AWARD NUMBER: W81XWH-15-1-0287

TITLE: Vibratory Stimuli, A Novel Rehabilitation Method for Preventing Post – Traumatic Knee Osteoarthritis

PRINCIPAL INVESTIGATOR: Troy Blackburn

CONTRACTING ORGANIZATION: University of North Carolina at Chapel Hill
CHAPEL HILL, NC

REPORT DATE: AUGUST 2019

TYPE OF REPORT: Annual (Year 4)

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
AUGUST 2019	Annual	1 August 2018 - 31 July 2019

4. TITLE AND SUBTITLE
Vibratory Stimuli, A Novel Rehabilitation Method for Preventing Post – Traumatic Knee Osteoarthritis

5a. CONTRACT NUMBER
W81XWH-15-1-0287

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Troy Blackburn

E-Mail: troyb@email.unc.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
UNIVERSITY OF NORTH CAROLINA
AT CHAPEL HILL
HAMILTON BROWN
104 AIRPORT DR STE 2200
CHAPEL HILL NC 27599-5023

8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Development 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

The purpose of this study is to determine the acute effects of whole body vibration (WBV) and local muscle vibration (LMV) on quadriceps function, proprioception, and gait biomechanics in individuals with anterior cruciate ligament reconstruction (ACLR). We hypothesize that both forms of vibration will enhance the outcomes in manners that would potentially reduce the risk of developing post-traumatic knee osteoarthritis (PTOA). The primary goals for Year 4 were to complete data analysis and development of dissemination materials. We have completed testing in the entire sample of 75 participants, and have completed the primary analyses. We have been granted a no-cost extension for the project which we will use to finalize data analysis and dissemination materials. To date, the project has resulted in 3 peer-reviewed manuscripts and 8 conference abstracts, and we anticipate at least 1 additional manuscript will be submitted for peer review in the near future.

The study has been highly successful. In particular, we have demonstrated that vibration acutely improves gait biomechanics linked to development of PTOA. Specifically, WBV increased the sagittal plane knee moment, an outcome that is consistently reduced following ACLR and is lower in patients who develop PTOA within 5 years compared to those who do not. Additionally, LMV reduced the vertical loading rate, which is greater in the reconstructed limb and is associated with cartilage structural and biosynthetic degradation.

15. SUBJECT TERMS
Knee, Osteoarthritis, Anterior Cruciate Ligament, Quadriceps, Inhibition, Muscle Dysfunction, Proprioception, Gait Biomechanics, Rehabilitation

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified	7	USAMRMC

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

INTRODUCTION

Osteoarthritis (OA) is a leading cause of medical discharge from military service during both peacetime and armed conflict. Quadriceps dysfunction and proprioceptive deficits following traumatic knee injuries alter walking gait biomechanics in manners linked to development of knee OA. Current rehabilitation techniques are minimally effective for addressing these complications and preventing knee OA. Anterior cruciate ligament reconstruction (ACLR) dramatically increases the risk of knee OA and represents an ideal model for evaluating novel rehabilitation techniques for preventing knee OA. Direct (local muscle vibration - LMV) and indirect (whole body vibration - WBV) vibratory stimuli enhance quadriceps function and proprioception, and may improve rehabilitation outcomes and reduce the risk of knee OA. The purpose of this study is to determine and compare the acute effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR. We hypothesize that WBV and LMV will equally enhance quadriceps function, proprioception, and gait biomechanics in manners that would potentially reduce the risk of developing knee OA.

KEYWORDS

Knee, Osteoarthritis, Anterior Cruciate Ligament, Quadriceps, Inhibition, Muscle Dysfunction, Proprioception, Somatosensory, Gait Biomechanics, Rehabilitation

ACCOMPLISHMENTS

- **Major goals of the project for Year4**
  - The primary goals for Year 4 were to complete data analysis and development of dissemination materials.

- **Accomplishments under goals**
  - To date we have completed enrollment of the total sample of 75 participants, all of whom have competed their participation in the study with no adverse events or unanticipated problems.

  - Primary analysis is complete, and we are in the process of developing dissemination materials.

- **Opportunities for training and professional development**
  - Nothing to Report

- **Dissemination**
  - The project has resulted in 3 peer-reviewed manuscripts and 8 conference abstracts.

- **Plans for achieving goals in the next reporting period**
  - We anticipate at least 1 additional manuscript will be submitted for peer review in the near future. Additionally, we have begun the process of using the data derived from the current project to inform development of the next step in this line of research, which is a clinical trial evaluating the effects of the vibratory interventions of indicators of PTOA following ACLR. We are currently developing multiple grant proposals to achieve this goal.

