Insight

indiana university medical student research journal

Insight

April 2023 / Vol 5 / Issue No. 1

Questions?

Feel free to contact us at: insightj@iupui.edu

Front cover photo: "green leaf plant closeup photography" by Yusuf Evli is licensed with CC BY-SA 2.0

In this issue:

The Imagination in Medical Education

Richard Gunderman, MD, PhD

Richard Gunderman, MD, PhD is the Chancellor's Professor and John A. Campbell Professor of Radiology, and the faculty advisor of Insight Medical Student Research Journal.

> Next year's going to be even bigger, days will be brighter, nights longer and darker, more people dying, more babies born, and me in the middle of it all.
>
> Ray Bradbury,"Dandelion Wine"

The medical school curriculum as it exists today cannot, by itself, provide the full education medical students need to become the best versions of themselves as physicians and human beings. Like every professional curriculum, it is focused on a narrow body of knowledge – in this case, medicine, and there is certainly a great deal of knowledge that every medical student needs to assimilate to qualify as a physician. But physicians are not mere technicians, who sit at a desk, laboratory bench, or computer console, eyes fixed all day on data streams. Instead, physicians get to know and care for human beings, and to do this well, it is necessary to explore and connect with persons, whether they be patients, families or colleagues. It requires not just a large fund of knowledge and battery of skills, but a well-honed moral imagination, the capacity to understand how health and life look to another human being.

Why don't medical school curricula excel at fostering moral imagination? There is simply too much anatomy, physiology, and pathology, too much medicine, pediatrics, and surgery to get across. Moreover, the instructional methods of medical education, such as pre-recorded lectures and solitary study, are not conducive to the development of essentially interpersonal capacities, a problem severely exacerbated recently by the COVID-19 pandemic. Perhaps most problematic is the contemporary regime of medical assessment, with its heavy reliance on multiple-choice tests, which by their very nature hardly engage the moral imagination at all. There is a big difference between selecting the one best response and asking good questions, listening attentively, formulating and testing different hypotheses, and all the while learning about one's fellow human beings as one goes along.

To enable medical students to become the best physicians and human beings they can be, they need to extend their education beyond the walls of the contemporary medical school into families, communities, and ultimately, the human condition. The key to caring well for patients is to genuinely care for patients, and this means getting to know patients deeply – the ways in which each patient is both totally distinctive and shares certain essential attributes with every other. And this is where the arts come into

"There is a big difference between selecting the one best response and asking good questions, listening attentively, formulating and testing different hypotheses, and all the while learning about one's fellow human beings as one goes along."

play. In enabling us to get beyond the technical aspects of medicine into its human dimension, the arts have more to offer than science. To see why this is so, it is helpful to focus on a single form of art and a single artist. Consider a largely unknown resource located less than a block from the Indianapolis campus of the Indiana University School of Medicine.

This resource is the Ray Bradbury Center, which houses his office and library. Bradbury, who was born in Waukegan, Illinois in 1920 and died in Los Angeles, California in 2012, was one of the nation's foremost writers of fantasy, horror, science fiction, and mystery stories. As such, he loved books and believed deeply in their power to engage and enhance the imagination. Of course, these books were not textbooks or test preparation manuals, the learning resources with which the attention of many contemporary medical students is glutted, but something very different. Bradbury was thinking of novels, collections of short stories, and the like. He knew that to become fully human, a prerequisite to becoming a health professional in full, we must become more imaginative, and his writing aimed to expand and deepen the human capacity to see human situations and the world from alternative perspectives.

Bradbury spent his life with books, not because he was a bookworm but because he knew they are the best resources available to expand the human imagination. We can never become another person, but we can imagine how another person sees the world, feels about it, and wishes it would be. Imaginative literature allows us to glimpse the full range of human possibility, to consider how our lives might turn out if we pursued different paths, what it is like to give in to and resist various forms of temptation, and what, ultimately, we aspire to contribute through our lives. It is impossible to become a good investigator, whether in the examination room, the laboratory, the classroom, or the boardroom, without continually nurturing and developing one's imagination. We must imagine how life could be different before we can fully appreciate what it is.

Consider perhaps Bradbury's best-known work, Fahrenheit 451, named after the temperature at which book paper ignites. Superficially about book burning, this 1953 novel imagines a dystopian world in which human imagination has been criminalized. "Schools," he writes, "are turning out more runners, jumpers, racers, tinkerers, grabbers, snatchers, fliers and swimmers instead of examiners, critics, knowers, and imaginative creators," and the world "intellectual" has become a "swear word." To prevent people from discontent, they are molded to consider only one side of a question. The burning of books represents the effort to destroy the human imagination. To this poisonous, dehumanizing vision of human life Bradbury offers a powerful antidote: "Stuff your eyes with wonder. Live as if you'd drop dead in ten seconds. See the world. It's more fantastic than any dream made or paid for in factories."

Our most valuable resources in medicine are not the budgets by which we too frequently presume to set boundaries on the possible, the physical plants of office buildings and hospitals that would be nothing more than empty shells if patients and those who care for them did not report there, or the sophisticated equipment found in intensive care units and operating rooms. Instead, our most valuable resources are people and the stories they tell, which teach us what we really are, how we fit into the greater scheme of things, and what it means to be really grateful for it all. ››

"It is impossible to become a good investigator, whether in the examination room, the laboratory, the classroom, or the boardroom, without continually nurturing and developing one's imagination. We must imagine how life could be different before we can fully appreciate what it is."

Consider these words of Bradbury:

> Every so often, late at night, I come downstairs, open one of my books, read a paragraph and say, My God. I sit there and cry because I feel that I'm not responsible for any of this. It's from God. And I'm so grateful, so, so grateful. The best description of my career as a writer is "at play in the fields of the Lord." It's been wonderful fun and I'll be damned where any of it came from.

Applied to health professions education, we should focus less on students' capacities to reproduce countless facts and operations and more on nourishing their imaginations. They must learn not only to extract relevant facts from the patient's history, physical examination, and laboratory findings, but to imagine themselves in the place of their patients, to glimpse what a disease, injury, or disability means in the larger context of the patient's life, and above all in situations where hopes for recovery and cure have been exhausted, to give them their full attention and be fully present with them. Bradbury wants us not only to act, to fix, and to make, but to witness, imagine, and wonder. A career in the health professions is a profound human privilege, a ring-side seat at the human drama, and it would be a terrible waste if students' capacities to recognize and respond to it languished untapped.

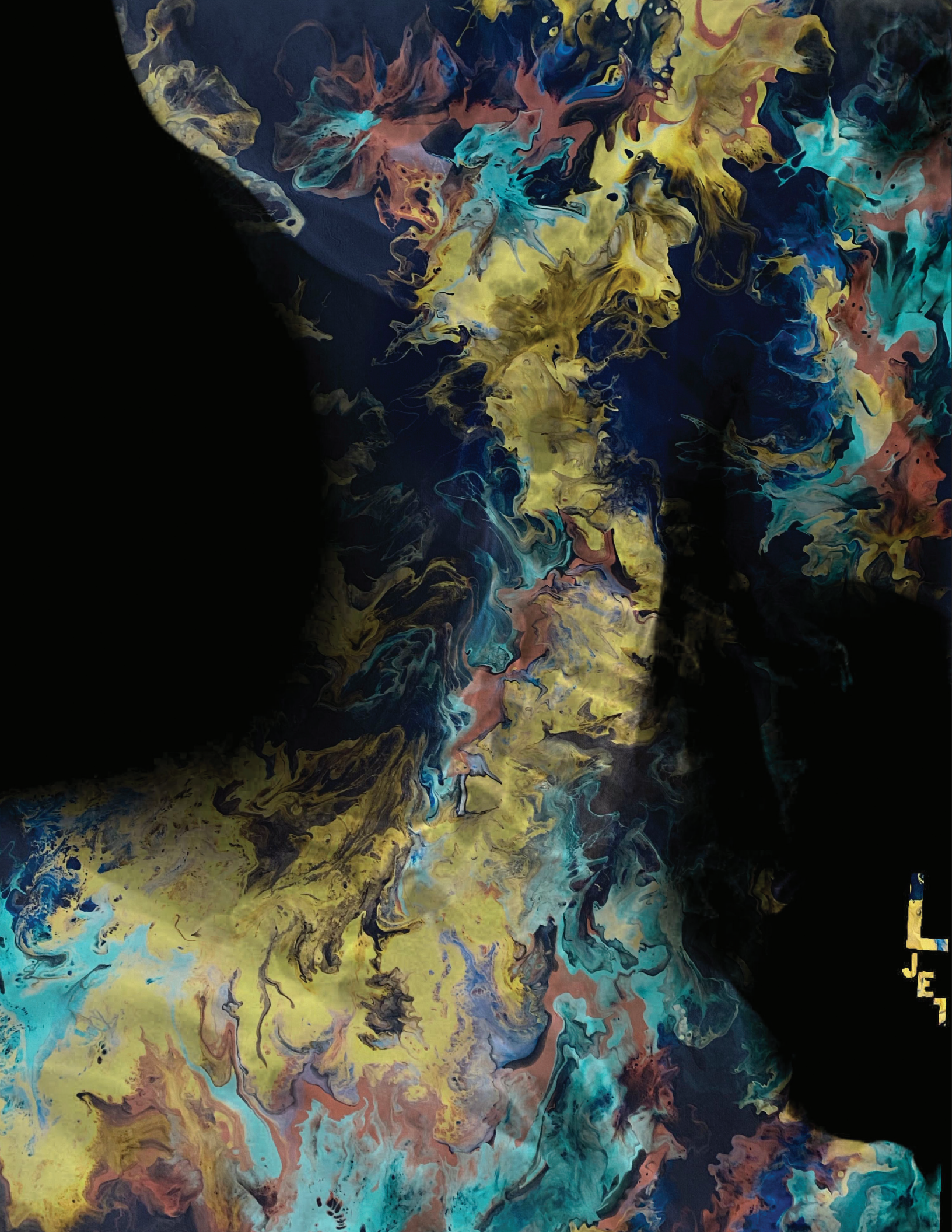
In the field of medicine, what books might best promote this goal? To understand the implications of our shared vulnerability to disease and injury, the ineluctability of mortality, and the range of ways human beings can respond to them, medical students can turn to no better source than Homer's "Iliad." To understand how a physician's good intentions can be warped by outside pressures and decline from neglect, there is no better text than George Eliot's "Middlemarch." To glimpse what it is like to pass through the gauntlet of mortal illness and some of the insights it can spawn on how to live, it would be difficult to beat Tolstoy's "The Death of Ivan Ilych." And Albert Camus' "The Plague" does a superb job of confronting its readers with the question whether physicians as healers are fundamentally aligned with or fighting against the forces of nature.

Short stories have an equally important role to play. Consider, for example, the shorter works of two great Russian authors, Anton Chekhov and Mikhail Bulgakov, both of whom were practicing physicians. Chekhov, who kept practicing medicine long after he had become a successful writer, composed such masterpieces as "Longing," often mistranslated "Misery," which beautifully explores the human need for someone with whom to share our difficulties and suffering in life, a call that all physicians should be well prepared to answer. Likewise, Bulgakov's "A Young Doctor's Notebook" contains the story "Morphine," showing how overwork, discouragement, and confusion can drive a physician to doom. In the same league are the short stories of William Carlos Williams, an American physician, whose tale "Jean Beicke" explores the indomitable will to life amid even the most desperate of human circumstances.

To burn books is to destroy ideas, and to destroy ideas is to miniaturize and superficialize the human mind and heart. Bradbury wants not sterile efficiency but life in full, and he wants it in abundance. In each human being, each patient and health professional, we find all of life refracted, and our mission as educators is not to simplify and streamline but to welcome and glory in this plenitude, helping health professions education and practice awaken, challenge, and nurture full human beings. To learn to be enthused about what is most worthy says far more about imagination than memorization. We must focus less on what is easy to teach and assess and more on what really matters most. In doing our part to foster such a vision of health professions education, we sustain and develop what is ultimately best in patients, physicians, and humankind.

Arts and Humanities

The following works were submitted by IUSM medical students and include artwork, narratives, poems, opinion pieces, critiques, and more.



Feature: Visual Art

Griffin Elzey, MS3 blends photography with acrylic paint to create original artwork

"I've spent the last 15 years in the military, 12 of them as an Air Force Pararescueman (PJ). This career field, that I still currently serve in as a member of the Air National Guard, exposed me to so many incredible sights and experiences ranging from the unimaginably horrific to the unbelievably beautiful; both of which I was able to document through amateur photography on occasion. Somewhere along the way I also started doing acrylic painting which I wasn't great at but enjoyed. In the last few years I found that the pleasure I get from combining the two art forms is greater than either individually, and the end products usually look better than the lone forms too. Not only do I find this to be an enjoyable way to decompress from the rigors of medical school, but I have been fortunate enough to have sold a few works and 100% of the proceeds have gone to the very worthy cause of the Pararescue Foundation which I will shamelessly plug here. Also, here are three recent works related to medicine."

See Spine

My own X-Ray blended with my wonderful wife's acrylic work. Who knew that cervical spine issues could look so good?

Hospital Sunset: Demolition of the St. Joe Hospital in Fort Wayne, IN

St. Joseph Hospital, or what remained. As a native born resident of Fort Wayne, IN this hospital was a staple of the downtown area and its newfound absence is even more eerie to me than this photo acrylic blend.

A Little Pick Me Up

Everyone needs a little pick me up on occasion. It is true. This is an acrylic splashed shot that I took of a team of Air Force Special Operations Medical (PJs) loading patients onto a CH47 Chinook helicopter during a training event in Michigan.


BRITT
For Admittance
CALL
339-0332

Feature: Visual Art

Kathleen Ho, MS2 showcases her artwork

Changing of the Seasons

Oil Paint
8 x 10" each

This series of paintings reflects on the human experience and the different seasons of life that shape and mold us, both as individuals and as a community. As I painted each piece, I was reminded of the inherent beauty that exists within ourselves and in the world around us, even during difficult times.

In fact, I began this series during a time of personal grief after the loss of a family member. Painting allowed me to process my emotions and find solace in the beauty that can still be found in each season of life, even in the midst of sorrow. Each painting in this series represents a different stage of my journey, from the pain of loss to the hope of healing and growth.

Through this process, I have come to realize the power of art in helping us cope with difficult emotions and shift our perspective to focus on the light and positivity in life. I hope that these paintings can inspire others to find their own sources of beauty and light during their own seasons of life.

Abyss

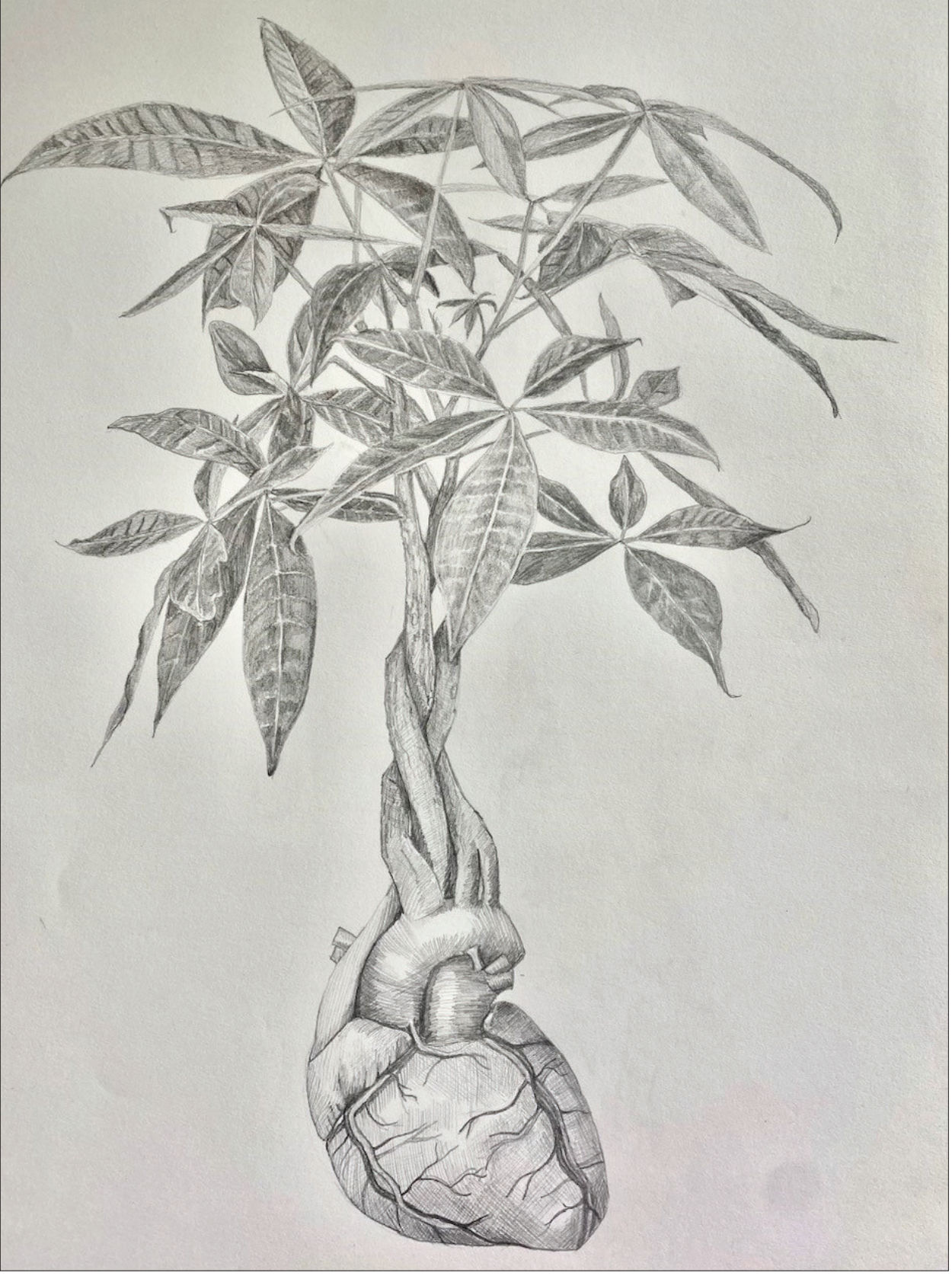
Oil on canvas
18 x 20"

I aspire to unite the realms of art and medicine by capturing the awe-inspiring intricacies and captivating beauty of the human eye, a true manifestation of life's enigmatic wonder.

The Inner Garden

Oil Paint
18 x 24″

I began creating this artwork shortly after studying Human Structure, and completed it in April of my first year of medical school. This large-scale project provided me with a much-needed outlet outside of my academic studies, allowing me to focus on something outside of the classroom while still stimulating my creativity and passion. Through this piece, I gained a newfound appreciation for the beauty and colors of nature, and learned the importance of slowing down and taking time to appreciate the simple things in life.



Truncus Arteriosus

Graphite

18 x 24″

I created this piece during our cardiology block, with inspiration from a plant in my room. I found that drawing the anatomy of the heart helped me perceive the dimensionality of the organ, its chambers, and blood flow. I titled the piece after the pathology of truncus arteriosus, the failure of the pulmonary artery and aorta to separate in fetal development. In this drawing, these vessels spiral upwards into the tree trunk, as medicine can help those with this pathology live and grow resiliently.

The Mediating Effects of Prayer on the Anterior Cingulate Cortex's Regulation of Anxiety

by Peyton Estes, MS1

In The Screwtape Letters Screwtape writes to Wormwood, "There is nothing like suspense and anxiety for barricading a human's mind against the Enemy. He wants men to be concerned with what they do; our business is to keep them thinking about what will happen with them" (1). Without directly stating it, C.S. Lewis made a profound connection between neurobiology and spiritual formation.

It has been supported that The Lord's Prayer has correlation with activation in several areas of the brain, one of which is the anterior cingulate cortex (ACC), a structure involved with emotions, particularly anxiety, as well as decision-making (2). Furthermore, when a person prays, the same regions of the brain are activated as those which are stimulated during conversations with others (3). Based on this observation, it can be hypothesized that the brain has come to view conversations with God, on a neurobiological level, as quite similar to those that one may have with a close friend or family member. These same regions of the brain are also heavily involved with assessing the past and future experiences of your own life (3). As someone who has struggled with anxiety, I know first hand that it is rooted in an over evaluation of the past and an overthinking of what is to come. Even though Neubauer does not directly reference anxiety, he does highlight the connectivity between prayer and the structures of the brain which impact how you think about yourself. Using functional magnetic resonance imaging (fMRI), the study demonstrated patterns of activation within the ACC during prayer, which provides a theoretical basis for the hypothesis that prayer can mediate feelings of anxiety and/or, impact the way a person evaluates and dwells on previous life choices, as well as future ones that may be hanging over his/her head (3).

This hypothesis is backed by research that has explored the relationship between spirituality and meditation. A two-week meditation study that evaluated pain, anxiety, mood, and spiritual health pre- and post-test found that those who identify as religious reaped greater benefits from prolonged periods of meditation (4). At the end of the study, the individuals who were classified as spiritual reported significantly larger decreases in anxiety and significantly greater increases in positive mood (4). In contrast to the Neubauer study, this research did not directly reference the ACC, though it did specifically include anxiety as an endpoint. Nevertheless, because of the physiological role of this structure and common activation by emotions (e.g. anxiety), self-reflection on past and future decisions, and prayer, there is a theoretical basis for the hypothesis that the ACC may be heavily involved in the alleviation of anxiety by spiritual meditation and prayer. It is time that meditation, prayer, and the ACC, as a unit, receive the recognition they deserve for the potentially significant impact they may have on the health and well-being of individuals across the world.

References

1. Lewis, C.S. (2015). The Screwtape Letters. HarperOne.

2. Mercadillo, R. E., Fernandez-Ruiz, J., Cadena, O., Domínguez-Salazar, E., Pasaye, E. H., & Velázquez-Moctezuma, J. (2017). The Franciscan Prayer Elicits Empathic and Cooperative Intentions in Atheists: A Neurocognitive and Phenomenological Enquiry. Frontiers in Sociology, 2. Available from: https://www.frontiersin.org/article/10.3389/fsoc.2017.00022

3. Neubauer, R. L. (2014). Prayer as an Interpersonal Relationship: A Neuroimaging Study. Religion, Brain & Behavior, 4(2), 92–103. Available from: https://doi.org/10.1080/2153599X.2013.768288

4. Wachholtz, A. B., & Pargament, K. I. (2005). Is Spirituality a Critical Ingredient of Meditation? Comparing the Effects of Spiritual Meditation, Secular Meditation, and Relaxation on Spiritual, Psychological, Cardiac, and Pain Outcomes. Journal of Behavioral Medicine, 28(4), 369–384. Available from: https://doi.org/10.1007/s10865-005-9008-5

Trading Stress for Stress

by Kennedy Stoll, MS 2

As a second-year medical student, I'm constantly reminded by upperclassmen and faculty alike how lucky I am that the USMLE Step 1 exam is now pass/fail. At times, I find myself slightly more relaxed knowing if I have a bad test day, I won't receive a three-digit score reflecting what I perceived to be a poor performance. As long as I pass, with or without flying colors, I can breathe a little easier. This all sounds great on paper; at first glance, it appears a stressor has been eliminated. I too was initially under this impression but have recently become concerned the stressor has simply changed hats.

