diseases. This pilot study may lead to larger studies into whole genome-based blood biomarker approaches for monitoring abstinence and other clinical co-morbidities to be addressed in cocaine addiction recovery.

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Using Computer Vision and Wearable Devices to Improve Care of Parkinson's Disease

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OBJECTIVES/GOALS: Inexpensive, accurate home monitoring is the standard-of-care in many diseases like hypertension or diabetes; however, it has yet to be widely used in neurodegenerative diseases. We used wearable activity monitors and computer-vision evaluated assessments to estimate Parkinson's disease (PD)-related disease burden. METHODS/STUDY POPULATION: We recruited 22 people from the University of Iowa Movement Disorders Clinic. Each person completed a standardized set of 3 fine motor tasks using their hands. We recorded a video of this activity, which was evaluated using MediaPipe - an open-source pose classification program from Alphabet - as well as had an nurse-practitioner evaluate the performance on a validated scale (UPDRS). Participants wore a Fitbit Inspire 3 activity tracker at home for the next two weeks. We quantified disease burden using the Parkinson's Disease Questionnaire 39 - a validated 39-item survey about the intensity of PD-related impairment. Using data from the videos and activity trackers, we estimated 1) the standardized UPDRS assessment of motor impairment and 2) the total PDQ-39 score. RESULTS/ANTICIPATED RESULTS: We found observationally recorded fastest sustained (at least 5 minutes) walking speed was a strong predictor of PDQ-39, explaining over one third of the variability in the measure. Range of motion in the videos was a significant predictor of UPDRS scores; however, was only weakly related to the overall PDQ-39 score. Further processing of the signals from the video, including wavelets and frequency domain analysis, may provide better predictive capabilities. PDQ-39 subscores (e.g., cognition, social support, mobility) will be the subject of further analysis. DISCUSSION/SIGNIFICANCE: Home monitoring has become the standard in other fields because of the better generalizability of home measurements. Improving the detection and evaluation of PD using home monitoring will lead to more timely and accurately changes in medication and less need for clinic visits - especially off levodopa.

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Utility of [89Zr]Trastuzumab-PET/MRI Imaging for Quantitative Assessment of Tumor Heterogeneity In HER2+ Breast Cancer

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OBJECTIVES/GOALS: This study was performed to explore the capabilities of simultaneous [89 Zr]trastuzumab-PET/MRI acquisition in a cohort of metastatic HER2+ breast cancer. The insights derived provide additional noninvasive characterization and precise intratumoral analysis tools for healthcare providers. METHODS/STUDY POPULATION: A total of 13 patients, aged between 40 and 70, diagnosed with HER2-positive breast cancer, were selected to participate in this study. Whole-body [89 Zr]trastuzumab-PET/MR imaging was performed 5 ± 1 days post-injection of the radiopharmaceutical during ongoing HER2-directed therapy. Concurrently acquired T1-weighted MRI facilitated the identification of normal organ and tumor regions of interest, which were further analyzed for mean ADC and mean standardized uptake value. Multiparametric intratumoral habitat analysis was performed. Utilizing the median metric values, tumors were evaluated for heterogeneity, specifically assessing high and low HER2 expression through an image processing framework in conjunction with ADC metrics. Long-term treatment response evaluation is ongoing. RESULTS/ANTICIPATED RESULTS: Initial analysis indicate all tumors exhibited higher overall uptake of [89 Zr]trastuzumab across various sites including the bone (p=0.019), brain (p=0.014), and breast (p=0.069), when compared to corresponding normal organs. Additionally, increased ADCmean values were observed in all regions besides brain tumors (bone: p=0.002, brain: p=0.5, breast: p=0.03, juxtapulmonary: p=0.037), indicating distinct patterns of cellularity. Notably, one of five patients with a breast lesion, who exhibited a complete response to HER2-targeted therapy, exhibited the highest breast lesion SUVmean. Brain and lymph node lesions demonstrated intratumoral heterogeneity of HER2 expression. Qualification of multi parametric maps is anticipated to inform on intratumoral heterogeneity DISCUSSION/SIGNIFICANCE: Despite limitation in clinical applications of quantitative approaches due to lack of standardization of processing, initial investigations, in combining molecular imaging of HER2 and quantitative MRI demonstrate potential in characterizing metastatic HER2+ breast cancer for intratumoral classification and therapeutic stratification.

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Application of human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) for modeling of Ankyrin-2 p.R990Q variant-induced ventricular arrhythmia and personalized medicine

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OBJECTIVES/GOALS: The cytoskeletal protein α^2II spectrin interacts with actin and ankyrin-2 in cardiomyocytes which is essential to orchestrate ion channels and membrane proteins in the cardiac dyad. Our goal is to understand molecular mechanism causing severe ventricular arrhythmias due to spectrin dysfunction and explore novel therapies to treat such conditions. METHODS/STUDY POPULATION: We previously published a case of a 36-year-old woman with an ankyrin-2 p.R990Q (ANK2) variant, presented with severe ventricular arrhythmias and sudden cardiac arrest, caused by a novel mutation in the ankyrin-B gene (c.2969G>A) that disrupts the interaction of ankyrin-B/βII spectrin. To model the condition, we will use human induced pluripotent stem cell (DF 19-9-7T, WiCell)-derived ventricular cardiomyocytes (iPSC-CMs) having ANK2 variant, engineered using CRISPR/Cas9 method (Synthego Corp.). We will validate the differentiation of iPSCs into ventricular lineage and characterize the ANK2 ventricular phenotype. Next, we will express light-gated cation channel Channelrhodopsin (ChR2) in the ANK2 iPSC-CMs and investigate the potential role of

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