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Reproducibility of Maximum ATP Production Following Isotonic versus Isometric Exercise[†]

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OBJECTIVES/GOALS: This project aimed to investigate differences between isometric and isotonic systems for low and high frequency contractions. Intracellular changes in pH caused by the rate of exercise differ in their effect on PCr. The project assessed the reproducibility between these exercise methods. METHODS/STUDY POPULATION: Four subjects were studied (2F/2M, avg. age 27 years). 31P-MRS spectra were measured in the vastus lateralis (VL) using a 3T MRI scanner using a 31P/1H surface coil. In the isometric studies, the (supine) subjects legs were supported by a wedge pad and restrained by straps over the hips and knee with a resistance strap over one ankle. In the isometric studies, the (prone) subjects legs were fit into machine designed to induce isometric exercise. There were 4 exercise bouts that differed by exercise type and frequency and, consequently, duration. 31P-MR spectra were acquired from a 25mm slab of leg positioned parasagittal along the VL. Analyses were done using jMRUI and R. RESULTS/ANTICIPATED RESULTS: With an increase in sample size, we expect differences between recovery time constants, tau, of PCr between the different exercise frequency groups alluded to by other studies investigating recovery rates in bicep skeletal muscle. From the preliminary data, we obtained large limits of agreement of tau = 0.053 s-1 & tau =-0.074 s-1 from using Bland-Altman analysis. As we increase our sample size, we anticipate that we will see differences of PCr recovery rates between the exercise types as well. DISCUSSION/SIGNIFICANCE: Current studies that investigate the differences in PCr recovery rates between different metabolic states differ in the exercise methods employed on subjects. This study aims to standardize PCr recovery assessment in the VL for more interpretable and applicable assessments of metabolic function.

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Parenting Stress and Drinking to Cope Association with Early Childhood Risk Behaviors*,[†]

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OBJECTIVES/GOALS: Parent stress and coping impacts reward and motivation circuits during child development which influence self-regulation. One well known maladaptive coping response is alcohol or drinking-to-cope (DTC). This study assessed differences in stress and child behaviors among DTC parents as compared to non-DTC parents. METHODS/STUDY POPULATION: Baseline data was used from parents of a 2-5-year-old who were screened for a larger study assessing a mindfulness-based parent stress reduction intervention to improve healthy choices for themselves and their families. The sample included 172 parent-child dyads, mean parent age was 34.4 (6.1) years old, 56.3% white, mean child age was 3.6 (1.2) years old, 52.3% male. Subjective stress was assessed using the Perceived Stress Scale (PSS), parent-specific stress was assessing using the Parenting Stress Index (PSI), DTC was assessed using the COPE inventory, and child behaviors were assessed using the Devereux Early Childhood Assessment. To investigate the differences in stress and child behaviors between DTC parents and non-DTC parents independent samples t-tests were conducted. RESULTS/ANTICIPATED RESULTS: DTC was significantly correlated with PSS (r= 0.23, p<.01), PSI (r= 0.26, p<.01), child self-control (r= -0.16, p= .03), child attention problems (r= 0.22, p<.01), and total behavioral concerns (r= 0.16, p=.04). After excluding those who do not drink alcohol at all, we found significantly higher perceived stress among DTC parents (M= 27.83, SD= 9.79) compared to non-DTC parents (M= 23.79, SD= 8.40), t(80)= 2.02, p= .02. For children, we found significantly higher aggression scores for children of DTC parents (M= 47.16, SD= 31.69) compared to children of non-DTC parents (M=35.83, SD=25.72), t(84)= 1.83, p= .04. And greater attention problems among children of DTC parents (M= 73.97, SD= 26.77) compared to children of non-DTC parents (M= 56.71, SD= 34.09), t(84)=2.63, p=.01. DISCUSSION/SIGNIFICANCE: Stress and DTC may contribute to negative behaviors in children. An intervention designed to decrease stress and increase adaptive coping mechanism in parents could benefit health child socioemotional and behavioral development. Future analyses will examine third variable effects in the relationship between stress, coping, and child behaviors.

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Adaptive Capacity and Preparedness of CTSAs: The Environmental Scan Approach and Findings

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OBJECTIVES/GOALS: Illuminate processes and findings of the Environmental Scan of Adaptive Capacity and Preparedness of CTSAs done by the CTSA Working Group. Share challenges, strategies, and lessons learned for CTSAs to build Capacity to address clinical and translational barriers while responding to emergencies. METHODS/STUDY POPULATION: An Environmental Scan approach for searching, collecting, analyzing and using information from diverse sources regarding CTSA hubs experiences during emergency as related to research implementation, translation, support, adaptation, and preparedness: - Triangulating multiple data sources and mixed methods (e.g., literature review, document/RPPR analysis, and expert review); - Secondary analysis of the JCTS COVID-19 Survey of the CTSAs: challenges, lessons learned, and practices that work in various program components/areas; - Using feedback of CTSA professionals from multiple disciplines to enhance our knowledge of emergency preparedness

