AWARD NUMBER: W81XWH-17-1-0424

TITLE: Sensory Integration Balance Deficits in Complex mTBI: Can Early Initiation of Rehabilitation With Wearable Sensor Technology Improve Outcomes?

PRINCIPAL INVESTIGATOR: Dr. Laurie King

CONTRACTING ORGANIZATION: Oregon Health and Science University, Portland, OR

REPORT DATE: October 2021

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE
October 2021

2. REPORT TYPE
Annual report

3. DATES COVERED
30Sep2020-29Sep2021

4. TITLE AND SUBTITLE
Sensory Integration Balance Deficits in Complex mTBI: Can Early Initiation of Rehabilitation With Wearable Sensor Technology Improve Outcomes?

5a. CONTRACT NUMBER
W81XWH-17-1-0424

5b. GRANT NUMBER
PT160104

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Dr. Laurie King (PI); Dr. Kody Campbell; Shelby Martin

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)

Oregon Health & Science University
3181 SW Sam Jackson Park Road
Portland, Oregon 97239

Veteran Affair Portland Health Care System
3710 SW US Veteran Hospital Rd,
Portland, OR 97239

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Objectives: 1) To determine the role of timing in rehabilitation of balance deficits in people with mTBI 2) To determine if home monitoring improves outcomes 3) To develop a novel feedback system using wearable sensors to provide physical therapists with real-time information about quality of head and trunk movement during exercise.

Plan: This is an interventional study on people with mTBI. Aim I examines whether initiating interventional physical therapy earlier rather than later improves outcomes. Aim II, nested within Aim I, examines whether home monitoring of vestibular rehabilitation improves outcomes. Aim III develops a system capable of delivering real-time feedback on quality to improve outcomes.

Aims and Hypotheses:
Aim I. Early Intervention: To determine the effects of early versus late rehabilitation for balance deficits in mTBI. We hypothesize that early rehabilitation will improve outcomes more than standard of care.
Aim II. Home Monitoring: To compare traditional balance rehabilitation versus balance rehabilitation with sensor-based home monitoring. We hypothesize that providing physical therapists with objective measures on performance of prescribed exercises at home will improve outcomes in rehabilitation.
Aim III. Real-time Monitoring for Training: To develop and evaluate a novel sensor system that provides real-time feedback to physical therapists. We hypothesize that real-time feedback on head and trunk movements during exercise will be feasible for use by a physical therapist.

Methods:
Aims I & II: These aims involve 160 participants who have sustained an mTBI. They will complete questionnaires to identify their perceived problems, as well as undergo clinical tests of vestibular function and balance and gait. Motion sensors, force platforms, and clinical assessments will be used to measure balance and gait.
Intervention: Participants will be randomly assigned to begin physical therapy immediately or within the standard of care timeline. During these sessions, the participant will be evaluated by the physical therapist while performing exercises around common impairments after concussion. People will perform either standard vestibular rehabilitation exercises or standard vestibular rehabilitation exercises using wearable sensors to track head movements.
Aim III: Three physical therapists from the study team will use the biofeedback sensor system, along with six mTBI subjects, and they will be asked to provide feedback about the system. 50 people without mTBI will be asked to perform specified exercises that require head movements during standard balance and vestibular exercises to obtain normative values.

Results: For Aims I & II we have screened 199 subjects and enrolled 148 subjects in this study. For Aim III, 50 healthy control subjects and six mTBI subjects have completed testing.

15. SUBJECT TERMS mTBI, Rehabilitation, Brain Injury, Inertial Sensors, Balance, Central Sensory Integration, Concussion, Eye Tracking					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified	Unclassified	22	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

Mild traumatic brain injury (mTBI) is common both in civilian and military populations and can be debilitating if symptoms do not resolve after injury. Balance problems are one of the most common complaints after sustaining an mTBI and often prevent people from returning to their previous quality of life. However, we currently lack clear guidelines on when to initiate physical therapy rehabilitation and it is unclear if early physical therapy is beneficial. We believe that the underlying problem of imbalance results from damage to parts of the brain responsible for interpreting sensory information for balance control. We hypothesize that retraining the brain early, as opposed to months after injury, to correctly interpret sensory information will improve recovery. We also believe this retraining is limited when rehabilitation exercises are performed incorrectly, and that performance feedback from wearable sensors, can improve balance rehabilitation. The researchers in this project are experts at understanding and treating complex balance problems and have developed novel and portable ways to measure balance using new technology. There are three of objectives of this proposal: 1) To determine how the timing of rehabilitation affects outcomes after mTBI 2) To determine if home monitoring of balance exercises using wearable sensors improves outcomes and 3) To develop a novel feedback system using wearable sensors to provide the physical therapist information, in real-time during training, about quality of head and trunk movements during prescribed exercises.

2. KEYWORDS:

mTBI, Rehabilitation, Brain Injury, Inertial Sensors, Balance, Central Sensory Integration, Concussion, Eye Tracking

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Goal	Target Completion Date	Percentage of Completion
Specific Aim 1 & 2 (Assessment of late vs early intervention & home monitoring)		
Major Task 1: Launch Study Activities	*March 2018*	100%
Major Task 2: Recruitment and Testing	*March 2021*	85%
Major Task 3: Randomized Interventions	*March 2021*	76%
Major Task 4: Assess Efficacy of Interventions	*March 2021*	44%
Major Task 5: Data Analysis &	*September 2021*	88%

Publications		
Specific Aim 3 (Real-Time Monitoring)		
Major Task 1: Develop & Evaluate the wearable system for feedback	*September 2021*	100%
Major Task 2: Launch Study Activities	*September 2020*	100%
Major Task 3: Data Collection	*September 2019*	100%
Major Task 4: Data Analysis & Publications on Interventions	*September 2021*	93%

What was accomplished under these goals?