Step 1 anxiety still exists. Making the exam pass/fail might've decreased stress to some degree, but those studying can confirm the exam is still a challenge. Step 2, on the other hand, has become not only the more important standardized test, but also the only standardized quantitative metric residency programs have to compare applicants. People have always disliked the idea of residencies initially filtering applicants based on Step 1 and Step 2 scores. This is understandable as the filtration process seemingly prematurely evaluates the capacity of a resident based on two, three-digit exam scores. Without Step 1 scores, programs may begin filtering applicants based on one exam alone. Though applicants are further evaluated based on third-year clerkship grades and numerous other metrics, a lower Step 2 score could get an application thrown out prior to any comprehensive review and have a drastic impact on career trajectory. As a result, research, letters of recommendation, and extracurricular activities are more important than ever. Unfortunately, active and meaningful participation in these activities is quite a feat, requiring time and energy that busy medical students often lack.

Timeline now also has greater emphasis. Step 1 exam scores previously provided insight by the end of second-year into medical students' future competitiveness for residency. With Step 2 now as the only scored standardized test in medical school, objective performance level and subsequent impacts on competitiveness for residency are now unknown until the end of third-year or beginning of fourth-year. This is well after fourth-year schedules have been submitted and finalized, which students build largely based off the specialty they anticipate applying to in the fall. Backup plans must now be made as one bad test day could decrease competitiveness in an intended specialty. This uncertainty unfortunately means students may need to add rotations in multiple different fields throughout their fourth-year schedule, consuming elective spots.

I think it is rather apparent that new issues have arisen as a result of Step 1 changes. Perhaps I have overestimated importance in some areas and underestimated it in others. Regardless, I believe the stress of medical school has not changed but merely shifted. While one source of stress has decreased, many others have increased to an equal or further extent. Of course, time is always needed to evaluate results after change, but I believe students will report a similar, if not greater, level of stress in the years to come. I am happy to see administration within medicine attempting to decrease stress for medical students, but my concern is that this was not the best method and other alternatives need continued pursuit. I challenge medical students, administrators, and faculty clinicians to critically evaluate the changes made to Step 1 and consider the resulting ripple effect.

Chronic Eye Floaters: An Opportunity for Progress

by Michael Smith, MS3 and Matthew Mazewski, PhD

Medical education places a strong emphasis on discussing barriers to care and underserved patient populations. As a new matriculant to medical school, I did not fully appreciate how this could manifest, and I never imagined that I would soon face these challenges myself. During my first year of medical school, I developed what are commonly known as eye floaters. While my case was not severe, it led me to discover a unique subset of patients who not only suffer from a very real and potentially debilitating disease, but also from a general lack of knowledge about how to objectively diagnose and treat their condition.

Eye floaters, also known more technically as myodesopsia, have been associated with many conditions ranging from benign age-related changes of the eye like posterior vitreous detachments to acute processes like uveitis and trauma to idiopathic causes. The pathophysiology of myodesopsia involves an aggregation of collagen fibers within the vitreous of the eye, which casts visible shadows on the retina and is best seen when contrasted against a bright surface. Though floaters may be a warning sign of serious pathologies like retinal detachment, especially floaters with an acute onset, often no such pathology is present and, once ruled out, patients are sent on their way. However, the long-term impact on quality of life must not be discounted, particularly for patients with numerous floaters or floaters of large size. This can manifest as patients choosing not to venture outside due to visual disturbances that are worse in more brightly lit or higher-contrast settings; socially isolating themselves; experiencing difficulties performing tasks that require quick saccadic eye movement, such as reading or driving; and experiencing higher rates of mental health issues as a result of their condition (1).

Unfortunately, both patients with chronic floaters and physicians treating chronic floaters are put in an unenviable position. Because it is difficult to objectively quantify how badly someone's floaters are affecting their vision, physicians must rely on subjective reports from these patients. This problem exists even in light of emerging data regarding vitreous echodensity as obtained by quantitative ultrasound and measures like contrast sensitivity function, both of which have been shown to correlate with subjective symptoms (2). Additionally, the only curative treatment for eye floaters is with vitrectomy, which is an invasive procedure that many physicians are not keen on performing when a patient's eye is otherwise healthy, even when these patients report a high subjective degree of suffering (3-4). This even further limits treatment options and may lead this patient population to feel that their struggles are not being appreciated or taken seriously. A well-documented outgrowth of this is "doctor-shopping behavior," which has been studied by Tseng. Patients' experiences of receiving an inadequate explanation of the disease, as well as a high degree of concern about their condition, were correlated with this behavior (5). This raises questions about whether our current patient interactions around this condition could

be modified in some way to either better equip patients with evidence-based understanding, or at the very least, help to better align goals of care between the patient and physician.

Another complicating factor is the paucity of data on myodesopsia. While there is research demonstrating the negative impact that it can have on quality of life, there is little work exploring how many patients are affected and to what degree they are affected (6). This leads to a lack of corporate or governmental incentives to research treatments for the condition. There is also a general sense among physicians that floaters are common and that since most people can adapt to life with them, then so can the patients who are severely afflicted (7,8). This is likely not the case, and more study of this specific patient population could be of immense benefit. This begins by obtaining better data on prevalence and the fraction of patients with significant visual impairment, and by intensifying efforts to provide physicians with better diagnostic and therapeutic tools.

Patients suffering from chronic eye floaters face many hurdles. They often struggle to help their physicians understand the severity of their condition, they grapple with visual changes that can potentially impact them for the rest of their life, and they face a reality of few treatment options and little prospect of large-scale research to develop new therapeutic strategies. As a medical community we must do more to avoid letting this population slip through the cracks.

References:

(1) Senra H, Ali Z, Aslam T, Patton N. Psychological implications of vitreous opacities - A systematic review. J Psychosom Res. 2022 Mar;154:110729. doi: 10.1016/j.jpsychores.2022.110729. Epub 2022 Jan 25. PMID: 35091262.

(2) Mamou J, Wa CA, Yee KM, Silverman RH, Ketterling JA, Sadun AA, Sebag J. Ultrasound-based quantification of vitreous floaters correlates with contrast sensitivity and quality of life. Investigative Ophthalmology & Visual Science. 2015 Mar 1;56(3):1611-7.

(3) Cohen MN, Rahimy E, Ho AC, Garg SJ. Management of symptomatic floaters: Current attitudes, beliefs, and practices among vitreoretinal surgeons. Ophthalmic Surg Lasers Imaging Retina. 2015;46:859-865

(4) Cunningham MA, Kumar JB. Surgical Considerations for Vitreous Opacities. Retina Today. Jan/Feb 2022. https://retinatoday.com/articles/2022-jan-feb/surgical-considerations-for-vitreous-opacities?c4src=topic:surgery:topic-hero

(5) Tseng GL, Chen CY. Doctor-Shopping Behavior among Patients with Eye Floaters. Int J Environ Res Public Health. 2015 Jul 13;12(7):7949-58. doi: 10.3390/ijerph120707949. PMID: 26184266; PMCID: PMC4515702.

(6) Wagle AM, Lim WY, Yap TP, Neelam K, Au Eong KG. Utility values associated with vitreous floaters. Am J Ophthalmol. 2011 Jul;152(1):60-65.e1. doi: 10.1016/j.ajo.2011.01.026. Epub 2011 May 12. PMID: 21570045.

(7) Sebag J. Vitreous and Vision Degrading Myodesopsia. Prog Retin Eye Res. 2020 Nov;79:100847. doi: 10.1016/j.preteyeres.2020.100847. Epub 2020 Mar 6. PMID: 32151758.

(8) Zou H, Liu H, Xu X, Zhang X. The impact of persistent visually disabling vitreous floaters on health status utility values. Qual Life Res. 2013 Aug;22(6):1507-14. doi: 10.1007/s11136-012-0256-x. Epub 2012 Oct 11. PMID: 23054488.

The Complexity of Medical Training: Helping Loved Ones Understand

by Maria Feucht, MS3

The structure of medical training, from medical school to residency and beyond, is complicated. While we as medical students work with residents, fellows, and attendings every day, our loved ones who don't have as much experience with the medical field may have never even heard of these terms, much less understand their roles in a clinical environment. It's hard to explain medical school, residency, the matching process, etc., to people who haven't lived through it—simply put, it's complicated, as many of us have told our family and friends. Because of this, I often find myself struggling to answer questions about the structure of medical training and my future plans. Despite the challenges, it's worth the time and effort to help our loved ones understand the complex process we're going through.

Medical education can be isolating. Many trainees find themselves growing apart from family and friends during medical school and residency; this is due, in large part, to the tremendous demands on their time. Most people hold the perception that medical school is hard, but that doesn't mean they understand the true nature of its demands. Helping our loved ones gain a deeper comprehension of the realities of medical education and the associated time constraints may help them better understand why it's more difficult—or sometimes impossible—to attend family gatherings or social events with friends. Additionally, many loved ones take an interest in the process expressly because they want to learn how they can best support us. Taking the time to explain what you're going through can provide insight into how they can help you, whether it's making sure you have an environment conducive to studying for exams or distracting you from the stress of Match Week.

To make such a complicated system more comprehensible to your loved ones, look no further than the skills you already use to explain diseases and physiological mechanisms to patients. Use terms they can understand and analogies that relate to their lives. Do they watch medical shows? Tell them you'll be like J.D. from Scrubs once you graduate medical school. Struggling to help your relative understand the matching process and why you don't just get to pick where you'll work for the next three to seven years? Tell them that it's a little more like the NFL draft than it is a normal job search. Use humor; send them Dr. Glaucomflecken's sketches about Match Day and the matching algorithm.

Beyond the tools that we use to make complicated concepts more accessible to patients, though, we can also help our loved ones understand by being honest about our experiences. Be vulnerable with the people you trust about your struggles and allow them to see how medical training impacts you.

Ultimately, while you may help your loved ones better understand medical training and its demands, it's important to be cognizant that your loved ones also have a lot of demands on their time. Remember that they need your support and to know that you care about them, too.

Visual Art: Pain and Pills

Alyssa Iurillo, MS2

Sickle cell disease results in episodes of acute severe pain. Also, chronic pain can develop. Currently, sickle cell pain is not adequately managed. There needs to be more research to improve pain management in sickle cell disease. Overall, there is limited evidence for using analgesic in acute pain crises.

References

(1) Aich A, Jones MK, Gupta K. Pain and sickle cell disease. Curr Opin Hematol. 2019 May;26(3):131-138. doi: 10.1097/MOH.0000000000000491. PMID: 30893088.

(2) Brandow AM, Carroll CP, Creary S, Edwards-Elliott R, Glassberg J, Hurley RW, Kutlar A, Seisa M, Stinson J, Strouse JJ, Yusuf F, Zempsky W, Lang E. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain. Blood Adv. 2020 Jun 23;4(12):2656-2701. doi: 10.1182/bloodadvances.2020001851. PMID: 32559294; PMCID: PMC7322963.

(3) Katsivalis KV, Kosacz J, Austin Szwak J. Opioid Use in Vaso-Occlusive Crisis During Intravenous Opioid Drug Shortage. Hosp Pharm. 2022 Dec;57(6):721-726. doi: 10.1177/00185787221095894. Epub 2022 Jun 4. PMID: 36340631; PMCID: PMC9631012.

(4) Dunlop RJ, Bennett KC. Pain management for sickle cell disease. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD003350. doi: 10.1002/14651858.CD003350.pub2. Update in: Cochrane Database Syst Rev. 2014;4:CD003350. PMID: 16625580.

Listening Closely

by Sabin Karki, MS1

(This short story describes my experience volunteering in a local pediatric emergency department as part of a study to collect pulmonary recordings for the development of a smart stethoscope. Patient and physician names have been changed.)

In the pediatric emergency department (ED) of Johns Hopkins Hospital, two patients share a single room, their beds arranged in parallel. Each bed is flanked by chairs for family members and an opaque blue curtain bisects the room, its spongy texture attracting the curious hands of more than one toddler on any given day. After spending several weeks recruiting patients for a study testing a new stethoscope, I began shadowing Dr. H, a young pediatrician in the pediatric ED. I felt accustomed to the general comings and goings of the throngs of doctors, nurses, PAs, and patients streaming through the maze-like facility. Evenings were noisier than mornings, and now, at 5:30 pm on a Wednesday evening, even the fax machines and telephones were drowned out by the cries of children. As I followed Dr. H from room to room, I tried my best to keep out of the way while listening to and learning about each of her patients.

As Dr. H and I stood in front of Room 05, she articulated stories about the highest acuity, most contagious patients she had seen throughout her career in encyclopedic detail. Today, she was telling me about her preparations for coronavirus, should a patient arrive with the associated symptoms. Regimented, clear protocols laid out before the event — that's how you prevent panic and infighting for resources, she said. Our conversations always pushed me to think about medicine from a broader perspective, and the energy and passion Dr. H brought to patient care were palpable. She squeezed one of the countless hand sanitizer dispensers lining the walls, rubbing her hands together almost unconsciously as we waited for the nurse to finish charting on the bedside laptop.

Dr. H leaned against the wall. "It's been a long week -- but here, I'm always learning, always teaching. In a way, it's a privilege." The nurse exited the room, signaling our cue to enter. Dr. H stood upright, squeezed the Purell dispenser again, rubbed her hands together, and turned the aluminum door handle to Room 05. Inside, an exhausted mother lay asleep, cradling her infant in white sheets on one side of the room. In the other bed, a toddler sat upright in her mother's arms before tossing a stuffed dinosaur at my feet. I laughed and gingerly returned it to an empty chair.

"Maddie!" Dr. H smiled. "It's been a while. You've gotten so big." The mother flashed a brief smile, and they exchanged pleasantries for a few moments. "Can I listen to her heart and lungs?" Dr. H asked.

"Yes," murmured the mother, positioning Maddie so she faced the physician. "She's been doing good for a couple days. No more coughing." Dr. H squeezed the toddler's hand, and Maddie's eyes flitted toward Dr. H, but only for a moment. The child's face suddenly twisted and she began to wail. Dr. H cooed and soothed her within seconds, flashing a stethoscope retrofitted with a plastic clicking frog. Maddie stopped mid-wail, examining the frog intensely, as the doctor placed another

stethoscope on her chest and back.

After a brief pause to auscultate, Dr. H issued an exciting assessment. "She sounds clear! I don't hear any more crackles or wheezing, so this is a great sign." The mother perked up; her shoulders visibly relaxing. "I'm always happy to see Maddie," Dr. H continued as she leaned forward, gently taking one of the child's fingers in her hand and waggling it, "But I'd be even happier to not see you in the hospital for a while. Now, go home and get some rest. Your nurse will be here soon to go over her paperwork." The mother was ecstatic. She thanked Dr. H profusely, glancing up intermittently as her fingers rapidly tapped out a text on her phone, presumably to her spouse.

We exited the room, and I heard the heavy door slide close behind Dr. H. I turned and was shocked to see a look of frustration on Dr. H's face. "She shouldn't even be here in the emergency room" she said. I nodded as she clarified: "Coming into the ED presents its own risks to the most vulnerable patients I see, but for many families it's the only way they can get care. Maddie's lungs sound great and she has a greater chance of catching something just by being here." As we left the room, I wondered aloud: Why had Maddie's mother brought her all the way to the ED when she appeared to be nearly recovered from her sickness? Perhaps Maddie had no pediatrician, or the ED was the closest source of medical care for her daughter in East Baltimore? There are no easy answers, said Dr. H, and I agreed. She reached for the hand sanitizer dispenser. Squeeze. We walked down the hall to the next room.

A Place to Heal

by Christopher Schorr, MS2

Streaming down my face, they fall,
Invisible to all but me.
Silent tears that speak it all,
Of pain, hurt, and misery.

I lay here in this sterile room,
With machines that beep with every breath.
Each tear a symbol of my woe,
A sign of what lies beneath.

One day, a stranger walked in,
A soul with wounds just like my own.
We shared our pain, our hope, and then,
A friendship was born, a bond that's grown.

Together, we laughed and cried,
We shared our joys and fears.
In this place where sickness prevails,
We found a home, a place to heal and cheer.

And now, as I look back and see,
How far I've come, I'm filled with pride.
For I have found a family,
In this hospital, where tears once cried.

Disparities in Our Medical Education: Our Curriculum is Not Equitable

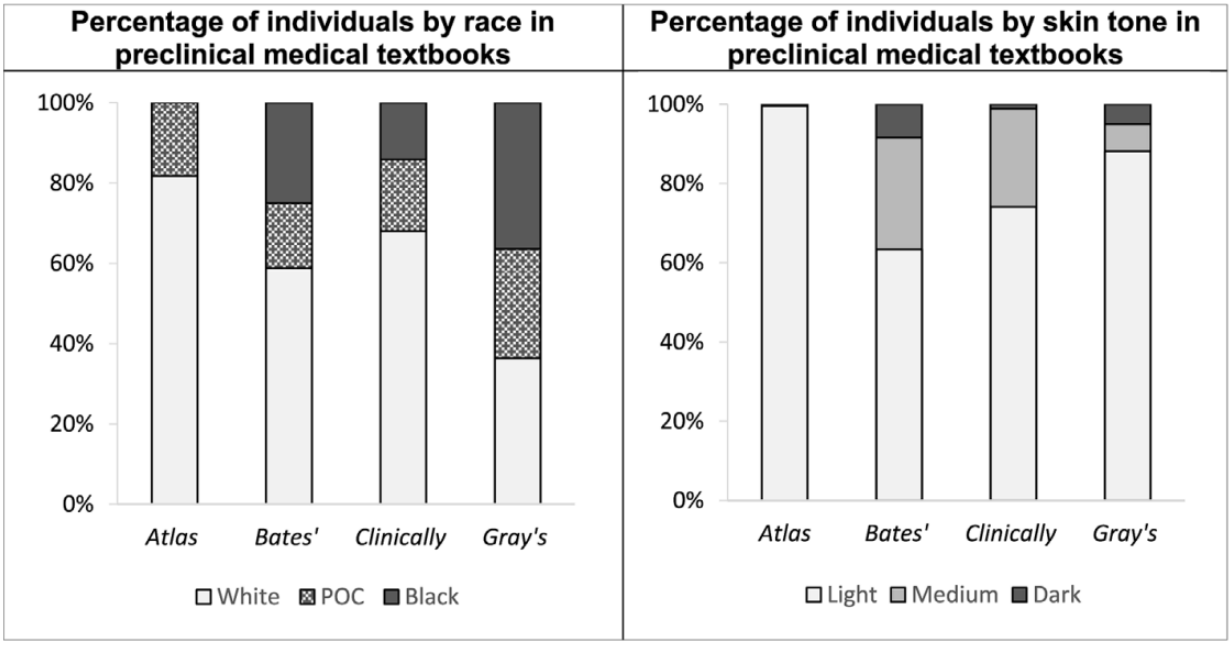
by Brianna Harvey, MS2

Medical schools across the country, including our own Indiana University School of Medicine (IUSM) have failed us drastically in one category: diagnosis of skin conditions for all skin tones. As a rising 3rd year medical student with rotations looming around the corner and as the thoughts of residency begin to creep into my mind, I have started to reflect on the quality of my medical education. Wherever you are in your medical education journey, think back to any time in which you were learning about a disease which was presented with some sort of skin manifestation. When has that manifestation been described or shown on skin that was non-white? Impetigo, blanching lesions, purpura, and even APGAR scores are all taught to us through the lens of white physicians practicing on white patients. If I was born either pink or blue, both would have been abnormal as the child of two Black parents.

During my first semester of medical school, in the trials of human structure and anatomy lab, a professor was talking about physical changes that happen during pregnancy. He mentioned that most areolas are pink unless the person has been pregnant before, in which they turn brown. At that moment, my G0P0 self had to pause the video and conduct a self-examination to make sure that I hadn't been seeing my body wrong my entire life. After battling with the internal struggle of if I wanted to speak up and possibly risk tainting my professional reputation before I even created one, I decided to reach out. The professor responded, without judgment, saying that "no one had ever caught that error before." With IUSM being the largest medical school in the country, the fact that no one has caught the error in the many years of that presentation being used speaks to the huge problem we face. In addition to the lack of representation, there's also a lack of people willing to address that issue for the sake of our future patients.

That story is just one example of the many times in which I, as a Black woman, have not felt like my "standardized" medical education has prepared me to practice medicine with a diversified population. According to the latest census data, the US population is 57.8% white, 18.7% Hispanic/Latino, 12.1% Black, and 5.9% Asian[1]. Of those ethnicities, a variety of skin tones are represented, many of which we are not prepared to accurately diagnose based on our current educational materials. A recent national study of dermatology residents reported that there was a significant difference in their confidence in diagnosing dermatologic conditions on skin of color[2]. The study also found that those residences with specific curricula for skin of color reported higher confidence in their diagnosing skills.

Medical schools are not the only ones at fault for this lapse in education; this issue extends beyond the lectures presented in the classroom. The majority of the commonly cited textbooks that medical students use also disproportionately represent skin tones in pictures. The heralded Atlas of Human Anatomy, Bates' Guide to



Note. Reprinted from Representations of race and skin tone in medical textbook imagery, Louie, P and Wilkes R. 2018, Social Science and Medicine.

Physical Examination & History Taking, Clinically Oriented Anatomy, and Gray's Anatomy for Students were found to display 74.5% light, 21% medium, and 4.5% dark skin tones when placed into a computer algorithm using a total of 10 skin tones classifications[3].

I am certainly not the only medical student sounding the alarm on this growing problem in medical education. In 2020, a medical student at St. George's University of London, Malone Mukwende, had the similar concerns and created a database called Mind the Gap: A Handbook of Clinical Signs in Black and Brown Skin[4]. Since its creation, not only has he achieved international awareness of the problem but also created tools to fix it. Other databases like visualDx are taking notice, but change is a slow process. As students at IUSM, it is up to each of us to follow the lead of our colleague and advocate for our quality of education, helping us become doctors better suited to confidently diagnose and treat patients of different skin tones and backgrounds. Being an ally is a verb — be the student who questions what a dermatological manifestation may look like on different skin tones, the professor who includes pictures of all skin tones in their presentations, or the person who advocates for representation of skin tones in the curriculum. The quality of care for our diversified patient population depends on it.

References:

(1) United States Census Bureau. Racial and Ethnic Diversity in the United States: 2010 Census and 2020 Census. Census.gov. Published August 12, 2021. Accessed May 15, 2022. https://www.census.gov/library/visualizations/interactive/racial-and-ethnic-diversity-in-the-united-states-2010-and-2020-census.html.

(2) Gupta R, Ibraheim MK, Dao Jr H, Patel AB, Koshelev M. Assessing dermatology resident confidence in caring for patients with skin of color. Clinics in Dermatology. 2021;39(5):873-878. doi:10.1016/j.clindermatol.2021.08.019. Accessed May 15, 2022.

(3) Louie, P and Wilkes R. Representations of race and skin tone in medical textbook imagery. Social science & medicine. 2018;202:38–42. doi:10.1016/j.socscimed.2018.02.023. Accessed May 13, 2022.

