current study presents the optimization of a Comprehensive Rehabilitation Assessment summary report that is used by clinicians to individualize treatment. METHODS/STUDY POPULATION: A multi-aim approach was taken that utilized aspects of various implementation science frameworks. Participants were clinical staff (N = 7; female = 71%). A quantitative survey was used for aims 1 and 2 to assess motives and context around the report as well as evaluate the design of it. Aim 3 focused on optimization via semi-structured interviews. Descriptive and modified content analyses were utilized appropriately for each aim. RESULTS/ANTICIPATED RESULTS: Five versions of the assessment report were created between February 2021 and August 2022, the most recent of was adapted into patients'electronic medical records based on study results. Each report version, participants'results/feedback, and researchers'perceived barriers to this translational process will be discussed. DISCUSSION/SIGNIFICANCE: The current study highlights a replicable approach for optimizing the translation of assessment data into treatment for patients with disorders of addiction.

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Using autism symptom profiles at intervention baseline to predict social cognitive outcomes

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Rush University Authorship has not yet been determined and finalized, but all will be at Rush University.

OBJECTIVES/GOALS: 1) Investigate the utility of pragmatic communication profiles in a sample of children with autism at baseline to predict response to treatment in a randomized clinical trial (RCT) of oxytocin augmentation and social cognitive skills training at week 12. 2) Determine if levels of anxiety or hyperactivity moderate child outcome performance. METHODS/STUDY POPULATION: 40 children (37M, 3F), aged 8-11(M=9.25, SD=1.10), with confirmed autism spectrum disorder (ASD), enrolled in an RCT(NCT02918864) were evaluated at baseline on: an assessment of ASD (Autism Diagnosis Observation Schedule, ADOS-2), a task of perspective taking, Theory of Mind ToM, (Reading the Mind from the Eyes Task), pragmatic communication (Pragmatic Rating Scale-School Aged; PRS-SA), IQ (WAIS_I, WISC-V) and anxiety and hyperactivity (Behavior Assessment Scales for Children-3; BASC-3). A Tobii T60 XL was used for eye-tracking visual patterns and attention during the RMET. The PRS-SA was coded by trained, reliable clinicians. Parent ratings indicated over half of the participants' had At Risk levels or higher on anxiety and hyperactivity on the BASC-3. Week 12 measures included all but the PRS-SA and ADOS-2. RESULTS/ANTICIPATED RESULTS: Baseline preliminary analysis indicated the participants spent more time looking at words (.41ms) than eye images on the RMET(.15ms, p DISCUSSION/SIGNIFICANCE: Findings at baseline suggest pragmatic communication skills are more related to ToM than gaze and attention on the RMET. This relationship will be further investigated over the time of the trial. Mental health indicators need to be considered further in this population. Child profiles at baseline may inform appropriate triage and treatment targets.

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Utilization of machine learning approaches on multimodal and ambulatory data to predict individualized symptom course in adults with obsessive-compulsive disorder.

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OBJECTIVES/GOALS: This study will collect multimodal and longitudinal data in adults with obsessive-compulsive disorder and healthy controls. A mixed effects random forest machine learning approach will be taken to develop a model that can predict individualized longitudinal OCD symptom burden. METHODS/STUDY POPULATION: Baseline resting state functional MRI (rsfMRI) and measures of symptom burden will be collected in adults with OCD and healthy controls. Longitudinal measures of behavior and physiology–such as heart rate, activity, and sleep metrics - will be collected using Fitbit Charge 5 tracker. Daily assessments of symptom burden and functional status will be collected through a smartphone app. Individuals with OCD will start pharmacotherapy during the study period and all participants will be followed for a total of 10 weeks. Repeat rsfMRI imaging will occur at study conclusion. Data will be analyzed using a mixed effects random forest machine learning algorithm with assessment of model performance. RESULTS/ANTICIPATED RESULTS: Prior studies of symptom severity in psychiatric illness and affect in non-clinical populations have found longitudinal features - such as lexical and acoustic measures, participant context, heart rate, and sleep metrics–that were predictive of these states over time. It is anticipated that the present study will extend these results to individuals with OCD and identify physiologic and behavioral features that track personalized symptom burden longitudinally in this patient population. A model able to predict when symptoms are elevated could allow for provision of additional treatment or interventions targeted to times of high symptom burden. DISCUSSION/SIGNIFICANCE: This study will be the first to collect and analyze longitudinal measures of behavior, symptoms, and physiology in patients with OCD with a goal of predicting symptom burden. Identification of elevated symptom burden would allow for implementation of just-in-time treatment, during these periods.

