AWARD NUMBER: HT9425-23-1-0047

TITLE: Transfemoral Osseointegrated Prosthesis Limb-Load Symmetry Training

PRINCIPAL INVESTIGATOR: Cory Christiansen, PT, PhD

CONTRACTING ORGANIZATION: Regents of the University of Colorado – University of Colorado Denver

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6. Authors
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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14. ABSTRACT

This Phase I clinical trial has been successfully initiated, with the first year of study implementation now complete. The goals of testing the feasibility and gathering data to optimize the protocol of a limb-load biofeedback training intervention for people with lower-limb osseointegrated prostheses is progressing as planned for the current project. The fourth quarter progress has resulted in enrolling a total of **nine** participants, randomizing **four** of those participants into the study protocol (five participants currently in the pre-randomization phase), completing T1 testing with **four** participants, beginning study intervention with **four** participants, and making progress on major tasks as expected.

15. SUBJECT TERMS
Amputation, Osseointegration, Rehabilitation, Biofeedback

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Introduction

This trial will inform osseointegrated (OI) prosthesis rehabilitation by examining a prosthetic training innovation, which aligns with the Orthotics and Prosthetics Outcomes Research Program (OPORP) *Strategic Goal* to Optimize patient-specific rehabilitation regimens for the Warfighter/Veteran.

This Phase I clinical trial will test the feasibility and optimize the protocol of a limb-load biofeedback training intervention for people with OI lower-limb prostheses. OI prostheses create a direct femur-prosthesis connection as a novel alternative to traditional socket-based prostheses for people with transfemoral amputation. Initial evidence demonstrates improved physical function following femoral OI prosthesis placement. OI prostheses are attractive to many people with transfemoral amputation as they address common debilitating problems that occur with traditional socket prostheses, such as skin irritation and wounds, poor sitting tolerance, poor weight-bearing tolerance, and limited proximal joint mobility. In addition, OI prostheses also provide direct bone-prosthesis force transmission and the bone-prosthesis attachment provides the ability to directly perceive pressure and vibrotactile bone stimuli (i.e., osseoperception) through the prosthesis. Removal of socket-related problems, direct bone-prosthesis force transmission, and improved osseoperception promotes functional loading that will more closely resemble a healthy intact limb condition than a socket prosthesis.

Transfemoral socket prosthesis users have the challenge of controlling the prosthesis due to excessive movement between the socket and femur. As a result, people using a socket prosthesis present with gait pattern asymmetry, commonly overloading the non-amputated limb while underloading the amputated limb, resulting in a nearly 14-fold increased risk of developing hip osteoarthritis than their healthy counterparts. Limb-load asymmetry negatively influences long-term musculoskeletal health by both overloading the non-amputated limb and underloading the amputated limb. Overtime, cumulatively non-amputated limb overloading increases risk of hip osteoarthritis while amputated limb underloading limits the stimulus for promoting bone and joint structural health. Our preliminary evidence from OI rehabilitation demonstrates that the more normative ground to residual limb load transmission through the OI prosthesis results in improved hip muscle function and joint loading compared to socket prosthesis use, yet asymmetries persist. Persistent between-limb asymmetrical functional loading suggests a need to improve OI prosthesis user training. The proposed intervention targets habitual movement behavior to optimize between-limb loading symmetry during daily function.

Current OI prosthesis rehabilitation protocols are based on very limited evidence and lack validation, with focus on highly controlled progression of prosthesis loading to minimize risk for prosthesis loosening, prosthesis fracture, and bone fracture. Once full-weight bearing is allowed, there is no evidence to guide the necessary functional movement training for free-living prosthesis use. We hypothesize that the persistence of asymmetrical lower-limb loading for OI prosthesis users is due in part to a lack of intentional training that changes movement behaviors to optimize between-limb symmetrical loading. We propose limb-load biofeedback training based on behavior change theory, motor learning evidence, and use of wearable technology to optimize mechanical loading of the prosthesis, lower-limb joints, and lumbar spine during free-living physical task performance for people with transfemoral OI prostheses.

This document will summarize the progress that has been made in the first year of this Phase I Clinical Trial.

Keywords

Amputation

Osseointegration

Rehabilitation

Biofeedback

Accomplishments

What were the major goals of the project?

Specific Aim 1: Determine feasibility, acceptability, and safety of implementing targeted limb-load biofeedback training by measuring: 1) participant retention, 2) intervention fidelity, 3) participant acceptability, and 4) safety.

Major Task 1 Determine feasibility of implementing targeted limb-load biofeedback training by measuring participant retention.

