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TITLE: Epidemiological Study of Mild Traumatic Brain Injury Sequelae Cause by Blast Exposure During Operations Iraqi Freedom and Enduring Freedom

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<b>13. SUPPLEMENTARY NOTES</b>											
				<b>14. ABSTRACT</b>  Preliminary Results: Accomplishments include initial and ongoing IRB review & approval of all initial submissions, protocol amendments, recruitment advertisements, serious adverse events reporting, and ongoing Richmond VAMC and off-site recruitment activities. We continue to submit to both McGuire and WRAMC IRBs. During Year-4, USMC Camp Lejeune and Richmond VAMC have been our most productive recruitment sites. The appropriate US Navy IRB agreed to accept the findings of the WRAMC IRB. Research assistant positions were reduced from 3 to 2 full time employees. Study procedures, recruitment, data management, and analyses have been refined through meetings, reviews, consultations, and through lessons learned during completed data collection efforts to date. Through 8/31/2012, two hundred and seven (207) subjects have been enrolled through RVAMC Polytrauma Network Site Clinic screening and Polytrauma Inpatient Rehabilitation Center, recruitment letters mailed, radio advertisements, posters in the clinics, and on-site enrollment at Fort Lee, VA, USMC Base Camp Lejeune, USMC Base Quantico, and Fort Lee, VA. Pending data analysis, most subjects appear to meet symptom criteria for PCS. Conclusions to Date: Enrollment has commenced and continues. Study personnel continue to work with the military partners to improve access to post-deployed service members. To ensure a sample representative of the target population, we continue to improve access to active duty service members at additional recruitment sites. At the time of this report, we have four active recruitment sites (see body of report). Due to now chronic radiology technician shortages at McGuire VAMC, Dr. Walker has cancelled plans for the proposed Diffusion Tensor Imaging sub-study. Any study outcomes (conclusions) await data analysis phase.							
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## **I. INTRODUCTION:**

Blast related Traumatic Brain Injury (TBI) is an important source of morbidity in Operations Iraq Freedom and Enduring Freedom (OIF/OEF). Mild TBI (MTBI) may go unrecognized and persist as post-concussion syndrome (PCS). Given that available information is largely anecdotal, the identification, characterization, and prediction of individuals who have PCS with persisting effects from blast-related MTBI are the focus of this series of epidemiological investigations. Multiple hypotheses are being tested including:

- a significant proportion (>18%) of service members experiencing blast events during OIF/OEF sustain a MTBI that leads to persisting symptoms consistent with PCS;
- multiple predictive factors for developing PCS can be identified;
- returnees with PCS will display objective impairments on neuropsychological testing, computerized posturography and/or quantitative electroencephalography; and,
- those with PCS will demonstrate improvement over time but will continue to display significant long-term disability.

A cross-sectional sample of 747 OIF/OEF returnees, who experienced a blast event on tour within the past two years, will undergo three phases of evaluations as follows:

- Phase-I: will determine the sample prevalence of PCS after blast related MTBI, characterize the constellation of related symptoms and problems, and allow predictive modeling.
- Phase-II: will utilize a case-control design to evaluate objective abnormalities among the subjects with PCS after MTBI.
- Phase-III is a longitudinal design using repeated measures for analysis of outcomes over time (baseline, 6 months, and one year).

## **II. BODY OF REPORT: Accomplishments relative to our Statement-of-Work (SOW):**

### **A. SOW Task 1 - Objective: prepare and initiate the overarching research study plan.**

#### **1. Obtain IRB approval for project [Research Assistants, Mr. Heimiller, Dr. Walker]:**

Approval from the primary institutional review board, the McGuire IRB was obtained on August 15, 2008. Secondary IRB approval from USAMRMC (Fort Detrick IRB) was received on September 27, 2008. Virginia Commonwealth University IRB approval was received on March 5, 2009.

