Clinical Trials Cover Page: Study Protocol and Statistical Analysis Plan

Document Date: 11/5/2021

Peripheral Nerve Stimulation for Subacromial Impingement Syndrome

NCT03752619

Date: Friday, November 05, 2021 2:14:38 PM
View: 01-00 Study Information

Print Close

1.0 Study Information:

1.1 * **Short Title:** PNS for SIS (R01)

The Short Title Should be the sponsor protocol number. If there is no sponsor protocol, then enter 3-5 words or numbers that capture the important study characteristics and help identify the study.

1.2 * **Full Title of Research Project:**
Peripheral Nerve Stimulation for Subacromial Impingement Syndrome

Enter the Full Title of the study.

1.3 **Principal Investigator:** Richard Wilson

HSR Certification Status: Certified **HSR Certification Expiration Date:** 8/10/2022 ;

COI Expire Date: 7/3/2022 ; **COI Yes or No:** No ; **COI Management Plan:** No ; **PI Non-Compliance:**

The PI must be a MetroHealth Staff person or have privileges to practice at MHS. The PI must assume full responsibility for the conduct of the study.

1.4 Key Personnel:

Add additional Staff as needed.

Update to add Study Roles

If using Epic, add role of DRA to one person

	Name	CREC Status	CREC Expiration	COI	COI Expire	Management Plan?	Study Roles	Employer Name	Non-Compliance
View	Terri Hisel	Certified	10/18/2022	no	6/5/2022		Research Support Staff Interviewer (Survey, Focus Group)	Physical Medicine and Rehabilitation	
View	Douglas Gunzler	Certified	12/1/2022	no	7/2/2022		Co-investigator	The MetroHealth System	
View	David DiLorenzo	N/A	8/3/2024	no	8/9/2022		Co-investigator	The MetroHealth System	
View	Steven Lewis	Certified	1/27/2023	no	1/27/2022		Co-investigator	The MetroHealth System	
View	John Chae	Certified	9/1/2022	yes	7/2/2022	yes	Co-investigator	The MetroHealth System	
View	Chong Kim	Certified	8/28/2024	no	7/30/2022		Co-investigator	The MetroHealth System	
View	Victoria Whitehair	Certified	4/11/2022	no	7/2/2022		Co-investigator	The MetroHealth System	
View	Kristine Hansen	Certified	4/6/2023	no	7/7/2022		Research Support Staff Interviewer (Survey, Focus Group) eIRB Notification Recipient Study Coordinator	Physical Medicine and Rehabilitation	

	Name	CREC Status	CREC Expiration	COI	COI Expire	Management Plan?	Study Roles	Employer Name	Non-Compliance
View	Amy Friedl	Certified	3/16/2023	no	7/2/2022		Research Support Staff Interviewer (Survey, Focus Group) Obtaining Informed Consent	The MetroHealth System	
View	Shannon Hogan	Certified	2/23/2023	no	6/4/2022		Research Support Staff Obtaining Informed Consent	The MetroHealth System	

1.5 Type of Research:
Clinical Device Trial

1.6 If "Other" Type of Research Please Explain:

View: 01-01 Study Information

1.1 Study Information:

1.7 * Department-What Department approvals are required?
Name
Physical Medicine and Rehabilitation

1.9 Definitions to keep in mind when selecting the degree of risk:

Minimal Risk is defined in 45CFR46 and in FDA regulations 21CFR50.3 as:
Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

*** Degree of Risk: (This is the investigator's assessment of the risks involved in the research which will informed the IRB Decision but which will not automatically be accepted. The Board is the final arbiter of risk. The risk level will be set by the IRB staff at the time of approval.)**

Select most appropriate one.

Name

- (•) Risk
- ( ) Not Greater Than Minimal Risk

1.10 * Type of IRB Review Requested:
Full Board

Select one. If you select Exempt or Expedited you will be taken to that section when you hit continue.

View: 01-02 Study Information

1.2 Study Information:

1.11 **Will you require access to Epic to conduct this study?** ◉ **Yes** ○ No

If you answer this question yes you will need to identify a Designated Records Administrator one person only.

The DRA's employee number must be listed on their registration form.

Please add the role of "DRA" to one study staff member on page 1 of the application.

1.12 **Is the Principal Investigator a resident or trainee?**

○ Yes ◉ **No**

Please check yes or no.

NOTE: Residents, Fellows, and non-MHS Personnel cannot be listed as the Principal Investigator

View: 01-03 Study Information

1.3 Study Information:

1.13 * **Will CRU Be Used:**

Yes *If you answer yes to this question this application will be sent to the CRU for review after departmental review and before it is submitted to the IRB.*

Will the CRU be used?

1.14 * **Has this research protocol ever been submitted to another CASE affiliated IRB (i.e. UH, CCF, VA or CASE)?**

No

If this study has been reviewed at another CASE affiliated IRB you should answer yes.

1.15 **If yes, was it:**

Select one from drop down menu.

1.16 **Please supply the following information: At which institution was it approved? If it was disapproved, why was it disapproved?**

What institutions have approved this study. If it has been disapproved, please give a brief explanation of why study was disapproved.

Please attach the Approval letter/letters from other IRBs (i.e. UH, CCF, VA or CASE):

Name	Description
There are no items to display	

Please attach approval letter/letters.

1.17

View: CRU 01-01 Application

Please Note: If you are using the CRU you must adhere to the following New NIH Public Access Policy:

Please review the information provied by theis link regarding enforcement of the NIH Public Access Policy that will begin on April 1, 2013. The most recent changes to the NIH Public Policy are explained in the attached Power point presentation from the NIH (January 15, 2013) and the attached MS-Word document, "Manuscript Submission to PubMed Central for a PMCID".

All studies that utilize the MetroHealth CRU resources (space, nursing, lab, bionutrition) that are non-industry funded, are required be NIH Public Access Policy compliant by obtaining a PMCID number. The PMCID number is an separate index from the PMID - the PMCID number indexes the entire publication while the PMID indexes the abstract, only. In addition to the PMCID number, investigators are required to post their publications on 'My Bibliography' and link their publications to grant numbers.

Attention to this policy is important because the NIH will halt the process of renewals, re-submissions and certain progress reports if relevant publications are non-compliant with the PMCID number and My Bibliography. Continued use and funding of the CRU may be jeopardized if appropriate publications are not fully compliant.

In addition, please ensure that studies utilizing the CRU also acknowledge the CTSC grant in their publications and cite the CTSC grant number, **UL1TR000439**. This is a NEW NIH CTSC grant number that went into effect on June 1, 2012. The acknowledgment and grant number can also be found by going to the Cleveland CTSC website acknowledgments page. (This page also has information about the NIH Public Access Policy.)

Thank you in advance for ensuring that all publications from studies utilizing CRU resources (that are not-industry supported) are compliant with these requirements as soon as possible.

1.00 CRU Application [*Since you have indicated in your application that you want to utilize the resources of the CRU Please complete the following pages of the IRB Application. Hit the continue button to move from page to page in that way you will be able to take advantage of the built in branching logic to complete your CRU application.]*

1.01 Is this an HIV/AIDS Project: ○ Yes ◉ **No** — HIV/AIDS?

1.02 Are you currently Funded by NIH? ○ Yes ◉ **No** — If yes please add grant or contract number.

1.03 Would you like to conduct your study on the CRU? ○ Yes ◉ **No** — Yes or No

1.04 What is your eRA Commons Name?
RDWILSON — eRA Commons Name required for all non- industry studies

1.05 Anticipated Start Date:
1/1/2018 — *Anticipated Date Study to Begin (1st Patient)*

Anticipated End Date:
12/31/2022 — *Anticipated End Date*

1.06 Approximate Inpatient Days Per Subject:
0 — *Enter approximate numbers*

Approximate Outpatient Visits Per Subject:
18

1.07 *After August 2010 this is a read only copy of the paper CRU Resource Application:* — Old CRU Application forms

Name	Version
There are no items to display	

1.08 **These are your target enrollment numbers for the ethic and racial categories below:** — Enter anticipated numbers for this protocol

Ethnic Category

	Sex/Gender		
Ethnic Category	Females	Males	**Total**
Hispanic or Latino	5	4	9
Not Hispanic or Latino	53	54	107
Ethnic Category Total of All Subjects	58	58	116

Racial Category

	Females	Males	**Total**
American Indian/Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	20	20	40
White	37	37	74
Racial Categories Total of all Subjects	58	58	116

View: CRU 01-02 CRU Resource Needs

2.00 CRU: Resource Needs

Hospital Lab Tests = CRU draws

Hospital Lab Tests: ◉ **Yes** ○ No

blood and send it to Hospital Lab or forwards blood already drawn to Hospital Lab

Human Performance Lab Tests and Measurements: ○ Yes ◉ **No**

Human Performance Lab Tests and Measurements

Research Nutrition Services: ○ Yes ◉ **No**

Research Nutrition Services

CRU Laboratory Services: ○ Yes ◉ **No**

Core Laboratory Services (7:00 am to 5:30 pm, weekdays)

Use of CRU Facilities or Equipment Only: ○ Yes ◉ **No**

Use of CRU Faciities or Equipment Only

Nursing Resources: ○ Yes ◉ **No**

Use CRU Nurses

Spanish Translation Services: ○ Yes ◉ **No**

Translation is the rendering of a written text in one language in a comparable written text in another language

Spanish Interpertation Services: ○ Yes ◉ **No**

Interpreting is the oral rendering of spoken or signed communication from one language into another.

View: CRU 01-05 Hospital Lab Tests

1.05 CRU: Hospital Lab Tests

Required for research purposes. Include Standard of Care test to be drawn and sent to the MHMC central lab here.

5.01 CRU Hospital Lab Tests:

Please give the details of any Lab tests needed.

	EPIC Order Code	Hospital Lab Test Name	Number Of Tests Per Subject
View	81025	Urine hCG	1
View	85610	INR/PT	1

View: CRU 01-09 Additional Notes or Requests

1.09 CRU: Additional Notes or Requests

9.01 If you have any additional notes or requests from the Clinical Research Unit that have not been covered, please describe them here:
CRU assists us with scheduling and Hospital Lab Tests only.

View: 01-04 Study Information

1.4 Study Information

These Questions are specifically about the adequacy of resources, are there the necessary resources to complete this study? There are two questions which focus on nursing resources. If this research will require the use of nursing resources then the Nursing Resources Form found on the IRB Home Page under forms and templates will need to be completed and attached to this research application.

1.18 Can you assure the IRB that there are adequate numbers of qualified staff to conduct this research?
◉ **Yes** ○ No

Please answer yes or no. This is an assurance to the IRB.

1.19 How will the investigator ensure that persons assisting with the research were adequately informed about the protocol and their research-related duties and functions and requirements for maintaining the confidentiality of all data?
Meeting between PI and participating staff will take place to ensure that all are appropriately informed of their roles and responsibilities. Parties will meet regularly after the initiation of the protocol to maintain communication and ensure proper equipping and training of persons assisting with the research.

i.e. investigator meeting, formal protocol review with PI, monitor, sponsor.

1.20 Will the PI and study staff have sufficient time to conduct and complete the research?
(●) **Yes** ( ) No

Please answer yes or no. This is an assurance to the IRB.

1.21 What facilities are available to conduct the research? Are they adequate? Please describe.
Visits will take place in our labs in PM&R at OBHC.

Please describe the facilities, i.e. lab, procedure room, chemo treatment room.

Nursing Resources:

1.22 Is this study using MetroHealth staff nurse time or labor ? (i.e. giving medcations, teaching, or additional documentation)

( ) Yes (●) **No**

This is in addition to the time of the study/research nurse.

1.23 Attach Nursing Resources Form here:

Click here for Nursing Resources form

Open the form, Complete the form and save it to your files then attach it to the study by hitting the browse file and selecting the file and hitting OK.

Click here for the MHS Policy

View: 04-00 Scientific Review

4.0 Scientific Review:

All Studies need a Science Review. Has your study been reviewed by any of the following?

4.1 Please Check all that Appy to this study so that the IRB may make a determination if there needs to be further scientific review:

Select all that apply. Note FDA Approval does not equal science review.

Review Type

- [ ] Initiated and sponsored by industry under an IND, IDE, HDE, or 510K exemption issued by the FDA for which no scientific integrity concerns were identified during the FDA review process
- [ ] Trial initiated and sponsored by industry that has undergone a scientific merit review by the sponsoring agency, but is not being conducted under an IND, IDE, HDE, or 510K exemption
- [ ] Sponsored by a Cooperative Group
- [ ] Proposed research has been awarded funding by a federal agency
- [x] Peer reviewed by a federal funding agency and received a favorable funding score
- [ ] Peer reviewed by a federal funding agency with the acknowledgment of scientific merits, but not likely to be funded for reasons unrelated to scientific merit
- [ ] Sponsored by a foundation or a private agency that requires a separate scientific merit review process at the sponsoring agency
- [ ] No Science Review

4.2 Do any of the following apply to your study? Please check all that apply:

Check all that apply your answers will assist the IRB in

Additional Reasons Why Science Review May Be Required

Additional Reasons Why Science Review May Be Required
Investigator-initiated study

deciding if further science review is necessary.

4.3 Does this study require review by the Biosafety Committee?
No

All studies involving vaccines, potentially hazardous materials or genetic research must go to the biosafety committee at CASE.

4.4 Does this study require review by the Radiation safety committee? No

If a study involves more than routine exposure to radiation on the part of subjects the study must go to the radiation safety committee.

4.5 Does this study require Review by the Nursing Committee?
No

The nursing committee must review all studies where the PI is a nurse, and all studies which have as the primary objective to contribute to nursing knowledgebase, and/or have implications for nursing practice.

View: 05-00 Funding Information I

5.0 Funding Information I:

All Research Projects must have an identified funding source!

5.1 Is this research externally funded? Yes

Check one

Research can be both externally and internally funded so you can answer yes to both 5.1 and 5.6.

5.2 Types Of External Funding:
Name
Government / Federal

Check all that apply.

5.3 If other, external funding please explain:

If other please describe.

5.4 Sponsor Information:

Please supply this information as your application can not be processed without it.

Name Sponsor/Agency	Address	Telephone FAX	Contact Person
NIH: National Institute of Child Health and Human Development	6710B Rockledge Drive Room 2161C, MSC 7002, Bethesda, MD 20817	301-435-6838	Susan Marden

5.5 Have you received and/or submitted a Notice of Award or Contract?
Yes

Select one from drop down menu.

Attach notice of award.

If yes, attach your Notice of Award letter here (not your grant):

Name	Version
PNS for SIS Notice of Award	0.01

View: 05-01 Funding Information II

5.1 Funding Information II

5.6 ***Is Research Internally Funded (internal funding is any MetroHealth System or MetroHealth Foundation funds):***

Check one, research can be both externally and internally funded so you can answer yes to both 5.1 and 5.6.

○ *Yes* ◉ ***No***

5.7 Internal Funding Sources List:
Internal Funding Source
There are no items to display

Check all the apply.

5.8 If a MetroHealth Foundation funds or any MetroHealth System funds are being used, has department approval been received?
○ Yes ○ No

Check yes or no.

5.9 If a MetroHealth Foundation funds or any MetroHealth System funds are being used indicate the Account Number:

Please enter the account number if this applies.

5.10 *** Are there current Conflict of Interest Forms for all Key Personnel? [It is the responsibility of the Principal Investigator to ascertain this information and check this box.]**

◉ **Yes** ○ No

This question is not asking if there are COI forms for all Key Personnel it is asking if all Key Personnel have current COI forms so that any SFI is reported and can be dealt with if a management plan is need or reporting to NIH is required.

In order to submit a new protocol all COI Forms for key personnel and investigators must be current = provide up to date information.

5.11 **Please check below any Conflicts of Interest (Financial) you as Principal Investigator or your study staff [Co-Investigator, Coordinators, Other Study Staff] may have on this Study:**

Potential Conflict of Interest

You or your co-investigators have a significant financial interest in the sponsor of this research, the manufacturer of the drug or device being tested, or in the drug or device itself, including any share of potential future profits or royalties.

This question pertains to this study and is not a general question. Check all that apply.

You and/or your study staff will need to file a Conflict of Interest Disclosure Form annually.

If anyone working on this study has a Conflict of Interest or a perceived conflict. This information will need to be included in the consent form i.e. company is paying MHS to do this study.

5.12 **Please attach a copy of your grant application here:**

Name	Description
PNS for SIS Grant Narrative	
PNS for SIS Grant Narrative(TRACKED).docx	

You must attach a copy of your grant application here (i.e. NIH Grant Application).

You have the option to attach a copy of the budget, clinical trial account authorization form, contract and Approval letter(s) now or you can email them to your grants management specialist in the RABO office.

Copies of all RABO forms are available at:

http://www.metrohealthresearch.org/raboforms.html

View: 06-00 Performance Site Information

6.0 Performance Site Information:

6.1 **At what sites will the study team be performing this research, (please enter information about all non-MHS sites in 5.2):**

Name

The MetroHealth System

FES Center

Other

Select all that apply. If you select other please enter information about that site in question 6.2.

If this study is being done at MetroHealth where is it being done give the physical location (i.e. 8B, ED, Broadway, Old Brooklyn, PICU, Cath Lab):

Visits will take place in our labs in PM&R at OBHC.

If immediate hazard to subject to come to the labs in PMR at OBHC the visit will be completed via telephone, email or telehealth

Where is the research going to be done? What physical location on the Main campus or the community health centers?

