytes to gain immunosuppressive phenotypes. Recent work has also shown that prior exposure to pro-inflammatory cytokines, TNF-α and IFN-ɣ, alters the response of MSCs to pro-apoptotic drugs, accelerating the rate in which MSCs die and are cleared by monocytes. Knowing that MSC viability is vital for the acquisition of immunosuppressive responses of monocytes from efferocytosis, and that the exposure to pro-inflammatory cytokines alters their apoptosis, we hypothesized that MSC efferocytosis could be enhanced using cytokine priming with TNF-α and IFN-ɣ.

Methods: To study the effects of cytokine priming on MSC phenotype, we cultured umbilical cord MSCs with the pro-inflammatory cytokines, TNF-α and IFN-ɣ, each at a concentration of 10ng/mL, for 24, 48, or 72 hours to study time-dose dependent effects on the rates of immunomodulatory molecule production and other changes in MSC phenotype. We measured MSC surface marker expression of immunoregulatory molecules, CD73 and HLA-DR, through flow cytometry. We also measured the anti-inflammatory IDO enzymatic activity of MSCs through a kynurenine colorimetric assay. We then assessed the efficiency of MSC uptake by monocytes through a Cell Brite Orange phagocytosis assay. MSC apoptosis in a non-adherent environment was also assessed through flow cytometry characterization of Propidium Iodide and Apotracker Green cell apoptosis markers.

Results: We found that viable MSCs cultured with TNF-α and IFN-ɣ for 72 hours had the largest change in immunomodulatory molecule production and IDO enzymatic activity compared to those primed only for 24 or 48 hours, and this phenotype was significantly different compared to non-primed MSCs. MSCs primed for 72 hours also resulted in a significant ~40% increase in CBO fluorescence intensity of monocytes indicating increased uptake by monocytes compared to their non-primed counterparts. However, primed MSC apoptosis in a non-adherent environment did not differ significantly from their non-primed counterparts.

Conclusion: Priming MSCs with pro-inflammatory cytokines increases immunomodulatory molecule production and pro-inflammatory enzymatic activity in a time-dependent manner. MSC priming also increases the rate of efferocytosis by monocytes. While there were no apparent changes to apoptosis of primed cells in a non-adherent environment, further technical experiment optimization and looking at differences between innate vs. drug-induced apoptosis should be studied. Further study is also needed to assess any differences in T-cell suppression that results from monocyte efferocytosis of primed MSCs.

Machine Learning with Multiple Modalities of Brain Magnetic Resonance Imaging to Predict Prior Suicidal Behavior Among Participants with Bipolar Disorder

Student: Lubin R. Deng
Mentor: Vincent A. Magnotta

Background: Bipolar disorder (BD) is a chronic psychiatric mood disorder that is associated with a high rate of suicide attempts. Evaluation of suicide risk is generally based on patients' self-reported information, which can be unreliable. In recent years, a handful of studies have attempted to use machine learning (ML) to create predictive models for suicidality in BD based on data from brain magnetic resonance imaging (MRI). Most of these studies have focused on a single modality of MRI data (e.g., functional connectivity) and have reported a wide range of classification accuracies, most commonly 70%-80%. Stronger prediction performance may be achievable by combining information from multiple modalities of MRI.

Purpose and hypothesis: In this study, we used ML to differentiate between BD type I patients with and without a prior suicide attempt by combining information from structural, functional, and diffusion-weighted MRI of the brain. We hypothesized that a moderate prediction performance would be observed using each of the modalities individually, and higher accuracy would be achieved by combining information from all three modalities.

Methods: Participants with BD type I were recruited into a multimodal MRI study. We obtained volumetric data, resting state connectivity data, and diffusion-weighted imaging data on 108 participants (51 with a prior suicide attempt, 57 without); 22 participants were randomly selected as an independent test set. For each of the three modalities of MRI data, a ML model was selected by performing holdout validation on the non-test subjects. The selected model was then trained on all non-test subjects and used to generate a prediction of each test subject's class (suicide attempter or non-attempter). Voting was performed with the three models' predictions; the final predicted class of each test subject was the one predicted by at least 2 of 3 models. The prediction performance was determined, and the most important predictor variables were explored.

Results: The selected ML model for each modality and its performance were (modality—model, test accuracy/F1 score/ROC AUC): volumetric—neural network, 0.773/0.737/0.650; connectivity—AdaBoost of decision trees, 0.727/0.720/0.700; diffusion—neural network, 0.773/0.737/0.767. Voting resulted in an accuracy of 86.4%, F1 score of 0.842, and ROC AUC of 0.896. Voting with only 2 of the 3 modalities did not achieve metrics as high. Important predictors included gray matter volumes in the frontal lobe, functional connectivity involving the prefrontal cortex and the cerebellum, and diffusivity in the corpus callosum and internal capsule.

Conclusion and significance: It is possible to predict a history of suicidal behavior with relatively high accuracy in our sample by combining structural, functional, and diffusion-weighted MRI data. All modalities were integral to the strong performance. Several important predictor variables are consistent with what is currently thought to be altered in suicidal individuals.

Title: Factors Influencing Time of Presentation Among Children with Myelomeningocele in Zambia. A Prospective Study

Authors: Allison Dodds, BS[1]; Kutha Banda, MPH[2]; Linder Wendt, MS[3]; Brooks Jackson, MD, MBA[4]; Humphrey Kunda, MD[5]; Rebecca Reynolds, MD[6]

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Introduction: Although myelomeningocele (MMC) remains a leading cause of infant disability and death in low-resource settings, data regarding access to timely neurosurgical care remains limited. Initial investigations in Zambia show median age at MMC repair is 21 days.

Objective: To characterize factors associated with delayed presentation for surgical repair of MMC in Zambian infants.

Methods: Infants with MMC presenting to the major tertiary academic hospital in Lusaka, Zambia for MMC repair between May 1, 2024, and May 31, 2025, were enrolled in a prospective cohort study. The primary outcome was delayed presentation for postnatal MMC repair, defined as > 72 hours from birth. Univariate and multivariate logistic regression models were fit to assess the impact of demographic factors on late presentation to clinic.

Results: Eighty-nine infants (54% male, n=48) were enrolled with 74% (n=66) born at term. Seventy percent (n=62) presented for MMC repair after 72 hours of birth. Average age of the infant's mother was 25.6 ±7.3 years with an average 2.9 pregnancies (SD 2.0). The median monthly household income was 8.75 USD (4.37, 21.87). Mean distance from the primary referring center to the major tertiary care center was 459.6 kilometers (SD 269.4) or 285.6 miles (SD 167.4). Infants whose mothers had received at least one antenatal ultrasound (OR 0.26, p=0.046) and infants with any monitored comorbidity (OR 0.311, p=0.039), were less likely to present late. Further, the multivariable model showed that infants who travelled longer distances to care (OR 1.748 for 100 km increase, p<0.001) and those who were born preterm (OR 4.903, p=0.031) were more likely to undergo late MMC surgical repair.

Conclusions: Longer distances to care, preterm birth, lack of co-morbidities, and lack of antenatal ultrasound were associated with delayed presentation for MMC repair in Zambia. A focus on improving antenatal/postnatal care and increasing transport access to neurosurgical tertiary care services warrant further investigation.

Title: Developing Polyurethane Nanocapsules to Deliver Pirfenidone for the Treatment of Subretinal Fibrosis

Authors: Chase Eastham, Narendra Pandala, and Budd Tucker

A hallmark characteristic of neovascular Age-Related Macular Degeneration (colloquially referred to as “wet AMD”) is abnormal vessel growth from the underlying choroidal connective tissue into the subretinal space. However, vascular leakage, sustained inflammation, and fibroblast activity causes an extracellular matrix buildup in the subretinal space secondary to the vascularization. So although angiogenesis is the target of multiple FDA-approved agents (such as anti-VEGF treatments), new vessel formation is not the sole cause of photoreceptor cell death in wet AMD. Fibrotic scaring can lead to permanent vision loss despite successful anti-VEGF therapy.

Therefore, we explored the use of the common anti-fibrotic agent pirfenidone as a potential adjuvant therapy for subretinal fibrosis secondary to choroidal neovascularization. To deliver pirfenidone directly to the subretinal space, we employed polyurethane nanocapsules, a promising drug-delivery platform. These specific polyurethane nanocapsules were formed via an interfacial polymerization process using emulsion droplets formed from an oil-in-water system. Isocyanate groups from isophorone diisocyanate (IPDI) reacted with hydroxyl groups from 1,6-hexanediol to form a carbamate group, also known as a urethane linkage with pirfenidone physically entrapped within the capsule shell.

Excitingly, our preliminary data suggest that pirfenidone released from degraded capsules retains proper function, supporting this system as a potential therapy for subretinal fibrosis.

Switching JAK Inhibitors in Alopecia Areata: Real-World Evidence Suggests Insurance, Not Efficacy, Drives Treatment Changes

Author: Yumeng Engelking; **Mentor:** Ali Jabbari, MD; Collaborators: University of Iowa Department of Dermatology

Introduction:

Alopecia areata (AA) is a chronic autoimmune disorder characterized by nonscarring hair loss with substantial psychosocial burden. Janus kinase (JAK) inhibitors have emerged as effective treatments, yet clinical durability and predictors of response remain uncertain. Switching between JAK inhibitors is increasingly practiced, often assumed to reflect clinical decision-making. However, the real-world drivers of switching remain poorly defined.

Purpose:

We aimed to identify the primary reasons for JAK inhibitor switching in AA and evaluate whether switching improves clinical outcomes.

Methods:

We performed a retrospective chart review of 72 patients with AA treated with ≥1 JAK inhibitor at the University of Iowa (2018–2025). Patients were categorized as *switchers* (≥2 distinct JAK inhibitors sequentially) or *non-switchers* (remained on initial agent). Collected variables included demographics, alopecia subtype, treatment history, response, adverse events (AEs), and documented reason for switching. The primary outcome was the reason for switching (insurance/access, efficacy, AEs, other). Secondary outcomes included response rates, treatment durability, and AE frequency. Statistical comparisons were performed using chi-square/Fisher's exact tests; survival analysis was conducted with Kaplan–Meier methods.

Results:

Of 72 patients, 23 (31.9%) switched therapies while 49 (68.1%) remained on their initial agent. Insurance/access barriers accounted for nearly half of switching events (47.8%), whereas lack of efficacy (17.4%) and AEs were infrequent. Response rates were similar between switchers (56.5%) and non-switchers (55.1%, p=1.00). Notably, patients who failed to respond to their first JAK inhibitor did not achieve response with a second. Kaplan–Meier analysis showed most patients remained on their initial agent for >1 year, with no significant differences in drug survival between agents. AEs were reported in 20.8% of patients, but rarely influenced switching.

Conclusion/Significance:

In this real-world cohort, insurance-related factors—not clinical efficacy or safety—were the dominant drivers of JAK inhibitor switching in AA. Clinical outcomes were similar regardless of switching, and initial non-responders did not improve with subsequent agents. These findings highlight the outsized role of payer policy in shaping treatment decisions and emphasize the need for insurance practices that align with evidence-based, patient-centered care.

Title: Self-reported dietary changes lead to improved outcomes in newly diagnosed multiple sclerosis patients

Authors: Kim Fairhead, BS; Annie Noel, BS; Jordan Hook, BS; Landon Crippes, MD; Erika Dorff MD, MPH; Bridget Easler, MS; Mary Ehlinger, BS; Linda Rubenstein, PhD; Patrick Ten Eyck, PhD; Linda Snetselaar, PhD, RDN; Tyler Titcomb, PhD, RDN; Terry Wahls, MD

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Background: Multiple sclerosis (MS) is a chronic immune-mediated disease involving demyelination of the central nervous system. Approximately half of people with MS report following a special diet to manage their symptoms; however, there are no established dietary guidelines for those diagnosed with MS.

Purpose: To assess the association of self-reported diets on physician-reported MS-symptom severity with the goal of providing real-world evidence on the impact of diets in MS.

Methods: We performed a retrospective study of electronic health records from the Department of Neurology at UIHC among patients newly diagnosed with clinically isolated syndrome (CIS) or relapsing-remitting MS (RRMS) from 1/1/2008 to 8/3/2020. 527 patients were screened for eligibility. Inclusion criteria were age 18 to 56 y/o at diagnosis, able to walk ≥ 25ft without support, and had ≥ 2 MS-related clinical encounters at UIHC or had records accessible via CareEverywhere. Exclusion criteria were exposure to chemotherapy/radiation for cancer treatment in the past 3 months, psychiatric disorders in which psychosis could occur, or active eating disorders. After screening, 140 patients were eligible for inclusion and sorted into the 'dieter' group if they attested to following a special diet in an MS-related visit or into the 'nondieter' group if there was no mention of diet. Two participants were excluded due to having unclear diet status yielding 48 dieters and 90 nondieters. Areas of function impairment status (e.g., vision, walking, pain, bladder, mood, memory/cognition), disease-modifying therapy (DMT) usage, and other MS symptom-related medication changes were recorded up until 05/31/2024. Time-varying cox proportional hazard and competing risk analyses were conducted to assess the association of dieting with the time-to-event of extracted outcomes. Models included covariate information on age, sex, race, ethnicity, BMI, and time-varying DMT status.

Findings/Results: Compared to nondieters, dieters were more likely to experience reduced overall MS symptoms (HR=2.02, 95% CI: 1.30, 3.14) . Specific areas of improvement were memory (HR=2.29, 95% CI: 1.07, 4.91) and vision (HR=1.91, 95% CI: 1.32, 2.76). Additionally, dieters were less likely to experience worsened vision function (HR=0.42, 95% CI: 0.22, 0.80) and worsened pain burden (HR=0.50, 95% CI: 0.33, 0.76), when compared to the nondieter group. Lastly, dieters were less likely to experience improved bladder function (HR=0.43, 95% CI: 0.20, 0.92).

Conclusions: MS patients that changed their diet were more likely to experience improvements and less likely to experience worsening of several outcomes, apart from bladder function, in which dieters were less likely to experience improved outcomes. While this study provides real-world evidence for the impact of diet on MS outcomes, due to its limitations, additional research is needed to confirm these findings.

Quantifying Sensory Symptoms in Thyroid Eye Disease

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Purpose

Thyroid eye disease (TED) is an autoimmune inflammatory disorder that causes swelling and enlargement of the extraocular muscles and orbital tissue. Patients with TED report experiencing a variety of sensory symptoms, including, but not limited to, pressure and pain behind the globe and a foreign body sensation in the eye. However, descriptions of these sensory symptoms are limited, and there is a lack of literature describing differences in sensory experiences between men and women with TED. This study aims to evaluate the descriptors patients use to characterize their ocular and periocular sensory symptoms and to determine how these descriptors vary by gender.

Methods

An IRB-approved retrospective review was conducted of all patients with TED who were seen at the UIHC Oculoplastic Surgery Clinic between 1/1/2020 and 12/31/2024. Among these patients, appointments from 1/1/2010 through 12/31/2024 were eligible for review; the first and most recent appointments for each patient were reviewed, as well as appointments before and after completion of a course of oral steroid, methylprednisolone infusions (Kahaly Protocol), or teprotumumab infusions. Patient sensory symptoms reported in the History of Present Illness section were recorded. Data for men and women were compared using Fisher's exact test, the chi-square test, Welch's t-test, and Poisson rate ratio testing where applicable.

Results

Of the 798 patients initially screened, 631 were eligible for analysis, and 1,412 appointments were reviewed. Symptomatic patients (n = 562) used 48 unique descriptors to characterize their periocular, intraocular, retrobulbar, and generalized symptoms. *Pain with eye movement* (115 patients, 20%), *pain behind the globe* (53, 9%), *pressure behind the globe* (41, 7%), *generalized headaches* (40, 7%), and *generalized achiness* (32, 6%) were the most frequently expressed descriptors. The percentage of symptomatic men (85%, 145/170) and women (90%, 417/461) was similar (p = 0.09). However, women reported a significantly greater mean number of symptoms than men (2.83 vs. 2.45, p = 0.02). Among symptomatic men (n = 145) and women (n = 417), a significantly higher percentage of women reported *pain around the orbit* (7% vs. 1%, p = 0.01) and *pressure within the globe* (5% vs. 1%, p = 0.02). Nine ocular surface descriptors were separated from the others as the underlying etiology (e.g., TED, dry eye, exposure keratopathy) could not be reliably determined. The most frequently endorsed surface symptoms were tearing (311, 55%), dryness (273, 49%), and irritation (145, 26%), and men experienced significantly higher rates of tearing (63% vs. 53%, p = 0.03) and burning (13% vs. 6%, p = 0.02).

Conclusions

Patients with TED used forty-eight sensory descriptors to characterize their symptomatology. Women reported experiencing a greater mean number of sensory symptoms and had higher rates of *pain around the orbit and pressure within the globe* than men. Nine descriptors were used to describe ocular surface symptoms, and men experienced significantly higher rates of tearing and burning sensations than women. Future research is necessary regarding the symptom predictivity of more active or severe disease, symptom burden in relation to disease duration and treatment, and whether noted sensory symptom differences result from variable reporting by men and women.

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Body Composition–Driven Changes in Infrapatellar Fat Pad Composition: Implementing Bioimpedance-Guided Risk Assessment in Total Knee Arthroplasty

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Disclosures: None

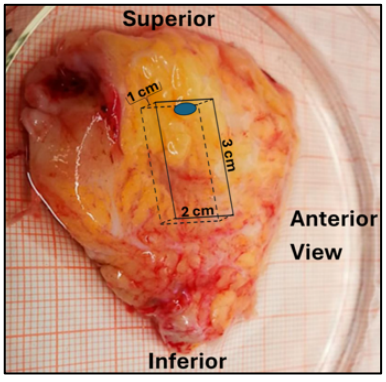
Introduction: The infrapatellar (Hoffa's) fat pad (IFP) is a metabolically active periarticular structure that supports load distribution, patellar tracking, and synovial fluid dynamics of the knee joint. Although mechanisms remain unclear, pathologic changes in the IFP have been linked to pain and osteoarthritis progression. Further, alterations in the balance of adipose tissue and fibrotic collagen in the IFP have been theorized to affect knee joint integrity and function. Because periarticular tissue quality and composition influence postoperative healing and surgical outcomes, characterizing IFP composition may provide insight into patient-specific risks associated with poor tissue quality such as impaired wound healing, infection, and poor suture integrity. This study analyzed fibrotic composition of the IFP in patients undergoing primary total knee arthroplasty (TKA) and evaluated its relationship with body composition metrics, aiming to identify factors with potential relevance for preoperative assessment and outcome prediction.

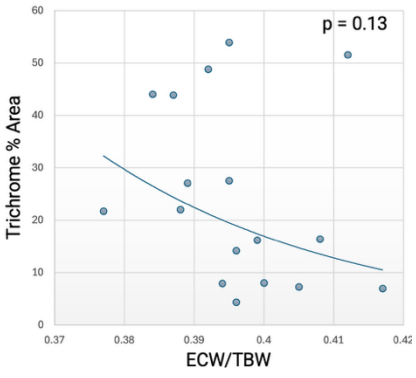
Methods: This study was approved by the University of Iowa Institutional Review Board, and informed consent was obtained from all participants. Infrapatellar fat pads, routinely excised during primary TKA, were collected from seventeen patients (9 male, 8 female) undergoing primary TKA. Ages ranged from 43–77 years, BMI from 24.7–51.7 (mean 38.3). Intraoperatively, the fat pad was removed with electrocautery and handed directly to a research team member for dissection. A central 3×2×1 cm section was excised to avoid electrocautery artifact, with superior and anterior aspects marked for consistent orientation during fixation and histologic processing. Samples were paraffin-embedded, coronally sectioned, and stained with hematoxylin and eosin (H&E) for general histological evaluation and Masson's trichrome to quantify fibrosis. Fibrosis was measured using ImageJ standardized color deconvolution thresholds to isolate collagen staining. Preoperative body composition was assessed using InBody bioimpedance scans, including BMI, fat mass, percent body fat, extracellular water to total body water ratio (ECW/TBW), and related measures. Fibrosis values and body composition metrics were compared to identify potential associations with periarticular tissue quality. The Wilcoxon rank-sum test was used to compare InBody metrics, operative limb-specific metrics, and fibrosis marker (Trichrome Area %) by age group (< 60 vs ≥ 60 years) and severe obesity status (BMI < 40 vs ≥ 40 kg/m²). Spearman's correlation was used to assess associations between Trichrome Area % and age, BMI, InBody metrics, and operative limb-specific metrics.

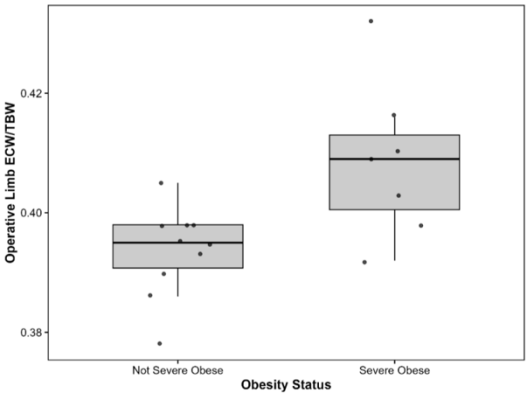
Results: Trichrome analysis revealed fibrosis ranging from 0.8–54% of tissue area, demonstrating wide interpatient variability. Fibrosis did not significantly correlate with BMI, age, or surgical laterality. Stratification by obesity class showed that severely obese patients (BMI ≥40) had significantly higher operative limb ECW/TBW while whole-body and contralateral limb ECW/TBW was not significantly different. No clear association was observed between fibrosis percentage and systemic body composition measures, though fibrosis remained a central feature of tissue heterogeneity.

Discussion: These findings emphasize two themes. First, fibrosis within the IFP is highly variable and not readily explained by systemic factors such as age or BMI, pointing toward localized or patient-specific remodeling processes independent of aging or systemic adiposity. Second, body composition analysis highlighted clear differences in operative limb ECW/TBW between severely obese and non-severely obese patients, suggesting that obesity may predispose to compromised periarticular tissue quality through mechanisms such as localized edema, altered extracellular matrix balance, or impaired lymphatic fluid homeostasis. While IFP fibrosis alone was not predictive of systemic body composition, bioimpedance-derived measures, particularly limb-specific ECW/TBW, may serve as reliable indicators of tissue vulnerability. Together, these data suggest that bioimpedance could complement standard demographic metrics in preoperative evaluation, offering a practical means of identifying patients at higher risk for wound complications or delayed recovery. Future directions include immunohistochemical staining for CD31 and CD45 to evaluate vascular and lymphatic changes, respectively, as well as prospective follow-up to track postoperative complications such as periprosthetic joint infection (PJI), revision procedures, and postoperative pain. Expansion to larger patient cohorts will further clarify the predictive utility of fibrosis heterogeneity and limb-specific ECW/TBW.

Clinical Significance: This study provides foundational insight into the relationship between periarticular tissue composition and body composition, suggesting a practical role for preoperative bioimpedance analysis in patient evaluation. Assessing localized fluid imbalance alongside tissue fibrosis may allow surgeons to identify patients at higher risk for complications such as impaired wound healing, infection, or poor suture integrity. By moving beyond traditional reliance on BMI or chronological age and instead leveraging quantitative measures of hydration and extracellular matrix status, clinicians may be better able to anticipate which patients are most vulnerable to poor postoperative recovery. Incorporating bioimpedance-derived metrics into routine orthopedic assessment therefore holds the potential not only to guide surgical planning and perioperative management, but also to inform broader efforts toward personalized, precision-based approaches in musculoskeletal care that directly link tissue quality with clinical outcomes.







Language Barriers Are Not Associated with Urine Specimen Contamination

Allison J. Frahm, BS, Adrienne L. Esposito, MD, Emily M. Conlin, BS, Abbey J. Hardy-Fairbanks, MD, Colleen K. Stockdale, MD, MS

Introduction

In patients presenting with urinary symptoms, presence of a urinary tract infection is typically confirmed using urinalysis and/or urine culture. These lab tests are often limited by contamination with skin flora, which is especially prevalent among female patients. There is concern that non-English speaking patients may not be receiving adequate instruction on how to properly collect urine samples. Determining if there is an association between non-English speaking patients and urine specimen contamination could provide support for the implementation of efforts to improve education on proper urine sample collection.

While prior studies have shown that factors such as female sex, pregnancy, and obesity were associated with contamination, there are currently no known studies that assess the relationship between language barriers and urine specimen contamination.

Purpose

Examine whether there is an association between non-English speaking patients and prevalence of urine sample contamination.

Methods

IRB approval was obtained to identify patients who provided urine samples at any UIHC OB/GYN location within the Iowa City region. Data from Tableau were associated with patient MRNs. MRNs were used to access outpatient charts within Epic electronic medical record. Relevant data from patient charts within Epic were aggregated and input into REDCap for statistical analysis. Statistical comparisons of the rates of contamination of urine samples were performed using SPSS. Data from English speaking vs. non-English speaking patients were compared to assess differences in rates of contamination.

Results

Of the 340 patients included in this study, 30 (8.8%) were non-English speaking. The contamination rate of all urine samples was 74.4%. There was not a statistically significant difference in contamination rates for non-English speakers compared to English speakers (76.7% vs. 74.4%; $p=0.3835$).

Interestingly, contamination was associated with younger age ($p<0.0000001$) and pregnancy ($p=0.0014$). Non-contamination was associated with antibiotic use within the last 30 days ($p=0.00014$) and vaginal estrogen use ($p=0.0004$).

Conclusion

Most of the urine samples were contaminated, regardless of the language spoken by patients. Language barriers do not appear to play a significant role in the contamination of urine specimens.

An ex-vivo approach to predict clinical response to CFTR modulator therapy or to rule out CF in individuals with rare CFTR mutations

Student: Ryan Gannon
Mentor: Alejandro Pezzulo

The combination of elexacaftor/tezacaftor/ivacaftor (ETI) is effective in people with cystic fibrosis (CF) with at least one *F508del-CFTR* allele; however, approximately 10% have variants without established ETI responsiveness and are ineligible for therapy. Additionally, diagnostic confirmation or exclusion of CF can be challenging in individuals with compatible symptoms, *CFTR* variants of unknown significance, and indeterminate sweat chloride or nasal potential difference (NPD) results. We implemented a minimally invasive method for "theratyping" in subjects with confirmed or clinically suspected CF and a *CFTR* variant currently ineligible for ETI therapy. We derived air-liquid interface epithelia from airway basal cells obtained via nasal brushings; we then assessed *CFTR* function at baseline and in response to ETI with Ussing chambers. We present six cases highlighting the value of our theratyping approach in guiding clinical decision-making. In two subjects, theratyping demonstrated substantial improvement in CFTR function and supported approval for ETI therapy, with subsequent clinical improvements in airway mechanics, weight maintenance, microbiology, and symptom burden. Conversely, theratyping identified two subjects with CF unlikely to respond to ETI, suggesting they may be candidates for future trials of new therapeutics. Finally, in two subjects with suspected CF, theratyping demonstrated normal-range *CFTR* function and decreased suspicion for CF. This work highlights our theratyping approach as a practical strategy for 1) predicting ETI response in people with CF and *CFTR* variant currently ineligible for ETI therapy and 2) aiding in the diagnostic confirmation or exclusion of CF in cases with inconclusive sweat chloride or NPD results.

Oral *Candida* as a novel biomarker for chemotherapy treatment response and survival in pancreatic cancer patients

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Background: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignancy with poor prognosis and limited response to systemic therapy. Chemotherapy outcomes remain highly variable, and no reliable biomarker currently exists to guide treatment decisions. Emerging evidence suggests that the microbiome influences tumor biology and chemoresistance, and we have recently demonstrated that *Candida* species within the biliary tract and tumor microenvironment are associated with advanced stage, worse survival, and poorer response to neoadjuvant chemotherapy in PDAC patients. Additionally, our experimental models have shown that *Candida* can directly impact cancer cell growth and promote epithelial-mesenchymal-transition (EMT), which contributes to chemotherapy resistance. However, detection of tumor- or bile-associated *Candida* requires invasive sampling. Given the accessibility and feasibility of oral sampling, we investigated whether oropharyngeal *Candida* colonization could serve as a non-invasive, reliable biomarker of chemotherapy response in PDAC patients, with potential to improve patient stratification and treatment personalization.

Methods: A prospective single-institution cohort of PDAC patients (2003-2025) enrolled under approved IRB protocol (GIMER: IRB#201202743) at the Holden Comprehensive Cancer Center was queried for clinical manifestation of oropharyngeal candidiasis (OC). Buccal swabs were collected from subjects returned in the cancer clinics between June and August 2025 and plated on CHROMagar™ Candida to identify common *Candida* species. Demographic, clinicopathological, treatment, and outcome data were abstracted from electronic medical records. Student t-tests and chi-squared tests were used to compare continuous and categorical variables, respectively, between patients with and without OC. Chemotherapy response was assessed radiologically using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria and pathologically via tumor regression grade (TRG) for patients receiving neoadjuvant therapy. Overall survival (OS) and recurrence-free survival (RFS) were estimated by Kaplan-Meier analysis, and associations of OC status with chemotherapy response, overall survival (OS), and recurrence free survival (RFS) were evaluated using multivariable logistic regression and Cox proportional hazards models.

Results: Of the 248 PDAC patients meeting inclusion criteria, 41 (16.5%) displayed evidence of OC. Demographics were similar between groups, though OC-positive patients were more likely to receive upfront chemotherapy (85.4% vs. 62.8%, p=0.005). After controlling for age, sex, and stage, OC was associated with lower odds of radiographic response (OR 0.47, p=0.10) and higher risk of disease progression (HR 1.28, p=0.28). In a subset of 31 surgical patients with both intraoperative bile and buccal samples, the detection of *Candida* in buccal samples showed fair agreement with intraoperative bile samples (κ=0.33), which improved to moderate among stented patients (κ=0.42; McNemar p=0.016). Among 27 patients receiving neoadjuvant therapy followed by surgery, the presence of buccal *Candida* trended toward poorer pathological response when TRG was grouped as 0-1 vs. 2-3 (OR 0.20, 95% CI 0.01-4.25; p=0.29). Patients with buccal *Candida* tended to have shorter median RFS (20.6 vs. 27.8 months, Gehan-Breslow-Wilcoxon test p=0.03)

Conclusions: Our findings suggest that oral *Candida* is associated with trends toward poorer chemotherapy response in PDAC and worse RFS. Buccal *Candida* demonstrates moderate concordance with biliary fungal colonization in stented patients, supporting its potential role as a non-invasive surrogate marker. While these findings are exploratory and limited by small sample size, they provide rationale for larger studies and future clinical trials stratifying PDAC patients by oral fungal signatures to guide treatment.

Preoperative Urodynamic Leak Point Pressure Measurements and Stress Urinary Incontinence After Pelvic Organ Prolapse Surgery

Samantha Ohlson Gardner, BA; Leanne Brechtel, MD; Joseph Kowalski, MD; Patrick Ten Eyck, PhD; Kimberly Kenne, MD, MCR; Catherine Bradley, MD, MSCE

Introduction

Pelvic organ prolapse (POP) is a common condition in which parts of the vagina and/or uterus descend, allowing herniation of nearby organs into the vagina. POP leads to uncomfortable symptoms for which surgery is a common treatment. Stress urinary incontinence (SUI) can occur independently of POP, and patients may elect to have concurrent surgery for treatment of both. SUI may also be masked in women with prolapse due to urethral obstruction or kink and subsequently revealed following POP surgery. Current clinical guidelines recommend women with POP should undergo preoperative SUI testing while reducing the prolapse to identify "occult" SUI and then offer concurrent SUI surgery if present. However, the literature disagrees on the degree to which presurgical urodynamic parameters are predictive of postsurgical SUI. During preoperative urodynamic tests (UDT), urine leakage during a cough/Valsalva is identified, and the pressure change in the bladder that results in leakage, the abdominal leak point pressure (LPP), is recorded. While urodynamic LPPs are associated with SUI severity in patients without prolapse, the significance of this measurement in women with POP and when assessed during prolapse reduction is unclear.

Hypothesis/Purpose

The purpose was to study the value of presurgical UDT in a cohort of POP surgery patients. We hypothesized that patients with lower urodynamic LPP measurements at UDT were more likely to experience postoperative SUI with or without concurrent SUI surgery.

Methods

This cohort study included patients from the Urogynecology Surgery Repository at the University of Iowa who had anterior and/or apical POP surgery and preoperative UDT. Baseline, surgical, and 3- and 12-month postoperative data were collected prospectively, including the Pelvic Floor Distress Inventory-20 (PFDI-20) questionnaire. Additional urodynamic and postoperative SUI data were collected via retrospective chart review. During UDT, urine leaks were elicited with and without prolapse reduction and intrinsic sphincter deficiency (ISD), a more severe type of SUI, was identified with LPP $\leq$60 cmH_2O. The primary (composite) outcome was SUI at 3 months, defined as SUI symptoms ("urine leakage related to coughing, sneezing, or laughing") rated at least "somewhat" bothersome (PFDI-20 item #17) and/or SUI treatment recommended. Secondary outcomes included 12-month postoperative SUI endpoints.

Results

164 women were included who had 3- (n=163) and/or 12-month (n=103) follow-up data (PFDI-20 or clinic visit). Median age was 64.5 years and 69 (48.2%) had stage 3-4 POP. 79 (48.2%) had preoperative SUI, and 88 (53.7%) leaked during UDT. Of those who leaked, 43 (48.9%) had ISD. 65 (39.6%) had concurrent SUI surgery. The composite SUI outcome (symptoms and/or treatment recommendations) at 3-months occurred in 44 (27%) and did not differ in those with or without UDT leak or with or without ISD, but SUI treatment was more often recommended at 3 months in those with preoperative ISD (7 (16.3%) vs 1 (2.2%), p=0.03). The association between preoperative ISD and 3-month SUI treatment recommendations was attenuated after adjusting for concurrent SUI surgery (ISD OR 6.9 (0.8-60.3, p=0.08)). At 12-months, the composite SUI outcome did not differ among those with UDT leak vs no leak (10 (17.9%) vs. 12 (25.5%), p=0.47), but, like 3-month results, was more common in those with vs. without ISD (8 (29.6%) vs. 2 (6.9%), 0.04).

Conclusion:

Among patients planning POP surgery who leak at preoperative UDT, lower LPPs indicating ISD were associated with more SUI after surgery, as indicated by SUI treatment recommendations at postoperative visits or by SUI symptoms (at 12 months). This finding suggests clinical value to LPP measurements during preoperative UDT. Our results may help surgeons in counseling POP patients about expected outcomes and the option of concurrent SUI surgery.

Clinicopathologic Features in an Institutional Cohort of Gastric Neuroendocrine Tumors

By Garza, KG, Bellizzi, AM, & Gosse, MD

Background

Gastric neuroendocrine tumors (G-NETs) are rare neoplasms that mostly arise from enterochromaffin-like (ECL) cells, which regulate gastric acid secretion by producing and releasing histamine. There are currently three established G-NET subtypes and a presumptive fourth G-NET subtype, which has been tied to chronic proton pump inhibitor (PPI) use. Each G-NET subtype has specific clinical associations and prognostic outcomes. It is generally difficult to distinguish Type III and Type IV G-NETs via histology alone. Thus, one objective of this study was to identify clinicopathologic features that can be used to more reliably differentiate between G-NET subtypes, especially Type III and Type IV.

Materials and Methods

Subjects were selected for the project if they had their procedure performed at the University of Iowa Hospitals & Clinics (UIHC) and were diagnosed with a primary neuroendocrine tumor of the stomach between January 1, 2000, and May 30, 2025. Slides from each patient case were reviewed to categorize G-NETs based on histology. These pathological diagnoses were later informed by a review of patient records.

A tumor was classified as a Type I G-NET if it possessed histological features typical of autoimmune atrophic gastritis and/or the condition was endorsed in the associated pathology report. Type II G-NETs were identified by the presence of elevated serum gastrin (>100 pg/mL) and a past medical history that included one of the following conditions: multiple endocrine neoplasia 1 (MEN1), Zollinger-Ellison syndrome (ZES), or gastrinoma. A tumor was classified as a Type IV G-NET if the patient was on a proton pump inhibitor (PPI) for at least 12 months. Additionally, the patient needed to have a history of elevated serum gastrin (>100 pg/mL) and/or neuroendocrine hyperplasia was present on the associated slide. If a tumor did not meet the criteria established for the other categories, it was classified as a Type III G-NET.

A Fisher's exact test and post-hoc pairwise Fisher's exact test (if applicable) were performed for statistical analyses involving categorical variables. Due to the limited number of Type II G-NET samples, a Kruskal-Wallis test and post-hoc Dunn test (if applicable) were performed for statistical analyses involving continuous variables. All statistical tests were two-sided using a p-value less than or equal to 0.05.

Results

The most statistically significant difference between G-NET subtypes was in mean serum gastrin (p-value=2.20×10^{-16}). Type I G-NETs had the highest mean serum gastrin at 809.3 pg/mL. Meanwhile, Type III G-NETs had the lowest mean serum gastrin at 82.0 pg/mL. Type II G-NETs had a mean serum gastrin of 639.9 pg/mL, while Type IV G-NETs had a mean serum gastrin value of 366.8 pg/mL.

Another notable difference between G-NET subtypes was in duration of PPI use (p-value=2.74×10^{-4}). As expected, the Type IV G-NETs had the longest mean PPI use at 60.8 months. Type III G-NETs followed with a mean PPI use of 27.8 months. Type I G-NETs had a mean PPI use of 18.8 months, while Type II G-NETs were associated with the lowest mean PPI use at 5.6 months.

Mean age at diagnosis significantly differed between G-NET subtypes (p-value=6.73×10^{-3}), with Type II G-NETs having the lowest mean age (at diagnosis) of 31 years old. Interestingly, there was not a significant difference in mean tumor size, focality, or male-to-female ratio between G-NET subtypes in our cohort.

Conclusions

Previous studies have relied on PPI use to differentiate between Type III and Type IV G-NETs; however, the results of this study suggest that mean serum gastrin may be a more reliable way to distinguish G-NET subtypes, including Type III and Type IV.

3D Lego model for Mohs Education, Anxiety, and Satisfaction

Student: Luke Geis
Primary Mentor: Jennifer G. Powers, MD
Collaborators: Daniel Haws, Christopher Langland, Nicole Negbenebor MD, Kirk Sidey MD MBA, Marta Van Beek MD MPH, and Elizabeth Cusick MD

Background: Previous studies have shown patient perioperative anxiety to be associated with increased postoperative pain and decreased satisfaction. Additionally, undergoing three or more stages of Mohs micrographic surgery (MMS) has been associated with reduced patient satisfaction. Many types of standardized patient education may be utilized preoperatively, including phone calls, pamphlets, videos, and analogies. 3D models in MMS have demonstrated the ability to reduce anxiety while improving patient understanding of surgery. It is unclear if specific education, focused on the necessity of additional stages, could improve a patient's education, anxiety, and satisfaction with the surgery.

Purpose: The primary goal of this study is to evaluate whether the use of a 3D Lego model can enhance patient understanding, reduce anxiety, and improve overall satisfaction with Mohs micrographic surgery by providing a tangible, visual representation of the procedural stages. The secondary objective of this study is to identify other factors associated with anxiety, satisfaction, and understanding of MMS.

