

laterality, and treatment, as well as other data, were collected. DICOM files of CT or MRI at presentation and all subsequent follow-up imaging up to 5-years post-ICH were obtained. Using a novel semi-automated image segmentation tool developed in MATLAB by our group, ICH volumes were segmented. Using T1w MRI data, ipsi- and contralateral brain volumes were segmented using NeuroQuant, a fully automated software for MRI volumetric processing, for both initial and follow-up MRIs. Ipsilateral and global cerebral volume changes over time were calculated using initial and follow-up MRI images. Spearman rank correlation between volume changes and ICH volumes were calculated for each patient. RESULTS/ANTICIPATED RESULTS: 75 spontaneous ICH patients with adequate imaging follow-up and both early and follow-up MRI comparisons were considered. Of these, 14 patients had MRIs adequate for segmentation by NeuroQuant. There was a positive correlation ( $R^2 = 0.72$ ,  $p=0.03$ ) between ABC/2, the traditional ICH volume measuring approach, and our semi-automatic segmentation tool, with ABC/2 tending to overestimate ICH volume. There was an average of -6.51% of total brain volume loss with respect to initial brain volume at follow-up. There was a negative correlation between ICH volume and both global (Spearman rank correlation coefficient ( $R$ )=-0.714,  $p=0.004$ ) and local atrophy ( $R$ =-0.785,  $p=0.0009$ ), meaning that as ICH volume increases, there is greater brain volume loss. DISCUSSION/SIGNIFICANCE OF FINDINGS: Greater ICH volume is associated with greater brain volume loss both ipsilaterally, reflected as encephalomalacia, and globally. These findings are important as encephalomalacia can result in focal neurologic deficit and other neurological symptoms over time, while global brain atrophy is associated with dementia and cognitive decline.

### Clinical Trial

79696

#### Reversible DNA Hypermethylation of the Interleukin-15 Promoter Induces IL-15 Expression, Drives the Pathogenesis of T-Cell Large Granular Lymphocytic Leukemia (T-LGLL) and Provides a Therapeutic Approach Using 5-Azacitidine

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**ABSTRACT IMPACT:** This work describes, for the first time, the methylome in patients with T-LGLL, focusing on the IL-15 promoter, and clearly demonstrates that 5-azacytidine decreases IL-15 production leading to T-LGLL cell death. These results form the basis a translational clinical trial in T-LGLL that will begin accrual in 2021 **OBJECTIVES/GOALS:** T-LGLL is an incurable leukemia with few treatment options driven by overexpression of IL-15. Our objective is to characterize the methylation status of the IL-15 promoter in T-LGLL patients and evaluate the potential use of 5-azacytidine (5-aza) in a translational trial by studying the effect of 5-aza in vitro on IL-15 levels, and the IL-15 promoter. **METHODS/STUDY POPULATION:** We sorted T-LGLL patient (n=3) and normal donor

