IMPRS Abstracts

A Qualitative Analysis of Participant Perceptions of a Human-Centered, Co-Designed Diabetes Prevention Program

Aders E, Pike J, Hannon T

Background: Youth weight management programs are effective for reducing risk factors for type 2 diabetes (T2D) but have poor rates of participation. Little research exists regarding program characteristics that promote engagement and health improvements. We evaluated perceptions of a co-designed youth weight management program (PowerHouse).

Project Methods: We interviewed five mother-child dyads (youth aged 7-18 years) who participated for 6 months in PowerHouse. Youth met criteria for overweight or obesity (BMI ≥85th percentile) and had two or more additional risk factors for T2D. One interviewer engaged each dyad separately. Each interview transcript was standardized using a predetermined format and words such as uhm and like were eliminated. Transcripts were uploaded into Atlas.ti qualitative analysis software. Emergent thematic coding was performed, and broad themes related to participant expectations, likes, and dislikes were identified.

Results: The following themes emerged: 1) Parent expectations focused on their children's actions and behaviors rather than their own. Parents want children to learn to make "good choices now so as they get older, they would potentially be in the situation of not having diabetes"; 2) Participants liked to "learn something new and to try something new" rather learning didactically and shared meaningful social interactions, realizing "a bunch of us are going through the same things"; 3) taking time away from a busy schedule when the whole family is not engaged is hard.

Potential Impact: This research suggests participants value socially engaging, experiential learning. Parents expect youth will take responsibility for their own health habits, which should be explored more fully in future work. Nonetheless, parental involvement and support is associated with better weight management outcomes in youth; thus, strategies that align parental and youth expectations are needed. Based on these findings, a strategy that includes shared-decision making, managed and aligned expectations, and goal setting with parent-youth dyads could further improve PowerHouse.

Extracellular DEK Treatment Increases Mitochondrial Dysfunction in the Mouse AML Cell Line MLL-AF9

Aguilar Neuville P, Ropa J, Gutch S, Capitano M

Acute myeloid leukemia (AML) is the most common kind of acute leukemia and the second most common type of leukemia in adults. Poor outcomes resulting from AML are thought to occur due to the inability to target the small pool of cancer-initiating cells that develop from cells within hematopoietic stem (HSC) and progenitor (HPC) cell compartments in bone marrow. DEK, a nuclear protein that can be secreted under stress conditions, plays a role in regulating HSC and HPC function. Extracellular DEK has been found to improve functional HSC expansion in in-vivo and ex-vivo mouse studies. Moreover, RNAseq experiments suggest that recombinant human DEK treatment causes the upregulation of the antioxidant gene programs. Indeed, DEK treatment reduces total reactive oxygen species (ROS) in human umbilical cord blood HSCs and HPCs. Thus, extracellular DEK enhances normal HSC function through antioxidant programs, but the role of the extracellular DEK in AML is unclear. We hypothesized that recombinant mouse (rm) DEK treatment of the mouse-derived AML cell line MLL-AF9 would affect mitochondrial function since mitochondria are an important source of ROS production. Since ROS production can contribute to mitochondrial dysfunction by causing damage to the organelles, we investigated the effects of DEK signaling on mitochondrial metabolism in MLL-AF9 cells using the Seahorse XF instrument, which can measure changes in metabolic flux. Compared to vehicle-treated control, cells treated with DEK demonstrated a decrease in basal and maximal mitochondrial respiration, proton leak, and non-mitochondrial oxygen consumption. Experiments to explore the effects of DEK treatment on the glycolytic function of MLL-AF9 cells are ongoing. Our data shows DEK treatment of MLL-AF9 cells alters mitochondrial function. In the future, we wish to investigate DEK's effect on proliferation and colony formation.

Altered White Matter Connectivity in Children with Prenatal Marijuana Exposure

Ahmad ST, Vishnubhotla RV, Zhao Y, Radhakrishnan R

Background: The potential health outcomes of cannabis use during pregnancy are currently not well-known. Several studies have shown an association between prenatal marijuana exposure (PME) and adverse neonatal outcomes. Specifically, cannabis use has been associated with an increased risk of cognitive deficits and neuropsychiatric disease. The aim of this project is to examine alterations in cerebral white matter connectivity of children with PME compared to unexposed controls based on diffusion tensor imaging (DTI). Identifying such microstructural alterations may help us better understand neurodevelopmental and cognitive effects of PME.

Hypothesis: We hypothesize that there will be differences in white matter connectivity in children with PME compared to controls.

Methods: DTI images for children with (n=88) and without (n=90) PME were obtained from the Adolescent Brain Cognitive Development (ABCD) Study database. Image quality assurance, preprocessing, and tractography were completed using DSI Studio. Fiber counts between 94 regions of interest were assessed. A groupwise comparison was performed to assess differences in structural connectivity in children with and without PME.

Results: The PME group and control group had 35 and 37 males, respectively. The mean age for both groups was 9.9 years. First level comparative analysis revealed alterations in microstructural connectivity between PME and control groups. Increased connectivity was found in the PME group compared to the control group in 51 tracts, while decreased connectivity was indicated in 22 tracts. However, significance was not maintained when corrected for multiple comparisons.

Conclusion/Impact: Although there were small alterations in brain structural connectivity in children with PME, these were not significant after correcting for multiple comparisons. It is possible that microstructural neuroplasticity in the developing brain lowers the impact of potential long-term adverse effects of marijuana exposure in utero. Further studies are required to understand longitudinal brain development and adverse neurodevelopmental and cognitive outcomes associated with PME.

Predicting Response to Polytrauma through Resolution of Immunologic Mediators

Ali I, McKinley T

Background/Objective: Traumatic injury can lead to hemorrhagic shock and hypoperfusion in patients precipitating multiple organ dysfunction. This study adopts a precision medicine approach to identifying biological markers in predicting patient response to polytraumatic injury. Clusters of cytokines can be used to model the immunologic response to traumatic injury. We hypothesized that analyzing the resolution of immunologic mediators in clusters would reveal differences among groups of patients identified to be sensitive/tolerant to hemorrhagic shock.

Methods: Patients were required to have a stay in the ICU, one surgical operation, and a lower extremity traumatic injury. Blood samples were collected on patients at 0, 1, 12, 24, and 48 hours after injury. Multiplex analyses of 33 immunologic mediators were performed. A square-root transformation was applied to Luminex data before calculating z-scores (scores > 3 eliminated). Z-scores were summed to calculate composite cluster scores. T-tests were conducted to determine statistical significance.

Results: High SHVL shows higher inflammatory cluster levels and lower orchestration than low SHVL. Low SHVL shows higher reparative cluster levels and lower orchestration than high SHVL. High SHVL shows higher proinflammatory 1 levels before 12 hr and at 48 hr than low SHVL. Low SHVL has higher proinflammatory 2 levels and less orchestration at 0, 12, and 24 hr. Low SHVL has higher type 2 cluster levels than high SHVL. SS shows higher lymphoid cluster levels at 0 hr and 1 hr than ST. SS has higher reparative cluster levels than ST, while ST has more orchestration. SS has higher proinflammatory 2 cytokine levels, while ST shows more orchestration. SS has higher type 2 cluster levels, while ST shows more orchestration.

Conclusions: Cumulative hypoperfusion at time of injury is correlated with higher inflammatory cluster and proinflammatory 1 and 2 cluster cytokine levels as shown by both high SHVL and SS groups. Sensitivity to hemorrhagic shock and lesser hypoperfusion correlate to higher reparative cytokine cluster levels. Proinflammatory 2 cluster cytokine levels can be used to predict organ dysfunction.

Clinical Impact and Implications: This work presents findings that can inform acute trauma care through immunologic mediators and patient characteristics.

Analysis of the Population and Distribution of Minorities in the State of Indiana that Utilize Dermatologic Care in the IU Health System

Arrocha D, Somani A

Background: Medical centers require reevaluations to appropriately adapt to everchanging societal needs. This study aims to disclose the extent to which IU Health (IUH) patient demographics represent Indiana's population. U.S. Census Bureau shows Indiana has had a 42.2% increase in its Hispanic population from 2010 to 2020. Via Cerner, thousands of patient demographics were obtained from the University Hospital (UH) and 4 other IUH dermatologic satellite locations – Zionsville, West, Meridian Crossing (MX), and Methodist – to assess whether patients who visit these locations accurately embody the drastically changing state population.

Methods: Cerner's "Kitchen Sink" tool generated a list of patients that had made an appointment at one of the 5 dermatological centers. The search was refined to 2021 and included ethnicity, preferred language, residential zip code, etc. This data was then crossreferenced with Indiana's Public Data, where 92 counties were grouped into 6 regions.

Results: Indiana's Public Data for 2021 revealed that 8.3% of the population identified as Hispanic. These Hispanics were localized into residential regions, with the majority being in region 1 (40%), followed by region 4 (29%), region 2 (10%), region 3 (9%), regions 5 (5%) and 6 (5%). Our analysis revealed that 0.6% of Hispanics in Indiana utilized an IUH dermatology facility. Interestingly, despite most Hispanics residing in region 1, only a total of 4% were seen by IUH (UH & MX).

Conclusion: Our preliminary findings show most Hispanics utilized an IUH facility in region 4, where they resided. Furthermore, we did not see any statistically significant differences in site preference within this group. However, we were surprised by the low number of Hispanics from other regions, especially region 1, utilizing IUH dermatologic care. This study raises the question of potential barriers (proximity, preferred language, lack of awareness, and need for dermatology services) to dermatologic care available to Hispanics within the IUH system. Further studies are needed to identify the cause and potential solutions to the discrepancies within the Hispanic community in Indiana and IUH Dermatology.

Brain folding increases in sharpness and complexity over third trimester-equivalent development
Basinski C, Garcia K

Background and Hypothesis: Gyrification, or convolution, of the cerebral cortex is a promising transdiagnostic marker for early neurodevelopment. Previous studies have related differences in sulcogyral shape to schizophrenia, bipolar disorder, and autism spectrum disorder, but the physical mechanisms underlying these differences remain poorly understood. The focus of this study was to explore decomposed curvature metrics, the principal curvatures, as physically meaningful quantitative biomarkers to track brain development. We hypothesize that the average sharpness and complexity of sulci and gyri, reflected by principal curvatures, increase throughout third trimester-equivalent development.

Methods: Cortical surfaces generated from magnetic resonance imaging (MRI) were obtained from the developing Human Connectome Project. Global sharpness was calculated from the principal curvature of maximum magnitude, with average sharpness defined separately for gyral (positive) and sulcal (negative) curvatures. Global complexity of folds (eg., curviness along the length of a fold) was calculated from variance in the principal curvature with minimum magnitude. Trajectory of each summary metric was fit over time using polynomial regression.

Results: Forty-three subjects were removed due to incomplete curvature analysis or missing subject information, such that 541 preterm and term-born infants were evaluated with scan age ranging from 27 to 45 weeks postmenstrual age (PMA). Across this developmental range, sharpness and complexity increased until a plateau around term-equivalent. Average sharpness of gyri was best correlated with age of scan ($R2 = 0.877$).

Conclusion and Potential Impact: During the pre- and postnatal development period, total cortical surface area continues to increase after birth, but the overall sharpness and complexity of folding plateaus at $\sim$37 weeks post-menstrual age. Exploring these physically meaningful curvature metrics can provide improved parameters for comparison to mechanistic models of brain folding.

Standardizing Virtual Curriculum – Examination of Slide Content to Improve Student Utilization
Bassett S, Husmann P

Background/Objective: The COVID-19 pandemic forced educational institutions to adapt their courses for a completely virtual experience within a matter of weeks. Instructors rose to the challenge although many were lacking experience in virtual instruction and had modest framework to guide their content creation. Several studies have been conducted examining the efficacy of virtual courses however, guidance for content creation is still not widespread. This study aimed to examine guidance for creation of virtual slide decks to determine if standardizing slide decks would improve student interaction with course materials.

Methods: This research used a retrospective analysis of Indiana University School of Medicine slide decks utilizing guidance from the IUPUI Center for Teaching and Learning to determine how existing slide decks aligned with pedagogical recommendations. Content examined included number of slides with more than six bullets, number of bullets with more than ten words, and graphic utilization. Overall number of slides and recording length were also analyzed. Number of "plays" was used as a metric to determine what content students accessed more frequently to examine the relationship between slide deck content and utilization.

Results: The relationship between bullets with more than ten words and number of plays demonstrated a negatively trending relationship whereby slide shows containing more slides exceeding ten words per bullet were played fewer times. Metrics concerning graphic utilization, slides with more than six bullets, recording length, and overall slide number did not yield conclusive results.

Conclusion and Potential Impact: This study demonstrated that the negatively trending relationship between content utilization

and exceeding ten words per bullet should be further explored. Examining this and other data points utilizing more accurate metrics will better elucidate the relationship between slide deck content and student utilization. This research will provide guidelines for instructors to streamline content delivery and improve the virtual education experience.

Prevalence and Clinical Characteristics of Adult Strabismus

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Purpose: Strabismus is a condition in which the eyes are misaligned causing double vision. While it primarily affects pediatric patients, adults may also present with strabismus due to various etiologies, but the occurrence of these are not well-established. This study aims to elucidate the prevalence of adult strabismus and its clinical risk factors.

Methods: This retrospective study reviewed charts of 1705 adult patient seen by the Indiana University School of Medicine Department of Ophthalmology between June 2016 and October 2020 for potential strabismus. Exclusion criteria included no diagnosis of strabismus or diplopia (n=42), not an adult patient (n=3), no charts available for review (n=105), and personal relation with a patient (n=3). Patient demographic, co-morbidity, ophthalmologic risk factor, and strabismus characteristic data was collected. Prevalence was calculated for each subclassification of strabismus, and clinical characteristics were discovered through calculation of odds ratios (OR).

Results: 1551 patient charts were included. The prevalence of esotropia (ET), exotropia (XT), and hypertropia (HT) was found to be 42.41%, 43.8%, and 44.04%, respectively. Combined vertical and horizontal strabismus was seen in 29.91% of patients. Patients 65 years and older had increased odds of having ET and HT (OR 1.67, 95% confidence interval (CI) (1.35, 2.05); OR 1.79, CI (1.45, 2.20)) but lower odds of having XT than their younger counterparts (OR 0.40, CI (0.32, 0.50)). Women had reduced odds of having ET compared to men (OR 0.63, CI (0.51,0.78)). Patients with low visual acuity (logMAR≥1) had much lower odds of having ET and HT (OR 0.43, CI (0.24, 0.78); OR 0.06, CI (0.02, 0.20)) but over four times greater odds of having XT (OR 4.34, CI (2.41, 7.84)). Hypertension, diabetes, and hyperlipidemia also affected the odds of having strabismus.

Conclusion: Adult strabismus remains a poorly understood condition; further research is necessary to facilitate individualization of care.

Ethanol Induces Blood-Brain Barrier Dysfunction in a Familial Alzheimer's Human Stem Cell-Derived Model

Bell KT, Hughes JM, Canfield SG

Background: The World Health Organization has linked alcohol consumption to neurodegenerative diseases, including Alzheimer's disease (AD). Additionally, heavy consumption of alcohol has been shown to cause a faster cognitive decline in AD patients. A subset of studies demonstrated that alcohol can diminish BBB integrity and independently AD patients have suppressed barrier properties, but the direct effect of alcohol on barrier integrity in AD patients remains unclear. In this study, we utilize a human stem cell-derived AD BBB model with near in vivo properties to investigate the effects of alcohol on critical barrier properties.

Methods: Brain microvascular endothelial cells (BMECs) were derived from healthy (IMR90) and AD (PSEN 1, PSEN 2, and APP) human-induced pluripotent stem cells (iPSCs). Healthy and AD cell lines were treated with physiologically relevant concentrations of alcohol (5, 25, and 50 mM). Following exposure, several critical barrier properties were monitored, including trans-endothelial electrical resistance (TEER) sodium fluorescein permeability, and tight junction localization. TEER was monitored following 30 minutes to 5-days post exposure. Permeability assay was performed at 24 hours and immunochemistry was conducted at 1 and 6 hours after treatment with ethanol.

Results: Moderate to severe alcohol exposure (25mM and 50mM) decreased barrier integrity in both healthy and AD-derived BMECs, as observed by an increase in sodium fluorescein permeability and a reduction in TEER. Furthermore, alcohol increased the number of discontinuous tight junctions directly contributing to the diminished barrier integrity. Interestingly, our preliminary results demonstrate that AD-derived BMECs are more susceptible to ethanol-induced barrier injury at lower concentrations of ethanol (5mM) compared to healthy-derived BMECs.

Conclusion and Potential Impact: Our results indicate that alcohol can diminish critical barrier properties in healthy-derived BMECs similarly to other non-human established BBB models. For the first time, we observed an increase sensitivity to alcohol-induced BBB dysfunction in a familial AD-derived BBB model. These data suggest that mild alcohol consumption could significantly alter the BBB and contribute to the development or exacerbation of AD-induced barrier dysfunction.

Gene Expression Data Points to a Role for Hypoxia in Medulloblastoma Pathogenesis

Blocher WA, Cooper SH, Richardson AM

Background: Medulloblastoma (MB) is the most common intracranial tumor in children. While molecular classification of MB is well-established, detailing cell origin, biological properties, and biomarkers, little research has been performed concerning the MB tumor microenvironment. Hypoxia is significantly associated with tumor spread, poor prognosis, malignant phenotype, and resistance to radiotherapy and chemotherapy in numerous cancer types. The aim of the present study was to assess a possible role for hypoxia in MB and the potential effect on clinical outcomes.

Methods: We, therefore, performed a systematic review examining the role of hypoxia in MB as well as pediatric brain tumors in general. In vitro studies have identified a role for HIF-1α in chemotherapy resistance, while patient samples suggest hypoxia-induced changes in gene expression as well as proteomic, metabolomic, and lipidomic profiles. Based on this literature review, 55 candidate hypoxia-related genes were identified. The PedcBioPortal for Integrated Childhood Cancer Genomics was used to assess expression differences in pediatric patient samples for these genes of interest.

Results: RNA expression was analyzed for correlation with survival, molecular group, and Chang stage. Expression of DDAH1, HYOU1, MYC, and RBX1 were significantly associated with survival. ANOVA and Ttest with a Bonferroni correction were used to assess for expression differences between groups and Chang stage. Multiple hypoxia candidate genes (ARNT2, BHLHE40, CYP3A5, DDAH1, DDIT4L, EGLN3, MT3, MYC, MYCN, TGFBR2, TP53, VEGFA) were significantly correlated with molecular group. Expression levels of TGFBR3 and GPR37 were associated with Chang stage.

Conclusion and Potential Impact: The results of our systematic review and gene expression analyses support a role for hypoxia in the pathogenesis and potentially the clinical outcomes of children with MB. Future studies comparing gene expression levels at normal oxygen tension (21%) and physiologic oxygen tension (1-3%) will allow us to assess the role of hypoxia in medulloblastoma pathogenesis.

Predicting Cognitive Impairment in Long-COVID Patients: A Demographic and Comorbid Analysis Using BrainCheck Cognitive Assessment

Bohn C, Li J, Todd N, Pater J, Carroll J, Henriksen B, Chang F

Introduction: Coronavirus disease (COVID-19) was declared a global pandemic by the World Health Organization (WHO) on March 11, 2020. From the onset in early January 2020 until now, we have made monumental steps toward combatting the deadly virus.