(4) Mukwende M, Tamony P, and Turner M. Mind the Gap: A handbook of clinical signs in Black and Brown skin. St George's, University of London. 2020. doi:10.24376/rd.sgul.12769988.v1. Accessed May 13, 2022.

What Medical Students Should Know About Artificial Intelligence, From a Former Instructor

by Kali Konstantinopoulos, MS1

It's no secret that artificial intelligence (AI) in healthcare is a hot topic. AI has already found its way into multiple medical specialties, such as radiology and pathology, in which machine learning algorithms are able to identify possible diagnoses from image features. Now, with further advancements in the technology, physicians may be able to use AI to inform diagnoses based on patient vitals and lab results, predict which treatments will be most effective, and assist with documentation. Since AI has great potential to aid physicians in clinical decision-making and shift the future of medicine, the question of how best to incorporate AI into medical education arises: What do medical students need to know about AI? As a former teaching assistant for an introductory AI course at Indiana University (IU) Bloomington, this question is of great personal interest to me. Having reflected on my time teaching the subject and my experiences as a medical student, I believe that the most important thing medical students should know about AI is the foundational workflow of training and testing models, no matter how easy it is to get lost in the technical details.

International Business Machines (IBM) defines AI as "a field, which combines computer science and robust datasets, to enable problem-solving" (1). It can be thought of as a machine that can complete tasks that normally require human cognition, such as distinguishing objects in pictures or writing a piece of text. The subfield of AI that may be most relevant for medicine is machine learning, in which algorithms typically find patterns in provided data to classify items or identify subgroups within the dataset. The basic workflow of machine learning involves choosing and processing the data, using a subset of that data to train the model to find patterns, testing the algorithm on similar data it has not seen before, and then evaluating its performance. In medicine, a machine learning program may take in images of histological slides or radiological scans and use image features like color and shape to determine a potential pathology. In the future, we may use machine learning to help identify diagnoses, prognoses, and treatment options from physical exam and testing results.

When I was teaching machine learning in an engineering context, students' main concerns were usually related to technical details: preparing and analyzing the data, writing code, and optimizing the algorithm for improved accuracy. However, in a clinical setting, patients are front and center. In a 2020 article on AI medical education by McCoy et al., the authors reasoned that physicians should be able to "identify when [AI] is appropriate for a given clinical context...understand and interpret the results with a reasonable degree of accuracy, including awareness of sources of error, bias, or clinical inapplicability" and "be able to communicate the results and the processes underlying them in a way that others (e.g. allied health professionals and patients) can understand" (2). The authors advocate for an educational model in which AI topics necessary for everyday clinical practice are integrated into the medical school curriculum, while quantitative skills necessary to advance the technology are incorporated into extracurricular activities. There are some existing models for computing-related extracurricular and curricular activities in medical school. The University of Toronto, for example, created a Computing in Medicine certificate for medical students, which included programming classes, medical computing projects, and

seminars with experts in the field (3). At the IU School of Medicine, the Terre Haute campus offers an elective called Advanced Topics in Biomedical Informatics and Technology, which covers, among other topics, "principles of biomedical data representation, software design…mathematical modeling…[and] big data" (4). While not specific to AI, these options address the computing literacy that would be necessary for medical students interested in becoming leaders in the medical software space.

From all this discussion on AI in medical education, it seems easy to conclude that all medical students need lessons in coding. However, when I think about machine learning concepts that could be applied to clinical practice, I don't envision memorizing the mathematical structure of a model or optimizing an algorithm. Instead, I go back to the basic workflow of machine learning: data acquisition and processing, training, testing, and evaluating. Even when teaching undergraduates majoring in engineering, I always returned to this framework to focus on critical analysis of the software. From a clinical perspective, the workflow may be the most important concept that a physician could explain to a patient, as it covers how patient data will be used and assuages fears that the AI will replace the physician. After all, the algorithm cannot think for itself and makes decisions based on how it was trained. Thinking beyond the exam room, understanding these foundational concepts also allows physicians to better collaborate with technologists to meet clinical needs. Having a baseline understanding of the machine learning process aids in the cross-disciplinary communication necessary to establish clinical relevance and ensure that new technologies meet the needs of both physicians and patients. This can include evaluating sources of bias, as physicians can use their knowledge of social determinants of health and related disparities to recognize bias in the dataset or features used to train the model.

The world of AI can seem like a black box (and for some algorithms, that may be true). However, when AI comes into the clinic, knowledge of the field cannot be left solely to computer scientists and engineers. With a basic understanding of the machine learning workflow, future physicians can be poised to evaluate new algorithms for clinical use, explain basic concepts to patients, and communicate with technical experts. So, while diagnoses of algorithmic bugs are left to the programmers, medical students can still be well-equipped to face the changing landscape of healthcare. No coding experience required.

References:

(1) International Business Machines. What is Artificial Intelligence (AI)? [Internet]. IBM: [cited 2023 Mar 1]. Available from: https://www.ibm.com/topics/artificial-intelligence.

(2) McCoy LG, Nagaraj S, Morgado F, Harish V, Das S, Celi LA. What do medical students actually need to know about artificial intelligence?. NPJ Digital Medicine [Internet]. 2020 Jun 19 [cited 2023 Mar 1];3(1):86. Available from: https://www.nature.com/articles/s41746-020-0294-7.

(3) Law M, Veinot P, Campbell J, Craig M, Mylopoulos M. Computing for medicine: Can we prepare medical students for the future?. Academic Medicine [Internet]. 2019 Mar [cited 2023 Mar 1];94(3):353. Available from: https://journals.lww.com/academicmedicine/Fulltext/2019/03000/Computing_for_Medicine__Can_We_Prepare_Medical.26.aspx.

(4) Indiana University School of Medicine. 2022-2023 Electives. IUSOM: [cited 2023 Mar 1]. Available from: https://iusom.sitehost.iu.edu/electives/.

Professionalism Policies at IUSM: A Conceptual Analysis and Critique

by Eli G. Schantz, MS2, Afsheen Mansoori, Jonathan Harris, and Clayton Hicks

Introduction: The notion of professionalism informs policy-making at all levels of medical practice, from national organizations and licensing boards to hospital disciplinary committees. The creation of policies to promote professionalism, however, is made all the more complex in the context of undergraduate medical education, where the notion of professionalism not only acts to govern behavior, but also to shape the professional identity of physicians-in-training.

Objectives: Given the importance of professionalism policies, our goal here is to characterize, both descriptively and prescriptively, how the notion of professionalism manifests in the policies governing undergraduate medical education. We seek to offer a critique of this characterization and propose potential strategies for reforming these policies.

Methods: To present a review of the professionalism policies currently in effect at Indiana University School of Medicine (IUSM), we reviewed IUSM's Mission Statement, Physician's Oath, Honor Code, Statement of Professionalism Competencies, Professional Conduct Policy, and Dress Code Policy as they all spoke to professionalism. After identifying key themes present across these policies, we present two main shortcomings evidenced from our review: (i) the frequent use of circular definitions, giving rise to considerable ambiguity, and (ii) pronounced conflict between policies which seek justice and policies which maintain institutional power structures. Finally, we conclude by proposing strategies to combat these shortcomings and discuss the potential continued work on this important topic.

Results: From our review of IUSM's policies that speak to professionalism, the following particular themes were found repeatedly across many policies: the primacy of patient welfare, probity, justice, collaboration, and accountability. In our review we found many examples of tautological definitions and circularity in IUSM professionalism policies (e.g. the Professional Conduct Policy requiring "medical students consistently conduct themselves in a professional manner"). Further, we found that IUSM's policies create dissonance regarding IUSM policy's duties to justice and collegiality. This dissonance is contradictory as the policies may point students to two opposite decisions in a situation regarding justice in healthcare.

Conclusion: We conclude that these conceptual inadequacies represent significant barriers which can both hinder the professional growth of medical students and hamper their ability to navigate their professional obligations, and we offer a number of recommendations for refining and reforming these policies. We recommend the following changes to IUSM's professionalism policies: (i) organization around justice as the primary principle of medicine and (ii) offer a clear definition of professionalism that does not rely on circularly using "professional" in its definition.

For access to the full version of this article, scan the QR code.

Spotlights

Articles written by our editorial board members.

New Technology and Infrastructure: A Look at the Future of Medical Education

by Amrit Parihar, MS3

On October 19, 2022, IU School of Medicine (IUSM) broke ground on the new medical education and research building, which is slated to finish construction by the end of 2024. Not only is this $230 million project the largest in IUSM's 120-year history, but it's also the first new classroom space IUSM has built in Indianapolis since 1959. Even though I will have graduated by then, it's exciting to see what future IUSM students have in store. I sat down with Dr. Jay Hess, Dean of IUSM since 2013, to talk more about the new building and how it may spur new ideas regarding medical education. ››

The construction timeline for the new medical education building coincides with a multibillion-dollar project by IU Health to build a new downtown hospital on 16th St and Capitol Ave. However, proximity to the new hospital wasn't the only reason for IUSM's new space, according to Dean Hess. "There's been many changes in medical education, moving away from large lecture halls to streamed lectures and small group learning. We wanted to optimize the building for the kind of education students will receive in the future."

Future medical education will almost certainly place an increasingly heavier emphasis on technology. Applications of technology in healthcare, such as telemedicine during the COVID-19 pandemic, have already proven invaluable in helping to meet the dynamic needs of both patients and physicians. The new facility accounts for this increasing importance, incorporating infrastructure that will allow students to practice interacting with patients through a virtual medium.

IUSM's new building will also include technology that makes me wish I was back in Human Structure, the first-year anatomy course. "Learning anatomy is hard with just cadaveric dissection, so there will be more virtual reality and more ways of connecting things like radiographic imaging to what you're actually seeing," says Dean Hess. Furthermore, there will be robotic simulators for various surgical procedures, which may serve as an interesting way for students to apply their anatomical knowledge.

"There's been many changes in medical education, moving away from large lecture halls to streamed lectures and small group learning. We wanted to optimize the building for the kind of education students will receive in the future."

Outside of these futuristic educational features, students can also look forward to a beautiful architectural layout and design, according to Dean Hess. "One of the things we've needed in the School of Medicine in Indianapolis is a common gathering area. A place where you can grab a cup of coffee, meet with other people, and enjoy the view. The new building has a spectacular three-story sunlit atrium that looks like the Guggenheim Museum."

Beyond the atrium, the building was designed with the intention of creating a sense of cohesion and teamwork. This aligns with the school's plan to group future students into 12 learning communities. On the second and third floors, the new building will have individualized lockers, study areas, practice exam rooms, and kitchenettes for the groups. "It goes beyond the facility," adds Dean Hess. "We're planning to have faculty assigned to each learning community to make it similar to the regional campuses. They will be right there where the students are, which will facilitate getting advice and help with study material."

It's clear that the new building is only one part of the equation for IUSM. Dean Hess emphasized that even with all the new technology and educational opportunities coming to IUSM, student experience remains at the core. "I've always wanted the School of Medicine to be a place where each learner can discover and begin to realize their dream for their career."

Exciting times are ahead. Students will be able to experience the new building in 2025.

Scan the QR code for a livestream of the construction of the new medical education and research building.

Student-Run Free Clinics: With Great Impact Comes Great Responsibility

by Nirupama Devanathan, MS3 and Amrit Parihar, MS3

There's no shortage of stories about exorbitant medical bills in the United States, one of the few industrialized economies with a lackluster medical safety net. With the complex web of in-network and out-of-network providers, rejected prior authorizations, and expensive copays, even insured patients face medical costs that can empty entire checking accounts. Given the unreliability of certain options, such as a "GoFundMe's" or schoolchildren's fundraisers for catastrophic injuries, many individuals must resort to desperate measures, such as filing for bankruptcy (1).

What then is done for patients without medical insurance, whether due to unemployment or undocumented immigration status? Or for those who are underinsured and unable to afford copays?

While the passage of the Affordable Care Act in 2010 extended affordable healthcare to many Americans, about 30 million people still remain uninsured, according to a 2022 Kaiser Family Foundation report (2). From the same report, one in five uninsured adults puts off needed medical care due to cost.

It is evident that healthcare, especially preventative medical services, is out of reach for many Americans. In medical school, we learn about the United States Preventative Services Taskforce (USPSTF) guidelines but are then faced with patients suffering from advanced pathologies due to delayed care. It's a vicious cycle. Patients delay preventative healthcare due to finances but are then faced with the astronomical financial burden of emergent lifesaving procedures.

Student-run free clinics (SRFCs) have been constructed to help address the moral injury of inaccessible healthcare. There are 152 member SRFCs across 31 states, including the Indiana University Student Outreach Clinic (IUSOC) here in Indianapolis. The IUSOC was founded in partnership with the Neighborhood Fellowship Church to serve as a transitional care center for the North Eastside community. Our patients are mostly uninsured, and many speak English as a second language. The insured patients we see often have insurmountable medical debt, which may have soured their outlook on traditional healthcare facilities.

To better optimize services offered to the community, the IUSOC Research Team strove to understand the impact of the clinic. The financial impact was analyzed using data from the Centers for Medicare and Medicaid Services to assign costs to medical visits and lab services. Preliminary data from this analysis shows that 70% of medical visits seen at the IUSOC in 2021 were for returning patients. This is of little surprise; on a given clinic day, many of our volunteers and patients know one another on a first name basis. Apart from quantifying the type of visits, this study also

considered lab services. Of more than 3,600 lab tests performed in 2021, almost half were for routine labs, including BMPs, CBCs, and lipid panels, supporting the longitudinal patient care model.

From the data, it's clear the IUSOC has evolved from a stopgap solution to a source of consistent, primary care for many patients. We provide hundreds of patients with insulin and glucometers, anti-hypertensive medications, free, no-questions-asked contraception and Pap Smears, and physical therapy sessions for longstanding musculoskeletal pain.

And yet, despite our best intentions, we cannot perform cataract surgeries or administer chemotherapy infusions.

If patients come seeking services from us initially, we must help guide them to other, robust resources in the community that were purposefully built for longitudinal care, such as the county hospital or Federally Qualified Health Centers. At the IUSOC, this has taken shape with the involvement of Patient Navigators (PNs), who work to connect patients to affordable healthcare programs that provide access to these resources, like our local Eskenazi Health Advantage or the statewide Healthy Indiana Plan.

Though the IUSOC serves many of the same neighbors on a weekly basis, much of the work that advances care for these patients occurs under the purview of PNs. A core component of practicing medicine is having humility, understanding our limitations, and seeking assistance when necessary.

"If patients come seeking services from us initially, initially, we must help guide them to other, robust resources in the community that were purposefully built for longitudinal care..."

SRFCs, like the IUSOC, provide medical services to community members who may lack many other initial options. However, when formal, longitudinal options exist, we owe it to our patients to walk with them and explore the possibility of affordable, routine healthcare.

It all goes back to the Physician's Oath we took together during orientation:

"I will practice my profession with conscience and dignity; the health of my patient will be my first consideration."

References:

(1) Woods, E. (n.d.). Health Care Costs Number One Cause of Bankruptcy for American Families. American Bankruptcy Institute. https://www.abi.org/feed-item/health-care-costs-number-one-cause-of-bankruptcy-for-american-families

(2) Tolbert, J., Drake, P., & Damico, A. (2022, December 19). Key Facts about the Uninsured Population. KFF (Kaiser Family Foundation). https://www.kff.org/uninsured/issue-brief/key-facts-about-the-uninsured-population/

IMPRS: Indiana Medical Student Program for Research and Scholarship

The following works represent a selection of the student research that took place at the 2022 IMPRS summer internship program–a collaboration of Indiana University School of Medicine and The Indiana CTSI–including finalists who were selected to give oral presentations to a panel of judges.

IMPRS Award Winners

Design Improvement and Deployment Efficacy of Novel 3D-Printed Bioresorbable Vascular Scaffolds in Coronary Artery Atherosclerosis

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

Background: Endovascular stents are an effective treatment for coronary stenosis. However, the permanent presence of metal stents can hamper normal vasomotion, limit adaptive arterial remodeling, and provoke long-term foreign-body responses. Bioresorbable stents are designed to circumvent these issues. To maintain commensurate radial strength, polymeric bioresorbable stents require 2-4-fold thicker struts than metal stents, leading to increased risk of cardiovascular complications. To address this issue, a low-profile bioresorbable vascular scaffold (BVS) was produced by a citrate-based polymer and 3D printing technique. The patency of the BVS was compared to the metal Abbott Xience stent, employing swine with metabolic syndrome (MetS) as a clinically relevant translational model for coronary disease in humans.

Methods: Stents were deployed in coronary arteries of MetS swine. BVS vs metal selection and artery placement were randomized. Angiography was conducted pre- and post-stent deployment to determine target site, accuracy of stent placement, and degree of vasospasm. Intravascular ultrasound (IVUS) was performed to determine target vessel diameter and assess percent deployment. MetS was substantiated by obesity, dyslipidemia, and hypertension. IVUS quantified coronary atherosclerosis.

Results: MetS swine exhibited increased atherosclerotic coronary artery wall coverage (37 ± 9%, N=5) compared to lean swine (11 ± 2%, N=4). BVS required increased time of deployment (24.8 ± 2.4 min, N=9) compared to metal (11.8 ± 2.8 min, N=7). BVS demonstrated a deployment success rate of 88% (N=6) compared to metal 100% (N=8). BVS exhibited suboptimal expansion with an average percent of target diameter deployment at 74 ± 0.4% (N=8) compared to metal at 94 ± 0.4% (N=6). Coronary intervention with BVS generated increased frequency of electrocardiographic T-wave abnormalities compared to metal.

Conclusion: The metal stents outperform the BVS with shorter time of deployment and increased average percent of target deployment. Future analysis following long-term recovery will assess hypothesized benefits of BVS, including reduced inflammation and in-stent restenosis compared to metal.

[Support: NIH R01 HL141933 T35 HL110854]

Hazel and Tommy Thompson Cardiac Research Scholarship Award

Creating a Patient Registry for the Parkview Vein Clinic

Fliotsos K, GeRue M, Sowden D

Background/Objective: The Parkview Vein Clinic provides individualized care to patients suffering from venous disease by providing assessment, education, treatment, ultrasound imaging, and surgical interventions all under one roof. The Vein Clinic has experienced a consistent increase in patient volume since opening in 2019, creating a need for tracking patient outcomes. Patient registries are useful tools for tracking high volumes of patients, assessing outcomes, and improving treatment guidelines. The main objective of this quality improvement project is to define the workflow for creating a patient registry for the Vein Clinic and determine which data points are feasible to collect.

Methods: This is a retrospective chart review of patients with the diagnosis of "venous stasis ulcer" seen at the Vein Clinic from September 2019 to July 2022. A total of 84 data fields were collected on each patient, including information on demographics, medical history, ulcer descriptions, imaging, procedure information, and post-procedure follow-up. The Society for Venous Surgery Vascular Quality Initiative was used as a template for registry design, with the goal of merging the registry with the national database in the future.

Results: Venous ulcer information, including number of healed ulcers, duration of ulcer, and largest diameter active ulcer, was not readily accessible within the chart and required expanded review find and quantify. All other categories were readily accessible in the chart.

Conclusions: The data collected by the registry will be useful for future quality improvement purposes of the Vein Clinic. Creation of a structured reporting template in Epic would help facilitate the ease and accuracy of data extraction and help maintain the internal validity of the registry. More detailed follow-up assessments should be implemented to track patient outcomes, which could include use of the Venous Clinical Severity Score or a patient-reported outcomes assessment.

Hazel and Tommy Thompson Cardiac Research Scholarship Award

Katrina Fliotsos is a third-year medical student, who is currently undecided about her future specialty; however, she knows she wants to integrate research into her future medical practice.

"I really enjoyed learning more about venous disease and the incredible impact that non-invasive surgical techniques can have on a patient's quality of life. This was my first time participating in quality improvement research, and I was given a lot of freedom to choose which parameters to include in the registry. Through this experience, I learned about the vital role that quality improvement research has in driving medical innovation, enhancing patient outcomes, and improving the standard of care."

Methionine's Role in Hyperoxia-Induced Pulmonary Dysplasia

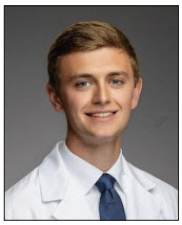
Nisen N, Ranasinghe D, Schwarz M

Background/Objective: Following preterm birth in the saccular stage of lung development, 24 weeks gestational age to term, infants are forced to navigate the further development of their lungs with the abnormal environmental influences of oxygen. This disruption of normal development of alveoli is the etiology of bronchopulmonary dysplasia (BPD), which is a chronic pulmonary disease of preterm infants. We hypothesize that this lung dysplasia is based upon the disruption of the role of one of the lung metabolites, Methionine, that is utilized during this period. Specifically, we postulate that Methionine's role in this dysplasia could be used as a rescue of normal lung development if undeterred.

Methods: Endothelial Colony Forming Cells (ECFCs) were utilized to measure angiogenesis in vitro in the presence of a variety of concentrations of Methionine. A WST-1 Assay, Crystal Violet Assay, and Scratch Assays were performed to quantify the amount of ECFC proliferation and migration in the presence/absence of Methionine. Western blotting analysis was performed to measure the expression of enzymes of the one carbon metabolism pathway. A murine model was utilized to contrast methionine's dietary role lung development in hyperoxia and normal oxygen conditions.

Results: We have seen that the presence of Methionine increases endothelial cell proliferation and migration. We found that the expression of the enzymes in the one carbon metabolism pathway are significantly impacted by the presence of Methionine. Histological studies have further shown Methionine's role as a rescue of hyperoxia induced alveolar dysplasia, identifying Methionine as a crucial metabolite in lung development.

Conclusion and Clinical Implications: Through these studies, we believe that new therapeutic targets are elicited that will guide and improve the ability to improve lung development of a premature infant.



Hazel and Tommy Thompson Cardiac Research Scholarship

Noah Nisen is a third-year medical student, who is currently undecided about his future specialty. Outside of school, he is married and has a 6-month-old daughter.

"The most important takeaway from my summer of research was gaining an appreciation of the translation of the molecular discoveries in the lab and how they are able to impact patient care down the line. I think this was related to me in a unique way in that my research mentor, Dr. Schwarz, is a physician scientist that brought a clinical perspective to what was being done at the lab level. It was enjoyable to be able to learn from her about the role metabolism plays in lung development and how alterations in that could be therapeutic to pathologic processes such as bronchopulmonary dysplasia."

The Effect of Large Femoral Heads and Acetabular Cup Position on PROMs after Modern Posterior Approach THA

Darden A, Deckard ER, R. Michael Meneghini RM

Introduction: Use of large femoral heads (≥40mm) in total hip arthroplasty (THA) decreases postoperative dislocation by increasing impingement-free range of motion, however, may leave patients more susceptible to groin pain. Also, limited data exist for the effect of large femoral heads and acetabular cup position on modern patient-reported outcome measures (PROMs). Therefore, the purpose of this study was to evaluate the effect of large femoral heads (≥40mm) and acetabular cup position on PROMs after primary THA.

Methods: 328 primary THAs performed by a single surgeon were retrospectively reviewed. Acetabular cup inclination and anteversion were measured using Martell Hip Analysis Suite software. Femoral head and acetabular cup sizes were recorded from the electronic medical record. Prospectively collected PROMs (and covariates) related to activity level, satisfaction, and overall hip health were evaluated.