(ND) samples (n=3) for CD3+/CD8+/CD5-/dim for T-LGLL immunophenotype. We analyzed DNA methylation and gene expression profiling using reduced representation bisulfite and RNA sequencing and determined differential methylation and gene expression using 1-way ANOVA analysis. To determine the functional significance of differential methylation, we evaluated MOTN-1 T-LGLL cell viability in vitro with 5-aza at increasing concentrations. Next, we evaluated IL-15 gene expression in MOTN-1 cells treated with 5-Aza versus MOTN-1 with control using western immunoblot. Finally, we exposed MOTN-1 cells to a novel IL-15 inhibitor, IBI-15, and compared cell viability against MOTN-1 cells exposed to an inactive control. RESULTS/ANTICIPATED RESULTS: There was significant differential methylation ( $P=0.0178$ ) and expression ( $P=0.0059$ ) in T-LGLL patients vs ND. These data revealed significant differential hypermethylation of gene promoters, including an increase in DNA methylation of the IL-15 promoter in T-LGLL cells vs ND. In MOTN-1 cells treated in vitro with 5-Aza at 24 and 48 hours, a dose-dependent decrease in the viability of T-LGLL cells was observed, from 100% to 49.5%,  $p=0.037$ . Further, a marked decrease in IL-15 expression was observed at all concentrations of 5-aza compared to control ( $p=0.0001$ ). Finally, a decrease in cell viability was observed utilizing the IL-15 inhibitor IBI-15 vs control. These results confirm that 5-aza leads to decreased transcription of the IL-15 gene, possibly due to hypomethylation of the IL-15 promoter. DISCUSSION/SIGNIFICANCE OF FINDINGS: Hypermethylation of the IL-15 promoter and subsequent increase in IL-15 is critical to the pathogenesis of T-LGLL. Inhibition of the IL-15 promoter by 5-aza leads to down-regulation of the IL-15 gene transcript, which is sufficient to induce T-LGLL cell death. Based on these results, a phase I trial will be conducted using CC-486 (oral 5-Aza) in T-LGLL.

### Data Science/Biostatistics/Informatics

23154

#### Electrical stimulation of hippocampus and amygdala produces multiple distinct responses in human ventral temporal cortex

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**ABSTRACT IMPACT:** This study characterizes interactions between human limbic circuitry and ventral temporal cortex using single pulse electrical stimulation, which may inform emerging stimulation therapies for epilepsy. **OBJECTIVES/GOALS:** The goal of electrical brain stimulation treatment is to modulate brain network function. However, stimulation inputs to different brain sites alter the network in a variety of ways. This study examines that variability by characterizing responses in a target region while stimulating multiple other brain sites. **METHODS/STUDY POPULATION:** We measured voltages in intracranial EEG in 6 patients who had electrodes implanted for epilepsy monitoring. We stimulated pairs of electrodes at multiple sites in the brain with a single pulse every 5 to 7 s and measured the resulting corticocortical evoked potential (CCEP) responses in the ventral temporal cortex (VTC). Using a novel clustering method, we uncovered sets of distinct canonical

response shapes from the 20 to 500 ms post-stimulation period. This allowed us to group stimulation sites that evoked similar responses. We then related each group to high frequency, broadband, changes in spectral power as a reflection of local neuronal activity. RESULTS/ANTICIPATED RESULTS: We found that the VTC receives strong inputs specifically from the amygdala and hippocampus, both in terms of amplitude and broadband spectral power change. However, inputs from the hippocampus produced a different canonical shape than those from the amygdala. We also observed that VTC responses to inputs from the insula clustered in shape with those from the amygdala. These clustering patterns were consistent across subjects, although the actual shapes of the clusters showed variability. We further observed that some shapes were more associated with increases in overall neuronal activity than others, as reflected by broadband spectral power change. DISCUSSION/SIGNIFICANCE OF FINDINGS: Stimulation of connected sites may drive excitability at the target region in ways that are described by sets of full-time-course responses. By capturing their shapes, we can begin to decipher canonical input types at the circuit level. This approach might identify how stimulation inputs can be tailored to therapy while mitigating adverse effects.

86057

### High Screening Efficacy Using Wearable Seismocardiography to Identify Aortic Valve Disease Patients, Potential to Tailor MRI Exams to Patient Needs\*

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ABSTRACT IMPACT: A single seismocardiography (SCG) parameter has been shown to accurately classify aortic valve disease (AVD) status in healthy controls and AVD patients. This could support development of SCG as a quick, inexpensive screening tool to better tailor MRI examination to patients' needs. OBJECTIVES/GOALS: MRI is used commonly for monitoring of aortic valve disease (AVD), but it has high costs. We hypothesize that energy in seismocardiograms (SCG) "signals from chest surface vibrations" is different between healthy controls and AVD patients, and we evaluate potential efficacy of using SCG to recommend MRI only for patients with flow abnormalities. METHODS/STUDY POPULATION: With IRB approval, 45 healthy control subjects (47 ±18years, 18 female) and 9 patients (63 ±16years, 2 female) with aortic valve disease history and known flow abnormalities were recruited. SCG signals were acquired supine, immediately prior to MRI of thoracic aortic blood flow at 1.5T with a time-resolved phase contrast (4D Flow) sequence. The SCG was processed to calculate late-systole high-frequency (120-240Hz) RMS energy. MR velocity images were analyzed to measure peak velocity and trace pathlines of flow.