Methods: The study utilized an unblinded, randomized control trial design with patients split between:1) a standardized education (SE) via script (control group) and 2) standardized education utilizing a Lego model (experimental group). Patients filled out preoperative surveys for visual analog scale (VAS) procedure understanding, VAS anxiety, and short-form state-trait anxiety index (STAI). Following the first stage of Mohs surgery, patients filled out VAS understanding and anxiety, STAI, patient satisfaction questionnaire (PSQ) 18: short form, and a 5-question knowledge assessment.

Results: 100 patients were recruited with 50 each in the control and experimental groups. Both recruited groups had similar mean demographics: age (72.24 years) ($p = 1.0$), sex (61% male) ($p = .54$), prior MMS experience (56%) ($p = .23$). Both groups experienced a statistically significant reduction in VAS Anxiety, STAI forms, and an increase in VAS understanding pre-operatively vs after the 1st stage. The Lego model group performed better on the knowledge assessment, answering 90.4% correctly, with the standard education alone group answering 86.8% correctly, though this difference was not statistically significant ($p > .05$). Patients who were married were more likely to experience increased satisfaction as reported by PSQ 18 ($p<.05$).

Conclusion: There was a trend towards improved performance in the Lego group compared to SE group, but there was no statistical significance. More research is needed to understand how a higher knowledge base impacts patient experience during Mohs micrographic surgery and if 3D models improve spatial reasoning for patients. Individuals who stated they were married were associated with increased satisfaction during the visit and decreased anxiety post-stage.

Limitations: Overestimations of baseline anxiety via STAI-trait, limited and simple questions in the knowledge questionnaire, multiple educators.

Outcomes in stage IIB and IIC cutaneous melanoma treated with wide local excision and adjuvant pembrolizumab without sentinel lymph node biopsy

Mahaasrei Ghosh; Brandon Toliver, MD; Mohammed Milhem, MD; Hisakazu Hoshi, MD

Introduction: The Multicenter Selective Lymphadenectomy Trial-1 (MSLT-1) reported no significant difference in overall survival (OS) but poorer disease-free survival in patients who had wide local excision (WLE) versus WLE with sentinel lymph node biopsy (SLNB) with subsequent complete axillary dissection if SLNB was positive. With expanded immunotherapy recommendations for stage IIB and IIC melanoma from the KEYNOTE-716 trial, what are the expected survival outcomes? Thus, we studied patients who had WLE without SLNB for stage IIB/C melanoma and adjuvant Pembrolizumab to determine RFS and OS.

Hypothesis: The expected recurrence-free and overall survival outcomes with adjuvant immunotherapy for stage IIB/C melanoma will not be significantly different in patients who undergo WLE only and patients who undergo WLE with SLNB.

Methods: We performed a single-institution retrospective chart review and included patients with stage IIB/C cutaneous melanoma who were treated with WLE and adjuvant pembrolizumab. The primary endpoint was recurrence-free survival (RFS), and the secondary endpoint was OS. Recurrence was defined as local, regional lymph node, or distant metastasis; new primary melanoma not considered recurrence. Survival was estimated via a Kaplan-Meier survival analysis.

Results: Twenty-nine patients met inclusion criteria between 2021-2025. Our sample was 59% male, 100% White, non-Hispanic, and median age at operation was 58.0 ± 11.7 years. Twenty-two (75.9%) patients were clinical group stage IIB. Twenty-seven underwent WLE and two had toe amputation. Tumor subtypes included acral lentiginous (3.4%), desmoplastic (3.4%), nodular (38%), spindle cell (3.4%), and superficial spreading (27.6%). Median follow-up was 24.0 ± 11.2 months.

Mean RFS was 25 ± 11.3 months. We observed 10 recurrences (34.5%), 5 (17.2%) occurred in regional lymph nodes at 3, 7, 7, 20, and 34 months, and 5 (17.2%) were distant metastases at 6, 11, 19, 20, and 25 months. At 11 months, the RFS probability was 80.5% and 42.7% at 34 months. Three deaths occurred at 11, 17, and 32 months, and the OS probability was 95.5% at 11 months and 79.4% at 32 months. Mean OS was 35.9 ± 1.9 months. Of the 5 patients with regional node recurrences, 4 modified their immunotherapy regimen to nivolumab/relatlimab and experienced complete radiologic response with no subsequent recurrence or death.

Conclusion: In our cohort treated with WLE and adjuvant pembrolizumab, OS at 3 years was comparable to OS reported in the observation arm of MSLT-1. RFS was comparable to KEYNOTE-716 at 1 year but declined beyond 2 years. This suggests that adjuvant pembrolizumab may maintain survival outcomes in the early period; however, a larger, more heterogeneous sample studied over a greater amount of time is needed to substantiate this conclusion.

Eye-Opening Transfers: Eye Complaints seen in the Emergency Department

Heath Gibbs
Mentor: Kaila Pomeranz DO, MME
Collaborators: Kanwal Matharu MD; Erin Shriver MD, FACS; Peter Sanchez MD; Eliezer Santos León; Katie Schneider MSN, RN

Introduction: Emergency department (ED) overcrowding remains a persistent challenge in the United States, contributing to inefficiency, prolonged wait times, and patient dissatisfaction. Between 2010 and 2017, there were over 16 million eye-related ED visits nationwide. Emergency medicine physicians report limited training and confidence in managing ocular disease, and it is hypothesized that many rural hospitals lack the equipment or ophthalmic specialists required for accurate evaluation. Consequently, patients are frequently transferred to tertiary care centers such as the University of Iowa Healthcare (UIHC). However, a recent study found that only 13.4% of orbital fracture cases presenting to UIHC required emergent intervention, suggesting that many transfers may not be truly emergent.

Purpose: To characterize the frequency, transfer status, diagnoses, and follow-up of patients presenting with eye complaints at UIHC's ED. This analysis aims to identify ocular conditions emergency physicians must be prepared to evaluate and assess whether potentially avoidable transfers contribute to ED overcrowding.

Methods: We reviewed the charts of 894 patients who received an ophthalmology consult in the UIHC ED during 2024. Data collected included diagnosis, transfer status, referral source (eye clinic, urgent care, other outpatient clinics), ophthalmology clinic follow-up within 14 or 28 days, and same-day clinic evaluation. Patients seen for papilledema in the context of systemic disease and those without an eye-related diagnosis were excluded. Patients with eye related complaints who did not have an ophthalmology consult were not included. Of 743 eligible patients, 17 (2.3%) required hospital admission and were excluded. The final cohort consisted of 726 discharged patients.

Results: Among the discharged cohort, 226 (31.1%) were transferred from outside EDs, 108 (14.9%) were referred from eye clinics, 56 (7.7%) from urgent care, and 24 (3.3%) from other outpatient clinics. Same-day ophthalmology follow-up occurred in 115 (15.8%) cases. Follow-up within 14 and 28 days occurred in 348 (47.9%) and 396 (54.5%) patients, respectively. The most common diagnoses included orbital fracture (68), retinal detachment/tear (60), eyelid laceration (49), corneal abrasion (45), posterior vitreous detachment (44), corneal ulcer (36), hyphema (28), motility disturbance/diplopia (22), chemical injury (21), foreign body (20), and vitreous hemorrhage (20). Notably, 40 of 60 retinal detachments/tears (66.6%) were transferred from eye clinics; all were discharged, with 61.6% seen same-day at the UIHC eye clinic and 93.3% within 14 days.

Conclusion: The vast majority of patients with eye complaints (96.7%) were discharged from the ED, many with rapid follow-up in ophthalmology clinic. These findings suggest that a proportion of cases, though urgent, were not emergent. Nearly one-third of patients were transferred from other EDs and another quarter from outpatient clinics, indicating that some referrals may have been more appropriately managed in urgent ophthalmology settings. Improved triage and referral pathways may help reduce unnecessary ED transfers and alleviate overcrowding at tertiary centers. Additional education can be provided to our own ED residents for evaluation of ophthalmologic complaints to enhance comfort with subsequent practice in a community or rural setting.

Recovery coaching outcomes in patients with co-occurring liver disease and substance use disorders

Mikayla Gibson, BS, Andrea Weber, MD, MME, Frankline Matanji, Ph.D., Vickie Roesner

Background: Since the pandemic, the prevalence of alcohol use disorder (AUD) in the U.S. has nearly doubled. Over the past two decades, mortality from alcohol-associated liver disease (ALD), a common complication of AUD, has also nearly doubled. Despite evidence-based treatments, AUD remains highly untreated, particularly for those in rural areas. Recovery coaching, when integrated into the healthcare team, could be a solution to increasing treatment engagement and mitigating stigma between healthcare professionals and those with substance use disorders (SUD). Recovery coaches (RC) are qualified individuals with lived experience who support those in recovery by offering hope, resources, personalized recovery plans, and guidance in setting goals and navigating challenges. Recovery coaching is a low-cost, low-barrier intervention that reduces healthcare costs, decreases hospitalizations, and improves relapse rates, recovery capital, and treatment adherence. To our knowledge, the effectiveness of recovery coaching has not been studied in individuals with co-occurring ALD and SUD, nor has it been evaluated when delivered primarily via telehealth with a rural population. We hypothesize that hybrid recovery coaching delivered in a healthcare team will be accepted, feasible, and improve recovery outcomes in a medically complex population.

Methods: This study evaluates outcomes of the Integrated Liver Recovery Service (ILRS), a three-year pilot grant funded by SAMHSA. ILRS enrolls Iowans with SUD and ALD and provides them an array of treatment options, offered both in-person and virtually, which include case management, therapy, recovery coaching, and medication for addiction treatment. Participants completed the Government Performance and Results Act (GPRA), the Brief Addiction Monitor (BAM), and the Assessment of Recovery Capital (ARC) surveys upon enrollment, six-month follow-up, and discharge. Additionally, Model of End-Stage Liver Disease–Sodium (MELD-Na) scores, used to estimate 90-day mortality in those with liver disease, were obtained from the electronic health record. A satisfaction survey was administered at six-month follow-up. To analyze the data, we ran Wilcoxon signed-rank test for paired samples, McNemar's test, Spearman's rank correlation test, and descriptive statistics using SPSS 29.0.1.1.

Results: Of the 84 participants enrolled between September 30, 2022, and March 31, 2025, the majority were male (69.0%, n=58), white (88.1%, n=74), non-Hispanic (94.0%, n=79), and heterosexual (91.7%, n=77). Thirty-eight percent resided in rural counties (n=32). All participants had been diagnosed with AUD and ALD, and nearly half had decompensated cirrhosis (DC) (n=39). Seventy-five of 84 participants (89.3%) met with the RC at least once. The RC provided 3,342 services, with the most popular services being recovery support (47.7%, n=1593) and goal setting (22.5%, n=753). The RC engaged with clients most commonly via phone call (59.6%, n=1992) and text (31.5%, n=1053). Of the 47 participants who utilized recovery coaching and completed a 6-month follow-up, the median number of RC encounters per client was 45 (range 3-310). For this subset of participants, Wilcoxon signed-rank test demonstrated a significant decrease in MELD-Na scores (36.2%, n=17, $p<0.05$), past 30-day alcohol consumption (48.9%, n=23, $p<0.05$), and past 30-day binge drinking (50%, n=8, $p<0.05$), and a significant increase in ARC scores (70.2%, n=33, $p<0.001$). The median ARC score increased from 36 to 41. McNemar's test revealed a significant decrease (60%, $p<0.01$) in past 30-day emergency department visits. Higher volumes of recovery coaching were positively correlated with relationship satisfaction and negatively correlated with alcohol consumption and MELD-Na scores but were not significant. Those with DC and those with less advanced ALD had similar proportions of high utilizers of RC services (45.9%, n=17 vs. 56.7%, n=17). Satisfaction rates were high with the types (91.7%, n=33) and quality (94.4%, n=34) of services offered. When asked "what services were most helpful," 61.1% (n=22) mentioned recovery coaching in their open-ended responses.

Conclusion: Our study demonstrates that recovery coaching, delivered virtually within an integrated team is feasible and accepted in a medically complex, rural population. Participants showed significant improvement in multiple domains: increased recovery capital, improved liver function, reduced alcohol consumption and binge drinking, increased abstinence, and reduced ED utilization. These findings correlate with reduced mortality and increased life quality and suggest improved social capital and health management. While these outcomes cannot be directly attributed to recovery coaching alone, nearly 90% of participants engaged with the RC, and most reported it as integral to their recovery. Patients with DC participated at similar rates to the others, highlighting that coaching is both accessible and desirable among those with severe illnesses. These findings align with current literature and contribute new evidence that recovery coaching is practical and well-received in virtual, rural, and medically complex contexts, promoting its expansion in to broader medical environments. Study limitations include sample size, self-reported data, and potential confounding variables. Future research should explore causal pathways and evaluate recovery coaching in larger, more diverse populations.

Structural Brain Lesions and Delirium in Geriatric Emergency Department Patients: A Matched Case-Control Study

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Abstract

Background: Delirium is a common and serious condition affecting up to one-third of older adults in the emergency department (ED). While often attributed to reversible causes, structural brain lesions may be associated with delirium risk. This study evaluated whether structural brain abnormalities on head CT are associated with delirium in older ED patients.

Methods: We conducted a retrospective matched case-control study of adults aged ≥65. Cases were defined as patients who screened positive for delirium and underwent head CT within 24 hours. Each case was matched 1:1 to a control without delirium based on age, sex, Emergency Severity Index, and chief complaint. Structural lesions were identified throught radiology report review. Associations between lesion presence and delirium were assessed using conditional logistic regression, adjusting for dementia and comorbidity burden.

Results: A total of 244 patients were included (122 cases, 122 matched controls). Structural brain lesions were more common in delirium cases than controls (55.7% vs. 37.7%). The presence of a lesion was associated with increased odds of delirium (unadjusted OR = 2.2, 95% CI: 1.3 – 3.7; adjusted OR = 2.1, 95% CI: 1.1 – 3.8). Ischemic lesions were the most frequently observed lesion type.

Conclusion: Older adults with delirium had significantly higher odds of structural brain lesions on head CT compared to matched controls. These findings suggest that brain lesions may contribute to delirium pathogenesis and highlight the value of neuroimaging in selected geriatric ED patients. They also reinforce the importance of early delirium screening to inform diagnostic workup and guide care planning.

Evaluation of the Concordance and Discordance in Urine Parameters on the Risk of Cystine Stone Activity

Carson Godbersen BS, Chad Tracy MD, Ryan Steinberg MD

Introduction: Cystinuria is a rare, autosomal recessive disease that leads to the formation of cystine stones. The mechanism of action is due to a mutation on the SLC7A9 or SLC3A1 gene, which disrupts kidney reabsorption of four amino acids: cysteine, ornithine, lysine, and arginine. Unlike the others, cysteine's low solubility allows for crystal precipitation, and therefore leads to stone formation. Because of its genetic nature, patients often experience stone formation and the symptoms related to stones before the age of thirty. The lifetime risk of recurrent stone episodes is high and places these patients at an increased risk for chronic kidney disease. Currently, cystinuria patients are monitored with 24-hour collections which assess the chemistry of their urine. Specifically, the cystine concentration and cystine capacity are the most important parameters. While cystine concentration is a simple measurement, it does not account for all possible molecules that can affect cystine stone formation. Cystine capacity does account for these molecules but is a proprietary test offered by only one lab. Many patients will progress to needing Thiol-Binding Drugs (TBDs) to make their urine less likely to form stones. The medication works by binding cysteine in its monomeric form. In the presence of TBDs, a cystine concentration will be artificially low due to the medication, which can make it hard to assess whether medical treatment is working to decrease the risk of stone formation. In many circumstances, these two parameters (cystine concentration and cystine capacity) will be in discordance which can make it hard to assess the patient's risk for recurrent stone formation.

Purpose: To characterize adult cystine stone patients cared for at UIHC over the past 15 years and see if stone activity differs when cystine capacity and cystine concentration are concordant or discordant.

Methods: We performed a retrospective chart review of all patients who were seen at UIHC with a diagnosis of cystinuria or stone analysis demonstrating cystine composition between 1/1/2010 and 1/1/2025. We collected patient demographics, surgical and medical histories, interventions performed at UIHC, blood labs, urine labs (including 24-hour urine collections (24U)), medications, and imaging studies performed during the review date. Descriptive statistics were generated. Only 24-hour urine collections that included all cystine stone parameters, including cystine concentration (CCon) and cystine capacity (Ccap), were included in the stone activity analysis. CCon and Ccap was labeled as favorable (+) or unfavorable (-) based upon previously established cut offs (favorable included CCon<250 and Ccap >90). Chi squared statistics were performed to compare stone activity amongst groups. P-value <0.05 was considered significant

Results: A total of 52 patients were identified, of which 32 were greater than 18 years old and thus included in data analysis. The median age was 33 (IQR 22-54), with 15 males and 17 females. 31 were white, and 1 was ethnically Hispanic. The median BMI was 35.1 (IQR 28.3-38.5), and 18 (56%) patients had hypertension and/or diabetes. Eight (25%) patients had a family history of cystine stones, nine (28%) patients had a family history of non-cystine stones, and 15 (47%) patients had no family history of stones. 29 (91%) patients had at least one stone surgery prior to establishing care at UIHC. 19 (59%) patients had at least one stone surgery at UIHC, with 12 (38%) patients receiving a ureteroscopy and 13 (41%) receiving percutaneous nephrolithotomy. The median follow up time was 58 months (IQR 5-125). We identified 16 patients who completed a 24U with a median number of 4 (IQR 2-5) collections per patient. A total of 64 24U were identified, though only 24 were appropriate for analysis. We identified 1 24U classified as +CCon/+Ccap, 5 classified as +CCon/-Ccap, and19 classified as –CCon/-Ccap. Stone activity for +Ccon/+Ccap was 0%. There was no statistical difference between the stone activity for +CCon/-Ccap (20%) and –Ccon/-Ccap (64%, p=0.11). When comparing to -Ccon/-Ccap, +CCon/-Ccap collections had higher median urine volume (+0.66), lower pH (-0.09), lower citrate (-19), more favorable cystine capacity (+42), and more favorable cystine concentration (-167).

Conclusions: In patients treated at Iowa over the past fifteen years, only 38% of urine collections contained the critical parameters for cystine patients. Of those that were correct, discordant parameters were found in 20% of the results. While not statistically significant, a clinically significant difference was noted in the stone activity rate between those with concordant unfavorable parameters and discordant parameters, which may be due to the increased median urine volume. This suggests that the combination of both parameters may be best to provide an accurate risk for stone formation. Further analysis of large populations is needed to confirm these findings.

Title: Revisiting the risk of complications from hepatic adenomas

Authors: Sean Michael Gomendoza, Dr. Kyle Brown

Background and aim:

Hepatic adenomas (HAs) are benign liver tumors that are usually asymptomatic and are most often found incidentally on abdominal imaging. These lesions have a strong female predilection and are associated with exposure to estrogens. Serious consequences of HAs, such as hemorrhage or malignant transformation to hepatocellular carcinoma (HCC), are infrequent but the risk of these complications is uncertain. The literature suggests that the risk of rupture is 25%, while the risk of malignancy is 5%; however, these figures are derived from surgical series, in which HAs requiring surgical intervention are likely to be over-represented. The aim of this project was to determine the rate of complications in all patients with HAs seen at UIHC by a variety of specialists over 20 years.

Methods:

We reviewed the records of patients seen at UIHC for a benign liver neoplasm from 2005 to 2025, using a list of all patients diagnosed with the ICD-10 code D13.4. Patients whose lesions were determined to be HAs comprised the study group. All information was manually reviewed and stored in Excel and descriptive statistics were then performed.

Results:

Of 741 patients with liver or biliary tree neoplasms, 245 were confirmed to have an HA. 233 patients (95.1%), were female, with an average age at diagnosis of 38 yrs. 210 female patients (90.1%) had a documented history of use of oral contraceptives (OCPs). A majority of HA patients were seen by adult GI/Hepatology (155 [63.3%]) or by surgery (68 [28.2]) with a smaller number of patients seen by Heme-Onc (4), Peds GI (5), Interventional Radiology (2), OB/Gyn (1), Internal Medicine or Family Medicine (6). Of the 242 cases in which the circumstances surrounding the identification of the liver lesion could be ascertained, 202 (83.5%) HAs were found incidentally. 234 patients had sufficient information to assess whether a complication was present at the time of initial evaluation or later, during the average follow-up period of 4.46 years. The classical picture of an adenoma rupture with hemorrhage occurred in 15 patients (6.5%); in 14/15 cases, the hemorrhage was the initial presentation of the HA. In 2 patients, or 1.0% of the overall sample, an HCC arose out of an HA. Finally, of 227 patients with at least one follow-up visit, the treatment plans included observation (145 [63.9%]), embolization (20 [8.8%]), surgical resection (48 [21.1%]), or some combination of these (15 [6.6%]).

Conclusions:

The overwhelming majority of HA patients in this series were females with a history of OCP use, consistent with the current understanding of the genesis of HAs; that is, the development of these tumors is linked to the growth-inducing effects of estrogens on hepatocytes as well as the naturally higher levels of estrogen in reproductive age women.

Our data suggest that when patients with HAs followed by non-surgical specialists are included, rates of HA-related complications are substantially lower than the literature indicates. It is also worth noting that complications of HAs were often the presenting symptom of the HA. The usual approach to management of incidentally-discovered HAs that are <5 cm in size is to discontinue OCPs and monitor with periodic imaging. With the exception of 2 patients that were initially lost to follow-up, no patients experienced a serious complication with regular monitoring across the mean follow up time of about 4 1/2 years. Finally, over 60% of our sample did not require any intervention; this information will hopefully enable providers to make more informed decisions on the management of HAs as well as provide patients with HAs with better information about this condition.

Developing an Assay for tRNA-Fragment Mediated Suppression of Herpesvirus Replication in Macrophages

Nicholas Gorman, Jessica Tucker

Introduction: Gammaherpesviruses (gHV) like Kaposi Sarcoma--Associated Herpesvirus and Epstein-Barr Virus are linked to many human cancers. gHVs are known to have a biphasic lifestyle, in which they can lytically replicate or establish latent reservoirs in many cell types (including macrophages). A unifying feature of these viruses is their modification of host transcription during infection. Specifically, gHVs cause increased expression of pre-tRNAs by enhancing RNA Pol III activity, as well as depleting host tRNA processing machinery by host shutoff—a virus-induced mechanism that depletes host mRNAs and protein. Tsen2 and Clp1 have been identified as important tRNA processing factors that are perturbed during gHV infection, and small RNA sequencing confirms that tRNAs are cleaved into tRNA fragments (tRFs) in response to gHVs. Our data suggest that accumulation of tRFs correlates with decreased viral replication and decreased viral gene expression. One hypothesis is that tRFs are directly responsible for suppression of viral replication through one of many possible effector mechanisms, including cytokine stimulation, RNA binding protein sponging, or RNA interference.

Purpose: To develop an assay that can be used to directly introduce tRFs into macrophages by transfection, then evaluate whether these tRFs attenuate viral replication or gene expression in the host.

Methods: Murine immortalized bone marrow-derived macrophages (iBMDMs) were cultured and transfected with tRFs and control single stranded RNAs. Six hours after transfection, one subset of samples were collected for qPCR analysis, and another subset was infected with MHV68, a murine gHV used as a gHV model virus. 48 hours after infection, supernatant was collected for viral titering using the 50% tissue culture infectious dose (TCID50) assay, and cells were lysed for RT-qPCR analysis. Transfection efficiency was verified in six-hour samples by TNFα induction and stem-loop RT-qPCR (SL-qPCR). Viral replication was measured by TCID50 and endogenous viral gene expression of the viral ORF50 gene. All qPCR used the $\Delta\Delta C_t$ relative quantitation method relative to an 18S rRNA control gene.

Results: The HIV ssRNA40 positive control demonstrated upregulation of TNFα corresponding to successful entry of small RNAs into the cell. SL-qPCR also demonstrated strong recovery of tRFs corresponding to a ~1,000-10,000-fold increase in tRF levels above background, which was stable over the course of the experiment. TCID50 assay revealed no reduction of viral titer in cells transfected with tRFs compared to those treated with negative control. Quantitation of viral ORF50 mRNA transcripts also showed no observable reduction in viral gene expression, although some tRFs appear to mildly stimulate viral gene expression upon our first trial.

Conclusion: We developed an assay in which tRFs can be reproducibly introduced into macrophages and transfection can be verified in two ways. Despite efficient delivery, individual tRFs alone do not appear to be sufficient to substantially reduce viral gene expression or replication of MHV68. Future studies should explore alternative outcomes of tRNA cleavage, such as changes to the overall tRNA pool.

Evaluating Outcomes and Return to Sport of Ulnar Collateral Ligament Injuries in Wrestlers

Student: Eli Gregory, BS

Mentor: Robert Westermann, MD

Collaborators: Richard J. VanTienderen, DO, Brandon J. Marshall, MD, Brain R. Wolf, MD, Shannon Ortiz, MPH.

Introduction:

Ulnar collateral ligament injuries are under-studied in wrestlers despite high injury rates. Unique biomechanical demands may create distinct injury profiles and treatment plans compared to the overhead athlete.

Methods:

This study is a retrospective review of wrestlers, 12 and older, treated for UCL injuries at UIHC between 2014-2023. All wrestlers with UCL injuries were included. Patients with unrelated elbow pathology or injuries sustained in other sports were excluded. Data collected included demographics, competition level, injury mechanism, physical exam and imaging characteristics, and treatment modality. Key outcome was ability to return to sport (RTS).

Results:

We found 46 wrestlers that met inclusion criteria. Average age was 18, BMI ranged from 23.0 to 27.6. Ten athletes were female. 7% were competing in middle school, 52% in high school, 33% in college, 9% in a wrestling club, and 2% at the national level. 89% (41/46) were primarily indicated for non-operative treatment and 11% (5/46) underwent primary surgery. 41% (17/41) of the non-operative treatment group failed conservative management and 44% (18/41) ultimately required surgery.

The non-operative treatment group consisted of 3 middle school, 21 high school, 14 collegiate, and 3 club athletes. Of these, 1 middle school, 11 high school, 4 collegiate, and 1 club athlete failed conservative treatment after an average of 124 days, requiring subsequent surgery. Tear characteristics included 22 proximal, 10 distal, 2 midsubstance and 5 combined proximal/distal tears. The group that failed non-operative management tended to have complete tears, or tears involving both proximal and distal aspects of the UCL. Surgical management included 15 reconstructions and 3 augmented repairs. RTS occurred in 71% of the non-operative group at an average of 42 days, versus 76% of the surgical group at 180 days post-op.

The primary surgery group consisted of 3 high school, 1 collegiate, and 1 national level athlete. Tear characteristics included 3 proximal, 1 proximal/distal, and 1 proximal/midsubstance/distal tear. All tears were complete. 4 underwent UCL reconstruction, and 1 received augmented repair with internal bracing. These athletes saw 100% RTS at an average of 154 days.

Conclusion:

Wrestlers showed high RTS rates following both nonsurgical and surgical UCL treatment; however, primary non-operative management failed in 44% of patients, particularly those with complete tears, necessitating subsequent surgery. While nonoperative treatment led to faster RTS, successful outcomes were achieved with surgical intervention, particularly reconstruction.

Analysis of quantitative sonographic echogenicity and renal measurements with differential renal function in infants with unilateral congenital hydronephrosis

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INTRODUCTION: Hydronephrosis is the most common urologic abnormality discovered on prenatal ultrasound. Current practice includes postnatal renal ultrasonography and nuclear renal scans to assess differential renal function (DRF). Previous research showed kidneys with hydronephrosis and renal medullary pyramid <3mm in length were at significantly increased risk of a DRF < 40%. In addition, kidneys with parenchyma that is more echogenic than the liver or spleen are at increased risk for decreased renal function, however, this is a subjective determination.

PURPOSE: This project explored whether sonographic quantification of echogenicity in the renal parenchyma or renal pyramids correlated with the relative kidney function as determined by nuclear renal scan and could therefore better identify children with compromised renal function.

METHODS: We retrospectively reviewed 71 children with unilateral hydronephrosis who underwent both a renal ultrasound and nuclear renal scan. Adobe Photoshop was utilized to quantify the echogenicity of the renal pyramids, parenchyma, and pelvic fluid as well as the parenchyma of the adjacent liver or spleen. The echogenicity of the renal pyramid and parenchyma measurements were normalized by dividing them by the renal pelvic fluid measurement. The ratio of these values compared to the liver and spleen were then assessed for correlation to the DRF from the nuclear scans using T-tests and with a 40% DRF threshold for Fisher's exact analysis.

RESULTS: The parenchyma echogenicity/pelvic fluid ratio was not significantly associated with a DRF threshold of 40% ($p = 0.21$), and the inclusion of the Liver or Spleen echogenicity decreased the association ($p = 0.61$). All other analyses that were run failed to show meaningful correlational relationships ($r < 0.3$).

CONCLUSIONS: We were unable to identify a significant correlation between echogenicity and renal function in any category, nor an echogenicity value predictive of a DRF < 40%. Our study's results may have been limited due to a small sample size, a single reviewer, and lack of severely compromised kidney function. The data points we had from the few compromised kidneys appeared to support our hypothesis, but more evidence is needed to determine whether quantifiable echogenicity could work as a reliable method for predicting DRF.

Surgical Management Patterns of Iris Lesions Suspicious for Melanoma at a Tertiary Referral Center

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Purpose: To evaluate the incidence of iris lesions and characterize clinical decision-making, surveillance duration, and timing of surgical interventions for lesions suspicious for melanoma at a tertiary care center.

Methods: This was a retrospective, IRB-approved study of 280 eyes of patients referred to the University of Iowa for iris lesions suspicious for melanoma. Kaplan-Meier analysis was applied to estimate time from initial evaluation to time of surgical intervention.

Results: 280 eyes were included in the analysis. 44 (16%) had surgical intervention, while the majority (84%) were managed with observation alone. Among the 44 eyes that had intervention performed, interventions included iridocyclectomy (59%), plaque brachytherapy (16%), and enucleation (11%).

Conclusions: At this tertiary academic referral center, the majority of iris lesions suspicious enough for surgical intervention were treated with iridocyclectomy. Most surgical interventions were recommended within the first two years of surveillance.

Title: Transient Skeletal Muscle Loss After Cervical Decompression for Myelopathy
Student: Isaiah Gritters
Mentor: Dr. Catherine Olinger
Collaborators: Reagan Grieser-Yoder, Dr. Bradley Hindman, Dr. Matthew Howard, Dr. Andrea Strayer, and Dr. Natalie Glass
Introduction with background: Degenerative cervical myelopathy (DCM) is a prevalent spinal cord disorder in older adults that causes neurologic symptoms such as gait instability and disruption of fine motor control. The goal of surgical decompression for DCM is to halt or reverse neurologic dysfunction as measured by the modified Japanese Orthopaedic Association (mJOA) scale, but factors influencing postoperative recovery remain incompletely understood. Sarcopenia, defined as abnormally low skeletal muscle mass and/or strength, is common in older adults and is linked to accelerated functional decline, increased mortality, and may negatively affect outcomes in cervical spine procedures. Bioelectrical impedance analysis (BIA) is a guideline-accepted, noninvasive method for quantifying skeletal muscle mass, and can be used to calculate the appendicular skeletal muscle index (ASMI) and detect sarcopenia at presurgical baseline and postoperative changes over time.
Purpose: To determine the prevalence of sarcopenia and characterize longitudinal changes in ASMI in patients undergoing surgical decompression for DCM.
Methods: In this prospective study, patients between 18 to 100 years of age undergoing non-emergent cervical decompression for DCM were enrolled after providing written informed consent. Exclusion criteria were emergent surgery, cardiac electronic devices, and inability to stand unsupported for 60 seconds. ASMI was measured using BIA with the InBody 770 and 970 preoperatively and at 3, 6, 13, and 26 weeks postoperatively. Functional status was assessed at the same time points using mJOA scores calculated from questionnaires. Repeated measures generalized linear models were used to model longitudinal change in ASMI following surgical decompression using follow-up week as the predictor variable. Estimated marginal means for each follow-up time-point were compared with baseline and simulation adjustment was used to account for multiple comparisons. Analyses were repeated using sex, mJOA score, and surgical invasiveness as model covariates. Surgical invasiveness was defined as the number of vertebral levels fused (1, 2-3, or ≥ 4 levels).
Findings/Results: Data was analyzed from 31 patients undergoing surgical decompression for DCM. Preoperative characteristics included age, body mass index (BMI), BMI group, obesity status, sex, ASMI, mJOA score, sarcopenia status, osteoporosis status, and the number of vertebral levels fused. Prior to surgery, 6.5% (n=2) of patients met the criteria for sarcopenia. Postoperatively, ASMI was significantly different from baseline at weeks 3, 6, and 13 ($P = 0.002$, 0.001, and 0.008, respectively) but did not differ from preoperative values by week 26 ($P = 0.71$). Males had a significantly greater ASMI than females ($P = 0.001$); however, the interaction between sex and week was not statistically significant ($P = 0.78$), indicating that changes in ASMI over time were similar between sexes. mJOA score was not associated with ASMI ($P = 0.66$).
Conclusion/Overall significance/Broader perspective: ASMI decreased significantly in the three months following cervical decompression surgery but appeared to return to presurgical baseline levels by week 26. The early decline is consistent with expected decreases in postoperative activity and lifting restrictions and suggests transient, rather than persistent, muscle loss. Continued follow-up to one and two years will reveal any long-term changes in ASMI or sarcopenia prevalence.

Neuroanatomical and Imaging Evidence of Brain Alterations in Hemophilia A

Kevin Gubner, Danielle York, David Li, Daniel Thedens, Eric Axelson, Lauren Hopkins, Dr. Janice Staber

Background: Hemophilia A (HA) is a hereditary bleeding disorder caused by a deficiency in clotting Factor VIII (FVIII). Lack of this cofactor of the coagulation cascade leads to severe bleeding complications, including hemarthrosis, muscular hematomas, and intracranial hemorrhage. Beyond its physical manifestations, people with HA carry significant psychological burdens, with affected individuals showing increased rates of depression, anxiety, and attention deficit hyperactivity disorder (ADHD). In addition to psychological burdens, children with HA demonstrated impairments of executive function, specifically pointing to challenges in cognitive flexibility. These findings, paired with smaller cerebellar volumes in children with HA, suggest an undetermined neuroanatomic or systemic role of FVIII.

In this study, we aimed to investigate the physical manifestations of FVIII deficiency on neuroanatomical development and tissue composition. Using T2-Star (T2*) weighted Magnetic Resonance Imaging and immunofluorescent imaging, we examined tissue inhomogeneities in children with HA and to aid in mechanistic studies a -FVIII-deficient murine model. Here we focus on cerebellar architecture due to prior data demonstrating smaller cerebellar volumes in children with HA.

Methods: Murine T2 Imaging and Analysis:* 6-month-old male and female HA (n=21) and WT (n=20) mice underwent T2* weighted MR imaging. Relaxation values were mapped onto the DSURQE mouse brain atlas, covering 356 anatomical regions of interest and 294 sub-regions. Mean non-zero relaxation times were extracted for each region of interest (ROI). Linear modeling was applied with group (HA or control) as the predictor variable and mean non-zero ROI relaxation time as the outcome, and adjustments made for age and sex. Group differences were estimated using standardized coefficients with 95% confidence intervals. Analysis performed using RStudio version 2023.06.2+561 "Mountain Hydrangea" and GraphPad Prism.

Murine Purkinje Cell Analysis: Brains with specific focus on the cerebellum from 6-month-old male and female HA and WT mice were sectioned at 50 μm. Cerebellar slices were stained for Calbindin and Parvalbumin to identify Purkinje cells. Subregions with known volumetric differences were imaged at 40x. Once the Purkinje cell (PC) layer was delineated, Purkinje cells were classified as normal, partially ectopic, or ectopic. Once Purkinje cell enumeration and classification was completed, gaps between Purkinje cells and within the PC layer were measured.

Human T2 Imaging and Analysis:* Male participants with HA and unaffected controls ages 6-16 years underwent T2* MR imaging. Relaxation values were mapped to a standardized brain atlas to delineate ROIs. Mean non-zero T2* relaxation times were extracted for each ROI, and linear modeling was applied with status (HA or unaffected control) as the predictor variable, mean non-zero ROI relaxation time as the outcome, and adjustments for age, height, and weight. Group differences were quantified using standardized coefficients with 95% confidence intervals. Analysis performed using RStudio version 2023.06.2+561 "Mountain Hydrangea" and GraphPad Prism.

Results: In the murine model, significant variations in mean T2* relaxation times were detected within subregions of the hippocampus, entorhinal cortex, and cerebellum. Compared to wild-type controls, several areas exhibited increased mean T2* values, while others showed decreased values. Quantification and classification of Purkinje cells across cerebellar subregions- including the parafloculus, lobule IV/V, simple lobule VI, crus I and crus II- revealed differences in the presence of ectopic Purkinje cells and discontinuities between cells.

In the human model, prolonged mean T2* relaxation times were identified in 33 regions of interest, notably the lingual gyrus, cuneus, and the cerebellum. All significant findings indicated higher T2* times compared to unaffected healthy controls. Overlap between mouse and human T2* differences were observed in several subregions of the cerebellum.

Conclusions: These findings highlight region specific alterations in T2* relaxation times and Purkinje cell organization in the cerebella of a murine model of HA. Observed variations in T2* times of the human model indicate the presence of neuroinflammation or edema, as indicated by the increased mean T2* times. Both Purkinje cell patterns and findings through T2* MRI suggest underlying structural or physiological differences that may result from FVIII deficiency.

A Comparative Investigation of Patient Outcomes Across Multiple Total Joint Arthroplasties

Student: Daniel X. Haws
Primary Mentor: Brendan M. Patterson MD
Collaborators: Maria Bozoghlian MD, Garrett Christensen MD

Background: Total joint arthroplasty (TJA) is among the most common surgical procedures in the United States. Decades of evidence support total hip (THA) and total knee arthroplasty (TKA) as effective for pain relief, mobility restoration, and high patient satisfaction. In contrast, total shoulder arthroplasty (TSA) and reverse TSA (RTSA) are newer procedures and less consistent evidence on long term outcomes. Despite rising utilization of TSA, formal comparative data with THA and TKA remain limited. Defining recovery curves and patient-reported outcomes for TSA is critical to contextualize its performance and better inform patient expectations.

Purpose: The purpose of this study is to conduct a comprehensive comparison of self-reported recovery curves across total shoulder arthroplasty (TSA), total knee arthroplasty (TKA), and total hip arthroplasty (THA). By quantifying these factors, the study aims to generate clear comparative data to better inform patient education and clinical counseling. This analysis will provide a framework for understanding the relative complexities of each procedure and create comparisons that can guide expectations and support shared decision-making in total joint arthroplasty.

Methods: This retrospective cohort included patients undergoing primary anatomic or reverse TSA from 2021–2024 with up to two years of follow-up. Patient-reported outcome measures (PROMs) and PASS responses were analyzed to assess recovery and satisfaction, and results were compared with published THA and TKA benchmarks. Revision and fracture cases were excluded.