Aim I & II

~~**Major Task 1: Launch Study Activities**~~

Major Task 2: Recruitment & Testing
Subtask 2: data collection & management (0/5 tasks completed)

- Complete vestibular testing at OHSU and VA for data collection; Total Day 1's completed is 148 out of the anticipated 160- 92% complete
- Complete gait and balance testing for data collection at OHSU and VA; Total Day 2's completed is 143 out of the anticipated 160- 89% complete
- Data back-up onto server including manual data entry into Redcap; Data has been placed on the server and also manually entered into REDCap for all study participants- 89% complete
- Screen and verify data on server and check for accuracy; The last data check was completed June 2021. The next data check will be completed December 2021- 80% complete
- Validate and submit forms to FITBIR quarterly; We submitted all data thus far to FITBIR during September 2021. Data will continue to be submitted yearly, as required- 75% complete

Major Task 3: Randomized Interventions on 160 mTBI Patients
Subtask 1: intervention (1/4 tasks completed)

- Enroll subjects in rehabilitation intervention; As subjects enroll they are being randomized in to either early or standard of care rehabilitation- 89% complete
- Complete 6 week interventions; 95 total subjects (including 15 telehealth subjects) have completed the 6-week intervention. Six subjects stopped rehabilitation early due to Covid restrictions. Two subjects are currently participating in the intervention. There are five subjects randomized to the delayed group and are waiting to start the intervention- 59% complete

- Physical therapist's document compliance, adverse events and progression of exercise for each subject; Physical therapists are keeping a detailed record of progression through rehabilitation and are required to fill out a summary sheet for each visit documenting any protocol deviations and progression of exercises- 59% complete

Major Task 4: Assess Efficacy of Interventions
Subtask 1: intervention assessment (0/2 tasks completed)

- Complete immediate posttest after intervention; Ninety-two subjects have completed the posttest- 57% complete
- Complete long-term assessment 6 months later to assess retention; Fifty-one subjects have completed the long-term assessment- 31% complete

Major Task 5: Data Analysis and Publications
Subtask 1: data analysis (0/1 task completed)

- Perform all analysis according to proposal and share all findings with investigators; Data is continually being organized in preparation for analysis as we continue with data collection. This organization includes self-reported questionnaires, neurocognitive testing, eye-tracking, postural sway, gait, and mobility data from our testing sessions. We will prepare statistical analysis scripts for data analysis. We are continuing preliminary analyses on the demographic distribution of our participants enrolled into the 4 intervention arms to track progress and project needs. This quarter we determined the percentage of our sample that responded well to the rehabilitation and described responders to the rehabilitation according to their ocular motor and vestibular impairment profiles. We also investigated changes in cardiovascular and autonomic function from rehabilitation. (see significant results)- 60% complete

Subtask 2: manuscripts, presentations and other output (3/5 tasks completed)

- Disseminate findings (abstracts, presentations, papers, DoD); We revised and resubmitted a manuscript in the *Journal of Neurologic Physical Therapy*, which is comparing remote rehabilitation for mTBI to in-person rehabilitation. Another manuscript to *Frontiers in Bioengineering and Biotechnology* that compared eye movements made during walking in healthy people and people with mTB was accepted October 2021. Our research group submitted 3 abstracts and had all 3 accepted to the American Physical Therapy Combined Sections Meeting, with one being accepted as a platform presentation. Additionally, we had 2 other abstracts submitted, accepted, and presented this quarter at the 2021 National Center for Rehabilitative Auditory Research Conference in Vestibular Disorders: From Cause to Cure. An abstract from each meeting – CSM and NCRAR – used data from the current grant and other abstracts used data from previously DoD funded grants (see products)- 50% complete
- Integrate new protocols and head movement metrics into APDM Mobility Lab system; New protocols for measuring head and trunk range of motion, and velocities during gaze stabilization movements (Vestibular Ocular Reflex and Visual Motion Sensitivity) were created and implemented into Mobility Lab system. These protocols are used for testing, data collection, and providing performance results to the users. We continue to monitor and address any issues or feedback we receive from users to improve the usability of the system. A new Opal DataHub for sharing and transferring data remotely has been implemented and

will be tested to address intermittent issues that arise with the use of the access point. Testing and verification will continue throughout the study- 90% complete

- Submit manuscript presenting APDM algorithm and validation results; A manuscript detailing the reliability of inertial sensors and algorithms developed by APDM at measuring head movement metrics for vestibular rehabilitation therapy was published in the *Journal of Physiotherapy Research* this quarter (see products)- 100% complete

Aim III

~~**Major Task 1: Technology Development**~~

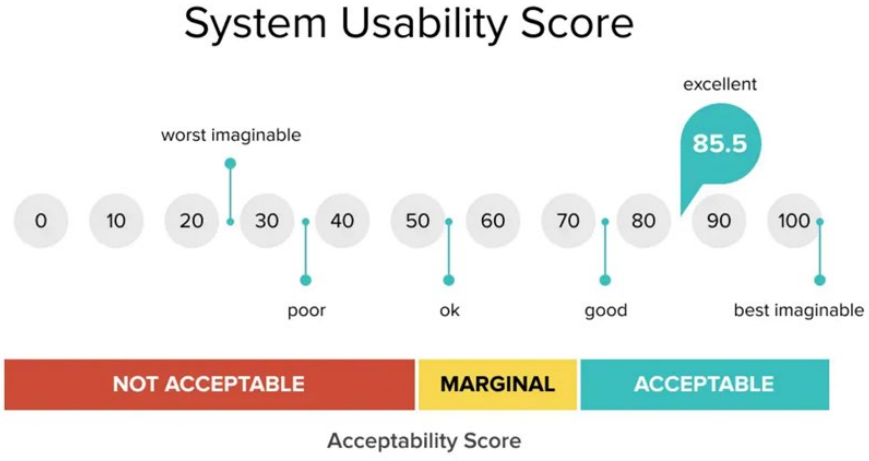
Major Task 2: Launch Study Activities
Subtask 1: train and recruit (2/2 tasks completed)

- Identify patients from physical therapy to evaluate vestibular rehabilitation feedback system; Each physical therapist (total of three) will use this on two of their patients, for a total of six mTBI subjects. Feedback forms for system usability has been created and 3 physical therapists have utilized the system, each testing 1-2 mTBI patients. System usability forms have been completed by individual physical therapists- 100% complete

~~**Major Task 3: Data Collection**~~

Major Task 4: Data Analysis and Publications on Intervention
Subtask 1: data analysis (4/4 task completed)

- Perform all analysis according to proposal and share all findings with investigators; -100% complete
    - System Usability Scale: PTs scored an average of 80 points (SD +/- 3.5). Scores below 68 point to issues with the design that need to be researched and resolved, while scores higher than 68 indicate the need for minor improvements to the design.



