TECHNICAL ABSTRACT – PI: C. Mac Donald – The ADAPT Study

Background: Traumatic brain injury (TBI) affects approximately 3.5 million individuals annually in the United States [1] and approximately 75% are due to 'mild' or concussive events[2]. In the US military, it is estimated that roughly 20% of the deployed force suffered a head injury[3] in the wars in Iraq and Afghanistan, 83.3% of whom endured a mild, uncomplicated TBI or concussion[4,5]. The long term impact of these injuries is just beginning to be appreciated. Many of these service members are young males, 20-30 years old who have decades of life to live with the complex and often debilitating impact of war-time brain injury. The total lifetime health care costs are largely unknown. Although substantial effort has been placed on trying to better understand this type of injury, much research has been forced to rely largely on self-reporting[6-13], retrospective medical records review [14-18], or evaluations of only later stages of injury[19,20]. No study to date has prospectively followed active-duty US military from injury to long term outcome with advanced MR imaging and clinical evaluation.

Objective and Hypothesis: The overall goal is to investigate long-term advanced MR imaging and clinical outcome measures of concussive traumatic brain injury (TBI) in US military personnel injured during deployment. We will relate these findings to prospectively acquired longitudinal imaging and clinical data from the acute/sub-acute, and early chronic stages following concussion collected on these patients as part of previous collaborative efforts. We hypothesize that early clinical and imaging measures will correlate with late stage clinical outcome.

Specific Aim #1: Explore long-term progression of neurological, neuropsychological, and psychiatric effects of mild-concussive blast-related brain injury in US military personnel by analyzing clinical outcome data to be collected 3-5 years post-injury and previously acquired early clinical data.

Specific Aim #2: Quantify the relationship between imaging biomarkers of brain injury from early and long-term advanced MRI data in US military personnel with mild-concussive blast-related TBI by analyzing DTI data acquired 3-5 years post injury and previously collected acute/sub-acute and early-chronic imaging data.

Specific Aim #3: Develop a predictive model from combined acute/sub-acute, and early-chronic clinical and imaging data for long-term clinical outcomes following mild-concussive blast-related TBI in US military personnel.

Study Design: As part of previous collaborative efforts, we have successfully completed early prospective, longitudinal studies enrolling active-duty US military at 0-7 days (median 4), 0-30 days (median 8), and 0-90 days (median 14) post-injury[21-23] where early advanced MR imaging and clinical data were collected. All TBI subjects met the DoD definition for mild-uncomplicated traumatic brain injury. At 6-12 months imaging was repeated and a battery of neurological, neuropsychological and psychiatric evaluations were completed. In total, 575 subjects were enrolled through these efforts; 54% TBI, 46% control. We propose to re-examine control and TBI subjects now 3-5 years post-injury and compare their current clinical and imaging presentation with the previously acquired longitudinal data. We believe that this population offers a unique opportunity to rigorously evaluate the long term impact of war-time concussive blast-related TBI. Two groups of subjects will be studied: 1) subjects with concussive brain injury from blast during deployment, 2) subjects with no history of blast exposure and no diagnosis of brain injury from deployment.

Impact: This proposal has the potential to strongly impact the field of Neurotrauma by offering new insight into the etiology of long term outcome following concussive war-time brain injury. The knowledge gained could better inform the recovery profiles of this type of injury motivating new recommendations for the management and care of these patients. This will offer predictive insight into the long term impact of war-time concussive TBI thereby guiding new recommendations for clinical management, decisions regarding return to duty, and therapeutic intervention.