Results: A total of 343 patients were included (mean age 68 years, 53.1% male). The mean preoperative ASES score was 38.5, and baseline pain intensity was 6.2/10; 66.7% underwent reverse TSA and 33.3% anatomic TSA. Recovery trajectories showed progressive improvement over 2 years: 19% achieved MCID by 2 weeks, 38% by 6 weeks, 58% by 3 months, 69% by 6 months, 76% by 1 year, and 78% by 2 years, while 22% never did. Pain scores followed similar trends, with most improvement in the first 6 months. Compared with published benchmarks, THA demonstrated the fastest recovery, TKA intermediate, and TSA the slowest trajectory toward MCID attainment.

Conclusion: This study demonstrates that recovery following TSA remains slower and less consistent than that observed after TKA or THA, though the majority of patients ultimately achieve clinically meaningful improvement. Using a 21-point ASES threshold, nearly 40% of TSA patients reached MCID by 6 weeks and 58% by 3 months, compared with more rapid gains reported in hip and knee arthroplasty. In contrast, most TKA and THA patients surpass MCID within the first 1–3 months, with recovery curves plateauing by 6 months. TSA recovery lagged hip arthroplasty by 20–60% and knee arthroplasty by 6–38%, depending on timepoint, with the most pronounced delays in the early postoperative period. These findings underscore that functional recovery after TSA often extends beyond the early postoperative period and highlight the importance of setting realistic patient expectations, as well as targeting interventions for the subset who fail to achieve meaningful improvement.

Surgical outcomes of Urinary Diversion for End-stage Bladder Secondary to Pelvic Radiation Disease

Student: Timothy Hays
Mentor: Bradley A. Erickson, MD, MS

Introduction
Pelvic malignancies, including prostate, bladder, rectal, and cervical cancers, often require radiation therapy, which can induce sarcopenia and long-term sequelae necessitating reconstructive urological surgery. With improved cancer survival, radiation-induced complications increasingly impact long-term surgical outcomes. Psoas Muscle Thickness (PMTH) on CT has been recently studied as a practical measure of sarcopenia. This study evaluates the association between PMTH-measured sarcopenia and surgical outcomes following urinary diversion for end-stage bladder disease secondary to pelvic radiation.

Hypothesis
Higher degrees of sarcopenia (reduced PMTH) correlate with higher rates of complications after reconstructive urinary diversion surgery in patients treated for pelvic malignancies.

Methods
A retrospective review of urinary reconstruction cases performed by a single surgeon at University of Iowa Health Care (2013–2025) was conducted. PMTH was measured using built-in software at the L3-level on CT, normalized to patient height. Acute complications (≤30 days) included reoperation, readmission, infection, DVT, and surgical injury. Chronic complications (>30 days) included conduit complications and infections. Data were analyzed by cancer type with “other” cancers excluded. Comparisons were made using ANOVA and t-tests; odds ratios (OR) were calculated using 2×2 tables.

Results
N=90 patients underwent urinary diversion after pelvic radiation: 61 prostate, 13 cervical, 12 rectal, and 7 other cancers. Mean age was 68.8 years (SD=12.2), with median time from radiation to complications 6.31 years (SD=8.33). PMTH did not differ significantly between cancer types ($p=0.323$). Prostate cancer: mean PMTH 12.09 (SD 1.92). Acute complications occurred in 49.2%, chronic complications in 75.4%, 29.5% required reoperation. PMTH was significantly lower in patients with chronic complications ($p=0.013$) and specifically conduit complications ($p=0.008$). PMTH below the median was associated with increased odds of conduit complications (OR=3.26, 95% CI 1.08–9.78). Cervical cancer: mean PMTH 11.34 mm (SD 1.44). Acute complications 46.2%, chronic 53.8%, 30.8% reoperation. No significant PMTH differences between complication groups ($p=0.317$). Rectal cancer: mean PMTH 12.36 mm (SD 1.53). Acute complications 50%, chronic 50%, 33.3% reoperation. PMTH was significantly lower in patients with acute complications.

Conclusion
Lower PMTH, indicative of sarcopenia, is associated with increased risk of chronic and conduit-specific complications following urinary diversion in patients with prior pelvic radiation, particularly in prostate cancer. PMTH may serve as a useful preoperative risk stratification tool for reconstructive urologic surgery. This information will benefit the counseling of patients and allow providers to more appropriately explain the potential risks and benefits when considering treatment

Title: Operative Time in Cephalomedullary Femoral Nailing: A Retrospective Analysis of Nail Length and Patient Demographics

Student: Jared J. Hill M3
Research Mentor: Matthew Karam MD

Introduction: Cephalomedullary nails (CMNs) are widely used for proximal femoral fractures, with short and long variants each offering unique advantages in surgical efficiency and fracture protection. While shorter CMNs have been associated with reduced operative time, patient-specific variables that influence procedure length are often overlooked. This retrospective study investigates how patient-specific factors such as BMI, age, and sex influence procedural duration, aiming to guide more patient-centered CMN selection and improve surgical outcomes.

Purpose: This study aims to 1) evaluate differences in procedural time between short and long cephalomedullary nail (CMN) procedures and 2) examine the influence of patient-specific factors such as body mass index (BMI), sex, and age on operative time.

Methods: A retrospective study was conducted using structured query language (SQL) programming to access the Epic electronic medical record (EMR) system, exporting data on orthopedic procedures involving intramedullary nailing of the femur between August 2012 and August 2024. Patient BMI, sex, and age, as well as procedure time were collected from the EMR. Procedure time was compared between short and long nails, and within short and long CMN cohorts, procedure time was compared between males and females. These comparisons were evaluated using Mann-Whitney U test. BMI was categorized into four categorical variables (underweight, normal weight, overweight, and obese). These groups were tested for significant differences using Kruskal-Wallis test for multiple independent variables. Spearman Correlation test evaluated correlation between age and procedure time among short and long CMNs.

Results: A total of 744 CMN cases were evaluated, comprising of 421 long nails and 323 short nails. Procedure time was significantly longer for long CMNs (median: 104 minutes, IQR: 81-133) compared to short CMNs (median: 62 minutes, IQR: 51-76, $p<0.001$). Among patients receiving a short CMN, obese individuals (median: 66 minutes, IQR: 58-86) had significantly longer procedure times than overweight (median: 59 minutes, IQR: 49-73, $p=0.028$), and normal weight individuals (median: 61 minutes, IQR: 49-73, $p=0.011$). For patients receiving a long CMN, obese individuals (median: 112 minutes, IQR: 89-148) had significantly longer procedure times compared to normal weight patients (median: 97 minutes, IQR: 79-128, $p=0.005$). When comparing procedure time based on sex, men receiving a long CMN (median: 108 minutes, IQR: 88-137) had significantly longer procedure times than women receiving a long CMN (median: 98 minutes, IQR: 78-128, $p=0.002$). Age and procedure time had a weak relationship in long nails (correlation coefficient: -0.34, $p=0.001$) and a very weak negative relationship in short nails (correlation coefficient: -0.19, $p=0.001$).

Conclusions: Procedure time for cephalomedullary nailing was significantly influenced by nail length, BMI, sex, and patient age. Patients receiving a long CMN had significantly longer operative time than those receiving a short CMN. Obese patients experienced longer procedure times both long and short CMN groups when compared to their normal weight counterparts. Men receiving a long CMN had longer procedure times than their female counterparts. Age had weak, however statistically significant negative correlations with procedure times. These findings highlight the importance of considering patient-specific factors such as BMI, sex, and age when planning operative strategies to improve efficiency and optimize outcomes in CMN procedures.

Title: PREDICTIVE POWER OF MODIFIED, QUANTITATIVE FLUORESCENCE IN SITU HYBRIDIZATION (FISH) ASSAY FOR HIGH-GRADE TUMOR RECURRENCE IN BLADDER CANCER PATIENTS TREATED WITH GEMCITABINE-DOCETAXEL

Jackson Hofland, Mohamad Abou Chakra, Ian McElree, Michael O'Donnell

Introduction:

Intravesical therapy with Gemcitabine and Docetaxel (Gem/Doce) has demonstrated clinical promise in managing non-muscle invasive bladder cancer (NMIBC), particularly in patients who are BCG-naïve. Despite its growing adoption, reliable tools to predict tumor recurrence and guide optimal sequencing of intravesical therapies remain limited. Conventional surveillance methods—such as cystoscopy, urine cytology, and biomarker assays—are routinely employed; however, no biomarker has achieved universal validation or consistent clinical integration. The UroVysion FISH assay has been evaluated in BCG-treated cohorts, with meta-analyses reporting a sensitivity of 54%, specificity of 85%, and an AUC of 0.78 for recurrence prediction. Prior studies have primarily relied on 16% binary interpretations of either baseline or post-instillation FISH results.

Purpose:

In this study, we aim to assess the predictive value of a modified FISH assay in a Gem-Doce–treated, BCG-naïve NMIBC cohort by incorporating longitudinal post-treatment FISH results from all surveillance timepoints.

Methods:

We retrospectively reviewed BCG-naïve NMIBC patients treated with intravesical Gem/Doce at our institution between 2013 and 2025. Inclusion criteria were an intention to complete 6 weekly Gem/Doce instillations, recurrence-free at initial surveillance after induction, and subsequent surveillance with UroVysion FISH, cystoscopy, and urine cytology. Maintenance therapy was given for up to 24 months. The FISH assay followed the standard UroVysion protocol with 3 institutional modifications: (1) cell collection via barbotage during cystoscopy to enhance sample cellularity, (2) assay processing by our cytogenetics laboratory, and (3) reporting of the percentage of abnormal cells from samples of up to 50 cells, enabling quantitative analysis. The time-dependent ROC curve method using the cumulative cases and dynamic controls approach was used to construct ROC curves and estimate the AUC at 24 months after the initiation of Gem/Doce.

Results:

A total of 181 BCG-naïve patients with NMIBC were included (96% White, 84% male, median age 74). Before starting Gem/Doce therapy, 38.1% had T1 high-grade (HG) disease, 26.5% had Ta HG, 13.8% had Ta HG with carcinoma in situ, 13.3% had T1 HG with CIS, and 8.3% had CIS alone. The first post-treatment FISH test yielded an AUC of 0.62. When all FISH results within 24 months were considered, the AUC improved to 0.72. Sensitivity and specificity varied by abnormality threshold: at a 5% cutoff, the first FISH showed 35% sensitivity and 85% specificity, while the all-FISH approach showed 53% sensitivity and 90% specificity. Raising the threshold slightly improved specificity but reduced sensitivity. When we analyzed our FISH cohort in quantitative groups, we found that low-abnormal FISH results (0-5% abnormal) recurred after 2% of tests in the following 6 months. High-abnormal FISH results (81-100% abnormal) recurred after 72% of tests in the following 6 months.

Conclusion:

Our findings challenge the conventional binary FISH model and support the predictive value of modification of current FISH analysis practice for recurrence in BCG-naïve NMIBC patients treated with Gem/Doce. Longitudinal monitoring, combined with a lower abnormality threshold, enhances detection accuracy. Additionally, when we grouped FISH results based on the degree of cellular abnormality, a clear pattern emerged. Patients with minimal abnormalities on FISH testing rarely experienced tumor recurrence in the short term. In contrast, those with highly abnormal FISH profiles were much more likely to show recurrence within six months. This trend reinforces the potential of quantitative FISH analysis to stratify recurrence risk and guide follow-up intensity. Given the limited data on FISH performance in Gem/Doce-treated cohorts, the distinct mechanism of action compared to BCG, and active treatment of highly abnormal patients, optimal thresholds remain undefined and warrant further investigation.

Efficacy of *Ask Ana* Chatbot for Prenatal Questions

Erica Hsu, Megan Aucutt, Emily Price, Mark Santillan, MD, PhD, Donna Santillan, PhD

Background:
Easy access to AI chatbots has changed the way that information is consumed by the general population. This creates an opportunity to implement fine-tuned chatbots into a promising and accurate way to distribute personalized medical information to patients. A way in which medicine has started to achieve this is to verify the efficacy of ChatGPT or by training AI chatbots to specifically utilize a certain set of trusted and verified data. The chatbot *Ask Ana* within *Count the Kicks*, a pregnancy-related app, was specifically trained from trusted sources to answer questions related to prenatal health.

Purpose:
Our primary objective was to determine whether *Ask Ana* provided answers that were correct and complete.

Methods:
Retrospective cohort study of prompts and answers of *Ask Ana* users. De-identified data was collected from the Ask Ana database were provided from Healthy Birth Day, Inc. on user demographics, question prompts, and chatbot responses. Prompts not relevant to prenatal healthcare were excluded. Non-English responses were translated using Google translate. This work was determined not to be human subjects research by the University of Iowa Institutional Review Board. Responses were analyzed via Likert scales for accuracy (1-excellent response not requiring clarification to 4-unsatisfactory requiring substantial clarification) and completeness (1-incomplete, addresses some aspects of the question, but significant parts are missing or incomplete to 3-comprehensive, addresses all aspects of the question, and provides additional information or context beyond what was expected). Readability grade level was determined by Hemingway Editor.

Results:
There were 4325 prompts asked originally with 3117 included concerning prenatal health. Questions and responses were 99% in English and about 1% Spanish. Screening completed by a third-year medical student showed a mean accuracy score of 1.25 (SD=0.57). 3% were rated 3 or 4, while 91% were rated a 1. The mean completeness score was 1.13 (SD=0.45). 7% were rated 3, while 81% were rated a 1.

Conclusions:
The availability of AI chatbots can help bridge gaps in health education and serve as a supplement to in-person clinical care, particularly for questions that arise after appointments or patients in resource-limited settings. The specially trained *Ask Ana* chatbot offers good accuracy and completeness of responses to prenatal health questions. Thus, it offers a promising free resource for delivering information to expecting mothers.

Perinatal experiences in mental health and support among BIPOC women in Iowa and Indiana: A Thematic Analysis

Anjali Iyangar, Morolake Agadeabo, DeShauna Jones, Jaime Hamil, Darius Tandon, Maiti Peters, Karen Tabb Dina, Kelli Ryckman, Elissa Faro

Introduction with background/rationale
The perinatal period, which is defined as the time from the start of pregnancy up to one year after birth, is a high risk period for the development of mental health illnesses such as depression and anxiety. Studies show that the prevalence of maternal mental health conditions ranges between 25% and 50%, underscoring the importance of support in this period. Furthermore, BIPOC (Black and Indigenous People of Color) women are affected by perinatal mental health conditions at a disproportionately high rate due to social determinants of health, such as socioeconomic status and structural factors. Despite this, there is a gap in ethnographic research about the perinatal mental health experiences of BIPOC women. Qualitative studies of BIPOC experiences and perspectives here in the Midwest will ultimately help tailor interventions for women that are at highest risk for perinatal mental health conditions.

Hypothesis/Purpose
The purpose of this study is to understand the experiences of perinatal mental health and support needs of BIPOC women in Iowa and Indiana.

Method
Semi-structured interviews were conducted with women in Iowa and Indiana (n = 9) from November 2024 to February 2025. Interviews were recorded and first transcribed via a transcription software, then confirmed and revised manually. Interview data were analyzed using the Braune and Clarke method of thematic analysis.

Findings/Results
Four themes with 2-3 subthemes each emerged among the 9 interviews: experiences of mental health (impact on mental health, social connection as a mediator), what good support means (methods of support, individualized care), trust as a critical guide (the trusted ally, mistrust repels, the systemic erosion of trust), and valued outcomes (informed agency, reduced mental burden, time for self).

Conclusion/Overall significance/Broader perspective
While the impact of experiences during the perinatal period on participants' mental health ranged from very positive to negative, it was clear that increased social connection was a mediator for positive mental health outcomes. Through these social connections, participants benefitted from a wide range of support, whether it be from medical professionals, community resources, or from family and friends. However, the unifying characteristic of support that was valued by a majority of participants is person-centered care from trusted individuals. Ultimately, these findings underscore the importance of community, trust-building practices, and individualized care when providing support in the perinatal period.

Impact of Screw Diameter on the Mechanical Performance of Cement-Augmented Lumbar Spinal Fusion Constructs

Akar Jani, BSE[1], Nicole DeVries Watson, PhD[1], Doug Fredericks, BS[1], Catherine Olinger, MD, MS[1]

Introduction: Lumbar spinal fusion using pedicle screw instrumentation (PSI) is a well-established surgical approach to treat degenerative spine conditions. PSI improves fusion rates and construct stability, facilitating earlier mobilization and reducing complications. However, osteoporosis severely compromises bone quality, reducing screw fixation strength—biomechanically measured as pullout strength—by up to 80%, increasing the risk of loosening and failure. Cement augmentation with polymethylmethacrylate (PMMA), delivered via fenestrated pedicle screws, reinforces the screw-bone interface and can improve pullout strength up to twofold. Prior literature supports that increasing screw diameter enhances fixation strength by increasing surface area of the screw-bone interface. However, in osteoporotic vertebrae where cortical bone is thinner and weaker, the benefit of larger screws may be limited when combined with cement augmentation. Cement augmentation increases construct rigidity and alters force distribution, potentially concentrating stress at the screw-bone interface and reducing the mechanical advantage of larger diameter screws. Thus, the benefit of larger screws in cement-augmented fixation remains unclear. In this study, we utilized anatomically accurate osteoporotic-grade synthetic L3 lumbar vertebrae (Sawbones®, Pacific Research Labs) to evaluate how increased screw diameters in cement-augmented constructs affect mechanical performance following dynamic cyclic loading. We hypothesize that (1) larger-diameter fenestrated screws will demonstrate higher pullout strength than non-fenestrated screws after physiologic cyclic loading, and (2) larger diameter screws will increase cement distribution within cancellous bone, strengthening the construct and enhancing resistance to pullout following cyclic loading.

Methods: Fifty-millimeter length titanium polyaxial fenestrated pedicle screws of either 5.5 mm (n=8) or 6.5 mm (n=8) diameter were bilaterally implanted into osteoporotic-grade L3 lumbar vertebrae Sawbones. Screws were placed using 3D-printed guides to ensure a consistent trajectory within the pedicle, parallel to the vertebral endplates. Each fenestrated screw was augmented with 3 cc of PMMA, delivered through the screw's inner cannulation. Non-fenestrated 6.5 mm screws (n=8) were used for non-augmented constructs. All constructs were stabilized with 100 mm pre-bent bilateral rods and mounted to a Material Testing System (MTS) following a modified ASTM F1717-21 protocol. Implants underwent 90,000 cycles of compression in force control between 100–200 N at 3 Hz (approximating 3 months of walking at 110 steps/min), with simultaneous axial rotation in displacement control (±1.50°) at 1.8 Hz. Additional cement-augmented fenestrated screws (5.5 mm and 6.5 mm, n=2 each) not subjected to loading served as passive controls. High-resolution CT scans were obtained pre- and post-loading to assess macroscopic damage, screw hole volume changes, and cement distribution within cancellous bone. Pullout strength was measured according to modified ASTM F543-23 by applying axial force until screw extraction.

Preliminary Results: After bilateral implantation of pedicle screws, initial CT imaging demonstrated intact cortical shells without pre-existing cracks or fractures for all samples. Cement injection caused superior endplate rupture and extravasation in one of four vertebrae with 5.5 mm fenestrated screws and three of four vertebrae with 6.5 mm fenestrated screws. All screws withstood cyclic preloading and rotation. Paired comparisons between left and right pedicle screws showed no significant differences in pullout strength for 5.5 mm screws (left: 1726.23 ± 333.12 N, right: 1672.72 ± 285.36 N, $p = 0.64$) or 6.5 mm screws (left: 1806.20 ± 314.90 N, right: 2033.68 ± 106.70 N, $p = 0.12$). This lack of side-to-side difference indicates that cement volume loss through extravasation did not affect pullout strength and confirms that the MTS machine did not preferentially load one screw over the other. When comparing screw diameters, 6.5 mm screws demonstrated higher mean pullout strength than 5.5 mm screws (1919.94 ± 249.37 N vs 1699.47 ± 288.73 N), but this difference did not reach statistical significance ($p = 0.124$).

Discussion: These findings suggest that increasing pedicle screw diameter does not appear to confer a significant biomechanical advantage in cement-augmented fixation after three months of simulated walking. Larger screws were associated with more frequent endplate rupture, indicating that increasing diameter may elevate structural risk without improving fixation strength. This study builds on prior work through the novel use of osteoporotic-grade Sawbones, standardized screw placement, and combined compression with axial rotation to better replicate physiological conditions. Compared with cadaveric or synthetic block models, this approach reduces variability in bone mineral density and preserves vertebral anatomical complexity, providing a controlled, clinically relevant evaluation of cement-augmented pedicle screw constructs.

Clinical Relevance: This study establishes a reproducible biomechanical protocol to evaluate pedicle screw diameter in cement-augmented spinal fusion constructs. As research advances in the management of degenerative spinal diseases, findings from this study may help generate clinically relevant guidelines to optimize implant selection and surgical techniques, ultimately improving outcomes for patients with osteoporotic bone.

Quantitative Finger Tapping Reveals Differential Effects of Subthalamic Nucleus Deep Brain Stimulation in ON vs OFF States

Student: Sonia Jeon
Mentor: Jeremy D.W. Greenlee, MD

Background: Deep brain stimulation (DBS) efficacy in Parkinson's disease (PD) is traditionally assessed using the Unified Parkinson's Disease Rating Scale (UPDRS), a standardized clinical scale with limitations for detecting subtle motor changes. Early and accurate assessment of motor symptoms is crucial for PD diagnosis, disease monitoring, and treatment optimization. We used quantitative goniometric finger tapping analysis to gather objective measurements of subthalamic nucleus DBS (STN-DBS) effects and examine correlation with UPDRS scores.

Methods: We performed within-subject comparisons in 59 patients with idiopathic Parkinson's disease receiving bilateral STN-DBS with assessment at baseline (pre-surgery), 6-month, and 12-month post-operative timepoints (2,557 total observations). Three trials of 10 second finger tapping were measured with stimulation ON vs OFF, following an 8+ hour levodopa off period to isolate DBS effects from medication. Each patient served as their own control in this within-subject design, eliminating inter-individual variability. A wireless goniometric device captured tap frequency (Hz), movement speed (degrees/s), and amplitude variability (CV%)—metrics relevant to bradykinesia and dysrhythmia assessments critical for PD diagnosis. UPDRS motor scores were collected in both the ON and OFF states.

Results: Within-subject analysis (n=59) compared DBS ON vs OFF states at 6 and 12 months post-operatively. While tap frequency showed minimal change (OFF: 3.48 ± 0.94 Hz vs ON: 3.56 ± 0.85 Hz; +2.4%, $p= 0.17$, $d= 0.18$), significant improvements emerged in movement speed (OFF: 219.49 vs ON: 244.87 degrees/s; +11.6%, $p= 0.001$, $d= 0.45$) and motor consistency (amplitude variability decreased from 37.35% to 33.58%; $p= 0.0006$, $d= 0.47$). Analysis of individual responses revealed 78% of patients improved in speed and 72% in consistency despite only 59% showing increased tap frequency. From baseline (pre-surgery) to 12 months post-op, patients showed stable tap frequency in the OFF state (3.25 ± 0.89 to 3.48 ± 0.94 Hz), but ON stimulation revealed additional benefit (3.56 ± 0.85 Hz). UPDRS scores correlated moderately with quantitative changes ($r= 0.6$), yet 20% of patients (n= 12) showing quantitative improvement were not shown by UPDRS changes. This suggests potential benefits detected by objective measures.

Conclusions: Our longitudinal within-subject analysis in 59 DBS patients demonstrates differential motor responses to stimulation in the medication off state with speed and motor consistency improvements exceeding frequency changes. These findings collected post-operatively have important implications for PD management: (1) Early diagnosis could benefit from multidimensional motor assessment beyond simple frequency measures; (2) Quantitative metrics showed improvement in 20% more patients, suggesting UPDRS may underestimate treatment response; (3) Objective goniometry measures could guide DBS programming by identifying individual responses.

Student Name: Aditya Joglekar, BS

Mentor Name: Nitin J. Karandikar, MD, PhD

Collaborators: Chakrapani Vemulawada, PhD, and Michael Crawford, MD

Title: Interferon-gamma (IFNγ) – IFN-γ Receptor axis controls the suppressor function of $CD8^+$ T-cells and effector resistance of $CD4^+$ T-cells

Abstract

The role of $CD8^+$ T-cells in autoimmune pathology is poorly understood. Previous studies have shown that acute relapses of multiple sclerosis (MS) are associated with impaired $CD8^+$ T-cell suppression of pathogenic $CD4^+$ effectors. Interferon-gamma (IFN-γ), a critical cytokine in T-cell biology, has been implicated in this process. Prior work from the Karandikar lab showed that deletion of IFN-γ in $CD8^+$ T-cells disrupts their suppressive ability, and that exogenous IFN-γ cannot restore this function, suggesting a requirement for intrinsic IFN-γ signaling. To investigate whether $CD4^+$ and $CD8^+$ T-cells require IFN-γ sensing, we examined the role of T-cell–intrinsic IFN-γ and IFN-γ-receptor (IFNγR) in both $CD4^+$ and $CD8^+$ T-cells. PBMCs from healthy human donors were acquired and $CD4^+$ and $CD8^+$ T-cells were isolated, which were then subjected to CRISPR/Cas9-mediated IFN-γ or IFNγR knockdown. The WT and knockdown cells were co-cultured in immune suppression assays and $CD4^+$ T-cell proliferation was quantified using flow cytometry.

Our data confirmed that IFN-γ-deficient $CD8^+$ T-cells had significantly diminished ability to suppress the proliferation of effector $CD4^+$ T-cells. Interestingly, IFN-γ-deficient $CD4^+$ T-cells showed greater resistance to suppression by WT $CD8^+$ T-cells. Importantly, IFNγR-deficient $CD8^+$ T-cells were also diminished in their ability suppress $CD4^+$T cell proliferation, indicating that IFN-γ signaling is required to induce a suppressive phenotype. Conversely, IFNγR-deficient $CD4^+$ T-cells exhibited resistance to suppression, demonstrating that CD4-instrinsic IFN-γ signaling is also necessary for $CD4^+$ susceptibility to immune suppression. Together, these results highlight that both $CD4^+$ and $CD8^+$ T-cells must “see their own” IFN-γ for suppression to occur, likely in an autocrine or paracrine manner.

In the future, we plan to perform single-cell RNA sequencing on IFN-γ and IFNγR-deficient T-cells to define the transcriptional changes underlying these defects. Our studies highlight the dual role of IFN-γ in shaping suppressive and responsive T-cell states, offering potential therapeutic avenues for autoimmune diseases like MS.

Student: Connor Johnson, M2G

Mentor: Christopher Petkov

Gene expression signature of electrical stimulation in the human brain

Direct electrical stimulation has been used for decades as a gold standard clinical tool to map cognitive function in neurosurgery patients. However, the molecular impact of electrical stimulation in the human brain is unknown. Here, using transcriptomic and epigenomic sequencing techniques, we define the molecular changes in bulk tissue and at the single-cell level in the human cerebral cortex following direct electrical stimulation of the anterior temporal lobe in patients undergoing neurosurgery. Direct electrical stimulation has a robust and consistent impact on the expression of genes related to microglia-specific cytokine activity, an effect that was replicated in mice. Analysis was performed using multimodal genomic tools (multiomics), including scRNAseq, pseudo-bulk RNA constructed from distinct cell populations, and chromatin analysis using ATACseq. Using a newly developed deep learning computational tool, NEUROEstimator, we further demonstrate cell type-specific molecular activation, which underscores the effects of electrical stimulation on gene expression in microglia.

Glaucoma Genetics: Exploring the Molecular Mechanisms of the CDKN2B Gene

Preston Johnson

Mentor: John Fingert MD, PhD

Department of Ophthalmology and Visual Sciences

Introduction: Glaucoma is a genetically complex neurodegenerative disorder that affects retinal ganglion cells (RGCs) within the retina. Over the last few decades, genome-wide association studies have begun to identify single-nucleotide polymorphisms (SNPs) that are associated with primary open-angle glaucoma (POAG), the most common form of glaucoma. Despite the discovery of hundreds of SNPs associated with POAG, very little work has been done to unravel the molecular mechanisms of these SNPs and their role in the pathogenesis of glaucoma. One of these SNPs (rs4977756) is located within the CDKN2B gene cluster. The CDKN2B gene encodes the p15ink4b protein, which is involved in cell cycle regulation and is regulated by the CDKN2B-AS1 cis-regulatory element.

Hypothesis/Purpose: The purpose of our study was to examine the expression levels of p15ink4b in sections from three human donor eyes homozygous for the risk allele and three homozygous for the non-risk allele. We hypothesized that p15ink4b expression would be upregulated in the donors homozygous for the risk allele within the ganglion cell layer (GCL) since the SNP is located within the CDKN2B-AS1 region of the CDKN2B gene cluster.

Methods: Expression levels of p15ink4b protein were detected using DAB chromogenic immunohistochemistry (IHC). The p15ink4b polyclonal antibody used for IHC was validated using a synthetic blocking peptide prior to staining with donor sections.

Results: Using our synthetic blocking peptide and a no primary control, we determined that our polyclonal p15ink4b antibody is specific for the p15ink4b protein. With this, our preliminary results qualitatively indicate that there is increased expression of p15ink4b within the GCL of sections homozygous for the risk allele, albeit a rather modest increase.

Conclusions: Our findings indicate that p15ink4b expression may be increased in donors homozygous for the CDKN2B-AS1 risk allele. Moving forward, we plan to increase our sample size and quantify our expression levels using ImageJ. These steps will help us improve our statistical power and provide a more detailed description of p15ink4b expression within the retina. Beyond this, we intend to perform single-cell RNA sequencing to look at how different subtypes of RGCs are affected by SNP rs4977756 and if there are any pathways that are up or downregulate in response to this SNP.

Characterizing the incidence and risk factors behind duodenal hematoma as an endoscopy complication in pediatric patients

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Introduction: Esophagogastroduodenoscopy (EGD) is a powerful tool used to diagnose and characterize a variety of conditions, including gastroesophageal reflux disease, peptic ulcer disease, esophageal strictures, and celiac disease, among other diagnoses. Given that over 6 million EGDs are performed each year in the United States, it is important to characterize and understand the complications associated with the procedure. Among rare complications, patients are informed about the risk of duodenal hematoma. A duodenal hematoma is a pooling of blood in the wall of the first part of the small intestine and is seen almost exclusively in children. Duodenal hematoma is more commonly known as a potential secondary effect of blunt force abdominal trauma but over the last few decades has also been described as a complication following an endoscopy. In these cases, the limited literature proposes anticoagulant use, clotting disorder, and receipt of a transplant as potential risk factors.

Hypothesis: In our patient population we expect to find duodenal hematomas as a rare complication of pediatric endoscopies. The complication will likely be found at a higher rate in patients with prior coagulopathies and transplants.

Methods: This is a retrospective cohort study on pediatric patients undergoing EGD at the University of Iowa between 2010 and 2025. Based on a list of applicable CPT billing codes we requested data from the Institute for Clinical and Translational Science (ICTS). This data was organized through Python scripts and different risk factors were isolated and categorized. Potential cases of duodenal hematoma were determined by a keyword search followed by a manual review. A duodenal hematoma event was then identified when a patient presents with signs and/or symptoms of an upper GI obstruction with radiologic confirmation by an imaging modality (US and/or CT).

Findings:
Our data request identified 13,394 applicable EGDs over the last 15 years. While review of the data is ongoing, based on past literature we expect to find around 7 cases in our dataset. Once we have identified these cases, we will calculate the incidence rate in our hospital system. We can then look for patterns within the cases and compare the incidence of risk factors in these cases to risk factors in EGDs without a hematoma.

Significance: Our analysis is ongoing, but through this research we aim to determine patterns in incidence, risk factors, presentation, diagnosis, and treatment. These results will enhance our understanding of the causes behind this rare but potentially life-threatening procedural complication, enabling better patient education on associated risks and more effective strategies for its prevention.

A Community-Engaged, Mixed-Methods Approach to Defining the Role of Preventive Measures and Access to Care for Kidney Disease in Iowa

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DeShauna Jones, PhD; Martha Carvour, MD, PhD

Introduction: Chronic medical conditions, such as diabetes mellitus and hypertension, are increasingly prevalent in the United States. Without effective management, these conditions may lead to chronic kidney disease and, in some cases, lead to end-stage renal disease requiring kidney dialysis or kidney transplantation. There is a need for targeted interventions to improve access to care, strengthen preventive strategies, and ultimately enhance health outcomes for patients who are at risk for kidney disease.

Purpose: The purpose of this study is to identify modifiable gaps in the kidney care continuum among adults with diabetes, hypertension, or both, and examine the relationship of factors such as transportation and health insurance with access to care. Using a mixed-methods approach that combines quantitative analysis of electronic medical record data with community-engaged qualitative data collection, the study is intended to inform future strategies to improve kidney health awareness, care access, and care outcomes.

Methods: We used the TriNetX database to obtain de-identified patient information from Iowa Health Care. The study population included adults (≥18 years) with a diagnosis of diabetes mellitus (any type), hypertension (any type), or both, between January 1, 2014, and December 31, 2024. Using these three cohorts, we constructed three separate continua of care models to illustrate the preventive measures, medications, complications, and procedures that patients experienced. To provide context for these continua from a patient's perspective, we conducted focus groups and interviews, recruiting community members (≥18 years) in Iowa who have personal experience with, or have connections to individuals affected by diabetes, hypertension, and/or kidney disease, to share their experiences with care.

Results: In the TriNetX database, upstream measures such as glucose monitoring, kidney function assessment, and preventive education (including exercise and dietary counseling) were documented at substantially lower rates than medication prescriptions for diabetes and hypertension. Patients with limited access to transportation or health insurance received lower levels of care, with transportation exerting a marked negative influence across the care continuum. In focus groups and interviews with community members, similar themes emerged. Community members identified transportation and financial costs, including insurance coverage, as barriers to care. Community members also noted that kidney health education and awareness efforts were scarce in their local communities, in contrast with more widespread efforts related to other chronic conditions, such as heart disease.

Conclusion: Kidney care in Iowa may be strengthened by increasing the emphasis on preventive measures, including primary prevention of kidney disease before it occurs and secondary prevention of advanced or end-stage kidney disease once earlier stages are recognized. This study identified three opportunities to enhance prevention. First, preventive screening and counseling should be routinely incorporated into clinical encounters for diabetes and hypertension, including encounters in which medications are prescribed. Second, health-related practical needs, such as transportation and health insurance, may substantially impact care and should be addressed as part of the care process. Finally, kidney health education and awareness efforts should be more widely available in community settings in Iowa.

Reducing Alert Burden in Inpatient Care: Transitioning a Medication on Hold Alert from Interruptive to Non-Interruptive Format

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Background:
Clinical decision support (CDS) alerts are integral to modern medical care, yet excessive interruptive alerts contribute to alert fatigue and may reduce alert effectiveness. The alert demonstrated minimal clinical value while contributing significantly to alert fatigue.

Objective:
To evaluate if transitioning a high-firing medication on hold alert from an interruptive to a non-interruptive storyboard format would affect provider behavior or increase safety risks.

Methods:
We conducted a pre-post cohort study comparing provider practices six months before and after the transition. The alert fired when ≥2 medications or ≥1 anticoagulant were held for >48 hours. A comparison was made to evaluate provider practices in resuming medications during these periods. Data was extracted from the EHR (Epic) and institutional risk reporting system (Riskonnect). A large language model (Microsoft Co-pilot) was used to analyze free-text reports in Riskonnect for medication-related adverse events. All identified events were manually reviewed for relevance and independent keyword-based free-text queries were conducted to identify any missed events.

Results:
Following the transition, the number of alert interactions decreased from 33,632 (3.0 clicks per hospital encounter) to 305 (0.02 clicks per hospital encounter) in a six-month period. There was no significant difference in the median hold duration of medications (81.5 hours v. 85.6 hours p-value 0.22) or in the proportion of medications never resumed before discharge (43% in both cohorts). No increase in reported safety events related to medications on hold was identified.

Conclusions:
Transitioning the alert to a non-interruptive format substantially reduced alert burden without compromising patient safety. These findings highlight the importance to routinely evaluate CDS tools and suggest that alerts lacking demonstrated benefit may warrant redesign or retirement to reduce clinician fatigue and preserve alert effectiveness. Additionally, this study demonstrates the utility of large language models as a support tool for efficient, scalable review of safety report narratives.

Patients Treated at Tertiary Care Centers For Periprosthetic Joint Infections of the Hip or Knee Have Similar Outcomes to Patients Initially Treated at Smaller Local Hospitals Before Completing Treatment at a Tertiary Center

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Investigation performed at University of Iowa Orthopedics and Rehabilitation, Iowa City, Ia

Background: Periprosthetic Joint Infection (PJI) treatment in THA/TKA requires specialized surgery and culture directed antibiotics. Such care is typically offered at tertiary care centers by multidisciplinary teams consisting of arthroplasty surgeons, infectious diseases specialists and occasionally plastic surgeons. Patients from rural areas often present first to smaller/critical access hospitals where full PJI care may not be available. The purpose of this study was to compare treatment outcomes between patients with hip or knee PJI who were entirely treated at a tertiary care center and patients who were partially treated at a smaller local hospital before completing treatment at a tertiary center.

Methods: We retrospectively reviewed all cases of hip and knee PJI definitively treated at our tertiary care center from 2013-2023. Patients were divided into two categories based on their treatment history (partially medically or surgically treated at an outside hospital (group 1 = OSH) vs totality of treatment at our center (group 2 = all-tertiary)). Treatment outcomes were categorized based on previously defined tiers set by the Musculoskeletal Infection Society (MSIS). The total number of surgeries patients had to treat their infection was recorded. Patient reported outcomes (PROs) were also analyzed to assess patient satisfaction with their PJI treatment.

Results: 324 patients treated for hip or knee PJI at out center were included in this study. 201 in the OSH group and 123 in the all-tertiary group. The percentage of patients within each post-operative MSIS tier was similar across both groups. There was a trend, however, toward better outcomes with complete care at our center, with a $p=0.07$. There was no difference in the percentage of patients in tiers 1 and 2 representing successful treatment (62% OSH vs 60% all-tertiary) and patients in tiers 3, 3E and 4 representing treatment failure (38% OSH vs 40% all-tertiary). The average number of surgeries across the two groups was similar (1.3 surgeries OSH vs 1.5 surgeries all tertiary). Regarding treatment satisfaction, all most-recent PRO measures were similar between the two groups (mean KOOS score: 64 OSH vs 58 all-tertiary; mean HOOS score: 14 OSH vs 13 all-tertiary; mean PROMIS global physical health score was 41 for both groups; mean PROMIS global mental health score of 46 for both groups; mean MCID score was 3 for both groups; mean PASS score was 54% satisfied OSH vs 43% satisfied all-tertiary).

Conclusions: The results of this study indicate that there was no significant difference in treatment outcomes nor in the satisfaction of treatment for patients who were treated for PJI of the hip or knee, first at local hospitals before presenting to a tertiary care center compared to patients who were entirely treated at a tertiary center. These results help to inform treatment protocols for PJI patients living in rural areas and signal that it may be appropriate for these patients to receive initial evaluation at smaller hospitals, before transferring to a tertiary care facility for definitive PJI care.

