LIMBIC CONCUSSION NEURIMAGING TOOL

- *These variables are completed at Initial and Comprehensive Re-Evaluations, except as noted. Collection Schedule – baseline, 1-year-post-index mTBI, 3-year-post-index mTBI, 5-year-post-index mTBI, then every 5 years afterwards*

- *The self-report questionnaires may be completed prior to visit, reviewed by study staff for completeness and reviewed with subject at visit; alternatively, they may be collected remotely, such as over the telephone, if the participant is logistically unable to come in person to a post-baseline comprehensive visit to achieve partial data collection instead of entirely missed visit.*

Advanced Brain Imaging (Structural & Physiological)

- *Mock Scanner Training*. To mitigate fear, enhance comfort, and reduce motion artifact, participants expressing apprehension or anxiety about scanning will be invited to undergo mock scanner training with guided imagery and relaxation techniques to become desensitized to scanning environment.
- *Urine (women of child-bearing age only)*: depending on local MRI policies procedures, sites may obtain specimen solely for pregnancy testing in premenopausal females to confirm nongravid status. Specimens are tested locally and destroyed after testing.
- *Neuroimaging Data Acquisition*. Volumetrics, FLAIR white matter hyper intensity analysis, DTI/DKI, fcMRI, and ASL done at comprehensive evaluation time points. The specific protocol sequence that each participant will undergo is as follows:
    - Localizer: Calibration/Reference Scan
    - Sagittal 3D T1 MPRAGE/IR-SPGR
    - Axial 3D T2* GRE/SWAN/SWI
    - Axial DTI
    - Axial Resting State fMRI - Subjects should have eyes OPEN.
    - Axial 3D T2-FLAIR (CUBE/SPACE/VISTA)
    - Sagittal 3D T2 (CUBE/SPACE/VISTA)
    - Axial ASL
    - HDFT protocol (SAMMC and MEDVAMC only)
    - *All scans are performed in straight orthogonal planes*
- *Primary Imaging Variables.* Numerous variables are generated from acquisition and analysis and will be readily available for specific exploratory analysis at little additional effort. However, to reduce the number of variables and analyses for the primary aims of the grant, the following measures will be used
    - Volumetrics (volume in cubic millimeters): Total frontal gray matter and white matter (GM, WM), total temporal GM/WM, total parietal GM/WM, right and left cingulate GM/WM, right and left hippocampus and amygdala, right and left caudate, right and left thalamus, right and left cerebellum GM/WM, total GM, total WM, ventricle-to-brain-ratio.
    - DTI tractography (fractional anisotropy [FA] and mean diffusivity [MD]: right and left cingulum bundles, fornix, total corpus callosum, uncinate fasciculus, ventral striatum, anterior thalamic radiation.

- FLAIR white matter hyperintensity analysis: total lesion volume and count, anterior cerebral middle cerebral, posterior cerebral, and vertebral basilar system (feeding brainstem and cerebellum) vascular territories
- ASL cerebral blood flow (CBF) in the same vascular territories as detailed above as well as whole brain GM and WM CBF, and CBF of the thalamus and posterior cingulate
- fcMRI connectivity changes in seedpoints involving anterior cingulate cortex, lateral prefrontal cortex, default mode network, posterior cingulate cortex, and hippocampus.
- Common Data Elements: presence or absence of potentially clinically-relevant pathology.