Percutaneous Peripheral Neuromodulation for Postoperative Analgesia

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Written, informed consent will be obtained using an IRB-approved ICF prior to any study procedures. Lead insertion may occur up to 2 weeks prior to surgery within the CTRI or orthopedic clinic, or the morning of surgery in the CTRI or regional anesthesia induction area (it just depends on subject and surgeon preference, as well as logistical issues such as the time of the surgery and availability of the investigators). Baseline muscle strength will be measured with a pressure transducer.

Preoperative lead insertion (approximately 1-3 hours). A percutaneous, helically-coiled, insulated electrical lead will be inserted via an introducer needle at least 2 cm proximal or distal to the perineural catheter site along the target nerve using real-time ultrasound guidance:

Surgical Procedure Location	Perineural Catheter Location	Electrical Lead Location
Shoulder	Interscalene	Interscalene, supraclavicular, or suprascapular
At or distal to the elbow	Infraclavicular	Interscalene, supraclavicular or terminal nerve(s)
Foot or ankle	Popliteal-sciatic [adductor canal optional]	Subgluteal-sciatic [femoral optional]
Knee or distal thigh	Adductor canal [popliteal-sciatic optional]	Femoral [subgluteal-sciatic optional]

It will be optional for a conducting probe to be used prior to lead insertion—this allows identification of the optimal lead tip location relative to the target nerve by passing electrical current via the insulated probe. The desired end point is a pleasant paresthesia in the distribution of the target nerve reported by the subject. If used, the probe will be completely withdrawn following target location identification, and a lead subsequently inserted to the target location. Following needle removal, the percutaneous helical lead will have electric current passed using the SPRINT (SPR Therapeutics, Cleveland, OH) pulse generator to ensure accurate placement (a pleasant paresthesia in the distribution of the target nerve). It will be replaced, if necessary. The pulse generator will then be removed and the lead affixed to the skin using an occlusive dressing.

With the subject's permission we may photograph or videotape the procedures described above for educational, training, or publication purposes. The photos or video will focus only on the lead insertion site and affected limb. Ultrasound images from the procedure may also be collected. Every effort will be made to protect the subject's privacy and the photos or video will not include the subject's face or any other personal identifiers such as birthmarks. Subjects and their caretakers will be trained in device care and management, and given written instructions as well. Following successful lead insertion, a perineural catheter may be inserted, if the patient desires a catheter (with normal saline injection and not local anesthetic via the inserting needle). This will be used to deliver perineural local anesthetic as a rescue analgesic method postoperatively in case the SPRINT system provides inadequate analgesia.

Randomization. Within the recovery room, the surgeon often performs a standard neurologic examination (variable depending on the surgeon and surgical procedure), after which time the subject will have baseline end points measured, including a pain score at the surgical site using the Numeric Rating Scale (NRS, 0-10), pain score (NRS) within the target nerve distribution, and

sensory deficits (measured with alcohol pads and von Frey filament, compared to the contralateral limb within the cutaneous distribution of the target nerve). For their first pulse generator—"Stimulator A"—subjects will be randomized to one of two treatments—current or sham—using computer generated lists and opaque, sealed envelopes. The stimulator will then be attached to the lead and switched "on" (sham stimulator produces no current). The end points will be measured per the table below. Subsequently, the stimulator will be replaced by the alternative (current or sham)—"Stimulator B". The subject will have the end points measured and the stimulator replaced with a unit set to deliver active current for the remainder of study participation ("Stimulator C"). Operating and recovery room pharmacologic analgesic requirements will be recorded. Of note, if a lead fails to provide paresthesias within the target nerve distribution with either Stimulator A or B (adjustment of stimulator settings allowed), the lead may be replaced at the discretion of the subject and investigators.

Of note, the data derived from the chronic pain literature suggests that there is a "carry over" effect following stimulation: analgesia is provided even after the cessation of electrical current. It remains unknown if this is true following surgery in the acute postoperative pain period. For subjects randomized to active current from Stimulator A, the data collected for Stimulator B placebo treatment may be lowered due to the carry over effect. Therefore, this data will not be compared with the baseline or Stimulator A outcome measures. However, it is valuable data to possibly detect and quantify the carry-over effect of the initial stimulation.

At any time, subjects may choose to have their perineural catheter bolused with local anesthetic and a perineural local anesthetic infusion begun (if they desired a catheter with subsequent insertion). Therefore, subjects will not risk receiving inferior analgesia by participating in this study. However, subjects also have the option of leaving their infusion pump off and using neuromodulation as their primary analgesic if the latter proves adequate—the decision is completely each subject's and may be made any time prior to perineural catheter removal.

Subjects and their caretakers will be trained in device care and management, and given written instructions as well. Pain scores (resting and dynamic worst and average) will be collected daily for two weeks, along with oral analgesic requirements, perineural local anesthetic use, and sensory/motor deficits (all specific to the previous 24 hours). Perineural catheters will be removed at home upon subject request, after 3 days, or upon local anesthetic reservoir exhaustion, whichever comes first (standard-of-care). The electrical leads will be removed upon subject request, or after 30 days, whichever comes first. The leads will be removed at home by subjects or their caretakers (standard-of-care for perineural catheter withdrawal) or by investigators, depending on both investigator and subject preference. If removed by subjects or their caretakers, a picture of the extracted lead tip must be texted/emailed to investigators, or the physical lead returned to investigators for inspection. Subjects will be contacted no less than every 5 days following the initial 2-week period until their lead is removed; and, will then be contacted 1 and 3 months postoperatively and the end points again verbally collected.

Sample Size Estimation and Statistical Analysis Plan. This is a feasibility study to demonstrate proof-of-concept and generate data to help design and power subsequent definitive, randomized, controlled clinical trials. Therefore, a convenience sample of 40 subjects will be enrolled (10 additional subjects permitted to account for any drop-outs for a total of 50 subjects). Although this is a feasibility—and not definitive—investigation, we will treat as the primary end point the difference between the baseline pain score and pain score 5 minutes after the active (non-sham) electrical stimulator is first turned on.