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Waste not, test more: Innovations in tissue processing to expand the testing of clinical specimens

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OBJECTIVES/GOALS: Clinical tissue specimens are primarily destined for formalin fixed, paraffin embedded processing to create a basis for diagnosis by microscopic examination. Innovations in specimen processing are required to expand its availability for inclusion as the substrate in assays that can contribute to the further development of

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Precision Medicine. METHODS/STUDY POPULATION: Transurethral resection of bladder tumors were selected for testing based on availability and tissue composition. A wash step was used to generate daughter aliquots composed of dislodged cells and a solution with prior contact to the parent tissue. This wash step served two purposes: 1) reduce the amount of contaminating material from spreading to other cases, a problem known to be associated with this type of specimen; and 2) create aliquots from which additional informative data could be generated. These daughter aliquots were then examined to determine their value as a source for exosome profiling, metabolomic studies, molecular characterization and organoid development. The parent tissue was not compromised, was able to undergo conventional processing and yielded results equivalent to unwashed specimens. RESULTS/ANTICIPATED RESULTS: Exosomes secreted by the tumor cells were identified to be present in the daughter aliquots by a combination of their isolation using CD31 and detection of miR-21 expression. These exosomes were confirmed to be not related to fragmented cells from testing for beta-tubulin. A global/discovery-based approach using mass spectrometry provided insights into early characterization of metabolomic profiles present in these tumor cells. Ample amounts of high quality DNA (226 ng/ul concentrations; 11.3 ug total) were recovered from the dislodged, excess cells in the wash for molecular studies. Finally, from viable cells recovered in one of the daughter wash aliquots, the ability to grow organoids was proven to be possible and reproducible. DISCUSSION/SIGNIFICANCE: Based on these results, the value of the clinical specimen can be markedly expanded for utilization in research and possible clinical use without detracting from the parent tissue. This non-destructive, easy to adopt wash procedure can potentially lead to an influx of data that may ultimately prove useful in improving patient care.

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WDR5 represents a therapeutically exploitable target for cancer stem cells in glioblastoma

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OBJECTIVES/GOALS: Glioblastomas (GBMs) are heterogeneous, treatment-resistant tumors that are driven by populations of cancer stem cells (CSCs). In this study, we perform an epigenetic-focused functional genomics screen in GBM organoids and identify WDR5 as an essential epigenetic regulator in the SOX2-enriched, therapy resistant cancer stem cell niche. METHODS/STUDY POPULATION: Despite their importance for tumor growth, few molecular mechanisms critical for CSC population maintenance have been exploited for therapeutic development. We developed a spatially resolved loss-of-function screen in GBM patient-derived organoids to identify essential epigenetic regulators in the SOX2-enriched, therapy resistant niche. Our niche-specific screens identified WDR5, an H3K4 histone methyltransferase responsible for activating specific gene expression, as indispensable for GBM CSC growth and survival. RESULTS/ANTICIPATED RESULTS: In GBM CSC models, WDR5 inhibitors blocked WRAD complex assembly and reduced H3K4 trimethylation and expression of genes involved in CSC-relevant oncogenic pathways. H3K4me3 peaks lost with WDR5 inhibitor treatment occurred disproportionally on POU transcription factor motifs, required for stem cell maintenance and including the POU5F1(OCT4)::SOX2 motif. We incorporated a SOX2/OCT4 motif driven GFP reporter system into our CSC cell models and found that WDR5 inhibitor treatment resulted in dose-dependent silencing of stem cell reporter activity. Further, WDR5 inhibitor treatment altered the stem cell state, disrupting CSC in vitro growth and self-renewal as well as in vivo tumor growth. DISCUSSION/SIGNIFICANCE: Our results unveiled the role of WDR5 in maintaining the CSC state in GBM and provide a rationale for therapeutic development of WDR5 inhibitors for GBM and other advanced cancers. This conceptual and experimental framework can be applied to many cancers, and can unmask unique microenvironmental biology and rationally designed combination therapies.

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A Novel Animal Model of Radiation-Induced Heart Disease Using Photon Radiation

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OBJECTIVES/GOALS: The purpose of this study is to develop a clinically relevant mouse model of Radiation-Induced Heart Disease (RIHD) and characterize the resulting phenotype to find biomarkers and therapeutic targets as well as to understand the changes in cellular and molecular mechanisms of bioenergetics. METHODS/STUDY POPULATION: We used a two-beam method in the axillary region targeting the heart to irradiate male BALB/c mice at an isodose of 22, 16 and 8 Gray (Gy). We examined cardiac damage (i.e., vacuolization), inflammation, and DNA damage at 10 days post irradiation using histology and immunohistochemistry of heart tissue and cardiac function at day 35 by echocardiography. Additionally, cardiac tissue of mice irradiated at 22 Gy was collected at day 10 and day 35 post irradiation and sent for RNA sequencing. Data from RNA sequencing was analyzed using gProfiler, GSEA, and Cytoscape to enrich and visualize differentially expressed genes. RT-qPCR was performed to validate findings of significantly differentially expressed genes. RESULTS/ANTICIPATED RESULTS: Significantly increased phosphorylation of H2A.X indicated that irradiated mice were undergoing DNA double strand break repair indicating cardiac damage. Additionally, we found that regulators of mitochondrial function were decreased in the heart at day 10 for all doses. We found

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