    - Key findings:
        - PTs most strongly agreed that they "would like to use this system frequently" and most strongly disagreed that "the system was very cumbersome/awkward to use."

        - PTs reported neutral scores regarding "need assistance to be able to use this system" and "need to learn a lot of things before I could get going with this system."
    - Open field feedback from PTs: "I liked using it with patients where I was questioning what was limiting them most gaze stability versus postural instability. It helped." As well as; "My patient really valued the feedback. It motivated them to participate in [their] home exercise program!"
- Optimize system user interface and reports based on input from users; Further optimization of system user interfaces and reports will coincide with data collection for Major Task 2 Subtask 1 for Aim III- 100% complete
- Summarize qualitative data from PT and patients and provide to APDM; Data collection has been completed and qualitative data has been shared with APDM. We have had weekly meetings with APDM on designing and optimizing the biofeedback user interface and reports for Aim III. No further changes were required for the real-time biofeedback system- 100% complete

Subtask 2: manuscripts, presentations, and other output (1/2 task completed)

- Disseminate findings (abstracts, presentations, papers, DoD), including APTA, ACRM and MHSRS rehabilitation journals to share with clinicians; 100% complete
    - A manuscript presenting the reliability of wearable sensors for vestibular rehabilitation has been published in the *Journal of Physiotherapy Research*
    - Results used as pilot data for proposal of randomized clinical trial
    - Findings presented at conferences: OHSU Research Week, NIH Rehabilitation Research
- Initiate the process to obtain FDA clearance to market the feedback system; The APDM team continues to follow the Quality Management System procedures to complete the system verification and validation in preparation for FDA 510(k) clearance to market. The APDM team implemented the technical File for the Clinical-Grade Opal System. This Technical File is implemented to meet the Medical Device Regulation (MDR). The File is now under review to certify the system Declaration of Conformity to MDR requirements- 60% complete

<u>Significant Results/ Key outcomes:</u>

Aims I & 2	DoD2 In-Person Subjects	DoD2 Telehealth Subjects	Total
Screened	178	21	**199**
Enrolled	130	18	**142** 122 VA/OHSU 26 only OHSU
Day 1	130	18	**148**
Day 2	125	18	**143**
Posttest	73 (+4 remote visits)*	15	**92**
6-month follow up	27 (+12 remote visits)*	12	**51**

*These participants were enrolled in the study before COVID restrictions were executed. These visits were performed over the phone and no in-person data collection occurred.

Quarter 4 Key Results

A larger proportion of people with abnormal vestibular system function responded to vestibular rehabilitation therapy than those with no vestibular or only ocular motor abnormalities. There is a growing consensus that identifying symptom profiles can facilitate care following mTBI. This quarter, we explored if abnormal vestibular and/or oculomotor function after mTBI could predict responsiveness to vestibular rehabilitation. Seventy-two subjects (age 35.0±12.6; 58 F) with mTBI completed vestibular and oculomotor assessments based on eye movement recordings on the Dx NOTC system (Rotary Chair; Neurolign USA) protocols. Normative cutoffs (NOTC system) and published cutoffs classified abnormal measures. Subjects were classified as abnormal oculomotor-only, vestibular-only, or oculomotor and vestibular. Subjects then attended 8 rehabilitation visits over 6 weeks that included cervical therapy, cardiovascular exercise, and vestibular rehabilitation. After rehabilitation, physical therapists rated participants on Global Impression of Change as responders (>= 6) and non-responders (<= 6) to therapy. Seventy-four percent of the entire cohort were responders to rehabilitation. **Figure 1** provides the proportions of responders and non-responders according to symptom profile subgroup. Although those with both vestibular/oculomotor deficits had a higher percentage of responders, results were not significantly associated with responsiveness to rehabilitation. Further exploration of individual performance across tests and logistical modeling to control for days since injury will provide additional clinical recommendations.

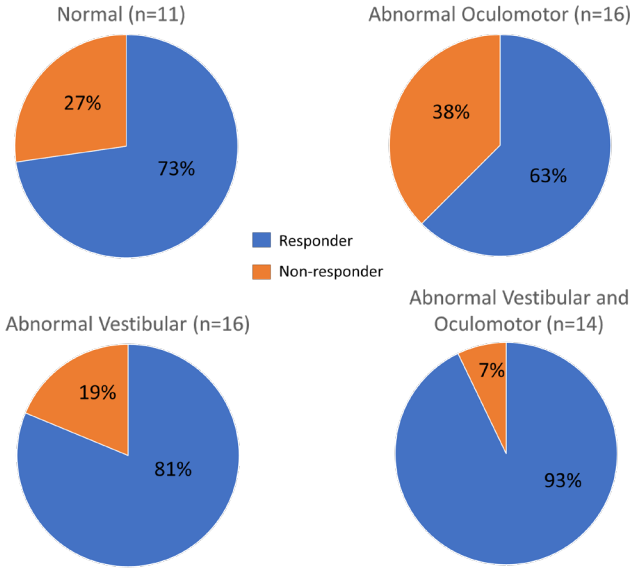


Figure 1: Proportions of vestibular rehabilitation responders (blue) and non-responders (orange) according to symptom profile subgroups.

