Clinical Evaluation of an External Neuromodulation Device (VibraCool) to Reduce Pain and Opioid Use After Anterior Cruciate Ligament Reconstruction

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Neuromodulation to Reduce Pain After ACLR

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Introduction:

Opioid use after surgery has been identified as a primary contributor to addiction, both directly and through increased opioids in circulation [1]. The incidence of opioid addiction increases three days after outpatient use [2, 3], and the average duration of opioid use for many surgical patients exceeds this duration [4]. As such, opioid-sparing pain relief options are needed to address this issue and reduce the potential for dependence and global misuse.

While opioid-reducing consensus statements exist for hip and knee arthroplasty [12], no similar guideline exists for ACL reconstruction (ACLR) [13]. Current methods to decrease ACLR pain include surgical techniques and post-operative medications including non-steroidal anti-inflammatory medications and opioids [14]. Prescription amounts varied widely by geographic region, with an average of 87% of patients filling an opioid prescription within 30 days of surgery in 2017 [14].

Cryotherapy has also been used as an adjunctive post-operative therapy to reduce pain and inflammation following UCLR. It has been shown to decrease local metabolism, resulting in reduced pain and inflammation [cite Crystal et al]. Multiple studies have shown the benefits of using cryotherapy after ACLR [cite Raynor et al, Blakeley et al], and more recently dynamic intermittent compression has been shown to improve circulation while reducing the risk of skin necrosis associated with static permanent compression [cite Khanna et al, McGuire et al]. A recent meta-analysis including ten RCTs found significant reductions in post-operative VAS pain scores and breakthrough opioid consumption when using cryotherapy, such as Game Ready ice therapy, following ACLR [cite Davey et al].

Multiple studies have shown that vibration sources applied to muscles prior to exercise reduced soreness and lactate dehydrogenase production, and increased range of motion at 48 and 72 hours [5-11]. Acute pain results from fast A nerves transmitting nociceptive information to the dorsal column, where the substantia gelatinosa's interneurons prioritize competing A mechanoreceptor and C-fibers to slow pain transmission. Melzack and Wall observed that stimulation of A mechanoreceptors "shut the gate" on pain transmission, an inhibitory mechanism known as "gate control" [5]. Multiple physical methodologies leverage gate control physiology for pain relief, such as vibratory massage therapy and electrical stimulation to varying degrees [7]. However, the use of vibratory massage to improve pain control and reduce opioid use following ACLR has not been well studied, and to our knowledge there are no RCTs evaluating the use of this modality compared to standard ice or cryocompression.

Therefore, the primary objective of this study is to test the effects of the FDA-approved VibraCool mechanical stimulation and neuromodulatory therapeutic device on post-operative pain and opioid use following ACLR, compared to standard ice therapy and cryotherapy. Our secondary objective was to determine the degree these treatment modalities reduced the amount of residual opioids in circulation.

Methods:

Study Design:

Surgeons participating in the study will agree to a standard prescription amount of opioids (the standard of care, 15 tablets post-operatively with instructions for every 6 hours as needed) and a standardization of postoperative ice therapy (i.e., ice pack application usage to 20 minutes 3 times per day). The standard ice packs control group will apply the ice pack as usual,

while the remaining treatment arms will place the ice pack in the VibraCool or Game Ready machines and place it on their leg for 20 minutes 3 times per day. Pediatric and adult subjects with surgical plans to undergo ACL reconstruction will be identified and approached.

Subjects were randomized to one of the three treatment arms. Subjects randomized to the intervention VibraCool group will still receive the standard of care in addition to the intervention. Subjects randomized to the intervention groups will be given a one-sheet instruction for use of a VibraCool Pro at their pre-operation visit and a link to a video explaining its use. The same will be done for the Game Ready treatment arm. Questions about use will be answered by a study coordinator, video instruction, or a provider. Study personnel will instruct patients in both groups on a 10 cm visual analog (VAS) pain scale using a script, and on a daily analgesic diary. Both groups will then record daily logs of pain and opioid use for 7 days. The home pain diary will include a Numeric Rating Scale of 0-10 which will be explained prior to discharge, as well as daily ratings of pain prior to any pain relief interventions, additional medications and dosages, and any comments detailing pain related activities. Qualitative assessment of pain will also be completed. On day seven, subjects will complete the patient-reported outcomes measurement information system (PROMIS) instrument 8a (adult form for ages 18+ or the pediatric form) for pain interference will be completed. The study will be complete at 7 days.

REDCap was used to record patient responses on a daily basis, with daily patient portal or phone call reminders. The daily survey also contained a video on how to use the device so patients have easy access to detailed information on how to use the device, in addition to our team being available to address any issue. Multiple factors have been shown to influence pain, including anxiety and/or depression, age, severity of preoperative pain, smoking, alcohol use, and socioeconomic status [16-20]. These characteristics were collected for each patient in our

study to account for potential confounders. Classically, pain has been rated on a numerical scale, which gives little perspective into the degree of impact on an individual's function and quality of life. A more insightful measure may be Pain Interference (PI), known as “pain impact,” which has been shown to be a more insightful measure into how pain interferes with an individual's physical, mental, and social quality of life and has been deemed a key outcome in pain clinical trials, especially in orthopedics [21-23].

Potential subjects are identified as those pediatric and adult patients who are indicated for ACL reconstruction surgery. Pediatric iliotibial band (ITB) ACLR and non-English speakers were excluded secondary to xxx and limitations of our study group. Patients (and in appropriate cases, their parents or guardians) will be notified of the study and its procedures by the treating orthopedic surgeon or other study member listed on this IRB. Consent will be obtained either in the office or via phone a telehealth visit, the study will be explained in full during visit, then re-explained with consent to be signed in the pre-operative area, at which time the patient will be randomized as described above. The informed consent process as a whole presents information in sufficient detail relating to the research study, and informed assent was also obtained for every subject below the age of 18.

Statistical Analysis:

The primary outcome will be daily mean VAS pain scores over the first seven post-operative days and percent of patients discontinuing opioid use by or on post-operative day three, compared to those who continue after day three. Secondary outcomes include mean reduction in opioid use in milligrams of morphine equivalents per day (MMOD) of 30% from patients not using the device over the 7-day period and pain interference scores. A descriptive analysis of the demographic and physiological data will be performed using proportions, frequency

distributions, medians, and confidence intervals. Statistical testing will include ANOVA analysis and unpaired t-tests for continuous variables between the treatment arms, while chi squared analysis will be used for categorical variables. Subgroup analysis by graft type was conducted similarly.

Based on a previous ACL pilot study using a single vibration unit, 71% discontinued opioids by day 3, compared to only 40% in a published cohort. Therefore, 38 patients will be needed in each group. Assuming a 15% drop-off, 44 patients will need to be recruited for the device versus nothing group to give 80% power, or 88 subjects total. Previous studies comparing two modalities suggest a standard deviation of 1.8. 20 patients in each group will have power of 0.87 to detect a difference in the means of 1.8 cm mean VAS pain score reduction between nothing and study device with the same alpha criterion. The study will be underpowered to detect an overall difference in opioid use based on the assumed effect size of .58 (Cohen's D) – 0.62 (Hedges' g) for the primary outcome variable (opioid use) based on 10.1+/- 10.3 (n=14) compared to 15.6+/-8.5 (n=77). The criterion for significance (alpha) is 0.05

Results:

Discussion:

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