Validating Within-Limb Calibrated Algorithm Using a Smartphone-Attached Infrared Thermal Camera for Detection of Arthritis in Children

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Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease in children. It causes joint swelling and stiffness and can last for months to years. Current methods to screen for JIA include Magnetic Resonance Imaging (MRI) and Musculoskeletal Ultrasound, both of which are often time-consuming and expensive. Using our developed thermal imaging algorithm, the ability to screen for JIA would become more accessible, affordable, and less time-consuming to kids and their families. The goal of our study was to determine if using a smartphone-attached thermal camera was reliable for image detection of arthritis in children. We also wanted to test the effect that physical activities, such as walking, would have on lower extremity temperature data within our imaging algorithm. Using an industrial-grade thermal imaging camera, we took thermal images of the lower extremities from the anterior, posterior, medial, and lateral views. We also repeated this using the smartphone-based thermal imaging camera. The temperature data was extracted from the thermal images and analyzed for temperature fluctuations in the regions of interest. Even though the smartphone-attached camera had lower resolution and less precision than the industrial-grade camera, both performed well in their sensitivity and specificity to detect the inflamed joints compared to the common standard of doing a physical joint exam. In addition, the cohort which performed physical activity demonstrated significant temperature changes which were consistent over time and did not return to pre-activity levels. The results of this study show potential for faster and more accessible JIA imaging platforms in the future.

How to Measure School Functioning in Youth with Chronic Pain During a Pandemic: A Topical Review of Evidence-Based Assessment Tools

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As many as 1 in 4 children suffer from chronic pain. Around 5% of children with chronic pain experience severe pain-related disability, which can impact nearly all aspects of daily life. Youth with chronic pain are more likely to experience chronic school absenteeism and bullying than their healthy peers. Most recently, the Covid-19 pandemic has drastically changed school experiences for youth across the U.S. due to prolonged school closures and changes in school policies. However, the impact of these policy changes on the school experiences of youth with chronic pain is largely unknown. The purpose of this study was to conduct a topical review in order to identify evidence-based assessment tools for evaluating school functioning in youth with chronic pain that would be appropriate for use in the context of the ongoing pandemic. We reviewed abstracts to identify manuscripts that met the following inclusion criteria: a) peer-reviewed paper, b) published in the last 20 years, and c) had a stated aim to evaluate school functioning in youth with chronic pain. We identified 10 papers that met our inclusion criteria. We extracted 13 separate measures of school functioning, which we classed into six domains including: school attendance, academic performance, perceived academic competence, frequency of school nurse visits, dissatisfaction with school, and receipt of special education services. Results from our topical review indicate that there are several existing, evidence-based measures of a wide variety of domains of school functioning. In terms of evaluating school functioning during the pandemic, we recommend administering measurement of multiple domains (rather than a focus on a single domain). All of the objective domains have become harder to accurately assess throughout major widespread crises such as a pandemic. Further research
is needed to develop an objective domain that is able to fit the nuanced experience of school.

**Smart Asthma-Inhaler**

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**Response Following Use of VetChange**

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Asthma, a chronic disease of the lungs, affects approximately 262 million people and caused 461,000 deaths worldwide, just in 2019. Asthma can result in frequent emergency department visits, hospitalizations, and premature deaths. To effectively manage their condition, asthma patients need to accurately track their medication usage. But it is a manual task, prone to human error. To improve the lives of asthma patients, we built a smart asthma-inhaler system to automatically record patients’ use of medication. Our system is made of a Bluetooth-enabled inhaler, a smartphone app, and a Bluetooth-enabled wearable sensor. The inhaler records when the patients took their medications and sends the data to the smartphone app. The app retrieves weather information including temperature, humidity, and air quality index from the web. The wearable sensor measures the particulate matter in the air surrounding the patient when the inhaler was used. This system should allow patients to accurately record when and why they used their inhalers. Physicians can then use this information to better diagnose and treat asthma. We hope to marketize this system to mitigate the damages of asthma.