Multimodal physical therapy for subacute mTBI may promote cardiovascular autonomic adaptations and reduce mTBI-related symptoms during sub-maximal exercise. Cardiovascular autonomic function can be impaired following mTBI leading to prolonged recovery. We explored if a multimodal physical therapy program for people with subacute mTBI improved cardiovascular function and reduced mTBI-related symptom provocation during sub-maximal exercise. Sixty-five people with subacute mTBI completed pre- and post-rehabilitation assessments on the Buffalo Concussion Treadmill Test (BCTT). The BCTT evaluated the maximal heart rate achieved during

incremental sub-maximal treadmill running by participants before terminating the test due to symptom provocation (>2) or completing the test duration. Subjects attended 8 rehabilitation visits over 6 weeks that included cervical therapy, cardiovascular exercise, and vestibular rehabilitation. The average maximal heart rate increased from 73 ± 10.82 bpm to 80.06 ± 8.31 bpm with 65% of the subjects increasing their symptom provoking max heart rate. Subjects had lower average symptom severity when performing the BCTT following rehabilitation (pre: 5.9 ± 4.03 vs post: 3.05 ± 3.27) with 75% of subjects reporting lower symptom severity after completing rehabilitation. Future analyses will determine the number subjects that failed the BCTT pre-rehabilitation (max heart rate > 85% of age predicted maximum) and any associations of subjects failing the BCTT pre-rehabilitation with time since injury, symptom profiles, pre-injury fitness level estimates, and quality of life.

Quarter 3 Key Result

People with sub-acute mTBI exhibit balance deficits by domain determined by the Mini Balance Evaluation Systems Test – MiniBESTest. We compared Mini-BESTest total scores and domain scores on our sub-acute mTBI group to age- and sex-matched healthy controls (HC). The sub-acute mTBI group had significantly lower Mini-BESTest total scores compared to the healthy control group (median and [interquartile range]: 24 [3] for mTBI, 27 [3] for HC; $p < 0.0001$; **Figure 2**). Further, the mTBI group had significantly lower reactive stepping (5 [2] for mTBI, 6 [1] for HC; $p = 0.0026$) and dynamic gait (8 [5] for mTBI, 9 [1] for HC; $p < 0.0001$) domain scores compared to the healthy group (**Figure 3**). The Mini-BESTest may be suitable for detecting balance control system differences between people with subacute mTBI and healthy controls. Future analyses will determine differences in instrumented measures from the Mini-BESTest between groups.

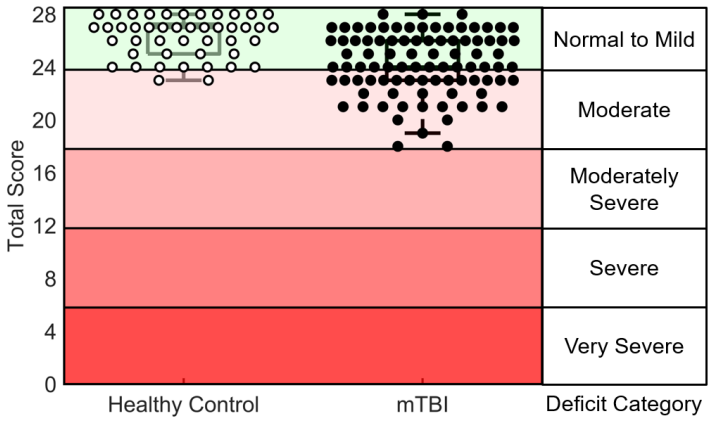


Figure 2: Mini-BESTest total score distributions with box-whisker plots for healthy controls (white open circles) and mild traumatic brain injury (mTBI – black closed circles) participants. Shading in figure corresponded to previous established Mini-BESTest deficit categories – indicated on right side of figure.