IMPACT

- **Impact on development of the principal discipline**
  - In general, this study has been highly successful. Consistent with our hypotheses, we demonstrated that vibration improves gait biomechanics that have been linked to PTOA development following ACLR. Specifically, WBV increased the sagittal plane knee moment during walking. This outcome is consistently reduced following ACLR and is smaller in ACLR patients who develop PTOA within 5 years compared to those who do

not. The minimal clinically important difference (MCID) in the peak sagittal plane moment reported in the literature is 0.04 Nm/kg*m. A single exposure to WBV in our pre-clinical study increased the peak sagittal plane knee moment by 0.03 Nm/kg*m. As such, repeated exposure to vibration such as would occur during ACLR rehabilitation would likely resulted in substantial improvements. Additionally, LMV delivered via our prototype stimulator decreased loading rate during gait. Higher loading rates have been observed in the ACLR limb during gait compared to contralateral and healthy control limbs, and disrupt cartilage structure and biosynthesis, potentially contributing to PTOA development. Aberrant gait biomechanics are considered a primary contributor to the development of PTOA, thus the results of our study potentially inform development of future intervention strategies. These findings are the centerpiece of future clinical trials for which we are currently developing grant proposals.

- **Impact on other disciplines**
  - Nothing to report

- **Impact on technology transfer**
  - Our prototype LMV acutely improved gait biomechanics linked to the development of PTOA. Preliminary analysis also indicate that it improved somatosensory function. These findings provide strong rationale for its use in the clinical setting and advancement to a commercial product. We are working with the University's Office of Technology Commercialization to pursue a patent and FDA Investigational Device Exemption, and identify commercial licensing partners.

- **Impact on society beyond science and technology**
  - Nothing to report

CHANGES/PROBLEMS

- Nothing to report

PRODUCTS

- **Publications, conference papers, and presentations**
  - **Journal publications**
    - Blackburn JT, Padua DA, Pietrosimone B, Schwartz TA, Spang JT, Goodwin JS, Dewig DR, Johnston CD. Vibration improves gait biomechanics linked to post-traumatic knee osteoarthritis following anterior cruciate ligament injury. *Journal of Orthopaedic Research* (In Review)
    - Blackburn JT, Pietrosimone BG, Spang JT, Goodwin JS, Johnston CD. Somatosensory function influences aberrant gait biomechanics following anterior cruciate ligament reconstruction. *Journal of Orthopaedic Research* 2020 (In Press).
    - Blackburn JT, Pietrosimone B, Goodwin JS, Johnston C, Spang JT. Co-activation during gait following anterior cruciate ligament reconstruction. *Clinical Biomechanics* 67: 153-159, 2019.

  - **Conference papers and presentations**
    - Blackburn T, Pietrosimone B, Dewig D, Goodwin FJ, Johnston C. Vibratory stimuli improve gait biomechanics linked to post-traumatic osteoarthritis in individuals with anterior cruciate ligament reconstruction. *2019 Osteoarthritis Research International World Congress on Osteoarthritis*, Toronto, Canada.

- Blackburn T, Pietrosimone B, Dewig D, Johnston C. Improvements in somatosensory function with vibration do not influence gait biomechanics in individuals with anterior cruciate ligament reconstruction. *2019 American College of Sports Medicine Annual Meeting*, Orlando, FL.
- Dewig D, Johnston C Pietrosimone B, Blackburn T. Somatosensory function and gait biomechanics in individuals with anterior cruciate ligament reconstruction. *2019 American College of Sports Medicine Annual Meeting*, Orlando, FL.
- Blackburn T, Pietrosimone B, Dewig D, Goodwin J, Johnston C. Somatosensory deficits influence gait biomechanics linked to post-traumatic osteoarthritis in individuals with anterior cruciate ligament reconstruction. *2019 ACL Research Retreat VIII*, Greensboro, NC.

o **Inventions, patent, applications, and/or licenses**

- We are working with the University's Office of Technology Commercialization to pursue a patent and FDA Investigational Device Exemption for our prototype LMV stimulator. Additionally, we are working with the group to identify potential commercial licensing partners.

PARTICIPANTS & OTHER COLLABORATIN ORGANIZATIONS

- **What individuals have worked on the project?**

The following individuals devoted at least one person month to the project:

Name	Troy Blackburn
Project Role	Principal Investigator
Nearest Person Month Worked	3
Contribution to Project	Dr. Blackburn performed work related to the primary duties associated with the project including data reduction and analysis; software development for data reduction; and supervision of RAs. He has also been responsible for the overall coordination of the project.

Name	Brian Pietrosimone
Project Role	Co-Investigator
Nearest Person Month Worked	1
Contribution to Project	Dr. Pietrosimone aided with data analysis and interpretation, as well as drafting of dissemination materials.

Name	Chris Johnston
Project Role	Graduate Student/Research Assistant
Nearest Person Month Worked	8
Contribution to Project	Mr. Johnston has performed work related to data reduction, analysis, and drafting of dissemination AMTEIRALS; and calibration and maintenance of research equipment.

Name	Derek Dewig
Project Role	Graduate Student/Research Assistant
Nearest Person Month Worked	8
Contribution to Project	Mr. Dewig has performed work related to subject recruitment; data collection and reduction; and calibration and maintenance of research equipment.

- **Change in active support of PD/PI or senior/key personnel**
  - Nothing to report

- **Other organizations**
  - Nothing to report

SPECIAL REPORTING REQUIREMENTS

- Please see attached updated Quad Chart

APENDICES

- Please see attached journal articles