**Renal Outcomes in Post-Liver Transplanted Patients Treated With Tenofovir Alafenamide Compared With Tenofovir Disoproxil Fumarate and Entecavir**

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Liver transplantation (LT) is the only curative treatment for advanced chronic hepatitis B (CHB), however, these patients are at significantly higher risk of developing chronic kidney disease (CKD) post-LT. Therefore, it is important to understand the renal impacts of life-long antiviral therapies for CHB, commonly including tenofovir alafenamide (TAF), tenofovir disoproxil fumarate (TDF), and entecavir (ETV). To study this, I conducted a retrospective cohort study in collaboration with five multinational LT centers of 298 LT recipients who received TAF (n=112), TDF (n=51), or ETV (n=135) monotherapy for at least 12 months post-transplant. To measure changes in renal function, I analyzed CKD stage and estimated mean glomerular filtration rate (eGFR, mL/min/1.73 m²) data, where higher eGFR indicates better renal function. I found that at baseline, TAF patients compared to TDF and ETV patients were older (P=0.02), had higher rates of hypertension (P=0.048), and had lowest eGFR (P=0.01). However, from baseline to the 24th month of follow-up, the proportions of patients with normal renal function (CKD stage 1) and mild renal impairment (stage 2) remained stable for the TAF and TDF groups but significantly shifted towards poorer renal function in the ETV group (CKD stage 1: 35.56% to 18.18%, P=0.002; stage 2: 35.29% to 49.59%, P=0.006). TAF patients also had the smallest decline in mean eGFR from baseline to the 24th month of follow-up (1.46 vs. 2.97 (TDF) vs. 4.57 (ETV)). In conclusion, I found that patients treated with TAF had baseline characteristics correlated with poorer renal function, however, their CKD stages remained stable and had the smallest eGFR decline throughout follow-up. These trends reveal an interest in further investigating the renal impacts of TAF treatment in post-LT patients.
Type of Immunosuppression Matters: Efficacy of Immunotherapy in Immunosuppressed Merkel Cell Carcinoma Patients

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Merkel cell carcinoma (MCC) is a rare skin cancer with a high propensity for recurrence. Persons with chronic immunosuppression have a higher risk of developing MCC and a more aggressive disease course. Immuno-therapy treatment enhances the immune system’s ability to fight MCC and is associated with improved disease-specific survival. However, the immunotherapy efficacy in immunosuppressed MCC patients is not well categorized. This study explores and aims to compare differences in immunotherapy efficacy between different forms of immunosuppression, and between immunocompetent versus immunosuppressed MCC patients. In this project, I determined the patient cohort from a Seattle-based prospective registry of 1,529 MCC patients and identified 36 patients treated with immunotherapy and who had chronic immunosuppression. I collected treatment response data from medical records, and analyzed the results. Of the 36 patients, 13 patients (36%) had a complete response (CR), 3 patients (8%) had a partial response (PR), and 20 patients (56%) had progressive disease (PD). Disease progression and survival status varied greatly among different types of immunosuppression. Five types of chronic immunosuppression were represented in these 36 patients and were evaluated for an objective response (CR or PR): chronic lymphocytic leukemia (CLL, 3/13, 23%), autoimmune disorders (AD, 3/9, 33%), solid organ transplant (SOT, 2/4, 50%), HIV/AIDS (2/3, 67%), and other hematologic malignancies (OHM, 6/7, 86%). In comparison, in a study of immunocompetent patients, 28 of 50 (56%) had objective responses to immunotherapy. Toxicities were also high in immunosuppressed patients, as 9/36 (25%) patients stopped treatment due to toxicities. Immunotherapy efficacy in patients with chronic immunosuppression appears to be dependent on the type of immunosuppression. While there is reason for optimism for patients with certain types of immunosuppression, MCC treatment for patients with CLL remains a major concern.

