Gait Modification Treatments for Knee Pathology
NCT: 03116230
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Study Protocol and Statistical Analysis Plan

Project Title. Analysis of Pain, Function, and Joint Mechanics in Response to Two Treatments for Knee Pathology

Purpose. The objective of this project proposal is to complete a longitudinal clinical study of a cutaneous stimulation device in a target population of subjects with knee pathology. This work will determine the longer-term effect of the intervention on pain/function, gait/muscle function, and patient comfort.

Scientific Rationale. Knee injuries and pathologies such as anterior cruciate ligament (ACL)/ meniscus tears and knee osteoarthritis (OA) are prevalent musculoskeletal conditions that cause functional limitations, pain and disability affecting patient quality of life and healthcare cost. Individuals with knee injuries who had undergone a meniscectomy or ACL reconstruction surgery and knee OA patients exhibit significant alterations in lower extremity muscle patterns involved in gait, including a weakness in the quadriceps muscle. Over the long term, an impairment in muscle activity may result in a change in mechanical stress loading of a joint and have adverse effects on the knee joint, and research increasingly suggests that such alterations may be significant predictors of onset and progression of knee OA.

Clinical guidelines for management of knee OA and associated joint injuries recommend non-pharmacological conservative interventions such as physical therapy, use of braces, elastic wraps, electrical stimulation and taping. These interventions are commonly used to improve muscle strength, joint stability and mitigate pain. However, treatment is often discontinued because of time constraints and cost involved, and hence there are limited long-term improvements.

To address these limitations, we have developed a device which utilizes a novel design to activate deficient lower extremity muscles through the somatosensory system and cutaneous stimulation. This device exploits the cross modal plasticity of the somatosensory system that controls touch, pain and proprioception. By applying intermittent cutaneous stimulation to the thigh and shank through vibration, it may activate the mechanoreceptors in the leg and thereby induce improved muscle contraction and a functional response during walking. This study aims to assess the changes in gait patterns and pain/function resulting from the intermittent cutaneous stimulation of afferent nerves on the surface of the thigh and shank.

Focus. Using a cross-over study design, this study aims to assess the influence of the cutaneous stimulation device versus a commercially-available knee sleeve on pain, function, and knee joint mechanics.

Anticipated Impact. Knee injuries and disease cause substantial pain and disability, and their high prevalence necessitate simple interventions. Clinical guidelines for management of knee OA and associated joint injuries emphasize the importance of non-pharmacological conservative strategies. Gait modification through cutaneous stimulation may offer a low cost alternative to rehabilitation programs and current treatments to address pain, deficient muscle activation in knee OA and conditions related to development of the disease.

Methods. The objective of this study is to conduct a cross-over study to assess the influence of the cutaneous stimulation device versus a commercially-available knee sleeve. We will use a single-center, single-blind, randomized, crossover study design. Participants will be told only that we are comparing two types of treatment for their knee pain.

Interventions will include: (A) Control treatment consisting of an off-the-shelf neutral knee sleeve and (B) Active treatment consisting of the cutaneous stimulation device.

Individuals with prior ACL injury/surgery, meniscus injury/surgery, and/or physician-diagnosed medial compartment knee osteoarthritis will be recruited. The participants will be 18 years or older, and both males and females will be recruited. Individuals below the age of 18 years old are excluded as they may not have reached skeletal maturity. Knee pathology subjects may be recruited through direct referrals from clinicians in primary care, rheumatology, physical medicine and rehabilitation, physical therapy, radiology, and orthopedic surgery. The group has successfully used advertising flyers to recruit subjects and we will also employ these methods for knee pathology subjects.

Subjects will be telephone screened for inclusion criteria. If the subject meets the designated criteria, he/she will be scheduled to visit the gait lab and enrolled in the study. The procedures will take approximately 2-3 hours.

At baseline testing, eligible subjects will be randomized to receive either treatment A or B for the initial 4 weeks and will receive a gait test. After the 4 weeks, the assigned treatment will be removed and a second gait test performed, and the participants will receive no treatment for 2 weeks. Following this 2-week washout period, the second randomized treatment will be

assigned for a 4-week period and a gait test performed. At the end of the 4-week period, another gait test will be performed. For each subject, the trial will last for a total of 10 weeks.