Modeling complex airway procedures using a novel subglottic airway device for selective lobar ventilation: a mannequin-based study

Dennis Kobuzi, Roberta Garberi, Luiz Maracaja, Franklin Dexter, David W. Kaczka

Introduction:
Acute respiratory distress syndrome (ARDS) is a form of sudden hypoxemic respiratory failure associated with pulmonary edema, regional inflammation, and airspace consolidation. It is also associated with high mortality, as well as substantial morbidity in survivors. Given its heterogeneous pathology, ARDS also presents with variable compliance across different lung regions. Traditional lung-protective ventilation strategies, such as low tidal volumes and driving pressures, fail to account for this, increasing the risk of ventilator-induced lung injury. Our group has developed a new technique, termed selective lobar ventilation (SLV), that offers a promising alternative management strategy for ARDS by delivering targeted mechanical ventilation to specific lung lobes. It remains unclear, however, how readily SLV can be translated into routine clinical practice without delaying care, given the time requirements for successful placement of lobar endobronchial tubes.

Purpose:
This study aimed to assess the procedural time requirements for clinicians to perform an endobronchial intubation for SLV after being provided stepwise instructions on a high-fidelity airway mannequin. Our goal was to determine the probability distribution of the time required for successful endobronchial intubation and explore the implications for clinical workflow and safety thresholds. We hypothesized that intubation times would follow a log-normal distribution, given the nonlinear skill acquisition and procedural variability associated with complex airway techniques.

Methods:
This prospective study recruited 52 participants with varying levels of experience in clinical airway management. Participants performed simulated endobronchial intubation using a novel subglottic "shuttle" endotracheal tube (ETT) system in conjunction with a GlideScope and fiber-optic bronchoscope. Once proper placement of the shuttle ETT occurred, a fiber-optic bronchoscope loaded with an endobronchial tube was passed through the shuttle ETT and into the left lower lobe bronchus. Independent inflation of the designated left lower lung lobe, while the other lobes remain uninflated, confirmed successful placement for SLV. We recorded times from initial tube insertion to the successful establishment of SLV. We also assessed operator experience by asking participants to estimate the number of endotracheal and double-lumen intubations performed within the year 2024.

Results:
Of the 52 participants, six reported performing <5 endotracheal intubations in 2024. These participants also exhibited longer procedure times, suggesting an experience-based threshold for future studies. For the remaining 46 participants with ≥5 endotracheal intubations performed in 2024, procedure times followed a log-normal distribution (Shapiro-Wilk $W = 0.98$, $P = 0.75$). The mean procedure time for this group of participants was 135.5 seconds with a standard deviation of 26.7 seconds. The 95% upper confidence limit for the probability of exceeding a 5-minute safety threshold was 0.02%, supporting procedural feasibility.

Conclusion:
Our simulation-based study demonstrates that SLV using a novel subglottic airway device can be performed within clinically acceptable timeframes by clinicians with basic airway management experience when provided with stepwise instructions. Characterizing the log-normal distribution of procedure times allowed for the calculation of confidence intervals for exceedance probabilities – findings critical for planning clinical trials, guiding training strategies, ensuring clinical readiness, and reducing procedural risk.

Title: Impact of Tumor Hypoxia on Lipid Nanoparticle Mediated-mRNA Transfection

Student: Shruthi Kondaboina

Mentor: James Byrne

Background: Tumor hypoxia remains a critical barrier to effective therapeutic delivery, suppressing nanoparticle uptake and reducing transgene expression. Despite the growing use of lipid nanoparticle (LNP) platforms in over 120 active cancer clinical trials, the mechanistic limitations imposed by the tumor microenvironment—particularly hypoxia—are underexplored. Malignant peripheral nerve sheath tumors (MPNSTs), characterized by poor vascularization and limited oxygen diffusion, exemplify this challenge and underscore the need for strategies that overcome these delivery bottlenecks.

Objective: To evaluate the impact of hypoxia on LNP-mediated mRNA transfection and to assess whether hyperbaric oxygen therapy (HBOT) can improve transfection efficiency under hypoxic conditions.

Methods: MPNST cells were cultured under three conditions: normoxia (~20% O_2), hypoxia (1% O_2), and HBOT (3 atmospheres for 90 minutes). LNPs encapsulating GFP mRNA were applied, and transfection efficiency was quantified via cell imaging and flow cytometry.

Results: Flow cytometry revealed that hypoxia significantly reduced mRNA translation, with only 6.66% GFP-positive cells compared to 18.5% under normoxia. HBOT showed transfection levels of 16.5%, comparable to normoxic controls. Imaging coroborated markedly reduced protein expression in hypoxic cultures, while HBOT-treated samples exhibited protein-expression levels comparable with normoxic controls.

Conclusion: Hypoxic stress reduces mRNA transfection efficiency in MPNST cells. Hyperbaric oxygen shows potential as an adjunct therapy to enhance nanoparticle efficacy. These findings support further in vivo validation and suggest that oxygenation strategies may improve therapeutic mRNA delivery in therapy-resistant tumor types. If further validated, these findings may pioneer the integration of tumor oxygenation strategies as adjuncts to existing therapeutic modalities—establishing a new framework for enhancing treatment efficacy in hypoxic malignancies.

Keywords: mRNA transfection, tumor hypoxia, hyperbaric oxygen, lipid nanoparticles, MPNST, therapeutic resistance

Morning Headache and Vivid Dreams in Parkinson's Disease

Student: Brittany Koontz / Mentor: Deema Fattal, MD / Data Analysis: Linder Wendt

Introduction
Morning headache (MH) is a common condition that affects 1 in 13 individuals, and this prevalence further increases with various comorbid conditions. Frequent headaches greatly affect an individual's daily functioning. For example, one literature review found that patients with primary headache disorders have diminished quality of life compared to controls. This may be due to a correlation between MH and daytime sleepiness. However, the pathophysiological basis of MH remains unclear.

The relationship between MH and various sleep parameters, such as the presence of apnea, is multifaceted and contradictory. Several theories propose MH may be caused by disturbances in sleep. For example, it has been suggested there is a potential link between MH and rapid eye movement (REM) sleep. In research, individuals with a higher amount of REM sleep were more likely to report vivid dreams. At the same time, clinically, patients with REM sleep behavior disorder complain of MH after sleep with vivid dreams. Therefore, there may be an indirect correlation between vivid dreams and MH.

Sleep issues are a common comorbid feature of Parkinson's disease (PD) and are found in approximately 84% of PD patients. REM sleep behavior disorder is common among patients with PD, with prevalence ranging 33-47%. Based on clinical observations, REM sleep behavior disorder is known to be associated with vivid dreams. The prevalence of MH in individuals with PD is unknown.

Hypothesis:
We hypothesize that MH and vivid dreams co-exist in patients with PD, as REM sleep behavior disorder is a common feature of the disease.

Methods:
We supplied an optional, anonymous survey to PD patients in the waiting room at the University of Iowa Health Care (UIHC) Neurology Clinic. The survey asked whether the patient had experienced MH or vivid dreams, and asked about further details regarding the timing of these events. The survey was filled out by PD patients who did not have a dementia diagnosis, within the ages 18–89 years old, as well as control patients who accompanied patients to their appointments. We collected the surveys approximately twice a week to record the results in a password-protected drive; surveys were collected from November, 2024 through August, 2025. This project was approved by the University of Iowa Institutional Research Board (#202408539).

Results:
We received 46 total responses from 18 PD patients and 28 controls. Among the control patients, 13 (48%) of participants endorsed having morning headaches, compared to 7 (41%) of the PD patients ($p = 0.7$). Regarding vivid dreams, 16 (59%) of controls and 9 (56%) of PD patients endorsed these ($p = 0.8$). 7 (64%) control patients reported morning headaches that occurred immediately following sleep with vivid dreams, compared to 3 (43%) of PD patients ($p = 0.6$).

Discussion:
Overall, there was no statistically significant difference between PD patients versus controls reporting MH or vivid dreams. It is possible that the previously observed clinical correlation between MH and vivid dreams could be due to comorbidities that are prevalent among older neurology patients, such as sleep apnea, which has an established correlation with MH. A limitation of this study is the small sample size. To increase the overall power of our research, we would need to increase the number of participants. Future studies could evaluate MH in a larger sample of patients with REM sleep behavior disorders including PD and other related conditions.

Project Title: Forebrain Modulation of the Hypercapnic Ventilatory Response in Humans Undergoing Intracranial Monitoring

Student Name: Thomas Krapfl

Mentor Name: Dr. Brian Dlouhy

Background:
The regulation of breathing is classically attributed to brainstem centers; however, emerging evidence suggests that the forebrain—including limbic and thalamic structures—may play a role in modulating ventilatory and affective responses to hypercapnia. This study aimed to investigate how forebrain regions influence the hypercapnic ventilatory response (HCVR) in patients undergoing intracranial monitoring for epilepsy.

Hypothesis:
Forebrain sites including the amygdala and thalamus will inhibit the hypercapnic ventilatory response and the CO_2 drive to breathe.

Methods:
We studied both pediatric and adult patients with drug-resistant epilepsy undergoing phase II stereoelectroencephalography (sEEG) for seizure focus localization. Participants completed the Read rebreathing protocol, in which they rebreathed from a closed circuit to gradually increase inhaled CO_2 over a 4-minute period. Ventilation, end-tidal CO_2, subjective dyspnea, and galvanic skin conductance (GSC) were recorded. To assess forebrain modulation, electrical stimulation was applied to specific sEEG-implanted regions, including the amygdala and thalamus, during the HCVR protocol.

Results:
As expected, rising levels of end-tidal CO_2 produced a robust increase in ventilation, confirming the typical hypercapnic ventilatory response. However, during electrical stimulation of the amygdala and thalamus, this ventilatory response was markedly blunted. Participants reported less dyspnea and air hunger during these stimulation trials. In parallel, GSC—a marker of sympathetic arousal—was also reduced during stimulation, suggesting attenuation of autonomic and emotional responses to hypercapnia.

Conclusions:
These findings provide direct evidence that the forebrain—including the amygdala and thalamus—can inhibit brainstem-driven respiratory responses to hypercapnia. In addition to dampening the physiological ventilatory drive, stimulation of these regions suppressed the associated affective experience of dyspnea and autonomic arousal. This highlights a potential forebrain network that modulates both the sensory and emotional components of breathing, with implications for understanding conditions such as anxiety, panic disorders, and sudden unexpected death in epilepsy (SUDEP).

Title: Investigating ion channel function in serotonin-mediated central chemosensitivity
Student Presenter: Campbell Krusemark
Faculty Advisor: George Richerson
Introduction: Breathing is one of the most essential tasks for maintaining human life. As such, the brain tightly regulates this process to ensure we avoid the catastrophic effects that are brought about by an inability to breath. Breathing is primarily regulated in the brain through serotonin (5-HT) neurons acting as central chemoreceptors. These neurons are located in midbrain raphe nuclei and are highly sensitive to acidosis, or a decrease in pH. As carbon dioxide levels rise during breathing, 5-HT neurons in the brain can sense this intracellular decrease in pH and initiate a response. The close association of 5-HT neurons with other brainstem nuclei allows these neurons to stimulate the centers in the brain that are responsible for coordinating the muscles required for inspiration. Despite what we know about serotonin-mediated breathing control, the mechanisms behind this pathway have yet to be fully elucidated. While a calcium-activated nonselective cation current linked to the stimulation of these neurons has recently been identified, the specific channel responsible for the current remains a mystery. Identification of this channel will be crucial to advancing our knowledge of the neural mechanisms which control breathing. Critically, identification of this channel would provide a target for intervention in conditions of impaired breathing, such as SUDEP and SIDS.
Hypothesis/Purpose: We hypothesized that at least one of the ion channels commonly found in raphe serotonin neurons is responsible for the calcium-activated nonselective cation current which confers chemosensitivity to this neuronal population. Inactivation of the gene encoding this protein will lead to an inability of the neuron to sense and respond to changes in pH.
Methods: Using a CRISPR-Cas9 system, individual candidate channel genes were inactivated in 5-HT neurons harvested from neonatal mice. The chemosensitivity of cells lacking candidate channels was tested using *in vitro* whole-cell patch-clamp recording. To control pH, cells were bathed in 5% CO_2 or 9% CO_2 solutions during recording.
Results: Experiments are still ongoing, but we continue to optimize our experimental protocols and make progress by testing candidate channel genes, including those channels most commonly associated with serotonin circuitry.
Conclusion: Here, we outline a project with immense implication in breathing control and central chemosensitivity. Upon identification of this channel, further work must be done to characterize its expression and its role in breathing disorders and conditions of sudden death. In addition to this application, once the channel responsible for chemosensitivity is identified, it may be a target for future therapies across the spectrum of serotonin-mediated disease.

Investigating the Role of Cardiac Sodium-Glucose Co-Transporter 1 (SGLT1) in Diabetic Cardiomyopathy

Vooha Kumar, Dr. Ferhaan Ahmad, Michael Cicha, Mia Michel

Background: Diabetic cardiomyopathy (DM) is a heart condition characterized by abnormal structure and function of the myocardium associated with the disease process of diabetes mellitus. 11.6% of the US population suffers from diabetes and are therefore at a 20% increased risk of developing heart failure due to DM. This risk is independent of other risk factors for heart failure, such as atherosclerosis and hypertension. Prior studies have implicated the sodium-dependent glucose transporter (SGLT1) as a major contributor to ischemia-related myocardial injury through its interactions with epidermal growth factor (EGFR). EGFR is known to cause increased reactive oxygen species which damage the heart muscle. Previous murine studies revealed phosphorylated SGLT1 was upregulated under ischemic conditions and SGLT1-knockout mice were protected from ischemic damage compared to wild-type mice.

Hypothesis/Purpose: Since SGLT1 expression increases in enterocytes during diabetic hyperglycemia, it may also play a role in diabetes-related cardiomyopathy. The purpose of our study was to investigate SGLT1 expression in the heart during various glycemic conditions to identify potential causes, and thus interventions, of DM. We hypothesized that there would be an increase of both total SGLT1 and the percent of phosphorylated SGLT1 in the cells grown in glucose media compared to control media.

Methods: We grew a culture of immortalized HL-1 cells in control media, mannitol (an osmotic control), and high glucose. We then used Western blots to measure the levels of total SGLT1 and the percentage of phosphorylated SGLT1 in each state. We also used immunofluorescence to visualize the location of the protein in the cells.

Results/Conclusion: Using an unpaired two-sample t-test there was not a statistically significant difference in SGLT expression between cells in the high glucose environment and the control ($p > 0.05$). This suggests that SGLT1 may not behave the same way in cardiomyocytes and enterocytes, or the theorized connection between diabetes and cardiomyopathy needs further refinement. Future directions for this study should involve murine studies as the HL-1 cells in vitro may not be an exact model for diabetic conditions as cardiomyocytes in vivo. Furthermore, it would be beneficial to measure other steps in the pathway such as EGFR or extracellular signal-related kinase (ERK), a signaling protein that phosphorylates and upregulates SGLT1, to investigate if the other steps of the proposed mechanism are valid.

Successful maturation of stem cell derived islet from RUES2 cell line in the presence of fatty acids

Dat Lam, Siming Liu, & Yumi Imai

Introduction: Diabetes is a prevalent metabolic disease globally, characterized by the loss of pancreatic beta cell mass and function. While transplantation of human donor islets can restore functional insulin secretion, application is limited by scarcity of donor tissue. Pluripotent stem cells, therefore, offer a promising solution as source for generating functional islets. However, stem cell derived islets (SC-islet) behave differently compared to human islets, with less potent glucose-stimulated insulin secretion. It has been proposed that activation of PPARα and PPARγ could improve maturity of SC-islet.[1] We tested differentiation protocol of pancreatic islets using RUES2 cell line, which has not been previously reported, and investigated whether small concentration of non-esterified fatty acids (NEFA), natural ligands for PPAR receptors, at the final differentiation stage can enhance functional maturation of SC-islet.

Hypothesis:

1) RUES2 is a viable source of stem cell for the generation of SC-islet.

2) Supplementation of NEFA can improve the maturity and glucose-stimulated insulin secretion (GSIS) of RUES2-derived islets.

Method: RUES2 cells (kindly provided by Dr. Amy Ryan of Department of Anatomy and Cell Biology) were differentiated through seven stages using protocol from Dr. Kieffer.[2] Islets were further matured at the end of stage 7 following Dr. Otonkoski protocol[3] with and without 0.05 mM palmitic/oleic acid (2:1). Differentiation was followed using Taqman and SYBR qPCR of stage 4 (pancreatic progenitor) and stage 7 (SC-islet). Immunohistochemistry of PDX1/NKX6.1 was performed for stage 4 and INS/GCG for stage 7. Perifusion was performed using BioRep Perifusion System and insulin secretion was assessed using human ELISA. Functional assessment was characterized by area under the curve of first and second phase insulin secretion. Student's t test was performed with $p<0.05$ as statistically significant.

Result: Successful differentiation toward pancreatic progenitors was confirmed through expressions of PDX1 and NKX6.1 in isolated S4 RNA sample. Immunostaining revealed 83.3 ± 6.4% PDX^+ cell and 42.2 ± 19.7% $NKX6.1^+$ cells (n=4). SC-islet showed strong expression of INS and GCG gene, with 63.9 ± 11.9% INS^+ cells and 25.9 ± 3.6% GCG^+ cells through immunostaining (n=2). Perifusion of S7 islets demonstrated insulin secretion in response to high concentration of glucose and KCl. We determined that IHC and perifusion data from this method is similar to previously mentioned publication.[2,3] NEFA-treated SC-islets exhibited subtle but statistically significant enhancement in GSIS, with higher AUC first-phase secretion (mean difference = 0.34 fold, 95%CI: 0.10-0.58, p = 0.014) and second-phase secretion (mean difference = 0.19 fold, 95%CI: 0.006-0.364, p = 0.045).

Conclusion: RUES2 cell line is a viable source for generating functional SC-islets. Low-dose NEDA exposure during maturation modestly improves insulin secretory function. Analysis of NEFA effect was limited to insulin secretion due to small scale production during the culture process. Further studies, including transcriptomic and extended immunostaining analyses, are warranted to better define the role of NEFA in SC-islet maturation.

Reference:

1. PMID: 39211191
2. PMID: 37323565
3. PMID: 35241836

Association between dietary factors and environmental factors with melanoma incidence in the Agricultural Health Study cohort

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Introduction and Purpose: Cutaneous melanoma (CM) rates are rising nationally — in 2024, there were 100,640 estimated new cases of invasive disease making up 5% of all new cancer cases. Iowa has the 5th highest melanoma incidence in the United States with an age-adjusted incidence rate of 31.4 cases per 100,000. Given that occupational and lifestyle factors may contribute to elevated melanoma risk and may present a modifiable risk factor, the role of dietary has begun to be explored. Previous studies have shown alcohol and citrus fruit consumption to be associated with increased melanoma risk, while tobacco, caffeine, and red meat have been shown to have protective effects. This study examines associations between dietary factors and melanoma incidence among private pesticide applicators and spouses in the Agricultural Health Study (AHS) cohort.

Methods: Since 1993, the AHS has been a prospective cohort that includes 89,655 pesticide applicators and spouses recruited in Iowa and North Carolina to explore how agricultural, lifestyle, and genetic factors affect the health of farmers. Exposures were assessed through self-reported data collected via questionnaires from Phase 1 (1993-1997) and Phase 2 (1999-2003 including dietary health questionnaire DHQ) of the AHS. Melanoma incidence was calculated using regular links from the State Vital Statistics and Cancer Registries. Time to Melanoma (TTM) was calculated from the date of DHQ completion to the date of first melanoma diagnosis. Subjects were censored at their date of death, date of other cancer diagnosis, or the date they moved out of state. Multivariable Cox regression was used to evaluate the association between demographic and dietary characteristics and the risk of melanoma. Estimated effects were reported as hazard ratios (HR) and assessed for significance at the 5% level.

Results: Out of the 32,709 subjects analyzed, 18,279 were applicators (commercial and private combined) and 14,430 were spouses. 74.6% of the subjects were from Iowa, with the remaining being from North Carolina. On multivariable analysis, applicator status ($p<0.01$), age at DHQ completion ($p<0.01$), and absence of regular, caffeinated soft drink consumption ($p=0.02$) were significantly associated with TTM, after accounting for smoking status. The average risk of melanoma was 90% greater in applicators compared to spouses (HR=1.90, $p<0.01$), 12% greater for every 5-year increase in age (HR=1.12, $p<0.01$), and 25% lower for every 500g increase in the daily consumption of regular, caffeinated soft drinks (HR=0.75, $p=0.02$).

Conclusion: This study supports age as a known risk factor for melanoma. Preliminary findings show higher rates of melanoma in pesticide applicators v. spouses as well as lower rates associated with daily consumption of regular caffeinated soft drinks in an agricultural population based in Iowa and North Carolina. Previous studies have hinted at a protective effect regarding caffeine and melanoma. The AHS uniquely allows dietary data to be correlated with major health outcomes, allowing for further inquiries regarding modifiable risk factors for melanoma. Future analyses will explore additional dietary factors and pesticide exposures in the setting of melanoma incidence as well as inquiries regarding mechanism.

Investigating Patient Perspectives on Robotic-Assisted Knee and Hip Arthroplasty

Chase Larsson, Silvana Velasquez-Marin, Victoria Tappa, Natalie Glass, Krit Petrachainan, Nicolas Noiseux, Jacob Elkins, **Dallas Vanorny**

INTRODUCTION: Robotic-assisted total knee (rTKA) and total hip arthroplasty (rTHA) have gained popularity due to purported enhanced precision and improved patient outcomes. However, limited research exists on patient perceptions, expectations, and perceived trust with rTKA and rTHA. Understanding these factors may optimize patient pre-surgical education, set realistic expectations on postoperative outcomes, and improve patient satisfaction. This study primarily evaluated whether patients undergoing rTKA/rTHA differ from those undergoing traditional TKA/THA in their preoperative expectations and perceptions of robotic technology.

METHODS: This was a prospective, cross-sectional pilot study of 30 adult patients (mean age 63.2 years) undergoing primary TKA or THA with either robotic assistance or traditional methods. Patients completed a preoperative survey at their work-up visit. The survey included four components: 1. patient demographics and experience with previous arthroplasty surgery, 2. assessment of patient priorities regarding surgical outcomes, 3. Likert scale questionnaire measuring perceptions of rTKA/rTHA, and 4. HOOS-JR or KOOS-JR surveys accessing joint function. To analyze baseline differences, group comparisons were performed on patient perceptions, priorities, and HOOS/KOOS-JR scores. Statistical analysis of primary outcomes was done using Wilcoxon rank sum test.

RESULTS: We found no significant baseline differences in priorities between robotic-assisted and traditional TKA/THA patients. Both groups ranked “moving better after surgery” and “less pain after surgery” as top priorities, while “use of newest technology” and “lower cost” ranked lowest. Perception of robotics scores were generally neutral to mildly positive across the cohort. Patients undergoing rTKA/rTHA showed slightly greater agreement that rTKA/rTHA could improve long-term function (mean 3.53 vs. 3.13) and less concern about the loss of surgeon control (mean 2.40 vs. 3.00); however, these differences were not statistically significant. Patients undergoing rTKA/rTHA did show a significantly greater confidence that surgeon experience with robotics leads to better outcomes. Baseline HOOS-JR and KOOS-JR scores showed no significant differences in functional status. Familiarity with robotic-assisted surgery was low: 16 patients (55%) reported no familiarity, 12 (41%) reported some familiarity, and only one was very familiar.

CONCLUSIONS: This pilot study found no significant differences in perceptions or functional status between robotic-assisted and traditional TKA/THA patients but did find that patients undergoing rTKA/rTHA did have some more positive views of robotic-assisted surgery. The neutral perception responses may reflect low familiarity with robotic-assisted surgery rather than established opinions. These findings highlight the need for enhanced preoperative education to address knowledge gaps and support informed decision-making. Further studies should explore how perceptions evolve postoperatively, and influence satisfaction as robotic-assisted arthroplasty sees increased utilization.

Title: Impact of Sonographic Training on Prenatal Myelomeningocele Diagnosis Across Rural and Urban Settings in Zambia

Authors: Mei Lietsch, Rya Muller, Roxanna Garcia, Brooks Jackson, Humphrey Kunda, Rebecca Reynolds

Introduction: Prenatal myelomeningocele (MMC) diagnosis, primarily by ultrasound, is essential for timely surgical intervention and better patient outcomes. However, recent data shows 3% (2/69) of mothers in Zambia receive a prenatal diagnosis.

Objective: To identify challenges to prenatal ultrasound diagnosis of MMC in Zambia.

Methods: A cross-sectional written survey of 60 prenatal care providers in rural and urban healthcare settings in Zambia was conducted between May-July 2025. Provider confidence in diagnosing spina bifida was assessed using a 5-point Likert scale. Data were analyzed using Fisher's exact test and Spearman correlation.

Results: Sixty respondents completed the survey: 28 physicians, 29 non-physician providers (sonographers, midwives, and nurses), and 3 unspecified. Rural providers included 20 physicians and 16 non-physicians. Urban providers included 8 physicians and 13 non-physicians. Most providers (98.3%, 58/60) reported access to prenatal ultrasound equipment. Thirty-eight percent (23/60) of providers obtained formal sonographic training. Training was more common in urban (67%, 14/21) than rural settings (23%, 9/39, $p=0.0002$). Specific obstetrics training (urban 57% vs. rural 18%; $p=0.005$) and congenital anomaly training (urban 38% vs. rural 10%; $p=0.017$) was more available to urban providers. Spina bifida diagnostic ability and confidence did not differ significantly by region ($p=0.38$; $p=0.288$) or provider type ($p=0.389$; $p=0.5673$). Provider confidence increased with years of experience ($\rho=0.34$, $p=0.010$) but was not associated with obtaining sonographic training ($\rho=-0.009$, $p=0.95$). No significant differences were found between physicians and non-physicians, except urban physicians (38%, 8/21) were more likely to have higher training rates than urban non-physicians (62%, 13/21; $p=0.018$).

Conclusion: Despite near-universal access to ultrasound equipment and higher training rates in urban areas, sonographic obstetric and congenital anomalies training remains limited, particularly in rural areas in Zambia. This gap may contribute to low prenatal MMC diagnostic detection, which highlights a need for more qualified obstetric sonographers and warrants further investigation.

Battlefield Acupuncture as a non-pharmacologic treatment for pain and nausea in hospice patients

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Introduction: Patients enrolled in hospice often experience pain and nausea from a variety of causes. Side effects from prescribed opioids are also common. The aim of this study is to investigate the effects of implementing a nonpharmacological treatment, Battlefield Auricular Acupuncture (BFAA), for the management of pain and nausea associated with the end of life.

Methods: Patients experiencing unmanaged pain and/or nausea were enrolled in the study. This study had one primary outcome: pain intensity measured by visual analog scale pain score, and one secondary outcome: opioid consumption in daily dose of oral morphine equivalent (DOMED) up to one month prior to treatment, and up to one month after the BFA treatment. Statistical analysis was performed utilizing Wilcoxon Ranked-Sign test for nonparametric pain scores.

Results: A total of 34 subjects were included in this study. With preliminary results, statistical analysis found there was no significant change in reported pain scores after treatment (Wilcoxon signed-rank $p = 0.625$, small effect size $r = 0.22$). While the average difference in reported pain score was -1.6 points, the variation in changes was large. Due to the constrained sample size, the test had low power to detect any effect.

Conclusion: The results from this study reveal the potential clinical benefits of using BFAA for reducing pain intensity and opioid use in hospice patients, although firm conclusions cannot be made. Enrollment for this study is ongoing, and with a greater sample size an effect may be measured. A future direction of study that may offer some benefit consists of a tolerability and perceived benefit survey administered to patients receiving BFAA. Ultimately, the potential benefit of non pharmacologic pain control methods at the end of life remains an important and under researched are of medicine, and this study provides one step toward improving the human experience of dying.

Pretreatment with Auranofin Sensitizes KEAP1 Knockout Non-Small Cell Lung Cancer Cells to the Antitumor Effects of P-AscH$^-$ by Inhibiting Enhanced Peroxide Metabolism

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Introduction: Approximately 11 - 27% of non-small cell lung cancer (NSCLC) cases harbor KEAP1 (Kelch-like ECH-associated protein 1) mutations, resulting in constitutive activation of nuclear factor-erythroid factor 2 (NRF2) transcription factor. This leads to upregulated expression of antioxidants and promotes resistance to standard of care chemo- or radiotherapy. Previous studies show that FDA-approved antirheumatic drug, auranofin, is a thioredoxin reductase inhibitor that enhances the anti-cancer effects of pharmacological ascorbate (P-AscH$^-$) presumably by inhibiting peroxiredoxin-mediated metabolism of hydrogen peroxide produced by the oxidation of ascorbate by peroxiredoxins. Considering these cancer-specific biological effects, auranofin and P-AscH$^-$ have significant potential as adjuvant therapies for sensitizing KEAP1 mutant NSCLC to radio-chemotherapy.

Hypothesis: (1) CRISPR-mediated KEAP1 knockout (KO) in KEAP1 WT NSCLC cells induces resistance to auranofin monotherapy, and (2) auranofin pretreatment sensitizes the KEAP1 KO NSCLC cells (relative to normal lung epithelial cells) to the antitumor effects of P-AscH$^-$ by inhibiting enhanced peroxide metabolism.

Methods: This project used two NSCLC cell lines, specifically H1299T KEAP1 partial KO cells and H1299T sgRNA negative control cells, which were created from H1299T cells (KEAP1 WT), utilizing the Alt-R^{TM} CRISPR-Cas-9 system. Approximately 150,0000 cells were plated in 60 mm dishes. All cells were maintained at 21% oxygen with RPMI 10% FBS media. For the dose-response experiments, clonogenic survival assays were performed after treatments with 0.1, 0.5, 1, and 2 μM auranofin for 24 hours to assess whether growth inhibition or loss of cloning efficiency was induced. The cells were then treated with the dose of auranofin that resulted in approximately 60 - 80% cloning efficiency (0.5 μM) for 24 hours, followed by treatments with P-AscH$^-$ for 1 hour in FBS-free RPMI media. The doses of P-AscH$^-$ that resulted in approximately 60 - 80 and 30 - 40 % cloning efficiency respectively (H1299T sgRNA negative control cells: 5 pmol/cell (2.5 mM) and 10 pmol/cell (5 mM), H1299T KEAP1 partial KO cells: 5 pmol/cell (2.5 mM) and 25 pmol/cell (8.75 mM)) were applied based on previous results. Clonogenic survival assays were performed after treatments to assess whether growth inhibition or loss of cloning efficiency was induced by auranofin + P-AscH$^-$ treatments. Western Blots were performed to ensure consistent gene expression. All cell counts were collected with a Coulter Counter.

Findings: CRISPR-mediated partial KO of KEAP1 in H1299T cells (KEAP1 WT) results in slightly enhanced resistance to auranofin. Additionally, pretreatment with auranofin sensitizes both H1299T KEAP1 partial KO cells and H1299T sgRNA negative control cells to P-AscH$^-$.

Conclusion: CRISPR-mediated partial KO of KEAP1 in H1299T cells (KEAP1 WT) resulted in a slightly enhanced resistance to auranofin monotherapy, and pretreatment with auranofin sensitized both H1299T KEAP1 partial KO cells and H1299T sgRNA negative control cells to P-AscH$^-$. These findings support the hypothesis that KEAP1 mutations contribute to cancer cell resistance to standard therapies and targeting peroxide metabolism enhances NSCLC therapeutic outcomes in KEAP1 mutants. Future studies will test (1) if KEAP1 mutant NSCLC cells are more resistant to irradiation compared to KEAP1 WT cells, (2) if irradiation sensitizes KEAP1 and KEAP1 WT NSCLC cells to P-AscH$^-$, (3) if CRISPR KO of KEAP1 in H1299T (KEAP1 WT) and CRISPR KO of NRF2 in A549 (KEAP1 mutant) enhance resistance/sensitization to combination treatments (irradiation + P-AscH$^-$ / auranofin + P-AscH$^-$), and (4) if HBECs (normal lung epithelial cells) are more resistant to auranofin, irradiation, and P-AscH$^-$ compared to NSCLC cells. This research will contribute to the improvement of therapeutic strategies for cases of NSCLC with KEAP1 mutations.

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Disrupted Salience Network Dynamics Linked to Anxiety in Parkinson's Disease

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Introduction: Patients with Parkinson's disease (PD) experience debilitating nonmotor symptoms, including depression and anxiety which often go undiagnosed and untreated. These symptoms contribute to worse cognitive outcomes, faster disease progression, lower quality of life, and greater caregiver burden. Despite their clinical impact, the neural correlates of psychiatric symptoms in PD remain poorly understood.

Objective/Hypothesis: We aimed to identify functional neural correlates of anxiety in PD using resting-state fMRI and task-based EEG. fMRI was used to link anxiety to canonical cortical networks, while EEG was used to evaluate the electrophysiological dynamics of these networks in a separate cohort of patients with PD. We hypothesized that anxiety in PD would be associated with changes in frontal activity

Method: We analyzed fMRI data from the patients with PD ($N = 87$), focusing on canonical frontal networks such as the salience (SAL), frontoparietal (FPN), and default mode networks (DMN). We also analyzed EEG data collected during the Simon Task in a separate cohort of patients with PD ($N = 84$) focusing on low-frequency delta (1-4 Hz) and theta (4-8 Hz) activity at the midfrontal cortex overlying the anterior cingulate node of the SAL. Linear models tested the relationship between State-Trait Anxiety Inventory (STAI-S/T) scores and brain network activity.

Results: In our fMRI study, decreased intra-SAL connectivity was strongly linked to higher state anxiety ($r = -0.34$, $p = 0.001$, $\eta^2 = 0.13$), while trait anxiety showed no reliable associations. Higher state anxiety also correlated with worse cognitive performance on the Montreal Cognitive Assessment (MoCA) ($r = -0.37$, $p = 0.0004$). In our EEG study, reduced cognitive control-related delta power was linked to higher anxiety scores ($r = -0.3$, $p = 0.005$). Higher anxiety was, again, associated with worse cognitive performance on the MoCA ($r = -0.26$, $p = 0.02$) and lower accuracy on the Simon Task ($r = -0.2$, $p = 0.05$).

Conclusions: Our multimodal analysis of the neural correlates of anxiety in PD revealed a key role for the frontal networks. Notably, our findings underscore the comorbidity of anxiety and cognitive impairment, highlighting the importance of comprehensive assessment and treatment of nonmotor symptoms in PD.

Sleep Quality and Neurovascular Correlates of Lifelong HIV Infection: A Sub-Study of Neurovascular Health in Perinatally Infected Young Adults with HIV in Uganda

McKenna Major, Linder Wendt, Katherine Timboe, Rita Nakalega, Juliane Etima, J. Brooks Jackson, Julie C. Gudenkauf

INTRODUCTION: As of 2023, there was estimated to be 39.9 million people living with HIV globally, and of which, 30.7 million were accessing antiretroviral therapy (ART). In the present era of ART, more people are living with HIV as a chronic condition, especially individuals who acquired the infection perinatally. Studies consistently show that people living with HIV (PLWHIV) are prone to significant sleep disturbances that adversely impact quality of life.

OBJECTVIVES: The primary objective of this study is to determine correlations between perinatal HIV infection and sleep-related issues, as a sub-study of a larger project investigating correlates of carotid arterial pathology and neurocognitive function in young adults with perinatal HIV infection.

METHODS: The parent study was a cross-sectional study of young adults in Kampala, Uganda, living with and without HIV. Participants were included in the variable group if they were age 24-30 from the Youth Generation Alive (YGA) group living with HIV contracted perinatally. Exclusion criteria consisted of inability to provide informed consent or speak English/Luganda and inability to undergo carotid ultrasound. Sleep quality was evaluated using the Epworth Sleepiness Scale (ESS), select items from the Patient Health Questionnaire-8 (PHQ-8) and General Anxiety Disorder-7 (GAD-7), and data on sleep duration. Participants also completed blood work for markers of inflammation and vascular risk factors, a medical history questionnaire, a screening assessment for mood symptoms, and a cognitive battery. The primary endpoint was the **Epworth Sleepiness Scale (ESS) score**. Additional endpoints included sleep duration and select items from PSQ-8 and GAD-7 regarding **sleep quality**.

RESULTS: 58 participants were included in this study with 29 living with HIV and 29 controls. The two groups were similar in age, sex, and race. The primary endpoint analysis showed higher mean ESS scores in PLWHIV relative to controls (4.0 vs. 2.3); however, this difference was not statistically significant ($p = 0.3$). Interestingly, a greater number of PLWHIV had an ESS ≥10 compared controls (14% vs 0%; $p = 0.11$). For additional endpoints, sleep duration was similar between groups; 72% of PLWHIV and 69% of the controls obtained 6-9 hours of sleep ($p = 0.8$). Furthermore, both groups reported similar rates of "trouble staying sleep, staying asleep, or sleeping too much" (21% in PLWHIV vs. 24% in controls; $p = 0.8$) and "feeling tired or having little energy" (62% in PLWHIV vs. 41% in controls; $p = 0.11$) on the PHQ-8, and higher rates of "trouble relaxing" (21% in PLWHIV vs 10% in controls; $p = 0.5$) on the GAD-7.

CONCLUSIONS: Young adults with perinatally acquired HIV in Kampala, Uganda, demonstrated overall ESS scores comparable to age- and sex-matched uninfected controls; however, a greater proportion of PLWHIV had severe ESS (≥10), suggesting excessive daytime sleepiness and potential underlying sleep disturbances warranting medical evaluation. Based on the parent study, mood symptoms were not strongly associated with sleep quality; however, larger studies are needed to further elucidate those relationships. Further research is needed to determine the extent of the relationship of sleep quality in PLWHIV and potential long-term implications.

Key words: HIV, sub-Saharan Africa, perinatally infected, ESS, sleep quality

Incidence and Prevalence of Ventricular Tachycardia has Increased in Most Demographics over the past Decade

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Introduction: Ventricular tachycardia (VT) is a potentially fatal cardiac arrhythmia that originates in the heart's ventricles and restricts the heart's ability to pump blood effectively. This study provides the first large-scale, global analysis of temporal and demographic trends in VT.

Question: How have the incidence, prevalence, and demographic patterns of VT over the past decade changed globally and within the United States?

Methods: This study is a retrospective, observational cohort study using de-identified electronic health record data from the TriNetX Global Collaborative Network. It analyzes VT incidence, prevalence, and incidence proportion from 2015 to 2024 across 142 healthcare organizations, sampling over 120 million patients worldwide. Demographics of sex, age decile (0-80+), and race were compiled through TriNetX and used as the basis for group comparisons.

Results: In the last decade, there has been a 155% increase in the US incidence of VT and a 114% increase in VT in the global incidence. Global incidence has increased across all age deciles and remained highest in older age deciles. The change in incidence was greater in deciles less than 50 than in deciles over 50 with the exception of the 0-9 decile. The incidence of VT was higher in males compared to their female counterparts while the change in incidence was higher in females (153% increase) than in males (120% increase). Native Hawaiian or other Pacific Islanders had the highest incidence of VT while Asians had the lowest incidence of VT over the last decade. Incidence rate and prevalence showed similar results as incidence proportion.

Conclusion: VT incidence has increased over the past decade across all age, sex, and racial groups, with the highest rates observed in older adults, particularly US men, and Native Hawaiian or Other Pacific Islander populations. These findings highlight a growing global arrhythmia burden likely driven by rising cardiometabolic risk factors, increased longevity, and improved detection. Understanding these demographic trends is critical for developing targeted prevention strategies, informing healthcare policy, and guiding future research into the underlying causes and disparities in VT risk.

