

AWARD NUMBER: W81XWH-18-1-0083

TITLE: Addressing Neuromuscular Deficits for Improved Outcomes in Ankle Rehabilitation

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# REPORT DOCUMENTATION PAGE

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<b>6. AUTHOR(S)</b> Gribble, Phillip; Soute, Shawn; Wikstrom, Erik; Heebner Nick; Hoch, Matt; Johnson, Nathan; Powell, David  E-Mail: phillip.gribble@uky.edu				<b>5d. PROJECT NUMBER</b>	
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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The primary purpose of this study will seek to identify lateral ankle sprain (LAS) patients that do not respond to physical rehabilitation under a traditional medical model and who subsequently develop chronic ankle instability (CAI). The proposed study will evaluate established clinical outcomes along with innovative measures of brain and spinal cord function and ankle joint stability during a one-year follow-up after injury. Our hypothesis is that patients who develop CAI within one-year after injury will demonstrate poorer clinical outcomes, larger alterations in innovative measures of brain and spinal cord function, and early ankle joint cartilage turnover compared to the LAS patients that develop into Copers. The secondary purpose of this study will be to transition the results to methods that can be applied in multiple rehabilitation settings across civilian and military treatment facilities. We will determine which clinical measures are most related to the advanced brain and spinal cord measures.					
<b>15. SUBJECT TERMS</b> Lateral ankle sprain; sensorimotor; musculoskeletal treatment; physical readiness					
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## **1. INTRODUCTION**

Lateral ankle sprains (LAS) are the most commonly reported injury in military and civilian populations. Up to 70% of those who sustain a LAS will develop chronic ankle instability (CAI), with re-injury and persistent functional disability. In the military, those who suffer from CAI typically have less service time prior to discharge as a function of the physical limitations imposed by the ankle injury. Many with LAS history will develop ankle joint degeneration, marked by changes in its cartilage and has been shown even in young adults. This suggests the need to determine why some individuals follow the cascade of events of sustaining a LAS, to developing CAI, to developing osteoarthritis. A strong contribution to CAI appears to be related to lingering changes in the structure of the brain, which impacts efficient cortical regulation of overall body control. Standard of care (SOC) for LAS typically consists of symptom management or activity modification and a recovery protocol to improve motion and strength of the ankle but does not typically address central nervous system (CNS) deficiencies. However, the high rate of CAI suggests the SOC may not be sufficient. The purpose of this study is to compare the success of an innovative sensorimotor ankle rehabilitation training (SMART) protocol to mitigate the CNS deficiencies that likely lead to CAI and ankle joint degeneration. Ultimately, this study will utilize an integrative medicine approach (brain/spinal cord influence on neuromusculoskeletal injury rehabilitation) to address a common issue (why some people respond to treatment and are able to return to normal activities, while others do not) associated with LAS. This will improve the ability to disrupt the cascading transition from LAS to potential joint degeneration. This innovative and integrative approach to rehabilitation will significantly impact the short and long-term health and well-being of those affected by LAS.

## **2. KEYWORDS**

Lateral ankle sprain; sensorimotor; musculoskeletal treatment; physical readiness

### 3. ACCOMPLISHMENTS

#### Major Goals and Accomplishments

SOW Goals	Timeline	Achieved
<b>Major Task 1: Administrative Objectives</b>	Months	Y/N
Refine eligibility criteria, exclusion criteria, screening protocol	1-3	Y
Finalize consent form & human subjects protocol	1-3	Y
Coordinate with Sites for IRB protocol submission	1-3	Y
Coordinate with Sites for University of Kentucky IRB review	1-6	Y
Coordinate with Sites for University of North Carolina IRB review	1-6	Y
Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO)	1-6	Y
<i>Milestone Achieved: Local IRB approval at UK, UNC and BAMC</i>	3	Y
<i>Milestone Achieved: HRPO approval for all protocols and local IRB approval through University of Kentucky.</i>	18	Y
Coordinate with Sites for job descriptions design	1-4	Y
Advertise and interview for project related staff	1-5	Y
Coordinate for space allocation for new staff	1-6	Y
Coordinate with Sites for Independent Evaluators hiring and trainings	5-11	Y
Coordinate with Sites for training Independent Evaluators until 100% concordance	8-11	Y
<i>Milestone Achieved: Research staff trained</i>	8-11	Y
Quarterly Reports to USAMRMC	Quarterly	Y
Annual Reports to USAMRMC	Annually	Y
<b>Major Task 2: Technical Objectives</b>		
Finalize assessment measurements	1-4	Y
Coordinate with Sites for flow chart for all study steps, web data collection and database requirements	4-6	Y
<i>Milestone Achieved: 1<sup>st</sup> participant consented, screened and enrolled at each site</i>	7-8	Y
Subject recruitment. Participants complete follow-up assessments upon completion of physical therapy for acute LAS	7-32	Y
Complete follow-up assessments 6 months after completion of physical therapy	13-38	Y
Complete follow-up assessments 12 months after completion of physical therapy	19-44	Y
Milestone Achieved: All participants enrolled and follow-up assessments completed	44	N
Data Analysis: Clinical, CNS, and MRI outcomes	7-48	Y
Data interpretation and dissemination	36-48	N
<i>Milestone Achieved: Report findings from completed assessments</i>	36-48	N
Coordinate with Sites for annual IRB report for continuing review	Annually	Y
Submit amendments, adverse events and protocol deviations as needed	As Needed	Y

## Summary

### Human Subject Protections

Summary from Year 1: Approval of human subject protections was initiated on MAY 18 between the IRB offices of UK, UNC and WBAMC. Reliance agreements were discussed to recognize UK as the primary site for the study for all IRB offices. Initial approval of the study was obtained by the UK IRB on 10 MAY 18. Initial HRPO documents were submitted 4 JUN 18. Notification of receipt and initiation of review was received from Brittane Foy at MPMC on 11 JUN 18. Initial HRPO Administrative Review was received 2 AUG 18. Responses and supporting documents were returned to Brittane Foy 10 AUG 18. Second HRPO Administrative Review was received 5 NOV 18. Much of the 2<sup>nd</sup> Administrative Review required coordination and revisions to documents relative to WBAMC. From NOV 18 to JAN 19, Dr. Gribble coordinated with Larissa Schmersal, WBAMC Human Protections Administrator, to address requested revisions, as well as begin preparing CLAR materials to be submitted from WBAMC after HRPO review. By the end of Year 1 period (15 MAR 19), HRPO approval was not yet received.