During each treatment, subjects will maintain a daily wear log, pain diary, and medication usage. Subjects will record the number of hours of brace wear each day and will be instructed to wear the brace during the active part of the day (greatest number of gait cycles).

During gait testing, each subject may be asked to walk at a variety of speeds and perform activities of daily living. A motion capture system consisting of infrared cameras and small reflective balls (markers) attached to the subjects using small double sided stickers and force platforms embedded in the floor will be used estimate subjects kinematics and kinetics during gait following the point cluster method protocol and standard inverse kinetics calculations. Pressure sensors may also be used to provide a 2 dimensional map of the pressure distribution in the stance phase of gait. EMG may be used to provide information on muscle activation. Additionally, inertial sensors may be placed on the bodies of the subjects to measure their kinematics. The markers and sensors will be placed on the bodies so that they do not impede the subject's movements in any way. Moreover, these elements do not impart excessive force. Ideally, the subject will forget that they are wearing the system. The walkway in the laboratory is well lit and free of obstacles. Outdoor testing may occur in a selected outdoor location that is also safe and unobstructed. There is little to no risk to the subjects beyond the normal risks associated with walking.

Subjects will be asked to complete questionnaires regarding pain, function, and physical activity.

Statistical Analysis Plan. Paired two-tailed t-tests will be used to assess changes in patient-reported outcomes and joint loading parameters (e.g. peak knee flexion moment) with each treatment from pre-treatment control.

Results.

- Mean +/- SD KFM at baseline for all 38 subjects : 3.14 ± 1.31
- Mean +/- SD KOOS Pain at baseline for all 38 subjects 66.25 ± 13.4
- Mean +/- SD KOOS Function at baseline for all 38 subjects 72.31 ± 15.98
- Mean +/- SD KOOS Symptoms at baseline for all 38 subjects 59.8 ± 15.58
- Mean +/- SD *change* in KFM (%Bw*Ht) separately for Treatment A and Treatment B from control (and # of subjects analyzed for each). For slow walking

Treatment A mean +/- SD change in KFM (%Bw*Ht) relative to control= 0.197 ± 0.374

Treatment B mean +/- SD change in KFM (%Bw*Ht) relative to control= 0.018 ± 0.725

- Statistical test used to compare the KFM and the p-values from it (separate p-values for Tx A and Tx B vs. control)
- T-test Treatment A P=0.005
- T-test Treatment B P=0.64

- Mean +/- SD *change* in KOOS Pain separately for Treatment A and Treatment B from control (and # of subjects analyzed for each).

Treatment A mean +/- SD change in KOOS Pain relative to control= 1.476 ± 12.286

Treatment B mean +/- SD change in KOOS Pain relative to control= -0.391 ± 9.714

- Statistical test used to compare KOOS Pain and the p-values from it (separate p-values for Tx A and Tx B vs. control)
- T-test Treatment A P=0.5
- T-test Treatment B P=0.82

- Mean +/- SD *change* in KOOS Function separately for Treatment A and Treatment B from control (and # of subjects analyzed for each).
  - Statistical test used to compare KOOS Function and the p-values from it (separate p-values for Tx A and Tx B vs. control)

Treatment A mean +/- SD change in KOOS Function relative to control= 4.48 ± 12.56

Treatment B mean +/- SD change in KOOS Function relative to control= 0.64 ± 7.903

- T-test Treatment A P=0.05
- T-test Treatment B P=0.65

- Mean +/- SD *change* in KOOS Symptoms separately for Treatment A and Treatment B from control (and # of subjects analyzed for each).
- Treatment A mean +/- SD change in KOOS Symptoms relative to control= 3.571 ± 9.47
- Treatment B mean +/- SD change in KOOS Symptoms relative to control= -0.781± 10.876

- Statistical test used to compare KOOS Symptoms and the p-values from it (separate p-values for Tx A and Tx B vs. control)
- T-test Treatment A P=0.04
- T-test Treatment B P=0.68