Efficacy of Novel Insulin Tablets on Reducing Blood Glucose

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Insulin release normally leads to the reduction in blood glucose levels; type 1 diabetes mellitus is a disease caused by a lack of insulin production by the pancreas that affects millions of people around the world. Diabetic patients are tasked with injecting insulin daily to support optimal blood sugar levels. Recently, a gastric-resistant fast dissolving tablet form of insulin has been synthesized, which can ease the process of intaking insulin. The purposes of our in vivo studies are to test the efficacy of the novel oral insulin formulation in lowering blood glucose levels and to compare the blood glucose lowering effects of oral versus conventional subcutaneous insulin. We hypothesized that the oral administration of the novel insulin will reduce blood glucose levels more efficiently than both oral and subcutaneous administrations of conventional, non-encapsulated insulin since the insulin tablet mimics the pathway of natural insulin release within the body. We used a rodent model using a sample size of 10 mice to test the pharmacodynamic effects of the novel insulin - in other words, how the formulation affects the body. To do so, I compared the efficacy of the novel insulin to conventional insulin through insulin tolerance tests using intraperitoneal injections of the administration of novel insulin of 1 U/kg body weight. Furthermore, I performed glucose tolerance tests using an oral gavage to analyze the time course for normalizing blood glucose levels. We expect preliminary results to show a statistically significant difference in effectively lowering blood glucose levels in response to the novel formulation relative to the conventional insulin. The results of these studies are crucial to determining proper dosing concentrations and viable insulin administration schedules that can aid prospective human clinical trials.
GHSR-1a Modulates Tumor-Induced Lipid Oxidation Independently of Ghrelin in Cachectic Mice
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Mentor: Jose Garcia, VA PSHCS, Univ of Washington
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Cachexia is a debilitating syndrome that accelerates muscle and fat wasting, affecting up to 80% of cancer patients with no current effective treatment. This condition is associated with weakness, fatigue, and poor tolerance to chemotherapy. Recently proposed as a therapeutic option due to its anabolic effects on preserving muscle and adipose tissue, ghrelin has been reported to attenuate Lewis Lung Carcinoma (LLC)-induced weight loss and lipolysis, also partially regulated by its only known receptor growth hormone secretagogue receptor (GHSR-1a). Tumor-induced lipolysis is associated with an alteration of substrate utilization. However, the extent to which these effects of ghrelin relate to substrate utilization (lipid oxidation and carbohydrate oxidation, LO and COX) remains unclear. This project seeks to determine if ghrelin’s effect on LO and COX in the LLC-induced cachexia model is dependent on GHSR-1a. Adult male C57BL/6J GHSR-1a knockout (KO) and wild-type (WT) mice were treated with or without LLC tumor, then injected with vehicle or ghrelin (0.8 mg/kg). Metabolic parameters were evaluated by the Comprehensive Lab Animal Monitoring System, in which I analyzed LO and COX (calculated mean values and performed statistics). Tumor implantation led to an increase in LO and a decrease in COX in tumor-bearing mice. GHSR-1a KO mice had a greater increase in LO compared to WT, highlighting the receptor’s essential role in maintaining normal levels of LO during cachexia, with no genotype effect for COX. Ghrelin did not prevent the LLC-induced response regardless of GHSR-1a expression, hence its mitigating effects for lipolysis in cachexia are not dependent on the regulation of LO or COX. In conclusion, GHSR-1a plays a role in modulating LO in tumor-induced cachexia, and these effects are independent of ghrelin. More studies are needed to further characterize the pathways involved, including alternative receptors of ghrelin or its adjacent mechanisms.

Regional Identification of Activated Neurons following Brain Immune Cell Inflammation
Connor Chong Rhee, Senior, Biochemistry
Mentor: Kelly Ness, Medicine, Division of Metabolism, Endocrinology, and Nutrition

Microglia, the immune cells of the brain, interface closely with neurons and become activated and inflamed in response to pathogens or neuronal injury. Accumulating evidence suggests that microglia also play a role in a number of diseases and disease pathology, including obesity: when mice are fed a high fat diet (HFD), there is a rapid increase in microglial activation. Blocking this diet-induced microglial activation curtails HFD weight gain in mice compared to controls. Evidence from our lab suggests that HFD microglial activation may moderate diet-induced disturbances in glucose tolerance, possibly via a neuronally mediated mechanism. To test the hypothesis that microglial activation stimulates a change in neuronal activity we generated a mouse model wherein microglia express the hM3Dq (Gq) designer receptor exclusively activated by designer drugs (DREADD). In this model, administration of the DREADD agonist, clozapine N-oxide (CNO) acutely and specifically activates microglia. Mice with the DREADD receptor (Gq+) and mice without the receptor (Gq-) were injected with 5 mg/kg CNO and sacrificed one hour later. The brains were fixed in 4% paraformaldehyde (PFA) and immunohistochemistry for Dapi, GFP, iba1, and c-fos was performed. Matched sections were imaged on a Keyence BZ-X800 microscope and c-fos, an early response gene used as a marker of elevated neuronal activity, was assessed. We anticipate significant regional differences in c-fos expression between Gq+ and Gq- mice, identifying areas of the brain where microglial activation has stimulated downstream neuronal activity. Future studies will investigate these regions-of-interest and demonstrate a novel role for microglia in peripheral glucose homeostasis.