Summary from Year 2: During Year 2, after a 4<sup>th</sup> HRPO Administrative Review was completed in MAY 19, initial HRPO approval was received 5 JUL 19. During JUL and AUG 19, Dr. Gribble prepared and submitted substantive changes to the protocol, including a site-PI change at WBAMC (CPT Golden) and modifications to the shared consent form. The Amendment Approval was received 6 SEP 19. Enrollment commenced in OCT 19. In JAN 20 during the UK IRB annual review, an oversight was discovered in the previously approved consent form related to HIPAA language that was not allowable by UK. Dr. Gribble worked with UK IRB, Dr. Schmersal and HRPO personnel during JAN 20 to modify the consent form to remove the HIPAA language and an Amendment Request was submitted 1 FEB 20, and approval of this amendment was received 11 MAR 20. Previously enrolled participants at all sites were re-consented with the new consent form. The HRPO Continuation Review was submitted in conjunction with the Amendment approval described above and was approved 11 MAR 20.

Summary from Year 3: During Year 3, modifications to improve recruitment and maintain study operations during COVID-19 restrictions were successfully submitted and approved. This allowed resumption of research that could be conducted in person while following COVID-19 mitigation guidelines, or to use a telehealth option temporarily. Personnel changes at WBAMC, including the departure of the site PI and the Clinical Research Coordinator, created further delays. Appropriate substantive changes submitted by Dr. Gribble were approved by UK IRB and HRPO to indicate this change in site PI corresponding with the addition of MAJ Stoute in this role at WBAMC starting in DEC 20. The HRPO Continuation Review was received and approved.

Summary from Year 4: During Year 4, several modifications were submitted and approved. To expand recruiting efforts, the study team discussed a modification of the inclusion criteria with our Science Officer, which allowed to have participants with a previous ankle sprain, but no signs and symptoms of chronic ankle instability. This proposal was approved by the UK IRB and HRPO in MAY 21. A

new Clinical Research Coordinator at WBAMC, Ms. Sarah Tolley, joined the project in JUN 21. A modification to the IRB to reflect this was approved 13 JUL 21. A modification to the IRB to reflect an update to the consent form to reflect that the intervention did not have a finite time period for completion was approved 17 AUG 21. A modification to the IRB to reflect an update to the consent form to reflect MAJ Stoute's promotion from CPT with the updated rank was approved 14 OCT 21. Dr. Gribble ensured that all subject personnel maintained appropriate CITI training and submitted the continuation review that was approved by the UK IRB 25 OCT 21. The HRPO Continuation Review was approved in DEC 21.

During Year 5, Dr. Gribble ensured that all subject personnel maintained appropriate CITI training and submitted the continuation review that was approved by the UK IRB 31 AUG 22. The HRPO Continuation Review was received and approved in 27 OCT 22.

In NOV 22, Dr. Gribble communicated with HRPO to notify of the approved UK IRB MR that reflected personnel changes at WBAMC (see Personnel section for more detail) and the addition of undergraduate student, Ms. Bailey Bunn, that would be engaging in study recruitment efforts. In this communication (see Appendices), Dr. Gribble submitted this as a potential substantive change as it would prohibit the ability to deliver the intervention at WBAMC in absence of the CRC. Given the time it would take to find and onboard a replacement, Dr. Gribble expressed that after consideration and discussion with the study team and Science Officer Jason Ghannadian, he wished to carry out any remaining follow-up testing under the guidance of the Site PI MAJ Stoute, but suspend any further enrollment at WBAMC. This email was acknowledged by Human Subjects Protection Scientist Kelsey Kilmon. Dr. Gribble has remained in contact with Ms. Kilmon and Dr. Ghannadian to prepare any further necessary documentation.

## **Personnel**

MAJ Shawn Stoute, the site PI at WBAMC, alerted Dr. Gribble in MAY 22 he would be leaving WBAMC in APR 23 to transition to a new post. MAJ Stoute will continue to oversee scheduled follow-up testing of WBAMC participants until his departure. His departure would necessitate identifying and on-boarding a new site PI.

On 3 NOV 22, the CRC at WBAMC, Ms. Sarah Tolley, submitted her resignation to Dr. Gribble effective 18 NOV 22 (see Appendices). There had been no prior discussion of this by Ms. Tolley with Dr. Gribble or the Site PI MAJ Stoute. On a follow-up video call with Dr. Gribble and MAJ Stoute, Ms. Tolley expressed no concerns about the CRC position, her work environment or personnel on the project. She expressed a desire to return to clinical practice again and there was an opportunity to begin working in the H2F program at Ft. Bliss. Ms. Tolley was compliant and helpful in assuring proper documentation and data access was available to Dr. Gribble and MAJ Stoute, and a transition plan was carried out.

After discussions among the study team, and between Dr. Gribble and Science Officer Jason Ghannadian, it was determined best not to replace the CRC position. All agreed that relative to the projections for how long it would take to find a suitable replacement and onboard the new CRC, it would not be worth the

investment of resources to replace the CRC relative to the return on study outcomes given the study's remaining timeline.

For the same reasons mentioned above relative to the CRC departure, the study team, along with input from Science Officer Ghannadian, recommend that a new site PI not be pursued. Subsequently, no new enrollments will be pursued at WBAMC. MAJ Stoute will oversee the 6 and 12-month follow-up testing of existing enrolled participants through remote communications.

### **Equipment Acquisition**

No equipment acquisitions took place in Year 4 of the project.

### **SOP Procedures and Site Visit**

Dr. Gribble conducted a site visit at WBAMC 17-19 MAY 22. During this time, he met with MAJ Stoute and Ms. Tolley, toured facilities in WBAMC where study outcomes were conducted, as well as H2-F facilities in 3 brigades where study recruitment and participant rehab interventions were conducted. During the visit, Dr. Gribble observed Ms. Tolley conduct a rehabilitation session of an enrolled participant. Additionally, Dr. Gribble observed MAJ Stoute conduct a 6-month follow testing session of an enrolled participant. Dr. Gribble observed compliance with SOP for intervention and outcome testing.

### **Opportunities for Training and Professional Development**

Nothing to Report

### **Dissemination of Results to Communities of Interest**

Dr. Gribble participated in the MOMRP conference in SEP 22. He presented the preliminary findings at this on-line conference, and received positive feedback about the project and the trajectory of findings to date.

### **Plan for Next Reporting Period**

As of this report, 25 participants have been enrolled across the three sites (UK: 9, UNC: 8; WBAMC: 8).

Due to an 18-month delay in initial HRPO approval followed by a two-year interruption from COVID-19 restrictions that began in MAR 20, enrollment and completion of interventions timelines had to be modified. While we continued to aggressively recruit during this reporting year, our sites have been experiencing considerable reductions in expected referrals since the global pandemic began. In DEC 22, we petitioned for and were granted a second No Cost Extension year (NCE) to continue study operations beyond the study ending date (15 MAR 23). Many aspects of musculoskeletal-related research enterprises have experienced significant interruptions and declines during this time period. We are encouraged that during this reporting period, new enrollments did continue, with 6 new enrolled

participants, and study activities continued, such as some 6-month and 12-month follow-up sessions were completed at UK, UNC and WBAMC. We anticipate that additional follow-up sessions of previously enrolled participants will proceed successfully during this next reporting period. We anticipate that our enrollment numbers will increase in the second NCE period, but our total enrollment may likely fall short of our intended enrollment goals. Our study team still believes that our data will provide valuable and impactful information that will contribute to the intended deliverables.