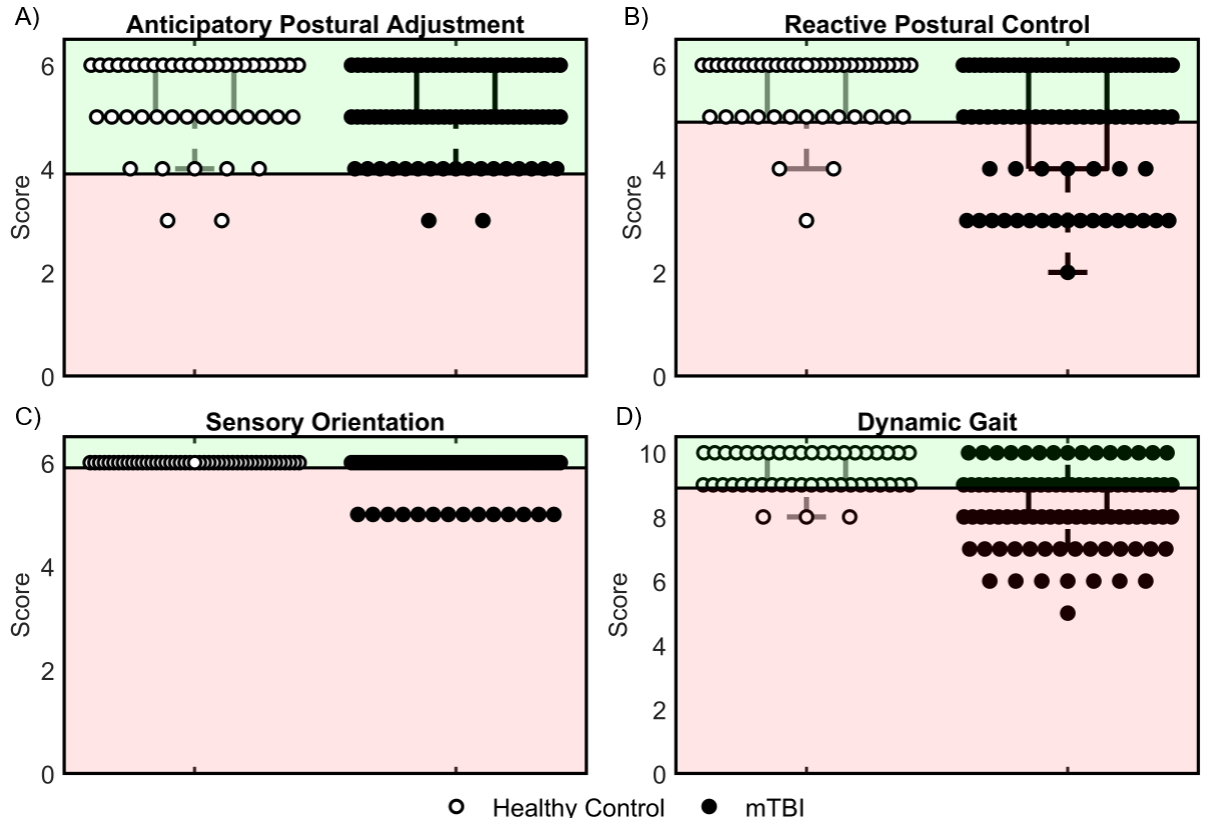


Figure 3: Healthy control (white open circles) and mild traumatic brain injury (mTBI – black closed circles) score distributions with box-whisker plots for A) Anticipatory Postural Adjustment, B) Reactive Postural Control, C) Sensory Orientation, and Dynamic Gait domains from the Mini-BESTest. Individual participants within the green shading indicate normal performance determined from a 90th percentile cutoff derived healthy control data and those in red indicate abnormal performance.

Quarter 2 Key Result

Saccadic eye movements during walking are impaired in people with subacute mTBI. We evaluated differences in eye-tracking measures during walking between healthy controls (HC) and patients with mTBI using a mobile eye-tracking system. Thirty-seven HC participants and 67 individuals with mTBI completed a single trial of walking back and forth over 10-meters for 1 minute. Gait was assessed using six inertial sensors and gait velocity was selected as the primary outcome. Eye-tracking measures included saccadic (frequency, mean and peak velocity, duration, and distance) and fixation measurements (frequency and duration). Individuals with mTBI had significantly reduced saccadic frequency (p = 0.003, SMD = 0.599), duration (p = 0.006, SMD = 0.560) and peak velocity (p = 0.007, SMD = 0.549) compared to the HC group. These findings have implications in real-world function including return to sport for athletes and return to duty for military service members. Future research should investigate whether or not saccade outcomes are influenced by rehabilitation.

Quarter 1 Key Result

Quality of life and post-mTBI symptoms improve following in-person- and tele-rehabilitation, but in-person rehabilitation improve post-mTBI symptoms to a larger extent than tele-rehabilitation. We quantified post-mTBI symptoms (using the Neurobehavioral Symptom Inventory - NSI) pre- and post-rehabilitation for participants that received and completed in-person rehabilitation prior to the research restrictions due to COVID and participants that received tele-rehabilitation during the

restrictions. We described these groups at pre- and post-rehabilitation time points with means and standard deviations (SD) and calculated effect sizes in the change from pre- to post-rehabilitation. For post-mTBI symptoms, both groups improved following rehabilitation (**Table 1**) but in person changes were larger, both for total score and the subscales of the NSI -somatosensory, affective and vestibular related symptoms (**Table 1**). Rehabilitation program differences between in-person and tele-rehabilitation could explain differences in our results. For the tele-rehabilitation program, we were unable to provide symptom managed aerobic exercise, and balance exercises were less challenging due to limited equipment and safety considerations. This data suggests the importance of a challenging exercise program within a multimodal rehabilitation program post mTBI for greater symptom recovery.

Table 1: Means and Standard Deviations (SD) for the Quality of Life After Brain Injury (QOLIBRI) and Neurobehavioral Symptom Inventory (NSI) with subscales at pre-rehabilitation and post-rehabilitation time points on participants receiving in-person or tele-rehabilitation (Tele-Rehab) care. Effect sizes from pre rehabilitation to post rehabilitation and 95% confidence intervals (CI) are presented for each group.

	Pre – Rehabilitation		Post – Rehabilitation		Effect Size (95% Lower, and Upper CI)	
	In-Person N = 49	Tele-Rehab N = 15	In-Person N = 49	Tele-Rehab N = 15	In-Person	Tele-Rehab
Variable	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**		
NSI						
Somatosensory	9.67 (5.15)	8.8 (4.46)	5.65 (3.76)	6.53 (3.62)	-0.86 (-1.12, -0.65)	-0.54 (-1.07, -0.02)
Affective	10.96 (5.17)	10.2 (5.25)	6.57 (4.81)	7 (3.87)	-0.85 (-1.22, -0.59)	-0.67 (-1.2, -0.27)
Cognitive	7.38 (3.81)	7.67 (2.29)	4.73 (3.53)	5.47 (3.81)	-0.69 (-0.97, -0.45)	-0.67 (-1.55, -0.25)
Vestibular	4.17 (2.61)	3.4 (2.06)	2.71 (2.1)	2.73 (1.94)	-0.58 (-0.86, -0.35)	-0.32 (-0.76, 0.03)
Total Score	34.33 (15.24)	31.4 (11.79)	20.71 (12.7)	22.53 (11.46)	-0.94 (-1.27, -0.7)	-0.73 (-1.32, -0.31)

Blue shading indicates a small effect size (0.2 to 0.5); Yellow Shading indicates a moderate effect size (0.5 to 0.8); Green indicates a large effect size (> 0.8).

What opportunities for training and professional development has the project provided?

Members of the research team had the opportunity for training and professional development through virtual attendance at conferences this year. Several members of our research team attended and presented at the 2021 International Conference on Ambulatory Monitoring of Physical Activity and Movement (2 postdoctoral scholars) and the 2021 National Center for Rehabilitative Auditory Research Conference on Vestibular Disorders (1 postdoctoral scholar and 1 physical therapist). Dr. Peterka (Co-I), virtually presented at the 2021 Vestibular Oriented Meeting. Additionally, several research team members presented work at an internal institutional conference – OHSU Research Week.

