



Abstracts

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Title: Risk Factors for Pickleball-Related Orthopedic Injuries: A 10-Year Analysis of Injury Patterns in a Rapidly Growing Sport.

Authors: Reed Adajar, Robert Westermann.

Introduction: In 2025, it is estimated that 24.3 million Americans played pickleball and the sport has grown 171% between 2022 and 2025 alone. The rise in pickleball-related emergency department visits per the National Electronic Injury Surveillance (NEISS) showed a case increase of about 750% since 2016. Current literature focusing on orthopedic pickleball injuries extends through 2022; however, there were cumulatively more estimated injuries within the last three years than from 2016 to 2022.

Purpose & Hypothesis: The purpose of this study was to describe the types and mechanisms of pickleball-related orthopedic injuries identified through existing injury surveillance data in different age groups. We hypothesized significant increases in pickleball-related orthopedic injuries to reflect growth in the sport, and a significant increase in injuries in people below the age of 50 due to the shift in the sport's demographics.

Methods: This retrospective study utilized the NEISS database to collect information about emergency department visits pertaining to pickleball. Using standard NEISS coding for type of injury, body part, etc., custom keyword-based formulas were utilized to code for variables of interest, including mechanism of injury (fall, paddle strike, etc.), non-orthopedic cases (cardiovascular events, heat stroke, etc.), region injured (shoulder/upper extremity, spine, foot/ankle, etc.), and more. Cases were included if they matched predefined criteria (fracture, strain/sprain, etc.) and excluded if they could not be clearly identified as a pickleball injury or if there was a non-orthopedic diagnosis. Weighted national estimates, 95% confidence intervals, descriptive statistics, survey-weighted contrasts, and trend analyses were generated with R version 4.6.1 using RStudio 2026.7.1.147. Survey statistics were calculated from the NEISS variables “stratum”, “primary sampling units (PSU)”, and “weight” using the survey package, version 4.5.

Results: From 2016–2025, a total of 2,013 pickleball-related orthopedic cases were identified, yielding an overall national estimate of 109,272 ED visits for the 10-year span. Mean age decreased from 63.7 to 56.6, and the proportion of injuries in people under the age of 50 has increased from 7.9% in 2016 to 28.7% in 2025. Injury types have remained similar, with fractures and strains/sprains most common. However, within the last three years there has been a decreased proportion of fracture cases, with more other/rare diagnoses consisting of differing injury types, including musculoskeletal pain. When stratified into age groups, the pickleball players under 60 years old predominantly arrive at the ED with complaints of strains/sprains whereas those over 60 are seen most with fractures. It is also noteworthy that the players under 50 have a much smaller proportion of fracture cases. Cases among individuals aged 20–49 were 10%–15% fractures, but those in the 60–79 age range had about 40% fracture cases. By grouping injuries by people under 50 and people 50 and older, the proportion of injuries in younger patients increased significantly between 2016 and 2025 ($P < .001$). There was a much larger percent increase in cases seen in people 20–29 and 40–49 between 2021 and 2025, whereas national estimates of injuries in those over 50 have not significantly increased.

Conclusion: This up-to-date retrospective analysis highlights two major points. The first is the rapid increase in pickleball-related orthopedic injuries reflecting the sport's growth in popularity. Second, injury trends in younger athletes are reflective of a shifting demographic of pickleball players. The present study offers insight for clinicians into the mechanism, types of injuries, and difference in injuries between age groups. This will better prepare providers to anticipate diagnoses, develop treatment plans, and educate patients on the risks of pickleball.

pH-Mediated Changes in Antiarrhythmic Efficacy

The Effect of pH on Flecainide Inhibition of Na channels in the Heart.

Daniel Akinremi, Christian Anderson, MD-PhD, Alex Dou, Christopher Ahern, PhD, Barry London, MD, PhD

Introduction: Ventricular arrhythmias are a common complication of myocardial infarction (MI)¹ and are found to be a predictor of late mortality in post-MI patients.² Class 1c antiarrhythmic medications like flecainide are used to treat arrhythmias and block the predominant sodium channel in the heart, Nav1.5. The CAST trial tested to see if giving antiarrhythmic medications (flecainide) to post-MI patients to treat these arrhythmias would improve their mortality. Surprisingly, they found that patients given flecainide had a higher rate of arrhythmia-related deaths compared to placebo.³ This has been attributed to an increase in reentrant arrhythmias.⁴ However, the precise mechanism by which flecainide seemed to produce a pro-arrhythmic response is unclear.

Hypothesis: We suspect that there are two mechanisms working in concert to produce these results in these patients. Firstly, we suspect that long-term flecainide treatment increases the Nav1.5 current density. Secondly, we suspect that the acidic condition created in an MI may affect how flecainide works on the Nav1.5 channel.

Method: To test this hypothesis, we transfected HEK293T cells with the SCN5a gene to stably express the Nav1.5 protein. Then we used automated patch-clamp electrophysiology to measure the Nav1.5 current in HEK293T cells.

Result: Firstly, previous work in the lab has been able to show that long-term flecainide treatment increases the Nav1.5 current density in mice. But our work this summer showed that an acidic environment is enough to reduce the Nav1.5 current. We also showed that flecainide has an increase in the IC₅₀ at an acidic pH, which is statistically significant. In other words, flecainide has a lower potency in an acidic condition. These two results seem to have opposing effects on the Nav1.5 current. On the one hand, an acidic condition reduces the Nav1.5 current, but on the other hand, it also reduces flecainide potency, which should increase the Nav1.5 current. To elucidate which pathway weighs more, we treated cells with a significant dose of flecainide at physiological pH and then gave those same cells the same dose of flecainide but now in an acidic condition. The net effect of flecainide in an acidic environment is a slight but significant 10% increase in the Nav1.5 current.

Conclusion: This finding, combined with the net increase in Nav1.5 current density in long-term flecainide treatment, proposes a complementary molecular mechanism as to why flecainide seemed to be pro-arrhythmic in post-MI patients in the CAST trial. Thus taking us a step further in fully understanding the shocking results of the CAST trial.

¹ Ruberman, W., Weinblatt, E., Goldberg, J. D., Frank, C. W., & Shapiro, S. (1977). Ventricular premature beats and mortality after myocardial infarction. *The New England journal of medicine*, 297(14), 750–757. <https://doi.org/10.1056/NEJM197710062971404>

² Bigger, J. T., Jr, Fleiss, J. L., Kleiger, R., Miller J. P., & Rolnitzky, L. M. (1984). The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. *Circulation*, 69(2), 250–258. <https://doi.org/10.1161/01.cir.69.2.250>

³ Echt, D. S., Liebson, P. R., Mitchell, L. B., Peters, R. W., Obias-Manno, D., Barker, A. H., Arensberg, D., Baker, A., Friedman, L., & Greene, H. L. (1991). Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. *The New England journal of medicine*, 324(12), 781–788. <https://doi.org/10.1056/NEJM199103213241201>

⁴ <https://www.sciencedirect.com/book/edited-volume/9780323497985/kaplans-essentials-of-cardiac-anesthesia>

Prehospital Care Needs Assessment in Riobamba, Ecuador

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BACKGROUND: Prehospital care systems vary widely across resource settings. Barriers to clinical training, equipment reliability, and system coordination potentially affect provider readiness. In Riobamba, Ecuador, emergency medical services are delivered by multiple agencies with distinct organizational structures and resources. This project sought to characterize clinical preparedness, training needs, and system-level barriers identified by frontline EMS clinicians in Riobamba as a needs assessment to guide the development of future educational programs.

METHODS: A 31-item mixed-methods survey was administered to six frontline EMS clinicians recruited through local EMS and hospital contacts. These included providers representing a variety of professions including Técnicos en Emergencias Médicas (TEM), paramedic, nursing, and physician respondents. Survey topics included clinical preparedness, procedural exposure, equipment and operational barriers, access to protocols and medical direction, continuing education, and preferred training modalities. The survey was translated by local medical Spanish faculty and reviewed by Ecuadorian emergency medicine physicians for accuracy and cultural relevance. Descriptive statistics summarized quantitative responses, and qualitative comments were reviewed for recurring themes.

RESULTS: Six clinicians completed the survey. Pediatric emergencies were the most frequently selected priority for training (3/6), and five respondents included pediatric training among the three interventions most likely to improve patient care. Exposure to pediatric and obstetric emergencies was limited, with 5/6 reporting rare or no pediatric cases and 4/6 reporting rare or no obstetric cases in the past year. Simulation-based training was selected by all respondents as a preferred educational modality, yet 4/6 reported that their EMS system did not provide simulation or skills training. Three respondents reported hesitating to perform interventions within their authorized scope of practice. They cited limited opportunities for practice, inadequate training, equipment limitations, limited medical direction, and unclear protocols as contributing factors. Access to physician or supervisory support was reported as rare or absent by 4/6 respondents. Institutional support was the most frequently identified barrier to additional training (5/6), followed by cost (4/6).

CONCLUSIONS: This preliminary needs assessment identified gaps in training, pediatric preparedness, procedural exposure, and access to system support among EMS clinicians in Riobamba. Findings suggest that sustainable EMS education initiatives should prioritize hands-on and simulation-based training as well as pediatric and obstetric emergency preparedness. As a next step, these findings support the development of a pilot simulation-based training program to be offered to a larger cohort of EMS personnel. A future study could entail a pilot simulation educational program with assessment of effectiveness.

Home Versus Office Foley Catheter Removal Following Routine Urologic Surgery: A Retrospective Cohort Study

Ryan Albright and Amanda A. Myers

Introduction

Many common urologic surgeries involve postoperative indwelling urinary catheterization to facilitate healing of the urinary tract and prevent acute urinary retention. Longer indwelling catheterization leads to decreased patient satisfaction, greater clinical resource utilization, and increased risk of urinary tract infection (UTI). Catheter removal may be performed either in the clinic with a formal voiding trial or at home by the patient. Our objective was to assess complication rates and healthcare utilization in patients undergoing home versus office foley catheter removal after urologic surgery.

Materials and Methods

A retrospective review of consecutive patients undergoing urologic surgery between November 17, 2025, and April 3, 2026, was performed. Included patients underwent an eligible procedure and had a foley catheter placed that remained indwelling for at least one day. Eligible procedures included radical and simple prostatectomy, transurethral resection of bladder tumor (TURBT), transurethral resection or incision of prostate (TURP, TUIP), cystoscopy, holmium laser enucleation of the prostate (HoLEP), irreversible electroporation (IRE) of the prostate, laser vaporization of the prostate, and Rezūm therapy. Patients were excluded if no Foley catheter was placed postoperatively (n=23), the catheter was removed on the day of surgery (n=20), or the patient was catheterized at baseline (n=10). The primary outcome was post-catheter removal complications. Complications included clean intermittent catheterization (CIC), UTI within 14 days of catheter removal, failed trial of void, foley reinsertion, urinary retention, and emergency room visits for catheter removal. Patients were grouped based on actual catheter removal location and outcomes were compared between groups.

Results

Of 258 included patients, 110 (43%) removed their catheter at home, 81 (31%) underwent catheter removal at UIHC, 15 (6%) had removal at a local clinic, and 49 (19%) underwent catheter removal while inpatient. Sixteen patients (15%) in the home-removal group experienced at least one complication compared with 18 patients (19%) in the office-based removal group. Complication rates had no statistically significant difference between groups ($p = 0.417$). Patients undergoing home catheter removal avoided an estimated 13,470 miles of round-trip travel, representing an average savings of 122 miles per patient.

Discussion

Most patients assigned to home catheter removal were able to successfully complete it without increased complications compared to office removal. Home catheter removal substantially reduced patient travel burden. These findings support the use of home catheter removal as a patient-centered strategy that may reduce healthcare utilization while maintaining comparable clinical outcomes.

Genome-wide DNA Methylation Analysis of Delirium and Clinical Outcomes in Postoperative Hip Fracture Patients

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Background: Delirium is associated with postoperative complications including prolonged hospital length of stay (LOS), resource utilization, increased morbidity and mortality. Our group previously showed epigenetic signatures associated with delirium. Epigenetic variation may also provide insight into biological processes associated with recovery or poor outcomes following surgery. We performed an exploratory epigenome-wide association study (EWAS) to identify DNA methylation patterns associated with hospital LOS and examined biological pathways represented among the strongest associations.

Hypothesis: Genome-wide DNA methylation signatures are associated not only with delirium but also with clinically meaningful postoperative outcomes such as hospital length of stay and mortality, reflecting underlying biological mechanisms.

Methods: Genome-wide DNA methylation was assessed using the Illumina EPIC v2 array in hip fracture patients with available clinical outcome data. Associations between CpG methylation and log-transformed hospital LOS were evaluated separately using preoperative samples and the first available postoperative sample. EWAS statistics were adjusted for potential test-statistic inflation using BACON. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were subsequently performed using the 1,500 CpGs with the strongest BACON-adjusted associations with LOS. Because no individual CpGs reached genome-wide significance, pathway analyses were considered exploratory and hypothesis-generating.

Results: The preoperative EWAS included 56 patients and the first postoperative EWAS included 48 patients, with 867,766 CpGs evaluated at each timepoint. No individual CpGs reached BACON-adjusted FDR <0.05 in either analysis. Despite this, exploratory pathway analysis identified biologically relevant signals based on the top LOS-associated CpGs. Notably, pathways related to mitotic spindle organization, microtubules, and chromosome alignment emerged among the potentially intriguing signals. Other pathways identified included regulation of glutamate metabolic process and positive regulation of circadian sleep/wake cycle, non-REM sleep. These pathways are of particular interest given the established roles of glutamatergic signaling and circadian dysregulation in delirium and their recurrence in previous studies.

Conclusions: Although no individual CpG associations reached genome-wide significance, exploratory pathway analysis identified potentially meaningful enrichment in glutamate metabolism and circadian sleep/wake regulation among CpGs associated with hospital LOS. The biological relevance and recurrence of these pathways across cohorts support their consideration as candidate mechanisms underlying postoperative recovery. Larger cohorts and independent validation will be necessary to determine whether these epigenetic pathways represent reproducible biomarkers or mechanisms associated with prolonged hospitalization after surgery.

The Invasive Proliferative Gelatinous Mass is a Specialized Inflammatory Niche of Hidradenitis Suppurativa

Tatiana Anderson¹, Hang Sun¹, Tanya Henry MD, Taylor Johnson, Britt Mariman, Zeina Miari, Ahmed Baig, Trevor Jackson, Jacob Belardo, Thoi D Tran, Alexander Kurjatko MD, MPH, Nicole Negbenebor MD, Lucy Wibbenmeyer MD, Michal Kidacki MD, PhD

¹Authors contributed equally and share first authorship

Background: Hidradenitis suppurativa (HS) is a debilitating inflammatory skin disease that manifests as deep-seated nodules, abscesses, sinus tracts, and scarring primarily of the intertriginous areas of the skin, including the axillae, inframammary, inguinal, and anogenital regions. The dysregulated inflammatory nature of HS leads to the formation of dermal tunnels, which are typically resistant to current therapies. Within these epithelialized tunnels is an underrecognized beefy-red jelly-like material known as the Invasive Proliferative Gelatinous Mass (IPGM). This mass appears to be central to disease pathogenesis, with removal in deroofing procedures yielding lesion resolution; however, it remains uncharacterized at the cellular level. The underappreciation of IPGM may contribute to limited and modest efficacy in current biologic therapies.

Purpose: To characterize the immunophenotype of IPGM by identifying immune cell populations distinct from inflamed lesional dermis.

Methods: Paired IPGM and adjacent lesional dermis were collected by deroofing procedures or wide local excision surgeries performed on patients with Hurley stage III HS. Immediately following tissue collection, each donor sample was enzymatically dissociated into single-cell suspensions for analysis through a 20-color flow cytometry panel. Linear mixed effects models were applied using tissue type and biologic treatment status as fixed effects and subject as a random effect. P-values were calculated by t-tests on model estimates, using Satterthwaite's method to estimate degrees of freedom.

Results: The IPGM was not composed solely of acellular debris but contained viable leukocytes, with viability comparable to that observed in adjacent lesional dermis (estimate: 1.907 ± 3.766 , $p=0.631$). Within the lymphoid compartment, IPGM was enriched for CD8⁺ T cells (estimate: 4.059 ± 0.907 , $p=0.004$) and NK-like T cells (estimate: 0.565 ± 0.265 , $p=0.077$), but diminished in CD4⁺ T cells (estimate: -2.967 ± 1.124 , $p=0.039$), with similar downward trends for Tregs (estimate: -3.667 ± 2.646 , $p=0.215$), and B cells (estimate: -6.161 ± 3.831 , $p=0.159$) when compared to lesional dermis. IPGM exhibited a nonsignificant trend toward higher T-cell activation levels defined by CD38^{high} and HLA-DR^{high} expression (CD4⁺ estimate: 3.442 ± 2.286 , $p=0.183$; CD8⁺ estimate: 1.806 ± 1.592 , $p=0.300$). Across myeloid subsets, IPGM showed reduced macrophage (estimate: -1.304 ± 0.511 , $p=0.044$) and dendritic cell proportions (estimate: -0.230 ± 0.108 , $p=0.055$).

Conclusions: Our findings identify the IPGM as a viable, immunologically active compartment within HS-affected skin rather than passive intraluminal debris. Compared with adjacent lesional dermis, the IPGM exhibited a distinct immune composition characterized by enrichment of CD8⁺ T cells, relative depletion of CD4⁺ T cells, and trends toward increased T-cell activation and reduced regulatory populations. In contrast, lesional dermis contained higher proportions of macrophages and dendritic cells. Together, these findings demonstrate that the IPGM is immunophenotypically distinct from surrounding inflamed tissue and support the hypothesis that it represents a specialized inflammatory niche with a potentially active role in sustaining HS pathogenesis.

Medical Student Research Conference Poster Presentation Abstract

- Title of the presentation- Strabismus as a Presentation of Stickler Syndrome: A Case Series
- Your name, your mentor's name, and any other collaborators: Susan Anil (M4), Dr. Alina Dumitrescu (Mentor), Dr. Valencia Potter, Tara Bragg
- Introduction with background/rationale: Stickler Syndrome is a connective tissue disorder resulting from gene mutations in collagen production. There are multiple types of Stickler Syndrome, each associated with unique gene mutations and ocular and non-ocular phenotypes. Stickler Syndrome types 1 and 2 are the most common subtypes that have ocular manifestations, which are due to mutations in the COL2A1 and COL11A1 genes respectively. Common ocular manifestations of Stickler Syndrome include progressive, bilateral high myopia, lattice degeneration of the retina, vitreous syneresis, cataracts, and non-traumatic retinal detachment. While patients may have additional symptoms of a connective tissue disorder that may prompt further investigation, many patients go undiagnosed for years, causing gaps in Ophthalmologic care.
- Hypothesis/Purpose: Although less common than the above ocular manifestations of Stickler Syndrome, it has been observed that there are patients who initially present to care due to strabismus from high myopia, known as Heavy Eye syndrome. This case series describes patients' path to diagnosis with Stickler Syndrome who first presented to care due to strabismus. The goal of this study is to recognize additional presentations of Stickler Syndrome to reduce diagnostic delays and care gaps.
- Method: The inclusion criteria for this study include patients having strabismus as their initial presenting concern that led to suspicion of Stickler Syndrome as well as a later positive genetic diagnosis. Patients who presented with strabismus without the result of an investigation for Stickler Syndrome were excluded from the study. Patients who had a clinical, but no formal genetic diagnosis were also excluded. 71 patient records were reviewed, with only 3 patients meeting criteria for study involvement. Data collected for each patient is as follows: age at presentation, chief concern at presentation, age at first strabismus diagnosis, age at first suspicion of Stickler Syndrome, age at genetic diagnosis of Sticklers Syndrome.
- Findings/Results:
 - Case #1: This patient presented to care at age 11 for a new onset of esotropia and diplopia, anisocoria, and ptosis of the left eye. Ocular history also included bilateral high myopia. The patient was first diagnosed with strabismus at age 11, and the clinician became concerned about a connective tissue disorder starting at age 12. This prompted genetic testing, and the patient received a genetic diagnosis of Stickler Syndrome at age 12.
 - Case #2: This patient presented at age 35 for evaluation of esotropia. The patient first had strabismus as a baby, with the exact age not documented. Ocular history and notable other medical history at the time of presentation included bilateral high myopia/ glaucoma/ cataracts in addition to hearing loss. The clinician became concerned about a connective tissue disorder starting at age 35, and the patient received a genetic diagnosis of Stickler Syndrome at age 35.
 - Case #3: This patient first presented to care and was diagnosed with strabismus at age 1. The patient then re-presented at age 9 for evaluation of bilateral high myopia, micrognathia, and cleft palate. The clinicians were concerned for a connective tissue disorder at age 9, and the patient received a genetic diagnosis of Stickler Syndrome at age 9.
- Conclusion/Overall significance/Broader perspective: The time in years between age of diagnosis with strabismus and genetic diagnosis of Stickler Syndrome ranges from 1-30+ years for the patient cases. While the pathway to diagnosis varies between these patients, this case series supports that strabismus can be an initial presentation of Stickler Syndrome. Further research is needed to quantify the prevalence of patients that initially present with strabismus, leading to the suspicion and subsequent diagnosis of Stickler Syndrome. Furthermore, this research is also needed to encourage prompt recognition and Ophthalmologic monitoring of Stickler Syndrome prior to the development of serious, vision-threatening disease manifestations.

Blunt cerebrovascular injury in trauma patients presenting with mandible fractures

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Student: Olivia Grace Arter, BA

Mentors: Dionne Skeete, MD; Colette Galet, PhD

Introduction. Symptomatic Blunt Cerebrovascular Injuries (BCVI) carry a high mortality rate and often incur permanent neurological damage. Research indicates that mandible fractures are a significant and independent risk factor for BCVI, along with cervical spine, basilar skull, occipital, and LeFort 2 and 3 fractures. However, the association between mandible fracture location and BCVI type, specifically blunt carotid artery injury (BCAI) versus blunt vertebral artery injury (BVAI), remains unexplored.

Purpose/Hypothesis. This study aims to address the gaps in literature by examining the association between mandible fractures and the presence of BCAI or BVAI in adult trauma populations, paying particular attention to mandible fracture locations, mechanisms of injury, and outcomes such as hospital length of stay (LOS), and in-hospital mortality. We hypothesized that there will be a stronger association between mandible fractures and BCAI compared to BVAI.

Methods. This is a retrospective cohort study including adult blunt trauma patients who suffered a mandible fracture. We gathered data on 574 cases with mandible fractures and BCVI from the TQIP database from 2019-2024 and 704 blunt trauma patients with mandible fractures from the Iowa Healthcare Trauma Registry from 2019-2025. We obtained information on demographics, injury severity, mandible fracture location, BCVI subtype, hospital course, and outcomes. Using univariate analysis, we assessed the association between mandible fractures and BCAI versus BVAI. We used logistic regression analysis adjusting for sex, age, race, and injury severity score (ISS) to assess the association between mandible fracture type and risk of BCAI versus BVAI. We compared our trauma registry data to national TQIP data to assess whether Iowa Healthcare trends were similar to national ones. $P < 0.05$ was considered significant.

Results. BCVI rate in patients who presented with mandible fractures was lower in our center (1.7%) than that reported in TQIP (3.1%). Of the 574 TQIP cases with mandible fractures and BCVI, 126 cases presented with isolated, unique mandible fractures. Most cases suffered injuries from high energy mechanism of injury (85.7%), 10.3% from assault, and 4% from low energy mechanisms of injury. Of the 126 cases, 29 (23.0%) were diagnosed with BVAI, 81 (64.3%) with BCAI, and 16 (12.7%) with both BVAI and BCAI. Demographics, mechanisms of injury, and ISS were similar between the groups. On univariate analysis, fracture pattern differed by BCVI subtype ($p=0.032$), with condylar fractures more likely to be associated with BCAI and angle fractures more likely to be associated with BVAI. These associations were not significant in multivariate analysis. ICU LOS and time on a ventilator were significantly different between the groups (5.5 days [2.25-10.75] vs. 6 days [3-14] vs. 3 days [2-3], $p = 0.001$ and 3.5 days [2.75-8.75] vs. 5 [3-9] vs. 2 [2-2.75], $p = 0.001$, respectively) with patients with both BCAI and BVAI. Hospital LOS was not significantly different between the groups (7 days [4-11] vs. 8 days [4-21] vs. 4 [3-8], $p = 0.208$). Despite a trend, mortality rates were not significantly different between the groups. (6.9% vs. 9.9% vs. 25%, $p = 0.152$).

Of the 704 blunt trauma cases with at least one mandible fracture from our center, 108 patients (15.3%) were screened for BCVI; 12 (11.1%) were diagnosed with BCVI. Among patients with BCVI, mandibular symphysis fractures were the most common (50.0%). However, none of the fracture locations were significantly associated with BCVI. BCVI resulted from high-energy mechanisms of injury in 10 cases (83.3%), assault for one case (8.3%), and a low energy mechanism of injury for one case (8.3%). Five (41.7%) patients with BCVI suffered neurological deficit, two (16.7%) suffered a stroke, and one (8.3%) died. BCVI was also significantly associated with a longer total hospital stay (13 days versus 6, $p = 0.024$) and a longer total days on a ventilator (6 days versus 4, $p = 0.005$).

Conclusion. In the TQIP cohort, BCAI was more common than BVAI among patients with isolated mandible fractures. While some association between mandible fracture type and BCVI type were observed on univariate analysis, the significance was lost when adjusting for age, sex, race and ISS in multivariate analysis. Similarly, no association between mandible fracture location and BCVI was identified in the Iowa Healthcare Trauma Registry cohort. This may be due to lower volume of injuries compared to the national database. Given that the presence of BCVI was associated with increased hospital resource utilization and substantial neurologic morbidity, a low threshold for BCVI screening should be maintained in patients with mandibular fractures to minimize missed opportunities for diagnosis and intervention.

Food Insecurity and Diabetes in Foot and Ankle Orthopedics: Implications for Risk Stratification and Care

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Introduction

Food insecurity, defined as inconsistent access to sufficient, safe, and nutritious food, affects an estimated 13.7% of U.S. households and disproportionately impacts low-income, single-parent, and racial and ethnic minority households. Food insecurity is associated with increased risk of type 2 diabetes and poorer glycemic control, potentially through reliance on inexpensive, nutrient-poor foods that promote obesity and insulin resistance. Diabetes-related foot disorders, including ulcers, infections, Charcot neuroarthropathy, and fractures, are common causes of disability and hospitalization. Malnutrition, a potential downstream consequence of food insecurity, is an established risk factor for wound complications, readmission, and mortality in orthopedic populations. Despite the plausible overlap between food insecurity, diabetes, and foot and ankle pathology, this intersection remains understudied, and reported rates of food insecurity in orthopedic populations vary widely (13.3–37%). This study aimed to (1) determine the prevalence of food insecurity in a foot and ankle orthopedic population and (2) identify disparities in food security between diabetic and non-diabetic patients. We hypothesized that food insecurity would be more prevalent among diabetic patients presenting with foot and ankle conditions and that food-insecure patients would experience higher rates of delayed healing and complications than food-secure patients.

Methods

This prospective cross-sectional study surveyed patients presenting to the foot and ankle orthopedic clinic of a Level I trauma center and tertiary hospital from May 2026 to the present. Eligible patients were ≥ 18 years old and either new patients, undergoing preoperative evaluation, or returning for conservative management. Study activities included patient-reported outcome measures (PROMs) and medical record review. Food security was assessed using the 18-item USDA Household Food Security Survey, and psychological factors were evaluated using the Patient Health Questionnaire-9. Additional measures included a food consumption questionnaire, and demographic and socioeconomic characteristics, including education level, annual household income, and insurance status.

Findings/Results

To date, 63 patients have been enrolled, with a mean age of 53.2 ± 19.1 years; 67.3% were female. Three patients (4.8%) met USDA criteria for low or very low food security. Patients with high food security ($n=50$) were compared with those with marginal, low, or very low food security ($n=13$), designated as the food insecure/at-risk group. Six patients (9.5%) had diabetes; 1 of 6 diabetic patients (16.7%) had food insecurity compared with 2 of 57 non-diabetic patients (3.5%). Household size was significantly larger in the food insecure/at-risk group (median 4 vs. 2 members, $p=0.0031$), as was the ratio of household members to income-earning members ($p<0.0001$). Patients in the food insecure/at-risk group were more likely to report annual household income below \$50,000 (28% vs. 3%, $p=0.0352$) and to be uninsured or enrolled in Medicare/Medicaid (31% vs. 5%, $p=0.0307$). Per-capita weekly grocery spending was also lower in the food insecure/at-risk group (median \$45.80 vs. \$75.00, $p=0.0090$).

Conclusion/Significance

Marginal, low, or very low food security was present in 20.6% of patients presenting to a foot and ankle orthopedic clinic and was strongly associated with socioeconomic disadvantage, including larger household size, lower household income, public insurance or lack of insurance, and lower per-capita grocery spending. Among the small subset of diabetic patients, food security risk was observed in 16.7% compared with 3.5% of non-diabetic patients; however, the limited diabetic sample precludes meaningful inference regarding this association. These findings suggest that food security risk may identify a population with broader socioeconomic vulnerabilities relevant to orthopedic care. Screening for food insecurity may help identify patients who could benefit from connection to food assistance programs and nutritional resources. Continued enrollment, particularly of diabetic patients, is needed to determine whether food insecurity is associated with delayed healing and postoperative or disease-related complications. These preliminary findings support consideration of socioeconomic screening as part of comprehensive risk assessment in foot and ankle care.

Title: Characterization of Mucin 5B Expression in Hidradenitis Suppurativa

Authors:

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Introduction/Background:

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterized by recurrent nodules, abscesses, and epithelialized dermal tunnels. Mucins are high-molecular-weight glycoproteins that contribute to epithelial barrier function, tissue hydration, and innate immune defense. In other chronic inflammatory diseases, dysregulated mucin production has been associated with persistent inflammation, neutrophil recruitment, and extracellular trap formation. However, mucin deposition and the specific mucins present within HS lesions have not been well characterized.

Hypothesis/Purpose:

We hypothesized that mucins are present within the HS inflammatory microenvironment and that specific mucin subtypes are selectively expressed in HS lesions. To explore this, we initially screened MUC3, MUC5AC, MUC5B, and MUC19, with particular interest in the gel-forming mucins MUC5AC and MUC5B. Based on the initial staining pattern, MUC5B was selected for expanded evaluation in additional HS tissue.

Methods:

Formalin-fixed, paraffin-embedded HS tissue was initially screened by immunohistochemistry for MUC3, MUC5AC, MUC5B, and MUC19 (n=5), with corresponding positive-control tissues used to confirm antibody performance. Alcian blue pH 2.5 staining was also performed to identify mucin-containing material. Based on the initial screening results, MUC5B was selected for expanded evaluation in additional HS tissue samples and a 52-core tissue microarray. Mucin expression was assessed across lesional dermis, tunnel-associated tissue, inflamed follicular cysts, and normal skin.

Findings/Results:

Alcian blue staining demonstrated mucin-containing material within the initial HS specimens. Immunohistochemical screening of MUC3, MUC5AC, MUC5B, and MUC19 demonstrated distinct mucin expression patterns. Among the gel-forming mucins evaluated, MUC5B showed reproducible expression in HS tissue, particularly in areas of dermal and tunnel-associated inflammation, whereas MUC5AC was not detected despite appropriate staining of positive-control tissue.

Conclusion/Overall Significance:

HS lesions contain mucin-rich material and selectively express MUC5B. These findings identify mucins as previously underrecognized components of the HS inflammatory microenvironment and support further investigation of their cellular source, spatial distribution, and potential roles in epithelial dysfunction, neutrophilic inflammation, tunnel persistence, and disease progression.

Reversing Aging-Associated Epigenetic Silencing in Endometrial Cancer Using Combined 5-Azacytidine and Romidepsin

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Introduction: Endometrial cancer (EC) is the most common gynecologic malignancy in the United States and frequently develops resistance to progestin therapy. Aging is associated with progressive increases in DNA methylation, which can epigenetically silence genes involved in tumor suppression and hormone signaling. Progesterone signaling is the major tumor suppressor pathway in the endometrium. This pathway is regulated through the FOXA2 → PR → HAND2 axis, in which FOXA2 functions as an upstream chromatin-opening transcription factor that promotes progesterone receptor (PR/PGR) expression, whereas HAND2 acts as a downstream mediator of progesterone-dependent stromal tumor suppression. Aging-associated promoter hypermethylation of genes within this pathway may reduce their expression, disrupting progesterone signaling and contributing to treatment resistance. The reversibility of DNA methylation and associated histone deacetylation provides a rationale to suggest that DNMT and HDAC inhibition may restore this aging-associated loss of progesterone signaling and suppress endometrial cancer growth.

Hypothesis: Combined treatment with the DNMT inhibitor 5-azacytidine (5-AZA) and the HDAC inhibitor romidepsin would reverse epigenetic silencing of the FOXA2 → PR → HAND2 axis, restore progesterone signaling, and suppress endometrial cancer growth.

Methods: Public patient datasets were analyzed to examine age-associated promoter methylation and expression of FOXA2, PGR, and HAND2. Age-stratified FOXA2-PGR and PGR-HAND2 expression correlations were also evaluated. Patient-derived EC cell lines PDC69 and PDC112 were treated with vehicle, 5-AZA, romidepsin, or combination therapy. Crystal violet staining assessed cytotoxicity, while Western blotting evaluated PR expression and PARP cleavage. Patient-derived xenograft (PDX) models were treated with vehicle or combination therapy, and tumor growth was monitored to evaluate *in vivo* antitumor activity.

Results: Increasing age was associated with progressive promoter hypermethylation accompanied by decreased FOXA2, PGR, and HAND2 expression, supporting age-associated epigenetic silencing of progesterone signaling. FOXA2-PGR and PGR-HAND2 expression were positively correlated across age groups, further supporting coordinated regulation of the pathway. Because increasing promoter methylation was associated with reduced expression of FOXA2, PGR, and HAND2, it was next tested whether inhibiting DNMT-mediated DNA methylation with 5-AZA and histone deacetylase-mediated gene repression with romidepsin could restore the expression of the epigenetically silenced progesterone signaling pathway. These findings provided the rationale for testing whether combined 5-AZA and romidepsin could restore progesterone signaling. *In vitro*, combined 5-AZA and romidepsin produced greater cytotoxicity than single-agent treatment and increased PR expression and PARP cleavage, consistent with restoration of progesterone signaling and induction of apoptosis. Combination therapy also reduced tumor growth across three PDX models, reaching statistical significance in PDX100 ($p = 0.02$) and showing favorable trends in PDC69 ($p = 0.09$) and PDC112 ($p = 0.17$). Immunohistochemistry analysis of PDX100 tumors further demonstrated increased PR expression following combination treatment.

Conclusion: Age-associated hypermethylation and downregulation of FOXA2, PGR, and HAND2 identify epigenetic silencing of progesterone signaling as a potentially reversible therapeutic target in endometrial cancer. Consistent with this rationale, combined DNMT and HDAC inhibition increased PR expression and apoptosis and demonstrated antitumor activity in patient-derived models. Clinically, restoring progesterone signaling could provide a therapeutic approach for patients whose tumors have lost hormone responsiveness through epigenetic silencing and may expand treatment options by targeting a reversible mechanism of resistance. Further validation using additional patient-derived models, immunohistochemistry of FOXA2, PGR, and HAND2, qPCR, RNA sequencing, and expanded *in vivo* studies with individual and combination treatment groups will help define the broader therapeutic potential of this approach.

Title: Differences in self-reporting nicotine use in pregnant people: comparing survey responses to paired clinical data

Names: Jordan Bayles (M2), Donna Santillan, PhD (Mentor)

Background: The negative effects of nicotine exposure in pregnancy are well-known and considered to be the leading preventable cause of pregnancy complications. Nicotine use during pregnancy is heavily stigmatized in the United States. The American College of Obstetricians and Gynecologists (ACOG) recommends that all perinatal providers screen for nicotine use, inform patients of the many risks associated, and advise cessation. Many people tend to quit nicotine use during pregnancy, but we propose that a significant amount of pregnant people are choosing not to disclose their nicotine use due to shame, guilt, and fear of judgement from their medical provider. Studies comparing self-reports to biological cotinine levels have found significant nondisclosure in pregnant people, but no studies exist comparing self-reports in research surveys to the same self-reports in the medical record.

Hypothesis: There will be a statistically significant difference between participants' self-reported nicotine use on a research survey and their self-reported nicotine use documented in the medical record.

There will be no significant difference between self-reported race and ethnicity on a research survey and their documented race and ethnicity in the medical record.

Methods: A survey on demographics, lifestyle habits, and exposures was provided to Perinatal Family Tissue Bank participants (IRB#200910784). Participants with any current or former nicotine use were identified, and self-reported nicotine use data from the medical record was extracted from the Iowa Intergenerational Health Knowledgebase (IRB#201902830). Self-reports from the survey and from the medical record for each participant were compared to identify discrepancies indicative of nondisclosure of nicotine use. A chi-square test was performed to determine significance. A similar analysis for self-reported race and ethnicity was performed on the entire cohort to compare.

Results: 200 participants self-reported current or former nicotine use in the survey. Of 165 former nicotine users, 57 (35%) did not disclose their status on the medical record. Inconsistent responses included having only passive smoke exposure and never using nicotine. All results are statistically significant, which supports the hypothesis. Of 35 current nicotine users, 13 (37%) did not disclose the same nicotine use status on their medical record. Inconsistent responses included being a former nicotine user, having only passive smoke exposure, and never using nicotine.

Of 1007 participants who self-reported their race on the survey, 34 (3%) of participants' self-reported race did not match that of their medical record. Of 990 who self-reported their ethnicity on the survey, 10 (1%) of participants' self-reported ethnicity did not match their medical record. These results were statistically significant, which does not support our hypothesis.

Conclusions: Results support the idea that a significant amount of pregnant people may choose not to disclose nicotine use status to their medical provider but may choose to do so on a research survey. This result is clinically significant as patients who do not disclose are not receiving the appropriate support and counseling. Differences in real or perceived stigma surrounding nicotine use, pressure to appear healthy, and lack of comfortability with providers are possible reasons for nondisclosure in the clinical setting compared to the research setting. Race and ethnicity results indicate a significant discrepancy between self-reports and the medical record, introducing suspicion regarding the accuracy of these reports in a clinical setting. Discrepancies may be due to clerical errors or changes in clinical practices over the five-year period in which this data was collected.

Effect of Treatment Timing with Losartan on Auditory Recovery after Noise Overexposure

Authors: Bhinu, A., Salehpour, S., Fuller, B., Bennion, D. M.

Background: The renin-angiotensin-aldosterone system, a widespread regulator of cardiovascular and fluid homeostasis, has emerging and significant roles in inner ear physiology. Angiotensin II can bind to type I angiotensin receptor to drive inflammation and fibrosis; conversely, binding to type II angiotensin receptors promotes vasodilatory, anti-fibrotic, and neuroprotective effects. Preliminary data from the Bennion lab supports the protective effects of angiotensin receptor blockers (ARBs), observing that pre-treatment of young adult CBA/CaJ mice with losartan preserved hair cell and spiral ganglion synapse and provides protection against shifts in auditory brainstem responses against noise-induced trauma.

Hypothesis: We hypothesized earlier administration of an ARB would provide greater protection against noise-induced hearing loss compared to delayed treatment, resulting in smaller auditory threshold shifts and improved preservation of cochlear hair cells and synaptic connections.

Methods: Mixed male and female mice were assigned to six groups. Each group was treated with losartan at various timepoints relative to noise exposure. All treatments were administered via intraperitoneal (IP) injection at a dose of 4 mg/kg losartan (or equivalent saline vehicle). Following the initial IP injection, mice were maintained on either losartan-infused chow (120 ppm) or matched control chow for the remainder of the study. The groups were as follows:

- Group A: Noise control, no losartan before or after noise exposure (n=13)
- Group B: No-noise control, no losartan and no noise exposure (n=8)
- Group C: Losartan pretreatment (48hrs) before noise exposure (n=8)
- Group D: Losartan treatment immediately after noise exposure (n=8)
- Group E: Losartan treatment 4 hours after noise exposure (n=8)
- Group F: Losartan treatment 24 hours after noise exposure (n=8)

Auditory brainstem responses (ABR) (measured at 8, 16, and 32 kHz from 90-10 dB) and distortion product otoacoustic emissions (DPOAE) measurements (at 8, 16, and 32 kHz) were measured prior to noise exposure and at 1- and 14-day timepoints following noise exposure. 8-16 kHz octave band noise was delivered at 105 dB SPL for males and slightly higher at 107.5 dB SPL for females due to the protective effects of estrogen against noise induced hearing loss. ABR and DPOAE threshold shifts were analyzed using mixed-model ANOVA with time and treatment group as fixed effects and animal as a repeated measure. Tukey's post hoc tests were used for multiple comparisons between groups at each time point. Significance was set at $p < 0.05$.

Results: Noise exposure resulted in elevated ABR thresholds in all groups compared to uninjured no-noise controls (Group B) by Day 1. At 8 kHz, losartan pretreatment (Group C) produced the smallest acute threshold shift, and by Day 14, the losartan pretreatment group (Group C) and the 4-hour losartan treatment group (Group E) exhibited the lowest residual threshold shifts compared with the untreated noise control Group A (3.8dB and 5.7dB versus 23.9 dB, respectively). At 16 kHz, losartan pretreatment (Group C) again showed the greatest acute protection, and both this pretreatment group (Group C) and the 4-hour losartan treatment group (Group E) recovered significantly better than Group A (C vs. A: $p=0.0427$; E vs. A: $p=0.0340$). At 32 kHz, 4-hour losartan treatment (Group E) demonstrated the best recovery.

Conclusion: The overall pattern suggests that losartan has both protective and restorative effects following noise-induced hearing loss. Pretreatment appears to reduce the magnitude of the initial injury, whereas administration 4 hours after noise exposure provides the greatest long-term preservation of auditory function. Delaying treatment to 24 hours substantially reduces efficacy, resulting in hearing outcomes that are not significantly better than untreated noise-exposed controls. Collectively, these findings reveal a therapeutic window following acoustic injury and identify early post-exposure ARB treatment as an effective strategy for preserving hearing after noise trauma. Future studies including cochlear wholemount analysis of ribbon synapses and hair cell survival will be necessary to determine whether the functional benefits of early ARB treatment arise from preservation of cochlear synapses, sensory hair cells, or both.

Body Mass Index and Psoas Muscle Index as Predictors of Outcomes Following Single-Level Lumbar Fusion for Degenerative Spine Disease

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Introduction:

Obesity is common among patients undergoing lumbar fusion and has been associated with adverse perioperative outcomes. However, most studies classify patients as obese or non-obese, potentially masking differences in obesity severity. Body mass index (BMI), the most commonly used measure of obesity, does not distinguish adipose tissue from skeletal muscle mass and may inadequately reflect physiologic reserve. Psoas muscle index (PMI), a radiographic measure of skeletal muscle mass, has emerged as a potential complementary marker of surgical risk. This study evaluated associations between BMI classifications, PMI quartiles, and outcomes following single-level lumbar fusion for degenerative spinal disease.

Hypothesis:

We hypothesized that increasing BMI classification and lower PMI quartiles would be associated with longer operative times, increased perioperative complications, prolonged hospitalization, and worse postoperative functional outcomes.

Methods:

A retrospective cohort study was performed of 520 patients undergoing primary single-level lumbar fusion for degenerative spinal pathology between 2010 and 2025. The cohort was 55.8% female with a mean age of 57.4 years. BMI was categorized according to Centers for Disease Control and Prevention classifications, and PMI was stratified into quartiles. Outcomes included operative time, estimated blood loss, length of stay, complications, readmission, reoperation, mortality, and patient-reported outcomes. Multivariable logistic and linear regression models were used to evaluate independent associations.

Results:

Compared with normal BMI, overweight, Class I obesity, Class II obesity, and Class III obesity were independently associated with operative times 20-44 minutes longer (all $p \leq 0.01$). Class III obesity was also associated with greater estimated blood loss ($\beta = 72$ mL, $p = 0.042$). Higher PMI was associated with shorter hospital length of stay (Q3: $\beta = -0.72$ days, $p = 0.049$; Q4: $\beta = -1.1$ days, $p = 0.005$) and lower odds of cerebrospinal fluid leak (Q2: OR=0.39, $p = 0.039$; Q4: OR=0.34, $p = 0.031$). Neither BMI nor PMI was associated with readmission, reoperation, mortality, or improvement in patient-reported outcomes.

Conclusions:

BMI and PMI demonstrated distinct associations with perioperative outcomes. Increasing BMI classification was associated with longer operative times and greater blood loss among Class III obesity patients, whereas higher PMI was associated with shorter hospitalization and lower odds of cerebrospinal fluid leak. Neither measure was associated with long-term functional improvement. These findings suggest that BMI and PMI provide complementary information for preoperative risk stratification.

Exploring the Association Between Adverse Childhood Experiences and Clinical, Physiological, and Self-Reported Outcomes in Multiple Sclerosis

Student: Drew Bolisay, M2

Mentor: Terry Wahls, MD, Departments of Internal Medicine and Neurology

Background

Emerging evidence suggests that early-life stress caused by adverse childhood experiences (ACEs) may alter immune regulation, potentially contributing to risk and disease progression of autoimmune diseases such as multiple sclerosis (MS). However, the true extent of this connection has not yet been determined, and quantitative analyses are needed to better characterize how a history of ACEs may relate to disease burden and disease outcomes in MS.

Objective

To compare and examine whether baseline clinical, cognitive, and metabolic outcomes differ between individuals with MS who report a history of ACEs and those who do not.

Methods

A retrospective chart review of medical records collected (MRC) from individuals with MS who enrolled in the clinical trial “Efficacy of Diet on Quality of Life in Multiple Sclerosis” (NCT05007483, IRB ID: 202104639) was performed. MRC data retrieved included neurology, primary care, urgent care, and emergency room visits for any MS-related care that occurred during two years of study participation. MRC data was inputted into a REDCap database, and cognitive function was documented as stable, improved, or worsened for each visit. Each individual’s information was protected by a study ID to ensure privacy. Baseline ACE exposure was assessed using the Adverse Childhood Experience (ACE) Questionnaire. Participants were compared based on whether or not they reported a history of ACEs. Clinical trial baseline outcomes include disability progression from the Multiple Sclerosis Functional Composite (MSFC), walking ability from the Patient-Determined Disease Steps (PDDS), cardiometabolic measures including baseline glucose, hemoglobin A1C, insulin, and triglyceride/HDL ratio, and criteria for metabolic syndrome such as baseline abdominal circumference and blood pressure. Descriptive analyses were performed on the entire participant pool without stratifying participants based on their diet assignment, to assess the impact of ACEs on MS outcomes rather than the impact of diet on MS outcomes. These analyses were conducted using SAS 9.4 software (SAS Institute, USA), and statistical significance was determined using a p-value of < 0.05 .

Results

There were no statistically significant differences between individuals with MS who reported a history of ACEs and those who did not in scores on the MSFC ($p = .6014$) or PDDS ($p = .1688$). There were no statistically significant differences in baseline glucose ($p = .1895$), hemoglobin A1C ($p = .4908$), insulin ($p = .8377$), triglyceride/HDL ratio ($p = .7359$), abdominal circumference ($p = .1818$), systolic blood pressure ($p = .9801$), or diastolic blood pressure ($p = .5156$).

Conclusion

There were no significant differences in clinical, physiological, or self-reported outcomes between individuals with MS who reported a history of ACEs and those who did not. These results may partially be affected by the small number of participants that did not report ACEs ($n = 53$), contributing to the belief that ACEs may impact MS development. Additional research is necessary to determine the association between MS and ACEs, with preference to a larger sample size and a wider range of MS outcomes.

Same target, worse aim: how aging alters cognitive precision

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Introduction: Aging affects us all and carries significant health consequences. As we age, executive function and working memory decline, significantly impacting quality of daily life. With an aging population, the prevalence of age-associated cognitive impairments is rapidly rising. While cognitive decline is often viewed simply as "slowing down," an equally critical but understudied aspect of aging is increased cognitive variability.

Purpose: To investigate how aging affects cognitive precision and accuracy using an interval timing task in a mouse model.

Methods: Young (5 mos) and old (17 mos) mice were food-restricted to ~85% of free-feeding weight and trained on an interval timing task, which required mice to estimate an interval of several seconds by making a motor response. Timing intervals required working memory for temporal rules and attention to the passage of time. We quantified timing accuracy by the mean temporal estimate and variability by the coefficient of variation across trials. During interval timing, we plan to record prefrontal activity via neuronal ensemble recordings and both dopamine and calcium dynamics via fiber photometry.

Results: Young and old mice both learned the interval timing task. When examining temporal accuracy, there was no significant difference between young and old mice. However, when analyzing trial-by-trial variability, there was an elevation in the coefficient of variation (%) in old mice, indicating decreased temporal precision. Other parameters, such as the total number of switch trials, number of rewards, and average number of responses per switch trial also showed no difference between the two groups.

Conclusion: These findings indicate a decrease in interval timing or response precision, but not overall accuracy, in aged versus young mice, suggesting that aging selectively impairs temporal consistency rather than mean timing capability. Future directions include utilizing dual photometry to map prefrontal cortex (PFC) circuit dynamics and targeted optogenetics to stimulate the ventral tegmental area (VTA) to PFC pathway to rescue cognitive precision. These data will help advance our understanding of how age changes brain circuits relevant to cognition.

AI-Derived Volumetric Intraretinal Fluid Predicts Anti-VEGF Treatment Response Beyond Central Subfield Thickness in DME

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Introduction

Diabetic macular edema (DME) is the leading cause of central vision loss in diabetic retinopathy (DR). However, response to therapy is variable, with some eyes demonstrating persistent fluid despite treatment. Predicting treatment response could facilitate earlier therapeutic escalation in incomplete responders with persistent fluid. Spectral-domain optical coherence tomography (SD-OCT) is routinely used to monitor treatment response in DME, most often via central subfield thickness (CST). However, CST reflects the combined thickness of fluid and retinal tissue at a central location and does not capture spatial distribution of fluid across the macula. Deep learning (DL)-based segmentation instead allows fluid itself to be quantified volumetrically, which may capture treatment-relevant information that thickness alone does not. We applied DL segmentation to quantify volumetric OCT fluid and tested whether baseline intraretinal fluid improves prediction of anti-VEGF treatment response beyond central subfield thickness and clinical variables.

Methods

A total of 69 eyes from 52 patients with non-proliferative DR and DME were analyzed. A previously validated DL model quantified intraretinal fluid (IRF) and subretinal fluid (SRF). Response at 2 years was defined as a $\geq 50\%$ reduction in IRF volume or $\geq 30\%$ reduction in en face IRF area from baseline. Eyes not meeting this threshold were classified as having an incomplete response. A patient-grouped 5-fold cross-validated XGBoost model identified baseline features associated with treatment response. Predictive performance was assessed using area under the receiver operating characteristic curve (AUC-ROC) for baseline IRF, central subfield thickness (CST), and clinical variables (age, sex, smoking status, BMI, HbA1c, and diabetes duration). SHapley Additive Explanations (SHAP) identified the features contributing most to model predictions.

Results

Of 69 eyes, 46 (67%) were responders, and 23 (33%) were incomplete responders. Responders demonstrated greater CST and IRF at baseline ($p=0.036$, $p=0.043$), but lower at 2 years, than incomplete responders ($p=0.039$, $p=0.023$). In cross-validated XGBoost models, clinical variables alone predicted 2-year response with an AUC of 0.58, increasing modestly to 0.64 with baseline CST but substantially to 0.77 with baseline IRF volume, indicating that volumetric fluid carries prognostic information not captured by thickness. SHAP identified baseline IRF volume as the strongest predictor of treatment response, followed by age, BMI, and diabetes duration.

Conclusions

Baseline volumetric IRF improved prediction of 2-year anti-VEGF response beyond central subfield thickness and clinical variables, indicating that AI-derived fluid volume captures prognostic information that retinal thickness does not. Higher baseline IRF was associated with greater fluid reduction at 2 years, with responders reaching lower absolute volumes despite starting with more, a pattern consistent with active, treatment-amenable disease. These findings support AI-derived IRF as a prognostic imaging biomarker that adds value over conventional thickness-based monitoring in DME.

Title: Impact of a Multidisciplinary Thoracic Outlet Syndrome Clinic on Surgical Outcomes Following First Rib Resection

Authors: Paisley Bryant, MS4, Dorcie Ann Gillette, MD, Maen Aboul Hosn, MD

Introduction: Neurogenic thoracic outlet syndrome (nTOS) is a challenging pathology due to its varied and nonspecific symptoms that overlap with other neurological disorders. There are currently no standardized diagnostic or treatment protocols for nTOS, and patients experience varying degrees of symptom improvement following surgical decompression. In 2018, our institution developed a multidisciplinary thoracic outlet syndrome (TOS) clinic to improve diagnosis and outcomes following first rib resection.

Purpose: To describe our TOS clinic, where a multidisciplinary management algorithm has been adopted, and to compare surgical outcomes before and after the development of the clinic.

Methods: A retrospective review was conducted of patients who underwent thoracic outlet decompression via first rib resection for TOS between 2008 and 2026, both before and after the creation of the TOS clinic.

Results: At our institution, the pre-clinic group included 35 patients who underwent 37 first rib resections. The post-clinic group consisted of the remaining 284 patients who underwent 318 first rib resections. In the pre-clinic group, of the 37 first rib resections performed for nTOS, 12 (32%) reported a complete symptom improvement, 17 (46%) reported partial symptom improvement, and 8 (22%) reported no symptom improvement. Of the 243 patients with nTOS in the post-clinic group, 175 (72%) reported complete improvement, 57 (23%) reported partial improvement, and 10 (4%) reported no improvement.

Conclusion: nTOS is a complex pathology whose workup should follow a standardized algorithm utilizing a multidisciplinary approach. Establishing a TOS clinic in which this approach is efficiently applied expedites the diagnosis and management of this pathology, especially for patients with equivocal examinations, ultimately leading to improved outcomes. Given the success of the multidisciplinary clinic model for the management of TOS, the same principles can be applied to improve the management of other complex pathologies.

Prediction of Ovarian Cancer Chemo-Response with Multimodal Deep Learning Analysis Integrating Clinical, Pathological, and CT Imaging Data

Ashley Callaghan, Katherine Sawaya, M.D., Rebecka Ernst, M.D.,
& Jesus Gonzalez Bosquet, M.D., Ph.D., M.Sc.

ABSTRACT

Background: Ovarian cancer remains one of the most lethal gynecologic malignancies, with approximately 70-80% of patients with high-grade serous histology responding to first-line platinum-based chemotherapy. Early, non-invasive prediction of chemotherapy response could enable personalized treatment strategies and improve clinical outcomes. Prior studies using CT-based radiomics and machine learning have demonstrated moderate predictive performance (AUC 0.65-0.87) for platinum sensitivity, but most rely on handcrafted radiomic features of 2D imaging analysis. We hypothesized that a convolutional neural network (CNN) applied to 3D-formatted CT images could more accurately distinguish platinum-sensitive from platinum-resistant ovarian cancer.

Methods: We conducted a retrospective study of patients with ovarian cancer who received standard platinum-based chemotherapy. Pretreatment contrasted-enhanced CT scans of the abdomen and pelvis were acquired and processed using novel 3D Normalized Imaging Feature Transform (NIFTI) formatting pipeline. Patients were classified into two groups based on clinical response; responders (N=211, platinum-sensitive) and non-responders (N=110, platinum-resistant). A CNN architecture was developed and trained on the NIFTI-processed 3D CT volumes. Additionally, we used multimodal models with early and late integration of clinical data, to improve model performance. The dataset was split into training and testing cohorts, 80% and 20% respectively. Model performance was evaluated using AUC.

Results: The CNN model demonstrated excellent discriminative performance for predicting platinum chemotherapy response. The training cohort achieved an AUC of 0.98, while the testing cohort achieved an AUC of 1.00, indicating near-perfect classification of responders versus non-responders. Multimodal models of chemo-response did not improve prediction performance.