#### **4. IMPACT**

##### **Impact on Principal Disciplines of the Project**

Nothing to Report

##### **Impact on Other Disciplines**

Nothing to Report

##### **Impact on Technology Transfer**

Nothing to Report

##### **Impact on Society Beyond Science and Technology**

Nothing to Report

#### **5. CHANGES/PROBLEMS**

##### **Changes in Approach and Rationale**

Nothing to Report

##### **Actual or Anticipated Problems or Delays**

During Year 5, limitations in additional enrollment due to the COVID-19 outbreak that began to affect the United States in FEB 20 persisted. In-person research allowances were maintained at all three sites, but referrals to our study continued to be low, which we attribute to the societal restrictions in place. We began using the expanded inclusion criteria adopted in Year 4 to allow for a previous ankle injury history without evidence of the development of chronic ankle instability. Access to some critical recruiting portals, such as in-person recruiting by our study personnel in the ED, continued to be restricted due to COVID-19 protocols. In spite of these restrictions, we were able to enroll 6 new participants during this reporting period.

As described above, the Clinical Research Coordinator at WBAMC site was vacated 18 NOV 22. The timing of this absence relative to the remaining timeline of the study led to the decision to cease enrollment at WBAMC.

Despite our efforts and alternative strategies, the COVID-19 pandemic has created significant, unanticipated delays in study operations in the lifespan of the study, including over the last 12 months. These delays justified our request for an initial and now a second No Cost Extension period to continue study activities. We are hopeful that in the coming year, these barriers will lessen and our trajectory of accomplishing study objectives will resume.

### **Changes in Expenditures**

During this reporting period, Dr. Gribble increased his effort from 16% back to 20% that was originally budgeted to more closely match effort with project responsibilities.

With the vacancy of the Clinical Research Coordinator starting 18 NOV 22, there were no study related expenditures on the Geneva Foundation sub-award related to this position during these months. These has led to creating some surplus in the operating budget which Dr. Gribble as PI will be using to help support study efforts in the second no-cost extension period that has been granted.

### **Changes in Use or Care of Human Subjects**

Nothing to Report

## **6. PRODUCTS, INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES**

### **Publications, Conference Papers, and Presentations**

Dr. Gribble participated in the MOMRP conference in SEP 22. He presented the preliminary findings at this on-line conference, and received positive feedback about the project and the trajectory of findings to date.

### **Websites or Other Internet Sites**

Nothing to Report

### **Technologies or Techniques**

Nothing to Report

### **Inventions, Patent Applications, and/or licenses**

Nothing to Report

### **Other Products**

Nothing to Report

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### Individuals Working on Project

<b>Name:</b>	<b>Phillip Gribble</b>
Project Role:	Principal Investigator
Nearest person month worked:	2
Contribution to Project:	Provide scientific oversight to the project and direct activities at UK, UNC and WBAMC. Assumes responsibility for the scientific integrity of the project; works closely with the site-PIs to ensure validity of the data and observations from the investigators. Ensure compliance with specific terms and conditions of the award as stated in the award notification. Supervise and co-mentor graduate student researchers.
Funding Support:	N/A
<b>Name:</b>	<b>Nick Heebner</b>
Project Role:	Co-Investigator
Nearest person month worked:	1
Contribution to Project:	Assist with data collection, interpretation and analysis
Funding Support:	N/A
<b>Name:</b>	<b>Matt Hoch</b>
Project Role:	Co-Investigator
Nearest person month worked:	0
Contribution to Project:	Assist with data interpretation and analysis
Funding Support:	N/A
<b>Name:</b>	<b>Nathan Johnson</b>
Project Role:	Co-Investigator
Nearest person month worked:	1
Contribution to Project:	Assist with data collection, interpretation and analysis
Funding Support:	N/A

<b>Name:</b>	<b>David Powell</b>
Project Role:	Co-Investigator
Nearest person month worked:	0
Contribution to Project:	Assist with data interpretation.
Funding Support:	N/A
<b>Name:</b>	<b>Kyle Kosik</b>
Project Role:	Co-Investigator
Nearest person month worked:	9
Contribution to Project:	Coordinate data collection sessions at UK. Assist with recruitment. Assist with data collection, interpretation and analysis
Funding Support:	N/A
<b>Name:</b>	<b>Erik Wikstrom</b>
Project Role:	Co-Investigator
Nearest person month worked:	1.75
<b>Contribution to Project:</b>	Site PI at UNC. Provides oversight to all activities at UNC. Maintains communication with PI. Contributes to data interpretation and analysis from all sites.
Funding Support:	N/A
<b>Name:</b>	<b>Sarah Tolley</b>
Project Role:	Co-Investigator
Nearest person month worked:	3
Contribution to Project:	Clinical Research Coordinator. Coordinate intervention sessions at WBAMC. Assist with recruitment at WBAMC. Assist with data collection, interpretation and analysis at WBAMC. Maintains communication with site-PI at WBAMC and study PI at UK.
Funding Support:	N/A

**Change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period**

**Matt Hoch, PhD**

**NEW Title: Visual-Motor Coordination Assessments for Patients with Chronic Ankle Instability: Decision Support Tools to Optimize Return to Duty**

**Role:** Principal Investigator

**Time Commitments:** 17%, 2.04 person months

**Supporting Agency:** Army Medical Research and Materiel Command

**Performance Period:** 09/01/2022 – 08/31/2026

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** The purpose of this proposal is to establish a novel outcomes assessment paradigm focused on visual-motor coordination (VMC) in patients with CAI.

**Aim 1:** VMC assessments will more effectively identify residual motor dysfunction.

**Aim 2:** Exhibit associations with brain connectivity, cognitive performance, and injury-related fear. **Aim 3:** Demonstrate strong test-retest reliability in CAI patients.

**Point of Contact:** Jennifer Shankle (Grants Management Specialist)

**Title: Musculoskeletal Health Considerations to Improve Resiliency and Lethality in Female Marines**

**Role:** Principal Investigator

**Time Commitments:** 28%, 3.4 person months

**Supporting Agency:** United States Department of Defense, Office of Naval Research

**Performance Period:** 08/30/2021 – 08/29/2024

**Level of Funding:**

**Sub-Awards:** Naval Health Research Center, University of North Carolina Charlotte

**Goals:** The purpose of this study is to compare musculoskeletal injury and healthcare utilization patterns between male and female Marines. This study will also examine sex-specific contributing factors to musculoskeletal injury and threats to resiliency following musculoskeletal injury.

**Aim 1:** Examine differences in musculoskeletal injury risk between female and male service members across different occupations and phases of the deployment cycle. **Aim 2:** Compare healthcare utilization as a result of musculoskeletal injury in female and male service members in combat and non-combat occupations. **Aim 3:** Identify sex-specific factors for musculoskeletal injury in active-duty service members. **Aim 4:** Determine the effect of musculoskeletal injury on resiliency in female and male service members. **Aim 5:** Explore field-based physiologic and biomechanical data captured using remote monitoring technology to assess musculoskeletal injury risk and recovery.

