**Title:** PRMRP Norms: Iterative Design of Custom Dynamic Orthoses and Comprehensive Design of Musculoskeletal Model.

**NCT Number:** NCT04800510

**Date:** November 7, 2023

**Study Protocol:**

Purpose and Procedures:

The purpose of this study is to determine the effect of external bracing, in the form of a carbon fiber dynamic orthosis, on joint contact stress, muscle forces, physical function, and gait biomechanics. The effects of external bracing on gait mechanics, mobility, and muscle and joint forces are poorly understood. Collected data will include patient demographics and anthropometrics, ankle range of motion and stiffness data, plantarflexion strength data, CT images, CDO stiffness data, physical performance measures, patient reported outcomes, gait kinematics and kinetics, plantar pressures, and electromyography data. The knowledge that will be gained from this investigation has the potential to substantially improve the understanding of how external bracing impacts limb function and inform future investigations to advance the clinical prescription of ankle foot orthoses.

Objectives and Specific Aims:

Specific Aim 1: Determine the effect of CDO design modifications on ankle contact stress in a cohort of healthy able-bodied individuals.

Specific Aim 2: Determine the effect of CDO design modifications on physical function and gait biomechanics in a cohort of healthy able-bodied individuals.

Specific Aim 3: Determine the effect of CDO design modification on muscle forces during gait

Specific Aim 4: Refine methods of integrating data from multiple sources into musculoskeletal model to evaluate ankle contact stress.

Background and Significance:

Post-traumatic osteo-arthritis (PTOA) is a significant problem caused by chronic, increased, contact stress and fracture severity. Surgical fracture reduction has been the mainstay of intra-articular fracture (IAF) treatment for decades, but it is not the only factor influencing joint contact stresses. Furthermore, even with the best surgical effort, there often remains residual incongruity that leads to elevated contact stress. Numerous studies have explored the relationship between elevated contact stresses and the development of osteoarthritis following traumatic injury of the ankle. CDOs, such as the Intrepid Dynamic Exoskeletal Orthosis (IDEO) developed at Brooke Army Medical Center, have been used to dramatically improve function and reduce pain in hundreds of service members with traumatic limb injury. CDOs are comprised of a proximal cuff sitting just below the knee, a posterior strut used to store and return energy, a semi-rigid foot plate, and in some cases a heel cushion between the footplate and shoe [11]. These design components can be varied to influence the forces and motions experienced by the limb [11-14], which in turn influence the forces on the foot and the activation of muscles that cross the ankle [8, 15, 16]. Recent findings indicate that this can decrease load transfer across the ankle, which implies that CDOs may be able to be effectively tuned to reduce articular contact stress. A key mechanism by which may articular contact stress may be reduced is the reduction of force produced by muscles around the ankle.

The multiple data sources collected in this study will serve as inputs for creating a comprehensive musculoskeletal model using OpenSim modeling software. OpenSim is an extensible software package that has been developed over decades to combine knowledge of computational modeling and biomechanical system simulations in order to calculate muscle forces generated from movement, kinematic adaptations during gait, and human-device interactions [78]. The use of OpenSim will allow for accurate simulations of gait, as well as calculation and prediction of variables that are difficult to measure experimentally [78].

Inclusion/Exclusion Criteria:

Patient Inclusion Criteria

- Between the ages of 18 and 50

- Shoe size between women’s 8 and 13.5 or men’s 6.5 and 12

- Healthy individuals without a current complaint of lower extremity pain, spine pain, or medical

or neuromusculoskeletal disorders that have limited participation in work or exercise in the last 6 months

- Full active range of motion of the bilateral lower extremities and spine
- Ability to hop without pain
- Ability to perform a full squat without pain
- Ability to read and write in English and provide written informed consent

Patient Exclusion Criteria

- Diagnosed moderate or severe brain injury
- Prior lower extremity injury resulting in surgery or limiting function for greater than 6 weeks
- Diagnosis of a physical or psychological condition that would preclude testing (e.g. cardiac condition, clotting disorder, pulmonary condition)
- Visual or hearing impairment that would interfere with instructions given during testing
- Require an assistive device
- Wounds to the foot or calf that would prevent CDO use
- BMI greater than 35
- Pregnancy – Per participant self-report. Due to the expected small number of pregnant individuals and resulting inability to account for its effect on resulting outcomes, participants will be withdrawn from the study

Design and Methods:

Patients will wear generic sized CDOs provided by Bio-Mechanical Composites (Des Moines, IA). Personal/demographic and anthropometric information will be used to fully characterize the study participants. We will collect multiple variables that have been previously associated with outcomes including race, ethnicity, and education. Anthropometric and demographic information such as age, biological sex, study limb (left or right), height, weight, leg length, shoe type, shoe length and width will also be used to characterize the cohort. Multiple outcomes measures will be used to characterize patient-centric outcomes.