Bullous Pemphigoid Blister Fluid, Sera, and Antibodies Drive Regulatory T Cell Dysfunction and Langerhans Cell Activation

Britt Mariman, BS and Kelly Messingham, PhD

Introduction: Bullous Pemphigoid (BP) is an autoimmune blistering disease that primarily affects the elderly. Because the basic mechanisms of disease are not understood, targeted therapies cannot be developed, leaving broad-based immune suppression as first line treatment. Autoimmunity develops because tolerance mechanisms fail. Within the skin, Langerhans cells (LCs) and regulatory T cells (Tregs) are critical for maintaining peripheral tolerance.

Methods: An in vitro skin organ culture model was used to test whether LC and Treg populations are modulated by BP-associated autoantibodies or inflammatory factors. Skin from Mohs surgeries was cut into 6-mm punch biopsies and cultured ~40 h in media containing BP blister fluid (BF), BP sera (BPS), control sera (CS), or BP180 antibodies/IgG controls at defined doses. Biopsies were digested to single-cell suspensions, and flow cytometry was used to assess LC and Treg phenotypes.

Results: LC and Treg frequencies remained unchanged across conditions. BP BF increased Treg IL-10 and reduced CCR6, while LCs upregulated Ki-67, IL-10, IL-2, and CCR2. BPS had dose-dependent effects: 20% BPS reduced CD127 and TGF-β and increased Ki-67 and CCR6; 5% BPS decreased CD127, CLA, and CCR6 but increased Ki-67 and IL-10. BPS also enhanced LC expression of OX40L, IL-2, IL-10, Ki-67, IL-15Rα, and CCR2, with 20% BPS decreasing CD80 and CCR6 while increasing Ki-67, PD-L1, IL-10, and CCR2, and 5% BPS increasing CD80, CCR2, Ki-67, and PD-L1 while reducing ICOSL. BP180 antibodies decreased Treg CD127 and increased Ki-67, CD73, and IL-10, with the 50 ng/ml dose lowering CD39 and elevating CCR4. In LCs, both antibody doses reduced CD80 and ICOSL while increasing IL-10 and IL-15Rα, with the 50 ng/ml dose additionally increasing Ki-67, PD-L1, CCR2, and IL-2.

Discussion: BP blister fluid, sera, and BP180 antibodies promote Treg dysfunction and LC activation. Rather than changing cell frequencies, BP stimuli shift Tregs toward a less suppressive, activated state and reprogram LCs to deliver stronger costimulatory and cytokine signals. This imbalance may impair immune regulation and sustain autoreactivity, consistent with mechanisms common to autoimmunity.

Title: Extent of Centralization of Cancer Surgery in the United States

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Introduction: Centralization of cancer surgery has been increasingly recognized as a correlate of improved surgical outcomes in the United States. Prior research demonstrates that procedures such as pancreatectomy, esophagectomy, and cystectomy have become increasingly centralized over time, with care shifting toward major teaching hospitals and tertiary centers, which are associated with lower perioperative mortality rates. Existing studies have largely focused on individual cancers or regional datasets, leaving a gap in understanding the broader national landscape of centralization across multiple oncologic surgeries.

Purpose: To quantify the distribution of oncologic surgery volumes for common cancers across hospital centers and to examine the characteristics of hospitals providing surgical management of these cancers in the United States.

Methods: The authors conducted a retrospective cross-sectional analysis using the Nationwide Readmissions Database for 2021–2022. The study population included all patients admitted for surgical resection or excision for laryngeal, lung, colon, rectal, kidney, or uterine cancers. Procedure distribution was visualized using Lorenz curves, which depict the distribution of operations performed within volume quintiles, with each operation analyzed separately. Centralization was quantified using the Gini index, a measure of inequality in a dataset. Hospital characteristics—including bed count (designated threshold for large, medium, and small varied based on hospital's location and teaching status), urban designation, and ownership—were compared between quintile 5 (highest-volume) and quintile 1 (lowest-volume) hospitals.

Results: A total of 138,794 patients undergoing oncologic surgery were included. The sample size for each cancer site was as follows: larynx (n = 2,264), lung (n = 30,834), colon (n = 62,007), rectum (n = 9,513), kidney (n = 23,237), and uterus (n = 11,939). Across all cancer types, a substantial proportion of procedures were concentrated in the highest-volume hospitals. The share of procedures performed in Quintile 5 hospitals ranged from 57.6% for colon surgery to 61.1% for uterine surgery, while other cancer sites were in between. Gini coefficients were from 0.584, 0.566, 0.552, 0.541, 0.564, and 0.591 for larynx, lung, colon, rectum, kidney, and uterus, respectively. Additionally, Lorenz curve analyses demonstrated a highly clustered quintile-by-quintile distribution of oncological procedures across all sites. Hospital characteristics were broadly consistent across cancer sites. Across all sites, between 54.5% and 82.9% of procedures were performed at large hospitals, and 55.2%–68.4% of procedures were conducted at hospitals in large metropolitan areas. Regarding ownership, most procedures (78.3%–84.5%) were performed at private non-profit hospitals. Larynx cancer procedures demonstrated the highest concentration in large bed size hospitals and metropolitan areas and the highest proportion of procedures in government, nonfederal hospitals.

Comparisons between quintile 1 (lowest-volume) and quintile 5 (highest-volume) hospitals highlighted consistent differences. Bed size distributions differed substantially, with Q5 hospitals overwhelmingly large compared to Q1. Urban designation also varied, with Q5 hospitals much more likely to be in large metropolitan areas, whereas Q1 hospitals had relatively higher proportions in small metropolitan and micropolitan areas. Notably, no Q5 hospitals were in micropolitan areas except for colon and kidney procedures, with less than 2.5% of cases in these settings. Ownership categories did not vary markedly between Q1 and Q5, although Q5 hospitals consistently had fewer private investor-owned hospitals compared to Q1. For larynx cancer surgeries specifically, no procedures in Q5 hospitals occurred at government nonfederal facilities.

Conclusions: This study provides a comprehensive overview of common cancer management in the United States in relation to hospitals that provide oncologic surgeries. We found that across diverse cancer sites—including larynx, lung, colon, rectum, kidney, and uterus—oncologic operations were similarly and consistently centralized, with more than half of procedures performed in the highest-volume hospitals. These findings suggest that, regardless of cancer type, patients increasingly receive surgical care in large, metropolitan, and predominantly private hospitals, reinforcing a national trend toward centralization. While such concentration of care may support improved outcomes by leveraging high-volume expertise, it also highlights the importance of ensuring equitable access to these centers, particularly for patients in smaller or rural communities.

Impact of Obesity on Severity and Outcomes of Acute Pancreatitis in Children

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Introduction: Acute pancreatitis (AP) is the leading cause of gastrointestinal-related hospital admissions in the United States. While mild cases often resolve with minimal intervention, moderately severe to severe cases can lead to significant complications and frequently require intensive management due to organ failure. Despite the rising incidence of pediatric AP (~1 in 10,000 children per year), the predictors of disease severity and outcomes remain poorly understood. Evidence suggests that obesity may be associated with more severe disease in children, possibly acting as an important modifier of AP outcomes in the pediatric population. Given the rising incidence of both obesity and AP in children, and the existing gaps in the pediatric literature, this study aims to evaluate the impact of weight status on the severity and outcomes of pediatric AP at University of Iowa Health Care.

Hypothesis: Overweight and obese children admitted with AP are more likely to have worse outcomes when compared to children of normal weight. These worse outcomes include increased disease severity, complications, therapies used, mortality, and length of stay.

Methods: This retrospective cohort study was conducted on patients aged 0-17 who were admitted to the University of Iowa Health Care and diagnosed with AP between January 1, 2015 and December 31, 2024. Overall, 137 individual hospital encounters were identified and used in data analysis. Each AP episode was identified using the 2012 Revised Atlanta Classification and local and systemic complications were defined as outlined in the 2017 Clinical Report from the NASPGHAN Pancreas Committee. Participant BMI was calculated as a percentile by age and divided into categories of normal weight, overweight, and obese as defined by the Centers for Disease Control and Prevention. Data points such as mortality, length of stay, intensive care admissions, interventions, lab values, and ancillary services were among those recorded for each encounter.

Findings/Results: Out of all encounters, 61/137 (44.5%) were with patients of normal weight, 20/137 (14.6%) were overweight, and 56/137 (40.9%) were obese. In encounters with patients of normal weight, 36/61 (59.0%) had a mild episode with no local or systemic complications. The other 25/61 (41.0%) had a moderately severe or severe episode, with 19/25 (76.0%) experiencing local complications and 9/25 (36.0%) experiencing systemic complications. In encounters with overweight patients, 14/20 (70%) had a mild episode with no local or systemic complications. The other 6/20 (30%) had a moderately severe or severe episode. In encounters with obese patients, 24/56 (42.9%) had a mild episode with no local or systemic complications. The other 32/56 (57.1%) had a moderately severe or severe episode, with 28/56 (87.5%) experiencing local complications and 14/32 (43.8%) experiencing systemic complications. Further data analysis is pending at this time.

Conclusions: While further data analysis is pending, the preliminary results seem to suggest that obese patients are more likely to experience a moderately severe or severe episode of AP with a higher likelihood of developing both local and systemic complications. However, no solid conclusions can be drawn until data analysis is complete.

Integrating Genomics and Deep Learning OCT Analysis to Predict Treatment Response in Neovascular AMD

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Introduction: Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in elderly worldwide. In the neovascular form (nvAMD), choroidal neovascularization leads to retinal fluid accumulation and rapid visual decline. Although anti-vascular endothelial growth factor therapy remains the standard of care, a significant proportion of patients exhibit incomplete or poor response to treatment. The *MMP9* locus is the only gene independently associated specifically with the neovascular subtype of AMD. This study aimed to characterize the clinical phenotypes and treatment responses of *MMP9* variants in patients with nvAMD.

Methods: We genotyped subjects with nvAMD for the rs4810482 single nucleotide polymorphism that received care at University of Iowa Healthcare. These patients were categorized into the following groups: homozygous TT, CC, and heterozygotes (TC). Retrospective chart review was performed on these patients. We collected and analyzed corrected distance visual acuity (CDVA in logMAR) and injection interval at four time points: initial visit, 4th injection, 2-years, and final visit. To objectively quantify anatomical outcomes, we developed a novel deep learning algorithm of OCT images to automatically quantify intraretinal fluid (IRF), subretinal fluid (SRF), and pigment epithelial detachment (PED). Generalized estimating equations (GEE) were used to analyze dependent variables, adjusting for age, sex, BMI, and smoking history.

Results: 56 eyes (TT = 20, CC = 10, TC = 26) from 38 patients were included. The mean age at the initial visit was 75.6 ± 8.8 years. 60.5% of our subjects were female. Patients with the TC genotype showed a decrease in visual acuity from 20/40 to 20/50 while the TT genotype demonstrated an improvement from 20/50 to 20/40 (mean change in logMAR VA from baseline to final visit: 0.1 ± 0.28 vs. -0.1 ± 0.24, respectively; P = 0.03). Automated segmentation revealed higher volumes of IRF in the second year with each additional risk allele (CC: 0.01 ± 0.02 mm3, TC: 0.02 ± 0.05 mm3, TT: 0.03 ± 0.07 mm3, P = 0.003), although this was not observed at other time points. The total combined fluid burden was highest for the TC genotype group, which also had the greatest reduction in total fluid from initial visit to final (-0.68 ± 1.38 mm3), whereas the TT group had the least improvement in fluid volume (-0.16 ± 0.28 mm3, P = 0.03). SRF and PED volume changes did not differ by genotype.

Conclusions: This is the first study to demonstrate that MMP9 rs4810482 heterozygosity is associated with distinct structural and functional treatment responses in nvAMD. Our findings suggest *MMP9* genotype may be a biomarker of disease severity and could inform prognosis or therapeutic strategies.

Impact of General Anesthesia Exposure in Early Childhood on Neural Activation and Working Memory during Adolescence: The Role of Exposure Characteristics and Surgery Severity

Julie Mathews, BS; Amy L. Conrad, PhD; Timothy Koscik, PhD; Robert Block, PhD

Background: General anesthesia (GA) can cause neurotoxic effects in the central nervous system that may impair the developing brain. This is likely due to its ability to induce neuronal apoptosis via either NMDA receptor-blocking or $GABA_A$ receptor-enhancing properties. As 1.5 to 2 million children under the age of 3 undergo anesthesia annually in the United States, it is important that we understand potential long-term effects, with a major concern being learning and memory.

Purpose: We aimed to determine how a) number of GA exposures before age 4, b) age of first GA exposure, and c) total duration of GA exposure before age 4 affect children's working memory (WM) and neural activation (via fMRI) across various brain regions, including the pre-frontal cortex (PFC) and cerebellum. Further analysis evaluated if d) invasiveness/severity of surgery moderated the relationship of exposure to memory outcomes.

Methods: In this cross-sectional study, adolescents (12-15 years old) exposed to GA before age 4 were identified from patient lists at the University of Iowa, and those born full-term without major CNS diagnoses or relevant medications were included. At a single visit, participants completed a cognitive battery, including the Children and Adolescent Memory Profile (ChAMP), and underwent structural and functional MRI using the previously published Sternberg WM task in a 3T MRI scanner. Retrospective chart review provided GA exposure and surgery severity information (classified using CPT codes and the Surgery Flags Software-Services and Procedures v2024). Participants were grouped by their highest surgery severity before age 4, with the most severe categorized as "narrow", the mid-tier as "broad," and the least severe as "neither broad nor narrow" ("neither"). Multivariate linear regressions assessed main and interaction effects of the three exposure variables and surgery severity on Blood Oxygen Level-Dependent activation in the regions of interest (ROIs) and across the brain during the task. Multiple comparisons were controlled for with a cluster-based threshold ($\geq$8 voxels, 216 mm^3, $p<0.05$). Univariate and multivariate analysis of covariates assessed effects of the exposure variables and severity on ChAMP scores.

Results: The final sample included 360 adolescents (mean age 13.7 ± 1.1 years; 57% male). Surgery severity was categorized as "neither" (n=51), "broad" (n=58), or "narrow" (n=251, most severe). Age of first GA exposure was significantly lower in the narrow group. Mean ChAMP Total score (93.0 ± 12.0) was in the average range, with no significant severity-group differences (p=0.787). 342 of the participants completed at least part of the fMRI Sternberg WM task, with a ceiling effect for accuracy across all groups. Significant activation was observed across many brain regions, with $p<0.001$ for all the following. Of the hypothesized ROIs for the Sternberg task, the PFC showed increased activation within the L. superior frontal gyrus with longer GA duration (β=0.005), and decreased activation in both the R. superior frontal gyrus (β=-1.859) and L. rostral middle frontal gyrus (β= -1.359) with increasing age of first exposure. All of these effects were attenuated by increasing surgery severity. The R. cerebellar cortex showed increased activation with longer GA duration, also weakened by increasing severity (β=0.011). Beyond ROIs, several cortical regions showed multiple exposure-related effects. Among these were the R. precuneus, which showed increased activation with age (β=0.791) and decreased activation with more exposures (β=-.666), both weakened by increasing severity. The R. inferior parietal lobe showed increased activation with both age (β=0.819) and number of exposures (β=1.295), with the positive effect of age strengthened by increasing severity. The R. precentral gyrus and R. posterior cingulate showed increased activation with age (β=1.37, 1.13), weakened by increasing severity, and with longer duration (β=0.012, 0.015).

Conclusion: Early-life anesthesia exposure was linked to region-specific differences in brain activation during an fMRI WM task but not to out of scanner WM performance. All three measures of anesthesia exposure had some relationship to activation patterns, with most activations found bilaterally or in the right hemisphere. Most exposure–activation relationships were attenuated by greater surgery severity (i.e., aspects of exposure had more of an impact for *less* severe surgeries). Some regions reflected diminished activation related to greater anesthesia exposure (e.g., R. precuneus) and other regions demonstrated increased (potentially compensatory) activation (e.g., R. cerebellum and L. superior frontal gyrus (of the PFC)). Given uniformly high WM performance across groups (outside of scanner), these activation differences may have limited clinical significance. A post hoc analysis examining the effect of any GA exposures after the age of 4 on these same outcomes is in progress. Future work should explore other measures of executive functioning, such as attention or concentration, in adolescents with early childhood anesthesia exposure.

Paraneoplasia risk and prevalence quantification of paraneoplastic dermatoses by TriNetX data network analysis.

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Introduction with background/rationale: Paraneoplastic dermatoses (PNDs) are a heterogeneous group of rare skin conditions characterized by their potential association with an internal neoplasm (IN), a concept first proposed by the Austrian physician, Von Hebra, in 1868. PNDs exhibit a remarkable spectrum of clinical presentations, incidences, types of associated neoplasms, and timing of the PND relative to the associated neoplasm. Moreover, the risk of any PND to be actually associated with an IN, varies significantly. Current estimates of risk of internal neoplasia for PNDs largely extrapolates from limited case series and reviews providing indirect data. In order to obtain more accurate and precise quantification of internal neoplastic association for PNDs, systematic analysis of large populations is required. TriNetX, a global data network including over a thousand unique health-providing locations, offers access to de-identified electronic medical records from millions of patients, and therefore a unique platform to address PND-IN quantification. Calculation of this specific risk of IN for any given PND is critical in informing prognosis and guiding optimal evaluation for internal neoplasia when facing a PND.

Hypothesis/Purpose: This study primarily aims to determine the prevalence of internal neoplasms in populations diagnosed with the top eight most common PNDs. A secondary aim of the study is to elaborate the relative timing of diagnosis between the PND and IN. Furthermore, this study seeks to uncover particular clinical features for patients with PND which would suggest a higher risk of IM.

Methods: Following institutional IRB-approval, a retrospective cohort study was performed using the de-identified electronic database, TriNetX. Each cohort consists of individuals diagnosed with a unique PND, resulting in eight total groups. The prevalence of IM within these individuals was then obtained from the database and categorized based on the extent of neoplasm prevalence as either obligate (>50%) or facultative (<50%). PND-neoplasm relationships were also studied temporally, measuring the rates of neoplasm diagnoses within 1 and 3-year windows, respectively, following an initial PND diagnosis. Additionally, the relative order of PND vs IM diagnoses was recorded and quantified.

Findings/Results: Prevalence data for the eight PNDs examined, individually and collectively were found to differ from historical literature estimates. Specifically, TriNetX data demonstrated an overall neoplasm prevalence higher than what has been previously reported. Sweet syndrome, for instance, historically with an IN prevalence of 20%, demonstrated a 61% IN (47% benign) prevalence measured through TriNetX. Although overall IN rates were generally found higher with the TriNetX data, many specific neoplasms showed lower prevalence lower than previous estimates. For example, in prior studies, patients with paraneoplastic pemphigus have an estimated NHL prevalence of 38.6%; however, in TrinetX, only 23.7% of these patients were found to have a type of NHL. The analysis of relative timing between PNDs and their associated IN is currently in process.

Overall significance: Using a new data source with cohort sizes much larger than prior PND-neoplasm prevalence analyses, this study reveals that historical data may have underestimated the presence of benign neoplasms in populations with PNDs, leading to higher overall neoplasm percentages in TriNetX. Additionally, the findings of this study suggest that previous data on specific neoplasms have possibly been overestimated, particularly in the case of NHL for paraneoplastic pemphigus. These new insights can help guide optimal screening for internal neoplasia for these PNDs.

Organizational Structures, Systems, and Processes for the Dermatologic Care of Skin Cancer Patients: A Literature Review

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Background:
Physicians, dermatologists, and Mohs surgeons work to meet the needs of skin cancer patients every day. Much time and energy are rightly spent acquiring the individual knowledge and skills necessary to provide the best possible patient care. However, even the most brilliant physician is ineffective without the necessary organizational processes and structures in place. From specialized skin cancer transplant clinics and tumor boards to telehealth outreach and digital educational material, organizational systems have an immense impact on patient care.

While several studies have described the utility of specific organizational structures and systems related to skin cancer patients (e.g. multidisciplinary tumor boards), little work has been done to summarize the array of interventions. The purpose of this study will be to do just that – summarize the organizational structures and systems currently utilized in caring for skin cancer patients in various practice settings. To the authors' knowledge, there are no published reviews on skin cancer management processes.

Purpose:
This review is an exploratory project that aims to determine the state of research related to skin cancer management organizational processes and structures and identify gaps in the literature. An evaluation of the currently utilized structures and processes will provide a valuable reference for providers and institutions looking for ways to improve the care of skin cancer patients.

Methods:
This project is following the methodological framework of narrative literature and will include identifying the research question, identifying relevant studies, study selection, charting the data, collating, summarizing, and reporting results, and consultation. The Hardin Library team has been involved with development of the project protocol and search strategy. Thus far in the project, identification of research questions, determination of search terms, and an initial search of relevant databases have been completed. A challenge that is currently being addressed is determination of the inclusion and exclusion criteria and solidifying the scope. Subsequent steps of the project are yet to be completed.

Findings:
Initial database search performed on 8/18/25 returned 3,547 articles. These articles are currently being analyzed by the research team, and search terms will be further refined and narrowed. After terms are refined, another search will be completed and articles will be evaluated for inclusion/exclusion criteria.

Summary and significance of the research:
Caring for patients with skin cancer is a complex task. From the time a suspicious skin lesion is identified through diagnosis, treatment, and long-term surveillance, significant specialty expertise and skill are required. Throughout a patient's care journey, numerous organizational processes, systems, and structures are needed to provide care. The purpose of this study is to summarize these processes, systems, and structures, which will serve as a helpful resource for individuals and institutions hoping to implement or alter organizational structures and systems to better serve patients. Additionally, this study will help uncover gaps in care and will aid in generating new ideas and potential interventions.

Targeting GPx4 to Induce Ferroptosis in Patient-Derived Tumoroids

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Introduction: Patients with colon cancer are traditionally treated with chemotherapy regimens that include FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) and FOLFIRI (5-fluorouracil, leucovorin, irinotecan). However, some tumors are resistant to these treatment regimens. In many of these therapy-resistant tumors, a glutathione peroxidase 4 (GPx4)-dependent state exists. GPx4 is a selenoprotein that is protective against oxidative stress in cell membranes, preventing an iron-dependent form of cell death called ferroptosis.

Hypothesis: Ferroptosis-inducing agents that can overcome the GPx4-dependent state present a promising therapeutic target for therapy resistant colon cancers, which can be demonstrated using primary, patient-derived tumoroids.

Methods: Tumoroid lines were cultured from patient tumor samples in order to provide a 3D model that closely reflects the pathophysiology of the cancer. A fluorescence-based organoid viability assay was utilized to determine effectiveness of a traditional chemotherapy treatment 5-fluorouracil (5-FU) on these patient-derived organoids. Using the same assay, effectiveness of ferroptosis inhibitor RSL3 was tested on the same organoid lines. Finally, a combination of the two drugs was assessed.

Results: Sensitivity to 5-FU varied in the tumoroids. Response to the drug has no correlation with treatment naivety. All five of the tumoroid lines decreased in viability by treating with RSL3. The combination of 5-FU and RSL3 did not reveal any synergy.

Conclusions: Ferroptosis inhibitors, specifically RSL3, appear to successfully decrease viability in patient-derived colon tumoroid lines that are both sensitive and resistant to traditional treatment 5-FU. Because of the low bioavailability of RSL3, we will search for other compounds that can act on glutathione peroxidases in a similar mechanism. As a next step, we will try to optimize the 5-FU and RSL3 combination experiment, as well as overlay RSL3 with tumoroids with a loss of glutathione peroxidases. Additionally, we will continue using the tumoroids to experimentally determine which other compounds may modify 5-FU sensitivity.

Ventriculoperitoneal shunt catheter tip migration in pediatric skull growth.

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Background: Deep Brain Stimulation (DBS) is a neurosurgical procedure that involves implanting electrodes into specific brain sites depending on the pathology of intertest. In epilepsy, FDA-approval for DBS only covers adult patients, which leaves many pediatric patients that may receive a seizure control benefit from DBS outside the bounds of FDA-approval. Part of the concern for implanting pediatric patients with DBS leads at young ages arises from the potential for significant skull growth, and the effect this may have on lead position and thus DBS effectiveness. Ventriculoperitoneal (VP) shunt placement is a widely used procedure to treat hydrocephalus in pediatric patients. Common clinical practice is to have regular clinic follow up with repeat imaging every 1-2 years making this a desirable population to study.

Objective: We aim to determine if the position of the tips of the proximal (intraventricular) shunt catheters will migrate relative to the midpoint of the anterior commissure - posterior commissure (AC-PC) line over time due to the normal cranial development of children. Measuring shunt catheter tip migration in the brain as patients age will allow us to predict how the position of a DBS lead may be expected to change as patients age and the skull grows.

Methods: Retrospectively, charts of pediatric patients (0-18 years) who underwent VP shunt placement at UIHC were reviewed. Patients with supratentorial tumors or craniofacial conditions were excluded. 200 patients were initially screened, those that had several shunt revisions or lack of follow-up scans were excluded. Ultimately, a total of 85 patients was further analyzed. Serial CT and/or MRI scans from each patient were reviewed. In each post shunt-implantation scan, we calculated the distance from the tip of the ventricular shunt catheter to the midpoint of the anterior AC-PC line and analyzed the differences in this distance over time.

Results: Our included study population was 55.3% male and 44.7% female ($p=0.1674$). The median age at first procedure was 0.53 years (range 0.01-12.09 years) and the median number of shunt procedures was 1 (range 1-2). The median age at last follow up was 10.43 years (range 1.81-23.95) and median total length of follow up was 8.75 years (range 0.44-14.30 years). A parietal approach (61.2%) compared to frontal approach (38.8%) ($p=0.0036$) was more common and VP shunts were more commonly placed for obstructive hydrocephalus (75.0%) compared to communicating (24.7%) ($p<0.0001$) with the most common pathologies being posterior fossa tumor and neonatal intraventricular hemorrhage. Infants (0-1 years) had the highest average rate of migration per year of 3.27 mm/year, followed by those in early childhood (3-5 years), 2.01 mm per year. Those in late childhood (9-12 years) and adolescents (12-18 years) had the lowest average rate of migration per year of 0.88 mm/year and 0.60 mm/year respectively. Infants had significantly higher rates of migration compared to both of those later age groups ($p<0.001$)

Conclusion: Ventricular catheter tip migration was highest in infants and stabilized to a low yearly rate in late childhood and adolescents, suggesting that DBS leads may be relatively stable in these lateral pediatric age groups and DBS for epilepsy treatment and seizure control may be considered. However, this study has significant inherent limitations, and further investigation will be necessary.

Patterns and predictive factors of local recurrence in benign bone tumors

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Background: Benign bone tumors represent a heterogeneous group of nonmalignant lesions that are often treated surgically when symptomatic or at risk of pathological fracture. Although local recurrence is a known risk, comparative data on how recurrence timing and presentation vary across histologic subtypes remain limited. This knowledge gap contributes to the absence of standardized surveillance protocols for most benign bone tumors.

Purpose: To examine locally recurrent benign bone tumors after surgical treatment, with the goal of defining recurrence patterns by histology. Our findings aim to provide evidence-based recommendations to optimize the frequency and duration of postoperative surveillance tailored to tumor subtype.

Methods: We performed a single-center retrospective cohort study of 329 curative-intent procedures for benign bone tumors treated at the University of Iowa Hospitals and Clinics between 2010 and 2024. Eligible histologies included giant cell tumor (GCT), aneurysmal bone cyst (ABC), unicameral bone cyst (UBC), osteoid osteoma (OO), chondroblastoma (CB), osteoblastoma (OB), non-ossifying fibroma, and chondromyxoid fibroma. Local recurrence was defined by histologic confirmation or radiographic features consistent with recurrence. Our primary outcome was the mode of recurrence presentation (symptomatic or radiographic). Secondary outcomes included time to recurrence and recurrence by bone filler type. Analyses included Wilcoxon rank-sum, Fisher's exact, and Spearman correlation tests, with $p < 0.05$ considered significant.

Results: Forty-two episodes of recurrence (12.8%) were identified. Recurrence presentation differed significantly by histology ($p = 0.001$). Individually, OO and OB recurred exclusively symptomatically (100%) while CB recurred more symptomatically (66.7%). ABC (80.0%), UBC (78.9%), and GCT (62.5%) more frequently recurred asymptomatically and were detected radiographically. No recurrences occurred of non-ossifying fibroma and chondromyxoid fibroma. No associations were observed between recurrence timing and age, sex, tumor site, or surgical method. In GCT treated with curettage, recurrence was significantly more common with allograft than cement (33.3% vs. 3.4%, $p = 0.007$). Recurrence timing was earliest for OB and OO with 100% and 83.3% having recurred by year one respectively. By year three, all cases of OO had recurred with >75% of GCT, ABC, and UBC having done so and 66.6% of CB. By year five, 100% of all tumor histologies had recurred except for CHB with 66.6% of cases still having recurred.

Conclusion: Recurrence behavior in benign bone tumors is strongly influenced by histologic subtype. Symptomatic recurrence predominates in OO and OB with nearly all recurrences in the first year after treatment. Limited clinical follow up is reasonable for these tumor types following operative removal as surveillance imaging is of limited utility to recognize a recurrence. In contrast, UBC, GCT, and ABC more often recure asymptomatically and most tumor recurrences will have occurred within the first three years with all those tumors in this study having done so by five years. It is our recommendation to follow these tumors with structured imaging surveillance for 3-5 years. Use of cement in GCT appears protective compared with allograft. CB was represented by a small sample size and recurred symptomatically more than radiographically with a wide range of time to recurrence. We recommend physicians follow these tumors conservatively with structured imaging surveillance for 3-5 years until more data is obtained regarding CB recurrence behavior.

Outcomes for Adult Mechanically Ventilated Patients Receiving an Analgesia – First Sedation Protocol

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Abstract

Introduction:
Mechanical ventilation includes the use of analgesics and sedation medications to manage pain, agitation, and maintain ventilator compliance. The process is not without potential concerns. Over-sedation can increase the incidence of Intensive Care Unit (ICU) delirium, mortality, post-traumatic stress disorder, and prolonged ventilation, which can be associated with pneumonias. Long-term or high-dose opioid use in the ICU can increase risks of developing opioid dependence, tolerance, addiction, and other physiological effects.
Objectives:
To investigate whether the adoption of a structured analgesia-first sedation protocol can decrease morphine milligram equivalents (MMEs) of analgesics administered during an ICU stay. Secondarily, examine the impact of the protocol on ICU stay duration, mortality, episodes of delirium, ventilator duration, and adverse events.
Methods:
A pre-/post-design was used to study the adoption of an analgesia-first sedation protocol as standard care. The change was implemented on February 1st, 2025 in the Critical Care Units (CCU) in two Des Moines hospitals within the same health system. Patients admitted on/or after this date served as the experimental group. Patients admitted prior to this date during a similar time-period within the previous year, who did not receive any particular sedation protocol, served as the pre-implementation control group. Differences in hourly MMEs between the groups was determined using a quantile regression model with standardized inverse propensity score weights based on baseline covariates. The study received Institutional Review Board approval including a waiver of consent.
Results:
Study data revealed the upper quantile values of the MME distribution in patients in the post-implementation group were significantly lower than the values for patients in the pre-implementation group. In particular, patients in the 90^{th} percentile received 8.89 (95% CI: -22.3509, -0.6789) fewer MMEs per hour during their CCU stay than the control group. Secondary outcomes were mixed, with delirium incidence increasing at 24-hours post-extubation in the experimental group, and a failure to see a difference at 48-hours post-extubation. The duration of CCU stays and mortality increased appeared higher in the post-implementation group. There was no discernible increase in adverse events across groups.
Conclusions:
Study findings demonstrated the primary benefit of the analgesia-first protocol in a documented reduction in the number of mechanically ventilated patients receiving inappropriately high doses of opioids. Study limitations include a lack of patient randomization, which could result in residual confounding if patient severity characteristics were not fully balanced. The study was designed to study the primary outcome, so secondary measures may be limited and require additional research.

Surveying Quality of Life After Liver Resection at a Single Center from 2020-2023

Abdullahi Mohamed, Linda Peng, Ethan Angle, Hassan Aziz

Background:

While liver resection has become safer with advances in surgical technique, long-term quality of life (QoL) following these procedures remains poorly characterized. Identifying clinical and socioeconomic factors that impact postoperative well-being is critical. This study aims to investigate self-reported QoL after liver resection and identify factors associated with poorer health in this population. We hypothesized that patients who experienced surgical complications, were unpartnered, or lived farther from the hospital would report having lower QoL.

Methods:

We surveyed patients who had previously undergone liver resection at a single academic institution between 2020 and 2023. A 32-item survey incorporating the Patient-Reported Outcomes Measurement Information System (PROMIS-10) was administered to assess patients' current QoL. Patients were contacted via email and phone call. Demographic information, comorbidities, preoperative treatment, intraoperative factors, and postoperative outcomes were extracted from the electronic medical record. Relationship status was divided into two groups: partnered (married or life partner), and not partnered (single, separated, widowed, or divorced). Equal variance t-tests were used to analyze differences between patient groups.

Results:

Among all 38 survey respondents, mean Global Physical Health (GPH) and Global Mental Health (GMH) scores were comparable to the general population. 54% of respondents were able to complete daily physical tasks without limitation, and 58% stated they were rarely or never bothered by emotional issues. Postoperative complications did not have a significant effect on reported QoL. Patients who were partnered scored slightly higher in GMH (51.71±3.7) compared to patients who were not partnered (45.43±3.6), but both groups were within one standard deviation of the general population (50.0). Patient home-to-hospital distance and patient gender had no significant effect on reported QoL.

Conclusion:

Patients who have undergone liver resection report having QoL that is comparable to the general population when surveyed 2-5 years after their index operation, despite the physiologic and psychological stress of major hepatic surgery. Patients who have postoperative complications also appear to maintain similar QoL as patients who have an uncomplicated hospital course. Ongoing data collection will allow for more robust modeling of factors that impact recovery and well-being after liver resection.

Title: The Role of Chronic Anemia and Hemorrhage in Perinatal Transfusions in Rural Iowa

Presenter: Alex Murra, MPH

Mentor: Dr. Stephanie Radke MD, MPH

Collaborators: Dr. Grace Chabal MD, Dr. Debra Kane PhD

Introduction: Rural residents in Iowa have a 55% greater risk of severe maternal morbidity (SMM) compared to their urban counterparts. The elevated rate of SMM is theorized to be influenced by social and structural determinants of health, limited access to specialty care, and possibly variations in healthcare quality, with recent reports of higher SMM experienced in low-volume obstetrical hospitals. Receipt of a blood transfusion is the largest contributor to the SMM aggregate measure and anemia during pregnancy is known to increase the likelihood of needing a transfusion. In Iowa, there have been informal reports of elevated rates of maternal anemia among subpopulations in several rural and micropolitan communities. In this study, we examined the rates of maternal anemia and blood transfusion among the Iowa birthing population by patient characteristics and by obstetric facility volume.

Purpose: To understand if there is an increased rate of transfusion among non-metropolitan residents giving birth in Iowa and, if so, if that relates to higher rates of anemia complicating pregnancies or the birth volume of the facility where they delivered.

Methods: Hospital billing dataset was obtained from Iowa Department of Health and Human Services on Iowa occurrent births from 2022-2024. Descriptive statistics were performed to obtain the proportions of individuals who had anemia (acute or chronic), obstetric hemorrhage, and/or received a blood transfusion by maternal age, race/ethnicity, primary payment source, and residence. Frequencies of anemia types, hemorrhage, and blood transfusion were determined by obstetric facility volume. Associations between patient demographics, transfusion rates, anemia types, and hemorrhage rates were estimated using chi-square tests of independence.

Results: Of the 95,655 deliveries that occurred between 2022-2024, 21% occurred to rural residents. Chronic or pregnancy-related anemia was more prevalent among persons under the age of 19 at delivery (21%) or 20-24 years old (17%), non-Hispanic Black residents (26%), those with public/self-pay insurance (17%), and residents in rural or micropolitan areas (13%). Postpartum hemorrhage rates were elevated for persons aged 25-29 (31%), NH White race/ethnicity (70%), those on public insurance (97%), and those living in metropolitan areas (63%). Micropolitan residents had elevated transfusion rates compared to metropolitan and rural residents at 3% compared to 2.3% and 2.4% respectively. Transfusion rates did not significantly differ by obstetric facility volume (<250 births=2.5%, 250-500 births=2.5%, 501-1000 births=2.8%,>1000 births=2.4%, standard error 0.19%). Chi-square tests showed statistically significant associations between anemia type and patient residence ($\chi^2 = 320.5$, $p < 0.0001$), maternal age ($\chi^2 = 575.6$, $p < 0.0001$), race/ethnicity ($\chi^2 = 1633.1$, $p < 0.0001$), and payment source ($\chi^2 = 965.5$, $p < 0.0001$). Stratified analyses of anemia type and residence by transfusion status resulted in significant associations of anemia type among both patients who received a transfusion ($\chi^2 = 83.47$, $p <0.0001$) and those who did not ($\chi^2 = 281.38$, $p <0.0001$).

Conclusion: In Iowa, non-metropolitan residents (micropolitan and rural) have higher rates of anemia complicating their pregnancies, however only micropolitan residents also have increased receipt of blood transfusion associated with childbirth. While elevated rates of chronic anemia may contribute to increased blood transfusion, and therefore SMM, it does not fully explain the difference. However, there is little variation in the transfusion rate by facility volume, suggesting that variations in care practices are also not primarily driving this disparity. These results suggests that patient-level factors, rather than facility-level differences in clinical care, may drive the elevated rate of SMM events seen among rural patients in Iowa.

Effect of catheter ablation with vein of Marshall ethanol infusion vs catheter ablation alone on persistent atrial fibrillation.

Student: Sarah Nacos
Mentor: Paari Dominic, MD

Background: Atrial fibrillation (AF) is when there is rapid and irregular beating of the atria due to abnormal electrical impulses (Brundel), and it poses a major health risk as it has been shown to be a strong risk factor for other health complications such as stroke, heart failure, and myocardial infarctions. Ablations of the myocardium are employed for patients that continue to have AF despite other medical interventions and is usually done around the ostia of the pulmonary veins. However, a significant proportion of patients that undergo an ablation will still have recurrent AF, thus other forms of treatment such as ethanol infusions into the Vein of Marshall (VOM) are being pursued. The VOM is an embryological remnant located on the posterior left atrium, and several studies have provided evidence that is the trigger of ectopic beats leading to AF.

Hypothesis: We hypothesize that there will be a decrease in atrial fibrillation reoccurrence when de novo catheter ablation is accompanied by infusion of ethanol into the vein of Marshall.

Methods: 102 patients between the ages of 18 and 85 from February 2023 until August 2025 at the University of Iowa were included in the study. Qualitative information was collected at several time intervals from patient records in EPIC and documented in a REDCAP database. First, Patient's demographic information, comorbidities, and other medical information prior to their respective procedure were collected and compared. Next, ablation procedure information and VOM attempts and success rates were collected. Patients that had a failed VOM infusion were used as the controls for the study. Other data such as discharge disposition was also collected. Lastly, three-month, six-month, and twelve-month post-procedure follow up information was collected for each patient to document AF recurrence and post-procedural complications, if any.