Now a subset of individuals are experiencing post-acute sequelae of COVID-19, more colloquially known as Long-COVID. Research surrounding the long-term consequences of COVID-19 is now at the height of importance as approximately 25-56% of individuals who were initially diagnosed with COVID-19 will go on to display new neuropsychiatric symptoms [5]. Mind long consequences of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection include brain fog, difficulties with memory, and focusing [3]. The burden of disease is substantial. Approximately 5.8% of individuals will be diagnosed with new psychiatric illnesses [8]. While many of the symptoms associated with Long-COVID have been summarized, the cognitive impairment that takes place because of COVID-19 infection were quantified in this study using BrainCheck cognitive assessment.

Methods: A retrospective chart review was conducted on subjects' data that was included in the Parkview Post-COVID Clinic (PPCC). BrainCheck cognitive assessment measures were the main cognitive metric utilized to assess cognitive impairment in patients. BrainCheck cognitive assessment compares patient's current cognitive levels to the national average by using normalizations and standard deviations. Subcategories of the BrainCheck cognitive assessment include attention, mental flexibility, executive functioning, and memory. Age, gender, weight, BMI, and hospitalization status were the demographic and predisposing factors that were analyzed, looking for correlations with levels of cognitive impairment experience by patients. Pearson Correlation Coefficient calculations were conducted on the continuous variables, and Point-Biserial Correlation Coefficient calculations were conducted on the dichotomous variables. Furthermore, ANOVA and chi-squared analysis was done to assess for differences among stratified groups.

Results: There is a correlation between age and mental flexibility (p-value = <.001, correlation = 0.3131), indicating that with increased age there is a less impairment in the mental flexibility aspect of cognitive function. There is a correlation between age and executive functioning digit symbol substitution (p-value = 0.03431, correlation = 0.1601), indicating that younger individuals will have worse cognitive impairment in complex attention and processing speed. There is also a correlation between age and executive functioning stroop color interference (p-value = 0.01904, correlation = 0.1661), indicating that younger individuals will experience a worse impairment in their judgement and decision making. There is a correlation between hospitalization status and immediate memory recognition (p-value = 0.01107, correlation = 0.1742), indicating that being hospitalized at the onset of COVID-19 infection leads to worse short-term memory. Lastly, when stratifying the sample by BMI, the chi-squared analysis yielded significance (chi-squared = 14.00, p-value = <.001) when comparing to BrainCheck mental flexibility scores. This would suggest that BMI has implications for differing levels of cognitive impairment in Long-COVID patients.

Conclusion: The aim of this study was to utilize the PPCC database to analyze levels of cognitive impairment in Long-COVID patients, looking for correlations between predisposing factors, as well as demographics. It was determined that age, BMI, and hospitalization status have indications for differing levels of impairment in certain aspects of cognition for patients experiencing Long-COVID symptoms. The goal is to inform clinicians on what levels of cognitive impairment to expect from Long-COVID patients and shed light on COVID-19's effect on the central nervous system.

Assessing the Impact of Physician Pain on Motivation to Provide Longitudinal Osteopathic Manipulative Therapy to Patients and its Correlation to Opioid Prescribing: A Cohort Study

Braly T, Jefferson E, Henriksen B

Background/Objective: In recent years physician wellness has become a priority. Current well-being initiatives focus on the emotional and spiritual components of health. However, physical pain and its relationship to wellbeing and patient care has not been examined. We hypothesize that reduction in resident physical pain would impact enthusiasm for providing OMT services and reduce opioid prescribing tendencies.

Methods: Both allopathic and osteopathic residents were offered biweekly OMT treatments from external osteopathic physicians. Pain scores were evaluated prior to each treatment session. The osteopathic resident cohort was surveyed regarding motivation to perform OMT. Subsequent patient OMT encounters were evaluated by tracking the number of body systems and the complexity of each OMT treatment. Patient BMI was also monitored as a measure of patient bodily habitus. Finally, the opioid prescribing habits of all enrolled resident participants were evaluated to correlate these scripts with participant pain levels.

Results: This study did not identify any statistically significant correlation between the regularity of delivered OMT services and physician physical wellness. Additionally, the PIs for this study did not observe a statistically significant correlation between volume or complexity of OMT services but did find a correlation between patient BMI and participants' reported pain.

Conclusion/Impact and Implications: Longitudinal OMT did not improve provider pain over time. Patient BMI did correlate with later DO pain scores after delivering OMT. There remains a need for physical wellness interventions to improve provider wellness.

Relationship of Trust and Research Engagement

Bruns R, Vinaixa C, Haywood A, Ridley-Merriweather KE, Sotto-Santiago S

Background/Objective: Lack of trust is a major barrier to research participation and can lead to disparities in health outcomes. Scales that measure trust in healthcare organizations and biomedical research have never been synthesized into a single tool, nor has such a scale been used to assess attitudes regarding trust in a more focused community. This project aims to measure trust in medical researchers and healthcare institutions in Indiana.

Methods: A survey was created by combining previously validated trust scales (Shea et al., Mainous et al., and Hall et al.), along with questions about demographic backgrounds. Cognitive interviewing was conducted in three focus groups to finalize survey questions. The questionnaire was sent to participants recruited via email from the All IN for Health registry, a statewide database of volunteers interested in research participation.

Results: At the time of analysis, 481 participants had completed the survey. About half of respondents were age 60+, and almost three times more women participated than men. The majority had bachelor's degrees or higher (72.5%). About half of participants agree that healthcare organizations cover up their mistakes. Half disagreed that patients get the same medical treatment regardless of race/ethnicity. Almost one in five respondents (17.4%) believe that medical researchers conduct experiments on people without their knowledge.

Conclusion: Preliminary results suggest additional efforts may be needed to foster trust in healthcare research and organizations. Results may not be generalizable to the entire population due to differences in gender, race/ethnicity, and level of education across initial respondents. One limitation is that recruitment using the All IN for Health registry may have produced biased results. Further studies are needed to understand factors that may influence trust.

Scientific/Clinical/Policy Implications: Results may influence public outreach and research recruitment to gain trust from Indiana residents and enhance participation in medical research.

Combinatorial Inhibition of Epigenetic Regulators to Treat Glioblastoma

Burket N, Koenig J, Saratsis A

Background: Glioblastoma multiforme (GBM) is a deadly primary brain cancer that is diagnosed in 12,000 patients in the US annually with a median survival time of 15 months. Temozolomide is the standard-of-care for GBM; however, many tumors are resistant, necessitating the expansion of therapeutic options. EZH2 and JMJD3 are two proteins responsible for epigenetic regulation of the genome

via histone methylation, with EZH2 also affecting non-histone targets. Prior studies showed that inhibition of these proteins decreased cell counts and induced radiosensitivity in GBM. Thus, we investigated combined use of EZH2 inhibitor, EPZ-6438, and JMJD3 inhibitor, GSK-J4, in the treatment of temozolomide-resistant GBM10 cells.

Methods: Non-irradiated cells were treated with both drugs singly or combined, and counted at 24-, 48-, and 72-hour intervals. Irradiated cells were pre-treated with each drug or combination therapy for three days, irradiated, and then counted at 24-, 48-, and 72-hour intervals. Western blot allowed investigation of dsDNA damage biomarker yH2AX, gene-silencing modification H3K27me3, total H3, tumor suppressor p53, EZH2, JMJD3, ySTAT3, and total STAT3 expression in non-irradiated and irradiated cells following drug treatment.

Results: Single EPZ-6438 and GSK-J4 treatment decreased cell count in a dose and time dependent manner. GSK-J4 was more effective than EPZ-6438, and combinatorial treatment was most effective. Western blot revealed that GSK-J4 but not EPZ-6438 treatment followed by radiation increased H3K27me3 expression. EPZ-6438 treatment increased yH2AX expression, but this was not further increased by radiation. Meanwhile, GSK-J4 treatment increased yH2AX, but only after radiation.

Discussion: Decreased cell count following GSK-J4 treatment may be due to increased gene silencing resulting from the inhibition of H3K27 demethylation. Additionally, increased dsDNA breaks observed in EPZ-6438 and GSK-J4 treatments supports their roles in radiosensitizing GBM cells.

Potential Impact: This study highlights the importance of further investigation into GSK-J4 and EPZ-6438 combination therapy in temozolomide-resistant GBM tumors.

Metrics Assessing Biofilm Infection in Clinically Translational Wound Models: A Systematic Review
Chaudhry N, Steiner SS, Singh K, Sen CK

Background and Hypothesis: The challenge of antibiotic-resistant bacteria perpetuating biofilms infections has shifted a focus to innovating wound therapies. Regarding cutaneous wounds, biofilm is regarded as a prominent contributor of slowed wound healing. 80% of human infections deemed chronic are associated with biofilm formation. However, there is no continuity in metrics used to assess biofilm infection due to a lack of standardized protocol. This discrepancy prevents equitable comparison between studies to understand the efficacy of different therapies. Furthermore, certain tests will deem biofilm infection eradicated at the wound when it is still present. Through a systematic review of literature 2020 onwards, we set forth to establish an understanding of various metrics used to assess biofilm interventions.

Project Methods: The systematic review was registered on the COVIDENCE database adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA). Of 906 reports identified, 72 were analyzed under the inclusion/exclusion criteria. A biofilm therapy was defined as an intervention eradicating or lessening, not preventing, a mature biofilm infection at the wound site. We included animal (ex-vivo, in-vivo, pre-clinical) and human studies. In-vitro studies were excluded due to poor translational qualities in clinical settings.

Results: Of the plethora of biofilm metrics identified, the most commonly used in studies regardless of therapy type was colony forming units (CFU), followed by histological analysis of the wound site's inflammation and healing with H&E staining for neutrophils. Other methodologies included scanning electron microscopy (SEM), MT staining for collagen deposition, CD31 immunohistological assays, wound size, bioluminescence, etc.

Potential Impact: The data of this systematic review identifies an issue in the lack of uniformity in measuring biofilm infections. It speaks to the strengths and limitations of different metrics to make an argument for adopting a single protocol, as well as detailing new biofilm treatments.

Validation of Spinal Cord Injury Sensory Deficit Model with Head-Fixed Rat
Chinthala AS, Slack JC, Yadav AP

Background/Objective: Numerous studies have reported restoring motor function through spinal cord stimulation in a rodent spinal cord injury model; however, replicating sensory information through spinal cord stimulation has not been thoroughly tested. We have previously trained rats to detect artificial sensations which lead to the question if this can be generated in a spinal cord injured rat. Our study begins to address this question by first validating a spinal cord injury model to test. Our hypothesis is if a decrease in the percent correct response compared to pre-procedure is observed, then this will verify sensory loss in this dorsal column lesion model of spinal cord injury.

Methods: We use sensory detection in a head-fixed rat to verify a spinal cord injury sensory deficit model. We begin by placing a water-deprived rat into a custom-made head-fix set up where two water spouts are placed in front of the rat. Vibration stimuli is applied to the hind paw via a vibration motor set at 200 hz $\pm$ 50 hz. The rat is trained to associate stimulus with left spout and no stimulus with right spout. Correct percent response is recorded, and once the rat demonstrates detection, the rat undergoes a dorsal column hemi-section procedure. Post procedure, the rat will be placed back in the head-fix set up to repeat the behavioral experiment.

Results: We have been able to train rats in detection training to a correct response rate of 85% indicating the rat has learned the

association of the vibration stimulus to the left spout. The next step is to perform a dorsal column hemi section and perform the detection training again to measure a difference in correct response rate.

Conclusion and Potential Impact: This is a crucial step for spinal cord injury research as this confirms sensory loss and will allow further testing to restore sensation. After validation, we can begin testing to restore sensation using stimulation of the spinal cord.

Longitudinal Study of COVID-19 Impact on Breast Cancer Screening in Lake County Indiana
Crowe N, Green D, Han A

Introduction: During the COVID -19 pandemic, elective procedures such as mammography were suspended from late March to late April. Previous analyses done by Green and Han revealed that mammography screenings continued to be down in 2020 and 2021 from their baseline in 2019 prior to the pandemic. Continued efforts in monitoring how mammography screenings have been affected following the pandemic is crucial especially in understudied cities with predominantly black populations such as Gary, IN.

Methods: Data was provided from "Hospital A" on 22,693 mammography encounters and this data was analyzed to determine how mammography screenings have changed after the suspension period.

Results: Following the lift on the suspension of elective procedures on April 27, 2020, there was a sharp increase of mammograms the following 8 weeks to near pre-pandemic levels. However, after this 8-week post suspension period of elective procedures on April 27, 2020, the weekly average began to decrease starting at the beginning of 2021. The weekly average went from 171 (SD 21.9) mammograms in 2019 to 108 (SD 40.0) mammograms in 2021. Furthermore, the weekly average has continued to decrease in 2022 with 101 (SD 46.8) mammograms.

Conclusion: "Hospital A" successfully returned mammography procedures to pre-pandemic levels initially during the 8 weeks following the suspension on elective procedures. However, strategies should be implemented to mitigate the continuing decrease in mammography procedures following the COVID-19 pandemic.

The Efficacy of Cyranose in Detecting In Vitro Volatile Organic Compounds
Dalis C, Shelley C, Brokaw J, Markel T

Background and Hypothesis: Electronic-noses are a subtype of electronic-sensing technology designed to reproduce human smell via sensor arrays and pattern recognition algorithms. Specifically, they can detect headspace volatile organic compounds (VOCs), which are end products of human metabolism (normal and disease-specific) mainly excreted in the breath, urine, and feces. VOCs are often emitted before the onset of clinical symptoms of many diseases, making them useful screening biomarkers. Additionally, the portable, inexpensive, and non-invasive nature of e-noses allows for easy clinical implementation for point-of-care (POC) disease screening/diagnosis. We hypothesize that Cyranose, one e-nose model, can differentiate headspace VOCs between healthy cells and cells stressed with an in vitro inflammatory state.

Project Methods: Human Intestinal Epithelial Cells (HIEC-6s) and Umbilical Stem Cells (USCs) were cultured in their respective 50 mL complete media at 37o C in 5% CO2. Upon reaching appropriate confluence, cells were washed using PBS and passaged with TrypLE Express. Cells were counted with a hemocytometer and Trypan blue exclusion, then added to a 12 well plate and exposed to either TNF-α (50 ng/mL), LPS (200 ng/mL), or hypoxia (5% O2) for 24 hours. Supernatant (1.5 mL) was added to Eppendorf tubes, sealed with parafilm, and heated to 40o C for 30 minutes. Headspace VOC profiles were analyzed with Cyranose and compared to controls.

Results: Using the "identify" function on Cyranose, it was unreliable in correctly distinguishing VOCs between HIEC-6s and USCs from their controls under all treatment conditions. While Cyranose sensors did generate smellprint profiles that showed differences between HIEC-6s and USCs against controls with LPS treatment, small sample sizes limit these results.

Conclusion and Future Directions: This study demonstrates that new method designs are necessary when identifying in vitro VOC profiles using Cyranose. Future considerations should include the concentration of treatments/cells, cell types, treatment duration, supernatant volume, number of samples prepared, heatblock temperature, and/or a different e-nose model.

Applying Cyclical Loading Parameters for In-Vitro Neo-Tendon Development
Darden K, Jenkins T, Little D

Annually, over 300,000 rotator cuff tear repair surgeries are performed in the USA. Current surgical methods have varied success, due to factors such as tear size and patient age. The fibrotic repair tissue that results from repairs is susceptible to re-tear: the overall retear rate following rotator cuff tendon repair is around 20%, and up to 94% for large tears. Therefore, there is an unmet need for better surgical options. Tendon tissue engineering is a potential solution. Previous work evaluated meltblown polylactic acid scaffolds but found it cannot withstand physiological strains. In this study, we evaluated poly(ε-caprolactone) (PCL) meltblown scaffolds for responses to cyclical tensile loading in-vitro and anabolic responses to neo-tendon development. To accomplish this, we characterized the baseline viscoelastic mechanical properties of PCL. Then we seeded PCL with human adipose stem cells and cultured for 28 days with

cyclic loading to 6% strain three times per week in culture for 0 or 10,000 cycles using a bioreactor to mimic loading in physically active individuals. After culture, we performed viscoelastic testing followed by load to failure and used Picrosirius red stain to investigate collagen alignment in histologic sections. We found that seeding cells increases the viscoelastic properties but loading at 10,0000 cycles did not improve mechanical properties or collagen alignment. We will perform biochemical assays to characterize cell proliferation and extracellular matrix synthesis. Lastly, we will do additional cultures that will be cyclically loaded at 6% strain for 120 and 5,000 cycles three times per week, which represents the number of fetal kicks per day as would occur during fetal tendon development, and an estimate of moderate daily upper extremity movements, respectively. Together our data will establish if 3D meltblown scaffolds are viable to move into preclinical studies and will begin to inform rehabilitation protocols for engineered tendon development.

Factors Influencing Disease Recurrence After Primary R0 Resection of Masaoka Stage I and II Thymoma
Davis H, Heldman E, Laniak L, Wuthrich B, Loehrer P, Kesler K

Background: The available research has demonstrated that the best treatment for early thymoma is surgical resection, with the goal of an R0 (complete) resection and an associated cure rate of 90-95%. The standard approach is a median sternotomy with en bloc resection of the thymoma, though minimally invasive approaches (video-assisted and robotic-assisted thorascopic surgery; VATS/RATS, respectively) have recently gained popularity. These techniques remain controversial as tumor spillage into the pleural space is difficult to control and increased tumor manipulation during minimally invasive surgery may increase risk of drop metastases.

Purpose: This study analyzes factors influencing disease recurrence after primary R0 resection of Stage I/II thymoma, with a specific focus on the effect of surgical approach on probability of disease recurrence.

Methods: A database of 1023 thymic neoplasm patients seen at IU was established. From this database, 109 patients with stage I/II thymoma and primary R0 surgical resection were identified. Cerner records were reviewed retrospectively, and the following data were collected: (1) WHO histologic type, (2) biopsy prior to surgery (yes/no), (3) surgical approach, (4) recurrence status/location, and (5) location of surgery (IU or outside institution).

Results: Of the 109 patients, 30 had recurrence/progression after surgery. 25 VATS/RATS surgeries were performed, with 7 cases of recurrence (28%), and 81 open surgeries were performed, with 20 cases of recurrence (24%); 3 patients with recurrence did not have sufficient records to determine surgical approach. For the VATS/RATS patients with recurrence, 100% had pleural recurrence ipsilateral to the surgical approach. 57 surgeries were performed at IU, with 2 patients having recurrence (96.5% cure rate at IU), while 52 were performed outside IU, with 28 patients having recurrence. Biopsy prior to open sternotomy was associated with a 38.9% recurrence rate, whereas open sternotomy without biopsy had a 17.1% recurrence rate. Lastly, WHO types B1, B2, and the mixed B2/B3 type were associated with increased risk of recurrence.

Conclusions: Surgical approach, performance of biopsy prior to surgery, WHO histologic type, and surgical institution, are all factors that may influence recurrence probability in stage I/II thymomas. In addition, this study demonstrates that pleural recurrences after VATS/RATS tend to occur ipsilateral to the surgical approach. This finding further supports the concern that there could be greater risk of pleural recurrence with minimally invasive surgery as a result of increased tumor manipulation; a similar mechanism is theorized to be responsible for increased recurrence risk with biopsy. Lastly, the low recurrence rates at IU suggest thymoma resection should be performed at centers with extensive thymoma experience.

