Non-invasive Interactive Neurostimulation (InterX®) as an adjunct in pain control for patients following Total Knee and Total Hip Arthroplasty: a Randomized Placebo Controlled Trial

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Introduction:

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are painful procedures that have seen the postoperative implementation of a number of strategies to advance patient comfort and early mobilization. The aim of postoperative analgesia is to make patients as comfortable as possible with the lowest possible morbidity from analgesic modalities, such as cardiorespiratory or central nervous system depression [1]. Thus, the development and study of a non-drug, non-invasive means of delivering pain relief is warranted for the purpose of improved patient comfort and potential cost-savings relating to better patient outcomes with some suggesting that the next major development in TKA technology will be a pain relief modality. It has previously been demonstrated that a 25% reduction in opioid consumption can lead to as much as a 66% reduction in clinically meaningful events/side-effects [2] .

The InterX is a non-invasive interactive neurostimulation device manufactured by InterX Technologies, Richardson, Texas, USA. It is an advancement of neurostimulation technology which delivers a more powerful and more targeted stimulation to optimize the treatment parameters and significantly improve the physiological and clinical benefits. The interactive, impedance sensitive waveform allows for the delivery of stimulation through small, closely spaced electrodes to optimal treatment points at an amplitude 4-5 times higher than other neurostimulators and without the risk of painful muscle contraction. These characteristics activate a powerful and consistent pain relieving effect and have even been shown to reduce inflammation[4], a mechanism not generally associated with transcutaneous electrical stimulation. InterX technology has demonstrated significant clinical efficacy in two published trials of Level One therapeutic evidence [3,4].

This randomized, placebo controlled, prospective study was designed to research this technology on total joint replacement patients; a population which has previously proven difficult to treat with neurostimulation due to poor efficacy[5] and risk factors.

Hypothesis:

In this study it is hypothesized that active InterX Therapy added as a compliment to usual in-patient rehabilitive care of post-operative hip and knee replacement will:

Primary:
Reduce pain severity on a 0-10 scale when compared to sham therapy over time, or reduce use of pain medication when compared to sham therapy over time

Secondary:
Reduce length of time required to achieve discharge goals when compared to sham therapy over time

Study Population
87 consecutive patients presenting for admission to the Presbyterian Rehabilitation Unit following hip or knee primary joint replacement and meet the entry criteria will be elegible. Patients were randomized to be treated with the InterX device or to the placebo group which used a sham device. All patients gave informed consent and the protocol received formal approval from the institutional review board. Participants were randomized using a block randomization schedule.

Inclusion Criteria:
40 years of age or older
Postoperative primary hip or knee replacement at Presbyterian Hospital of Dallas
Willing to abide by protocol and treatment schedule
Able and willing to give informed consent

Exclusion Criteria:
Implants, insulin pumps, or patient incompatible with electrical stimulation
History of epilepsy or seizure
Preganancy
Medical management issues that delay active physical therapy upon admission
Bilateral joint replacements
Revisions and/or traumatic joints

Method:

The groups received InterX treatments 2 times per day starting 72 hours after surgery. Treatment with the device was approximately 20 minutes per session. Patients were treated with an active InterX or sham InterX. Therapists giving "sham" treatments followed the same treatment protocols as when using the active devices. The therapists instructed the patients that they may or may not experience the stimulation. Therapists were trained to respond in the same manner whether or not the stimulation was felt so the patients remained blinded. Part of the use of the device involves scanning for points of low impedance around the surgical site as these represent optimal treatment points for neurostimulation. This procedure was also followed with the sham device. Data on pain medication was documented daily. Parental morphine equivalent (PME) conversion was performed by the pharmacist.

Parental Morphine Equivalent (PME) conversion:

The IV conversion will be: Morphine IV 10mg = Hydromorphone 1.5mg IV = Fentanyl 0.1mg IV
The oral opiate medications will be converted as follows: Morphine IV 10mg = Hydrocodone 30mg PO = Oxycodone 20mg PO
Transdermal fentanyl (note the equivalence is based on a 24 hour amount): Morphine IV 22mg per 24 hours = 25mcg/hr fentanyl patch

References:

1. **Zhao S.Z., PhD, MD, et al.** Dose-Response Relationship Between Opioid Use and Adverse Effects after Ambulatory Surgery, journal of Pain and Symptom Management 2004; 28:35-46
2. **Ranawat A.S., MD, et al.** MDyz Pain Management and Accelerated Rehabilitation for Total Hip and Total Knee Arthroplasty, The Journal of Arthroplasty Vol.22 No. 7 Suppl.3 2007
3. **Gorodetskyi G.I., et al,** Non-invasive interactive neurostimulation in the post-operative recovery of patients with a trochanteric fracture of the femur. *J Bone Joint Surg (Br) 2007;89-B:1488-94*
4. **Gorodetskyi G.I., et al:** The effects of non-invasive interactive neurostimulation on pain and edema during post-surgical rehabilitation following internal fixation of unstable bi-malleolar ankle fractures. J Foot Ankle Surg 2010; 49:432-437
5. **Breit R, et al.** Trancutaneous Electrical Nerve Stimulation for Postoperative Pain Relief after Total Knee Arthroplasty, The Journal of Arthroplasty 2004; 19: 45-48