and efficient adaptation to public health and other crises. RESULTS/ANTICIPATED RESULTS: The E-scan approach helped identify challenges, successful practices, and evidence-based strategies for building adaptive capacity and preparedness of CTSAs across various scientific sectors of the translational science spectrum. Some of the findings include: - Roadmaps for the creation of new collaborative research resources (biobanks; data repositories, etc.); - Rapid clinical and research decision making during public health crises; - New community-based research strategies to facilitate communication, research dissemination, and participant recruitment based on existing trust-based networks; - Innovative resource allocation to guarantee continuity of training and research opportunities for trainees. DISCUSSION/SIGNIFICANCE: The Environmental Scan of the Adaptive Capacity of CTSA hubs provides useful knowledge and tools to diverse clinical research stakeholders for mitigating the impact of a disaster via adjusting programs, practices, and processes, and building capacity for effective, emergency-ready and responsive research, training, and community engagement.

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Dysfunctional leukocyte mitochondrial metabolism is associated with immune paralysis in critically ill septic patients

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OBJECTIVES/GOALS: The host immune response during sepsis is now recognized to have anti-inflammatory pathophysiology. We aim to determine whether mitochondrial dysfunction of leukocytes predicts which critically ill septic patients develop immune paralysis and to identify differences in cellular metabolites between patients with and without immune paralysis. METHODS/STUDY POPULATION: Critically ill septic and control adult patients were recruited from one of 6 ICUs in a single-center tertiary care academic hospital. After enrollment, peripheral blood mononuclear cells (PBMCs) were isolated from a tube of whole blood on day 0-1 after ICU admission. Flow cytometry to quantify monocyte HLA-DR was performed to determine whether patients were immune paralyzed or not. Mitochondrial functional assays of PBMCs were performed with inhibitors of the electron transport chain to assess for differences in oxidative phosphorylation and glycolysis utilization. Metabolic profiling of cell pellets was performed to evaluate for specific metabolites and pathways associated with immune paralyzed patients. RESULTS/ANTICIPATED RESULTS: A total of 101 patients were recruited, including 62 control and 39 septic patients. 81 patients had immune paralysis status available for analysis. 52% of all recruited subjects were immune paralyzed. Of these, 58% were controls and 75% were septic. Immune paralyzed septic and control patients showed features of reduced utilization of oxidative phosphorylation (ox phos) including reduced basal respiration, ATP production and maximal respiration compared with non-immune paralyzed septic and control patients. Immune paralyzed septic patients showed diminished glycolysis utilization compared with septic non-immune paralyzed patients. Finally, cellular kynurenine and quinolinate levels were low in both immune paralyzed control and septic patients compared with non-immune paralyzed patients. DISCUSSION/SIGNIFICANCE: The PBMCs of immune paralyzed septic patients show evidence of mitochondrial dysfunction, with reduced ox phos and glycolysis utilization. Low levels of kynurenine and quinolinate, metabolite precursors to NAD+, in immune paralyzed

patients may signal key deficiencies and targetable therapeutic avenues for reversal of an immune paralyzed state.

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A Novel High Dose Rate Brachytherapy Device for Preventing Local Recurrence of Pancreatic Cancer Dosimetry Verification

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OBJECTIVES/GOALS: To demonstrate safety and limit damage to off-target organs, we will be determining dosimetry parameters through experimentation and Monte Carlo simulations with our brachy therapy applicator designed to improve upon current designs to treat a 3-dimensional volume. METHODS/STUDY POPULATION: Low-cost materials were used to manufacture our High Dose Rate (HDR) applicator and a readily available after loading system was used to load our configuration with a radioactive source. The dosimetry of our device was analyzed using commercially available software and external beam therapy films to generate depth dose profiles and superficial dose distribution. Additionally, we attempt to confirm Task Group No. 43 (TG-43) dosimetry parameters using Monte Carlo simulations for our device. These data were compared with currently available applicators used for intraoperative radiotherapy. RESULTS/ANTICIPATED RESULTS: We anticipate that we will be able to validate dosimetry parameters for our device in preparation for clinical use. We aim to show our dose distributions align well with proposed target volumes while considering the composition and shape of our applicator. We hope to demonstrate that, unlike current applicators, our design is more effective at treating a 3-dimensional target volume. DISCUSSION/SIGNIFICANCE: By 2040, pancreatic cancer will be the second-largest cause of cancer-related deaths. Even with current brachytherapy applicators, 30-40% of pancreatic cancer seems to recur near the surgical site after surgery. By preventing local recurrence, we hope to improve patient outcomes.

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Convolutional Neural Networks and Machine Learning in the Identification of Ultrasonographic Features of Ovarian Morphology

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OBJECTIVES/GOALS: To develop a two-staged convolutional neural network to identify the ovary and antral follicles within ovarian ultrasound images and determine its reliability and feasibility compared to conventional techniques in 2D and 3D ultrasonography image analysis. METHODS/STUDY POPULATION: De-identified and archived ultrasonographic images of women across the reproductive spectrum (N=500) will be used in the study. These ultrasound images will be labeled by experienced raters to train a two-staged convolutional neural network (CU-Net). CU-Net will first separate the entire ovary from the background and subsequently identify all antral follicles within the ovary. Following