Conclusions: A CNN model utilizing NIFTI 3D-formatted pretreatment CT images demonstrated outstanding performance in predicting response to platinum-based chemotherapy in ovarian cancer, substantially exceeding previously reported models using conventional radiomics and deep learning approaches. The 3D volumetric approach may capture spatial heterogeneity features that are lost in 2D or handcrafted radiomic analyses. If validated in prospective, multicenter cohorts, this tool could serve as a non-invasive imaging biomarker to guide individualized treatment planning in ovarian cancer. Limitations include the retrospective design, potential overfitting given the high AUC values, and the need for external validation.

Title: Clinical Data Artificial Intelligence Platform for Real-Time Chart Abstraction of Prostate Cancer in the Electronic Health Record

Student: Sean Carroll, M2

Mentor: Kenneth Nepple, MD

Collaborators: Jessica D. Beetner, BS; Demir J. Tuken, MS; Richard Hoffman, MD; Sarah L. Bell, MS; Colleen Campbell, PhD, MS, LGC; Madeline VanDerGraaf, MS, LGC; Alfredo Camargo Rodrigues, MD; Kathryn Marchetti, MD; Jim Blum, MD

Introduction: The rapid expansion of artificial intelligence (AI) has presented opportunities for use in clinic, quality improvement, and research. Conversational ambient AI tools have become common, but do not address the burdensome process of electronic health record (EHR) information retrieval. Comprehensive chart abstraction in cancer is particularly challenging due to the complex and longitudinal nature of data. Prior evaluation of generative AI in this context has been limited by use in specific clinical contexts and research informatics environments.

Hypothesis/Purpose: An unmet need exists to develop AI-enabled workflows for efficient and accurate real-time retrieval of data from the EHR. To address this need, we evaluated a clinical data AI platform (CDAIP) capable of ingesting the extensive charts of prostate cancer (PC) patients and creating custom summary data tables.

Method: We evaluated an institution-wide, EHR-embedded CDAIP (Evidently). At the encounter level, the platform retrieves data from structured and unstructured sources, maps to a knowledge graph, and allows user prompts to generate custom summaries. One brief, 14-variable and one comprehensive, 56-variable PC-specific prompt were developed in clinical practice for creation of PC data summary tables. For a cohort of 50 consecutive PC patients, each prompt was input and concurrent manual chart abstraction of the same PC variables was performed to establish a “ground truth.” The abstraction was performed on an initial platform (Model 1.0) and then following an update to the underlying large language model (Model 2.0) and again following an update to the specialized context layer (Model 3.0) for a total of three AI abstraction rounds. Subsequent analysis was performed to assess overall accuracy, comparison between two prompts, accuracy over time across platform models, and accuracy for each PC variable.

Results: The CDAIP generated a summary table in all patients in an average of 12.2 seconds. Evaluation across the 50-patient cohort of 10,500 data points demonstrated an overall AI abstraction accuracy of 89.3%. AI abstraction with brief prompting was 86.2% accurate; comprehensive prompting was 90.0% accurate. Overall accuracy of AI abstraction was 90.6% with Model 1.0, 88.7% with Model 2.0, and 88.7% with Model 3.0. At the PC-specific variable level, accuracy ranged from 47.3% (evaluation of specific National Comprehensive Cancer Network PC risk group) to 100% for some variables. Higher accuracy was demonstrated with variables that were structured and/or less complex.

Conclusion: We performed the initial evaluation of an EHR-embedded CDAIP with short execution latency and moderate to high accuracy for PC chart abstraction. Notably, use of a longer, more complex prompt did not degrade performance of the same variables relative to a brief prompt. The platform remained consistent over time but did not have significant improvement with technical upgrades, which implies that cancer-specific refinement learning will be needed beyond just technical advances. Variable-level analyses demonstrate both the promise of the AI platform for high-fidelity retrieval of cancer variables and areas of improvement in prompt development and the underlying model. (Work supported by AUA/Pfizer/Astellas QI grant)

Perioperative pembrolizumab increases wound healing complication rates following high grade soft tissue sarcoma resection

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Abstract

Introduction

Immune checkpoint inhibitors are increasingly being incorporated into multimodality treatment strategies for soft tissue sarcoma (STS). Among these immunotherapeutic agents, pembrolizumab, a programmed cell death protein-1 (PD-1) inhibitor, has demonstrated promising antitumor activity in sarcoma subtypes. However, their effect on postoperative wound healing remains poorly understood.

Methods

A single-surgeon, single-institution retrospective cohort study was conducted of patients undergoing STS resection between January 2020 and March 2026. Inclusion criteria included intermediate- or high-grade, deep, and ≥ 5 cm. Patients receiving perioperative pembrolizumab were compared with a control cohort without pembrolizumab exposure. The primary outcome of the study was return to the operating room (ROR) for irrigation and debridement. Secondary outcomes included admission for IV antibiotics, >4 months of wound care, or oral antibiotic usage for presumed cellulitis. Statistical analysis included multivariate logistic regression adjusted for tumor size, metastatic disease, preoperative radiation therapy, and tumor location.

Results

Data collection yielded 112 patients, with 25 receiving pembrolizumab and 87 serving as controls. ROR occurred in 40% of pembrolizumab-treated patients compared with 18% of controls ($p=0.028$). After adjustment, pembrolizumab exposure was independently associated with increased odds of ROR (OR 3.19, 95% CI 1.06-9.58; $p=0.039$). Overall wound healing complications occurred in 60% of pembrolizumab-treated patients versus 40% of controls (OR 3.04, 95% CI 1.03-8.92; $p=0.043$). Rates of intravenous and oral antibiotic use did not differ significantly between groups.

Discussion

Perioperative pembrolizumab exposure was associated with significantly increased odds of ROR and overall postoperative wound healing complications following STS resection. As immunotherapy becomes increasingly integrated into sarcoma care, patients and providers should be aware of the potential benefits (oncologic control) and risks (wound healing complications). This is a limited single-center retrospective study which supports additional multi-institutional data collection to further explore the relationship between immunotherapy and surgical outcomes.

Patients' Expectations and Education Surrounding Shoulder Surgery

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INTRODUCTION: Previous research shows that patients undergoing shoulder and upper extremity surgery frequently seek health information before surgery, commonly through internet use and non-physician sources in addition to surgeon counseling. Understanding what patients know and where they obtain information about their surgical procedures is important, especially since information found on the internet has been shown to shape surgery expectations and decision making. The purpose of this study is to investigate patients' current knowledge and information seeking behaviors surrounding their shoulder surgical procedure and pathology. Specifically, the study aims to uncover the current resources that are being utilized by patients to educate themselves regarding their surgery, patients' thoughts on the usefulness and quality of these resources, and gaps in educational resources.

METHODS: This cross-sectional survey study included patients attending the Shoulder Surgery Clinic who had recently undergone shoulder surgery. Patients were asked to fill out an anonymous survey at their 2-week postoperative visit, which was developed with the Office of Patient Experience. Specific inclusion criteria were patients at least 18 years old, able to read, and fluent in English. The survey contained 11 multiple choice questions and assessed information-seeking patterns, perceived quality and trustworthiness of the information that was available to the patient, and how prepared the patient felt for surgery. Patients rated the helpfulness and trustworthiness of each internet resource on a five-point scale ranging from "not at all" to "extremely." Data from the survey was analyzed using jamovi and RSudio.

RESULTS: A total of 130 patients completed the survey. Procedures included shoulder arthroplasty in 64 patients, shoulder arthroscopy in 51, other procedures in 9, and an unknown procedure type in 6. Mean age was 69 years for arthroplasty patients, 56 years for arthroscopy patients, 47 years for the "other procedure" group, and 55 years for those unsure of procedure type. Internet resources were used by 65 (50%) of patients. Among internet users, 54% rated the resource as very or extremely helpful, whereas 69% rated it as very or extremely trustworthy. Fifteen patients (12%) reported not knowing how to obtain additional information about their procedure; 10 (67%) of these patients underwent shoulder arthroscopy. 22 patients (17%) reported feeling underprepared for surgery; 13 of these patients (59%) underwent shoulder arthroscopy. On multivariable analysis, younger age and higher education level were independently associated with internet use, whereas surgery type was not. Education level and surgery type were independently associated with preparedness; patients undergoing shoulder arthroscopy had lower odds of feeling prepared than those undergoing shoulder arthroplasty. Internet use, surgeon discussion, and outside information sources were not associated with preparedness.

CONCLUSION: The present study provides insight into how shoulder surgery patients seek information and identifies potential gaps in current educational strategies. Internet-based health information is commonly utilized and generally trusted by patients, but its use alone does not appear sufficient to ensure preparedness for surgery. Moreover, with half of the patients using internet resources, an effort should be made to provide accurate and helpful information. Patients undergoing shoulder arthroscopy who reported difficulty obtaining information and feeling underprepared may represent a particularly important population for targeted educational interventions. By characterizing information-seeking behavior, this study can inform the development of targeted education that emphasizes postoperative pain management, activity restrictions, and wound care which may improve perceived patient preparedness before shoulder surgery.

Effects of a Very Low-Calorie Diet on Metabolic and Microbiome Profiles in Women with Obesity and Metabolic Dysfunction-Associated Steatotic Liver Disease

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Background / Hypothesis: Weight loss is the primary therapeutic strategy for patients with metabolic dysfunction-associated steatotic liver disease (MASLD). However, the impact of weight loss on the gut microbiome in individuals with MASLD remains poorly characterized. We hypothesized that a very low-calorie diet (VLCD)-induced weight loss would lead to significant changes in metabolic, hepatic, and microbiome profiles from baseline in women with obesity and MASLD.

Method: In this prospective, non-parallel intervention study, 10 women with obesity and MASLD [median age 42 years (IQR 37-46); controlled attenuation parameter (CAP) ≥ 248 dB/m] consumed an 800 kcal/day VLCD for 8 weeks. Anthropometric, metabolic, and hepatic measures were assessed pre- and post-intervention. Hepatic steatosis and stiffness were quantified by transient elastography. Stool samples were collected before and after weight loss. Microbial DNA was extracted and V3-V4 regions sequenced (Illumina MiSeq 2 $\times$ 300 bp). Fecal microbiomes were annotated using the Greengenes Databases, respectively. Longitudinal analyses were performed using TimeOmics, with each participant serving as her own control.

Results: Adherence to VLCD was 76%. Mean weight decreased by 12.7 ± 1.1 kg (11% from baseline; $p < 0.0001$), with significant reductions in waist (-9.3 ± 1.5 cm) and neck circumference (-2.1 ± 0.2 cm). Body fat percentage per bioimpedance declined by $2.0 \pm 0.5\%$ ($p = 0.0006$). Systolic and diastolic blood pressures decreased by 12.7 ± 3.6 mmHg and 9.0 ± 1.6 mmHg, respectively. HbA1c ($-0.32 \pm 0.07\%$) and HOMA-IR (-1.95 ± 0.6) improved significantly. CAP decreased by 106.1 ± 16.3 dB/m ($p = 0.0001$), indicating marked reduction in hepatic steatosis. Liver stiffness did not change. Across oral and gut niches, post-diet samples demonstrated no differences in alpha diversity and distinct niche-specific microbial remodeling. Taxa that increased in abundance included health-associated species (*A. muciniphilia*, *P. distasonis*, *A. hadrus*, *C. catus*, and *O. splanchnicus*), but also taxa linked to obesity and MASLD (*Collinsella spp.*, *Blautia spp.*, *R. gnavus*, and *Dorea spp.*). In contrast, taxa that decreased in abundance included disease-associated species (*B. wadsworthia*, *P. vulgatus*, and *D. invisus*), as well as beneficial short chain fatty acid-producing taxa (*A. rectalis*, *A. butyriciproducens*, *R. hominis*, *E. ramulus*, *A. shahii*, *B. fusiformis*, *B. caecimuris*, *L. eligens*, *F. prausnitzii*, and *P. faecium*).

Conclusions: VLCD-induced weight loss and lower fat masses were associated with reductions in hepatic steatosis, insulin resistance, and cardiometabolic risk in women with obesity and MASLD. Despite alpha and beta diversity stability, post-VLCD fecal microbiome showed distinct niche-specific remodeling. Microbiome remodeling was not unidirectional, with increased or reduced taxa abundance being potentially associated with metabolic health or dysfunction. Fecal microbiome metabolites, rather than taxa remodeling alone, might be associated with mechanisms of improved hepatic steatosis. These findings suggest that dietary weight loss may concurrently modulate metabolic and microbial pathways relevant to MASLD pathophysiology.

Weight-Bearing CT Reveals Differing Restoration of Tibiofemoral Rotational Stability and Screw Home Mechanics Following ACL Reconstruction

Justin T. Crawmer, BA; Tyce C. Marquez, MS; Brian Wolf, MD/MS;
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Introduction: Anterior cruciate ligament reconstruction (ACLR) has been shown to restore anterior-posterior stability of the knee joint; however, evidence supporting restoration of rotational stability under functional loading remains limited. We utilized tibiofemoral rotation (TFR) measured from weight-bearing CT (WBCT) to assess axial rotational stability of the knee joint in the screw-home mechanism (SHM), defined as the natural rotation that locks the knee into maximum stability during terminal extension.

Purpose: The objective of this study was to assess whether modern surgical techniques restore TFR and the SHM compared to the contralateral uninjured knee at 3 and 12 months post-ACLR. A secondary objective was to determine whether these relationships vary by the type of graft used.

Methods: Bilateral weight-bearing CT (WBCT) scans were acquired at approximately 3 and 12 months post-ACLR in semi-flexed ($\sim 20^\circ$) and fully extended poses. TFR was measured in the axial plane, and patients were excluded if TFR could not be accurately measured; patients were included even if they had knee measurements at only one time point. 3D joint space width (JSW) analyses were used to compute the center of contact (CoC) to evaluate joint loading mechanics. TFR was used to assess pure rotational aspects of loaded knee kinematics, while CoC translation was used to assess combined SHM kinematics. Restoration of tibiofemoral rotational stability was evaluated by comparing TFR and CoC between ACLR and intact knees, with sub-analysis by graft type.

Results: 67 patients (134 knees) were analyzed at 3 months, including 42 quadriceps, 15 Bone-Patellar Tendon-Bone (BTB), and 10 hamstring grafts, with an average age and BMI of 23.5 years and 25.2 kg/m². 63 patients (126 knees) were analyzed at 12 months, including 39 quadriceps, 17 BTB, and 7 hamstring grafts, with an average age and BMI of 23.0 years and 24.29 kg/m². At 3 months, ACLR knees demonstrated a significantly reduced TFR in a semi-flexed pose compared to intact knees (8.85° vs. 10.85° ; $p=0.020$), while there were no differences in TFR for the fully extended pose. The difference in TFR between the semi-flexed and fully extended poses was significantly reduced (10.36° vs. 13.12° ; $p=0.001$). By 12 months, semi-flexed TFR normalized ($p=0.442$), but the difference in TFR between poses remained deficient (11.57° vs. 13.58° ; $p=0.012$). Stratifying by ACLR graft type, the 3-month difference in TFR between poses was significantly reduced for quadriceps (10.54° vs. 12.98° ; $p=0.031$) and hamstring grafts (8.54° vs. 13.44° ; $p=0.019$), while BTB grafts showed no deficit ($p=0.37$). By 12 months, semi-flexed TFR normalized across all three graft types, and the difference in TFR between poses normalized for both BTB and hamstring groups ($p=0.41$ and $p=0.66$, respectively). There remained a significant difference in TFR deficit at 12 months for quadriceps grafts (10.70° vs. 13.10° ; $p=0.021$). Loading mechanics (CoC translation) for BTB grafts demonstrated a trend toward increased lateral translation in the medial compartment compared to quadriceps and hamstring grafts.

Conclusion: Modern ACLR largely restores normal knee rotational stability in static semi-flexed and fully extended poses by 12 months postoperatively. Rotational deficits at 3 months may be largely explained by post-surgical deconditioning, yet overall rotational TFR between poses remains significantly altered at 12 months and differs by graft type. The persistent rotational deficits and trend toward lateral translation of the CoC in the medial compartment highlight potential mechanical factors that may contribute to long-term joint wear, instability, and post-traumatic osteoarthritis risk.

Title: Relationship between Neo-ossification and Neo-angiogenesis after cochlear implantation

Student: Edward Cuao

Mentor: Andrew Claussen

Relationship between Neo-ossification and Neo-angiogenesis after cochlear implantation

Background: Cochlear implants (CIs) restore hearing by electrically stimulating the auditory nerve, but, up to 40% of recipients with residual hearing experience hearing loss following implantation. A foreign body response characterized by fibrosis and neo-ossification develops around the electrode array and may increase electrode impedance, impair electrical current spread, and compromise long-term CI performance. Neo-angiogenesis also occurs within normally acellular regions of the implanted cochlea. Although angiogenesis is a normal component of wound healing, persistent vascular remodeling may promote inflammation and pathological bone formation. This study investigates the relationship between neo-angiogenesis and neo-ossification following cochlear implantation. Throughout this investigation we used 3Dslicer and Imaris to examine temporospatial relationships between post-CI angiogenesis and ossification

Methods: PECAM-GFP reporter mice will undergo unilateral cochlear implantation and be evaluated at 10, 28, and 56 days post-implantation. Following cochlear harvest, 3D X-ray microscopy (3DXRM) will quantify the volume and distribution of neo-ossification and fibrosis. Specimens will then undergo sectioning and confocal microscopy to visualize and quantify newly formed vasculature via PECAM-GFP expression. Three-dimensional reconstructions of neo-angiogenesis will be co-registered with 3DXRM datasets to evaluate spatial relationships between vascularization, neo-ossification, and fibrosis. Regression analyses will assess correlations between these measures and comparisons between 10-, 28-, and 56-day cohorts will evaluate changes over time. Understanding the relationship between angiogenesis and the cochlear foreign body response may identify potential therapeutic targets to improve CI performance, implantation, and preserve residual hearing.

Results: Throughout the experiment, we observed a progressive increase in neo-ossification over time and growth of neo-angiogenesis directly following cochlear implantation. At earlier time points, limited new bone formation were present, while later time points showed more extensive bone remodeling. When analyzing neo-angiogenesis, we saw the most amount of vascularization at 10 days, with it stabilizing in both the 28 day and 56-day mark post implantation. Importantly, neo-ossification and neo-angiogenesis showed similar distributions within the cochlea, with both processes identified in the basal turn and ganglion regions. The basal turn, corresponding to the region of initial electrode insertion, demonstrated particularly prominent post-implantation changes. Areas of increased vascularization were observed in proximity to regions of new bone formation, suggesting a potential spatial relationship between angiogenic activity and the development of the cochlear foreign body response. The increase in neo-ossification, as well as the new vascular formation seen from 10 to 56 days, and the localization to similar cochlear regions, supports further research into whether vascular remodeling may contribute or accompany bone formation following cochlear implantation.

Conclusions: Our findings demonstrate that neo-ossification progressively increases from 10 to 56 days following cochlear implantation, whereas neo-angiogenesis is seen the most directly after implantation, and then stabilizes over time. Both of these processes occur within similar regions of the cochlea, particularly the basal turn and ganglion regions. The temporal and spatial association between vascular remodeling and new bone formation suggests that these processes may be interconnected components of the cochlear foreign body response. Although these findings do not establish a causal relationship, they support further investigation into the role of angiogenesis in post-implantation neo-ossification. For future studies, an investigation that would be able to quantify the overlap between neo-ossification and neo-angiogenesis could better establish the relationship these two factors can have in the cochlear foreign response, even though they are imaged under two different modalities. A better understanding of this relationship may help identify therapeutic targets to reduce the foreign body response, improve the performance of cochlear implants, and preserve residual hearing following implantation.

Title: Transport of neonates in extremis: Exploring goals of care conversations**Name: Kip Cullinan****Mentor: Dr. Samuel Wong (samuel-wong@uiowa.edu)****Department: Pediatrics****Background**

Throughout the United States, there are numerous neonatal intensive care units, but due to the regionalization of higher levels of care, neonates are frequently transported in critical condition. No research has examined the frequency of neonates who are transported *in extremis*, or nearing death. Additionally, no research has explored whether clinicians discuss family goals of care during neonatal transport. We propose that the transportation of neonates *in extremis* occurs on a regular basis, and family goals of care are minimally discussed between sending and receiving clinicians on transport calls.

Methods

A retrospective chart review from 2023 to 2026 was performed on institutional data from University of Iowa (UI) Health Care. The number of neonates in whom transport was requested then subsequently canceled due to death or hemodynamic instability was determined, as was the number of neonates who died within 72 hours of transport. Each patient's electronic medical record was used to qualitatively analyze their documented transport note from the receiving institution (UI Health Care). The rate of clinical notes documenting goals of care, redirecting care, withdrawing care, and stopping a resuscitation were subsequently determined for canceled transports and neonates who died within 72 hours of transport.

Results

From 2023 to 2026, UI Health Care received approximately 250 neonatal transport requests per year. During this time, 14 neonatal transfers were canceled due to patient death prior to the arrival of the transport team or during stabilization. An additional 3 transfers were canceled secondary to hemodynamic instability of the neonate, and 8 neonates died within 72 hours of being transferred to UI Health Care Stead Family Children's Hospital. Of these 25 transfers, a discussion with the referring clinician about the family's goals of care was documented in transport notes 16% of the time. Of the remaining transport notes, 33% made recommendations for redirecting care, withdrawing care, or stopping a resuscitation.

Conclusion

Transport requests for neonates *in extremes* are an infrequent, but regular occurrence that warrants further exploration. For neonates *in extremis*, our institutional data show that receiving neonatologists are rarely documenting a discussion of family goals of care with the sending clinician. Additionally, end-of-life care transitions are documented less than half the time. Further research is needed on transporting neonates *in extremis* and whether a framework can be used to train neonatologists to discuss family goals of care during transport calls.

CFTR Modulators Alter the Metabolism and Growth of Pancreatic Cancer Cells

John Davelaar, Yunxia O'Malley, Anna Prouty, Akansha Jain, Henry L. Keen, Ian M. Thornell, Andrew W. Norris, and Aliye Uc

Background: People with cystic fibrosis have significantly increased risk of pancreatic ductal adenocarcinoma (PDAC) with CFTR mutations found in approximately 12% of patients with PDAC. CFTR modulators have recently received FDA approval for targeting patients with homozygous deletion of phenylalanine at position 508 (F508del). This mutation is one that is commonly reported in PDAC. CFTR modulators are highly effective in treatment of cystic fibrosis, however, their impact on tumor biology of PDAC remains undefined. As the life expectancy of patients with cystic fibrosis continues to increase with CFTR modulators, there will be additional utility in delineating this relationship. Here we hypothesize that CFTR modulators (brand name Trikafta, abbreviated ETI) will have negatively affect cell growth and migration, increase oxidative stress, and decrease cellular metabolic rate in PDAC cell lines.

Methods: We evaluated human PDAC cell lines with intact expression of CFTR (PANC-1) and cell lines with Cells were cultured in monolayer and with 3D organoids on Matrigel. Proliferation, organoid growth, and cell migration (scratch assay) were tracked longitudinally. Oxidative stress and metabolic potential were measured using flow cytometry. Cellular metabolic rate was measured in real time using Seahorse XF assays.

Results: ETI suppressed cellular proliferation, migration, and organoid expansion in both PDAC cell lines. Additionally, we demonstrated the reversible nature of this effect when ETI treatment is substituted with control treatments. Seahorse analysis revealed that ETI downshifted cellular energy production, significantly attenuating basal and maximal mitochondrial respiration, spare capacity, and ATP coupling efficiency without disrupting mitochondrial membrane integrity. ETI also increases ROS concentration within cells treated with ETI compared to control.

Conclusions: CFTR modulation shifts the functional phenotype of pancreatic cancer cell lines in vitro, by reducing cellular respiration, replication, and migration. These findings identify an intersection between CFTR function and cellular bioenergetics, suggesting that CFTR-targeted therapies can influence pancreatic cancer cell biology per se in addition to restoring HCO₃⁻ secretion to the ductal epithelial cells.

Understanding the Impact of VEGFR2 Inhibition on Neoangiogenesis Following Cochlear Implantation in Mice

Dr. Alexander Claussen, Riley DeJohn, Fahad Hossain

Hybrid cochlear implants have been an effective rehabilitative option for patients with severe-to-profound high-frequency hearing loss and usable low-frequency hearing since their FDA approval in 2005. Although most patients initially preserve residual acoustic hearing following implantation, up to 40% subsequently experience delayed loss of residual acoustic hearing (DLRAH). The mechanisms underlying DLRAH remain incompletely understood; however, the foreign body response (FBR), characterized in part by robust neoangiogenesis, may contribute to delayed implant-associated hearing loss. Vascular endothelial growth factor (VEGF) plays a central role in angiogenesis, and anti-VEGF therapies have been shown to reduce neovascularization surrounding implants in animal models. Targeting VEGF receptors may further modulate downstream angiogenic pathways, with VEGFR2 playing a prominent role in mediating VEGF-induced angiogenesis through downstream signaling pathways, including STAT3.

This study investigated the effects of the VEGFR2 inhibitor DC-101 on neoangiogenesis following hybrid cochlear implantation in mice over a 10-day period. We hypothesized that DC-101 treatment would reduce post-implantation neoangiogenesis. Specifically, we anticipated that DC-101-treated mice would demonstrate reduced PECAM/CD31-associated GFP signal within the scala tympani, reflecting decreased endothelial-associated neoangiogenesis, compared with control mice.

Eight-week-old male transgenic PECAM-GFP mice were randomly assigned to an experimental or control group ($n = 3$ per group). The PECAM-GFP reporter line was used to identify endothelial-associated neoangiogenesis, as GFP expression is driven by the PECAM/CD31 promoter in endothelial cells. Mice in the treatment group received DC-101 (40 mg/kg; Bio X Cell, USA) by intraperitoneal injection once every three days for 10 days, beginning 24 hours before surgery. Control mice did not receive intraperitoneal injections. All animals underwent left cochlear implantation and survived for 10 days, a time point at which preliminary data demonstrated extensive cochlear neoangiogenesis. The implanted and contralateral unimplanted cochleae were subsequently harvested and processed for histologic analysis.

Cochleae from both groups were imaged using confocal microscopy. GFP signal within the scala tympani was quantified using Imaris and normalized to scala tympani volume to determine relative endothelial-associated neoangiogenesis. An unpaired t-test comparing normalized GFP signal between the DC-101-treated and control groups did not demonstrate a statistically significant difference ($p > 0.05$). These preliminary findings therefore did not demonstrate a significant reduction in post-implantation neoangiogenesis following VEGFR2 inhibition with DC-101.

One potential explanation for this finding is that alternative VEGF-mediated signaling pathways may continue to promote angiogenesis despite VEGFR2 inhibition. Future studies will investigate the effects of combined VEGFR1 and VEGFR2 inhibition to determine whether a more comprehensive blockade of VEGF-A-mediated signaling can more effectively suppress post-implantation neoangiogenesis. Given the limited sample size of this preliminary study, additional experiments with larger cohorts will be necessary to determine whether VEGFR2 inhibition produces biologically meaningful effects on the foreign body response and preservation of residual hearing following hybrid cochlear implantation.

Treating Inherited Retinal Diseases with Next-Gen CRISPR Gene Editing Technology

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Background: Inherited retinal diseases (IRDs), including choroideremia, Leber congenital amaurosis, and retinitis pigmentosa, represent a major cause of blindness worldwide. These disorders arise from mutations in several well-characterized genes, many of which present opportunities for genetic correction. While patient-derived human induced pluripotent stem cells (hiPSCs) hold significant therapeutic potential for autologous cell replacement in some of these blinding diseases, correcting disease-causing mutations in hiPSCs prior to differentiation and transplantation could provide a durable therapeutic strategy capable of addressing the underlying genetic cause of disease through a potentially one-time treatment.

Purpose: The aim of this study is to engineer specific CRISPR prime editing (PE) strategies to target disease-causing variants in *CHM*, *RPE65*, and *RHO*.

Methods: Patient-derived hiPSC lines harboring disease-causing variants in *RPE65*, *CHM*, and *RHO* were established for development and evaluation of prime editing strategies. For each target, pegRNAs and nicking single-guide RNAs (nsgRNAs) were designed to facilitate precise correction of the disease-associated variant. Prime editing strategies targeting *RPE65* were evaluated through transfection screening of seven pegRNA/nsgRNA combinations in patient-derived hiPSCs, and editing efficiency was assessed to identify the most effective guide combinations.

Results: Screening of seven pegRNA/nsgRNA prime editing combinations targeting the mutant *RPE65* allele identified two lead strategies that achieved approximately 35% correction in patient-derived hiPSCs. These results demonstrate efficient correction of the disease-causing *RPE65* variant using prime editing in a patient-derived cellular model. Prime editing strategies targeting *CHM* and *RHO* have been designed, with screening in the corresponding patient-derived hiPSC lines pending.

Conclusions: These findings demonstrate the potential of CRISPR prime editing to precisely correct disease-causing variants in patient-derived hiPSCs and support its development as a strategy for generating genetically corrected cells for autologous transplantation. The identification of lead *RPE65* editing strategies provides a foundation for further optimization and validation, while ongoing studies targeting *CHM* and *RHO* will determine the broader applicability of this approach across genetically diverse IRDs.

Quantitative Laryngoscopic Assessment of Vocal Fold Bowing in Presbyphonia

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Background/Objectives: Presbyphonia is an age-related voice disorder characterized by perceptual vocal changes such as hoarseness, breathiness, reduced vocal intensity, and pitch changes. Although vocal fold bowing is commonly associated with presbyphonia, quantitative comparisons of vocal fold bowing between older adults with presbyphonia and age-matched controls without voice complaints remain limited. The purpose of this study is to quantitatively compare vocal fold bowing between older adults with presbyphonia and age-matched controls.

Methods: Adults aged 65 years and older with presbyphonia and age-matched controls were enrolled as part of an ongoing prospective study on the impact of presbyphonia on social interaction. At the time of analysis, 32 participants ($n=9$ presbyphonia, $n=23$ controls) had completed study procedures and were included in the analysis. Videostroboscopy was performed using a KayPentax digital video system via a flexible endoscope. High-definition still images were obtained during quiet respiration when the vocal folds were fully abducted and again during the stroboscopic exam at maximum closure of the vocal folds during sustained vowel phonation. ImageJ software was used to measure the membranous vocal fold length (L) and displacement (d) of both vocal folds, and the area (a) of the glottal gap, to calculate the bowing index (BI) and the normalized glottal gap area (NGGA), respectively. Descriptive statistics were calculated for BI and NGGA, and group differences between presbyphonia and age-matched controls were evaluated using Welch's independent t-tests.

Results: Mean BI was 8.956 ± 3.622 in the presbyphonia group and 1.540 ± 2.894 in the controls. NGGA was 1.112 ± 1.645 in the presbyphonia group and 0.155 ± 0.385 in the controls. BI was significantly greater in participants with presbyphonia (Welch's $t(12) = 5.49$, $(p < 0.001)$), while there was no significant difference in NGGA between participants with presbyphonia and controls (Welch's $t(8) = 1.73$, $p = 0.122$).

Conclusions: Preliminary findings demonstrate greater vocal fold bowing in older adults with presbyphonia compared to age-matched controls, supporting the use of quantitative laryngoscopic measures to characterize structural and functional laryngeal differences associated with presbyphonia. Recruitment is ongoing, and future analyses will aim to correlate acoustic measurements with anatomical changes associated with presbyphonia and evaluate changes in these measures following behavioral voice treatment (Phonation Resistance Training Exercises, PhoRTE).

Title: Association of epithelialized status of spinal defects with postoperative complications in infants with myelomeningocele in Zambia

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Introduction: At birth, myelomeningocele (MMC) lesions characteristically lack epithelial coverage. However, in some low- and middle-income countries, it has been conjectured that allowing MMC defects to epithelialize before surgery is associated with better outcomes. The study objective was to determine rates of postoperative infection, wound healing, and MMC closure within 6 weeks of surgery, stratified by preoperative epithelialization status.

Methods:

In this prospective cohort study, infants underwent MMC surgery at a tertiary center in Zambia as part of standard of care between October 2023 and June 2026. Infants were prospectively followed and assessed post-surgery with a minimum of 6-week follow-up. Ninety-six infants met the inclusion criteria. The primary outcome was surgical site infection (SSI), defined by clinical assessment of the treating surgical team. Secondary outcomes included wound dehiscence, central nervous system (CNS) infection, and death.

Results: The median infant age at MMC surgery was 18 days old [IQR 3–121], and 54 (56%) were male. At time of surgery, 26 (27%) infants had epithelialized MMC (EMMC) and 70 (73%) had non-epithelialized MMC (NEMMC). Infants with EMMC underwent surgical repair at a significantly older age than those with NEMMC (median 144 [IQR 107–217] vs. 8 [IQR 2–23] days, $p < 0.001$). Hydrocephalus was diagnosed before MMC repair in 73 (77%) infants and was more common among those with EMMC than NEMMC (96% vs. 70%, $p = 0.006$). There were no significant differences in SSI (19% vs. 37%, $p = 0.14$), wound dehiscence (31% vs. 33%, $p = 0.8$), CNS infection (0% vs. 2.6%, $p = > 0.9$), or mortality (12% vs. 20%, $p = 0.5$) between the EMMC and NEMMC groups, respectively.

Conclusion: In this prospective study of infants with MMC in Zambia, epithelialization status was not significantly associated with 6-week postoperative complications rates including wound infection, wound dehiscence, CNS infection, or mortality. In LMICs where delays in accessing surgical care are often unavoidable and healthcare resource access is variable, future studies regarding optimal MMC surgical timing and patient clinical factors should be considered within the broader clinical and resource constraints of the setting.

Brief Health Literacy Identifies Differences in Patient-Reported Health Status, but Not Surgical Improvement.

Braiden DeSchryver

Mentor: Dallas Vanorny, M.D. Ph.D.

Collaborators: Elizabeth Meyer, Silvana Mohr

Hypothesis/Purpose:

For patients undergoing primary total hip arthroplasty (THA) or total knee arthroplasty (TKA), those with higher perceived health literacy will have better overall health outcomes than those with lower perceived health literacy. Health literacy may represent a meaningful area for intervention to improve patient-reported outcome (PRO) scores in both THA and TKA.

Methods:

A retrospective cohort study was conducted among patients at the University of Iowa Hospitals and Clinics who underwent either THA or TKA between May 2025 and December 2025 and completed the Brief Health Literacy Screening (BHLS) survey (n = 206). Patients were separated into three groups based on their BHLS scores: low health literacy (score <12), moderate health literacy (score 12–16), and adequate health literacy (score 17–20). PROMIS Global, Knee PASS, Knee SANE, Hip PASS, Hip SANE, KOOS JR, and HOOS JR scores were then compared across groups.

Findings/Results:

Of the 206 patients, 11 were categorized as having low health literacy, 21 as having moderate health literacy, and 174 as having adequate health literacy. Higher BHLS scores were associated with better PROMIS health status, with the strongest association observed for early postoperative mental health (Pearson $r = 0.42$, $n = 186$, $FDR\ q < .000001$). Early postoperative mental health scores increased stepwise from 38.0 in the low-literacy group to 45.9 in the moderate-literacy group and 52.1 in the adequate-literacy group. BHLS scores were not associated with HOOS JR or KOOS JR improvement ($r = 0.11$ and 0.07 , respectively) or with achievement of clinical benefit across literacy groups (HOOS $p = .427$; KOOS $p = .549$).

Conclusion:

Higher perceived health literacy was associated with better overall patient-reported mental, physical, and social health among patients undergoing primary THA or TKA, supporting the hypothesis that health literacy is associated with health outcomes in arthroplasty populations. Although health literacy did not predict the magnitude of postoperative HOOS JR or KOOS JR improvement, these findings suggest that patients with lower health literacy may enter and progress through the surgical episode with broader health disadvantages. Health literacy therefore represents a potentially modifiable area for targeted education, communication, and perioperative support aimed at improving patient-reported outcomes and promoting equitable recovery after total joint arthroplasty.

Co-occurring Autoimmune and Immune-Mediated Diseases in a University of Iowa MS Cohort Reveal a Broad Systemic Inflammatory Phenotype

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Background:

Multiple sclerosis (MS) is a chronic immune-mediated autoimmune disease of the central nervous system arising from interactions among genetic, environmental, and immune factors. Although autoimmune diseases are traditionally classified by the primary organ affected, emerging evidence suggests that clinically distinct diseases may share underlying mechanisms of immune dysregulation. We examined the prevalence and spectrum of co-occurring autoimmune and immune-mediated diseases in a well-characterized MS cohort to determine whether MS is associated with a broader systemic inflammatory phenotype.

Methods:

Clinical records from 196 individuals with MS enrolled in an ongoing observational cohort at the University of Iowa Hospital and Clinics were reviewed for physician-documented autoimmune and immune-mediated diseases. Diagnoses were classified as endocrine, systemic/rheumatologic, dermatologic, gastrointestinal, or neuro-ophthalmic. Only confirmed diagnoses were included in the primary analysis. Hypothyroidism or hyperthyroidism without documented autoimmune etiology and unconfirmed systemic autoimmune disease were analyzed separately. Inflammatory MS activity was assessed using available longitudinal clinical and MRI records.

Results:

Twenty-four of 196 individuals with MS (12.2%) had at least one additional confirmed autoimmune or immune-mediated disease, representing 26 diagnoses across multiple organ systems. Endocrine autoimmunity was most common (13 diagnoses; 6.6% of the cohort), followed by dermatologic (5; 2.6%), systemic/rheumatologic (4; 2.0%), gastrointestinal (2; 1.0%), and neuro-ophthalmic (2; 1.0%) disorders. Hashimoto's thyroiditis was the most frequent individual condition (8/196; 4.1%), followed by type 1 diabetes (3; 1.5%), Graves' disease (2; 1.0%), Sjögren's disease (2; 1.0%), psoriasis (2; 1.0%), and celiac disease (2; 1.0%). Additional conditions included systemic lupus erythematosus, localized scleroderma/morphea, chronic urticaria, vitiligo, pyoderma gangrenosum, chronic inflammatory demyelinating polyneuropathy, and panuveitis with retinal vasculitis. No confirmed rheumatoid arthritis or inflammatory bowel disease was identified. Seven additional individuals had acquired hypothyroidism without confirmed autoimmune etiology, while isolated cases of unspecified hyperthyroidism and possible systemic lupus erythematosus were also identified.

Conclusions:

More than one in ten individuals with MS in this cohort had an additional confirmed autoimmune or immune-mediated disorder, spanning endocrine, cutaneous, rheumatologic, gastrointestinal, and neuro-ophthalmic systems. The breadth of these co-occurring conditions suggests that MS may occur within a broader phenotype of systemic immune dysregulation rather than representing exclusively CNS-restricted autoimmunity. In alignment with emerging NIH priorities aimed at identifying mechanisms shared across autoimmune and inflammatory diseases, these findings provide a clinical foundation for investigating common immune, genetic, environmental, and microbiome pathways across these diseases.

Title: A prospective evaluation of the impact of early antibiotic initiation in infants with myelomeningocele in Zambia

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Introduction: Although patients with myelomeningocele (MMC) are at high risk of infection, prospective data regarding the impact of extended preoperative antibiotic use on MMC surgical outcomes remain limited.

Objective: This study aims to understand the impact of preoperative antibiotic administration on postoperative infection and mortality in infants with MMC.

Methods: Infants with MMC who presented to the major tertiary hospital in Lusaka, Zambia for surgical defect closure between April 2, 2024, and March 10, 2026, were enrolled in a prospective cohort study. Patients were categorized into ‘Early’ and ‘Late’ groups based on the timing of pre-operative antibiotic initiation. The Early group comprised patients who received 1+ antibiotic dose within three days of life, whereas the Late group included those who received 1+ antibiotic dose after three days of life. The primary outcomes for this study were the presence of surgical site infection (SSI), central nervous system (CNS) infection, or death within 6 weeks postoperatively.

Results: One hundred infants were enrolled in this study; 59% male (n=59) and 41% female (n=41). Median age at hospital presentation was 3 days (IQR 2-5) for the Early group and 10 days (IQR 3-30) for the Late group (p=0.001). Twenty-six infants (26%) were in the Early group. Median age at MMC repair was 7 days (IQR 3-45) for the Early group versus 30 days (IQR 9-128) for the Late group (p=0.024). History of sepsis prior to surgery occurred in 31% (n=8) of Early infants compared to 18% (n=13) in Late infants (p=0.2). A preoperative antibiotic regimen consisting of third generation cephalosporins was used in 11 Early infants (42%) and 10 Late infants (14%; p=0.004). Postoperative SSI, CNS infection, or death occurred in 49 (49%) patients, 14 (54%) Early infants and 35 (47%) Late infants (p=0.7). There was no significant association between timing of preoperative antibiotics and risk of postoperative SSI, CNS infection, or death (p>0.05). Timing of surgical repair of MMC was not a study confounder.

Conclusions: In this prospective study of infants with MMC in Zambia, initiation of preoperative antibiotics within 3 days of life was not significantly associated with reduced postoperative infection or mortality. Future prospective studies should evaluate indications for and types of preoperative antibiotic coverage for prophylactic purposes in this population.

Studying the Mechanism of Action of Small Neurotrophic Molecules trans-Banglene and 4,10-ARDD

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Despite therapeutic breakthroughs, neurodegenerative dementias have remained untreatable, leaving patients to suffer mental and physical decline. As such, the synthesis and study of small molecules that can pass through the blood-brain barrier and facilitate neuritogenesis continues to be an important and influential area of research. Previous work in the Williams Lab studied small neurotrophic molecule trans-banglene (t-BG) and its enantiomers, finding they exhibited neuritogenesis and NGF-potential in the PC 12 cell line (a model neuronal cell line). To further elucidate the mechanism of NGF-potential, the neuritogenesis and potential properties of (-) trans-banglene were tested in the presence of Erk 1/2, PkC and Akt inhibitors. It was found that (-) trans-banglene rescued neuritogenesis in the presence of Erk1/2 and PkC inhibitors. This poster will outline further investigations, including the synthesis of a photolabile crosslinker to identify the cellular target of t-BG. This photolabile crosslinker contains a diazirine which will bind to the cellular target in the PC 12 cells upon irradiation, as well as a terminal alkyne which can couple to biotin and allow for extraction from the cell lysate. Fluorescent labeling will also be used to determine where the target of t-BG localizes in the cell. In addition, synthetic work to access another neurotrophic compound, (-)9,10-aromadendranediol [(-)-ARDD] will be outlined. Previous and current work on t-BG is important to the (-)-ARDD project, as much of the same neuritogenesis and potential properties will be tested. With these current aims, a strong hypothesis for the mechanisms of actions for these small neurotrophic molecules can be constructed, which will aid new therapeutic strategies.

Establishing an Approach to Study Dopaminergic Regulation of D1- and D2-MSN Activity During Interval Timing

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Timing is essential for coordinating everyday behavior and depends on cognitive processes including working memory, attention, and executive function. Disruptions in temporal processing are associated with neurological and psychiatric disorders, including Parkinson's disease and schizophrenia. Medium spiny neurons (MSNs) in the dorsomedial striatum encode temporal intervals via time-related ramping activity (i.e., monotonic increases or decreases in firing rate). These neurons can be classified by their predominant dopamine receptor expression as D1- or D2-MSNs. Nigrostriatal dopamine is a key modulator of time perception, and inhibiting dopamine in rodents disrupts MSN ramping. However, how dopamine differentially regulates D1- and D2-MSN activity remains unclear. Addressing this gap in knowledge is predicted to reveal therapeutic strategies aimed at increasing quality of life for those suffering from neurologic and psychiatric disorders.

We hypothesized that nigrostriatal dopamine differentially regulates D1- and D2-MSN ramping activity during interval timing. To test this hypothesis, we aim to record calcium activity from D1- or D2-MSNs with fiber photometry while inhibiting nigrostriatal dopamine neurons with optogenetics while mice perform an interval timing task. In this task, mice estimate intervals of several seconds by switching responses between nose pokes. This recording strategy requires the use of a genetic mouse line to specifically target a fluorescent calcium sensor to D1- or D2-MSNs. In these experiments, we sought to identify an approach that could be combined with this strategy to selectively inhibit nigrostriatal dopamine neurons. First, we tested the use of a retrograde virus to express Cre-recombinase in nigrostriatal projection neurons, which would allow us to selectively express an inhibitory opsin via a Cre-dependent virus in these neurons.

The retrograde viral approach expressed in cortical and hippocampal projection neurons but did not produce strong expression in nigrostriatal dopamine neurons, indicating that this approach was insufficient for selective targeting of the nigrostriatal pathway. Therefore, we implemented an alternative strategy using a non-Cre-dependent optogenetic virus targeted to the substantia nigra. Ongoing experiments are evaluating if terminal inhibition of nigrostriatal dopamine neurons is sufficient to 1) suppress dopamine release in the dorsomedial striatum (measured with the fluorescent dopamine indicator dLight) and 2) affect timing behavior in the interval timing task.

Establishing an effective strategy for manipulating nigrostriatal dopamine signaling during interval timing will provide a foundation for future work examining how dopamine differentially regulates ramping activity in D1- and D2-MSNs during temporal processing.

Feasibility of Zwitterionic Conditioning of the Decompressive Craniectomy Site for Early Cranioplasty

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Decompressive craniectomy (DC), is an important treatment for moderate to severe traumatic brain injury (TBI). Subsequent cranioplasty is necessary to restore the closed cranial vault anatomy, though its timing remains controversial. Benefits of early cranioplasty have been shown, but residual brain swelling, soft tissue inflammation and scar fibrosis can create an unsuitable environment for successful early cranioplasty. Zwitterions (ZIs) are net neutral polymers with positively and negatively charged particles that reduce inflammation, swelling, and scar fibrosis, qualities that make them ideal for early cranioplasty considerations. We hypothesize that the application of a ZI hydrogel to the site of DC may promote a suitable environment for successful early cranioplasty.

A validated “hit and run” closed cortical impact was used to induce TBI. CD1 mice were randomly assigned to 4 groups: sham, TBI only, TBI with DC, and TBI with DC and ZI hydrogel. Trunk blood was collected 24-hours following the designated intervention for each group and GFAP, NfL and UCH-L1 concentrations were quantified via ELISA. Long-Evans rats were randomly assigned to 3 groups: sham, TBI with DC and TBI with DC and ZI hydrogel. A beam walk task was performed prior to intervention and at 7 and 14 days post intervention with time to cross the beam and number of slips per crossing recorded. Long-Evans rats were randomized into 2 groups: DC or DC and ZI. Scalp and cranial soft tissue were harvested at 6 weeks for histological analysis by the University of Iowa Histology Research Lab using H&E and Masson’s Trichrome stains.

GFAP and UCH-L1 were significantly increased in TBI relative to sham (GFAP: 0.609 ± 0.073 vs. 0.339 ± 0.035 , $p = 0.0014$, UCH-L1: 0.332 ± 0.057 vs. 0.206 ± 0.016 , $p = 0.0471$), while neither DC alone nor DC with ZI hydrogel differed significantly from sham for any biomarkers (TBI/DC: GFAP: $p = 0.9899$, UCH-L1: $p = 0.9899$, NfL: $p = 0.9152$; ZI hydrogel: GFAP: $p = 0.9124$, UCH-L1: $p = 0.9979$, NfL: $p = 0.7104$). This suggests that ZI hydrogel application does not negate the benefits of DC and still permits the brain to swell outside the confines of the cranial vault. The TBI with DC group showed persistent motor deficit with increased completion time compared to baseline (1.00 ± 0.08) at both day 7 (1.73 ± 0.29 , $p = 0.0267$) and day 14 (1.68 ± 0.48 , $p = 0.0434$) as well as increased slips from baseline (1.00 ± 0.28), at day 7 (2.79 ± 0.52 , $p = 0.0246$) and day 14 (2.74 ± 0.65 , $p = 0.0302$). The DC with ZI hydrogel group showed improved motor outcomes with no significant increase in completion time or slips compared to baseline at day 7 or day 14. Qualitative histological assessment of the DC only group showed increased scar fibrosis and disruption of the normal tissue architecture of the scalp consistent with increased fibrotic activity. In comparison the DC and ZI group demonstrated improved tissue organization with preserved tissue architecture, supporting the hypothesis of ZI reducing fibrotic remodeling.

This study supports the preliminary benefits of ZI hydrogel application at the time of DC to facilitate early cranioplasty and improve neurotrauma outcomes. Further studies should continue to assess the properties of ZI hydrogel and its suitability for use during DC to promote early cranioplasty.

Synergistic Trends Between New Targeted Therapeutics for Malignant Peripheral Nerve Sheath Tumors

Chase Eastham, Ellen Voigt, Rebecca Dodd, and Dawn Quelle.

Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive soft tissue sarcomas initiated by dysregulation of the RAS-MAPK pathway. No effective therapies exist for these tumors. SHP2, a protein tyrosine phosphatase that promotes RAS activation through recruitment of guanine nucleotide exchange factors (GEFs), has emerged as a promising therapeutic target. However, inhibition of signaling downstream of RAS may be necessary to enhance sensitivity to SHP2 inhibitors and concurrently block the development of therapy resistance. The transcription factor FOXM1, a powerful oncoprotein that acts downstream of RAS-MAPK signaling, is upregulated in MPNSTs and its expression correlates with poor patient survival. To test for synergistic effects on tumor inhibition between SHP2 and FOXM1 inhibitors, a patient-derived MPNST cell line was exposed to dose matrices of multiple drugs targeting those pathways. The synergy assays included two distinct FOXM1 inhibitors, selected based on either high target affinity (NB-73) or favorable bioavailability (NB-115), with both compounds designed to increase the proteolytic sensitivity of the transcription factor. All three SHP2 inhibitors contain motifs designed to allosterically inhibit SHP2 by stabilizing the phosphatase domain in its closed, inactive conformation. The relative affinity for SHP2 increases from SHP099 to TNO-155 to JAB3312. Both TNO-155 and JAB3312 are currently being evaluated in early-phase clinical trials as single agents and in combination therapies. Cell viability was evaluated 72 hours after drug exposure using Alamar Blue staining and drug synergy was analyzed with SynergyFinder3.0. The results demonstrate synergy between these targeted therapies although often within narrow therapeutic windows, suggesting conditions can be further optimized. These data support the potential of jointly targeting SHP2 and FOXM1 as a new therapeutic strategy for treating MPNST patients.

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

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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 ≥ 25 ft 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.

From Vessel to Viable Ring: Establishing a Living Human Coronary Plaque Platform for Disease Modeling

Will Fairman BS, Deven Strief BS, Kane Zemo BS, Lu Persaud BS, Madhu Singh PhD, Jennifer Streeter MD PhD

Introduction/Rationale: Coronary artery disease remains the leading cause of heart disease worldwide, yet progress toward better therapies has been limited by models that fail to preserve the native coronary microenvironment. Existing approaches rely on isolated plaques or cultured endothelial cells, which strip away cell-cell communication, extracellular matrix interactions, and the plaque-vessel architecture that defines human disease.

Hypothesis: 300 μ m cross-sections of Human Coronary Arteries with Plaques (HuCAPs) can maintain viability in culture and serve as a high-fidelity model to study coronary artery disease.

Methods: Whole coronary arteries were excised from freshly explanted hearts from patients receiving heart transplant or donor hearts. Excised arteries were embedded in agarose and sliced into 300 μ m cross-sections using a precision vibratome. HuCAP slices were kept in culture for 30 days. Viability was assessed using the resazurin reduction assay. Structural integrity was assessed using immunofluorescence (IF) staining/confocal microscopy for markers of vessel architecture and cell identity. Vasoreactivity was tested using wire myography. Gene expression changes were assessed by RNA-seq in response to a pro-resolving mediator, Ac2-26, for 72 hours.

Results: Resazurin viability assays showed HuCAPs remain metabolically active for at least 30 days in culture. IF staining of internal elastic lamina, smooth muscle myosin heavy chain (smooth muscle cell marker), and von Willebrand factor (endothelial marker) demonstrated that plaque and vessel wall architecture remained stable in culture. Vasoreactivity assays showed HuCAPs respond appropriately by contracting in response to treatment with potassium chloride and relaxing in response to nitric oxide. However, HuCAPs paradoxically contract instead of relaxing in response to acetylcholine, suggesting endothelial dysfunction, which is a known characteristic of coronary artery disease. Transcriptomic profiling verified preserved molecular integrity suitable for transcriptomic analysis and demonstrated gene expression changes consistent with vascular repair in response to Ac2-26.

Significance: HuCAPs preserve defining features of human coronary plaque tissue, including viability, vessel wall architecture, vasoreactivity, endothelial dysfunction, and transcriptional responsiveness while converting a single coronary artery specimen into hundreds of experimentally tractable living sections. This platform bridges the gap between oversimplified cell culture and intact human coronary disease, enabling scalable, high-fidelity testing of plaque biology in its native vessel context. HuCAPs provide a new foundation for studying mechanisms of coronary artery disease and evaluating therapeutic strategies that promote vascular repair and plaque resolution.

Title: Interaction Between Maternal Medical and Obstetric Complications and Early Breast Milk Feeding Practices: A Retrospective Study

Authors: Sophie Fisher, BS, Meghan Funk, BA, Sarah Upton, MS, Donna Santillan, PhD, Mark Santillan, MD, PhD, and Noelle Bowdler, MD

Introduction: Breast milk feeding (BMF) has numerous benefits for both the mother and infant. The WHO recommends that hospitals should promote BMF to support both infant and maternal health. However, many women face difficulties initiating and continuing BMF, particularly those who experience medical and obstetric complications. Despite the knowledge that conditions can impact BMF success, there is a lack of research into the specific reasons for these gaps in outcomes. Particularly, there is a lack of knowledge on how mothers with complications compare to mothers without complications with respect to the prevalence and timing of factors that promote BMF.

Purpose: The purpose of this research is to understand factors that may impact BMF success in populations who experience complications, including hypertensive disorders of pregnancy, diabetes, chorioamnionitis, and obstetric hemorrhage.

Methods: This study combines a secondary analysis of a dataset from the UI Intergenerational Health database as well as retrospective chart review of mothers who gave birth in the year of 2022 at UIHC and expressed an intention to breastfeed. Data were collected on type of medical or obstetric complications experienced, time to first skin-to-skin contact (SSC), time to first BMF, and infant feeding status at discharge. Of 471 mother-infant dyads who met inclusion criteria and did not meet exclusion criteria, data were collected for an opportunity sample of the first 250 mother-infant dyads based on delivery date. Subjects with any complication, and with specific complications, were compared to a control group with none of the specified complications (“no complications” group). Chi-squared tests were used for comparison of categorical variables, and two-tailed student’s t-tests were used for comparison of continuous variables. Linear regression was used to assess the significance of covariates, and multiple logistic regression was used to compare demographic information. Statistics were considered significant at a level of $p < 0.05$.

Results: There were no significant differences between the complications and no complications groups with respect to rurality, insurance type, race, or ethnicity. The complications group was significantly older (29.9 +/- 4.9 vs 28.7 +/- 3.9 years, $p = 0.037$) and was more likely to have undergone a cesarean delivery ($p = 0.004$) compared to the no complications group. With respect to feeding status at discharge, there were no differences in BMF in any capacity at discharge between the complications and no complications groups as a whole. Patients who experienced chorioamnionitis were less likely to BMF in any capacity at discharge compared to patients who didn’t experience this complication ($p = 0.017$). For the primary outcome of time to SSC, there was a significant difference between the complications and no complications groups ($p = 0.0028$). Analysis of each type of complication revealed a significantly longer time to SSC for hypertensive disorders ($p = 0.004$), hemorrhage ($p < 0.001$), and chorioamnionitis ($p < 0.001$). For our other primary outcome of time to first BMF, time was significantly longer for patients with hypertensive disorders ($p < 0.001$), hemorrhage ($p = 0.023$), chorioamnionitis ($p = 0.009$), and diabetes ($p = 0.034$). When controlling for any complication, cesarean delivery had an effect on time to first SSC ($p = 0.012$), and race had an effect on time to first BMF ($P = 0.008$).