Results: Age, covariates related to PROMs, and acetabular cup position did not differ between ≥40mm and <40mm femoral head groups ($p \geq 0.177$). The ≥40mm head group had significantly higher mean BMI and proportion of males ($p \leq 0.022$). UCLA Activity level and satisfaction scores did not differ preoperatively or postoperatively at 4-months or minimum 1-year follow-up between femoral head groups ($p \geq 0.209$). Preoperative HOOS JR scores did not differ by femoral head groups ($p = 0.538$). At 4-months, mean HOOS JR score was significantly higher in the ≥40mm head group compared to the <40mm head group ($p = 0.027$); however, both groups achieved similar mean HOOS JR scores by minimum 1-year follow-up ($p = 0.956$). HOOS JR score >90 and being 'very satisfied or satisfied' correlated with wide ranges and several combinations of acetabular cup inclination and anteversion.

Conclusion: Patients achieved comparable PROMs regardless of femoral head size suggesting large femoral heads may not leave patients susceptible to groin pain in addition to reducing the risk of postoperative dislocation. Excellent patient outcomes correlated with wide ranges of acetabular cup position.

General Excellence Award

Austin Darden is a third-year medical student, who is currently interested in orthopedic surgery. He appreciates that the field offers quick gratification and loves the thought of being able to use his hands to help people gain functionality back.

"The most important takeaway from my research this summer is that no matter how perfect a technology or procedure may seem, there is always room for improvement. I really enjoyed diving deep into my research topic and learning about all the advancements taking place and avenues for future work."

The Relationship Between Loneliness and Quality of Life in Older Adults

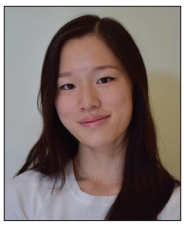
Li C, Perkins A, Nicole Fowler N

Background: Loneliness is the self-perceived discrepancy in an individual's desired and actual social relationships. Loneliness is common among older adults and is associated with chronic illness and poorer mental health outcomes. Our objective was to determine the relationship between loneliness and quality of life (QOL) in older adult patients, controlling for depression and anxiety.

Methods: Secondary data analysis was conducted on baseline data from the Caregiver Outcomes of Alzheimer's Disease Screening (COADS) Trial, an ongoing trial evaluating benefits and risks of Alzheimer's disease and related dementias (ADRD) screening. Patients were ≥65 years old with no history of ADRD. Measures include the 5-item NIH Toolbox Loneliness measure, QOL, measured by the physical (PCS) and mental health component (MCS) scores of SF-36, and depression and anxiety, measured by PHQ-9 and GAD-7, respectively. We conducted a Spearman correlation and ran unadjusted and adjusted linear regression models to assess the relationship between loneliness and QOL.

Results: Patient mean (SD) age was 73.7 (5.1) years; 44.8% male; 91.5% white; 7.5% black. We found that loneliness was moderately correlated with QOL measured by SF-36 MCS ($r = -0.43$, $p<0.001$), anxiety ($r = 0.44$, $p<0.001$), and depression ($r = 0.42$, $p<0.001$), while weakly correlated with QOL measured by SF-36 PCS ($r = -0.15$, $p<0.001$). Loneliness was associated with lower MCS ($p<0.001$) and PCS ($p<0.001$). After adjusting for depression and anxiety, only MCS ($p<0.001$) was reduced by loneliness. Additionally, we found a positive association between PCS and patient report of comfortable level of income, before ($p=0.002$) and after ($p= 0.002$) adjustment.

Conclusion: We found that loneliness was significantly associated with worse quality of life as measured by mental health constructs among older adult primary care patients. Therefore, we recommend primary care providers assess loneliness with their older adult patients and if present, consider interventions aimed at reducing loneliness such as activities that maintain meaningful social relationships.



General Excellence Award

Claudia Li (she/her) is a third-year medical student, who is currently interested in neurology and psychiatry.

"My past research experiences were rooted in basic science, so I was excited about this opportunity to learn something new and explore what goes into health outcomes research. Being involved in this project gave me valuable insight into the topic of mental health in older adults and some of the unique challenges that impact this population. I have thoroughly enjoyed working with such a welcoming team and appreciate their guidance and mentorship."

Relationships Between Health Behaviors, Social Determinants of Health, and Patient Demographics in an Urban Northwest Indiana Hospital

Nosbusch S, Love E, Ryan E, Guerrero J, Muvuka B

Background: Social determinants of health (SDOH) contribute to over 50% of health outcomes and inequities. Healthcare institutions are increasingly implementing SDOH screenings and referrals. St. Mary Medical Center (SMMC) in Northwest Indiana was the first acute care hospital to implement a comprehensive SDOH pilot screening and referral program in Indiana using the validated Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE). This study is part of a three-phased Community-Based Participatory Research (CBPR) partnership between IUSM-NW and SMMC to examine and address SDOH within SMMC's service area from January 2022-January 2025. This study's research question is: What are the relationships between SDOH, behavioral, and demographic factors in SMMC's inpatients?

Methods: This descriptive study analyzed a limited dataset generated by SMMC from EPIC™ with SDOH, demographic, behavioral (tobacco use, alcohol use, physical activity), and health outcomes data for adult inpatient visits from January 2021 to June 2022. Data analysis was conducted in SPSS 28.0 using descriptive statistics (i.e., frequencies and central tendency) and tests of association including Chi-square, Fisher's Exact, Wilcoxon-Mann Whitney, and Kruskal Wallis H ($p<0.05$). This study was exempted by Indiana University Human Research Protection Program (IRB # 14040).

Results: This study included 4370 inpatients, who were predominantly White (75.7%), older adults (65 ± 24), and publicly insured (76.3%). There were significant relationships between SDOH and tobacco use, alcohol use, and physical activity. Tobacco use was significantly associated with the majority of SDOH including insurance type ($p<.001$), housing risk ($p<.001$), financial resource risk ($p<.001$), unmet transportation needs ($p<.001$), and overall social risk ($p=.012$).

Conclusions: Understanding how SDOH influence health behaviors will inform efforts to develop, implement, and evaluate multi-level interventions. The next phases of this CBPR will use advanced statistical techniques to further explore these relationships, evaluate SMMC's pilot program, and co-develop SDOH interventions.

General Excellence Award

Sydnye Nosbusch (she/her/hers) is a third-year medical student, who is currently interested in OBGYN and women's health.

"Being able to participate in research addressing social determinants of health, particularly in Northwest Indiana where I grew up, was the most rewarding part about this summer. I've enjoyed learning more about the patients that IU serves and the multifaceted aspects of health and well-being."

Therapeutic Effects of Benzoylacetonitrile on Microglia Activation in Multiple Sclerosis

Zhao A, Kuo P, Scofield BA, Yen JJ

Background: Multiple Sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). Pathogenic T cells, such as Th1 and Th17, infiltrate the CNS, resulting in neuroinflammation, demyelination and axonal damage. Th1 activates microglia (MG) in the CNS and Th17 acts as a chemokine to recruit immune cells into the CNS. MG is a resident immune cell in the CNS and its activation is associated with destruction of myelin and secretion of inflammatory cytokines such as IL-12, IL-23 and IL-1β. IL-12 and IL-23 are important for Th1 and Th17 differentiation and reactivation, respectively. IL-1β is a key mediator of the inflammatory response. Benzoylacetonitrile (BTN) has been shown to reduce disease severity in mouse model of MS and reduce Th1 and Th17 differentiation in vitro. However, the effects of BTN on MG are unknown, and this study was aimed to investigate the effects of BTN on MG activation in vitro. We hypothesize that BTN can suppress MG activation and decrease the production of inflammatory cytokines.

Methods: Primary MG were pretreated with BTN at concentration of 200μM or 300μM for 2 hours or with DMSO (vehicle), followed by lipopolysaccharide (LPS) 100ng/ml stimulation for 1.5 or 3 hours. RNA was isolated from MG and mRNA expression levels of IL-12, IL-23, IL-1β were measured using Q-PCR.

Results: Our results showed that BTN suppressed MG activation and reduced inflammatory cytokine production. The mRNA expression levels of IL-12, IL-23, and IL-1β in LPS and BTN-treated MG were significantly lower than LPS-treated MG.

Conclusion: This study demonstrated that BTN was able to suppress MG expression of inflammatory cytokines in vitro, suggesting that BTN exhibits immunomodulatory effects on MG activation in vitro. BTN has a potential to attenuate neuroinflammation in MS through the reduction of inflammatory cytokines.

General Excellence Award

Angela Zhao is a third-year medical student, who is currently interested in neurology and family medicine.

"Research has been a valuable experience during which I was able to gain more knowledge about the immune system and how modulation of the inflammatory response can affect disease progression. This experience emphasized the integral role research plays in advancing medicine and patient care. I am looking forward to continuing research during medical school and incorporating research in my future medical career."

EPHA2 is a Potential Target for the Treatment of NF2-/- Vestibular Schwannoma

Foster K, Mitchell DK, Flint A, Rodriguez B, Mang H, Davis C, Angus SP, Clapp DW, Yates C

Neurofibromatosis type 2 (NF2) is an autosomal dominant cancer predisposition syndrome characterized by the development of bilateral vestibular (VS) and spinal schwannomas secondary to loss of heterozygosity of NF2 in Schwann cells or their precursors. While these tumors are largely benign, they can cause considerable morbidity due to compromised auditory, vestibular, facial, and vertebral nerve function. This may result in deafness, vertigo, facial muscle weakness, chronic neuropathic pain, and even death. There are currently no pharmacotherapies for VS, and surgical resection remains the standard of care, which is associated with significant morbidity. Thus, there is an urgent need to develop pharmaceutical approaches to halt or reverse the progression of tumor growth in NF2 patients who develop VS. Our lab previously identified the receptor tyrosine kinase inhibitors brigatinib and dasatinib as potentially efficacious agents for the treatment of VS and demonstrated that both agents targeted the Ephrin A2 receptor (EPHA2). EPHA2 is a transmembrane receptor tyrosine kinase that is involved in cell contact-mediated motility, adhesion, and migration. Additionally, EPHA2 modulates axon guidance, and synaptogenesis in developing brain. Here we demonstrate that EPHA2 expression is increased in NF2-/- Schwann cells and NF2-/- cancers. We identify ponatinib, a receptor tyrosine kinase inhibitor targeting ABL1 that is FDA-approved for CML, as an additional agent that targets EPHA2. We demonstrate that ponatinib treatment impairs the viability of both human and murine NF2-/- Schwann cells in vitro and decreases EPHA2 protein expression. Accordingly, pharmacologic, and siRNA-mediated inhibition of EPHA2 also impaired the growth of human NF2-/- Schwann cells in vitro. Lastly, we demonstrate that both ponatinib and EPHA2 inhibition induce morphological changes in NF2-/- Schwann cells. Our findings suggest that ponatinib or the direct targeting of EPHA2 may be efficacious for the treatment of NF2-associated vestibular schwannoma. Future in vivo efficacy studies are warranted.

Marvella Bayh Memorial Scholarship

Kéyana A. Foster is a third-year medical student, who is currently interested in otolaryngology. She attributes her interest to her love for head/neck anatomy and oncology.

"I want to be a physician who can treat a patient in all aspects of their care. To me, that means translating groundbreaking research from the lab to the clinic/OR space. That was my most important takeaway from my summer research experience. We were doing the work to find new methods of treating a patient's vestibular schwannomas by targeting cancer cells with currently FDA approved chemotherapies. In addition to that, the numerous skills I gained as a researcher is something I will take with me throughout my entire career. I am tremendously grateful for the opportunity to learn from my mentors during this project".

Clinical Features Distinguishing Diabetic Retinopathy Severity Using Artificial Intelligence

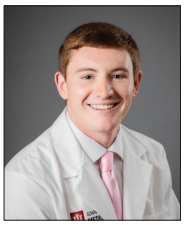
Happe M, Gill H, Salem DH, Janga SC, Hajrasouliha A

Background and Hypothesis: 1 in 29 American diabetics suffer from diabetic retinopathy (DR), the weakening of blood vessels in the retina. DR goes undetected in nearly 50% of diabetics, allowing DR to steal the vision of many Americans. We hypothesize that increasing the rate and ease of diagnosing DR by introducing artificial intelligence-based methods in primary medical clinics will increase the long-term preservation of ocular health in diabetic patients.

Project Methods: This retrospective cohort study was conducted under approval from the Institutional Review Board of Indiana University School of Medicine. Images were deidentified and no consent was taken due to the nature of this retrospective study. We categorized 676 patient files based upon HbA1c, severity of non-proliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR). Retinal images were annotated to highlight common features of DR: microaneurysms, hemorrhages, cotton wool spots, exudates, and neovascularization. The VGG Image Annotator application used for annotations allowed us to save structure coordinates into a separate database for future training of the artificial intelligence system.

Results: 228 (33.7%) of patients were diagnosed with diabetes, and 143 (62.7%) of those were diagnosed with DR. Two-sample t tests found significant differences between the HbA1c values of all diabetics compared to diabetics without retinopathy ($p<0.007$) and between all severities of DR versus diabetics without retinopathy ($p<0.002$). 283 eyes were diagnosed with a form of DR in this study: 37 mild NPDR, 42 moderate NPDR, 56 severe NPDR, and 148 PDR eyes.

Potential Impact: With the dataset of coordinates and HbA1c values from this experiment, we aim to train an artificial intelligence system to diagnose DR through retinal imaging. The goal of this system is to be conveniently used in primary medical clinics to increase the detection rate of DR to preserve the ocular health of millions of future Americans.



NIH NEI-T35 Award

Michael Happe is a third-year medical student, who is currently interested in ophthalmology due to its blend of surgery, patient care, and immediate impact on the lives of patients.

"The most important takeaway from my research has been that there are always improvements to be made. As an Ophthalmologist, it will be my job to provide the best possible care to patients, and I believe that my research is a perfect example of enhancing diagnostic tests in order to ultimately improve the health outcomes of patients. I have enjoyed working alongside experts in the field and learning more about ophthalmology through my research. I look forward to more opportunities of continued learning in the future."

Protease-Activated-Receptors 1 and 2 are Essential in the Initiation of Food Allergy Early in Life

Miller J, Martin A, Cook-Mills J

Background and Hypothesis: Because food allergies can be life-threatening, it is imperative to investigate the underlying pathways of food allergy initiation to progress towards treatment and prevention. Food allergies occur at an increased rate in children with altered skin barriers. Previous RNAseq studies have identified increased ApoE gene expression in mouse pups with skin barrier mutations sensitized with house dust mite and peanut allergens. Furthermore, PAR2 has been shown to be involved in the synthesis pathway of ApoE when activated by household allergens. We hypothesize that PAR2 is necessary for the initiation of food allergy in mice with skin barrier mutations.

Project Methods: Pups heterozygous for skin barrier mutations in FLG and Tmem79 were sensitized with Alternaria alternata (Alt) and peanut extract (PNE) on postnatal days 3, 6, 9, 13, and 15. Pups received injections of PAR1 or PAR2 antagonist, no antagonist, or saline before each sensitization. At day 17, the pups received a PNE oral gavage. Rectal temperatures were incrementally measured for 80 minutes after the gavage to monitor anaphylaxis. Tissues were collected 8 hours after the gavage. Skin punches and intestine are currently being processed and analyzed by qPCR for IL33, OSM, and Areg.

Results: Statistical analysis was completed using area under the curve by summation of average temperature changes for each pup. Pups that received PAR1 or PAR2 antagonists and application of Alt and PNE did not exhibit significant temperature drops whereas pups that received no inhibitor and Alt and PNE did undergo anaphylaxis, indicating blocking PAR1 and PAR2 blocked anaphylaxis. There were no statistically significant differences between male and female pup responses.

Conclusion: The results of this study indicate that PAR2 and PAR1 are essential for development of food allergy and are potential cellular targets for treatment and prevention of food allergy early in life.

NIH NHLBI-T35 Award

Jessica Miller is a third-year medical student, who is currently interested in internal medicine.

"Completing research in an animal model for the first time gave me a deep appreciation for the time, effort, and sacrifice that goes into the biomedical discoveries that shape medicine. Although I will not be continuing research involving animals in the future, I am grateful for the animals and the researchers who work with animals to discover the pathology, physiology, and pharmacology that leads to improved healthcare. Additionally, I will always be grateful for Dr. Cook-Mills and her lab for teaching me the basic ropes of allergy/immunology research as well as the importance of team collaboration within a research laboratory."

Evaluating the Effects of Targeted Drug Therapies for 8q24.3 Amplified Breast Cancer

Phipps S, Khatpe A, Nakshatri H

Background/Objective: Cancer studies have helped us understand recurrent chromosome abnormalities leading to tumor progression. One such recurrent genomic aberration found in breast cancer is chromosome 8q24.3 (Chr. 8q24.3) amplification. We identified Tonsoku Like, DNA Repair Protein (TONSL) located within this amplicon as an immortalizing oncogene, with TONSL-overexpressing cells exhibiting distinctively upregulated homologous recombination (HR). Further experiments have shown that cancer cells with TONSL amplification are sensitive to the FACT inhibitor CBL0137, which is in early phase of clinical development. Based on known functions of TONSL in promoting dsDNA repair, we hypothesized that drug combinations targeting multiple pathways of DNA repair would synergize to kill chromosome 8q24.3 amplified breast cancer cell lines.

Methods: Chr.8q24.3-amplified breast adenocarcinoma cell line TMD436 was utilized in this study. Cells were treated with various drugs targeting DNA repair pathways such as ATR inhibitor (VE-822), PARP inhibitor (Talazoparib), and PI3K inhibitor (BYL719). Cell proliferation rates were measured using bromodeoxyuridine incorporation ELISA.

Results: Thus far, the use of PI3Ki and PARPi combination has had an additive effect - the combined effect of the two drugs is equal to the sum of the effect of each agent given alone. The effect of ATRi and PARPi combination was antagonistic.

Conclusion/Potential Impact: This study establishes the potential feasibility of using DNA repair signaling inhibitors in the treatment of TONSL-overexpressing breast cancer. Future studies extending the range of drug concentrations and newer combinations may ultimately lead to translation of these drugs to in vivo models and clinical trials. By targeting multiple DNA repair pathways, similar approaches may sensitize patients to lower doses of chemotherapeutics, thus decreasing unwanted side effects. Moreover, negative data concerning the ATRi/PARPi combination helps to further refine which drugs may be used to treat Chr. 8q24.3 amplified tumors and to understand signaling pathways active in TONSL-overexpressing breast cancer.

NIH NHLBI-T35 Award

Savannah Phipps (she/her) is a third-year medical student, who is currently undecided about her future specialty, though she is drawn towards the idea of caring for patients of all ages and backgrounds.

"Connecting with my patients on a personal level and being their partner and advocate in healthcare is one of the most important parts of medicine for me, no matter what specialty I decide to pursue. My biggest takeaway from this research experience has been a newfound appreciation for the detail and rigor that goes into basic science research. Without the dedicated individuals who devote their lives to scientific research, we would not be able to provide our patients with the quality of care they deserve."

A Cancer Cell's Toolbox for Conquering Other Organs: Discovering and Combating the Secretome of a Metastasis Capable Cancer Cell

Spivak S, Adebayo A, Batic K, Nakshatri H

Background and Hypothesis: Previous studies have recognized that abnormal signaling by RAS oncogenes is predominantly observed in metastatic breast cancer. A hypothesis was developed: the cancer cells with abnormal RAS genes release protein factors into the blood stream which can reorganize the signaling of non-breast tissue in a way that mimics breast tissue therefore making this organ prone to metastasis. These RAS-dependent factors can be targeted therapeutically to decrease metastasis.

Experimental Design: Three cell lines were plated for the experiment: KTB-hTERT immortalized cell line as the control line, KTB-hTERT transformed derivatives TKTB RAS + SV40, which forms metastatic adenocarcinomas in NSG mice, and TKTB PIK3CA + SV40, which forms non-metastatic adenocarcinoma in NSG mice. Three Western Blots were conducted with protein readings for phospho-PAK4, PAK4, phospho-PIK3CD, and PIK3CD. These experiments were done to begin to test the hypothesis that phospho-proteome unique to RAS transformed cells regulate secretome with an effect on distant organs. These cell lines were examined for sensitivity to PIK3CD inhibitor Idelalisib and MEK1/MEK2 inhibitor Trametinib, which mediates signals downstream of RAS that regulate PIK3CD, using BrdU-incorporation ELISA proliferation assay.

Results: Through the western blot analysis, it was consistently shown that there is a significant increase in the production of phospho-PIK3CD and PIK3CD in RAS over PIK3CA which shows that PIK3CD could be a protein that leads to metastasis of RAS transformed cells. Idelalisib did not display activity in any cell lines. Trametinib showed decreased growth of all cell lines and RAS transformed cells were less sensitive to the drugs suggesting hyperactivation of this pathway in RAS-transformed cells

.

Conclusion and Impact: This study brings breast cancer research closer to pinpointing which proteins, in this case PIK3CD, can be targeted to decrease metastasis. The development of a drug that is specific to PIK3CD should be pursued to discover a treatment that decreases breast cancer metastasis.

NIH NHLBI-T35 Award

Sarah Spivak is a third-year medical student, who is currently interested in neurosurgery. She wants to advocate for patients experiencing difficult diagnoses, and is intrigued by how much has yet to be discovered about the human brain.

"Research is a lot of trial and error, but when you get that one promising result after so many fails it feels like you are on top of the world. I love knowing that the work we are doing could lead to a future treatment that could impact so many people. It is extremely rewarding."

Histologic Diversity of Thymic Epithelial Tumors in Patients with Myasthenia Gravis

Heldman EM, Davis HO, Laniak LJ, Wuthrich BS, Loehrer PJ, Kesler KA

Background and Objective: Thymic epithelial tumors (TETs) include thymic carcinomas and thymomas, the latter of which can be further categorized by the World Health Organization (WHO) histologic classification based on the morphology of epithelial cells and the ratio of lymphocyte to epithelial cells (WHO types A, AB, B1, B2, and B3). TETs are rare malignancies with an incidence of 0.15 per 100,000 person-years in the United States. While their etiologies remain unknown, these tumors are associated with distinctly high rates of autoimmune disorders and paraneoplastic syndromes. The most common comorbid autoimmune disorder is myasthenia gravis (MG), affecting approximately 30% of patients with thymoma; thus, evaluating the risk of MG in patients with TETs of various histologies is important clinically. For the present retrospective study, we created a database of patients with TETs and examined prevalence of each histologic subtype in patients with MG.

Methods: Drs. Patrick Loehrer, Kenneth Kesler, and colleagues have collaborated at the Indiana University Simon Cancer Center to care for over 1000 patients with TETs. The electronic health records of these patients were accessed via Cerner and used to input demographic, diagnostic, and histologic data into a REDCap database. The TETs were further categorized by WHO classification, and heterogenous tumors were categorized by their most aggressive histologic type (i.e. mixed type B2 and B3 categorized as B3).