Months 1-2:

Subtask 1: IRB Approval (percent complete: 100%)
Milestones Achieved: IRB approval received 12/07/2022, OHRO approval received 01/18/2023, and ClinicalTrials.gov submission complete (02/01/2023)
Subtask 2: Personnel Training (percent complete: 100%)
Milestones Achieved: Personnel trained including physical therapists, outcomes testers, and interventionists (04/30/2023)

Months 1-34

Subtask 3: Participant Recruiting & Retention (percent complete: 60%)
Milestones Achieved: First nine participants have been enrolled; no loss to follow-up

Major Task 2 Determine acceptability of implementing targeted limb-load biofeedback training by measuring intervention fidelity and participant acceptability

Months 3-34

Subtask 1: Monitor fidelity of telehealth providers (percent complete: 17%)
Milestones Achieved: Completed fidelity checks of providers during randomly-selected telehealth sessions for three enrolled participants on (10/27/23), (12/1/23), and (1/19/24).
Subtask 2: Monitor fidelity of outpatient physical therapy (percent complete: 22%)
Milestones Achieved: Completed fidelity checks of outpatient PT of first four enrolled participants on (3/21/23), (4/24/23), (5/01/23), (5/02/23)
Subtask 3: Measure participant acceptability of intervention

Major Task 3 Determine safety of implementing targeted limb-load biofeedback training

Months 1-34

Subtask 1: Monitor adverse events by participant (percent complete: 6%)
*Milestones Achieved: Ongoing. We have monitored and documented eight adverse events on 3/16/23, 6/22/23, 7/11/23, 8/7/23, 9/29/23, 10/24/23, 11/28/2023, and 12/14/23 all **unrelated** to the study participation and five serious adverse events on 6/27/23, 6/29/23, 7/08/23, 7/21/23, and 1/24/2024 all **unrelated** to the study participation.*

Subtask 2: Assign an independent safety monitor (percent complete: 100%)
Milestones Achieved: Complete. Dr. Susan Ladley was appointed in the first quarter of the study and has been reviewind study progression and safety outcomes on a quarterly basis with quarterly safety reports.

Specific Aim 2: Assess if the limb-load biofeedback training has a signal of efficacy for loading symmetry and standard of care outcome measures

Months 2-36

Major Task 4 Cumulative loading

Subtask 1: Daily step count (percent complete: 30%)

<u>Milestones Achieved:</u> Collected daily steps across 10 days with ActivPal from seven participants at the T1 test point and two participants at the T2 test point.

Subtask 2: Calculate ground reaction force impulse (percent complete: 17%)

<u>Milestones Achieved:</u> Calculated at the T1 timepoint using ground reaction forces measured from the force plates within the motion capture laboratory for five participants.

Subtask 3: Analyze cumulative loading (percent complete: 20%)

<u>Milestones Achieved:</u> Analyzed cumulative loading (product between daily steps and ground reaction force impulse) at the T1 timepoint in 6 participants. Manuscript detailing methodology currently in revision in Gait & Posture.

Major Task 5 Joint loading

Months 2-34

Subtask 1: Collect motion capture data (T1, T3) (percent complete: 17%)

<u>Milestones Achieved:</u> Motion capture data collected at T1 for five study participants.

Subtask 2: Musculoskeletal modeling (T1, T3) (Percent complete: 13%)

<u>Milestones Achieved:</u> Models have been developed and validated for four participants at the T1 timepoint.

Subtask 3: Analyze low back, bilateral hip, and intact knee joint loading outcomes

Major Task 6 Collect and analyze patient reported outcomes (PLUS-M, WHODAS 2.0, ABC, and PSFS) and functional outcomes (daily step count, Colorado Limb Donning + Timed-Up and Go, 30-second sit to stand, and gait speed) collected as standard of care.

Months 2-36

Subtask 1: Collect all participant reported outcomes (T1, T2, T3) (percent complete: 22%)

<u>Milestones Achieved:</u> Participant reported outcomes collected at T1 for eight study participants and T2 for two study participants.

Subtask 2: Collect measures of functional performance (T1, T3) (percent complete: 30%)

<u>Milestones Achieved:</u> Functional performance outcomes collected at T1 for nine study participants.

Subtask 3: Analyze patient reported and functional outcomes

Specific Aim 3: Identify the key functional movement priorities for participants who choose OI prosthesis.

Major Task 7 Perform participant exit interviews after one year of OI prosthesis use

Month 1

Subtask 1: Develop semi-structured interview guide for use in exit interviews (percent complete: 100%)

<u>Milestones Achieved:</u> We have developed the interview guide, and have successfully received IRB approval to use this during exit interviews after the T3 testing timepoint.

Months 2-34

Subtask 2: Perform exit interviews with participants

Months 34-36

Subtask 3: Analyze exit interviews for movement priorities

What was accomplished under these goals?

.