All amendments, updated staff rosters, SAEs, and continuing reviews have been submitted to primary and secondary IRBs as required.

#### **2. Establish Military site screening/recruitment options [ Dr. Walker & Research Assistants]:**

After extensive planning and preparation, full Walter Reed AMC IRB approval, as required by the Fort Lee base commander, was received on June 10, 2009. The CDMRP research team began the recruitment and screening process at Kenner Army Health Clinic at Fort Lee on 6/19/2009. Fort Lee on-site recruitment is temporarily suspended due to staff changes in the site clinic. We continue to place recruitment flyers at the Kenner Clinic.

Active recruitment efforts will resume at Fort Lee Army Base once a dedicated clinic nurse is appointed. To date, 19 subjects have been recruited from Fort Lee.

The military recruitment site at US Marine Corps Base (MCB), Quantico, Virginia, remains active (since June 9, 2010), but has turned out to have fewer eligible subjects than originally anticipated. As previously reported, the Department of Navy Human Research Protection Program (DON HRPP) determined that an additional Navy IRB review would not be necessary as protocol has already been reviewed/approved by the following: McGuire IRB, VCU IRB, WRAMC IRB and USAMRMC. At that time, the McGuire VAMC and McGuire Research Institute added an FWA addendum as requested by DON HRPP. To date, 11 subjects have been recruited from this site.

Because the above sites were not meeting enrollment expectations, the addition of a third external recruitment site was deemed necessary and MCB Camp Lejeune, NC was added as an additional site. All necessary letters of support and regulatory approvals, following a subsequent amendment to the original protocol, were obtained. Recruitment at MCB Camp Lejeune commenced in April 2011 and is ongoing. The research team conducted two recruitment trips in 2011 (April, November), and two trips to date in 2012 (April, May). Next enrollment visit is tentatively scheduled for September, 2012. To date, 83 subjects have been recruited from MCB CL. An amendment expanding study procedures conducted on base received regulatory approval. This change has been appreciated by the military command as the most recent groups were able to complete Phase 2 testing on base with minimal disruption to their duties.

**3. Establish availability and content of acute injury (war-zone) variables. [Dr. Walker]**

After determining that acute injury documentation was not reliably available post-acutely, we refined our injury situation and experience questionnaires to be as thorough and specific as possible. Additionally, we chose to add two structured interviews to help cross-validate some of our key diagnostic screening questionnaires. These processes were completed during award year-3.

**4. Finalize Data collection forms including TELEforms. [Drs. McKinney, Cifu, Manning Franke & Walker]**

Completed during Year One for initial study approval. Changes to data collection instruments, including TELEforms have been made to remain consistent with protocol amendments and our data auditing findings and conclusions. All form revisions were submitted for respective IRB approvals, as part of the amendment submission packets. No changes since last report.

**5. Complete set-up of data management software system. [Mr. Bush]**

Accomplished.

**6. Establish logistics (when, where, workspace) for study screening and recruitment of military personnel at Central Virginia PDHA clinic sites. [Dr. Cifu, Dr. Walker, Dr. Manning Franke & Research Assistants]**

Thus far, the volume of eligible subjects identified at Kenner Army Health PDHRA clinics has been far below anticipated. Therefore we have continued to explore and pursue recruitment opportunities outside of the PDHRA clinics. We continue to work on this effort. At Fort Lee we have sent staff to all large group briefings and the PDHRA clinic one to three times per week. We were notified that effective September 2011, our POC will be moved to another area and we will no longer have the same level of access. We have created a pamphlet to leave on site with the clinic personnel and in the waiting

rooms. Once a Registered Nurse is hired for the clinic, Dr. Walker and Dr. Manning Franke will schedule a meeting to address recruitment needs on base. We continue to have the support of the Fort Lee Site PI. At MCB Quantico, we continue to collaborate with the Wounded Warrior Regiment and Command to facilitate access to Marines. Dr. Walker and the study staff continue collaborations with the Command at MCB Camp Lejeune to facilitate access to additional battalions. We continue to screen all patients seen within the Polytrauma program at the McGuire VAMC and send recruitment letters to all individuals who have registered as having served in OEF/OIF conflicts.