Physical performance measures provide an objective and responsive assessment of an individual's functional mobility. Activities of daily life require performance of a range of functional tasks that require balance, agility, speed, and power. The four square step test (4SST) is a widely used test of functional mobility that requires rapid changes in direction that are often problematic following lower limb injury. The measure has good to excellent reliability and validity across multiple patient populations and groups and is a key dependent measure in most CDO-related studies to date and has demonstrated ability to detect changes in function in individuals with limb trauma and CDOs [7, 9, 27, 36]. The sit to stand 5 times (STS5) test is a well-established measure of lower limb muscle strength, endurance, and mobility [39]. The STS5 test has excellent reliability and good validity across a broad range of patient populations [35, 39-48].

Patient-reported outcomes questionnaires will be used to evaluate participant physical function, activity level, pain, comfort, satisfaction, and preference in addition to multiple other relevant outcomes. The Orthotics Prosthetics Users' Survey (OPUS) is a leading measure for evaluating satisfaction with orthotic devices and services [49]. It is a self-report questionnaire, with the full battery consisting of 88 questions and five modules. The satisfaction with devices portion will be used to evaluate device comfort, form, and fit using a four-point Likert scale and has good to excellent reliability, internal consistency, and validity for individuals with a wide range of diagnoses requiring orthotic and prosthetic services [49]. Comfort and smoothness will also be assessed using a modified version of the Socket Comfort Score, a reliable, valid, and sensitive measure of device fit and comfort [50]. These measures have been shown to effectively capture patient perception, are

responsive to simple modifications to CDO device function, and will be applied in a manner consistent with a prior publication by the research team [11]. Participants will be asked to report their pain using a standard 11-point numerical pain rating scale, in which 0 = no pain and 10 = worst pain imaginable, at the start of each session, and at multiple points while walking in each condition. Participants will be asked to rate the three braces (CDO-A, CDO-B, and CDO-C) on a standard 11-point scale, where 0 = worst imaginable device and 10 = best imaginable device. The University of California, Los Angeles (UCLA) activity score is a 10-level rating scale that is used to both qualitatively and quantitatively define an individual's current and/or desired level of activity and has been shown to be reliable with no floor effects [53]. The Patient Reported Outcomes Measurement Information System (PROMIS) is a group of patient-centered tests, developed through funding from the National Institutes of Health, which can be used to characterize physical, mental, and social health and function. The PROMIS instruments use modern measurement theory to reliably and validly assess patient-reported outcomes. We will use PROMIS to evaluate physical function. Semi-structured interviews will also be used to fully capture the patients' perspectives, experience, and opinions associated with the device options they experienced as part of the study.

Impairment, biomechanical, and device data will be used to compare devices, characterize limb and device function, and to provide insight in a manner not commonly found in comparative studies. Bending stiffness will be measured using a custom-made orthotic stiffness testing device designed specifically for quantifying CDO bending stiffness in Nm/degree. Ground reaction force and motion capture data will be used to evaluate the motion and loading of the lower limb and CDO devices as participants walk on an over ground walkway at self-selected speed and a controlled speed based on leg length [54, 55]. Muscle activity will be measured using DELSYS EMG sensors. EMG data will be collected bilaterally in the lower limbs and data will be analyzed over regions throughout the gait cycle. In-shoe plantar pressure distribution will be measured using the LoadSol system which interfaces with the foot and shoe insole and has been found to be accurate, precise, and repeatable in measuring plantar pressures during normal gait [60, 61]. Ankle range of motion and stiffness will be assessed using the Iowa Ankle Range of Motion device. Ankle strength will be assessed using the Standing Heel-Rise Test. Subjects will perform as many standing heel-rises as they can, while their ankle motion and body/limb alignment are carefully monitored.

**Statistical Analysis Plan:**

Analysis Methods:

Data quality will be rigorously examined over the course of this study. The distributions of study measures will be characterized using descriptive statistics. For descriptive statistics, univariate statistical approaches will include careful review of data frequencies, measures of central tendency, and distribution shapes. Additionally, identification of out of range data, determination of the quantity of missing data, and accurate description of the study population will be achieved.

Power Analysis:

The proposed sample size for this study is 10 subjects. Since the primary purpose of this study is to refine procedures for inputting multiple data sources into a musculoskeletal model, the study does not call for a total number of participants consistent with prior investigations by Dr. Wilken. In a 2017 study conducted by Blazkiewicz et al, data was collected from 10 healthy subjects and incorporated into a generic OpenSim musculoskeletal model [79]. The results of the study showed some inter-individual variation as expected, but identified a common theme of muscle peak force regularities acting on the ankle joint across subjects, indicating that a 10 subject sample size is sufficient for the protocol design of similar investigations [79].

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