Pentacam-Derived Higher-Order Aberrations for Early Pediatric Keratoconus Screening: Toward Low-Cost, Point-of-Care Detection

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Introduction: Keratoconus is a progressive thinning disorder of the cornea that leads to irregular astigmatism, glare, blurred vision, and impaired night vision. In advanced cases, patients may require rigid contact lenses or corneal transplantation to restore functional sight. Because vision loss is closely tied to disease progression, early detection and timely intervention are essential. Corneal collagen cross-linking (CXL) is the current gold standard for halting progression, but its effectiveness depends on diagnosis before significant steepening or scarring has occurred. Existing tomographic tools such as the Pentacam are accurate but costly and resource-intensive, limiting widespread use in primary care and low-resource settings. Our study evaluates whether higher-order aberrations (HOAs), captured during Pentacam imaging, can serve as an alternative low-cost diagnostic marker for early keratoconus.

Hypothesis: We hypothesize that elevated HOAs on Pentacam imaging will correlate with pediatric keratoconus, supporting their use in inexpensive handheld devices for early screening.

Method: This was a retrospective cross-sectional study of 28 patients with keratoconus and 65 controls (ages 4–18) who underwent Pentacam imaging at the University of Iowa between 2015–2025. Patients with prior ocular trauma, corneal surgery, infection, or scarring were excluded. For each eye, we evaluated HOA RMS, vertical coma, spherical aberration, cylinder, spherical equivalent, Kmax, Km, central corneal thickness (CCT), thinnest corneal point, and demographic and clinical variables. Group comparisons and ROC/regression analyses were performed to assess diagnostic accuracy and the incremental value of HOAs.

Results: Pediatric keratoconus eyes demonstrated significantly higher total corneal HOA RMS than age-matched controls, independent of refraction and corneal thickness. The increase was driven primarily by vertical coma, which achieved an AUC >0.90 on ROC analysis; a coma-RMS threshold of ~0.20–0.25 μm distinguished keratoconus from normal eyes with ~90% sensitivity and specificity.

Conclusion: This study demonstrates that pediatric keratoconus eyes exhibit a significantly elevated HOA burden, particularly vertical coma, independent of myopia and stromal thinning. To our knowledge, this is the first study to demonstrate this relationship in a purely pediatric cohort, extending adult findings to children. Moreover, pediatric keratoconus often progresses more aggressively than adult disease, making early identification before overt clinical symptoms beneficial for preserving vision. HOA analysis provides a sensitive and specific marker that can be obtained from less expensive and potentially handheld devices, supporting its use in vision screenings for school-age children and expanding access to diagnostic tools in resource-limited settings.

Investigating the Role of Dynorphinergic LJA5 Neurons in Post-Surgical Pain Modulation

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Post-surgical pain remains a significant clinical challenge affecting millions of patients annually. The transition of pain from post-surgery to recovery is poorly understood, and current treatments often have limited efficacy and significant side effects, including opioid dependency and tolerance. Descending pain modulation pathways are emerging as critical regulators of pain states, yet much remains unknown about their precise roles in post-surgical pain and the complex organization of neural circuits controlling nociception. The recent discovery of prodynorphin-expressing neurons in the rostral ventrolateral pons (LJA5 neurons) provides a novel avenue for exploring pain modulation. LJA5 neurons project to spinal and brainstem pain-processing regions, suggesting an important role in post-surgical pain regulation. We hypothesized that chemogenetic activation of LJA5 neurons would reduce post-surgical pain behaviors in a mouse model of plantar incision.

Pdyn-Cre-GFP mice received bilateral stereotaxic delivery of excitatory (hM3Dq-mCherry), inhibitory (hM4Di-mCherry), or control (mCherry) DREADDs targeted to LJA5 neurons. Mice then underwent plantar hindpaw incision to establish a model of post-surgical pain. Behavioral assessments were performed before and after surgery, including: mechanical sensitivity (von Frey), dynamic mechanical sensitivity, spontaneous guarding, thermal sensitivity (Hargreaves), and cold allodynia. On testing days, LJA5 neurons were selectively modulated by intraperitoneal (i.p.) injection of clozapine-N-oxide (CNO) or saline. Behavioral assessments were performed at baseline and at 1-, 3-, and 5-hours post-injection across post-operative days 1, 3, 6, 12, and 24.

Chemogenetic activation of LJA5 neurons suppressed post-surgical mechanical hypersensitivity, whereas chemogenetic inhibition enhanced post-surgical mechanical hypersensitivity. No changes were observed in dynamic mechanical sensitivity, spontaneous guarding behavior, thermal sensitivity, or cold allodynia. Control (mCherry-only) injections produced no behavioral differences. At the study endpoint, mice were euthanized, and brainstem tissue was collected. Immunohistochemistry and imaging for GFP and mCherry fluorescence colocalization is underway to confirm accurate targeting of LJA5 neurons.

LJA5 neurons were shown to selectively regulate the mechanical component of post-surgical pain without broadly altering other pain modalities. These findings identify LJA5 neurons as a novel descending pain modulatory pathway and suggest they may represent a promising target for improving post-operative pain management and reducing the burden of chronic pain.

Association of dieting with MRI outcomes in patients with multiple sclerosis

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Background: Up to half of patients with multiple sclerosis (MS) report using dietary modification to manage symptoms and improve wellness. Preliminary trials suggest that healthy diets improve symptoms, but there is a lack of real-world observational evidence supporting these findings.

Purpose: To evaluate the impact of self-reported diets on MRI outcomes (new enhancing lesions, new non-enhancing lesions, total number, lesion burden, and brain volume) in newly diagnosed patients with MS.

Methods: A retrospective chart review was performed of all newly diagnosed patients with MS at the UIHC Department of Neurology between 1/1/2008 to 8/3/2020. Demographics, clinical notes, radiology, and medication data were extracted from electronic medical records. Extracted MRI data included brain, cervical spine, and thoracic spinal cord scans. Time-dependent cox proportional hazards models were used to compare the time-to-event between MS dieters and non-dieters for MS outcomes including MRI. All models were adjusted for age, sex, race, ethnicity, body mass index, and time-varying MS disease modifying therapy status.

Results: 138 EMRs were eligible and abstracted (90 non-dieters and 48 dieters) with a mean follow-up of 3.42 ± 1.46 years. Participants who adopted a diet did so on average 1.02 ± 1.26 years after baseline. Self-reported dieting was not significantly associated with any MRI outcomes. Patients who reported following a diet had an HR (95% CI) of developing new brain lesions of 0.76 (0.37, 1.56) and 1.24 (0.40, 3.85) for new spinal lesion compared with non-dieters. Furthermore, no differences were observed for relapse requiring hospitalization 1.18 (0.68, 2.07), DMT change 0.97 (0.74, 1.26), or walking aid escalation 0.59 (0.33, 1.04).

Discussion: This study suggests that adopting a diet as a complementary therapy for MS does not lead to worse disease progression among people with newly diagnosed MS; however, given the small sample size, the observed trends warrant further investigation with a larger sample size.

Stepan Orlovskiy

Mentor: Dr. James Byrne

Title: Impact of hyperbaric oxygen therapy on malignant peripheral nerve sheath tumors

Tumor hypoxia is a hallmark of many solid tumors, which causes pathological changes in cancer cell metabolism that promote cancer growth, development of resistance to therapy, and invasion of surrounding tissues. One way to modulate tumor hypoxia is via hyperbaric oxygen therapy (HBOT), where patients receive 100% oxygen under higher-than-normal atmospheric pressures (2-3 atmospheres) to increase levels of dissolved oxygen in blood and tissues. Previous studies have demonstrated the clinical benefit of HBOT, especially as an adjunctive treatment for hypoxic tumor types. Our study aims to delineate the effects of HBOT on cancer cell metabolism. We exposed malignant peripheral nerve sheath tumors, a hypoxic tumor type, to HBOT and evaluated the impact using Seahorse analysis, tumor growth assessment, histology, and protein detection/quantification through Western blotting. We found that HBOT resulted in significant changes in tumor metabolism and delayed tumor growth. Overall, HBOT represents a promising strategy that can be used as an adjunctive treatment.

Maternal Exposure to Environmental Contaminant Perfluorooctanesulfonic Acid Disrupts Metabolic Pathways Critical for Placental Function and Fetal Growth

Sydney Pearl, BS; Donna Santillan, PhD; Brandon Schickling, PhD.

Exposure to per and poly-fluoroalkyl substances (PFAS), such as perfluorooctanesulfonic acid (PFOS), is associated with adverse maternal and fetal health outcomes including preeclampsia and low birth weight; However, the mechanisms by which PFAS may induce these conditions are not fully understood. During pregnancy, metabolic shifts are necessary to provide sufficient nutrients to sustain mother and child, indicating metabolic dysfunction may serve as a key mechanism in PFAS-related poor pregnancy outcomes. This study mimics the common route of human exposure to PFAS via contaminated drinking water, investigating the effects of maternal oral PFOS exposure on gene expression levels in a murine model. Results indicate dams exposed to PFOS had offspring with significantly reduced birthweights compared to controls ($p<0.05$), establishing a phenotypic difference in the experimental condition. Findings support metabolic stress, and corresponding deficiencies in oxygen/nutrient delivery to the fetus, as the underlying cause of low birthweight in the PFOS condition. Results suggest global metabolic dysfunction, with both placental and liver tissues from the PFOS condition exhibiting paradoxical upregulation of genes important to mitochondrial beta oxidation, lipogenesis, and glycolysis. Metabolic dysregulation is a well-established cause of excess reactive oxygen species (ROS) formation. Consistent with ROS overproduction, the metabolic dysregulation observed in the PFOS group was accompanied by increases in expression of placental genes that respond to oxidative stress including heme oxygenase-1 (5.3-fold increase), nuclear factor erythroid 2-related factor 2 (6.5-fold increase), catalase (6.2-fold increase), superoxide dismutase 2 (4.3-fold increase), and glutathione peroxidase 1 (4.0-fold increase). Despite these adaptive responses, the estimated relative mitochondrial DNA copy number in PFOS-treated hepatic tissue was reduced to 0.741 compared to controls, suggesting mitochondrial DNA loss or damage consistent with oxidative stress. Published studies also link metabolic dysfunction with placental insufficiency. The present study supports this connection, with an observed increase in expression of Hypoxia-inducible Factor 1-Alpha (HIF1α) in placental tissue from PFOS exposed mice compared to controls (6.952-fold increase vs 1.668, respectively). In vitro experiments with HTR-8 cells, a trophoblast cell line, additionally associate direct PFOS exposure with poor trophoblast migration which can hinder the trophoblast spiral artery invasion necessary for proper placental formation. Overall, this study adds to a growing body of research connecting PFAS to poor pregnancy outcomes, highlighting a preliminary connection between PFOS-induced oxidative stress and metabolic dysfunction, with important long-term implications for maternal and child cardiovascular health.

Iris Lesion Characteristics: Differentiating Pigmentation from Melanoma

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Introduction: Pigmented iris lesions are diagnostically challenging because intervention for suspected melanoma has major visual consequences. Shields et al. proposed the ABCDEF mnemonic (Age ≤ 40, Blood in anterior chamber, Clock hour inferior, Diffuse configuration, Ectropion uveae, and Feathery margins) as a clinical guide to melanoma risk, but external validation is limited.

Hypothesis: Iris melanomas would demonstrate increased prevalence of ABCDEF and related features compared to benign lesions.

Methods: An IRB-approved retrospective cohort study was conducted at the University of Iowa, a tertiary referral center. Patients with documented iris lesions were provided by the Ophthalmology Department. Exclusion criteria included non-pigmented lesions and age <18 years. Variables included ABCDEF features, intrinsic vessels, ≥3 clock hour involvement, angle seeding, and tumor dimensions. Wilcoxon rank-sum and Fisher's exact compared features by group. Logistic regression and ROC analysis assessed independent predictors and diagnostic accuracy.

Results: Among 262 iris lesions, 37 (14%) were biopsy-confirmed melanoma. Melanoma demonstrated greater largest diameter (median 3.15 vs 1.80 mm, $p<0.001$) and thickness (1.4 vs 1.00 mm, $p=0.005$). Among ABCDEF features, ectropion uveae was the most predictive (64.7% vs 31.8%, $p<0.001$). Additional strong predictors included intrinsic vessels (78% vs 13%), ≥3 clock hours (75% vs 19%), and angle seeding (86% vs 27%), (all $p<0.001$). In multivariable analysis, ectropion uveae (OR 4.3, $p=0.012$) and thickness (OR 2.9 per mm, $p<0.001$) remained independent predictors. ROC AUC improved from 0.73 (ABCDEF alone) to 0.85 when thickness was added.

Conclusion: Ectropion uveae is the most reliable ABCDEF feature for melanoma, while thickness substantially improves diagnostic accuracy. Although vascular and angle features are strong univariate indicators, incorporating thickness and ABCDEF criteria yields the most robust predicative framework for iris melanoma risk stratification.

Title: “Nitrous Oxide GEMs for Accelerated Wound Healing in Diabetic Mice”
Katerina Petroff
Mentor: James Byrne, MD, PhD - Department of Radiation Oncology
Collaborators: Emily Witt, MS; Milad Arzani, MS; Jianling Bi, MS; Lindsey Culver, BS

Introduction: Diabetic patients often present with delayed wound healing including increased pain and inflammation, and it is therefore critical to find ways to accelerate wound healing in diabetic patients. Topical therapies, including acellularized matrices and negative pressure wound therapy, have mixed benefit in patients and are costly. To overcome these limitations, we have developed topical low cost, gas-entrapping materials (GEMs) for delivery of gases that are known to play a role in the wound healing cascade or can positively impact wound healing. In particular, nitrous oxide (N_2O), which is often administered via inhalation for anesthetic effects, is known to modulate inflammation, promote angiogenesis, and support cell proliferation that can be beneficial in wound healing. However, the effects of topically delivered N_2O on wound healing and pain have yet to be studied.

Purpose: The purpose of this study was to develop a foam GEM containing N_2O and determine if this N_2O-GEM accelerated wound healing in diabetic mice. We hypothesize that the N_2O-GEM treatment group will show a greater reduction in wound diameter after 10 days of treatment compared to the control and N_2-GEM groups.

Methods: We developed nitrous oxide gas-entrapping materials (N2O-GEM) using hyaluronic acid foam formulations and characterized foam stability at 37°C. Male C57BL/6 mice were rendered diabetic via streptozotocin injection (50 mg/kg IP for 5 days) and received 6 mm excisional wounds. Mice were treated daily for 10 days with 0.3 mL foam injections: control (no treatment), N2-GEM (anoxic control), or N2O-GEM (treatment group). Wound diameter was measured using ImageJ software and analyzed with GraphPad Prism.d diameter was measured using ImageJ software and graphs were created using GraphPad Prism.

Results: For GEM characterization, we found that increasing the weight percent of HA in the prefoam solution enhanced foam stability over time. The 0.5 weight% HA foam collapsed completely after 1 hour, while the 1.0 weight% HA foam collapsed fully at 24 hours, and the 1.5 weight% HA foam did not completely collapse after 24 hours. In diabetic wound healing studies, the N_2O-GEM treatment group demonstrated a statistically significantly higher percent of wound area healed after 10 days compared to the N_2-GEM anoxic control group ($P = 0.0023$). A visual difference could also be seen between the control and N_2-GEM treatment groups ($P = 0.0587$). While the N_2O-GEM showed a higher percent of wound area healed compared to the control group, the N_2O-GEM - control test was not statistically significant ($P = 0.0705$) **.**

Conclusion: These findings indicate that the N_2O-GEM treatment significantly accelerated wound healing in diabetic mice relative to a wound in anoxic conditions. This finding is crucial to improving the speed and efficacy of diabetic wound healing - often, diabetic wounds become hypoxic or anoxic due to physiologically impaired blood supply. It is possible that N_2O could stimulate angiogenesis and provide a topical analgesic effect to wounds, though the mechanism for this action has yet to be determined. The development of an N_2O-GEM could provide relief and improve the prognosis of diabetic patients, though further study is needed to optimize and confirm the mechanism of this treatment.

Half Oxytocin Infusion Rate Does Not Improve Fetal Heart Rate Changes After Labor Analgesia

Spenser Pfannenstiel, BS, Cynthia A. Wong, MD, Unyime S. Ituk, MBBS, FCARCSI, MBA

Background: Oxytocin is used during labor to increase the frequency of contractions and augment uterine contractile strength, thereby supplementing a regular pattern of labor. However, the administration of exogenous oxytocin in the presence of an uncoordinated labor pattern confers a risk for increase in uterine contraction frequency and inadequate relaxation periods, termed tachysystole. Initiation of combined spinal-epidural (CSE) labor analgesia causes a decrease in circulating maternal epinephrine levels. This decrease in β_2-adrenergic activity in turn results in increased worsening tachysystole, leading to decreased placental perfusion and nonreassuring FHR. The optimal oxytocin management at the time of initiation of CSE labor analgesia in terms of effects on uterine activity, uteroplacental perfusion, and fetal oxygenation, is not known. We hypothesized that decreasing the exogenous oxytocin infusion rate before CSE analgesia would lower the incidence of nonreassuring FHR tracings caused by uterine tachysystole in the first 60 minutes following initiation of analgesia.

Methods: Eligibility criteria were healthy women age ≥ 18 years, English speaking, ≥37 weeks' gestation, singleton pregnancy who request CSE analgesia, and received oxytocin augmentation per institutional protocols. Exclusion criteria included chronic use of analgesic medications, a nonvertex fetal presentation, contraindications to neuraxial analgesia, category III FHR tracings prior to initiation of CSE analgesia, and systemic opioid analgesia ≤2 hours before CSE analgesia. In this randomized, controlled, and blinded trial (patients and obstetrician), patients were randomized to one of two groups: decreasing oxytocin infusion rate by half (50%) or 2) maintaining the current infusion rate. All patients received an intrathecal injection of bupivacaine 1.25 mg and fentanyl 20 µg followed by insertion of an epidural catheter and initiation/maintenance of epidural analgesia with bupivacaine 0.08% and fentanyl 2 µg/mL. Per standard protocol, FHR was continuously monitored for 60 minutes and assessed using National Institute of Child Health and Human Development (NICHD) criteria. The primary outcome was the FHR category (scores I to III), evaluated by an obstetrician blinded to patient group. Secondary outcomes were the number of times oxytocin was stopped/decreased within the first hour after CSE and any emergent deliveries during the study period.

Results: In total, 227 patients were randomized: median age was 31 y (IQR 28-34) and BMI was 34.4 kg/m^2. Median pain score at time of CSE was 7 (IQR 5-8) (0-10 scale). FHR tracings for 215 patients were available for review. For the standard treatment group, 55/111 (49.5%) had nonreassuring FHR (category II/III FHT) after CSE, compared to 47/104 (45.2%) in the oxytocin reduction group (P=0.4094, 95% CI 4.36% (-8.93% - 17.65%)). Oxytocin was decreased or stopped within one hour of CSE in 26 (11.5%) patients: 12 for nonreassuring FHR, 2 for uterine tachysystole, and 12 for unknown/uncharted reasons. Five patients delivered within the study period, all were in the standard treatment group, and all had spontaneous vaginal deliveries.

Discussion: The FHR is one clinical sign of fetal well-being used to guide obstetric management during labor. This study standardized analgesia to determine whether high- or low-dose oxytocin is implicated in nonreassuring FHT changes within the first hour of analgesia. Management of labor is a complex process; both oxytocin and labor analgesia have been implicated in nonreassuring FHTs, and the optimal management of labor seems to remain multifactorial as this study did not find that reducing the oxytocin infusion rate is beneficial to the FHT.

Exploring the Mechanism of SETDB1 in Obesity-Enhanced Endometrial Cancer: A Pilot Study

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SET domain bifurcated histone lysine methyltransferase 1 (SETDB1) functions as an epigenetic silencer by catalyzing di- and tri-methylation of histone H3 lysine 9, promoting heterochromatin formation. SETDB1 is overexpressed in endometrial cancer (EC) and correlates with worse patient outcomes. Previous studies from the Yang Laboratory found that SETDB1 knockout (KO) in a mouse EC cell line (Mouse Endometrial Cancer PTEN-deleted K-Ras activated, MECPK) significantly decreased tumor progression and improved survival in C57BL6 mice. Additionally, 70% of EC patients have obesity, which has been linked to oncogenesis and tumor progression. As EC's incidence and mortality rates have been climbing since the mid-2000s, the mechanism by which SETDB1 may promote obesity-enhanced EC warrants further research.

Our objective was to explore the mechanism by which SETDB1 contributes to tumor progression in obesity-enhanced EC. We hypothesized that SETDB1 promotes tumor growth by dysregulating mitochondrial function through H3K9 methylation. First, we performed an enrichment analysis using The Cancer Genome Atlas (TCGA) data to identify pathways correlated with SETDB1 in 11 obesity-related cancers and in EC. In both groups, SETDB1 had the strongest reverse correlation with the oxidative phosphorylation pathway (normalized enrichment score, NES: -5 and -4, respectively). This finding may be related to the results obtained from a collaboration between the Yang Laboratory and Griguer Laboratory: SETDB1 knockout (KO) in the Ishikawa (ISH) EC human cell line led to significantly decreased reactive oxygen species (ROS) levels.

Next, we used past chromatin immunoprecipitation sequencing (ChIP-seq) data to identify oxidative phosphorylation genes displaying H3K9 methylation in ISH cells with SETDB1 wild-type (WT) and KO. H3K9 methylation peaks were present on the promoters of two genes: oxidase assembly 1-like protein (OXA1L) and succinyl-CoA ligase α-subunit (SUCLG1). Both genes had a significant negative correlation with SETDB1 expression per the EC-TCGA dataset by the University of California Santa Cruz Xena browser, which corroborated that they are potential SETDB1 targets.

We then performed Western blotting to determine the effects of SETDB1 WT, KO, and knockdown (KD) on protein expression of OXA1L and SUCLG1 in MECKPK, ISH, and Patient-Derived Primary Carcinoma 10 (PDC10) cells. PDC10 cells originated from a patient at the University of Iowa confirmed to have obesity (BMI: 35.84). ISH cells, on the other hand, originated from a patient with an unknown obesity status. In the KO system, OXA1L showed subtle upregulation in MECPK KOs and subtle downregulation in PDC10 and ISH KOs. SUCLG1 showed no change in MECPK KOs and subtle downregulation in PDC10 KOs and in one ISH KO. The downregulation in the ISH and PDC10 human cell lines was contrary to our expectations. For the KD system, in PDC10 cells, OXA1L showed downregulation in the 96-hour KD but no changes with KD release at 48 and 72 hours. Interestingly, OXA1L was upregulated at SETDB1 0-hour KD. SUCLG1 showed no change in expression.

Despite our efforts, our Western blot studies showed variable results for the effect of SETDB1 KO and KD on OXA1L and SUCLG1 expression. Further studies are needed to determine whether SETDB1 is responsible for methylation of OXA1L and SUCLG1 and/or how SETDB1 affects mitochondrial function. We plan to repeat Western blots to confirm our data, particularly in EC models with SETDB1 overexpression. Additionally, we will perform RNA-seq and ChIP-seq on PDC10 cells to gain deeper insights into SETDB1's regulatory mechanism in an obesity-confirmed EC model.

Title: Developing a research program for reevaluating emotional tasks in fMRI
Student: Corey Plate, PM1
Mentor: Jing Jiang

The study of human emotion and its neurophysiological correlates is of great interest in both basic sciences and clinical practice, but the tools to investigate the neurobiology of emotions, like functional magnetic resonance imaging (fMRI) are still relatively new and finding their footing. One concern of note is whether the sorts of activities patients are asked to complete in the investigation of human emotion are truly tasks that engage emotional processing networks in the brain. Using cytoarchitectural and functional imagining in conjunction, we can define areas that work in tandem to support emotions, and then use these in fMRI experiments with tasks that purportedly engage with emotion processing in the brain. In particular, we investigated whether the Multisource Interference-Task (MSIT) is an emotion processing localizer in the brain for individuals by looking at whether MSIT sensitively and selectively inhibited previously identified areas of the brain, such as insula and amygdala, subserving this function at the group level. If it fails to do so at the group level, then this disclaims the initial assertion by the MSIT literature that MSIT is useful as an emotion localizer because it antagonizes a less emotion-specific area of the brain, the anterior cingulate cortex. Results from fMRI analysis demonstrate that while MSIT can sensitively inhibit some emotion-processing specific areas of the brain, it does not do so selectively, instead reliably inhibiting the default mode network, which is antagonized by any positive task. This calls into question whether classical experiments used to identify and investigate emotion-processing specific areas of the brain are doing what they purport to, and requires careful investigation to assure that these tasks are not generating false conclusions about emotion processing and the brain.

EBL and MAL-II-binding in the retina and choroid

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Purpose: Complement Factor H (CFH) is a key player in the complement alternative pathway and has been implicated in various conditions including age-related macular degeneration. To protect host cells from complement bystander injury, this glycoprotein recognizes sialic acid glycoconjugates with α-2,3 linkages present on cells and matrix. CFH itself also contains many α-2,6 sialoglycoconjugates. Sialoglycoconjugates with α-2,6 and α-2,3 linkages can be identified with EBL (Elderberry Bark Lectin) and MAL-II (*Maackia amurensis* lectin II), respectively. Identifying glycoconjugates with α-2,6 and α-2,3 linkages may prove beneficial for understanding complement regulation in the eye.

Methods: Corresponding 8mm retina and choroid punches were taken from both the macula and supratemporal region of 5 human donors and protein was extracted. Western blots labeling with EBL and MAL-II were then performed on the samples. EBL identifies bands with α-2,6 sialic acid linkages, and MAL-II identifies α-2,3 sialic acid linkages. Sections from cryopreserved blocks of both the macula and periphery from 3 different donors were collected and labeled with EBL and MAL-II lectins individually and imaged with epifluorescence. Additionally, 2D gel electrophoresis was performed on two separate soluble and insoluble fractions collected from bulk choroid, with subsequent EBL and MAL-II labeling. A precipitation of human choroid proteins with EBL-bound beads was also performed, with subsequent Western Blot labeling with EBL and MAL-II.

Results: Differences in EBL and MAL-II lectin binding within the submacular choroid were noted, with EBL more dominantly binding intercapillary pillars and MAL-II binding the endothelial cell surface. From the precipitation, MAL-II bound to 2 bands within the protein fraction that had been selected via EBL-binding, indicating that those bands contained proteins with both types of sialic acid linkages. There was some variation between individuals in regards to EBL-binding bands in the choroid. However, there were no major observed differences between EBL and MAL-II labeled bands between the macula and superotemporal fractions.

Conclusion: Identifying sialoglycoconjugates with α-2,6 and α-2,3 linkages may give insight into complement regulation within the eye. A number of protein spot candidates from the 2D gel have been selected for and are awaiting mass spectrometry.

Title: Computational Characterization of Poroviscohyperelastic Material Properties of Porcine Cartilage Using Finite Element Analysis of Mechanical Indentation Tests

Presenter: Dominic J.L. Rivas, M1

Mentor: Jessica E. Goetz, Department of Orthopedics and Rehabilitation

Collaborators: Joshua E. Johnson, Marc J. Brouillette, Maxwell Sayki

Introduction: Osteoarthritis (OA) is a degenerative joint disease that reduces the mechanical stiffness of articular cartilage, which in turn can alter how forces are transferred across the affected joint. Post-traumatic osteoarthritis (PTOA) is the rapid onset of OA following a traumatic injury. High-energy impacts that result in intra-articular fractures (IAF) frequently lead to the rapid development of PTOA. Quantifying changes in the material properties of cartilage early after IAF may improve our understanding of joint function after injury and help identify patients who could benefit from mechanically favorable PTOA interventions.

Hypothesis/Purpose: We hypothesized that in the first week after intra-articular fracture, cartilage in the fractured joint would begin to exhibit reduced stiffness compared to the intact contralateral joint. Our second hypothesis was that in malreduced fractures with an articular step-off, overloaded cartilage would have stiffer cartilage, and underloaded regions would have even less stiff cartilage than that in joints with anatomically reduced fractures.

Method: A unilateral, single-fragment IAF was created in the distal tibia (hock/ankle joint) of n=16 Yucatan mini-pigs. Half of the animals (n=8) had the fracture reduced anatomically (AR group), with the repair performed to most closely reproduce the original joint surface. The remaining animals (n=8) had the fracture repaired with the anterior fragment intentionally displaced distally to create an anterior step-off (AS) group with intentional overloading of the displaced fragment. Minipigs were euthanized one-week after surgical fixation of the fracture, and the distal tibia and talus of both the fractured and intact contralateral joint were harvested. Cartilage thickness in 3 regions of both the tibia and talus was measured via ultrasound. Mechanical indentation tests were performed at each measured location using a 3.175 mm diameter spherical indenter. Tests consisted of 3 progressive step-strains followed by a period of relaxation. Using a reverse iterative fitting finite element (FE) analysis technique, coefficients of a poroviscohyperelastic material model were numerically optimized until the FE-derived force-time curve replicated the experimentally measured force-time curve. Mann-Whitney non-parametric tests were performed to determine differences in FE-optimized stiffness values and peak reaction forces during the third strain step of the indentation test. Statistical significance was set at $p \leq 0.05$, and data are reported as medians.

Findings/Results: Cartilage stiffness on the posterolateral tibial surface was comparable (3.1 vs 3.4 MPa; p=1.0000) between fractured and unfractured joints. Cartilage on the anteromedial tibia of fractured joints was stiffer (2.5 vs 1.8 MPa p=0.1824) and had higher peak reaction forces (1.5 vs 1.0 N; p=0.0770) than cartilage from the same location in an intact joint. However, posteromedial tibial cartilage trended to be less stiff in fractured joints than in intact joints (1.7 vs 2.5 MPa p=0.1615). Similar trends were found for talus cartilage in fractured joints, with the posteromedial stiffness being lower (0.6 vs 1.7 MPa; p=0.0315) and the anteromedial stiffness being higher (1.2 vs 0.6 MPa; p=0.2673) than in intact joints. Stiffness of the anterolateral talus cartilage was not different (1.2 vs 1.2; p=0.4088) between fractured and intact joints.

Comparing between fracture reduction types, there were no regional differences in cartilage stiffness found between the AR and intact groups for either the tibia (p=0.4286 – 0.5035) or the talus (p=0.1483-0.5014). Overloaded tibial cartilage in the AS group also had no difference in stiffness (2.5 vs 2.0 MPa; p=0.9524) compared to the AR group. Underloaded tibial cartilage in the AS group was moderately stiffer (2.9 vs 2.3 MPa; p=0.4598) compared to the AR group. On the talus, the AS group was stiffer in the overloaded region (1.3 vs 1.0 MPa; p=0.2000) and less stiff in the underloaded region (0.4 vs 0.8 MPa; p=0.5556) compared to the same locations in the AR group.

Conclusion: These findings demonstrate that cartilage mechanical response varies as a result of the joint being fractured, by anatomical region, and by reduction quality following IAF. These initial comparisons were based on 10 of the 16 specimens. We anticipate that incorporation of the remaining specimens will strengthen our findings that IAF alters cartilage stiffness by 1 week after injury, and that underloading after fracture (as was the case in the posterior region of joints with AS) contributed to cartilage softening. Immunohistochemistry sections of the cartilage at the mechanically measured joint locations can be used to quantify chondrocyte mitochondrial metabolism and oxidative damage at these locations. Correlation of these markers with the FE analysis derived mechanical stress and strain data may yield cellular mechanisms driving tissue dysfunction, damage, and altered mechanics.

Identifying Risk Factors for Inpatient Falls in Burn Patients: A Retrospective Cohort Analysis

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Student: Ana Rivera Juarez, BS
Mentors: Alexander Kurjatko MD, MPH, Colette Galet, PhD
Collaborator: Sadaf Akbari Kharazi, MD

Background: Inpatient falls are a significant source of morbidity and mortality among hospitalized patients, particularly in high-risk populations. Prior studies have associated falls with prolonged hospital stays and increased complications. Falls also contribute to a substantial economic burden on healthcare systems. Burn patients may be uniquely vulnerable to falls due to impaired mobility, systemic stress responses, and motion limitations from dressings. Despite this, the risk factors and outcomes associated with inpatient falls in burn units remain underexplored.

Objective: This study aims to evaluate the impact of inpatient falls on adult burn patient outcomes and identify predictors of fall risk within this population. The findings will inform fall prevention strategies and guide quality improvement initiatives within burn care settings.

Methods: This is a retrospective cohort study. Information on all patients admitted for a burn injury between July 1, 2015 and June 30, 2024 were obtained from the University of Iowa Burn Registry. Adult burn patients who experienced falls during hospitalization were identified through an internal auditing system (Riskonnect). Their information was merged to the Burn Registry data. Fall patients were then propensity matched 1:2 to non-fall controls based on age, sex, total burn surface area (TBSA), and inhalation injury using SPSS 28.0. Data collected on our final cohort included demographics, comorbidities, medication use, Fall Risk Assessment Score (FRAS), physical therapy (PT)/occupational therapy (OT) assessments, and fall safety measures. Univariate analyses were conducted to identify significant difference between fall and non-fall patients. Receiver Operating Characteristic (ROC) curve was conducted to determine the optimal FRAS score cutoff. Stepwise multivariate logistic regression was performed to identify factors associated with risk of falls in the unit. $P < 0.05$ was considered significant.

Results: A total of 132 patients were included (45 fallers, 87 non-fallers). Fallers were significantly more likely to have been on antihypertensives and antiarrhythmics (62.2% vs. 39.1%, $p = 0.016$ and 75.6% vs. 52.9%, $p = 0.014$, respectively) and to require greater mobility assistance on admission (Basic mobility score 16 [11.3-20] vs. 20 [14-24], $p = 0.002$). Among fallers, 57.8% fell before their first surgery, with a median time from admission to fall of 9 days. The FRAS demonstrated moderate predictive value (AUC = 0.653, $p = 0.009$) with a cutoff score of 15 yielding 50% sensitivity and 72–74% specificity. OT assessments at admission reflected significantly reduced activities of daily living (ADL) independence in fallers (Daily activity total score 19 [14-22] vs 16 [12-19], $p = 0.004$). Multivariable analysis showed that burn surgery requirement indicative of a more severe injury (Odd Ratio [OR] = 3.35 [1.12-10.1]; $p = 0.031$] and FRAS (OR = 1.12 [1.04-1.20]; $p = 0.003$) were associated with increased risk of fall.

Conclusion: In the burn unit, inpatient falls are preceded by identifiable functional deficits and commonly prescribed medications. The FRAS and early PT/OT assessments can provide valuable insight into fall risk. These findings underscore the importance of functional risk stratification, interdisciplinary care coordination, and proactive fall prevention protocols tailored to the unique needs of burn inpatients.

Assessing Pain Control and Satisfaction in Spine Surgery Amidst COVID-19 Staff Shortages: A Retrospective Study on Patient-Controlled Analgesia

Emma Bechler, Kristina Rossmiller, Reagan Grieser-Yoder, Jill Corlette, Krit Petrachaianan, Natalie Glass, Catherine Olinger

Abstract

Purpose: To evaluate the impact of patient-controlled analgesia (PCA) versus non-PCA pain strategies on opioid consumption and pain control in spine surgery patients before and during the COVID-19 pandemic.

Patients and methods: This retrospective cohort study included 5,528 adult patients who underwent one of four spine procedures between January 2018 and December 2023. Patients were stratified by analgesia type (PCA vs. non-PCA) and time period (pre-COVID vs. post-COVID). Primary outcomes included total opioid consumption (measured in morphine milliequivalents, MME) and average Visual Analog Scale (VAS) pain scores in the first 24 hours postoperatively. Multivariable regression adjusted for demographics including age, sex, obesity, and smoking.

Results: PCA use was associated with a 52.1% reduction in opioid consumption compared to non-PCA ($p < 0.001$). This effect was most pronounced post-COVID (74.2% reduction), though not statistically significant. Despite reduced opioid use, PCA patients reported slightly higher VAS scores (+0.814, $p = 0.0013$). Subgroup analyses revealed higher opioid use and pain scores among smokers and obese patients, while male sex predicted lower pain scores. PCA was particularly beneficial in more invasive procedures, and its expanded use in less complex surgeries post-COVID did not increase pain scores**.**

Conclusion: PCA significantly reduced opioid use following spine surgery, though pain scores were modestly higher. During staffing shortages, PCA may offer operational and clinical advantages. Patient-specific risk factors should guide individualized pain protocols.

Title: When Air Becomes a Risk Factor: PM2.5 Exposure and Lung Transplant Outcomes

Authors: Thomas Rush, Anuradha Gore, Ashten Sherman, Raul Villacreses, Julia Klesney-Tait, Tahuanty Pena, Spyridon Fortis, Josalyn L. Cho

Background: Chronic lung allograft dysfunction (CLAD) is the primary driver of morbidity and mortality in patients who survive at least one year following lung transplantation. CLAD develops as a result of injury to the small airways, leading to aberrant tissue repair that causes fibrotic obliteration of the small airways and airflow obstruction. Unlike other solid organs, transplanted lungs are continuously exposed to ambient air. Inhaled particulates, including fine particulate matter (PM2.5) and diesel particulate matter (DSLPM), reach the small airways and alveoli. Although the effects of air pollution on lung transplant outcomes are not fully understood, particulate exposures have been shown to induce oxidative stress and airway inflammation. These processes could plausibly induce injury to the small airways. We therefore hypothesized that lung transplant recipients with CLAD have higher residential exposure to PM2.5 and DSLPM compared to those without CLAD.

Purpose: To quantify residential exposure to air pollution, PM2.5, and DSLPM in lung transplant recipients with and without CLAD

Methods: We performed a retrospective cohort study of lung transplant recipients with ≥ 1 year of follow-up data at UIHC between January 2007 and December 2024. Home addresses of recipients at the time of transplant were geocoded and linked to census tract-level air pollution indicators from the Environmental Justice Index. We used two EJI metrics per pollutant: a concentration “score” for PM2.5 and diesel particulate matter (µg/m³; E_PM and E_DSLPM) and a state percentile rank (unitless; 0–1; EPL_PM and EPL_DSLPM). The EJI air-pollution composite is also a unitless percentile rank (0–1). Lung transplant recipients with CLAD were defined as those with a reduction in the forced expiratory volume in 1 second (FEV1) to ≤ 80% of the post-transplant baseline based on two measurements ≥ 3 months apart in the absence of another cause. No imputation was made for missing data. Univariate comparisons were made using the Chi-squared test, one-way analysis of variance, or Mann-Whitney test. Post-hoc comparisons between groups were performed using the Dunn test for multiple comparisons. Differences were considered statistically significant when $P < 0.05$ based on a two-sided test.