Conclusions: Our study showed that various medical and obstetric complications are associated with longer times to SSC and first BMF. In particular, hypertensive disorders of pregnancy, obstetric hemorrhage, chorioamnionitis, and diabetes had significantly longer times to factors that have been shown to improve BMF outcomes. Addressing the prolonged times to SSC and first BMF may improve the overall success of BMF in these individuals, particularly for individuals experiencing chorioamnionitis, given that they also had lower rates of BMF at discharge.

Upper Extremity Osteomyelitis: A Multicenter, Retrospective Cohort Analysis with In-Depth Assessment of Patient-Centered Outcomes at Iowa Health Care

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Introduction: Upper extremity osteomyelitis (UEOM) is a serious bone infection that can cause substantial disability and reduced quality of life. Previous osteomyelitis research has focused on cases involving the lower extremities and spine, but research on UEOM has been scarce.

Purpose: The purpose of this study was to define the epidemiology of UEOM and understand patients' experiences with serious upper extremity infections, including UEOM.

Methods: UEOM cases between January 1, 2015 and December 31, 2025 were identified using TriNetX, a large multicenter database. The annual incidence of UEOM was calculated and stratified by diagnostic subcategories (acute, chronic, and other), presence of prior upper extremity surgeries and wounds, and known clinical risk factors for osteomyelitis, such as diabetes mellitus and peripheral vascular disease. The incidence of amputation among patients with UEOM was assessed over the same period. Odds ratios for amputation were calculated for clinical risk factors as well as health-related social needs, which were defined using statistical models that estimate patients' likelihood of health insurance and transportation. To complement the quantitative analysis with qualitative context about the patient experience, interviews were conducted with adults hospitalized with upper extremity infections at the University of Iowa.

Results: The incidence of UEOM and the incidence of amputation among patients with UEOM both increased >50% over the study period (test for trend $p=0.004$, $p=0.006$, respectively). Increases in UEOM incidence were concentrated in patients with diabetes mellitus and upper extremity wounds. Amputation had significantly higher odds in patients with peripheral vascular disease [unadjusted odds ratio (OR): 3.07; 95% confidence interval (CI): 2.88, 3.28, $p<0.001$], diabetes mellitus (OR: 2.33; 95% CI: 2.19, 2.48, $p<0.001$), and kidney disease (acute or chronic; OR 2.05; 95% CI: 1.92, 2.18, $p<0.001$) compared to patients without each condition. Health insurance was inversely associated with amputation, with a 2-3-fold increase in the odds of amputation among patients with low versus high likelihood of insurance. Preliminary results from patient interviews highlighted the impact of upper extremity infections on motor function.

Conclusion: The incidence of UEOM and associated amputation is increasing over time, particularly in cases associated with diabetes mellitus and upper extremity wounds. Amputation is more often observed among patients with peripheral vascular disease, diabetes mellitus, kidney disease, and limited insurance access. These findings support the general importance of preventive care for chronic conditions and chronic wounds. Future research is needed to enhance prevention, early detection, and treatment for limb-threatening infections of the upper extremity, with attention to the impact of upper extremity functions on motor function, activities of daily living, and patients' quality of life.

Long-term Assessment of Foot and Ankle Structure and Function in Adults Treated with the Ponseti Method for Clubfoot Deformity

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Introduction: Congenital clubfoot deformity affects 1 child every 1,000 births. The Ponseti method, developed by Dr. Ignacio Ponseti at the University of Iowa, is the standard of care in the treatment of clubfoot and has been well-studied in short to mid-term follow-up during infancy and adolescence. However, long-term assessment of the Ponseti method has been less well characterized and is limited to 2D radiographs. Weight bearing computed tomography (WBCT) enables advanced evaluation of complex foot and ankle deformities in a functionally loaded position. When combined with dynamic plantar pressure mapping (PPM) these technologies may provide complementary insights into structural deformity and functional loading, advancing our understanding of long-term outcomes in clubfoot treatment. Therefore, the objective of this study was to evaluate the long-term structural and functional characteristics of adults with a history of Ponseti-treated congenital clubfoot and compare them with healthy controls using WBCT and PPM to better understand the long-term biomechanical consequences of clubfoot deformity.

Methods: Following IRB approval and informed consent, 19 adults with confirmed diagnosis of congenital clubfoot treated with the Ponseti method during infancy (n=28 feet, age: 33.3±13.9 y, BMI: 30.4±7.7) and 20 healthy controls (n=40 feet, age: 34.6±10.4 y, BMI: 29.3±4.8) received a bilateral standing WBCT scan (CurveBeam AI) and completed functional assessment through dynamic PPM while walking barefoot over a plantar sensor platform (Novel EMED). 3D and 2D measurements of foot structure were performed on WBCT scans in all three imaging planes. Peak pressure, pressure-time integral (PTI), and contact area were obtained from the dynamic PPM and analyzed across the whole foot and regionally using a five-region mask based on foot length and width. Center of pressure (COP) trajectories were also calculated from dynamic PPM. WBCT measures and dynamic PPM values were compared using a clustered Wilcoxon rank-sum test to account for non-normality from inclusion of bilateral and unilateral clubfoot participants. A linear mixed-effects model was used to quantify the association of clubfoot deformity contribution to altered plantar loading characteristics.

Results: Ponseti-treated clubfeet demonstrated no significant differences in 3D structural measures compared to controls (Foot-ankle-offset: p=0.939, Calcaneal-offset: p=0.5769, Hindfoot alignment angle: p=0.9302). For 2D WBCT measures, Ponseti-treated clubfeet demonstrated significantly decreased calcaneal inclination angles (p<0.001), increased talonavicular coverage angles (TNCA: p<0.001), and increased axial plane talus first metatarsal angles (TFMA: p=0.03). PPM assessment revealed clubfeet have increased contact area in all five regions (all p<0.05). Furthermore, clubfeet demonstrated significantly decreased plantar loading in terms of peak pressure and PTI in the medial (p=0.0031, p=0.0051) and lateral (p=0.0113, p=0.0056) forefoot with significantly increased peak pressure and PTI in the lateral midfoot (p<0.0001, p=0.0028). Ponseti-treated COP trajectories exhibited increased loading time in the midfoot and decreased loading in the forefoot. The linear mixed-effects model indicated clubfoot progression into a flatfoot deformity with metatarsal adduction was significantly associated with increased plantar loading in the lateral midfoot and decreased loading in both forefoot regions.

Conclusions: This long-term follow-up study demonstrated the effectiveness of the Ponseti method in restoring the 3D foot and ankle alignment that presents in clubfoot deformity. However, decreased calcaneal inclination angles and increased plantar contact area may indicate an over-correction of clubfoot deformity into a flatfoot deformity, and increased TNCA and TFMA may indicate residual forefoot adduction that is under-corrected. Additionally, clubfoot patients exhibit altered plantar loading through the midfoot and forefoot that is associated with flatter feet and more severely adducted metatarsals. This study is the first to evaluate both 2D and 3D structure of Ponseti-treated clubfeet, and the first to correlate structure to function through the correlation of WBCT structure to PPM analysis. These findings provide further insight into the long-term outcomes of the Ponseti method and advance our understanding of the structural and functional characteristics of Ponseti-treated clubfoot into adulthood. Future studies with larger cohorts and advanced PPM across the stance phase may further define the relationship between residual deformity and functional loading.

Tirzepatide activates GIPR-mediated signaling and enhances tyrosine kinase inhibitor sensitivity in gastroenteropancreatic neuroendocrine neoplasm cells

Sarah Fu, BS; Camilla Koczara, MD; Caleb Morgan, BS; Eugene Kang; Joseph Dillon, MD; James Howe, MD; Po Hien Ear, PhD

Introduction/Background:

Gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) are tumors derived from hormone-secreting cells of the pancreas and gastrointestinal tract. The majority are low-grade, well-differentiated neuroendocrine tumors (NETs), but some are high-grade, poorly-differentiated neuroendocrine carcinomas (NECs). Most GEP-NENs express somatostatin receptors on their cell surface, which is a valuable target for imaging and therapy. Many of these tumors also express glucose-dependent insulintropic polypeptide (GIPR), and to a lesser degree, glucagon-like peptide 1 receptor (GLP-1R). Incretin mimetic therapies targeting these receptors have become extremely popular for treating diabetes and obesity, with 14% of the United States population having taken one of these agents. A boxed warning has been issued against GLP-1R agonist use in patients with medullary thyroid cancer, a type of NET, due to preclinical reports that they promote C-cell proliferation in mice. Our group has reported that NET cell lines expressing GLP-1R have increased cell growth when treated with the corresponding agonist. This study seeks to determine GIPR/GLP-1R expression in NEN cell lines and patient-derived spheroids (PDS) and define the effects of the dual GLP-1R/GIPR agonist tirzepatide in these models.

Methods/Results:

We screened five GEP-NEN cell lines (BON, GOT1, NEC-1583, NEC-913, and QGP-1) for GIPR and GLP-1R expression via quantitative polymerase chain reaction and immunofluorescence (IF). All cell lines were found to be GIPR positive at both the mRNA and protein level, while only NEC-913 exhibited GLP-1R positivity. Additionally, IF of patient-derived spheroids cultured from three patient specimens, from both primary and metastatic small bowel and pancreatic NETs, showed GIPR positivity with a lack of GLP-1R expression. Having confirmed expression of at least one incretin receptor in each cell type, we treated them with tirzepatide and assessed downstream MAPK/Erk and PI3K signaling, pathways canonically associated with growth and/or survival in cancer cells. After treatment with 100 nM Tirzepatide for 0, 2, 5, 10, 15, or 30 minutes, GOT1, QGP-1, and NEC-913 cells showed a time-dependent activation of the MAPK/ERK pathway as evidenced by increased p-ERK/total ERK ratio on Western blot (WB). Furthermore, QGP1 cells demonstrated increased p-FoxO1 levels on WB, and export of p-FoxO1 from the nucleus on IF, indicating engagement of the PI3K-Akt pathway. Despite activation of downstream signaling pathways, extended treatment with tirzepatide did not increase proliferation of BON, QGP-1, GOT1, or NEC-913 cell lines as measured by AlamarBlue assay. 24-hour pretreatment with tirzepatide did, interestingly, enhance sensitivity of QGP-1 cells to the FDA-approved tyrosine kinase inhibitor (TKI) therapy, sunitinib, lowering IC₅₀ from 9.2 μ M to 2.6 μ M (n=5).

Conclusion:

In the present study, we confirmed GIPR expression in several GEP-NEN preclinical models and documented activation of signaling pathways canonically considered to be pro-oncogenic in response to tirzepatide treatment. However, the functional consequences of tirzepatide treatment in GEP-NENs remain unresolved as tirzepatide did not affect proliferation, but sensitized QGP-1 cells to TKI therapy. These findings suggest a complex relationship between incretin signaling and drug sensitivity that warrants additional mechanistic studies. Further understanding the effects of incretin agonists on GEP-NENs will help to inform the risks of managing GEP-NEN patients with incretin-based therapies.

Title: Impact of oral cavity and velopharyngeal dimensions on sleep disordered breathing and pre-speech language metrics in infants with oral cleft

Student: Alejandro Garay

Mentor: Amy L. Conrad, PhD - Stead Family Department of Pediatrics

Co-Mentor: Jamie Perry, PhD – East Carolina University

Introduction

Orofacial clefts (OFCs) are the most common congenital craniofacial malformations in the United States, affecting approximately 1 in 1000 births. Normal function of the velopharyngeal system is essential for speech and respiration, creating a direct pathway between anatomical differences in OFC and speech impairment. An additional indirect pathway can be proposed that connects anatomical differences to sleep disordered breathing (SDB), impacting development and ultimately speech and language function. Using structural MRI acquired as part of an ongoing infant study, we combined functional and anatomical approaches by quantifying oral cavity and velopharyngeal anatomy to examine relationships with SDB and pre-speech language measures.

Purpose

To examine associations between MRI-derived oral cavity and velopharyngeal anatomy, SDB, and early pre-speech language measures in 2-month-old infants with oral clefts and unaffected controls. We hypothesized that reduced oral cavity and airway dimensions would be associated with greater SDB severity and poorer early speech outcomes.

Method

This secondary analysis used parental ratings of development and emerging language, overnight pulse oximetry measures of SDB, pre-speech vocal acoustic (PSVA) recordings, and high-resolution structural MRI. Oral cavity and velopharyngeal anatomical measurements were derived from MRI using 3D Slicer. Shapiro–Wilk tests assessed normality. Between-group differences were evaluated using Mann–Whitney U tests with rank-biserial correlations as effect sizes, and associations between variables were assessed using Spearman correlations.

Results

Of the 20 infants enrolled in the original study, MRI quality was sufficient for analysis in 16 infants (iCLP: n=5; iCLO: n=2; unaffected: n=9). The iCLO group was excluded from statistical analysis due to insufficient sample size. Hard palate width was the only variable to demonstrate a statistically significant between-group difference ($p = .014$, rank-biserial correlation = -0.66 ; large effect). Percent time with $\text{SpO}_2 \geq 90\%$, pharyngeal depth, and effective VP ratio demonstrated medium effect sizes but did not reach statistical significance. Spearman correlation analyses identified significant associations between oral cavity dimensions and SDB. Smaller VP port gap, VP port area and hard palate length were associated with greater oxygen desaturation, while greater LVP length and origin-to-origin distance were associated with improved oxygenation ($|p| = 0.62\text{--}0.76$, $p < .05$). Associations between hard palate and LVP dimensions with pre-speech vocal acoustic measures and receptive language growth residuals trended toward significance ($|p| = 0.49\text{--}0.56$, $p = .055\text{--}.078$).

Conclusion

MRI-derived oral cavity and velopharyngeal anatomy demonstrated significant associations with sleep-disordered breathing and showed trends toward associations with early speech and receptive language outcomes. Although exploratory due to the limited sample size, these findings suggest that early craniofacial anatomy may influence both respiratory and developmental outcomes and warrant confirmation in larger, adequately powered studies.

***MMP9* Genotype and Systemic Immunophenotype in Neovascular Age-Related Macular Degeneration**

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Introduction:

Age-related macular degeneration (AMD) is a leading cause of vision impairment worldwide. Neovascular AMD (nvAMD) is an advanced form, characterized by pathogenic blood vessel growth resulting in fluid accumulation and irreversible vision loss. While intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections are the standard of care, treatment response is variable and often incomplete. There are many genes associated with the development of AMD, but *MMP9* is the only validated locus associated specifically with development of nvAMD. *MMP9* encodes a protease that remodels extracellular matrix components of Bruch's membrane. Beyond its structural role, *MMP9* modulates immune cell activity by regulating T cell surface receptors and participating in a positive feedback loop with VEGF. Elevated plasma *MMP9*, increased circulating T cell subsets, and dendritic cell (DC) *MMP9* expression have all been implicated in nvAMD immunopathogenesis. Recent data also suggest worse fluid and visual outcomes in *MMP9* heterozygotes. We hypothesized that *MMP9* genotype is associated with distinct immunophenotypes in nvAMD, with genotype-dependent differences in *MMP9* expression driving downstream differences in immune cell function.

Methods:

We retrospectively analyzed 53 patients with nvAMD treated at the University of Iowa. We genotyped patients for the *MMP9* single nucleotide polymorphism rs4810482 (TT=28, TC=18, CC=7). We stimulated their whole blood samples (n=30) with candidate peptide epitopes that interact with *MMP9* and measured interferon-gamma (IFN- γ) production. We defined peptide reactivity as the percentage of peptides eliciting a positive IFN- γ response. We analyzed immune cell populations with 40-color flow cytometry, quantifying cell counts (n=49) and *MMP9* geometric mean fluorescence intensity (gMFI; n=42). We assessed associations between genotype and peptide reactivity using Fisher-Freeman-Halton tests with post hoc Fisher's exact tests. We compared cell counts and *MMP9* gMFI using Kruskal-Wallis tests with post hoc Dunn's tests. We applied Benjamini-Hochberg false discovery rate adjustment across all immune cell analyses.

Results:

Dendritic cells (DCs) demonstrate a monotonic gene-dose gradient in *MMP9* expression, with gMFI highest in TT, intermediate in TC, and lowest in CC (p=0.03). No other immune cell population showed significant genotype-associated differences in *MMP9* expression. Median peptide reactivity was highest in the TC genotype (53% [9.38-85.16%]) and lowest in the CC genotype (16% [9.38-28.13%]), although the difference was not significant (p=0.20). Flow cytometry revealed significant genotype associated differences in total innate lymphoid cells, CD4⁺ T cells, natural killer cells, and B cells (all p < 0.05), with the TC genotype consistently exhibiting the lowest cell counts.

Conclusion:

MMP9 genotype is associated with a DC-specific gene-dose effect on *MMP9* expression (TT>TC>CC), while TC heterozygotes exhibited a trend toward greater autoreactivity to Bruch's membrane-derived peptides and the lowest immune cell counts. These findings are consistent with a model in which genotype-driven *MMP9* expression in DCs shapes downstream adaptive immune responses in nvAMD. It is unclear if reduced circulating immune cell counts may reflect increased tissue infiltration and a more active disease state, warranting further investigation, including spatial tissue-level analyses currently underway.

Title: Web-based multi-variable computational models predicting early spontaneous resolution in children with vesicoureteral reflux

Student: Bailey Garnica, M4

Mentor: Dr. Christopher Cooper, MD, Urology

Collaborators: Logan Harris, PhD, Bridget Zimmerman, PhD, Knute D. Carter, PhD

Introduction: Primary vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder to the upper urinary tract due to dysfunction of the ureterovesical junction (UVJ). VUR is a common pediatric urological condition where management remains a challenge because many children spontaneously resolve without serious complications, but others may develop pyelonephritis which can further progress to renal scarring, hypertension, and chronic kidney disease. In a previous study, computational models used variables from 205 patients including age, laterality, grade of reflux, bladder volume at the onset of reflux, ureteral duplication, and bladder-bowel dysfunction to help predict chances of early resolution in children with VUR. Since the creation of this model, the distal-ureteral-diameter ratio (UDR) has been recognized as a prognostic factor of resolution and risk of UTI. The goal of this project was to create updated computational models that included the previous predictive variables in addition to UDR to better predict 1 and 2-year reflux resolution.

Methods: We reviewed medical records and voiding cystourethrography's (VCUG) of 828 children diagnosed with primary VUR between 1982 and 2018 at our institution. Predictive factors included in the computational models were age, sex, presenting symptom, laterality, reflux grade, bladder volume at onset of reflux, and UDR. The UDR was calculated by dividing the largest ureter diameter within the false pelvis by the distance from the bottom of L1 to the top of L3 vertebral bodies on the VCUG. Not all measurements or variables were available for all patient visits, so separate models were built based on the availability of each measurement and were fit using PROC GENMOD in SAS with a binomial distribution, logit link, and an exchanged correlation structure to account for repeated measurements within patients.

Results: Reflux grade, bladder volume at onset of reflux, and UDR each improved prediction of VUR resolution as compared with covariates alone. The model combining bladder volume at onset of reflux and reflux grade had the highest predictive performance at 1 year (AUC=0.777) and 2 years (AUC=0.758). At 1 year, the model combining UDR and reflux grade performed significantly better than the reflux grade alone ($p=0.044$). The resulting models were then created into a web-based user-friendly application that generates patient specific predictions at 1 and 2 years after diagnosis including the corresponding sensitivities and specificities. The web-based user-friendly application can be seen here: https://ph-ivshiny.iowa.uiowa.edu/loharris/reflux_prediction_app.

Conclusion: The integration of UDR into our computational models provides a more objective and reliable variable for predicting likelihood of resolution as compared to previous models. These updated computational models are able to integrate routinely available clinical data to provide more individualized estimates of early spontaneous VUR resolution. These models can help clinicians and families make more informed management decisions.

MiR-23a-3p mimics modulate GPX4 expression in corneal endothelial cell lines

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Introduction: Fuchs endothelial corneal dystrophy (FECD) is a genetic disorder of the corneal endothelium and the leading indication for corneal transplant in the US. Healthy corneal endothelial cells (CECs) are essential for maintaining visual clarity through barrier functions and ion pumps that maintain the water balance in the cornea and prevent it from becoming edematous and causing poor vision. In FECD, the CECs lose their normal morphology and function and eventually die through a process called ferroptosis, leading to corneal edema and reduced visual clarity. There are currently no treatments to slow or stop the progression of FECD, and corneal transplant remains the only curative measure for this condition. Developing a treatment to slow the progression of FECD could prolong or eliminate the need for corneal transplant, improving visual outcomes without the risks and resources associated with surgery. Prior studies have demonstrated that microRNA (miRNA) expression is significantly altered in FECD, and restoring expression of some miRNAs that are deficient in FECD has been shown to protect CECs against ferroptosis, but more work must be done to identify the best miRNA to treat FECD prior to rigorous drug development.

Purpose/Hypothesis: In this study, we aimed to identify a strong candidate miRNA to treat FECD and test its ability to protect CECs against ferroptosis. We also performed experiments to elucidate the genetic modulation of GPX4 in immortalized CECs transfected with miR-23a-3p mimics to determine effectiveness in modulating GPX4 protein expression, a potent inhibitor of ferroptosis. We hypothesized that transfecting immortalized CECs with miR-23a-3p mimics would increase expression of GPX4.

Methods: We submitted corneal endothelial peels from surgical patients with FECD (N=10) as well as healthy controls (N=10) to Novogene to perform miRNA sequencing to determine which miRNAs are most differentially expressed in FECD. For the transfection experiments, we grew immortalized healthy CEC lines (B4G12 cells) as well as immortalized FECD CEC lines (F35T cells) to 70% confluency in biological triplicates and transfected them with miR-23a-3p for 24 hours before replacing the transfection materials with normal F35T growth media for an additional 48 hours. We collected cell lysates, analyzed GPX4 expression using a microfluidics Western blot, and used one-way ANOVA, Tukey's post-test, and Welch's t-test to determine statistical significance. These results will later be used in comparison to the therapeutic potential of the miRNA identified in the sequencing results in finding the best candidate for treating FECD.

Findings: So far, we found that miR-23a-3p transfection significantly increased GPX4 protein expression in B4G12 cells compared to negative and scramble sequence controls (Tukey adjusted $p=0.0026$ and 0.0203 respectively), but did not have a significant effect on GPX4 expression in F35T cells (ANOVA $p=0.11$). For all treatment groups, GPX4 expression was significantly higher in F35T cells than in B4G12 cells (Welch's t-test $p<0.05$ for all groups).

Conclusion: These results demonstrate our transfection protocol effectively increases expression of anti-ferroptosis proteins in B4G12 cells, but our transfection protocol or our miRNA of choice must be changed to see a similar effect in F35T cells. When we receive our miRNA sequencing results, we will analyze them and decide if we wish to continue optimizing the miR-23a-3p transfection protocol for F35T cells, or if we will proceed with another candidate miRNA for follow-up experiments.

Analysis of Electrode Migration After Cochlear Implant in Dexamethasone Eluting Electrodes

Agam Gill, B.S.E., Aseem Jain, M.D., Alexander Claussen, M.D.

Cochlear implants (CIs) work to restore hearing in those with profound sensorineural hearing loss by bypassing the damaged inner ear and providing direct electrical stimulation to auditory neurons. However, the surgical trauma and chronic foreign body response elicited by electrode insertion drive intracochlear fibrosis and inflammation, which can raise electrode impedance, degrade the electrode-neural interface, and contribute to loss of residual hearing over time. Dexamethasone eluting CIs (Dex-CIs) are an emerging innovation in CIs that were developed to address this limitation by reducing inflammation and electrical impedance in CIs through sustained and localized intracochlear steroid release. As Dex-CIs undergo clinical validation, it is important to evaluate their effect on electrode migration (EM), defined as postoperative movement of the electrode array (EA) within the cochlea, since reduced intracochlear fibrosis could theoretically allow greater EA movement over time. EM is reported to be the second leading cause of revision surgery in CI, and its consequences include drop in hearing performance, pain, increased electrode impedance, and facial nerve stimulation. The purpose of our study was to assess for differing rates of EM in standard (non-Dex) CIs vs Dex-CIs over 12 months using CT imaging to determine whether dexamethasone elution is associated with greater EM.

This study used an IRB-approved retrospective cohort of 30 patients (15 Dex-CI, 15 non-Dex-CI) who underwent perimodiolar (CI632 or CI632D) electrode insertion between 2022-2024 and had CT imaging performed preoperatively, at initial activation, and at 12 months postoperatively. A previously developed cochlear implant positional analysis tool was used to (1) segment the EA from postoperative CT scans and (2) estimate intracochlear regions and cochlear duct length (CDL) from preoperative imaging. These results were co-registered to measure EA position relative to intracochlear structures, including distance from the EA to the modiolus and to the lateral wall expressed as a function of CDL. This tool was applied to each patient at each postoperative time point and results between the two groups were compared. Additionally, to further measure EM, the 12-month CT was registered to the initial-activation CT. EA segmentations were then qualitatively assessed for migration, and surface distance between the registered EA segmentations was calculated as a quantitative measure of EM. Finally, a Mann-Whitney U test was used to assess differences in EM, distance from EA to modiolus, and distance from EA to lateral wall between the Dex-CI and non-Dex-CI groups.

There was no statistically significant difference between the Dex-CI and non-Dex-CI groups in distance from the EA to the modiolus or to the lateral wall ($p = 0.836$ and $p = 0.868$, respectively). Quantitative EM was also similar between groups (median = 0.104 mm for Dex-CI vs. 0.081 mm for non-Dex-CI; $p = 0.263$). However, qualitative assessment did show two Dex-CI patients with notable EA misalignment (migration of 0.169 mm and 0.240 mm, respectively). In both patients, the EA moved toward the modiolus between 10–25% of CDL and shifted toward the lateral wall between 25–50% of CDL, where the largest displacement occurred.

Overall, these findings suggest that dexamethasone does not have a statistically significant impact on EM. However, the wider variability within the Dex-CI group including two cases of clinically notable migration warrants continued monitoring. Future research should be done to better understand the mechanisms behind EM.

Exploring the Association Between Adverse Childhood Experiences and Fatigue, Quality of Life, and Mood Among People with Multiple Sclerosis

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Background

Adverse childhood experiences (ACEs) are known to impact long-term health into adulthood. While ACEs as early stressors have been studied as a cause of neuronal dysfunction and a predictor of healthy lifestyle in adulthood, it is unknown how ACEs specifically affect adults with multiple sclerosis (MS), especially their symptoms and quality of life (QoL). It is essential to understand how factors beyond disease pathology, such as early life stressors, can impact fatigue, mood, and overall QoL in patients with MS.

Purpose

To investigate anxiety, depression, fatigue, and QoL among adults with MS with or without a history of ACEs.

Methods

Individuals aged ≥ 18 with relapsing-remitting MS (RRMS) enrolled in the EDQ-MS study (IRB: 202104639) completed baseline online surveys assessing ACEs and patient-reported outcomes (PROs). Survey instruments included the 10-item ACE questionnaire for ACE, Hospital Anxiety and Depression Scale (HADS-A and HADS-D) for mood, Multiple Sclerosis Quality of Life-54 (MSQOL-54) for mental and physical QoL, and both the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS) for fatigue. Data was deidentified, and differences between groups based on ACE category were examined using Fisher's exact, ANOVA, and Kruskal-Wallis tests. A p -value of <0.05 indicated statistical significance.

Results

Baseline MFIS – cognition scores were poorer between individuals with MS who had history of 1+ ACEs (scores: 15 vs 14, $p=0.0434$). Baseline scores of the mental health composite of the MSQoL-54 measure were worse in individuals with MS who had a history of ACEs than those who did not (scores: 79 vs 74, $p=0.0337$). No significant associations were observed with mood, fatigue severity, physical and psychosocial function, or physical health with regards to daily activities.

Conclusion

A history of ACEs among people in the MS community was associated with a greater impact on fatigue and cognitive function. Additionally, individuals with MS and a history of ACEs had worse mental health within the aspect of daily activities. The findings suggest that a history of ACEs affects the health and daily activities of individuals with MS.

Plaque Enhancement on High-Resolution MRI and its association with Recurrent Ischemic Stroke in Intracranial Atherosclerotic Disease: A Multicenter Longitudinal Study

Student: Caleb Greene

Mentor: Edgar Samaniego, MD, MS, Clinical Professor of Neurology

Collaborators: Giancarlo Campodonico, Martin Cabarique, Chengcheng Zhu, Bing Tian, Mirjam Heldner,

Background

Intracranial atherosclerotic disease (ICAD) is a major cause of ischemic stroke, with the degree of stenosis currently used to assess the risk of recurrent ischemic stroke. However, the degree of stenosis does not always correlate with symptoms and does not convey the structure of complex plaques. This limitation highlights the need for additional biomarkers to characterize atherosclerotic plaques that may become symptomatic. Plaque enhancement (PE) on high-resolution MRI (HR-MRI) following gadolinium administration has been identified as a potential biomarker of symptomatic plaques, as plaques that have more enhancement are more likely to be present in patients who have suffered an acute ischemic stroke (AIS) or a transient ischemic attack (TIA). In this multicenter study, we evaluated the potential association between plaque morphology and PE, and the risk of recurrent AIS or TIA in patients with ICAD.

Hypothesis

Increased PE may be associated with recurrent AIS and TIAs in patients with underlying ICAD.

Methods

Patients from three institutions in Switzerland, China, and the United States, who suffered an AIS and/or TIA attributed to ICAD were included. They underwent imaging on a 3T HR-MRI at baseline and one-year follow up. Atherosclerotic plaques were localized, and only symptomatic plaques, defined as those within the vascular territory of the index AIS or TIA, were included in the analysis. Following multiplanar image review, three-dimensional (3D) segmentations of each symptomatic plaque were conducted. Signal intensity (SI) was quantified, 3D heat maps, and enhancement histograms were generated. SI directly correlates with PE after the administration of contrast, with plaques that exhibit more SI, being brighter after the administration of contrast. Plaque morphological metrics, including degree of stenosis and plaque burden, were also obtained. The primary outcome was new AIS or TIA related to ICAD. Changes in plaque enhancement and plaque morphology were analyzed as secondary outcomes.

Results

A total of 151 patients with AIS and TIA attributed to ICAD were included. During one-year follow-up, 24/151 patients (15,9%) developed a new AIS and TIA. On multivariable logistic regression, increased degree of stenosis (OR 0.97, 95% CI 0.55–1.72, $p=0.92$) or increased plaque burden (OR 0.59, 95% CI 0.10–3.35, $p=0.70$) were not associated with recurrent AIS or TIA. However, an increase in PE on follow-up 3T HR-MRI was associated with a higher risk of recurrent AIS (OR 3.66, 95% CI 1.01–13.22, $p=0.04$). Patients with poorly controlled hyperlipidemia, reflected in higher low-density lipoprotein (LDL) at one year compared to baseline were more likely to show higher PE on follow-up HR-MRI (OR 1.38, 95% CI 1.01–1.91, $p=0.04$). No association was found between smoking, aspirin use, administration of dual antiplatelet therapy, or changes in hemoglobin A1c with PE, degree of stenosis, or plaque burden ($p>0.05$).

Conclusion

Increased PE on follow-up imaging is associated with a higher risk of recurrent AIS or TIA and is correlated with higher LDL levels over a one-year period. These findings suggest that PE may serve as a potential biomarker for risk stratification and therapeutic monitoring in patients with ICAD.

Droperidol vs. Ketamine for Out-of-Hospital Agitation Management

Student: Kendall Haefele, M4

Mentor: Dr. Peter Georgakakos, DO, FAEMS

Collaborators: Taeuk Kang MSc, MBiotech; Sydney Krispin, MA, MPH; Priyanka Vakkalanka, PhD

ABSTRACT

Background: Emergency Medical Service (EMS) providers routinely administer ketamine to manage acutely agitated patients; however, recent ketamine shortages and safety concerns have increased interest in alternative approaches to agitation management. Droperidol is recommended by the National Association of EMS Physicians (NAEMSP) as an alternative to ketamine, although comparative out-of-hospital data remain limited.¹ We evaluated whether droperidol use by EMS in the out-of-hospital setting for agitated patients was associated with improved patient outcomes compared with ketamine in the emergency department (ED).

Methods: This was a retrospective cohort study of patients who received chemical sedation by a single ambulance service in a midwestern state between January 2019 and August 2024. Data were collected from hospital and EMS electronic medical record systems. We included adult patients (≥ 18 years) who presented with agitation and received droperidol or ketamine in the out-of-hospital setting. Our primary outcome was the need for airway support; secondary outcomes included the use of physical restraints, adjunctive medication and patient disposition. We measured the association between medication administration and outcomes using multivariate logistic regression, adjusting for clinical characteristics.

Results: Among 178 screened patients, 152 patients met eligibility criteria. One hundred patients (65.8%) received droperidol and 52 (34.2%) received ketamine. Few patients were intubated in the hospital setting (four received droperidol, six received ketamine), and there was no association between medication administration and intubation (adjusted odds ratio [aOR]: 0.4; 95% CI: 0.2-1.1). Use of adjunctive medications was lower among patients receiving droperidol compared to the ketamine (aOR: 0.4; 95% CI: (0.2-0.9), but there was no observed difference between medication given and use of physical restraint or ED disposition.

Conclusion: Among agitated patients receiving chemical sedation in the out-of-hospital setting, droperidol and ketamine were associated with similar patient safety outcomes after adjustment for clinical characteristics. Droperidol use was associated with reduced adjunctive medication administration. Further multicenter, prospective studies are needed to better understand the comparative safety and effectiveness of these medications in the out-of-hospital setting.

Title: Tumor-Associated Macrophages Modulate Proliferation and are Altered by Treatment in Vestibular Schwannoma

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Introduction: Vestibular schwannoma (VS) is the most common tumor of the peripheral nervous system and causes progressive hearing loss, tinnitus, imbalance, and, in large tumors, brainstem compression. Treatment options remain largely limited to surgical resection and radiotherapy (RT), and tumor recurrence or progression remains a concern, particularly in patients with Neurofibromatosis type 2. Recent research into the tumor microenvironment (TME) of VS demonstrates an association between increased levels of tumor-associated macrophages (TAMs) and more rapid VS growth. However, the functional contribution of TAMs to VS proliferation and their response to treatment are not well understood and may inform better treatment strategies and targeted therapies for patients.

Purpose: To determine the role of TAMs in promoting VS growth and to characterize the changes in macrophage and schwannoma cell populations following RT and CSF-1R inhibition.

Methods: To assess the role of TAMs in driving the growth of VS, primary human VS cells and autologous macrophages derived from peripheral blood collected at the time of surgical resection were cultured *in vitro*. Cultures were randomly assigned to one of three groups (n=8 per group): 1) VS culture only, 2) VS and resting macrophage co-culture, and 3) VS and lipopolysaccharide (LPS)-activated macrophage co-culture. VS cells and macrophages were cultured separately for 7 days and subsequently co-cultured for an additional 7 days. 5-Ethynyl-2'-deoxyuridine (EdU) was administered during the final 72 hours to assess cellular proliferation. Immunofluorescence (IF) staining for S-100 and CD68 identified VS cells and macrophages, respectively, and cultures were imaged using confocal microscopy. EdU incorporation in VS cells was quantified.

To assess whether macrophage-mediated effects were dependent on soluble factors, VS cells were cultured with 1) control medium, 2) resting-macrophage-conditioned medium, or 3) LPS-activated-macrophage-conditioned medium, followed by EdU quantification using the same IF-based approach.

To evaluate treatment-associated changes *in vivo*, fresh human primary VS tissue from surgical resection was implanted subcutaneously between the scapulae of 8 to 16-week-old nude mice. Five weeks after tumor implantation, mice were randomly assigned to one of four conditions (n≥3 per group): 1) no treatment (control) 2) 12.5 Gy RT 3) PLX5622 diet (PLX), or 4) 12.5 Gy RT and PLX5622 diet (RT-PLX). PLX5622, a CSF-1R kinase inhibitor used to reduce macrophage populations, was administered for 1 month before xenograft harvest, and RT was delivered 1 week before harvest. 72 hours before xenograft harvest, EdU was administered to all mice. Tumor xenografts were then fixed as frozen samples, sectioned, and IF stained with SOX10 and Iba1 as markers of schwannoma cells and macrophages, respectively. After imaging with confocal microscopy, SOX10 and Iba1 cell counts were performed and colocalization of SOX10 and Iba1 with EdU was analyzed to assess differences in cell populations.

Results: Direct co-culture with LPS-activated macrophages significantly increased VS cell proliferation compared to VS with resting macrophages (mean EdU uptake 10% vs 3%; p=0.04). In contrast, LPS-activated macrophage-conditioned medium was associated with lower VS proliferation than resting-macrophage-conditioned or control medium (mean EdU incorporation, 3%, 13%, and 14%, respectively). In xenograft models, PLX and RT-PLX treatment groups showed a significantly reduced proportion of Iba1+ cells compared to RT mice (p=0.0006 and p=0.0074, respectively). RT-treated xenografts also demonstrated a trend toward a greater proportion of Iba1+ compared to untreated controls. No significant differences in EdU+SOX10+ or EdU+Iba1+ cells were observed among treatment groups.

Conclusions: This study provides an initial investigation into the role of TAMs in the growth of VS and their response to radiation and chemotherapy treatments. Direct co-culture of VS and LPS-activated macrophages *in vitro* resulted in greater tumor proliferation while conditioned media alone from LPS-activated macrophages inhibited VS proliferation, suggesting that a physical interaction between VS cells and macrophages may be required for a protumorigenic effect rather than soluble factors alone. A successful xenograft model of RT and CSF-1R inhibition chemotherapy for VS was also created which demonstrated that PLX treatment successfully depletes Iba1+ TAMs *in vivo* but does not acutely alter VS cell proliferation. RT was associated with a trend toward increased macrophage abundance, warranting further investigation into treatment-induced macrophage recruitment. Future studies will characterize the mechanisms underlying macrophage-VS interactions and determine the longer-term effects of RT and CSF-1R inhibition on VS growth.

It's Not All Your Fault: Paternal Health Status and the Impact on Preeclampsia Development

Gwen Harty BS, Madison Seda BS, Alexa Rivera, Ashlyn Kenney BS, Nicole Essig BS, Meghan Funk BS, Heath Davis MS, Donna Santillan PhD, Brandon Schickling, PhD, Mark Santillan, MD, PhD

Introduction

Each year there are 600,000 deaths worldwide that are due to preeclampsia. Preeclampsia is thought to develop through the incorrect remodeling of spiral arteries in the placenta which leads to reduced blood flow, decreased nutrient delivery, and increased oxidative stress. It is important to note that paternal imprinting occurs in placental genes, specifically in placental growth and modulating the placenta's nutrient transport capacity, which are important aspects in preeclampsia (PreE) development. Despite previous links demonstrating maternal-paternal immune incompatibility increasing PreE risk, the role of paternal health remains understudied. We hypothesize that poor paternal health will lead to poor pregnancy outcomes and impacts on fetal development.

Methods

This retrospective cohort study included a subset of participants in the University of Iowa Women's Health Tissue Repository (WHTR) that underwent artificial reproductive technology (ART) to achieve pregnancy and who had seminal fluid samples available for later analyses. This cohort of participants included 56 individual fathers and 74 unique pregnancy episodes. All coded clinical data were obtained from the banks within the WHTR including Reproductive Endocrinology and Infertility Bank (IRB# 201709794), Perinatal Family Tissue Bank (IRB# 200910784), and the Intergenerational Health Knowledgebase (IRB# 201902830, 202102473). We examined the health status of the father, specifically their cardiovascular health and analyzed that in relation to matched pregnancy outcomes in the mother. Paternal cardiovascular disease (CVD) was defined as hypertension, multiple elevated blood pressure readings, type I and II diabetes, and mixed hyperlipidemia. Descriptive, univariate, and multivariate regression analyses were conducted ($\alpha = 0.05$).

Results

In an uncontrolled analysis, there were significant differences in the rates of PreE (39% vs. 15%, $p = 0.019$) and age (37.071 vs 34.37, $p = 0.01$) in fathers with cardiovascular disease compared to those without cardiovascular disease. Unsurprisingly, as these variables have already been associated with increased rates of PreE, preexisting hypertension (OR = 11, $p < 0.001$) and depression (OR = 13.6, $p < 0.001$) with PreE as the dependent variable. Pregnancies resulting from fathers with CVD placed the mother/pregnancy at increased risk of developing PreE (OR=3.6, $p = 0.02$). Even after controlling for known clinical covariates such as preexisting hypertension in the mother and diabetes during pregnancy, paternal CVD is independent risk factor for PreE development (aOR=3.6, $p = 0.02$).

Conclusions

Our data demonstrate that paternal cardiovascular disease is an independent risk factor for preeclampsia development. Future studies will focus on the molecular mechanisms that link paternal exposure to pregnancy to the development of the short- and long-term risk of preeclampsia in mothers.

Clinical, Histologic, and Molecular Insights into Wound Healing Under Systemic Immunosuppression

Grace P. Haugstad, Rachel Heinrich, Jodi Jin, Trenton Grief, Vincent Liu, Jennifer Powers, Kelly N. Messingham

ABSTRACT

Background:

Wound healing is a tightly regulated process that requires a balance between inflammatory and reparative signaling. Immunosuppressive therapies, commonly used in organ transplantation, are often considered a surgical risk factor, yet there is evidence that their use improves cutaneous healing in some patients.

Hypothesis:

We believe the inflammatory cytokines, profibrotic mediators, and growth factors in the wound milieu after Mohs micrographic surgery will differ between immunosuppressed and non-immunosuppressed patients.

Methods:

We conducted a prospective study of 23 patients undergoing Mohs micrographic surgery for non-melanoma skin cancer, including 8 patients receiving systemic immunosuppression for organ transplant rejection and 15 non-immunosuppressed controls. Surgical discard tissue was collected on Day 0, and wound biopsies were obtained on Day 14. Histologic scoring evaluated inflammation, fibroblast density, collagen deposition, vascularity, and macrophage populations. RT-qPCR quantified inflammatory cytokines (IL-1 β , IL-6, TNF- α), profibrotic mediators (TGF- β family), and growth factors (FGFs, EGF, VEGFs, PDGFA). Clinical outcomes were assessed through serial wound photography, scar measurements, and patient- and observer-reported scar scales on days 0, 14 and at follow-up (3-6 months).

Results:

Histologic scoring revealed significantly reduced inflammatory infiltrates in immunosuppressed wounds ($p = 0.014$) without impairment of collagen maturation or vascular remodeling. While TNF- α remained stable over time in both groups, IL-1 β and IL-6 were reduced at D14. In immunosuppressed wounds, IL-1 β levels were significantly reduced compared to controls by Day 14 ($p \leq 0.05$). Immunosuppressed wounds demonstrated greater downregulation of TGF- β 1, TGF- β 2, and TGF- β R1, whereas TGF- β 3 appeared increased. Growth factor analysis revealed reduced FGF2, FGF3, EGF, VEGFA, VEGFC, and PDGFA expression in immunosuppressed patients, while FGF1 and VEGFB remained stable or increased, suggesting compensatory pathways.

Conclusions:

Systemic immunosuppression was associated with reduced inflammation and downregulation of profibrotic signaling, while key reparative growth factor pathways were preserved, resulting in wound healing outcomes comparable to controls. These findings suggest that immunosuppression rebalances the wound environment by limiting inflammation without abolishing regenerative mechanisms. Targeted modulation these pathways may represent a therapeutic strategy to optimize cutaneous repair and reduce fibrosis.

Title: Hospital rurality, CoC accreditation status and timeliness of adjuvant radiation in patients with head and neck squamous cell cancer

Authors: Lauren Herrington, Bryan Palis, Xuan Zhu, Ingrid Lizarraga, Mary Charlton, Ronald J. Weigel, Xiang Gao

Introduction: Adjuvant radiation is a mainstay of treatment for patients with head and neck squamous cell cancer (HNSCC) and receiving post-operative radiation therapy (PORT) within 6 weeks of surgery is a quality measure for hospitals accredited by the Commission on Cancer (CoC). Previous analyses demonstrated that non-adherence was higher among patients who received surgery and PORT at different facilities and patients who lived in rural areas. One important factor to consider with these observations is the rurality of the hospital and its role in ensuring timely delivery of PORT. Currently, this quality measure is assessed only for CoC hospitals who perform the surgery and not for hospitals who only deliver PORT. Without knowledge of their adherence on this metric, hospitals who only provide PORT are limited in their ability to identify and address delays in PORT.

This study examined measure adherence by hospital rurality and CoC-accreditation status to gain insight into whether providing data on measure adherence for PORT represents an opportunity for improving timely receipt of PORT in rural hospitals.

Methods: Eligible cases of HNSCC who underwent surgery and PORT between 2018 and 2023 were abstracted from the National Cancer Database (NCDB). CoC hospital location was determined by geocoding the hospital postal code to its corresponding latitude and longitude coordinates. Rurality was classified using the Rural-Urban Continuum Codes (RUCC), with counties assigned RUCC codes 4–9 classified as rural. Measure adherence (start of PORT $\leq$ 42 days after surgery) were calculated by rurality and CoC-accreditation status of the hospital(s) where surgery and PORT were performed.

Results: The study included 23,498 cases. Measure adherence for CoC hospitals performing the surgery was 35%, while adherence for all hospitals regardless of surgery site was 33% ($p < 0.01$). Overall, 11% of cases received PORT at a rural hospital and 62% received PORT at a CoC hospital. Among rural PORT cases ($n=2479$), 68% received surgery at an urban hospital, 30% received PORT at a CoC hospital, and 76% received surgery at a CoC hospital. Among urban PORT cases ($n=19,375$), 97% received surgery at an urban hospital, 71% received PORT at a CoC hospital, and 75% received surgery in a CoC hospital. Among cases where both PORT and surgery were in rural hospitals, 70% received PORT at a CoC hospital but surgery at a non-CoC hospital. Measure adherence was highest (40%) when both surgery and PORT were performed at urban CoC hospitals. Measure adherence was lower for cases of PORT at CoC and surgery at non-CoC (26%) compared to PORT at non-CoC and surgery at CoC (29%, $p < 0.05$). Among cases that received both surgery and PORT in a rural hospital, measure adherence was lower (25%) if PORT was at a CoC hospital and surgery was not, compared to 34% if surgery was at a CoC hospital and PORT was not ($p = 0.096$).

Conclusion: This study uses novel data from the NCDB to analyze adherence of timely PORT for HNSCC by hospital rurality and accreditation status. Compared to their urban counterparts, rural PORT cases less often received PORT in a CoC hospital but had a similar proportion of receiving surgery at a CoC hospital. Additionally, for rural cases, measure adherence was lower when PORT was at a CoC hospital and surgery was not. Taken together, these findings represent an opportunity to support CoC accreditation in rural settings and suggest that providing rural hospitals who perform PORT with data on their measure adherence may result in a decrease in PORT delay.

Title: *Vaccine Hesitancy Among US Adults and the 7C Psychological Antecedents Model: A Cluster Analysis*

Name: Jacob Hill

Mentor: Natoshia Askelson

Collaborators: Aaron Scherer, Knute Carter, Anna Miller

Abstract (367 words):

Purpose: Declining public confidence in vaccines has become a global crisis. In 2019, the WHO declared vaccine hesitancy one of the most salient threats to global health. Most current strategies to increase vaccine acceptance focus on providing pro-vaccine information, but these have proven to be largely ineffective at changing behavior. Alternatively, some research has focused instead on elucidating the psychosocial components of vaccine hesitancy. In 2022, Geiger et al. compiled previous research into the “7C” model, which contains three components (that is, psychological antecedents of behavior) associated with higher vaccine acceptance and four components associated with higher vaccine hesitancy. While subsequent studies have validated the 7C model, they have not considered the potential value of identifying shared variance between 7C components in order to tailor vaccine advocacy to specific populations. We propose that qualifying the multivariable nature of vaccine hesitancy using the 7C model will allow for more targeted interventions.

Methods: The research team conducted a survey from July 10 to August 5 of 2025 utilizing a national, demographically diverse panel of American adults recruited by Dynata. Participants answered questions about their demographics, the short-form 7C model questionnaire, and other medical, psychological, and political measures. Participants who did not complete each analyzed variable were excluded from the study. The research team then used K-means clustering (N=3244) to identify subgroups of respondents with similar profiles across the included variables. Four clusters were selected based off of the within-cluster sum of squares (WSS) elbow method. Differences across clusters were assessed using the Kruskal-Wallis rank sum test and Pearson’s chi-squared test.

Results: Preliminary analysis demonstrated four clusters with distinct vaccination readiness and demographic profiles. This is the first phase in a larger 3-phase study. In the second phase, focus groups tailored to the four identified vaccine readiness and demographic profiles will be conducted by the research team. The findings of these focus groups will be used to create vaccination promotion strategies utilized in the third phase of the study, a survey-based experiment that evaluates the efficacy of the vaccination promotion strategies. The ultimate goal of this 3-phase study is to create an interactive vaccination promotion website that provides evidence-based, personalized content based off of the self-identified characteristics of the user.

Improvements in non-rapid eye movement sleep parameters correlate with improvements in treatment-resistant depression among individuals receiving electroconvulsive therapy

Student: Margaret Huang, BS

Mentor: Mark Niciu, MD, PhD

Collaborators: Bengi Baran, PhD, Hazal Arpacı, MS, and Isabella Martinez, BS

Background: Major depressive disorder (MDD) is one of the leading causes of morbidity and mortality globally. Treatment for MDD typically consists of psychotherapy and antidepressant medication. Treatment resistant depression (TRD) is typically defined as MDD that has not improved (measured by a 50% or greater reduction in standardized rating scale scores) after two or more trials of antidepressant medication at adequate doses and durations. TRD individuals can pursue interventional psychiatric modalities including electroconvulsive therapy (ECT). Individuals with MDD and especially so with TRD tend to experience sleep disturbances, and issues with sleep are known to exacerbate depressive symptoms and quality of life issues of affected individuals.

Purpose: The aim of this project was to study how non-rapid eye movement (NREM) sleep is impacted by ECT, with a secondary goal of exploring whether changes in sleep early in the treatment course can predict eventual antidepressant response. We expected ECT to improve sleep measures in individuals and early improvements in sleep to predict later improvements in mood.

Methods: Participants were recruited from the patient population receiving interventional psychiatric therapies as second-line treatment for TRD. We included individuals within the ages of 18-65 who had a diagnosis of MDD and were receiving ECT for depression. Each participant was evaluated at 2-3 time points: a baseline evaluation before treatment and a post-treatment evaluation occurring at the end of the course (after 6-12 sessions). At each visit, the participant completed questionnaires assessing mood and sleep. A researcher administered the Montgomery-Åsberg Depression Rating Scale (MADRS), which measured changes in depression. The EEG monitor was set up for the participant to wear during sleep and data was collected in the morning to be uploaded to the Sleep Profiler software.

Results: Pre- and post- treatment sleep and mood data were obtained from 10 patients receiving inpatient ECT treatment. Within-subject analyses using Student's t-test on RStudio and Jamovi were used to compare participants' variables at baseline versus at the two-week follow-up. Sleep parameters of interest included total sleep time, sleep efficiency, and sleep latency, and the NREM features of sleep spindles and slow wave oscillations. At the follow-up, TRD participants were found to have increased percentage of time spent in NREM3 (deep sleep); decreased percentage of time spent in NREM2 (light sleep); decreased NREM3 latency (time spent to reach stage 3 of NREM sleep); and increased N2N3 delta power (a proxy for slow wave activity). Pearson's correlation coefficient was used to explore associations between changes in sleep variables and changes in mood. An increase in MADRS score is considered a worsening of mood while a decrease in MADRS is considered an improvement in mood. Three sleep variables—N2N3delta power (a proxy for slow wave activity), N2N3 sigma power (a proxy for sleep spindles), and spindle duration—were negatively correlated with MADRS scores. As they increased, MADRS score decreased.

Conclusion: These findings were consistent with our hypothesis that with ECT, TRD individuals would see improvements in sleep and that these improvements in sleep would accompany improvements in mood. Limitations of our study included a small sample size, reliance on the automatic sleep scoring of the sleep software, and multiple statistical analyses performed with uncorrected p-values. Thus, any findings from our study are preliminary and should emphasize potential directions to explore. In the future, studies should expand the sample size and consider investigating whether the NREM sleep parameters of slow wave activity and sleep spindles have a causal effect on treatment efficacy and whether these sleep improvements last long-term.

Development of an Intraoperative Bone Quality Assessment Tool for Total Knee Arthroplasty

Trevor B. Hughes, BS, Michael C. Marinier, MD, Jacob M. Elkins, MD, PhD

Introduction:

Total knee arthroplasty (TKA) is one of the most common orthopedic procedures performed worldwide, with the annual number of cases expected to grow exponentially. Additionally, the population of patients undergoing TKA has shifted to include patients who are younger, more obese, and living longer. Cemented fixation has historically been the gold standard in TKA; however, the changing patient population has led to concerns with the longevity of the bone-cement interface and the possibility of long-term aseptic loosening in cemented implants. This concern has led to renewed interest in cementless fixation, which had previously fallen out of favor due to poor patient outcomes. However, modern cementless implants have shown good survivorship rates, particularly in younger and more obese patients, due to advances in surgical technique and implant technology. Unlike cemented implants, cementless implants rely on biological ingrowth from the host bone for fixation and stabilization. Poor bone quality at the knee joint can therefore lead to early failure, making selection of patients with sufficient bone quality crucial to success in cementless TKA. Intraoperative assessment of mechanical suitability for cementless fixation in TKA is largely subjective, relying on tactile feedback, palpation, and visual grading. Therefore, a need exists for an objective intraoperative measure to provide surgeons with improved feedback and aid in making informed decisions on choice of fixation.

Purpose:

The aim of this study was to design, construct, and evaluate the repeatability of a simple prototype device capable of applying a controlled force intended to be used on discarded cancellous bone during TKA via indentation testing.

Methods:

The device was constructed to perform impact-based testing of the mechanical resistance of the specimen being measured, which is an established method for material characterization. A vertical drop was utilized, as gravity is a reproducible and constant force. A 25 mm steel ball bearing attached to a steel rod free falls to impact a 10 mm steel ball bearing to apply a concentrated force. The rod is held upright on a ring stand by a 3D printed cylindrical cap that stabilizes the rod while still allowing for the rod to move unimpeded to apply the indentation force. Repeatability testing was performed on three commercial foams, performing 5 trials on each foam and measuring indentation depths for each trial. Indentation depth measurements were taken using the depth gauge on a Pittsburgh Digital Caliper (accuracy: $\pm 0.03\text{mm}$). Mean indentation depth, standard deviation, and coefficient of variation (CV) were calculated for each foam to assess the repeatability of the device.

Results:

A total of 15 indentation trials were performed across three commercial foam materials ($n=5$ per material). Repeatability testing demonstrated low within-material variability, with CVs of 1.0%, 4.2%, and 4.7% across the three materials. Mean indentation depths were 5.09 ± 0.053 mm, 2.73 ± 0.114 mm, and 2.38 ± 0.111 mm, respectively.

Conclusion:

A functional prototype indentation device was successfully developed and demonstrated repeatable measurements across different commercial foams. These findings support further validation of the device as a potential objective method of assessing mechanical suitability for cementless fixation in TKA. Future goals include completing testing on polyurethane foams from Sawbones that mimic cancellous bone properties, with known hardness, densities, and compression moduli to calculate device sensitivity to changing mechanical properties. Eventually, testing should progress toward use on cadaver specimens and clinical testing in the operating room.

Improving geometric and dynamic fluid modeling of the optic nerve head with a nerve-centered image segmentation approach

Treyton Hveem; Zhi Chen; Saikat Mukherjee, PhD; Edward Linton, MD

Introduction:

Optical coherence tomography (OCT) is used to assess the optic nerve by measuring retinal nerve fiber layer (RNFL) thickness; however, conventional segmentation methods interpolate retinal structures across the optic nerve head (ONH) and do not accurately represent patient-specific ONH anatomy. These limitations reduce the ability to characterize three-dimensional nerve geometry, which is increasingly recognized as an important determinant of optic nerve biomechanics, glymphatic fluid dynamics, and disease progression in conditions such as papilledema, ischemic optic neuropathy, and spaceflight-associated neuro-ocular syndrome (SANS). Development of anatomically accurate volumetric segmentation models may improve disease characterization and enable more robust predictive modeling.