**Point of Contact:** Joshua Swift (Program Officer), Office of Naval Research, 875 North Randolph Street, Arlington, VA 22203-1995.

**CLOSED Title: Optimizing Musculoskeletal Health Outcomes through High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT)**

**Role:** Co-Investigator

**Time Commitments:** No measurable effort

**Supporting Agency:** Office of Naval Research

**Performance Period:** 10/01/2021–09/30/2022

**Level of Funding:**

**Goals:** The scientific objective is to acquire high-resolution peripheral quantitative computed tomography (HRpQCT) to enable our team to make significant leaps forward in several identified areas where musculoskeletal injuries limit the readiness of military personnel's ability to return to duty.

**Specific Aims:** 1) Prospectively assess the effect of trabecular and subchondral bone microarchitecture on the development of post-traumatic osteoarthritis (PTOA); 2) Evaluate measures of trabecular and cortical bone tissue integrity following recovery of a tibia fracture; 3) Investigate the relationship of alterations of bone tissue integrity in patients that have sustained mild traumatic brain injury; 4) Improve the education of clinicians and clinician scientists engaged in the treatment, recovery and prevention of common skeletal tissue injuries and conditions.

**Point of Contact:** Joshua Swift

### Nick Heebner, PhD

**NEW Title: Visual-Motor Coordination Assessments for Patients with Chronic Ankle Instability: Decision Support Tools to Optimize Return to Duty**

**Role:** Co-Investigator

**Time Commitments:** 5%, 0.60 person months

**Supporting Agency:** Army Medical Research and Materiel Command

**Performance Period:** 09/01/2022 – 08/31/2026

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** The purpose of this proposal is to establish a novel outcomes assessment paradigm focused on visual-motor coordination (VMC) in patients with CAI.

**Aim 1:** VMC assessments will more effectively identify residual motor dysfunction.

**Aim 2:** Exhibit associations with brain connectivity, cognitive performance, and injury-related fear. **Aim 3:** Demonstrate strong test-retest reliability in CAI patients.

**Point of Contact:** Jennifer Shankle (Grants Management Specialist)

**NEW Title: Safety, Health, and Injury Mitigation in Firefighter Training (SHIFT)**

**Role:** Co-Investigator

**Time Commitments:** 10%, 1.2 person months

**Supporting Agency:** Federal Emergency Management Agency

**Performance Period:** 09/22/2022 – 09/21/2025

**Level of Funding:**

**Sub-Awards:** Georgia Southern

**Goals:** The focus of our research team is to minimize musculoskeletal injury and promote safe activity in physically active populations. The objective of our research is to better quantify musculoskeletal injury mechanisms in structural firefighters in order to inform evidence-based prevention strategies designed to decrease injury risk. The purposes of this proposal are to examine specific mechanisms of musculoskeletal injury sustained by firefighters during occupational and physical training activities and explore the role that HCPs have on improving care for these injuries.

**Aim 1:** Describe the injury mechanisms and risk factors associated with physical training and occupational operations in firefighters. **Aim 2:** Compare firefighter

occupational time-loss outcomes due to musculoskeletal injury between departments that use different integrations of health care providers to manage injury. **Aim 3:** Identify the most common barriers to implementation of the model of direct access to HCP in Fire Departments.

**Point of Contact:** Julia Barron (Preparedness Officer)

**Title: Musculoskeletal Health Considerations to Improve Resiliency and Lethality in Female Marines**

**Role:** Co-Investigator

**Time Commitments:** 28%, 3.4 person months

**Supporting Agency:** United States Department of Defense, Office of Naval Research

**Performance Period:** 08/30/2021 – 08/29/2024

**Level of Funding:**

**Sub-Awards:** Naval Health Research Center, University of North Carolina Charlotte

**Goals:** The purpose of this study is to compare musculoskeletal injury and healthcare utilization patterns between male and female Marines. This study will also examine sex-specific contributing factors to musculoskeletal injury and threats to resiliency following musculoskeletal injury.

**Aim 1:** Examine differences in musculoskeletal injury risk between female and male service members across different occupations and phases of the deployment cycle. **Aim 2:** Compare healthcare utilization as a result of musculoskeletal injury in female and male service members in combat and non-combat occupations. **Aim 3:** Identify sex-specific factors for musculoskeletal injury in active-duty service members. **Aim 4:** Determine the effect of musculoskeletal injury on resiliency in female and male service members. **Aim 5:** Explore field-based physiologic and biomechanical data captured using remote monitoring technology to assess musculoskeletal injury risk and recovery.

**Point of Contact:** Joshua Swift (Program Officer), Office of Naval Research, 875 North Randolph Street, Arlington, VA 22203-1995

**CLOSED Title: Optimizing Musculoskeletal Health Outcomes through High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT)**

**Role:** Principal Investigator

**Time Commitments:** No measurable effort

**Supporting Agency:** Office of Naval Research

**Performance Period:** 10/01/2021–09/30/2022

**Level of Funding:**

**Goals:** The scientific objective is to acquire high-resolution peripheral quantitative computed tomography (HRpQCT) to enable our team to make significant leaps forward in several identified areas where musculoskeletal injuries limit the readiness of military personnel's ability to return to duty.

**Specific Aims:** 1) Prospectively assess the effect of trabecular and subchondral bone microarchitecture on the development of post-traumatic osteoarthritis (PTOA); 2) Evaluate measures of trabecular and cortical bone tissue integrity following recovery of a tibia fracture; 3) Investigate the relationship of alterations of bone tissue integrity in patients that have sustained mild traumatic brain injury; 4) Improve the education of clinicians and clinician scientists engaged in the

treatment, recovery and prevention of common skeletal tissue injuries and conditions.

**Point of Contact: Joshua Swift**

**Phillip Gribble, PhD**

**NEW Title: Visual-Motor Coordination Assessments for Patients with Chronic Ankle Instability: Decision Support Tools to Optimize Return to Duty**

**Role:** Co-Investigator

**Time Commitments:** 2%, 0.24 person months

**Supporting Agency:** Army Medical Research and Materiel Command

**Performance Period:** 09/01/2022 – 08/31/2026

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** The purpose of this proposal is to establish a novel outcomes assessment paradigm focused on visual-motor coordination (VMC) in patients with CAI.

**Aim 1:** VMC assessments will more effectively identify residual motor dysfunction.

**Aim 2:** Exhibit associations with brain connectivity, cognitive performance, and injury-related fear. **Aim 3:** Demonstrate strong test-retest reliability in CAI patients.