Members of our team meet monthly with multiple departments within our university and the Portland VA, including Family Medicine, Rehabilitation, and the National Center for Rehabilitation and Auditory Research (NCRAR). This is a great opportunity for study team members to hear clinical perspectives and to stay educated on mTBI rehabilitation approaches.

One of our postdoctoral scholars, Dr. Kody Campbell, was awarded a grant by the Medical Research Foundation (MRF) in 2020 titled "Can continuous monitoring of mobility with wearable sensors measure recovery after mTBI with and without rehabilitation?"

This project has allowed training for our Exito student who has directly been working with the data in this project. She recently had an abstract accepted at the APTA annual meeting, as well as providing training for completion of her honors thesis.

How were the results disseminated to communities of interest?

Information regarding the study has been documented on the following websites, which are available to the public:

- ClinicalTrials.gov
- ResearchMatch.org
- Fitbir.nih.gov

This reporting period we have submitted one manuscript and have one in preparation, along with conference abstracts, poster and virtual presentations, and attended a large community outreach event (see products below).

What do you plan to do during the next reporting period to accomplish the goals?

No Cost Extension: We received a no-cost extension expiring September 2022, which will allow us to finish data analysis and disseminating results in the next year. We have two manuscripts we are preparing and will submit in the next reporting period.

Recruitment & Enrollment: We plan to finish enrollment by March 2022 to allow enough time to finish data analysis.

APDM: Working to complete the DataHub and gait speed algorithm for real-time feedback (see technology below).

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

This project will influence the base knowledge and theory of physical therapy treatments for people who suffer from mTBI. This project will give insight on patient recovery for those receiving early intervention versus those receiving standard of care treatment. Clinical practice may also be impacted through the implementation of wearable sensors to more accurately measure and assess gait and balance during both at-home activity, as well as in clinical and rehabilitative settings.

What was the impact on other disciplines?

Our research team meets monthly throughout the year with a wide range of practitioners who treat patients with mTBI. These meetings allow our team to disseminate research findings, and help to

translate knowledge into clinical practice. Meeting with clinicians also allows our team to gain insight and discuss how research can help influence clinical practice.

What was the impact on technology transfer?

Throughout this reporting period we have been working closely with APDM Wearable Technologies to 1) validate an algorithm capable of tracking head, neck and trunk motions, and 2) generate an easy user interface for providing objective information to physical therapists and the patient. The technology is only being used within this study and we believe this is a large step toward being able to monitor mTBI recovery in the home environment. The inertial systems in use provide information beyond the typical activity tracker, by providing information not only on quantity (e.g. of steps), but on quality of movement. In the next reporting period the study team will work with physical therapists to implement this system within a clinic setting and get feedback on user experience.

What was the impact on society beyond science and technology?

Our research team has continued to help mentor the development of young researchers completing undergraduate and high-school programs of education. Specifically, we have had students engage in projects relating to the validation of the inertial sensors, rehabilitation outcomes, and eye-tracking procedures. Two students were selected to work in our laboratory from NIH Build Exito to work on this project. Build Exito is an undergraduate training program that supports underrepresented students interested in a career in science.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

We have modified Aim III due to COVID restrictions. (See goals for next reporting period section)

Actual or anticipated problems or delays and actions or plans to resolve them

No problems or delays.

Changes that had a significant impact on expenditures

We received a no-cost extension through September 2022. We plan to complete enrollment, data analysis, and dissemination of results in the next year.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

Significant changes in use or care of human subjects

No significant changes have been made.

6. PRODUCTS:

Publications, conference papers, and presentations

Journal publications.

Accepted Manuscript:

Martini DN, Pettigrew NC, Wilhelm JL, Parrington L, & King LA. (2021) Wearable sensors for vestibular rehabilitation: a pilot study. *J Physiother Res* Vol.5 No.8:31. doi:10.36648/ippr.21.5.31

Parrington L, Popa B, Martini DN, & King LA (2020). Instrumented balance assessment in mild traumatic brain injury: Normative values and descriptive data for acute, sub-acute and chronic populations. *Journal of Concussion.* doi:10.1177/2059700220975605

Lirani Silva E, Stuart SS, Parrington L, Campbell KR, & King LA. (2021) Saccade and Fixation Eye Movements during Walking in Mild Traumatic Brain Injury and Healthy Controls. Planned submission to *Frontiers in Bioengineering and Biotechnology*.

Manuscripts in Review:

Campbell KR, Wilhelm JL, Pettigrew NC, Scanlan KT, Chesnutt JC, & King LA. (2021) Tele-rehabilitation after mild traumatic brain injury; a pilot study on its feasibility and efficacy. *Journal of Neurologic Physical Therapy*. (Resubmitted: 8/11/2021)

Martini D, Wilhelm J, Lee L, Chesnutt J, Brumbach B, Skorseth, P, King LA. Exploring age and gender patterns for care after concussion; a retrospective analysis. Planned submission to *Archives of Physical Medicine and Rehabilitation.* (Invited for Revise and Resubmit)

Manuscripts in Preparation:

Campbell KR, Scanlan KT, Wilhelm JL, Pettigrew NC, Neilsen A, Parrington L, & King LA. Mini Balance Evaluation Systems Test: balance deficits by domain after mild traumatic brain injury. *Target Journal TBD*

Campbell KR, Gallun F, Kampel S, Chesnutt JC, Mabry J, & King LA. Auditory spatial processing in civilians with mild Traumatic Brain Injury. *Target Journal TBD*

Campbell KR, Mabry J, & King LA. Cognitive Deficits after mTBI: Do Standard Clinical Tests Relate to Real World Deficits? *Target Journal TBD*

Antonellis, P, Campbell KR, Wilhelm JL, Pettigrew NC, & King LA. Multimodal physical therapy for subacute mTBI may promote cardiovascular autonomic adaptations after mTBI. *Target Journal TBD*

Books or other non-periodical, one-time publications.