Results: Of 1023 total patients in the REDCap database, 626 were found to have sufficient documented information regarding TET diagnosis and histology as well as the presence or absence of MG (thymoma – 468; thymic carcinoma – 158). 112 of these patients carried diagnoses of both MG and a TET confirmed by pathology report (thymoma – 110; thymic carcinoma – 2). 77 (68.75%) patients were diagnosed with MG prior to TET, while 30 (26.79%) were diagnosed with MG after TET ($p < 0.0001$). The greatest prevalence of WHO histologic type in patients with thymoma and MG was Type B3 (36, 32.14%), followed by Type B2 (33, 29.46%), Type B1 (19, 16.96%), Type A (7, 6.25%), and Type AB (7, 6.25%) ($X2 = 37.41$, $p < 0.0001$). Notably, only 2 of 158 (1.27%) total patients with TC had comorbid MG in contrast to 110 of 468 (23.50%) with thymoma and MG; this suggests a uniquely favorable microenvironment of thymoma in patients with MG.

Clinical Impact and Implications: A distinct link exists between myasthenia gravis and thymoma, particularly those of more aggressive WHO histologic types (Type B3 and Type B2). Future work will aim to determine whether histologic classification has a predictive value for tumor prognosis in patients with and without MG. Furthermore, patterns of gene expression associated with thymoma in patients with and without MG may elucidate the etiologic mechanisms for the development of this autoimmune disorder.

William H. and Fern L. Hardiman Scholarship

Targeted Inhibition of the HGF/c-Met Pathway by Merestinib Augments the Effects of Albumin-Bound Paclitaxel in Gastric Cancer

Kaurich Q, Huang J, Awasthi N

Introduction: Combination chemotherapy regimens are commonly used to treat gastric adenocarcinoma (GAC), but the median survival time remains less than one year. Nab-paclitaxel has demonstrated high antitumor activity in previous GAC studies. Many growth factors and their receptors are overexpressed in GAC and have been implicated in its pathophysiology. We hypothesize that merestinib, a small-molecule inhibitor targeting c-Met, Axl, and DDR1/2 pathways, will have significant antitumor effects and will enhance the response to nab-paclitaxel in GAC preclinical models.

Methods: In vitro proliferation and protein expression were assessed using WST-1 and immunoblot assays. Subcutaneous xenografts of MKN-45 and SNU-1 cell lines were implanted in mice to study tumor growth inhibition. Immunohistochemistry was performed to examine intratumor proliferation and microvessel density.

Results: In vitro assays showed that nab-paclitaxel and merestinib decreased cell proliferation in all three cell lines, with an additive effect in combination. Reduction in cell proliferation at low doses of nab-paclitaxel (10 nM), merestinib (100 nM), and their combination was 87%, 82%, and 94% (MKN-45 cell line, high phospho-c-Met expression), 59%, 50%, and 82% (SNU-1 cell line, low phospho-c-Met expression), and 53%, 19%, and 66% in gastric fibroblasts. Immunoblot analysis of merestinib treated MKN-45 cells revealed increased expression of apoptotic proteins and decreased expression of phospho-c-Met, phospho-EGFR, phospho-IGF-1R, phospho-ERK, and phospho-AKT. In gastric fibroblasts, merestinib decreased phospho-ERK and increased apoptotic protein expression. Phospho-c-Met and phospho-EGFR were not detected in SNU-1 immunoblots; however, phospho-ERK, phospho-VEGFR, and apoptotic protein expression increased after treatment. In MKN-45 xenografts, net tumor growth in control, nab-paclitaxel, merestinib, and combination groups was 503 mm3, 115 mm3, 91 mm3, and -9.7 mm3. Immunohistochemistry analysis of tumor cell proliferation and microvessel density corroborated tumor growth study results.

Conclusion: The data suggest that merestinib in combination with nab-paclitaxel carry a promising potential for improving clinical GAC therapy.

William H. and Fern L. Hardiman Scholarship

Quinn Kaurich is a third-year medical student, who is currently interested in internal medicine.

"My most important takeaway from my research is the realization that preclinical research plays a critical role in the biomedical research process. Although it is not always easy to see its connection to benefiting real patients, it is a necessary step in the process. Preclinical research is also exciting because it gives us the opportunity to try out new things without the fear of causing any harm. I am extremely grateful for the opportunity to contribute to the field of targeted cancer therapy, and I am hopeful that this work may one day help people with gastric cancer."

Characterization of a Conserved Cysteine Residue in the Papillomavirus E2 Protein

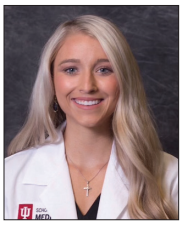
Stoll K, Gonzalez J, Androphy E

Background: Human papillomaviruses (HPVs) are DNA tumor viruses that infect cutaneous and mucosal epithelium. While most infections are self-limiting, a small subset that infects the mucosal epithelium progresses to cancer. All papillomaviruses encode the protein E2 which regulates viral transcription and replication; a highly conserved cysteine residue in the DNA contact helix of E2 plays an unknown role. Previous research suggests the residue is not necessary for replication or binding to DNA. We hypothesize that post-translational modification of this conserved cysteine residue leads to release of viral DNA during packaging of progeny virions.

Methods: Mutations of the murine papillomavirus conserved E2 C307 residue to serine and phenylalanine were used to investigate its role in E2 function. C33A, HPV negative cervical cancer cells, were transfected with an E2-responsive luciferase reporter and either wild type or mutant C307 E2 vectors; luciferase assays were performed 48 hours post-transfection to assess transcriptional activity. Whole cell lysates from overexpressed C307 mutants were separated by SDS-PAGE and immunoblotted to assess expression levels relative to wild type. To examine protein localization, C33A cells were transfected with equal amounts of wild type or mutant E2 and fixed 48 hours post-transfection for immunofluorescence.

Results: C307S and C307F mutants are both capable of weakly activating transcription. Overexpression of the mutants resulted in a dose dependent increase in transcriptional activity. Both mutants are expressed at levels comparable to wild type E2 and are correctly localized to the nucleus.

Conclusion/Impact: The deficient transcription function displayed by the C307 mutants cannot be explained by poor expression or mislocalization. Continued study of this conserved cysteine will help to further understanding of papillomavirus biology and may offer insight into novel avenues for treatment or prevention of HPV-associated cancers.



NIH NHLBI-T35 Award

Kennedy Stoll is a third-year medical student, who is currently interested in dermatology. She is drawn towards the idea of improving a patient's physical health and mental well-being.

"I find the medicine behind dermatology fascinating and enjoy the connections made while working to better a patients' condition. My summer research highlighted the role and necessity of physician scientists in advancing preventative medicine, specifically within the realm of HPV."

Correlation of Outcomes Following Mechanical Thrombectomy in Covid-19 Patients with Ischemic Stroke

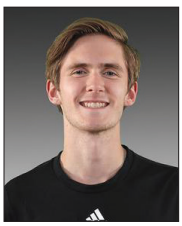
Masterson R, Troja W, Bohnstedt B, Kovoor J

Background/Objective: SARS-CoV-2 is a respiratory virus most well-known for causing acute respiratory failure. COVID-19 can cause a variety of conditions with poor prognoses, such as cerebrovascular accidents (CVA). COVID-19 is believed to cause a prothrombic state and can cause large vessel occlusions (LVO) and acute ischemia in brain parenchyma. As such, our goal is to compare the outcome of stroke patients, who were either COVID positive or negative, who underwent mechanical thrombectomy (MT), which serves as the gold-standard for treatment of an LVO.

Methods: Modified Rankin Scores (mRS) at 90 days post-MT were collected from 281 patients (17 COVID+ and 264 COVID-) who underwent MT due to LVO in the IU Health network. Pertinent risk factors, LVO sites, and suspected etiology of strokes were collected from 223 (17 COVID+ and 206 COVID-) of these patients' EMRs as secondary objectives. mRS values were analyzed via two-tailed t-test, and the averages of secondary objective occurrences were compared between groups.

Results: A two-tailed t-test revealed $t(279) = 1.969$; $p = 0.236$, indicating no statistical significance between the two groups. Stroke risk factor occurrence was relatively similar between groups, with cardiovascular factors (HTN, HLD, etc.) being most common. COVID- patients showed increased rates of a-fib and prior CVAs. COVID+ patients showed a higher degree of M3 LVOs. Etiology of strokes remained largely embolic between both groups, with sub-types being mostly atherothrombotic and cardioembolic in COVID+ and COVID-, respectively.

Conclusion and Potential Impact: By comparing outcomes and various aspects of stroke patients, several conclusions can be made. Mechanical thrombectomy is shown to be equally effective in producing similar long-term outcomes in stroke patients due to LVO, regardless of COVID status. Furthermore, smaller, more distal vessel occlusions (M3 vs. M1) are increasingly seen in COVID+ stroke patients. A caveat of our study is the low COVID+ sample size from whom we could obtain an mRS value from, and this may warrant investigations into the variance in emboli sub-type and thrombi penetrance in more distal arteries.



The Phillip A. Hoskins Foundation

Reid Masterson is a third-year medical student, who is currently interested in diagnostic/interventional radiology because of the special role that imaging can play in the diagnosis and treatment of various conditions.

"Being able to perform a minimally invasive, image-guided procedure to treat a patient not only improves the care of the patient, but also represents the rapid advancements in medicine. The experience of this research project has been incredibly valuable to not only show how effective IR procedures are in treating stroke patients, but also has allowed me to further my understanding of how a research project goes from an idea to fully fleshed-out data. It has allowed me to work with other medical students, residents, and attendings in multiple specialties, proving that it really does 'take a village' to continue pushing medical knowledge forward."

Tmprss3 deficiency does not affect auditory neuron differentiation: Implications for cochlear implantation

Moawad J, Chen J, Cabrera E, Nelson R

Background and Hypothesis: TMPRSS3 variants are one of the most common genetic causes of hearing loss in children and adults undergoing cochlear implantation (CI). Controversy exists regarding the success of CI in patients with TMPRSS3-mediated hearing loss as a prior immunolabeling study localized TMPRSS3 to the spiral ganglion (SGN) neurons. Type I SGNs transmit sound information to the CNS, while Type II SGNs are thought to play a role in amplification. Sensory hair cells (HC) that synapse on the SGN appear normal at birth but rapidly degenerate at the onset of hearing (postnatal day 12) in Tmprss3-mutant mice implicating an extrinsic process in HC death. During development, the precise pattern of SGN subtypes requires spontaneous firing of HCs prior to the onset of hearing. We hypothesize that Tmprss3 does not impact HC mechanotransduction or SGN subtype patterning.

Project Methods: Cryosections of control and Tmprss3 mutant (Tmprss3Y260X/Y260X) mice at P11 and P21 were immunolabeled with antibodies specific for SGN subtypes and all neurons. Cell counts were analyzed including two-tailed unpaired t test with significance of $p < 0.05$ ($n=3$ for each condition). Whole mount cochlea from P7 mice were used to test HC mechanotransduction using FM1-43 uptake assay. Tmprss3 gene expression was determined using hybridization chain reaction.

Results: There was no difference in subtype patterning at P11 or P21 except Tmprss3 mice had less Type II SGNs at P21. Tmprss3 is not expressed in Type I SGNs and has limited expression in Type II SGNs. FM1-43 uptake was unaffected in Tmprss3-mutant mice.

Conclusion/Potential Impact: SGN patterning is normal in Tmprss3-mutant mice suggesting that TMPRSS3 plays no physiologic role in the spontaneous firing or mechanotransduction of HCs. The limited expression of Tmprss3 within SGNs and normal SGN patterning supports CI as an effective treatment option for patients with TMPRSS3-mediated hearing loss.

Claude Smith Black, MD, Award for Outstanding Work in Research

Jasmine Verena Moawad is a third-year medical student, who is currently interested in otolaryngology.

"My most important takeaway from summer research was the ability to gain exposure to my field of interest. I grew up seeing cochlear implantation from the patient perspective, so I really enjoyed the opportunity to learn more about inner ear physiology and cochlear implantation from the laboratory side."

A Mixed Methods Analysis of Patient Utilization and Trust of Emergency Medical Services (EMS)

LaShell AK, Musey P, Alexander A, Glober N

Background: Little is known regarding patients' decisions to come to the emergency department (ED) via emergency medical services (EMS) versus privately owned vehicle (POV) and no studies have investigated patients' trust of the EMS system as it varies by race.

Methods: Patients who came to one urban, academic ED were given a mixed methods survey at bedside. Qualitative data identified patient reasoning for utilization of EMS versus POV. Quantitative data included patient demographics, medical and social history, and two validated scales to assess trust and perceived empathy of EMS providers (the Group-Based Medical Mistrust Scale and the Jefferson Scale of Patient Perception of Physician Empathy). Descriptive statistics showed characteristics of patients who came in via EMS versus POV and an unpaired t-test described the difference in EMS trust as it varied by race.

Results: Qualitative: Patients who came via EMS reported lack of access to a POV, inability to drive, and the inability to move secondary to the chief presenting medical complaint. Patients who came in via POV based their selection on speed, high cost of EMS transport, the ability to drive themselves safely, or lack of perceived emergency.

Quantitative: 9/23 (39.1%) patients utilized EMS transport and 14/23 (60.9%) utilized POV. 56.5% of patients were Black and 39.1% were White. Of those who came in by EMS, only 5/9 (55.5%) felt they had an immediate threat to life, organ or body function. The Group-Based Medical Mistrust Scale indicated that Black patients had less trust in the EMS system than White patients ($p=0.04$), while the Jefferson Scale of Patient Perception of Physician Empathy demonstrated no significant difference ($p=0.60$).

Conclusion and Potential Impact: Hopefully, this data will inform policy makers attempting to make the emergency care system accessible to all patients and provide appropriate non-emergent options for optimal medical care.

General Excellence Award

Alex LaShell is a third-year medical student, who is currently interested in emergency medicine and intensive care. She enjoys the acuity of care and breadth of patients offered in these settings.

"My most important takeaway from this research has been learning more about qualitative studies, especially in the area of health equity. I like to understand the thought processes people have and this type of study is a really interesting way to understand the 'bigger picture' of patient perspective and how it impacts their care."

Immunoreactive Trypsinogen Levels in Infants Born to Women with Cystic Fibrosis Taking Elexacaftor-Tezacaftor-Ivacaftor

Patel P, Yeley J, Brown C, Wesson M, Lesko B, Slaven J, Chmiel JF, Sanders DB

Background/Objective: Cystic Fibrosis (CF) is a lethal autosomal recessive disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene affecting people of every race and ethnicity in the US. Highly effective modulator therapies (HEMT), such as elexacaftor-tezacaftor-ivacaftor (ETI), correct misfolding and/or improve functioning of the abnormal CFTR protein to lessen disease severity. Most people with CF are diagnosed following abnormal newborn screening (NBS), which involves measuring levels of immunoreactive trypsinogen (IRT). There have been case reports of falsely low IRT levels among infants with CF exposed to ETI in utero, but an overall assessment of IRT levels among these infants has not been conducted. We hypothesize that infants born to mothers with CF taking ETI (ETI-exposed) may have lower IRT levels than newborns with CF, CFTR-related metabolic syndrome (CRMS), or CF carriers.

Methods: NBS data from infants born between 2020-22 in Indiana with at least one CFTR mutation were collected and compared to infants born to mothers with CF taking ETI followed at Indiana University, regardless of CFTR mutation status. Infants were categorized as: CF, CRMS, Carrier, ETI-exposed, and Unknown (i.e., diagnosis not determined). An ANOVA test was performed on log-transformed data, with p-values adjusted for Dunnett's to compare IRT levels of infant groups to ETI-exposed group.

Results: There were 51 children with CF, 21 with CRMS, 489 CF carriers, and 19 ETI-exposed infants. Compared to other groups, ETI-exposed infants had a lower median IRT value and IQR ($p<0.0001$). To our knowledge, there are no CF diagnoses among ETI-exposed infants.

Conclusion: IRT levels for ETI-exposed infants, who are obligate CF carriers, were lower than for other infants with CF-related diagnoses, raising the likelihood of false normal NBS results. ETI-exposed infants should have CFTR mutation analysis performed to correctly categorize them as CF, CRMS, or CF carriers.

General Excellence Award

Payal Patel (she/her/hers) is a third-year medical student, who is currently interested in OBGYN and pediatrics because of the variety of care in both fields, as well as the ability to develop long-term relationships with patients. She also loves the huge focus on education and advocacy in both patient populations.

"I was amazed how closely the pediatric physicians worked with social workers, pharmacists, etc. to develop a whole patient picture to provide the best care in and out of the office especially for a condition as involved as Cystic Fibrosis. Not only that, but so much of healthcare is beyond just one body system, so it was a great realization to see how a pulmonary issue related to GI and Endocrinology issues requiring doctors to sometimes step back and look more holistically. The best part of pediatrics was seeing the not so serious side of all the adult doctors while they laughed and played as if they were kids again so they could connect and communicate better with their patients."

IMPRS Finalists

Challenges of Recruitment of Diverse Populations in Clinical Research

King C, Witting H, Hoffman S, Edmonds BT

Objective: The recruitment of diverse populations in research is essential for representing marginalized groups. We discuss the successes and challenges of recruiting pregnant-parent dyads for a study examining neonatal decisional authority within diverse partnerships.

Methods: We aimed to recruit 30 adult, first-time pregnant people between 18-26 weeks gestation, along with their partner. Heterosexual, same-sex, married, and unmarried partnerships were recruited to ensure a sample of diverse partnerships. Study advertisements were shared on pregnancy-related Reddit and Facebook groups. Flyers were distributed to OB/GYN clinics, LGBTQ+ healthcare providers, public events, and coffee shops. In-person recruitment at local clinics began in July 2022. Ads included a hyperlink or QR code to direct individuals to a brief screening questionnaire. If deemed eligible, the research team contacted the candidate to confirm eligibility and to schedule interviews. Virtual interviews lasted 1-hour and each participant received a $50 gift card.

Results: A total of 88 (51.4%) individuals were initially eligible. Of those, 35 (39.8%) did not leave contact information and 23 (26.1%) did not respond. To date, 20 parent dyads have been interviewed, with most recruited from Reddit (n=17, 85%). The majority of dyads were white. Four (10%) participants were non-white and four were Hispanic/Latinx. Additionally, 4 (10%) participants identified as LGBTQIA+. All eligible dyads were married. Challenges to recruitment include lacking access to private social media groups, a high prevalence of scammers, unresponsiveness, and difficulty getting buy-in from clinicians to share study ads with patients. In-person recruitment is promising but difficult to coordinate and limits the study's generalizability.

Conclusions: Online recruitment provides potential for recruiting diverse populations but yields several challenges. This presentation can provide insight for studies needing to recruit these populations.

Trends in Metastases among Patients with Masaoka-Koga Stage IV Thymic Epithelial Tumors

Laniak LJ, Davis HO, Heldman EM, Wuthrich BS, Kesler KA, Loehrer PJ

Background: Thymic epithelial tumors (TET's), including thymomas (5 histological subtypes) and thymic carcinomas, are rare tumors with an estimated incidence of 0.15 per 100,000 person-years in the United States. While their etiologies remain largely unknown, some are associated with uniquely high rates of paraneoplastic syndromes and an elevated risk of secondary malignancies. And, though thymomas were once thought to be benign tumors, it is now well-documented that all TET's can metastasize. The gold-standard in TET staging, the Masaoka-Koga system, defines metastatic disease as Stage IV, further specifying pleural/pericardial metastases as Stage IVa and lymphatic/hematogenous metastases as IVb. Unfortunately, little is known about patient prognosis as it relates to metastasis location. Here, we assemble and analyze one of the largest single-institution databases of TET patients in the world and seek to examine trends in metastases and their correlation with patient prognosis.

Methods: Files of 1023 TET patients seen at Indiana University Hospital were accessed via Cerner, after which a standardized information list including demographics, diagnostics, tumor histology, treatments used, disease course, and patient outcome at last follow-up was extracted and input into a RedCap database.

Results: Stage IV disease cases were filtered, yielding a total of 428 patients. Of these patients, 122 (29%) had carcinoma, making carcinoma the single largest histology represented in Stage IV. Locations of metastases also varied, with 284 patients (66%) having pleural metastases, 171 (40%) having lung, 71 (17%) liver, 58 (14%) bone, 56 (13%) pericardium, 37 (9%) neck lymph nodes, 12 (3%) brain, and 5 (1%) kidney. Moreover, 98 (23%) patients presented in stage IVb without any pleural/pericardial metastases. At last follow-up, 10% (19) of Stage IVa patients had no recurrence compared to only 3% (7) of IVb patients.

Potential Impact: These data altogether suggest that disease spread outside the thorax occurs much more commonly than previously reported, and that rates of metastasis vary with tumor histology. Future analysis will elucidate the exact differences in the patterns of spread among histological types, how these patterns correlate with prognosis, and the implications of this on screening and treatment options.

Improving Family and Surrogate Research Engagement in Nursing Homes

Mungcal L, Unroe K

Background: Nursing homes (NHs) are important sites of care for people with cognitive and physical disabilities; nearly half of NH residents have dementia. Unfortunately, NHs continue to be plagued with quality-of-care issues including lack of person-centered care and under- treatment of symptoms. The UPLIFT-AD (Utilizing palliative Leaders In Facilities to Transform care for Alzheimer's Disease) stepped wedge trial aims to address these issues by using palliative care (PC) specialists in NHs. Measuring the impact of this intervention is challenging because people with dementia often have difficulties communicating, and thus, much research relies on the observations of staff and surrogate decision-makers (usually family members). The latter has yielded a low response rate for the first timepoint of the UPLIFT-AD project.

Project Methods: A brief literature scan for similar PC NH interventions and surrogate engagement in NH research was performed, with support from a medical librarian, and revised strategies for surrogate recruitment were utilized during the second timepoint survey for two first-wave NHs.

Results: Two first-wave NHs (n=47 and 43) had surrogate baseline survey completion rates of 42.6% (n=20) and 34.9% (n=15). Following the implementation of the additional strategies– calling surrogates from NH phones, calling at varied times, and emailing research information– the overall survey completion rate was relatively unaffected–42.6% (n=20) and 37.2% (n=16). Of the surrogates from these facilities (n=90), 30.0% (n=27) refused to participate and 17.8% (n=16) were "unable to contact." The reasons for refusal included "not interested" (37.0%), "too busy" (18.5%), "no reason" (11.1%), "hung up" (11.1%), and "other" (22.2%). The literature scan yielded few published articles containing strategies to improve engagement of surrogates in NH PC research.

Conclusion: Strategies to enhance surrogate engagement in NH research are underdeveloped. Engaging surrogates in research requires multiple strategies and presents an ongoing challenge but represents a critical perspective for studies involving people with dementia.

Inhibition of CaMKK2 Decreases Progression of Post-traumatic Osteoarthritis in a Rabbit ACL Transection Model

Riggs K, Dilley J, Sankar U

Background and Hypothesis: Post-traumatic osteoarthritis (PTOA) is a multifactorial degenerative disease of the joint affecting 20-50% of all joint injuries with a total annual cost of $15 billion. There are no current disease-modifying therapies for PTOA. Mechanical stress due to ligament tear or impact injury triggers the release of inflammatory mediators in the joint. Resulting collagen damage, loss of proteoglycans, and cell death triggers further release of inflammatory mediators and reactive oxygen species. This cycle of inflammation leads to PTOA. We hypothesize that inhibition of Ca2+/CaM dependent protein kinase kinase 2 (CaMKK2), a kinase associated with the inflammatory effects in PTOA, will mitigate the disease-propagating mechanisms.