Limitations: The cohort analyzed here had a higher recurrence rate than reported elsewhere for stage I/II thymoma. This is likely a selection bias based on IU's experience with advanced thymoma.

Impacts of Interprofessional Spiritual Care Education Within a Healthcare Team: a Qualitative Analysis
Davis J, Oyedele O, Lion AH, Szilagyi C, Puchalski C

Background: Spirituality is frequently utilized by patients experiencing cancer and blood disorders to maintain their well-being and cope with their diagnosis. The provision of spiritual care is a critical aspect of whole person care and is associated with increased quality of life and positive coping with pain. Generalist aspects of spiritual care may be provided by any team member trained to do so. The Interprofessional Spiritual Care Education Curriculum (ISPEC©) is an online program which provides this training.

Methods: We utilized ISPEC© for the training of Pediatric Hematology-Oncology team members. From 21 team members who were trained, a convenience sample of 8 participants were interviewed regarding their experience. Using a phenomenological approach for interview and analysis, we explored the experience of interprofessional spiritual care training. Through iterative review of interview transcripts, themes representing the essence of the lived experience were identified. Theme saturation was reached through the interviews of the 8 participants.

Results: Three major themes emerged. These themes were (1) Knowledge gained, (2) Barriers to Providing Spiritual Care, and (3) Impact on the Healthcare Team. While the experience of interprofessional spiritual care training mitigated one barrier (lack of training), it also revealed barriers within the standard workflow, which participants became interested in changing. Through education

on generalist spiritual care, there were both benefits to patients whose spiritual needs could be better addressed, and an increased understanding of the team member's own spiritual needs.

Conclusion: Interprofessional spiritual care education, utilizing ISPEC©, has a strong potential to develop pediatric hematology-oncology team members' capabilities to attend to the spiritual aspect of whole-person care. In addition to contributing to the well-being of patients, the experience of training in spiritual care also holds benefits to the team members as they are learning to recognize their own spiritual needs and resources.

Biomarker Profiles and Immunologic Predictors of Neurodevelopment in Children who are HIV Exposed Uninfected

Egler A, Jang JH, Li W, McHenry M, Oyungu E, Yu Q, Khaitan A

Background: Children who are HIV-exposed uninfected (HEU) have higher morbidity and mortality rates than their unexposed uninfected counterparts (HU). HEU also exhibit lower neurodevelopmental outcomes. Previous studies show that HIV-induced immune dysregulation can be linked to decreased neurodevelopment in HIV+ children. However, the role of inflammation on neurodevelopment in HEU remains unclear.

Methods: This study investigated the plasma levels of 81 biomarkers in 82 Kenyan children between the ages of 18 and 36 months. Neurodevelopment was measured using the Bayley Scales of Infant and Toddler Development, 3rd edition. Bayesian model averaging was used to identify significant biomarkers.

Results: HEU showed lower levels of 12 different proinflammatory cytokines/chemokines/growth factors: IL-12, leukemia inhibitory factor (LIF), macrophage migration inhibitory factor (MIF), TNF-related weak inducer of apoptosis (TWEAK), and A proliferation inducing ligand (APRIL); BLC, eoxtaxin-2, I-TAC, monokine induced by gamma interferon (MIG), and MIP-3a; fibroblast growth factor-2 (FGF-2) and granulocyte colony-stimulating factor (G-CSF). HEU showed higher levels of 2 inhibitory soluble immune checkpoints: T-cell immunoglobulin and mucin-domain containing-3 (TIM-3) and CD40. Bayesian model averaging identified the biomarkers to best predict HEU vs. HU status were IL-12, IL-13, and CD40. In HU children, hepatocyte growth factor (HGF) and IL-5 predicted cognitive scores, BLC and IL-7 predicted motor outcomes, and IL-1a, IL-2R, IL-5, and maternal education predicted language scores. In HEU, FGF-2 predicted language scores, and IL-22 predicted motor development. Statistical analysis identified IL-2R and IL-22 as the strongest predictors of neurodevelopmental outcomes in HU and HEU, respectively.

Conclusion/Potential Impact: This study shows that HEU exhibit an immune suppressive biomarker profile, rather than an inflammatory profile as indicated in previous studies. The significant biomarkers we found may be used to determine children at risk of decreased poor neurodevelopmental outcomes, allowing more time for intervention.

"We Don't Know What We Don't Know" – A Qualitative Study of Medical Student Perceptions of Student Affairs

Fromke M, Starr B, Haywood A, Walvoord E, Longtin K

Background: The Indiana University School of Medicine (IUSM) Office of Student Affairs (OSA) is designed to address students' concerns and facilitate their personal and professional development (PPD). LCME accredited medical schools are evaluated on these areas using a nationally normed AAMC Graduation Questionnaire of graduating medical students. As the largest medical school in the U.S. with nine regional campuses, OSA faces a unique challenge in achieving high levels of satisfaction in these measures.

Objective: This study used focus groups to better understand second-year students' expectations, experiences, and ideas related to PPD programming and relationships with the OSA.

Methods: Given the individualized and complex nature of personal and professional development, we used a qualitative approach to gather data on students' experiences. All second-year medical students were invited to participate in a focus group in exchange for a modest meal and school-branded merchandise. The first and second author conducted seven, hour-long, semi-structured focus groups (3-8 participants each) with a total of 39 students representing eight of nine IUSM campuses. Discussions were recorded and transcribed verbatim. Three authors used NVivo™ qualitative analysis software to perform inductive thematic analysis according to established methods.

Results: Four themes were identified focusing on students' expectations of faculty and staff and relevance and timeliness of information.: 1. Two-Way Communication: students expect accessibility to faculty who can affect change, and ongoing responsiveness about inquiries that have been submitted. 2. Proximally-Relevant Information: students described types of information they need for their professional development, including ideas about when and how to communicate the information most effectively. 3. Guidance for the Future: students desire mentorship from individuals who truly understand physicians career paths. 4. In the Classroom and Beyond: students want relevant topics and formats for PPD. Participants also provided insights into existing, valuable programming.

Conclusion: Second-year medical students have specific desires for their development, including clinical experience, discussion of current events, and mentorship; and they appreciate events and opportunities that addressed these needs. Students expressed concern that opportunities for development are not comparable across all campuses. In their relationships with OSA, students desire

easy access to faculty and staff in order to voice inquiries and receive robust responsiveness to conflict resolution. Students also indicated a desire for earlier communication of information for short and long-term planning. Results of this study can be used at institutions with a regional campus model to shape future programming for PPD and improve channels of communication with all students.

Cholestasis in the First Trimester Associated with Rare ABCG5/8 Variants: A Case Study

Ganapaneni S, Arul Dhas BW, Raj Vuppalanchi R, Sara Quinney S

Background: Obstetric cholestasis, or intrahepatic cholestasis of pregnancy (ICP), is a liver disease that usually presents in the third trimester of pregnancy. It is characterized by pruritis that is associated with elevated liver enzymes and bile acids. This condition can have potentially serious effects on the fetus due to the buildup of serum bile acids resulting from the obstruction of bile flow.

Case Overview: A 28-year-old patient, who was pregnant for the third time, developed pruritis in the first trimester and presented with blood work that showed elevated total bile acids and liver enzymes. A medical history revealed similar symptoms amongst her female relatives during their pregnancies as well as the patient's own previous pregnancies, suggesting a genetic component in the etiology of the disease. Genetic testing supported this hypothesis and showed variants of unknown significance that indicated a duplication in the ABCG5 and ABCDG8 genes.

Discussion: This finding was rather unusual as these genes have not yet been clinically associated with ICP. The ABCG5 and ABCG8 genes code for canicular bile transporters in the liver that transport cholesterol into the bile. Overexpression of these transporters due to the duplication in her genes may result in increased transport of cholesterol into bile, disrupting the regular composition of bile. The resulting increased bile viscosity may cause bile stasis or blockage, and this proposed mechanism can possibly explain the pathophysiology behind this unusual case of cholestasis.

Conclusion and Potential Impact: ICP can have potential serious effects on the developing fetus, and its etiology is still being understood. The novel ABCG5/8 gene duplication is a novel variant that may lead to earlier onset of ICP than commonly known variants.

Examining the long-term efficacy and tolerability of netarsudil as an adjunctive glaucoma medical therapy

Gannamaneni K, Cantor L

Background and Hypothesis: Glaucoma is a group of progressive optic nerve neuropathies that commonly cause vision loss or blindness. The most prevalent of these neuropathies is known as primary open-angle glaucoma. POAG is caused by increased intraocular pressure (IOP) in the anterior chamber of the eye, due to increased resistance to outflow of aqueous humor. Netarsudil is a recently developed novel medication for lowering intraocular pressure. The aim of this study is to assess the long-term efficacy and tolerability of netarsudil as an adjunctive therapy in patients with POAG.

Methods: In this study data was collected through a retrospective chart review of patients being treated for POAG. Efficacy was measured by using the difference in intraocular pressure over the course of treatment. Tolerability was assessed using a Kaplan-Meier estimator, measuring the time to failure of treatment. Failure in this case is defined as either a termination in treatment due to adverse effects, or termination in treatment from lack of efficacy in lowering IOP. Data was separated into groups of either 2nd, 3rd, or 4th line treatments. In patients where both eyes were treated, one eye was randomly selected to be followed for measurements.

Results: Probability of failure curves, based on the tolerability and efficacy of netarsudil treatment, were constructed for each group. IOP reduction (mmHg) was found to be: 3.00 (3.09 95% CI) for 2nd line, 7.05 (4.65 95% CI) for 3rd line, and 5.31 (1.38 95% CI) for 4th line.

Conclusion and Impact: These results give context to netarsudil as a therapy in terms of its long-term implications. As the drug was only approved for use in late 2018, there is limited data on its long-term efficacy and tolerability, and this information helps to give clinicians a better idea of whether it will be a helpful treatment for patients.

Determining Barriers to Care in Pediatric Patients with SLE or JIA

Garcia GE, Kwan O, Rodríguez M

Background and Hypothesis: Every year in the US 5,000-10,000 children develop child-onset systemic lupus erythematous (SLE), while 294,000 children are diagnosed with Juvenile idiopathic arthritis (JIA). Among the affected, it remains unknown if barriers to care affect pediatric patients with rheumatic diseases. It is the goal of this study to identify what barriers to care pediatric rheumatology patients mention during focus group sessions.

Methods: This is a qualitative focus group study. 13 focus groups, 60 minutes each with 3+ participants. Patients aged from 5-22

and their caregivers were recruited from different demographics and purposively selected for a more representative sample. Focus groups were conducted via the videoconference program Zoom and led by one facilitator in either English or Spanish. All meetings were recorded, transcribed, analyzed, and were independently coded using the constant comparison method and the NVIVO program.

Results: Thus far, we have recruited 14 parents and 17 patients. Demographics are shown in Table 1. Guardians/parents have concerns with cost of medications and future challenges once their child reaches age 26. Among the patients, almost all expressed problems with school attendance, and adjustments to their daily life. Most concerning however, was the impact that SLE and JIA have on their social life. There were topics that participants felt they were satisfied with such as communication with medical staff and health literacy.

Conclusion and Potential Impact: The preliminary information collected in this study showed different concerns among caretakers and patients. However, both groups suggested that a social group for children with SLE and JIA be created. The next phase of this study is to develop a survey based on these responses to try to identify patients' and caregivers' perspectives on barriers to care with the final goal of improving patient quality of life.

Assessment on the Current State of Survivor-Focused Cancer Care in Southwestern Indiana
Gass B, Garcia K, Sajdyk T

Background/objective: In 2019, the Commission on Cancer (CoC) released updated standards for 2020. The 2020 standards deliberately focused on improving long-term outcomes and quality of life for survivors. The new standards went one step further and introduced requirements for staffing and programming to meet these goals. This study aims to qualitatively assess the current state of survivorship-focused care through direct interviews with survivors, community leaders and healthcare providers in Evansville, Indiana.

Methods: This is a qualitative study to understand survivorship care in southwestern Indiana. We conducted qualitative interviews with healthcare providers, community leaders, as well as survivors with an overall goal of learning what the needs and barriers are in providing or receiving long-term care. Our team worked to analyze qualitative data from the interviews to identify common themes within this community, as well as to compare the viewpoints and experiences of survivors with healthcare providers and community leaders. This study design is based on the Tri-Ethnic Center for Prevention Research model for implementing a community readiness assessment, and is the first step in a long-term appraisal of survivorship-focused care in the southwestern Indiana region.

Results: From this early assessment, it is determined that although awareness and efforts exist to address long-term survivorship care, there is room for improvement. Survivors and providers alike recognize gaps that exist in the transition of care, in patient education, and in awareness of and access to available resources.

Conclusion and potential impact: This study provides key information that will be utilized to further assess the readiness of the community of survivors and care providers. The themes drawn from this assessment will be utilized to determine high-impact areas for improvement in care, analyze availability of relevant resources, and to address barriers to care and resources.

Evaluating the Need for Surgical Intervention Following 360 Degree Trabeculotomy
Gill M, Smith H

Introduction: Pediatric glaucoma consists of congenital glaucoma and secondary glaucoma. The etiology of congenital glaucoma is attributed to defects in the trabecular meshwork, whereas secondary glaucoma encompasses a variety of causes including juvenile arthritis, Sturge-Weber syndrome, and aphakia.[1-4] The mainstay of treatment for primary congenital glaucoma is surgical intervention, which includes goniotomy or trabeculotomy.[6] A trabeculotomy involves opening Schlemm's canal into the anterior chamber to create an alternative pathway for aqueous outflow. A recently developed procedure is the 360-degree trabeculotomy, in which a suture is utilized to traverse Schlemm's canal 360 degrees as opposed to partial opening of the trabecular meshwork in a partial trabeculotomy.[5] 360-degree trabeculotomies have been shown to result in lower rates of surgical reoperation and improved control of intraocular pressure than partial trabeculotomies.[6] The purpose of this retrospective study was to evaluate the need for surgical intervention following 360-degree trabeculotomy in patients with congenital and secondary glaucoma.

Methods: IRB approval was received from the Indiana University School of Medicine to access digital patient charts from Riley Children's Hospital's department of ophthalmology. The Kruska-Wallis test was utilized to evaluate the average number of days between the initial 360 trabeculotomy and secondary glaucoma surgery. The chi-squared test was performed to evaluate surgical success rates. Surgical failure was defined by the patient needing additional surgical intervention or having more than two eye exams that demonstrated an intraocular pressure greater than 21. A 5% significance level was used for each test.

Results: The surgical success rates for 360 trabeculectomies in patients with congenital and secondary glaucoma were 64.70% and 25%, respectively ($p = .0002$). The average values for the number of days after which secondary surgery was needed were 818.20 and 259.00 days for patients with congenital and secondary glaucoma, respectively ($p = .28$). The average values for the number of days after which an intraocular pressure lowering drop was needed for patients following the initial procedure were 311.83 and 51.56 for patients with congenital glaucoma and secondary glaucoma, respectively ($p = .06$).

Conclusion: The rate of single surgical success was much higher for patients with congenital glaucoma than secondary glaucoma. This could be attributed to the anatomic variability, inflammatory processes, and pathophysiological mechanisms that contribute to secondary glaucoma. The small number of cases presents a limitation to this study. Although the data for the number of days between initial and secondary surgical intervention is not statistically significant, this study still demonstrates that a significant number of patients achieve intraocular pressure control following a 360-degree trabeculotomy.

Temporal Trends in Primary Total Hip and Knee Arthroplasty Preoperative PROMs from 2013-2021

Hamersly J, Deckard E, Meneghini RM, Sonn K

Background: Patient reported outcome measures (PROMs) are utilized in total joint arthroplasty (TJA) to objectively evaluate patient function and track progress over time. Limited data exists on temporal trends of preoperative PROMs and any specific effect of COVID-19 on preoperative functional status. The objective of this study was to identify changes in preoperative PROMs over time, and determine the influence of COVID-19 on patient function prior to TJA.

Methods: All patients undergoing unilateral primary total hip (THA) or total knee arthroplasty (TKA) by a single surgeon from 2013-2021 were retrospectively reviewed. Joint-specific preoperative PROMs and relevant covariates were compiled and evaluated. Time series, univariate, and multivariate analyses were performed to identify predictors of preoperative PROMs.

Results: After exclusions, 1,105 THAs and 1,909 TKAs were available for analysis. Preoperative activity level steadily increased from 2015 to 2021 for THA patients. For TKA patients, PROMs similarly increased from 2015 to 2019, however, a decrease in activity level occurred in 2020. No time series differences were observed for HOOS JR or Knee Society "knee normal" scores. KOOS JR scores increased from 2016 to 2019, then decreased in 2020 and 2021. Knee pain with level walking and stair climbing steadily increased from 2013-2019 with an increase in 2020 for both scores. The COVID-19 era (cases performed from 2020 onward) was a significant predictor of higher UCLA scores for THAs (p=0.020); and worse pain with level walking, and KOOS JR scores for TKAs in multivariate analysis (p≤0.038).

Conclusion: This study demonstrated detrimental effects of COVID-19 on preoperative patient functional status, particularly for TKA patients. Providers should consider the effects of surgical delays and how trends in preoperative PROMs are changing over time. These include rising activity levels of preoperative TJA patients overall and worsening knee pain and function in TKA patients during the COVID era.

Examining the Bone Marrow Niche in a Fracture Healing Model with the Use of Multiplex Imaging and Transcriptomics Technologies

Hartman ML, Karnik SJ, Khurram I, Gulbronson CJ, Dunn KW, Srour EF, Kacena MA

Background: In the US, 6.3 million fractures occur annually. Additionally, 5-10% of fractures do not heal without additional interventions. The bone microenvironment is comprised of cells such as osteoblasts (OBs), megakaryocytes (MKs), and endothelial cells (ECs). Traditional technologies, such as flow cytometry, immunofluorescence (IF), and qPCR have limitations that prevent studying the bone microenvironment as a whole.

Project Methods: Some of the advanced multiplexed technologies that can be useful tools in studying a complex microenvironment such as bone are the PhenoCycler™, previously known as CODEX (CO-Detection by indEXing) and Nanostring nCounter which use fluorescent probe hybridization to either visualize the tissue or quantify gene expression, respectively. Phenocycler addresses the limitations of IF by imaging up to 60 cell markers, thus, allowing for better identification of cells within the bone microenvironment. This complex information can then be used for image analysis with the HALO image analysis software, providing the spatial context as well as functional aspects of cell interactions during homeostatic, disease, and injury states. Nanostring nCounter maps out hundreds of genetic pathways without requiring amplification or the need to convert mRNA to cDNA. This process is highly reproducible and decreases variability.

Results: In the current study, we are standardizing and optimizing protocols for both of these technologies for bone which are more difficult to process than soft tissues. Regarding Nanostring, samples have been submitted to the SNRI Biomarker Core and are awaiting processing.

Potential Impact: We anticipate that both the multiplexed technologies will allow us to determine which interconnected pathways, such as angiogenesis, inflammation, and immune response are differentially regulated during normal fracture repair, repair using new therapies, and repair in aged or diseased animal models.