**Point of Contact:** Jennifer Shankle (Grants Management Specialist)

**NEW Title: Safety, Health, and Injury Mitigation in Firefighter Training (SHIFT)**

**Role:** Principal Investigator

**Time Commitments:** 14%, 1.68 person months

**Supporting Agency:** Federal Emergency Management Agency

**Performance Period:** 09/22/2022 – 09/21/2025

**Level of Funding:**

**Sub-Awards:** Georgia Southern

**Goals:** The focus of our research team is to minimize musculoskeletal injury and promote safe activity in physically active populations. The objective of our research is to better quantify musculoskeletal injury mechanisms in structural firefighters in order to inform evidence-based prevention strategies designed to decrease injury risk. The purposes of this proposal are to examine specific mechanisms of musculoskeletal injury sustained by firefighters during occupational and physical training activities and explore the role that HCPs have on improving care for these injuries.

**Aim 1:** Describe the injury mechanisms and risk factors associated with physical training and occupational operations in firefighters. **Aim 2:** Compare firefighter occupational time-loss outcomes due to musculoskeletal injury between

departments that use different integrations of health care providers to manage injury. **Aim 3:** Identify the most common barriers to implementation of the model of direct access to

HCP in Fire Departments.

**Point of Contact:** Julia Barron (Preparedness Officer)

**CLOSED Title: Optimizing Musculoskeletal Health Outcomes through High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Role:** Co-investigator

**Time Commitments:** No measurable effort

**Supporting Agency:** Office of Naval Research

**Performance Period:** 10/01/2021–09/30/2022

**Level of Funding:**

**Goals:** The scientific objective is to acquire high-resolution peripheral quantitative computed tomography (HRpQCT) to enable our team to make significant leaps forward in several identified areas where musculoskeletal injuries limit the readiness of military personnel's ability to return to duty.

**Specific Aims:** 1) Prospectively assess the effect of trabecular and subchondral bone microarchitecture on the development of post-traumatic osteoarthritis (PTOA); 2) Evaluate measures of trabecular and cortical bone tissue integrity following recovery of a tibia fracture; 3) Investigate the relationship of alterations of bone tissue integrity in patients that have sustained mild traumatic brain injury; 4) Improve the education of clinicians and clinician scientists engaged in the treatment, recovery and prevention of common skeletal tissue injuries and conditions.

**Point of Contact:** Joshua Swift

### Kyle Kosik, PhD

**NEW Title:** Visual-Motor Coordination Assessments for Patients with Chronic Ankle Instability: Decision Support Tools to Optimize Return to Duty

**Role:** Co-Investigator

**Time Commitments:** 15.5%, 1.86 person months

**Supporting Agency:** Army Medical Research and Materiel Command

**Performance Period:** 09/01/2022 – 08/31/2026

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** The purpose of this proposal is to establish a novel outcomes assessment paradigm focused on visual-motor coordination (VMC) in patients with CAI.

**Aim 1:** VMC assessments will more effectively identify residual motor dysfunction.

**Aim 2:** Exhibit associations with brain connectivity, cognitive performance, and injury-related fear. **Aim 3:** Demonstrate strong test-retest reliability in CAI patients.

**Point of Contact:** Jennifer Shankle (Grants Management Specialist)

**CLOSED Title:** Optimizing Musculoskeletal Health Outcomes through High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) **Role:**

Co-investigator

**Time Commitments:** No measurable effort

**Supporting Agency:** Office of Naval Research

**Performance Period:** 10/01/2021–09/30/2022

**Level of Funding:**

**Goals:** The scientific objective is to acquire high-resolution peripheral quantitative computed tomography (HRpQCT) to enable our team to make significant leaps forward in several identified areas where musculoskeletal injuries limit the readiness of military personnel's ability to return to duty.

**Specific Aims:** 1) Prospectively assess the effect of trabecular and subchondral bone microarchitecture on the development of post-traumatic osteoarthritis (PTOA); 2) Evaluate measures of trabecular and cortical bone tissue integrity following recovery of a tibia fracture; 3) Investigate the relationship of alterations of

bone tissue integrity in patients that have sustained mild traumatic brain injury; 4) Improve the education of clinicians and clinician scientists engaged in the treatment, recovery and prevention of common skeletal tissue injuries and conditions.

**Point of Contact:** Joshua Swift

### **David Powell, PhD**

**NEW Title:** Strategies for targeting astrocyte reactivity in Alzheimer's disease and related disorders

**Role:** Core Co-Leader, Cores B & C

**Time Commitments:** Core B: 5%, 0.6 person months; Core C: 10%, 1.2 person months

**Supporting Agency:** NIA

**Performance Period:** 9/1/2022 – 8/31/2027

**Level of Funding:**

**Goals (Core B):** The central purpose of our Core B is to support the proposed projects by providing our reliable routine service on functional assays in living animals.

**Core B Specific Aims:**

(1) Coordinate for small animal surgeries and intravital imaging techniques, including training and oversight. (2) Coordinate all brain slice electrophysiology experiments. (3) Coordinate and provide service for microelectrode arrays experiments. (4) Coordinate and provide service for Magnetic Resonance Imaging experiments.

**Goals (Core C):** The Human Studies Core functions to serve and complement the P01 Projects.

**Core C Specific Aims:**

1: Optimize clinically-relevant study design and manage an ongoing data streams incorporating human biomarker and autopsy data. 2: From existing autopsy material and data, generate a set of samples from human cases from the UK-ADRC that encompasses the ADRD phenotypes studied in all 4 Projects (AD, VCID, LATE+HS, and controls) and provides a common basis for downstream biochemical and neuropathological endpoint assessments relevant to the Projects. 3: From existing clinical material, generate a set of biomarker (in vivo) data from human subjects that represents a common basis for downstream biofluids and neuroimaging endpoint assessments relevant to the projects.

**Point of Contact:** Lisa A. Opanashuk, NIA [\\_\\_\\_\\_\\_](#)

**NEW Title: KSCHIRT: Pharmacological Intervention Targeting Mitochondrial Respiration for the Treatment of Traumatic Brain Injury**

**Role:** Other Significant Contributor

**Time Commitments:** N/A

**Supporting Agency:** KY Spinal Cord and Head Injury Research Trust

**Performance Period:** 02/01/2023 – 01/31/2024

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** The central hypothesis of this proposal is that AuPhos can afford neuroprotection following TBI by directly interacting with mitochondrial complex I to enhance mitochondrial biogenesis and to elucidate the mechanism(s) underlying neuroprotection.

**Specific Aims:** Aim 1: To determine the optimal dosage and therapeutic window of opportunity for AuPhos to maintain enhanced mitochondrial biogenesis post-injury (PI) and optimize AuPhos via synthetic chemistry to obtain an improved drug candidate to treat TBI. Aim 2: To determine the mechanism by which AuPhos affords neuroprotection by testing the hypothesis that the therapeutic benefit of AuPhos is mediated through interactions with mitochondrial complex I that enhances mitochondrial biogenesis.

