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

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14. ABSTRACT

The purpose of this study is to determine and compare the acute effects of whole body vibration and local muscle vibration on quadriceps function, proprioception, and gait biomechanics in individuals with anterior cruciate ligament reconstruction. We hypothesize that both forms of vibration will equally enhance quadriceps function, proprioception, and gait biomechanics in manners that would potentially reduce the risk of developing knee osteoarthritis. While the specific aims will not be realized and cannot be analyzed until the study's completion due to the single-blind randomized controlled trial design, Years 1, 2, and 3 of the project were highly successful regarding progress toward the study aims. The primary goal for Year 3 was to recruit and enroll the final cohort of 15 subjects and complete data analysis. September 25, 2018 will mark the 3-year anniversary of HRPO approval and initiation of research activities in earnest. The proposed sample included 75 individuals with anterior cruciate ligament reconstruction. To date we have enrolled 65 subjects who have completed all testing and 2 who are currently participating, have scheduled 1 potential subject for the initial screening session, and have recruited 5 potential subjects who are in the scheduling cue for the screening session. These data are in agreement with the target enrollment rate of 6-8 subjects per quarter specified in the SOW. We have been granted a no-cost extension for the project, and anticipate complete subject enrollment in the next two months. There have been no unanticipated problems, and data collection has proceeded as planned.

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

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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 Year 3**
    - Recruit and enroll the 3rd cohort of 15 subjects
        - As of 31-08-2018, 67 of 159 identified potential subjects have been enrolled in the study
            - 20 subjects were enrolled in Year 1
            - 22 subjects were enrolled in Year 2
            - 22 subjects were enrolled in Year 3
            - 3 subjects have been enrolled in Year 4 (no-cost extension)
                - 61 subjects did not meet the inclusion criteria and were excluded
                - 21 subjects declined to participate
                - 4 subjects enrolled but later dropped out
                - 65 subjects have completed their participation in the study (i.e. all 3 testing sessions)
                - 2 subjects are currently engaged in data collection
                - 1 subject is currently scheduled for the initial screening session
                - 5 subjects are pending scheduling for the initial screening session

- **Accomplishments under goals**
    - As of 31-08-2018 we have enrolled 67 subjects of whom 65 have completed their participation in the study and 2 are currently participating, and 6 subjects are currently either scheduled or pending scheduling for the initial screening session. This represents substantial progress toward the goals of the project and enrollment of the total sample of 75 subjects.

    - Data collection has progressed as planned with no adverse events or unanticipated problems. Four subjects screened into the study, but later withdrew. One of these subjects reported to the laboratory for the first testing

session, but stated during testing "This reminds me too much of physical therapy and I don't want to continue." No adverse or unanticipated events occurred - the subject simply no longer wanted to participate. Two subjects screened into the study but were “no-shows” for the first testing session, and have not responded to multiple attempts to reschedule. One subject withdrew due to time commitments.

    - Analysis of the study aims is not possible at this time due to the single-blind randomized controlled trial design of the study. The aims will be evaluated following completion of data collection.

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

- **Dissemination**
    - Nothing to Report – the specific aims of the study will not be realized until its completion due to the single-blind randomized controlled trial design.

- **Plans for achieving goals in the next reporting period**
    - Recruit and enroll the remaining 8 subjects
        - Classes for the fall semester began at UNC-Chapel Hill on 21-08-2018, and we have initiated recruitment efforts. In the first week of recruitment we have identified 8 potential subjects, 2 of whom are currently enrolled in the study, and will be recruiting heavily in the coming months.
    - Data reduction and analysis
    - Preparation of dissemination materials

IMPACT

Per the SOW, all of the specific aims will be evaluated via the same randomized controlled experimental design at the conclusion of data collection. As such, the study’s primary reportable outcomes will not be available until completion of the project.

- Development of the principal discipline
    - Nothing to Report
- Other disciplines
    - Nothing to Report
- Technology transfer
    - Nothing to Report
- Society beyond science and technology
    - Nothing to Report

CHANGES/PROBLEMS

- Though within the projected range of 6-8 subjects per quarter per the SOW, the overall recruitment rate is slightly behind schedule. We anticipated enrolling 75 subjects by the end of Year 3, but have enrolled only 67 to date. This discrepancy is due to 2 factors:
    1. Though funding for the project was initiated on 01-08-2015, HRPO approval was not received until 25-09-2015. As such, the project was ongoing in earnest for only 10 months of Year 1.
    2. As our laboratory is part of a university, recruitment incurs time intervals during which our convenience sample is minimized (e.g. winter break, summer break).