Role of Rap1 GTPases in Growth, Differentiation, and Migration of Myeloid Cells

Hemmerlein T, Kanumuri R, Ramdas B, Kapur R

Background: Rap1 is a Ras-like small-molecular-weight GTP-binding protein involved in signal transduction cascades. It cycles between a GDP-bound inactive and a GTP-bound active form. This switching is regulated by specific GEFs and GAPs. Rap1 exists in two isoforms - Rap1a and Rap1b. While Rap1 has been implicated in regulating several hematologic disorders, including chronic

lymphocytic leukemia, its role in the development and function of hematopoietic stem cells and progenitors (HSC/Ps) has not been investigated. Macrophages play an essential role in the retention of hematopoietic cells in the mesenchymal niche. Resident macrophages in the spleen retain HSCs through VCAM1 adhesion. Previous studies have shown that loss of both isoforms of Rap1 in mice results in enhanced peripheral blood leukocyte counts and mobilization of primitive hematopoietic stem cells (Lin-KIT+Sca1+) into peripheral blood circulation. Given this loss of retention of primitive hematopoietic cells in the bone marrow, we hypothesized that perhaps Rap1 plays an essential role in adhesive interactions of HSC/Ps in the bone marrow.

Methods: To test this hypothesis, we derived macrophages from the bone marrow of wild-type (WT) and Rap1a/b double knockout (DKO) mice and compared their growth, survival and differentiation using proliferation and adhesion assays, as well as flow cytometry to assess apoptosis, macrophage differentiation, MCSF receptor expression, and expression of integrins.

Results: Our studies show that macrophages derived from Rap1 DKO mouse bone marrow show impaired growth, survival and differentiation along with impaired adhesion in response to extracellular matrix components including fibronectin.

Future Directions: In the future, we hope to study macrophage adhesive interactions in response to SDF1, collagen, and other extracellular matrix proteins in myeloid-specific deletion of Rap1 in mice, and to study the role of Rap1 in different lineages of hematopoietic cells using different CRE drivers.

Comparison of Chiropractic Manipulation Therapy and Functional Movement-Based Myofascial Release in Shoulder Range of Motion of Collegiate Athletes: A Pilot Study

Heumann R, Waltz M, Garcia-Hosokawa M, Chlebowski AL

Background: Shoulder pain is the third most common presentation of musculoskeletal pain in the clinic with a lifetime prevalence of up to 70%. In athletes, shoulder dysfunction is often due to the extreme forces experienced by the joint during sport participation. Studies have shown that a deficit of 5 degrees in total arc of motion, 20 degrees in internal rotation, and 15 degrees in horizontal adduction can increase an athlete's chances of injury by a factor of four.

Methods: Student athletes with shoulder pain and decreased range of motion (ROM) in their dominant arm were separated into cohorts and received twelve therapy sessions. One cohort received chiropractic manipulation (CM) and the other received functional movement-based myofascial release (FMMR) with CM. ROM of the shoulder was measured during the first, sixth, and last sessions using goniometry and video capture. Cohorts were compared using statistical analyses on data collected.

Results: A total of four participants have completed at least the first six sessions of participation in study. Initial results show there is no statistical difference in improvement in shoulder ROM between cohorts. Student T-tests comparing cohorts' improvements in six of the seven specific ROM tests resulted in no statistical significance (p-values ≤ 0.05). The two participants that completed all twelve intended therapy sessions showed evidence of positive trajectory for increased ROM and qualitatively expressed improvement in shoulder motion.

Conclusion: This study shows that there was no statistically significant difference in treating athletes with CM versus FMMR combined with CM. This can mainly be attributed to the study's current size (n=4). Even with the small participant size, and lack of statistical significance several trends of the individual range of motion measurements provide questions that would benefit from the continuation of the study towards the full cohort participation.

Transplantation of human derived retinal ganglia cells as potential treatment for glaucoma

Ho K, Hameed SS, Sharma T

Purpose: Glaucoma is a group of optic neuropathies characterized by retinal ganglion cell (RGC) death and visual field loss. A degenerative mechanism associated with RGC death is disrupted delivery of neurotropic factors from the brain to RGC somas due to characteristic axonal damage in glaucoma. This transport is critical for protection of long-term neuronal function. Thus, we investigate a potential therapeutic target, human Neuritin 1 (NRN1), which has demonstrated neuroprotective effects within in vivo rodent axonal injury models. Further, the advent of induced pluripotent stem cell (iPSC) technology allows iPSC-RGCs to be generated in-vitro from commercial iPSCs and reprogrammed corneal fibroblasts. We hypothesize delivery of NRN1 and transplantation of iPSC-derived RGCs will sustain survival of RGCs and ultimately slow the progression of glaucoma-induced neuronal death in our translaminar autonomous system (TAS) perfusion model system. This will allow us to analyze a potential therapeutic approach for both early-stage glaucoma (NRN1 therapy) to protect dying RGCs, and late-stage glaucoma (iPSC-RGCs) when most RGCs are lost.

Methods: Human donor eyes were obtained from eye banks according to Declaration of Helsinki. To model glaucomatous insult in an ex-vivo environment, dissected human posterior cups were cultured in TAS model under pressurized conditions for 7 days with and without transplantation of iPSC-derived retinal organoids and NRN1. Survival of iPSC-RGCs, gliotic and fibrotic pathways were measured through expression by qRT-PCR, immunohistochemistry, and western blot analyses. Retinal function post-treatment was measured through electroretinogram analysis.

Results: We successfully maintained the human posterior eye cups in translaminar differentials for 7 days. In contrast to controls,

we observed increased RGC survival and retinal function with decreased gliosis and fibrosis after combination therapy of NRN1 and iPSC-RGC. Additionally, we found differential gene expression of apoptosis, inflammation, and RGC survival markers.

Conclusion: Our study identified that NRN1 in conjunction with iPSC-RGC transplantation treatment promotes RGC survival under glaucomatous conditions. This suggests that NRN1 and iPSC-RGCs could be utilized as a potential combination therapy to save retinal neurons and prevent neurodegeneration in glaucoma patients.

Cellular Fractionation to Characterize the Interaction of Nucleolin with Alpha-COP

Iurillo A, Custer S, Androphy E

Background and Hypothesis: The goal was to further characterize the interaction between Nucleolin and the alpha subunit of the COPI coatomer complex. Nucleolin contains a C-terminal dilysine motif, which mediates interactions between the WD40 domain of alpha-COP and COPI-interacting proteins. Previous work in the lab showed that this C-terminal dilysine is required for co-immunoprecipitation of alpha-COP with Nucleolin. Because alpha-COP is exclusively found in the cytoplasmic compartment, we hypothesized that the interaction between alpha-COP and Nucleolin is exclusively cytoplasmic but previous co-immunoprecipitations had only been performed from whole cell lysates. Alpha-COP has been shown to bind mRNA, but it was unclear whether this interaction was direct or whether alpha-COP was binding an RNA binding protein (RBP) which would act as a bridge between the mRNA and alpha-COP. Nucleolin acts as an RBP in both the nuclear and cytoplasmic compartments. We hypothesize that some of the mRNA bound to alpha-COP are present due to their association with Nucleolin.

Experimental Design or Project Methods: The first aim of the project was to optimize a reproducible cell fractionation protocol to reliably separate nuclear and cytoplasmic compartments. The second goal of the project was to identify mRNA that would co-immunoprecipitated with Nucleolin in HEK293T cells where we can easily express tagged versions of alpha-COP. Nucleolin-bound mRNA had previously been identified in Hela cells. We began by testing for the expression of these mRNAs in 293-TT cells using the published RT-PCR primers.

Results: After these tests identified Ftl (Ferritin light polypeptide) as a highly abundant transcript in 293- TTs, we performed RNA immunoprecipitation from cells expressing epitope tagged Nucleolin or alpha-COP. We confirmed that both Nucleolin and alpha-COP are in complex with Ftl mRNA.

Potential Impact: Future experiments will use short-hairpin RNA to knockdown Nucleolin and determine whether the levels of Ftl mRNA that co-immunoprecipitated with alpha-COP are reduced in the absence of Nucleolin.

Impact of Metastatic Bone Disease on the Progression of Cachexia in Lung Cancer

Jines ST, Kambrath AV, Poirier JL, Collier CD

Background/Objective: Cachexia is a systemic wasting syndrome characterized by skeletal muscle mass loss and is estimated to affect 80% of lung cancer patients. Previous studies have shown that metastatic bone disease may have a role in inducing cachexia, which is mediated by cytokines such as IL-6, TNF-α, and TGF-β. To develop therapies for cachexia, a better understanding of the impact of metastatic bone disease and these cytokines on cachexia is needed.

Methods: Patients diagnosed with lung cancer were identified from an institutional database and were designated to one of three cohorts: local disease (n=63), osseous metastatic disease (n=39), and extraosseous metastatic disease (n=39). Body mass index (BMI) at diagnosis and follow up were collected. Change in BMI per year was calculated and the Kruskal-Wallis Test was used to compare groups. In a parallel study, ELISA was performed for IL-6, TNF-α, and TGF-β on supernatant collected after 48 hours from the cell lines BEAS-2B (normal lung epithelia), H1299 (lung cancer), and A549 (lung cancer). These groups were compared using a one-way ANOVA.

Results: Median change in BMI was not statistically different (P=.79) among any cohort. The cytokine level varied by cell line. H1299 had significantly increased levels of TGF-β as compared to BEAS-2B (P=.004). A549 had elevated, but not a statistically significant different level of IL-6 as compared to BEAS-2B (P=.17). TNF-α was not present in any cell line.

Conclusion: BMI was not associated with disease state with the numbers available. The parallel study showed cell line specific elevation of TGF-β and IL-6 in lung cancer compared to noncancerous tissues. Together, these findings are inconclusive but support continued investigation into the pathogenesis of cachexia in lung cancer. Future studies will employ imaging-based body composition measurements in these disease cohorts and explore interactions between tumor, bone, and muscle in vitro.

Clinical Characteristics and Complications in Patients with Complex Vascular Anomalies

Johnson M, Haggstrom A

Background/Objective: Vascular anomalies are rare complications of development, with some forms affecting less than 1% of the population. In addition to visible manifestations, they may cause pain, swelling, bleeding, thrombosis, and infection. These conditions often require more than one field of medical expertise, so incorporating multidisciplinary care is essential for optimizing management strategies. In an effort to better describe a cohort of these patients requiring complex interventions and understand the spectrum of care they need, we captured demographic, clinical, and quality-of-life data to serve as a launching point for future studies.

Methods: We designed a RedCap database and conducted a retrospective chart review of 100 patients who presented at the Vascular Lesions Clinic (VLC) at Riley Children's Hospital from May 2020 to May 2022. Demographic, clinical, and quality-of-life data using the OVAMA scale was obtained from Cerner and captured on RedCap. Excel and RedCap software were used to characterize this patient population.

Results: The majority of patients had diagnoses of venous malformations and lymphatic malformations. These anomalies showed no male or female predominance and most lesions were segmental. Sclerotherapy was the most common intervention, with venous malformations receiving a higher median number of treatments than lymphatic malformations. Lymphatic malformations were associated with lower appearance satisfaction and a younger median age at the time of the VLC visit than venous malformations. Older age, larger lesion size, female sex, and lesion location on the lower extremities also correlated with worse quality-of-life outcomes.

Conclusion and Potential Impact: The characterization of this cohort will guide broader studies of treatments and quality-of-life trends among patients with complex vascular anomalies. Future directions could explore patient outcomes, complication rates, and influences on quality-of-life in a prospective study design.

Traumatic Brain Injury in a Level II Trauma Center Network Serving Rural Northeastern Indiana: A Cross-Sectional Study

Kipfer I, Zhu T, Hollister L, Opoku D

Background: CDC reports a need to fill gaps in current Traumatic Brain Injury (TBI) epidemiology research for at-risk populations and rural residents to help understand injury mechanisms, burden, and elucidate preventive resources. Patients aged 65 (Seniors) and above have worse outcomes after TBIs.

Objectives: This study aimed to characterize the epidemiological picture of TBI in a level II trauma center network serving rural county residents. Secondarily, we sought to determine predictors associated with senior post-TBI mortality.

Methods: A cross-sectional study of TBI in northeastern Indiana was conducted with 2019 TBI cases from five counties and patients at Parkview hospitals. Incidence rates (IR) and age-adjusted IR were examined by age and gender respectively. We analyzed TBI type, mechanism of injury (MOI), intent of injury, and hospital transfer by age group and patient type (ED, hospitalization, deaths). We used multivariable logistic regression to analyze post-TBI mortality for seniors.

Results: Males and age 75+ had the highest IRs per 1,000 residents. Concussions were the mildest TBI only causing 17% of hospitalizations and were the most common TBI in all age groups

except for seniors which had 71.7% intracranial bleeds and/or skull/orbit fractures. Falls and unintentional injuries were the highest frequency MOI and intent for all age groups, with seniors having 88.3% and 96.7% respectively. Binary regression results were significant for anticoagulant therapy, skull/orbit fracture, severe TBI, CCI, male sex, and age as predictors for senior post-TBI mortality.

Conclusion: Incidence, severity, and mortality matched high-risk groups including males and seniors. Unintentional falls were the most common MOI indicating the study population would benefit from a fall prevention program. Anticoagulant therapy and skull/orbit fracture on admission were predictors for senior mortality within one month of admission, which adds to the current understanding that these factors are associated with higher risk of TBI progression acutely.

Phone-Based Memory Test Predicts In-Clinic Memory, MCI Diagnosis, and Alzheimer's Neuroimaging & Plasma Biomarkers

Lawrence B, Deardorff R, McDonald BC, Dage JL, Wang S, Unverzagt FW, Moore PD, Apostolova LG, Saykin AJ, Risacher SL

Background: Early detection of dementia has become important for interventions that are developed to slow disease progression. Due to technological advancements, healthcare is trending toward using more telehealth screenings due to the convenience it provides patients. In our research, we evaluate the accuracy of a phone-based memory screen at diagnosing mild cognitive impairment.

Methods: 181 participants from the Indiana Alzheimer's Disease Research Center (IADRC) were screened using the Memory and Aging Telephone Screen (MATS) and diagnosed as cognitively normal (CN), subjective cognitive decline (SCD), or mild cognitive impairment (MCI). 177 underwent Rey Auditory Verbal Learning Testing (RAVLT); 103 received Aβ PET scans ([18F]florbetapir or [18F]florbetaben); 91 had plasma tau levels measured; and 140 received MRI scans (Freesurfer v6). ANCOVAs were used to evaluate differences between diagnostic groups covarying for age, sex, and education. ROC analysis and logistic regressions were used to predict MCI and Aβ positivity. Partial correlations covarying for sex and age (and education for RAVLT) were conducted to evaluate relationships between MATS scores with RAVLT, brain atrophy, pTau level, and amyloid deposition.

Results: MCI patients showed significantly lower MATS scores for immediate ($p<0.001$) and delayed recall ($p<0.001$) compared to controls. Scores on the MATS correlated well with clinical based testing (MATS learning vs RAVLT learning: r2= 0.318, $p<0.001$). MATS scores showed strong associations for Alzheimer biomarkers: amyloid and tau deposition, hippocampus atrophy, and temporal atrophy. The accuracy of MATS to predict MCI was found to be about 75% with cutoffs of ≤ 16 for learning and ≤ 4 for delayed recall.

Conclusion and Potential Impact: The findings support that the phone memory screen can be used to detect dementia early in disease progression. By establishing cutoffs for this screening tool, physicians can easily and quickly detect signs of early Alzheimer's disease, thus allowing for early intervention to slow disease progression.

Electromyographic Motor Evoked Potentials for Assessment of Laryngeal Innervation: Porcine Model Validation with Human Application

Libke M, Chen S, O'Bryan R, Takas S, Calcagno H, Zhang L, Brookes S, Voytik-Harbin S, Stacey Halum

Objective/Background: There is a paucity of information in the literature about use of electromyography (EMG) with motor evoked potentials (MEPs) in the field of neurolaryngology. For patients with early unilateral vocal fold paralysis (UVFP), it is difficult to determine appropriate interventions due to the inability of current diagnostic testing to differentiate normal conduction, neuropraxia (reversible nerve injury), and irreversible recurrent laryngeal nerve (RLN) injury. The goal of this study is two-fold: 1) to determine if the MEPs in a porcine model are reflective of underlying neurolaryngeal pathophysiology, and 2) to determine if EMG with MEPs can be used to assess patients with laryngeal denervation injuries clinically.

Methods: Yukatan minipigs with normally innervated larynges or unilateral laryngeal paralysis underwent general anesthesia and EMG with MEPs assessment via direct stimulation of the RLN (open surgical exposure) to establish normative and neuropathologic MEP profiles. In total, 11 normal vocal folds were measured, along with 3 RLN injury vocal folds and 3 compensatory vocal folds. Findings were then applied to 7 patients with RLN injury who had previously undergone transcutaneous EMG with MEPs assessment.

Results: MEPs assessment in the porcine model was reflective of underlying neuropathology. Similar findings were noted clinically in patients, although the data was more variable because of the small sample size and transcutaneous needle placement. The results from both the porcine and patient model suggest that EMG with MEPs assessment may serve as a useful tool to differentiate normal conduction, neuropraxia and irreversible RLN injuries.

Conclusion: This study demonstrates that the porcine model can be clinically translated to investigate UVFP. Because different measurements of nerve conduction were detected in the porcine versus clinical model, further clinical studies collecting EMG with MEPs data are needed to better understand the clinical utility and predictive value in the management of UVFP.

Kinetics of Measures Guiding Decongestive Therapy in AHF: Comparison of Lung Ultrasound to Conventional Markers

Line TA, Montelauro NJ, Ferre R, Brenner D, Herbert A, Kaine J, Kennedy S, Nti B, Pallansch J, Rood L, Russell F, Rutz M, Setrakian H, Zahn G, Desai A, Harrison NE

Introduction: Lung ultrasound (LUS) scoring of pulmonary edema severity has been proposed as a marker to track treatment response in acute heart failure (AHF), with a hypothetical advantage of detecting changes in congestion more quickly than traditional markers of treatment response. We compared change in LUS congestion score to contemporaneous changes in daily weight, natriuretic peptides, subjective score of worst AHF symptom (WSS), and clinical/exam findings in hospitalized heart failure patients from ED arrival to discharge, to determine which measure showed the most dynamic reduction during decongestive therapy.

Methods: This is a preliminary analysis of an ongoing prospective observational cohort study. ED patients were enrolled if they were being treated for presumed AHF diagnosis and if a LUS met diagnostic criteria for pulmonary edema. LUS, BNP, body weight, WSS, and clinical congestion score (CCS) (calculated based on orthopnea, JVD, hepatomegaly, and peripheral edema) were assessed at ED arrival and daily through discharge. Random effects models of percent change were fit for each measure, adjusted for initial value, to estimate magnitude and speed of change during ED and in-hospital decongestion.

Results: 78 observations of 21 patients were analyzed. Median age and NYHA score were 66 y/o and 4, respectively. LUS score dropped the most quickly, showed greatest mean change from ED to discharge, and showed the greatest change prior to transition to PO diuretics (initial 24-60 hours). BNP did not fall below ED values until day 3, and did not reach its nadir until day 6. The CCS correlated well with LUS, but showed a smaller magnitude of change from ED to discharge. Weight and WSS showed no significant change.

Conclusions: LUS score showed a more rapid and larger change in response to diuretic therapy, suggesting it may be a more dynamic measure of decongestion than conventional measures of treatment efficacy.