Other publications, conference papers and presentations.

Accepted Conference Abstracts:
Peterka RJ, Campbell KR, Parrington L, & King LA. Deficits in Standing Balance Control Following Mild Traumatic Brain Injury. Poster Presentation. Military Health Systems Research Symposium, August 23-26, 2021. (Not Presented due to COVID-19)

Campbell KR, Peterka RJ, Hullar TE, & King LA. Are We Measuring What We Say We are Measuring? Subjective and Objective Assessment of Vestibular and Ocular Motor Function in People with Mild Traumatic Brain Injury. Poster Presentation. Military Health Systems Research Symposium, August 23-26, 2021. (Not Presented due to COVID-19)

Campbell KR, Gallun F, Kampel S, Chesnutt JC, Mabry J, & King LA. Auditory spatial processing in civilians with mild Traumatic Brain Injury. Poster Presentation. Military Health Systems Research Symposium, August 23-26, 2021. (Not Presented due to COVID-19)

Scanlan KT, Wilhelm JL, Pettigrew NC, Neilsen A, Parrington L, & King LA. Mini Balance Evaluation Systems Test: balance deficits by domain after mild traumatic brain injury. Poster Presentation. Academy of Neurologic Physical Therapy Annual Conference (Virtual), Oct 1-3, 2021.

Mabry J, Campbell KR**,** & King LA. Does Dual Task Gait Relate to Cognitive Deficits in People with Mild Traumatic Brain Injury. Poster Presentation. 2022 Combined Sections Meeting – American Physical Therapy Association. San Antonio, TX, US. Feb 2 -5, 2022.

Wilhelm JL, Koch J, Pettigrew NC, Campbell KR**,** & King LA. Exploring Vestibular/Ocular Motor Screen (VOMS) in Adults As a Potential Outcome after Concussion Vestibular Rehabilitation. Podium Presentation. 2022 Combined Sections Meeting – American Physical Therapy Association. San Antonio, TX, US. Feb 2 -5, 2022

Pettigrew NC, Campbell KR**,** Parrington L, Peterka RJ, Wilhelm JL, Scanlan KT, & King LA. (2021) Vestibular Rehabilitation Is Facilitated By Audio Biofeedback after Mild Traumatic Brain Injury. Poster Presentation. 2022 Combined Sections Meeting – American Physical Therapy Association. San Antonio, TX, US. Feb 2 -5, 2022

Podium Presentations:
Gallun F, Campbell KR, Kampel S, Chesnutt JC, Mabry J, & King LA. Auditory processing after mild Traumatic Brain Injury. Podium Presentation. OHSU Research Week (Virtual), May 4-6, 2021.

Campbell KR, Peterka RJ, Hullar TE, & King LA. Are We Measuring What We Say We are Measuring? Subjective and Objective Assessment of Vestibular and Ocular Motor Function in People with Mild Traumatic Brain Injury. Podium Presentation. OHSU Research Week (Virtual), May 4-6, 2021.

Lee L, Martini D, Wilhelm J, Chesnutt J, Brumbach B, Skorseth, P, King LA. Exploring age and gender patterns for care after concussion; a retrospective analysis. Podium Presentation. OHSU Research Week (Virtual), May 4-6, 2021.

Neilsen A, Scanlan KT, Wilhelm JL, Pettigrew NC, Parrington L, & King LA. Balance deficits by domain on the Mini Balance Evaluation Systems Test following mild traumatic brain injury. Podium Presentation. OHSU Research Week (Virtual), May 4-6, 2021.

Peterka RJ, Campbell KR, Parrington L, & King LA. Deficits in Standing Balance Control in mTBI Subjects with Chronic Balance Complaints. Vestibular Oriented Research Meeting. February 2021. *(Virtual)*

Scanlan KT, Wilhelm JL, Pettigrew NC, Chesnutt JC & King LA. Is evidenced-based multimodal rehabilitation for mild traumatic brain injury using telehealth possible? American Physical Therapy Association Combined Sections Meeting. February 2021. *(Virtual)*

Wilhelm JL, Parrington L, Pettigrew NC, Scanlan KT, Martini DN, Chesnutt, JC, King LA. Cervical proprioception and neck dysfunction in people with subacute mild traumatic brain injury American Physical Therapy Association Combined Sections Meeting. February 2021. *(Virtual)*

Poster Presentations:
Lirani Silva E, Stuart SS, Parrington L, Campbell KR, & King LA. Saccade and Fixation Eye Movements during Walking in Mild Traumatic Brain Injury and Healthy Controls. *International Conference on Ambulatory Monitoring of Physical Activity and Movement* (Virtual), June 23-24, 2021.

Campbell KR, Mancini M, & King LA. Identifying Digital Biomarkers of Mobility During Daily Living in People Recovering from Mild Traumatic Brain Injury. *International Conference on Ambulatory Monitoring of Physical Activity and Movement* (Virtual), June 23-24, 2021.

Campbell KR**,** Peterka RJ, & King LA. Deficits in Standing Balance Control Following Mild Traumatic Brain Injury. 2021 National Center for Rehabilitative Auditory Research: Vestibular Disorders; From Cause to Cure, Portland, OR, US, Sept 29 – Oct 1, 2021.

Wilhelm JL, Campbell KR, Pettigrew NC, Kampel SD, Putterman DB, Peterka RJ, & King LA. Exploring the relationship between vestibular and oculomotor deficits and responsiveness to rehabilitation after concussion. 2021 National Center for Rehabilitative Auditory Research: Vestibular Disorders; From Cause to Cure, Portland, OR, US, Sept 29 – Oct 1, 2021.