**Point of Contact:** Jennifer Bobbitt (Administrative Specialist)

**NEW Title: Establishing the Role of MMP9 in Amyloid-Immunotherapy-Induced ARIA**

**Role:** Co-Investigator

**Time Commitments:** 5%, 0.6 person months

**Supporting Agency:** National Institute of Neurological Disorders &

Stroke **Performance Period:** 09/15/2022 – 08/31/2025

**Level of Funding:**

**Sub-Awards:** N/A

**Goals:** To test the novel hypothesis that anti-A $\beta$  immunotherapy triggers ARIA through inflammatory sequelae involving activation of the matrix metalloproteinase MMP9, degrading tight junction/basement membranes of vasculature inducing ARIA.

**Specific Aims:** Aim 1: Define neurovascular and neuroimmune responses to A $\beta$  immunotherapy in the humanized-A $\beta$  mouse model; Aim 2: Determine the role of MMP9 in ARIA development resulting from A $\beta$  immunotherapy; Aim 3: Evaluate the potential of MMP9 inhibition to eliminate ARIA.

**Point of Contact:** Roderick A. Corriveau (Program Director)

**Title:** Reduced BBB Water Exchange as a Preclinical Biomarker of Small Vessel Disease

**Role:** Co-investigator

**Time Commitments:** XX

**Supporting Agency:** NINDS

**Performance Period:** 2/1/2022 – 1/31/2025

**Level of Funding:**

**Goals:** This project will identify relations between a promising new biomarker of preclinical small vessel disease (SVD), cognition and brain connectivity patterns over time.

**Point of Contact:** Bruce Phillip Mertz, NINDS \_\_\_\_\_

Other Involved Partner Organizations

Nothing to Report

## 8. SPECIAL REPORTING REQUIREMENTS


### Collaborative Awards

Nothing to Report

### Quad Chart

**Addressing neuromuscular deficits for improved outcomes in ankle sprain rehabilitation**  
 Program: Joint Program Committee 8/Clinical & Rehabilitative Medicine Research Program  
 Funding Opportunity Number: W81XWH-17-DMRDP-CRMRP-NMSIRRA

**PI:** Gribble, Phillip A      **Org:** University of Kentucky      **Award Amount:** \$2.5 million

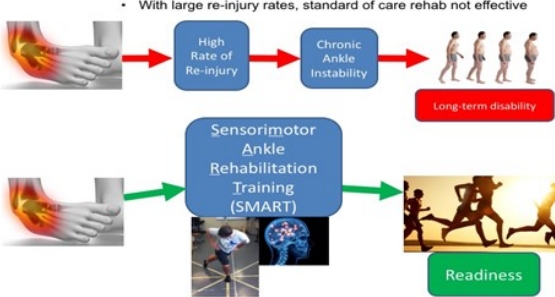


**Study/Product Aim(s)**

- Aim #1:** Determine if a novel sensorimotor ankle rehabilitation training (SMART) protocol improves clinical outcomes (patient-reported function and quality of life, lateral ankle sprain (LAS) re-injury rates, postural control, ankle ROM) and ankle joint integrity (articular cartilage turnover) in LAS patients.
- Aim #2:** Determine if SMART improves innovative measures of central nervous system (CNS) function (corticospinal excitability and brain white matter integrity) in LAS patients.
- Aim #3:** Delineate the association between explanatory mechanistic measures (corticospinal excitability and brain white matter integrity) and the hypothesized improvements in clinical and ankle joint integrity in LAS patients receiving SMART.

**Approach**  
 We will compare SMART protocol against a standard of care protocol to demonstrate successful 1-year outcomes and lower rates of re-injury and disability. We expect improvement in clinical outcomes, CNS function and joint health, improving health in LAS patients, bringing translational application to military personnel.

- LAS = Most common injury in military & civilians
- > \$7.5 billion in annual costs for LAS
- Re-injury and disability = decreased activity and health
- With large re-injury rates, standard of care rehab not effective



**Timeline and Cost**

Activities	CY	18	19	20	21
Regulatory/human subjects					
Participant enrollment, intervention implementation, post-testing					
1-year follow up testing					
Analysis of clinical, sensorimotor and MRI outcomes					
<b>Estimated Budget (\$K)</b>		<b>\$745</b>	<b>\$565</b>	<b>\$580</b>	<b>\$610</b>

**Goals/Milestones**

**CY19 Goal** – 25% enrollment

- Post-testing complete on 25% of sample
- Analysis of outcomes begins

**CY20 Goals** – 100% enrollment

- Post-testing complete on 100% of sample
- 1 year follow up complete on 50% of sample
- Analysis of outcomes continues

**CY21 Goal** – Completion of follow-up and outcomes analysis

- 1 year follow up complete on 100% of sample
- Analysis of outcomes at all time points of 100% of sample

**CY22 Goal**

- Dissemination of data

**APPENDICES**

- A. Letter of approval of Continuation Review – University of Kentucky IRB
- B. Email communication – HRPO approval of Continuation Review
- C. Resignation letter – Clinical Research Coordinator at WBAMC
- D. Email communication – Dr. Gribble alerting HRPO of the IRB modification and potential substantive change from the personnel changes at WBAMC



XP Continuation Review

Approval Ends:  
8/30/2023

IRB Number:  
44172

TO: Phillip Gribble, PhD, ATC  
Health Sciences - Rehabilitati  
PI phone #: 859- 218-0885  
  
PI email: phillip.gribble@uky.edu

FROM: Chairperson/Vice Chairperson  
Medical Institutional Review Board (IRB)

SUBJECT: Approval for Continuation

DATE: 8/31/2022

On 8/31/2022, the Medical Institutional Review Board approved your protocol entitled:

Addressing Neuromuscular Deficits for Improved Outcomes in Ankle Rehabilitation

Approval is effective from 8/31/2022 until 8/30/2023 and extends to any consent/assent form, cover letter, and/or phone script. If applicable, the IRB approved consent/assent document(s) to be used when enrolling subjects can be found in the "All Attachments" menu item of your E-IRB application. [Note, subjects can only be enrolled using consent/assent forms which have a valid "IRB Approval" stamp unless special waiver has been obtained from the IRB.] Prior to the end of this period, you will be sent a Continuation Review (CR)/Administrative Annual Review (AAR) request which must be completed and submitted to the Office of Research Integrity so that the protocol can be reviewed and approved for the next period.

In implementing the research activities, you are responsible for complying with IRB decisions, conditions and requirements. The research procedures should be implemented as approved in the IRB protocol. It is the principal investigator's responsibility to ensure any changes planned for the research are submitted for review and approval by the IRB prior to implementation. Protocol changes made without prior IRB approval to eliminate apparent hazards to the subject(s) should be reported in writing immediately to the IRB. Furthermore, discontinuing a study or completion of a study is considered a change in the protocol's status and therefore the IRB should be promptly notified in writing.

For information describing investigator responsibilities after obtaining IRB approval, download and read the document "[PI Guidance to Responsibilities, Qualifications, Records and Documentation of Human Subjects Research](#)" available in the online Office of Research Integrity's [IRB Survival Handbook](#). Additional information regarding IRB review, federal regulations, and institutional policies may be found through [ORI's web site](#). If you have questions, need additional information, or would like a paper copy of the above mentioned document, contact the Office of Research Integrity at 859-257-9428.

see blue.