Histological Examination of the Effects of Thrombopoietin Mimetic Peptide (TMP) and High-Fat Diet on Femur Fracture Healing

Majety S, Zike S, Staut CA, Alentado V, Mostardo S, Nazzal M, Blosser R, Kacena MA

Background and Hypothesis: In the US, 11.3% of the population are diabetic. Impaired bone healing is a complication of diabetes that dramatically impacts quality of life. Thus, it is imperative to

find effective, low-risk treatments for patients that can accelerate fracture healing. We propose treatment of femur fractures using a thrombopoietin (TPO) analogue, TMP, will expedite healing, reduce adverse side effects compared to FDA-approved BMP-2, and improve quality of life of diabetic fracture patients.

Experimental Design or Project Methods: Tie2CreERT+ mice were bred with Mplfl/fl mice to generate mice in which the TPO receptor (Mpl) was deleted in cells of the endothelial lineage (Tie2 expressing cells) following tamoxifen induction (3 consecutive daily 10mg/kg doses). Tie2CreERT+; Mplfl/fl and Tie2CreERT+; Mpl+/+ mice served as experimental and control mice, respectively. Eight-week-old male mice of both genotypes were placed on a low-fat diet (LFD) or high-fat-diet (HFD) for 12 weeks. One week prior to surgery, mice were injected with tamoxifen to induce Cre-recombination. Mice were then subjected to femur fracture and treated with saline or TMP (33nmol/kg/day) for the first week post-surgery. Mice were euthanized at 1-, 2-, and 4-week post-surgery and injured femurs were isolated for histological evaluation of the fracture callus size and composition.

Results: To date only Tie2CreERT+; Mplfl/fl specimens have been processed. As expected, untreated HFD mice exhibited impaired fracture healing compared to similarly untreated LFD mice. As would also be expected, no differences were observed in fracture healing histological parameters between saline and TMP treated Tie2CreERT+; Mplfl/fl mice at similar time points post-surgery.

Conclusion and Potential Impact: While ongoing, this study explores the efficacy of using thrombopoietic agents for fracture healing in type 2 diabetes. If promising, thrombopoietic agents could replace, BMP-2 treatment, and may improve the quality of life for individuals experiencing impaired fracture healing.

Retraumatization in Undergraduate Medical Education: Evaluating the Prevalence and Support Resources Available to Students
Makhecha K, Doster DL, Standfest M, Ritter EM, Stefanidis D

Background: Retraumatization is the conscious or unconscious reminder of past trauma that results in a re-experiencing of the initial traumatic event. This phenomenon has been well-studied in primary and secondary education and has been shown to negatively impact the learning environment. Retraumatization in the context of undergraduate medical education has yet to be evaluated. Therefore, we sought to explore the prevalence of retraumatization in medical students, identify specific areas of UME that are retraumatizing, and evaluate effectiveness of psychological support available to students.

Methods: A survey was created by a multidisciplinary team of health professions educators, revised through an iterative process, and distributed to all medical students at a single, large, academic institution. Respondents who endorsed prior trauma exposure met inclusion criteria for completing the survey. Data was analyzed using Microsoft Excel.

Results: Of the school's 1400 students, 93 responses were recorded for a response rate of 6.64%; this consisted of 20 males (21.5%), 47 females (50.5%), 3 nonbinary (3.2%) students, and 23 (24.7%) students that did not report a gender identity. 27 (29.0%) students reported no prior trauma and 8 (8.6%) students opted not to complete the survey. Of the 58 (62.4%) students completing the survey, retraumatization was experienced by 33 students (56.9%), which represents a prevalence of 35.4% among all medical students surveyed. 51% of females (n=24), 10% of males (n=2), and 100% of nonbinary (n=3) students reported retraumatization. Of the students that reported retraumatization, clinical rotations were identified as a retraumatizing setting by 66.7% (n=22) of students. Despite the availability of support services, 12 students (36.4%) reported being unaware of them when experiencing retraumatization. When asked about utilization of services, the majority of those who had experienced retraumatization did not utilize them (66.7%, n=22).

Conclusion: Retraumatization is occurring in undergraduate medical education, particularly in the clinical years. Medical schools should attempt to enhance the ease of utilization of support resources to improve the learning environment for students.

Impact of pre-existing conditions on peri-procedural coronary diameters
McClaine C, Vora K, Dharmakumar R

Background: Reperfusion therapy for acute myocardial infarction (AMI) by percutaneous coronary intervention (PCI) with stent implantation is associated with a significant reduction in immediate mortality. A long-term critical complication of PCI is in-stent restenosis (ISR). However, the factors leading to restenosis remain unclear, albeit changes in coronary diameters post-PCI have been suggested to be important in stent restenosis. We hypothesize that pre-existing conditions such as hypertension, diabetes, dyslipidemia, and smoking can affect the coronary artery diameters after PCI and contribute to in-stent restenosis.

Project Methods: We recruited 26 AMI patients (age: 50-70 years; male 22) who were revascularized with PCI and studied whether pre-existing hypertension (HTN; n=10), type II diabetes mellitus (DM; n=5), dyslipidemia (DLP; n=3), and smoking (n=8) had independent contribution to changes in coronary artery diameter pre- and post-PCI. We measured segment-wise end-diastolic luminal cross-sectional diameter of left main (LM), left anterior descending (LAD), left circumflex (LCx), and right coronary arteries (RCA) from invasive coronary angiograms before and after PCI.

Results: We found that the LM showed insignificant change in cross-sectional diameter in HTN, DM, and smoking groups. However, DLP group of patients showed an increase in diameter post-PCI. Proximal

segment of LAD in HTN patients and all LAD segments in DM group were significantly increased in diameter. Proximal LCx was reduced in diameter in DLP group. RCA distal and PDA segments in HTN group as well as PDA segment in DM group were reduced in diameter post PCI.

Potential Impact: Although following PCI, proximal and mid segments increase in diameter by 5-20%; and distal segments by 20-30%, our early findings indicate that changes in cross-sectional diameter of the coronary segments can fall outside these ranges when pre-existing conditions are present. Follow-up studies are needed to evaluate the relation between changes in coronary diameters and in-stent restenosis.

Direct Inspection of Primary Aortic Cell Transcriptomes Identifies Candidate Causative Variants in Patients with Thoracic Aortic Aneurysm

Mederos AV, Landis BJ

Background: Thoracic aortic aneurysm (TAA) is an aortopathy that predisposes to life-threatening aortic dissection. Autosomal dominant disorders associated with TAA include Marfan syndrome (FBN1), Loeys-Dietz syndrome (TGFBR1/2, SMAD3, TGFB2), and vascular type Ehlers-Danlos syndrome (COL3A1). Our objective was to identify single nucleotide variants (SNVs) in these six genes within the transcriptomes of primary aortic cells acquired from patients with aortopathy.

Methods: Primary aortic cell lines were cultured directly from the medial layer of surgically explanted aortic tissues in 63 unrelated aortopathy patients. RNA samples were extracted from aortic cells for mRNA sequencing. RNA reads aligning to the 6 selected TAA genes were directly inspected using Integrative Genomics Viewer (Broad Institute), and the identified SNVs were filtered for downstream analysis.

Results: Study patients were predominantly male and of European ancestry with a mean age of 52 ± 18 years. Thirty-three (52%) patients had a bicuspid aortic valve, and 10 (16%) had family history of TAA or dissection. A total of 3740 SNVs were identified in patient transcriptomes, and these occurred at 905 distinct genomic coordinates. There were 111 SNVs that were unique within the cohort, not located within a 3'-untranslated region, and had ≥ 20 aligned reads at the SNV's position. Using the application Franklin (Genoox) to estimate clinical interpretation, 8 unique SNVs were classified as pathogenic (P) or likely pathogenic (LP). Five of these P/LP SNVs were associated with reduced allelic expression, and gene expression level was below the 20th percentile of study samples for 6 P/LP SNVs. Eighty-six unique SNVs were classified as variants of uncertain significance (VUSs). A total of 41 patients (65%) had at least one SNV classified as P/LP/VUS.
Conclusion: Transcriptomic analysis of primary aortic cells identified candidate causative SNVs and their relative allelic expression. Further

analyses will investigate additional TAA-associated genes and integrate transcriptional abnormalities with genetic variants.

Granule Cell Layer Morphology and Wnt Signaling in Temporal Lobe Epilepsy

Nickerson M, Mardones M, Gupta K

Background and Hypothesis: Temporal lobe epilepsy (TLE) is the most common human seizure disorder and can develop after neurologic insults such as trauma or infection. No treatment exists to prevent the development of epilepsy during this critical period. Epileptogenesis is characterized by pathological neuronal network remodeling in the hippocampal dentate gyrus (DG). Previously, we found that Wnt pathway signaling is dysregulated in the kainate (KA) mouse model of TLE, such that Wnt antagonism exacerbated epileptogenic DG remodeling. We hypothesize that Wnt agonism will mitigate pathological DG remodeling of the granule cell layer (GCL) during epileptogenesis.

Project Methods: TLE was induced by unilateral intrahippocampal KA injection in POMC-eGFP transgenic mice, while controls received saline. Mice received injections of vehicle or Wnt agonist Chir99021 daily. eGFP+ immature dentate granule cells were characterized by confocal microscopy. GCL width and immature dentate granule neuronal migration in the ictal/ipsilateral and peri-ictal/contralateral DG were quantified. Quantitative analyses were performed to compare means of the 4 groups.

Results: We found that GCL width significantly increased in the ictal zone 2 weeks after seizure induction in both KA groups and was not mitigated by Chir treatment. Immature dentate granule cell migration also increased in the ictal zone in the KA groups and was not altered by Chir treatment. In the peri-ictal zone, GCL width and cell migration were unchanged across KA and saline control mice.

Conclusion and Potential Impact: The Wnt agonist Chir99201 did not appear to alter GCL morphology in control or KA mice. It is likely that Wnt signaling may impact neuronal functioning rather than morphology in DG remodeling, and this will be explored through future electrophysiological studies. The Wnt pathway remains a potential therapeutic target in the prevention of the development of epilepsy.

Mitochondrial Phenotypic Variability in Inbred Mouse Strain Tissues

Olchawa N, Anderson M, Dosunmu S, Graham B

Abstract: Mitochondrial inherited diseases are primarily inherited genetic disorders from the mother that cause mitochondrial dysfunction, which results in inadequate energy production to allow for a cell to thrive. A common cause of mitochondrial dysfunction is the pathological depletion of the mitochondrial genome, known as mitochondrial depletion syndrome (MDS). MDS refers to a group of complex and diverse multiorgan disorders that typically result in a poor prognosis for patients, and often ends in fatality. There are interventions that have been designed only for symptom management and supportive care, as there are currently no curative treatments available for MDS. Mitochondrial DNA (mtDNA) copy number is a unique way in which cells to determine their overall mitochondrial health and functionality. However, the molecular mechanisms that modulate mtDNA content in both healthy and non-healthy tissues are still poorly understood. Thus, further research into the regulatory control of mtDNA copy number may elucidate valuable information to further advance the management and treatment of MDS. In order to investigate the natural variability of mtDNA copy number across healthy tissues, Citrate Synthase and qPCR assays will be performed to quantify overall mitochondrial function and mtDNA copy number in various tissue segments of four inbred mouse strains that will elucidate mitochondrial phenotypic expression.

Continuous Glucose Monitoring for Cognitively Impaired Older Adults with Type 2 Diabetes: Workflow Analysis

Pamidimukkala U, Savoy A

Background: Older adults with Alzheimer's disease or Alzheimer's disease-related dementia (ADRD) and type 2 diabetes mellitus often have difficulty detecting hypoglycemic events. Over time, recurring hypoglycemic events increase the risk of severe consequences such as hospitalization. Previous studies have shown continuous glucose monitoring (CGM) to be one of the best ways to detect hypoglycemia. With CGM devices or sensors, a small needle is inserted under the skin to monitor glucose levels continuously, every 5-15 minutes. After 1-2 weeks the CGM devices need to be replaced. Glucose data from the device can be viewed by patients and shared with caregivers and clinicians. Latest models of CGM devices are advertised to patients and caregivers as easy to use with simple instructions or workflows. However, CGM use in the ADRD population has not been widely practiced or reported.

Objective: The goal of this project is to conduct a systematic review and analysis to develop a better understanding of the steps or tasks patients must complete to correctly set up and use CGM and identify potential barriers for patients with ADRD and type 2 diabetes.

Methods: In the summer of 2022, a workflow analysis with a narrative review of how CGM systems are currently used by patients and caregivers was conducted using the databases PubMed and Google Scholar, as well as CGM device manufacturers' user manuals, including FreeStyle Libre, DexCom, and MedTronic. We searched literature from 2000-2022, and search terms included "continuous glucose monitoring", "Alzheimer's disease and diabetes", and "continuous glucose monitoring barriers" to best address the objective of the search. Information from the articles regarding CGM barriers and how they manifest in the ADRD population was independently extracted to address the main research objective. Subsequently, a workflow extrapolated to patients with ADRD was created based on these sources.

Findings: A total of 118 articles, websites, and guides were obtained through the literature search, and 63 articles were excluded because they were irrelevant or outdated. A total of 55 articles were included in the review. Reported patient tasks for CGM can be described as workflows consisting of only 3-9 steps. Based on findings of the literature review, we constructed a more detailed workflow of expected tasks for patients with ADRD. There are 9 tasks: (1) healthcare visit, (2) CGM education, (3) CGM pick-up from a healthcare office or manufacturer, (4) sensor insertion, (5) scanning, (6) evaluation of glycemic data to guide patient care, (7) sensor replacement every 10-14 days, (8) next healthcare visit, and (9) pharmacist modifications of insulin or medication dosing. Additionally, we identified five potential areas for improvement, including (1) patient access to ADRD-friendly educational materials for CGM, (2) sensor insertion, (3) frequent sensor scanning to retain data, (4) CGM data interpretation and response, and (5) notifications to replace sensors.

Conclusion: Current patient workflows for CGM are oversimplified and do not detail tasks that can be complicated for patients with ADRD or their caregivers, including tasks that rely on patients' comprehension of instructions or data and patients' memory to scan data or replace sensors. More research is needed to determine the severity of the identified barriers and potential interventions to integrate diabetes management into ADRD care.

Advanced ultrasound imaging of the brain in neonatal hydrocephalus using a rat hydrocephalus model

Patwari N, Blazer-Yost B, Forbes-Amrhein M

Background and Objective: Preterm infants are at risk of developing post-hemorrhagic hydrocephalus. Earlier detection and intervention via placement of an intraventricular catheter improves neurologic and cognitive outcomes. However, intraventricular catheter placement is invasive with many risks, including hemorrhage and infection. Currently, invasive placement of an intraventricular pressure monitor is the only means to diagnosis hydrocephalus. Magnetic resonance imaging (MRI) can be used to detect ventriculomegaly and suggest hydrocephalus but cannot diagnose it; and MRI is challenging to obtain in premature infants, making it unfeasible as a monitoring tool. Shear wave elastography (SWE) is an ultrasound technique performed at bedside which measures tissue stiffness and could serve as a rapid way of detecting hydrocephalus. We hypothesize that SWE stiffness measurements will positively correlate to MRI-derived ventricular volume measurements.

Methods: The hydrocephalic rat model Tmem67 was bred to produce wild-type (n=10), heterozygous (n=9), or homozygous (n=10) rat pups. The point mutation causes non-obstructive hydrocephalus. The wild-type rat pups are without hydrocephalus. The heterozygotes manifest with a milder, slower progressing hydrocephalus. The homozygotes manifest a severe, rapid-onset hydrocephalus. SWE and MRI (3 Tesla) images of the rat pups were obtained at 7 and 14 days postnatally. Stiffness was measured using the Aixplorer SWE analysis tool with measurements taken in the coronal plane of the periventricular white matter. Lateral ventricle volumes were measured from the T2-weighted MRI images in the sagittal plane by planimetric analysis using the Q Image analysis program.

Results: Stiffness and ventricular volumes were compared between genotypes via Kruskal-Wallis test at 7 and 14 days. SWE stiffness measurements were significantly different between genotypes at 7 at 14 days, H = 12.94 (p < 0.05) and H = 17.58 (p < 0.001), respectively. MRI volume comparisons were significantly different between genotypes at 7 and 14 days, H = 18.78 (p < 0.001) and H = 19.01 (p < 0.001), respectively. MRI volume measurements were correlated to the SWE measurements via Spearman's rank correlation at 7 days (r = .53948, p < 0.05), 14 days (r = .57, p < 0.05). SWE and MRI measurements also significantly correlated when the data from days 7 and 14 were combined (r = 0.565, p < 0.001). In all correlations, the Spearman's r was consistent with a moderate correlation.

Conclusion and Potential Impact: This pilot study shows that SWE-derived brain stiffness has a significant, moderate correlation with ventricular volumes in the setting of hydrocephalus. SWE has the potential to be used as a bedside tool for detecting neonatal hydrocephalus in preterm newborns. SWE could reduce the need for MRI exams and invasive intraventricular catheter placements, allowing for more rapid diagnoses and interventions for fragile newborns with hydrocephalus. Further studies are needed using a larger sample size and a direct measure of intracranial pressure to establish the ability to use SWE clinically.

The Impact of Propofol on Blood-Brain Barrier Efflux Protein Activity in Alzheimer Disease Genotypes

Pavelka M, Hughes J, Reddy K, Canfield S

Introduction: Propofol is a common induction anesthetic that recently has been shown to diminish the integrity of the blood-brain barrier (BBB) while maintaining efflux protein expression and activity. Efflux transporters, notably MRP-1, BCRP, and P-gp, mediate clearing cytotoxic metabolites. The role of propofol on the activity of efflux proteins in Alzheimer's Disease (AD) patients is unknown. The goal of this study was to utilize human induced pluripotent stem cell (iPSC)-derived brain microvascular endothelial cells (BMECs) differentiated from familial AD iPSCS (APP, PSEN1, and PSEN2) and healthy iPSCs to determine the effects of propofol on efflux activity and expression.

Methods: To measure the effect of propofol on efflux activity, treated cells were exposed to 50μM propofol for three hours, and then protein-specific efflux fluorescent substrates and inhibitors were utilized to determine efflux activity (P-gp: Rhodamine 123/CsA; MRP-1: DCFDA/MK571; BCRP: Hoechst/KO143). Cells were lysed and the fluorescent substrate was quantified by a plate reader and normalized to the uninhibited group. Efflux protein expression was also qualitatively assessed using immunostaining.

Results: Our preliminary results demonstrated that propofol did not affect efflux activity similar to previous literature. Interestingly, PSEN1 and PSEN2 had suppressed baseline efflux transporter activity and did not show any change following propofol exposure. APP-derived BMECs displayed suppressed P-gp activity and similarly to PSEN 1/2-derived BMECs were not altered by propofol.

Conclusion: Our preliminary results implicate that AD-derived BMECs have suppressed baseline efflux activity; however, propofol exposure did not further alter activity level. Additional studies are needed to determine the role of anesthesia-induced injury on efflux activity and expression.

Measuring Denatured Collagen Debridement After in vivo ACL Cyclic Loading in Mice
Phan K, Loflin B, Ahn T, Schlecht S

Background/Objective: Anterior cruciate ligament (ACL) injuries are one of the most common and debilitating injuries in sports. Once thought to be caused due to acute stress events, recent research has demonstrated that this could be from chronic overuse and fatigue. We hypothesized that the estimated time that denatured collagen removal occurs is around 6 days to start ACL repair and there will be no changes between right and left knee mechanical parameters.