- We have 1 subject scheduled for the initial screening session and 5 potential subjects who we are attempting to schedule for this session. Additionally, we will intensify recruitment efforts in an attempt to enroll the remaining 8 subjects in September and October of 2018.

PRODUCTS

Portions of the preliminary pre-intervention/baseline data were presented at the annual meetings of the American College of Sports Medicine, Athletic Trainers' Osteoarthritis Consortium, and National Athletic Trainers' Association. We anticipate that these preliminary data will lead to peer-reviewed journal publications with the addition of more subjects and increased statistical power when data collection is complete.

- Johnston C, Pietrosimone B, Goodwin JS, Blackburn T. Quadriceps-hamstrings co-activation during gait following anterior cruciate ligament reconstruction. *2018 Athletic Trainers' Osteoarthritis Consortium Annual Meeting* New Orleans, LA.
- Johnston C, Goodwin JS, Pietrosimone B, Blackburn JT. The relationship between joint position sense and quadriceps function following anterior cruciate ligament reconstruction. *2018 Athletic Trainers' Osteoarthritis Consortium Meeting*, New Orleans, LA.
- Johnston C, Goodwin JS, Pietrosimone B, Blackburn JT. Gait biomechanics at different time periods following anterior cruciate ligament reconstruction. *2018 American College of Sports Medicine Annual Meeting*, Minneapolis, MN.
- Goodwin JS, Johnston C, Pietrosimone B, Blackburn T. Quadriceps function does not differ between subjects with ACL reconstruction with impulsive vs. non-impulsive loading. *2018 American College of Sports Medicine Annual Meeting*, Minneapolis, MN.

PARTICPANTS & OTHER COLLABORATING ORGANIZATIONS

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

Name	Troy Blackburn
Project Role	Principal Investigator
Nearest Person Month Worked	2
Contribution to Project	Dr. Blackburn has performed work related to the primary duties associated with the project including data reduction and analysis; software development for data reduction; subject recruitment; 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 has played a vital role in oversight of the randomization process. He has also supervised the delivery of the interventions to preserve blinding for both the PI and RAs who are conducting data collection.

Name	Todd Schwartz
Project Role	Co-Investigator
Nearest Person Month Worked	1
Contribution to Project	Dr. Schwartz played a vital role in preliminary analysis of the intervention data for presentation at the DHA meeting at Fort Detrick, MD in May 2016.

Name	Jonathan Goodwin
Project Role	Research Assistant
Nearest Person Month Worked	2
Contribution to Project	Mr. Goodwin has performed work related to subject recruitment; data collection and reduction; and calibration and maintenance of research equipment.

Name	Chris Johnston
Project Role	Research Assistant
Nearest Person Month Worked	2
Contribution to Project	Mr. Johnston has performed work related to subject recruitment; data collection and reduction; and calibration and maintenance of research equipment.

Changes in active support

- Following the initial funding decision, Drs. Blackburn and Pietrosimone received additional funding and changes in active support via the following two grants:
    - Pietrosimone (PI) – *Improving disability in knee osteoarthritis by targeting neuromuscular deficits*
        - National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) – Pilot and Feasibility Clinical Research Grants Program (R21)
        - Funding Awarded: $418,000
            - This grant provides funding in the amount of 22% effort for Dr. Pietrosimone and 7% effort for Dr. Blackburn.

    - Pietrosimone (PI) – *Posttraumatic Osteoarthritis: Establishing a Comprehensive Evaluation Strategy*
        - National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) – Small Grant Program for New Investigators (R03)
        - Funding Awarded: $152,000
            - This grant provides funding in the amount of 11% effort for Dr. Pietrosimone and 0% effort for Dr. Blackburn.

These projects have concluded, thus they do not impact our ability to carry out the associated aims. The only notable influence on the current project is with respect to Dr. Pietrosimone's

support. The university employs faculty on 9-month appointments, and limits the amount of additional income (e.g. via grants, contracts, summer school teaching, consulting, etc.) to 1/3 of the 9-month salary. For Years 1 and 2 of the project, the 33% summer funding detailed in the budget (i.e. 1 calendar month) would have exceeded Dr. Pietrosimone's total salary limit when combined with funding from the other sources. As such, this funding ($10,556 for Year 1, $10,846 for Year 2) has not been utilized. This cost savings was used to support the no-cost extension for the project. No other changes occurred.