405 Kinkead Hall | Lexington, KY 40506-0057 | P: 859-257-9428 | F: 859-257-8995 | [www.research.uky.edu/ori/](http://www.research.uky.edu/ori/)

An Equal Opportunity University

**Subject:** E04036.1 Series - Continuing Review Acknowledgement Memorandum (Proposal Number DM170430, Award Number W81XWH-18-1-0083)

**Date:** Thursday, October 27, 2022 at 11:17:21 AM Eastern Daylight Time

**From:** Kelsey Kilmon

**To:** Wikstrom, Erik A., CPT Shawn Stoute, Gribble, Phillip A.

**CC:** Kimberly Odam, Andrea Kline, IRB Reliance, Dr. Kim Carter, Tracey Harris, Kelsey Kilmon, D. Jason Ghannadian, David Adosci

**CAUTION: External Sender**

SUBJECT: Acknowledgement of the Continuing Review documents for the Protocol, "Addressing Neuromuscular Deficits for Improved Outcomes in Ankle Rehabilitation," Submitted by Phillip A. Gribble, Ph.D., University of Kentucky, Lexington, Kentucky, Proposal Log Number DM170430, Award Number W81XWH-18-1-0083, OHRO Log Number E04036.1 Series

1. The U.S. Army Medical Research and Development Command (USAMRDC), Office of Human and Animal Research Oversight (OHARO), Office of Human Research Oversight (OHRO) approved the following institutions which all rely on the University of Kentucky for review, approval, and oversight of the above-referenced multi-site protocol. The OHRO received a continuing review report for the protocol on 10/25/2022. The University of Kentucky IRB approved continuation of the protocol at the following sites on 08/31/2022; this approval will expire on 08/30/2023.

- a. OHRO Log Number E04036.1a, University of Kentucky, Phillip Gribble, Ph.D.
- b. OHRO Log Number E04036.1b, University of North Carolina at Chapel Hill, Erik Wikstrom, Ph.D.
- c. OHRO Log Number E04036.1c, William Beaumont Army Medical Center, CPT Shawn Stoute

2. This correspondence serves to acknowledge OHRO receipt of the continuing review documents for the protocol. No further action related to this continuing review is needed. The documents in support of this continuing review will be placed in the OHRO file.

3. The Principal Investigator must provide the following post-approval submissions to the OHRO via email to [usarmy.detrick.medcom-usamrmc.other.hrpo@health.mil](mailto:usarmy.detrick.medcom-usamrmc.other.hrpo@health.mil). **Failure to comply could result in suspension of funding.**

a. Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the OHRO for approval prior to implementation. The USAMRDC OHARO OHRO defines a substantive modification as a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change in the IRB of Record, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in study design (i.e. would prompt additional scientific review), or a change that could potentially increase risks to subjects.

b. A copy of the IRB continuing review approval letter must be submitted to the OHRO as soon as possible after receipt of approval. Please note that the OHRO conducts random audits at the time of continuing review and additional information and documentation may be requested at that time.

c. The final study report submitted to the IRB, including a copy of any acknowledgement documentation and any supporting documents, must be submitted to the OHRO as soon as all documents become available.

d. The following study events must be promptly reported to the OHRO by telephone (301-619-2165), by email ([usarmy.detrick.medcom-usamrmc.other.hrpo@health.mil](mailto:usarmy.detrick.medcom-usamrmc.other.hrpo@health.mil)), or by facsimile (301-619-7803) or mail to the U.S. Army Medical Research and Development Command, ATTN: MCMR-RP, 810 Schreider Street, Fort Detrick, Maryland 21702-5000.

(1) All unanticipated problems involving risk to subjects or others.

(2) Suspensions, clinical holds (voluntary or involuntary), or terminations of this research by the IRB, the institution, the sponsor, or regulatory agencies.

(3) Any instances of serious or continuing noncompliance with the federal regulations or IRB requirements.

(4) The knowledge of any pending compliance inspection/visit by the Food and Drug Administration (FDA), Office for Human Research Protections, or other government agency concerning this clinical investigation or research.

(5) The issuance of inspection reports, FDA Form 483, warning letters, or actions taken by any government regulatory agencies.

(6) Change in subject status when a previously enrolled human subject becomes a prisoner must be promptly reported to the USAMRDC OHARO OHRO. The report must include actions taken by the institution and the IRB.

e. Events or protocol reports received by the OHRO that do not meet reporting requirements identified within this memorandum will be included in the OHRO study file but will not be acknowledged.

4. Please note: The USAMRDC OHARO OHRO conducts site visits as part of its responsibility for compliance oversight. Accurate and complete study records must be maintained and made available to representatives of the USAMRDC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

5. Do not construe this correspondence as approval for any contract or grant/cooperative agreement funding. Only the Contracting Officer/Grants Officer can authorize expenditure of funds by notice of official award documentation. It is recommended that you contact the appropriate contract/grants specialist or Contracting/Grants Officer regarding the expenditure of funds for your project.

6. The OHRO point of contact for this study is Mrs. Kelsey Kilmon, B.S., Human Subjects Protection Scientist

Mrs. Kelsey Kilmon, B.S.  
Contractor - General Dynamics Information Technology  
Human Subjects Protection Scientist  
Office of Human Research Oversight  
USAMRDC Office of Human and Animal Research Oversight (OHARO)

November 3, 2022

Dear Dr. Gribble,

Please accept this as a formal resignation from The Geneva Foundation supporting the Addressing Neuromuscular Deficits and Improved Outcomes in Ankle Rehabilitation project as Clinical Research Coordinator. My last day will be November 18<sup>th</sup>, 2022, two weeks from tomorrow November 4<sup>th</sup>, 2022. I have learned a lot since this role, I am thankful for the opportunity I was given working on the project.

Please let me know what I can do to help transition process as I leave the role.

Best Wishes and Thank you for the opportunity.

Sincerely,

A handwritten signature in black ink, appearing to read 'Sarah Michaela Tolley', with a long horizontal flourish extending to the right.

Sarah Michaela Tolley

**Subject:** RE: E04036.1 Series - Continuing Review Acknowledgement Memorandum (Proposal Number DM170430, Award Number W81XWH-18-1-0083)  
**Date:** Wednesday, November 30, 2022 at 9:50:28 AM Eastern Standard Time  
**From:** Gribble, Phillip A.  
**To:** Kelsey Kilmon  
**CC:** Ghannadian, D Jason CIV USARMY CDMRP (USA)  
**Attachments:** image001.png, 83992\_ApprovalLetter\_809782.pdf, 83992\_Stamped Consent Form\_809781 (1).pdf, 83992\_ProtocolPdf\_809783.pdf

Good morning Kelsey,

I wanted to inform you of a potential substantive change to our protocol. The individual serving as the Clinical Research Coordinator at one of our testing sites (WBAMC), Ms. Sarah Tolley, submitted her letter of resignation to me earlier this month to take a new employment opportunity. With her absence, this prevents us from enrolling new participants at that site unless there is a replacement as the design involves the CRC being unblinded to the initial allocation, but the site PI, who is still in place, remains blinded.