Results: Of 277 lung-transplant recipients identified between January 2007 and December 2024, 44 were excluded (n=31 ≤ 1 year of follow-up data, n=13 unable to resolve residential geocodes), leaving 233 recipients to be analyzed. Residential air-pollution levels for recipients mirrored the statewide distributions for composite air pollution exposure, PM2.5, and DSLPM, indicating that the cohort’s exposures were representative of the state of Iowa. No differences were observed in age, sex, or race and ethnicity between recipients with and without CLAD. Compared to lung transplant recipients without CLAD, those with CLAD had similar air pollution exposure based on a composite percentile rank relative to all other US census tracts. Similarly, no differences in diesel particulate matter concentration (µg/m³) or percentile rank were observed in recipients with and without CLAD. However, recipients with CLAD had higher residential PM2.5 exposure than those without CLAD (median 9.17 µg/m³ [IQR 8.39-9.44] vs 8.67 µg/m³ [8.35-9.19]; p=0.0197). Airway inflammation can trigger acute rejection (AR), which is a major risk factor for CLAD. We therefore asked whether residential air pollution exposure was associated with the number of AR episodes among lung transplant recipients with CLAD. Although we did not observe differences in AR within the CLAD cohort based on composite air pollution or PM2.5 exposure, recipients with high DSLPM exposure had more episodes of AR compared those with lower DSLPM exposures (median 2.0 episodes [IQR 0-3] vs 1.0 episodes [0–2]; p = 0.0375).

Conclusions: In this single-center retrospective cohort study, residential PM2.5 exposure was higher among lung transplant recipients with CLAD, whereas DSLPM and composite air pollution exposure did not differ by CLAD status. Within the CLAD subset, higher DSLPM exposure was linked to a greater number of acute rejection episodes. These unadjusted findings suggest neighborhood particulate exposure may be an important risk factor for CLAD and AR, supporting the need for larger, adjusted, and time-varying analyses.

Outcomes for Adult Mechanically Ventilated Patients Receiving an Analgesia – First Sedation Protocol

Owen Millers*; Caitlin Sanderman*; Hayden Smith, PhD; Jonathan Hurdelbrink, PhD; Sarah Pandullo, APRN; Carlos Pelaez-Gil, MD; Matthew Trump, DO (*Authors contributed equally)

Abstract

Introduction:
Mechanical ventilation includes the use of analgesics and sedation medications to manage pain, agitation, and maintain ventilator compliance. The process is not without potential concerns. Over-sedation can increase the incidence of Intensive Care Unit (ICU) delirium, mortality, post-traumatic stress disorder, and prolonged ventilation, which can be associated with pneumonias. Long-term or high-dose opioid use in the ICU can increase risks of developing opioid dependence, tolerance, addiction, and other physiological effects.
Objectives:
To investigate whether the adoption of a structured analgesia-first sedation protocol can decrease morphine milligram equivalents (MMEs) of analgesics administered during an ICU stay. Secondarily, examine the impact of the protocol on ICU stay duration, mortality, episodes of delirium, ventilator duration, and adverse events.
Methods:
A pre-/post-design was used to study the adoption of an analgesia-first sedation protocol as standard care. The change was implemented on February 1st, 2025 in the Critical Care Units (CCU) in two Des Moines hospitals within the same health system. Patients admitted on/or after this date served as the experimental group. Patients admitted prior to this date during a similar time-period within the previous year, who did not receive any particular sedation protocol, served as the pre-implementation control group. Differences in hourly MMEs between the groups was determined using a quantile regression model with standardized inverse propensity score weights based on baseline covariates. The study received Institutional Review Board approval including a waiver of consent.
Results:
Study data revealed the upper quantile values of the MME distribution in patients in the post-implementation group were significantly lower than the values for patients in the pre-implementation group. In particular, patients in the 90^{th} percentile received 8.89 (95% CI: -22.3509, -0.6789) fewer MMEs per hour during their CCU stay than the control group. Secondary outcomes were mixed, with delirium incidence increasing at 24-hours post-extubation in the experimental group, and a failure to see a difference at 48-hours post-extubation. The duration of CCU stays and mortality increased appeared higher in the post-implementation group. There was no discernible increase in adverse events across groups.
Conclusions:
Study findings demonstrated the primary benefit of the analgesia-first protocol in a documented reduction in the number of mechanically ventilated patients receiving inappropriately high doses of opioids. Study limitations include a lack of patient randomization, which could result in residual confounding if patient severity characteristics were not fully balanced. The study was designed to study the primary outcome, so secondary measures may be limited and require additional research.

Detecting Visual Field Defects Using Size Modulation Perimetry: A Cost-Effective and Optimized Approach to Test the Visual Field

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Mentor: Edward Linton, MD, Department of Ophthalmology and Visual Sciences
Co-Mentor: Michael Wall, MD, Department of Ophthalmology and Visual Sciences
Collaborators: Andrew Pouw, MD, Department of Ophthalmology and Visual Sciences; Ronak Singh, Carver College of Medicine; and Ivan Marin-Franch, Valencia, Spain

Introduction:
Glaucoma is a leading cause of irreversible blindness, and its diagnosis and monitoring rely heavily on visual field (VF) testing with standard automated perimetry (SAP). Traditional SAP devices such as the Octopus 900 (O900) are limited by poor reproducibility in advanced disease (at low thresholds), high costs, and restricted accessibility. Head-mounted devices (HMD) provide a portable, low-cost alternative capable of both luminance and size modulation, with prior studies showing strong validity, repeatability, and patient preference in individuals without known defects. Building on this work, our study evaluates the repeatability of size modulation in patients with optic neuropathies such as glaucoma, with the goal of validating HMD-based size-modulation perimetry as a practical alternative or adjunct to fixed size, luminance-increment SAP and expanding access to VF testing for earlier detection and improved follow-up of visual loss.

Hypothesis:
The Iowa Head-Mounted Phone Display (HMD) Open-Source Perimetry, employing size modulation, demonstrates comparable, if not reduced variability, to standard automated perimetry (SAP) that relies on luminance modulation for measuring visual thresholds.

Methods:
We tested 31 patients with visual field defects from glaucoma or other optic neuropathies. Each completed six examinations: two each with Octopus 900 luminance modulation (SAP/O900), HMD luminance modulation (HMDl), and HMD size modulation (HMDs), in randomized order. Testing used the Open Perimetry Interface with size V stimuli, a custom grid, and the ZEST (Zippy Estimation by Sequential Testing) algorithm. Sensitivity values were age-adjusted using device-specific mean sensitivities derived from a normative database. Total deviations (TDs) were then calculated by subtracting these expected values from the observed sensitivities *(observed – age-corrected 50^{th} percentile value from the normal database)* and dividing by standard deviations to enable cross-device comparison. Agreement between devices was assessed with linear correlation and Bland–Altman analyses stratified by O900 sensitivity bins, while test–retest variability was compared using ANOVA of absolute retest differences and pointwise repeatability coefficients (RCs), dichotomized at 25 dB.

Findings/Results:
Thirty-one patients (186 tests; 62 per modality) were analyzed. A scatter plot of total deviations comparing SAP and HMDs at each location demonstrated a significant linear correlation ($r = 0.70$, $R^2 = 0.49$, $p < 2.22\times10^{-16}$), though the slope (0.43) indicated that the HMDs underestimated the depth of loss compared to SAP. Bland–Altman analysis showed that HMDs exhibited lower variability at locations with reduced sensitivity. When stratified at 25 dB based on average O900 sensitivity, a bimodal effect emerged. ANOVA confirmed this pattern: at high-sensitivity locations (>25 dB), O900 showed smaller retest differences (mean difference −1.63 dB, 95% CI −1.89 to −1.37, $p < 0.000001$), whereas at low-sensitivity locations (≤25 dB), O900 showed larger retest differences compared to HMDs (mean difference +3.91 dB, 95% CI 2.75–5.07, $p < 0.000001$). Pointwise repeatability coefficients (RCs) reflected the same trend: at >25 dB, O900 had a lower RC (5.68) than HMDs (11.89), while at ≤25 dB, O900 had a higher RC (19.94) than HMDs (8.23). Statistical testing of RC differences was not performed.

Conclusion/Overall Significance:
This study establishes that head-mounted perimetry utilizing size modulation demonstrated comparable overall repeatability to SAP, with significantly lower variability in regions of severe field loss (≤ 25 dB). Conversely, at higher sensitivities, SAP tended to remain more stable. These results support the emerging view that perimetry may benefit from switching from luminance to size modulation around the 25 dB threshold. While HMDs may underestimate sensitivity at normal locations (based on O900 values), this could reflect greater sensitivity to subtle damage. Together with its lower cost and portability, HMDs perimetry represents a practical complement or alternative to conventional SAP.

Improving and Modernizing Massive Transfusion Protocol at a Level 1 Trauma Center

Jacob Sharafuddin, BA; Harnoor Singh Bhardwaj, MD; Colette Galet, PhD; Charles Knudson, MD; and Dionne Skeete, MD

Introduction. Hemorrhage is a leading cause of death after trauma, secondary only to nervous system injury. Clinicians must therefore act rapidly to restore homeostasis in hemorrhaging patients. To ensure a rapid and organized delivery of blood to hemorrhaging patients, hospitals have implemented massive transfusion protocols (MTPs) that define predetermined numbers of packed red blood cells (RBCs), platelets, plasma, and cryoprecipitate (cryo).

Purpose. In April 2023, our institution's Blood Bank initiated a quality improvement project (QI) to update the MTP from a shipment containing 4 RBCs, 3 plasma, and 1 platelet or cryo every other shipment to shipments containing 6 RBCs:5 plasma:1 platelet. We hypothesized that, although the newer shipments would take longer to prepare, there would be fewer returned blood products, particularly cryo. We also speculated that blood product ratios would be closer to 1:1:1, in line with evidence found in transfusion literature. Secondly, we assessed whether patients with severe hemorrhage could be better defined using newer bleeding definitions such as the modern bleeding definition (10 or more pRBCs within 6 hours) and substantial bleeding definition (1 RBC within 2 hours *and* 5 RBCs or death within 4 hours). Patients have traditionally been considered massive transfusions if they receive ≥ 10 RBCs within 24 hours, although this definition's usefulness has been called into question, as it is affected by survival bias. Thirdly, we sought to determine if indicators like lactate or the Shock Index (heart rate divided by systolic blood pressure) could be used to trigger MTPs instead of clinical gestalt.

Methods. All MTPs from March 2021 to March 2025 were reviewed. Changes in our MTP were implemented on April 1st, 2023. We queried our institution's Blood Bank Database and medical records to collect data from each instance of an MTP called at our institution. Shipment preparation time and usage as well as return of cryo, plasma, pRBCs, and platelets were collected to assess the impact of the QI on preparation time and blood product return. pRBC usage at 2, 4, 6 and 24 hours as well as if the patient died within 4 hours due to hemorrhage were collected to determine whether other bleeding definitions would be useful. We assessed trauma MTPs separately from non-trauma MTPs. Univariate analysis was performed to compare the pre- and post-implementation period. Concordance and Fleiss Kappa tests were used to assess agreement between bleeding definitions. Receiver operating characteristic (ROC) curve analysis was used to compare clinical gestalt to selected lab values and Shock Index. $P < 0.05$ was considered significant.

Results. Shipment preparation time and the number of sets prepared did not significantly increase ($p = 0.707$ and 0.774, respectively). The number of sets shipped decreased ($p < 0.001$). Additionally, blood products were returned more frequently, except for cryo, which instead decreased (RBCs: 4 [2-6] to 7 [4-11]; plasma: 3[2-5] to 6[4-9]; platelets 0 [0-1] to 0 [0-2]; and cryo 0 [0-1] to 0 [0-0], respectively, per shipment; $p < 0.001$). For trauma patients: both RBC:plasma and RBC:platelets ratios decreased (1.3 to 1 [$p = 0.007$] and 0.89 to 0.67 [$p = 0.018$], respectively). For non-trauma patients: both RBC:plasma and RBC:platelets decreased ratios (1.33 to 1.17 [$p = 0.001$] and 1 to 0.75 [$p = 0.001$], respectively). The substantial bleeding definition captured the most patients (55.2%). There was a low concordance (27.1%) and interrater agreement between the 3 definitions (Fleiss Kappa = 0.494, $p < 0.001$). Lactate and Shock Index scored the highest on ROC for trauma patients (0.757 and 0.756, respectively; $p < 0.001$). For non-trauma, only lactate was significant (0.685; $p < 0.001$). For trauma, a cut-off of 1.3 was determined for the Shock Index (sensitivity: 61.1%, specificity: 72.7%, positive predictive value: 88.5%, and negative predictive value: 35.3%). Two cut-offs for lactate were determined, 3.05 mmol/L for non-trauma (67.1%, 56.7%, 88.4%, and 26%) and 5.05 for trauma (64.8%, 71.9%, 88.3%, and 38.3%).

Conclusion. Changes to our MTP did not significantly lengthen shipment preparation time, but significantly reduced use and return of cryo. However, all other blood products were returned more often, which could lead to wastage if returned out of temperature and not utilized. Additionally, for future audits of MTP protocols, the substantial bleeding definition may be more useful to use than the traditional one, as it appears to capture more patients who had received MTPs. Finally, we found that lactate and Shock Index can each be individually used in place of clinical gestalt as initial triggers of MTPs for trauma patients. Doing so would help standardize how MTPs are initiated.

Loss of Nicotinic Receptor Innervation Increases Cell Proliferation in Acute Airway Injury

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Introduction: Lung transplantation, an effective treatment for patients with end stage lung diseases, is hampered by poor long-term survival compared to other organ transplants. The lungs receive cholinergic stimulation from the vagus nerve along the bronchial tree. This stimulation is severed during lung transplantation. Understanding the role of parasympathetic stimulation in airways is vital when trying to understand any deleterious effects denervation has in the progression of disease in lung transplant patients.

Hypothesis: We hypothesized that loss of activation of nicotinic receptors due to vagal denervation may contribute to unregulated cell proliferation in response to acute injury.

Methods: Tracheas were harvested from ferrets (n=6), rubbed with a stiff nylon brush to induce a partial scratch injury, and cut into 1 cm pieces. Explants were cultured for five days in F-medium and pulsed every 48 hours with treatment conditions and EdU. Conditions included control, nicotine (NIC) (nicotinic receptor agonist, 10μM), acetylcholine (ACH) (muscarinic and nicotinic receptor agonist, 10μM) and mecamylamine (MEC) (nicotinic receptor antagonist, 10μM). On day 5, tissues were fixed with 2% paraformaldehyde and stained for EdU (marker of proliferation), alpha-tubilin (ciliated cell marker), and keratin 5 (basal stem cell marker). Stained tissue was imaged using confocal microscopy with Z-stacking in order to obtain 3D visualization of the tracheal surface. After submucosal glands (SMGs) were identified through SMG morphology, EdU positive pixel area was quantified as a percentage of total gland area. The surface plane was identified as the Z slice superficial to the gland slices, and EdU positive area was quantified as a percentage of total nuclei stain area; this was used to assess surface airway epithelial (SAE) proliferation.

Results: Preliminary data results (n=4), using paired t-tests, show a significant decrease in EdU+ area as a percentage of glandular area compared to control in the tracheal tissue cultured with ACH (ACH 2.45% *vs.* Control 9.34%, P=0.02). This trend also holds true for the tissue treated with NIC co-treatment with MEC did not rescue proliferation in the glandular tissue. In the surface epithelium, NIC and ACH treatments inhibited proliferation (NIC 9.5% *vs.* Control 34.4%, P<0.05; ACH 10.5% *vs.* Control 34.4%, P=0.03). MEC did not rescue proliferation in the surface epithelium when combined with either the NIC or ACH groups.

Discussion: Previous work produced by the Parekh lab, using the same methodology, demonstrated that acetylcholine treatment decreases proliferation in the glandular and surface epithelium, while muscarinic specific agonism, using bethanechol, only decreased proliferation in the surface epithelium. This experiment also demonstrated that acetylcholine decreases proliferative capacity~~,~~ but also showed that nicotinic agonism specifically decreases proliferation in both glandular and surface epithelium. This study suggests that the nicotinic branch of the cholinergic pathway of the vagal parasympathetic input to the lungs serves a vital role in proliferative regulation of SMGs and SAE and could be a therapeutic target for lung transplant recipients in the hopes of preventing the development of advanced lung diseases.

Exploring lysosome acidification defects in Parkinson's disease

Sydney Skuodas, Shreya Ghimire, Satya Tadinada, Weijie Du, Sarah Ernst, Thomas Moninger, Michael Welsh, Alejandro Pezzulo

Parkinson's disease (PD) is the second-most common neurodegenerative disorder and affects 1% of the population over the age of 60. There is a lack of treatment to prevent onset or slow disease progression. Most cases are sporadic, and the mechanism of pathophysiology is unclear. However, evidence supports a complex interplay between amyloid aggregation, pathologies, and neuronal loss and dysfunction. Work from Ghimire and Pezzulo showed that PD fibroblasts have an abnormal transcriptome that closely mirrors that of fibroblasts from patients with a familial form of PD with a mutation in a lysosome biogenesis gene, LRKK2. We therefore asked if lysosome biogenesis or function was altered in lysosomes from PD fibroblasts. We hypothesized that PD lysosomes would have mass changes and/or acidification defects.

To evaluate lysosome mass and lysosome acidity, I studied human dermal fibroblasts with LysoPrime Deep Red and pHLys Red to detect lysosomes and acidic cellular compartments, respectively. I examined the cells using confocal microscopy and used image processing software for a quantitative analysis of lysosome phenotypes. I imaged lysosomes and found no significant differences in cell size or number of lysosomes. However, I found fewer acidic compartments in PD fibroblasts compared to control fibroblasts. I also found decreased co-localization between lysosome and acidic compartment markers. These experiments suggest that fibroblasts from patients with sporadic Parkinson's disease have lysosome acidification defects. This is congruent with the decreased expression of genes important for lysosome acidification in PD fibroblasts compared to age-matched controls. These results suggest that additional studies of lysosomes in PD fibroblasts may yield insights into PD mechanisms. Further investigation may also yield potential novel diagnostic markers and detect PD during the presymptomatic development period before irreversible neuronal loss occurs.

The Role of Arhgap29 in Orofacial Morphogenesis

Jessica Smith
Mentor: Martine Dunnwald

Orofacial clefting (OFC) is a complex craniofacial anomaly arising from both genetic and environmental factors. One specific type of orofacial cleft, cleft palate, results from a failure of palatal shelf fusion during embryonic development. While it has been demonstrated that mutations in *RhoA GTPase Activating Protein 29* (ARHGAP29) are linked to cleft palate, the cellular and molecular mechanisms by which this gene contributes to tissue morphogenesis are not well understood. Based on previous work showing that Arhgap29 forms functional complexes with IRF6 and Rab11a, we aim to elucidate novel binding partners of Arhgap29 using immunoprecipitation and mass spectrometry. These binding partners will serve as avenues of further investigation aimed at characterizing the mechanisms by which Arhgap29 functions in palatogenesis.

Author: Jackson Snyder
Mentor: David Bedell

Abstract: **Perceptions of Diabetes Risk Factors in Ecuador and Iowa**

Background: Diabetes is a growing public health concern in Ecuador, affecting approximately 553,000 individuals. How communities perceive the risk factors for diabetes can directly influence both prevention strategies and disease management. This study examined perceptions of diabetes risk across three communities—Cacha and Riobamba, Ecuador and Independence, Iowa—while considering the influence of personal or family history of diabetes.

Methods: A structured survey of primary care patients assessed perceived importance of nine diabetes risk factors (diet, genetics, exercise, sleep, weight, tobacco use, alcohol consumption, stress, and social factors) on a 5 point scale. Responses were compared between participants with a personal or family history of diabetes and those without, and subgroup analyses were conducted by city. Independent-samples *t*-tests were used to evaluate differences.

Results: Across the three sites, most surveyed risk factors were rated as moderately to highly important. In Riobamba, participants with a family history of diabetes rated **social factors (mean 2.24 vs. 1.57, p = 0.013)**, **stress (2.87 vs. 2.23, p = 0.021)**, and **genetics (2.47 vs. 1.67, p = 0.036)** as significantly more important compared to those without a family history. No statistically significant differences were observed in the Cacha or Independence communities.

Conclusions: These findings suggest that personal or family exposure to diabetes influences perceptions of non-lifestyle risk factors, particularly in Riobamba. Stress, genetics, and social determinants were seen as more important by those with a family history, underscoring the role of lived experience in shaping health beliefs. Tailored education strategies may be needed to address both lifestyle and non-lifestyle risk perceptions to improve diabetes prevention in Ecuadorian communities.

Title: Diagnostic utility of ultrasonography in diagnosing carpal tunnel syndrome vs. electrodiagnostic studies

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Background: Carpal Tunnel Syndrome (CTS) is the most prevalent peripheral nerve entrapment neuropathy in the U.S., affecting 3% of the general population and 15% of the workforce. Electrodiagnostic studies (EDX), electromyogram and nerve conduction studies, are the current diagnostic gold standard; however, since they are more invasive, uncomfortable, and expensive, ultrasonography (US) has emerged as a promising alternative. US is non-invasive and affordably provides real-time anatomical imaging with no known risks. Although US is gaining traction as a diagnostic tool for CTS, this area of research is relatively uncharted, prompting physicians to investigate its diagnostic utility compared to EDX.

Purpose/Hypothesis: This study aims to assess the diagnostic utility of US in comparison to EDX, identify ultrasound findings that correlate with CTS diagnosis, and determine cross-sectional area thresholds at specific anatomical locations for diagnosing CTS. We hypothesize there is no significant difference in the detection of CTS between US and EDX, making US a feasible alternative to EDX.

Methods: A retrospective chart review was conducted to evaluate the diagnostic performance of ultrasound (US) findings compared to EDX for CTS. Ultrasound reports from UIHC patients between 2019-2023 were extracted from the Electronic Medical Record (Epic) based on the CPT code for upper extremity ultrasound and cleaned to remove duplicates, reports lacking median nerve examination, and patients without any EDX studies or EDX studies corresponding to the limb evaluated by US. All US and EDX studies were extracted that had corresponding reports, regardless of number of studies per patient; however, if a patient had more than one scan done on each side, then scans were checked for matching diagnoses, and only the combination closest in time were included in statistical analysis. EDX reports ranging from 2003 to 2025 were manually reviewed for their EMG/NCS impression. US reports, all performed by the same ultrasound technician, were manually reviewed to extract quantitative and qualitative sonographic descriptors of the median nerve. Ultrasound reports were considered indicative of CTS based on predefined criteria: cross-sectional area of median nerve ≥ 11 mm^2 at specified anatomical locations OR mention of focal compression on long axis imaging. To our knowledge, this is the largest single center cohort of US reports being evaluated for CTS that were compared to both institutional and external EDX impressions.

Results: Our final dataset included 514 patients, 533 US reports, and 522 EDX studies. We are currently awaiting final statistical analysis, but our study revealed that when held against the current gold standard of EDX, ultrasound had about an 82% sensitivity and 45% specificity. This means that US was successful at ruling in CTS when EDX said it was present, but not great at ruling CTS out when EDX said it was not present. PPV and NPV were 75% and 55%, respectively, revealing similar findings that US was more reliable when EDX tests indicated CTS than when EDX tests did not indicate CTS. Total congruence between all EDX and US interpretations was about 70%, which is a fair agreement.

Ultrasound diagnoses were made utilizing CSA criteria, either as a standalone or in conjunction with focal compression, 97.6% of the time; though focal compression was rarely used as a standalone criterion, it was still important to consider since it was involved in 1/3rd of all diagnoses, and accuracy was at its highest when both criteria were met.

Conclusion/overall significance/broader perspective: Our study's preliminary results demonstrated that ultrasound has acceptable sensitivity but poor specificity for diagnosing carpal tunnel syndrome. The large number of false positives suggest we should re-evaluate our US diagnostic criteria and adjust thresholds based on demographic information to improve accuracy. Ultrasound could be considered as a front-line diagnostic tool for CTS, reserving EDX testing for patients with negative US results. A prospective study with standardized ultrasound protocols and CTS-6 forms would allow for more consistent variables being reported as well as comparison to clinical symptoms, which are essential to diagnosis. Finally, US remains a useful complement to EDX studies due to its benefit in both pre-operative planning and post-operative comparison.

Assessment of pre-operative imaging to identify the etiology of ureteropelvic junction obstruction: an opportunity for continued diagnostic improvement

Tyler Stallman BS, Chad Tracy MD, & Ryan Steinberg MD

Background: Ureteropelvic junction obstruction (UPJO) refers to a blockage at the junction where the renal pelvis meets the ureter. This can impede the flow of urine out of the kidney, causing it to back up into the kidney. There are many causes of UPJO, including intrinsic and extrinsic causes. The work up for a UPJO often includes a CT scan and Mag3 renal scan. While the Mag3 renal scan will confirm the presence of obstruction, it is common that the CT does not definitively identify the cause. A robotic pyeloplasty is the most common procedure performed to reconstruct the UPJ and relieve the obstruction. During surgery, the definitive etiology of the obstruction can be identified.

Purpose: We aim to assess the sensitivity of cross-sectional imaging for various etiologies of UPJO, as well as assess whether differences in Mag3 parameters exist between different UPJO etiologies.

Methods: We conducted a retrospective chart review of adult patients that underwent robotic pyeloplasty between 1/1/2010 and 1/1/2025. Data collected included demographics, operative findings, radiology imaging, lab results, and clinical outcomes. Radiology imaging was reviewed by a single reviewer (TS). Descriptive statistics were generated. Confusion matrices were also constructed. Comparison of Mag3 renal data was performed using the ANOVA test with significance defined as $p<0.05$.

Results: A total of 141 patients were included in the analysis (40% male, 60% female, mean age 45 years, 93% White). Nearly 47% had a history of prior endoscopic procedures, while 10% had undergone open, robotic, or laparoscopic interventions. Among pyeloplasty procedures, 99% were performed robotically. The most common etiologies were crossing vessel (46%), stenotic segment (35.5%), and high insertion (10.6%). Computed tomography (CT) demonstrated limited sensitivity across etiologies (crossing vessel 0.35, stenotic segment 0.18, high insertion 0). Although, CT maintained high specificity (crossing vessel 0.91, stenotic segment 0.94, high insertion 0.99). Analysis of Mag3 renal scans using ANOVA revealed a significantly longer mean time to maximum activity in patients with high insertion (29 min) as compared to crossing vessel (20.7 min) or a stenotic segment (17.4 min, $p = 0.015$). Differences in upslope across etiologies were not statistically significant.

Conclusion: In our analysis, CT imaging displayed poor sensitivity but excellent specificity for predicting the etiology of UPJO prior to surgery highlighting the diagnostic limitations of CT. Among etiologies, high insertion was associated with a significantly prolonged time to maximum activity on Mag3 renal scans. This suggests that subtle functional differences may aid in preoperative etiology assessment.

Radiation exposure during sacral neuromodulation implantation procedures

Student: Summer Struve
Mentor: Annah Vollstedt, MD
Collaborators: Sydney Houlton, MS, Joanna Orzel, MD

Background: Sacral neuromodulation is an established treatment for various pelvic floor conditions, including urinary urgency incontinence, nonobstructive urinary retention, and fecal incontinence and can provide significant improvements in quality of life. Sacral neuromodulation involves placing a lead next to the S3 nerve root in the operating room to treat these conditions. The use of fluoroscopy during sacral neuromodulation implantation has been associated with decreased intra-operative time and has improved lead placement. However, there is currently no standardized protocol regarding fluoroscopy use during these procedures, leading to substantial variability in fluoroscopy time and radiation exposure across surgeons, institutions, and specialties.

Purpose: This study aims to characterize fluoroscopy time and radiation exposure during sacral neuromodulation implantation and to identify key risk factors and potential interventions to minimize exposure for all operating room personnel.

Methods: We conducted a prospective study collecting intraoperative radiation exposure data during sacral neuromodulation implantation at 5 institutions for 6 months. Variables collected included patient clinical information, surgeon and institution identifiers, stage of procedure (stage 1 vs full implant), presence of trainees (residents or fellows), fluoroscopy time, radiation dose, and dosimetry measurements. Study-specific dosimeters were worn by primary surgeons, trainees, and medical device representatives.

Results: Data has been collected from 14 surgeries at one institution over 2.5 months. The mean fluoroscopy time was 71.75 seconds (range: 33.2-134.2; SD 30.97). The mean total radiation dose was 65.57 mGy (range: 18.64-134.52; SD 32.08). The average total procedure time was 69 minutes, (range: 69-118.2; SD 20.4). Dosimetry data showed an average exposure of 24.13 mRem (range: 11-33; SD 11.6) with one surgeon reaching 5% of their yearly 5000 mRem exposure limit in 9 surgeries.

Conclusions: These results show significant variability in fluoroscopy time and radiation dose between the surgeries included. Further investigation with multi-institutional data is warranted to identify modifiable factors and develop standardized protocols to reduce radiation exposure during sacral neuromodulation implantation.

Title: Changes in Meteorologic Variables Impact the Incidence of Latent Tuberculosis Infections among Children in Vietnam

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Background: Tuberculosis (TB) is a prevalent and deadly disease caused by Mycobacterium tuberculosis (Mtb). TB is seasonal, with meteorologic changes in climate having documented effects on disease incidence. However, the effects of specific meteorologic variables are unclear, with different studies reporting opposing effects of the same meteorologic variable. In addition, current studies primarily study the incidence of active tuberculosis, not latent TB. In our study, we propose a method to study the effects of meteorologic variables on latent tuberculosis infection incidence in our pediatric household contacts cohort in Hanoi, Vietnam.

Hypothesis: We predict that increasing levels of heat, precipitation, particulate matter (PM2.5), and relative humidity will be associated with an increase in the risk of LTBI conversion. In contrast, we predict increasing levels of UV and wind speeds will be associated with a lower risk of LTBI conversion.

Methods: Initially, individuals in our study catchment area within Hanoi city limits and recently diagnosed with active TB infection were designated as index cases. A prospective cohort of healthy children that were household contacts of these index cases, lived with index cases within two months of enrollment, and were less than 16 years of age were enrolled. Those with a history of a positive tuberculin skin test (TST) or known adverse reaction to a TST were excluded. This cohort was followed from 2017-2020, with individuals undergoing a TST every 3 months to determine LTBI conversion status.

A climate reanalysis model, ERA5, was accessed from the European Centre For Medium-Range Weather Forecasts' (ECMWF) Climate Data Store (CDS) for all meteorologic data other than air quality. PM2.5 data, a measurement of air quality, was extracted from the Global High-resolution and High-quality Air Pollutants (GHAP) dataset utilizing the Argon High-Performance Computing (HPC) system at the University of Iowa.

Chi-square and t tests were applied to describe baseline characteristics by LTBI status. Confounders for our regression models were determined by use of direct acyclic graphing (DAG). For the prospective cohort component of the study, multivariable GEE logistic regression models were fit, with TB infection as the dichotomous outcome and meteorologic variables as predictors, using an exchangeable correlation structure with household ID as the grouping variable. To account for lagged effects of our meteorologic variables, a cross basis for each exposure was built utilizing a distributed lag nonlinear model (DLNM) framework and applied to its respective GEE regression model.

Results: Our study cohort consisted of 109 children (38% female, mean age 7 years). 39% of children lived in a household which had an individual that completed college/university, 61% of children lived with at least one smoker, 54% of children lived in a household that owned at least one motorcycle, and 28% of participants slept on the ground floor, with the rest sleeping on at least the second level or higher.

Hanoi is a subtropical city as evidenced by an average daily temperature of 24.7 °C (10.1 °C – 34.6°C), average daily UV exposure of 1574.9 kJ/m^2 (157.3 kJ/m^2 - 3264.6 kJ/m^2), and total daily rainfall that averages 5.8mm a day, but can reach as high as 191mm. Odds ratios derived from GEE model analysis suggest that lower temperatures (between 15-22°C) have a lagging protective effect at 1-2 months, in line with our hypothesis. In contrast, the odds ratios increased for the same temperature range at lag 0-2 days. UV exposure between 2000-3000 kJ/m^2 displayed increased odds ratios at a lag of 2-3 months, refuting our initial hypothesis. Low UV exposure (below 1000 kJ/m^2) displayed mixed effects: between lagged months 0-1 and 2-3, it increased the odds of LTBI conversion. However, at lag 1-2 months, this same range displayed a strong protective effect. Increasing precipitation consistently displayed an increased odds ratio at lag 1 months, aligned with our hypothesis.

Conclusion/Discussion: Initially, we anticipated that heat would be predictive of LTBI conversion given Mtb's ideal growth conditions. Through our analyses, we found that cooler temperatures were protective within a specific lag window (1-2 months). We also predicted that moisture in the air would be associated with increased risk of conversion when considering Mtb's primary method of transmission via airborne droplets; this was supported by our findings at lagged 1 month. While analyzing UV exposure, we found our hypothesis was not supported. We attribute this to host behavioral changes associated with high UV exposure: with increased UV exposure, we postulate that individuals are more likely to spend time indoors in close quarters, potentially increasing the risk of disease transmission. Limitations of this study are important to note, as statistical power was limited due to small sample size, and exact LTBI conversion timeframes are unclear within each 3-month gap between testing instances. Moving forward, GEE analysis will be performed on additional variables (relative humidity, wind speed, and PM2.5). In addition, we will fit multivariable COX proportional hazard models, with TB infection as the outcome and meteorologic predictors as variables, using the same selection criteria for the confounders as the multivariable GEE logistic regression models to acquire and represent time to event data.

Light Exposure Correlates with Disease Severity and Retinal Function in X-Linked Retinoschisis

Jacob M. Thompson, Arlene V. Drack MD

Introduction: Juvenile X-linked retinoschisis (XLRS) is a vitreoretinal disorder and the leading cause of juvenile macular dystrophy in males. Lack of functional RS1 protein leads to structural changes within the retina such as retinal layer separation, known as retinoschisis, which separates the bipolar cells (inner nuclear layer) from the photoreceptors (outer nuclear layer). Optical coherence tomography (OCT) enables visualization of retinal structure and cyst presence. Absence of RS1 also leads to changes in the full-field electroretinogram (ERG) which measures the mass electrical response of the photoreceptors and bipolar cells to light stimulation. Previous reports in the literature have shown that patients with XLRS experience some diurnal variation with cysts being most prominent in the morning. These studies have also investigated the effect of these fluctuations on clinical measures such as best corrected visual acuity (BCVA) and microperimetry with no significant associations found. Interestingly, although ERG is an important diagnostic tool and endpoint in animal model studies, there is no literature on the effect of these diurnal fluctuations on ERG amplitudes in patients with XLRS. Our study aims to elucidate both the association between cyst severity and ERG amplitudes, as well as diurnal changes in both metrics. These results will inform both how the timing of imaging/ERG can affect endpoint results in treatment trials as well as the link between light and retinal characteristics in XLRS which may present opportunity for novel treatments.

Hypothesis: There is a negative correlation between retinal thickness, a proxy for cyst severity, and time of day. There is a positive correlation between the time of day and amplitudes on electroretinogram. There is a negative correlation between BCVA and time of day.

Methods: Retrospective chart review of individuals being followed at the University of Iowa with molecularly diagnosed XLRS. Metrics gathered include OCT, ERG, and BCVA. The macula was imaged using Heidelberg OCT. Full-field ERGs were obtained with the Diagnosys system using the standard International Society for Clinical Electrophysiology of Vision (ISCEV) protocols. Central macular OCT images were analyzed using the Heidelberg OCT Software. A linear mixed model was run using R Studio (RStudio 2025.05.1) to test if there were significant correlations between time of day and ERG, OCT, and BCVA values while controlling for age and eye sidedness.

Findings/Results: On OCT measurements in the central macula are significantly correlated with time of day, showing decreasing retinal thickness throughout the day. This region, responsible for sharpest vision, is also typically the first area XLRS patients lose vision. In ERG the dark adapted 0.01 b-wave amplitudes, representing rod response, show significance with amplitudes increasing throughout the day. IOP was not correlated with time of day. Distance BCVA trended toward significance ($p=0.0568$), though it did not meet the conventional threshold.

Conclusion: These data are important as they closely follow observations in our mouse model of XLRS that demonstrate how light exposure affects schisis severity. In the current human study, time of day is likely a surrogate for hours of light exposure. Additionally, our study suggests there may be an association between time of day and BCVA in XLRS patients which has not previously been reported. This finding warrants further investigation to determine to what extent light exposure can be used to improve patients' condition. This could lead to drastic changes in recommendations to patients and could even result in new treatments for this condition.

Title: Exploring Prevalence of Mood Disorder Symptoms in those with Lifelong HIV Infection: A Sub-Study of Neurovascular Health in Perinatally Infected Young Adults with HIV in Uganda

Authors: Katherine Timboe, McKenna Major, Linder H. Wendt, J. Brooks Jackson, Juliane Etima, Rita Nakalega, Julie C. Gudenkauf

Introduction: HIV remains a major public health issue, affecting approximately 41 million people worldwide, with the highest burden in countries in sub-Saharan Africa. Since the beginning of the HIV epidemic, an estimated 11 million individuals have been born with perinatally acquired HIV (PHIV). Thanks to expanded access to antiretroviral therapy (ART), many of these children have survived into adolescence and young adulthood. As they mature, young adults with perinatally acquired HIV encounter novel psychosocial and health-related challenges.

Mental health disorders commonly onset during adolescence, with about 75% presenting by the mid-20s. Young adults with PHIV face unique stressors compared to their HIV-negative peers, including increased risks of poverty, homelessness, parental loss, and stigma related to their HIV status. Evidence suggests that youth living with HIV may bear a higher burden of anxiety and depression compared to uninfected peers. Although studies have shown that Ugandan adults living with HIV experience higher rates of mood disorders compared to the general population, such comparative studies have not yet been conducted among a population of perinatally infected young adults.

Hypothesis/Purpose: This study aims to describe the prevalence of mood disorder symptoms among young adults with perinatal HIV infection in Kampala, Uganda, compared to age- and sex-matched HIV-negative controls, as a sub-study of a larger project investigating correlates of carotid arterial pathology and neurocognitive function in young adults with perinatal HIV infection.

Methods: The parent study was a cross-sectional study of young adults in Kampala, Uganda, living with and without HIV. Participants were included in the variable group if they were age 24-30 from the Youth Generation Alive (YGA) group living with HIV contracted perinatally. Exclusion criteria consisted of inability to provide informed consent or speak English/Luganda and inability to undergo carotid ultrasound.

The study enrolled 58 participants: 29 participants had a documented perinatal HIV infection, and 29 participants were age and sex matched HIV negative controls. Depression and anxiety were assessed using validated psychometric instruments, the Patient Health Questionnaire-8 (PHQ-8) and Generalized Anxiety Disorder 7-item (GAD-7), respectively, with continuous score data collected from participants in both groups. Participants also completed a basic questionnaire regarding health behaviors. A two-tailed t-test (alpha = 0.05) was employed to determine whether there was a statistically significant difference in mean depression or anxiety scores between the two groups.

Results: Depression scores were significantly higher among individuals with PHIV compared to controls (mean PHQ-8: 3.66 vs. 1.90, $p = 0.0009$). By contrast, anxiety scores did not differ significantly between groups (mean GAD-7: 2.41 vs. 2.14, $p = 0.65$).

Conclusions: This study highlights an increased burden of depressive symptoms among young adults in Uganda living with perinatal HIV infection, compared to their HIV-negative peers in Kampala, Uganda. These findings underscore the need for more research on mood symptoms in the population living with HIV and whether routine mental health screening and integration of psychosocial support within HIV care programs might improve overall health outcomes and quality of life in this population.