6.2 **Please provide information about other external sites here:**

Name of Site	Address	Telephone Number
University of Texas Southwestern Medical Center	5323 Harry Hines Blvd., Dallas, TX 75390-8843	214-648-3378

Please enter contact information. Please include name of facility, address and department.

6.3 **If you are doing this research at an external site does this site have an IRB?**

◉ **Yes** ○ No

Select yes or no.

6.4 **If the External Site has an IRB will that IRB defer review to the MHS IRB?**

◉ **Yes** ○ No

This only applies if there is no IRB or if there is a legal agreement between institutions permitting a reciprocal review, i.e. CASE.

6.5 **Attach letter from external site agreeing to permit the MHS to review this protocol:**

Attach letter.

Name	Description
Determination_Letter_University_of_Texas_Southwestern_Medical_Center.pdf | History	

6.6 Has the external site granted permission for the research to be conducted?
(●) **Yes** ( ) No

This applies to sites where there is no IRB and the investigator must get a letter from the site that gives permission to conduct the research at the site.

6.7 Attach letter from external site granting permission for the research to be conducted:

Attach letter of support.

Name	Description
There are no items to display	

View: 06-01 Performance Site Information

6.1 Performance Site Information

6.8 Is MHS the lead institution of a multi-site study? (●) **Yes** ( ) No

Please answer yes or no.

6.9 If yes, is there a plan to communicate information obtained through research that might be relevant to the protection of human subjects, including a plan to provide the IRB with information on unanticipated events, interim results, and protocol modifications.
(●) **Yes** ( ) **No**

Please answer yes or no.

6.10 Please give a detailed explanation of the above plan:

This plan must give the IRB enough information to decide if the plan is appropriate and adequate.

University of Texas Southwestern Medical Center will serve as a second performance site.

The Investigators and respective project staff will meet or confer at least semiannually to review all adverse events and study data collected since the previous meeting. All adverse events will be reviewed to determine a course of action. Events are categorized according to severe/not severe, expected/unexpected, and related/unrelated.

IRBs at each participating institution will be informed of progress, AEs, unanticipated events and protocol modifications per their policies.
Smart IRB will be used

6.11 Will the Principal Investigator conduct this study at any location outside the United States of America?
( ) Yes (●) **No**

Answer these questions only if there are research sites outside the USA.

6.12 Country, City, and address:

Give country and location.

Country	Address of Research Facility
There are no items to display	

View: 07-00 Research Objectives and Background

7.0 Research Objectives and Background:

7.1 * **ABSTRACT: Please give the IRB a 500 word Abstract that contains the specific objectives of the study.**

This is your abstract also known as a synopsis from an industry sponsored study. Please limit to 500 words.

Shoulder pain accounts for 16% of all musculoskeletal complaints in the healthy adult population [1], and results in 12 million visits to physician offices per year. [2] Subacromial impingement syndrome (SIS) is the most common cause of shoulder pain. [3, 4] Conservative treatments include rest, non-steroidal anti-inflammatory drugs, physical therapy, and corticosteroid injections. [5-9] Approximately 65% respond to conservative management [7, 10]; when this fails, patients are often referred for surgical subacromial decompression. [7, 10, 11] Unfortunately, randomized controlled trials (RCTs) have shown surgery to be no better than conservative therapy. [12-17] Presently, there are no established practice guidelines for the management of chronic SIS in healthy adults refractory to conservative management.

The primary objective of this application is to determine the efficacy of percutaneous intramuscular (IM) peripheral nerve stimulation (PNS) in reducing shoulder pain secondary to SIS refractory to conservative management. IM PNS involves the percutaneous placement of a single IM electrode to stimulate the axillary nerve motor points of the deltoid muscle. The PI and collaborators developed the technique and completed a case series to demonstrate its feasibility for the treatment of SIS. [18, 19] Unlike spinal cord stimulation [20, 21], peripheral nerve field stimulation [22, 23] and transcutaneous electrical nerve stimulation (TENS) [24], IM PNS can maintain pain reduction for up to 12-mo after cessation of stimulation. IM PNS is proposed as an alternative to surgical subacromial decompression, which may be less risky, less costly and more effective. We propose a multisite, double-blinded, placebo-controlled RCT of percutaneous IM PNS for the treatment of refractory SIS in those with SIS with outcomes focusing on pain reduction, shoulder impairment, activities of daily living (ADLs) and quality of life (QoL).

The secondary objective is to investigate the mechanism underlying IM PNS mediated pain reduction. First, the initiation of SIS is likely due to the repetitive trauma of the supraspinatus tendon and subacromial bursa by the undersurface of the acromion resulting in nociceptive pain [25]; however, as patients fail conservative management and pain becomes more chronic, central sensitization may have the more dominant role. [26-29] To evaluate the role of IM PNS in reducing central sensitization, an assessment of the sensory system is proposed using mechanical and thermal quantitative sensory testing. Second, this study will also determine the phenotype that differentiates responders from non-responders. It is known that pain perception is influenced by multiple factors and not reliant on structural pathology alone, thus psychological traits, mood, demographics, physical examination, structural anatomy, and sensory testing will be measured. Determining the phenotype of responder will provide insight into mechanism, as well as improve patient selection for treatment.

7.2 *** What are the specific aims of this study i.e. what are the question(s) this research intends to answer? Provide at a maximum 3 primary and 3 secondary aims.**

This is your Hypothesis also know as your aims (NIH) or safety and efficacy aims (industry). Please list no more than 3 primary and 3 secondary clearly label these aims primary and secondary.

AIM 1: Determine the Efficacy of IM PNS in Treating SIS Refractory to Conservative Management. The trial will enroll 116 participants who will be treated for 7-wks with IM PNS or placebo and followed for 6-mo.
Hypothesis 1: The IM PNS participants will experience greater pain reduction and shoulder impairment, and greater improvements in ADLS and QoL than controls.

AIM 2: Quantify the Relationship between IM PNS Mediated Pain Reduction and Central Sensitization. As an initial step toward determining the role of IM PNS in modulating central sensitization, pain thresholds will be characterized using mechanical and thermal quantitative sensory testing.
Hypothesis 2: Pain thresholds will increase in the IM PNS group relative to controls at the affected shoulder (primary hyperalgesia) AND at the contralateral shoulder or tibialis anterior (secondary hyperalgesia).

AIM 3: Determine the specific phenotype characteristics will differentiate responders to IM PNS from non-responders. Baseline measurements of psychological traits, mood, demographics, physical examination, structural anatomy, and sensory testing will be utilized to determine the phenotype of those subjects who have successful pain relief from treatment with IM PNS.
Hypothesis 3: Specific phenotype characteristics can be identified to differentiate responders to IM PNS from non-responders.

7.3 **Please provide a summary of the present knowledge relevant to the research and make citation to any applicable scientific literature:**
See attached.

This is your literature search and bibliography. Also known as Background and significance (NIH) or Introductory Section from industry sponsored trial.

7.4 **Option to Upload Documents related to question 7.3:**

Name	Description
PNS for SIS 8 week/60 day tx justification | History	
PNS for SIS Background and Prior Studies | History	
PNS for SIS References | History	

If it is easier to attach your response to question 7.3 please do so here. *Please limit to three pages.*

View: 08-00 Methods and Procedures I

8.0 Methods and Procedures I:

8.1 **Will this research involve the following Social-Behavioral Procedures:**

Check all that apply.

Name
Surveys/Questionnaires

8.2 **Will this research involved any of the following Medical Procedures/Considerations:**

Check all that apply.

Name
Collection of Biohazardous Substances
Study of Human Biological Materials (i.e. Urine Collection)
Investigation/Approved Devices
Study of Existing Data
Medical Tests, Comparisons, Evaluations
Clinical Assessments (EEG, EKG, SCID, etc.)
Venipuncture (Blood Draw)
Magnetic resonance imaging (MRI) without contrast
Use of investigational devices

8.3 Identify Data Collection types for this study:

Check all that apply.

Name
Audio-Recording/Video-Recording/Photographs
Chart Review - Prospective
Existing/Retrospective Data/Specimens
Interviews, questionnaires or psychological tests

Note if you are doing, recordings, Video-Recording/Photographs then subjects will need to sign the MetroHealth Audio-Video Consent form. See the IRB Forms and Templates.

View: 08-01 Methods and Procedures II

8.1 Methods and Procedures II:

8.4 * **Please specify in detail the methods and procedures that are involved in this research:**

If this field is not completed your protocol will not be reviewed. Do not enter N/A. Please describe what methods and procedures will be involved in this research.

Study Summary: This is a multi-site, placebo controlled, double-blinded RCT that evaluates the efficacy of a new treatment for chronic shoulder pain to conservative management in otherwise healthy adults. One- hundred-sixteen participants are randomized to receive IM PNS or placebo treatment. All participants receive a single IM lead, and receive 6-hrs of daily PNS for 7-wks. The IM PNS group receives active stimulation while the control group receives placebo stimulation. All participants will also receive a course of PT during the treatment period to improve upper limb function and prevent re-injury by educating and training participants in the biomechanics and proper use of the shoulder and the upper limb. Measures of pain, shoulder impairment, pain interference with ADLs, ADLs, QoL and pain thresholds are assessed at baseline, time of implantation, at the start of treatment, at the EOT, 12, 24-wks treatment..

Baseline Variables and Randomization: Baseline data are collected so that the balance of covariates across the two groups can be evaluated. Each participant is characterized with respect to pain-related psychological traits, mood, demographics, comorbidities, and medication use. All participants will undergo a MRI(unless they are available in the ipsilateral shoulder) to evaluate for rotator cuff tears, tendonopathy and subacromial bursa fluid. Study outcome measures (see Outcomes Assessment) are administered to establish baseline levels. Participants are assigned to treatment groups using a stratified, block randomization scheme to minimize group imbalances on key patient characteristics: site, baseline pain (> 6 or ≤ 6), duration of pain (≥18 months or < 18 months). The randomization sequence is contained within the RedCap database..

Percutaneous IM PNS System: The Sprint PNS System (SPR Therapeutics, Cleveland, OH) is used to deliver the IM PNS. The System consists of a small external stimulator, percutaneous IM lead, and pad. The external stimulator “snaps” on to the pad. The pad serves as the anode. The pad is replaced regularly based on treatment parameters, allowing the investigative team to prescribe the total dosage based upon the number of pads. The single-channel stimulator outputs a biphasic current waveform with current pulse parameter ranges that are suitable for IM PNS. The IM electrode, originally developed at the Cleveland FES Center, has a coiled helical configuration wound from a 7-strand type-316LVM stainless-steel wire insulated with a poly-fluorocarbon, similar to Teflon®. These electrodes have been used extensively to deliver percutaneous IM PNS to shoulder muscles. [19, 36, 37, 39-42, 62, 75]

Lead Placement Procedure:

IM PNS Group: The procedure is performed under a sterile condition. The location and depth of the electrode implant site are determined by monopolar needle stimulation with demonstration of strong contraction of both the middle and posterior deltoid muscles. [18, 19, 39, 42] The introducer loaded with the IM lead is inserted perpendicular to the skin surface and advanced to the depth (3-4 cm) defined by the monopolar test stimulation. The introducer is then withdrawn with the electrode retained in the muscle by a barb at its tip.

Control Group: In order to facilitate blinding, control participants receive an IM electrode placed between the middle and posterior deltoid muscles similar to the IM PNS group. The only difference is that the monopolar electrodes are not used to guide IM electrode implantation so that no electrical stimulation is ever provided.

PNS Treatment Protocol:

IM PNS Group: After one week for lead stabilization [87] the Sprint System is programmed for stimulation. Based on over 30-yrs of experience, the Cleveland FES Center established parameters for safe and effective delivery of IM PNS (pulse frequency = 12 Hz; The amplitude (0.2-30 mA) and pulse duration (10-200 μsecs) is set to produce strong, comfortable contraction of both the middle and posterior deltoids; duty cycle = 2-sec ramp-up, 16-sec plateau, 2-sec ramp down, 10 sec off; daily dose = 6 hrs/day). [88] These parameters provide strong fused comfortable muscle contraction with minimal fatigue. [19, 36, 37, 39-42, 61, 62, 75, 89-91] Stimulation frequency and amplitude are fixed. The pulse duration is set to produce strong, comfortable contraction of both the middle and posterior deltoids. A balanced biphasic waveform allows an equal amount of current to flow in either phase, creating a safe net zero charge. [92] Participants receive a total of 6 hrs of stimulation per day in their home. The stimulator keeps an electronic log for compliance monitoring. There are no formal dose response studies to provide guidance on the optimal dose of IM PNS; however, the selected duty cycle and daily dose of 6-hrs were used in our prior studies [19, 36, 37, 39-42] and by others with robust results. [75]

Control Group: Control participants will receive an identical stimulator that will be placed in sham-stimulation mode by the nurse coordinator. The stimulator appears to function identically to that used in the active stimulation group and the battery drains with use, although no stimulation is delivered. All participants are queried at their final visit to determine the success of blinding. The implanted electrode poses minimal risk to control participants. The probability of serious adverse event (e.g. infection) for IM electrodes is 0.0006 per electrode. [41] The implantation of electrodes is no more painful than subcutaneous infiltration of lidocaine.

Electrode and Electrode Site Surveillance and Electrode Removal: All caregivers and participants are trained in the assessment of electrode site and the daily placement of the Sprint device. The caregiver conducts daily inspections to detect complications. The nurse coordinator inspects the site for infection and performs motor/sensory threshold testing for lead migration and lead integrity, respectively, at the following times: at the beginning of treatment, and at the EOT. Inspection and testing of motor/sensory thresholds and impedance may also occur anytime during the 7-wk PNS treatment period as deemed necessary. At the EOT, the electrode is removed by gently pulling on the external portion. All participants undergo radiographic surveillance for retained electrode fragments.

Standardized Physical Therapy: With pain reduction, it is anticipated that participants will use their limbs more aggressively; however, as observed in Preliminary Study 4, this may lead to re-injury and pain recurrence. Thus, all participants will receive eight 1.0 hr. sessions of PT over a 8-wk period from a physical /occupational therapist. Each participant also performs home exercises. The primary objective of PT and the home exercise program is to prevent re-injury by educating and training participants in the biomechanics and proper use of the shoulder and upper limb. The standardized therapy protocol was adapted from Holmgren et al.93 The protocol consists of 6 exercises: two eccentric exercises for the rotator cuff, 3 concentric/eccentric exercises for the scapular stabilizers and a posterior shoulder stretch. During each in-lab session, participants are trained in the implementation of these exercises, which are individually adjusted and progressed with increasing external loads by using weights and elastic rubber bands. Each strengthening exercise is repeated 15 times in 3 sets twice daily for 8-wks. The posterior shoulder stretch is performed for 30-60 s and repeated 3 times twice daily. Participants are not allowed to exceed pain level of 5 on a 0-10 pain NRS when performing the exercises. After completion of an exercise session, pain has to return to the pre-session level before the next session; otherwise, the external load is decreased.

Blinded Outcomes Assessment: The primary outcome measure is the worst daily pain (BPI 3) score recorded over the 7-d prior to each in-lab assessment. Secondary measures include daily least pain (BPI 4), average pain (BPI 5), present pain (BPI 6) after morning ADLs, and pain interference with ADLs (BPI 9) averaged over the 7-d prior to each in-lab assessment; shoulder impairment; ADLs; QoL; and mechanical and thermal QST. Details for each measure are presented below. The outcomes are administered face-to-face in a blinded manner.

Brief Pain Inventory (Short Form, Aims 1,2,3): The BPI has excellent psychometrics [94-100] and is recommended by the IMMPACT group for the assessment of pain in clinical trials. [79] The developers of the BPI recommend BPI 3, the “pain worst” rating, as the primary response metric. The question asks participants to rate their worst pain in the prior 24-hrs OR prior 7-d on a 0 to 10 NRS, where “0” indicates “No pain” and “10” indicates “Pain as bad as you can imagine.” In our prior studies, we used the 7-d version of BPI 3. However, in order to minimize recall bias and improve accuracy, the 24-h version collected over 7-d prior to each in-lab assessment is proposed. The primary pain outcome metric is the worst BPI 3 during the 7-d period. In order to gain a more comprehensive assessment of participants’ pain experience, daily

least pain (BPI 4), daily average pain (BPI 5) and daily present pain (BPI 6) after morning ADLs are also collected. Pain interference with ADLs (BPI 9) is described below. Since pain varies from day to day, the average over the 7-d prior to each assessment is proposed as secondary pain outcome metrics. The investigative team has extensive experience with the BPI. [36, 38, 40, 41, 75, 101-103]

ADL capacity – Functional Impairment Test-Hand and Neck/Shoulder/Arm (FIT-HaNSA) (Aims 1, 3): The World Health Organization defines capacity as what an individual can do in an idealized or standardized environment, whereas performance is defined as what an individual actually does in the community. [109] The FIT-HaNSA is a laboratory based objective measure of ADL capacity. The FIT-HaNSA is a timed test that provides a brief measure of functional ability of the upper limb while performing multi-level tasks that require grip/manipulation of the hand, elbow/shoulder reaching, sustained overhead work, and sustained positioning with an emphasis on assessing the limitations in functional capacity attributable to shoulder and neck disorders. The measure has been shown to be both valid and reliable among patients with shoulder pathology and matched controls. [110]

ADL performance – Shoulder Pain and Disability Index (SPADI) (Aims 1, 3): In contrast to the FIT-HaNSA, The Shoulder Pain and Disability Index (SPADI) is a self-administered questionnaire that consists of two dimensions, one for pain and the other for functional activities. The pain dimension consists of five questions regarding the severity of an individual's pain. Functional activities are assessed with eight questions designed to measure the degree of difficulty an individual has with various activities of daily living that require upper-extremity use. The SPADI takes 5 to 10 minutes for a patient to complete and is the only reliable and valid region-specific measure for the shoulder.