We are still carrying forward on follow-up assessments that the site PI is able to complete.

I have filed an IRB modification to the UK IRB to remove Ms. Tolley from the protocol and the approval letter for this IRB modification with copies of consent form and protocol are attached.

I have discussed this with my Science Officer, Jason Ghannadian, and also the research study team members, and have elected that going forward with our limited timeline remaining, it doesn't make sense to try and replace the CRC. Additionally, the site PI, MAJ Stoute, has informed me he will be transferring to West Point in either MAR or APR 23. Therefore, I believe the prudent thing to do is to phase-out study operations at WBAMC; starting with no new enrollments given the departure of the CRC, and carrying out the remaining follow-up testing of completed participants until MAJ Stoute's departure. The other two sites, UK and UNC, will remain active in all facets of pursuing the study objectives.

I assume I will need to submit a revised SOW for the project? Please let me know what documentation will be needed and when this should be submitted. FYI, I will be submitting a request for a NCE by mid-December, but I wanted to make sure I coordinated all of these moving parts with HRPO, starting with this potential substantive change relative to halted enrollment at WBAMC.

Please let me know what information you need from me at this time.

Thank you,  
Phillip



**Phillip Gribble, PhD, ATC, FNATA**

Chair and Professor

University of Kentucky

Department of Athletic Training & Clinical Nutrition, College of Health Sciences

210-G Charles T. Wethington Building

Lexington, KY 40536-0200

[859-218-0885](tel:859-218-0885)

[phillip.gribble@uky.edu](mailto:phillip.gribble@uky.edu)

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**From:** Kelsey Kilmon <kelsey.a.kilmon.ctr@health.mil>  
**Sent:** Thursday, October 27, 2022 11:17 AM  
**To:** Wikstrom, Erik A. <ewikstro@email.unc.edu>; CPT Shawn Stoute <shawn.m.stoute.mil@mail.mil>; Gribble, Phillip A. <phillip.gribble@uky.edu>  
**Cc:** Kimberly Odam <kimberly.l.odam.civ@health.mil>; Andrea Kline <andrea.j.kline.civ@health.mil>; IRB Reliance <IRBReliance@uky.edu>; Dr. Kim Carter <kcarter.1@uky.edu>; Tracey Harris <tracey.e.harris.civ@health.mil>; Kelsey Kilmon <kelsey.a.kilmon.ctr@health.mil>; D. Jason Ghannadian <darius.j.ghannadian.civ@health.mil>; David Adosci <david.n.adosci.civ@health.mil>  
**Subject:** E04036.1 Series - Continuing Review Acknowledgement Memorandum (Proposal Number DM170430, Award Number W81XWH-18-1-0083)

**CAUTION: External Sender**

SUBJECT: Acknowledgement of the Continuing Review documents for the Protocol, "Addressing Neuromuscular Deficits for Improved Outcomes in Ankle Rehabilitation," Submitted by Phillip A. Gribble, Ph.D., University of Kentucky, Lexington, Kentucky, Proposal Log Number DM170430, Award Number W81XWH-18-1-0083, OHRO Log Number E04036.1 Series

1. The U.S. Army Medical Research and Development Command (USAMRDC), Office of Human and Animal Research Oversight (OHARO), Office of Human Research Oversight (OHRO) approved the following institutions which all rely on the University of Kentucky for review, approval, and oversight of the above-referenced multi-site protocol. The OHRO received a continuing review report for the protocol on 10/25/2022. The University of Kentucky IRB approved continuation of the protocol at the following sites on 08/31/2022; this approval will expire on 08/30/2023.
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  - b. OHRO Log Number E04036.1b, University of North Carolina at Chapel Hill, Erik Wikstrom, Ph.D.
  - c. OHRO Log Number E04036.1c, William Beaumont Army Medical Center, CPT Shawn Stoute
2. This correspondence serves to acknowledge OHRO receipt of the continuing review documents for the protocol. No further action related to this continuing review is needed. The documents in support of this continuing review will be placed in the OHRO file.
3. The Principal Investigator must provide the following post-approval submissions to the OHRO via email to [usarmy.detrick.medcom-usarmmc.other.hrpo@health.mil](mailto:usarmy.detrick.medcom-usarmmc.other.hrpo@health.mil). **Failure to comply could result in suspension of funding.**
  - a. Substantive modifications to the research protocol and any modifications that could potentially increase risk to subjects must be submitted to the OHRO for approval prior to implementation. The USAMRDC OHARO OHRO defines a substantive modification as a change in Principal Investigator, change or addition of an institution, elimination or alteration of the consent process, change in the IRB of Record, change to the study population that has regulatory implications (e.g. adding children, adding active duty population, etc.), significant change in study design (i.e. would prompt additional scientific review), or a change that could potentially increase risks to subjects.
    - b. A copy of the IRB continuing review approval letter must be submitted to the OHRO as soon as possible after receipt of approval. Please note that the OHRO conducts random audits at the time of continuing review and additional information and documentation may be requested at that time.
    - c. The final study report submitted to the IRB, including a copy of any acknowledgement documentation

and any supporting documents, must be submitted to the OHRO as soon as all documents become available.

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(3) Any instances of serious or continuing noncompliance with the federal regulations or IRB requirements.

(4) The knowledge of any pending compliance inspection/visit by the Food and Drug Administration (FDA), Office for Human Research Protections, or other government agency concerning this clinical investigation or research.

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(6) Change in subject status when a previously enrolled human subject becomes a prisoner must be promptly reported to the USAMRDC OHARO OHRO. The report must include actions taken by the institution and the IRB.

e. Events or protocol reports received by the OHRO that do not meet reporting requirements identified within this memorandum will be included in the OHRO study file but will not be acknowledged.

4. Please note: The USAMRDC OHARO OHRO conducts site visits as part of its responsibility for compliance oversight. Accurate and complete study records must be maintained and made available to representatives of the USAMRDC as a part of their responsibility to protect human subjects in research. Research records must be stored in a confidential manner so as to protect the confidentiality of subject information.

5. Do not construe this correspondence as approval for any contract or grant/cooperative agreement funding. Only the Contracting Officer/Grants Officer can authorize expenditure of funds by notice of official award documentation. It is recommended that you contact the appropriate contract/grants specialist or Contracting/Grants Officer regarding the expenditure of funds for your project.

6. The OHRO point of contact for this study is Mrs. Kelsey Kilmon, B.S., Human Subjects Protection Scientist

Mrs. Kelsey Kilmon, B.S.  
Contractor - General Dynamics Information Technology  
Human Subjects Protection Scientist  
Office of Human Research Oversight  
USAMRDC Office of Human and Animal Research Oversight (OHARO)