Purpose:

To develop a manually labeled dataset and manually traced segments of ONH OCT images to support training and validation of an automated three-dimensional segmentation model, evaluate labeling reproducibility through inter-rater agreement, and establish a framework for longitudinal assessment of optic nerve edema progression.

Methods:

A retrospective dataset of OCT scans from eyes with normal anatomy, optic nerve edema, and other optic neuropathies was assembled. Manual segmentation of the optic nerve head, lamina cribrosa, and Bruch's membrane was performed using the University of Iowa Deep-LOGISMOS framework with Just Enough Interaction (JEI)-assisted refinement. A chart review was conducted to assign reference labels for normal and abnormal optic nerves. Nerve scans were independently segmented by a second reviewer to assess inter-rater agreement of manual segmentation. Longitudinal OCT studies from selected patients were manually traced across multiple time points to evaluate changes in optic nerve geometry and edema progression.

Results:

Manual segmentation of the study dataset and chart review for clinical labeling have been completed. Longitudinal tracings of selected optic nerves are in progress. Inter-rater analysis shows 0.893 ± 0.056 , 0.537 ± 0.095 , and 0.925 ± 0.059 agreement between tracings of the ONH, lamina cribrosa, and Bruch's membrane opening respectively. The manual-versus-automated mean B-scan Dice score of 0.927 is greater than the inter-observer ONH mean subject-level Dice score. Chart review revealed the number of eyes diagnosed with raised ICP, inflammatory optic neuropathy, ischemic optic neuropathy, compressive optic neuropathy, glaucoma, and miscellaneous causes of optic disc edema are 76, 32, 26, 9, 20, and 132 respectively.

Conclusions:

This work establishes a high-quality, manually annotated volumetric OCT dataset with clinically validated labels and longitudinal imaging to support development of anatomically accurate ONH segmentation. Future analyses will determine whether three-dimensional nerve-centered segmentation improves automated modeling of optic nerve anatomy, edema progression, and patient-specific risk prediction compared with conventional OCT segmentation methods.

Evaluation of Subsequent Fetal Outcomes Following Chorioamnionitis Diagnosis in a Prior Pregnancy.

Delaney Ita, Jillian Janssen, Jennifer Bermick MD, Jeremy Sandgren MD, PhD; Heath Davis MS, Donna Santillan PhD, Mark Santillan MD, PhD

Objective: Chorioamnionitis is a common perinatal infection involving the fetal membranes during labor or late pregnancy. Inflammatory diseases in pregnancy, like chorioamnionitis, are associated with short and long-term poor maternal-child outcomes. While there is a known association between chorioamnionitis and poor immediate newborn outcomes, there is little known about the effects that chorioamnionitis have on neonatal outcomes in a subsequent pregnancy. This study aimed to evaluate the association between the diagnosis of chorioamnionitis in a first pregnancy and adverse neonatal outcomes in the subsequent pregnancy.

Hypothesis: We hypothesize that pregnancies affected by chorioamnionitis will have a higher rate of poor neonatal outcomes in an immediately subsequent pregnancy.

Study Design: This retrospective cohort study (IRB#201902830) collected data on 46,372 pregnancies at the University of Iowa Health Care from 2000 to 2026 from the Iowa Intergenerational Health Knowledgebase (IIHK). Among these episodes, 629 mothers were identified and confirmed in the electronic health record (EPIC) of having chorioamnionitis as well as an immediate subsequent pregnancy. Exclusion criteria included deliveries at outside institutions, diagnoses of “at risk for chorioamnionitis,” and patients without a true subsequent pregnancy. Neonatal outcomes and later childhood diagnoses were evaluated via paired t-tests, χ^2 tests, and logistic regression models ($\alpha=0.05$).

Results: Neonates from a subsequent pregnancy of a previous chorioamnionitis affected pregnancy had higher mean birthweight (3437 vs. 3319 grams, $p<0.001$), lower 1- and 5-minute APGAR scores (7.33/7.66, $p<0.0001$ vs. 8.58/8.68, $p=0.014$), and more often required positive pressure ventilation (13.2% vs. 10.2%, $p=0.017$), total body cooling (2.9% vs. 1.3%, $p=0.002$), and treatment for hypoglycemia (19.9% vs. 15.4%, $p=0.003$).

Discussion: These findings suggest that there may be an association between a prior history of chorioamnionitis and adverse neonatal outcomes in the subsequent pregnancy. Further research is needed to evaluate the influence of concurrent maternal comorbidities as well as if there are associations to long-term health outcomes.

Assessment of the Performance of Large Language Models in the Diagnosis and Management of Cutaneous T-Cell Lymphoma

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Introduction: Cutaneous T-cell lymphoma (CTCL) can often resemble common inflammatory skin conditions such as atopic dermatitis and psoriasis, leading to delay in diagnosis and treatment. Whether artificial intelligence large language models (LLM) can effectively aid in diagnosing CTCL has been explored in a limited number of studies to date. These studies have largely focused on the pathology role in diagnosis, evaluating the ability of AI models to render a CTCL diagnosis based upon interpretation of H&E (hematoxylin and eosin) stained skin biopsies. The potential ability of AI models to assist the clinician by raising a differential diagnosis of CTCL based upon clinical scenarios, and by developing treatment plans currently remains uninvestigated.

Purpose: To assess the current ability of available LLMs to recognize, diagnose, and advise management of CTCL.

Methods: Three LLMs were tested: ChatGPT 5.6-Sol (publicly available), Claude Opus 5 (publicly available), and OpenEvidence (available to clinicians). ChatGPT and Claude “effort” level was set to “high. Following institutional IRB approval, fifteen standardized format clinical vignettes were created from medical records of patients diagnosed with CTCL (mycosis fungoides (MF) or Sezary syndrome (SS)), selected from the University of Iowa Healthcare (UIHC) CTCL registry. Patient clinical data preceding and immediately before the diagnosis of CTCL was anonymized and distilled into a vignette, including demographic information, history of present illness, past medical history, and physical exam details for the initial encounter. Each vignette was offered to each LLM, which was prompted for its ranked differential diagnoses (including % confidence) and recommendations for next steps. If requested by the LLM, results from skin biopsies, bloodwork, and if available, radiographic and other pathologic data were given. The LLM was then prompted again for its ranked differential diagnoses (including % confidence) and asked to create a treatment plan for the patient. For each LLM, the same patient vignette was run three times to evaluate reproducibility. The LLMs were run on modes that did not allow learning from or reference to the other vignette trials. Analysis of LLM responses for diagnosis, staging, and treatment was conducted by measuring frequency of CTCL inclusion in the differential diagnosis at both the initial and secondary prompts, and by comparing LLM suggested stage, work-up, and treatment responses with recommendations by the National Comprehensive Cancer Network (NCCN) guidelines for CTCL and with actual UIHC management.

Results: In 100% of these trials (n=135), the learning models requested a skin biopsy and, upon reviewing biopsy results, placed MF at the top of their updated differential diagnosis list. LLMs were also generally able to advise further work-up and treatment strategies for CTCL in accordance with NCCN guidelines. However, limited internal LLM reproducibility was observed upon repeated iteration with respect to specifics of treatment. Compared to the publicly available LLMs, OpenEvidence was seen to include CTCL in the preliminary differential diagnosis less frequently and to exhibit more internal variation of treatment strategy. Additionally, differences between LLMs were noted, in terms of precision, detail, and tone confidence of recommendations.

Conclusion: The demonstration of LLMs to correctly suggest CTCL in the differential diagnosis for provided clinical scenarios showcases the potential of such models as diagnostic aids. Although models also recommended NCCN-approved treatment, variable internal inconsistency raises caution for their current role in treatment guidance.

Finger Tapping Performance Before and After Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease

Student: Sonia Jeon

Mentor: Jeremy 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 74 patients with idiopathic Parkinson's disease receiving bilateral STN-DBS with assessment at baseline (pre-surgical), 6-month, and 12-month post-operative timepoints. 42 control or non-DBS patients that were matched with the surgical patients, using the same inclusion/exclusion criteria. 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. A wireless goniometric device captured tap frequency (Hz), movement speed (degrees/s), and amplitude variability —metrics relevant to bradykinesia and dysrhythmia assessments critical for PD diagnosis. UPDRS motor scores were collected in both the ON and OFF states at 6- and 12-months.

Results: DBS ON versus OFF comparisons showed minimal change in tap frequency ($p = 0.17$, $d = 0.18$) but significant gains in movement speed ($+11.6\%$, $p = 0.001$, $d = 0.45$) and motor consistency (amplitude variability, $p = 0.0006$, $d = 0.47$), indicating stimulation acts on movement speed and regularity more than tapping rate. Benefit was largest in the more-affected hand and at 6 months, attenuating by 12 months. Compared with matched controls, untreated patients differed most in motor consistency rather than speed; stimulation restored speed to near-control levels while a consistency deficit persisted. Quantitative changes correlated moderately with UPDRS scores ($r = 0.6$), though some patients showed objective change not captured by UPDRS.

Conclusions: Our longitudinal within-subject analysis in 74 DBS surgical and 42 control subjects demonstrates differential finger tapping 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, suggesting UPDRS may underestimate treatment response; (3) Objective goniometric finger tapping measures could guide DBS programming by identifying individual responses.

Preoperative Median Nerve Cross-Sectional Area Is Not Associated with Recovery After Carpal Tunnel Release: An Analysis of Clinical, Anatomic, and Operative Factors

Student: Aditya Joglekar, BS

Mentor: Dr. Joseph A. Buckwalter V, MD, PhD

Purpose

Although electrodiagnostic studies have been the gold standard for diagnosing carpal tunnel syndrome (CTS), ultrasound has emerged as a rapid and noninvasive adjunct for diagnosing CTS. Median nerve cross-sectional area (CSA) is widely used as a diagnostic tool, but its ability to predict outcomes after Carpal Tunnel Release (CTR) remains unclear. The goal of this study was to determine whether preoperative CSA is associated with time to Resolution of Symptoms (RoS) after CTR. Secondary analyses evaluated additional patient-level clinical and anatomical factors associated with postoperative RoS.

Methods

We conducted a single-center retrospective cohort study that analyzed 1,359 patients who had MN US imaging and met inclusion/exclusion criteria. Clinical documentation was reviewed to extract US findings, determine time to RoS, and potential covariates. This data was analyzed using a Weibull accelerated failure time (AFT) regression model.

Results

374 cases were included in the final cohort. 63.9% of cases (n=239) were female, average age was 51.7 (± 14.8) years, and mean body mass index (BMI) was 32.7 (± 7.7) kg/m². No association was found between CSA and time to RoS (p=0.643), even when normalized for BMI, weight, height separately (p=0.675, 0.676, and 0.696, respectively). 8.0% of cases (n=30) had a bifid median nerve which was not associated with time to RoS (p=0.076). Similarly, 30.7% of cases (n=115) had at least one corticosteroid injection prior to the CTR which was not associated with time to RoS (p=0.217). 19.5% of cases (n=73) had a concomitant ulnar nerve decompression and were associated with prolonged time to RoS compared to isolated CTR (AF=2.936, p<0.001). Likewise, 6.4% of the cases (n=24) were revision CTR which were associated with a delayed time to RoS (AF=3.057, p=0.038).

Conclusions

Although CSA is well established for the diagnosis of CTS, our findings suggest that CSA is not associated CTR outcomes, even after normalization for patient body habitus. Recovery appears to be multifactorial and associated with patient-level anatomical and clinical factors. These findings may improve patient counseling regarding expected recovery following CTR.

Safety and Efficacy of Atrial Antitachycardia Pacing with a Plugged Ventricular Port in Patients with Congenital Heart Disease

Alex Johnson, Ben Hale, MD, Mark Olson, Abdelrahman Masri, MD, Ashley Kimball, Maja Palmroos, and Ian Law, MD

Introduction/Background:

Intra-atrial reentrant tachycardia (IART) is an arrhythmia frequently experienced by patients with congenital heart disease (CHD). Although antiarrhythmic medications and catheter ablations may decrease the arrhythmia burden and improve the quality of life of some CHD patients, these treatments are less effective in patients with complex CHD. Atrial antitachycardia devices (ATDs) provide atrial antitachycardia pacing (ATP) and have successfully treated arrhythmias like IART, in complex CHD. When the ventricular lead is present the ATD can detect 1:1 A:V conduction, which automatically disables ATP therapy. “Plugging” the ventricular (v) port of an ATD blinds the ATD from determining if there is 1:1 AV conduction, allowing ATP intervention. However, when the v port is plugged it prevents the detection of potential rapid 1:1 AV conduction, which could result in hemodynamic compromise. To date, there have been no long term studies evaluating the efficacy and safety of “blinded” (plugged v port) ATP pacing in the CHD population.

Purpose/Hypothesis:

The goal of our study is to evaluate the safety and efficacy of ATP with plugged ventricular ports in the CHD population. We hypothesized that ATP therapy would be both safe and effective.

Methods:

This retrospective and prospective study analyzes data on CHD patients at the University of Iowa, Children’s Hospital of Orange County, the University of Louisville, and the University of Wisconsin who have received an ATD implant with the v port plugged and ATP enabled.

Results:

17 patients underwent ATD implantation for a combined 105 patient years with a median follow up time of 4.5 years. Indications for ATD implantation included: IART (17 patients), sinus node dysfunction (13 patients), and complete heart block (1 patient). Patients were programmed with both Ramp and Burst+ therapies, and if one did not terminate the arrhythmia, the other would attempt to pace terminate. There were a total of 2366 attempted treatments for AT/AF and 1777 successful pace terminated AT/AF episodes for a success rate of 75.0% (95% CI: 73.3% - 76.8%). Patient-level success rate was 60.2% (95% CI: 40.4% - 80.0%), with a median success rate of 72.5%. Burst+ had a success rate of 57.2% (651/1138) and Ramp had a success rate of 52.1% (392/752). While the number of cardioversions decreased post implantation, the change was not statistically significant ($P=0.2020$, Wilcoxon test). The number of ablations decreased significantly after implantation ($P=0.0479$, Wilcoxon test), with only one patient requiring an ablation post implantation. The number of antiarrhythmic medications did not change after implantation ($P=1.0$, Wilcoxon test). There were no instances of cardiac arrest or other life-threatening events related to ATP. One patient had a stroke, and two patients were hospitalized due to sustained AT/AF after ATD implantation.

Conclusion:

This retrospective and prospective study supports the safety of ATP therapy with a plugged v port in the CHD population despite a theoretical risk of rapid AV conduction.

Kidney Dysfunction and Nephrology Referral Patterns in Adolescents and Young Adults with Eating Disorders

Eleanor Johnson, Jason Misurac, Patrick Ten Eyck, Linder Wendt, Emily Steinbach Swehla, Lyndsay Harshman

Background: Impaired renal function has been observed as a significant consequence of eating disorders due to chronic malnutrition and purging behaviors, yet studies on the prevalence of renal dysfunction among individuals with a history of eating disorders are limited to small, single-center cohorts. Furthermore, no studies to date have characterized how nephrology referral timing affects patient outcomes.

Methods: A retrospective analysis leveraging Epic Cosmos, a de-identified database of Epic's health records, was conducted to identify the prevalence of acute kidney injury (AKI), chronic kidney disease (CKD), and end-stage kidney disease (ESKD) among patients aged 9–25 years at the time of an eating disorder diagnosis. Kidney and electrolyte outcomes were defined by ICD-10 codes and were compared across eating disorder subtypes. Nephrology referral timing was examined in relation to the rate of eGFR change and the development of end-stage kidney disease.

Results: Among 191,368 adolescents and young adults with an eating disorder diagnosis (median age 17 years [IQR 14–21]; 83% female; 77% White), the most common diagnoses were unspecified (49%) and other specified (24%) eating disorders, followed by restricting anorexia nervosa (13%), binge-eating disorder (12%), avoidant/restrictive food intake disorder (11%), bulimia nervosa (11%), and binge-eating/purging anorexia nervosa (5.0%). Kidney dysfunction was identified in 6,811 patients (3.6%), including AKI in 2.1% and CKD in 1.4%; electrolyte disturbances occurred in 12%, most often hypokalemia (8.0%). Median eGFR was 79 mL/min/1.73 m² (IQR 37–122) at first measurement and 111 (81–126) at last, with a median annual change of +1. Kidney and electrolyte complications were most severe among patients with combined restricting and binge/purge anorexia nervosa compared with the restricting type alone (AKI 8.1% vs 3.0%; CKD 2.6% vs 1.0%; hypokalemia 26% vs 8.8%; all $p < 0.001$). Only 4,691 patients (2.5%) were referred to nephrology, at a median of 519 days (IQR 106–1,273; ≈ 1.4 years) after diagnosis. Advanced (stage 3–4) CKD and ESKD were identified far more often among referred than non-referred patients (7.2% vs 0.4% and 5.7% vs 0.5%, respectively), yet 46% of patients with ESKD were never referred. Patients referred within one year of diagnosis had a more favorable median annual eGFR change than those referred later (+3 vs +1 mL/min/1.73 m²/year; $p < 0.001$).

Conclusions: In this population-based cohort of adolescents and young adults with eating disorders, kidney dysfunction affected 3.6% of patients and was most pronounced among binge/purge phenotypes. Nephrology referral was uncommon and typically delayed beyond one year, and nearly half of patients with end-stage disease were never referred, suggesting that kidney complications may be under-recognized in this population. Earlier referrals were associated with a more favorable eGFR trajectory; because these associations may reflect confounding by indication, prospective validation is warranted.

Role of Microglia in Thalamic Neurodegeneration Following Traumatic Brain Injury

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Introduction: Traumatic Brain Injury (TBI) is a leading cause of death and disability among children and young adults. Despite over 200,000 hospitalizations a year due to TBI, there are currently no available neuroprotective therapeutics. Over the last few decades, it has been well established that neuroinflammation plays a major role in the secondary injury cascade following TBI via type 1 interferons. Microglia, the resident immune cells of the central nervous system, are upregulated following TBI, including in areas outside of the primary injury site. The goal of this project was to identify the spatiotemporal timeline of microglia expression in a mouse model of TBI and track subsequent neuronal loss.

Hypothesis/Purpose: The purpose of this project is to determine the molecular mechanisms underlying the secondary injury response in TBI. We hypothesized that microglia upregulation would persist at least 28 days post TBI and coincide with neuronal loss in the thalamus.

Methods: For this project, we utilized the lateral fluid percussion (FPI) injury model to induce TBI in C57BL/6 mice. At days 3, 7, 14, and 28 post injury, mouse brains were perfused, collected, and sectioned at 10 μ m. Non-surgical control animals matched each timepoint and received anesthesia. Immunofluorescence was then performed using the microglia marker IBA1 and the neuronal marker NeuN. Neuronal cell counts were determined in Olyvia.

Results: FPI mice showed an upregulation of microglia surrounding the cortical injury site and hippocampus at 3 days post injury compared to the diffuse expression pattern seen in non-surgical control mice. As early as 7 days post injury, the thalamus showed signs of increased microglial accumulation that persisted through 28 days post injury. Interestingly, neuronal loss was observed in the thalamus only starting at 7 days post injury, coinciding with microglia upregulation.

Conclusions: Our findings indicate that following TBI, microglia accumulation begins near the site of injury; however, over time, this accumulation extends to areas beyond the site of primary injury, including the thalamus where significant neuronal loss was observed. These observations may help to explain the worsening of clinical symptoms seen by patients months to years following TBI. Future work is aimed at identifying how blocking type 1 interferon signaling pathways affects the spatiotemporal expression of microglia following TBI, which neuronal cell populations are lost, and the mechanisms underlying this neuronal cell death.

Title: Limited Health Literacy is Associated with Reduced Healthcare Engagement and Worse Patient-Reported Outcomes in Orthopedic Patients

Student: Alana Jones, M2

Mentor: Dr. Natalie Glass, Associate Research Scientist/Engineer, Orthopedics and Rehabilitation, Carver College of Medicine, University of Iowa; Dr. Michael Willey, Associate Professor of Orthopedics and Rehabilitation

Background: Health literacy is an important determinant of healthcare engagement and outcomes, yet its prevalence and clinical associations among orthopedic patients remain incompletely characterized.

Purpose: This study evaluated health literacy across multiple orthopedic subspecialties and examined associations between limited health literacy, patient characteristics, healthcare engagement, and patient-reported outcomes

Methods: A retrospective analysis was conducted of adult patients evaluated across six orthopedic services between April 2025 and June 2026. Health literacy was assessed using the BRIEF Health Literacy Screen and patients were categorized as having inadequate/marginal (scores ≤ 16) or adequate health literacy (scores ≥ 17). Demographic and clinical characteristics, healthcare engagement measures, and patient-reported outcome measures (PROMIS Physical Health, PROMIS Mental Health, PROMIS Pain Interference, Pain Catastrophizing Scale [PCS]) were compared between health literacy groups using chi-square tests for categorical variables or Wilcoxon Rank sum tests for continuous variables due to non-normal distributions.

Results: Among 2,788 patients assigned the BRIEF Health Literacy Screen, 2,173 (78.0%) completed the assessment, with completion rates ranging from 70.2% to 79.1% across orthopedic subspecialties. Among 2,169 patients with classifiable scores, 542 (25.0%) had inadequate/marginal health literacy and 1,627 (75.0%) had adequate health literacy, although prevalence varied by service. Compared with patients with adequate health literacy, those with inadequate/marginal health literacy had greater obesity prevalence (55% vs 48%, $p=0.009$), medical comorbidity (53% vs 46% with Charlson Comorbidity Index score >2 , $p=0.005$) and longer travel distances (median[IQR]=52[14-69] vs 36[7-67], $p=0.003$), and were more likely to be male (56% vs 41%, $p<0.001$), current smokers (10% vs 5%, $p<0.001$), unmarried (48% vs 40%, $p<0.001$), Medicaid-insured (15% vs 8%, $p<0.001$), and rural residents (32% vs 26%, $p=0.009$). Limited health literacy was also associated with lower MyChart activation (85% vs 95%, $p<0.001$) and higher no-show rates (6% vs 3%, $p=0.002$). Among patients who completed patient reported outcomes, those with inadequate/marginal compared with adequate health literacy had a greater prevalence of below normal PROMIS Physical Health scores (47% vs 31%, $p<0.001$), Mental Health score (32% vs 16%, $p<0.001$), and Pain Interference scores (65% vs 48%, $p<0.001$) as well as severe levels of pain catastrophizing (47% vs 25%, $p<0.001$).

Conclusions: Approximately one in four orthopedic patients exhibited marginal or inadequate health literacy. Lower health literacy was associated with demographic and socioeconomic disparities, greater comorbidity, reduced engagement with digital health tools, and significantly worse physical and mental health outcomes. Routine health literacy screening may help identify patients who could benefit from targeted educational interventions and communication strategies to improve orthopedic care and patient-reported outcomes.

Abstract Title

Large Scale Lesion and Lesion Network Localization of Chronic Hemispatial Neglect

Akshaj A Joshi, Joseph C Griffis, Joel E Bruss, Carrie N Brandauer, Aaron D Boes

Background

Hemispatial neglect (HN) is a common and debilitating consequence of focal brain damage involving impaired awareness of stimuli on one side of space. While most patients recover, persistent neglect may continue for years and substantially impair independence. Although acute neglect has been associated with lesions involving the ventral attention network, much less is known about the anatomical basis of chronic neglect. Prior studies have been limited by small samples, selection biases, and methodological heterogeneity.

Purpose

In one of the largest analyses to date, we sought to characterize the neuroanatomy of chronic HN using multimodal lesion and lesion-network localization in a less-selected cohort.

Methods

Participants were drawn from the Iowa Neurological Patient Registry ($n = 241$) and a Washington University in St. Louis stroke cohort ($n = 104$). Chronic HN (≥ 3 months post-lesion, $n = 34$) was defined by clinician-rated neglect, $\geq 70\%$ lateralized misses on the Line Cancellation Test, or a Behavioral Inattention Test Center of Cancellation ≥ 0.1 . All participants underwent research-grade MRI. Lesions were manually traced, confirmed by a neurologist, and normalized to a common brain template. Using the Iowa Brain-Behavior Toolkit, we performed voxel-based lesion-symptom mapping (VLSM), functional lesion network mapping (FLNM), and structural lesion network mapping (SLNM) while controlling for lesion size in both hemispheres. Permutation testing (1000 iterations) was used to determine statistical significance (family-wise error-corrected $p < 0.05$).

Results

VLSM yielded the strongest results, identifying regions in the dorsal and ventral attention networks, including the superior parietal lobule (peak partial $r = 0.27$), inferior parietal lobule (peak partial $r = 0.25$), and inferior frontal gyrus (peak partial $r = 0.25$). VLSM also identified the cingulum (peak partial $r = 0.21$). FLNM extended these results by identifying a lesion-associated functional network spanning dorsal attention and default-mode regions. SLNM findings did not survive permutation testing.

Conclusion

To our knowledge, this is one of the largest lesion/network analyses of chronic HN to date. Chronic neglect localized to a distributed system involving dorsal and ventral attention regions, with functional network involvement potentially extending into the default mode network. Because recovery from neglect has been associated with normalization of dorsal attention connectivity and dorsal attention–default mode interactions, direct damage to these regions may limit network normalization and contribute to the persistence of neglect. These findings extend network models of neglect beyond its acute origins and highlight the cingulum and other underemphasized regions for future prognostic and therapeutic investigation.

Title: Pre-Transplant Pulmonary and Cardiac Function as Predictors of Outcomes After Autologous Stem Cell Transplantation in Multiple Myeloma.

Student: Vivek Joshi

Mentor: Hira Shaikh

Background/Introduction

Pulmonary function tests (PFTs) and echocardiography are routinely obtained before autologous stem cell transplantation (ASCT) in multiple myeloma (MM), but the prognostic value of pre-ASCT cardiopulmonary testing remains uncertain. We evaluated associations of pre-ASCT pulmonary and cardiac function with early post-transplant complications, prolonged hospitalization, and 1-year survival.

Methods

We retrospectively analyzed adults undergoing first ASCT for plasma cell malignancies at a tertiary academic center between January 2012 and August 2024. Pre-ASCT FEV1, DLCO, ejection fraction (EF), cardiopulmonary comorbidities, performance status, and post-transplant outcomes were abstracted from the electronic health record. Outcomes included abnormal events within 100 days, prolonged hospitalization (>21 days), and 1-year overall survival. Logistic and Cox regression models were used; FEV1 and DLCO were evaluated in separate multivariable models because of expected collinearity.

Results

Among 686 patients, 95.2% had MM; median age was 61 years and 58.7% were male. Prior pulmonary and cardiac diagnoses were present in 23.7% and 33.5%, respectively. Abnormal 100-day outcomes occurred in 35.1%. Rates were 31.7% versus 45.6% for FEV1 >80% versus ≤65% and 24.7% versus 41.7% for DLCO >80% versus ≤65%. Prolonged hospitalization occurred in 18.4% versus 39.2% across the same FEV1 groups and 15.7% versus 30.3% across the same DLCO groups; 12-month survival was 94% versus 77% and 96% versus 85%, respectively.

In univariable analyses, FEV1 ≤65% (OR 1.81, 95% CI 1.11–2.93) and DLCO ≤65% (OR 2.18, 95% CI 1.45–3.27) were associated with abnormal 100-day outcomes relative to >80%. In separate multivariable models, FEV1 ≤65% was associated with abnormal 100-day outcomes (OR 1.75, 95% CI 1.06–2.88), prolonged hospitalization (OR 2.86, 95% CI 1.67–4.88), and 1-year mortality (HR 4.93, 95% CI 2.54–9.55) relative to >80%. DLCO ≤65% was similarly associated with abnormal 100-day outcomes (OR 2.09, 95% CI 1.38–3.18), prolonged hospitalization (OR 1.96, 95% CI 1.21–3.18), and 1-year mortality (HR 4.00, 95% CI 1.67–9.59) relative to >80%. Abnormal EF was associated with 100-day complications (adjusted OR 1.45–1.48) but not prolonged hospitalization or 1-year mortality.

Conclusion

Pre-ASCT pulmonary impairment, indicated by reduced FEV1 and DLCO, was independently associated with early complications, prolonged hospitalization, and 1-year mortality. Reduced EF was less consistently associated with adverse outcomes. These findings support cardiopulmonary risk stratification and prospective study of commonly used PFT thresholds.

Upper-Extremity Functional Recovery After Breast Reconstruction: A Longitudinal Comparison of Implant-Based and DIEP Flap Reconstruction

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Background and Aims

Upper-extremity dysfunction is an important component of recovery after breast reconstruction, but the functional burden of implant-based reconstruction versus deep inferior epigastric perforator (DIEP) flap surgery remains incompletely characterized. We compared longitudinal changes in upper-extremity disability following implant-based reconstruction and DIEP surgery.

Methods

We retrospectively analyzed postmastectomy reconstructive episodes with preoperative Disabilities of the Arm, Shoulder and Hand (DASH) scores and postoperative follow-up. Episodes were categorized as immediate implant-based reconstruction (tissue expander or direct-to-implant, anchored to the mastectomy) or DIEP flap reconstruction (immediate or delayed). Baseline was the most recent preoperative DASH, and the primary outcome was change from that baseline across prespecified intervals (0–2 weeks through >1 year), with positive values indicating greater disability. Trajectories were compared using Gaussian generalized estimating equations with patient-level clustering and robust standard errors, adjusted for baseline DASH, age, BMI, bilaterality, preoperative radiation, nodal surgery, and pre-existing upper-extremity conditions.

Results

Analysis included 156 reconstructive episodes (124 implant-based, 32 DIEP) and 997 postoperative DASH assessments. Mean preoperative DASH was 4.9 in the implant-based group and 8.7 in the DIEP group. At 0–2 weeks, adjusted mean postoperative DASH increased from baseline by 37.5 points in the implant-based group and 36.3 points in the DIEP group, declining to 7.5 and 3.3 points, respectively, by 7–12 weeks. By 3–6 months, adjusted DASH was 2.8 points above baseline in the implant group and 1.9 points above baseline in the DIEP group. Overall recovery trajectories did not differ significantly (group-by-phase interaction, $p=.096$), and no individual phase-specific difference reached statistical significance. Nonetheless, patients undergoing DIEP reported less disability at 7–12 weeks (DIEP-minus-implant difference, -4.2 points; 95% CI, -9.2 to 0.8 ; $p=.100$) and >1 year (DIEP-minus-implant difference, -4.8 points; 95% CI, -10.7 to 1.1 ; $p=.111$). Preoperative radiation was more common among DIEP flap patients (43.8% vs 7.3%).

Conclusions

Implant-based and DIEP flap breast reconstruction produced substantial early upper-extremity disability followed by rapid functional recovery. Although longitudinal trajectories were not statistically different, the lower reported disability after DIEP at later time points warrants further investigation. These findings may improve preoperative counseling by providing patients with realistic expectations regarding the magnitude and duration of postoperative functional impairment. Future analyses should evaluate the contribution of radiation to upper-extremity recovery and follow implant-based patients longer to determine whether their DASH scores return fully to baseline.

Impact of Treatment on Prevalence of Mental Health Disorders in Children with Hemophilia A

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Introduction: Hemophilia A (HA) is a rare X-linked bleeding disorder caused by factor VIII deficiency, leading to increased bleeding, and is treated with factor VIII replacement or factor VIII-mimetic therapies. The efficacy of current hemophilia therapies is commonly assessed using annualized bleeding rates (ABR), but substantial variation in the ABR definition and calculation limits its utility for evaluating treatment effectiveness. The emphasis on joint health as the primary target of prophylactic FVIII replacement has led to a paucity of research regarding detection, treatment, and prevention of effects on other end-organs, such as the brain. Additionally, higher rates of depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD) have been reported in people with hemophilia which reduce quality of life and treatment adherence, increasing morbidity and mortality. It is essential to understand the consequences of repeated “microbleeds” to the brain and utilize this knowledge to determine the ability of current and future therapies to provide protection of end-organ systems. Therefore, it is important to identify correlations between mental health disorder prevalence and treatment options to identify an alternative measure of outcomes and efficacy for current and future therapies.

Method: We conducted a retrospective cohort study of all children with hemophilia A (0 to <18 years old). Comparisons were conducted between PWH treated with factor products compared to those treated with mimetic products and PWH treated with recombinant factor products compared to those treated with plasma-derived factor products. Data were collected from UIHC electronic health records spanning from 1/1/1990 to 1/1/2025 and entered using Research Electronic Data Capture (REDCap). Collected variables included age, sex, hemophilia type, hemophilia severity, hemophilia treatment, type of mental health disorder, and mental health disorder treatment. Patients were stratified based on the extent of time on medications (minimum 1 year of treatment). Differences between groups were assessed via Chi-squared and Fisher Tests (RStudio). Statistical significance (probability of error) will be fixed at $p < 0.05$.

Findings: Of the 93 children with HA identified, 64 were identified in the factor replacement medication group and 16 were identified in the factor mimetic medication group. 22/93 (23.66%) were identified as having a diagnosis of a mental health disorder (MHD). Of the 64 in the factor replacement group, 47 (73.43%) did not have a MHD, while 17 (26.56%) did. Of the 16 in the mimetic group, 12 (75%) did not have a MHD, while 4 (25%) did. There was no significant difference ($p=1$) in the prevalence of MHD between factor replacement and factor mimetic treatment. There was a significant difference ($p=0.0000124$) in severity of hemophilia between treatment groups. Of the 64 patients in the factor replacement group, 25 (39.06%) had moderate/severe hemophilia A. Of the 16 patients in the mimetic group, 15 (93.75%) had moderate/severe hemophilia A. There was no significant difference ($p=0.985$) in MHD prevalence between patients with mild and moderate/severe hemophilia A. In a stratified analysis comparing MHD prevalence in factor replacement and mimetic treatments, patients were grouped based on severity. In patients with moderate/severe hemophilia A, 7/25 patients (28%) in the factor replacement group had a MHD while 3/15 patients (20%) in the mimetic group had a MHD. In patients with mild hemophilia A, 10/39 patients (25.64%) in the factor replacement group had a MHD, while 1/1 (100%) in the mimetic group had a MHD. In both moderate/severe ($p=0.715$) and mild ($p=0.275$) patients, there was no significant difference in MHD prevalence between treatment groups. Of the 80 patients taking factor replacement, 76 were placed into the recombinant group, and 4 were placed into the plasma group. 19 (25%) of the 76 patients in the recombinant group had a MHD, while 2 (50%) of the 4 patients in the plasma group had a MHD. There was no significant difference ($p=0.281$) in MHD prevalence between the recombinant and plasma groups. There was no significant difference in severity between the recombinant and plasma groups.

Conclusion: In this preliminary study, there was no significant difference between treatment groups in the prevalence of Mental Health Disorders (MHD). There was also no difference in MHD between severity of hemophilia. This contrasts with a previous publication by Schmitt *et al.* which revealed significant differences in MHD across hemophilia severities, with higher rates of MHD in moderate/severe hemophilia compared to mild. There was an anticipated significant difference in treatment types between mild and moderate/severe hemophilia within our patient population, with a higher prevalence of severe hemophilia patients within the mimetic group. This could potentially indicate that factor mimetics reduce the prevalence or prevent MHD which would normally be increased in patients with moderate/severe hemophilia. More research is needed to validate these findings in a larger sample size.

Body Image Distress and Psychosocial Well-Being Following Implant-Based Breast Reconstruction: A Preliminary Cross-Sectional Analysis

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Background: Breast reconstruction aims to restore physical form and psychosocial wellbeing following mastectomy. Although validated patient-reported outcome measures assess satisfaction and quality of life following reconstruction, surgical restoration may not fully resolve persistent body image distress. Whether body image distress and positive patient reported outcomes represent inverse constructs or may coexist following reconstruction remains poorly characterized. This preliminary study evaluates the relationship between body image distress and psychosocial well-being among patients following implant-based breast reconstruction.

Methods: In this cross-sectional study, adult patients (≥ 18 years) 1–5 years following unilateral or bilateral mastectomy with implant-based breast reconstruction completed surveys comprising the BREAST-Q Reconstruction Module (Psychosocial Well-Being, Satisfaction with Breasts, and Sexual Well-Being) and the 54-item BIMS. BIMS outcomes included total symptoms experienced (0–54) and overall severity (0–50), calculated from five symptom domains. BREAST-Q scores were Rasch-transformed to a 0–100 scale. Associations between BIMS and BREAST-Q domain scores were assessed using Spearman rank correlations.

Results: Preliminary data were available for 13 patients (mean age 49.7 ± 8.6 years; 76.9% bilateral reconstruction). Mean BREAST-Q scores were 64.5 ± 20.3 for Psychosocial Well-Being, 57.8 ± 14.1 for Satisfaction with Breasts, and 38.8 ± 23.0 for Sexual Well-Being. Patients endorsed a mean of 5.0 ± 4.7 BIMS symptoms. Greater BIMS symptoms experienced was associated with lower Psychosocial Well-Being ($\rho = -0.59$, $p = 0.034$) and demonstrated negative, although nonsignificant, associations with Sexual Well-Being ($\rho = -0.50$, $p = 0.078$) and Satisfaction with Breasts ($\rho = -0.40$, $p = 0.171$). In contrast, BIMS overall severity demonstrated little association with Psychosocial Well-Being ($\rho = -0.18$, $p = 0.550$) or Satisfaction with Breasts ($\rho = -0.02$, $p = 0.938$).

Conclusion: Preliminary findings suggest that greater body-image symptom burden is associated with poorer psychosocial well-being following implant-based breast reconstruction. However, the severity of body-image distress demonstrated little relationship with satisfaction with breasts, suggesting that these measures may capture related but distinct areas of postoperative recovery. These findings highlight the potential value of assessing both positive patient-reported outcomes and persistent body-image concerns following reconstruction. Larger datasets are needed to determine whether these measures provide complementary information that may inform preoperative counseling and targeted psychosocial support.

Identifying Novel Variants and Genotype-Phenotype associations in Charcot-Marie-Tooth and Hereditary Spastic Paraplegias using Long-Read Sequencing

Madelyn Klemmensen, Tiffany Grider, Miranda Keith, Thomas Woodford, Viviane Banion, Amanda Dragon, Leidewei Van de Vondel, Stephan Züchner, Michael E Shy

Background and Problem

Charcot-Marie-Tooth (CMT) and Hereditary Spastic Paraplegia (HSP) are neurodegenerative diseases classified based on clinical characteristics, electrophysiological features, metabolic defects, and specific genetic loci. Despite recent advances in genetic testing, the genetic diagnosis of CMT and HSP can be challenging, potentially leading to a diagnostic odyssey for patients and families. Long read whole genome sequencing (LRS) provides much longer genetic readouts than whole exome or short read whole genome sequencing, ultimately improving variant detection through improved mapping of complex regions. LRS enables identification of new pathogenic variants that previous methods could not identify.

Hypothesis

LRS will allow for the identification of novel variants in CMT and HSP. Utilizing genotype-phenotype information with novel variants can aid in future diagnostic and prognostic information.

Methods

Patient Enrollment: 13 patients clinically diagnosed with Charcot-Marie-Tooth disease (4 female, 8 male) or Hereditary Spastic Paraplegia (1 male) were recruited from the existing GENESIS database and all had LRS (PacBio HiFi) available. Informed consent was obtained from all participating subjects, and all patient information is protected under the Health Insurance Portability and Accountability Act (HIPAA). All patient information is encrypted and assigned to a random university unique identifier (UUID) upon registration. Analysis of long read sequencing: GENESIS and their integrated pipeline were used for LRS analysis to call candidate variants. GENESIS utilizes a variety of AI pathogenicity and constraint predictions including CADD, GERP, Maverick, SpliceAI, etc. Transcripts are aligned with GRCh37. Genotype-Phenotype relationship: Clinic evaluation including general health information, neurological examination, CMT examination score (CMTES), and CMT Functional Outcome Measure (CMTFOM)/CMTPedS, were used in review.

Results

Candidate variants were identified in all 13 patients. There were two pairs of siblings with the same variant (MPV17: UIA-76098-0001 and -0100; GJB1: UIA-100850-0001 and -0101) and two pairs of individuals with variants in the same gene (HADHB: UIA-103056-0001 and WSU-75600-0001; DOCK9: UIA-103102-0001 and UIA-94895-0001). 4 candidate genes are associated with human disease: MPV17 – CMT2EE, HADHB - mitochondrial trifunctional protein deficiency, GJB1 – CMT1X, KIF5A – SPG10. Remaining candidate genes (DOCK9, EIF4A3, ACER3, AGO3, PPTC7, KDM4B, SON) are expressed in the PNS/tibial nerve and have characterized roles in neuron development or maintenance, and/or mitochondrial function. Phenotypic similarities and differences were observed between different candidate genes, different variants within the same genes, and even within siblings with the same variant.

Summary and Significance

In summary, utilizing LRS in combination with clinical phenotype allows for the identification of novel variants in CMT and HSP. Although candidate genes are thoroughly vetted with combination of the GENESIS analysis pipeline, pathogenicity and conservation AI measures, protein function and expression information, and patient phenotype, functional studies are required to confirm or deny each candidate. Given that CMT and HSP are challenging to genetically diagnose, this project highlighted the value in utilizing LRS to identify novel variants that alternative genetic panels could not identify, aiding in the diagnostic odyssey. By linking these findings with patient phenotype, we provide insights on prognosis and pathophysiology of these variants.

Validity of surgical pathology collection times and closing count documentation times as milestones related to the start of surgical closure for operating room status boards

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Introduction: The start of surgical closure is a useful milestone for operating room (OR) management decision-making, including the assignment of add-on cases, choosing staff breaks and relief, and coordinating post-anesthesia care unit admissions. Knowing when surgical closure has started is especially useful because the proportional variability in the time remaining in surgical cases increases progressively as cases advance. At our institution, circulating nurses do not document the start of surgical closure because they are occupied with patient safety responsibilities, including surgical specimen management and closing counts. We evaluated whether existing electronic health record (EHR) documentation of surgical pathology collection and closing count documentation times could serve as milestones related to the start of surgical closure.

Purpose: To evaluate whether surgical pathology collection times and closing count documentation times are valid milestones associated with the start of surgical closure by assessing concurrent, predictive, and construct validity, and to determine the novelty of displaying these milestones on OR status boards.

Methods: A prospective observational study evaluated concurrent validity by comparing the observed start of surgical closure with closing count documentation times in 24 pediatric surgical cases. A retrospective cohort study of 44,841 surgical cases quantified the frequency of documented closing count and specimen collection times and their timing relative to OR exit to assess predictive validity. Construct validity was evaluated using 964 adult thoracic surgery cases as a positive control. Systematic literature searches of PubMed, Scopus, Web of Science, and Google Scholar were performed to assess whether similar applications had previously been reported.

Results: Closing count documentation occurred a mean of 5.5 minutes after the observed start of surgical closure, supporting concurrent validity. In the retrospective cohort, closing counts were documented in 49.6% of cases a mean of 38 minutes before OR exit, while specimen collection was documented in 27.5% of cases a mean of 69 minutes before OR exit, supporting predictive validity. At least one milestone was documented in 62.0% of all cases and in 97.0% of thoracic surgery cases, supporting construct validity. Systematic literature searches identified no prior reports describing the display of specimen collection or closing count documentation times on OR status boards.

Conclusion: Surgical pathology collection times and closing count documentation times are valid milestones related to the start of surgical closure. When available, these milestones provide earlier warning that a case is nearing completion than waiting for the end of surgery, without requiring additional work by circulating nurses. Displaying these existing EHR milestones on OR status boards represents a feasible technological innovation that improves communication of case progress and supports real-time OR management decision-making. Based on our results, these milestones were added to Iowa Healthcare's OR status boards and q5 minute data extracts for real-time decision making.

This research project has been accepted for publication in: *A&A Practice*.

Pediatric Cannabis Exposures at an Academic Medical Center in Iowa: A 23-year Retrospective Review

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Abstract

Introduction

The first decades of the 21st century have seen considerable change in the regulation of cannabinoids in the United States. Previous studies have reported an increase in unintentional pediatric cannabis exposures in the United States associated with expanded legalization of cannabis and related psychoactive cannabinoids.

Purpose

This study investigates trends in pediatric cannabis exposures over a 23-year period at the largest medical center in the state of Iowa. A timeframe in which this state introduced a Medical Cannabis Program, the 2018 Farm Bill allowed for distribution of THC-containing hemp-derived products within the state, and several bordering states legalized recreational cannabis use.

Methods

A retrospective analysis covering the timeframe from October 1, 2002 to October 16, 2025 was conducted of all cases involving children less than 12 years of age who had positive testing for THC in urine, for which THC exposure was the primary reason for care. A detailed chart review was performed and the following data elements were abstracted for each case: calendar year of visit, age in years at time of clinical presentation, legal sex, self-reported race, suspected source of THC exposure, location at the time of exposure, clinical symptoms, diagnostic workup, medical interventions, highest level of care, and duration of hospitalization.

Results

A total of 47 cases were identified with positive urine THC testing. Of these, 16 cases involved THC detection that was incidental to the reason for care and were excluded. Among the 31 remaining cases, all occurred between 2018 to 2025, 18 (58%) were in children 1-3 years old, and 16 (52%) were admitted to the pediatric intensive care unit. Accidental consumption of gummy products comprised the most common source of THC exposure (14/31, 45%). An estimated ingested dose of THC was available for 13 cases, and ranged from 70 to 8000 milligrams. The most common symptoms included altered level of consciousness, irritability, ataxia, seizure-like activity, respiratory depression, mydriasis, and emesis, typically with return to baseline within 48 hours.

Conclusion

In a large medical center, symptomatic cannabis exposures in children less than 12 years of age were mostly attributed to accidental ingestion of THC-containing edible products in the last 8 years, a timeframe in which several changes occurred to make cannabis and hemp products more accessible in this state. These findings highlight the need for clinicians to recognize THC exposure as a source of toxicity in children.

Glyphosate exposure in pregnancy

Mallory Lafever; Alexis Faudel; Heath Davis MS; Darrin Thompson MPH, PhD; David Cwiertny PhD; Mark Santillan MD, PhD; Donna Santillan, PhD

Abstract

Glyphosate was originally introduced in the United States in 1974 and is currently a widely used pesticide that controls broad-leaf weeds and grasses. As a state, Iowa is in the top 3 for total glyphosate usage because of its role in agriculture. Because it is a water-soluble chemical, human exposure to glyphosate primarily occurs through surface and groundwater contamination. Interest and concern about possible impacts of the chemical on human health have increased since a 2015 study by the World Health Organization's International Agency for Research on Cancer concluded that glyphosate is "probably carcinogenic in humans." Given the widespread use of glyphosate in Iowa and its potential health impacts, the purpose of this study was to determine if rural populations were at higher risk of exposure and adverse outcomes in pregnancy. Coded biological samples were provided by the University of Iowa Perinatal Family Tissue Bank (IRB#200910784). Paired third trimester maternal plasma and umbilical cord blood plasma samples were chosen for analysis based on the availability of samples and the maternal address during delivery being either in a Rural-Urban Commuting Area (RUCA) code of either 1 (most urban) or 10 (most rural) (IRB# 202512319). Glyphosate concentrations in the samples were quantified by Gold Standard Diagnostics' Glyphosate Enzyme-Linked Immunosorbent Assay (ELISA). Total protein concentration was measured using a Bicinchoninic Acid Assay (BCA, Pierce). Glyphosate concentrations were significantly higher in cord blood samples compared to maternal samples with no significant difference between RUCA codes ($P>0.05$). No difference was measured in maternal blood plasma glyphosate concentrations based on RUCA codes. Future analyses will include year of sample collection. Long-term health effects of glyphosate exposure in pregnancy will need to be monitored.

Outcomes of Budesonide Compared to Prednisone for Immune Checkpoint Inhibitor Hepatitis and Immunotherapy Rechallenge

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Background: Immune checkpoint inhibitors (ICIs) have transformed cancer treatment but can cause immune-mediated hepatitis that may require interruption of cancer therapy and treatment with systemic corticosteroids. Although systemic corticosteroids are effective, their systemic adverse effects and potential impact on subsequent ICI therapy highlight the need for alternative treatment approaches. Budesonide undergoes extensive first-pass hepatic metabolism and may provide more localized anti-inflammatory effects with less systemic exposure. However, data regarding the use of budesonide for ICI-associated hepatitis and its impact on subsequent ICI rechallenge remain limited.

Methods: We conducted a retrospective study of adult patients who received ICI therapy between 2019 and 2025 and subsequently developed ICI-associated hepatitis. Patients were identified through the TriNetX database, with clinical data abstracted from electronic medical records and entered into REDCap. Patients were categorized according to corticosteroid treatment with budesonide monotherapy, prednisone monotherapy, or both. Clinical outcomes included hepatitis remission, duration of hepatitis, successful ICI rechallenge, and recurrence of hepatitis following rechallenge. Univariable and multivariable logistic regression analyses were performed to evaluate factors associated with extended hepatitis duration and successful PD-1/PD-L1 rechallenge. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using SAS version 9.4.

Results: Among 116 patients with ICI-associated hepatitis, 78 (67.2%) received prednisone alone, 11 (9.5%) received budesonide alone, and 27 (23.3%) received both agents. Hepatitis remission was achieved in 86.2% of patients, and 56.0% underwent PD-1/PD-L1 rechallenge. In univariable analysis, prednisone-containing regimens were associated with increased odds of hepatitis lasting ≥ 1 month compared with budesonide monotherapy. After adjustment for BMI, patients receiving prednisone alone had higher odds of treated hepatitis lasting ≥ 1 month (OR 2.63, 95% CI 0.64–10.88), as did patients receiving both prednisone and budesonide (OR 11.10, 95% CI 1.72–71.88), compared with budesonide monotherapy. Among patients who underwent PD-1/PD-L1 rechallenge, hepatitis recurred in 25.4%. In multivariable analysis adjusting for hepatitis severity, patients receiving prednisone had significantly lower odds of PD-1/PD-L1 rechallenge compared with those receiving budesonide alone (OR 0.12, 95% CI 0.01–0.97; $p=0.05$). Higher-grade hepatitis was also independently associated with lower odds of rechallenge (OR 0.36, 95% CI 0.15–0.85; $p=0.02$). Among rechallenged patients, recurrence occurred in 34.1% of those treated with prednisone, compared with 0% of those treated with budesonide monotherapy and 16.7% of those receiving both agents ($p=0.06$).

Conclusions: In this retrospective cohort of patients with ICI-associated hepatitis, prednisone-containing regimens were associated with longer duration of treated hepatitis and lower likelihood of subsequent PD-1/PD-L1 rechallenge compared with budesonide monotherapy. Hepatitis severity was also independently associated with reduced likelihood of rechallenge. Although budesonide monotherapy was associated with more favorable rechallenge outcomes, the small number of patients receiving budesonide alone limits definitive conclusions regarding comparative treatment efficacy. These findings support further investigation of budesonide as a potential alternative to systemic corticosteroids for ICI-associated hepatitis and warrant validation in larger, prospective cohorts.

Medical Student Observations of Imaging Stewardship and Radiology Consultation During Clinical Rotations

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Introduction: Diagnostic imaging is essential to modern clinical care but is also an important source of healthcare utilization. Low-value imaging can increase costs, expose patients to unnecessary radiation or contrast-related risks, and lead to additional downstream testing. Strategies such as the American College of Radiology Appropriateness Criteria, clinical decision support, and direct radiology consultation can improve imaging utilization. Medical students develop many clinical habits through behaviors modeled during clinical rotations, yet it is unclear whether they observe these resources being used in routine care. Limited exposure to visible imaging reasoning and radiologist consultation may represent an educational gap through which suboptimal ordering practices are learned.

Purpose: This study aimed to assess whether clinical-year medical students observe radiologists being used as consultants during imaging decision-making and whether appropriate imaging practices are visibly modeled during clinical rotations. We also assessed exposure to imaging guidance resources and potentially inefficient imaging practices.

Methods: IRB exempt status was obtained for a cross-sectional survey of M3 and M4 students at the University of Iowa CCOM. Students reported imaging-related behaviors observed throughout their clinical rotations. Survey items assessed imaging rationale and modality selection, risks and patient burdens, unnecessary or duplicative imaging, imaging guidance resources, and radiology consultation. Students reported observed behaviors rather than judging whether individual imaging decisions were appropriate. The questionnaire underwent cognitive pretesting with students from the target population and was revised as needed before implementation in REDCap. Responses will be summarized using descriptive statistics. Follow-up cognitive interviews will explore students' experiences with imaging decision-making during clinical rotations, with qualitative analysis used to identify recurring themes.

Results: Survey development, cognitive pretesting, IRB exemption, and REDCap implementation were completed prior to broader distribution. Data collection among eligible M3 and M4 students is ongoing. Final analyses will characterize students' exposure to radiology consultation, imaging guidance resources, appropriate imaging practices, and potentially inefficient imaging behaviors during clinical rotations. Final response distributions and exploratory subgroup analyses will be presented at the conference.

Conclusions: Medical students learn imaging utilization not only through formal instruction but also through the clinical behaviors they observe. If radiologists are rarely seen functioning as consultants or the reasoning behind imaging decisions remains largely invisible, students may come to view radiology primarily as a report-generating service rather than as a clinical resource that can guide imaging decisions and reduce unnecessary or suboptimal imaging. Combining survey findings with students' qualitative experiences may identify gaps in clinical training and inform targeted education that better integrates imaging stewardship and radiologist consultation.

Title: Through the Wormhole: Conservatively Managed Clot-in-Transit Across a Patent Foramen Ovale With Systemic Embolization

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Background: Clot-in-transit (CIT) across a patent foramen ovale (PFO) represents a rare, high-risk form of venous thromboembolism with competing risks of pulmonary and systemic embolization. When the thrombus straddles a PFO, it creates an additional hazard of paradoxical systemic embolization which carries a high risk of early mortality, rates approaching 18-20%, and lacks guideline-directed management pathways. Treatment choices that reduce right-ventricular afterload (thrombolysis, catheter-based therapy, and surgical intervention) may simultaneously increase the risk of systemic embolization, generating a therapeutic conflict that must be resolved by individualized, multidisciplinary decision-making.

Hypothesis/Purpose: To describe the clinical course and outcomes of a high-risk patient with bi-atrial CIT across a PFO who was managed conservatively with selective escalation of therapy, and to illustrate the competing risks that arise when guideline-supported pulmonary embolism (PE) reperfusion strategies intersect with the threat of systemic embolization.

Method: A 60-year-old man with multiple cardiovascular comorbidities (HFpEF, HTN, HLD) presented five days after urologic surgery with intermediate-high risk (category C3R) PE, right-heart strain, and extensive acute lower-extremity deep-vein thrombosis evidenced by venous duplex imaging. Computed tomography angiography revealed acute bilateral saddle PE involving central, lobar, and segmental arteries and morphologic evidence of right heart strain (RV:LV ratio 1.8). Transthoracic echocardiography demonstrated a large (>8cm) mobile thrombus extending from the right atrium across a PFO into the left atrium and left ventricle during diastole.

Findings/Results: A multidisciplinary PE response team (PERT) was engaged, and therapeutic anticoagulation with heparin was started. Surgical embolectomy and catheter-directed thrombectomy were deferred because of the patient's prohibitive perioperative risk (severe obesity - BMI 56.6 kg/m² and elevated EuroSCORE II - 9.51%) and procedural risk of provoking further embolization. Thrombolysis was relatively contraindicated due to recent urologic surgery. However, subsequent clinical deterioration to high-risk (Category D2R) PE prompted a brief trial of systemic thrombolysis with alteplase, which was stopped early due to respiratory and hemodynamic compromise. Management thereafter remained conservative. Serial imaging and clinical observation documented spontaneous systemic embolization (subclavian artery occlusion, acute renal infarcts) without cerebrovascular events. Despite progression from intermediate-high to high-risk PE physiology, development of an apical right-ventricular thrombus, and documented systemic embolization, the patient achieved gradual hemodynamic and respiratory recovery with anticoagulation alone after the abbreviated thrombolysis attempt. No stroke occurred. He was discharged on hospital day 30 to inpatient rehabilitation on indefinite anticoagulation, with plans for outpatient pulmonary hypertension evaluation and consideration of eventual PFO closure. Hypercoagulability work-up and malignancy screenings were unremarkable.