Methods: Forty B6 female 10-wk old mice were used in a custom setup that cyclically loads to 60% of the ACL's max force for 500 cycles. All right legs were tested, and the specimens were randomly separated into four equal cohorts for rest times in 3-day increments. Following each cohort's rest time, the left knee was loaded in the same manner (n=7) and the remaining from each group (n=3) were used as untested contralateral controls. Immediately after each cohort was tested, they were euthanized, and legs were harvested, fixated, and decalcified for paraffin infiltration. Tissue was sectioned and deparaffinized for staining with R-CHP for immunofluorescence, followed by Raman spectroscopy to examine proteoglycan activity.

Results: Current results demonstrate the mechanical data of all tested ACLs via measures of hysteresis and stiffness. No statistical differences were found, except for the hysteresis of the left ACLs between cohorts 2 and 3 and upper stiffness of the right ACLs in all mice compared to the left ACLs in cohort 3. The results from CHP staining will be analyzed in future work.

Conclusion and Implications: Ultimately, this study will help narrow down when denatured ACL collagen from fatigue begins as an indication of the repair process taking place. This knowledge may be used in athletes with strained ACLs to know how long to adequately rest before continuing sport activity.

Effects of Gemcitabine/Nab-Paclitaxel and DMAPT in PDAC Cachexia in vivo and in vitro
Philleo SA, Brittany R. Counts BR, Jean S, Gowan AE, Narasimhan A, Nakshatri H, Zimmers TA

Cachexia is the involuntary wasting of skeletal muscle and adipose tissue, affecting over 80% of patients with pancreatic ductal adenocarcinoma (PDAC). Gemcitabine and nab-paclitaxel (GemNP) combination are commonly given as first-line treatments for PDAC. Data from our lab showed GemNP reduced tumor growth and prevented muscle and fat wasting. Dimethylaminoparthenolide (DMAPT), a small molecule inhibitor, prevented muscle wasting and prolonged survival in a genetic murine model of breast cancer. It has yet to be determined if GemNP in combination with DMAPT

can improve indices of cachexia and overall survival. Therefore, I hypothesize that GemNP in combination with DMAPT will improve indices of cachexia and overall survival in a murine model of pancreatic cancer.

Male 10-week-old C57BL/6J mice underwent orthotopic injection of 5x104 KPC cells or SHAM surgery. Mice were randomly assigned to 1 of 4 groups (N=10/group): SHAM+Vehicle, KPC+Vehicle, KPC+GemNP, KPC+GemNP+DMAPT. Gemcitabine (120 mg/kg) and Nab-paclitaxel (10 mg/kg) were injected intraperitoneally starting on day 4 and continued every 6 days. DMAPT (100 mg/kg) was administered by gavage Monday-Friday. To determine the role of GemNP and DMAPT in vitro, KPC cells were treated with GemNP and/or DMAPT and cell viability evaluated. Additionally, we treated myotubes with GemNP with/without DMAPT to assess myotube diameter in an established KPC conditioned media.

In KPC mice, GemNP (24.4days) increased survival compared to Vehicle (16.8 days, p=.0007). However, the combination GemNP+DMAPT did not extend survival over GemNP alone (25.4 days, p=.693). Tumor mass was similar between all groups (p=0.411). Interestingly, at the time of sacrifice, all KPC treated mice independent of treatment had similar reduction in adipose tissue and muscle mass compared to SHAM.

In conclusion, the addition of DMAPT to GemNP did not extend survival over GemNP alone in an aggressive pancreatic tumor cell line. Future studies should determine if less aggressive tumor cell lines might benefit from GemNP and DMAPT.

Characterization of a Chimeric MmuPV1 Genome with HPV-16E6E7
Pyles J, DeSmet M, Jose L, Androphy E

Background/Objectives: Papilloma Viruses (PVs) are double-stranded DNA viruses that infect cutaneous and mucosal epithelium. In humans, there are over 100 types of PVs. HPV-16 is a high-risk type that causes ~50% of cervical cancers and ~70% of oropharyngeal cancers by expressing viral oncogenes E6 and E7 in replicating keratinocytes. The mouse PV, MmuPV1, displays species tropism and causes neoplastic lesions. Its discovery in 2011 introduced the opportunity to study PVs from early stages of infection to cancer development. Such an in vivo model of HPV-16 could uncover novel mechanisms for treatment intervention and disease prevention. Our study aims to characterize a small-animal infection model using a chimeric MmuPV1 genome with HPV-16 E6 and E7 in place of mouse E6 and E7 (MmuPV1-16E6E7). The goal of our study is to investigate the genome's ability to express the HPV-16 oncogenes in vitro and to cause tumors in vivo.

Methods: To increase selective pressure in vitro, we replaced the MmuPV1 L1 and L2 genes with a neomycin cassette (MmuPV1-16E6E7neo). We packaged these genomes into infectious

quasiviruses using a HEK 293TTF viral packing cell line. After isolating quasiviruses, we infected two donor human foreskin keratinocytes (HFK) cell lines. Forty-eight hours post infection, we isolated mRNA for qPCR to quantify HPV-16 E6 expression. To investigate whether MmuPV1-16E6E7 can cause tumors in in vivo, we infected athymic nude (N/J) mice orally with quasiviruses to evaluate infection and viable genome persistence.

Results: HPV-16 E6 cDNA was detected in three HFK isolates.

Conclusions/Future Directions: The presence of HPV-16 E6 cDNA indicates that the gene can be successfully transcribed from MmuPV1-16E6E7neoin HFKs. Future studies will assess this ability in primary mouse keratinocytes. If tumors are observed, we can use this model to study the efficacy of antiviral compounds to inhibit HPV16 E6 in vivo.

Investigating Longitudinal Continuity of Persistent White Matter Alterations in Sport-related Concussion Using Individualized Analyses

Ramirez LA, Yang H, Wen Q, Dzemidzic M, Harezlak J, Wu Y

Background: Sport-related concussion (SRC) has been shown to lead to acute and long-term alterations in white matter (WM) organization. The Centers for Disease Control estimates around 283,000 children each year seek medical attention for SRC/recreation-related traumatic brain injury. However, literature on subject-specific longitudinal WM abnormalities in SRC is limited.

Purpose: Given the heterogeneous nature of SRC on WM microstructure, the goal of this study is to investigate the longitudinal continuity of persistent white matter alterations using a subject-specific approach.

Methods: MRI is a non-invasive imaging modality suitable for detecting neuropathophysiological changes after SRC. Compared to conventional anatomical MRI, using diffusion MRI to probe WM microarchitecture may provide additional sensitivity. The diffusion MRI data from 50 participants were obtained from the CARE consortium, a prospective multisite study examining the natural history of concussion. Each concussed athlete underwent MRI scan at three time points: (1) 24-48 hours after concussion, (2) asymptomatic state, and (3) 7-days after returned to play. Diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) metrics were computed and Z-scored based on a normal distribution template created from non-contact sport controls. Potential WM alterations indicated by extreme deviations of Z-score maps were calculated for all diffusion metrics in each concussed participant and time point.

Results: WM alterations persistent across all three timepoints manifested in 76%, 62%, and 82% of the participants as quantified by increases of mean, axial, and radial diffusivity, respectively.

58% of the participants had fractional anisotropy decreases. For NODDI metrics, 82% and 86% of the participants showed increases of isotropic volume fraction and orientation dispersion index, respectively.

Conclusion: This study demonstrated that by applying subject-specific analysis, extreme Z-score voxels can be identified across time in the same or spatially proximal brain regions suggesting persistent WM abnormalities beyond apparent clinical recovery.

Role of the XPC Gene Expression in the Prevention of Oxidative and DNA Damage to Lung Squamous Carcinoma Cells

Randall D, Zhou H, Sears C

Background and Hypothesis: Xeroderma pigmentosum group C (XPC) is a DNA repair protein involved in the detection and repair of DNA damage caused by oxidative lesions through global genomic repair. Carcinogens, chemotherapeutics, and UV-lesions require repair of DNA by XPC. Exposure to one environmental toxin, cigarette smoke (CS), leads to cancer development and can worsen outcomes of those with cancer, however, the precise mechanisms and why susceptibility varies individually remains poorly understood. This study examines the role of XPC in cell survival in human lung squamous cancer cells (H520) and hypothesizes that XPC protects against DNA damage and cell death after exposure to cigarette smoke extracts (CSE).

Methods: Lentiviral vector transduction for XPC knock-down (XPCKD) was completed in H520 cells. Transfection efficiency was measured by green fluorescence protein to determine multiplicity of infection (MOI); puromycin resistance was measured by CCK. XPC was targeted at two sites (Mission shRNA 118 and 119, Sigma), and gene knock-down efficiency determined by qRT-PCR. Survival of unmodified and H520-XPCKD cells to CSE exposure was determined by CCK and clonogenic survival assays.

Results: Lentiviral knock-down decreased XPC gene expression by 68-78% in H520-XPCKD as measured by RT-qPCR, with protein knock-down confirmed by Western blot. There was increased susceptibility of H520-XPCKD to CSE with decreased cell survival in XPCKD compared to non-transduced H520 cells.

Conclusion: XPC protects H520 cells against cell death due to exposure to cigarette smoke. Future studies will be performed to confirm the degree of protection and to determine the mechanism of XPC protective effect. These findings could be important for the discussion of risk factors with patients to understand the risks of smoking in patients with lung cancer and help physicians determine patient specific susceptibility.

Air Pollution as a Predictor of Asthma in Sickle Cell Disease Patients in Indiana

Reese E, Dixon B

Background: Sickle Cell Disease (SCD) is a recessive condition that predominantly affects Black individuals. It contributes to a plethora of poor health outcomes and events such as multiple organ failure, and chronic hypoxia. Additionally, SCD patients disproportionately have asthma as a comorbidity when compared to the general population. This pairing of SCD and asthma increases the likelihood of health complications like acute chest syndrome. Although some of the inflammatory mechanisms in SCD and asthma overlap, they have distinct pathophysiologies. This study explored the potential link between air quality and the prevalence of asthma in hopes of contributing to the understanding of the disproportionate prevalence of asthma amongst the SCD population in Indiana.

Methods & Results: This study conducted Poisson and Logistic regressions on county-level EPA TRI data and SCD patient comorbidity data to address these gaps. Our study yielded inconclusive results for a link between air emissions, total onsite-emissions, risk scores, and asthma. It showed that while these variables were significantly, but minimally, linked to increased prevalence of asthma when our analysis controlled for the number of SCD patients in each county the link became insignificant. Additionally, none of our variables were significantly predictive of the presence of asthma in SCD patients. We believe that either these variables are not significant contributors to the development of asthma in SCD patients, or the analysis should be repeated with data at a zip code level to increase the geographical precision and accuracy of pollution exposure.

Implications: Although we were unable to conduct this analysis, due to constraints involving data availability, future work should examine if air quality is associated with asthmatic events and hospitalizations for SCD patients. This work could be relevant for the implementation of preventative measures to improve health outcomes for SCD patients with asthma.

Lutheran Children's Hospital Neonatal Follow-Up Clinic: Risk of Developmental Delay of Preterm Neonates as a Function of Gestational Birth Age

Russell A, Stace S, Soldner SA

Background/Objectives: About 1 in 10 babies are born prematurely, a number that increased from previous years because more resources are available and fertility treatments are effective. Children born prematurely have a higher risk of developmental delays that are associated physically, socially, linguistically, and neurodevelopmentally. With these delays being commonly associated with preterm infants, there is the need to continuously study the longitudinal effects caused by being born prematurely. Our objectives include creating a more comprehensive care plan, comparing gestational age with developmental delay levels, and noting correlations between delays and their respective cohort. We hypothesis the more premature the child was born, the higher the likelihood of developmental delay(s).

Methods: Two main tests were used to look for a correlation between the delay or lack of a delay with the child's adjusted age. TIMP, Test of Infant Motor Performance, was used at two different age intervals to measure infant motor capacity. The ASQ, Ages and Stages Questionnaire, was used to screen several different developmental areas of concern, including social and behavioral abilities.

Results: The data shows the developmental delay decreasing over time in all preterm cohorts with an exception being the late preterm cohort, likely due to its small sample size. The Chi-square test is not significant for the TIMP1 and TIMP2 comparisons of preterm cohorts. The ASQ data sets did not have a clear consensus of data.

Conclusions: There is an increase of developmental delay in neonatal infants in comparison to the standard developmental milestones. A positive finding is that there is an overall decrease in developmental delay as the child progresses in age.

Potential Impact: This research may promote other hospitals to implement a NFC for patient care and research considerations.

Dynamic and Stimuli-Responsive Hydrogel Systems for Controlled Release of Proteins

Sammour Y, Dimmitt N, Lin C

Background and Hypothesis: Hydrogels have been extensively used as biomaterials for controlled release applications due to their biocompatibility and tunable networks. Stimuli-responsive, or smart, hydrogels are of interest due to their potential for localized release based upon local stimuli such as pH. In addition to smart materials, dynamic hydrogels have been utilized to obtain unique release profiles such as biphasic release curves. We hypothesized that by leveraging dynamic and stimuli-responsive click chemistry we can fabricate hydrogels with unique and controlled release profiles.

Project Methods: A new reversible addition fragmentation chain transfer (RAFT) polymer known as PADO, was synthesized bearing a ketone functional group allowing for crosslinking with hydrazide bearing motifs to form a pH labile acylhydrazone bond. In addition, polyethylene glycol (PEG) based hydrogels have been extensively used in controlled release applications due to their biocompatibility and antifouling properties. Previously, we have developed a novel conjugation technique for functionalizing norbornene onto hydroxyl-terminated PEG through a cyclic desymmetrization reaction with carbic anhydride. The new polymer, PEGNBCA, was further conjugated with dopamine via amide conjugation to form PEGNBD. Mass loss and protein release analysis were conducted for PADO and PEGNBD hydrogels, respectively.

Results: Mass loss studies confirmed that PADO hydrogel degraded

faster at mildly acidic pH of 6 compared to physiological pH of 7.4. In addition, the rapid hydrolysis of PEGNBD crosslinked via inverse electron demand Diels-Alder reaction demonstrated higher protein release compared to conventional PEGNB hydrogels, which are hydrolytically resistant.

Conclusion/Impact: The sensitivity to degradation PADO hydrogels in an acidic environment, and the hydrolytically sensitive PEGNBD hydrogels, can be utilized for targeted therapeutic release. For example, the pH-sensitive hydrogel system can be utilized for therapeutic release into an acidic neoplasm while having minimal release in neutral pH tissues.

Acute Effects of Metal vs. Bioresorbable Vascular Scaffold Deployment on Coronary Arteries in Metabolic Syndrome

Sansone J, Arnold J, Byrd J, Ding Y, Sun C, Alloosh M, Ameer G, Sturek M

Background: Metabolic syndrome (MetS) and type 2 diabetes are common patient populations requiring cardiovascular interventions, while also showing increased complications. Bioresorbable vascular scaffolds (BVS) have great potential to mitigate complications associated with permanent metallic stents, including hampered vasomotion and long-term foreign body responses. We compared the first critical steps in deployment of novel BVS and everolimus-eluting metal stents in coronary arteries of Ossabaw miniature swine having MetS.

Methods: MetS swine were stented in each of the 3 major epicardial arteries. Metal vs BVS selection and artery placement were randomized prior to procedures. Angiography and intravascular ultrasound (IVUS) were performed before and after stenting. Pulse oximetry and electrocardiography were used to evaluate the stability of the animal. Verification of cardiovascular MetS Ossabaw was done through serum chemistries and through IVUS quantification of atherosclerosis by circumferential wall coverage (CWC).

Results: MetS swine (n=6) showed typical obesity, dyslipidemia, and hypertension, and average CWC 3.5-fold greater than lean swine (n=4). In arteries stented with BVS (n=8), 88% had spasm(s), while 29% of arteries with metal stents (n=7) had spasm(s). There was thrombus noted during IVUS after BVS deployment in two pigs.

Conclusion: MetS swine showed increased atherosclerosis and serum markers consistent with MetS. Arteries stented with BVS had 3-fold more spasms than with metal stents. The BVS deployment mechanism, requiring more time spent in arteries than metal stents, or increased device size could have caused this spasm increase. Future analysis after long-term recovery will determine whether this BVS is superior to metal stents in attenuating neoatherosclerosis and in-stent restenosis.

Machine Learning as a Tool in Detecting Rib Fractures in Pediatric Patients

Satoor V, Marine MB

Background/Objective: Rib fractures are one of the most specific fractures in child abuse and are among the most common identified, reported in up to 45% of cases. Given rib fractures can be subtle and difficult for even experienced radiologists to identify, a diagnostic tool to improve the detection accuracy would provide value in evaluation of child abuse. The objective of this investigation is to create a machine learning algorithm with the ability to recognize the presence or absence of rib fractures on chest radiographs in pediatric patients less than 3 years old.

Methods: The IU Health radiology archive (DORIS) was searched for reports (Jan 2020-June 2022) for skeletal surveys in patients less than 3 years of age. 3 view chest radiographs (frontal and bilateral oblique) from the surveys were fit into two datasets: no rib fracture or presence of rib fracture. A machine learning model was trained and tested using the constructed datasets with Histogram of Oriented Gradients (HOG) features extracted to refine the prediction accuracy.

Results: The study group contained 100 patients (40 females, mean age 8 months) with 299 radiographs with reported rib fractures. The gender and age-matched control group included 100 patients who had 300 radiographs without reported rib fractures. The overall performance accuracy of the trained model was 95.9%. PPV, NPV, sensitivity, and specificity were 96.83%, 88.32%, 87.32%, and 97.09%, respectively.

Potential Impact: Given the demonstrated effectiveness of the machine learning model, it could serve as an aid to be used in the interpretation of skeletal surveys for child abuse. More importantly however, it may also be considered as a screening tool in identifying rib fractures in unsuspected patients, such as chest radiographs in the emergency room setting where ribs may not be the primary focus of evaluation and fractures may go overlooked.

Geriatric Trauma Patients and Firearm Ownership: Planning for Cognitive Decline

Scanameo L, Redilla N, Swartwood B, Smith H, Levin J, Meagher A

Background/Objective: It's estimated that roughly 13 million older adults will suffer from dementia in the United States by 2050 and over 30% of adults $\geq$65 years own a firearm. There is a lack of information on the attitudes of older adult firearm owners in the Midwest regarding management of firearms and dementia. The study's aim was to survey geriatric trauma patients about firearm ownership, storage, and planning for cognitive decline.

Methods: Patients were approached for study participation if they were admitted to the trauma service at an urban academic level I trauma center, aged $\geq$60 years, and own or live with a firearm. Participants were approached in person and if they agreed to participate, an anonymous survey was conducted during their

admission. Our primary outcome was rate at which participants would consider having a planning conversation following survey participation if they had not already done so. Results were analyzed for thematic trends.

Results: Over the study, 50 patients were approached with 19 (38%) meeting inclusion criteria. Of the eligible participants, 10 (~53%) were successfully enrolled. There was an equal male-to-female participation rate with an age range of 61-85 years. Twenty percent (n=2) of participants had previous conversations with family members about firearm management and dementia. After survey participation, 70% (n=7) of participants intended to have planning conversations. A theme of giving firearm responsibility to others emerged in response to prompting participant's biggest concern of firearm management and dementia.

Conclusion and Potential Impact: Sixty percent (n=6) of participants expressed a desire to have new planning conversations with family after survey participation, which met the primary outcome of the study. Further work to assess barriers to study participation is ongoing. These results have the potential to better inform educational interventions for adult firearm owners to guide conversation and outline available resources.