Results:

While there were fairly large variances between groups and genders, the overall reduction in medication taken by the InterX group was statistically significant. We used analysis of covariance methods (ANOCOVA) that adjusted for differences in BMI. There was significant treatment effect on total pain medication intake (p=0.029) in the InterX Group. The estimated means were 80.6mg vs. 50.6mg (Control vs. InterX)for hips and 104.1mg vs. 74.0mg (Fig.1) (Control vs. InterX) for knees.

We also looked at the effect of therapy on number of days in the rehab unit. Considering all patients and using the non-parametric Mann-Whitney test, InterX patients spent significantly fewer days in rehab, p=0.011 (Fig.2).

Fig. 1

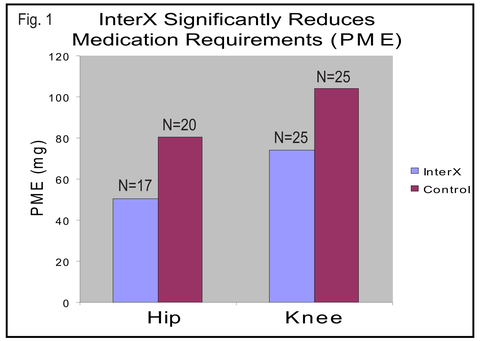
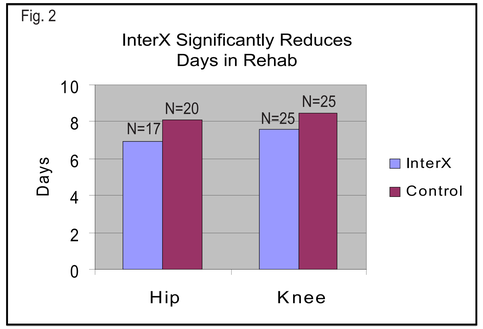


Fig. 2



This was against a back-drop of pain scores which remained around 4/10 for the duration of the in-patient stay in both groups. This demonstrates the clear ability to maintain adequate analgesia for patient comfort while needing significantly less drugs when InterX Therapy is included as an adjunctive treatment. This effect was even more marked when looking at the knee group over the first 7 days (the average length of stay in the treated group, thus providing the most data points for comparison), with a 47% reduction in medication in the InterX Group compared to Control (p<0.05). This is clinically significant as pain following TKA is particularly severe and has proven to be resistant to other forms of neurostimulation in the past [5] .

Fig. 3

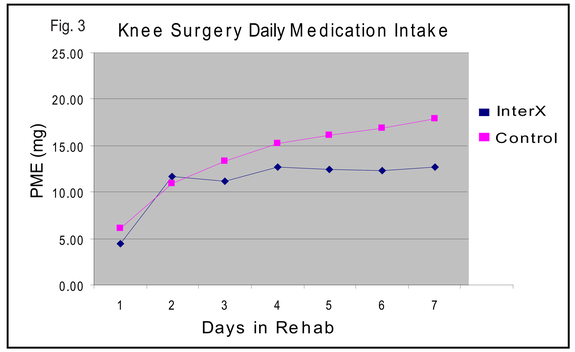
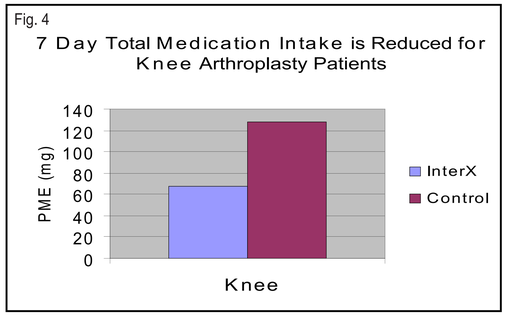


Fig. 4



Conclusion:

The effects of InterX treatment on TKA and THA patients is statistically significant and also has clear clinical and financial implications. The cost of in-patient rehabilitation ranges from $600.00 to $1,000.00 per day, so the cost savings for early discharge on this study population offer significant potential. This study alone demonstrates a potential saving of in-patient costs of between $25,200 and $42,000. The case for inclusion of InterX is furthered by the fact that the manufacturer has recently developed a patient-administered version of the technology which does not require the continual attendance of a therapist and can be self administered for between two to six times per day.

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