Pain interference with ADLs – BPI 9 (Aim 1): BPI 9 assesses pain interference with 7 domains of daily activity over a 24-hr period: general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life on a 0-10 NRS, where 0 indicates “does not interfere” and 10 indicates “completely interferes.” [111] The BPI 9 score is the average of the scores for the 7 domains. Psychometrics have been evaluated as part of the BPI battery. [94-97] BPI 9 has been used to evaluate the impact of percutaneous IM PNS mediated pain reduction on ADLs. [18, 36, 41, 42] BPI 9 is averaged over a 7-d period prior to each assessment.

QoL – SF 12(Aim 1): SF-12 is a health related QoL measure that assesses physical functioning, role limitation because of physical health problems, bodily pain, social functioning, general mental health, role limitations because of emotional problems, vitality (energy/fatigue), and general health perception.112 It is the only reliable and valid measure previously used to assess change in QoL associated with the treatment of shoulder pain with IM PNS.39, 42, 43, 75 Mechanical QST (Aims 2 ,3):

Primary, Secondary Hyperalgesia: Pressure Pain Thresholds or PPTs (Type III, IV afferents) are measured with a hand-held Wagner Instruments FPIX Pain Test Algometer (Wagner Instruments, Greenwich, CT) with 1 sq cm rubber tip. The 3 sites are the mid-belly of the deltoid muscle of the affected and non-affected limb and the mid-belly of the tibialis anterior of the contralateral limb. Three readings are averaged at each site. The reliability and validity of the pressure algometry to evaluate deep somatic tissue sensitivity have been demonstrated [113-115], and the method has been used to evaluate central sensitization in numerous pain conditions [51, 116-125], including SIS. [26-29]

Pinprick pain thresholds (A-fibers) are measured at the same sites using weighted pinprick stimuli that exert forces of 8, 16, 32, 64, 128, 256, and 512 mN (PinPrick Stimulators, MRC Systems GmbH, Heidelberg). [126, 127] The stimulators are applied at a rate of 2 sec on, 2 sec off in an ascending order until the first percept of sharpness is reached. The final threshold is the geometric mean of five series of ascending and descending stimuli. Pinprick pain threshold has been used to evaluate central sensitization in numerous conditions [128-131], including SIS [27], and has been shown to be reliable. [132]

Central Integration of Pinprick Stimuli (Aim 3): The perceived magnitude of a single pinprick stimulus will be compared with that of a train of 10 pinprick stimuli of the same force (256mN OR 512mN) repeated at 1/s rate at the same sites. The use of the larger stimuli will be made if, when presented at the first test site, the perceived pain rating is “0” for the lesser of the two. Thus, a greater differentiation of response may be possible, but will not present a significant discomfort to the subject. In all tests, the subject can stop the testing procedures. Single pinprick stimuli will be alternated with a train of 10 stimuli until both are done at three different sites: affected shoulder, unaffected shoulder, and unaffected tibialis anterior (lower leg). The mean pain rating of trains divided by the mean pain rating to single stimuli will be calculated as wind-up ratio (WUR

Other: Four other surveys also are collected for potential correlative data analysis. These are the

Beck Depression Inventory (BDI), the Pain Catastrophizing Scale (PCS), the Fear Avoidance Beliefs Questionnaire (FABQ) and a Patient Global Impression of Change (PGIC) Assessment. They are collected at Eligibility, except for PGIC which is done at EOT).

Concomitant Therapies: Participants may not receive additional PT or OT during the treatment period or during follow-up. Similarly, they may not receive any injections, opioids, membrane stabilizers or any other forms of electrical stimulation, including TENS or surface PNS, to the affected shoulder. Due to ethical considerations, they may use nonopioid analgesics for pain management. They may adjust dosing of these medications, but they may not change or add medications during the protocol. Participants will maintain their dosage during the week prior to each visit to match the recall period for assessment of BPI 3 and 9. Medication use is monitored via subject report

8.5 Does this study only involve the use of existing/retrospective data/specimens?
No

Check yes or no.

8.6 Describe in <u>detail</u> the study design also known as the experimental flow. Include all study procedures a subject will go through, in order of sequence and timing, including frequency of visits, duration of visits, length of subject participation etc. *Please Note this needs to be written for an educated person who is not an expert in the field, do not exceed 300 words*:
The duration of each subject's participation will be ~8 months.

This is also known as NIH Experimental Procedure section or Clinical Trial Procedure/Experimental Flow section. Do not just attach documents in response to this question you must do a study design summary for IRB Review.

Visit 1 – Consent/Eligibility: Consent form signed. Assessed for eligibility per inclusion/exclusion criteria. , MRI(prn per exclusion criteria) . BDI, PCS & FABQ administered. BPI administered. Medical history, demographics, comorbidities, and medication use recorded. Pregnancy test (in applicable subjects). (~4 hrs)

Visit 2 – Baseline Outcomes Assessment: Study outcomes assessment measures (see Outcomes Assessment) administered to establish baseline levels. (~4 hrs)

NOTE: VISITS 3 THROUGH 10 WILL OCCUR DURING A 60 DAY WINDOW -/+ 5 days.

Visit 3 - BPI administered. Subject queried for medication usage and adverse events. Sprint MicroLead (Electrode) Implant Procedure: Testing of muscle response with Sprint Test Needles; Implantation of percutaneous Sprint MicroLead. Subject given instructions on care of Lead exit site and bandage change instructions. Randomization to treatment group. Physical Therapy Treatment (~2.5 hrs)

Visit 4 –BPI administered. Post-Implant Safety Check. Check the Lead exit site and dressing change(prn). Start of Stimulation: Programming of external stimulator (Sprint Stimulator). Subject given instructions on use of System and care of Lead exit site. Subject queried for medication usage and adverse events. Physical Therapy Treatment (~1.5 hours)

Visit 5-10 Therapy Visits: Skin check/dressing change(prn), medication and adverse events query.

Visit 11 - EOT Outcomes Assessment & Explant Procedure: BPI, SF-12, SPADI & PGIC administered. Skin checked. Study outcomes assessment measures administered. Subject queried for medication usage and adverse events. Lead Removed. X-rays performed (may be done as separate clinical visit). (~3 hrs)

Phone call: Post-Explant check up. (15 min): Queried about skin and x-ray results reviewed.

Visit 12 - End of Treatment + 12 wks Outcomes Assessment: Skin checked. Study outcomes assessment measures administered. Subject queried for medication usage and adverse events. (~2 hrs)

Visit 13 – End of Treatment + 24 wks Outcomes Assessment: Skin checked. Study outcomes assessment measures administered. Subject queried for medication usage and adverse events. (~2 hrs)

Provision for lead replacement: If, in the judgement of the Investigator, the Sprint MicroLead becomes significantly displaced or fully dislodged, it is possible that the Investigator may elect to place another lead which would require an unscheduled visit. Other visits may be repeated as appropriate.

Unscheduled Visits are conducted if/as needed.

*some visits may be combined to accommodate subject or staff scheduling
*Visits may be completed via telephone, telehealth or email as determined by the principle investigator in case of immediate hazard to the subject

*Visits 12 and 13 : These visits include questionnaires and can be completed via telehealth, telephone or email at the discretion of the PI

Email will only be used with subject who sign the Alternative Means HIPAA

8.7 Please attach study design/subject visit schedule here:

If you have an electronic schedule of study visits and/or procedures please attach here.

Name | Description

PNS for SIS Visit Schedule Table | History

View: 09-00 Inclusion/Exclusion Criteria

9.0 Inclusion/Exclusion Criteria:

9.1 What are the inclusion criteria? Put this information in bullet form:

Please list inclusion criteria.

- Shoulder pain of >3 months
- Age>=21-90
- Worst pain in the last week>=4 (0-10 scale)
- Ability to check skin and perform dressing changes, independently or with assistance
- Stable dose of pain medication (Not taking more than than 1 opioid or 1 non-opioid analgesic)

9.2 What are exclusion criteria? Put this information in bullet form:

Please list exclusion criteria.

- **Current shoulder joint or overlying skin infection, or current bacterial infection requiring antibiotics**
- **Other chronic pain syndrome (Pain in another area of the body 15 or more days in the last 30 (more than half of the time) or taking daily analgesics for another pain syndrome)**
- **Prior shoulder surgery to ipsilateral shoulder joint (glenohumeral, rotator cuff, AC joint, etc.)**
- **Corticosteroid injection in the ipsilateral shoulder or any pain relieving procedure at the shoulder in the last 12 weeks**
- **Uncontrolled bleeding disorder**
- **Medical instability based on physician opinion after review of medical information**
- **Pregnancy**
- **Neurological condition affecting ipsilateral upper limb (add (such as central neurologic injury/illness, active radiculopathy, diabetic amyotrophy, Complex Regional Pain Syndrome, etc.)**
- **Current Worker's compensation claim for the ipsilateral shoulder**
- **Diagnosis of shoulder instability, adhesive capsulitis or severe glenohumeral OA based on current patient symptoms and physical examination**
- **Ipsilateral shoulder injury due to severe trauma (Fall from greater than standing height; Motor vehicle crashes; Struck by vehicle or other fast-moving projectile (e.g., bullet, baseball, etc.); Assault (i.e., injuries intentionally inflicted by another person))**
- **osseus fracture in ipsilateral arm in the last year**
- **Ipsilateral upper limb amputation other than a single digit (digits 2-5, partial or full)**
- **Patient is a candidate for shoulder surgery based on physician opinion**
- **Compromised immune system (immunodeficiency or immunosuppression)**
- **Current use of a Deep Brain Stimulation (DBS) system, implanted active cardiac implant (e.g. pacemaker or defibrillator), any other implantable neuro-stimulator whose stimulus current pathway may overlap with that of the SPRINT System**
- **Patients who have a tape or adhesive allergy**
- **Contraindication to MRI (metal in body, claustrophobia, body habitus, etc) – exclude from MRI only**
- **Severe problems with maintaining follow-up expected (such as but not limited to history of substance abuse, homelessness/incarceration, dementia, brain injury, and psychotic disorders)**

9.3 How will subject eligibility be determined and by whom?

Please describe in detail.

Subject eligibility will be initially assessed by the study coordinator and will be confirmed and reviewed by the Investigator. Eligibility will be determined from:

- review of medical history available in the chart;
- review of inclusion/exclusion criteria;
- physical examination of shoulder;
- pregnancy urine or serum test in applicable female subjects;
- MRI scans reviewed by study physician if available.
- completion of the Brief Pain Inventory Short Form at Visit 1 (to confirm baseline degree of pain of ≥ 4).

9.4 Will you exclude women and minorities, or persons under 21 from enrollment?

Check yes or no.

Yes

9.5 If yes, which groups are you excluding? Provide justification for your decision.

List groups to be excluded then provide justification.

Pregnant women: Pregnant women will be excluded since the effect of electrical stimulation on the fetus is not known.

Persons under 21: Children are excluded based on scientific considerations as they represent a fundamentally different population substantially different from the adult population. Individuals that are at least 21 years of age possess additional maturity beyond those that are 18. The study involves the use of an external stimulator and requires the maintenance of a percutaneous exit site. As such, we believe that this additional level of maturity is a valid reason to extend the minimum age of enrollment to 21.

9.6 Attach Documents:

If you are unable to fit your answers in the text boxes provided please attach as a word document.

Name	Description
There are no items to display	

View: 10-00 Risk/Benefits

10.0 Assessment of Risk I:

10.1 Identify and distinguish between those procedures that are standard versus those that are experimental. Include the frequency and duration of each activity and the total length of subject participation:

Please distinguish between those procedures that are standard versus those that are experimental. Describe in detail all experimental procedures.

• Physical Exam and Range of Motion of shoulder (standard): A physical exam and range of motion assessment is standard for patients with shoulder pain and will be done at Visit 1. The shoulder will be physically inspected during each visit. ROM also is an outcomes measure assessed during 4 Outcomes Assessments Visits.
• Collection of bloodwork (standard): A pregnancy test will also be administered in applicable subjects and can either be urine or serum pregnancy test.
• EMG needle electrode testing (experimental): EMG needles are commonly used to evaluate muscle physiology and strength of muscle contractions. In this study however, EMG needle (Sprint Test Needle) testing will be used to deliver test stimulation during the lead implant procedure.
• Placement of Percutaneous Fine Wire Intramuscular Lead and Use of Electrical Stimulation (experimental): The placement of the lead during the lead implant procedure and the use of stimulation during the treatment phase are FDA-cleared but considered experimental for this study. Local anesthetic will be used.
• MRI (standard): MRI are used for eligibility determination/characterization if available. Also, shoulder x-rays will be conducted following the removal (explant) of the electrode lead, to determine and document the presence of any retained fragments.
• Physical Therapy: Standard PT (standard) will be used during the study. There are 8 PT Visits.
• Collection of surveys and questionnaires: The BPI, SF-12 & SPADI (standard) surveys are used for research, but also are commonly used in clinical practice. These surveys will be collected as defined elsewhere in this protocol, including during 7 Outcomes Assessments Visits. The BDI and PCS (standard) are used for research, but also are commonly used in pain patients. They will be collected at Visits 1, . The FABQ (experimental) also will be collected at Visits 1,. The PGIC (experimental) also will be collected at Visits 11.
• Other outcomes measures (experimental): FIT-HaNSA, Pressure pain thresholds, pinprick pain thresholds, and central integration of pinprick stimuli are used for research but some also are used in clinical practice as well. They will be used as defined elsewhere in this protocol during 7 Outcomes Assessments Visits.

10.2 Describe any therapeutic alternatives to the research that may exist. How are they different from those procedures that subjects would normally undergo?

Describe any therapeutic alternatives. Can subjects receive this drug or device outside of a research study?

This summary includes an emphasis on post-stroke shoulder pain, but applies to shoulder pain in general.

Numerous interventions exist for the treatment of shoulder pain following stroke. This is due to the large number of possible etiologies, the diversity of clinicians that treat stroke patients, and the lack of consensus regarding a standard of care. None of the following interventions have been shown to reduce pain reliably in randomized controlled trials.

Slings and other supports: Arm slings and other mechanical supports, such as wheelchair trays, are often used to support the forearm and distribute its weight to one or both shoulders in an effort to prevent or reduce subluxation. Although slings may reduce subluxation, they often fail to reduce shoulder pain as subluxation recurs once they are removed and may slow rehabilitation by reducing arm mobility.

Strapping: Strapping is the application of non-stretch tape to the affected limb to support the glenohumeral joint while allowing free movement of the arm. In a randomized controlled study of 33 patients, those who received strapping reported reduced average pain compared to those who received no therapy (inactive control group). However, strapping fails to produce a significant benefit compared to active control groups, who received either sham strapping or standard physiotherapy without strapping. In addition, the tapes must be replaced at least every three days, and skin irritation is common.

Local Injection Techniques: Corticosteroid injections address pain by treating inflammation. Approximately 50% of clinicians who treat patients with poststroke

shoulder pain believe that steroid injections are effective. However, there are only two randomized controlled trials of corticosteroid injections for the treatment of post-stroke shoulder pain and they have mixed results. A recent trial of subacromial injections reported significant benefit over placebo. However, an earlier placebo controlled trial of intra-articular injections showed no benefit. Post-stroke shoulder pain has a variety of possible etiologies and does not always arise from inflammation, explaining why steroid injections do not consistently outperform placebo in stroke patients. In addition to uncertain efficacy, repeat corticosteroid injections are associated with frequent adverse events, making them a poor treatment option.

Botulinum toxin causes local paresis of muscles by blocking cholinergic transmission at the neuromuscular junction. It has been widely used to treat spasticity and some data suggest that it may also help to relieve pain. Six of nine patients in a small uncontrolled study receiving an injection of botulinum toxin to the affected limb reported pain reduction. However, the effect of botulinum toxin is known to diminish after 3-4 months, making repeated injections necessary. Little data exist regarding the repeated use of botulinum toxin for shoulder pain relief.

Oral analgesic medications: The use of opioid and nonopioid analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs) to manage shoulder pain is common practice. Unfortunately, extended use of opioids can lead to dependence and side effects such as headache, skin rash, dizziness, and gastrointestinal symptoms. Though NSAIDs may reduce shoulder pain in the general population, their efficacy has not been demonstrated in the stroke population.

Therapeutic exercises: Therapeutic exercises under the supervision of a trained professional are generally considered to be an important part of poststroke rehabilitation. Although they prevent immobility and improve the range of motion (ROM) of the hemiplegic arm, studies have found that some exercises, such as the use of an overhead pulley, can cause soft tissue damage and thereby worsen shoulder pain. In fact, exercises are generally associated with a worsening of pain or no change, rather than an improvement. In a study investigating static positional stretches, the treatment group showed increasing levels of pain.

Acupuncture/Electroacupuncture: Acupuncture has been used for centuries to treat various types of pain and is believed to improve cutaneous and muscle blood flow and to increase pain thresholds. Electroacupuncture, a therapy in which traditional acupuncture needles are used in conjunction with electrical stimulation, has been evaluated as a therapy for shoulder pain in post-stroke subjects in a randomized study comparing electroacupuncture plus occupational/physical therapy to therapy alone. Although statistically significant improvements in pain reported via a Visual Analog Scale were observed in the treatment group, the study did not follow the group beyond the conclusion of the treatment. Thus it is not clear how often the therapy must be reapplied. In addition, electroacupuncture requires repeated clinic visits (at least 3 visits per week for 1 month). Traditional acupuncture has also been evaluated as a treatment for shoulder pain; however subjects in these studies had non-stroke shoulder pain etiologies.

