Medial Branch Peripheral Nerve Stimulation for Refractory Axial Back Pain

Protocol Summary

IRB Approval Date of Current Version:	10/21/2020
University of Utah IRB #:	IRB_00127414
Sponsor:	
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Background and Introduction

Low back pain is one of a few conditions which affects all individuals through the lifespan. The etiology of low back pain is multifactorial and in many cases self-limiting, however it also is the leading cause for working age adults to be disabled with more than $87 billion spent on low back pain disorders in 2013. Listhesis of a vertebral body, chronic compression fractures, lumbar disc herniation, and internal disc disruptions are some primary anatomical abnormalities that can cause back pain and do not have great targeted treatments. that may more common in these younger age groups reaching 39-42% with a predicted probability above 60% until age 50y. While the natural history of back pain suggests most individuals will return to a prior level of function in 3-6 months, there is a high rate of recurrent episodes which can cause short-term disability. Continued back pain can lead to decreased activity levels and accelerate degenerative changes in the disc and facet joints as described by Kirkaldy-Willis.

Current guidelines for treatment of axial low back pain include a 6-12-week course of conservative care including medications, therapy, acupuncture, chiropractic and exercise before an interventional paradigm of injections and/or surgical treatment. For those individuals who do not improve with conservative care and have predominately axial pain, options are limited as success rates from epidural steroid injections and surgery are 50% or less. Other treatments include chymopapain injection, intradiscal electrothermal annuloplasty (IDET), nucleoplasty, methylene blue injection. All of which have 50% or less likelihood of reducing pain more than 50%, although much of this data is from uncontrolled or prospective case-control studies only.

Peripheral Nerve Stimulation (PNS) recently gained FDA approval as an interventional treatment of chronic back pain. PNS involves a minimally invasive percutaneous microelectrode connected to an external impulse generator that adheres to the skin for up to 60 days and then the entire system is removed. It is theorized that the neuromodulatory effects of PNS interrupts the chronic pain cycle and allowing healthy recovery of afferent signaling and limiting and perhaps reversing the maladaptive cortical plasticity involved in chronic pain. There have been two prospective cohort studies published this year, both of which showed meaningful clinical improvement in pain and function scores. One of these studies (Cohen et al.) showed that more than 50% of the patients had greater than 50% improvement in pain at one year after undergoing 2 months of implanted PNS treatment.

Purpose and Objectives

To assess changes in pain, physical function, health-related quality of life, and cost-effectiveness in patients with low back pain, without symptoms of radiculopathy, that have not responded to conservative or traditional interventional measures and are having a SPRINT percutaneous peripheral nerve stimulator placed as standard of care. Patients will be assessed periodically (by questionnaire) after the placement of the SPRINT, FDA approved 60 day, percutaneous peripheral nerve stimulator, targeting the bilateral medial branches at the

suspected level of pain generation. Neither the manufacturer nor the FDA are involved or will have access to data from this study.

Study Population

Age of Participants: 18+

Sample Size:
At Utah:
All Centers: 120

Inclusion Criteria:

1. Age greater than or equal to 18 years of age at day of enrollment.
2. Clinical diagnosis of refractory low back pain for >3 months.
3. Magnetic resonance imaging pathology consistent with clinical symptoms/signs at one or two levels.
4. Back pain of at least 4/10 or higher using the Numerical Rating Scale (NRS).
5. Pain duration of more than 12 weeks despite trial of conservative therapy (medications, physical therapy, or chiropractic care) for 2 months.

Exclusion Criteria:

1. Refusal to participate, provide consent, or provide follow-up information for the 24-month duration of the study.
2. Contraindications to medial branch targeted PNS (active infection, bleeding disorders, current anticoagulant or antiplatelet medication use, allergy to iodinated contrast, penicillin or clindamycin and pregnancy or breastfeeding).
3. More than 2 levels of clinical proven pain.
4. Active moderate to severe lumbar radiculopathy.
5. Intradural disc herniation.
6. Spinal fracture of posterior elements within the past 6 months.
7. Steroid injection in the spine within the last 30 days.
8. Any intradiscal injection other than contrast dye or anesthetic in the last 30 days.
9. Prior fusion at level considered to be the source of the pain.
10. Prior lumbar spine surgery within the last 6 months.
11. AP diameter of spinal canal less than or equal to 9mm at level to be treated.
12. Severe uncontrolled medical condition.
13. Severe psychological illness.
14. History of Inflammatory arthritis.
15. Malignancy within past 5 years except basal cell or squamous cell skin cancer.
16. Current use of equal to greater than 45mg morphine-equivalent per day of opioid use.
17. A history of alcohol or drug abuse within past 5 years.
18. Use of any investigational drug within past 30 days.

19. Severe anaphylactic/anaphylactoid reaction to any medications used.
20. Pending litigation involving subject's back pain.
21. No insurance coverage for any subsequent tests or procedures.
22. Inability or unwillingness to continue rehabilitation protocols.

Design

Prospective Biomedical Intervention or Experiment

Study Procedures

Recruitment/Participant Identification Process:

Our intended subject demographic includes an active population between the ages of 18 and 90 years on the day of enrollment.

In-PERSON CONTACT: Participants will be recruited from the practices of the Principle Investigator and the Co-Investigators, the clinics of the University of Utah Orthopaedic Center, University of Utah Farmington Clinic, and the University of Utah South Jordan Health Center, and other University of Utah Hospital and Clinic locations. If the participant appears to be a candidate, he or she will be invited to participate.

WRITTEN OR ELECTRONIC CHART REVIEW will also be used to identify potential study participants on the PI and Co-PIs clinical and procedure schedules. The PI, Co-PIs, Clinical Research Coordinator, and Study Coordinator will perform the chart review to determine eligibility.