**7. Hire and train study coordinator and other TBH study personnel. [Hiring: Mr. Heimiller, Dr. Walker. Training: Drs. Nelson, Walker & McDonald]:**

Please see the table below for study staff name, role, and effort. Mr. Heimiller helped write/prepare the original application, and has been continually involved in this project from its inception. Dr. McDonald, research psychologist joined us in August, 2008, as a part time employee NTE 10% effort. In 2011, Dr. McDonald transitioned to an “as needed” consultant status and continues to contribute to various aspects of the project. After award and funding were received, the above individuals continued in part-time paid roles. Lonnie A. Nelson, PhD., Research Psychologist, Fort Carson DVBIC, Fort Carson, Colorado, is an expert in the field of qEEG applications and analysis. Dr. Nelson is assisting, as a consultant, with interpretation and analysis of qEEG testing. There have been no subaward (VCU) staff changes since our last annual report.

**CDMRP/Walker: Study Staff (Compensated) Summary**

<b>NAME &amp; ROLE</b>	<b>MONTH/YEAR HIRED</b>	<b>% EFFORT</b>
<b>William C. Walker, MD, Principal Investigator</b>	<b>September, 2008</b>	<b>20 (see: VCU sub-award)</b>
<b>David X. Cifu, MD Co-Investigator</b>	<b>September, 2008</b>	<b>5 (VCU sub-award)</b>
<b>Jessica McKinney-Ketchum, PhD, Biostatistics</b>	<b>September, 2008</b>	<b>10 (VCU sub-award)</b>
<b>Brian J. Bush, MSMT Data Manager</b>	<b>June, 2009</b>	<b>5 (VCU sub-award)</b>
<b>Huan Wang Data Analyst</b>	<b>Subaward: Year-3</b>	<b>20 (VCU sub-award)</b>
<b>Michelle Nichols, MSN, RN, Co- Investigator &amp; Clinical Research Coordinator</b>	<b>September, 2008. (Departed program in March, 2012)</b>	<b>20</b>
<b>Jerome Heimiller, RPH, MPA, Administrator</b>	<b>September, 2008. (Departs program in Oct., 2012)</b>	<b>(up to) 10</b>
<b>Tiffany Clory, BS, Research Assistant</b>	<b>November, 2008 (Departed Program: July, 2010)</b>	<b>100</b>

April Dean, BS, Research Assistant	January, 2009.	100
Tammy Searles, RN, Lead Research Assistant	June, 2009 <i>(Departed Program: Jan., 2009)</i>	100
Scott McDonald, PhD., Research Psychologist	September, 2008	Consultant psychologist, prn NTE 5%
Emily Lynn, BA Research Assistant	April, 2010. <i>(Departed program: July, 2012)</i>	100
Jasmine Smith, BA Research Assistant	June, 2010 <i>(Departed Program: Sept, 2011)</i>	100
Judy Pulliam Research Assistant	June, 2012	100
Laura Manning Franke, PhD Co-Investigator	March, 2012	Up to 20%

**B. SOW Task 2 - Objective: Determine the prevalence of PCS after blast related MTBI in OIF/OEF to better define the scope of residual injury and determine early factors predictive of PCS after blast injury to aid the development of better secondary prevention and treatment strategies. Timeline for all subtasks: Gradually accrue over 4 years 747 subjects total (50 subjects by end Year 1, 325 subjects by end Year 2, 600 subjects by end Year 3, 747 subjects by end Year 4) into Phase-I. Responsible personnel: listed below for each subtask [ ].**