Involvement of Other Organizations

We have partnered with the Veterans Affairs Medical Center in nearby Durham, NC in an effort to recruit military veterans into the study as described in the original proposal. This partnership was made possible via collaboration with Dr. Kelli Allen who has a dual appointment at UNC-Chapel Hill and the Durham VA. Unfortunately, this collaboration was not successful due to the fact that only 47 potential subjects were identified, of which 22 did not meet the inclusion criteria and 17 were uninterested in participation primarily due to the requirement to travel large distances to the laboratory for multiple visits.

Vibratory Stimuli: A Novel Rehabilitation Method for Preventing Post-Traumatic Knee Osteoarthritis

MR140103-Neuromusculoskeletal Injuries Research Award

Funding Opportunity Number: W81XWH-14-DMRDP-CRMRP-NMSIRA

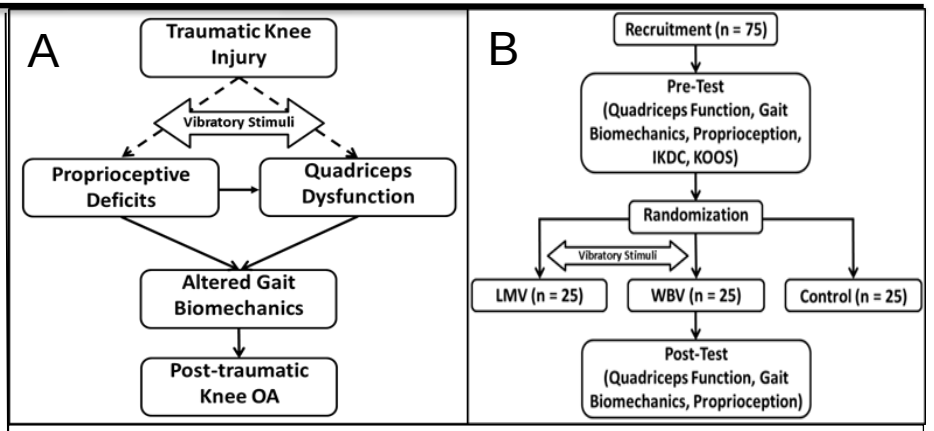
PI: Blackburn, J. Troy **Org:** University of North Carolina at Chapel Hill **Award Amount:** $772,058

Study/Product Aim(s)

- To determine the 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)
- To compare the effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR
- To identify factors that predict the effects of WBV and LMV on quadriceps function, proprioception, and gait biomechanics in individuals with ACLR

Approach

Individuals with ACLR within the past 5 years will be randomized to WBV, LMV, and Control groups (Figure B). Quadriceps function, proprioception, and gait biomechanics will be assessed prior to and following WBV and LMV interventions we demonstrated previously to improve quadriceps function, or a Control intervention.



A) Theoretical framework. Traumatic knee injuries (e.g. ACLR) result in proprioceptive deficits and quadriceps dysfunction which alter gait biomechanics in manners that contribute to post-traumatic knee osteoarthritis. We demonstrated that LMV and WBV improve quadriceps function, and WBV improves proprioception, thus these vibratory stimuli may also prevent alterations in gait biomechanics and reduce the risk of post-traumatic knee osteoarthritis. **B) Experimental design**

Timeline and Cost

Activities / CY	16	17	18
Subject recruitment			
Data collection			
Data reduction and analysis			
Develop dissemination materials			
Estimated Budget ($K)	**$253**	**$258**	**$261**

Goals/Milestones

CY16 Goals

☐ Enroll initial cohort of 30 subjects
- 20 subjects enrolled in CY16

CY17 Goal

☐ Enroll second cohort of 30 subjects
- 22 subjects enrolled in CY17
- 42 total subjects enrolled as of 30-08-2017

CY18 Goal

☐ Enroll final cohort of 15 subjects
- 22 subjects enrolled in CY 18
- 67 total subjects enrolled as of 31-08-2018

CY18 Goal
- Enroll final cohort of 8 subjects

☐ Complete data collection, reduction, and analysis

☐ Develop dissemination materials