REFERRALS: Additional recruitment from University of Utah Hospitals and Clinics will have flyers posted and information readily available for primary care providers to refer to the PM&R spine clinic. Flyers will be posted in waiting rooms, and clinic bulletin boards.

Participants will be personally invited to participate by either the PI or the Co-PI's in person while in their respective clinics.

Follow up surveys will be made at 1, 2, 3, 6, 9, 12, 24, and 36 months.

Informed Consent:

Description of location(s) where consent will be obtained:

University of Utah Orthopaedic Center University of Utah South Jordan Health Center

Description of the consent process(es), including the timing of consent:
As participants are identified by the PI or CO-I's as being possible candidates for this study they will invited to participate. It is anticipated that most subjects in this study will be identified mainly through the regular flow of the University of Utah clinics. The informed Consent process will occur either at the time the subject is in clinic or the participant may elect to complete the process at a later time. The patient will be greeted by the investigator or one of the study staff team members while in clinic. Patients will be given an IRB approved informed consent. All elements of the consent will be discussed with the participant, asking questions to assure they understand what is being asked of them. The patient will be allowed as much time as needed to consider fully if they would like to participate in the study. The patient will be encouraged to ask questions and if necessary take the consent home to discuss with family members and or other health care providers. The subject will be given sufficient time needed to review, ask and have his or her questions answered for a full understanding of the study and the procedures along with the risks and benefits. When the participant's questions have been fully answered, we will have the patient sign consent prior to their planned procedure. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Procedures:
Screening Visit:As participants are identified by the PI or CO-I's as being possible candidates for this study they will invited to participate. Main inclusion requirement, as listed in inclusion criteria, is that the patient is being scheduled by their treating physician for placement of a peripheral nerve stimulator as standard of care. If patient states interest in the study and wishes to discuss in more detail a research coordinator will call and answer any questions. If patient is interested, and does meet inclusion/exclusion criteria, and does not have time to do the baseline questions at time of appointment a qualified research staff member will call the patient to complete by phone. It is anticipated that most subjects in this study will be identified mainly through the regular flow of the University of Utah clinics. The informed Consent process will occur either at the time the subject is in clinic or the participant may elect to complete the process at a later time. Eligibility is determined by the inclusion and exclusion criteria. Qualifying volunteers will be asked to provide both written and verbal informed consent once a standard of care treatment plan has been agreed upon by the patient and treating physician.

Baseline: Participants who meet inclusion and exclusion criteria will be enrolled into the study after consenting to participate and before placement of the peripheral nerve stimulator. Surveys and results will be administered and recorded through REDCap, at the time of collection data will be coded by replacing the participant's name and other identifying information with a study ID number. This interventional procedure is considered standard of care and is typically based on physician preference. Baseline data will be collected within 2

weeks prior to the scheduled procedure, this will include information from their examination and baseline questionnaires which include the following:

1. Physical function (ODI)

2. Analgesic use (MQS III score30)

3. PROMIS Physical Function CAT version 2.0 (PF CAT)

4. PROMIS Global 10

5. Global impression of change (PGIC)

6. The Pain and Sleep Questionnaire (PSQ-3)

7. Numeric Rating Score (NRS) for back and legs

8. Patient Satisfaction Score ((5 point: 1, very dissatisfied; 2, dissatisfied; 3, neither satisfied nor dissatisfied; 4, satisfied; and 5, very satisfied).

Questionnaires will be administered and collected from the participant through the University of Utah approved survey system of REDCap. PGIC and Patient Satisfaction Score will only be collected on post procedure surveys.

Demographics will be collected in the baseline questionnaire and include the following information:

1) Age (years).

2) Sex.

3) Height (cm).

4) Weight (Kg).

5) Duration of pain (weeks).

6) Radiologic diagnosis based on MRI of the Lumbar Spine.

Following the Standard Treatment Procedure visit, routine scheduled follow-up (surveys) will occur at 1 month (+/- 1 week), 2 months (+/- 2 weeks), 3 months (+/- 2 weeks), 6 months (+/- 2 weeks), 9 months (+/- 2 weeks), 1 year (+/- 2 weeks), 2 years (+/- 2 weeks), 3 years (+/- 2 weeks), at which times all follow-up measures will be obtained. These questions will be administered over the phone or be sent to you using a secure REDCap survey by email. If received by email it will be in the form of two e-mail links in which you will again be asked questions regarding your pain level, changes in activity limitations, symptoms, emotions and

overall quality of life related to your painful condition and to record current use of opioid and non-opioid analgesic use. This part of the survey should take 10 minutes.

The study start date and the outcome assessment timeline will begin at the date of the participant's initial procedure when peripheral nerve stimulator was placed.

This study is intended to monitor outcomes for 3 years following peripheral nerve stimulator placement.

Procedures performed for research purposes only:

Survey Questionnaires will be given to all patients who qualify for, and are being schedul by their treating physician for, peripheral nerve stimalutor placement and are willing to en Within the survey questionnaire, pre-procedure and post-procedure NRS pain scores for b back and leg will be obtained for research purposes. Also, current pain medications of pat throughout treatment will be obtained for research purposes.

Statistical Methods, Data Analysis and Interpretation

Means and standard deviations of subject demographic data, as well as pain, functional, and treatment satisfaction scores will be calculated in addition to survival analysis. Intergroup differences will be assessed by t test for numerical data and Chi Square or Fisher Exact test for categorical data. Regression modeling will be implemented using ANOVA to assess for patient traits and characteristics that increase the likelihood of efficacy using one technique as opposed to the other.