**1. Consent & Enroll 747 Subjects Total. [Dr. Walker, Dr. Manning Franke, Research Assistants]**

Through August, 2012, 2,935 potential subjects have been screened, and 207 subjects have been enrolled. Please see "Appendix #1" for a demographic breakdown of enrolled subjects. Enrollment started slowly due to the lag time between selection and meeting USAMRAA pre-funding requirements, and the period devoted to recruiting/appointing our three full-time study staff. As noted previously, the requirement for an additional army IRB review delayed enrollment at Kenner Health Clinic. We found that many of the patients screened at VAMC Polytrauma Network Clinic who screened positive for blast exposure during OIF/OEF deployment were not eligible because the exposure was more than 2 years prior. We expanded our Richmond (McGuire) VAMC recruitment through outreach letters to registered patients and created a poster (previously submitted) to be displayed to enhance subject recruitment efforts. Through August 31, 2012, we have mailed out 12,384 recruitment letters to subjects/patients who were registered at the Richmond VA Medical Center, and had served in OIF or OEF. And as noted previously, we also opted to pursue an additional military recruitment site (Quantico, Virginia US MCB). Neither of the added military sites has yielded the anticipated volume of eligible subjects, so we continued to pursue additional recruitment opportunities (besides PDHRA clinics) at Fort Lee and Quantico. During Year-3, we completed the necessary approvals for advertisement and recruitment at Camp Lejeune Marine Base, NC, and enrollment visits began. During award years 3 & 4, Camp Lejeune became our second most productive enrollment site. We continue to use the approved advertisement (flyer) to aid recruitment efforts in the Central Virginia area. As previously reported, a radio advertisement was created, received full IRB approval, was implemented and

subsequently discontinued due to insufficient response (yield = 1 subject) to justify continued expense.

Due to slower than anticipated subject enrollment(s), Dr. Walker requested, and USAMRAA/CDMRP have approved a one-year, cost neutral study extension.

2. For each subject above, complete standardized current state questionnaires for qualitative and quantitative measurement of: Post-concussion syndrome (PCS) using the Rivermead Post-Concussion Symptoms Checklist (RPQ) (King, 1995), Combat Stress using the PTSD Checklist Military Version (PCL-M) (Weathers et al, 1991), pain using both the McGill Pain Questionnaire short form (MPQ-SF) (Melzak, 1987) and the 11 point Numerical Scale (Jensen MP et al, 1989), and affective disorder using the Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977). The ICD-10 criteria for PCS will be used to categorize the cases with PCS for the prevalence numerator, subjects with PCS after OIF/OEF blast exposure Injury (Boake, 2005; WHO, 1992; WHO, 1993). The International Classification of Diseases is published by the World Health Organization (WHO). The ICD-10 criteria for PCS are 1) a history of MTBI and 2) a minimum of 3 of following symptoms (present to a moderate degree compared to pre-morbid): headache, dizziness, fatigue, irritability, insomnia, poor concentration, memory problems, or intolerance of stress, emotion, or alcohol. The RPQ is being utilized to standardize this diagnostic assessment. [Oversight: Research Coordinator, Dr Walker and Dr Cifu. Scheduling: Research Assistants. Monitoring and facilitation of subject form completion: Research Assistants]

Accomplished on the 207 subjects enrolled through August 31, 2012.

3. For each subject, collect blast injury and individual characteristics data including: dazed, memory gap (injury, pre-injury, and post-injury), lost consciousness, stress, pain, helmet wearing, shrapnel injury, tympanic membrane rupture, hearing loss, type of blast, immediate blast effects, number of blast exposures, demographic, education level, psychiatric history, medical history, and time since injury. These variables will be collected using a series of questionnaires including: Full Blast Questionnaire (modified version of Walter Reed Blast Inventory (Scherer et al, 2007), see Protocol), a Health History Questionnaire (see Protocol), the recalled immediate psychological stress of the blast event using the Impact of Events Scale (IES) (Horowitz et al, 1979), the recalled physical pain level of the blast event using the 11 point Numerical Scale and the Alcohol Use Disorders Test-Consumption (AUDIT-C), a brief screening tool for heavy drinking and/or active alcohol abuse/dependency (Bradley et.al., 2007). [Oversight: Dr Walker and Dr Cifu. Scheduling: Research Assistants. Monitoring and facilitation of subject form completion: Research Assistants]

Accomplished on the 207 subjects enrolled through August 31, 2012.