Surface electrical stimulation: Surface electrical stimulation uses skin surface electrodes applied to the shoulder to deliver stimulation from an external stimulator. Baker and Parker published the first results from a randomized controlled trial of surface electrical stimulation for the treatment of poststroke shoulder pain. The authors found a treatment effect for subluxation but inconclusive results regarding pain relief. The investigators of a later study hoped to obtain more conclusive results than Baker and Parker by enrolling a larger population of 120 and following the subjects for two years. Pain was noted as present or absent at rest during passive motion and during active motion. Subjects were also asked to rate their pain using a visual analogue scale (VAS). For a subject to be classified as having no pain, all four variables had to be negative. A significantly higher proportion of subjects receiving electrical stimulation had no pain at 3, 6, 12, and 24 months compared to the control group (80.7% vs. 55.1%, $p<0.01$). The treatment subjects also showed a greater reduction in subluxation and a significant improvement in the recovery of arm motion.

The results of four additional studies investigating surface electrical stimulation are summarized in a Cochrane review. Although the authors found a significant improvement in pain-free range of motion (ROM) in the treatment groups, the data did not support a significant reduction in pain intensity or incidence. The authors concluded that larger randomized controlled studies would be necessary to fully examine the effects of electrical stimulation in the post-stroke shoulder pain population.
Another literature review including six trials found that electrical stimulation paired with conventional therapy is not superior to conventional therapy alone for pain prevention.

However, they noted that this may be due to the indirect way in which most studies measured pain (as "pain-free range of shoulder external rotation"). When pain was measured directly, using a VAS, electrical stimulation was found to be more effective in preventing pain than conventional therapy.

The results regarding the efficacy of surface electrical stimulation as a treatment for post-stroke shoulder pain have been promising, leading to its recommendation by several recently published guidelines. In addition, a literature review proposed that surface electrical stimulation combined with gentle clinician guided exercises should be considered the "best practice" for acute stroke survivors. However, several authors have noted that even with further evidence of the efficacy of surface electrical stimulation, it is unlikely that it will ever be the standard of care due to the discomfort caused by stimulation of cutaneous pain receptors, the potential for skin irritation under multiple surface electrodes, the need for skilled personnel to place the surface electrodes on a daily basis, and muscle fatigue that commonly occurs due to the high frequency of stimulation. Baker and Parker noted that either an implantable or a percutaneous system would have to be developed before electrical stimulation could become the preferred treatment. For these reasons, researchers have turned their attention to the use of intramuscular electrical stimulation.

bion® microstimulator (investigational): Due to the effectiveness of electrical stimulation but the difficulties associated with surface electrical stimulation, researchers have begun to investigate direct muscle and nerve stimulation. The bion® microstimulator used by Bioness, Inc. (Valencia, CA), is currently being investigated for the treatment of post-stroke shoulder pain and subluxation. Although the bion has technical advantages, including its small size and self-contained electrode, it also suffers from considerable disadvantages. First, the device does not utilize a trial stage to evaluate whether a candidate is likely to experience pain relief from long term use prior to implantation. Second, implantation of the bion requires fluoroscopy and precise placement in close proximity to the deep axillary nerve trunk. Third, the device must be recharged daily using a large, stationary charging apparatus, to which the patient must be tethered during the recharging session. In addition, the bion's extraction requires open surgery. Finally, the bion requires precise placement due to its bipolar configuration, as the stimulus current density (and efficiency of nerve recruitment) drops off rapidly with distance from the target nerve. Even a small migration of the bion could significantly diminish its effectiveness. Data regarding the safe and effective use of the bion for post-stroke shoulder pain have not yet been published.

10.3 **What are the outcome variables and how will they be analyzed? What are the statistical and analytical methods that will be used?** ***Note this section can be copied from the NIH Grant Application or from the Statistical and Analytical Methods section of the industry trial protocol.***

Define outcomes and describe data analysis, please include a power calculation.

See attachments below.

10.4 **If the above requested information does not fit in the text box please attach a word document here:**

If the requested information does not fit in the text box please attach a word document.

Name	Description
PNS for SIS Outcomes Measures and Data Analysis (inc. Power Analysis) | History	
Shoulder MRI Protocol_PNS for SIS 2018_11_20.docx | History	

View: 10-01 Risk/Benefits

10.1 Assessment of Risk II:

10.5 **List and quantitate the risks involved for each experimental procedure in bullet form. Identify risks as common (greater than 10%) uncommon (greater than 1% up to and including 10 %) rare (1% or less). This must match the risks listed in the Consent Form:**

Select all that apply.

1) Risks associated with needle insertion for Lead placement
Tissue damage, such as puncturing a blood vessel, irritating a nerve, or temporary bruising or pain at the insertion site may occur when the needle is placed.
• The risks of bruising and pain are common.
• The risks of puncturing a blood vessel or irritating a nerve are uncommon.
• It is possible, but rare, that you could feel dizzy or faint during the procedure.
To reduce this risk, the needles will be placed carefully by a trained doctor. In addition, local anesthesia (numbing medication) will be used to reduce the risk of pain. If you have a history of fainting, the procedure will be done with you lying down on your side.

It is possible that it may take more than one try to place the Lead (wire) in your shoulder. If this happens, you will have a needle placed in your shoulder more than once.

2) Risk of skin irritation, infection, or inflammation at the Lead exit site

Skin irritation, infection, or granuloma formation (mild tissue inflammation) may occur at the Lead exit site.
• Skin irritation is common.
• Infection and granuloma are rare.
Symptoms include redness, swelling, or pain. To reduce this risk, you should keep your shoulder clean and dry. After the Lead has been placed (Visit 3), it is important that the exit site remain clean and dry and be monitored as long as the Lead remains in place. You should notify the study staff if you see changes in skin color or have any discomfort where the Lead exits your skin.

To minimize the risk of infection:
To minimize the risk of infection, you must follow the specific instructions for the care of the electrode site.
• After electrode placement, the transparent dressing should be changed 3 days after the placement procedure or if the dressing becomes wet. This initial dressing will also be changed by study staff one week after the placement procedure.
• To minimize the risk of infection after this period, you should keep the electrode exit site clean and dry, and look for changes in skin color or sensitivity.
• You will be asked to change the dressing every 2-3 days or if the dressing becomes wet.

• If an infection occurs, it must be treated promptly. Untreated or delayed treatment of infection is very dangerous and could lead to severe complications including kidney failure, heart attack, stroke, blood clots or death. One participant who developed an infection did not follow the specific instructions for the care of the electrode site and did not come in for his scheduled follow-up appointment after the implantation. The participant was hospitalized, but subsequently died during the hospitalization. The cause of death is thought to be a heart attack, but the exact cause and its relationship to the infection are not known.
3) Risk of the Lead breaking beneath the skin
There is a possibility that the Lead may break beneath your skin either during stimulation or during the procedure to pull the Lead out at the end of the treatment period. This risk is uncommon. When a Lead breaks, one or more Lead pieces could stay in your body. An x-ray will be taken to see if any pieces remain in your body. Dr. Wilson will use his judgment to decide if the Lead pieces should be removed.

4) Risk of tissue infection from a piece of the Lead remaining in your shoulder
An infection or granuloma can happen during the study (as mentioned above) or after the study if a piece of the Lead stays in your body. This risk is uncommon. Symptoms of an infection or granuloma include swelling, pain, or fever. If this happens, Dr. Wilson, or an appropriately qualified doctor, will remove the piece of Lead and/or give you the necessary treatment (such as antibiotics) for this infection.

5) Risks of removing pieces of the Lead from your body
If Lead pieces need to be removed, Dr. Wilson will make a small cut in your skin and pull out the Lead pieces, which are usually right under the skin. The risks of doing so include discomfort during the procedure and skin irritation or infection where the pieces were removed. Call the study staff if you see any signs of redness, swelling, or pain. This risk is rare.

6) Risk of the Lead moving from its original position or coming out
It is possible that the Lead may move from its original location or come out during the treatment period. This risk is rare.
• If the Lead moves from its original position slightly and the stimulation is still comfortable, nothing will be done.
• If the Lead has moved a lot or come out of your shoulder, you may be asked if you are interested in having another Lead placed in your shoulder. Whether or not you get another Lead will depend upon your length of time in the treatment period, whether or not your shoulder is healthy enough to have another Lead placed, and if you agree to it.
• The risk of the Lead moving from its original location is that you could feel discomfort from the stimulation or "pins and needles".
If your Lead comes out or moves from its original location and you decide to have another Lead placed, you would again be exposed to the same risks of placing the original Lead.

7) Risk of skin irritation under the Sprint Pad, or bandages
The skin under the Sprint Pad, or bandages can get irritated. Skin irritation is common. Symptoms include redness and itching. To reduce this risk, medical grade tapes and bandages will be used. The Sprint Pad, and bandages should not be applied to unhealthy skin (such as skin that has scars or recent surgical incisions) to avoid irritation. If there is irritation, the Sprint Pad, or bandages will be moved slightly to a different area of your shoulder, or different bandages will be used.

8) Risk of the Sprint Stimulator working incorrectly
There is a small chance that the Sprint Stimulator may stop working correctly. It is very unlikely that this will be harmful to you. This risk is rare. If there is a problem with the Sprint Stimulator, electrical stimulation will turn off automatically. You should call the study staff if the Sprint Stimulator shows an error message or you can't turn the stimulation on.

9) Risks for pregnant women
The effects on the developing child of using electrical stimulation during pregnancy and the risk of birth defects are unknown. Therefore, women who are pregnant may not participate in this study. Women should not become pregnant while participating in this study. If you are a woman of childbearing age and potential, you should use birth control during the treatment phase of the study. Your doctor can discuss birth control methods with you. If you become pregnant during the study, notify the study staff immediately. Electrical stimulation will be turned off, the Lead will be removed, and you will be withdrawn from the study.

10) Risk of discomfort due to electrical stimulation
• The small amounts of electricity delivered to your shoulder muscle could feel like a tingling or vibrating sensation.
• You could also feel pain or discomfort if the level of stimulation is too high or if your muscle becomes tired from stimulation (known as muscle fatigue).
This risk is uncommon. The study staff will carefully choose a level of stimulation that is comfortable for you during set up of the system.
• You may also feel a tingling sensation under the Sprint Pad.
This is not expected to be uncomfortable. If stimulation is painful, you should turn off the stimulation and notify the study staff.

If the Lead starts to come out of your body, you may feel electrical stimulation near your skin surface, which could feel like "pins and needles" and may be uncomfortable. If you think your Lead has started to come out, you should turn off the Sprint Stimulator and notify the study staff.

11) Risks associated with Diathermy
Tissue damage can happen if you receive diathermy, a form of short-wave or microwave therapy that may be used to apply deep therapeutic heat for the treatment of selected medical conditions such as relief of pain, muscle spasms, and joint contractures. Diathermy over or near the Lead may heat it and hurt the tissue. You must not receive diathermy during the study. You also must not receive diathermy after the study if a piece of the Lead remains in your shoulder. This risk is rare.

12) Risks associated with MRI
If you have an MRI procedure while the Lead, or a piece of the Lead, is in your body, you could have tissue damage. You can tell that you might be having tissue damage because you might feel warming, burning, or muscle contraction. To minimize this risk, you should always tell study staff before you schedule an MRI. Study doctor, or an appropriately qualified doctor, will remove the Lead and may remove any remaining pieces of the Lead. During the treatment period, you should carry this consent with you to show to medical staff to explain that you have a metal Lead in your shoulder if you need an emergency MRI. This risk is rare.

13) Risk of allergic reaction to anesthetic (numbing) medication and/or risk of accidental injection of anesthetic into a vein
• There is a risk that you might have an allergic reaction to the local anesthetic used just before the Lead is inserted. You could feel itching, have problems breathing, or get a swollen tongue (common signs of an allergic reaction).
If you were to have an allergic reaction, it would probably happen while you were still at MetroHealth. If you feel these things after you leave, notify the study staff right away. This risk is rare.
• There is also a risk that the numbing medication (anesthetic) could be accidentally administered into a blood vessel. If this happens, it could affect your heart, blood vessels, and/or nerves. This could cause your heart and/or breathing to stop.
This risk is rare. Your doctor is trained on how to administer the numbing medication correctly.

14) Risk of worsening of pain symptoms
Your shoulder pain may get worse during this study. The risk of your pain getting worse is uncommon.

15) Risks of Therapy and performing shoulder exercises
Your shoulder pain may be worse during therapy or during home exercises. This risk is common. All exercises will be done under the supervision of a trained therapist during Therapy Visits and you will be trained to perform home exercises as safely as possible.

16) Risks of Outcomes Assessments
• The questionnaires present no risks other than a rare risk of psychological harm since answering some of the questions may make you feel uncomfortable or uneasy. You have the right to review these surveys before you begin participating in the study and you may skip any questions that you do not wish to answer.
• The assessments of range of motion, strength and functional ability may be uncomfortable.
• The assessments of your sensitivity to pain are uncomfortable and may cause brief skin irritation. This risk is common.

17) Risk of MRI visit
For the MRI visits, there are no expected risks associated with the MRI itself. However, these visits will be treated like any clinically-prescribed MRI visit. The usual common concerns associated with MRI will be explained at each visit. Because the MRI machine acts like a large magnet, it could move metallic objects in the MRI room during your examination that could possibly harm you. Precautions have been taken to minimize such an event from happening.

For example, loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you cannot have an MRI. Body piercing jewelry must be removed for scanning. Some tattoos could experience localized heating, although patients having tattoos are routinely scanned without problems. Cold compresses could be applied if heating were to occur.
Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia [being closed in a small space] and by the loud banging noise during the test. Temporary hearing loss has been reported from this loud noise. This noise will be diminished by the headphones you will be asked to wear to follow verbal commands. If you would also like to wear earplugs, they will be provided as long as you can still hear commands through the headphones. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

The MRI scan being done is designed to answer research questions, not to examine your shoulder medically. This MRI scan is not a substitute for one a doctor would order. However, if we believe that we have found a medical problem in your MRI scan, we will refer you to your primary care physician for further assessment. Since it is possible that an MRI abnormality could be suspected during this study, it is possible that you could experience worry or anxiety regardless of whether the abnormality was later confirmed.

18) Risks associated with X-ray
You are agreeing to participate in a research project that involves the use of imaging procedures that exposes you to radiation. This section will discuss the risks associated with imaging procedures that are for research only. Your doctors may order additional imaging procedures as part of your normal patient care that also expose you to radiation. Those normal imaging procedures are not included in the risk discussion below. Please discuss those procedures and radiation risks with your doctors.

As part of this research study, you may be asked to have imagining procedures that involves two x-ray images of your shoulder. This will help to ensure there are no pieces of an implant left in your body. The x-ray procedure exposes you to radiation. The amount of radiation that you could receive is approximately 0.06% of the amount allowed annually for persons exposed to radiation as part of their work or about 1% of the amount that we are all exposed to annually as part of our natural background radiation exposure.

19) Other
Since you will not know which treatment group you are in, there is a rare risk of psychological
harm.

Lastly, there may be risks and discomforts that are not yet known.

When PHI is involved there is the rare risk of a privacy breach.

There may be other risks as yet unknown.

10.6 **Are there defined stopping rules?** ◉ **Yes** ○ No

Describe in enough detail for the IRB to assess safety.

What are the stopping rules for the study? What are the conditions under which a subject will be withdrawn from the study for safety reasons, i.e. disease progression?
The study could be terminated at any time for valid scientific reasons or reasons related to the protection of subjects participating in this study. A reason for study termination includes but is not limited to the discovery of an unexpected, significant, or unacceptable risk to the participants enrolled in the study.

What findings, events, or conditions would require a research subject to be removed from the study? (i.e. disease progression)
The research subject may be removed if they develop any condition during the course of the study which would preclude the safe use of stimulation or otherwise impair their safe participation in any study activity.

10.7 **What Category of risk will study participants be exposed too?**

Should be consistent with risks listed in the Consent Form.

Name
Psychological
Physical
Privacy

10.8 **If Other listed above please specify:**

A text box is provided for further explanation.

10.9 **Describe the availability of medical or psychological services that participants might require as a consequence of participation in this the research:**

A text box is provided for further explanation.

It is not expected that participants would require medical or psychological services as a consequence of participation in this research. If that were to occur, appropriate referrals would be made for the subject.

10.10 **Describe in detail any measures in place to minimize or protect against the exposure of study subjects to these risks:**

Discuss any provisions for intervention in the event of an Adverse Event i.e. stopping rules.

1) Risks associated with needle insertion for Sprint MicroLead placement

To minimize the risks associated with percutaneously placing fine wire leads, only appropriately trained physician investigators will perform the procedure. Finally, the risk of discomfort during the procedure will be reduced by the use of an appropriate amount of local anesthetic.

Some participants may experience a vasovagal (“fainting”) response due to the discomfort or anxiety associated with of the procedure, especially among those with prior history of “fainting.” This risk is rare and may be associated with symptoms of lightheadedness, dizziness and or diaphoresis with concomitant reduction in blood pressure and heart rate. For those with prior history of “fainting” the procedure will be performed with the subject in the lateral decubitus position.