Abstract Title: **Speech Outcomes After Deep Brain Stimulation of the Subthalamic Nucleus in Parkinson's Disease**

Mentor: Dr. Jeremy D. W. Greenlee, Professor of Neurosurgery, Department of Neurosurgery

Student: Gabriel Toea

Introduction: The subthalamic nucleus (STN) is an important structure located within the basal ganglia. It plays an important role in various cognitive, motor, and limbic functions, making it an important target for the treatment of Parkinson's disease (PD). Up to 89% of PD patients experience hypokinetic dysarthria resulting from damage to the basal ganglia. In these patients, speech is characterized by a monotone, harsh or hoarse voice quality, imprecise articulation, and a variable speaking rate. Currently, Deep Brain Stimulation (DBS) of the STN is an effective treatment that helps alleviate some of the motor impairments seen in patients with advanced PD. However, STN-DBS treatment negatively impacts patient speech outcomes as demonstrated by declines in patient semantic and phonemic verbal fluency. Furthermore, there is evidence showing that > 30% of PD patients have speech deteriorations that do not improve once DBS stimulation is turned off and that speech changes are more prominent with bilateral and left STN stimulation. Despite the current understanding regarding the effects of DBS treatment on speech outcomes in PD patients, the structural and functional connectivity profiles of patients with worsening speech following DBS treatment are still being analyzed. The purpose of this project was to analyze the structural and functional connectivity profiles of 38 PD patients undergoing STN-DBS treatment as it relates to speech intelligibility, listener effort, and speech severity measures.

Methods: DBS electrode leads were localized for each patient using LeadDBS, an open-source software specifically designed to recreate DBS electrodes within deep subcortical structures. Volume of tissue activated (VTAs) were then calculated for each patient based on their DBS electrode stimulation settings. The resulting VTAs were used as seeds for fiber tracking and network connectivity analyses. Meanwhile, postoperative speech measures were obtained at 6- and 12-month intervals for each patient. The structural and functional connectivity profiles for each patient were computed using a normative connectome containing fMRI and DTI data from 85 PD patients. Cross validation analyses using leave one patient out and k-fold methods were used to ensure model robustness.

Results: A structural connectivity profile was created from a 38 patient dataset using three separate speech outcome measures. The models analyzing patient speech intelligibility, listener effort, and speech severity were internally robust and the model analyzing speech intelligibility yielded a strong predictive capacity when evaluated on a small out of sample dataset. A functional connectivity model was also generated using the listener effort and speech severity measures highlighting brain regions associated with higher and lower speech outcome scores.

Conclusion: The current project demonstrated the ability to use patient specific STN-DBS data to accurately generate structural and functional connectivity models that might help explain the speech outcomes seen in patients undergoing STN DBS treatment. Future projects should aim at utilizing individual patient DTI data to create more robust structural connectivity models that also consider individual patient anatomy. Additionally, larger patient datasets are needed to create better models that have a robust predictive capacity.

Enhancing Melanoma Patient Education Through Animation: A Prospective Study of Patient Comprehension and Anxiety

Jaden Troxel; Daniel Haws; Maggie Landherr; Luke Geis; Nicole Negbenebor, MD; Vincent Liu, MD; Jennifer Powers, MD

Background:
Video-based education is increasingly used in medicine as a tool to make complex information more accessible. Prior studies suggest it can improve patient comprehension and reduce anxiety, but its overall effectiveness has yet to be clearly established. Melanoma provides a particularly important context in which to study this approach. Patients often face substantial anxiety at diagnosis and throughout surveillance, while uncertainty about risk, follow-up, and self-examination can compound distress. Assessing how video-based interventions influence comprehension and anxiety in melanoma patients will help shape evidence-based approaches to patient education.

Purpose:
This study aimed to develop a five-minute animated video to educate melanoma patients about their diagnosis, management, and long-term expectations, and to evaluate its impact on patient understanding and anxiety.

Methods:
A five-minute animated melanoma education video was created by a medical student in collaboration with dermatologic physicians and residents to ensure accuracy and relevance. The video was embedded in a Qualtrics survey assessing demographics, baseline understanding, and anxiety, with repeat measures following the video. Eligible participants included adults with a current or prior melanoma, those undergoing biopsy for a suspicious lesion, and individuals at elevated melanoma risk attending routine surveillance. Surveys were administered in dermatology clinics at the University of Iowa main campus and Iowa River Landing, with options to complete on clinic iPads, personal devices, or at home via QR code. The primary investigator and three supervised medical students assisted with in-person survey administration. In addition, schedulers distributed links and QR codes to patients referred for melanoma excision or Mohs surgery.

Results:
A total of 102 participants completed the survey (53% female; mean age 58.6 years). Most reported a prior (52%) or current (32%) melanoma diagnosis. Self-reported understanding of melanoma improved significantly after the video, with mean scores increasing from 3.86 to 4.16 on a 5-point scale ($p < .0001$). Nearly all participants (95.9%) reported the video improved their understanding ($p < .0001$). Older age was modestly associated with smaller gains in understanding ($\rho = –0.24$, $p = .02$). Anxiety also improved, with mean scores increasing from 2.73 to 3.32 ($p < .0001$), and 61.0% reported reduced anxiety ($p = .034$). Composite anxiety scores improved modestly ($p = .047$), with no significant differences by gender or other demographic factors. Overall, 96% of participants indicated they would recommend the video to other melanoma patients, and 60% wished they had received it earlier in their care.

Conclusion:
A brief animated video significantly improved melanoma patients' understanding and modestly reduced anxiety, suggesting its greatest value lies in education. Variability in anxiety response highlights the need to examine why some patients derive greater benefit than others. These findings support video-based education as a valuable adjunct in melanoma care and point to opportunities for tailoring future interventions to diverse patient needs.

Title: Effects of healthcare personnel support on the likelihood of breast milk feeding in the postpartum period

Authors: **Sarah Upton, MS**, Donna Santillan, PhD, Meghan Funk, BA, Sarah Costello, MD, Mark Santillan, MD, PhD, and Noelle Bowdler, MD

Introduction: Health organizations including the World Health Organization, American Association of Pediatrics and the American College of Obstetricians and Gynecologists all recommend exclusive breast milk feeding (eBMF) for the first 6 months of an infant's life. In the United States >80% of parents initiate breast milk feeding (BMF), however only 27% continue exclusively BMF through 6 months postpartum. Factors shown to affect parental infant feeding decisions include intention to breastfeed, clinician advice, myths about breastfeeding, trouble breastfeeding, attitudes and social norms, and self-efficacy. Previous research has shown that providing adequate breast milk feeding support decreases the likelihood that a mother will experience BMF difficulties.

Purpose: To evaluate the effect of support from health care personnel for breast milk feeding during the pre- and post-natal period on the likelihood of continuing to breast milk feed at and after hospital discharge.

Methods: This study involves a secondary analysis of an existing data set extracted from University of Iowa Health Care's Maternal Child Knowledgebase, as well as a retrospective cross-sectional chart review to gather additional variables on the same patient population. The existing database includes mother-infant dyads who delivered at the University of Iowa Hospitals in 2022 and had documented they intended to BMF. Data on primary outcome (Infant feeding status at discharge, 2-5 day follow up, 2 week follow up, and 2 month follow up) and co-variables that may influence BMF were collected from the existing data set and manually extracted from the electronic health records (EHR) of 140 mother-infant dyads who met the inclusion criteria of delivery at term (> or equal to 37 weeks' gestation), mother 18 years of age or older at delivery, first time mothers (para = 0), and both mother and infant(s) living at discharge. Statistical analysis was done using logistic regression and one way ANOVA, and significance was determined using $p<0.05$.

Results: Of the 140 mother-infant dyads analyzed, at hospital discharge 120 infants (85.7%) were exclusively BMF (eBMF), 13 (9.3%) were BMF and formula feeding (FF), and 7 (5.0%) were exclusively formula feeding (eFF). At their 2 month follow up, 87 infants (62.1%) were BMF, 21 (15.0%) were BMF and FF, 25 (17.9%) were eFF, and feeding status was unknown for 7 infants (5.0%). Preliminary analysis showed an infant was more likely to be eFF at hospital discharge if mother ($p<0.001$) or infant ($p<0.001$) had an increased length of hospital stay (LOS), or if there was a longer length of time between birth and first recorded skin to skin event ($p<0.001$) or first recorded BMF event ($p<0.001$). At 2 month follow up, infants were more likely to be eFF if their mother had a longer hospital LOS ($p=0.042$) and if there was a greater length of time between birth and first recorded BMF event ($p=0.002$). More lactation consultant visits in the postpartum period were associated with an increased likelihood of infant being eBMF compared to eFF at 2 month follow up ($p=0.021$). Lastly, vaginal delivery ($p=0.045$), having private insurance ($p=0.042$), and the infant having a physician as their primary care provider ($p=0.043$) were all associated with an increased likelihood that an infant would be fed breast milk at all (eBMF or FF), compared to eFF during the postpartum period.

Conclusion: Initial data analysis indicates that support from healthcare personnel, specifically lactation consultants during the postpartum period, increases the likelihood that first time mothers will continue to BMF through 2 months postpartum when compared to support prenatally and during the hospital stay for delivery. Results from this study could help to identify the type of healthcare personnel support that is most likely to lead to increased BMF. This may help guide future decisions on resource allocation and help support policy changes to improve women's and children's health in the state of Iowa.

Radiomics-based biological assessment of clots to predict mechanical thrombectomy outcomes

Student: Alexander Van Dam, M2
Mentor: Edgar Samaniego, MD, MS
Collaborator: Andres Gudino, MD

Background
The biological composition of clots may affect outcomes in mechanical thrombectomy (MT), including, but not limited to, the first pass effect (FPE).

Objective
We aim to biologically profile clots on non-contrast computed tomography (NCCT) through radiomics to assess mechanical thrombectomy outcomes.

Methods
Ten clots were retrieved following MT and imaged with micro-Computed tomography (micro-CT) and histologically analyzed. Micro-CT slides were paired with histological cuts. Red blood cells (RBCs), fibrin, white blood cells were identified and matched on micro-CT. 3D Slicer was used to isolate the clot elements and radiomics features (RFs) were retrieved. Multivariate logistic regression was conducted to identify RFs associated with these components. Spearman's rank correlation was used to correlate Micro-CT RFs with percentage of biological composition. The ten clots were identified in NCCT and NCCT RFs were retrieved. Similarly, micro-CT and NCCT RFs were then correlated. Receiver operating characteristic (ROC) sensitivity (SN) and specificity (SP) analysis was conducted to retrieve optimal thresholds for RFs associated to biological components in NCCT. Moreover, a large set of NCCT images of clots retrieved after MT were biologically evaluated through radiomics. Finally, a logistic regression was conducted to find an association between clots biological composition and mechanical thrombectomy outcome measures.

Results
The features Total Energy (*TE*) (OR: 1.35, 95% CI: 1.20-1.54, P= <.001) and Large Dependence High Gray Level Emphasis (*LDHGLE*) (OR: 1.18, 95% CI: 1.07-1.32, P= 0.01) were associated with RBCs in micro-CT. Additionally, *TE* and *LDHGLE* were correlated with histological slides with > 70% of RBCs (Rho 0.654 and Rho 0.721, respectively) and NCCT *TE* and *LDHGLE* (Rho 0.687 and Rho 0.657, respectively) of clots that had > 70% of RBCs per histology. No association was found between RFs and remaining clots components. ROC analysis showed that *TE* and *LDHGLE* were sensitive (67% and 67%, respectively) and specific (71% and 86%, respectively) to identify RBCs clot composition higher than 70% in NCCT. *TE* and *LDHGLE* thresholds were applied in 243 NCCT images of clots showing that 98/243 (40%) of clots had RBCs as the main component. The presence of more than 70% of RBCs among clots was associated with higher odds of achieving FPE (OR: 2.1, 95% CI: 1.07-4.4, P= 0.02).

Conclusion
RBC rich clots (>70% RBCs) show a statistically significant positive association with experiencing FPE during MT. Radiomic analysis of clot composition can therefore be used to estimate the likelihood of experiencing FPE during MT.

Outcomes Following Endovascular Aneurysm Repair for Ruptured Abdominal Aortic Aneurysm: A Single-Center Experience

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Department of Vascular Surgery

Background:

Endovascular aneurysm repair (EVAR) has emerged as a less invasive alternative to open repair for ruptured abdominal aortic aneurysm (rAAA). However, outcomes remain variable, and survival benefit in real-world practice continues to be evaluated. We aimed to describe baseline characteristics, early outcomes, and mid-term survival in patients undergoing EVAR for rAAA at our institution.

Methods:

We performed a retrospective review of all patients who underwent EVAR for rAAA between 2015 and 2025. Patients with previous endovascular repair, infection, and patients who expired before arriving to the operating room were excluded. Baseline demographics, comorbidities, and outcomes were collected. Kaplan–Meier survival analysis was performed to assess short- and mid-term survival.

Results:

A total of 41 patients were included. The mean age was 76 years (range 65–87), and the majority were male (93%) and White (93%). Cardiovascular risk factors were highly prevalent, including hypertension (93%), smoking history (95%), coronary artery disease (44%), and chronic obstructive pulmonary disease (39%). In-hospital mortality was 10% (n=4), and 59% of patient were discharged home. At one year, mortality reached 22% (n=9). Kaplan–Meier survival analysis demonstrated the steepest decline in survival during the early postoperative period, with relative stabilization after hospital discharge. Re-intervention was required in 22% (n=9) of patients, 6 of which required an open procedure.

Conclusions:

In this contemporary single-center series, EVAR for rAAA was associated with favorable in-hospital survival compared with historical open repair cohorts. One-year survival remained over 75%, highlighting the potential of EVAR to improve outcomes in this critically ill population. The majority of survivors were discharged home, underscoring functional recovery in many patients.

PSYCHOLOGICAL DISTRESS IN ORTHOPEDIC TRAUMA PATIENTS

Medical Student: Lauren Vande Kamp
Mentor: Michael Willey, MD
Collaborators: Christopher Eberlin, MD, Yumeng Gao, MS, Ashley Kochuyt, BS

INTRODUCTION: Psychological distress is common after musculoskeletal trauma. Elements of psychological distress including depression, anxiety, and post-traumatic stress disorder can negatively impact pain and functional outcomes after trauma. The Optimal Screening for Prediction of Referral and Outcomes Yellow Flag (OSPRO-YF) and Patient Health Questionnaire-9 (PHQ-9) can predict mental health outcomes following injury. This study aims to document the incidence and risk factors for psychological distress in the orthopedic trauma population.

METHODS: Electronic health records were reviewed for patients who underwent surgery for orthopedic trauma between December 1, 2023, and January 1, 2025. The primary outcomes were the presence or absence of moderate or greater depression symptoms and psychological distress level based on the PHQ-9 and OSPRO-YF, respectively. Six potential risk factors–age, sex, BMI, length of stay, extremity, and polytrauma status–were evaluated using logistic regression. Multivariable models included predictors significant in univariable analysis after checking for multicollinearity.

RESULTS: Among the 805 patients in our population, 18.4% had moderate or greater depression symptoms and 29.9% experienced severe psychological distress. Patients aged 10-18 years (relative risk [RR]=0.42, p=0.012) and 80+ years (RR=0.33, p=0.004) had significantly lower risk of moderate distress, while female sex (RR=1.47, p=0.039) and hospital stays of 1-2 days (RR=1.72, p=0.025) were associated with higher risk. For severe psychological distress, lower risk was observed among patients aged 10-18 years (RR=0.28, p=0.002), 65-79 years (RR=0.49, p=0.013), 80+ years (RR=0.37, p=0.011), and those with pelvic (RR=0.11, p=0.004) or lower extremity injuries (RR=0.55, p=0.015). Higher risk was associated to female sex (RR=1.63, p=0.012) and longer hospital stays (RR=2.11, p=0.002).

CONCLUSION: This study demonstrates the high incidence of mental health challenges following orthopedic trauma and the need for effective screening tools. Patients aged 10-18 and patients over 65 were less likely to experience psychological distress than adults aged 19-64, suggesting age-related resilience or varying coping mechanisms. Female patients were more likely to report distress, consistent with research on gender disparities in mental health. Longer hospital stays were associated with increased distress, showing the psychological impact of prolonged recovery. Upper extremity injuries were associated with increased distress compared to lower extremity or pelvic injuries, suggesting differences in perceived disability or recovery expectations. These findings support the effectiveness and need for screening in the orthopedic trauma population as certain patient groups are disproportionately affected.

PRICE TO PAY FOR FREEDOM TO RIDE: DEREGULATION OF ATV/UTV OPERATION IN IOWA ASSOCIATED WITH INCREASED CRASHES AND HEALTHCARE COSTS

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Background. Effective July 1, 2022, Iowa enacted House File 2130 (H.F. 2130), authorizing ATV and UTV use on secondary roadways and eligible state highways. This legislation directly contradicts established ATV/UTV safety guidelines, which identify roadways as a significant risk factor for injuries and fatalities. We hypothesize that the implementation of H.F. 2130 has led to an increase in ATV/UTV-related trauma, resulting in more severe injuries and worse clinical outcomes among riders.

Methods. This was a retrospective cohort study. Data on ATV/UTV crashes from January 1, 2020, and December 31, 2024, were obtained from the Department of Transportation (DOT). Our institution's trauma level 1 center registry was queried to identify patients admitted for ATV/UTV crash-related injuries for the same period. Patients admitted from January 1, 2020, to June 30, 2022, were included in the pre-legislation cohort and patients admitted from July 1, 2022 to December 31, 2024 were included in the post-legislation cohort. DOT data were analyzed to assess number of crashes during the pre- and post-legislation periods and crash circumstances. Demographics, injury-related information including injury severity scores, abbreviated injury scores by body region, comorbidities, drug and alcohol use, complications, intensive care unit (ICU) length of stay (LOS), ventilator days, hospital LOS, complications including return to the operating room (OR) and unplanned ICU admission, in-hospital mortality, discharge disposition, and hospitalization cost were obtained from trauma registry. Univariate analyses were performed to compare the pre- and post-legislation data $P < 0.05$ was considered significant.

Results. According to the DOT, 580 ATV/UTV crashes occurred during the study period, reflecting a 40.7% increase following legislation (339 post-legislation vs. 241 pre-legislation). Crashes on concrete/asphalt/bituminous surfaces rose significantly (61.1% vs. 48.5%; $p = 0.004$), alongside increased crashes on state highways (7.1% vs. 1.7%; $p = 0.047$) and a notable shift in crash timing ($p = 0.023$), particularly during morning (15.3% vs. 11.6%) and evening hours (27.4% vs. 20.7%). The incidence of fatal crashes nearly doubled following implementation (11.8% vs. 6.2%; $p = 0.008$). Assessing our center admissions related to ATV/UTV crashes, we observed an 11.3% increase in ATV/UTV admissions (207 post-legislation vs. 186 pre-legislation). The incidence of abdominal (26.1% vs. 12.9%; $p = 0.001$), chest (37.7% vs. 27.4%; $p = 0.032$), and upper extremity injuries (67.6% vs. 45.2%; $p < 0.001$) increased significantly post-legislation. Post-legislation, trauma center transfers increased (34.3% vs. 24.7%; $p = 0.047$). Trends observed in the post-legislation cohort included a higher proportion of chest surgeries following index encounter (2.4% vs. 0%; $p = 0.063$), more crashes involving male drivers (74.9% vs. 66.7%; $p = 0.076$), an increase in neck injuries (2.4% vs. 0%; $p = 0.063$), longer hospital stays (median 2 days [IQR 1–6] vs. 2 days [IQR 1–4]; $p = 0.084$), and more ventilator days (median 5 days [IQR 2–10] vs. 2 days [IQR 1.5–6.5]; $p = 0.090$). Unplanned returns to the operating room and unplanned ICU admissions increased significantly, both rising to 7.2% from 0.5% ($p < 0.001$). Average hospitalization costs increased to $49,218 post-legislation from $31,859 pre-legislation ($p < 0.001$).

Conclusion. The implementation of ATV legislation has been associated with increased ATV/UTV crashes, more severe injuries, higher mortality, changes in rider behavior, and greater unplanned medical interventions, leading to increased hospitalization costs. These results suggest that expanded roadway access for ATV/UTVs has adversely impacted public safety and healthcare resources.

Disease Activity in Still's Disease: A Longitudinal Data Analysis

Student: Khoa Vu, M2
Primary Mentor: Aleksander Lenert, MD MS FRCPC

Background/Purpose: Autoinflammatory syndromes (AIS) are rare rheumatic diseases that remain under-recognized. Adult-onset Still's disease (AOSD) and systemic onset juvenile idiopathic arthritis (SJIA) represent a disease continuum, sharing many features such as daily fevers, evanescent salmon-colored rash, arthritis and other systemic manifestations driven by the innate immune system. We analyzed demographics, clinical characteristics and treatments at baseline, and disease activity longitudinally in a cohort of adults with AOSD/SJIA.

Methods: We analyzed 73 patients (16 years and older at baseline) with a confirmed diagnosis of AOSD/SJIA previously identified through an *International Classification of Diseases* (ICD-10) code screening of the EMR at the University of Iowa Hospitals and Clinics (UIHC) and the Stead Family Children's Hospital from 2009 through 2022. We collected patient demographics, clinical characteristics, laboratory studies and treatments. We performed longitudinal analyses (mean response profiles) of acute phase reactants (APR) and validated disease activity scores (DAS) over 6 months for the whole cohort and stratified by risk group. All analyses were done in SAS.

Results: Baseline characteristics and treatments of the cohort are presented in Table 1. The cohort was predominantly female (66%), non-Hispanic (88%), and white (71%) with a mean age of 36.1 (16.4) years. Sixteen subjects had pediatric-onset disease (<18 years) with a mean age of 13.5 (5.9) years at diagnosis, while 57 subjects were diagnosed in adulthood with a mean age of 39.0 (14.5) years. Arthralgia (90%), fever (82%), skin rash (81%), and myalgia (60%) were the most common presenting symptoms. Disease-related complications were notable for pleural effusion (18%), macrophage activation syndrome (15%) and renal insufficiency (12%). Related to disease activity, the cohort's mean Pouchot's Systemic Score (PSS) was 4.1 (2.3), Modified PSS (MPSS) was 4.4 (2.2) and Still's Activity Score (SAS) was 5.5 (1.7). At baseline, patients were treated with glucocorticoids (75%), anakinra (44%), NSAIDs (36%), and methotrexate (26%). Pertinent laboratories demonstrated elevated mean white blood count, ESR, CRP and ferritin (Table 2). Mean response profiles of ESR, CRP and ferritin over 6 months, in the entire cohort and stratified by DAS risk group, are presented in Figures 1-3. All three APRs decreased over time for the whole cohort ($p<0.05$). We observed significant differences in mean response profiles between low-risk and high-risk groups stratified by SAS for ESR and by MPSS and SAS for CRP; however, no significant differences between groups were observed for ferritin. Similarly, mean response profiles of disease activity scores (PSS, MPSS, and SAS) all decreased over time ($p<0.05$), and remained significant in stratified analyses ($p<0.05$ for time*group term) (Figure 4). Overall, risk stratification by SAS consistently identified two distinct groups of disease activity trajectories over time.

Conclusion: In this large cohort of adults with AOSD/SJIA, we characterized the trajectories of key inflammatory markers and composite scores. We identified two distinct groups of adults, low and high inflammatory disease, with differing mean response profiles over time. Future analyses will focus on the relations between inflammatory groups and disease-related outcomes.

Title: *Effect of ATF4 Deletion in Brown Adipose Tissue on GDF-15 Secretion Following Myocardial Infarction*
Student Name: Caden M Washburn
Mentor/Department: Dr. Renata Pereira Alambert, Internal Medicine
Contributors: Ayushi Sood, Jayashree Jena, Josh Peterson, and Vamsi Challa

Introduction: Myocardial infarctions (MI) are the most common cause of cardiovascular disease (CVD) mortality worldwide. Therapies for CVD underwent a renaissance in the 1960s which led to a sharp decline in patient mortality. The mortality rate for CVD began to plateau in 2011 and research has expanded to identify additional mechanisms to induce cardioprotection post MI. Brown adipose tissue (BAT) has drawn interest due to the known cardioprotective properties associated with uncoupling protein 1 (UCP1)-mediated thermogenesis and the release of batokines, such as fibroblast growth factor 21 (FGF21), which has been shown to mediate cardioprotection. Growth Differentiation factor 15 (GDF15) is a recently discovered batokine which is secreted by BAT in response to mitochondrial stress and β-adrenergic receptor agonism. Circulating GDF-15 levels are elevated in patients and in animal models with heart failure. Dr. Alambert's lab has discovered BAT secretion of GDF-15 contributes heavily to the increase in serum GDF-15 levels shortly after MI in mice and established that mice lacking GDF-15 in BAT have reduced survival following MI. Dr. Alambert's lab has also shown that in response to mitochondrial stress, GDF15 secretion from BAT is regulated by the transcription factor activating transcription factor 4 (ATF4). However, how GDF-15 is transcriptionally controlled within the BAT in response to cardiac stress is currently unknown and is the focus of my current project.
Hypothesis: ATF4 expression in BAT is required to induce transcriptional regulation of GDF-15 in BAT following MI, thereby promoting cardioprotection.
Method: We generated mice lacking ATF4 selectively in BAT by crossing ATF4 floxed mice with mice harboring the Cre recombinase under control of the UCP1 promoter to test this hypothesis. Myocardial infarctions were induced in the mice at approximately 10 weeks of age through ligation of the left anterior descending artery. Mice were sacrificed 3 days post MI, and tissues were collected for subsequent qPCR analysis of GDF-15, pathological hypertrophy markers (ANP, BNP, β-MHCB, etc.), pro-inflammatory markers (TNFα, F4/80, Il1β, IL6, etc.) and fibrosis markers (Col1a1, Col1a2, Col3a1). Serum was collected prior to and post MI to determine GDF15 circulating levels via ELISA. Echocardiography was performed prior to and after MI to determine cardiac geometry and systolic function. Statistical analysis was performed using GraphPad Prism Software.
Results: Mice with confirmed ATF4 deletion in BAT (KO) were found to have significantly reduced mRNA expression of GDF-15 on day 3 post MI. Our data showed no significant differences in systolic cardiac function, pathological hypertrophy, inflammatory markers or fibrosis markers between wild type controls and KO mice.
Conclusions: Our results so far indicate ATF4 is a key regulator of GDF-15 transcriptional regulation in BAT post MI. Further studies using BAT cell cultures are underway to confirm the in vivo findings in a cell autonomous manner. Future studies will focus on expanding our preliminary data to include additional mice and determining if ATF4 deletion in BAT will reduce survival following MI, as observed in mice lacking GDF15 in BAT. Our data establishes ATF4 as an important regulator of ATF4 expression in BAT with important implication for cardiometabolic health and CVD protection.

The Immunomodulatory Effects of Lactate on Neutrophils exposed to *N. Gonorrhoeae*.

Gabriel Weigel*, Willis Barr, Dr. Aimee Potter (PI)

The sexually transmitted bacterium *Neisseria Gonorrhoeae* (Gc) is an obligate human pathogen that globally effects 80 million people annually. Due to widespread antimicrobial resistance, the antibiotic ceftriaxone is the only remaining recommended antibiotic. Gc successfully colonizes and survives on genital and oral mucosal surfaces, despite the large influx of neutrophils (PMNs) that localize to the site of infection. Gc resists immunity and the various methods of PMN killing – the oxidative burst, phagocytosis and NETosis. PMNs rely on glycolysis to carry out these immune functions and secrete lactate as a byproduct, which can cause the concentration of lactate within the genital tract to exceed 100mM. Lactate has gained recognition as an important immunomodulatory metabolite, known to promote immunosuppressive M2 macrophages within the tumor microenvironment, but little is known about the effects of lactate on PMN function.

We hypothesize lactate will have an anti-inflammatory effect on PMNs as measured by the production of reactive oxygen species (ROS). PMNs were isolated from healthy donors and pre-treated with increasing concentrations of D- and L-Lactate before stimulation with PMA (positive control) or Gc to induce an oxidative burst. We used a luminol-based chemiluminescence assay to measure the production of ROS.

We found a significant reduction of the oxidative burst when PMNs were pre-treated with 80mM lactate and stimulated with PMA. When PMNs were exposed to Gc, we saw a significant reduction in ROS at 20mM, 40mM, and 80mM in a dose dependent manner. There was no difference between D- or L-lactate. We also did not see a decrease in cell viability, which was assessed by trypan blue staining and Promega's RealTime-Glo™ MT Cell Viability Assay. To test if lactate is acting through signaling pathways or metabolic blockade, we removed the lactate and saw a recovery of the oxidative burst compared to conditions that had lactate added back.

In this study, we showed that lactate inhibits PMN function at physiologically relevant concentrations when stimulated with live Gc. When we removed lactate, the oxidative burst was recovered, which suggests a metabolic blockade type mechanism of inhibition. Future studies will examine the lactate receptor, GPR81, as a non-exclusive mechanism of inhibition, and REDOX homeostasis and enzyme activity to further explore the metabolic blockade.

Dual Energy CT Assessment of Pulmonary Arterial Structure Within a Population Based Multi-center Study: MESA-Lung

Zijie (Jed) Yang, Seyed Soheil Hosseini, Dr. Eric A. Hoffman, Ph.D.

Background:

Chronic Obstructive Pulmonary Disease (COPD) is a rapidly growing contributor to mortality worldwide. Recent investigations suggest that regional perfusion deficits (hypoxic pulmonary vasoconstriction) within local regions of parenchymal inflammation is a potential contributor to the disease etiology. Additionally, airway dysanapsis (small airway diameters relative to lung size) imparts significant risk of COPD even in non-smokers. A similar assessment of arterial to lung size has not been evaluated. The NIH-supported, multi-centered MESA-Lung study incorporated a full inspiration and full expiration non-contrast CT scan in addition to a dual energy CT (DECT) contrast-enhanced scan at functional residual capacity (FRC), targeted at exploring regional perfusion characteristics. In this project, we have used the FRC scan to extract the vascular tree and to separate the arteries from the veins. Participants ranged from 59-94 years old (mean age 71), with minority ethnic groups oversampled to obtain sufficient data for analysis. A representative subset of 727 subjects from this study were chosen for the present investigation.

Methods:

The primary techniques developed in this project consisted of 1) improving the segmentation of the arterial and venous trees using a self-configuring neural network framework, 2) modifications to the algorithm for finding the graph representation of the pulmonary arterial tree, and 3) a proposed standardized method to quantify the size distribution of the proximal portions of the pulmonary arterial tree.

Segmentation of the arterial and venous trees was performed using nnUNet, a self-configuring framework for semantic segmentation of medical images. Several configurations of U-Nets were trained from scratch using a training set consisting of 60 hand-annotated DECT images, with distinct labels for the pulmonary arteries (class 1) and veins (class 2). The artery class (class 1) was selected and passed through an image processing pipeline that extracted a representation of the vasculature as a directed tree with information about each arterial segment. An algorithmic method was also developed to measure the distribution of arterial diameters at standardized distances away from the pulmonary trunk.

Results:

Among the nnUNet configurations that were tested, the low-resolution configuration with patch size 128x112x160 and spacing 1.13mm x 1.13mm x 1.13mm yielded the best results. The accuracy of the graph extraction pipeline was improved from 80% to >95% by incorporating methods to automatically resolve a subset of cases that used to require manual correction, including erroneous cycles that appear in the segmentation, short branches originating from the root which were erroneously pruned, and a specific branching pattern where thin vessels pass close to a much wider vessel.

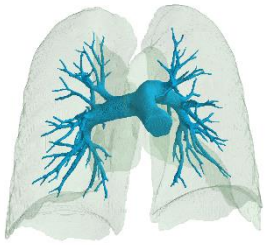

Figure 1: Segmented pulmonary arterial tree

Discussion:

The methods developed in this work can be applied to establish the relationships between pulmonary arterial geometry relative to lung size in comparison with similar features assessed to date for the airway tree. This comparison will help establish the relationships to, for instance, body mass index (BMI), smoking status, parenchymal characteristics, etc. By registering the DECT images at FRC via a deformable transformation to corresponding TLC images of the same subject we can standardize the measurement locations. When the same transformation is applied to the arterial graph, the arterial segments can be compared to their corresponding bronchial segments. The arterial size to airway size can be used as an index of downstream vascular resistance in a pre-COPD smoking population; additionally, we can establish the relationship between airway and arterial dysanapsis.

Separating DNA Synthesis and Pyrophosphatase Activities of DNA Polymerase Eta

Helen Yoo, Rem Quintin David, Zach Frevert, Sarah Jordan, Todd Washington

Translesion synthesis (TLS) is a mechanism that allows cells to continue replicating its genome in the presence of DNA damage. Non-classical polymerases, such as DNA Polymerase η (Pol Eta), with less constrained active sites are employed to replicate past the lesions. Recently, intrinsic pyrophosphatase activity has been discovered in some of these polymerases, which hydrolyzes pyrophosphate products released during DNA elongation, shifting the reaction equilibrium in the direction of continued DNA synthesis. Preliminary work in our lab suggests intrinsic pyrophosphatase activity of Pol Eta that is independent of DNA synthesis activity. This finding enables researchers to probe questions about the novel intrinsic pyrophosphate activity more directly. With this advantage, we explored what residues might be involved in the pyrophosphatase activity of Pol Eta. Using site-directed mutagenesis, mutant plasmids were generated, focusing on charged residues that might be involved in stabilizing the charged phosphate groups and polar residues that might be involved directly in the pyrophosphatase reaction. Future work in the lab will assay mutant Pol Eta activity to determine the residues involved in intrinsic pyrophosphatase activity. Since DNA replication is a fundamental process that occurs in nearly all living cells, understanding Pol Eta function has broad implications in medicine, including the role of non-classical polymerases in cancer or UV-damage response.

Pathologic extranodal extension: an undervalued prognostic factor in head and neck squamous cell carcinoma.

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Background

With 890,000 new diagnoses and 450,000 deaths each year, head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer worldwide. Pathologic extranodal extension (pENE)—defined as histopathologically-evident tumor growth beyond the lymph node capsule—is an important prognostic factor for HNSCC.

pENE-positive cancers are more aggressive, more difficult to remove surgically, and more likely to metastasize. Thus, pENE presently serves as an indication for more intensive treatment, including adjuvant chemoradiation. In this study, progression-free survival outcomes were compared by pENE status to determine whether current treatment approaches adequately address the increased risks posed by pENE+ cancer.

Methods

A retrospective review was performed of 146 patients with HNSCC, a subset of the Holden Comprehensive Cancer Center's BioMER cohort. Patients were excluded if their cancer was human papillomavirus (HPV)-positive, if they never received surgical intervention, or if they presented with recurrent disease originally treated at other institutions.

Data was extracted from clinical records in Epic, stored in a secure REDCap database, and anonymized prior to analysis in SPSS Statistics. Survival outcomes were compared using log-rank tests. The Cochran–Armitage test for trend or Fisher's exact test were conducted for all other comparisons, as appropriate.

Results

Patients who were pENE-positive had significantly worse progression-free survival outcomes than those who were pENE-negative ($P < 0.0001$). There was also a trend towards worse overall survival which did not reach statistical significance ($P = 0.2255$). Interestingly, macroscopic pENE (>2mm) was associated with significantly worse overall survival compared to microscopic pENE (≤2mm) ($P = 0.0387$).

In investigating correlations with other variables, tumors with poor differentiation ($P < 0.0001$), advanced T stage ($P = 0.0010$), and distant metastasis ($P = 0.0045$) were all significantly more likely to be positive for pENE.

Conclusion

Despite relatively rigorous treatment regimens, pENE-positive patients still suffer from significantly higher rates of recurrence. pENE status was also strongly associated with several other indicators of aggressive tumor behavior. One limitation of this study was the relatively short follow-up period, which may have limited the statistical power of some analyses.

Further research is needed to determine how we can fulfill this unmet clinical need and improve outcomes for patients with pENE-positive cancers. One promising approach involves radiologic ENE, which could potentially enable accurate risk stratification and treatment planning from the first diagnostic scan.

Weight Bearing CT Shows Altered Tibiofemoral Loading Following Combined ACL Reconstruction and Meniscus Treatment

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INTRODUCTION: The anterior cruciate ligament (ACL) and menisci act as stabilizers against anterior tibial translation. Failure to fully restore native knee kinematics and stability with ACL reconstruction (ACLR) is theorized to shift tibiofemoral loading to unconditioned cartilage regions, contributing to osteoarthritic joint degeneration. ACL-injured knees often have concomitant meniscal injuries, with certain types of meniscal pathologies known to accelerate joint space narrowing. The objective of this study was to analyze whether meniscus tears treated concurrently during ACLR shifted loading kinematics of the knee by measuring changes in the tibiofemoral center of contact (CoC).

HYPOTHESIS: The presence of a meniscus tear in an ACLR knee will cause a shift in the tibiofemoral CoC when compared to ACLR knees with no meniscus tears and non-surgical knees.

METHODS**:** Bilateral knee weight bearing CT (WBCT) scans were acquired for 66 patients (31M/35F, Age=23.07±12) approximately 12 months post-ACLR in semi-flexed (~20°) and fully extended positions. 3D joint space width (JSW) distributions in the medial and lateral compartments were calculated from WBCT using a semi-automated method. The center of contact (CoC), defined as the centroid of articular sites where the narrowest 10% of JSW values were measured in each compartment, was evaluated with respect to the overall compartment centroid. Concomitant meniscus tear type, location, and treatment were recorded. CoC location and translation between scan poses for patients with meniscal tears were compared to patients with no meniscal tears and to the patient's intact contralateral knee. Group differences in CoC medial-lateral (ML) and anterior-posterior (AP) translation were assessed using one-way ANOVA with post-hoc Bonferroni correction, significance set at p=0.05.

RESULTS**:** A concomitant meniscus tear was treated during ACLR in 43 patients. 3D JSW and CoC data were available for 32 patients with meniscus tears (medial meniscus=17, lateral meniscus=23; possible overlapping tears) and 17 patients without tears. In the medial compartment, the CoC for patients with medial tears shifted significantly more medially as the knee moved from flexion to extension, compared to intact knees (P=.02) and ACLR knees with no tear (P=.006). Although patients with lateral tears had a more medially shifting CoC in the medial compartment, it was not significant. There were no significant differences in AP translation between groups for medial and lateral tears.

DISCUSSION**:** ACL injury with meniscus tears altered tibiofemoral loading, despite meniscal treatment with either meniscus repair or partial meniscectomy during ACLR. Prior work showed that medial meniscus tears increase anterior tibial translation, while lateral tears increase rotation and translation, but only under a coupled valgus stress and internal-rotation torque/pivot shift test. The shift in CoC between poses that was observed with medial meniscal tears is consistent with these prior results. This CoC shift may be due to residual changes to the secondary stabilizing function of the menisci, despite treatment. The subsequent altered tibiofemoral loading may explain subsequent joint degeneration due to cartilage loading in unconditioned regions, and WBCT may be able to help in identifying knees at greatest risk in this regard. Accurate markers for changes in native knee kinematics, such as CoC shift, can also help predict the onset of joint degeneration, possibly leading to earlier intervention. One limitation of this study is the grouping of meniscus tears, where different tear types may have more pronounced influence on altered loading. Future work will analyze shifts in CoC in correlation to meniscus tear type and ACL graft type used.

CONCLUSION**:** In patients 1-year post-ACLR, medial tears significantly shifted CoC medially in the medial compartment.