4. For each subject, the study biostatistician will designate a group assignment (with PCS versus without PCS) using a predetermined threshold of MTBI symptom severity (ICD-10 diagnostic criteria applied to the RPQ data) in order to derive prevalence of PCS and to select subjects for Task 3 [Dr. McKinney]

Accomplished on the 207 subjects enrolled through August 31, 2011.

5. Study biostatistician will provide interval (monthly) updates of the ratio of PCS to no PCS group membership to the PI for the purpose of monitoring accrual targets and trends, but will otherwise will not reveal assignment to either subject or study staff (double blind). [Dr Ketchum]

Accomplished on the 207 subjects enrolled through August 31, 2012.

**6. Perform data audits after first subject completed Phase 1 and on 5% of accrual target (37 subjects) on a monthly basis. [Dr. McKinney]**

During the first year cycle, data auditing occurred on the first subject and has continued to date. This process has been maintained and has ensured data integrity and accuracy of new personnel in addition to inter-rater reliability. We are employing “Data Tracker” software that automatically audits every data file generated from study visits. Therefore, data audits far exceed our 5% goal. Phase I, II and III data audits have been performed on study visits through August 2012.

The study “consent” process has been audited by DVA Research Compliance Officers in May 2009, April 2010, May 2011, August 2011, and, most recently, in April 2012. To date, we have been 100% compliant with subject consent requirements.

**7. Using a case-control design (PCS versus no PCS) and adjusting for PTSD, several statistical analyses will be performed including two-way analysis of variance (ANOVA) (to compare quantitative variables), chi-square tests (to compare proportions of qualitative variables, and a multiple logistic regression model (to determine the predictive nature of these variables as a group). PTSD will be measured as a continuous variable using the PTSD Checklist – Military Version (PCL-M) total score. These analyses will determine factors associated with (or predictive of) developing PCS after blast related MTBI. [Statistics: Dr. Ketchum. Interpretation: all key investigators]**

Pending complete enrollment and data collection.

**C. Task 3 - Objective: Identify and describe objective cognitive performance and neuro-physical impairments in returnees with PCS after blast-related MTBI incurred during OIF/OEF (Study Phase 2). Timeline: Gradual accrual into Phase 2 of minimum of 284 total subjects over 4 years (30 subjects by end Year 1, 125 subjects by end Year 2, 225 subjects by end Year 3, 284 subjects by end Year 4). Responsible personnel: listed below for each subtask [ ].**

- 1. At least monthly, groups of subjects who completed Phase-I (Task 2 above), will be assigned to enter Phase-II evaluations as follows: With PCS (all), Without PCS (equal number to “With PCS” who are selected using described randomization scheme). [Research Assistants & Dr. Walker]**

Accomplished on the 207 subjects enrolled through August 31, 2012.

- 2. Study biostatistician will provide the study coordinator with a list (at least monthly) of de-identified subjects who are assigned for Phase-I evaluations, but will NOT reveal group assignment (With PCS versus Without PCS) to study staff or subject (i.e. to minimize bias of objective evaluations during Phase 2, double blinding of group assignment will be maintained). [Dr. Ketchum]**

Accomplished on the 207 subjects enrolled through August 31, 2012.