2) Risk of skin irritation, infection, or inflammation at the Sprint MicroLead exit site

These risks will be minimized by using sterile Leads and thoroughly cleansing the insertion site with antibacterial solution at the time of insertion. The insertion site will be covered with a dressing to keep it clean and dry, and the subjects and their caregivers will be instructed to inspect the site for signs of infection or irritation regularly and to inform the Investigator if they occur. If infection or skin irritation occurs, the Investigator will administer an antibiotic and/or remove the Lead. Infections are rare and typically resolve after Lead removal and antibiotic treatment.

It should be noted that in a completed clinical trial of percutaneous intramuscular electrical stimulation, one patient death occurred. The subject did not follow the instructions for the care of the Lead exit site and also did not return for his scheduled follow-up visit following electrode placement. He developed an electrode related infection and was hospitalized. The cause of death is thought to be a myocardial infarction or a pulmonary embolus, but the exact cause of the death and its relationship to the infection are not known. To mitigate the potential risk of serious infection, a 1 week safety check will be performed after the procedure.

Participants will return to the clinic and the exit site will be evaluated for signs of infection.

3) Risk of the Sprint MicroLead breaking beneath the skin

The risk of leaving a Lead fragment is minimized by reducing the amount of time the Lead remains implanted and the number of Leads implanted. In this protocol, a single Sprint MicroLead will be implanted for just 8 weeks.

4) Risk of infection associated with retained Sprint MicroLead fragments

Investigators at the Cleveland FES Center and Case Western Reserve University have over 30 years of experience with dozens of research participants and hundreds of implanted leads like those used in this study. Infections and granulomas of leads or lead fragments have been uncommon, which is attributed to the materials and procedures that have been developed as well as the extensive experience of the Investigators.

5) Risks associated with lead fragment removal

Subjects will be instructed to contact the Investigator if there are any signs of pain, redness, swelling, discharge, or the appearance of a pimple-like mass (skin abscess). Such signs indicate that the fragment has migrated to the skin surface. At that time, if clinically warranted, the fragment may be removed via an outpatient procedure which involves lancing the abscess and removing the fragment and application of a topical antibiotic.

6) Risk of Lead Replacement due to Lead Migration or Lead Becoming Dislodged

It is possible that the Lead may migrate from its original intended location or that the Lead may become dislodged (i.e. come out completely) during the treatment phase. Each time an additional lead is placed, the subject has an additional exposure to the same risks of lead placement described above in “risk of needle insertion for Sprint MicroLead placement”.

This risk of lead migration or the becoming dislodged is mitigated by instructions to the subject and their caregiver, as appropriate, to ensure careful handling of the Lead and Lead Connector during bandage changes. In addition, the risk of placing a new lead is further mitigated by ensuring that Investigators are trained in the lead placement procedure, ensuring that the shoulder tissue appears healthy prior to placing a new lead.
7) Risk of skin irritation under the Sprint Pad or bandages

The risks of skin irritation under the Sprint Pad (a modified surface electrode) and under the bandages surrounding the Sprint MicroLead exit site will be reduced by excluding patients with known sensitivity to skin surface electrodes and/or medical-grade adhesive tapes. Subjects and their caregivers will be advised to examine the electrode exit site at regular intervals to look for any signs of irritation. To avoid irritation under the Sprint Pad, subjects will be advised that the Sprint Stimulator and Sprint Pad may be moved to slightly different locations near the Lead insertion site throughout the treatment phase. In addition, subjects will be instructed to avoid placing the Sprint Pad or bandages on unhealthy skin.

8) Risk of mechanical or electrical failure of the Sprint Stimulator

There is a rare chance that the Sprint Stimulator may malfunction. It is very unlikely that a stimulator malfunction will be harmful. If there is a problem with the Sprint Stimulator or the Sprint MicroLead, the Stimulator will reset itself such that no stimulation is delivered.

The Sprint Stimulator will not deliver stimulation if it detects a high impedance level indicating a broken lead wire or a faulty lead connection. Subjects will be instructed to contact study staff in the event that an error message is displayed.

9) Risks for pregnant women

The risk of harm to a pregnant woman or fetus is unknown. The device will not be used in any subjects known to be pregnant. If a subject is known to become pregnant during the treatment phase, stimulation will be stopped and the Sprint MicroLead will be removed.

Potential risks of pregnancy will be reduced by administering a pregnancy test in females of reproductive potential at study enrollment. Additionally, the Informed Consent form will advise subjects that the risks of electrical stimulation during pregnancy are unknown and that they should immediately notify the Investigator if they suspect they have become pregnant during the study.

10) Risk of discomfort due to electrical stimulation

To minimize the risk of increased shoulder pain as the result of high intensity stimulation, the Investigator will set an appropriate intensity for the stimulation. Should a subject feel pain as the result of stimulation, he or she will be able to turn off the stimulation using the Sprint Stimulator controls. Although muscle fatigue is unlikely with six hours of daily stimulation therapy, subjects may also feel some discomfort if muscle fatigue occurs. If muscle fatigue is observed, the Investigator is able to prescribe several shorter stimulation sessions totaling six hours per day.

Discomfort or pain due to stimulation may occur if the Sprint MicroLead migrates from its original location. Stimulation near the skin surface may be perceived as a “pins and needles” or stinging sensation and may be uncomfortable.

The risk of pain due to a migrating electrode will be minimized by leaving stimulation off until the Sprint MicroLead has had time to stabilize. The Sprint MicroLead has a fine wire barb. In addition, the proximal portion of the Lead exits the skin which makes this Lead more susceptible to becoming dislodged during bandage changes. As a conservative measure, we allow one week for encapsulation of the Sprint MicroLead to ensure stability. Data on the Lead has shown that electrodes are fully encapsulated by the surrounding tissue.

A tingling sensation may be felt under the Sprint Pad but this sensation is not expected to be uncomfortable. If discomfort or pain is felt at the Sprint Pad site, the subject will be instructed to turn off stimulation and move the Sprint Pad and Stimulator to a different location.

11) Risks associated with Diathermy

The risk of diathermy will be reduced by informing subjects that diathermy must not be used. In addition, subjects will be informed to never undergo diathermy if a Sprint MicroLead fragment remains in the body.

12) Risks associated with MRI

Should a subject require a scheduled MRI during the treatment phase, the Sprint MicroLead will be removed. The decision to remove any remaining fragments will depend on a careful assessment of the benefits of the MRI, risks of MRI with retained fragments and risks associated with removing of electrode fragments.

13) Risk of allergic reaction to local anesthetics and/or risk of accidental injection of local anesthetic into a vein

The risks of allergy to local anesthetic agents will be reduced by excluding subjects with a prior known history of allergy or sensitivity to local anesthetic agents. In addition, prior to the procedure, subjects will be advised of the signs and symptoms of an allergic reaction. Because subjects will be awake during this procedure, they will be able to verbalize any itching or other signs of allergy to the local anesthetic. The risks of accidental intravascular injection of local anesthetic will be reduced by careful administration of the local anesthetic. Careful administration includes ensuring that a vein has not been punctured by the syringe prior to injecting the anesthetic and observing the subject after the injection. In addition, the physical location of the anesthetic injection (in the deltoid) combined with the injection technique would rarely result in an accidental intravascular injection.

Some subjects may experience a vasovagal (“fainting”) response due to the discomfort of needle insertion or anxiety associated with the procedure. The risk of fainting will be reduced by observing subjects during and following venipuncture to ensure that they feel comfortable rising from their seated position. Subjects with a history of vasovagal responses will be supine during venipuncture.

14) Risk of worsening of pain symptoms

It is possible that the subject may have a worsening of pain symptoms or that they may not obtain any therapeutic benefit from the treatment. The risk of worsening pain symptoms is uncommon. In addition, subjects will have the opportunity to discontinue treatment if their stimulation is too uncomfortable.

These risks are mitigated by clinical training on the safe limits. Subjects do not have access to make changes to the programming controls and thus could not advertently change the value.

15) Risks of Physical Therapy and Performing Shoulder Exercises

Shoulder pain may worsen during outpatient therapy or during home exercises. To minimize this risk, all exercises will be performed under the supervision of a trained therapist during outpatient therapies. Participants will be trained to perform their home exercise program to minimize the risk of further injuring the shoulder. The proper implementation of the home exercise program will be reinforced at each outpatient therapy visit. However, if shoulder pain persists during the home exercises, the home exercise program will be terminated.

16) Risks of Outcomes Assessments

If the subject feels discomfort, they may request that the outcomes assessments be paused. Measures will be taken to improve their comfort if possible. Skin irritation, should it occur, should resolved shortly after the cause is removed.
17 Risk of MRI(MH only): MRI will not be completed in subjects where the MRI in contraindicated. Subject will complete MRI Screen form which will be reviewed prior to the MRI.
18) Risk of x ray will be discussed with subject and subject will be given opportunity to discuss with their physician as needed. Subject can request x ray not be completed.
19) Other

The informed consent process ensures that subjects are aware of multiple treatment groups but acknowledges that there is a rare risk of psychological harm due to not knowing which group they are in. Subjects may choose not to answer survey questions that make them uncomfortable.

Privacy breach precautions are included in Sections 15-17.

There may be other risks as yet unknown.

10.11 Please add any documents related to the above questions:

If your answers to the above questions are too long for the space provided please attach them here.

Name	Description
There are no items to display	

View: 10-02 Risk/Benefits

10.2 Benefits:

10.12 Describe the potential benefits to the subject as a result of participating in this research. If there is no direct benefit to subjects please state that as well: *Note: payment or compensation to subjects for participation is not to be considered a potential benefit.*

Describe potential benefits to the study subjects.

Participants may experience substantial pain reduction, and all subjects are receiving active treatment.

10.13 Describe the potential benefits to society as result of this research:

Describe potential benefits to society.

The primary benefit will be the clinical and scientific knowledge gained.

10.14 What is the risk/benefit ratio of the research?

Discuss why the risks are reasonable in relation to the anticipated benefits.

The primary benefit will be the clinical and scientific knowledge gained as described above. Participants may experience substantial pain reduction, and all subjects are receiving active treatment. Due to the need for invasive procedures, participants will be exposed to greater than "minimal risk." However, the potential benefits to participants, other patients with SIS, and the scientific/rehabilitation community are substantial. Therefore, the risk benefit ratio is acceptable.

10.15 Attach Documents:

Attach documents here.

Name	Description
There are no items to display	

View: 11-00 Study Participant Information I

11.0 Study Participant Information I:

11.1 How will the Principal Investigator assure he/she has access to a population that would allow recruitment of the required number of study participants (i.e. prep for research):

How does the PI know he/she has the required number of subjects?

Please give the total #of subjects to be enrolled at all sites and anticipated subjects to be enrolled at MHS.

The participants needed for this study at MetroHealth are expected to be recruited from the clinics of the Investigators and via referral from other PM&R and Orthopedics physicians. Additionally, potential participants may be recruited from the Greater Cleveland area (as allowed for in the Recruitment section).

11.2

Request per NIH advisor:
Every site is eligible to enroll the entire sample, but total enrollment cannot exceed 116.

Anticipated number of subjects (all sites): [enter a number]
116

Anticipated number of subjects to be enrolled at MHS: [enter a number]
116

Anticipated number of potential subjects to be approached: [enter a number]
500

11.3 **If this is a multi-site study, how many sites will there be? [enter a number]** — How many total sites?
2

11.4 **Subject Characteristics:** — Check all that apply
Subject Population Categories
Outpatients
Patients with the "disease in question"

11.5 **Subject Source:** — Check all that apply
Subject Source Characteristics
Subjects from the Practice of the Principal Investigator
Subjects referred or recruited from other physicians practices
Public subject recruitment by advertisement, flyers, websites etc. (Note: required IRB review and approval)

11.6 **If "other" list above in either 11.4 or 11.5 please describe:** — *If applicable please describe.*

View: 12-00 Study Participant Information II

12.0 Study Participant Information II:

12.1 **Select age range of study participants:** — Check all that apply.
Subject Age Range
18 - 64
65 - 89

12.2 *** Will the study enroll vulnerable subject groups?** — Check yes or no.
No

*** Will you be enrolling Children?**
○ **Yes** ◉ **No**

*** Will you be enrolling Pregnant Women and/or Fetuses?**
○ **Yes** ◉ **No**

*** Will you be enrolling decisionally impaired subjects?**
○ **Yes** ◉ **No**

*** Will you be enrolling Prisoners?** ○ **Yes** ◉ **No**

12.3 **Please identify any vulnerable populations participating in the study:** — Check all that apply.
Vulnerable Populations
There are no items to display

12.4 **If you selected "other" above please describe:** — *Please describe other.*
The study does not target any of these groups although it is possible that some subjects would be associated with one or more of the groups (e.g., poor, elderly, minorities). — *Please enter a detailed plan.*

12.5 **If you are going to enroll <u>any</u> vulnerable populations please describe the safeguards you will put in place to protect these vulnerable Populations.**
All potential subjects will be assured that they may decline participation without jeopardizing their medical and rehabilitation care or compromising their relationship with their physician or MetroHealth Medical Center. All subjects have an opportunity to review the consent forms at home and discuss participation with family, friends, etc. PHI will remain at Metro, except enrolled research participants will be told that their names and contact information will be shared

with the device manufacturer for tracking purposes (addressed in HIPAA Authorization). Metro paper records with PHI are kept in locked cabinets in locked rooms. For PHI stored electronically, password protected secure MHS network drives will be used for electronic data in folders with access limited to those who are authorized by this protocol. Any data stored on portable media and/or removed from Metro would be deidentified.

View: 13-00 Recruitment I

13.0 Recruitment I:

All external advertisements (for radio, print media or TV) must be approved by MHS Communications Department prior to submission to the IRB so the IRB can see the final advertisement or script. All Advertisements on the MIV or On Hold messaging must be approved by the IRB before they are placed. You may not advertise a study which is not approved by the IRB. Please note that all studies which have a contract which an external sponsor must have that contract signed before any advertising can be done.

13.1 Recruitment Methods/Sources: *Check all that apply.*

Name
Internet/Web/MetroHealth Intranet
Telephone Scripts
Advertisements-Newspapers/Magazines, Television, Radio
Notices/Posters/Flyers
Letters
Epic Alerts
MetroHealth Face Book (no other Face Book recruitment is permitted)

13.2 If "Other" checked in 13.1 please explain: Please explain what other means.

13.3 Describe in detail all recruitment strategies for each subject group (as listed in Section 11.0) selected for this research: Please describe recruitment strategies in detail.

MetroHealth recruitment:
Subjects will be recruited from outpatient clinics at MetroHealth Medical Center (MHMC), as well as from the Greater Cleveland area. At MHMC, subjects will be recruited via direct referral from clinicians within the Departments of PM&R and Orthopedics.

Study subjects may be recruited from the following additional sources:
• All applicable MetroHealth Medical Center outpatient clinics and clinical departments (e.g., Family Practice, Internal Medicine, Neurology, etc.)
• University Hospitals and affiliate hospitals
• Cleveland Clinic and affiliate hospitals
• Other appropriate area physicians/hospitals/clinics/facilities
• Skilled nursing facilities/units
• Visiting nurse associations
• Nursing homes
• Assisted living facilities
• Support groups or forums
• Senior/community/recreation centers

Study subjects may be recruited using the following additional methods:
• Print advertisements (e.g., newspapers, periodicals, newsletters). May also be used for radio spots. Metro Communications will have approved.
• Craigslist advertisements. Metro Communications will have approved.
• Flyers and/or brochures.
• MetroHealth Voicemail and On-Hold Messaging. Metro Communications will have approved.
• Approved recruitment materials placed with permission on Bulletin Boards at appropriate locations in the MetroHealth System or at other locations (e.g., at other institutions, at conferences).
• In-service presentations at any of the locales listed above. Approved recruitment materials may be distributed or displayed.
• Research Introductory Contact Cards (the size of a business card) will be made available for inclusion with mailings, distribution by clinicians, distribution at inservices or other meetings, etc.
• Appropriate Informational Internet Sites (e.g., clinicaltrials.gov, MHS Clinical Trials Website). A recruitment campaign will be commissioned from Splash Clinical.

Initially, candidates who respond will be informally screened (possibly over the phone). Those who pass the informal screening will be scheduled for a formal, more detailed assessment of eligibility by the study team, usually including the PI or a physician co-investigator. An informed consent form will be provided for review, usually in advance. During the Eligibility visit, the clinical nurse coordinator will describe the research, review the consent form with the candidate, address all initial questions (with referral to the PI or a physician co-investigator as per the

candidate's request and the clinical nurse coordinator's discretion), and request participation in the study. Discussion is encouraged during the exchange to gauge subject comprehension. Candidates are free to take more time to think about it, consult with family or friends, and have additional questions answered if they wish. If and when a candidate agrees to participate, they sign the consent form, after which the formal assessment of eligibility takes place. Subjects may ask questions at any time. All questions will be answered.

UTSW: see attached 13.7
The following will be used to identify potential subjects:
1. Database search
2. Personal contacts
3. Referrals
4. Patients under the care of the research team
Patients being seen at the (Orthopedic as well as Rehab) shoulder clinic
There are two ways to initiate first contact:
1. The participants can reach out to the study team through email, online video call, or phone call to set an appointment to learn more about the study.
2. The research staff will contact the participant after identifying them from the screening process either in person, over the phone, online video, or email.
The participants will be approached either:
1. In person, immediately following consult with their provider, in the examination room
2. Over the phone/online video, when they have time to listen in a quiet room
By email

13.4 **What measures will be taken during the recruitment process to safeguard against the potential coercion or appearance of coercion of human subjects, particularly vulnerable subject groups?**

Please give an explanation of safeguards to be used.

