PROTOCOL TITLE:
A Post-Market Observational Case Series Study of Percutaneous Peripheral Nerve Stimulation (PNS) for the treatment of Chronic Shoulder Pain

BRIEF TITLE:
SPR PNS for Chronic Shoulder Pain

CLINICALTRIALS.GOV REGISTRATION
NCT05649917

DOCUMENT VERSION
Protocol V1.0, 12-APR-2022

PRINCIPAL INVESTIGATOR
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SPONSOR: International Spine, Pain and Performance Center

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Study Summary:

Investigational Agent(s) (Drugs or Devices)	None
IND / IDE / HDE #	NA
Indicate Special Population(s)	None
Sample Size	up to 20
Funding Source	SPR Therapeutics, Cleveland, OH
Indicate the type of consent to be obtained	Written
Site	International Spine, Pain & Performance Center (ISPPC)
Research Related Radiation Exposure	No
DSMB / DMC / IDMC	No

Background
Chronic degenerative changes in the shoulder are a frequent source of debilitating chronic pain. In particular, osteoarthritis of the shoulder has been estimated to affect up to 32.8% of the adult population over the age of 60, and OA in general is one of the most frequent causes of disability in the United States.[1] OA impacts the quality of life of tens of millions of Americans and carries a significant economic burden of over $60 billion in the U.S. each year.[2]

Degenerative joint disease in the shoulder is commonly managed with physical therapy and over-the-counter medications, but these modalities can be insufficient for pain management as degeneration progresses.[3] Corticosteroid injections, radiofrequency ablations, and even partial or total shoulder arthroplasty are used to treat advanced cases[3], and these interventions often

either have limited long-term effectiveness or are associated with significant invasiveness or other side effects and complications.

Peripheral nerve stimulation (PNS) is a neuromodulatory technique that seeks to provide pain relief through stimulation of the nerves that innervate the shoulder (e.g., the suprascapular nerve and axillary nerve). A novel, 60-day percutaneous PNS system that is FDA-cleared has shown effectiveness for chronic shoulder pain following stroke and shoulder impingement syndrome[4-15], and has demonstrated the potential to provide sustained relief following the short-term, 60-day treatment.[8, 15-18] The mechanism of action of neuropathic pain in osteoarthritis is proposed to be via peripheral sensitization (e.g., axillary and suprascapular nerves) that leads to subsequent upstream hypersensitization of the central nervous system; the proposed mechanism of long-term pain relief with 60-day PNS via reconditioning of the CNS to reverse hypersensitization therefore suggests that the treatment may be effective for degenerative shoulder including OA.[19, 20] However, no study has prospectively evaluated the use of 60-day, percutaneous PNS for the treatment of debilitating pain associated with degenerative changes in the shoulder. The goal of this study is therefore to collect data on the use of 60-day PNS for the treatment of chronic pain associated with degenerative shoulder.

Objectives
The study objective is to gather post-market data regarding the effectiveness of the SPRINT PNS System for the treatment of chronic shoulder pain due to degenerative changes of the shoulder.

Primary Outcome
The primary outcome is clinically significant reduction in shoulder pain as evidenced by ≥30% reduction in average pain intensity and/or average pain interference reported at 3 months post lead placement.

Secondary Outcomes
Secondary outcomes will include:
- Analysis of changes in pain intensity and pain interference individually
- Shoulder functional outcomes
- Range of motion of the shoulder

Hypothesis
It is hypothesized that a 60-day percutaneous PNS treatment will result in clinically significant reductions in shoulder pain and/or pain interference in a majority of patients.

Study Device
The SPRINT® Peripheral Nerve Stimulation (PNS) System (FDA 510(k) Cleared)

Study Population
The study will enroll up to 20 patients with pain due to degenerative changes in the shoulder scheduled for commercial placement of the SPRINT PNS System.

Procedures Involved

In qualifying patients scheduled for commercial implant of the SPRINT PNS System, leads will be placed percutaneously using ultrasound guidance to stimulate the suprascapular and axillary nerves and/or their branches. SPRINT PNS is chosen independently and without regard for this study as a part of the patient's standard of care management. Local anesthesia (e.g., Lidocaine) will be administered at the insertion site prior to lead placement. Testing will be performed during the lead placement procedure by adjusting stimulus parameters to verify that the patient obtains comfortable sensations in their regions of pain. Sterile, waterproof, covering bandages (e.g., Tegaderm by 3M) will be placed over the exit sites of the percutaneous leads. Patients will be instructed to use the SPRINT Stimulator continuously each day (except while bathing and during battery changes) during the 8-week treatment period. Stimulation may be administered at 12Hz targeting the axillary nerve to produce comfortable motor contractions and 100 Hz targeting the suprascapular nerve to produce comfortable stimulation-evoked sensations in the region of pain. At the end of the treatment period, patients will return to the clinic to have their leads removed.

Outcome Assessments

Primary and secondary outcomes will be evaluated using the following outcomes assessments:

- PROMIS-29 profile
- The Western Ontario Arthritis of the Shoulder (WOOS) Index
- Brief Pain Index Short Form Item 9 (BPI-9)
- Tracking of analgesic medication usage (i.e., medications affecting pain)
- Shoulder Range of Motion (ROM)

Study Timepoints

Patients will be evaluated according to the investigators' existing clinical practice for follow-up after commercial implantation of 60-day PNS leads. Study visits will include an eligibility and baseline evaluation followed by lead placement. Patients will receive follow-up visits at approximately Day 15, Day 30, and Day 60 of the PNS treatment period, and leads will be removed at Day 60. Patients will then complete follow-up assessments at 3, 6, and 12 months from the start of treatment (SOT) (1, 4, and 10 months from the time of lead removal).