- 3. For each Phase-II subject, conduct objective evaluations and collect data including full neuropsychological batteries (cognitive performance and fine motor assessment), quantitative electroencephalography (neurophysiologic cognitive assessment), and computerized posturography (balance impairment assessment). CPT will consist of The Sensory Organization Test (SOT), a composite index that defines abnormalities**

across somatosensory, visual, and vestibular systems. QEEG recordings will consist of baseline 10 minute eyes closed and a 10 minute eyes open resting period. There are multiple normative databases for comparison of individual electrocortical activity. The "life-span" database included with the Neuroguide® EEG analysis software consists of 625 records from normal individuals ranging in age from 2 months to 89 years. Neuroguide® also includes a discriminant function analysis to calculate the probability that a person has sustained a TBI based on their eyes closed resting baseline recording alone. In the initial validation study, a sensitivity of 95.45% and a specificity of 97.44% were reported for classification accuracy in comparison to normals. This discriminant function was developed based on the work of Thatcher and others with the Defense and Veterans Head Injury Program (DVHIP) in the 1990's and used a sample of veterans from what have become the lead Polytrauma centers within the Veterans Affairs health care system (Palo Alto, CA, Minneapolis, MN, Richmond, VA, and Tampa, FL). Thus, it is an appropriate comparison group for our purposes. The neuropsychological battery will consist of the following standardized, validated, tests of proven reliability: Wechsler Test of Adult Reading (WTAR, pre-morbid IQ estimate),(Mathias, Bowden, Bigler, & Rosenfeld, 2007) Conners Continuous Performance Test-II (CCPT-II, sustained attention),(Conners, 2000) Paced Auditory Serial Addition Test (PASAT, processing speed),(Vanderploeg, Curtiss, & Belanger, 2005) Halsted-Reitan Trail Making Test A & B (TMT, visual scanning and executive function),(Lange, Iverson, Zakrzewski, Ethel-King, & Franzen, 2005) Stroop classic test (target processing speed and divided attention),(Soeda et al., 2005) Grooved Pegboard to assess fine motor speed and dexterity (Hanna-Pladdy, Mendoza, Apostolos, & Heilman, 2002), Test of Memory Malingering (TOMM) (Tombaugh, 1997) California Verbal Learning Test-II (CVLT-II) (learning and working memory),(Vanderploeg et al., 2005) Wechsler Adult Intelligence Scale III (WAIS-III) items: Digit Symbol Coding, Digit Span, Letter-Number Sequencing, Symbol Search, & Arithmetic (processing speed, attention, and working memory),(McKay, Casey, Wertheimer, & Fichtenberg, 2007) Delis-Kaplan Executive Function System (D-KEFS) Category Fluency (Animals And Boys' Names) (Harrison, Buxton, Husain, & Wise, 2000):Controlled Oral Word Association Test single letter and category items (COWAT, verbal fluency),(Iverson, Franzen, & Lovell, 1999) Benton Visual Memory Test-Revised (BVRT-R) (visual perception and memory).(Morey, Cilo, Berry, & Cusick, 2003) [Test scheduling: Research Assistants; Neuropsychological testing: Trained Research Assistants, , & Drs. McDonald and Manning Franke. QEEG testing: research assistants.]

Accomplished on the 165 subjects who have completed Phase-II.

4. Use this data to perform and fit several two-way ANOVA models with main effects for PCS (present/absent) and cognitive or neurological impairment (present/absent). A separate model will be fit for each response variable. [Statistics: Dr. Ketchum. Interpretation: all key investigators]

Pending complete enrollment and data collection.

5. Determine the sensitivity and specificity for detecting neurophysiologic abnormalities after MTBI from blast injury during OIF/OEF using QEEG with the goal of assessing the accuracy of detection of mild TBI using a purely neuro-physical method of measurement. [Statistics: Dr. Ketchum. Interpretation: all key investigators]

Pending complete enrollment and data collection.

6. Determine the feasibility of a functional magnetic resonance and diffusion tensor imaging pilot descriptive study (anatomic/physiologic assessment) in a subset of cases and controls. [Dr. Walker]

Due to an ongoing, local shortage of radiology personnel, Dr. Walker has decided to cancel plans for this imaging pilot.