All potential subjects will be assured that they may decline participation without jeopardizing their medical and rehabilitation care or compromising their relationship with their physician or MetroHealth Medical Center or other relying sites. All subjects have an opportunity to review the consent forms at home and discuss participation with family, friends, etc.

13.5 **Incentives to Subjects: Will subjects receive any incentives (payments, free service, gifts, etc.) for participation in the research?**

This information must mirror the consent form language.

Yes

13.6 **If yes, please describe these incentives and how they will be disbursed:** ***Note: payment or compensation to subjects for participation is not to be considered a potential benefit.***

Describe incentives, if they are to be pro-rated based on visits completed please give that information. This information must mirror consent form language.

MetroHealth:
Transportation may be arranged for the study participant and covered by the study budget. Alternatively, subjects who are able to drive parking will be validated.

Participants will receive $15 for each physical therapy session, $50 for completing the 3 month and the 6 month study visit (for a total of $220). These payments are in appreciation of your time and effort and to cover costs of travel. All payments will be paid using a ClinCard which is a re-loadable debit card.

UTSW
Participants will receive $15 for each physical therapy session, $50 for completing the 3 month and the 6 month study visit (for a total of $220). These payments are in appreciation of your time and effort and to cover costs of travel. All payments will be paid using a ClinCard which is a re-loadable debit card.

13.7 **Please attach copies of all recruitment/advertising materials and verbal scripts:**

Attach copies of all recruitment and advertising materials.

Name	Version
MetroHealth Digital media verbage | History	0.02
PNS for SIS Appointment Reminder | History	0.02
PNS for SIS Brochure | History	0.04
PNS for SIS Consent Cover Form Letter | History	0.03
PNS for SIS Evaluation Cover Form Letter | History	0.03
PNS for SIS Fliery.3-2021.5.1 | History	0.04
PNS Study Patient Fact Sheet (60 days) - v1.3 - 2021.8.17.docx | History	0.03
Research Ad(newsletter) | History	0.01
Splash Clinical Marketing Information | History	0.01
Splash Clinical Privacy Policy | History	0.01
STU-2020-0352 Form C Population Recruitment 08Apr2020.doc | History	0.01

View: 13-01 Recruitment II

13.1 Recruitment II:

13.8 Expense to Subjects: Will subjects incur any expenses as a result of participation in the study or will they be billed for any study-related procedures?
No

Check yes or no, make sure this information is in the consent.

13.9 If yes, please describe the expenses or charges that subjects will be assessed:

Please provide information regarding expenses to subjects and add information to consent.

13.10 Compensation For Injury: If applicable, will funding be available to compensate subjects for injuries sustained as a result of participation in this research?
No

Check yes or no, make sure this information is in the consent.

13.11 Who will cover the costs related to any injuries sustained due to participation in the study?
The subject and his/her insurance carrier will be responsible for these costs.

Please describe in detail. Examples subjects or their insurance company, study sponsor.

View: 14-00 Data Collection

14.0 Data Collection:

14.1 A. What type of data will you be collecting as part of this research?

Existing data must be in place or on the shelf prior to the submission of the research protocol to the IRB.

Will you collect existing data?

Prospective data is collected in real time.

or

Will you collect prospective data?
○ Yes ○ No

or

Will you collect both existing and prospective data? ◉ **Yes** ○ No

Definitions: ***Data are considered to be existing data only if they were in place or "on the shelf" prior to the submission of the research protocol to the IRB. Data are considered prospective if they are created and collected as part of the research i.e. from surveys, questionnaires.***

Tell the IRB why you are collecting this data i.e. to verify inclusion criteria.

B. Why are you collecting this data?

What will be the purpose of collecting and/or reviewing the data (new data or existing data).
The data collected in this study will be used to determine and document eligibility and suitability for the study, to establish baseline data for the study, to document status throughout the study, and to determine the effects of the intervention provided during the study.

14.2 If you are collecting existing data:

Specify the types of existing data you will use in this study.

Specify the type(s) of existing data sources you will use (medical records, school records, publicly available records, existing database). If you are collecting data from an exisitng database and that database contains PHI, you must provide the IRB Approval letter (attach to Section 27.00 Additional Documents).
During the baseline visit, subjects will be queried for existing medical history, including, medication usage. In addition, data to collect descriptive characteristics (e.g, age, duration shoulder pain, ethnicity) will be collected from the medical record.

Time frame i.e. last 10 years or from 1990-2000.

What is the timeframe of the existing data you wish to review? (i.e. 2000-2006)
The timeframe will be patient-dependent, covering the time since their onset and/or first evaluation for shoulder pain.

14.3 If you are collecting prospective data:

Where or how will the data be obtained? (i.e. surveys, questionnaires, psychological tests)
Data will be collected during each visit to MHMC and during phone calls when visits are not necessary. Data that is collected is described in detail at 8.4, 8.6 and 10.4.
If immediate hazard to subject to come to the labs in PMR at OBHC the visit will be completed via telephone, email or telehealth

Where will data be obtained? i.e. survey.

14.4 How will the data you collect be identified?

Types of Data Identification:
Name
Deidentified/Confidential- Data will be linked to subject(s) via a code or indirect identifier (i.e. study IDs or numbers)
Identifiable- Data will be linked to subject(s) via direct identifier (names, medical records numbers, etc.)

Please select how your subject data will be identified.

14.5 Will the information collected from these records be linked to any research subjects by identifiers? (i.e. name, MRN#, DOB)
(●) **Yes** ( ) No

Will your data be linked to subjects?

Please answer questions about the security of the data in section 15.00

14.6 If subject data will be deindentified using a code will there be a link or a key? Please describe. Who will have the key and where will the key be kept?
Hardcopy data will be maintained by the study staff in study file and REDCap. Data will be deindentified and labeled with each subject's ID. RedCap will be used for electronic data and the subject ID Log (which provides a link between the subject ID and patient name) and will be accessible to study staff.

Under the HIPAA Regulations, deidentified key codes must be stores separately from data & must not be kept on paper, but electronically. The MetroHealth Research Informatics Support should be contacted at REDcap@metrohealth.org for assistance. They will assist personnel in developing a key in MetroHealth REDcap database. They can also assist with training & development for your study. REDcap is a free database provided in part by the Case CTSA.

Explain how Data will be linked.

14.7 Data Collection Form(s):

Name	Version
PNS for SIS Data Collection and CRF Plan | History	0.02

Add data collection forms and CRFs.

View: 15-00 Data Security I

15.0 Data Security I:

It is imperative that the IRB is proactive and consistent in protecting all research data containing Protected Health Information(PHI).

15.1 * Are the records for this study (some or all) electronic? (●) **Yes** ( ) **No**

What is Protected Health Information? The Privacy Rule protects certain information that covered entities use and disclose. This information is called protected health information (PHI), which is generally individually identifiable health information that is transmitted by, or maintained in, electronic media or any other form or medium. This information must relate to 1) the past, present, or future physical or mental health, or condition of an individual; 2) provision of health care to an individual; or 3) payment for the provision of health care to an individual. If the information identifies or provides a reasonable basis to believe it can be used to identify an individual, it is considered individually identifiable health information.

The following questions must be answered when submitting a new protocol.

15.2 * Are you collecting PHI? (●) **Yes** ( ) No

15.3 Is any PHI going to be stored as paper files? (●) **Yes** ( ) No

15.4 Is any PHI going to be stored in an electronic file format? (i.e. access, excel) (●) **Yes** ( ) **No**

15.5 Is your data being stored on a laptop computer? (●) **Yes** ( ) No

15.6 Will you be using RedCap to store your data? (●) **Yes** ( ) **No**

Which RedCap Database will you be using?
Name
MetroHealth
Case

15.7 Are you planning to store your data using a portable storage device?(i.e. jump drive, external hard drive, cd) (●) **Yes** ( )
No

Per current MetroHealth Policy PHI may not be stored on portable electronic devices.

15.8 Are there any circumstances under which you would want to remove data from MHS? (i.e. take data home to work on it) Give details below. Please note identified data can't be removed from MHS unless there is permission granted in the HIPAA Authorization. If you are unsure about what is identified data please consult the IRB staff. If you feel you will need access to your data when you are off campus you should ask the MHS IT Department located in Rammelkamp room R 134 about VPN access.

◉ **Yes** ○ No

If you answered yes to question 15.8, please explain?

PHI will remain at Metro. Any data stored on portable media and/or removed from Metro would be deidentified. Such data may be transported to work on elsewhere.

15.9 Where will the records pertaining to this research be stored? (give the actual physical location of the paper records i.e building name and room number); and/or the secure network drive where the data is being stored.

State the exact physical location of paper files and the network drive for electronic files.

Electronic records (inc. electronic photos & videos): For PHI stored electronically, password protected secure MHS network drives will be used for electronic data in folders with access limited to those who are authorized by this protocol. Most study data (deidentified) will be stored in a database on Case Redcap. For portable media or other computers such as laptops, only deidentified data will be stored.

Paper records (inc. non-electronic photos & videos): For this study, these records are stored in the following staff offices which are locked when unoccupied: N5-86, N5-43. Also, the PI's office is N2-19. These records with PHI are kept in locked cabinets in these rooms.

15.10 How will these records be secured (we are refering to both paper records and electronic records)? Examples for electronic records (i.e. secure drive, password protected documents, encrypted jump drive). Examples for paper records, must be double locked (i.e. locked office and locked file cabinet or a locked file box inside a locked cabinet). Offices, Labs and storage cabinets are kept locked. EPIC, which is secured, also will be used. For PHI stored electronically, password protected secure MHS network drives will be used for electronic data in folders with access limited to those who are authorized by this protocol. Only deidentified data will be stored on portable media. Non-electronic records are kept in locked cabinets in rooms that are locked when unoccupied.

i.e. locked cabinet, locked room.

15.11 Who will have access to the data?

Give name and title exclude study staff who are MHS employees.

If necessary, representatives of the Metro IRB, NIH, and FDA will also have access.

Please Note: All study documents must be retained for a minimum of four years after study completion (even when no subjects have been enrolled), twenty-two years if study involves children or pregnant women. Records for device studies must not be assigned a destruction date until the FDA approval status is determined, at which point records will be retained according to the scheme above (minimum of four or twenty-two years as appropriate). Under HIPAA regulations you must keep a record of all medical records where you looked at or recorded PHI (without a HIPAA Authorization) for 6 years (i.e. prep for research).

MHS Record Retention Policy VII-4

15.12 How long will you keep the records pertaining to this research? Where will these records be stored after the study has been completed?

Check the MHS Record retention policy for guidance.

You must have a plan for data destruction.

The PI will store these records indefinitely since it is unknown exactly how long it will be necessary to maintain the records for possible later review and potential additional analysis in response to post-publication inquiries from the funding or scientific communities, or in support of new grant proposals. After completion of the study, the records will continue to be stored as already described:

15.13

Electronic records (inc. electronic photos & videos): For PHI stored electronically, password protected secure MHS network drives will be used for electronic data in folders with access limited to those who are authorized by this protocol. Most study data (deidentified) will be stored in a database on Case Redcap. For portable media or other computers such as laptops, only deidentified data will be stored.

Paper records (inc. non-electronic photos & videos): For this study, these records are stored in the following staff offices which are locked when unoccupied: N5-86, N5-43. Also, the PI's office is N2-19. These records with PHI are kept in locked cabinets in these rooms.

Offices, Labs and storage cabinets are kept locked. EPIC, which is secured, also will be used. For PHI stored electronically, password protected secure MHS network drives will be used for electronic data in folders with access limited to those who are authorized by this protocol. Only deidentified data will be stored on portable media. Non-electronic records are kept in locked cabinets in rooms that are locked when unoccupied.

Where, when, and how will the information be destroyed?
If and when it is determined that the information is to be destroyed, paper and electronic records will be destroyed in compliance with MHS policies and methodologies.

*Please Note: There are EPA regulations surrounding the destruction of CDs, DVDs, Floppy discs and other portable storage media. If you want to destroy these types of media please contact Ron Wallace in Environmental Services at 778-4776.

View: 15-01 Data Security II

15.1 Data Security II:

15.14 **Who (non-study staff) will have access to the records? Give name and title of individuals. Where an individual's name is not known give title i.e. monitor from CRO.**
If necessary, representatives of the Metro IRB, NIH, and FDA will have access.

List all those not study staff who will see and have access to data.

15.15 **Will data be transmitted to the sponsor?** ◉ **Yes** ○ No

Are you sending CRFs to sponsor?

15.16 **If yes, describe what data will be sent to the sponsor and the provisions that have been made for preservation of confidentiality in the transmission of data to the sponsor:**
Deidentified information and results will be sent to the funding agency (NIH).

If necessary, FDA is authorized to review information.

Please describe i.e. will you be using encryption software?

15.17 **Will the data from this research project be transmitted to anyone other than the sponsor?**
○ Yes ◉ **No**

Check yes or no.

15.18 **If yes, to whom will this data be transmitted?**

Please describe organization or individual.

15.19 **Describe the data that will be sent to entities other than the sponsor and what provisions have been made for the preservation of confidentiality:**

Please describe data, and confidentiality provisions.

View: 16-00 Request for a Partial Waiver of HIPAA Authorization

16.00 Request For a Partial Wavier of HIPAA Authorization

An IRB, under certain circumstances, may allow researchers to forgo obtaining an authorization; this is called a waiver of authorization. A waiver of authorization may be full or partial:

- full waiver: an IRB waives the requirement for authorization for all uses of PHI for a particular research protocol (see Section 16.01 Request for a Waiver of HIPAA Authorization);
- partial waiver: an IRB waives the requirement for an authorization only for some uses of PHI for a particular research protocol. Researchers are required to obtain subjects' Research Authorizations after recruiting and enrolling subjects via a partial waiver and prior to creating or using PHI during research procedures.

Partial Waiver for Preparatory for Research Activities:
According to HHS guidance on the Privacy Rule the preparatory to research provision permits covered entities to use or disclose protected health information for purposes preparatory to research, such as to aid study recruitment. However, the provision at 45 CFR 164.512(i)(1)(ii) does not permit the researcher to remove protected health information from the covered entity's site. *As such, a researcher who is an employee or a member of the covered entity's workforce could use protected health information to contact prospective research subjects.* The preparatory research provision would allow such a researcher to identify prospective research participants for purposes of seeking their Authorization to use or disclose protected health information for a research study.

Under the preparatory to research provision, a covered entity may permit a researcher who works for that covered entity to use PHI for purposes preparatory to research. A covered entity may also permit, as a disclosure of PHI, a researcher who is not a workforce member of that covered entity to review PHI (within that covered entity) for purposes preparatory to research.

16.1 Are you requesting a Partial Waiver of HIPAA Authorization? ◉ **Yes** ○ No

Check yes or no.

Why are you requesting a Partial Waviver?

16.2 Is the purpose of the Partial Waiver Recruitment (including screening of Medical Records)?
◉ **Yes** ○ No

Check yes or no.

Is the purpose of the Partial Waiver to request access to PHI for Non-MetroHealth personnel?
◉ **Yes** ○ No

16.3 Will the use of Protected Health Information (PHI) involve more than minimal risk to the privacy

Check yes or no.

of the patients?
○ Yes ◉ **No**

16.4 The IRB as part of it's review of this request must have certain reassurances that Patient Privacy will be protected, please respond to the following questions true or false.

Check true or false.

1.) The PHI will be used solely to facilitate the research protocol as an aid to study recruitment or to expand the research study. The waiver would allow identification of prospective research participants for the purpose of seeking authorization to use or disclose PHI for a research study. Essentially, PHI will be used to identify and contact potential research participants. Only contact and screening information (race, age, medications, diagnosis, and primary physician) will be recorded, and no information will leave the premises of MetroHealth Medical Center. The information will not be disclosed outside the research group for this study. ◉ **True** ○ False

2.) Information about potential subjects who are not interested in participating will be destroyed after the patient declines enrollment. The information of patients choosing to participate will be further used to schedule an appointment. As soon as the research staff sees the participant, a full authorization will be obtained to collect, use and disclose PHI for the remainder of the study. ◉ **True** ○ False

3.) The PHI will not be reused or disclosed. Because the PHI belongs to individuals who are not yet in the study, oversight provisions do not apply. After subjects are formally enrolled, an authorization will be in effect and the waiver will no longer apply. ◉ **True** ○ False

16.5 If you did not answer true to all three parts of question 16.4 please explain:

Please explain your response to any statement where you have entered false.

16.6 Please give a detailed explanation as to why this research activity cannot be practicably conducted without a Partial Waiver or without access to PHI:
While most candidates for the study are expected to be identified via direct referral from the investigators and their colleagues, or via means whereby the candidates initially contact us, some prospective candidates for the study could be identified via review of the electronic medical record system.

Example: our study population has xxx disease and we rely on the EMR information to identify and contact potential subjects.

16.7 Who will have access to PHI? Please list below:

Add the names of persons who will have access to PHI.

Name	Employer	Department	Employer Name
John Chae	Metro	PM&R	The MetroHealth System
Amy Friedl	MetroHealth	PM & R	The MetroHealth System
Douglas Gunzler	MetroHealth	Medicine	The MetroHealth System
Kristine Hansen	MHS	Physical Medicine and Rehabilitation	Physical Medicine and Rehabilitation
Terri Hisel	MHS	PM&R Research	Physical Medicine and Rehabilitation
Shannon Hogan	MetroHealth	PM & R	The MetroHealth System
Richard Wilson	Metro	PM&R	The MetroHealth System

16.8 Are you or anyone who assists you Non-MetroHealth Personnel? ◉ **Yes** ○ No

Check yes or no.