Screening efficacy of the SCG energy metric was assessed, with hypothesis testing for differences in energy level distributions between controls and patients, and receiver-operator characteristic (ROC) analysis was used to calculate rates of correct/incorrect classification of disease. RESULTS/ANTICIPATED RESULTS: Healthy subjects had coherent flow pathlines through the aortic arch and mid-ascending aorta peak velocities of 106 ±21cm/s (cohort mean ±standard deviation). All valve disease subjects had flow abnormalities, such as jetting flow near the valve or swirling through the arch, as visualized by pathlines. Patients' peak mid-ascending aorta

velocities were 167 ±69cm/s. The SCG energy for healthy controls was significantly different than that of valve patients (-5.6 ±0.3dBmm/s/s vs. -4.0 ±1.2dBmm/s/s respectively; p<0.001). Thresholding SCG energy to distinguish patients from controls correctly classifies subjects with a high true-positive rate and low false-positive rate. The ROC for this classification has area-under-curve 0.956. DISCUSSION/SIGNIFICANCE OF FINDINGS: A high potential screening efficacy was observed using a single, linear SCG metric to identify AVD patients with flow abnormalities. If used to complement MRI surveillance protocols for AVD, this method has potential to serve as a quick, inexpensive tool for better tailoring MRI exams to patient needs.

### Dissemination and Implementation

30143

### Asymptomatic Thoracic Aortic Aneurysm Growth Rates and Predicting Factors: A Systematic Review and Meta-Analysis

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ABSTRACT IMPACT: Through conducting this systematic review and meta-analysis, we will elucidate which factors influence thoracic aortic aneurysm growth, which will further help clinicians to properly stratify and manage their patients with TAAs. OBJECTIVES/GOALS: Thoracic aortic aneurysms (TAA) are an indolent but fatal disease, and the patient characteristics that predict both overall growth and growth rate are still not well characterized. Our goal is to conduct a systematic review and meta-analysis in order to better describe different patient characteristics that predict TAA growth. METHODS/STUDY POPULATION: M.M. conducted a search of Ovid MEDLINE, Embase, and Scopus to identify articles. Inclusion criteria were any longitudinal study reporting asymptomatic TAA growth, growth rates, or clinical proxies for growth such as dissection, rupture, emergency surgery, and death. M.H and P.B. independently applied the criteria to the results of the search. Conflicts were resolved by N.B. Data was extracted and risk of bias assessed independently by M.H. and P.B. Summary estimates of the outcome variables are combined across studies using standard meta-analysis methods. Heterogeneity is assessed via forest plots, chi<sup>2</sup> test (Q test), and I<sup>2</sup> statistic. Sensitivity analysis is conducted to assess robustness of the findings. RESULTS/ANTICIPATED RESULTS: The literature search resulted in 3,419 abstracts, of which 176 were included and thus require a full text review. Cohen's Kappa coefficient was 0.64, indicating substantial agreement and high inter-rater reliability. We describe four categories of patient characteristics influencing the growth of asymptomatic TAAs: demographics, genetic or inheritable conditions, hemodynamic or biomechanical factors, and serum biomarkers. We describe the measure of effect for all variables. We anticipate there is a significant level of heterogeneity between studies, and potentially moderate risk of bias for many of the included studies as they are retrospective and observational in nature. Furthermore, we anticipate publication bias and evaluate