**D. Task 4 - Objective:** Assess the sensitivity and specificity within this sample of select key diagnostic questionnaires used in Phase 1 relative to “gold standard” structured interviews.

1. Structured interviews will be added to Phase-II measures for: Major Mental Health disorders (Major Depressive Disorder, Bipolar Disorder, Panic Disorder w/ w/o Agoraphobia Social Anxiety Disorder, Specific Phobia, Obsessive-Compulsive Disorder, Generalized Anxiety Disorder, and Psychotic Disorders) using the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998); PTSD using the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995); mild blast related TBI using an instrument newly developed for this study loosely based on existing interviews used in acute rehabilitation settings (e.g., Gioia et al., 2008). [Dr. McDonald, Dr. Cifu, Dr. Ketchum, and Dr. Walker]

Accomplished during reporting Year-2. Interviewer auditing and training continue as needed.

2. Collect these interview measures in the subsequent approximately 200 subjects entering Phase 2. [Dr. McDonald, Dr. Walker, Trained Research Assistants]

Phase-II activity (see D1 above). Structured interviews commenced in Year-Two and were completed on 14 subjects through August 2010, 67 subjects through August 2011, and 116 through August 2012.

3. Analyze findings and implications for the primary analyses described in Tasks 2 and 3. [Dr. Ketchum, Dr Walker, and all investigators]

Phase-II analytical activity (see D1 above). Not applicable to current progress report.

**E. Task 5:** Determine the trajectory of symptoms and social/vocational functioning in PCS after blast related MTBI (Study Phase-III). Timeline: Gradual accrual into Phase 2 of 225 total subjects over 4 years (25 subjects by end Year 1, 125 subjects by end Year 2, 2225 subjects by end Year 3). Responsible personnel: listed below for each subtask [ ].

1. On over 232 returnees (consecutive Phase-I enrollments described in Task 1 & 2), collect follow-up longitudinal data (6 months, and one year) on phase-I current-state measures, AND collect complete longitudinal outcome data (6 months and one year) using standardized and validated TBI specific outcome measures including: Extended Glasgow Outcome Scale (GOS-E) (Wilson et al, 1998) (global outcome), Mayo-Portland Adaptability Inventory-4 (MPAI-4)(Malec, 2004) (ability, participation, adjustment), and the Satisfaction With Life Scale (SWLS) (Diener et al, 1985) (quality of life). [scheduling: Research Assistants. Telephonic or in-person data collection: Research Assistants]

Completed Phase-III (6 month) evaluations, on 114 subjects through August 31, 2012.

Completed Phase-III (12 month) evaluations, on 106 subjects through

August 31, 2012. Completion of Phase-III evaluations has been hindered by subject relocation and or redeployment and is below our expectations. Thus, we have instituted additional strategies to optimize our Phase-III retention rate. These additional strategies have facilitated improvement of the collection of final outcome data. We continue to monitor progress on this and track those participants who are deployed at the time of study visits.

2. Describe the trajectory of symptoms and social/vocational functioning among returnees with PCS after blast-related MTBI. [Analysis by all key investigators]

Pending complete enrollment and data collection.

3. Conduct statistical analysis using repeated measures mixed-models for analysis of outcomes over time (baseline, 6 months, and one year). [Statistics: Dr Ketchum, Interpretation: All key investigators]

Pending complete enrollment and data collection.

#### **F. Task 6 – Objective: Disseminate Findings:**

1. Disseminate results via publication in peer reviewed journals. [All key investigators coordinated/led by Dr. Walker]

Walker, W., Nichols, M., McDonald, S., Ketchum, J., & Cifu, D. The identification of transient altered consciousness induced by military related blast exposure and it's relation to post-concussion syndrome. In Press: *Journal of Head Trauma Rehabilitation*.