Methods: We utilized a rabbit model of PTOA which involved surgical transection of the anterior cruciate ligament (ACL) to generate joint instability. Rabbits were then treated tri-weekly with either STO609 (CaMKK2 inhibitor, 0.033 mg/kg) or saline (control) for 16 weeks. Rabbits were sacrificed at 16 weeks post-surgery. Tibiofemoral joints were harvested for staining with safranin O fast green (SO) and PTOA grading via Osteoarthritis Research Society International (OARSI) guidelines. Apoptosis was assessed with terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL). RNA isolation of cartilage and subchondral bone tissue was conducted for qRT-PCR. Gene expression of MMP-13, IL-6, IL-1B, ACAN, COL2A1 was quantified and normalized to GAPDH.

Results: Histology and gross morphology showed increased PTOA severity in saline controls compared to STO-609 treated rabbits. There was no significant difference in chondrocyte apoptosis in STO-609 treated rabbits compared to saline controls based on TUNEL staining. Gene expression analyses are in progress.

Potential Impact: This study addresses the unmet clinical need for novel disease-modifying therapeutics for PTOA. Preliminary results show that inhibition of CaMKK2 has the potential to decrease cartilage degradation after joint injuries.

Husisha: Training Peer-Counselors in Adolescent Problem-Solving Therapy in Eldoret, Kenya: Implementation, Adaptation, and Outcomes

Vander Missen M, Barasa J, Jaguga F, Kwobah E, Turissini M, Ott M, Puffer E, Kusgei G, Rono W, Njiriri F, Giusto A

Background and Objective: In Kenya, youth needing mental health (MH) treatment vastly outnumber licensed mental health professionals. Task-sharing MH treatment to non-professionals has potential to reduce the treatment gap. For youth, non-professional peer counselors have the benefit of increasing engagement and reducing stigma. Problem-solving therapy (PST) is one treatment shown to alleviate MH symptoms even when delivered by non-professionals. Here we (1) evaluate the implementation of a PST training and (2) codify adaptations for PST implementation at a youth drop-in center at Family Health Options Kenya.
Experimental Design or Project Methods: A 2-week training for peer mentors was conducted. Curriculum included core counseling skills, overview of MH, and PST introduction and application.

Peer Outcomes: Mean scores from pre- and post-written exams were compared using paired t-tests. Standard role plays were evaluated

using the Working with children – Assessment of Competencies Tool (WeACT). Consensus WeACT scores from pre- and post-role plays were compared using paired t-tests.

Adaptations: Feedback on cultural acceptability, language comprehensibility, and intervention flow was collected. Proposed intervention changes were coded within the Ecological Validity Model framework.

Results: Based on a written exam, mentors' knowledge of MH conditions and core counseling skills improved after training (Pre: 10.88±4.36; Post: 15.38±2.88; p=.026). Competence in application of counseling skills evaluated with WeACT improved after training (Pre: 20.63±6.61; Post: 28±1.69). Examples of adaptations to PST include changes to address stigma for MH treatment in Kenya and redistribution of content between sessions.

Conclusion and Potential Impact: A 2-week PST training improved peers' counseling skills and ability to deliver a manualized PST treatment. Training allowed contextual, conceptual, and methodological adaptations to PST for use in a Kenyan context. Implementing and improving lay-counselor trainings for MH interventions in Kenya has the potential to increase access to preliminary MH treatment.

Evaluation of Chemotherapeutic Outcomes for Thymic Carcinoma Patients

Wuthrich B, Davis H, Laniak L, Heldman E, Loehrer P, Kesler K

Background and Hypothesis: Thymic Epithelial Tumors are uncommon tumors of the anterior mediastinum composed of thymomas and thymic carcinomas (TC). TC's are known to have worse disease outcomes and lower rates of survival in comparison to thymomas and are suspected to have lower response rates to chemotherapy as well. As these tumors are rare, little data exists assessing the true efficacy of chemotherapeutic regimens for TC patients. Due to this lack of data, and that the Indiana University Health Simon Cancer Center treats a high percentage of TET patients, a database of these patients covering a variety different disease characteristics and treatments has been established. We hypothesize, upon evaluation of this database, response rates to anthracycline based regimens (PAC) will be superior to non-anthracycline based regimens (i.e., PE, Carbo/Taxol) for TC patients.

Methods: In this project, a collection of patients seen by Dr. Patrick Loehrer and/or Dr. Kenneth Kesler was acquired, and a database was created using these patients in RedCap. Once established, we evaluated patient medical records in Cerner and entered data related to disease characteristics and treatments. These patients were then analyzed accordingly to evaluate chemotherapy response rates.

Results: The database yielded 123 instances of chemotherapy treatment for TC. Of which, the most popular treatments were PAC and Carbo/Taxol. The data suggests that PAC generates a higher response rate (65.5%) than other therapies (Carbo/Taxol: 27.6%, PE: 58.3%, etc.). Therefore, there is evidence that anthracycline based regimens may be more effective at generating response rates in comparison to non-anthracycline based regimens.

Conclusion and Potential Impact: This project will help elucidate the effectiveness of recommended systemic therapies for thymic carcinoma patients from one of the largest TET databases constructed. Ultimately, we hope that with clarity of the effectiveness of treatment, this can serve as a reliable reference for evidence-based medicine for the care of TC patients.

IMPRS Honorable Mentions

Intravital Microscopy Optimization for Murine Tail Lymphedema Model

Diaz S, Mohan G, Khan I, Sinha M, Sen CK, Hassanein AH

Background: Lymphedema is limb swelling caused by lymphatic dysfunction. It occurs in 30% of patients that undergo axillary lymph node dissection in the treatment of breast cancer. It can cause pain, impair function, and decrease quality of life. Lymphedema is treated with compression, excisional procedures and microsurgical physiologic procedures. There is no cure for this disease. The murine tail model of lymphedema is an established animal model for lymphedema. Visualization of lymphatics and functional assessment remains a challenge.

Project Rationale: Immunohistopathology and qRT-PCR are two commonly used in vitro techniques for molecular assessment of lymphatics in animal tissues. These methods provide incomplete information about the structure/function of lymphatics and introduce the confounder of harvested tissue. Methods of functional evaluation such as lymphoscintigraphy or lymphangiography show transit of dyes through lymphatics without high resolution imaging of the lymphatic vessels. Intravital two-photon microscopy (IVM) addresses these disadvantages through real-time imaging of subcellular level biological processes in live animals. The goal of this project is to optimize IVM methods for the assessment of functional lymphangiogenesis in the murine tail lymphedema model.

Methodology Development: A full-thickness skin excision is performed near the base of the tail in C57BL/6 mice. The lymphatic trunks are then surgically transected. Gene-based therapy is delivered to the tail at the surgical site. At 10 days post-treatment, a second full-thickness skin excision is made distal to the site of occlusion. FITC-Dextran (2000 kD) is injected at the distal tail for lymphatic uptake. Lymphatic vessels are visualized at the second skin excision site with the Leica SP8 Confocal/Multiphoton Microscope and assessed for number of branching points. Images are captured with Leica Application Suite Advanced Fluorescence Software and analyzed with Imaris Microscopy Image Analysis Software. This results in the ability of functional assessment of lymphatics and visualization of lymphangiogenesis following gene-based therapy.

Changes in Cortical Composition during Gyrification in the Developing Brain

Doherty S, Garcia KE

Background and Hypothesis: Abnormal brain folding has been implicated in neurodivergent conditions such as schizophrenia and autism, yet the mechanical and biological processes responsible for this process are not well understood. One current hypothesis is that cortex growth outpaces growth of the underlying white matter to drive mechanical buckling. However, mechanical stresses, such as those resulting from buckling, can also influence cellular behavior. In this study, we hypothesized that mechanical stresses from cortical folding influence processes of biological growth within the cortex, such as dendrite arborization within the neuropil and neuronal differentiation.

Methods: To quantify change in cell body size and neuropil over the period of cortical folding, sections of the developing ferret brain (postnatal days 20, 26, 32, and 38) were stained with FluoroNissl dye, imaged with confocal microscopy, and analyzed using Fiji software. Change in percent neuropil, cell area, cell density, and overall length were quantified at upper, middle, and lower thirds of the cortex to assess the influence of bending stresses within gyri and sulci during development.

Results: Preliminary analysis revealed a substantial increase in neuropil over time in the upper layers of the cortex. However, gyral regions expected to experience mechanical tension and increased expansion did not exhibit the hypothesized differences in neuropil or cell size. Though there was an overall increase in neuropil volume fraction and cell body size over time, throughout all layers of the cortex, these factors only accounted for roughly 2/3 of the physical growth quantified throughout these cortical layers.
Potential Impact: Findings indicate that neuropil and cell body expansion are insufficient to fully explain the growth observed during cortical folding. These results highlight a potential role for alternative cellular processes, such as the migration of other cell types into the cortex, to induce cortical growth and folding in gyrencephalic species.

Grounded Practical Theory Analysis of Patient-Provider Communication with Black Women Participating in Breast Cancer Clinical Trials

Okoruwa OP, Ridley-Merriweather KE

Background: Previous literature suggests breast cancer clinical trial participation among Black women has declined in recent years by as much as 35%. Though the literature identifies barriers to participation for this population, little has been studied about how researchers can address these barriers. This study investigates the communication between healthcare providers and Black women to illuminate how providers and researchers can positively influence their perceptions of breast cancer clinical trial participation.

Methods: Fourteen women (n=14) who self-identified as Black, Black American, or African American, were interviewed about their communication experiences with healthcare providers regarding breast cancer clinical trial participation. Each transcribed interview was coded using thematic analysis. Grounded Practical Theory was introduced to give insight into the patient-provider communication needs of Black breast cancer research participants.

Findings: The findings fell into four categories: (1) impressions of participants toward their providers, (2) reflections on the clinical trial recruitment experience, (3) communication relationships with medical and research providers, (4) and cultural aspects of patient-provider communication. One major finding was that an important way women learn about clinical trials is through conversations with their oncologists. However, only 29% of Black women interviewed were informed of their clinical trial by a healthcare provider, suggesting that Black women may not be receiving the information they need to participate in clinical trials.

Conclusion: By understanding existing patient-provider communication typologies, we can improve these methods of communication to increase the interest and participation of Black women in breast cancer clinical trials.

Implications: Clinical trials provide data to healthcare providers about treatment options for breast cancer. If minoritized populations are continually underrepresented in clinical trials, these treatments might not prove to be efficacious in Black women. Researchers must make the necessary investment of resources and effort to better understand the needs of Black women in clinical trial recruitment.

Complications in Burn Patients Following Fluid Over-Resuscitation

Peipert LJ, Kraatz J

Background/Objective: Over-resuscitation of burn patients leads to dangerous edema-related sequelae. The Parkland formula is commonly used to predict fluid requirements in the 24 hours following burn injury, yet studies report widely varying resuscitation rates. This study aims to assess fluid resuscitation practices at Lutheran Hospital and evaluate correlations between resuscitation rates and fluid-overload complications.

Methods: A retrospective chart review assessed fluid resuscitation of 36 adult patients with burns affecting at least 15% total surface body area (TBSA) between May 2020-May 2022 at Lutheran Hospital. Intravenous fluid rates and urine output (UO) were recorded for the first 24 hours of each patient's hospital stay. Complications and mortality were recorded for the entirety of a patient's hospital stay. Patients who received volumes exceeding those recommended by the Parkland formula were placed in the high-volume group whereas patients who received a lesser volume were placed in the low-volume group. Statistical analyses were performed using Microsoft Excel ($p = 0.05$).

Results: The study included 36 patients with an average fluid resuscitation of 4.13 ±2.14 mL/kg/%TBSA in the first 24 hours following hospital admission. Average UO in the high-volume group ($n=14$) was 1.33 ±0.76 mL/kg/hr compared to 0.75 ±0.47 mL/kg/hr in the low-volume group ($n=22$). Fluid complications were more common in the high-volume group (41.7%) compared to the low-volume group (19.0%), but this difference was not statistically significant ($p=0.230$). No difference in mortality was observed ($p=1.000$).

Conclusion: The high-volume group had an average UO exceeding the recommended range (0.5-1.0 mL/kg/hr) and experienced greater rates of fluid-overload complications (pulmonary edema, compartment syndromes, etc.). Due to the small sample size and limited power of this study, the difference in fluid-related complications was not statistically significant.

Clinical Impact and Implications: Physicians should limit fluid volumes exceeding the Parkland formula when resuscitating burn patients to avoid fluid overload sequelae.

Development of PET Tracers of Glutamine Metabolism

Rehman I, Arkin Cs, Knapek E, Snyder S, Schulte M

The labeling of amino acids with positron-emitting radionuclides (such as fluorine-18) has been a widely used approach for the imaging of tumors as it often provides higher diagnostic accuracy than what is observed with [18F]FDG. In particular, PET tracers of glutamine metabolism have garnered significant attention in recent years. O-(2-[18F]fluoroethyl-L-tyrosine (18F-FET) is a promising PET tracer in this regard and is currently under investigation at Indiana University (IU) through an expanded access IND for patients with brain malignancies. Clinical production of 18F-FET at IU previously required the use of HPLC for purification, following the reaction of fluorine-18 with the precursor molecule for FET. While this method has been successful in removing undesirable impurities and byproducts, HPLC significantly increases synthesis time and is a common failure point in the synthesis of FET on our current radiochemistry module. To address this issue, we aimed to deploy a solid-phase-extraction (SPE) method for the purification of FET, thereby eliminating the need for HPLC purification. Several methods for the SPE purification of FET have been previously reported; however, none of these strategies afforded pure [18F]FET on our synthesis module, thus development of new methods was required.

While several tracers capable of measuring different aspects of glutamine metabolism have been evaluated in both preclinical and clinical studies, there are metabolic liabilities that limit their utility and complicate data analysis. [18F]-4F-glutamine is one such tracer that has shown promise but has limitations due to undesirable metabolism in vivo. Herein we report our progress towards an improved synthesis of [18F]FET for ongoing clinical studies as well as our progress towards the development of a novel tracer that would

address metabolic liabilities associated with currently available PET tracers of glutamine metabolism.

Outcomes of Arterial and Caval Resection During Post-Chemotherapy Retroperitoneal Lymph Node Dissection in Metastatic Testicular Cancer

Smith R, Cary C

Background/Objective: In the United States, testicular cancer is the most common solid tumor in men aged 15 to 34. Fortunately, testicular cancer has a cure rate greater than 90% and a 97% five-year survival rate. For the men not cured, a relapse to the retroperitoneum (RP) is most common. Of the patients with RP metastases, a minimal number may require post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND) with resection of the aorta, external iliac, or inferior vena cava (IVC). We hypothesized this procedure would yield reasonable cure rates with acceptable levels of postoperative complications to warrant the indication for surgery.

Methods: Between 2000 and 2020, 2,054 patients with metastatic testicular cancer underwent a PC-RPLND; of those men, 39 also underwent an aortic, external iliac, and/or IVC resection. For the men with a PC-RPLND and vascular resection, demographic, clinical, pathologic, and operative information were reviewed. Next, a Kaplan-Meier curve was created to determine overall survival.

Results: In this retrospective cohort study of 39 patients, PC-RPLND and vascular resection occurred at a median age of 40. The median follow-up of the cohort was 9 months. The median pre-operative mass size was 9 cm and 19 cm in the RP and pelvis, respectively. At PC-RPLND, 54%, 13%, 18%, and 15% of patients demonstrated cancer, teratoma, teratoma and cancer, and necrosis, respectively. Following PC-RPLND and vascular resection, 22 (56%) patients recurred. The median (IQR) time to relapse was 4.2 (2.5 – 8.2) months. Recurrence to the lung was most common, followed by the RP and liver. In total, 17 (44%) patients died of disease with a median overall survival of 14.8 months.

Conclusion: With an overall survival rate of 45% at two years in this heavily pretreated patient population, PC-RPLND with resection of the aorta, external iliac, and/or IVC is reasonable in very select cases.

Targeting Arg-1 and PD-L1 in M2-Tumor Associated Macrophages Impairs Juvenile Myelomonocytic Leukemia (JMML) Cell Proliferation and Migration

Young K, Pasupuleti SK, Stieglitz E, Kapur R

Background and Hypothesis: Tumor-associated macrophages (TAMs) are a key component of tumor-infiltrating immune cells. They are largely characterized into M1 or M2 types. TAMs express an anti-inflammatory M2-like phenotype, promote tumor progression. However, the role of M2-TAMs in driving disease pathogenesis in patients with Juvenile myelomonocytic leukemia (JMML), a rare form of pediatric leukemia driven to a large extent by mutations in the PTPN11 gene, which encodes the phosphatase SHP2 is unclear. We hypothesized that in JMML, inflammatory myeloid cells including neutrophils and M2-TAMs express higher levels of arginase-1 (Arg-1) and PD-L1, which may contribute to the local suppression of immune responses and support the development of JMML.

Methods: To study how alterations in M1/M2 macrophages contribute to JMML development, we utilized a mouse model bearing Shp2E76K mutation (Ptpn11E76K/+) which manifests the cardinal features of human JMML. We hypothesized that Shp2E76K/+ mutations enhance the function of bone marrow derived macrophages (BMDMs), including M2-TAMs and contribute to T-cell suppression.

Results: Our analysis of the bulk RNA-sequence data from 90 JMML patients showed an increase in the expression of Arg-1 and PD-1. Furthermore, single cell RNA-seq analysis of macrophages from 4 JMML patients revealed higher expression of M2-macrophage markers/genes. Our results show that in M2-TAMs, Arg-1 and PD-L1 levels are elevated in BM and spleens of Shp2E76K/+ mice compared to WT. Moreover, M2-TAMs, Arg-1 and PD-L1 levels were also higher in BMDMs derived from Shp2E76K/+ mice compared to WT. The BMDMs from Shp2E76K/+ mice have greater proliferation and migration potential compared to WT BMDMs, which was significantly reduced by inhibiting the function of Arg-1 and PD-L1.

Conclusion: Our results show that M2-TAMs, arginase-1, and PD-L1 create a pro-tumor microenvironment, which likely contributes to the growth of JMML cells. Inhibition of Arg-1 and PD-L1 is a novel therapeutic approach to treat patients with JMML.

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 ~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

Belamkar AV, Haider KM

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 γH2AX, gene-silencing modification H3K27me3, total H3, tumor suppressor p53, EZH2, JMJD3, γSTAT3, 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 γH2AX expression, but this was not further increased by radiation. Meanwhile, GSK-J4 treatment increased γH2AX, 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 ± 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.

C**ase 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.

R**esults:** 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 ($p \leq 0.038$).

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

I**ntroduction:** 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.

Funding: This project was funded, in part, with support from the Indiana Clinical and Translational Sciences Institute funded, in part by UL1TR002529 from the National Institutes of Health, as well as by the National Institute On Aging of the National Institutes of Health under Award Number K01AG076971. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funders.

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 EPATRI 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

R**ussell 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.

[Support: NIH R01 HL141933 T35 HL110854]

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 ≥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 ≥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 ($p \geq .278$). 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

B**ackground 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.

Indiana University Student Research Symposium

The following works were accepted for presentation at the Indiana University Student Research Symposium, which serves to highlight student research from all levels of experience in order to ignite interest and support for scientific inquiry in the IUSM medical community.

Optimizing Outcomes for a Pregnant Patient with Congenital Heart Disease

Eckert NL, Jones TK, Okoruwa OP, Rouse CE

Case Description: A 24 yo F with complex congenital heart disease (CHD), modified WHO (mWHO) class III, presented for prenatal care in the first trimester. Her history was complicated by hypoplastic right heart syndrome with pulmonary atresia for which she had undergone multiple surgical procedures in childhood, including ultimately extracardiac lateral tunnel Fontan. Additional comorbidities included epilepsy, mild cerebral palsy, scoliosis, irritable bowel syndrome, asthma, and anxiety. Her pregnancy was managed by a multidisciplinary team, including Maternal-Fetal Medicine, Adult CHD Cardiology, Neurology, Obstetric Anesthesia, and Social Work. A cesarean delivery was performed at 32+4 weeks for fetal growth restriction with non-reassuring fetal testing without complications. Her postpartum course was complicated by pericarditis which was managed medically. The infant stayed in the NICU due to prematurity but was otherwise healthy.

Conclusion: A multidisciplinary team approach to the care of pregnant patients with complex CHD supports development of comprehensive, patient-specific assessments and plans for each stage of pregnancy, thereby minimizing risks of negative outcomes. Having extensive knowledge of high-risk care and applying the mWHO risk assessment helped the team ensure that the patient received appropriate counseling, monitoring, and management for a healthy pregnancy with minimal complications.

Clinical Significance: Prior to the utilization of high-risk multidisciplinary care teams, many women with congenital heart defects were discouraged from attempting pregnancy following the Fontan procedure. As the population of women who have undergone the Fontan procedure grows, it is critical to implement a multidisciplinary approach to care with intent to empower women with congenital heart defects to achieve successful pregnancies while minimizing pregnancy-related mortality and morbidity.

Approach to Treatment of Cervical Pregnancy: A Case Report

Campbell M, Chaudhary A, Pandhiri T, Tominack H, Rouse CE

Case Description: A 25 yo G1 at 11wk4d dated by last menstrual period and confirmed with a 10-week ultrasound presented with a possible cervical ectopic pregnancy. Past medical, surgical, and OBGYN histories were unremarkable. A cervical pregnancy was suspected on ultrasound due to low implantation of the gestational sac, and a significant posterior bulge with an hourglass shaped uterus. MRI suggested implantation of the placenta in the posterior uterine and cervical walls due to extreme thinning of these structures. Our institution had previously created a protocol for multidisciplinary management of cesarean scar and cervical pregnancies. The patient desired fertility preservation, and so consented to combined local and systemic treatment with methotrexate (MTX). Preprocedural Beta-hCG was 81,514.8 mU/mL. Ultrasound-guided transvaginal intra-gestational sac injection of MTX was performed without complication, though cardiac activity was still present at the conclusion of the procedure. The patient also received an intramuscular injection of MTX before discharge. Serial Beta-hCGs are still being followed and are trending towards 0.

Conclusion: The optimal management for cervical pregnancies is not known, and decisions around type of management are informed by the patient's desire for fertility preservation. In this case, a protocol created by a multidisciplinary team was used to guide treatment. This protocol using MTX successfully treated a cervical pregnancy at 11wk4d and avoided a surgery that could complicate future fertility.

Clinical significance: Due to the rare occurrence of cervical pregnancy, there is not a universally accepted treatment protocol. This case shows that medical management can be successful for cervical pregnancies. Clear guidelines must be established for cervical pregnancies to optimize outcomes, decrease maternal morbidity and mortality, and preserve future fertility.