Website(s) or other Internet site(s)

Nothing to Report

Technologies or techniques

Technology Development:

There were two stretch goals that were identified for optimizing the technology and are currently under implementation:

- DataHub: APDM developed and continues to verify the use of a charging unit that can be used to charge the sensors and wirelessly transfer the sensor data from the user home to a remote server for data analysis.
- Gait speed algorithm for real-time feedback: The algorithm to calculate gait speed from a lumbar and/or a trunk sensor is being implemented for off-line use. Depending on the timeline for implementation; verification; and results, the company will determine if real-time feedback on gait speed is attainable.

The development of the real time biofeedback has resulted in a grant application that will test this newly developed technology in a clinical population.

Inventions, patent applications, and/or licenses

Nothing to Report

Other Products

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Kody Campbell, PhD- no change
Josh Koch, BS- no change
Lindsey Lee, BS- no change
Daniel Putterman, Au.D. – no change
Natalie Pettigrew P.T, D.P.T – no change
Lucy Parrington, Ph.D – no change
Laurie King, Ph.D., P.T. – no change
Robert Peterka, Ph.D. – no change
James Chesnutt, M.D. – no change
Timothy Hullar, M.D. – no change
Jennifer Wilhelm, P.T., D.P.T., N.C.S. – no change
Shelby Martin, MA – no change
Edward King, MS – no change
Sean Kampel, Au.D – no change
Mahmoud El-Gohary – no change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Organization Name: APDM Wearable Technologies
Location of organization: 2828 SW Corbett Avenue, Portland, OR 97201
Partner's contribution to project: Partners have developed the Opals, which are the wearable sensors that detect movement, gait, and balance. They have developed kinematic algorithms and the home exercise interface for this study.

8. SPECIAL REPORTING REQUIREMENTS

9. APPENDICES

Rehabilitation of Complex TBI with Sensory Integration Balance Deficits; Can Early Initiation of Rehabilitation with Wearable Sensor Technology Improve Outcomes?

PI: Laurie King, PhD, PT **Org:** Oregon Health & Science University **Award Amount:** $4.6 million

Study/Product Aim(s)

Our central hypothesis is that rehabilitation after mTBI is suboptimal due to late initiation of and inadequate performance of exercises that do not adequately challenge vestibular and sensory integration function. Our long-term goal is to clarify best practices for the rehabilitation of balance deficits in people with mTBI by comparing early vs late (standard of care) initiation of physical therapy with and without wearable sensors on balance deficits after mTBI.

Aim I) Early Intervention: To determine the effects of early versus late rehabilitation for balance deficits in complex mTBI. Aim II) Home Monitoring: To compare traditional balance rehabilitation versus balance rehabilitation with sensor-based home monitoring of the quality of prescribed exercises. Aim III) Real-time Monitoring for Training: To develop and evaluate a novel, wearable sensor system to provide real-time feedback to physical therapists on head and trunk movement during training.

Approach

We will randomize, at the first physician visit (< 12 weeks post injury), 160 patients with mTBI to receive either early (within 2 weeks from physician visit) or late (standard of care ~60 days after physician visit) rehabilitation. People will be further randomized into either: 1) home exercise program or 2) the same home exercise program with wearable sensors worn on the forehead and trunk to monitor compliance and quality of performance during home exercises. Our primary outcome to measure efficacy of rehabilitation is the Dizziness Handicap Inventory (DHI). Secondary outcomes will be structured along the International Classification of Function and Disability (ICF) models framework and will include novel objective measures of balance and gait, central sensory integration and eye movements.

Timeline and Cost

Activities / CY	17	18	19	20
Study setup, Hiring, Training, Purchasing, IRB				
Recruitment				
Aims I and II: Balance Assessment and Rehabilitation 160 Randomized mTBI				
Aim III: Development and Evaluation of Real-time Monitoring				
Data Analysis				
Manuscript Preparation and Submission				
Estimated Budget ($K) $4,523	$1,007	$1,117	$1,148	$1,251

Updated: Portland, OR; October 27, 2021

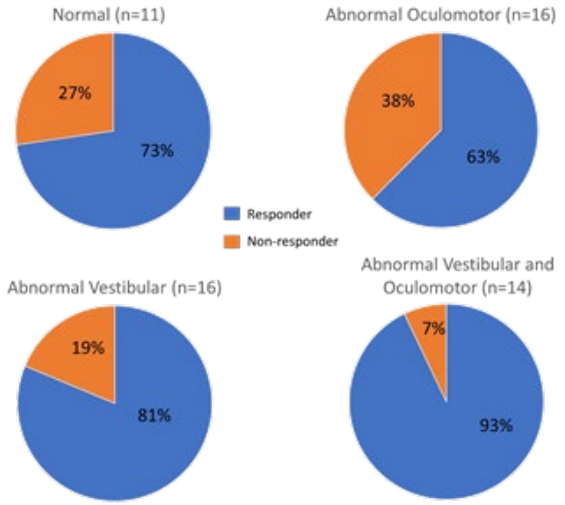


Figure 1: Proportions of vestibular rehabilitation responders (blue) and non-responders (orange) according to symptom profile subgroups.

Goals/Milestones

CY17 Goal – Study set up and launch
☒ All IRB, finalize protocols, order and test all equipment
☒ Begin balance assessment and rehabilitation (Aims I and II)
☒ Begin development of real-time feedback monitoring system (Aim III)
CY18 Goals – Clarify best practices for mTBI balance rehabilitation
☒ Continue testing and rehabilitation of subjects with mTBI
☒ Test and evaluate prototype feedback system on mTBI and control subjects
CY19 Goal – Clarify best practice for mTBI balance rehabilitation
☒ Continue testing and rehabilitation of subjects with mTBI
☒ Continue testing/evaluating feedback system and refine as directed
CY20 Goal – Complete all testing, analysis and dissemination of results
❑ Complete rehabilitation and all long term follow up testing
❑ Analyze results and disseminate findings

Comments: We received a no-cost extension to finish recruitment, data analysis, and dissemination through September 2022

Projected Expenditure: $4,652,124
Expenditures to Date: $3,169,426