**Note all Non-MetroHealth Personnel have to go through employee orientation, have a security clearance and Epic training before they can access the MetroHealth EMR. Also all all Non-MetroHealth Personnel must work under the control of a member of the MetroHealth Staff.*

If you filed a Prep for research form with IT and RABO please attach it here.

If you have previously completed an MHS **Prep for Research form** add that form here:

Name	Version
There are no items to display	

Partial Wavier Memos completed prior to 11/26/2010 will populate here.

Old Memos Requesting Partial Waivers (prior to 11/26/2010):

There are no items to display

View: 16-01 Request for a HIPAA Waiver of Authorization

16.1 Request For a HIPAA Waiver of Authorization:

16.9 **Are you requesting a Waiver of HIPAA Authorization?**
No

Check yes or no.

Check one, if you check no then hit continue and go to the next page.

If you are requesting a Waiver In order for the IRB to Grant a Waiver you must answer questions 16.10-16.16

16.10	**Disclosure of Protected Health Information (PHI) will not involve more than minimal risk to the privacy of the patients/subjects:**	Check true or false.
16.11	**What is the plan to protect patient/subject identifiers from improper use and disclosure?**	i.e. This unique identifier will be used on the data collection form. Only the PI will have access to the key linking the unique identifier to patient/subject names.
16.12	**What is the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research?**	i.e. The unique identifier key will be retained in Red Cap and will be destroyed two years after the study ends.
16.13	**Will PHI be reused or disclosed to others:**	Check yes or no.
16.14	**Please complete the following: Data will only be used to analyze...**	i.e. Data will only be used to analyze...
16.15	**Describe why this research can not be conducted without a waiver:**	i.e because many of the subjects who participate in this treatment are dead or have transferred to other treatment modalities, or are transient. To obtain HIPAA Authorization from these individuals would be a greater risk to their loss of privacy.
16.16	**Describe why this research could not be conducted without access to and use of PHI:**	i.e. It would not be possible to determine linkages between .....and clinical outcomes without the use of PHI.

View: 16-02 HIPAA II

16.2 HIPAA II:

16.11

Which of the following identifiers about subjects will be collected for this study?

Check all that apply, your answers will help the IRB to determine if your data is a limited data set.

Name
2. Telephone Numbers
3. Address - Street
4. Address - Town or City
5. Address - State
6. Address - Zip Code
8. Names or Initials
11. Full face photographic images or comparable images
15. Medical device identifiers or serial numbers
16. Medical record or prescription numbers
18. Email addresses
20. Social Security Numbers
21. Dates (except year) related to an individual (birth date, admission date, discharge date, date of death)

*These Questions deal with the collection of data and data use agreements. If you are **not** receiving data or sending data out to another entity this does not apply to you. If you have a signed contract with a sponsor or are in a cooperative group that has a signed agreement with MHS this does not apply to you. Data use agreements specify the conditions under which data can be shared between MHS and other organizations or individuals.*

16.12 **If you have selected only numbers 4, 5, 6, or 22 in question number 16.11 your research is considered to use a limited data set. If either of the**

Check one, please read carefully if you are not receiving data or sending

following conditions apply, you will need to obtain a Data Use Agreement and complete a waiver of authorization or obtain a HIPAA authorization from the subjects. (check one):
Name
There are no items to display

data out to another entity this does not apply to you, move on to 16.14. If you have a contract with a sponsor or you are in a cooperative group that has a signed agreement with MHS this does not apply to you. In all other cases please contact the MHS Legal Department with questions about data use agreements.

16.13 Attach a copy of the Data Use Agreement:
Name Description
There are no items to display

Attach Data Use Agreement.

View: 16-03 HIPAA III

16.3 HIPAA III:

16.14 If any other unique identifying number, characteristic or code is selected, please specify:

Please specify this question refers back to the list of 22 identifiers.

16.15 If a link to an identifier will be used (i.e. code numbers) is selected, please describe the coding mechanism that will be used:
Coding mechanism will be associated with sequential enrollment at each site. At Metro, numbers will be preceded by "MH-XX-PNS-xx". Thus, the enrolled subjects would be numbered MH-XX PNS-01, MH XX-PNS-02, etc. (At UTSW, numbers will be preceded "UT-XX-PNS-xx". Thus, the enrolled subjects would be numbered UT-PNS-01, UT-PNS-02, etc.) XX- screen # and xx= subject #

Describe the coding mechanism.

16.16 Will a certificate of Confidentiality be obtained for this study? No

Check yes or no.

16.17 If yes, please attach a copy the Certificate of Confidentiality:
Name Version
There are no items to display

Attach a copy of the Certificate of Confidentiality.

16.18 Describe how you will protect the privacy of participants. Describe specifically how you will gather information from or about them. *Please note while confidentiality concerns data, privacy concerns people. Example People may be uncomfortable answering questions about their employer in an open cubicle, so investigators may arrange for a more private location.*
Subject screening, informed consent, and eligibility determination procedures as well as medical histories will be conducted in a closed room with only the necessary study personnel present. Device deployment and data collection procedures will be done in labs with closed doors and only the necessary personnel present.

Please note while confidentiality concerns data, privacy concerns people.

View: 17-00 Waiver of Informed Consent

17.0 Request for a Waiver or Alteration of Informed Consent:

17.1 Are you requesting a Waiver of Consent [45 CFR 46.116(d)] OR a Waiver of Documentation of Consent [45 CFR 46.117 (c)].
No

Answer yes or no.

If no hit continue button and you will go to the next page.

If yes please Note:

Note: Waivers of consent are not applicable if the research is subject to FDA regulations, except the following.

FDA Exception from general requirements:

1. Emergency Ues: Waivers of Informed Consent in FDA-regulated studies are permissible in case of life-threatening situations, inability to communicate, not sufficient time and no alternative method, even if research presents more than minimal risk [21CFR50.23];
2. Planned Emergency Research: If the study satisfies the requirements under 21CFR50.24 “Exception from Informed Consent Requirements for Emergency Research.”

17.2 **Waiver of Consent: If you are requesting a waiver of consent, please provide the justification and address each of the following points for the IRB's consideration:**

Check true or false.

This research study involves no more than minimal risk:

The waiver will not adversely affect the rights and welfare of the subjects:

Note: practicably does not mean it would be inconvenient.

This research could not practicably be carried out without a waiver:

Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

○ **Yes** ○ **No**

17.3 **Please explain your answers to the above questions (You must provide the IRB with enough information to make a decision):**

Please explain in detail.

An IRB may **waive the requirement to obtain a *signed* consent form** for some or all subjects if it finds either of the conditions below. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

17.4 **(1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; OR**

Check true or false.

17.5 **(2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.**

Check yes or no.

○ Yes ○ No

17.6 **If you are requesting any Alteration to the standard consent form/process (written long form consent is the standard) please provide a detailed explanation or plan.**

Example of an alteration: verbal consent.

View: 17-01 Informed Consent Process I

17.1 Informed Consent Process I:

17.7 **Who will be approached to obtain consent/assent:**

Check all that apply.

Consent Method

Subjects will be asked to sign a study consent form after receiving a complete explanation of the study.

Idendtify all Staff obtaining consent on page 1 question 1.4 by selecting the corresponding role.

17.8 **Subject Comprehension: What measures will be taken to ensure that subjects fully understand the nature of their involvement in the research?**

Please give brief explaination.

***Note to Investigator*:**

To address issues of comprehension on the part of the participant or representative, and who is involved in obtaining consent, the answers to following questions should be addressed:

1. ***Once a potential participant is identified, what process is followed to inform the subject of the study prior to obtaining a signature on the informed consent form?***
   a. ***Who introduces the study to the potential subject?***
   b. ***Who reviews the informed consent document in depth?***
   c. ***Do you require the potential participant to have another person present during the presentation of the study?***
2. ***Who answers the questions presented by the potential participant and/or family?***
3. ***What method is used to determine if the potential participant fully understands the study, what is required from them, risk and benefits, and their rights as a participant?***
4. ***Is the principal investigator usually present during the presentation of the informed consent?***

The study is first introduced in general terms by staff listed on the study (physicians, nurses, therapists). Physicians may cite the study during a clinical visit if the patient seems appropriate. Nurses/Therapists may then follow-up with the candidate. They also may introduce the study to a candidate who responds to an ad or makes other inquiries.

Typically the Clinical Coordinator conducts Consent/Eligibility Visits, reviews the ICF in depth, and answers any questions presented by the candidate and/or their caregiver(s). Candidates are not required to have another person present during the presentation of the study, but they often do so. Typically, the PI and Co-Investigators are not involved in the entire lengthy process but they would be involved for a portion of eligibility determination and, as necessary, would address questions that cannot be otherwise addressed.

An ongoing dialogue takes place during the subject's introduction to the study and the informed consent process to ensure that the candidate fully understands the study, what is required from them, risk and benefits, and their rights as a participant. Questions are encouraged and answered.

See 17.10 for more details

17.9 **Capacity to Consent: How will capacity to consent be assessed?** ***This question is to be addressed for all subjects not just those with limited decision making capacity. Identify who will make this assessment? Suggested language....all subjects will be awake, alert and oriented, be able to read etc. It is important to address issues like ability to read and understand information in the consent.***

How will you determine capacity to consent?

All subjects will be awake, alert, and oriented. The PI or physician co-investigator will use their clinical discretion in making the final determination.

17.10 **Attach a description of the Consent Process: Explain the process of obtaining consent from subjects. Under what settings and conditions will consent be obtained? What will be the timing/waiting period? What measures will be taken to ensure that subjects will make decisions independently?** *Note to Investigator: The "informed consent process" should include sufficient time for the participant to review and consider participating with the assistance of family members, research partners or representative if necessary. Other items to consider regarding time / waiting periods are: Is the potential participant given a copy of the consent form to read prior to the discussion of the study? Is it presented in person or mailed (where they can review it in the privacy of their own home)? How much time elapses between the presentation of the study and informed consent form and the actual signing of the form? The answers to these questions will ensure the PI has considered this component of the process and will reassure the IRB that the PI is allowing adequate time for the participant to make an informed decision and minimize the possibility of coercion or undue influence.*

Attach a plan for consenting subjects. This must give detail about the consent process.

Name	Description
Informed Consent Process (01-09-2009) | History	
UTSW Informed Consent Process.docx | History	

17.11 **Parental Permission and Youth Assent: Complete this question only if enrolling minors. How will parental permission and youth assent (if applicable) be obtained?**

Give details of assent process and assent form.

View: 17-02 Informed Consent Process II

17.2 Informed Consent Process II:

17.12 **What method will be used to document the consent process (i.e. a note in EPIC)? Not how you will get consent only how you will document consent has been obtained, i.e chart note, note in study file.**

i.e chart note, note in study file.

Subjects will sign a consent form. The original consent form will be scanned into EPIC and placed in the study file. EPIC will be used to schedule subjects and to document the informed consent process.

17.13 **What type of Informed Consent will be used in this study? (check all that apply):**

Check all that apply

Consent Type
Written/Signed Consent by Subject
Video/Audio Consent Form

A non-return cover memo applies to a study in which you are sending out a questionnaire with a memo or letter that informs participants about the study but does not need to be signed and returned. If they complete and return the questionnaire they have given consent.

17.14 **If other, please specify:**

If other, please give specifics.

****Attach all consent forms (Informed Consent, Genetic Consent and HIPAA) here:****

17.15 Please attach a copy of each Informed Consent form(s) and HIPAA Authorization you are using for this study:

Attach Consent form(s) and HIPAA Authorization here

Name	Version
Metro - PNS for SIS Consent & HIPAA Authorization v1.7(track).doc	0.13
Metro - PNS for SIS Consent & HIPAA Authorization(1.7)	0.12
PNS for SIS HIPAA Alternative Means 1.1 (11-Sep-2019)	0.02
PNS for SIS HIPAA Alternative Means 1.1 (11-Sept-19) - tracked.doc	0.01
PNS for SIS Video-Photo Consent 1.0 (22-Aug-2017)	0.01
UTSW - PNS for SIS Consent & HIPAA Authorization v2.1(track).docx	0.04
UTSW - PNS for SIS Consent & HIPAA Authorization v2.1	0.07
UTSW - PNS for SIS HIPAA Alternative Means 1.2	0.02
UTSW - PNS for SIS HIPAA Alternative Means 1.2 (track).doc	0.01

17.16 Will non-English speaking subjects be enrolled?

Check one

○ Yes ◉ No Clear

If the answer to 17.17 is no we will not be enrolling non-English speaking subjects then tell the IRB why not?

Please give the IRB an explanation as to why non-English speaking subjects will not be enrolled.

There is a significant amount of patient documentation (consent forms, manuals, questionnaires) that would require translation. Also, the research, and the necessary interaction with the study team, requires understanding of

17.17 If non-English speaking subjects will be enrolled please provide information about the person(s) obtaining consent (what language they will speak)and how you will deal with written translation(s):

Provide information about translating consents and having interpertative services available for consent.

View: 18-00 Data Safety Monitoring I

Section 18.0 Data Safety Monitoring Plan

DATA AND SAFETY MONITORING PLAN GUIDE

WHEN DO YOU HAVE TO COMPLETE A DATA SAFETY MONITORING PLAN?

FOR THE IRB- **All interventional studies that are greater than minimal risk should have a Data Safety Monitoring Plan. The IRB reserves the right to require a Data Safety Monitoring Plan for any study.**

Archived IRB Data Plans - prior to 9/28/2010

FOR THE CRU- **ALL CRU PROTOCOLS [Recent NIH guidelines stipulate that all protocols that involve human subjects, a signed consent form and are conducted on, or use the resources of, the CTSA Clinical Research Unit - MHMC (CRU) are required to have a Data and Safety Monitoring Plan (DSM Plan).]**

What is a Data and Safety Monitoring Plan (DSM Plan)?

A DSM Plan is a prospectively defined strategy to assess the assumptions made in the trial design while the study is in progress. Its main purpose is to ensure the safety of participants in clinical research studies and the validity and integrity of research data collection. A properly designed DSM Plan improves the scientific quality and yield from a clinical trial and the protection of human subjects.

The DSM Plan needs to address the nature of the safety monitoring and who will be conducting that monitoring. It may be reasonable for a single individual to perform the monitoring in a small trial with minimal/low risk while a local independent or an external data and safety monitoring board (DSMB) may be required for more complex/high risk trials.

Key elements to be incorporated in a DSM Plan

- **Assessment of risks and monitoring level**
- **Safety contact: Who is responsible?**
- **Safety monitoring: Who will do it? How often?**
- **Informed consent process; consistency with the protocol**
- **Data collection process**
- **Adverse Events Monitoring: Anticipated and unanticipated**
  - **Description of anticipated adverse events**
  - **Grading and attribution method**
  - **Reporting of unanticipated adverse events**
  - **Plans for periodic reporting**
  - **Impact on termination of subjects from the study and study closure**

Step 1 - only for Investigators Using the CRU:

1.A Is your protocol approved and supported by the Ireland Cancer Center? ○ Yes ◉ **No**

If Yes - The Comprehensive Cancer Center Data and Safety Moniotoring Plan for Clinical Trials is on file. Proceed to Step 5.1.B If No, Proceed and complete Steps 2-5

****

Step 2 - all Investigators - Provide Information in order to determine the level of safety monitoring required

2.A List all data collection types and study procedures (this information will pull from Section 8 Methods and Procedures questions 8.1, 8.2, 8.3)

Data Collection types:
Name
Audio-Recording/Video-Recording/Photographs
Chart Review - Prospective
Existing/Retrospective Data/Specimens
Interviews, questionnaires or psychological tests

Social-Behavioral Procedures:
Name
Surveys/Questionnaires

Medical Procedures:
Name
Collection of Biohazardous Substances
Study of Human Biological Materials (i.e. Urine Collection)
Investigation/Approved Devices
Study of Existing Data
Medical Tests, Comparisons, Evaluations
Clinical Assessments (EEG, EKG, SCID, etc.)
Venipuncture (Blood Draw)
Magnetic resonance imaging (MRI) without contrast
Use of investigational devices

****

You must select the risk level Please read the information below, check the applicable boxes and select an appropriate risk level.

Level I: Minimal and Low Risk Studies (examples of studies that are minimal and low risk studies)

Types of Studies:
Name
Chart Review, interview, questionnaire

Level II: Moderate Risk Studies (examples of studies with populations, drugs, and procedures that are moderate risk)

Types of Studies:
Name
There are no items to display

Level III: High Risk Studies (examples of diagnostic procedures and drugs or device studies which are high risk)

Types of Studies:
Name
There are no items to display

2.B If you do not see your study procedures on the above list please add in the procedures being done for research purposes:

Add additional risk(s):

Procedure	DSMB Risk
Outcomes Assessments (questionnaires, tests of arm and shoulder movement & strength, pain thresholds)	Moderate
Percutaneous electrode implant procedure/short term implant and e-stim	Moderate
Percutaneous electrode removal	Minimal or Low
Physical Therapy	Minimal or Low
Venipuncture	Minimal or Low
X-Ray & Ultrasound	Minimal or Low

Select the Appropriate Level of Risk for this study based on the criteria above:

Level of Risk:
Risk Level II Moderate Risk Studies

Now Select the appropriate Level of Monitoring and give your justification:

2.C Rank Level of Monitoring (select one by checking the box)

Minimal/Low/Moderate Levels of Monitoring ☑

Justification for selecting Minimal/Low/Moderate Level of Monitoring Required:
The most notable study procedure is the short-term percutaneous electrode implantation and electrical stimulation. As detailed later in this application, the device is FDA Cleared via 510(k) and this is considered to be a Non Significant Risk procedure considering the time frame of less than 60 days. Also, the researchers have extensive experience with the associated procedures and risks, which are well tolerated by subjects. The risks are low, well understood and well managed. Thus, the lower level of monitoring will be sufficient.