Complications and Outcomes Associated with Two-Stage Treatment of Periprosthetic Total Hip Infection
Schmidt J, Ziemba-Davis M, Meneghini RM

Background and Hypothesis: Periprosthetic joint infection (PJI) is treated with implant resection, debridement, and component reimplantation after infection eradication. Treatment consists of either a single surgery or two-stage surgery with intravenous antibiotic therapy between stages. We replicated a recent study which concluded two-stage treatment is associated with high morbidity, hypothesizing that complication rates would be similar, but that morbidity is not always conclusively a consequence of two-stage treatment for PJI.

Project Methods: Prospectively documented data on all primary and revision hips undergoing two-stage treatment for PJI by a single surgeon were retrospectively reviewed. Surgical complications were quantified for the interstage and post-reimplantation periods. Chi-squared tests were used to compare current findings to published findings.

Results: Six of seven patient demographics and comorbidities were equivalent in the two studies (p ≥ .278). More complex infections characterized the current study as evidenced by significantly more polymicrobial infections (p < .001). Spacer retention rather than component reimplantation did not occur in the current study but characterized 32 patients (16%) in the comparison study (p = .002). There were no differences in the number of additional interstage

septic procedures (p = .402) and fewer post-reimplantation septic surgeries in the current study (p = .018). Using a proposed system which penalizes additional operations required to eradicate infection, treatment success rates at minimum one year follow-up were 73% and 71%, respectively (p = .856). Without these penalties, treatment success in the current study was 93% (equivalent proportion not available for comparison study). All-cause mortality was higher in the current study (18.2% versus 7.6%, p = .044) but only two deaths were related to PJI (unknown for comparison study).

Potential Impact: Study findings suggest that morbidity attributed to two-stage treatment reflects the inherent complexity of this patient group, and not the two-stage treatment itself.

The Effects of the COVID-19 Pandemic on IVC Filter Placement
Schneider D, Keltner K, White E

Background: IVC filters are self-expanding stents that have been used to prevent pulmonary embolisms when anticoagulants are contraindicated. Retrieval of filters is imperative to their success as prolonged dwell time can cause further complications such as filter erosion, displacement, or thrombus. The IVC filter clinic was created in July 2017 to improve patient outcomes, follow-up, and removal of filters.

Objectives: The purpose of this study is to determine differences in indication, removal rate, follow-up rate, dwell time, mortality, and general trends before and during the COVID-19 pandemic.

Methods: The current study is a retrospective chart review of patients who received an IVC filter between July 2017 and June 2022. In determining differences related to the COVID-19 pandemic, March 2020 was used as the start date, and it is ongoing through June 2022.

Results: There was a decrease in one year survival (86% vs 63%, p = .000412) when patients did not receive a follow-up office visit. There was a decrease in follow-up rate (86% vs 77%, p = .049762) after the onset of the COVID-19 pandemic. Patients who had their filter removed were more likely to be alive at one year than those who did not get their filter removed (95% vs 72%, p < .00001). There was no significant change in indication, removal rate, dwell time, or one-year mortality after the start of the pandemic.

Conclusions and Potential Impact: Patient survival can be improved if they attend a follow-up visit, and if they have their filter removed. We also identified patients whose filters did not improve their mortality because of other underlying medical conditions whereas other patients were successfully treated. This indicates the need for a more selective process in placing filters. This also confirms previous research that COVID-19 restrictions and fear caused secondary negative effects on patient outcomes.

Developing the Study Question: Relationship Between Cardiologist Age and Delivery of Aortic Valve Replacement

Shinnerl A, Torabi A, Knapp S, Breathett K

Introduction: Aortic stenosis (AS) is the most common valve disease worldwide, but intervention for symptomatic AS is variable and dependent on patient age, frailty, and co-morbidities. Recent studies have suggested that the greatest determinant of receipt of aortic valve replacement (AVR) is a supportive recommendation by the patient's cardiologist. Given that recommendations for cardiovascular therapies sometimes vary by clinician age, it is unclear whether cardiologist age is associated with referral for AVR.

Objective: To determine whether cardiologist age is associated with referral for AVR.

Hypothesis: We hypothesized that receipt of AVR is more likely to be associated with younger aged cardiologists ($</= 40$ years) than older aged cardiologists (>40 years).

Methods: Using the Centers for Medicare and Medicaid services (CMS) national database, we will use hierarchical logistic regression models to assess odds of AVR delivery according to cardiologist age group among patients hospitalized with primary diagnosis of AS. Models will be adjusted for patient-level covariates (demographics, insurance, comorbidities, comorbidity index) and hospital-level covariates (location, number of cardiologists per hospital). Secondary analyses will include stratifying odds AVR by type (transcatheter and surgical).

Discussion: We expect to find that physicians who have completed their training more recently may have higher rates of AVR referrals. This includes the use of transcatheter AVR, in patients with elevated surgical risk, which is an established non-inferior alternative to surgical AVR in many patients. While there are many factors which dictate intervention for AS, we hope that by performing this study, we will be able to promote a guideline directed approach to the management of symptomatic AS. We will be limited in the ability to classify severity of AS, selecting patients with primary admit diagnosis of AS will likely focus on patients with symptoms related to AS, which would support severe AS diagnosis.

Investigating the Role of Sterol Regulatory-Element Binding Proteins (SREBPs) in Age-related Macular Degeneration

Sivamohan A, Wang T, Pattabiraman P

Background/Objective: SREBPs are transcription factors involved in lipid biogenesis and are known to play a role in angiogenesis. Vascular endothelial growth factor (VEGF) also promotes angiogenesis, with VEGF inhibitors as the predominant treatment for age-related macular degeneration (AMD). AMD is the leading cause of permanent vision loss in the elderly population and is characterized by choroidal neovascularization (CNV). We hypothesize that VEGF can activate SREBPs in a SCAP-dependent manner.

Methods: Human retinal microvascular endothelial cells (HRECs) were grown in 5% media and treated at passage 7. Prior to treatment, cells were all starved for 1h in 0.5% media. To estimate the changes in SREBP activation - HRECs were treated with 50ng/ml VEGF for 1, 4, and 12h or with 20 µM fatostatin, an inhibitor of SREBP activation, translocation into the nucleus, and SREBP transcription for 6h and 12h. Post treatment cells were lysed and protein was collected in RIPA buffer and semi-quantitative changes in target proteins were analyzed using immunoblotting. Statistical analysis was done by t-test, with significance if $p < 0.05$, and sample size of n=2-3.

Results: HRECs treated with VEGF exhibited an increasing trend for SREBP-1 and SREBP-2 in the cytoplasmic and nuclear forms at all time points. SCAP did not show a clear trend. HRECs treated with fatostatin exhibited a decreasing trend for SREBP-1 and SREBP-2 in the cytoplasmic form and nuclear SREBP-1 form at both time points. The nuclear form of SREBP-2 increased at both time points.

Conclusion and Potential Impact: VEGF has demonstrated a role in SREBP activation, with both playing a role in angiogenesis. Fatostatin inhibition of SREBP indicated a potential antiangiogenic property. The downregulation of SREBP could provide a novel target in controlling and preventing angiogenesis in AMD. Further studies using animal models should elucidate the role of SCAP in VEGF activation of SREBPs.

Does Direct Anterior Approach Training During Residency and Fellowship Influence Clinical and Surgical Outcomes in Primary Total Hip Arthroplasty?

Sloat B, Ziemba-Davis Deckard ER, Buller LT

Background and Hypothesis: Total hip arthroplasty (THA) can be performed using various surgical approaches. The direct anterior approach (DAA) has been popularized due to fewer immediate postoperative functional restrictions. However, when transitioning from a posterior based approach, the DAA has a steep learning curve associated with higher early complication rates. The influence of formal residency and fellowship training on the DAA learning curve remains unknown. We hypothesized that formal training would reduce the learning curve associated with DAA THA resulting in better outcomes than previously reported.

Project Methods: Prospectively documented data on 726 unilateral primary THAs were retrospectively reviewed. Intraoperative, perioperative, and 90-day postoperative outcomes were compared for the index surgeon with formal DAA training and four surgeons

without formal DAA training. A Bonferroni-adjusted p-value of 0.004 denoted statistical significance. Fourteen additional covariates were examined in relationship to outcomes.

Results: Intraoperative fracture and nerve damage, calculated blood loss and blood transfusions, and 90-day emergency department visits, inpatient readmissions, reoperations, and wound complications did not differ between the two groups (p = .054 to .999). Mean procedure (140 versus 103) and anesthesia (192 versus 144) durations in minutes were significantly longer for index surgeon cases (p < .001). In multivariable analysis, statistically significant covariates of procedure and anesthesia durations were unreliable due to wide 95% confidence intervals.

Potential Impact: Excluding procedure and anesthesia durations, there were no significant differences in outcomes comparing a surgeon with formal DAA training to surgeons without formal training. Surgery durations may have been influenced by a difference in years of practice (first two years for the index surgeon and a mean of 16.5 years for comparison surgeons). Formal surgical training on the DAA may facilitate similar outcomes earlier in a surgeon's practice, reducing the learning curve associated with the DAA.

Evaluating the AMPATH Surgical App (ASAP): Open Appendectomy Module
Standfest M, Bhatia MB, Levy JS, Stefanidis D, Hunter-Squires JL, Saruni SI

Introduction: Due to paucity of surgical personnel and lack of resources in low- and middle-income countries (LMICs), general practitioners with little surgical education are often relied upon to complete emergent appendectomies. To address this concern, a smart phone app-based curriculum called AMPATH Surgical App: Open Appendectomy Model (ASAP) was created to enhance learner's appendectomy skills. The aim of this study was to evaluate the effectiveness of ASAP compared to standard curricula using Kirkpatrick's Learning Evaluation Model.

Methods: A randomized controlled trial was performed. Participants were randomized by simple, random allocation into the intervention ASAP curriculum education group, or the control standard education group. The intervention group was provided access to ASAP while the control group received traditional appendectomy instruction that included textbook and atlas chapters on appendicitis. All participants were assessed at weeks 0, 3, and 6 for appendectomy knowledge and surgical skill, both Kirkpatrick Level Two outcomes, and confidence, a Level One outcome.

Results: 10 students were enrolled into 2 groups: control (6/10, 60%), and intervention (4/10, 40%). At baseline there was no significant difference between control and intervention groups for knowledge pre-test, skills self-assessment, skills expert assessment, and operative time; demonstrating that the groups are similar in

baseline knowledge and skill. There was no significant difference in confidence between groups after the first simulation; both groups did increase in confidence from baseline. Both groups decreased operative from baseline to simulation 1, and despite no significant difference between groups for simulation 1 expert assessment, both groups increased points earned from baseline to simulation 1.

Conclusion: Preliminary results show ASAP to be an effective teaching tool, resulting in increased confidence and skills assessment improvements, corresponding to Levels One and Two of Kirkpatrick's Learning Evaluation Model, respectively.

Microplastic Effects on Thrombin-Fibrinogen Clotting Dynamics Measured via Turbidity
Stelflug N, Tran DQ, Hall A, Chakravarthula TN, Alves NJ

Background/Hypothesis: Widespread use of plastic has created a world where exposure to microplastics is inevitable leading to their presence in our circulatory system. This raises questions about microplastics' impact on thrombosis. Aminated polystyrene (aPS) plastics have been shown to increase platelet aggregation and thrombus formation in animal models. Given this, we hypothesized that aPS administration will increase the rate of fibrin clot formation in a simple thrombin-fibrinogen clot model.

Project Methods: We evaluated how concentrations of 25-200 μg/mL of 100 nm aPS particles affect fibrin clot formation using turbidity assays. To determine the effect of surface charge, experiments were also performed with non-modified polystyrene (nPS) particles. Microplastics were pre-incubated either with physiological concentrations of fibrinogen or thrombin and the clot formation was measured using turbidity at 405 nm every 10 seconds over 45-minutes. Clotting parameters such as maximum turbidity (TurbMax), time to 90% maximum turbidity (TurbTime), and clot formation rate (Vmax) were determined and compared to controls without microplastics.

Results: When increasing concentrations of aPS were preincubated with thrombin or fibrinogen, there was less than a 2-fold change in Vmax, TurbMax, and TurbTime. When increasing concentrations of nPS were preincubated with thrombin, there was up to a 27-fold decrease in Vmax, 2.4-fold decrease in TurbMax, and 4.36-fold increase in TurbTime compared to the control. Whereas preincubation of nPS with fibrinogen resulted in 1.86-fold decrease in Vmax, 1.63-fold decrease in TurbMax, and 2.30-fold increase in TurbTime.

Potential Impact: In this simplified clotting model, it was surprising to find inhibitory effects on clot formation and that they were more pronounced with nPS than with aPS. However, these results align with increase prothrombin time observed in literature in presence of aPS. Therefore, future studies with more complex clotting models need to be performed before claims can be made on the impact of microplastics on thrombosis.

Cutaneous Iontophoresis of Adrenergic Agonists can Mimic In Vivo Neural Effects on Vasodilation

Stout JA, Ungureanu CI, Miller OG, Metzler-Wilson K

Iontophoresis utilizes electrical current to non-invasively deliver agents through the skin. This pilot study sought to determine if iontophoresis could be paired with laser Doppler flowmetry (LDF) to administer adrenergic and cholinergic agonists and measure the subsequent changes in cutaneous blood flow. We hypothesized that iontophoresis administration would produce vascular tone changes consistent with those seen during other delivery methods. We iontophoresed phenylephrine, clonidine, isoproterenol, and acetylcholine to the forearm of one generally healthy 44-year-old female using existing or adapted protocols. We also created half-strength protocols with the goal of establishing dose-response relations. We quantified erythrocyte flux via LDF and beat-by-beat arterial blood pressure via finger photoplethysmography. After baseline, each drug was administered using its half and full-strength protocols, separated by a washout period. Finally, we stimulated maximal blood flow at each iontophoresis site via non-noxious local heating to 43°C. Cutaneous vascular conductance (CVC; laser Doppler flux/ mean arterial pressure) was calculated during baseline and following iontophoresis. We administered vehicle (deionized water) alone as a control, using the same protocols and analysis. The drug responses generally matched our predictions with the exception of phenylephrine, which caused vasodilation. Vehicle administration also caused vasodilation. Full-strength application generally led to a more pronounced change in CVC, suggesting that a dose-response relation might be established with additional data. Applications of certain agents led to a higher CVC than "maximal", possibly raising the need to alter the method for establishing maximal cutaneous blood flow. Overall, our findings indicate that iontophoresis and LDF can be used to effectively administer adrenergic and cholinergic agonists to non-glabrous skin and affect vascular tone. This non-invasive technique could be used to investigate responses to these agents in those whose cutaneous neural receptor characteristics have been altered as a consequence of disease.

Cellular Metabolism in B Cells in Type 1 Diabetes

Swar-Eldahab M, Conway H, Felton JL

 Background/**Objective**: Type 1 diabetes (T1D) is an immune-mediated disease that results in the destruction of pancreatic beta cells. While beta cell destruction is classically considered T cell mediated, autoreactive B cells play important roles in disease progression. B cell depletion prevents disease in non-obese diabetic (NOD) mice, and B cell depletion temporarily slows disease progression in individuals with new-onset T1D. However, mechanisms of autoreactive B cell function in T1D are not fully known. Cellular metabolism has been shown to drive autoimmune B cell development in other mouse models. We hypothesize that metabolic characteristics of B cells from NOD mice are distinct from metabolic characteristics of B cells from non-autoimmune C57BL/6J (B6) mice; therefore, making cellular metabolic pathways viable targets for therapeutic intervention.

Methods: Lymphocytes from spleen, pancreas, pancreatic lymph nodes, and mesenteric/lumbar lymph nodes were processed into single-cell suspensions. Glucose uptake was measured using fluorescent glucose analog 2-NBDG. Mitochondrial polarity was measured using fluorescent probes for mass and membrane potential. Cells were stained for surface markers and analyzed on an Attune Nxt flow cytometer.

Results: No statistically significant differences in glucose uptake or mitochondrial polarity for lymphocyte subsets in the spleen or PLNs of NOD and B6 mice were identified. In NOD mice, polarity was significantly higher in B cells in the pancreas compared to the spleen and PLNs. Polarity was also higher in B cells in PLNs compared to non-specific lymph nodes in NOD mice.

Conclusions/**Impact**: While no differences in glucose uptake or polarity in lymphocytes from NOD and B6 mice ex vivo were identified, future studies are needed to determine whether their activation drives metabolic alterations. Differences in polarity in the pancreas in NOD mice suggest that cellular metabolism is influenced by the islet microenvironment and has the potential to influence their function at the site of autoimmune attack.

Wireless Electroceutical Dressing Inhibition of Azole Sensitive and Resistant Strains of Aspergillus fumigatus

Swartz LE, Maupin AJ, Basaran-Akgul N, Steiner SS, Sen CK, Templeton SP

Background/**Objective**: The opportunistic fungus Aspergillus fumigatus is responsible for nosocomial infections, particularly in immunocompromised patients. Fungal infections are increasingly likely in burn victims, as the epidermis serves as the body's first line of defense against microbial pathogens. In an effort to utilize complementary methods of control, an electroceutical dressing containing geometrically patterned silver and zinc nanoparticles embedded in fabric was used. The dressing utilizes generates a weak electric field when moist to produce antimicrobial effects. Preliminary research showed that the dressing effectively inhibited Candida albicans. This foundational research has led us to hypothesize that the electroceutical dressing could also be an effective option for inhibiting A. fumigatus. The objective of this project was to establish the inhibitory effects of the dressing across multiple strains of A. fumigatus.

Methods: We used both radial growth on Aspergillus Minimal Media (AMM) agar plates and concentration in AMM liquid cultures to determine A. fumigatus growth rates. The plates were initially inoculated with 100 conidia of A. fumigatus. Liquid cultures were inoculated with 200,000 conidia/mL. The liquid cultures Radial growth was measured daily for 14 days, and concentration was measured every third day for 24 days.

Results: Our results show that the Wireless Electroceutical Dressing (WED) effectively inhibits A. fumigatus growth.

Summary: The data indicates that WED inhibits azole resistant and non-resistant strains of A. fumigatus. By illustrating the effectiveness of the electroceutical dressing, it presents additional options for controlling A. fumigatus infection. Additional research should be conducted to determine if the dressing is fungistatic or fungicidal, along with assessing its effectiveness in inhibiting other fungal infections.

Evaluation of Gait Parameters using Wearable Sensors in Simulated Freezing of Gait Episodes

Szilagyi H, Yadav AP

Background and Hypothesis: Freezing of gait (FoG), the failure to initiate or maintain locomotion, is a common symptom in Parkinsonism that severely impacts patients' quality of life. Wearable technology such as inertial measurement units (IMU) are being widely investigated as a method of detecting these episodes with increasing sensitivity and specificity. The aim of this initial study is to collect objective gait data using IMU sensors via Perception Neuron software and to develop an analysis pipeline for quick in-clinic calculation of gait parameters.

Experimental Design: 16 IMU's were attached to the feet, legs, arms, waist, back, and head in individuals without any gait abnormalities. Subjects were instructed to walk 10 meters normally, followed by 10 meters with interspersed, simulated FoG episodes. This data was processed and analyzed through Axis Studio and MATLAB to identify kinematic markers associated with gait. The correlation between the right and left foot gyroscopic data in the z-axis was determined and plotted against time, with any correlation less than 0.5 being considered a FoG episode. Further, parameters of gait including stride duration, stance duration, swing duration, and stride length were calculated from input of the raw data to establish a control comparison for future studies with Parkinson's patients.