Describe the Regulatory Protocol and Activity Status (if applicable).

(a) ***Human Use Regulatory Protocols***

PROTOCOL (1 of 1 total):

Protocol [HRPO Assigned Number]: E04316.1a

Title: **Transfemoral Osseointegrated Prosthesis Limb-Load Symmetry Training**

Target required for clinical significance: 15

Target approved for clinical significance: 25

SUBMITTED TO AND APPROVED BY:

- Colorado Multiple Institutional Review Board (COMIRB)
- Submitted 17 Nov 2022 Approved 07 Dec 2022
- OHRO: Submitted 12 Dec 2022 Approved 18 Jan 2023

Number of subjects screened/original planned target: 16
Number of patients enrolled/original planned target: 9/7
Number of patients completed/original planned target: 0

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:

- Amendment submitted to COMIRB 14 Mar 2023, Approved 29 Mar 2023.
  Amendment included adding a Co-Investigator, adding 3 questionnaires, a minor correction to consent form, and adding clarifying language to a questionnaire.

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:

Nothing to Report

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

There are four primary goals that we aim to accomplish during Y2Q1 of the award period. First, we plan for two participants to complete the study intervention at the T3 timepoint and plan for four participants to complete their respective T2 timepoints. Second, we hope to recruit and enroll at least one additional participant. Third, we will continue the analyses of dependent variables described in Major Tasks 4-6 (motion capture, cumulative loading, musculoskeletal modeling, and outcomes). To accomplish this, we plan to have all data processed from data collected from all enrolled participants collected at T1.

Impact

This Phase I clinical trial will be among the first randomized controlled rehabilitation trials for people with transfemoral OI prostheses. There is an immediate need to better understand the physical health benefits and factors that contribute to health outcomes for this population. A critical step in developing rehabilitation guidelines is to identify optimal methods for people to regain active lifestyles, best use their prostheses, and avoid secondary comorbidities. This novel limb-load biofeedback training program will provide the empirical evidence necessary to inform post-OI rehabilitation regimens designed to optimize outcomes. Importantly, data from this trial will also guide intervention refinement as we move toward a Phase II trial.

Changes/Problems

Nothing to Report

Products

Christiansen CL, Thomsen PB, Bade MJ, Melton DH, Gaffney BMM, Stoneback JW. Transfemoral Osseointegrated Prosthesis Limb-Load Symmetry Training: Study Protocol and 1-Year Progress. *2024 Military Health System Research Symposium*. [In Review]

Thomsen PB, Gaffney BMM, Tracy JB, Vandenberg NW, Awad ME, Stoneback JW, Christiansen CL. Cumulative Loading Increases but Loading Asymmetries Persist During Walking for People with a Transfemoral Bone-Anchored Limb. *Gait & Posture*. [In Revision]

Personnel

Name: Cory Christiansen, PT, PhD
Project Role: Co-PI (Primary Contact)
Researcher Identifier (ORCID ID): 0000-0003-3273-1169
Nearest person month worked: 0.90 calendar months of 0.70 FTE
Contribution to Project: Overseeing subject recruitment, protocol implementation, intervention delivery, evaluation and interpretation of results, Institutional Review Board approvals, progress reports, Independent Safety Monitor reports, preparation and presentation of scientific abstracts, and publications.

Name: Brecca Gaffney, PhD
Project Role: Co-PI
Researcher Identifier (ORCID ID): 0000-0003-4556-5868
Nearest person month worked: 0.90 summer months of yearly effort
Contribution to Project: Assessments of signals for efficacy, oversight of data collection, direction and implementation of joint biomechanics modeling, synchronization of research outcome assessments with the standard of care procedures, preparation and presentation of scientific abstracts, and publications.

Name: Jason Stoneback, MD
Project Role: Co-I
Researcher Identifier (ORCID ID): 0000-0003-0205-796X
Nearest person month worked: 0.24 calendar months of yearly effort
Contribution to Project: Assist development of the study protocol, conduct all surgeries for the research participants, direct the medical standard of care procedures, work closely with the rehabilitation team (Melton) and the research Co-PIs (Christiansen, Gaffney) to ensure tight coordination of care for the patient participants, oversee the clinical research documentation, work closely with the team to manage recruiting of participants, facilitate communication to assist with coordination from other physicians, the prosthetists, and clinicians, and assist with interpretation of the data and manuscript preparation.

Name: Michael Bade, PT, PhD
Project Role: Co-I
Researcher Identifier (ORCID ID): 0000-0002-7985-8565
Nearest person month worked: 1.2 calendar months of yearly effort
Contribution to Project: Led the development of the intervention protocol for the limb-load biofeedback training, provide direct oversight of the intervention as the primary interventionist, oversee fidelity assessments of the standard of care rehabilitation protocols and the control group attention control intervention, training of a back-up interventionist and control group interventionists, and assist in evaluation and interpretation of results and preparation/presentation of scientific abstracts and publications.