Conclusion/Overall significance/Broader perspective: CIT across a PFO creates a therapeutic conflict between guideline-directed escalation for PE and systemic embolization risk. This case was not without complications and underscores the inherent risk of conservative and selectively escalated management in this setting. Our patient developed systemic embolic events, including near-complete subclavian artery occlusion and renal infarctions, as well as transient clinical deterioration requiring ICU-level care. Conservative management likely allowed for these systemic embolic events, consistent with observational data demonstrating significantly higher rates of systemic embolism with non-surgical approaches to PFO-straddling thrombus. This case underscores the need for further data to guide therapy in this rare but high-stakes clinical scenario.

Test-Retest Repeatability of the Smart System Virtual Reality Perimetric Headset

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Purpose:

Perimetry is a vital tool for the characterization and monitoring of glaucomatous visual field defects. The Smart System Virtual Reality (SSVR) headset is a commercially available head mounted perimetry device with a short-term test-retest variance that has been characterized for patients without visual field deficits. The purpose of this study is to assess the test-retest variance of the device for patients who have been diagnosed with glaucoma.

Methods:

Participants completed two separate SSVR headset visual field tests within a minimum interval of one week to a maximum interval of one month. All participants were given a practice visual field test upon recruitment to mitigate potential learning effect. The mean deviation was compared between tests for each participant using Bland-Altman methodology to derive upper and lower limits of repeatability with 95% confidence intervals bootstrapped using n=1000 resamples, standard deviation, and confidence interval half-width. Subject feedback was collected using a custom SSVR Reality headset satisfaction survey and the NASA Task Load Index.

Results:

Preliminary results (n=27 of n=45 goal) show upper and lower limits of repeatability as +4.400 dB (95% CI: [3.052, 5.730]) and -4.224 dB (95% CI: [-5.837, -2.343]), respectively. Achieved limits of repeatability confidence interval half-width is 1.437 dB and test-retest standard deviation is 2.200 dB. Preliminary SSVR headset satisfaction survey feedback shows 96% of participants strongly agree that their overall experience with the SSVR headset was satisfactory and 81% of NASA Task Load Index responses indicate that using the SSVR headset was a very low workload experience.

Conclusion:

Preliminary test-retest variance of the SSVR headset is considerably higher than the gold standard Humphrey Field Analyzer, but similar to other novel virtual reality head mounted devices described in available primary literature. Subject perception of the device is strongly positive overall, and implementation of the device into routine clinical practice would likely improve patient's experience of performing perimetry. Further study is necessary to determine the effectiveness of the SSVR headset device for monitoring glaucomatous visual field defects over a longer interval, and to assess the device's ability to monitor patients with glaucoma of differing severities.

Regional Lung Reserve Assessed by Quantitative Computed Tomography Identifies Moderate-Risk Patients Requiring Supplemental Oxygen After Lobectomy

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Introduction: Patients undergoing lobectomy for lung cancer are often concerned about postoperative quality-of-life outcomes, including the need for supplemental oxygen. Predicted post-operative FEV1 (ppoFEV1) and DLCO (ppoDLCO) are used for risk assessment, but these global measures fail to capture regional heterogeneity in lung health. Quantitative computed tomography (CT) can quantify lobar-level differences in normal and diseased lung tissue. It remains poorly understood how these lobar-level CT biomarkers relate to post-lobectomy discharge with supplemental oxygen in a group of patients with similar ppoFEV1 or ppoDLCO.

Hypothesis: Quantitative CT-derived measures of regional lung composition, particularly those capturing the relationship between resected and remaining lobes, are associated with post-lobectomy supplemental oxygen requirement at discharge.

Method: With approval from the University of Iowa Institutional Review Board, adult patients who underwent elective single-lobe lobectomy for primary lung cancer between January 2020 and March 2026 were retrospectively identified from the Society of Thoracic Surgeons database. Patients with American Society of Anesthesiologists class IV or V, Eastern Cooperative Oncology Group performance status 4, or prior operation in the surgical field were excluded. Lobar segmentation masks were generated using TotalSegmentator from preoperative non-contrast CT scans obtained within one year before surgery. Then, CT lung texture analysis was performed using the Adaptive Multiple Feature Method (AMFM) implemented in the in-house-developed Pulmonary Analysis Software Suite (PASS) to classify lung texture patterns and quantify lobar tissue composition, including normal, emphysematous, ground-glass, and bronchovascular bundle patterns. For each texture pattern, measurements were calculated within the resected and remaining lobes, the difference between them, and the proportion contributed by the resected lobe relative to the whole lung. Derived imaging features were evaluated using Elastic-Net modeling across 100 iterations to identify predictors of new supplemental oxygen at discharge. Patients were stratified according to the 2025 European Respiratory Society guideline as normal risk [$\min(\text{ppoFEV1}, \text{ppoDLCO}) \geq 60\%$], moderate risk [$40\% \leq \min(\text{ppoFEV1}, \text{ppoDLCO}) < 60\%$], or high risk [$\min(\text{ppoFEV1}, \text{ppoDLCO}) < 40\%$]. Wilcoxon rank-sum tests were performed in each risk group to compare selected imaging features between patients discharged with and without supplemental oxygen ($p < 0.05$).

Results: Lobar quantitative CT analysis was successfully performed in 164 lobectomy patients, including 16 patients discharged with supplemental oxygen and 148 controls. Based on ppoFEV1 and ppoDLCO risk stratification, the oxygen group had a greater proportion of moderate-risk patients (75%, 12/16) than the control group (45.5%, 68/148), whereas normal-risk patients were less common (18.8% vs 47.9%) and high-risk patients were uncommon in both groups (6.2% vs 3.4%). The Elastic-Net identified seven predictive imaging features: bronchovascular volume in both lungs, normal tissue volume in the resected lobe, air volume in the resected lobe, fraction of resected-lobe normal tissue relative to both lungs, bronchovascular volume in the remaining lobes, and the resected-versus-remaining lobe differences in normal tissue% and ground-glass%. Among the moderate-risk patients, the difference in normal tissue percentage between the resected and remaining lobes was significantly greater in the patients requiring oxygen than in controls (1.25% IQR[-1.06%, 5.44%], vs. -1.80% IQR[-8.17%, 2.53%], $p = 0.048$). Patients requiring oxygen also showed trends toward greater air volume in the resected lobe and increased ground-glass and bronchovascular bundles in the remaining lobe, suggesting reduced functional reserve in the lung tissue left in place. Additionally, consolidation percentage in the remaining lobes was significantly higher among oxygen-requiring patients ($p = 0.024$).

Conclusion: Quantitative lobar CT analysis identified regional differences in lung health associated with postoperative supplemental oxygen requirement among patients with similar physiologic risk profiles. These findings suggest that CT-derived measures of regional lung reserve may complement ppoFEV1 and ppoDLCO, enabling more personalized preoperative risk assessment, surgical planning, and shared decision-making. Future prospective studies using standardized CT imaging protocols are warranted to validate and refine these imaging biomarkers for clinical decision support.

KEAP1-NRF2 Pathway Upregulates Thiol Antioxidants, NADPH Regeneration, and Iron Internalization that are Crucial for Survival and Proliferation in NSCLC Cells

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Introduction: Of all non-small cell lung cancer (NSCLC) cases, 11-27% harbor KEAP1 (Kelch-like ECH-associated protein 1) mutations. These mutations result in the constitutive activation of the nuclear factor-erythroid factor 2 (NRF2) transcription factor, leading to upregulated antioxidants that confer resistance to standard-of-care chemotherapy and radiotherapy. This study aimed to characterize the roles of the KEAP1-NRF2 pathway in NSCLC cellular phenotypes. Flow cytometry was performed to assess differences in reactive oxygen species (ROS) levels, cell cycle distribution and aneuploidy, mitochondrial quantity, labile iron levels, and mitochondrial membrane potential in NSCLC cell lines with or without genomic manipulation of KEAP1 and NRF2.

Hypothesis: The KEAP1-NRF2 pathway upregulates thiol antioxidants, NADPH regeneration, and iron internalization that are crucial for survival and proliferation in NSCLC cells.

Methods: H1299T sgRNA negative control, H1299T KEAP1 knockout (KO) 1, H1299T KEAP1 KO2, A549 sgRNA 1, A549 NRF2 KO2 (complete KO), A549 sgRNA 2, and A549 NRF2 KO3 (isoform-specific knockout) were created from the original H1299T (KEAP1 WT) and A549 (KEAP1 mutant) cells, utilizing the Alt-RTM CRISPR-Cas9 system. All cell lines were maintained and grown for 48 - 72 hours in 60 mm petri dishes to reach 1 - 1.5 million cells in 5% CO₂, 21% O₂, humidified in 37 °C, and in RPMI 10% FBS media. Cell counts were collected with a Coulter Counter, centrifugations were at 1,000 rpm in 4 °C for 5 minutes, and incubations after treatments except for propidium iodide (PI) were at 37 °C, 5% CO₂, and 21% O₂. [1] To assess aneuploidy, DNA content, and cell cycle distribution, cells were fixed in 70% ethanol and treated with 100 µL of RNase A (1mg/mL stock) for 30 minutes at room temperature (RT). 1 mL of 35 µg/mL PI stain was added to the samples, followed by a 1-hour incubation at RT in the dark. [2] To assess differences in mitochondrial mass, the cells were incubated with 100 nM MitoTracker Green (MTG) for 15 minutes with intermittent inversions. [3-5] Three assays detected ROS levels: dihydroethidium (DHE) for intracellular superoxides, MitoSOX for mitochondrial superoxides, and CellROX for general ROS levels. Cells were treated with 2 µM of MitoSOX, 5 µM of CellROX Deep Red, and 10 µM of DHE, respectively. The DHE and MitoSOX assays used Antimycin A (10 µM) for positive control and DMSO (0.1% v/v) for negative control. The CellROX Deep Red assay used tert-butyl hydroperoxide (400 µM) as a positive control. The treated samples were incubated for 15 minutes with intermittent inversions. [6] The JC-1 assay assessed mitochondrial membrane potential. The samples were incubated in 1 mL of RPMI media with 2 µM of JC-1 or 50 µM of CCCP + 2 µM of JC-1 in 60 mm dishes for 15 minutes. [7] The FerroFarRed assay detected cellular labile Fe²⁺ levels. Positive controls were treated and incubated with 40 µM of Ferrous ammonium sulfate, and negative controls were treated and incubated with 100 µM of deferoxamine for 3 hours. Next, the cells were stained and incubated with 5 µM FerroFarRed solution in HBSS for 1 hour. All assay samples were strained through a 30 µm mesh, and FACSDiva was used for data acquisition with the Flow Cytometer. Acquisition rates for the flow cytometer were maintained under 2,000 events/sec. FlowJo and GraphPad were used for data analysis.

Findings: The MitoSOX, DHE, and MTG assays showed no significant differences among the A549 cell lines or the H1299T cell lines. The CellROX assay indicated that the A549 NRF2 KO3 was significantly higher ($p \leq 0.05$) than A549 sgRNA 2 in ROS levels. No other significant differences were present. The PI stain data indicated no significant differences in ploidy and percentages of cells in cell cycle phases between the H1299T KEAP1 KO cells and the control. In contrast, A549 NRF2 KO2 displayed a significantly higher proportion of cells in the G1 phase and lower S phase than A549 sgRNA2 ($p \leq 0.05$), while the other A549 cell lines showed no significant difference. JC-1 data revealed that the A549 sgCTRLs displayed significantly lower red/green fluorescence ratios than the A549 NRF2 KOs ($p \leq 0.0001$). Additionally, H1299T KEAP1 KO1 had a significantly higher red/green fluorescence ratio than both the H1299T sgCTRL and KEAP1 KO2 ($p \leq 0.0001$). Lastly, FerroFarRed data indicated that the A549 sgRNAs had significantly higher labile Fe²⁺ levels than the A549 NRF2 KOs ($p \leq 0.0001$), while labile Fe²⁺ levels in the H1299T sgRNA were higher than the KOs with a significance of $p \leq 0.05$ for KO1 and $p \leq 0.01$ for KO2.

Conclusion: KEAP1 KO cells, compared to their control, showed increased mitochondrial membrane potential, decreased labile iron levels, but no difference in ROS levels or cell cycle progression. NRF2 KO cells, compared to their controls, showed increased mitochondrial membrane potential and decreased labile iron levels. In particular, A549 NRF2 KO2 cells showed a higher G1 population, and A549 NRF2 KO3 cells showed increased ROS levels. These results suggest that the KEAP1-NRF2 pathway is crucially involved in regulating iron metabolism and mitochondrial metabolism.

Title: Rapid Non-invasive Pediatric Solid Tumor Diagnosis through Liquid Biopsy Nanopore Sequencing

Student: Mikayla Lewis

Mentor: Dr. Andrew Groves, MD, Clinical Assistant Professor of Pediatrics - Hematology/Oncology, University of Iowa Stead Family Children's Hospital and Department of Pediatrics

Introduction: Central nervous system and extracranial solid tumors are the leading cause of cancer-related death in children. Diagnosis and molecular characterization often require invasive tissue biopsy, which may carry substantial risk depending on tumor location. Consequently, there is growing interest in circulating tumor DNA (ctDNA) analysis through liquid biopsy as a minimally invasive approach to diagnosis and molecular profiling, with the potential to guide tumor-directed therapy. In adult solid tumors, ctDNA has also been used to monitor clonal evolution, detect residual disease, and facilitate post-treatment surveillance. Nanopore sequencing is a state-of-the-art platform capable of directly sequencing long DNA and RNA molecules with rapid turnaround times, high throughput, and relatively low cost. Importantly, nanopore sequencing can simultaneously characterize epigenetic features, including DNA methylation, without requiring additional processing steps such as bisulfite conversion. Methylation profiles can be used to identify tissue of origin and tumor-specific molecular signatures, providing a unique "molecular fingerprint" based on CpG methylation patterns.

Hypothesis: We hypothesize that peripheral blood and CSF can be used as a source for liquid biopsy to using the Oxford Nanopore Technologies (ONT) nanopore sequencing platform.

Methods: Pediatric patients with solid tumors were consented under an IRB-approved protocol (ID #202212193). Tumor tissue underwent standard next-generation sequencing (NGS), while peripheral blood and cerebrospinal fluid (CSF) were collected and processed for cell-free DNA (cfDNA) isolation. cfDNA was extracted using the QIAamp circulating nucleic acid kit and quantified using the Qubit dsDNA High Sensitivity assay. Whole-genome sequencing was performed using the Oxford Nanopore PromethION P2Solo platform, and nanopore sequencing results were processed through the NanoDX pipeline and compared to the NGS clinical results taken from brain tumor specimens.

Results: To date, 59 pediatric patients have been consented to participate, including 52 with CNS tumors and 7 with extracranial solid tumors. A total of 52 peripheral blood samples and 22 CSF samples have been collected. The mean patient age was 8.63 years (range, 0.16 - 23.31 years). Among the neuro-oncology patients, detectable ctDNA of adequate quality was identified in 6 plasma samples and 7 CSF samples. For CNS tumors the mean ctDNA yield was 0.54 μ g in plasma 1.3 μ g in CSF, which was a statistically significant difference ($p = 0.0406$). Among all peripheral blood samples, extracranial solid tumors had a mean ctDNA yield of 0.089 μ g while CNS tumors had a mean of 0.034 μ g, which was also a statistically significant difference ($p = 0.0112$). We also investigated the yield differences among CSF samples obtained through lumbar puncture versus ventricular sampling. We had 5 ventricular samples with a mean DNA yield of 1.76 μ g and 2 lumbar samples with a mean of 0.16 μ g. While this represents a large difference, it was not statistically significant ($p = 0.19$), likely due to the small number of samples. Only one sample has undergone successful nanopore sequencing with bioinformatic analysis through the NanoDX pipeline. This participant is a now 8-year-old that presented at age 5 with a cerebellar mass in the context of several months of headaches. They underwent resection and it was identified to be a pilocytic astrocytoma, CNS WHO Grade 1, with a characteristic KIAA1549:BRAF fusion. A ventricular CSF sample from this patient underwent sequencing and classification was successful, matching the results determined from the biopsy specimen.

Conclusion: Collection of peripheral blood and CSF from pediatric patients with CNS and extracranial solid tumors is feasible. Consistent with prior reports, ctDNA yield is higher in CSF than peripheral blood for brain tumor patients, likely due to the presence of the blood-brain barrier. Ventricular samples also had higher ctDNA than those collected during lumbar puncture, which is likely due to proximity to the lesion. Further optimization of sequencing and bioinformatic workflows is needed to improve successful molecular classification. These efforts may ultimately enable minimally invasive diagnosis, molecular characterization, and longitudinal monitoring of pediatric solid tumors.

Project Title: Optic Atrophy 1 (OPA1) Deficiency in Brown Adipocytes Improves Cardiac Function Through Endocrine Signaling

Student Name: Jamille Lockhart

Mentor Department: Renata Pereira Alambert, Internal Medicine

Introduction: Cardiovascular disease remains the leading cause of death worldwide, highlighting the need for innovative approaches to improve cardiovascular health. Brown adipose tissue (BAT) has emerged as a potential therapeutic target because of its thermogenic and secretory functions. Mitochondrial dynamics within BAT are regulated by proteins that control mitochondrial fusion and fission, including optic atrophy 1 (OPA1), a key mediator of inner mitochondrial membrane fusion. Previous studies from our laboratory demonstrated that BAT-specific deletion of OPA1 induces mitochondrial stress and increases secretion of fibroblast growth factor 21 (FGF21) and growth differentiation factor 15 (GDF15) from BAT, resulting in elevated energy expenditure, adipose tissue browning, and resistance to diet-induced obesity. Although FGF21 and GDF15 have been independently linked to cardioprotective effects, it remains unknown whether mitochondrial stress originating in BAT can modulate cardiac function through endocrine signaling.

Hypothesis: We hypothesized that BAT-specific OPA1 deficiency improves cardiac function through FGF21 and GDF15 secretion.

Methods: To test this hypothesis, we assessed cardiac size, function, and mitochondrial bioenergetics in 10-12-week-old male and female BAT-specific OPA1 knockout (BKO) mice and BAT-specific OPA1/FGF21/GDF15 triple knockout (TKO) mice. Body weight and fasting blood glucose levels were also assessed. Cardiac performance was evaluated by echocardiography. Mitochondrial respiration supported by fatty acid and carbohydrate-derived substrates was measured in isolated cardiac mitochondria using high-resolution respirometry.

Results: Under basal conditions, male OPA1 BKO mice were significantly leaner with no changes in fasting blood glucose. These mice exhibited normal heart rate and cardiac mass but demonstrated improved cardiac contractility, characterized by increased ejection fraction and reduced end-systolic volume compared to wild-type controls. Male TKO mice showed no significant changes in body weight and had near significantly higher blood glucose levels. Of note, the improved contractility observed in BKO mice was absent in TKO male mice, suggesting that BAT-derived FGF21 and GDF15 contribute either directly or indirectly to the enhanced cardiac phenotype. Mitochondrial respiration analyses revealed a small but significant increase in palmitoyl-carnitine-supported respiration in male OPA1 BKO mice, while pyruvate-, glutamate-, and succinate-supported respiration remained unchanged. No changes in mitochondrial respirations were noted in the hearts of male TKO mice. Despite having reduced body weight, female OPA1 BKO mice showed no significant alterations in cardiac function or mitochondrial respirations. Female TKO mice lacked the reduction in body weight and displayed no changes in cardiac contractility or mitochondrial respiratory function.

Conclusions: These findings identify a previously unrecognized BAT-heart axis whereby mitochondrial stress in brown adipocytes influences cardiac physiology through endocrine communication. BAT-specific OPA1 deficiency improved cardiac contractile function in male mice and was associated with enhanced cardiac fatty acid-supported mitochondrial respiration. The absence of these benefits in OPA1/FGF21/GDF15 triple knockout mice suggests that BAT-derived FGF21 and GDF15 contribute to this cardioprotective phenotype. Notably, these effects were sexually dimorphic, as female OPA1-deficient mice exhibited no significant changes in cardiac function under basal conditions. Together, these data establish BAT mitochondrial dynamics as an important regulator of cardiac physiology and support a role for BAT-derived endocrine factors in mediating interorgan communication between adipose tissue and the heart. Future studies will focus on identifying the mechanisms by which BAT-derived FGF21 and GDF15 regulate cardiac function and determine the individual contribution of each factor to the improved cardiac phenotype observed in OPA1 BKO mice. We will also investigate the basis for the observed sex differences and test whether activation of the BAT-heart axis protects against obesity-, aging-, or injury-induced cardiac dysfunction. These studies may reveal novel therapeutic strategies targeting BAT endocrine signaling to improve cardiovascular health.

Title: A National Study of Pediatric Utility Task Vehicle Crashes and Fatalities on Public Roadways

Crystal Lore, BS, Taeuk Kang, MBiotech, MSc, Charles Jennissen, MD

Introduction: Utility task vehicles (UTVs), also known as side-by-sides and recreational off-highway vehicles, have become increasingly common over the past several decades and now outsell all-terrain vehicles (ATVs). Despite being designed for off-road use only, increasing numbers of municipalities, counties and states have passed laws allowing their use on public roadways. UTVs are widely used for both work and recreation and are being driven and ridden by individuals much younger than manufacturer recommendations. For most UTVs, manufacturers recommend drivers be at least 16 years old and passengers be at least 12 years old. Extensive work has been published characterizing the factors contributing to pediatric ATV crashes and injuries, but much less data exists assessing UTVs.

Hypothesis/Purpose: Our objective was to determine the number of pediatric UTV crashes occurring on public roadways, to identify risk factors that may contribute to crashes, and to compare and contrast several variables among pediatric crash victims including age, sex, occupant status, restraint use, and crash mechanism, in order to identify variables impacting crash and injury rates. In addition, we aimed to compare pediatric crash victims <16 years of age with those 16 years and older.

Methods: Information on UTV crashes was extracted from the Fatality Analysis Reporting System (FARS) database for the years 2017 through 2024. This was done using the person-level dataset and the vehicle body type code 96 (Recreational Off-Highway Vehicle). Crash mechanisms were grouped into four categories consisting of motor vehicle collisions, object collisions, primary rollover incidents, and primary ejection incidents. Frequency and bivariate analyses (Chi-Square or Fisher's exact test) were done in R and logistic regression analyses were performed using SAS.

Results: During the study period, 1398 UTV crashes involving fatalities on public roadways occurred impacting 2654 individuals, with increasing numbers over time. Of these, 590 were 0-17 years with 225 sustaining fatal injuries. Males comprised 62% of those involved. Over a third (34%) were drivers of the vehicle. Crashes involving youth occurred most frequently in rural areas (86%) and on minor roads (84%). Nearly four-fifths (78%) of crashes involved a rollover at some point, and about one-half (49%) of victims were ejected from the vehicle to some degree. Personal protection use was extremely poor, with 81% of children being unrestrained and only 3% documented as wearing helmets. Alcohol use was low overall, but 27% among drivers tested in the 16–17-year age group. Higher proportions of drivers had fatal injuries (59%) as compared to passengers (28%), $p<0.001$. Females were involved in a higher proportion of rollover crashes (83% vs 76%), $p=0.023$, while males had greater percentages of incidents occurring at night (68% vs 59%), $p=0.023$, and resulting in fatal injuries (41% vs 34%), $p<0.001$. Persons in vehicles colliding with an object had higher proportions of subsequent rollovers (65%) than those colliding with a vehicle (39%), $p<0.001$. Youth ejected from the vehicle to any degree had a higher percentage of fatal injuries (53%) than those not ejected (24%), $p<0.001$. Inappropriately restrained children and adolescents had significantly higher rates of being ejected (58%) compared to those appropriately restrained (5%), $p<0.001$. Moreover, inappropriately restrained youth also had higher rates of fatal injuries (43%) compared to those appropriately restrained (14%), $p<0.004$. Comparing <16-year-olds to those older, younger individuals had higher proportions of being female (38% vs 25%), $p<0.001$, being passengers (67% vs 42%), $p<0.001$, and driving during the day (66% vs 44%), $p<0.001$. Alcohol was involved in a higher proportion of cases for those 16 years and older (60% vs 1%), $p<0.001$. Older individuals also had higher proportions of object collisions (31% vs 22%) and motor vehicle collisions (20% vs 16%), while younger individuals had higher proportions of primary rollovers (58% vs 46%), $p<0.001$ for all. Fatal injuries were more common among older individuals (58% vs 37%), $p<0.001$.

Conclusion: Fatal public roadway UTV crashes are increasing in frequency and leading to the injury and death of many children. Restraint use was very low despite laws mandating use in many states. Being inappropriately restrained was associated with higher rates of ejection and worse injury severity including death.

Characteristics of High-Performing Low-Volume Birthing Facilities in Iowa

Lucy B. Kim; Mentor: Stephanie Radke, MD, MPH; **Collaborators:** Erin Wissler Gerdes, PhD, MA; Kristal Graves, DNP, MSN, RNC-OB

Introduction: Rural communities experience persistent maternal and neonatal health disparities compared with urban communities, including reduced access and delays in care from the loss of birthing facilities. Low obstetric volume has been cited as both a challenge to maintaining rural obstetric services and a potential risk factor for adverse outcomes. However, the relationship between birth volume and maternal and neonatal outcomes varies across measures, suggesting differences in performance among low-volume facilities may reflect modifiable strategies and practices.

Purpose: The purpose of this study was to characterize quality of care among Iowa birthing facilities with ≤ 250 average annual births and explore facility-level factors that may support high performance in low-volume obstetric settings.

Methods: We conducted an exploratory, mixed-methods analysis of Iowa birthing facilities with ≤ 250 average annual births from 2023–2025. Facility-level rates were calculated over the three-year period for seven maternal and neonatal performance indicators: severe maternal morbidity excluding transfusions, maternal transfusion, 3rd/4th-degree perineal lacerations, 5-minute Apgar scores < 7 , breastfeeding at discharge, nulliparous term singleton vertex cesarean rate, and infant transfer within 24 hours. Facilities were classified using quartile-based scoring across performance metrics, where facilities in the top quartile of overall scores were classified as high-performing (HP) and the rest classified as non-high-performing (NHP). To explore potential supportive practices, we reviewed 2025 MHI Needs Assessment survey responses and conducted semi-structured interviews with HP facilities. Rapid qualitative analysis was used to identify common themes and illustrative practice examples.

Results: Among 22 low-volume Iowa birthing facilities, six facilities were classified as HP based on maternal and neonatal performance indicators. Compared with NHP facilities, HP facilities had favorable performance on most indicators, including statistically significant differences in 5-minute Apgar scores < 7 among singleton live births (1.7% in HP facilities versus 3.0% in NHP facilities) and newborns breastfeeding at discharge (89.7% in HP facilities versus 85.0% in NHP facilities). Rapid qualitative analysis of a previously collected hospital needs assessment survey and interviews identified five consistent themes among HP facilities: experienced OB champions, embedded debriefing and review, repeated readiness-building through simulation and education, administrative and system support, and disciplined implementation of practice changes. These themes reflected practical strategies such as identifying and supporting cores of dedicated OB staff, integrating debriefing into everyday workflow, practicing low-frequency high-risk scenarios, and following up on implementation.

Conclusion: Overall, high performance in low-volume obstetric settings may be supported by systems that preserve unit readiness for high-acuity events, promote and reinforce staff learning, and maintain consistency in communication, education, and leadership. This study highlights potential strategies for supporting rural and low-volume birthing units so that we can preserve access to and maintain the quality of obstetric care across rural Iowa.

Complement system biomarkers and adverse cardiac outcomes in diabetic and non-diabetic kidney disease

Benjamin Madden

Mentor: Dr. Diana Jalal, Department of Internal Medicine, Division of Nephrology and Hypertension

Collaborators: Mingyao Sun, PhD; Patrick Ten Eyck, PhD; Trejahn Manning, Jack Mauter, Chloe Keideth

Introduction/Purpose: Chronic kidney disease (CKD) is a significant risk factor for cardiovascular events and mortality. Among individuals with CKD, death due to cardiovascular disease (CVD) is more likely than reaching end-stage kidney disease, underscoring the importance of elucidating the mechanism of vascular complications in this population. The complement system, specifically via the spontaneously active alternative pathway (AP), is dysregulated in CKD. The present study aimed to evaluate the association between the plasma level of AP biomarkers and cardiovascular events in diabetic and nondiabetic CKD. We hypothesized that biomarkers of AP activation would associate with cardiovascular disease in both diabetic and nondiabetic CKD.

Methods: Plasma samples from subjects with CKD were sourced from two clinical trials: NEPHRON-D, that included subjects with diabetes and CKD, and SPRINT, that included subjects with nondiabetic CKD. Cardiovascular events were the designated outcome and defined as a composite outcome of myocardial infarct, stroke, heart failure, or death. We measured plasma Ba, Bb, sC5b-9, Factor D, and Factor H using commercial ELISA according to manufacturer's instructions (Quidel and Hycult). Using demographical and risk factor data, subjects that developed the composite outcome were matched with subjects that did not within each trial (n=34 for NEPHRON-D, n=66 for SPRINT). Results for all 5 proteins were tested for significant changes between the composite and non-composite outcome groups from both trials using standard descriptive statistics and Welch's t-test.

Results: We observed no significant difference in plasma Ba, Bb, Factor D, or Factor H based on the composite outcome within NEPHRON-D nor SPRINT. Within NEPHRON-D, subjects who developed the composite outcome had significantly higher levels of sC5b-9 compared to those that did not (mean(SD)= 380.2(102.3) and 315.1(61.9) ng/mL respectively, p=0.04). While a similar trend was observed for sC5b-9 in SPRINT, this was not statistically significant.

Conclusion: Plasma level of AP biomarkers did not associate with adverse cardiac outcomes in diabetic or nondiabetic CKD. However, the terminal complement system marker sC5b-9 did associate with the composite cardiovascular disease outcome among those with diabetic CKD. These findings suggest increased activation of the complement system via another pathway in diabetic CKD.

Title: Left Atrial Appendage Geometry During Concomitant Pulsed-Field Ablation and Left Atrial Appendage Closure Using Four-Dimensional Echocardiography

Short Title: PFA and LAA Geometry by 4D ICE

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Background & Aims: Acute changes in left atrial appendage (LAA) geometry following pulsed-field ablation (PFA) for atrial fibrillation (AF) remain incompletely understood. We aimed to evaluate acute changes in LAA geometry following PFA using four-dimensional intracardiac echocardiography (4D ICE) in patients undergoing concomitant AF ablation and left atrial appendage closure (LAAC).

Methods: Single-center observational study of 55 consecutive patients undergoing concomitant PFA and Watchman FLX Pro implantation with 4D ICE assessment of the LAA before and after ablation. LAA diameters were measured using standardized imaging planes corresponding to 0°, 45°, 90°, and 135° imaging planes. Paired analyses and linear mixed-effects modeling were used.

Results: Mean age was 73.6 ± 8.0 years, and 61.8% were male. In a linear mixed-effects model, there was no overall effect of time on LAA diameter (p=0.893), but there was a significant time-by-angle interaction (p<0.001). Model-derived estimates demonstrated decreases in LAA diameter at 0° (-0.92 mm) and 90° (-0.96 mm), with increases at 45° (+1.12 mm) and 135° (+0.87 mm). In paired analyses, these changes reached nominal significance at 0° (p=0.027), 45° (p=0.007), 90° (p=0.022), and 135° (p=0.036), although after adjustment for multiple comparisons only the increase at 45° remained significant (adjusted p=0.026). No significant changes were observed in major and minor axis diameter, ellipticity, estimated elliptical area, or mean LAA diameter.

Conclusions: PFA was not associated with significant global changes in LAA geometry immediately following ablation. However, significant angle-dependent remodeling was observed across imaging planes, suggesting heterogeneous geometric responses following PFA.

BP180-Specific Autoantibodies and Localized Inflammation Remodel the Epidermal Tolerogenic Axis in Bullous Pemphigoid

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Introduction: Bullous pemphigoid (BP) is an autoimmune blistering disease of the elderly. Disease pathogenesis is initiated by autoantibodies against BP180; however, downstream mechanisms are not well understood.

Purpose: To determine how BP antibodies and inflammatory factors found in serum and blister fluid alter cutaneous populations of regulatory T cells (Tregs) and Langerhans cells (LCs).

Method: *Ex vivo* human skin explants generated from healthy donor skin were exposed to BP blister fluid (BF), BP serum (BPS), autoantibodies, or appropriate controls for 40 hours at 37°C, 5%CO₂. After tissue homogenization, cell suspensions were stained with fluorescent antibodies targeting cell lineage and activation markers which were measured using multicolor flow cytometric analysis of Treg and LC frequency and phenotype.

Results: All experimental treatments reduced cutaneous Treg frequency and induced phenotypic changes indicative of impaired suppressive function. LC frequency increased with concurrent changes in costimulatory, regulatory, and migratory molecules. BP BF produced broader and more pronounced effects than BP180 antibodies alone, suggesting that soluble inflammatory mediators amplify downstream immune remodeling beyond autoantibody binding.

Conclusion: These findings support a model in which BP autoantibodies and the inflammatory milieu found in BP sera and blister fluid remodel the epidermal LC-Treg tolerogenic axis. Our results identify disruption of local immune regulation as a potential contributor to BP pathogenesis and provide a framework for future mechanistic studies and therapeutic development.

Characterizing ferroptosis and mechanotransduction transcriptomic changes in corneal endothelial cells in Fuchs Endothelial Corneal Dystrophy

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Introduction: Corneal endothelial cells (CECs) form a confluent monolayer that comprises the posterior surface of the cornea, where they maintain corneal transparency and regulate fluid uptake by performing barrier and pump functions. CEC function is susceptible to disruption by mechanical stressors that disrupt cellular confluence, as well as oxidative stressors such as UV-A exposure that generate excessive intracellular reactive oxygen species. In Fuchs endothelial corneal dystrophy (FECD), the leading indication for corneal transplantation, CEC confluence is disrupted by excessive extracellular matrix deposits called guttae. Additionally, FECD is associated with ferroptosis, an iron-mediated form of cell death in which free ferrous iron destroys cellular membranes via lipid peroxidation. However, the differential gene expression in response to mechanical stresses in FECD remains understudied.

Hypothesis/Purpose: We hypothesize that there will be differential gene expression for mechanotransduction and ferroptosis pathway proteins in CECs. We expect transcriptional activity relating to maintenance of CECs barrier function, mediated by N-cadherin and beta-catenin, should be decreased with progressive confluence disruption. Likewise, we anticipate expression of antioxidant proteins such as glutathione peroxidase 4 (GPX4) will be decreased in FECD disease. Additionally, owing to the centralized concentration of guttae in FECD, we hypothesize that there is a spatial aspect to differential CEC gene expression, with centrally located CECs expected to have aberrant expression of genes that play critical pump and barrier functions compared to peripheral CECs. More complete characterization of transcriptional and translational profiles of FECD CECs topographically and in different states of confluency may uncover possible targets for future medical interventions.

Methods: Human corneal endothelial tissues were obtained from health donor corneas (Iowa Lions Eye Bank) or tissue explants from patients with FECD undergoing endothelial keratoplasty. Healthy tissues were divided into central and peripheral zones using a 4-mm tissue punch and underwent RNA extraction and purification. qPCR was performed in both biological and technical triplicate to quantify differential gene expression relating to ferroptosis and mechanotransduction pathways. Additionally, healthy immortalized CECs (B4G12 cells) were grown in biological triplicates at different target confluences (50%, 90%, and 100% confluence). mRNA sequencing (Novogene) was performed to assess differential gene expression of ferroptosis and mechanotransduction markers at differing confluence.

Results: N-Cadherin and tight junction protein ZO-1 increase in CECs with increasing confluency. Biologic triplicate samples of B4G12 cells grown to the target confluences (50% 90%, 100%) are currently being processed for mRNA-Seq (Novogene) to determine the mechanotransduction transcripts altered because of those cell-to-cell changes. Surgical tissue explants were dissected into central and peripheral FECD specimens successfully and stored in our biorepository for validation of disease dependent differences in mechanotransduction signaling due to topographical differences in cell dropout.

Conclusions/Future Directions: The goal of this novel study is to characterize the transcriptomic and proteomic profiles of FECD, a multifaceted disease process which has not fully been described. The quantification of differential gene expression in FECD may lay the framework for greater evaluation of the FECD process, which may involve the selection of targets for possible medical therapies. Ultimately, this study should be repeated for validation and to guide future studies into FECD.

Background

Antenatal depression is one of the most prevalent psychiatric conditions during pregnancy and is associated with adverse maternal, obstetric, and offspring outcomes, including preeclampsia, preterm birth, low birth weight, and long-term neurobehavioral developmental effects. Its mechanisms remain poorly characterized, with emerging evidence implicating neuroinflammatory, metabolic, and neuroendocrine pathways.

Molecular studies often rely on archived samples vulnerable to preanalytical handling deviations. In this study, PAXgene Blood RNA Tubes previously frozen at -80°C inadvertently experienced several days of thawing during shipment. While PAXgene Blood RNA Tubes are designed to stabilize RNA, the effects of prolonged thaw on RNA quality and downstream usability are poorly characterized.

Purpose

This study's primary aim is to evaluate whether PAXgene Blood RNA Tubes that underwent prolonged thaw (PT) differ in RNA quality and RT-qPCR performance from non-thawed (NT) tubes. Secondly, this study aims to assess feasibility of measuring candidate neuroendocrine and immunological gene expression in samples collected from pregnant people with and without antenatal depression at 28-32 weeks of gestation.

Methods

All Our Families is a longitudinal pregnancy cohort from Calgary, Alberta, Canada. Its data include participants' self-reported Edinburgh Postnatal Depression Scale score (>12 positive; <4 negative) and whole-blood samples collected in PAXgene Blood RNA Tubes at 17-23 weeks and 28-32 weeks of gestation. Exclusion criteria include age < 18, language insufficiency, multiple gestation, and non-viable pregnancy.

30 depression-negative PAXgene tubes collected at 17-23 weeks of gestation (10 PT, 20 NT) underwent two total RNA extractions (E1, E2), with refreezing between extractions. The 60 RNA samples were assessed for RNA Quality Number (RQN) by Fragment Analyzer and gene expression of housekeeping genes associated with less variability in pregnant populations: PPP1R15B, EXOC8, and ACTB. Linear mixed-effects models evaluated fixed effects of thaw status, extraction, and their interaction, with sample as a random intercept.

Simultaneously, 4 depression-positive and 8 depression-negative tubes collected at 28-32 weeks of gestation (NT) underwent total RNA isolation. Gene expression was assessed for the following neuroendocrine and inflammatory targets TLR4, NLRP3, NR3C1, BDNF, OXTR, and CRHBP.

Results

PT samples had significantly lower RQN than NT samples (-0.91 , $p < 0.001$); E2 samples had significantly lower RQN than E1 samples (-0.125 , $p = 0.0015$). No significant thaw x extraction interaction was observed ($p = 0.077$). Of the three housekeeping genes, only ACTB showed significant difference in Ct with PT $+0.732$ Ct higher than NT ($p = 0.006$). There were no significant extraction or interaction effects on Ct for any housekeeping gene.

Preliminary data from neuroendocrine-immune pilot show successful amplification of 5 of 6 targets; OXTR failed quality control in 10/12 samples. For the 5 usable targets, $\Delta\Delta Ct$ ranged from -0.04 to $+0.39$.

Conclusion

PT significantly reduced RQN, but PT samples still had model-estimated RQNs at approximately 8.3. One of three housekeeping transcripts showed a significant Ct difference. PAXgene Blood RNA Tubes subject to prolonged thaw may be suitable for targeted RT-qPCR gene expression studies, but thaw status should be accounted for in study design and analysis; results should be interpreted with caution.

Addiction Medicine After Burn and Traumatic Injury: Who is Offered Consultation and Who Accepts It?

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Mentors: Alexander Kurjatko, MD, MPH; Colette Galet, PhD; Hannah Jones, MD

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Introduction: Substance use is common among patients hospitalized with acute burn and traumatic injuries, making hospitalization an important opportunity to identify substance use disorders (SUD) and initiate treatment. Inpatient addiction consultation services may facilitate treatment initiation and engagement in outpatient therapy. Yet, little is known about how these services are utilized across different injury populations. We evaluated patterns of addiction medicine consultation among patients hospitalized with burn and traumatic injuries.

Hypothesis: We hypothesized that consultation delivery and patient acceptance would differ by injury type.

Methods: We conducted a retrospective cohort study of adult burn and trauma patients admitted to the University of Iowa between January 1, 2020 and July 31, 2022. Patients were identified through institutional Trauma and Burn Registries and included in the current analysis if drug and/or alcohol testing was positive. Patients who died within 24 hours of admission and those who had a pre-admission prescription explaining a positive drug test were excluded. Patients were categorized by injury mechanism as blunt trauma, penetrating trauma, or burn injury. Patient characteristics associated with consultation acceptance and initiation of pharmacologic SUD treatment were evaluated. Univariate analyses were performed to compare the groups. Binary logistic regression analyses were used to identify variables associated with offering addiction consultation and acceptance. Statistical significance was defined as $p < 0.05$.

Results: Data were collected on 1000 patients; 947 patients were included. Addiction medicine consultation was offered to 40.5% of patients with blunt trauma, 53.6% with penetrating trauma, and 60.3% with burn injury ($p < 0.001$). Among patients offered consultation, acceptance also differed by injury type: 42.8% with blunt trauma, 57.8% with penetrating trauma, and 74.5% with burn injury ($p < 0.001$). Compared with patients who declined consultation, those who accepted more frequently had documented alcohol abuse (60.4% vs. 34.3%, $p < 0.001$), drug abuse (31.6% vs. 17.4%, $p = 0.001$), depression (44.1% vs. 28.2%, $p = 0.001$), bipolar disorder (9.6% vs. 2.8%, $p = 0.004$), and alcohol withdrawal (28.4% vs. 14.1%, $p < 0.001$). Overall, 93.4% of patients with blunt trauma, 96.2% with penetrating trauma, and 97.1% with burn injury who were offered consultation met established criteria for SUD treatment. Inpatient initiation of SUD medication was uncommon but occurred more frequently among patients accepting consultation than among those who declined (5.3% vs. 0.5%, $p = 0.003$). Binary logistic regression showed that Black patients had lower odds of being offered consultation than White patients (OR = 0.56 [0.349–0.898], $p = 0.016$). Compared with patients with blunt trauma, those with burn injuries (OR = 1.94 [1.16–3.24], $p = 0.011$) or penetrating injuries (OR = 1.99 [1.2–3.32], $p = 0.008$) had greater odds of being offered consultation. Current smoking, documented alcohol or drug abuse, and prior psychiatric hospitalization were associated with greater odds of being offered addiction consultation. Among patients offered consultation, younger age (OR = 0.98 [0.97–0.997], $p = 0.015$) and burn injury (OR = 2.93 [1.41–6.12], $p = 0.004$) were associated with acceptance. Documented drug and alcohol abuse, depression, and antipsychotic medication use were also associated with greater odds of accepting the consult.

Conclusion: Addiction medicine engagement differed significantly across acute injury populations. Patients with burn injuries were the most likely to be offered addiction medicine consultation and, when offered, the most likely to accept it. Consultation was nearly universal among patients meeting established treatment criteria, suggesting that opportunities to improve addiction care may lie primarily in identifying patients who would benefit from intervention. These findings support systematic approaches to SUD identification, documentation, and consultation after acute injury and suggest that burn hospitalization may represent a particularly important opportunity to engage patients in addiction treatment.

Regional Proximal Tibial CT Attenuation by Fixation Method in Robotic Total Knee Arthroplasty

Elizabeth Meyer

Mentor: Dallas Vanorny, M.D. Ph.D.

Collaborators: Joshua Johnson Ph.D., Don Anderson Ph.D., Braiden DeSchryver, Silvana Mohr

Background:

Robotic-assisted total knee arthroplasty (rTKA) uses preoperative CT imaging for surgical planning, providing an opportunity to assess bone quality without additional imaging. Selection between cemented and press-fit fixation largely depends on the surgeon's assessment of patient factors and intraoperative bone quality. CT-derived Hounsfield units (HU) correlate with bone mineral density and may provide an objective measure of proximal tibial bone quality relevant to fixation selection.

Purpose:

To develop a reproducible method for quantifying trabecular CT attenuation in the proximal tibia using HU, and to evaluate regional HU differences between cemented and press-fit fixation cohorts undergoing primary rTKA.

Methods:

Twenty patients undergoing primary rTKA by a single surgeon were retrospectively evaluated (6 cemented, 14 press-fit). All CT scans were acquired on a single scanner platform. A standardized patient-specific coordinate system defined a 5-mm-thick region of interest (ROI) in the lateral proximal tibia 7 mm distal to the lateral plateau centroid, approximating the location of intraoperative tibial resection. This ROI was eroded inward by 3.5 mm to exclude cortical bone and divided into anterior-lateral and posterior-lateral subregions. Voxel-level HU distributions were normalized to account for variable ROI volume across patients. Patient-level mean HU values were compared between fixation cohorts using Welch t-tests, and anterior-posterior HU differences were assessed with paired t-tests.

Results:

Mean full-lateral HU values did not differ significantly between press-fit and cemented cohorts (168.9 ± 45.3 vs 174.8 ± 23.1 HU; $p=0.70$), with substantial overlap in normalized HU distributions. Press-fit patients had lower mean anterior-lateral HU (132.4 ± 40.2 vs 151.1 ± 51.8 HU) and slightly higher posterior-lateral HU (210.5 ± 60.5 vs 200.4 ± 51.2 HU), although neither difference was significant ($p=0.45$ and $p=0.71$, respectively). Posterior HU exceeded anterior HU in all 14 press-fit patients, with a mean paired difference of 78.1 ± 47.4 HU ($p<0.001$). The corresponding difference in cemented patients was 49.3 ± 92.1 HU, with no significant between-cohort difference in regional gradient ($p=0.49$). Cemented patients were older and more frequently female. No postoperative complications were observed in either cohort during available follow-up.

Conclusion:

Proximal tibial trabecular HU distributions substantially overlapped between cemented and press-fit cohorts, with no significant between-group differences in full or regional mean HU, suggesting that fixation cohorts are not readily distinguished by a single HU threshold. Regional analysis demonstrated pronounced anterior-to-posterior heterogeneity, indicating that whole-region averages may obscure spatial variation in bone quality. The absence of early postoperative complications among press-fit patients across this broad and overlapping range of HU values suggests that relatively lower proximal tibial attenuation may not, by itself, preclude successful press-fit fixation. Larger cohorts with demographic adjustment and longer-term outcomes are needed to determine whether regional HU patterns can inform fixation selection or predict implant performance.

Investigating Environmental PCBs, Adipocyte Crosstalk, and Matrix Mechanics in Macrophage Polarization During Tissue Repair

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Introduction: Impaired wound healing following surgery or trauma remains a significant clinical burden and can result in chronic wounds, fibrosis, and poor functional or cosmetic outcomes. These complications are especially relevant in reconstructive plastic surgery, where scarred or grafted tissues create altered mechanical and biochemical environments that may impair regeneration. Macrophages are important regulators of tissue repair, coordinating inflammatory responses, angiogenesis, and extracellular matrix (ECM) remodeling. Their phenotypes are strongly influenced by adipocyte-derived paracrine signaling and local environmental cues, including matrix stiffness and exposure to persistent environmental toxicants such as polychlorinated biphenyls (PCBs). PCBs accumulate in adipose tissue and have been shown to disrupt immunoregulatory signaling. Stiffer substrates have also been associated with more inflammatory macrophage phenotypes. We therefore aimed to determine how mechanically compliant (modeling healthy tissue) versus stiff environments (modeling scarred, fibrotic tissue) alter macrophage polarization in the presence of adipocyte-conditioned media (ACM) and dioxin-like PCB 126 exposure. We hypothesized that softer substrates would promote a pro-regenerative, M2 phenotype and anti-inflammatory factor secretion (increased IL-10 levels), whereas stiffer substrates would favor proinflammatory, M1-like responses. We further hypothesized that PCB 126 exposure would lead to enhanced proinflammatory macrophage signaling, particularly within stiff substrates.

Methods: Adipocyte spheroids were differentiated from mesenchymal stem cells, and ACM was collected following 10 days of differentiation. Monocytes were differentiated into M0 (naïve) macrophages and cultured on a collagen I-coated manufactured tunable-stiffness plate spanning 0.1–100 kPa, with tissue culture plastic (TCP) as a control. In parallel, collagen-agarose hydrogels were fabricated using varying concentrations of collagen I and agarose (% w/v) to generate a stiffness gradient spanning approximately 0.1–80 kPa, according to published literature. Macrophages cultured under each mechanical condition were treated with ACM made with complete RPMI (cRPMI), cRPMI vehicle control, 5 μ M PCB 126 diluted in low-serum RPMI (lsRPMI), or lsRPMI vehicle control. ELISAs were performed to quantify IL-8 and IL-10 as markers of pro- and anti-inflammatory macrophage responses, respectively. XTT and CellTiter assays assessed metabolic activity and relative cell density, and cytokine measurements were normalized against these values to account for differences in cell populations across experimental conditions.

Results: Similar overall stiffness-dependent trends were observed between the collagen-agarose hydrogels and manufactured tunable-stiffness plates. In the collagen-agarose condition, substrate stiffness significantly affected IL-8 and IL-10 secretion among ACM-exposed and cRPMI vehicle control groups (two-way ANOVA, $p < 0.0001$). ACM also significantly affected IL-10 secretion (two-way ANOVA, $p < 0.0001$) in this group. In the manufactured tunable-stiffness plate, Pearson correlation demonstrated a significant association between matrix stiffness and IL-8 secretion in the PCB 126-exposed group when normalized to TCP cRPMI cell density levels measured via XTT ($p = 0.0253$), with a similar trend shown for IL-10 secretion ($p = 0.0702$). Trends were also observed between matrix stiffness and IL-8 secretion in the lsRPMI vehicle control group ($p = 0.0875$) and following CellTiter normalization ($p = 0.0916$). An association between stiffness and IL-10 secretion was also observed in the CellTiter-normalized ACM group ($p = 0.0547$) in the manufactured tunable-stiffness plate condition. Overall, a general decrease in IL-10 secretion was noted with increased stiffness normalized to CellTiter TCP cRPMI levels.

Conclusion: Contrary to our initial hypothesis and previously published findings, ACM did not consistently demonstrate an anti-inflammatory effect across experimental groups, nor did PCB 126 consistently enhance inflammatory IL-8 signaling with increasing matrix stiffness. Similar findings between the collagen-agarose and manufactured tunable-stiffness plate conditions suggest that substrate composition may influence macrophage polarization alongside mechanical stiffness. These pilot findings highlight the importance of accounting for substrate composition and cell density when evaluating macrophage responses to mechanical and environmental stimuli, to better model macrophage responses to *in vivo* tissue environments when investigating repair responses. Repeating this series of experiments will further clarify how tissue mechanics, adipocyte-derived signaling, and PCB exposure interact to regulate macrophage polarization. These results may ultimately inform strategies to promote regenerative immune responses and reduce fibrosis and inflammatory signaling following tissue injury.

Long Term Quality of Life After Pancreatic Resection at a Single Center from 2020-2025

Abdullahi Mohamed, BS, Hassan Aziz, MD

Background:

Pancreatic cancer is among the leading causes of cancer-related mortality, associated with substantial morbidity and mortality. While advances in surgical techniques and perioperative care have enhanced outcomes following pancreatic resection, these procedures remain major abdominal operations that can substantially affect multiple dimensions of patients' quality of life (QoL), including physical, emotional, and social functioning. Despite the growing emphasis on patient-centered outcomes, the long-term impact of pancreatic resection on QoL remains poorly characterized. This study aims to identify preoperative, intraoperative, and postoperative factors associated with poorer long-term health outcomes following pancreatic resection, as assessed using self-reported European Organization for Research and Treatment of Cancer (EORTC) quality-of-life questionnaires. We hypothesized that patients who experienced postoperative complications, were unpartnered, had higher ASA scores, or had a diagnosis of pancreatic cancer would report lower QoL following pancreatic resection.

Methods:

Research participants who underwent pancreatic resection at a single academic institution between 2020 and 2025 were surveyed using a 32-item questionnaire incorporating the EORTC QLQ-17 to assess current quality of life across physical, emotional, social, cognitive, and role functioning. Patients were contacted via email for consent. A retrospective chart review was performed to collect demographic characteristics, comorbidities, treatment history, operative factors, and postoperative outcomes from the electronic medical record. Relationship status was categorized as partnered (married/life partner) or unpartnered (single, widowed, or divorced). Welch's unequal-variance t-tests were used to compare outcomes between groups.

Results:

Of the 408 patients who underwent pancreatic resection during the study period, 153 were deceased and 255 alive. Email invitations were sent to 221 patients with identifiable email addresses, of whom 43 completed the survey (19.5% response rate). Higher ASA scores (ASA 3 vs. 2) were associated with lower role functioning scores (80.0 ± 5.1 vs. 93.4 ± 2.7 , $p=0.026$). Partnered patients reported higher emotional functioning compared with unpartnered patients (82.2 ± 4.1 vs. 59.6 ± 7.4 , $p=0.015$). Hypertension was associated with lower physical functioning (83.6 ± 3.9 vs. 93.3 ± 2.7 , $p=0.046$). Patients who received chemotherapy also reported lower physical functioning (81.6 ± 4.9 vs. 92.8 ± 2.2 , $p=0.046$). No significant differences in QoL were observed based on age, surgical approach (minimally invasive vs. open), malignancy status, 30-day readmission, or post-surgical complications.

Conclusion:

Pancreatic resections, including pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy, are major operations that can impose substantial physiological and psychological stress. Our findings suggest that long-term quality of life following pancreatic resection is influenced by perioperative factors, with higher ASA scores and comorbidities such as hypertension associated with poorer physical and role functioning. Patients who received chemotherapy also demonstrated lower physical functioning, highlighting the potential long-term burden of systemic therapy. A partnered relationship appeared protective for emotional functioning. In contrast, no significant differences in quality of life were observed based on malignancy, surgical approach (laparoscopic vs. open), or other evaluated factors. Given the limited response rate and sample size, continued data collection and larger cohorts will enable more robust assessment of factors influencing long-term recovery and quality of life following pancreatic resection.

Short- and Long-Term Outcomes of Older Adult Patients with Burn Injuries

Jenna Mosnik, BS, Will Fairman, BS, Patrick Ten Eyck, PhD, Colette Galet, PhD, Lucy Wibbenmeyer, MD

Introduction: Burn injuries are serious, debilitating injuries with long recovery times. As medical treatments advance, survivability after burn injuries continues to increase. However, older adult patients with burn injuries continue to have lower inpatient life expectancy than younger cohorts. There are numerous factors that complicate the recovery of older adults including thinning skin, decreased peripheral angiogenesis, chronic inflammation, and various comorbidities. Impaired wound healing also complicates the treatment of burn injury in the older adult population by predisposing them to deeper burn wounds and sequela. Generally, inpatient survivability is related to age, burn size, and inhalation injury. However, as a person ages, survivability is more heavily influenced by comorbidities and frailty. Moreover, there is limited research on the impact of burn injury on subsequent quality of life and long-term survivability.

Hypothesis & Purpose: We sought to determine factors related to both in-hospital and long-term survival in an older adult burn population. We also evaluated hospital free days as a measure of quality of life (QOL) post burn injury. This information will help providers counsel families and patients about expectations following their injury. We hypothesized that in-hospital mortality rates will be significantly different between the two cohorts examined: 1977-1996 and 2009-2019. We also hypothesized that patients who survive their injury will have shorter life expectancy and more hospital admissions compared to controls.

Methods: Patients admitted between 1977-1996 were compared to patients admitted between 2009-2019 to determine trends in treatment and mortality. The following variables were abstracted: demographics, burn history, hospital course, complications, and resource utilization. Outcome variables include hospital length of stay (LOS), disposition, and in-hospital mortality. Charlson Comorbidity Index (CCI) was used as a measure to predict survivability post-index admission. Modified 5-item frailty index (mFI-5) and CCI were compared to Baux Score and ABSI to determine the best in-hospital mortality prediction method by a receiver operating curve. Chi square and Students' T test were used when appropriate. Significance was determined at $p < 0.05$ level.