2. Present at professional meetings to reach the variety of practitioners treating TBI and blast injured patients [All key investigators coordinated/led by Dr. Walker].

Oral Symposium presentation, Military Health Research Forum, Kansas City, MI, Sept 1, 2009 (previously submitted)

Poster presentation, Military Health Research Forum, Kansas City, MI, Sept 2, 2009 (previously submitted).

Kelly, N.R., McDonald, S., Ketchum, J.M., Nichols, M., & Walker, W. (2011, June 13-15). Balance and cognitive functioning: Associations following blast exposure. Poster presented at the 3<sup>rd</sup> Federal TBI Interagency Conference in Washington, D.C.

Walker WC, Nichols M, McDonald S, Cifu DX, Ketchum, J. The identification of transient altered consciousness induced by military related blast exposure and it's relation to post-concussion syndrome. Amer Academy Phys Med Rehabil Annual Assembly, November 2011, Orlando, FL. (Poster Hall presentation plus separate Oral Platform session presentation for "Neurologic Best Research Presentations" awardees)

Franke LM, Ketchum JM, Walker WC. Factor Analysis of the Rivermead Postconcussion Questionnaire Following Blast Exposure. Accepted for poster presentation at American Congress of Rehabilitation Medicine and American Society of Neurorehabilitation (ACRM-ASNR) Annual Conference, Oct 9-13, 2012, Vancouver BC, Canada.

### III. KEY RESEARCH ACCOMPLISHMENTS:

- Developed structured interview for the post-acute detection/diagnosis of mild TBI. Such an instrument did not previously exist in the published literature.
- Additional “key” research accomplishments are expected in year five. For year-four accomplishments, please see “II” above (pages 4-13).

IV. REPORTABLE OUTCOMES: Outcomes await data analysis and study closure.

### V. CONCLUSION:

When completed, this study will aid in developing targeted secondary prevention strategies by identifying factors that predispose service-members to PCS after blast-related MTBI. Characterization of the impairments and problems related to PCS will aid health care planning and development of targeted medical and rehabilitative treatment strategies.

### VI. REFERENCES:

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., et al. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress, 8*, 75-90.

Gioia, G. A., Collins, M., & Isquith, P. K. (2008). Improving identification and diagnosis of mild traumatic brain injury with evidence: psychometric support for the acute concussion evaluation. *Journal of Head Trauma Rehabilitation, 23*(4), 230-242.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry, 59 Suppl 20*, 22-33.

VII. APPENDICES:

**APPENDIX # 1:**  
**Subject Demographics through Year-IV**

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CDMRP W81XWH-08-2-0178 Demographic Summary Sheet

N = 199 (*at time of analysis*)

Variable	Mean	SD	Range
Age, years	27.51	7.75	19 – 60
	Count	Percent	
Sex			
Male	192	96.5	
Female	7	3.5	
Marital Status			
Married	92	46.2	
Divorced	17	8.5	
Single	90	45.2	
Race			
Caucasian	155	77.9	
African American	31	15.6	
Other <sup>1</sup>	13	6.5	
Ethnicity			
Hispanic	20	10.1	
Non-Hispanic	179	89.9	
Highest Level of Education			
Non-High School	2	1.0	
High School Graduate	104	52.3	
Some College	68	34.2	
College Graduate	22	11.1	
Post-Graduate Degree	3	1.5	
Prior Deployment Status			
Active Duty	150	75.4	
Selective Reserves – National Guard	29	14.6	
Select Reserves – Reserves	13	6.5	
Ready Reserves	4	2.0	
Civilian Government Employee	2	1.0	
Other (Contractor)	1	0.5	

<sup>1</sup> Other Race includes: 1 Black/White, 6 Hispanic, 2 Latino, 1 Native American, 1 Native American/Black, 1 White/Asian, and 1 unknown (missing).

**VIII. SUPPORTING DATA:** Please see table and figures above. No additional supporting data at this time (Year-IV).