Assaults in Schools: Findings Using a National Database

Loder RT, Farooq H, Gianaris JB

Background: Assaults can occur at schools/educational facilities involving students, teachers, and other school employees. The purpose of this study was to correlate injury patterns with patient demographics in school assault victims. Understanding injury patterns with their associated demographics will not only be useful for healthcare providers but can also assist in proposing prevention strategies for both students and school employees.

Methods: Emergency department (ED) data from the National Electronic Injury Surveillance System All Injury Pro-gram for years 2005-2015 were used in this study. Statistical analyses were performed with SUDAAN software to account for the weighted, stratified nature of the data.

Results: There were an estimated 852,822 ED visits for school assaults. The median age was 13.8 years, with 81.3% of participants between 5-19 years old. 64.4% of participants were male. After age 4, the number of females proportionately increased with increasing age. The most common diagnosis was a contusion/abrasion (38.6%). The injuries occurred in the head/neck (63.9%), upper extremity (19.0%), upper trunk (6.6%), lower trunk (5.5%), and lower extremity (4.9%). Firearm violence accounted for 0.1% of the assaults. Human bites occurred in 3.7%. Sexual assault was rare and proportionally the highest in those ≤4 years of age. Internal organ injuries were more common in females (13.1% vs 3.55%) and for those admitted to the hospital (29.9% vs 19.9%). The incidence of ED visits for school assault decreased 50% from 2005 to 2015.

Conclusions: This study analyzed ED visits due to assaults occurring in schools. Firearm violence accounted for only 0.1% of the injuries,

in contrast to media coverage regarding school assaults. The most common injury location was the head/neck, and the most common diagnosis was a contusion/abrasion. This data can also serve as a baseline for further studies and the impact of potential reduction strategies.

Utilization of Free Clinics by Underinsured and Uninsured Populations and their Impact on Community Health

Wickstrom M, Gong S, Burrow Z, Stoll K

Case: A 50-year-old female presented with suspected "thyroid issues," which consisted of lower extremity edema, insomnia, alopecia, dry skin, cold intolerance, extreme fatigue, and anxiety/depression. Review of systems was significant for pallor of skin and conjunctiva, thymus of normal size without nodules, alopecia, and bilateral lower extremity edema. Family history was significant for hypothyroidism. The patient was furloughed by her employer during the COVID-19 pandemic.

Conclusion: This patient was underinsured and furloughed by her employer, leaving her with no source of income and limited access to healthcare. Fortunately, with access to a free clinic, she was able to obtain lab work at zero cost to her, which revealed extremely low hemoglobin and hematocrit levels. She was advised to go to the emergency department the day that results were obtained, where she was diagnosed with a GI bleed, given iron supplementation, and 3 units of blood.

Clinical Significance: A survey conducted by the US Department of Health and Human Services estimated that 30 million Americans lived uninsured in the first half of 2020, leaving many Americans living without primary health care services due to fear of out-of-pocket expenses. Individuals lacking insurance are more likely to identify as African American or Latino, be young adults, have lower incomes, and live in states that have not implemented Medicaid expansion. Free clinics provide a number of basic medical services which can be of significant benefit to patients who are unable to regularly access healthcare. This case demonstrates a scenario in which a patient's life was likely saved due to her access to a free clinic and the services therein. As is evident, free clinics are an integral part of closing the uninsurance gap and ensuring quality healthcare access to those who require it regardless of ability to pay.

A Plan for Progress: Indiana Women's Health Center of Excellence Five-Year Plan

Clodfelter K, Emerick S, Farris K, Stoll K, Peipert J

Background: Strategic plans are useful for setting ambitious goals as they allow the organization of timelines, encourage interdepartmental collaboration, and create a basis for funding to reach goals. Indiana University Health and the Indiana University School of Medicine have developed a strategic five-year plan to enhance the Center of Excellence in Women's Health (WH-CoE). The vision for WH-CoE and the goal of the strategic plan is that the center will be a leader in women's health and a premier destination for the prevention, treatment, and cure of women's health disorders. Attention to Indiana women's health is necessary as certain health outcomes in the state fall low on national rankings. Indiana has an infant mortality rate 20% higher than the national average, ranks 28th for infants born preterm, and has the third highest maternal mortality rate in the United States.

Intervention: The five-year strategic plan aims to position WH-CoE as a recognized leader and primary destination for women's health disorders. This task will be accomplished through the completion of yearly goals established by the foundation in areas of clinical care, research, and education, which were identified by a committee of leaders from various women's health disciplines. The plan is broken down into six centers of focus: chronic pain, cardiovascular disease, breast health, endocrine/polycystic ovarian syndrome (PCOS), oncofertility, and substance use disorders.

Results: The timeline was developed to give priority to initiatives which were multidisciplinary and the most feasible for the given timeframe. Research efforts are built into the five-year plan to evaluate the plan's efficacy and impact on women's health.

Conclusion: As healthcare providers in Indiana, we have a duty to our patients to improve our women's healthcare. Our hopes are that the successes and failures of this plan may be built upon by other programs to improve women's healthcare across the nation.

Use of Nasal Septal Grafts in Substitution Urethroplasties: An Early Series

Arnold PJ, Soyster ME, Burns RT, Mantravadi AV, McDonald CJ, Mellon MJ

Overview: Substitution urethroplasty remains one of the most effective treatments of urethral strictures, especially in cases of elongated stricture length. While oral mucosa is the gold standard graft for repairs, buccal mucosa grafts (BMG) are associated with significant post-operative morbidity. This series is the first to review the use of nasal septal cartilage for augmentation urethroplasty.

Methods: All patients undergoing nasal septal graft substitution urethroplasty from December 2020 to February 2022 were identified. Institutional Review Board exempt status was granted for the conduct of this study. Septal graft harvesting was performed by two otolaryngologists, and urethroplasty was performed by a single surgeon at a tertiary care referral center. The novel nature of the technique was explained to all patients who expressed understanding and willingness to proceed. Descriptive analyses were performed, and postoperative retrograde urethrograms (RUG) were analyzed.

Results: Four patients were identified with an average follow-up time of 12 months. The average stricture length was 2.6 cm. Three patients had bulbar urethral strictures; one patient had a perineal urethrostomy stricture. The largest nasal perichondral harvest was 3x5 cm. At 4 weeks, two patients had no leak on RUG with successful catheter removal. One patient had a minor contained leak and catheter was removed at 6 weeks without imaging. One patient had a leak at their 4- and 6-week RUG, with no leak and catheter removal at week 10. Notably, this patient had a prior BMG urethroplasty. Patients reported associated pain ("2-4/10"), difficulty breathing, and epistaxis as side effects.

Conclusions: Further study of this technique and longer follow-up are required to determine long-term efficacy. Still, this initial data suggests that nasal septal substitution urethroplasty may be a viable surgical approach to treating urethral strictures, especially for patients wishing to avoid morbidity associated with BMG urethroplasty or those unable to undergo BMG harvesting.

A Case of Plaque-Like CD34+ Dermal Fibroma Masquerading as Granuloma Annulare

Skorobogatko V, Spaulding R, Alomari A, Umphress B

Background: Plaque-like CD34+ dermal fibroma, also known as "medallion-like dermal dendrocyte hamartoma (MLDDH)," is a rare cutaneous lesion found predominantly in females. It often presents as a solitary, erythematous, and circumscribed atrophic plaque. Histologically, lesions demonstrate a bandlike proliferation of bland fibroblast-like cells within the upper dermis. CD34 is positive with variable expression of FXIIIa. Here, we report the case of a patient who presented with a long-standing and asymptomatic erythematous, firm annular plaque without scaling. The plaque was located on the lower extremity and clinically resembled granuloma annulare. Biopsies revealed dermal spindle cell proliferation with interspersed collagen and CD34 reactivity. Given the findings, a diagnosis of plaque-like CD34+ dermal fibroma was favored with differential diagnostic considerations including fibroblastic connective tissue nevus and dermatomyofibroma.

Conclusion: Our aim is to increase awareness of this rare diagnostic entity, highlight distinguishing features from its histologic mimickers, and further illuminate one of the possible clinical presentations.

Analysis of Neutral Lipid Accumulation in Hepatic Lineage Cells to Study NAFLD/NASH

Bolujo I, Park Y, Isidan K, Lopez K, Cross-Najafi A, Li P, Zhang W, Ekser B

Background: Nonalcoholic fatty liver disease (NAFLD) is the leading cause of liver disease in the United States and is often associated with obesity and type 2 diabetes. NAFLD may progress to Nonalcoholic Steatohepatitis (NASH), which is characterized as lobular inflammation and apoptosis leading to fibrosis, cirrhosis, and/or hepatocellular carcinoma (HCC). Although it is well established that lipid deposition in hepatocytes plays a critical role in the pathogenesis of NAFLD/NASH, the effects of accumulation of neutral lipids in other liver cell types, including liver endothelial cells and cholangiocytes, are poorly understood.

Methods: Primary human hepatocytes, cholangiocytes, and liver endothelial cells were seeded on a collagen-coated plate prior to being incubated with vehicle alone (control, 1% BSA) or different concentrations of free fatty acids (FFA - oleic acid and palmitic acid 2:1; 160 M, 320 M, 500M and 1mM) for 24 hours. After treatment, the cells were subjected to BODIPY493/503 staining to determine lipid droplet accumulation within the cells. Hoechst was used to stain the cell nuclei. Images were captured with a Leica fluorescence microscope and imaging system. Fluorescence intensity was measured with Image J software.

Results: Following treatment, especially with higher FFA concentrations, lipid accumulation (BODIPY493/503, green fluorescence) was augmented in all three cell types (Figure 1). In addition, treating the cells with 1 mM FFA led to reduced Hoechst-labeled cell nuclei and increased cell detachment in all three cell types, which indicated high levels of lipid-mediated cell toxicity.

Conclusions: We developed an in vitro model to examine lipid accumulation in different liver cell types, which could be used to determine the adaptive responses within different hepatic lineage cells in NAFLD/NASH progression.

Patients Don't Read Textbooks: The Impact of Medical and Social Biases on the Diagnosis of Cushing's Syndrome

Patel S, Young A, Cooper S, Love E, Saeed Z

Background: We present the case of a 66-year-old African American female with severe Cushing's syndrome (CS) who remained undiagnosed for several years. The patient had a history of an unsuccessful Roux-en-Y gastric bypass nine years ago. The patient also had type 2 diabetes, hypertension, unexplained hypokalemia, and a past history of unprovoked PE and DVT. She presented with acute onset headache. MRI of the brain revealed a 1.4x1.7 cm macroadenoma. On exam, the patient did not have the classic Cushingoid appearance. In particular, she did not have "moon facies," facial plethora, supraclavicular fullness, or any evidence of a dorsocervical fat pad ("buffalo hump"). Work-up was consistent with severe ACTH-dependent CS with random serum cortisol of 58.6 mCg/dL, ACTH of 300 pg/mL (reference range 7.5-63 pg/mL), 24-hour urine free cortisol of 1,608 mCg (normal: <45 mCg), and 1 mg dexamethasone suppression test with no reduction in cortisol. The diagnosis was delayed for ten years, but the patient was later found to have a pituitary tumor causing excessive ACTH secretion which caused her symptoms.

Conclusions: Awareness of medical and social biases is crucial when evaluating a patient. CS is a treatable condition and delays in diagnosis correlate with increased morbidity and mortality (Neiman et al). This case demonstrates the importance of recognizing disease presentation beyond textbook characterization and recognizing potential biases held by providers. CS is caused by excessive production or exposure to glucocorticoids (Sharma et al). This disorder commonly presents with weight gain, "moon facies," and dorsal fat pads, although the presentation can be variable. Though patient sex, age, and disease etiology have not been found to influence diagnosis timing, the impact of race and bias has not yet been described (Rubinstein et al). Medical training may overemphasize "buzzwords" and textbook presentations causing physicians to misattribute a patient's symptoms to another pathology.

Establishment and Characterization of Patient-Derived Xenograft from Leptomeningeal Spread of Rare Pediatric Anaplastic Pleomorphic Xanthoastrocytoma (PXA) Bearing CDC42SE2-BRAF Fusion

Damayanti NP, Saadatzadeh RM, Dobrota E, Ordaz JD, Bailey B, Pandya P, Alfonso A*, Keir S, Zhang ZY, Balsara KE, Pollok KE

Background: Pleomorphic xanthoastrocytoma (PXA) is a rare subset of primary pediatric glioma with 70% 5-year disease-free survival. Up to 20% of cases can recur and/or undergo malignant transformation into a more aggressive type, anaplastic PXA (AXPA). The understanding of disease etiology and the mechanisms that drive PXA and APXA are limited. Therefore, there is a need to develop preclinical models to investigate molecular underpinning and guide therapeutic approaches.

Methods: We established and characterized a patient-derived xenograft (PDX) from a leptomeningeal spread of a patient with recurrent APXA bearing novel type of CDC42SE2-BRAF fusion. Characterization was done to assess the model fidelity in genomic, transcriptomic, and proteomic landscape.

Results: Histological features were conserved between the PDX and matched human tumors throughout serial passages. Whole exome sequencing (WES) demonstrated a high degree of conservation in small variants (Pearson's r=0.794-0.839), tumor mutational burden, and mutations in MAPK family genes between PDX and patient tumor. Chromosomal gain in chromosomes 4-9, 17, and 18 and loss in chromosome 9p associated with homozygous 9p21.3 deletion involving CDKN2A/B locus, were identified in both patient tumor and PDX sample. Chromosomal rearrangement involving 7q34 fusion; CDC42SE-BRAF t (5;7) (q31.1, q34) (5:130,721,239, 7:140,482,820) was identified in PDX tumor, xenoline, and matched human tumor. Transcriptomic profile of the original patient tumor was retained in PDX (Pearson r=0.88) and in xenoline (Pearson r= 0.63), as well as preservation of enriched signaling pathways (FDR Adjusted P<0.05). Both xenoline (IC50= 200nM) and PDXs did not respond to MEK inhibitor recapitulating patient insensitivity to similar treatments in the clinic. Multi-omics data integration was used to deduce potential actionable pathways (FDR<0.05) including; KEGG01521, KEGG05202, and KEGG05200.

Conclusion: This set of PDX and stable xenolines will serve as a preclinical resource for developing novel therapeutics for rare APXA and other pediatric high-grade gliomas bearing the BRAF fusion.

Translocation RCC: Progression-Free and Overall Survival by Tumor Stage and Surgical Procedure at a High-Volume Academic Center

Drake CJ, Farrow JM, Bahler CD, Sundaram CP

Background: Translocation Renal Cell Carcinoma (RCC) is a rare variant and is estimated to represent 2-5% of RCC diagnoses. Prior studies characterizing the clinical behavior of translocation RCC are limited and stage-by-stage prognostication for adult patients remains uncertain.

Methods: Patients diagnosed with localized translocation RCC that underwent either partial or radical nephrectomy between 2004 and 2021 were reviewed. Standard clinico-pathologic characteristics were included. Progression-free and overall survival were estimated using Kaplan-Meier curves. Non-parametric tests in SAS were used, with statistical significance set at 0.05.

Results: A total of 59 patients were identified. Age at surgery and body mass index were balanced across pathological stage. Tumor complexity increased with stage, as did adverse pathological features (Fuhrman Grade 3-4, lymphovascular invasion, and margin positivity). Both progression-free and overall survival were worse with higher stage disease. Of note, low-stage disease had favorable long-term survival, approaching 90%; there was no difference in overall survival between partial or radical nephrectomy for low-stage disease.

Conclusion: Translocation tumors predictably demonstrate worse pathological features with stage progression. Interestingly, those patients with low-stage disease had durable treatment responses with either partial or radical nephrectomy, suggesting minimally invasive approaches may be preferred to limit perioperative morbidity without sacrificing oncologic outcomes.

Participatory Design and Development of a Mobile App to Improve Kangaroo Mother Care in Kenya Using the People at the Center Of Mobile Application Development (PACMAD) Framework

Young A, Dolan M, Esamai F, Purkayastha S, Bucher S

Background: Prematurity is the leading cause of death worldwide for children under five. 15 million babies are born prematurely each year, and 2.4 million children die during their first month of life. Neonatal hypothermia is a contributing factor, particularly in low-and-middle income countries (LMICs), where incubators may be less available or overcrowded. To address the global burden of neonatal hypothermia among premature infants, the NeoInnovate Collaborative Consortium has developed a suite of innovations to provide automated thermal support and facilitate the uptake of and compliance to Kangaroo Mother Care/Skin-to-skin care (KMC/STS). This integrated intervention features a wearable baby warmer ("NeoWarm") and a suite of smart-phone applications to increase access to KMC/STS, as well as provide vital sign updates to healthcare workers. We describe on-going multidisciplinary efforts to utilize human-centered participatory design techniques to develop a feasible and acceptable mobile phone app ("NeoRoo") for parents and healthcare providers of premature infants in LMICs.

Methods: Participatory design is a human-centered design technique that involves stakeholders in the design process itself, with the goal of creating a solution that better addresses users' needs and context. For this study, 10 healthcare workers and 10 parents of premature infants from 3 hospitals in Western Kenya will be asked to navigate through the app as they "think aloud" about its features and function. Next, a facilitator will conduct semi-structured interviews while instructing participants to complete tasks. Their responses will be further analyzed using the People at the Center of Mobile Application Development (PACMAD) model.

Conclusion: Integration of direct stakeholder feedback into subsequent iterations of the application is anticipated to increase the functionality and usability of NeoRoo for targeted users. Results will be utilized to further iterate the existing NeoRoo prototypes, and then perform an A/B evaluation.

Candida Rugosa: An Atypical Cause of Vulvovaginal Candidiasis

Crawford JD, Weber L, Wickstrom MJ, Burrow ZM, Neal CM

Case Description: A 20-year-old female presented with recurrent bacterial vaginosis and incomplete resolution of symptoms after treatment. She reported multiple episodes of green vaginal discharge with odor and vaginal pruritus. Her symptoms began two years prior and never completely resolved after treatments with metronidazole. History and physical exam were noncontributory. Vaginal microscopy was normal. Culture and staining showed 1+ Candida albicans and 1+ Candida rugosa.

Conclusion: Because C. rugosa is an atypical pathogen for candidiasis, the treatment plan had to be altered, and the patient was placed on boric acid vaginal suppositories once daily for 14 days. As diagnoses and treatments for typical pathogens are well established, atypical pathogens are a growing problem, due in part to reduced susceptibility to normal treatments for candidiasis.

Clinical Significance: C. rugosa was first isolated in 1917. It is a poorly studied fungus and not typically implicated in vulvovaginal candidiasis (VVC), which is a challenging long term condition characterized by inflammation secondary to fungal colonization. Current challenges to treatment include social barriers to care, azole resistance, and emergence of new fungal species. Identification and research of emerging fungal strains are critical contributions to the literature since these strains are not well studied, continue to arise in practice, and are problematic for diagnosis and treatment. There are few reports in recent literature of patients diagnosed with C. rugosa VVC. However, there are numerous recent studies of C. rugosa using lipase as a means of the fungus' drug resistance, making this an important topic for further research. There have also been a growing number of fungi with similar characteristics identified in recent case

reports. Their susceptibility to antifungals is particularly important as it seems to be an emerging cause of both localized and disseminated fungal infections worldwide.

Multilevel Factors Underlying Adolescent Retention and Disengagement in HIV Care Across Global Settings: A Mixed-Methods Systematic Reviewl

Risk N, Toromo J, Bosma C, Misquith C, Apondi E, Wools-Kaloustian K, Vreeman RC, Enane LA

Background: Adolescents living with HIV (ALHIV, aged 10-19) are at risk for disengagement from care, resulting in poor health outcomes and potential for viral transmission. We investigated multilevel barriers and facilitators to retention in HIV care for ALHIV across global settings to inform strategies to better retain this group.

Methods: We conducted a systematic review of publications between 1994-2022 that reported factors associated with retention or disengagement from HIV care for ALHIV. Our search included terms for concepts of antiretroviral therapy (ART), treatment adherence, and barriers to care. Quantitative and qualitative barriers and facilitators to retention at multiple levels were synthesized using a convergent integrated approach, assessing themes, promising interventions, and needs for research or implementation.

Results: 8,564 records were screened, 333 full-text articles assessed, and 98 included. Studies were conducted in Africa (n=53), the Americas (n=36), Asia (n=5), Europe (n=2), and multiple regions (n=2). Barriers to retention included: older adolescence; female sex; pregnancy; racial, ethnic, sexual, or gender minority status; orphan status; no initiation of ART; advanced immunosuppression; mental health factors; lack of social support; financial challenges; unstable living conditions; nondisclosure of HIV status to the adolescent or household; negative experiences with providers; rural clinic site; school-related factors; and pervasive HIV stigma. Facilitators to retention included: adolescent disclosure; having a family member with HIV; supportive relationships with family or providers; adolescent-friendly services including peer support, dedicated clinic hours, and case management; appointment reminders and follow-up after missed appointments; and financial or social support interventions.

Conclusion: Improving adolescent retention requires addressing multilevel factors associated with disengagement, which reflect multiple axes of social, financial, and medical vulnerability. Beyond provision and scale-up of comprehensive adolescent-friendly services, peer, social, or financial support interventions may be promising to mitigate various challenges across settings. Rigorous intervention studies are needed as well as strategies for implementation and scale-up.

Food Banks and Food Insecurity: A Measure of Hope and Resiliency

Haas AN, Mulcahey CT

Background: Food bank utilization has increased in America due to the COVID-19 pandemic and is closely associated with food insecurity. The very state of being food insecure may affect one's outlook for a better future, their hope, or their ease in overcoming obstacles. To investigate these themes, two food banks in South Bend, IN were surveyed using validated stigma, hope, resiliency, and food insecurity scales. Additionally, special attention was given to the COVID-19 pandemic effects on relationships, given the resource shortage and collective emotional trauma experienced disproportionally by those of lower socioeconomic status.

Methods: This quantitative study was conducted between June-August 2021 in South Bend, IN at the Clay Church Food Pantry and the Food Bank of Northern Indiana. This study included 433 individuals and investigated hope and resiliency between stratified levels of self-reported food insecurity, as well as COVID-19 effects on relationships and quality of life.

Results: Of the total respondents, 33.8% reported being severely food insecure, 26.3% moderately, 23.4% somewhat, and 16.4% had no food insecurity. Hope was measured on the Trait Hope Scale, with a mean hope score of 43.7 (SD=12.9), in the hopeful range. There was no statistically significant difference in hope scores when comparing severity of food insecurity. Post COVID-19 effects on relationships show that family and friend relationships were worse in only 22.1% and 27.6% of respondents, respectively. Quality of life measures, physical health, mental health, and financial situation were worse in 23.5%, 24.2%, and 43.1% of respondents, respectively.

Conclusion: Most local food bank clients are severely food insecure. In addition, these clients rate overall in the "hopeful category." Although food insecurity remains a concern, food bank clients largely did not report negative COVID-19 effects on quality of relationships, physical health, mental health, or financial resources.

Surgeon Values vs Clinical Practice: Do We Assess the Right Clinical Factors when Deciding to Initiate Enteral Nutrition in Surgical Neonates?