Results: The 1977-1996 cohort consisted of 310 patients and the 2009-2019 consisted of 852 patients. The 2009-2019 cohort had decreased length of stay (5 vs 16 days, $p < 0.0001$), increased TBSA/LOS (1.0 vs 0.6 days/TBSA, $p = 0.0041$), decreased skin graft size (750 vs 1150 cm², $p = 0.0137$), increased ventilator days (1 vs 0 days, $p < 0.0001$), and decreased inhalation injury (8% vs 15.2%, $p = 0.0022$). Significantly fewer patients transitioned to comfort care (7.6% vs 16.5%, $p = 0.0002$) and died (8.5% vs 30.1%, $p < 0.0001$) during their hospital stay in the 2009-2019 cohort. The 2009-2019 cohort had significantly more comorbidities including: chronic kidney disease (8.9% vs 3.6%, $p = 0.0034$), chronic pulmonary disease (28.2% vs 10.1%, $p < 0.0001$), and peripheral vascular disease (8.5% vs 2.3%, $p = 0.0003$), and significantly less myocardial infarction (9.3% vs 38.1%, $p < 0.0001$).

Conclusions: As hypothesized, on univariate analysis, the 2009-2019 cohort had improved in-hospital survival and shorter LOS compared to the 1977-1996 cohort. Further analysis is ongoing to determine if survival is improved when adjusting for confounders. Data collection for life expectancy and hospital free days is ongoing and will be analyzed in the future.

Indications and Timing of Physical Therapy Referral and Upper Extremity Outcomes After Breast Reconstruction

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Introduction/Background: Upper extremity dysfunction following breast reconstruction is common and can adversely affect postoperative recovery and quality of life. Although physical therapy (PT) is frequently recommended, the optimal timing for referral remains uncertain and largely driven by clinical observations rather than protocol. This study evaluated whether earlier PT referral is associated with improved upper extremity function following breast reconstruction.

Hypothesis/Purpose: Early PT referral following breast reconstruction may be associated with improved recovery of upper extremity function. These findings may help guide postoperative rehabilitation protocols and identify patients most likely to benefit from early referrals.

Methods: We conducted a retrospective cohort study of patients undergoing breast reconstruction at a single institution. Patients who underwent tissue expander (TE) or implant placement during their index reconstructive surgery were categorized by PT referral timing relative to the index procedure as early (≤ 6 weeks), late (> 6 weeks), or no referral. Upper extremity function was assessed using the QuickDASH questionnaire at their preoperative baseline and four postoperative time points: 0-6 weeks, 7-12 weeks, 3-6 months, 6-12 months. Demographic, oncologic, and perioperative surgical variables were collected. Changes in postoperative QuickDASH scores were compared directly between PT referral groups, and multivariable adjustment was utilized to account for confounders and identify independent associations between PT referral timing and QuickDASH scores.

Findings/Results: A total of 125 patients who underwent breast reconstruction with TEs or implants were included. Of these, 67 patients (53.6%) received no PT referral, 26 patients (20.8%) had early referral, and 32 patients (25.6%) received late referral. All three groups were comparable in age, BMI, reconstructive laterality, and complication rate. Referred patients were more likely to have undergone axillary lymph node dissection and receive adjuvant radiation treatment ($p=0.002$). The median preoperative QuickDASH score for all groups was 2.3, which subsequently rose to a median of 50.0 between 0-6 weeks postoperatively ($p<0.001$). After 6 weeks, QuickDASH scores declined but remained above their preoperative baseline ($p=0.034$), however still below the QuickDASH minimal clinically important difference (MCID) threshold of 15 points. Unadjusted comparisons between referral groups revealed no difference in the change of QuickDASH scores at any time point. ($p>0.05$). Multivariate linear regression was performed to adjust for age, adjuvant radiation exposure, axillary lymph node dissection, and baseline preoperative QuickDASH, which revealed late referral was independently associated with an 8.1 point increase in 6-12 month QuickDASH scores (95% CI 0.6-15.7, $p=0.036$). Furthermore, early referral did not demonstrate any significant difference in 6-12 month QuickDASH scores ($p=0.223$). These associations remained significant even after further adjustment for early postoperative upper extremity dysfunction (95% CI 2.2-16.8, $p=0.012$).

Conclusion: In patients undergoing breast reconstruction with TEs or implants, upper extremity function worsened early after surgery and gradually improved over time. While PT referral timing was not associated with differences in unadjusted QuickDASH scores, late referral was associated with worse long term function after adjusting for relevant confounders. These findings suggest that delayed PT referral is associated with persistent functional deficits, although the retrospective nature of this study limits conclusions regarding causality. Future prospective studies with standardized PT referral and treatment protocols will be evaluated to better determine the role and optimal timing of PT after breast reconstruction.

From Expiration to Preservation: Reducing Plasma Waste by Incorporating Liquid Plasma in Trauma Resuscitation: A Before-and-After Evaluation

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Background: Trauma-related mortality increased by 91% from 2000 to 2020, exceeding the 18% population growth during the same period in the United States. Early administration of plasma can improve outcomes in some patient groups such as those with hemorrhagic shock. To avoid delays in transfusion, trauma centers maintain plasma products for immediate emergency use. However, trauma volumes can be unpredictable, resulting in plasma expiring before it is needed. Fresh frozen plasma (FFP) must be thawed before administration and once thawed, can be stored for approximately five days. Liquid plasma (LQP) is immediately available and can be stored for up to 26 days.

Objective: To evaluate changes in plasma waste and cost after LQP became the primary initial plasma product used in trauma resuscitation.

Methods: A single-center retrospective study was conducted at a Level I Trauma Center in the Midwestern United States. On December 1, 2025, the center changed its protocol from FFP to LQP as the primary initial plasma product in trauma resuscitation. During the study periods, FFP cost \$49.00 per unit through May 31, 2025, and \$54.05 per unit beginning June 1, 2025, while LQP cost \$116.25 per unit. An interim analysis was conducted to examine corresponding six-month periods before and after the protocol change (i.e., December 2024 through May 2025 and December 2025 through May 2026). Trauma volume, plasma waste, and associated product costs were compared between the two periods. Total plasma utilization was not available and not accounted for in the presented interim analyses. In addition, unused plasma could be used by other service lines in the hospital, though an unvalidated assumption was made that the two periods were exchangeable in regard to secondary product use and the overall trauma case mix.

Results: At the study center there were 1,199 trauma patient encounters in the pre-protocol period and 1,232 patient encounters afterward, representing a 2.8% increase in patient volume. FFP waste decreased from 98 units in the pre-protocol period to 48 units in the post-protocol period. The change represents an approximately 50% reduction. The post-protocol total included one wasted unit of LQP. Of note, all FFP units were discarded due to expiration, while the single LQP unit was discarded because of improper storage. Total waste cost decreased from \$4,802 to \$2,708, representing a 43.6% reduction and \$2,094 in savings.

Conclusion: The transition to LQP as the primary initial plasma product was associated with reductions in waste and cost despite an increase in the trauma volume. The low number of wasted LQP units suggests that its longer shelf life can reduce expiration-related waste while maintaining immediate plasma availability. The findings support LQP as a practical strategy for reducing plasma waste and associated costs without compromising product availability. Trauma centers seeking to reduce plasma waste should consider LQP as part of their blood product inventory. Ongoing study analyses will compare complete one-year periods and evaluate secondary clinical outcomes including 24-hour and 30-day survival, and ICU and hospital lengths of stay.

Oculocutaneous Albinism: Visual Outcome Predictors Among Genetically Tested Pediatric Patients
Sabah Munir, Advisor: Alina Dumitrescu, MD
Collaborators: Anthony Chen, Tara L. Bragg, Valencia L. Potter, Arlene V. Drack, Alina V. Dumitrescu

Background and Purpose: Oculocutaneous albinism (OCA) refers to a group of congenital disorders of melanin production. Different molecular subtypes have been identified based on the genes affected, including AR OCA1-7, X-linked ocular albinism, and multisystem conditions such as Hermansky-Pudlak syndrome. Prior studies demonstrated no genotype-phenotype correlations, but visual outcomes vary widely in OCA. We have access to a large cohort of OCA patients with extensive multimodal workups, including genetic testing, and we aim to develop predictive models that can inform visual prognosis, especially among pediatric patients. In the current analysis, we explored relationships between various clinical and imaging markers and the different molecular forms of OCA, focusing on visual acuity measured over time and relationships between molecular genotype, phenotype, and visual outcome.

Methods: We performed an IRB-approved retrospective chart review of patients who had received care in the pediatric ophthalmic genetic clinic in the UIHC Department of Ophthalmology and Visual Sciences between January 1, 1990, and December 31, 2025. We abstracted information regarding patient genetic reports, initial and recent visual acuity, and albinism-associated clinical and imaging features. Because Shapiro-Wilk test results showed that many continuous variables were not normally distributed, we used non-parametric statistical methods. All statistical tests were performed using R and were assessed using $\alpha = 0.05$.

Results: A previously described clinical albinism score (CAS) was used to quantify the severity of various clinical features of OCA. Across variables stratified by molecular diagnosis, we found that the presence of severe iris transillumination deficits was correlated with lower final visual acuity (Fisher's exact, $p = 0.017$). Final best corrected visual acuity (BCVA) values were significantly different based on optic nerve anomaly severity (Kruskal-Wallis rank sum, $p = 0.008$), clinical presence of foveal hypoplasia (Kruskal-Wallis rank sum, $p = 0.034$), nystagmus severity (Kruskal-Wallis rank sum, $p < 0.001$), and degree of foveal hypoplasia on optic coherence tomography by Thomas grade (Kruskal-Wallis rank sum, $p < 0.001$); BCVA values worsened at higher levels for these variables. While Kruskal-Wallis rank sum methods showed that different molecular diagnosis groups had similar initial and latest BCVA values, all groups demonstrated significant improvements in BCVA over time (Wilcoxon signed rank exact, overall $p < 0.001$, OCA1 $p = 0.001$, OCA2 $p = 0.003$, others $p = 0.018$). While changes in BCVA were not correlated with latest CAS ratios, changes in BCVA were negatively correlated with elapsed time between visits ($\tau = -0.187$, $p = 0.041$, $n = 62$). Most patients had hyperopia (65.2%) and astigmatism (97.2%); high astigmatism affected 64.8% of the overall sample. Among patients with myopia, changes in spherical equivalence were significantly correlated with elapsed time between visits for only the right eye ($\tau = -0.339$, $p = 0.031$, $n = 22$). Among patients with hyperopia, changes in spherical equivalence were positively correlated with elapsed time between visits for both the right eye ($\tau = 0.256$, $p = 0.026$, $n = 38$) and left eye ($\tau = 0.272$, $p = 0.018$, $n = 38$).

Conclusions and Significance: Past research suggested a trend of overall improvement of BCVA in children over time or with age. Our study validates those findings and quantifies the prognostic factors that contribute to final BCVA, and the findings support our hypothesis that younger patients would see larger improvements in BCVA over a longer follow-up time. Refractive errors were analyzed in this cohort; spherical equivalence changes and time between assessments varied in correlation direction based on whether patients had refractive errors. Future work may use a different statistical model to assess changes in BCVA or spherical equivalence over time.

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

Student: Sarah Nacos

Mentor: Paari Dominic

Abstract

Background

Adjunctive vein of Marshall (VOM) ethanol infusion has been shown to improve outcomes during catheter ablation for persistent atrial fibrillation (AF), although prior studies have routinely incorporated endocardial lateral mitral isthmus ablation. Data evaluating VOM ethanol infusion without routine lateral mitral isthmus ablation remain limited.

Objective

To evaluate the procedural success, acute electrophysiologic effects, and clinical outcomes of adjunctive VOM ethanol infusion performed without routine endocardial lateral mitral isthmus ablation during AF ablation.

Methods

We retrospectively evaluated consecutive patients undergoing attempted adjunctive VOM ethanol infusion during catheter ablation for AF at a single tertiary referral center. Procedural success, acute electrophysiologic effects of ethanol infusion, recurrent atrial arrhythmias, repeat catheter ablation, and lesion durability at repeat procedures were assessed.

Results

A total of 130 patients underwent attempted VOM ethanol infusion. Successful VOM cannulation and ethanol delivery were achieved in 110 patients (84.6%). Acute electrophysiologic effects included isolation of both left pulmonary veins in 23 patients (17.7%), isolated left inferior pulmonary vein isolation in 17 (13.1%), isolated left superior pulmonary vein isolation in 1 (0.8%), lesion formation around the left pulmonary veins without pulmonary vein isolation in 45 (34.6%), lesions extending below the left inferior pulmonary vein without pulmonary vein isolation in 15 (11.5%), and no demonstrable acute electrophysiologic effect in 9 (6.9%). Over a median follow-up of 10.9 months (interquartile range 5.3–12.6 months), recurrent atrial fibrillation occurred in 38 patients (29.5%), recurrent atrial flutter in 14 (10.9%), and recurrent atrial arrhythmias in 39 (30.2%).

Conclusion

61% of patients with persistent atrial fibrillation undergoing Vein of Marshall ethanol infusion without the use of endocardial mitral isthmus ablation were atrial arrhythmia free over a median follow up of 10.9 months.

TITLE: Comparing Surgical Outcomes of Osteochondritis Dissecans of the Knee With Minimum 5-Year Follow-Up

STUDENT: Troy Nation

MENTOR: Robert Westerman, MD

COLLABORATORS: Shannon Ortiz, Crystal Maldonado

BACKGROUND: Osteochondritis dissecans (OCD) of the knee is commonly treated surgically, but there is limited evidence to guide surgical decision-making. Joint-sparing procedures are generally preferred over excision techniques; however, their relative effectiveness, particularly in severe cases, is unclear. This study aims to evaluate the influence of surgical approach and initial lesion characteristics on need for reoperation, osteoarthritis development, and long-term knee function.

METHODS: We performed a retrospective review of patients who were treated surgically for OCD or osteochondral defects prior to June 2021. Patients with focal chondral defects, osteochondral defects unrelated to OCD, or pre-existing knee osteoarthritis were excluded from the study. Patient demographics (age, BMI, sex, and smoking status), lesion characteristics (size and stability), and surgical characteristics (procedure type, concomitant procedures) were collected from patient charts. Additionally, eligible patients were invited to complete a Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire. Long-term outcomes included reoperation, postoperative osteoarthritis, and KOOS subscale scores. We performed univariable analysis (significance set to $P < .05$) to identify associations between each outcome and the variables previously listed.

RESULTS: Of the 121 eligible patients (mean follow-up 12.1 ± 4.0 years), 31 (25.6%) underwent reoperation and 21 (17.4%) developed osteoarthritis (mean time to diagnosis 3.28 ± 3.63 years). At the time of analysis, 18 patients (14.9%) had completed KOOS questionnaires, with collection still ongoing for the remaining cohort. No variables were found to be significantly associated with reoperation, though procedure type approached significance ($P = .055$), with subchondral drilling demonstrating the highest reoperation rate (58.3%) compared to OCA/OATS (19.1% and 18.9%, respectively). Older age ($P < .001$) and higher BMI ($P = .004$) at time of initial surgery, as well as undergoing OCA/OATS versus other procedures ($P = .021$, OR 5.06, 95% CI 1.11 – 47.35), were significantly associated with postoperative osteoarthritis. There were no significant associations between the variables we assessed and KOOS subscale scores.

CONCLUSIONS: Age, BMI, and procedure type were shown to be significantly associated with the development of postoperative osteoarthritis. No variables were significantly associated with reoperation. Additional KOOS responses are needed to draw meaningful conclusions about long-term knee function following surgical treatment of OCD.

Spatial Proteogenomic Profiling of the Non-Small Cell Lung Cancer Tumor Microenvironment

Student: Natalie Nelson

Mentor: Dr. Christina Cho

Collaborators: Anna Hepfer, Francesc Lopez-Giraldez, Gavitt Woodard, David Rimm, Lieping Chen

Introduction: Lung cancer remains the leading cause of cancer-related mortality worldwide. Although lung cancer is resistant to most available therapies, immunotherapy has transformed the field of oncology by eradicating tumors and dramatically improving 5-year survival rates, making it the first-line treatment for advanced metastatic non-small cell lung cancer (NSCLC). Unfortunately, only a subset of patients achieve clinically durable benefits. Immune checkpoint inhibitors (ICIs) bolster immune responses in only 20% of patients, and 80% are left with few therapeutic alternatives. While the mechanisms driving non-response remain unclear, it is known that immune surveillance is linked to improved patient outcomes. Immune responses are governed by adequate infiltration of functional CD8⁺ T-cells within the tumor microenvironment (TME). When T-cells are dysfunctional or excluded from the TME, the immunotherapy response rate is poor.

Hypothesis: We hypothesize that soluble factors within the TME, termed T-cell excluders (TCEs), prevent cytotoxic T lymphocytes (CTLs) from infiltrating tumors; thus, facilitating immune evasion and limiting therapeutic efficacy.

Methods: Human NSCLC specimens were analyzed utilizing the GeoMx Digital Spatial Profiler (DSP), a powerful spatial multiomic instrument that combines immunohistochemistry (IHC), *in situ* hybridization, and barcoding technology of next-generation sequencing to evaluate RNA and protein expression within intact tissues. In contrast to traditional profiling tools, this platform can preserve tissue integrity and maintain high plexity when evaluating the TME. UV-directed micromirror technology enabled the selection of user-defined regions of interest (ROI) for compartment-specific profiling. This allowed us to independently evaluate the proteomic and transcriptomic profile of the vimentin-positive stromal compartment, panck-positive cancer cell compartment, and CD8⁺T cells. Using the number of CD8⁺T cells in each specimen, we grouped the tumors into T-cell exclusive “cold” and T-cell inclusive “hot” tumors, then compared the transcriptome and proteome of those two groups. The transcriptomic and proteomic profiles of T-cell exclusive (cold) and T-cell inclusive (hot) tumors were investigated.

Results: We identified 752 differentially expressed genes and 38 differentially expressed proteins. Molecules that were differentially expressed at both the gene and protein levels were selected for additional bioinformatic analysis. Ultimately, we identified 5 molecules that have potential to modulate T cell exclusion: MET, IL-33, WNT3A, ErbB3, and MUC5AC. Ongoing work with IHC, T-cell motility assays (TCMA), and T-cell activity arrays (TCAA) will assess the function of those candidate molecules and determine whether they are bonafide TCEs.

Conclusion: Spatial proteogenomic profiling serves as a powerful tool, allowing the study of complex molecular interactions while avoiding destruction of tissue architecture. Additional *in vitro* and *in vivo* studies will determine whether candidate molecules are T cell excluders or predictive biomarkers of response to immunotherapy.

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.

Dynamic Changes in Heart Rate Variability Following Mechanical Thrombectomy and Their Association with Neurologic Recovery

Baqir Noor (Student), Mario Zanaty (Mentor), Anderson Brito Alvarado, Nour Shaheen, William Davis Haselden

Introduction: Heart rate variability (HRV) is a noninvasive marker of autonomic nervous system function and has been associated with outcomes following ischemic stroke. However, most prior studies have focused on absolute HRV measurements, while the significance of dynamic changes following mechanical thrombectomy (MT) remains unclear. Because MT produces a defined transition from cerebral ischemia to reperfusion, characterizing early HRV trajectories may reveal physiologic responses to reperfusion that are not captured by single time-point measurements and could provide an early, noninvasive means of monitoring neurologic recovery and tissue injury after thrombectomy.

Purpose: To evaluate whether changes in HRV during the first 12 hours following MT are associated with neurologic recovery, functional outcome, and infarct burden after acute ischemic stroke.

Methods: Ten patients undergoing MT for large vessel occlusion stroke with available EKG recordings were retrospectively analyzed. Baseline HRV measurements obtained prior to thrombectomy were compared with measurements acquired at 1, 6, and 12 hours cumulatively following MT. Delta HRV values were calculated as post-procedure minus pre-procedure values. Time-domain metrics included SDNN, RMSSD, SD1, SD2, and pNN50. Frequency-domain metrics included LF, HF, LFnu, HFnu, and LF/HF ratio. Spearman correlation analyses evaluated relationships between HRV changes and neurologic improvement, defined as the change in NIHSS from pre-thrombectomy assessment to discharge, 3-month modified Rankin Scale (mRS), and early follow-up infarct volume (24h from MT). Univariate analyses compared five patients with favorable functional outcomes (mRS 0-2) and five with unfavorable outcomes (mRS 3-6) using Wilcoxon rank-sum and Fisher exact testing.

Results: Regarding neurologic recovery, greater improvement in NIHSS from pre-thrombectomy assessment to discharge was associated with lower ΔMeanHR at 1 hour post-MT ($\rho = -0.56$, $p = 0.09$). Greater NIHSS improvement also correlated with lower LFnu and higher HFnu at 1, 6, and 12 hours post-MT ($\rho \approx -0.59$ and $\rho \approx 0.59$, respectively). Although these associations did not consistently reach statistical significance, their persistence across multiple timepoints may suggest that improved neurologic recovery is accompanied by a relative shift toward parasympathetic predominance following reperfusion.

Associations between HRV measures and 3-month functional outcome were generally modest. In outcome-group analyses, patients with favorable outcomes required fewer thrombectomy passes than those with unfavorable outcomes (median 1 vs 3, $p = 0.025$), potentially reflecting the impact of procedural complexity on long-term recovery. Patients with favorable outcomes also demonstrated smaller changes in heart rate at 6 hours post-MT compared with those with unfavorable outcomes (ΔMeanHR 0.1 vs 13.8 bpm, $p = 0.095$). While not statistically significant, this trend may indicate that post-procedural heart rate elevation is associated with less favorable recovery trajectories.

Most HRV parameters demonstrated little association with follow-up infarct volume. However, increased SD1/SD2 at 1 hour post-MT was significantly associated with larger infarct volume ($\rho = 0.76$, $p = 0.016$), with similar directional relationships observed at 6 and 12 hours. This finding raises the possibility that early alterations in the balance between short- and long-term HRV components may reflect the extent of tissue injury after reperfusion.

Conclusion: In this pilot cohort, favorable neurologic recovery following MT was associated with lower post-procedural heart rate and consistent shifts in autonomic balance across the first 12 hours after reperfusion. In contrast, increased early SD1/SD2 was associated with larger infarct volume, suggesting that distinct HRV signatures may reflect separate aspects of neurologic recovery and tissue injury. These findings support the potential utility of dynamic HRV assessment as a physiologic biomarker following thrombectomy; however, given the small sample size, results should be considered preliminary and warrant validation in larger prospective studies.

The Feasibility, Challenges, and Facilitators of Implementing a Web-Based Behavioral Lifestyle Intervention to Improve Cancer-Related Fatigue and Quality of Life Among People with Cancer in Remission: A Mixed-Methods Study

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Background: Cancer-related fatigue (CRF) is defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. CRF is reportedly experienced by 70-80% of patients who have received cancer treatment and has been noted to have a negative impact on quality of life (QoL). Clear guidelines for pharmacological strategies to mitigate fatigue, as well as safety data for potential medications, are limited, prompting the investigation of non-pharmacological treatment options including lifestyle modification interventions.

Purpose/Hypothesis: This study aimed to evaluate the feasibility of implementing a web-based behavioral lifestyle intervention for individuals with cancer in remission and included one-on-one interviews to capture participants' experiences related to challenges and facilitators of implementing such a program. We hypothesized that qualitative analyses would reveal distinct facilitators of and barriers to participation in and engagement with a web-based behavioral lifestyle intervention.

Methods: The study used a mixed method, randomized, waitlist-controlled design to evaluate the feasibility of a web-based wellness intervention including diet, exercise, and stress management strategies among post-treatment fatigued cancer in remission patients after 6 months. Online questionnaires were sent to participants at months 0, 3, and 6 to assess outcomes of interest. After study completion, participants were invited to participate in a one-time, 30-minute, one-on-one interview to share their perspectives and experiences related to the study. A sample of four individuals was recruited for semi-structured interviews, with open-ended questions designed to characterize their experience with the online course. Analysis of interview transcripts was performed independently by two team members using MAXQDA software and followed a five-step thematic analysis approach. Themes were defined and summarized, with representative participant quotations selected to support the interpretation of findings.

Results: A total of 34 participants were enrolled, and four agreed to participate in virtual, one-on-one interviews. Thematic analyses revealed five major themes: personal readiness and health context, program content and experience, social and environmental factors, resource accessibility and lifestyle change feasibility, and program impact on fatigue and behavioral change. A Sankey diagram was created to visually depict the flow of coded responses into broader themes. Quantitative measures, including fatigue, QoL, and mood surveys completed by all participants will be analyzed and are anticipated to be complete by late 2026, when quantitative and qualitative results will be compared to interpret consistencies and discrepancies.

Conclusion: Qualitative analysis revealed five themes that represented facilitators of and barriers to engagement with a web-based behavioral lifestyle intervention for people with cancer in remission. These results will be further compared with quantitative data that will characterize participants' fatigue and QoL once analyzed. This will allow for a broader picture view of the feasibility and impact of a remotely-delivered lifestyle intervention which can be used to inform future interventions.

A Systematic Characterization of Tele-Buprenorphine Hotlines in the US

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Background/Introduction: Buprenorphine is a highly effective medication for the treatment of opioid use disorder (OUD) and is considered the preferred option for low-barrier treatment models. Legislative and regulatory changes introduced during the COVID-19 pandemic substantially expanded access to buprenorphine via telehealth, enabling patients to initiate and continue treatment remotely. As a result, tele-buprenorphine programs and on-demand treatment hotlines have emerged nationwide to increase access to evidence-based OUD care, particularly for rural and underserved populations.

Gap/Study rationale: Despite the rapid growth of tele-buprenorphine hotlines across the United States, no comprehensive characterization or consensus framework exists to describe their operations or service delivery models. This project addresses this critical gap by systematically describing the current tele-buprenorphine hotline landscape to inform more efficient and scalable models of care.

Methods: We conducted a cross-sectional study and developed a survey instrument (REDCap) to capture key characteristics of tele-buprenorphine hotlines and their operations, including funding sources, staffing models, service scope, and care delivery processes. Programs were identified using a wide-net recruitment strategy that incorporated internet searches, snowball sampling, and expert recommendations to ensure broad representation of tele-buprenorphine hotline programs. Respondents received compensation as an incentive for survey completion. Survey responses were analyzed using descriptive statistics and synthesized to identify common operational characteristics, areas of variation, and emerging models of tele-buprenorphine service delivery.

Findings/Results: Of the 30 invited pool of participants, 12 participants from tele-buprenorphine programs completed the survey. Most programs operated statewide (75.0%) and provided direct patient-facing services (91.7%), while 55.6% also offered provider-to-provider consultation. Core clinical services were highly consistent across programs, including buprenorphine dosing and induction guidance (100%), opioid withdrawal assessment support (100%), buprenorphine initiation support (91.7%), referral coordination (91.7%), and naloxone access support (91.7%). Most programs routinely provided buprenorphine prescribing (83.3%). Hotline operations varied substantially, with 33.3% offering 24/7 coverage, 50.0% operating during fixed hours, and 16.7% using on-call models. Staffing models were multidisciplinary, most commonly involving physicians (81.8%) and advanced practice providers (60.0%). Funding mechanisms were diverse, with state funding (60.0%) and billing or revenue generation (58.3%) reported most frequently. The most commonly cited barriers to utilization were funding (58.3%) and awareness (50.0%), while outreach (75.0%) was the leading facilitator.

Conclusions: Tele-buprenorphine hotlines represent an increasingly important mechanism for expanding access to low-barrier OUD treatment. While core clinical services were largely consistent across programs, substantial variation existed in operational structure. These findings suggest that tele-buprenorphine hotlines have evolved through diverse local approaches rather than a standardized model of care. Developing a consensus framework for characterizing and evaluating tele-buprenorphine hotlines may facilitate best-practice sharing, program evaluation, and broader dissemination of effective models for OUD treatment access.

Title: “The Microbiome’s Effect on Tissue Loss in *Klebsiella pneumoniae* Sepsis”

Katerina Petroff

Mentor: Dr. Kale Bongers, MD, PhD, Department of Internal Medicine - Pulmonary, Critical Care, and Occupational Medicine

Collaborator: Nicholas Gansemer, BS

Sepsis, a syndrome of organ dysfunction and immune dysregulation in response to infection, affects millions of patients worldwide each year and causes hundreds of thousands of deaths. Sepsis survivors are often left profoundly debilitated due to muscle weakness. Despite its prevalence and severity, sepsis treatments are largely limited to antibiotics and supportive care, and our understanding of its pathogenesis and sepsis recovery remains limited. One intriguing target for sepsis therapeutics is the gut microbiome, the community of bacteria living within the gut; recent work has shown that antibiotics targeting gut anaerobic bacteria are associated with worse clinical outcomes than antibiotics sparing gut anaerobes. Further, muscle loss is associated with increased mortality in sepsis; in health, the microbiome is an important regulator of muscle mass. However, the role of the microbiome in tissue loss in sepsis is poorly understood.

The purpose of this study was to identify differential loss of muscle and adipose tissue loss during sepsis with administration of either cefepime (a broad-spectrum antibiotic which spares gut anaerobes) or piperacillin-tazobactam (a broad-spectrum antibiotic with strong activity against gut anaerobes) after intranasal infection with *Klebsiella pneumoniae*. Administration of these antibiotics affects the patient’s microbiome in addition to the pathogen. We hypothesized that piperacillin-tazobactam administration would preserve muscle mass more than cefepime due to the elimination of anaerobic bacteria in the gut microbiome.

On Day 0, male C57BL/6 mice were intranasally infected with *Klebsiella pneumoniae*. Additional uninfected mice were used as a control cohort. Starting on Day 3, experimental mice received cefepime (30 mg/kg) or piperacillin-tazobactam (67.5 mg/kg) intraperitoneally once daily, while control mice received daily saline injections. Mouse weights were monitored daily; on Day 5, the tibialis anterior muscle, gastrocnemius-soleus complex muscle, perigonadal adipose tissue, and brown adipose tissue were harvested.

We found that *Klebsiella*-treated mice had significant weight loss compared to control animals prior to antibiotic administration (Day 0-3, cefepime: -3.7 g, piperacillin-tazobactam -3.8 g, control: -0.28 g, $p < 0.001$). After antibiotic administration, the experimental weights diverged, with cefepime-treated mice regaining weight while piperacillin-tazobactam-treated mice continued to lose weight (Day 3-5, cefepime: 0.62 g, piperacillin-tazobactam: -1.5 g). Further, piperacillin-tazobactam treated mice demonstrated higher mortality compared to cefepime-treated mice (Mantel-Cox test $P = 0.0023$). For the harvested tissue, both experimental groups had significantly reduced tissue weight compared to control ($p < 0.01$) for the two muscle groups (tibialis anterior and gastrocnemius-soleus complex muscles) and perigonadal adipose tissue. While the piperacillin-tazobactam group showed greater perigonadal adipose tissue loss compared to the cefepime group, this comparison was not statistically significant ($p < 0.08$). Finally, for brown adipose tissue, the piperacillin-tazobactam group had significantly lower tissue weight compared to control (control: 92.41 mg, piperacillin-tazobactam: 68.06 mg, $p < 0.01$).

These findings suggest that aerobic and anaerobic microbiome depletion with piperacillin-tazobactam significantly alters metabolic tissue mass and increases mortality compared to anaerobic microbiome-sparing antibiotics. This suggests that the microbiome plays an important role in regulating metabolism during the systemic stress of sepsis. Further studies are needed to elucidate the mechanisms underlying these effects and elucidate the role of anaerobic bacteria in the physiological response to infection.

Pregnancy-Relevant Autoantibody Profiles and Adverse Pregnancy Outcomes in Patients with Sjögren's Disease: A Retrospective Chart Review

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Background: Sjögren's disease (SjD), historically referred to as primary Sjögren's syndrome (pSS), is a systemic autoimmune disease characterized by sicca symptoms, extraglandular manifestations, and autoantibody production. Certain autoantibodies, including SS-A/Ro, SS-B/La, and antiphospholipid antibodies, are clinically relevant in pregnancy due to their associations with neonatal lupus, fetal/congenital heart block, pregnancy loss, preeclampsia, fetal growth restriction, thrombosis, and other adverse pregnancy outcomes.

Objective: To describe pregnancy-level adverse outcomes, pregnancy-relevant autoantibody profiles, complement status, and pregnancy medication exposure among patients with SjD, and to evaluate whether maternal serologic features or documented pregnancy medication exposure were associated with pregnancy outcomes.

Methods: We conducted a retrospective chart review of biologically female patients of child-bearing age (ages 18-50) with rheumatologist-confirmed SjD at a single academic center. Demographic characteristics, clinical manifestations, serologic profiles, complement status, pregnancy history, and pregnancy-specific medication exposures were abstracted from the medical record. The primary unit of analysis was pregnancy. We defined an adverse pregnancy outcome (APO) as miscarriage/pregnancy loss, preterm birth, preeclampsia/eclampsia, neonatal lupus, fetal heart block, or intrauterine/fetal growth restriction. Maternal factors included ANA positivity, high ANA titer, SS-A positivity, any antiphospholipid antibody positivity, lupus anticoagulant positivity, triple-positive aPL status, low C3 and/or C4 at any time, hydroxychloroquine exposure, and low-dose aspirin exposure. Odds ratios (ORs), 95% confidence intervals (CIs), and Fisher exact p-values were calculated using R version 4.6.0.

Results: A total of 95 unique patients with SjD were included, contributing to 215 pregnancies. Overall, 84/215 pregnancies (39.1%) had at least one APO. The most common APO was miscarriage/pregnancy loss, occurring in 60/215 pregnancies (27.9%), followed by preterm birth in 19/215 pregnancies (8.8%). APO proportions were not significantly increased among pregnancies from SS-A-positive patients compared with SS-A-negative patients (41/119, 34.5% vs 43/96, 44.8%; OR 0.65, 95% CI 0.36–1.17; p=0.16). Any aPL positivity was associated with a numerically higher APO proportion, though this was not statistically significant and was limited by small numbers (7/15, 46.7% vs 74/178, 41.6%; OR 1.23, 95% CI 0.36–4.07; p=0.79). ANA positivity, high ANA titer, low C3/C4 at any point, LAC positivity, and triple-positive aPL status were not significantly associated with APOs. Hydroxychloroquine and low-dose aspirin exposures did not demonstrate significantly lower pregnancy-level APO proportions.

Conclusion: In this single-center retrospective cohort of patients with SjD, APOs were common at the pregnancy level and were driven largely by miscarriage/pregnancy loss. Traditional maternal serologic markers and documented pregnancy medication exposures were not significantly associated with pregnancy-level APOs. These findings suggest that historical serologic profiles alone may not fully explain the observed APO burden in SjD and support the need for larger, pregnancy-specific prospective cohorts to identify factors and biomarkers associated with APOs in patients with SjD.

Integrating Advanced Practice Providers into 911 Response: A Retrospective Feasibility Analysis of Low-Acuity Calls

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Introduction

Emergency medical services (EMS) systems are designed for rapid treatment and transport of acute illness and injury, yet a considerable share of 911 calls involve non-acute conditions such as chronic disease management or medication refills. Patients with low-acuity needs disproportionately use ambulance transport due to limited transportation options and lack of primary care access. Because paramedics and EMTs are not licensed to diagnose or make field non-transport decisions, and because field determination of medical necessity carries added ethical and legal liability, the default response is transport to the emergency department (ED) regardless of clinical necessity. This pattern contributes to ED crowding, rising healthcare costs, and reduced 911 ambulance availability for higher-acuity calls. Embedding an Advanced Practice Provider (APP) in 911 response has been proposed to address this gap: prior work from the Grady Health System Mobile Integrated Health program found patients were 24 times more likely to be safely managed on-scene compared to a traditional EMS response. However, no data currently exist estimating how many of a given EMS agency's own low-acuity transports could plausibly be managed on-scene by an APP.

Hypothesis/Purpose

We hypothesize that a clinically meaningful proportion of low-acuity 911 transports within Johnson County Ambulance Service (JCAS) represent Potentially Avoidable Transports (PAT) that could be managed on-scene by an APP rather than transported to the ED. The purpose of this study is to describe and quantify this proportion, and to compare the population receiving avoidable ED transport to those with appropriate, non-avoidable transport. As secondary aims, we will compare the proportion of PAT across EMD dispatch complaint types to identify which call types are best suited to an APP response and compare the projected cost of an APP response to the cost of standard ambulance transport and an ED visit using national cost benchmarks.

Method

This is a retrospective, cross-sectional chart review linking JCAS Patient Care Records (ESOsuite) to corresponding University of Iowa Health Care (UIHC) emergency department records (Epic) by patient name, date of birth, and encounter date, for encounters between January 1 and December 31, 2025. Eligible patients were adults aged 18-70 who were dispatched and transported at non-emergent (Code 2) priority by JCAS to UIHC Medical Center-University Campus or UIHC Medical Center-North Liberty and received BLS-level care throughout. Encounters were excluded for Code 3 response or transport, ALS-level care, prior provider care (e.g., ED-to-ED or urgent care transfer), or law enforcement custody. Each encounter was classified as a Potentially Avoidable Transport only if it passed three sequential screening tiers: a primary impression screen excluding inherently high-acuity presentations (e.g., cardiac arrest, chest pain, stroke, sepsis, major trauma) and associated EMD codes; a physiologic vitals screen applying National Expert Panel field-triage criteria (respiratory rate under 10 or over 29, systolic blood pressure under 90 mmHg, or under 110 mmHg if age 65 or older, GCS under 14, room-air oxygen saturation under 90%); and an ED outcome screen requiring triage acuity of 3 or lower priority, point-of-care glucose testing only, and no imaging, consults, parenteral medications or procedures, hospital admission, or discharge against medical advice. Encounters failing any tier were classified as Appropriate Transport.

Findings/Results

Data linkage and encounter classification are currently in progress. There are 1,597 transports that meet inclusion/exclusion criteria. Findings characterizing the prevalence of Potentially Avoidable Transport, associated patient demographics, dispatch-complaint distribution, and the comparative cost of an APP response versus standard ambulance transport and ED visit will be reported upon completion of analysis.

Conclusion/Overall Significance

This study will provide the first agency-specific estimate of the proportion of low-acuity 911 call volume within a mid-sized county EMS system that could plausibly be managed on-scene by an Advanced Practice Provider. Findings will inform whether and how APP integration into 911 response might reduce avoidable ED transports, alleviate emergency department crowding, preserve ambulance availability for higher-acuity calls, and reduce downstream healthcare costs. More broadly, this work addresses the gap between the known burden of low-acuity 911 utilization and the field-level tools EMS providers currently have to safely redirect appropriate patients away from the ED, supporting future prospective validation of APP-staffed response models for flagged low-acuity calls.

Empathy: Organizing a Field

Corey Plate

Dr. Dan Tranel

Introduction

Empathy is reputed to be a cornerstone, if not the cornerstone, of human socialization, and folk wisdom holds that it lives at the heart of prosocial behavior. Yet, in spite of enjoying this en vogue status, there exists confusion about what empathy describes, both colloquially and in research. More challengingly, the research that has been done to elucidate empathy and how it affects social and emotional behavior has been siloed across relatively disjointed research programs in fields as varied as ethology, moral philosophy, social psychology, social and affective neuroscience, and even a prolific and growing catalog of publications in artificial intelligence.

Purpose

To begin to tackle this complexity, this investigation aimed to conduct a thorough conceptual mapping review of existing empathy literature, and to develop a tool-based strategy for organizing the sheer volume of publications unearthed in that effort.

Methods

This involved the application of a number of existing tools, including semantic search software (e.g., Consensus), bibliographic software (i.e., Zotero), and concept mapping software (i.e., Scapple), as well as the development of new tools with the assistance of generative AI (e.g., DeepSeek R1).

Results

Two novel Python-based tools were engineered to map out bibliographic databases, one for generating semantic network graphs using a UMAP, HDBSCAN and Natural Language Processing pipeline, and the other for producing citation network graphs using a Gephi and VOSviewer pipeline.

Conclusion

Used together, these tools offer considerable organizational power, particularly for a field as variegated as empathy. They open up new avenues for selecting the most pertinent research questions, integrating diverse theory, and tackling empirical shortfalls in empathy research, such as experimental realism and ecological validity. Ultimately, when combined with future empirical work in a clinical neuropsychology population, these well-posed questions, and experimental design that is informed by decades of multidisciplinary research, offer the possibility of uniquely veridical insights into the elusive construct of empathy.

Alternative Splicing in Hypertrophic Murine Cardiac Models

Remodeling of the Mediator kinase module with a focus on CDK8

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Background

Chronic hypertension or aortic valve stenosis forces the heart to contract against elevated resistance. This Pressure overload drives compensatory hypertrophy in the myocardium and ultimately, heart failure. Currently, no therapies exist to reverse this cardiac remodeling.

Transcriptomic studies of the stressed heart focus on quantifying gene expression while overlooking alternative splicing. The inclusion or exclusion of exons lets a single gene encode multiple protein isoforms independent of its expression level. Splicing dysregulation is an established cause of human cardiomyopathy, exemplified by RBM20-mediated mis-splicing of titin in familial dilated cardiomyopathy.

The Mediator kinase module, whose catalytic subunit CDK8 tunes RNA polymerase II transcription, lies on the pathways that drive hypertrophic gene programs, yet whether the diseased heart remodels CDK8 through splicing is unknown.

Objective

Validating the predicted alternative splicing of CDK 8 In Hypertrophic Murine Cardiac Models.

Methods

Cardiac pressure overload in mice was modeled by transverse aortic banding (TAB) - a surgical model in which a suture is tied around the transverse aorta to create a fixed constriction. Sham animals undergo the identical surgery without band tightening to control for the surgery itself. All study comparisons were TAB versus Sham in the left ventricle at a matched timepoint.

Left-ventricular RNA sequencing was analyzed with rMATS software to identify the predicted differential splicing events between groups. Candidate events within the Mediator kinase module were prioritized with a focus on CDK8.

Validation the predicted CDK8 alternative splicing was done using isoform-specific primer design, RT-PCR with densitometric quantification, and Sanger sequencing of amplicons. Product identity was confirmed by BLAST alignment to the Cdk8 reference genome.

Results

TAB produced cardiac hypertrophy accompanied by a canonical stress transcriptome, including increased heart mass and reactivation of the fetal gene program.

RMATS software predicted the Mediator kinase module was coordinately spliced. CDK8 exon 7, which encodes part of the kinase domain, showed increased inclusion in hypertrophic hearts (Δ PSI +17.2%).

RT-PCR confirmed the shift (exon 7 inclusion ratio 0.60 in Sham versus 0.89 in TAB; $p = 0.0079$), and Sanger sequencing of the amplicons aligned to the Cdk8 gene sequence, confirming product identity.

Conclusions

Pressure overload remodels alternative splicing across the cardiac transcriptome and converges on the Mediator kinase module, increasing inclusion of the CDK8 kinase-domain exon 7.

Because the affected exon lies within the catalytic domain, this splicing change may alter CDK8 activity. In turn, the heart's transcriptionally responds to hemodynamic load.

As a druggable enzyme with existing small-molecule inhibitors, CDK8 represents a potential therapeutic entry point. Future work will test the functional consequences of exon 7 inclusion.

Effects of Hemophilia A Severity and Mental Health Disorders on Healthcare System Usage

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Introduction: Hemophilia A is a rare X-linked bleeding disorder caused by decreased levels of clotting factor VIII, leading to spontaneous or trauma-related bleeding. Management relies on preventive measures through lifestyle modification and pharmaceutical intervention. People with hemophilia (PWH) experience higher rates of mental health disorders (MHDs), particularly depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD). MHDs negatively affect treatment adherence, increasing bleeding risk. The impact of MHDs as a comorbidity on healthcare utilization is poorly understood. Additionally, the relationship between hemophilia severity and MHD risk has not been well studied. Understanding how MHD risk varies by hemophilia severity may help identify high-risk groups and guide targeted interventions.

Purpose: To quantify the impact of MHDs in hemophilia on healthcare utilization and define the relationship between hemophilia severity and MHD risk.

Methods:

A single-center retrospective chart review of adults (>18 yo) with hemophilia A (HA) was conducted. Electronic health records were reviewed to confirm patient eligibility, including a congenital factor VIII deficiency confirmed by the Iowa Hemophilia and Thrombosis Center and at least one hematology encounter after age 18. Patients with additional coagulation disorders or factor VIII levels above 50% were excluded. Data were collected in REDCap and analyzed using RStudio.

MHD prevalence was compared across mild, moderate, and severe hemophilia using Pearson's chi-square test. Hemophilia-related emergency department (ED) visits and length of stay (LOS) were compared between patients with and without MHDs using Kruskal-Wallis rank-sum tests. Additional Kruskal-Wallis rank-sum tests evaluated the effects of anxiety, depression, and ADHD on ED visit frequency and cumulative LOS.

Findings/Results: Adults with HA (n=152) were included, of whom 53.9% (82/152) had one or more MHDs. Hemophilia severity did not significantly affect the prevalence of MHDs, with rates of 48.6% (34/70) among patients with mild HA, 47.8% (11/23) among patients with moderate HA, and 62.7% (37/59) among patients with severe HA ($\chi^2(2)=2.99$, $p=0.225$).

Patients with mild or moderate HA and MHDs did not experience significantly more hemophilia-related ED visits than those without MHDs (mild HA: median 3.0 [IQR 5.0] vs. 2.0 [IQR 2.0], $p=0.213$; moderate HA: median 5.0 [IQR 4.5] vs. 3.0 [IQR 4.5], $p=0.727$). However, patients with severe HA and MHDs experienced significantly more hemophilia-related ED visits than those without MHDs (median 3.0 [IQR 5.0] vs. 1.0 [IQR 1.0], $p<0.001$). Patients with mild or moderate HA and MHDs did not have significantly longer cumulative hemophilia-related LOS than those without MHDs (mild HA: median 1.0 [IQR 5.75] vs. 0.5 [IQR 3.25] days, $p=0.320$; moderate HA: median 2.0 [IQR 8.0] vs. 2.5 [IQR 9.25] days, $p=0.432$). In contrast, patients with severe HA and MHDs had significantly longer cumulative hemophilia-related LOS than those without MHDs (median 9.0 [IQR 16.0] vs. 3.5 [IQR 7.5] days, $p=0.003$).

Anxiety was not associated with increased ED utilization ($p=0.291$) or LOS ($p=0.408$). Depression was associated with increased ED utilization (median 4.0 [IQR 5.5] vs. 2.0 [IQR 4.0] visits, $p=0.003$) and longer LOS (median 5.5 [IQR 13.75] vs. 2.0 [IQR 8.0] days, $p=0.016$). ADHD showed the strongest association with increased ED visits (median 4.0 [IQR 5.0] vs. 2.0 [IQR 3.5] visits, $p=0.007$) and longer LOS (median 8.5 [IQR 14.75] vs. 2.0 [IQR 8.0] days, $p=0.007$).

Conclusion: Among the 152 people with hemophilia, more than half had a comorbidity of a MHD. Our data suggest a trend toward higher MHD prevalence with increasing HA severity. MHDs were associated with greater hemophilia-related healthcare utilization, including more hemophilia-related ED visits and longer hospital stays. Depression and ADHD were associated with the greatest increases in healthcare utilization. These findings support the need for routine mental health screening and stronger partnerships with behavioral health professionals within hemophilia treatment centers.

Phenobarbital Based Protocol for Alcohol Withdrawal Syndrome in the Emergency Department

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Introduction

Alcohol withdrawal syndrome (AWS) is a potentially life threatening condition frequently managed in emergency departments (ED). Phenobarbital may be used in addition to benzodiazepines for AWS, though standardized protocols remain limited. We aimed to measure clinical outcomes following implementation of a phenobarbital AWS protocol in the ED.

Methods

We conducted a single-center, retrospective quality improvement study using electronic health record data from a tertiary academic medical center. We included adult participants treated with phenobarbital (with/without benzodiazepines) and benzodiazepines only in the ED for AWS. The primary outcome was hospital length of stay (LOS), and secondary outcomes included ED LOS and complications. We estimated adjusted incident rate ratios (aIRR) and 95% confidence intervals (CI) to measure the relationship between ED treatment received for AWS and hospital LOS, adjusting for patient demographic and clinical characteristics.

Results

Of 626 adult participants for whom the alcohol withdrawal protocol was initiated, 62% (n = 386) met study eligibility criteria. Overall, 10% of patients (n = 38) received phenobarbital and 90% (n = 348) were treated with benzodiazepines alone; moderate-to-severe alcohol withdrawal scores were observed in 66% of the phenobarbital group (n = 25) compared with 35% of the benzodiazepine-only group (n = 121). Median hospital LOS was 70.3 hours (IQR: 55.9–113.5) for phenobarbital-treated patients and 76.3 hours (IQR: 45.4–122.2) for those receiving benzodiazepines alone; after adjustment, phenobarbital use was associated with a 30% reduction in LOS (aIRR: 0.70; 95% CI: 0.53–0.93). Phenobarbital-treated patients experienced higher proportions of withdrawal related complications, including delirium tremens (23.7% [n = 9] vs. 7.8% [n = 27]), alcohol withdrawal seizures (13.2% [n = 5] vs. 1.4% [n = 5]), and intubation (10.5% [n = 4] vs. 0.0% [n = 0]).

Conclusion

Patients who were treated with phenobarbital had worse AWS severity at baseline. After adjustment, we observed an associated 30% decrease in hospital LOS. Hospitals may consider implementing a phenobarbital protocol in the ED to treat patients with moderate-severe AWS when hospitalization is anticipated. However, further prospective research investing in alternative protocols is needed.

Title: Genetic and clinical contributors to speech perception outcomes after cochlear implantation

Student: Emily Riley

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Other Collaborators: Rachel Scheperle, Abin Kuruvilla-Mathew, Joshua Pizour, Hela Azaiez, Amanda Odell, Alexander Claussen, Richard Smith

Introduction: Cochlear implantation (CI) is the standard of care for patients with severe-to-profound sensorineural hearing loss. It bypasses impaired cochlear sensory transduction and electrically stimulates the spiral ganglion neurons (SGNs) and the auditory nerve (AN). Although CIs remain the most successful neural prosthesis to date, outcomes vary considerably among recipients. Clinical and environmental factors including residual hearing, duration of deafness, and neurocognitive functioning account for some of this variability. Genetic etiology has also been proposed as a determinant of CI performance, given that different causes of hearing loss affect distinct cochlear structures and biological mechanisms. However, genetic etiology can also influence the onset, severity, and progression of hearing loss, which in turn can affect age at implantation and duration of auditory deprivation. Therefore, the relationship between genetic etiology and CI outcomes may be more complex than a simple cochlear site-of-lesion model. The impact of genetic and clinical factors on CI outcomes remains poorly understood.

Purpose: We aimed to characterize speech perception outcomes across genetic etiologies in cochlear implant recipients and assess the contribution of genotypic and clinical characteristics to outcome variability. Given the variable CI outcomes and genotype-dependent hearing loss progression reported for the *TMPRSS3* gene, we also examined clinical and genotype-related factors associated with CI performance within this subgroup.

Methods: This retrospective study included CI recipients from the cochlear implant clinic who underwent genetic testing with the OtoSCOPE gene panel between 2014 and 2026. Of 116 patients with positive genetic findings, 89 met inclusion criteria and had postoperative speech perception testing; 75 had postoperative Consonant-Nucleus-Consonant (CNC) word scores obtained in everyday listening conditions. Descriptive statistics were used to summarize CNC performance across genetic etiologies. Median CNC word scores were calculated for each gene to evaluate CI performance. Within the *TMPRSS3* group, CNC performance was evaluated in relation to age at initial implantation and duration of CI use. CNC scores were also compared between missense/missense (M/M) and missense/predicted loss-of-function (M/pLoF) genotype groups.

Findings/Results: The most frequently affected genes were *TMPRSS3* (n = 17, 22.7%), *GJB2* (n = 16, 21.3%), *SLC26A4* (n = 10, 13.3%), and *MYO6* (n = 5, 6.7%). All remaining etiologies were represented by fewer than five individuals. Among the 75 participants, the median CNC word score was 86%. For genes with ≥ 5 affected individuals, median CNC word scores were highest for *MYO6* (94%) and *GJB2* (92%) followed by *SLC26A4* (80%) and *TMPRSS3* (74%). These groups also differed substantially in age at initial implant. Median age at initial implant was 59 years for *MYO6*, 41 years for *TMPRSS3*, 8 years for *SLC26A4*, and 2.5 years for *GJB2*. Across the cohort, increasing age at CNC testing was associated with poorer CNC performance ($R^2=0.265$). CNC outcomes varied significantly in individuals with *TMPRSS3*-related hearing loss (0% to 97%). Within this group, older age at initial implantation was strongly associated with poorer CNC performance ($R^2=0.539$), whereas duration of CI use showed little relationship with performance ($R^2=0.012$). Median CNC scores were 65% for M/M genotypes and 85% for M/pLoF genotypes, but this difference was not statistically significant ($p=0.12$).

Conclusions: Speech perception outcomes differed across genetic etiologies, but these groups also differed substantially in age, which was associated with CNC performance. These findings suggest that gene-specific differences in CI outcomes should be interpreted in the context of the natural history and clinical characteristics of hearing loss rather than through a simple model focused on cochlear site of lesion. *TMPRSS3* highlights this complexity: outcomes varied significantly and older age at implantation was associated with poorer speech perception. Genetic etiology may influence CI outcomes through both the underlying molecular defect and the resulting course of hearing loss and timing of implantation. The wide range of outcomes within the same genetic etiology may reflect additional genetic and clinical modifiers. Larger future studies integrating genetic etiology, natural history, clinical variables, measures of auditory-neural health, and background genetic variation are needed to determine whether a combined prognostic model can improve prediction of CI outcomes.

Title: Mitochondrial responses to simulated loading of articular cartilage

Presenter: Dominic J.L. Rivas, M2

Mentor: Mitchell Coleman, Department of Orthopedics and Rehabilitation

Collaborators: Madeline Hines, Marc Brouillette, Jessica Goetz, Jaycie O'Neill, Maxwell Sayki

Introduction: Post-traumatic osteoarthritis (OA) has been shown to demonstrate mitochondrial dysfunction and oxidative stress following severe joint injury. Previous work has demonstrated increased oxidative damage and reduced mitochondrial content in the articular cartilage after impact injury. While OA development is associated with chronic joint overuse, its effects on cartilage mitochondrial responses are not understood.

Hypothesis/Purpose: The purpose of this study was to determine whether physiologically relevant compressive and shear loading induced mitochondrial dysfunction in articular cartilage. We hypothesized that repetitive overloading would decrease markers of mitochondrial content.

Method: Bovine stifle joints were obtained from a local abattoir (Bud's Custom Meats, Riverside, IA, USA). Matched femoral and tibial osteochondral explants were harvested from non-meniscus covered regions. Explants were aligned in custom-built explant holders to recreate native articular surface contact. Explants were then placed into culture medium (45% Dulbecco's Modified Eagle's medium, 45% F-12, 10% fetal bovine serum, 100U/ml penicillin, 100µg/mL streptomycin, and 2.5 µm/mL amphotericin B) and kept in a tissue culture incubator maintained at 5% O₂, 5% CO₂, and 37°C overnight to equilibrate prior to testing.

Explants underwent one hour of mechanical loading (1800 cycles) using a custom build joint articulation simulator designed to replicate the forces and motions experienced during walking. The simulator was programmed to reproduce loading patterns measured from patients with instrumented knee replacements (Orthoload) and adjusted compression throughout each cycle to match instrumented knee forces. Cartilage explants were allowed limited movement during loading which was provided by springs that represent soft tissue and ligamentous constraints. Culture media covered the cartilage surface throughout testing to prevent drying and decrease friction.

Cartilage deformation that occurred during testing was measured using 3D geometry scans collected prior to and after loading by a structured-light 3D scanner (EinScan Pro 2X Pro-Shining 3D). Pressure-sensitive film (Prescale low) was used to evaluate changes in contact mechanics (area and pressure) before and after loading.