Name: Danielle Melton, MD
Project Role: Co-I
Researcher Identifier (ORCID ID): 0000-0002-1314-6426
Nearest person month worked: 0.24 calendar months of yearly effort
Contribution to Project: Assisted in development of the study protocol, oversee the rehabilitation research documentation in the clinical record, work with the rehabilitation team to manage the standard of care rehabilitation care for all research participants, is the study physiatrist, guides the classification and management of adverse events for research participants, work with Dr. Bade to ensure clear coordination of the limb-load biofeedback training into the standard of care protocol, while also ensuring coordination of the attention control sessions with the standard of care, facilitate communication among members of the rehabilitation, prosthetic, orthopedic, and research teams, and assist with interpretation of the data and manuscript preparation.

Name: Elizabeth Juarez-Colunga , PhD
Project Role: Co-I
Researcher Identifier (ORCID ID): 0000-0002-6369-2353
Nearest person month worked: 0.36 calendar months of yearly effort

Contribution to Project: Guided the study design and statistical analysis plan for the research study, provide expertise on issues related to study design, database management, quality control, and preparation of manuscripts, oversee all data analysis of the trial and guide monthly reports for progress with data collection and entry.

Name: Peter Thomsen, PT, DPT, MS
Project Role: Research Assistant
Researcher Identifier (ORCID ID): 0009-0007-8761-8901
Nearest person month worked: 1.2 calendar months of yearly effort
Contribution to Project: Responsible for participant outcome testing, test scheduling, data cleaning and entry, collection of data for intervention fidelity checks, and assisting in decisions related to data management and analyses, in concert with Dr. Juarez-Colunga (Co-I), oversee equipment and supply needs for the study, including software and hardware maintenance.

Name: Andrew Ebert, MS
Project Role: Research Assistant
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 1.2 months of yearly effort
Contribution to Project: Responsible for coordination of participant recruitment and scheduling, coordinating lab management activities [including guidance on regulatory procedures as they relate to data management and security, creating a study database using an approved data management system (e.g., REDCap), and participant reimbursement], interventionist for the control group participants to deliver the attention control intervention.

Special Reporting Requirements

Quad Chart (see Attachments)

Appendices

N/A

Transfemoral Osseointegrated Prosthesis Limb-Load Symmetry Training

Log Number: OP220013

PI: Cory Christiansen and Brecca Gaffney **Org:** University of Colorado, Anschutz Medical Campus **Award Amount:** $349,939

Study/Product Aim(s)

- AIM 1: Determine feasibility of implementing targeted limb-load biofeedback training by measuring: 1) participant retention, 2) intervention fidelity, 3) intervention acceptability, and 4) participant safety
- AIM 2: Assess if the limb-load biofeedback symmetry training has a signal of efficacy for: 1) symmetry in cumulative loading during free living activities 2) symmetry of multi-domain hip biomechanics during tasks increasing biomechanical demand and 3) on standard of care clinical outcome measures
- AIM 3: Identify the key functional movement priorities for participants who choose OI prostheses.

Approach

This study seeks to advance OI prosthesis training through a novel limb load biofeedback training approach with four primary areas of innovation: 1)target quality of life of people living with limb-loss using wearable technology, 2) assess real-life functional outcomes, 3) guide rehabilitation innovations with behavioral and motor learning, and 4) uses telehealth to remove access barriers.

Phase I Clinical Trial:

Limb-load symmetry biofeedback training via pressure insoles in patients with osseointegrated prostheses.

Primary Outcomes:

1) Intervention feasibility and 2) Changes in loading (free living and using motion capture data and musculoskeletal models)/clinical outcomes.

Timeline and Cost

Activities	CY '23	CY '24	CY '25
AIM 1: Implementation feasibility of limb-load biofeedback training			
AIM 2: Signal of efficacy analyses			
AIM 3: Key functional movement priorities identified			
Estimated Budget ($K)	$127	$132	$91

Goals/Milestones

CY '23 Goal – Project Initiation

☒Complete IRB Approval and ClinicalTrials.gov registration

☒Train personnel for testing & intervention delivery (Aim 1)

☒Begin enrollment of study participants

☒Intervention onset (Aim 1)

CY '24 Goals – Project Continuation

☐Complete data collection at all testing timepoints for first 7 participants

☐Finalize data processing methods

☐Finalize enrollment of all study participants

CY '25 Goal – Project Completion

☐Intervention completion for all participants (Aim 1)

☐Complete data collection and analyses of all outcome data (Aim 2)

☐Complete exit interview for all patients (Aim 3)