Results: Data analysis demonstrated increased stride duration, stance duration and swing duration with shorter stride length in the stimulated FoG episodes as compared to normal gait. The developed MATLAB code was further able to accurately distinguish the simulated FoG episodes from normal gait given the correlation parameter difference of <0.5.

Conclusion: Our findings showed that data obtained from Perception Neuron IMU can be processed to succinctly detect FoG episodes and calculate gait parameters. Ultimately, this data will be used as the baseline for a future study investigating the use of spinal cord stimulation as treatment for FoG in individuals with Parkinson's Disease.

Evaluating Waste Produced from a Day of Cataract Surgeries

Tharp M, Protopapas S, Gill M, Cantor L

Purpose: The goal of this descriptive study was to characterize and measure the waste produced by phacoemulsification procedures in order to develop interventions that will (1) reduce the environmental impact, (2) minimize financial waste, and (3) prioritize ease of adaptation for staff.

Methods: Waste produced from 15 phacoemulsification procedures conducted in a single day at the Ascension St. Vincent Outpatient Surgical Center in Evansville, Indiana was collected, sorted, and weighed in the following categories: hard plastics, soft plastics, wrapping, medications, textiles, metals, and miscellaneous. The same data were also collected for all other procedures performed that day consisting of 5 plastic surgery, 3 urologic, and 5 otolaryngologic cases.

Results: The 15 phacoemulsification procedures resulted in 95.4 lbs of waste divided among the 7 categories. The breakdown is as follows: 18.5 lbs hard plastic (avg. 1.2 lbs/case), 5.5 lbs soft plastic (avg. 0.4 lbs/case), 8.3 lbs wrapping (avg. 0.6 lbs/case), 13.5 lbs medications (avg. 0.9 lbs/case), 41.2 lbs textiles (avg. 2.8 lbs/case), 0.0 lbs metals, and 6.7 lbs miscellaneous waste (avg. 0.5 lbs/case). Relative to all other cases, the phacoemulsification cases consistently produced the least or second-least amount of waste per case, outside of medications, where ophthalmology was the greatest producer of waste. Though producing less waste per case relative to the other scheduled specialties, ophthalmology still produced the greatest amount of waste total due to the relatively high case volume.

Conclusion: The goal of this audit, following the waste characterization and practice analysis stages, is to develop interventions for reducing environmental and financial waste while prioritizing ease of adaptation for staff. Due to the high case volume, it is necessary to revise phacoemulsification practices. Planned interventions include (1) reducing the size of tetracaine bottles used during surgery. Currently, 4 mL bottles of tetracaine drops are used, of which only a fraction is needed. (2) Minimizing surface area of patient draping and (3) optimizing packaging of surgical supplies. A purported advantage to cataract surgery, however, is the use of IV sedation in contrast to anesthetic gases, many of which are known to be potent eCO2 emitters. The issue lends many complexities worth exploring for the greater purpose of waste reduction in acknowledging the contribution of the health sector to the growing climate crisis.

*** Abstract not from IMPRS, alt. abstract publication due to being unable to publish original

Evaluation of Gait Development Trajectory in Mice

Thayer A, Villarreal C, Chan D

Background/Objective: Movement and walking are huge facets in how we go about our lives and experience the world. Gait is compromised in numerous conditions, from injury and chronic pain to neurological conditions and arthritis. Movement biomechanics have therefore been studied extensively in humans for decades. Although animal models are often used to examine the progression

of various health conditions, translational gait research in animal models are less complete, and there is limited information on gait changes as mice grow.

Methods: We recorded video segments of wild-type C57Bl/6J mice during skeletal growth (5 weeks to 16 weeks) walking (n = 4 Female, n = 2 Male) at 20 cm/s on the DigiGait system, a transparent treadmill equipped with a high-speed camera. Videos captured a ventral view of the mouse and were processed using DigiGait Analysis software, which uses local thresholding and position-finding algorithms to examine paw placement on the treadmill belt. Manual adjustments were made to eliminate artifacts and confirm heel-strike and toe-off times. After these corrections, the software returns stride parameters that were compared between sexes.

Results: Over 30 gait metrics, including stride length, frequency, stance/swing times, and stance width, were calculated for all four limbs per animal for several time points. Stride length increased from 4.5 ± 0.5 cm at week 5 to 5.0 ± 0.8 cm at week 16, and frequency decreased from 4.6 ± 0.6 to 4.2 ± 0.6 steps per second. No notable changes in stance width, symmetry, or stance/swing ratio were identified.

Conclusion and Potential Impact: Future directions for this research include conducting a principal component analysis to investigate the variability within the gait data. Identifying trends in gait parameters will help create a more complete picture of gait maturation. Establishing this baseline data allows for its comparison against treatment groups and the potentially meaningful investigation of translatable therapeutics and interventions.

Complications and Outcomes Associated with Two-Stage Treatment
of Periprosthetic Total Knee Infection
Thomas J, Ziemba-Davis M, Meneghini RM

Background and Hypothesis: Periprosthetic joint infection (PJI) is treated with implant resection, debridement, and component reimplantation after infection eradication. Treatment consists of either a single surgery or two-stage surgery with intravenous antibiotic therapy between stages. We replicated a recent study which concluded two-stage treatment is associated with high morbidity, hypothesizing that complication rates would be similar, but that morbidity is not always conclusively a consequence of two-stage treatment for PJI.

Project Methods: Prospectively documented data on all primary and revision knees undergoing two-stage treatment for PJI by a single surgeon were retrospectively reviewed. Surgical complications were quantified for the interstage and post-reimplantation periods. Chi-squared tests were used to compare current findings to published findings.
Results: Patient demographics and comorbidities were equivalent

in the two studies ($p \geq .137$). More complex infections characterized the current study as evidenced by significantly more polymicrobial infections ($p < .001$) and greater use of static spacers due to bone loss ($p = .002$). Nonetheless, only 1.5% of cases in the current study did not undergo component reimplantation compared to 7.8% in the comparison study ($p = .129$). There were no differences in the number of additional interstage and post-reimplantation septic surgeries ($p \geq .492$). Using a proposed system which penalizes additional operations required to eradicate infection, treatment success rates at minimum one year follow-up were 64% and 71%, respectively ($p = .473$). Without these penalties, treatment success in the current study was 95.6% (equivalent proportion not available for comparison study). All-cause mortality was statistically equivalent in the two studies (15.6 versus 7.6%, $p = .144$) but no deaths from PJI were observed in the current study (unknown for comparison study).

Potential Impact: Study findings suggest that morbidity attributed to two-stage treatment reflects the inherent complexity of this patient group, and not the two-stage treatment itself.

Regional Differences in Human Skin Responses to Receptor Agonists: Implications for Differing Facial vs. Forearm Innervation
Ungureanu CI, Stout JA, Miller OG, Metzler-Wilson K

There is no consensus on the precise differences between non-glabrous and facial skin characteristics. Our lab identified similar responses to local heat stress in forearm and facial skin, while others identified differing responses to autonomic stressors within facial regions. Anatomical differences, such as the thinner nature of facial skin and specifically its thinner stratum corneum, may also impact facial autonomic responses. Considering this layer is a protective barrier, facial skin may be more sensitive to perturbations like drug administration. While non-glabrous skin is innervated by spinal nerves, facial skin is innervated by cranial nerves. Because of these anatomical and physiological differences between non-glabrous and facial skin, it is possible that their differing neural and receptor characteristics impact a key autonomic end-organ response: cutaneous blood flow. In this pilot experiment, we investigated possible regional differences between the forehead and forearm in response to adrenergic and cholinergic agonists. We hypothesized that drugs targeting adrenergic (phenylephrine, clonidine, and isoproterenol) and cholinergic (acetylcholine) cutaneous receptors would elicit similar vasomotor effects in both locations. One female subject underwent forearm and forehead iontophoresis of each agonist using adaptations of published protocols, as well as a control protocol using deionized water (vehicle) alone. We recorded blood flow via laser-Doppler flowmetry (Moor Instruments) and beat-by-beat arterial blood pressure via finger photoplethysmography (ADInstruments). We calculated baseline cutaneous vascular conductance (CVC) and plateau 43°C CVC to determine the change in skin blood flow resulting from drug administration. Our results indicate that while phenylephrine administration caused vasodilation,

opposing our hypothesis, administration of all other drugs caused responses in agreement with our expectations. Thus, these pilot data suggest that facial and non-glabrous skin may respond similarly to adrenergic or cholinergic agonists. These findings imply a potential use for topical dermatological drug treatments utilized on the trunk/extremities to benefit cutaneous facial diseases.

Putting Their Money Where Their Mouths Are: A Multidisciplinary Approach to Addressing Disparities in Health Research, Grant Funding, and Recruitment of Black Women to Breast Cancer Clinical Trials

Vogel K, Okoruwa OP, Ridley-Merriweather KE, Hoffman-Longtin K, Ashburn-Nardo L

Background and Objective: On this literature review and textual analysis, we apply theories from health communication and psychology to better understand the cultural and structural factors that may discourage Black women's participation in clinical trials, paying particular attention to the public and private organizations and agencies that fund this research. We use breast cancer clinical trials as an extended example to illustrate the wider issue of a lack of funding for formative and community-based research.

Design: We begin by reviewing the recruitment of Black women to breast cancer research and identifying themes in the literature where gaps exist. We then examine the social and organizational psychology literature on influencing the recruitment of women and racial/ethnic minorities, suggesting this field may be helpful for addressing the recognized gaps. Throughout the work, we identify points at which disparities may arise. We suggest that these theoretical approaches are helpful in reducing disparities and illuminating the structural factors that discourage participation from minoritized groups. Finally, we suggest future research opportunities for using these perspectives to increase participation of Black women in breast cancer and other health research.

Results: Researchers could benefit from employing psychology principles of contingency cues and identity safety when recruiting Black women into clinical trials, especially for breast cancer. Further, funding organizations such as the NIH must fund formative research which seeks out the voices of Black women and other marginalized populations to fully address and eliminate health disparities.

Conclusions: This work highlights the need for increased cross-sectional literature in the fields of communication and psychology. As scholars explore directions for future research, we encourage them to consider the expertise of Black women, themselves, in solving these problems.

Comparison of Goniometry and Video Analysis in Measuring Shoulder Range of Motion of Collegiate Athletes

Waltz M, Heumann R, Garcia-Hosokawa MM, Chlebowski AL

Background: The shoulder joint's multiplanar motion creates a challenge in measurement of range of motion (ROM). Goniometry is currently the most common tool for measuring ROM in the clinic due to its ease of use but is subjective in nature. Video capture rigs have become popular in all facets of motion monitoring, but they can be limited to large open spaces and user discrepancy. Further, motion capture with wireless wearable inertial measurement units (IMUs) has also become popular but is often cost/implementation prohibitive. Understanding the consistency between these recording methods must be established to understand if a therapy impacts the shoulder complex.

Methods: Student athletes with complaints of shoulder pain and decreased ROM in their dominant arm were separated into cohorts receiving twelve therapy sessions. One cohort received chiropractic manipulation therapy and the other received functional movement-based myofascial release therapy combined with chiropractic manipulation. Shoulder ROM was measured via seven standard tests during the first, sixth, and last sessions using goniometry, video capture, and IMUs. Following data collection, results of the measurement techniques were compared.

Results: Preliminary statistical analysis conducted between goniometry and video capture indicates measurement techniques differ for three of seven standard ROM tests, pronated flexion, supinated abduction, and internal rotation (p-value $\leq$ 0.05). Reliability between individuals analyzing video capture is strong, with an ICC of 0.994. This indicates consistency between individuals taking measurement of shoulder ROM using this method. IMU data has been collected with analysis forthcoming.

Conclusion: This study is limited by the number of participants (n=4). Preliminary results indicate that consistency in video analysis may make it preferable to standard goniometry. A larger, more comprehensive study is needed to provide conclusive results, including IMU data. These conclusive results could indicate that clinical use of video capture or IMUs should replace standard goniometry if other implementation hurdles can be reduced.

Determining the Best First-line Modality for Identifying and Localizing Skull Base CSF Leaks

Whitted C, Okecheku V, Koontz K

Background: Patients with skull base cerebrospinal fluid (CSF) leaks present with headaches, fluid in the ear(s), and/or rhinorrhea, which are vague symptoms. Beta-2-transferrin protein assays are the gold standard for identifying CSF leaks, but adequate samples cannot always be collected, and the results give no specific localizing

information. Medical imaging, including Computed Tomography (CT), Magnetic Resonance (MR), and Nuclear Medicine (NM) cisternography can be utilized to identify and localize CSF leaks, but are imperfect tests. This study aims to determine the best imaging modality for identifying and localizing skull base CSF leaks by comparing CT, MR, and NM Cisternogram results to beta-2-transferrin assay and intraoperative visualization as criterion standards.

Methods: In this ongoing study, patient cisternogram and pre-cisternogram imaging and results were acquired from the electronic medical record, radiology information system, and picture archiving and communication system. Inclusion criteria include age greater than 18, suspected skull base CSF leak, and CT, MR, and/or NM cisternogram performed. MR cisternogram procedure included intrathecal gadolinium and NM SPECT-CT cisternogram procedure included intrathecal Tc-99m Sulfur Colloid. These data will be analyzed for positive and negative predictive values, sensitivity, specificity, and ROC Curve comparing to beta-2-transferrin assay results and surgical findings.

Results: From 2018-2022, 30 patients with suspected skull base CSF leaks were evaluated. In this limited preliminary data set, MR was more sensitive than CT, CT was more sensitive than NM, there were three false negatives, and there were no false positives. Performing two types of cisternogram increased the chance of identifying leaks. More data is needed to draw stronger conclusions in this ongoing study.

Conclusion/Potential Impact: The initial data suggests that MR cisternogram with intrathecal gadolinium is superior to CT and SPECT-CT cisternogram for detecting skull base CSF leaks. Localizing skull base CSF leaks helps enable surgeons to perform less invasive corrective procedures.

Investigating a Closed Loop Neural Control System to Optimize Sacral Neuromodulation
Wood J, Lim J, Lee H, Ward M

Background and Hypothesis: Approximately 16% of the American population suffers from overactive bladder, with 25-40% of patients reporting unsatisfactory results following first line treatments. Sacral neuromodulation is a well-established, minimally invasive treatment option for several forms of bladder and bowel dysfunction that are non-responsive to first line pharmacologic or behavioral therapies. While more broadly applicable stimulus parameters are being investigated, the precise set of nerve fibers whose activity regulates optimal bladder function(s) is not known, leading to high levels of treatment variability between patients and within patients over time. We hypothesize that treatment efficacy and durability could be rapidly improved by continuously tuning the electrical stimulus waveform and pattern of stimulation to recruit the nerve fiber populations that mediate micturition.

Experimental Approach: We aim to access the sacral (S2-4) nerves and implant a set of recording and stimulating bipolar cuff electrodes (FNC-400-V-R-C-2C-30, Micro-Leads, Somerville, MA, USA) to measure the evoked CAP of the sacral nerves at various combinations of pulse amplitude and duration. Simultaneously, we will measure changes in bladder pressure using a pressure transducer attached to a bladder catheter and amplifier. By measuring how the bladder responds to all applied nerve stimulation parameters we will be able use an Autonomous Neural Control algorithm to identify the compound nerve action potential response that produces the most robust changes in pressure.

Results: We developed a surgical protocol, currently pending PACUC approval, that allows us to decode and encode specific CAP signatures that represent the firing activity of distinct subsets of nerve fibers, each differing in diameter, degree of myelination, activation threshold, conduction speed, and presumably function.

Conclusion and Potential Impact: This study aims to act as proof of concept for a system that selects stimulation parameters based on fibers required to produce a desired response rather than patient tolerance to stimulation parameters, ultimately improving efficacy of sacral neuromodulation therapy.

The Contribution of Genetic Risk for Alzheimer's & Cardiovascular Disease to Recovery from Traumatic Brain Injuries
Wood E, Nudelman K

Background: Polygenic risk scores (PRS) represent the genetic likelihood of developing a phenotype and represent an exciting opportunity for the development of personalized medicine. This study used PRS to determine if individuals at high-risk for Alzheimer's (AD) or cardiovascular disease (CVD) would recover differently after TBI compared to low-risk individuals.

Methods: GWAS with the Illumina Global Screening Array was performed on DNA available for a subset of the TBI-Model Systems cohort (N=189). PRS were chosen from the PGS Catalog (https://www.pgscatalog.org) and calculated using the Michigan Imputation Server. 1-year follow-up data (1Y) for the Functional Independence Measure (FIM) was used to evaluate TBI recovery. FIM represents the subject's self-care ability after TBI and includes a cognitive and a motor component.

ANCOVA models were used to elucidate the relationship between PRS risk groups (score in top 20% vs. 80%) and 1Y FIM scores. Covariates included age, education, FIM scores at discharge, injury severity, and genetic ancestry. Post-hoc analysis was conducted using 1Y FIM scores of subjects stratified by AD risk and APOE e4 carrier status, a major risk factor for AD onset. Additional post-hoc analysis evaluated hypertension at 1Y by CVD PRS groups using a cox survival model.

Results: Individuals with high AD PRS had lower 1Y FIM scores than those with low risk (p= 0.041). Post-hoc analysis showed a trend for APOE e4 carriers with high AD PRS performing worse on FIM motor testing (p=0.145). There was not a significant association between the CVD high-risk group and FIM scores (p=0.389). The cox survival model of hypertension trended towards an earlier age of onset in the high-risk subjects (p=0.155).

Conclusion: This pilot study shows the potential for PRS to identify individuals at risk for worse TBI recovery, allowing for future research on early interventions and their effects on TBI recovery.

Electrical Stimulation Insulation Pedestal for Peripheral Nerve Regeneration

Zaidi S, Yoshida K, Borschel G

Background/Objective: Peripheral nerve injuries are common, and nerve regeneration occurs slowly. Application of electric stimulation (ES) can accelerate nerve regrowth. Currently, ES involves a 30-minute application of current via needle electrodes that are bent into a hook around the injured nerve. The aim of this project was to design a 3D model of an accessory device that can supplement this electrode system and overcome the suboptimal characteristics of the ES apparatus, including bending of the electrodes, pooling of blood around the electrodes, and discontinuous stimulation.

Methods: PTC Creo 4.0 was used to design the ES insulation pedestal. Design requirements included fitting within the intended anatomical space, securing and minimizing the bending of electrodes, securing nerves, and isolating the nerve-electrode interface from the surrounding tissue. One design was submitted for 3D printing of a prototype hard model. A rough carving of this design was implemented in the OR using sterile Styrofoam.

Results: Four initial designs were developed and sized to the upper limit of the acceptable size range of the intended application. The design submitted for printing utilized a 5 mm diameter groove for nerve securement with evenly spaced electrode contact securement sites. The rough carving of the apparatus was implemented in the OR and showed feasibility by demonstrating continuous activation of the nerve, minimal pooling of blood, and minimal electrode bending.

Conclusions and Impact: This initial prototype phase of device design demonstrated feasibility of use for this device. The dimensions and component compatibility of the designs must be tested. During the next phase of the design, we will develop a soft model of the most acceptable design using a cast-molding technique with a known electrically insulating material (e.g., silicone). This device is intended to make ES more efficient, easy to use, and appealing to physicians.