Anderson C, Bhatia M, Fisher S, Joplin TS, Hunter-Squires J, Saula P, Gray B

Background: Enhanced Recovery After Surgery (ERAS) guidelines recommend enteral nutrition (EN) initiation within 48 hours following neonatal surgical procedures; however, this practice has not been widely adopted by pediatric surgeons. We aimed to understand if surgeon-ranked patient factors were similar to observed clinical factors when initiating EN in surgical neonates.

Methods: Following institutional review board approval, neonates (admitted at <30 days) treated at a quaternary referral center in July 2021 (n=10) were enrolled in an observational study. Clinical factors and nutrition status were recorded electronically for 30 days or until discharge. Results were analyzed using SPSS 27 and SAS 9.4, with $p<0.05$ indicating significance. Concurrently, pediatric surgeons and fellows from this and a neighboring institution (n=10, response rate 67%) completed an online survey to assess their feeding practices in surgical neonates.

Results: Patient diagnoses included congenital diaphragmatic hernia (n=2), gastroschisis (n=4), spontaneous intestinal perforation (n=3), and umbilical cord hernia (n=1). The average time until EN initiation was 11.2 ± 14.0 days. Only two neonates received EN within 48 hours of their operation. Univariate analysis demonstrated that top clinical factors predictive of EN administration were passage of stool (OR 12.99 [5.95-27.78], $p<0.001$) and hemodynamic stability (OR 8.62 [2.07-35.71], $p=0.003$). On average, surgeons (n=8) ranked hemodynamic stability and gastric tube output volume as the top two essential factors, respectively. When multiple clinical factors were combined in stepwise multivariate regression, stool within the past 24 hours (OR 27.02 [8-125], $p=0.022$), lower gastric tube output volume (OR 0.85 [0.79-0.90], $p=0.032$), and higher postoperative day (OR 1.09 [1.04-1.15], $p=0.001$) were significantly associated with EN.

Conclusion: Surgeon ranking of patient factors for initiation of EN did not exactly match clinical observations, emphasizing the subjectivity of the decision. Goal-based nutrition protocols may reduce variability and ambiguity when advancing neonatal nutrition.

Intramedullary Nailing Achieves Comparable Reductions to Plate Fixation in Complete Intraarticular Distal Femur Fractures

Poirier JL, Lopas L

Background: Intraarticular distal femur fractures (AO/OTA type 33C) are an uncommon and challenging injury to treat. Achieving adequate reduction while minimizing soft tissue injury requires balancing potentially competing interests. Traditionally, 33C type injuries have been treated with various plating constructs due to the belief that adequate reductions could not be obtained or maintained with alternative methods. Intramedullary nailing (IMN) is potentially more biologically favorable and is preferred to plate fixation in a variety of different orthopedic injuries. The purpose of this study is to evaluate the quality of the reduction obtained for 33C type injuries when treated primarily with a plate vs IMN.

Methods: This retrospective study identified patients 17 years of age who sustained a 33C type fracture from 2013-2020. Patients with incomplete radiographic follow-up were excluded from the study. 42 patients who underwent plating and 142 patients who underwent IMN met criteria. Patient demographics and radiographic data including posterior distal femoral angle (PDFA) and lateral distal femoral angle (LDFA) were collected. T-Tests and descriptive statistics were performed to assess difference; significance was set at $p=0.05$.

Results: Mean PDFA at most recent radiographic follow-up was not different between plating and IMN (82.8 vs 83.1, $p=0.706$). Mean LDFA at last follow-up was not different between plating and IMN (81.9 vs 82.8, $p=0.2684$). Mean follow-up for the plating cohort was 366 days and 307 days for the IMN cohort ($p=0.3178$).

Conclusion: Both radiographic measures showed no difference between the alignment obtained between IMN and plating. This suggests that based on radiographic alignment, plating and IMN may be similar. Future studies will compare the difference in LDFA and PDFA from initial postoperative imaging to last known follow-up as well as evaluate for differences in patient reported outcomes.

Instability Risk Factors for Conservative Therapy-Refractory Chronic Lateral Ankle Instability

Poirier JL, Porter D

Background: Most acute lateral ankle sprains are treated nonoperatively; however, up to 20% of acute sprains develop Chronic Lateral Ankle Instability (CLAI) requiring surgical reconstruction. CLAI risk factors have not been analyzed in the context of a multifactorial system. This study aims to identify a model to identify patients who are at increased risk for CLAI after acute lateral ankle sprains utilizing clinical and radiographic findings.

Methods: This retrospective study identified 78 patients who presented with acute lateral ankle sprains and 50 patients with CLAI who underwent lateral ankle reconstruction (LAR), diagnosed between 2010-2020. Patients' clinical exam findings and radiographic data were collected. Descriptive statistics were utilized to determine difference; significance was set at $p<0.05$.

Results: Of 50 CLAI patients who failed conservative therapies and required LAR, 48% had a clinical diagnosis of lateral ankle impingement (LAI) as compared to 18% of acute sprains ($p=0.0003$). A clinical diagnosis of subtalar instability was made in 32% of CLAI patients as compared to 2.5% of acute sprains ($p=0.0001$). Assessment of calcaneal pitch yielded a significant difference between CLAI [$\mu=30.7$, median=30.9] and acute sprains [$\mu=25.8$, median=25.8] ($p<0.0001$).

Conclusion: Clinical diagnosis of LAI is a significant risk factor for developing CLAI necessitating LAR. Furthermore, subtalar instability is a difficult clinical diagnosis that is nonetheless a significant risk factor for developing long term CLAI. High calcaneal-pitch angle is associated with CLAI and can be a prognostic indicator after acute sprain encounters. The presence of any of these risk factors at time of acute LAS necessitates closer patient follow-up, monitoring, and more extensive preventative intervention. Future studies aim to identify candidates for early surgical intervention.

Variables Contributing to Missed Appointments in a Free Clinic

Stoll K, Black M, Hopf B, Nunez A, Smeltzer K

Background: In a free clinic, missed primary care appointments often result in the absence of prevention and treatment of chronic diseases. Underserved communities are particularly vulnerable, and providers for this population have an obligation to contact patients for follow up and aid. Mollie Wheat Memorial Clinic (MWMC) performed a qualitative study to evaluate variables contributing to missed appointments. The results of this study can serve as a benchmark for deriving solutions used to provide a high quality of care to the Wabash River Valley.

Intervention/Innovation: MWMC is a student-run clinic open every other Saturday. Patients who presented from February 2021 to April 2022 with an appointment ("show") or as a walk-in ("walk-in") were surveyed on barriers to care and demographics. Patients who failed to present for a scheduled appointment ("no-shows") were contacted via phone for a brief interview highlighting reasons for missing the appointment. Comparisons between "show" and "no-show" groups were made to evaluate variables contributing to missed appointments.

Results: 53 "show/walk-in" patients have been surveyed and 6 "no-show" patients have been interviewed. Preliminary data analysis of surveys has highlighted several variables patients encounter when trying to attend appointments. Phone interviews have provided insight on ways that MWMC can work to mitigate some of the challenges patients are facing.

Conclusion: Transportation, lack of internet access, proximity to affordable healthcare, and socioeconomic status were all variables encountered by our patients. Since access to care at the clinic was presumably affected as a result, we proposed the introduction of a text message system reminding patients of their scheduled appointment and new clinic hours that differ from what we currently offer. The text messaging system was recently implemented, and missed appointments are repeatedly tracked to evaluate efficacy.

Acute Urinary Retention Seen in a Pediatric Male Patient After the Administration of Afrin During Intra-arterial Chemotherapy

Smith TE, Kritzmire S, Tejada JG, Martinez ML

Case Description: A 3-year-old male patient underwent selective ophthalmic artery infusion chemotherapy (SOAIC) for retinoblastoma (RB). A "generous amount" of intranasal oxymetazoline (INO) was administered via both nostrils after intubation. The patient underwent SOAIC twice without incident or adverse complications. After the third session, the mother of the patient noted he had issues with voiding over the next 24 hours, which eventually resolved on their own. The same experience was noted after SOAIC #4. However, the patient was unable to obtain relief from his symptoms and was taken to the emergency room, where a postvoid residual volume of >200 mL was noted. The symptoms resolved on their own. Prior to SOAIC #5, the parents brought this to the attention of the team. After completion of the procedure, the patient underwent straight catheterization and was kept for a period of observation. After awakening, the patient immediately complained of an inability to urinate and was found to have a postvoid residual volume of 100 mL. Upon returning home, the patient continued to have voiding issues and was subsequently prescribed Tamsulosin 0.4 mg daily. Approximately two hours after administration, he was able to urinate normally. The patient required three days of treatment with Tamsulosin.

Conclusion: Adverse events from adjunctive techniques used to optimize outcomes of SOAIC for the treatment of RB are rare. In the case of our patient, we suspect that oxymetazoline's affinity for adrenergic receptors played a role in the voiding dysfunction.
Clinical Significance: Although adverse events following INO administration during SOAIC procedures for RB are rare, increased awareness of adverse effects can help with prevention and/or treatment. Moreover, there is a need for more research pertaining to the pharmacokinetics, dosing, adverse effects, and benefits of common adjunctive agents being used in SOAIC.

Caregiver Experiences with Accessing Sickle Cell Care and the Use of Telemedicine

Feliciano A, Jacob SA, Daas R, LaMotte JE, Carroll AE

Background: Sickle cell disease (SCD) is associated with a wide range of complications. However, a multitude of barriers prevent SCD patients from receiving adequate healthcare, including difficulties with transportation and lack of provider knowledge about disease sequelae. Importantly, studies have demonstrated the benefits of telemedicine in addressing barriers to healthcare. While previous studies have identified barriers to care through quantitative methods, few studies have explored barriers which affect the pediatric SCD patient population in the Midwest, wherein the geographical landscape can prohibit healthcare access. Furthermore, few studies have established acceptability of telemedicine among caregivers and patients with SCD.

Methods: This study aims to increase understanding of barriers to care and
perceptions of telemedicine by caregivers of pediatric SCD patients in a medically under-resourced area in the Midwest. Researchers conducted semi-structured interviews with caregivers of children with SCD. The interviews were audio-recorded and transcribed. Thematic analyses were performed.

Results: Researchers interviewed 16 caregivers of 15 children with SCD. Thematic analyses of the interview transcripts revealed four broad themes regarding caregiver burden/stress, both facilitators and barriers to SCD healthcare, and general thoughts on the acceptability/usefulness of telemedicine.

Conclusion: This qualitative study describes common burdens faced by caregivers of SCD, barriers to and facilitators of SCD care in the Midwest, and caregiver perceptions of the usefulness and efficacy of telemedicine for SCD care.

Characterization of Voluntary Social Distancing and Vaccination Trends Among Workers From May 2020-June 2021

Waggoner C, Gidley S, Garcia K

Background: Vaccine hesitancy has become an important topic of discussion during the COVID-19 pandemic. The purpose of this study was to determine the relationship between early adherence to COVID-19 mitigation measures (before vaccine availability) and later vaccination status (after vaccines were widely available) in the Southwest Indiana workforce population.

Methods: This study focused on secondary analysis of existing data from two surveys of the same workforce population, spanning manufacturing, finance, healthcare, and service industries. As part of a COVID-19 prevalence study conducted in May 2020, participants were asked to provide information about demographics, social distancing behaviors, and health status. As part of a follow-up study conducted in June 2021, the same cohort was invited to complete an online survey focused on mental health. The latter survey also asked participants to report information about their work environment and vaccination status. Groups were compared using Chi Square and Kruskall-Wallis or Mann-Whitney U where appropriate.

Results: Significant differences in age ($p=0.016$) and education ($p=0.011$), but not rurality (rural, rural/mixed, or urban county based on zip code of residence), were observed between the vaccinated and unvaccinated groups. Furthermore, comparison of vaccinated and unvaccinated groups found significantly different responses to the degree of social distancing self-reported in early 2020.

Conclusions: Consistent with previous studies, we found that demographic characteristics such as age and education may influence vaccination status. Furthermore, our data suggest an association between willingness to socially distance at the beginning of the pandemic and willingness to receive the COVID-19 vaccine.

Sexual Dysfunction in Male Childhood Cancer Survivors (CCS) and Adolescent and Young Adult (AYA) Survivors of Hematologic Malignancies

Crist N, Bernie H

Abstract: Sexual health is an important aspect of overall health and quality of life (QoL) among adolescents and young adults (AYA), as well as childhood cancer survivors (CCS). Sexual health encompasses the psychosocial, physical, developmental, emotional, and relationship factors that impact sexual function. Cancer and its associated treatments are associated with negative effects on sexual health, body image, and relationships, as well as overall physical and mental health. Data shows that CCS are known to experience diminished QoL compared to their peers. However, limited information is available to guide the assessment and treatment of sexual dysfunction (SD) in AYA and CCS. Further, exploration into specific cancer types, treatment methods, and their resultant effects on sexual function within these populations is far more limited. We conducted an extensive review of the literature that focused on SD in male survivors of hematologic malignancies (HM). Our review identified an increased incidence of SD within male AYA and CCS of HM, and the negative impact this has on overall QoL. Our results show the degree to which survivors of HM experience increased SD, and the therapies and pathophysiologic mechanisms that may contribute to the development of SD within this population. These findings highlight the lack of research on this topic and the need for further exploration into AYA and CCS sexual health to improve patient care and close the knowledge gaps to better assess and treat SD in this patient population.

Systems Modeling of Gut Microbiome Regulation of Estrogen Receptor Beta Signaling in Ulcerative Colitis

Trinh A, Munoz J, Cross TW, Brubaker D

Introduction: A sex-bias exists in ulcerative colitis (UC), a chronic inflammatory disorder in the colon, with men 20% more likely to develop UC. A possible explanation for the difference is the anti-inflammatory and epithelial-protective role of estrogen signaling via estrogen receptor beta (ESR2) in the gut. To understand microbiome regulation of ESR2 signaling in UC, we developed a partial least squares path modeling (PLS-PM)-inspired microbiome multi-omic modeling framework.

Materials and Methods: Gut metabolomic, colorectal transcriptomic, and stool 16S rRNA-seq data from 35 unique UC or non-IBD controls subjects were obtained from the Inflammatory Bowel Disease Multi-Omics Database. We built regularized sparse PLS regression (sPLSR) models predicting ESR2DN scores from 16S or metabolomic data. A linear regression meta-model with independent variables consisting of patient LV scores of metabolites and 16S data variables, sex, and UC status was built to predict ESR2DN activity. Significance testing on regression coefficients identified LV interactions synergistically predictive of ERb pathway activity.

Results and Discussion: The meta-model was significantly predictive of ESR2DN pathway activity, implicating main effects of microbiotaLV1 ($p = 0.004$), metabolitesLV2 ($p = 0.004$), and diagnosis and the interaction effects of metabolites:microbiotaLV1 ($p = 0.005$), microbiota:UC in LV1 ($p = 0.014$), microbiota:sex in LV2 ($p = 0.017$), and metabolites:UC in LV2 ($p = 0.035$) in predicting ESR2DN pathway status. Utilizing the metamodel and loadings from sPLSR, many interesting metabolites were identified via spearman correlation of highly-loaded taxa and metabolites and Mann-Whitney tests of metabolite abundance by sex or disease status. L-histidine, a metabolite predicted by our model to have a differential effect on ESR2 activity based on patient sex, was validated in literature to show association with reduced colonic inflammation.

Conclusions: We demonstrated the effectiveness of a PLS-PM based meta-model for modeling relationships between host signaling and microbiome multi-omics data and quantified significant multi-omic microbiome interactions that can aid in identifying new therapeutics for UC.

Progression of Paraneoplastic Vitelliform Retinopathy: A Case Study

Minturn R, Minturn J

Case Description: A 62-year-old patient with metastatic cutaneous melanoma presented with difficulty seeing at night and blurring of vision, OS > OD. He had a past medical history of prostate cancer with no pertinent ocular, cardiovascular, or smoking history. Best-corrected vision at the initial visit was 20/30 OD and 20/25 OS. Indirect ophthalmoscopy showed evidence of multiple flat subretinal yellow foci, suspicious of vitelliform dystrophy. At 2-week follow-up, the patient noted persistent difficulty in low light and difficulty accommodating. Best-corrected vision worsened to 20/60 OS and indirect ophthalmoscopy showed increased layering of subretinal material in the inferior macula. At 8-month follow-up, the patient had no significant vision changes; however, best-corrected vision showed improvement to 20/25 OS. Indirect ophthalmoscopy showed resolution of the material in the inferior macula and continued absence of choroidal metastasis. However, there was presence of new lipofuscin material in the superior macula. At 26-month follow-up, the patient noted no significant vision changes, no changes in visual acuity, and complete resolution of subretinal deposits. This was the last visit with the patient, unfortunately, the patient passed 8 months later.

Conclusion: Paraneoplastic vitelliform retinopathy is a rare autoimmune phenomenon caused by antibodies targeting cancer cells which cross-react causing degradation of bipolar cells, rods, and cones leading to deposition of lipofuscin in the subretinal space. While it may lead to visual distortion, visual acuity changes are transient and resolve on their own as the lipofuscin deposits resolve.

Clinical Significance: Here, we reported the progression and subsequent regression of the macular-associated retinopathy over the course of a 2-year follow-up. While clinically paraneoplastic vitelliform retinopathy leads to visual disturbances such as vision color change, visual distortion, and blurred vision, given time it will regress without intervention. In this case, visual changes were mild with full resolution of subretinal deposits.

Non-metastatic Colon Cancer Model C26 Upregulates Glycolysis in Osteocytes in vitro and Bone in vivo

Tollar MR, Prideaux M, Pin F, Bonewald L

Background: Developing effective treatments for musculoskeletal complications in cancer patients requires understanding metabolic effects of cancer on bone, and particularly osteocytes, the most abundant bone cell and key regulator of bone remodeling. However, little is known regarding how cancer impacts normal osteocyte energy metabolic pathways, such as glycolysis. Given that changes in metabolism are important regulators of cellular function, it is essential to determine how osteocyte metabolism is disrupted by cancer and how this may impact skeletal and whole body health.

Methods: Mice inoculated with saline (N=5) or C26 cells (N=6) were sacrificed after 2 weeks. Bones were harvested for metabolic profiling by GC-MS, gene expression by RT-PCR, and bone morphology by μCT. Differentiated IDG-SW3 osteocyte-like cells were cocultured with C26 cells for 12-24hrs and metabolites and gene expression analyzed by GC-MS and RT-PCR.

Results: Trabecular bone mass was significantly decreased in the C26 mice. GC-MS analysis revealed decreased glucose in C26 mice tibiae, but no change in lactate. The bone resorption promoting gene Rankl was upregulated, whereas the inhibitor Opg was unchanged. Bone mineralization regulators Mepe and Phex were decreased. In vitro metabolic studies revealed increased glucose and lactate in IDG-SW3 cell lysate; culture media glucose levels were decreased whereas lactate was increased in the co-cultures with C26 cells. RT-PCR demonstrated increases in the glycolysis promoter Hif1-alpha in addition to glycolysis pathway genes including Glut1, Hk2, Slc16a3 and Pdk1. Rankl was also increased in the IDG-SW3 cells co-cultured with the C26 cells whereas Opg, Phex, and Mepe were downregulated.

Conclusion: Glycolysis is upregulated in mouse bone and in vitro IDG-SW3 cells exposed to cancer. Our study provides novel understanding for how cancer affects bone metabolism. Integrating these results with whole body metabolism will aid in the development of novel therapeutic strategies to target musculoskeletal and systemic complications of cancer.

The Importance of Sleep in Total Joint Arthroplasty: A Review

Gregory B, Deans C, Stahl SM, Buller LT

Background: Total joint arthroplasty (TJA) procedures are among the fastest growing and most cost-effective surgeries in the US. With the desire to optimize outcomes, the association of sleep and TJA has relatively little focus and requires proper assessment. This review serves to assess the current state of the literature regarding sleep in the perioperative period: importance of sleep, etiologies of sleep disturbance, and pre-operative, intraoperative, and postoperative interventions that may improve our patients' sleep quality and duration after surgery.

Methods: A review of the literature was conducted using the PubMed database. A total of 120 articles were used wherein inclusion criteria was determined based on the relevance of content pertaining to TJA and sleep. Preference was placed towards articles of recent publication.

R**esults:** Disturbances in normal sleep structure related to comorbid conditions and surgical intervention play a multifactorial part in TJA recovery, most notably with pain perception. Sleep and pain act in a bidirectional fashion, whereas a decline in one adversely affects the other, and vice versa. Several aspects play a role in sleep quality such as perioperative pain, alteration in sleep structure, and the body's physiologic response to surgery. Improvements of sleep focus on perioperative pain control, the type of anesthesia used, environmental conditions, and pharmacologic intervention, as well as cognitive therapy and meditation.

Conclusion: The findings from this review indicate the importance of sleep on recovery and outcomes in patients undergoing TJA. While sleep is a complex process, modifications to enhance sleep and thus decrease pain may prove to be a beneficial and necessary intervention in improving overall outcomes.

Relationship of Speech Language Pathology with Physical Outcomes in Spinal Cord Injury Patients with Cognitive-Communication Limitations and Traumatic Brain Injury: The SCIRehab Project

Leonard PM, Littell K, Whiteneck G, Foster J

Objective: Examine the impact of speech therapy (SLP) services on physical outcomes with acute traumatic spinal cord injury (SCI) during acute inpatient rehabilitation with concurrent diagnosis of cognitive-communication limitations (CCL) and traumatic brain injury (TBI).

Methods: Using the SCIRehab database from six participating rehabilitation centers, comparison was done with patients who had SCI with CCL that received SLP services during their acute inpatient rehabilitation stay and those who did not receive SLP. A propensity analysis was used to control for heterogeneity of the initial groups with n= 190 in each paired group. A subset was then completed to include the diagnosis of TBI with concurrent CCL, n=85 in each pair.

Results: Data was obtained from the SCIRehab database using a propensity score analysis and analyzed with a logistical regression model with variable predictors, including admission cognitive and physical FIM, ASI neurologic group, total PT/OT hours, and several other metrics. Patients receiving SLP were randomly matched with similar controls, forming nearest neighbor pairs. In total, for SCI/CCL with and without SLP, there were 380 subjects or 190 matched pairs for primary analysis. Pairs were formed similarly in the SCI/CCL+TBI group forming 85 pairs, or 170 subjects with and without SLP.

Differences in FIM motor scores between admission and discharge were analyzed using a one-sample t-test. In the SCI/CCL group, no significant difference was found in motor FIM improvement, with a p-value of 0.72. Similarly, with the SCI/CCL+TBI group, no significant difference was found in motor FIM improvement, with a p-value of 0.87.

Conclusion: SLP remains an important tool in the care for SCI and TBI patients with and without CCL. Though the impact of SLP was not shown in motor FIM improvement in this study, future studies may be better able to associate such treatment with improved outcomes.

Acknowledgements and Funding

We extend our deepest gratitude to Anne Nguyen, Dr. Brittney-Shea Herbert, and the Indiana Medical Student Program for Research and Scholarship (IMPRS) for their support and guidance since the founding of this journal. We also would like to recognize the Department of Medicine, the Department of Pediatrics, and The Indiana Clinical and Translational Sciences Institute (CTSI) for their generous contributions.

This publication was made possible with support from the Indiana Clinical and Translational Sciences Institute funded, in part by Award Number UL1TR002529 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.