Following loading, tibial explants were cut exposing the cross section of the cartilage and stained with Calcein AM Green to assess cell viability and Mitotracker Deep Red to evaluate mitochondrial content. Images were gathered using a Fluoview FV1000 confocal microscope (Olympus/Evident, Tokyo, Japan) with a 4x and 20x objective. Samples were imaged top-down and in cross-section at the site of injury.

Findings/Results: Mechanical loading produced localized cartilage deformation, with peak surface deformation exceeding 1 mm in concentrated regions. Post-loading pressure-sensitive film demonstrated increased contact area (144 mm² to 183mm²) and decreased contact stress (3.3 MPa to 3.0 MPa) relative to pre-loading measurements. Confocal imaging revealed extracellular matrix failure characterized by the presence of fissures near the loaded region and reduced cell viability at the articular surface. Additionally, imaging revealed areas with preserved Calcein AM staining but diminished Mitotracker signal, indicating loss of mitochondrial content despite continued cellular viability. These changes were spatially heterogeneous and associated with regions adjacent to matrix damage.

Conclusion: This study established cartilage injury and mitochondrial loss from a physiologically relevant bovine overloading model. Mechanical overloading resulted in extracellular matrix damage, chondrocyte injury, and region-specific decreases in mitochondrial content. We think regional loss of mitochondrial content in viable cells suggests the presence of stress-shielding, with higher amounts of load causing downregulation and loss of mitochondria. These findings suggest a mechanism whereby abnormal loading might contribute to OA pathogenesis through localized dysregulation of mitochondria. Future work will define thresholds for injury and characterize the biochemical pathways linking mechanical overloading to degeneration.

Title: Sodium Supplementation on Growth Outcomes in Premature Neonates with AKI

Student: Kallison Rochford

Mentor: Lyndsay Harshman

ABSTRACT

BACKGROUND

Preterm infants are susceptible to total body sodium depletion, which is associated with impaired somatic growth. An individualized sodium supplementation protocol based upon standardized urine sodium screening was established at the University of Iowa neonatal intensive care unit (NICU) in 2016; pilot data demonstrated increased weight gain in the first 8 weeks of life among supplemented infants versus controls. Acute kidney injury (AKI) affects up to 30% of extremely preterm infants and further impairs renal sodium handling, yet whether supplementation benefits infants with AKI has not been evaluated. We assessed whether this protocol is associated with improved somatic growth among premature infants with neonatal AKI.

METHODS

We studied 692 infants born between 26^{0/7} and 33^{6/7} weeks gestation and treated within the University of Iowa Stead Family Children's Hospital NICU (UISFCH NICU) between 2012 and 2020. Infants managed with the protocol (born 2016–2020) were compared to gestational age-, sex-, and birthweight-matched historical controls born prior to its institution (2012–2015). AKI was identified and staged using modified neonatal KDIGO criteria based on urine output and, when available, serum creatinine. Infants were categorized by AKI status and supplementation exposure (Groups 1–4, respectively): no AKI/no supplementation (n = 264), no AKI/supplementation (n = 356), AKI/no supplementation (n = 46), and AKI/supplementation (n = 26). Weight, length, and head circumference were obtained at birth and at 2-, 4-, 6-, 8-, and 16-weeks postnatal age, with Fenton z-scores at each timepoint. Hypertension, hypernatremia, bronchopulmonary dysplasia (BPD), sepsis, time on mechanical ventilation, and time to discharge were also compared.

RESULTS

Groups were similar in race, ethnicity, and sex. Infants with AKI were born at a lower gestational age ($p < 0.0001$), were more likely to be small for gestational age ($p = 0.02$), had lower 1-minute APGAR scores ($p = 0.0002$), and had longer time to discharge ($p < 0.0001$). Body weight and head circumference differed significantly across groups ($p < 0.0001$ for both). Group 3 demonstrated the lowest weight and head circumference trajectories at every timepoint, whereas Group 4 tracked with the non-AKI groups; weight differences between Groups 3 and 2 were significant from 2 through 16 weeks postnatal age. Raw body length also differed across groups ($p < 0.001$ at 16 weeks), but length z-scores did not differ at any timepoint; weight and head circumference z-scores remained significantly different across groups through 16 and 6 weeks, respectively. Among infants with AKI, supplementation was associated with fewer ventilator days, but this did not reach significance after adjustment. Supplementation was not associated with mild or moderate hypernatremia, hypertension, or BPD in adjusted models.

DISCUSSION

In a large single-center cohort of preterm infants, protocol-based, physiologically guided sodium supplementation was associated with better early-life weight gain and head growth, including among infants with neonatal AKI, and was well-tolerated apart from increased moderate hypernatremia. AKI remained an important risk factor for impaired growth, and individualized sodium replacement may address the changing renal sodium requirements of injured neonatal kidneys. These findings support consideration to nutrition strategies tailored to renal physiology and warrant prospective study in this high-risk population.

Understanding Breakthrough Pain During Labor Analgesia: The Role of Neuraxial Analgesia Duration in a Predominantly Combined Spinal-Epidural Practice Using PIEB/PCEA

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Background: Combined spinal-epidural (CSE) analgesia maintained with programmed intermittent epidural bolus (PIEB) and patient-controlled epidural analgesia (PCEA) is an effective contemporary approach to labor analgesia. Nevertheless, breakthrough pain remains common, decreasing maternal satisfaction and increasing anesthesia-team workload. We conducted a quality improvement project to determine the incidence of breakthrough pain and identify characteristics associated with its occurrence.

Methods: The University of Iowa Institutional Review Board determined that this quality improvement project did not meet the regulatory definition of human subjects research and did not require IRB review. The cohort analysis included all laboring patients who received neuraxial analgesia maintained with PIEB/PCEA at our teaching hospital, May 12 to July 22, 2026. Inadequate analgesia events were documented prospectively using standardized forms. Patient charts were reviewed contemporaneously to ensure complete data. Breakthrough pain was defined as inadequate analgesia that resulted in clinician-administered epidural supplementation, catheter manipulation or replacement, or an increase in the PIEB volume after initial establishment of effective analgesia. Candidate predictors were evaluated using exact Wilcoxon rank-sum tests treating $P < 0.01$ as significant for Bonferroni adjustment. Variables retained during multivariable modeling were evaluated using Poisson regression with robust standard errors.

Results: Of the cohort including 335 patients, 310 (92.5%) received CSE, 15 (4.5%) received dural puncture epidural (DPE), and 10 (3.0%) received conventional epidural analgesia. Breakthrough pain occurred in 78 patients (23%), with 121 total breakthrough-pain events. Fifty-four (69%) patients experienced one event. The mean number of breakthrough-pain events was 0.36 per patient (SD, 0.85). Including initial neuraxial placement, patients required a mean of 1.36 anesthesia-team interventions (SD, 0.85; 95% CI, 1.27–1.45). In unadjusted analyses, neuraxial-to-delivery duration, cervical dilation at neuraxial placement, and initial PIEB setting differed according to breakthrough-pain status. Neuraxial-to-delivery duration was the predictor retained in multivariable modeling. Among patients with breakthrough pain, median neuraxial-to-delivery duration was 10.9 hours [IQR, 6.1–16.7], compared with 5.6 hours [IQR, 3.3–9.1] among those without a subsequent intervention ($P < 0.0001$). Each additional hour from neuraxial placement to delivery was associated with a 5.8% higher relative risk of breakthrough pain (risk ratio, 1.058; 99% CI, 1.037–1.081; $P < 0.0001$). The observed overall 0.36 pain events per patient was the marginal expectation obtained by evaluating this log-linear model across the cohort's duration distribution.

Conclusions: Our quality improvement project findings provide an institution-specific estimate of anesthesia workload, with a mean of 1.36 anesthesia-team interventions per patient, including initial neuraxial placement, in our practice utilizing primarily CSE initiation and PIEB/PCEA maintenance. Longer neuraxial-to-delivery duration was independently associated with breakthrough pain, suggesting that institutions with different distributions of neuraxial-to-delivery times may experience different anesthesia workload requirements. In addition to our primary focus on staffing, secondary results suggest proactive reassessment of analgesia in patients with extended neuraxial duration may be a potential strategy to reduce urgent anesthesia-team interventions and improve the maternal experience.

Investigation of TGF- β mediated phenotypic switching of airway epithelial cells via EMT in Chronic Lung Allograft Dysfunction (CLAD)

Student: Santo Roy | Mentor: Kalpaj R. Parekh, MBBS | Collaborators: Kusum Devi, PhD

Introduction

Chronic lung allograft dysfunction (CLAD) is the leading cause of mortality after lung transplantation and represents the primary barrier to long-term allograft survival. CLAD is characterized by progressive airway remodeling and fibrosis. Transforming growth factor- β (TGF- β) is a central mediator of fibrosis, driving fibroblast activation, extracellular matrix deposition, and persistent tissue remodeling. TGF- β is also implicated in promoting epithelial-mesenchymal transition (EMT), whereby airway epithelial cells lose epithelial characteristics and acquire mesenchymal features, contributing to airway remodeling and fibrotic processes.

Hypothesis

Our central hypothesis is that sustained TGF- β signaling because of allo-immune response induces epithelial-mesenchymal transition (EMT) in the airway epithelium, drives epithelial plasticity and differentiation arrest, impairing normal epithelial repair and promoting profibrotic airway remodeling that contributes to the development of CLAD. Furthermore, we hypothesize that pharmacologic inhibition of TGF- β /SMAD signaling using a dual SMAD inhibitor or SB431542 will attenuate or reverse these EMT-associated phenotypic changes in our model.

Method

Human airway epithelial cells were cultured under air-liquid interface (ALI) conditions and indirectly co-cultured with either normal or activated fibroblasts in the basolateral compartment. Six experimental conditions were evaluated: (1) ALI control, (2) normal fibroblasts, (3) activated fibroblasts, (4) activated fibroblasts with a cytokine cocktail (TGF- β , IL-1 β , and TNF- α), (5) activated fibroblasts with cytokine cocktail and dual SMAD inhibitor, and (6) activated fibroblasts with cytokine cocktail and SB431542. Following treatment, immunofluorescence (IF) staining and quantitative PCR were performed to assess markers of epithelial-mesenchymal transition (EMT), epithelial differentiation, and fibrotic remodeling.

Results

Exposure to the cytokine cocktail condition (4) resulted in reduced expression of airway epithelial differentiation markers FOXJ1 and MUC5AC/CC10 by IF staining. Both dual SMAD inhibition and SB431542 partially restored these differentiation markers. Cytokine cocktail treated epithelial cells also demonstrated reduced E-cadherin and increased vimentin staining, along with upregulation of the stress-associated keratin KRT17. Both dual SMAD inhibition and SB431542 resulted in increased E-cadherin staining while reducing vimentin and KRT17 staining.

qPCR demonstrated increased expression of VIM (vimentin), FN1 (fibronectin), and COL1A1 (type I collagen) in the cytokine cocktail condition (4), supporting induction of an EMT-associated and fibrotic remodeling program. CDH1 (E-Cadherin) expression was paradoxically increased in the cytokine cocktail condition, suggesting a partial EMT or compensatory epithelial response rather than complete loss of epithelial identity. Both dual SMAD inhibition and SB431542 reduced expression of CDH1, VIM, FN1, and COL1A1.

Conclusion

Activated fibroblasts with cytokine cocktail (Condition 4) reproduced key features of CLAD in our ALI model, including disruption of airway epithelial differentiation and induction of EMT-associated and fibrotic remodeling. Attenuation of these changes with TGF- β pathway inhibition suggests that targeting TGF- β signaling may represent a promising therapeutic strategy for CLAD.

Immune Tolerance Induction Strategies for Tividenofusp Alfa in Mucopolysaccharidosis II

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Background: Mucopolysaccharidosis II (MPS II) is an X-linked lysosomal storage disorder caused by deficiency of iduronate 2-sulfatase (IDS). Tividenofusp alfa is an enzyme replacement therapy (ERT) engineered to cross the blood-brain barrier and address both peripheral and central manifestations of MPS II. However, clinical studies have demonstrated substantial immunogenicity, including development of anti-drug and neutralizing antibodies that may compromise therapeutic efficacy. Immune tolerance induction (ITI) has been successfully used to mitigate ERT-associated immunogenicity in infantile Pompe disease, but experience with ITI during tividenofusp alfa therapy in MPS II remains limited.

Purpose: To describe the clinical application and immunologic outcomes of two distinct ITI protocols administered during tividenofusp alfa initiation in two patients with MPS II, one ERT-naïve and one with prior ERT exposure.

Methods: We retrospectively reviewed two patients with MPS II who received tividenofusp alfa with concomitant ITI at the University of Iowa. Patient A was ERT-naïve and received prophylactic ITI with methotrexate, rituximab, and intravenous immunoglobulin (IVIG) beginning with tividenofusp alfa initiation. Patient B had prior ERT exposure and elected to receive a less intensive ITI protocol with tividenofusp alfa initiation. Clinical response, laboratory markers of disease burden, and immunogenicity were monitored longitudinally, including anti-drug and neutralizing antibody responses and B-cell reconstitution.

Results: Both patients tolerated tividenofusp alfa with concomitant ITI and demonstrated favorable clinical and laboratory trends during treatment. Patient A, who received prophylactic ITI in the ERT-naïve setting, demonstrated minimal immunogenicity, with sustained suppression of anti-drug and neutralizing antibody responses and favorable longitudinal disease-related laboratory markers. Patient B, who had prior ERT exposure, also demonstrated a favorable clinical and laboratory response following initiation of ITI, although immunogenicity was greater than that observed in the ERT-naïve patient. These findings suggest that initiation of ITI before development of an established immune response may provide more effective mitigation of tividenofusp alfa immunogenicity.

Conclusion: These two cases provide early clinical experience supporting the use of ITI to mitigate immunogenicity during tividenofusp alfa therapy in MPS II. Prophylactic ITI initiated in the ERT-naïve setting was associated with superior control of immunogenicity compared with ITI initiated after prior ERT exposure, while both patients demonstrated favorable clinical and laboratory trajectories. These findings support further investigation of prophylactic ITI as a strategy to preserve the efficacy of tividenofusp alfa and warrant continued investigation in patients with MPS II.

Clinical Implementation of OpenCap for Functional Biomechanical Assessment in Total Knee Arthroplasty

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Introduction: Total knee arthroplasty (TKA) is one of the most common orthopedic procedures worldwide, yet current postoperative assessments are limited in their ability to fully characterize functional recovery and dynamic biomechanics. Patient reported outcomes (PROs) provide valuable information about perceived pain and function but may not fully reflect objectively measured performance, limiting their use as a sole measure of recovery. While marker based motion capture can quantify 3-dimensional movement, its cost and complexity restrict its use. OpenCap is a markerless video based motion capture system that uses 2 smartphones and a web application to provide objective measures of movement and may offer a scalable approach to analyzing postoperative recovery. This study evaluated the clinical utility of OpenCap for characterizing functional movements such as walking and standing up from a chair following TKA in a real world clinical setting and examines how OpenCap derived biomechanical measures relate to established clinical assessments of postoperative function.

Methods: This study was approved by the University of Iowa Institutional Review Board and informed consent was obtained from each patient. 18 patients indicated for primary TKA (11 female; age 65.4 years; BMI 34.8 kg/m²; height 1.69 m) were enrolled preoperatively along with 19 postoperative patients returning for routine follow up (11 female; age 66.6 years; BMI 33.4 kg/m²; height 1.67 m) at 2-3 weeks (n=4), 1-3 months (n=8), and 7 months-1 year (n=7) post TKA. OpenCap motion capture was performed in a gait laboratory using two iOS devices positioned 3 meters from each other and calibrated at a 45° angle from the point of interest. Participants completed a 3 m walking trial at a self selected pace and a sit to stand task (STS) using an armless chair. Videos were processed in OpenCap using its HRNet based pose estimation model and OpenCap's processing python scripts were used to quantify gait speed, step length, cadence, peak knee flexion during swing, and double support time as well as postural movements and temporal characteristics during STS. The first successfully processed trial was analyzed, with participants excluded from analysis when 3 processing attempts were unsuccessful (1 preop and 2 postop excluded from STS). STS performance was quantified as the time from initiation of forward trunk lean to complete of the rise, with the transition from seat off to upward rise defining the onset of the rising phase. Clinic range of motion (ROM) was also collected from each patient. Outcomes were compared across preop and postop time points using Welch's Two Sample T-test and associations between biomechanical measures and KOOS Jr scores were evaluated using Spearman correlation (Pearson correlation was used for double support time), with statistical significance defined as $p < 0.05$.

Results/Findings: Postoperative patients demonstrated a trend toward faster gait speed when compared to preoperative patients (0.87 vs. 0.77 m/s, $p=0.113$), with higher KOOS Jr scores moderately correlated with higher gait ($\rho=0.404$, $p=0.013$). This increase in gait speed appeared to be driven primarily by changes in movement strategy, such as greater knee flexion during swing (56.2° vs. 49.6°, $p=0.118$) and statistically significant longer operative leg step length (56 vs 48 cm, $p=0.03$) (KOOS Jr correlation, $\rho=0.379$, $p=0.021$), rather than increased cadence. These findings may suggest that postop improvements in walking performance reflect more effective limb advancement and restoration of functional knee motion. Double support time was moderately correlated with KOOS Jr ($\rho=-0.42$, $p=0.009$), indicative of compensatory movement patterns with worse perceived knee function. During STS, there was no significant difference in overall STS timing between preop and postop patients. However, examination of postop recovery time points revealed a temporal pattern in rise time, with an initial worsening during the early post period followed by improvement at later postop time points. Forward flexion initiation times were generally similar across groups, although patients 7 months-1 year postop demonstrated faster initiation from start of forward flexion to the beginning of rise. Patient reported function was more closely associated with the time required to initiate rising ($\rho=-0.449$, $p=0.008$) than with total rise time. Clinic ROM was not significantly correlated with KOOS Jr ($\rho=0.243$, $p=0.141$).

Conclusion: OpenCap demonstrated clinical utility for objectively characterizing functional movement in patients undergoing TKA. It captured meaningful postoperative changes, particularly in gait biomechanics, including alterations in gait speed, knee flexion, and step length. Furthermore, because walking requires single leg stance on the operative limb, gait may provide a clearer assessment of operative limb function than a double legged STS task, during which compensatory movement strategies may be masked. These measures provide a more granular view of how patients perform functional tasks and may reveal altered movement strategies that are difficult to identify through PROs or conventional clinical assessment like non weight bearing ROM. Because KOOS Jr reflects how patients perceive their function while OpenCap provides information about how patients physically perform movement, the two approaches may provide complementary perspectives on recovery. OpenCap's relatively simple implementation and positive patient perception also support its potential use in a clinical setting. Future longitudinal studies at standardized postoperative time points are needed to further determine how OpenCap derived biomechanical measures can be used to identify specific functional deficits and guide individualized rehabilitation following TKA.

Title: Multidimensional Sleep and Movement Behaviors Across Pregnancy: a Pregnancy 24/7 Cohort Study

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Introduction: Pregnancy presents many physiologic and anatomic changes that can disrupt sleep and lead to sleep disorders. Sleep plays a critical role in maternal and fetal health, yet many pregnant women experience poor sleep. Given these risks, identifying modifiable factors to improve sleep in pregnancy is critical. In the general population, studies show that physical activity is associated with improved sleep, while increased sedentary behavior (SED) may increase the risk of sleep disturbances. The World Health Organization recommends that adults accumulate at least 150 minutes of moderate-vigorous physical activity (MVPA) per week and limit SED. Other studies have found that 10 or more hours of SED were associated with increased risk of sleep disorders. Thus, it is important to examine whether adherence to MVPA and SED guidelines is associated with sleep health during pregnancy, as these modifiable behaviors can be targets for future interventions. Prior studies rely on self-reported data and focus primarily on sleep duration, but other dimensions of sleep may also be important. This study addresses these gaps by examining how movement behaviors, individually or in combination, relate to multidimensional sleep health during pregnancy.

Hypotheses: We hypothesize that multidimensional sleep health would decline across pregnancy, with the poorest overall sleep health in the third trimester. Additionally, we hypothesized that women who met MVPA guidelines would have more favorable sleep dimensions, including longer sleep duration, greater sleep efficiency, better sleep satisfaction and daytime alertness, and a higher proportion meeting criteria for healthy sleep (RU-SATED composite score), especially in the first and second trimesters. Finally, we hypothesized that women who met SED guidelines (< 10 hours per day) would have higher sleep satisfaction and a larger proportion meeting criteria for healthy sleep.

Methods: This was a secondary analysis using data from the Pregnancy 24/7 cohort study. MVPA and SED were assessed using a thigh-worn accelerometer for 24 hours x 7 days each trimester. Participants were classified as meeting guidelines for MVPA (≥ 150 minutes/week) and SED (<10 hours/day). Sleep health was assessed via actigraphy and questionnaires in each trimester. The RU-SATED framework was used to define sleep health dimensions (regularity, satisfaction, alertness, timing, efficiency, and duration) and to create a composite score (0-6) based on meeting criteria for healthy sleep. Linear mixed-effects models and logistic regression models were used to examine associations between MVPA, SED, RU-SATED sleep dimensions and overall composite score.

Results: Women who met MVPA guidelines went to sleep 10 minutes earlier in the first trimester (02:50 [02:44, 02:57] vs 03:00 [02:53, 03:07]) and 14 minutes earlier in the second trimester (02:54 [CI: 02:47, 03:01] vs. 03:08 [03:01, 03:15]) compared to women not meeting guidelines. Adherent women also had shorter sleep duration compared to women who did not meet MVPA guidelines in the first (7.62 hours/day [7.53, 7.70] vs. 7.80 hours/day [7.71, 7.89] and second trimester (7.49 hours/day [7.40, 7.58] vs. 7.65 hours/day [7.56, 7.74]). Adherence to SED guidelines was associated with longer sleep duration (14 min) across pregnancy compared to non-adherence (7.69 hours/day [7.62, 7.76] vs. 7.46 hours/day [7.39, 7.53]). Adherence to MVPA or SED guidelines was not associated with healthy sleep (defined as an RU-SATED composite score ≥ 5).

Conclusions: Though meeting MVPA and SED guidelines were associated with RU-SATED sleep dimensions, mainly sleep timing and duration, the differences in sleep outcomes may not be clinically meaningful. MVPA and SED guideline adherence are still important for the many health benefits they are associated with, but interventions may need to focus on other behavioral targets to improve sleep health.

Influence of Seminal Plasma From Hypertensive Fathers on iPSC Differentiation: A Model of the Paternal Role in Preeclampsia

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Introduction: Preeclampsia (PreE) is a serious pregnancy complication characterized by new onset hypertension after 20 weeks gestation accompanied by proteinuria and/or maternal organ dysfunction. PreE is associated with long-term health consequences for both mother and child and contributes significantly to maternal and fetal morbidity and mortality worldwide. Although the pathogenesis of PreE is multifactorial, proposed mechanisms have largely focused on maternal factors, including immune dysregulation, abnormal placentation, and genetic susceptibility. In contrast, the role of paternal factors in PreE remains poorly understood. Importantly, analysis of existing data from fathers with seminal plasma in our biobank indicates paternal hypertension is an independent risk factor for the development of preeclampsia, (OR=4.159; p=0.037), supporting a potential paternal contribution.

The placenta plays a central role in the pathogenesis of PreE. Insufficient trophoblast invasion into the uterine decidua leading to incomplete remodeling of the spiral arteries can impair placental perfusion, resulting in reduced nutrient delivery, ischemia, oxidative stress, and the release of factors promoting maternal endothelial dysfunction. Hypertension is also associated with increased production of reactive oxygen species (ROS) and systemic oxidative stress. Because sperm are particularly sensitive to oxidative damage, paternal hypertension may alter sperm or seminal plasma in ways that influence early developmental processes. Given the paternal contribution to the fetal and placental genome, increased oxidative stress in hypertensive fathers presents one potential mechanism through which paternal health may influence PreE risk and fetal development.

Human induced pluripotent stem cells (iPSCs) provide a platform for modeling early developmental responses to environmental exposures due to their ability to differentiate into all three germ layers and further into a wide range of tissue types. Alterations in lineage-associated gene expression following exposure to different conditions can provide insight into how paternal-derived factors may influence early fetal and placental development.

Purpose: Using a human iPSC model, this study evaluated whether seminal plasma from hypertensive fathers alters early differentiation-associated gene expression compared with seminal plasma from normotensive fathers.

Methods: Banked seminal plasma samples were selected from patients with documented blood pressure measurements and/or a diagnosis of hypertension and classified as hypertensive or normotensive. Human iPSCs were cultured using an established workflow and plated in 12 well plates at 3.9×10^5 cells per well. Following 48 hours of recovery, cells were exposed to seminal plasma at a final concentration of 0.5% in culture media. After 24 hours of exposure, RNA was isolated and quantitative PCR was performed. Twelve genes representing pluripotency and ectoderm, mesoderm, and endoderm differentiation were evaluated.

Results: A log2 expression heat map generated from the mean expression values of replicate samples demonstrated differences in differentiation-associated gene expression between cells exposed to seminal plasma from hypertensive fathers and those exposed to seminal plasma from normotensive fathers or control conditions. Notable differences were observed in TBXT, HAND1, PAX6, and CDX2 genes, suggesting altered expression of markers associated with multiple developmental lineages.

Conclusion: These preliminary findings suggest seminal plasma from hypertensive fathers may alter early differentiation-associated gene expression in human iPSCs. In combination with the biobank data demonstrating increased risk of preeclampsia development in pregnancies involving hypertensive fathers, these findings support further investigation into paternal hypertension as a possible contributor to maternal PreE risk and fetal development. Future studies will evaluate pregnancy outcomes associated with the banked seminal plasma samples and will quantify oxidative stress and other candidate mediators within seminal plasma to identify mechanisms underlying the observed effects.

Diagnostic Utility of Ultrasonography in Diagnosing Carpal Tunnel Syndrome Versus 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) are the current reference standard for diagnosing carpal tunnel syndrome (CTS), but are invasive, costly, and time consuming. Ultrasonography (US) allows for point-of-care and cost-effective examination of the carpal tunnel and is a promising alternative to EDX.

Purpose/Hypothesis: The purpose of the study was to assess the diagnostic utility of US in comparison to EDX and identify ultrasonographic findings and cross-sectional area (CSA) thresholds associated with CTS diagnosis.

Methods: A retrospective chart review was conducted using 345 paired US and EDX studies performed within six months of each other. Both quantitative (CSA at the proximal wrist crease and pronator quadratus) and qualitative (mention of focal compression or edema) variables were compared to EDX impressions to evaluate their utility in diagnosing CTS. Logistic regression evaluated associations between US measures and EDX diagnosis of CTS. Receiver operating characteristic (ROC) analysis was used to estimate the area under the curve (AUC). For US measures of CSA with AUC values supporting threshold determination, optimal cut-points were identified using Youden's J statistic, and the corresponding sensitivity and specificity were estimated using EDX as the reference standard.

Results: ROC analysis identified an optimal proximal wrist crease CSA threshold of 11.5 mm² (Youden's J Statistic), which provided fair discrimination (AUC=0.75) between CTS and non-CTS cases. CSA at the pronator quadratus demonstrated poor discriminatory ability (AUC=0.59). Neither focal compression nor neural edema were independently predictive of CTS. Notably, 20% of patients demonstrated discordant findings of negative EDX and positive US.

Conclusion/overall significance: Median nerve CSA at proximal wrist crease demonstrated clinically meaningful diagnostic utility for CTS, supporting US as a cost-effective and noninvasive modality that may reduce reliance on EDX. Qualitative US features did not provide independent diagnostic value. Discordant cases suggest US may detect cases not identified by EDX.

Quantitative CT for Early Detection of Chronic Rejection in Lung Transplantation

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Introduction: Lung transplantation is a life-saving therapy for patients with end-stage lung disease. Despite rigorous surveillance and post-transplant care, approximately 50% of lung transplant recipients develop a persistent and irreversible decline in lung function known as chronic lung allograft dysfunction (CLAD). There are no established effective therapies to prevent CLAD or halt its progression. This is largely due to the lack of diagnostic modalities that can detect allograft damage at early stages. To diagnose CLAD, clinicians rely on standard pulmonary function tests, which identify disease only after significant and potential irreversible injury has occurred. The purpose of this study is to investigate the utility of quantitative computed tomography (qCT) in the early detection of allograft abnormalities prior to the development of CLAD, when earlier treatment may still prevent functional decline.

Methods: Patients who underwent bilateral lung transplantation between 2019-2025 at University of Iowa Health Care were included in the study. Clinical computed tomography (CT) scans using a coached inspiratory (TLC) and expiratory (RV) protocol were retrospectively analyzed in patients between 6 months and 2 years post-transplant to avoid the post-acute stage but prior to a diagnosis of CLAD. Imaging was acquired on a range of clinical Siemens scanners (Siemens Healthineers, Germany). Image registration and quantitative analysis were performed using *Insights* (VIDA Diagnostics, Coralville, IA, USA). Air trapping was assessed using the Disease Probability Measure (DPM), a probabilistic approach using deformation and density changes of matched voxel pairs between breath-hold volumes. Voxels are labeled as normal, emphysematous, or air-trapped. For patients with multiple scans, the scans with greatest air trapping were selected. Groupwise comparisons were performed using the Wilcoxon signed-rank test, using diagnostic criteria (>3 month persistent decline of >20% FEV₁ from patient's post-transplant maximum) to identify patients with rejection before July 1st 2026. The receiver operating characteristic curve for air trapping as a predictor of CLAD was calculated and used to extract thresholds. These thresholds stratified the cohort for a CLAD-free survival analysis using Kaplan-Meier curves. R Statistical Software (V4.6.0, R Core Team, 2023) was used for statistical analysis using the "pROC" and "survival" packages.

Results: 131 clinical inspiratory-expiratory CT pairs from 73 patients were identified. 42 patients had imaging performed within the defined timeframe. Five patients were excluded due to being diagnosed with CLAD before imaging occurred. In total, 37 patients (27M/10F, 59±10 yrs) indicated for lung transplant for idiopathic interstitial pneumonias (56%), obstructive diseases (30%), pulmonary hypertension (11%), or cystic fibrosis (3%) were included. Those who developed CLAD had 9.6% high air trapping than non-CLAD (34.9±12.4% vs 25.3±10.3%, p=0.07). The CLAD group also demonstrated regional differences, with significantly higher air trapping in the right lower lobe (31.4±11.9% vs 19.0±10.4%, p=0.01) and trended toward higher air trapping in the right middle lobe (36.4±12.0% vs 26.0±11.0%, p=0.06), and left lower lobe (30.6±14.0% vs 20.2±10.6%, p=0.06). A balanced threshold of 34% (sensitivity = 0.63, specificity = 0.79), and a high sensitivity threshold of 23% (sensitivity = 0.88, specificity = 0.41) were identified. Using the balanced threshold, patients in the low air trapping strata went significantly longer without developing CLAD (4.7±1.1 yrs vs 3.3±1.8 yrs, p=0.01). All patients in the high air trapping group (i.e. >34%) who developed CLAD did so within 3 years of their transplant. At the lower threshold (23%), only one participant in the low air trapping strata developed CLAD, greater than five years from transplant, and could serve as an upper limit of normal air-trapping post-transplant.

Discussion/Conclusion:

In this study, we observed that increased air trapping is associated with progression to CLAD, and presents with a lower lobe predominance. These results support the utility of qCT in detecting early regional small airway pathophysiology post-transplant, thus enabling early interventions, enhancing prognosis, and improving survival in lung transplant recipients.

Risk of Developing Atopic Conditions in Term Infants Exposed to Chorioamnionitis

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Background: Chorioamnionitis (CA) is a pregnancy complication characterized by inflammation of the amniotic fluid, placenta, and/or maternal and fetal tissues. CA often causes an *in-utero* inflammatory response in the fetus which is associated with the future development of atopic disorders (food allergies, allergic rhinitis, atopic dermatitis, and asthma) among pre-term infants (born <37 weeks' gestation). However, there are limited studies describing the association between chorioamnionitis and the development of atopic disorders for term infants (≥ 37 weeks' gestation). In addition, no study has examined the healthcare utilization of children born to mothers diagnosed with CA during their pregnancy.

Hypothesis: Term infants exposed to CA are more likely to develop atopic disorders compared to term infants without exposure, which will be associated with higher rates of healthcare utilization by 5 years of age.

Methods: This was a retrospective matched cohort study (n=67 CA, n=67 no CA) of term infants born at the University of Iowa between 2009 and 2021 with a clinical diagnosis of maternal CA compared to gestational age-, race-, mode of delivery-, and sex-matched patients without CA. Data was extracted from the electronic medical record through 5 years of age, including number of visits to the Emergency Department (ED) for respiratory illnesses, number of hospital admissions for respiratory illnesses, diagnosis of upper-respiratory infection induced wheezing, asthma diagnosis, number of medical visits for asthma, seasonal allergy diagnosis, atopic dermatitis diagnosis, food allergy diagnosis, and family history of atopy. Data were analyzed by Student's T-test for continuous variables and Chi-Squared analysis for categorical variables.

Results: Matched patients had similar pregnancy characteristics except for a higher incidence of maternal fever ($p<0.01$), elevated WBC count ($p=0.02$), and maternal antibiotic exposure ($p<0.01$). Likewise, neonatal characteristics were similar except for neonatal antibiotic exposure ($p<0.01$), length of stay ($p<0.01$), and 1- and 5-minute APGAR scores ($p<0.01$). There was significantly greater albuterol use for participants in the CA group compared to the controls ($p=0.05$). The CA group also demonstrated a non-significant association with more wheezing events ($p=0.11$), asthma management visits ($p=0.14$), ED respiratory visits (0.29), and respiratory admission ($p=0.14$). There was no association between CA and asthma diagnoses ($p=0.52$), food allergies ($p=0.38$), seasonal allergies ($p=0.55$), and dermatitis ($p=0.73$) compared to the control group.

Conclusion: With a limited patient population, CA was associated with trends towards more wheezing events, ED respiratory visits, respiratory admissions, and asthma visits compared to the controls. There was significantly greater use of albuterol for the CA group, which may be secondary to a predisposition for respiratory symptoms and reactive airways from CA *in-utero*. There was no association between CA and food allergies, seasonal allergies, and dermatitis, which is generally consistent in the previous literature for term infants. We have an additional 100 patients with CA to analyze, which will improve our power for assessing CA exposure and the development of atopy and healthcare resource utilization.

Outcomes of Budesonide Compared to Prednisone for Immune Checkpoint Inhibitor Colitis and Immunotherapy Rechallenge

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Introduction:

Colitis is among the most common adverse events of immune checkpoint inhibitors (ICI), affecting 8-27% of patients. For CTCAE grade ≥ 2 colitis, current guidelines recommend holding ICIs and initiating systemic glucocorticoids. However, high dose systemic steroids cannot be used prophylactically for colitis during ICI rechallenge. As a result, only 33% of patients with ICI colitis are rechallenged with ICIs, and among those rechallenged, colitis recurs in 34-37%. Budesonide, a locally acting glucocorticoid with selective action in the colon, has been shown to be effective in the treatment of ICI colitis. However, its role in preventing recurrent colitis during ICI rechallenge has not been characterized.

Hypothesis:

We hypothesize that patients treated with prednisone will have higher odds of colitis recurrence following ICI rechallenge than patients treated with concurrent prednisone and budesonide or budesonide monotherapy.

Methods:

We conducted a retrospective cohort study at University of Iowa Health Care of adult patients diagnosed with ICI colitis between January 1, 2019 and December 31, 2024. Using the TriNetX database, we identified 589 adult cancer patients who received ICI therapy, developed diarrhea, and were treated with prednisone or budesonide. Of these, 179 patients met CTCAE criteria for ICI colitis. Logistic regression models were used to evaluate factors associated with the odds of colitis recurrence after ICI rechallenge. Estimates are reported as odds ratios and 95% confidence intervals.

Results:

Among 179 patients with ICI colitis, the median age was 68 years, 104 (58.1%) were male, and 176 (98.9%) were white. Melanoma was the most common malignancy (n=65, 36.3%), followed by genitourinary (n=40, 22.3%), and then lung cancer (n=20, 11.2%). Steroid regimen for ICI colitis consisted of prednisone monotherapy in 76 (42.5%) patients, budesonide monotherapy in 38 (21.2%), and budesonide and prednisone combination therapy in 65 (36.3%). Overall, 88 patients (49.2%) underwent ICI rechallenge, including 37 (42.0%) treated with prednisone monotherapy, 26 (29.5%) with budesonide monotherapy, and 25 (28.4%) with combination prednisone and budesonide therapy. Recurrent colitis occurred in 26 (70.3%), 9 (34.6%), and 11 (44.0%) patients, respectively.

After adjusting for sex and year of treatment, steroid regimen was significantly associated with colitis recurrence after ICI therapy rechallenge ($p < 0.01$). Patients receiving prednisone monotherapy were at 5.95 (1.65-21.47) increased odds of colitis recurrence relative to patients who received budesonide monotherapy. No statistically significant difference in colitis recurrence was seen between budesonide monotherapy and budesonide and prednisone combination therapy.

Conclusion:

Our findings suggest that patients treated with budesonide have lower odds of colitis recurrence upon ICI rechallenge compared to patients treated with prednisone monotherapy. Given the limitations of the retrospective study design, prospective studies are needed to further validate our results. Based on our findings, we suggest that prospective studies evaluate the treatment of grade ≥ 3 ICI colitis with 1 mg/kg of prednisone and 9 mg budesonide. As symptoms improve, prednisone can be tapered and the patient rechallenged with an ICI while still on budesonide. For grade 1 or 2 colitis, we suggest evaluating 9 mg budesonide monotherapy. Finally, for steroid refractory ICI colitis, the prophylactic role of biologics such as vedolizumab in facilitating ICI rechallenge has yet to be characterized.

Early Respiratory Response and Extubation Success after Dexamethasone Burst V.S. DART in Extremely Preterm Infants with Evolving Bronchopulmonary Dysplasia

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Background: Bronchopulmonary dysplasia (BPD) is a common contributor to neonatal morbidity and long-term pulmonary and neurodevelopmental sequelae affecting more than 50% of surviving extremely premature infants. While corticosteroids are one of the most investigated medications in newborn medicine, the optimal protocol for dexamethasone administration to prevent and treat BPD is still unknown. In ventilator dependent, low birth weight, pre-term infants pulse doses twice daily for 3 days at 10-day intervals increased survival rates without oxygen supplementation ($p = 0.03$) and decreased chronic lung disease incidence ($p = 0.047$). The DART protocol administered a tapered dexamethasone regimen and demonstrated more preterm infants were extubated by 10 days vs saline control ($P < .001$). Our study evaluates extremely preterm infants who received DART over 10 days (0.075mg/kg oral BID X 6 doses, 0.05mg/kg oral BID X 6 doses, 0.025mg/kg oral BID X 4 doses, and 0.01mg/kg oral BID X 4 doses) or Burst (0.2mg/kg every 12 hours for 6 doses) to determine which has a greater impact on respiratory outcomes. Our hypothesis is Burst protocol allows for earlier visible impact on chest x-ray but higher rates of rebound inflammation leading to repeat courses while DART requires fewer courses prior to successful extubation.

Methods: University of Iowa NICU records from 2021-2025 were screened for infants born at or before 27 weeks, without major genetic or congenital anomalies, who received systemic dexamethasone courses. Courses were eligible if given between 30-90 days of life, the infant weighed ≥ 900 g at administration, and the infant was on high frequency jet ventilation at initiation. For each course, information was collected on dexamethasone dose, repeat courses or non- dexamethasone steroids given within 21 days, and reintubations within 21 days of extubation. Ventilator settings before, during and after course completion were gathered along with extubation success defined as maintaining extubation for ≥ 7 days. For statistical analysis, continuous variables were summarized as median [interquartile range] and compared using Mann–Whitney U tests; categorical variables were compared using Fisher exact or chi-square tests. Adjusted analyses accounted for repeated courses within infants and included baseline RSS, postmenstrual age, weight at treatment initiation, prior dexamethasone exposure, and calendar year. Separate multivariable models examined factors associated with regimen selection; RSS and FiO_2 were not included in the same model because of collinearity. An exploratory regimen $\times$ baseline RSS interaction was tested for extubation success. Outcomes unavailable after transfer were treated as missing. Sensitivity analyses included the first completed standard course per infant, first-ever dexamethasone courses, and exclusion of infants who received both regimens. Respiratory trajectory, fixed post-initiation landmark, and interaction analyses were considered exploratory.

Results: Among 158 completed standard dexamethasone courses, in 114 extremely preterm infants, 91 were burst and 67 were DART. Burst courses were initiated at later postnatal age, higher postmenstrual age and weight, and greater baseline respiratory severity score (RSS). Higher baseline RSS was independently associated with lower odds of DART use (aOR 0.76 per 1-unit increase, 95% CI 0.67–0.86; $p < 0.001$), consistent with preferential use of burst in infants requiring greater respiratory support. By 48 hours, transition to non-invasive respiratory support was more frequent after burst than DART (36.7% vs 20.9%; $p = 0.036$), with greater reductions in RSS (-33.6% vs -27.1% ; $p = 0.014$) and jet ΔP (-24.0% vs -15.4% ; $p = 0.008$) among infants remaining invasively ventilated. By 72 hours, the proportion on non-invasive support was similar (45.6% vs 46.3%). In contrast, DART was associated with more extubation within 7 days (79.1% vs 51.1%; $p < 0.001$) and greater extubation success (74.6% vs 42.2%; aOR 4.98, 95% CI 1.83–13.54; $p = 0.002$). Among infants still invasively ventilated at 72 hours, subsequent extubation by day 7 occurred after 61.1% of DART versus 10.2% of burst courses ($p < 0.001$). Repeat dexamethasone within 14 days was less frequent after DART (20.9% vs 46.7%; aOR 0.38, 95% CI 0.17–0.87; $p = 0.022$). At approximately matched post-initiation landmarks, non-invasive support was more frequent after DART at both ~ 10 days (88.1% vs 43.8%) and ~ 17 days (83.6% vs 53.9%; both $p < 0.001$). An exploratory regimen $\times$ RSS interaction suggested that the relative association between DART and extubation success increased at higher baseline RSS (p for interaction = 0.048), although this was not consistent across sensitivity analyses.

Conclusion: Burst appears to produce a faster initial lung response in some infants, however, among infants ventilated after 72 hours subsequent extubation within the following week occurred more frequently during DART. The variation in amount of repeat systemic steroid courses between those on Burst compared to DART may indicate need to give more medication to achieve successful extubation. However, this also needs to be considered in the context of typical institutional practice. It may be more likely that providers tend to prescribe multiple Burst courses more often than DART courses. The project is ongoing with plans to analyze each subject's lung imaging, corresponding steroid course, and respiratory outcomes to further elucidate patient extubation readiness at the time of steroid initiation.

Patterns in Substance Use-Related Presentations to the Emergency Department

Mentor: Hayden Smith

Student: Padraic Sullivan

Background: Substance-use related disorders (SRDs) represent a significant public health burden and contribute to the increasing strains placed on Emergency Departments (EDs). Patients who present with complaints related to substance use frequently have coexisting mental health and social needs, with their care often requiring substantial resources. Limited research has examined the characteristics and timing of these patients' ED presentations. A greater understanding of the temporal distribution of these visits may help improve resource allocation.

Methods: A retrospective descriptive study of patients with SRD at three Midwestern EDs for the year 2025 was conducted. Patients over 18 were included if their chief complaint or primary diagnosis was related to substance use. Patients were excluded if their visit involved intentional self-harm or accidental overdose of a prescription or over-the-counter drug. Demographic, temporal, clinical, substance use, treatment, and disposition data were collected from electronic medical records. The primary objective was to describe characteristics and the temporal distribution of visits by month, day of week, and time of day.

Results: The study sample included 1,358 individual SRD visits, represented by 964 unique patients. These visits made up 1.4% of the 97,478 total ED visits during the study period. Median patient age was 40 years, 67.4% were male, and 55.4% of patients had a documented mental health diagnosis. Nearly 6% of patients were unhoused, and this number rose to 11% when accounting for repeat encounters. Alcohol was involved in 83.4% of individual ED visits. Visits were most common from 12:00-17:59 (31.9%) and least common from 0:00-5:59 (16.5%). Saturday and Sunday had the highest concentration of visits (15.6% and 15.4%), while Friday had the lowest (12.7%).

Discussion: Substance use-related visits to the ED demonstrated temporal patterns, with the greatest concentration occurring in afternoon/evening hours and on weekends. There was a high prevalence of patients being unhoused and mental health disorders, highlighting the need for integrated care solutions. These findings and future work may help inform targeted resource allocation and linkage to ongoing, longitudinal care.

Title: Targeting Caspase-8 and the Extrinsic Apoptotic Pathway in Ewing Sarcoma Tumors

Authors: Mary Thomas, Stacia Koppenhafer, Annika Veit, David Gordon

University of Iowa Carver College of Medicine, Department of Pediatrics Hematology/Oncology, Holden Cancer Comprehensive Center

Introduction: Ewing sarcoma (ES) is a highly metastatic bone and soft-tissue sarcoma with peak incidence at age 14, primarily occurring in children and young adults. It is caused by chromosomal translocations resulting in a fusion oncogene that acts as abnormal transcription factor. 85% of tumors are associated with fusion of the *EWSR1* and *FLI1* genes from a t(11;22)(q24;q12) translocation. Current treatments for ES include combining cytotoxic chemotherapy, radiation, and surgery to increase the 5-year survival rate to about 70%. Despite this, the prognosis remains unfavorable, especially for patients with metastatic disease or recurrent disease. In recent work, we identified a distinct, CDK1- and caspase-dependent apoptotic mechanism in response to DNA replication stress, offering new insights into the molecular basis of a therapeutic vulnerability in Ewing sarcoma tumors.

Hypothesis: We hypothesize that activation of caspase-8, a key initiator of the extrinsic apoptotic pathway, is an untapped therapeutic approach to increase ES cell sensitivity to therapy. Current chemotherapy drugs, except for Irinotecan (SN38) which is used for relapsed/refractory ES, do not target caspase-8. Ozekibart, or INBRX-109, is a late-stage clinical trial drug that has demonstrated antitumor activity in patients with relapsed or refractory ES. It is a tetravalent agonist of Death Receptor 5 (DR5) that induces apoptosis via the extrinsic apoptotic pathway. By treating cells with INBRX-109, we aim to increase activation of this underutilized apoptotic pathway, ultimately increasing ES cell therapeutic vulnerability.

Methods: Multiple Ewing and non-Ewing sarcoma cell lines were treated with increasing doses of INBRX-109 to demonstrate sensitivity due to cleavage and activation of caspase-8. To assess the specificity of INBRX-109 to activation of the extrinsic apoptotic pathway, ES cells were treated with pan-caspase and caspase-8 inhibitors. Caspase-8 and DR5 CRISPR-knockout cell lines were also generated as a complementary method of confirmation. Lastly, INBRX-109-resistant cells were created in 4 different ES cell lines by repeated exposure to the drug.

Results: ES cells are uniquely sensitive to drugs that activate the extrinsic apoptotic pathway via DR5 and caspase-8. Treatment with either a pan-caspase or a caspase-8 specific inhibitor rescued cells from INBRX-109 toxicity. Furthermore, both caspase-8 and DR5 CRISPR knockout cell lines demonstrated near-complete resistance to INBRX-109 treatment, demonstrating specificity to the extrinsic apoptotic pathway. Finally, ES cells mediated resistance to INBRX-109 by downregulating DR5 and/or caspase-8, suggesting the need for INBRX-109 combination therapies.

Conclusions: Directly targeting Ewing sarcoma tumors has proven to be challenging. The standard treatment – cytotoxic chemotherapy, surgery, and irradiation – has improved survival outcomes for localized disease, but the 5-year survival rate for metastatic or relapsed patients has minimally changed in the past 20 years. By demonstrating that directly targeting caspase-8 and activating the extrinsic apoptotic pathway decreases cell viability, we believe we have uncovered a novel approach to increase ES therapeutic vulnerability. With this information, we hope to modify treatments to ensure activation of caspase-8 using drugs like INBRX-109, further improving survival rates especially for relapsed or refractory cases. Future work will focus on optimizing synergy with other drugs to overcome treatment resistance.

Title: Standardized Parotid Gland Subunit Classification Improves Interpretation of Multimodal Imaging in Salivary Gland Disease

Student: Abigail Townsend

Mentor: Henry Hoffman

Abstract:

Conventional imaging of the parotid gland typically describes abnormalities at the level of the entire gland, despite well-recognized regional variation in anatomy, ductal drainage, vascular supply, and disease involvement. This shortcoming limits comparison across ultrasound, CT, elastography, and sialography. We propose an ultrasound-determined classification that divides the parotid into five reproducible subunits: buccal, facial process (including accessory lobe), body (including hilar zone), tail, and deep lobe. We support this system with case presentations using ultrasound and multimodal imaging to address parotid gland injury.

A 41-year-old woman, 10 years after oral cavity external beam radiation, was evaluated with CT imaging showing attenuation of the right tail (−25 HU) and body (−27 HU) versus left tail (+46 HU) and body (+53 HU) to indicate fatty replacement in the more heavily irradiated right gland. Shear wave elastography (right tail 1.35 m/s, body 2.26 m/s; left tail 1.77 m/s, body 2.03 m/s) and sialography implicated changes to the left parotid suggestive of past sialadenitis.

A 22-year-old woman with salivary pain and swelling 7 years after high-dose (284 mCi) I-131 for papillary thyroid carcinoma was evaluated with sialography identifying complete right main ductal obstruction with preserved accessory lobe drainage and left parotid ductal pruning with an intact main duct. CT (right tail +40.6 HU, body +76.2 HU; left tail +47.8 HU, body +85.1 HU) and elastography (right tail 1.48 m/s; left 1.50 m/s) documented symmetric intraglandular heterogeneity.

Subunit-specific analysis in these cases revealed clinically meaningful dissimilarity not well represented by assessment of the glands as single units and enabled precise cross-modality localization. This five-subunit classification we have developed in application to specific cases is under review by the AAO-HNS Salivary Gland Committee to offer a standardized anatomic language for salivary gland imaging.

Epigenetic inflammatory memory in airway basal cells amplifies viral RNA responses in vivo

Lorena Tran

Mentor: Alejandro Pezzulo, M.D., Associate Professor of Internal Medicine, CCOM

Background:

Acute inflammation in the airways facilitates clearance of pathogens such as respiratory viruses; however, the airways of people with asthma and chronic bronchitis often respond to viral infection with excessive immune responses and persistent inflammation. Mechanisms of this inflammation vary; half of people with asthma and a third of people with chronic bronchitis have cytokine IL-13-driven goblet cell metaplasia (GCM) and mucus hypersecretion with plugging of airways. While IL-13-receptor-blocking antibodies such as dupilumab decrease exacerbations and severity, symptoms return upon treatment discontinuation. Understanding the mechanisms driving the heightened response to respiratory viruses in chronic lung diseases is critical to the development of curative treatments.

IL-13-induced GCM can persist for months in vitro. We previously found that GCM persistence in vitro is driven by epithelial epigenetic “memory”, which is acquired during adaptation to exposures and is similar to trained immunity in mononuclear immune cells. Moreover, IL-13 treatment induces changes in chromatin accessibility and DNA methylation that persist in the absence of IL-13, post-mitosis in human airway basal stem cells (“Memory_{IL-13} basal cells”) and the epithelia they form (“Memory_{IL-13} epithelia”). Compared to previously untreated (“Naïve”) cells, Memory_{IL-13} basal cells are prone to goblet cell differentiation and have pro-inflammatory gene expression both at baseline and in response to IL-13. However, when exposed to the viral RNA mimic polyinosinic:polycytidylic acid (poly I:C) alone, Memory_{IL-13} epithelia did not develop excessive GCM. Moreover, it was unclear whether Memory_{IL-13} basal cells would affect GCM and modulate immune cell activation in vivo.

Hypothesis: Memory_{IL-13} basal cells are sufficient to enhance the epithelial inflammatory response to viral exposures.

Methods: 1) Transplantation of Memory_{IL-13} and Naïve donor cells into recipient mice: I treated 6 tdTomato mice (“donors”) with intranasal IL-13 or PBS as a control, then harvested and cultured their tracheal epithelial cells. I then transplanted these cells into the airways of wild type mice (“recipients”). 2) Viral challenge: I treated mice with intranasal poly I:C or PBS as a negative control. Poly I:C is a synthetic dsRNA molecule which induces a viral immune response through Toll-like receptor 3 activation. 3) Confocal microscopy to assess GCM and immune response: I harvested mouse tracheae and proximal lungs. Using immunostaining, I assessed GCM with a goblet cell marker and airway morphology with ciliated and basal cell markers.

Results:

Our novel model of basal cell transplantation was an effective tool to assess epithelial inflammatory memory in vivo, as Memory_{IL-13} and Naïve basal cells had normal engraftment capacity in the recipient trachea, and engrafted basal cells could differentiate into ciliated and goblet cells. Tracheal epithelium originating from transplanted Memory_{IL-13} basal cells was skewed towards goblet cell differentiation, reinforcing our earlier in vitro findings. In contrast to our in vitro findings, intranasal challenge with the viral RNA analog poly I:C increased GCM in Memory_{IL-13} epithelia in vivo, while Naïve epithelia had no response. In poly I:C-challenged mice transplanted with Memory_{IL-13} basal cells, the recipient (non-transplanted) epithelia also had increased GCM compared to the same epithelia in mice transplanted with Naïve basal cells. This suggests that engrafted Memory_{IL-13} cells could affect recipient cells through paracrine or contact-mediated signaling involving non-epithelial cells (e.g., immune, mesenchymal).

Overall significance: Here, we demonstrate that Memory_{IL-13} in airway epithelial cells is sufficient for an enhanced response to poly I:C in vivo but not in vitro, suggesting that Memory_{IL-13} in airway epithelial cells intrinsically determines the outcome of viral respiratory infections in vivo. This highlights the need for epithelial-centered treatment development to cure asthma and other chronic inflammatory lung diseases.

A Comparison of Cadaveric and Synthetic Models For Testing Cement-Augmented Lumbar Spinal Fusion Constructs In Osteoporotic Bone

Kyle Trunnell , Nicole DeVries Watson, PhD , Doug Fredericks, BS , Catherine Olinger, MD, MS

Cadaveric bone requires both sensitive acquiring procedures and cooling techniques, making a synthetic bone model attractive. However, limited research has examined whether synthetic vertebral models accurately replicate pullout testing compared to cadaver bone. Studies in other bones have shown variability in testing metrics between their models and cadaver bone as well. This study examined whether there is a difference in pullout strength of cement-augmented fenestrated constructs in osteoporotic cadaveric bone and synthetic sawbones after physiologic cyclic loading.

Osteoporotic L3 and L4 vertebrae were instrumented with fenestrated 5.5 mm or 6.5 mm screws with 3 cc of polymethylmethacrylate cement, or 6.5 mm non-fenestrated screws without cement. These screws underwent cyclic loading to simulate three months of postoperative activity, then underwent pullout strength testing. CT images were used to quantify cement distribution and screw migration. Passive controls were included.

There was a significant decrease in the pullout strength of 6.5 mm fenestrated screws in the cadaveric bone as compared to the sawbone ($p < .01$) and in 6.5 mm non-fenestrated screws in the cadaveric bone as compared to the sawbone ($p < .05$). In sawbones, screw diameter did not have a significant change in pullout strength, but in cadaver bone there was a significant difference between fenestrated 5.5 mm screws and fenestrated 6.5 mm screws ($p < .05$) and between fenestrated 5.5 mm screws and non-fenestrated 6.5 mm fenestrated screws ($p < .01$). The mean pullout strength for the 5.5 mm fenestrated screws, 6.5 mm fenestrated screws, and 6.5 mm non-fenestrated screws were 2044 N, 1081 N, and 840 N respectively.

Sawbone synthetic models showed significant differences in pullout strength compared to cadaver bone in multiple screw types. Cadaveric bone models showed decreased strength, suggesting that force measurements pulled from sawbones may be estimated too high for actual bones. Cadaveric bones also showed a difference in pullout strength when screw diameter was changed, suggesting that the mechanical properties of the sawbone may not entirely reflect how actual bone behaves under stress.