Schedule of Visits

Visit	**1**	**2**	**3**	**4**	**5**	**6, 7, 8**
Event	**Eligibility Baseline**	**Start of Treatment (Lead Placement)**	**Day 15 Phone Call**	**30-Days post-SOT**	**End of Treatment (60-Days post-SOT, Lead Removal)**	**3, 6, 12 Months post-SOT**
Informed Consent	x					
Assess Eligibility	x					
PROMIS-29, WOOS & BPI-9	x	x	x	x	x	x
Opioid Assessment	x	x	x	x	x	x

ROM	x	x			x	x

Data Collection
Data will be collected and stored in the patient's EMR as a part of their regularly scheduled and documented visits. Surveys (e.g., PROMIS-29,WOOS Index, BPI-9) may be completed by patients on paper surveys or electronically by direct patient entry via a de-identified survey platform. Patients will be able to request documentation from their visits within the clinic at any time. Only those participating in the patient's care will have access to identifiable data.

Sharing Results with Participants
Any information related to the study or patients' participation in the study will be shared upon their request.

Study Timelines
This study will begin upon approval from the IRB. All patients who meet the criteria noted below will be considered for the study. Total involvement in the study will be up to 12 months. The expected enrollment period will be 6-12 months. The expected completion of primary analyses will take place in late 2022.

Inclusion and Exclusion Criteria
Inclusion:
- At least 21 years old
- Diagnosed with degenerative changes within the shoulder complex
- Scheduled for a commercial SPRINT PNS procedure
- Shoulder pain score at baseline ≥ 5 as demonstrated on the PROMIS 29
- Able to understand and willing to take part in study and comply with all study requirements

Exclusion:
- No shoulder pain at rest
- Pain exclusively in the anterior aspect of the shoulder
- Confounding conditions such as cervical radiculopathy, inflammatory arthritis, complete rotator cuff tear, or ipsilateral shoulder surgery in the past one year
- Daily opioid use >90 mg morphine equivalent at any point in the past month
- Opioids for any condition other than shoulder pain
- Deep brain stimulation (DBS) system, implanted active cardiac implant (e.g. pacemaker of defibrillator), or any other implantable neuro-stimulator whose stimulus current pathway may overlap the SPRINT system.
- Any other condition that may interfere with the ability to participate in a clinical trial (*e.g.,* anatomy that may interfere with lead placement, nerve damage, compromised immune system, uncontrolled DM) as determined by the Investigator
- Vulnerable populations (e.g., prisoners, minors, students, employees)
- Workers Compensation
- Pregnant

Vulnerable Populations
No vulnerable populations will be included in this study.

Recruitment Methods
Patients will be patients of, or referrals to, the investigator's clinical practice that are planning to undergo a commercial placement of percutaneous PNS treatment which will be covered by the patient's insurance. Patients that meet criteria may be asked during their routine visits if they would be willing participate in the study.

Compensation for Participation in Research Activities
Patients will be compensated $50 for completion of Visits 1, 2, and 7 and $25 for completion of Visit 3, 4, 5, and 6. Patients will be compensated $75 for completion of Visit 8. Patients who complete all visits will receive a total of $325.

Withdrawal of Participants
Patients may withdraw consent at any time from this study. Additionally, any patient that becomes unwilling to fully participate in all necessary steps will be removed from the study. Any collected information will remain within their EHR as a part of standard of care management.

Risks to Participants
A very remote chance of loss of confidentiality is the only risk associated with this research protocol and has been minimized to the furthest possible degree. All measures to ensure patient confidentiality will be employed. All patient information will be collected and maintained in their secure EHR and only accessible through onsite password protected computers.

All treatment procedures performed are a part of the patient's routine care and are not experimental in nature.

Potential Benefits to participants
Patients in this study may not receive any direct benefit by participating in this study. If the treatment is successful, patients may experience a reduction in the degree of pain (pain intensity) during and/or after stimulation. This research may also benefit future patients with chronic shoulder pain.

Data Management and Confidentiality
Data will be collected and stored in the patient's EMR as a part of their regularly scheduled and documented visits. Surveys (e.g., PROMIS-29 and WOOS Index) may be completed by patients on paper surveys or electronically by direct patient entry via a de-identified survey platform. Patients will be able to request documentation from their visits within the clinic at any time. Only those participating in the patient's care will have access to identifiable data. Patient data may be provided to SPR Therapeutics.

Provisions to Monitor the Data to Ensure the Safety of Participants
This research study involves no more than minimal risk to participants.

Economic Burden to Participants
Patients will not be responsible for any costs as a result of participation in this study. Patients will still be responsible for the cost of the routine care.

Consent Process
IRB approved written consent will be obtained for all patients who choose to enroll in the study. The consent process will take place at the time the patient chooses to participate in the study. Investigator or research coordinator will be present and participate in the consenting process as well as collecting all consent forms for storage. All consent forms will be printed in English and sufficient time will be provided to review all pertinent points included within the consent form and answer any/all questions. Patients will be asked to summarize the consent to ensure appropriate understanding.

Protected Health Information (PHI and HIPAA)
HIPAA Authorization form will be obtained for all study participants as part of the Informed Consent Form. Basic demographic information will be collected for all patients as a part of the standard of care management provided during clinical evaluation encounters.

Qualifications to Conduct Research and Resources Available
ISPPC currently has a full time research coordinator assisting with participation in 5+ clinical trials. Between the two ISPPC offices, there are roughly 10-15 shoulder pain appointments each week. The robust demographic of pain patients seen each week at this practice will provide ample recruitment opportunities. Additionally, given the current participation in multiple clinical trials, the infrastructure is already in place to carry out safe and compliant clinical studies.

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