Title: ***Impact of OPA1 Loss in Brown Adipose Tissue on Cardiac Function and Remodeling Following Myocardial Infarction***

Student Name: Caroline Van Bell

Mentor/Department: Renata Pereira Alambert, Internal Medicine

Contributors: Ayushi Sood, Jamille Lockhart, Jayashree Jena, Josh Peterson, Nikhil Namshamgari, and Vamsi Challa

Background: Myocardial infarction (MI) is a leading cause of cardiovascular mortality, highlighting the need for novel therapeutic strategies. Brown adipose tissue (BAT) is one such potential therapeutic target due to its cardioprotective effects through thermogenesis and endocrine signaling. Optic atrophy 1 (OPA1), a mitochondrial inner membrane protein regulating mitochondrial dynamics, is critical for BAT function. Previous studies demonstrated that BAT-specific OPA1 knockout (OPA1 BKO) mice exhibit altered BAT endocrine signaling, including secretion of fibroblast growth factor 21 (FGF21) and growth differentiation factor 15 (GDF15) and improved systemic metabolism. Because BAT-derived factors have been implicated in cardiovascular protection, we hypothesized that OPA1 deficiency in BAT would attenuate cardiac dysfunction and remodeling following MI.

Hypothesis: OPA1 BKO mice will exhibit attenuated MI-induced heart failure, characterized by reduced hypertrophy, fibrosis, inflammation, and preserved systolic function compared to littermate control mice.

Methods: To test this hypothesis, male mice with conditional deletion of Opa1 in Ucp1-expressing cells (brown and beige adipocytes) were generated by crossing Opa1-floxed mice with Ucp1-Cre mice (OPA1 BKO). Male OPA1 BKO mice and littermate controls underwent MI induction at approximately 10 weeks of age by left anterior descending coronary artery ligation. Cardiac structure and function were evaluated by echocardiography before and 3 days after MI. Seven days post-MI, hearts were collected for qPCR analysis of hypertrophic, fibrotic, and inflammatory markers and for histological assessment of fibrosis. Statistical analyses were performed using GraphPad Prism software.

Results: Under basal conditions, OPA1 BKO mice exhibited a slight but significant elevation in ejection fraction relative to controls despite smaller end-diastolic and end-systolic volumes, suggesting enhanced baseline systolic function. Conversely, following MI, OPA1 BKO mice demonstrated a near significant reduction in ejection fraction, decreased cardiac output and stroke volume and larger akinetic region consistent with greater functional myocardial impairment. Cardiac mass, end diastolic volume and end systolic volume as measured by echocardiography were unchanged between genotypes. Despite worsened systolic dysfunction, survival and transcriptional markers of pathological hypertrophy, inflammation and extracellular matrix remodeling were similar between control and OPA1 BKO mice.

Conclusions: Contrary to our initial hypothesis, BAT-specific OPA1 deficiency did not confer protection against MI-induced cardiac dysfunction. Although OPA1 BKO mice displayed modestly improved cardiac function under basal conditions, they experienced greater functional deterioration following myocardial infarction without corresponding changes in early remodeling markers or survival. These findings suggest that the favorable cardiometabolic adaptations associated with BAT OPA1 deficiency are insufficient to protect the heart from ischemic injury and may differentially influence cardiac function under physiological versus pathological conditions. Future studies will evaluate infarct size, cardiomyocyte survival, mitochondrial metabolism, and immune cell infiltration during the acute and chronic phases of post-infarction remodeling. These studies will provide mechanistic insight into how BAT mitochondrial stress influences cardiac responses to ischemic injury and whether BAT-heart communication can be therapeutically targeted in cardiovascular disease.

Title: GLP-1 Receptor Agonists and Hearing Outcomes in Metabolic Syndrome

Authors: VandeLune, E., Belding, E., Urdang, Z., Bennion, D.M.

Introduction: Auditory dysfunction is an understudied aspect of metabolic syndrome. Individual components of metabolic syndrome such as dyslipidemia, hyperglycemia, and hypertension, are associated with increased incidence of sensorineural hearing loss in review of large population studies. Pathophysiologic drivers of metabolic syndrome center around microvasculopathy including the accumulation of chronic systemic inflammation mediated by oxidative stress, mechanisms that also contribute to cochlear and auditory nerve damage and hearing loss. Glucagon-like peptide-1 (GLP-1) receptor agonists, increasingly used for diabetes and weight management, may interrupt this disordered inflammatory and oxidative signaling through and thereby result in oto-vascular protection. Using an ultra-large electronic health database, we tested the hypothesis that treatment with semaglutide, the most widely prescribed GLP-1 agonist in the U.S., associates with favorable hearing outcomes.

Hypothesis: We tested the hypothesis that semaglutide treatment among patients with metabolic syndrome associates with lower odds for developing tinnitus, sensorineural hearing loss (SNHL), and sudden sensorineural hearing loss (SSNHL). Subsequently, we delineated the dose-response for each individual metabolic syndrome criteria and each unique combination of criterion to test the hypothetical mechanistic relationship between metabolic syndrome and hearing health.

Methods: TriNetX is a de-identified, live, federated, electronic health records database representing 125 million patients across 95 healthcare organizations. Two complementary analyses were conducted. First, adults aged ≥ 40 years with metabolic syndrome who received semaglutide following diagnosis were compared with patients with metabolic syndrome who did not receive GLP-1 agonist treatment. Cohorts were propensity-score-matched for relevant medical comorbidities and ototoxic risk factors. Outcomes included tinnitus, SNHL, and SSNHL. Then, hearing outcomes were evaluated according to the number of metabolic syndrome diagnostic criteria, with propensity score matching (PSM) performed for age at index.

Results:

The semaglutide analysis included semaglutide-treated patients with metabolic syndrome (mean age, 56 years; 66.2% female) and propensity score matched controls ($n=24,714$ per group). Compared to untreated patients, semaglutide-treated patients had lower risks of SNHL (3.02% vs 4.22%; OR, 0.71; 95% CI, 0.64–0.78), tinnitus (2.00% vs 2.86%; OR, 0.70; 95% CI, 0.62–0.78), and SSNHL (0.11% vs 0.23%; OR, 0.47; 95% CI, 0.30–0.72), with only a minimal delay in time to diagnosis. An analogous 2024 analysis similarly demonstrated lower odds of tinnitus (OR, 0.65; 95% CI, 0.54–0.78) and SNHL (OR, 0.52; 95% CI, 0.46–0.59) with semaglutide treatment. Increasing numbers of metabolic syndrome diagnostic criteria were associated with a modest trend towards adverse hearing outcomes, although this trend was substantially attenuated following PSM for age at index.

Conclusion:

Semaglutide treatment associates with lower odds of tinnitus, SNHL, and SSNHL compared with propensity score-matched controls. These findings raise the possibility that the metabolic, vascular, anti-inflammatory, or antioxidant effects of GLP-1 receptor agonism may contribute to more favorable hearing outcomes. The potential confounding changes in BMI that may impart on these associations is a topic of ongoing and future study. Further prospective and mechanistic studies are needed to determine whether GLP-1 agonists confer direct otoprotective effects.

Neighborhood Socioeconomic Deprivation and Risk of Orofacial Clefts in Iowa: A Population-Based Study

VandeLune J, Qian V, Rhoads A, Romitti P, Conway K, Jensen J, The National Birth Defects Prevention Study

Background

Neighborhood socioeconomic deprivation has been associated with adverse pregnancy outcomes and selected congenital anomalies, but its relationship with orofacial clefts (OFCs) remains uncertain. We evaluated whether neighborhood deprivation during the periconceptional period (one month before through the third pregnancy month) was associated with risk of OFCs among Iowa participants in the National Birth Defects Prevention Study (NBDPS).

Methods

We performed a population-based case-control analysis of the 452 Iowa case and 1,269 Iowa control participants from the NBDPS (birth years 1997–2011). Maternal residential addresses during the periconceptional period were geocoded and linked to census tract-level socioeconomic data to generate a standardized neighborhood deprivation (ND) index. ND was categorized into quartiles using cutoffs derived from controls in the overall NBDPS population. Crude and adjusted odds ratios and 95% confidence intervals were estimated via logistic regression and generalized estimating equations for all OFCs, cleft lip with or without cleft palate (CL±P), and cleft palate only (CP). Models were adjusted for maternal age, race/ethnicity, education, and household income based on a directed acyclic graph with an exchangeable correlation matrix for census tract.

Results

Compared with controls, OFC cases differed in plurality and first-degree family history of OFCs, while mothers of cases differed in educational attainment, household income, gravidity, pregestational diabetes, and cigarette smoke exposure during the periconceptional period. Increasing ND was characterized by younger maternal age, higher proportions of non-Hispanic Black and Hispanic mothers, lower educational attainment and household income, higher prepregnancy obesity particularly among controls, and greater cigarette smoke exposure. Crude analyses suggested increased odds of OFCs overall and both OFC subtypes within some higher ND categories, with stronger patterns for CL±P than CP. However, these associations were attenuated after adjustment for individual-level socioeconomic and demographic factors, with adjusted confidence intervals including the null and no clear dose-response relationship. Similar findings were observed in analyses restricted to isolated OFCs.

Discussion

Neighborhood socioeconomic deprivation was not independently associated with risk of OFCs among Iowa NBDPS participants. Although crude associations suggested increased odds of OFCs and CL±P within some of the higher deprivation categories, these associations were attenuated after adjustment and did not demonstrate a consistent dose-response relationship. These findings suggest that observed crude associations may largely reflect differences in individual-level maternal socioeconomic and demographic characteristics rather than an independent effect of neighborhood deprivation.

Reducing Unnecessary Hospital Admissions After Routine Percutaneous Nephrostomy Catheter Placement

Veena Venkatesh, Andrea Rossman, Brent Yelton, Benjamin Plambeck, Gina Lockwood, Kenneth Nepple, and Chad Tracy

Department of Urology, University of Iowa Hospitals & Clinics

Introduction:

Patients undergoing routine percutaneous nephrostomy catheter (PCN) placement by interventional radiology (IR) have traditionally been admitted to the urology service overnight for post-procedural monitoring. However, many patients undergoing uncomplicated routine PCN placement have an uncomplicated recovery and are discharged the following morning. Routine overnight admission may contribute to increased urology patient census, resident workload, unnecessary utilization of hospital beds and resources, and increased patient costs. A standardized same-day discharge pathway may allow appropriately selected patients to safely recover at home while reducing unnecessary hospital utilization.

Purpose:

To develop and implement a standardized same-day discharge pathway for appropriately selected patients following uncomplicated routine PCN placement and to evaluate its safety, feasibility, and impact on hospital resource utilization and patient and resident experience.

Methods:

A retrospective chart review was performed of patients undergoing PCN placement from July through September 2023. Patients were screened using predefined eligibility criteria for same-day discharge, including unilateral PCN placement for routine indications and absence of higher-risk indications such as nephrolithiasis or infection. Patients undergoing bilateral PCN placement, those not admitted to urology, and those meeting other predefined exclusion criteria were excluded. Postoperative outcomes included vital sign stability, pain control, 72-hour readmissions, 30-day readmissions, and post-discharge complications. Findings from the baseline review were used to develop a multidisciplinary Urology-IR quality improvement initiative. Beginning in June 2026, eligible patients undergoing scheduled unilateral PCN placement are monitored for approximately 4 hours following the procedure and discharged if they demonstrate stable vital signs, controlled pain, no concerning bleeding, and an appropriate discharge plan. Patients with higher-risk indications or clinical features remain candidates for overnight admission. Prospective evaluation of length of stay, complications, emergency department visits, readmissions, and patient and resident satisfaction is ongoing.

Results:

Twenty-nine patients underwent PCN placement during the baseline review period; 10 were excluded, leaving 19 patients for analysis. All 19 patients (100%) had stable postoperative vital signs and controlled pain. Eighteen patients (94.7%) had no documented 72-hour readmission. Seven patients (36.8%) had a documented 30-day readmission, and seven (36.8%) had a documented post-discharge complication, most commonly urinary tract infection or dysuria. The baseline review identified approximately 1-2 routine PCN admissions per week. Based on patient volume and eligibility criteria, approximately 6 patients per month were estimated to potentially qualify for same-day discharge. These findings supported implementation of the standardized same-day discharge pathway in June 2026. Prospective outcome data are currently being collected.

Conclusion:

Implementation of a standardized same-day discharge pathway represents a potential opportunity to reduce unnecessary overnight admissions following uncomplicated routine PCN placement while maintaining patient safety. This initiative may decrease inpatient resource utilization, patient costs, and urology resident workload while allowing appropriately selected patients to recover in their homes. Continued prospective monitoring of complications, readmissions, emergency department visits, and patient and resident experience will determine the safety, effectiveness, and sustainability of this practice.

Patient Satisfaction and Tolerability of Intralesional Chemotherapy for Non-Melanoma Skin Cancer: Findings from a Single-Institution Survey

Mukund Viswanadha B.S., Esther O. Nwozo, BS, Olivia Lamberg, MD, Nicole A. Negbenebor, MD

Non-melanoma skin cancer (NMSC), including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and keratoacanthoma, represents the most common malignancy in the United States, with incidence continuing to rise annually. Treatment approaches include surgical excision and Mohs micrographic surgery, with non-surgical options reserved for select cases. Intralesional chemotherapy, including 5-fluorouracil, bleomycin, and methotrexate, has emerged as a less invasive alternative, particularly for patients who are poor surgical candidates or prefer to avoid surgery, with several chemotherapeutics demonstrating high cure rates and minimal scarring. Despite growing clinical use, patient-reported data on tolerability and satisfaction with intralesional therapy remain limited. The purpose of this study was to characterize patients' experiences with intralesional chemotherapy for skin cancer, including treatment preferences, perceived side effects, and overall satisfaction.

Patient data was gathered by compiling the contact information of every patient who had received treatment for BCC or SCC at UIHC over the past several years. We called and asked each patient a series of survey questions to understand their feelings towards intralesional chemotherapy, their personal history of skin cancer, and the ways in which intralesional therapy has affected their personal lives. We compiled data from every patient who successfully completed the survey and statistically analyzed the results to identify major factors influencing their opinion towards intralesional therapy.

The patients in this study skewed older, with around 59% being over the age of 80. Most patients reported skin cancers in the facial region (29%) and upper/lower extremities (83%) compared to other regions of the body, with a majority of patients reporting more than ten cancers. In addition to intralesional therapy, many patients also received Mohs surgery (80.5%) and cryotherapy (61%). Analysis of the cohort showed that 77% of the patients cited the minimally invasive aspect of the intralesional chemotherapy as a principal reason for preferring it over surgery, and 64% valued the lack of physical activity restrictions. Additionally, over 66% of patients reported a positive opinion of the treatment and stated that they would recommend this treatment to others. Patients generally expressed satisfaction with intralesional treatment compared to surgery, especially those who had previously undergone multiple surgeries with limited improvement. The findings suggest that several patients find intralesional therapy to have been a more convenient option compared to surgical treatment.

Future studies should evaluate larger, more diverse cohorts across multiple institutions and incorporate quality-of-life metrics and cross-modality comparisons of patient-reported satisfaction.

Association of Hormone Replacement Therapy with Foot and Ankle Tendon and Fascia Injury: An Electronic Health Record Database Study

Arielle Weber

Mentors: Ruth Chimenti, DPT, PhD and Bopha Chrea, MD

Abstract:

Background: Sex hormones play an important role in tendon homeostasis, yet the relationship between exogenous hormone therapy and foot and ankle tendon pathology remains poorly understood. This study evaluated the association between hormone replacement therapy (HRT), testosterone therapy, and the development of common foot and ankle tendon and fascia disorders.

Purposes/Hypotheses: The primary purpose was to determine whether HRT (estrogen-, progesterone-, or progestin-containing therapy) is associated with the risk of developing foot and ankle tendon and fascia disorders among peri-menopausal and menopausal women. The secondary purpose was to evaluate the association between testosterone therapy and foot and ankle tendon and fascia disorders among adult men and women. We hypothesized that both HRT and testosterone therapy would be associated with increased odds of developing these disorders.

Methods: A retrospective cohort study was conducted using the TriNetX Research Network, an international multicenter electronic health record database. The primary analysis compared peri-menopausal and menopausal women receiving HRT with matched women not receiving HRT. Secondary analyses compared adult men and women receiving testosterone therapy with matched controls. The primary outcome was the development of any foot or ankle tendon or fascia disorder identified using ICD-10 diagnosis codes. Propensity score matching was performed for age and body mass index. Odds ratios (ORs), 95% confidence intervals (CIs), and *p* values were calculated using the TriNetX comparative analytics platform.

Results: Following propensity score matching, HRT in menopause women was associated with significantly greater odds of developing foot and ankle tendon and fascia disorders compared with no HRT (3.59% vs. 1.75%; OR, 2.10; 95% CI, 2.05–2.15; $p < 0.0001$). Testosterone therapy was likewise associated with increased odds of tendon and fascia disorders in both men (3.84% vs. 1.40%; OR, 2.82; 95% CI, 2.65–3.00; $p < 0.0001$) and women (2.89% vs. 1.43%; OR, 2.05; 95% CI, 1.84–2.28; $p < 0.0001$).

Conclusions: Exogenous hormone therapy was associated with significantly increased odds of foot and ankle tendon and fascia disorders. These findings contribute to the growing understanding of hormone therapy and tendon health and may help inform clinician counseling while providing a foundation for future prospective investigations.

Pain Recognition and Rejection of Care in Hospitalized Persons Living with Dementia

Caitlyn Weeks, Clarissa Shaw, PhD, RN

Introduction: Persons living with dementia (PLWD) are frequently hospitalized and experience high rates of complications and rejection of care (RoC). Pain is often underrecognized and undertreated due to impaired self-reporting and inconsistent assessment. Improving pain recognition may help guide care, reduce RoC, and improve care for hospitalized PLWD.

Hypothesis/Purpose: The purpose was to (1) evaluate the relationship between RoC and pain in hospital dementia care, and (2) evaluate documented pain assessment accuracy at the nurse and provider level. Hypothesis 1: Shifts with more severe nursing-charted pain will be associated with RoC by PLWD. Hypothesis 2: Nurse and provider documented pain will not consistently capture patient pain compared to the gold standard nonverbal observational tools—PAINAD and CNPI.

Methods: To evaluate hypothesis 1, a secondary analysis of data collected from an ongoing Alzheimer's Association Research Grant was completed. Documented pain assessments and medication administration was extracted from the EMR. Pain was collapsed at the shift level and categorized as none, mild, or moderate–severe. RoC was rated by researcher evaluators using the RTC-DAT during nurse-patient care encounters. The association between pain and RoC was evaluated using a GEE while controlling for pharmacologic pain treatment and psychotropic medication use and accounting for within-patient effects. To evaluate hypothesis 2, a prospective case series of 18 patient shifts (38 care encounters) was conducted. Each encounter included PAINAD and CNPI pain assessments and a chart review of nurse and provider pain documentation.

Results: The secondary analysis consisted of 169 shift-level records within 43 unique patients. RoC was present in 54.4% of shifts. No pain (48.7%) was most frequently documented in the EMR, followed by moderate to severe pain (34.4%) and mild pain (16.9%). 15 shifts were excluded for having no pain documentation during the shift. Only 16.0% of shifts used a gold-standard non-verbal pain assessment tool. The GEE identified that nurse-documented pain was not associated with RoC. The odds ratios for mild (OR=1.4, 95% CI=0.4–2.7) and moderate-severe pain (OR=1.1, 95% CI=0.2–1.5) vs. no pain were both non-significant. This remained non-significant after accounting for pain and psychotropic medication use. Pain medication administration was significantly associated with RoC (OR = 2.7, 95% CI=1.0–6.93). The case series demonstrated 66.7% of observations as no pain, 11.1% mild pain, and 22.2% moderate to severe pain by the CNPI. Nurse charting matched the gold standard in 50.0% of the shifts, 38.9% did not match, and 11.1% there was no pain assessment charted. Provider documented pain assessment was present in 50% of daily progress notes. Providers failed to document pain in all shifts where the gold standard identified pain.

Conclusion: Although no association between nurse-identified pain and RoC was demonstrated, only 16.0% of nurse pain assessments used a gold-standard non-verbal observational tool, potentially contributing to under recognition of pain. Prior research evaluating the relationship between pain and RoC using observational pain tools have yielded different findings. Pain medication was the only significant predictor in this model suggesting that because more severe pain leads to treatment the true impact of pain on RoC may be captured through the medication administration record rather than nurse assessment in the EMR. The concern for accuracy of nurse-charted pain assessment was supported by evidence of disagreement between nurse documentation and the gold standard assessment. Additionally, the lack of documented pain assessment by providers in half of the shifts and failure to document pain in all cases captured by the gold standard suggests an area for improvement. These findings underscore substantial gaps in pain recognition and documentation that may impede appropriate pain management in PLWD.

Knock out of Lactate Transporters MCT1 and MCT4 Differentially Polarize T Cells Towards a Tfh and Th1 phenotype during *Plasmodium* Infection.

Gabriel Weigel, Taylen Nappi, Dr. Noah Butler

Introduction: *Plasmodium*, the causative parasite of malaria, is a global health burden infecting over 280 million people and killing 610,000 across 80 countries in 2024. A major challenge to eradicating the disease has been a lack of long-term sterilizing immunity both to infection and vaccines. Pathogenic species of the parasite have a complicated life cycle between mosquito, and the liver and blood stages of infected human hosts and evolved numerous mechanisms to subvert the immune response. In addition to protein polymorphism and antigenic drift, evidence suggests *Plasmodium* leverages metabolic disturbances to gain a competitive advantage over the immune system. Lactatemia and hypoglycemia are two metabolic symptoms of *Plasmodium* infection that can also be seen in mouse models to correlate with parasite burden. Data from the lab suggests that the mouse spleen, which plays a critical component in clearing *Plasmodium* in humans and mice, undergoes durable changes to the metabolome after infection. To clear the infection, Th1 and Tfh cells are indispensable for activating macrophages and B cells, respectively. Th1 and Tfh cells have distinct metabolic needs; Th1 cells are more glycolytic, and Tfh cells are more reliant on mitochondrial electron transport for energy. How metabolic disturbances, such as lactatemia and hypoglycemia, affect the balance of these two T cell populations during blood stages of *Plasmodium* is unknown. The Butler lab investigated two transporters of lactate called MCT1 and MCT4 to define their role in regulating metabolic homeostasis in Th1 and Tfh cells.

Hypothesis: Knock out of the high affinity lactate transporter, MCT1, will shift lactate out of the cells relative to controls leading to greater reliance on glycolysis and supporting a Th1 phenotype. Knock out of the low affinity lactate transporter, MCT4, will shift lactate into the cells relative to controls leading to a greater reliance on lactate as a source of energy and a Tfh phenotype.

Method: Four groups of transgenic CD4 T cells expressing the same TCR for *Plasmodium* (PbTII cells) will be injected via tail vein into C57BL/6J mice, who are then infected with *Plasmodium berghei* the following day. The PbTII cells will be isolated from the spleen and lymph nodes of MCT1-floxed mice with or without the expression of cre under the CD4 promoter. These two groups of PbTII cells will then undergo CRISPR with MCT4 or CD8 (control) gRNA. On day 12 of infection, the PbTII cells are isolated from the spleen and polarization towards the Th1 or the Tfh phenotype was assessed using flow cytometry.

Results: MCT1 KO PbTII cells were more polarized towards the Th1 phenotype as seen by an increase in CXCR6 and the transcription factor TBET. MCT4 KO and MCT1/MCT4 dKO PbTII cells were more polarized towards the Tfh phenotype as seen by an increase in CXCR5 and the transcription factor BCL6.

Conclusion: We show in these experiments that lactate transport in *Plasmodium*-specific T cells contributes to T cell differentiation. Leveraging these transporters could help health professionals tailor an immune response towards either Th1 differentiation to control parasite burden acutely or Tfh development during vaccination to stimulate a better antibody response.

Recurrence After Revision Shoulder Stabilization: Two-Year Results from the MOON Shoulder Cohort

Carter J. Weyman, Shannon F. Ortiz, MPH, Warren R. Dunn, MD, MPH, Carolyn M. Hettrich, MD, MPH, and MOON Shoulder Group, Brian R. Wolf, MD, MS

BACKGROUND: Revision anterior shoulder instability stabilization patients represent a distinct clinical subgroup, often presenting with a greater cumulative burden of instability events and altered glenohumeral anatomy, suggesting outcomes after revision surgery may not parallel those after primary stabilization. Therefore, revision anterior shoulder stabilization remains a complex and understudied clinical scenario, with prior studies predominantly small, retrospective, and single-center. The MOON Shoulder Instability Group was established to prospectively collect standardized demographic, clinical, surgical, and patient-reported outcome data across multiple centers in patients undergoing anterior shoulder stabilization, providing an opportunity to characterize outcomes in this understudied population.

PURPOSE: The purpose of this study was to report 2-year prospective multicenter outcomes in a large revision shoulder stabilization cohort, including rates of reoperation, recurrent dislocation, and subluxation, as well as patient and surgical risk factors associated with recurrent instability and patient-reported outcomes.

METHODS: Patients enrolled in the MOON Shoulder Instability database who underwent revision anterior shoulder stabilization were prospectively followed. Of the 275 enrolled patients, 228 (82.9%) had 2-year follow-up data. Primary outcomes included reoperation, dislocation, and subluxation at 2 years. Secondary outcomes included change in ASES and WOSI scores from baseline to 2 years. Patient factors analyzed included Beighton score, preoperative dislocation number, bone loss, and preoperative shoulder activity level. Surgical factors analyzed included revision procedure type, categorized as bony/Latarjet, open soft tissue, or arthroscopic.

RESULTS: Of the 228 patients with 2-year data, Bony revision trended toward lower reoperation ($p=.086$) and dislocation rates ($p=.062$) compared with arthroscopic revision, though neither reached statistical significance. Patients with more than 5 preoperative dislocations had significantly higher rates of glenoid bone loss $\geq 20\%$ (51.9% vs. 9.1%, $p=.0002$) and were significantly more likely to undergo bony/Latarjet revision (63.6% vs. 13.6%, $p<.0001$) compared with patients with no preoperative dislocations. Despite this greater bone loss burden, 2-year outcomes were equivalent between these groups (ASES $p=.88$; WOSI $p=.80$; composite failure $p=.81$). Higher preoperative shoulder activity level correlated with better 2-year ASES ($p=.037$) and WOSI ($p=.006$), with no correlation with baseline scores. Patients with bone loss had significantly lower mean Beighton scores than those without bone loss ($p=.0138$). Higher Beighton score predicted subluxation ($p=.0014$) but not dislocation ($p=.256$).

CONCLUSION: Bony revision demonstrated numerically lower reoperation and dislocation rates compared with arthroscopic revision, though these differences did not reach statistical significance. Appropriate surgical escalation toward bony procedures in patients with more frequent preoperative dislocations and greater bone loss appeared to normalize 2-year outcomes across severity groups. Higher preoperative shoulder activity level independently predicted better 2-year patient-reported outcomes without correlation with baseline scores, suggesting this reflects true recovery potential rather than a baseline difference. Higher Beighton score was associated with less bone loss and predicted perceived subluxation without predicting mechanical dislocation, which may inform preoperative counseling in hypermobile patients.

Patient Characteristics and Retention at Iowa's Only Same-Day Walk-In MAT Clinic

Collaborators: Karl Wilson, Sayeh Sabbagh, Nicholas Bormann, Benjamin Miskle, Andrea Weber

Background: A core principle of patient-centered treatment is meeting individuals where they are. Many individuals with substance use disorders (SUDs) do not receive treatment for a myriad of reasons, including lack of access, highlighting the importance of understanding different models of addiction care. One such model, Rapid Access Addiction Medicine (RAAM) walk-in clinics, provides low-barrier, rapid treatment for SUDs. This model differs from bridge clinics, which primarily focus on transitions between inpatient and outpatient SUD treatment settings. While prior studies have demonstrated the effectiveness of RAAM clinics in urban settings, this retrospective chart review describes patient characteristics, care patterns, and retention among patients from predominantly rural areas. These patients, seen between December 2021 and December 2025, visited the only RAAM-style clinic in Iowa offering same-day diagnosis and medication management for SUDs.

Methods: This retrospective chart review used Epic Reporting Workbench and SlicerDicer to collect electronic health record (EHR) data from adult patients seen at The University of Iowa Medication for Addiction Treatment (MAT) walk-in clinic between December 1, 2021, and December 31, 2025. Data were reviewed to examine trends in walk-in encounters over time, patient demographics, encounter diagnoses at intake, medications prescribed, and 1-year retention, defined as attending at least two follow-up visits within 365 days of intake. Logistic regression analyses were performed using RStudio to evaluate associations between demographic and clinical characteristics and treatment retention.

Results: Data analysis identified 566 adult patients who completed an intake visit at the MAT walk-in clinic between December 1, 2021, and December 31, 2025. The cohort included 386 males and 180 females with a mean age of 42.6 years (SD = 12.2). The cohort was predominantly White (82.2%), with smaller proportions identifying as African American/Black (7.6%), Multiracial (2.5%), Hispanic/Latino (2.3%), Asian (0.7%), and American Indian/Alaska Native (0.2%). Patients represented 51 counties across 8 states, including 31 rural and 20 urban counties, with the majority residing in Iowa and Illinois. The most common substance use disorder diagnoses at intake were opioid use disorder (n=378, 66.8%), alcohol use disorder (n=187, 33.0%), stimulant use disorder (n=153, 27.0%), and tobacco/nicotine use disorder (n=77, 13.6%), with the majority have more than 1 SUD. Patients frequently had multiple encounter diagnoses, including multiple diagnoses within the same SUD category. Buprenorphine-containing formulations (including buprenorphine-naloxone) were the most prescribed medications at intake (n=430), followed by naloxone, naltrexone, bupropion, and gabapentin, with some patients prescribed multiple medications. Among all patients, 417 attended at least one follow-up appointment. Among patients with at least one follow-up visit, the mean number of follow-up visits was 6.9. Retention, as previously defined, was met by 318 patients (56.2%). In logistic regression analyses, receipt of a prescription at the intake encounter was associated with greater odds of 1-year retention (OR 2.23, 95% CI 1.35–3.73, $p = 0.002$). Age, sex, rural versus urban residence, primary insurance coverage group (commercial, Medicare, Medicaid, Self-Pay/other), and distance from clinic were not significantly associated with retention.

Conclusions and Discussion: The University of Iowa MAT walk-in clinic is currently the only RAAM-style program in Iowa providing medication initiation for patients with co-occurring substance use and psychiatric disorders. Expansion of similar RAAM models into rural areas, particularly with the integration of tele-health services, may help reduce geographic and transportation-related barriers to care. Preliminary findings demonstrate substantial utilization of the MAT walk-in clinic across a largely rural geographic region, including patients from more than 40 counties across Iowa and Illinois. Retention rates were notable, with 56.2% of patients retained at one year. Additionally, patients who attended at least one follow-up visit averaged 6.9 follow-up appointments, suggesting sustained engagement in care following intake. These findings support the potential benefit and impact of RAAM clinics while also demonstrating that this treatment model can succeed in a largely rural setting. Retention analysis data suggests that timely initiation of treatment may support ongoing engagement in care, and that geographic barriers alone may not explain retention in this population. Limitations include the retrospective single-center design, reliance on electronic health record data that may be incomplete, and the potential for unmeasured confounding from clinical and social factors not captured in the dataset.

Title: CellSpy: A fully automated immunofluorescent image analysis tool.

Author List: Brett Wineinger, Amy L. Ryan

Introduction: Immunofluorescent (IF) imaging is a widely used technique for visualizing cell structure and behavior; providing detailed visualization of cell distribution, marker colocalization, morphology, and spatial organization. However, IF is inherently qualitative and converting these observations into reliable quantitative measurements remains a significant challenge. Although software platforms such as FIJI, CellProfiler, and QuPath facilitate image analysis, they often require substantial optimization and manual intervention, limiting reproducibility and accessibility. Consequently, a fully automated, accurate, and open-source solution for IF image quantification has yet to be established.

Purpose: The purpose of this project is to develop a fully automated immunofluorescence (IF) image analysis platform that combines ease of use and accuracy with minimal user intervention. Our solution is “CellSpy”, designed as a “click-and-go” solution that streamlines image quantification and substantially reduces the time researchers spend on routine analysis workflows.

Methodology: CellSpy was coded in Python using OpenAI’s ChatGPT 5.5 on Codex. Initially, the confocal microscope images are split into individual channels and transformed into maximum intensity projections in .TIF format. After preprocessing is the initial segmentation of the cell boundaries. This is done to identify and define the regions of interest (cells) in the image. This segmentation is done using CellPose’s cpsam_v2, which is a fine-tuned variation of Facebook Research's SAM (Segment Anything Model) designed to identify different cellular stains. After the initial segmentation is completed, the various stains of interest are overlayed on top of the newly defined regions of interest. From here CellSpy inspects the intensity of the pixels within the regions of interest and based on the settings defined by the user, classifies the cell as positive or negative for a given marker. This repeats every cell and every stain.

Results: CellSpy successfully performed the automated workflow and accurately quantified the IF images without user intervention. The platform generated measurements of cell count, cell area, colocalized (double-positive) cells, stain-specific area coverage, and the proportion of segmented versus unsegmented image area as a surrogate measure of cytoskeletal disorganization. Quantitative outputs were comparable to manual image analysis, demonstrating the accuracy of the approach. In addition, CellSpy analyzed each image in approximately two minutes, enabling rapid and efficient data processing.

Overall Significance: CellSpy addresses a critical unmet need for a fully automated IF image analysis workflow, enabling researchers to reduce the time and effort required for image quantification while maintaining high analytical quality. In addition to standard IF measurements, CellSpy can quantify cytoskeletal disorganization in images containing a cell boundary marker such as phalloidin, providing a novel metric that is not readily available in existing analysis platforms. CellSpy delivers automated, accurate analysis of IF images with performance comparable to manual quantification. The platform also offers customizable settings that can be tailored to diverse experimental applications while maintaining an intuitive, user-friendly interface that avoids unnecessary complexity

Improvements in Glaucoma Medication Reconciliation Using Structured Versus Free Text Entry

Student: Angela Wong, M2

Mentor: Andrew Pouw, MD

Introduction:

Medication reconciliation is the process of maintaining a complete and accurate medication list throughout the electronic health record (EHR). This is especially important in the glaucoma setting, where patients may use multiple medications with different doses, dosing frequencies, and laterality. In the glaucoma clinic at UIHC, medication lists and information is documented in several locations in Epic, including the discrete medication list, the provider's clinic note, and the after-visit summary (AVS), which is printed and given to the patient. Medication discrepancies can include missing medications or differences in dose, frequency, and laterality across these sources, resulting in inconsistent medication information for both patients and providers and potentially affecting quality of care. This study evaluates whether using a structured Epic medication documentation template improves medication documentation concordance and accuracy compared with free-text entry, which was previously the predominant documentation practice.

Methods:

This is a retrospective pre-post chart review of patient encounters and medications in the glaucoma clinic at UIHC. A structured medication documentation template using native Epic SmartLink functionality was implemented in the documentation workflow of a single glaucoma provider, replacing the free-text based medication documentation. At the time of analysis, approximately three weeks of pre-implementation and four weeks of post-implementation encounters were reviewed, with additional weeks currently being collected. For each eligible encounter, the "source of truth" list of medications was identified from the provider clinic note and compared with the discrete medication list for concordance of dose, frequency, laterality, and overall medication presence. Medication list inclusion in the after-visit summary (AVS) was evaluated separately as an additional outcome because medication documentation in the AVS was limited, particularly before implementation. Each concordance outcome was coded as concordant or discordant, and pre- and post-implementation rates were compared using two-sided Fisher's exact tests.

Results:

While data collection and analysis are still ongoing, 184 patient encounters were included in a preliminary analysis, including 253 pre-implementation and 174 post-implementation medication-level observations. Medication presence concordance increased from 92.9% (235/253) before implementation to 100% (174/174) after implementation ($p < 0.001$). Dose concordance increased from 92.1% (233/253) to 99.4% (173/174), frequency concordance increased from 87.0% (220/253) to 97.7% (170/174), and laterality concordance increased from 87.7% (222/253) to 97.7% (170/174) (all $p < 0.001$). Medication inclusion in the AVS, which was evaluated separately from the concordance measures, increased from 36.0% (91/253) before implementation to 82.2% (143/174) after implementation.

Conclusion:

Preliminary results suggest that structured medication documentation in Epic improves medication concordance and increases medication inclusion in the AVS compared with free-text documentation. These findings support structured documentation as a simple approach to improving medication accuracy and consistency in the glaucoma clinic.

Annualized Changes in Brain Structure and Function in Juvenile-Onset Huntington's Disease

Manar Yaseen; Peggy Nopoulos

Introduction: Juvenile-onset Huntington's disease (JoHD) is an advanced form of HD where symptoms occur before age 20, rather than middle age. Because JoHD accounts for approximately 5% of Huntington's disease (HD) cases, characterizing the disease trajectory for these patients is challenging. Because adult-onset HD (AOHD) changes gradually over years, identifying reliable short-interval markers of JoHD progression could improve characterization of disease progression and provide measurable outcomes for future therapeutic trials.

Hypothesis/Purpose: We quantified longitudinal change in motor function, inhibitory control, and striatal brain volume in JoHD. We hypothesized accelerated neurodegeneration and cognition over one year relative to gene non-expanded (GNE) controls and disease-stage-matched AOHD.

Methods: We compared our the yearly changes in our measures of interest between 16 JoHD participants (ages 6-30 years) and 1) 48 age- and sex-matched GNE individuals and 2) 48 AOHD participants matched on years since motor symptom onset. Motor severity was measured using the Unified Huntington's Disease Rating Scale Total Motor Score (TMS). Inhibitory control was assessed with Flanker in JoHD/GNE and Stroop Interference in AOHD and compared as percent change. Striatal volumes were obtained from structural MRI and normalized to estimated total intracranial volume (eTIV). ANCOVA was used for group comparisons, adjusting for baseline age, sex, and follow-up interval where applicable, and AOHD MRI change is annualized to account for differing follow-up intervals.

Results: The direct annualized change comparison showed nominally greater JoHD motor symptom worsening (+5.70 TMS points/year, 95% CI -0.18 to 11.57; $p=.057$) compared to GNE controls. Cognitive change did not differ between JoHD and GNE controls (+0.69 percentage points; $p=.878$). Striatal volume changes favored greater JoHD loss but were not statistically significant; the striatal adjusted difference was -0.042% eTIV (95% CI -0.141 to 0.058; $p=.387$). Compared with AOHD, JoHD did not show significantly faster motor change (+5.14 TMS points/year; 95% CI -0.0253 to 0.236; $p=.331$), cognitive change (+0.35 percentage points; 95%CI -13.36 to 14.06; $p=.959$), or annualized striatal volume loss (-0.001% eTIV; 95% CI -0.0253 to 0.236; $p=.944$).

Conclusion: The similar longitudinal changes observed between JoHD and AOHD suggest that greater impairment in JoHD may reflect differences present at baseline rather than a consistently faster rate of progression over the observed interval. These findings advance the longitudinal characterization of JoHD, with the observed pattern of greater short-interval motor worsening relative to controls supporting continued investigation of motor function as a potential marker of progression. The study also provides effect estimates and a foundation for larger longitudinal studies aimed at identifying sensitive outcome measures for future therapeutic trials.

Title: Mathematically Modeling Antisense Transcription in Cardiac Stress
Student: Hye-Lin Yoo
Mentor: Colleen Mitchell

Our group is developing a mathematical model for transcription of a gene locus implicated in cardiac stress. The Myh6/Myh7 locus codes for myosin heavy chain and when the heart is under stress, there is a switch from relatively higher production of Myh6 to relatively higher production of Myh7. On the antisense strand, there is the Mhrt gene, which overlaps the Myh7 locus by about 3,000 base pairs and is important in regulating transcription of both Myh6 and Myh7. Previous work in the group constructed a stochastic process model for transcriptional interference in that 3,000 bp overlap where RNAPs that are transcribing in opposite directions (antisense transcription) collide and are both dislodged, preventing successful transcription. This model was used to obtain probabilities of successful transcription of each gene, which was input into a comprehensive mathematical model of transcription at the gene locus, which has displayed notable mathematical behavior like bifurcation and hysteresis. Simulations of the present model produced an approximately all-or-nothing effect where if one gene has a non-zero probability of successful transcription, the other has a zero probability. However, when we added another layer to the simulation by accounting for promoter availability using a Markov-chain, we observed not only successful transcription of both genes but also a higher probability of successful transcription for both genes in certain cases, depending on the rate at which we modeled the promoter switching between the available and unavailable states. We suspect this may be due to the promoter remaining “available” for longer stretches of time, which promotes a “buffering” effect where an RNAP trailing behind multiple RNAPs is protected from collision. Additionally, the longer stretches of “unavailability” would allow RNAPs on the antisense strand to complete transcription. It would be interesting to incorporate these new probabilities into the comprehensive model and see how the system behaves. Ultimately, this work seeks to understand the dynamics of transcriptional interference in antisense transcription, which is relevant to 40-60% of transcribed mammalian genes, and furthermore, how the Myh6/Myh7 locus behaves, which may help us understand the pathological state of a stressed heart.

Comparing Outcomes in Distal Femur Fractures of the Native Femur and Peri-prosthetic Above Total Knee Arthroplasty: Distal Femur Replacement vs Open Reduction Internal Fixation

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Background: An aging population is expected to experience more distal femur fractures, both above native knee joints and total knee arthroplasties. Determining optimal surgical treatment is essential to improving outcomes. Patients experiencing poor surgical outcomes may suffer from infection, nonunion, and hardware failure, among other adverse outcomes. Given the mixed literature regarding Distal Femoral Replacement (DFR) vs Open Reduction Internal Fixation (ORIF), treatment decisions are often made based on hospital and surgeon preference. This study compares the surgical and functional outcomes of patients with native or periprosthetic distal femur fractures who were initially treated with ORIF or DFR in a large cohort over twelve years.

Hypothesis: ORIF and DFR are valid treatment options for distal femur fractures, with similar surgical and functional outcomes at the latest follow-up.

Methods: We retrospectively reviewed medical records of all eligible patients seen at UIHC from 2013-2025. Eligible patients were at least 18 years old, with a distal femur fracture between the metadiaphyseal junction and the articular surface. Patients were categorized by whether the distal femur fracture was above a native knee or an existing total knee arthroplasty, and by whether the primary surgical treatment was ORIF or DFR. Surgical success was defined as favorable clinical outcomes and healing after primary surgery. Flawed success was defined as patients requiring at least 1 additional surgery but still achieved healing and favorable outcomes. Failure was defined as patients never reaching healing or favorable outcomes, as well as DFRs converted to amputations, and ORIFs converted to DFR. Surgical outcomes were analyzed using Cox Proportional Hazard Regression. Additional variables collected included reoperation rate, ambulation status, range of motion, and PROMIS Global Physical Health T-score at the most recent follow-up date, which were analyzed using appropriate regression models.

Results: 390 total distal femur fractures were included in the study, including 191 Native ORIF, 5 Native DFR, 150 Periprosthetic ORIF, and 43 Periprosthetic DFR. Surgical success was achieved in 69.79%, 60%, 76.67%, and 83.72% of patients, respectively. Multivariable Cox regression adjusted for age, BMI, sex, laterality, and fracture type showed that ORIF was associated with a higher hazard ratio of failure or flawed success than DFR (HR: 2.096, CI 1.006-4.364, $p=0.0481$). When adjusted for joint status, ORIF had 1.67 $\times$ higher odds of not achieving satisfactory ROM than DFR (95% CI: 0.85–3.31, $p = 0.140$). Within the native cohort, reoperation rates were higher among DFR patients than among ORIF patients (40% vs 25%, though the small native DFR cohort limits interpretation), while reoperation rates were lower among periprosthetic DFR patients than among periprosthetic ORIF patients (16.3% vs 20%). After adjusting for joint status, DFR showed higher rates of independent ambulation than ORIF. ORIF was associated with 2.12 $\times$ higher odds of worse mobility than DFR (OR = 2.12, 95% CI 1.05–4.27, $p = 0.037$). The periprosthetic DFR cohort demonstrated higher rates of satisfactory range of motion than the periprosthetic ORIF cohort, at 56.4% and 41.4%, respectively, although this relationship was insignificant ($p=0.139$). PROMIS Physical Health T-Scores were higher among DFR patients than ORIF, but results were insignificant after adjustment ($p=0.30$).

Conclusions: Surgical success rates varied among DFR and ORIF of distal femur fractures in native femurs and above total knee arthroplasties, and ORIF was associated with higher hazard of failure or flawed success. DFR tends to display more favorable functional outcomes, with variable significance. Future directions include identifying risk factors for ORIF failure and increasing the size of the native DFR cohort. This study will encourage discussions between trauma and arthroplasty teams to determine the most appropriate treatment.

Chronic Kidney Disease Prevention in Iowa Primary Care: An Interview Study

Hannah Zadeh, PhD; Aloha D. Wilks, CPC; Martha L. Carvour, MD, PhD

Introduction: Primary care providers (PCPs) hold a central role in the identification of early-stage chronic kidney disease (CKD) and prevention of further decline in patients' kidney function. This role may be especially crucial in states like Iowa, which has one of the lowest numbers of nephrologists per capita.

Purpose: The aim of this study was to explore how Iowa PCPs navigate their role in kidney care, what challenges they encounter, and how differences in PCPs' practice setting (academic center vs. rural community) shape their experience.

Methods: Semi-structured Interviews were conducted with PCPs working in Iowa. Interviews covered a range of topics, including measures used to monitor kidney function, use of kidney care guidelines, experiences with subspecialty referrals, and barriers to kidney care prevention and treatment in the primary care setting. Interviews were recorded and transcribed. Thematic analysis was conducted.

Results: Interviews were conducted with 16 PCPs, 7 of whom were either currently working in or had previous experience working in a rural community setting. Four main themes were identified, all of which were concerned with time: that is, what kind of time is valued and/or what timeline takes precedence.

- *Time Available for Appointments:* PCPs emphasized short appointment times as a significant barrier. Specifically, they said that more time is needed for in-depth discussions about strategies to prevent kidney function decline and about why patients are struggling to execute those strategies. As one PCP put it: "It's very quick for me to say: Oh, you need to exercise. You need to eat better and lose weight. That took 6 seconds. But to really get at *why* they can't do those things is much more difficult."
- *Imminent vs Future Outcomes:* PCPs discussed the discordant time scales of progressive kidney function decline and patients' everyday lives. On the one hand, CKD is asymptomatic until kidney function declines to extremely low levels; and this progression typically happens on the scale of several years or decades. On the other hand, patients are often dealing with immediate symptoms, like chronic pain, and urgent life situations, like finding work, making rent, or providing for dependents. "You have somebody doing manual labor, and their back hurts, and Tylenol doesn't work for them, but NSAIDs do. And I say, [NSAIDs are] not the best for your kidneys. Okay, but if it gets them relief and then they can get up and work the next day, they're probably still going to take it."
- *Logistical Costs of Care:* PCPs highlighted the complex dynamics affecting patients' time, including time costs accrued by patients seeking care. PCPs in university and rural community settings reported that the main barrier to nephrology referrals was *not* a lack of available nephrologists or appointment slots. Instead, they emphasized logistical challenges to get to the appointments, including transportation and scheduling logistics related to patients' work and other responsibilities: "[Patients] can't just plan to be gone for a day next week, even if they could be seen [in the renal clinic]."
- *Timing of Referrals:* PCPs expressed concerns about timing their own referrals to nephrology. PCPs working in academic settings mostly indicated that they use glomerular filtration rate or CKD stages as benchmarks for referrals, whereas PCPs working in rural settings said they also frequently consider whether they think the patient will be able to make it to a referral appointment. Some PCPs also expressed hesitancy to refer to prevent "overburden[ing] an already taxed system," explaining that they learned to practice in a "culture" that trained them "to hold on to folks." Other PCPs expressed uncertainty about making referrals: "Like, are they gonna think I'm dumb if I put in this referral?"

Conclusion: PCPs' perspectives suggest that policies premised exclusively on short-term efficiency (e.g., squeezing in more patients per day, more relative value units) may run up against the goals of prevention and primary care and may, in turn, have important tradeoffs in care effectiveness and longer-term care efficiency. Importantly, PCPs reported that the main challenge to nephrology referrals was not a limited number of appointment slots but coordination between those slots and patients' lives. This finding may have important implications for optimizing referral systems and aligns with an enduring observation in the sociology of health and illness: control over one's time is a critical tool in disease prevention.

Ac2-26 Activates Concordant Plaque-Stabilization Programs in Reversa Mice and an Ex Vivo Human Coronary Atherosclerosis Model

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Background: Therapies that promote plaque stabilization in mouse models frequently lack direct evidence that the same molecular mechanisms operate in human coronary arteries, in part because intact living human coronary arteries cannot readily be studied experimentally. Ac2-26, an Annexin A1 mimetic, promotes plaque stabilization in murine atherosclerosis, but its transcriptional effects in human coronary arteries are unknown. We developed the Human Coronary Artery (HuCA) model, 300- μ m precision-cut sections of intact atherosclerotic human coronary arteries that permit controlled pharmacologic and transcriptomic interrogation *ex vivo*. This enabled comparison of Ac2-26 responses in HuCAPs and Reversa mice to identify concordant transcriptional programs across species.

Hypothesis: Ac2-26 induces concordant transcriptional programs associated with plaque stabilization in HuCAP tissue and murine atherosclerosis.

Methods: HuCAPs (300 μ m) were generated from coronary arteries from an explanted heart, incubated in low-cholesterol medium (LC) with or without Ac2-26 (2 μ M) for 72 hours, and analyzed by bulk RNA sequencing (edgeR, n=3/group). Aortic cross sections with atherosclerosis were collected from male Reversa mice after cholesterol lowering at 40 weeks with or without Ac2-26 treatment from weeks 44–48, and analyzed by Visium spatial transcriptomics (Seurat, n=3–4/group). Differential expression was defined as FDR<0.05. Of 17,258 human and 4,031 mouse genes tested, 3,683 orthologs were evaluable in both species. Cross-species concordance was assessed by Fisher's exact test and pre-ranked GSEA.

Results: Thirteen orthologous genes were independently upregulated at FDR<0.05 in both species, 3.7-fold more than expected by chance (3.53 genes; Fisher's exact OR 5.67, 95% CI 2.78–11.57; $P=1.4\times 10^{-5}$). Concordant genes included extracellular-matrix/remodeling genes COL3A1, COL4A1, COL4A2, COL5A1, COL6A1, SPARC, TGFB1, and the macrophage marker FOLR2. GSEA identified additional cross-species concordance in two independent programs, both significant after Benjamini-Hochberg correction across all tested gene sets: a contractile smooth-muscle program (human NES 2.01, q=0.001; mouse NES 1.76, q=0.003) and a published FOLR2⁺/LYVE1⁺ resident-like macrophage signature (human NES 2.05, q=0.001; mouse NES 1.61, q=0.011).

Conclusions: Ac2-26 elicited concordant extracellular-matrix, smooth-muscle, and FOLR2⁺/LYVE1⁺ resident-like macrophage transcriptional programs in Reversa atherosclerosis and HuCAP tissue. Concordance in this specific, literature-defined macrophage state, rather than a generic macrophage response, is consistent with Ac2-26's known pro-resolving mechanism of action. Significant gene-level overlap and concordant pathway enrichment provide initial human evidence that Ac2-26-responsive plaque-stabilization programs translate across species. Reproduction of an *in vivo* treatment response in HuCAP further supports this model as a biologically relevant platform for mechanistic and therapeutic studies of human coronary atherosclerosis.

Feasibility, Acceptability, and User Experience of the PACE-App: A Mixed-Methods Pilot Randomized Trial

By: Jennifer Zeng

Mentor: Dr. Nai-Ching (Allison Chi), PhD, RN, College of Nursing

Introduction: Chronic pain is the one that most significantly impairs quality of life in dementia and is significantly underdiagnosed and undertreated due to trouble identifying and communicating symptoms. Family caregivers often assume substantial responsibility for observing pain, documenting symptoms, and communicating with healthcare providers. Caregiver-centered tools that integrate assessment, tailored management strategies, tracking, and communication remain limited. The PACE-app (PAin Control Enhancement) is a web-based intervention developed to support caregivers in identifying and managing pain in individuals with dementia.

Purpose: To evaluate the feasibility and acceptability of the PACE-app in supporting pain management for persons with dementia and chronic pain, and to generate preliminary estimates of caregiver outcomes for a future randomized controlled trial.

Methods: We conducted a two-arm randomized feasibility trial in which family caregivers were assigned 1:1 to the PACE-app or usual care. Intervention participants used the app for 1 month; both groups completed assessments at baseline, 1 month, and 2 months. Feasibility and acceptability were assessed using recruitment and retention metrics, app-use analytics, surveys, and semi-structured interviews. Exploratory caregiver outcomes included pain-management self-efficacy, treatment adherence, burden, stress, and depressive symptoms.

Results: 79 caregivers were screened, 41 enrolled, and 18 completed the study. Among the 18 participants, the pain diary was the most highly used feature across all participants. Engagement was high for the first week but steadily declined over the four-week intervention. All interviewed caregivers (n=18) described the app as easy to use, and all identified improved communication or decision-making as a major benefit. Exploratory correlations suggested associations between higher care-recipient pain and poorer caregiver medication adherence and depressive symptoms.

Conclusion: The PACE-app demonstrated encouraging feasibility and acceptability, particularly for pain tracking and organization of information. Declining engagement and uneven use of lower-value features highlight priorities for refinement before a larger trial. These findings support continued evaluation of an integrated, caregiver-centered digital approach to pain management in dementia care.

Effect of surgical treatment of hydrocephalus on radiographic parameters and neurological development in pediatric myelomeningocele patients in Zambia

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Objectives: Infants born with myelomeningocele (MMC) develop an associated clinical manifestation of hydrocephalus in 57-86% of cases. Hydrocephalus is associated with elevated intracranial pressure, which can interfere with neurodevelopment or lead to death. The study objective was to determine the effect of surgical treatment of hydrocephalus on anterior horn width (AHW) and neurodevelopment in infants with MMC in Zambia.

Methods: This prospective cohort study included infants under 1 year of age with MMC who received surgical treatment of hydrocephalus (ventriculoperitoneal shunt (VPS) insertion or endoscopic third ventriculostomy (ETV)) at the University Teaching Hospital in Lusaka, Zambia between April 2024 and January 2026. Subjects were excluded for a history of hypoxic ischemic encephalopathy. The primary outcome was AHW, measured on head ultrasound preoperatively and at 7 months postoperatively. The secondary outcome was Malawian Development Assessment Tool (MDAT) Z-score as a proxy for neurodevelopmental status at 7 months post-hydrocephalus treatment.

Results: 18 infants met inclusion criteria and 50% were male (n=9). Median age at time of index hydrocephalus surgery was 117 [IQR 47-178] days. VPS and ETV were the index surgical treatment in 13 (72%) cases and 5 (28%), respectively. 3 required surgical revision (17%) within the 7-month study period. The median preoperative right AHW was 21 [IQR 15-33] mm and postoperatively was 21 [IQR 15-31] mm. Preoperative left AHW was 22 [IQR 14-33] mm and postoperatively was 22 [IQR 13-30] mm. There was no significant difference in postoperative AHW compared to preoperative AHW ($p>0.05$). The median global MDAT z-score was -2.23 [IQR (-2.89)-(-0.94)]. In the subsections, the median MDAT z-scores were -3.06 [IQR (-3.70)-(-2.45)], -0.03 [IQR (-0.97)-0.45], 0.89 [IQR 0.14-1.80], and -0.73 [IQR (-1.56)-0.54] for gross motor, fine motor, language, and social respectively. MDAT gross motor Z-score was inversely associated with preop AHW ($p=0.047$). There was no association between the other MDAT Z-scores and AHW.

Conclusion: Smaller preoperative AHW was associated with higher MDAT z-scores at 7 months post hydrocephalus repair in this prospective infant cohort in Zambia. This association suggests improved infant neurological development in Zambian children with MMC who have smaller AHW at 7 months postoperatively. Further study is warranted to assess causation and long-term outcomes.