High Level of Monitoring ☐

Justification for selecting Risk High Level of Monitoring:

View: 18-01 Data Safety Monitoring II

18.01 Data Safety Monitoring II

A designee will perform the safety monitoring:
◉ **Yes** ○ No

Identify the designee [provide contact information]:
At the study team level, the PI will have oversight. Safety monitoring at Metro also will be overseen by: Kristine Hansen, PT Study Coordinator; x73584; khansen1@metrohealth.org

A medical monitor or independent individual/safety officer will be performing the safety assessments.
○ Yes ◉ **No**

Identify who will be performing the safety assessments [provide contact information]:
In addition to PI oversight, medical safety monitoring will be a DSMB role (see below).

Has a Data Safety Monitoring Board or Committee been established for this study?
◉ **Yes** ○ No

Identify these members by name, title and qualifications. How often will the DSMB meet? How frequently will the DSMB report it's findings?) data prior to 9/28/2010 read only.

If there is a DSMB or DSMC is it a nationally constituted Data and Safety Monitoring Committee? ○ Yes ◉ **No**

Please enter the Name of Contact or Chair, Address and Phone or E-Mail:
DSMB Charter attached below.

Dennis Bourbeau, PhD; Chair
Researcher
MetroHealth Rehabilitation Institute of Ohio
4229 Pearl Rd
Cleveland, OH 44109
dbourbeau@fescenter.org
216-778-4414

Is there a locally constituted Data and Safety Monitoring Committee or Board that will perform the safety monitoring. Specify composition and responsibilities in the box below.
Note: Board Members should not have conflicts with this study or with study personnel. ○ Yes ◉ **No**

Names of Members of Local DSMB [provide contact information]:

3.B.1 Description of anticipated adverse events. Pulled from question 10.5.

1) Risks associated with needle insertion for Lead placement
Tissue damage, such as puncturing a blood vessel, irritating a nerve, or temporary bruising or pain at the insertion site may occur when the needle is placed.
• The risks of bruising and pain are common.
• The risks of puncturing a blood vessel or irritating a nerve are uncommon.
• It is possible, but rare, that you could feel dizzy or faint during the procedure.
To reduce this risk, the needles will be placed carefully by a trained doctor. In addition, local anesthesia (numbing medication) will be used to reduce the risk of pain. If you have a history of fainting, the procedure will be done with you lying down on your side.

It is possible that it may take more than one try to place the Lead (wire) in your shoulder. If this happens, you will have a needle placed in your shoulder more than once.

2) Risk of skin irritation, infection, or inflammation at the Lead exit site
Skin irritation, infection, or granuloma formation (mild tissue inflammation) may occur at the Lead exit site.
• Skin irritation is common.
• Infection and granuloma are rare.
Symptoms include redness, swelling, or pain. To reduce this risk, you should keep your shoulder clean and dry. After the Lead has been placed (Visit 3), it is important that the exit site remain clean and dry and be monitored as long as the Lead remains in place. You should notify the study staff if you see changes in skin color or have any discomfort where the Lead exits your skin.

To minimize the risk of infection:
To minimize the risk of infection, you must follow the specific instructions for the care of the electrode site.
• After electrode placement, the transparent dressing should be changed 3 days after the placement procedure or if the dressing becomes wet. This initial dressing will also be changed by study staff one week after the placement procedure.
• To minimize the risk of infection after this period, you should keep the electrode exit site clean and dry, and look for changes in skin color or sensitivity.
• You will be asked to change the dressing every 2-3 days or if the dressing becomes wet.

• If an infection occurs, it must be treated promptly. Untreated or delayed treatment of infection is very dangerous and could lead to severe complications including kidney failure, heart attack, stroke, blood clots or death. One participant who developed an infection did not follow the specific instructions for the care of the electrode site and did not come in for his scheduled follow-up appointment after the implantation. The participant was hospitalized, but subsequently died during the hospitalization. The cause of death is thought to be a heart attack, but the exact cause and its relationship to the infection are not known.

3) Risk of the Lead breaking beneath the skin

There is a possibility that the Lead may break beneath your skin either during stimulation or during the procedure to pull the Lead out at the end of the treatment period. This risk is uncommon. When a Lead breaks, one or more Lead pieces could stay in your body. An x-ray will be taken to see if any pieces remain in your body. Dr. Wilson will use his judgment to decide if the Lead pieces should be removed.

4) Risk of tissue infection from a piece of the Lead remaining in your shoulder

An infection or granuloma can happen during the study (as mentioned above) or after the study if a piece of the Lead stays in your body. This risk is uncommon. Symptoms of an infection or granuloma include swelling, pain, or fever. If this happens, Dr. Wilson, or an appropriately qualified doctor, will remove the piece of Lead and/or give you the necessary treatment (such as antibiotics) for this infection.

5) Risks of removing pieces of the Lead from your body

If Lead pieces need to be removed, Dr. Wilson will make a small cut in your skin and pull out the Lead pieces, which are usually right under the skin. The risks of doing so include discomfort during the procedure and skin irritation or infection where the pieces were removed. Call the study staff if you see any signs of redness, swelling, or pain. This risk is rare.

6) Risk of the Lead moving from its original position or coming out

It is possible that the Lead may move from its original location or come out during the treatment period. This risk is rare.

• If the Lead moves from its original position slightly and the stimulation is still comfortable, nothing will be done.

• If the Lead has moved a lot or come out of your shoulder, you may be asked if you are interested in having another Lead placed in your shoulder. Whether or not you get another Lead will depend upon your length of time in the treatment period, whether or not your shoulder is healthy enough to have another Lead placed, and if you agree to it.

• The risk of the Lead moving from its original location is that you could feel discomfort from the stimulation or “pins and needles”.

If your Lead comes out or moves from its original location and you decide to have another Lead placed, you would again be exposed to the same risks of placing the original Lead.

7) Risk of skin irritation under the Sprint Pad, or bandages

The skin under the Sprint Pad, or bandages can get irritated. Skin irritation is common. Symptoms include redness and itching. To reduce this risk, medical grade tapes and bandages will be used. The Sprint Pad, and bandages should not be applied to unhealthy skin (such as skin that has scars or recent surgical incisions) to avoid irritation. If there is irritation, the Sprint Pad, or bandages will be moved slightly to a different area of your shoulder, or different bandages will be used.

8) Risk of the Sprint Stimulator working incorrectly

There is a small chance that the Sprint Stimulator may stop working correctly. It is very unlikely that this will be harmful to you. This risk is rare. If there is a problem with the Sprint Stimulator, electrical stimulation will turn off automatically. You should call the study staff if the Sprint Stimulator shows an error message or you can’t turn the stimulation on.

9) Risks for pregnant women

The effects on the developing child of using electrical stimulation during pregnancy and the risk of birth defects are unknown. Therefore, women who are pregnant may not participate in this study. Women should not become pregnant while participating in this study. If you are a woman of childbearing age and potential, you should use birth control during the treatment phase of the study. Your doctor can discuss birth control methods with you. If you become pregnant during the study, notify the study staff immediately. Electrical stimulation will be turned off, the Lead will be removed, and you will be withdrawn from the study.

10) Risk of discomfort due to electrical stimulation

• The small amounts of electricity delivered to your shoulder muscle could feel like a tingling or vibrating sensation.

• You could also feel pain or discomfort if the level of stimulation is too high or if your muscle becomes tired from stimulation (known as muscle fatigue).

This risk is uncommon. The study staff will carefully choose a level of stimulation that is comfortable for you during set up of the system.

• You may also feel a tingling sensation under the Sprint Pad.
This is not expected to be uncomfortable. If stimulation is painful, you should turn off the stimulation and notify the study staff.

If the Lead starts to come out of your body, you may feel electrical stimulation near your skin surface, which could feel like “pins and needles” and may be uncomfortable. If you think your Lead has started to come out, you should turn off the Sprint Stimulator and notify the study staff.

11) Risks associated with Diathermy
Tissue damage can happen if you receive diathermy, a form of short-wave or microwave therapy that may be used to apply deep therapeutic heat for the treatment of selected medical conditions such as relief of pain, muscle spasms, and joint contractures. Diathermy over or near the Lead may heat it and hurt the tissue. You must not receive diathermy during the study. You also must not receive diathermy after the study if a piece of the Lead remains in your shoulder. This risk is rare.

12) Risks associated with MRI
If you have an MRI procedure while the Lead, or a piece of the Lead, is in your body, you could have tissue damage. You can tell that you might be having tissue damage because you might feel warming, burning, or muscle contraction. To minimize this risk, you should always tell study staff before you schedule an MRI. Study doctor, or an appropriately qualified doctor, will remove the Lead and may remove any remaining pieces of the Lead. During the treatment period, you should carry this consent with you to show to medical staff to explain that you have a metal Lead in your shoulder if you need an emergency MRI. This risk is rare.

13) Risk of allergic reaction to anesthetic (numbing) medication and/or risk of accidental injection of anesthetic into a vein
• There is a risk that you might have an allergic reaction to the local anesthetic used just before the Lead is inserted. You could feel itching, have problems breathing, or get a swollen tongue (common signs of an allergic reaction).
If you were to have an allergic reaction, it would probably happen while you were still at MetroHealth. If you feel these things after you leave, notify the study staff right away. This risk is rare.
• There is also a risk that the numbing medication (anesthetic) could be accidentally administered into a blood vessel. If this happens, it could affect your heart, blood vessels, and/or nerves. This could cause your heart and/or breathing to stop.
This risk is rare. Your doctor is trained on how to administer the numbing medication correctly.

14) Risk of worsening of pain symptoms
Your shoulder pain may get worse during this study. The risk of your pain getting worse is uncommon.

15) Risks of Therapy and performing shoulder exercises
Your shoulder pain may be worse during therapy or during home exercises. This risk is common. All exercises will be done under the supervision of a trained therapist during Therapy Visits and you will be trained to perform home exercises as safely as possible.

16) Risks of Outcomes Assessments
• The questionnaires present no risks other than a rare risk of psychological harm since answering some of the questions may make you feel uncomfortable or uneasy. You have the right to review these surveys before you begin participating in the study and you may skip any questions that you do not wish to answer.
• The assessments of range of motion, strength and functional ability may be uncomfortable.
• The assessments of your sensitivity to pain are uncomfortable and may cause brief skin irritation.
This risk is common.

17) Risk of MRI visit
For the MRI visits, there are no expected risks associated with the MRI itself. However, these visits will be treated like any clinically-prescribed MRI visit. The usual common concerns associated with MRI will be explained at each visit. Because the MRI machine acts like a large magnet, it could move metallic objects in the MRI room during your examination that could possibly harm you. Precautions have been taken to minimize such an event from happening.

For example, loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you cannot have an MRI. Body piercing jewelry must be removed for scanning. Some tattoos could experience localized heating, although patients having tattoos are routinely scanned without problems. Cold compresses could be applied if heating were to occur.
Having an MRI may mean some added discomfort for you. In particular, you may be bothered by

feelings of claustrophobia [being closed in a small space] and by the loud banging noise during the test. Temporary hearing loss has been reported from this loud noise. This noise will be diminished by the headphones you will be asked to wear to follow verbal commands. If you would also like to wear earplugs, they will be provided as long as you can still hear commands through the headphones. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

The MRI scan being done is designed to answer research questions, not to examine your shoulder medically. This MRI scan is not a substitute for one a doctor would order. However, if we believe that we have found a medical problem in your MRI scan, we will refer you to your primary care physician for further assessment. Since it is possible that an MRI abnormality could be suspected during this study, it is possible that you could experience worry or anxiety regardless of whether the abnormality was later confirmed.

18) Risks associated with X-ray
You are agreeing to participate in a research project that involves the use of imaging procedures that exposes you to radiation. This section will discuss the risks associated with imaging procedures that are for research only. Your doctors may order additional imaging procedures as part of your normal patient care that also expose you to radiation. Those normal imaging procedures are not included in the risk discussion below. Please discuss those procedures and radiation risks with your doctors.

As part of this research study, you may be asked to have imagining procedures that involves two x-ray images of your shoulder. This will help to ensure there are no pieces of an implant left in your body. The x-ray procedure exposes you to radiation. The amount of radiation that you could receive is approximately 0.06% of the amount allowed annually for persons exposed to radiation as part of their work or about 1% of the amount that we are all exposed to annually as part of our natural background radiation exposure.

19) Other
Since you will not know which treatment group you are in, there is a rare risk of psychological harm.

Lastly, there may be risks and discomforts that are not yet known.

When PHI is involved there is the rare risk of a privacy breach.

There may be other risks as yet unknown.

Additional Comments on anticipated adverse events:

3.B.2 Safety data/procedure used to preform evaluation:

Data to be evaluated:
Name
Subject interview and/or contact
Subject's physical exam
Subject's symptoms or performance status
Interim Assessment of AE (e.g. midway, quarterly, semiannually, etc.)

Who will evaluate safety data:
The PI and study staff meet at least semi-annually to review all adverse events and study data collected since the previous meeting. The staff reviews all adverse events to determine a course of action.

The Data and Safety Monitoring Board convenes semi annually to review and monitor the progress of the study with respect to enrollment, drop-outs, outcomes and safety.

Frequency of Monitoring:
Name
6 Months

3.C. Grading method and attribution for adverse event reporting:

Grading method and attribution for adverse event reporting

The PI must identify what scale will be used to grade adverse events (AEs) and indicate his/her attribution/assessment of the relationship between the adverse event and the protocol/intervention. Each protocol may have a unique approach to grading adverse events and the PI should consult the parent protocol and/or funding source for specific grading scales. Suggested guidelines for the grading of adverse events are available below:

Example A: Cancer Therapy Evaluation Program (CTEP) Common Toxicity Criteria (CTC II) available for viewing at http://ctep.info.nih.gov (see "Reporting Guidelines, Common Toxicity Criteria")

Example B: Common grading scale

0 No adverse event or within normal limits or not clinical significant
1 Mild AE, did not require treatment
2 Moderate AE, resolved with treatment
3 Severe AE, resulted in inability to carry on normal activities and required professional medical attention
4 Life threatening or disabling AE
5 Fatal AE

3.C.1 Identify the scale to be used to Grade AEs in this study:

CRU Safety Scale:
Name
AEs will be graded using another system (specify and attach description).

3.C.2 Identify the attribution scale to be used in this study:

CRU Attribution Scale:
Name
The PI will determine the relationships of AEs to test procedure/device/agent as not related, possibly related, or definitely related, using standard criteria for clinical trials.

3.D. Population being studied: (populated from your answers to Sections 11.00 and 12.00)

Vulnerable subject groups? No

Children? No

Decisionally Impaired Subjects? No

Pregnant Women and/or Fetuses? No

Will you be enrolling Prisoners? No

Other Populations being studied:

Vulnerable Populations
There are no items to display

The study does not target any of these groups although it is possible that some subjects would be associated with one or more of the groups (e.g., poor, elderly, minorities).

**** Note More Frequent monitoring intervals may be needed for vulnerable populations.***

4.A. Plan for Adverse Event Reporting:

All Reportable Events (Anticipated and Unanticipated events) from this protocol must be submitted using the MHA eIRB Reportable event form in a timely maner consistent with MHS IRB SOPs.

In addition to the MHS IRB adverse events and Uanticipated problems will be reported to:

Reporting Institutions (check all that apply):
Name
National Institutes of Health (NIH)

If other has been selected above please specify:

4.B Stopping Rules or Conditions under which Subjects can be removed from the Study [this information is from Section 10.01 of the Protocol Risks/Benefits Questions

Are there defined Stopping Rules? Yes

What are the stopping rules for the study? The study could be terminated at any time for valid scientific reasons or reasons related to the protection of subjects participating in this study. A reason for study termination includes but is not limited to the discovery of an unexpected, significant, or unacceptable risk to the participants enrolled in the study.

What findings, events, or conditions would require a research subject to be removed from the study? (i.e. disease progression)
The research subject may be removed if they develop any condition during the course of the study

which would preclude the safe use of stimulation or otherwise impair their safe participation in any study activity.

4.D. Additional Information (if Applicable):

Provide any other information relevant to the data and safety monitoring plan that was not already incorporated into this form.
The PI and respective project staff meet at least semi-annually to review all adverse events and study data collected since the previous meeting. The staff reviews all adverse events to determine a course of action.

The DSMB will meet at least semi annually.

The PM&R Research Team reviews study safety information (AEs) quarterly.

Attach A copy of your Data Safety Monitoring Plan or other relevant information related to this form:

Name	Version
DSMB Report to PI 12 December 2018.pdf	0.01
PM&R Research Team Routine Study Safety Review Procedure	0.02
Wilson - DSMB Charter - PNS for SIS - Final 12DEC2018	0.03

View: 19-00 Use of Human Biological Materials In Research I

19.0 Use of Human Biological Materials In Research I:

19.1 Will Human Biological Materials be collected as part of this study? (i.e. blood, tissue, fluids and substances etc.)
Yes

If no, hit continue and you will be taken to the next page.

Check yes or no.

19.2 Will the storage or transportation of study materials place anyone at a health risk? In other words, are these biohazardous materials? Will they put the staff collecting them or transporting them at risk?
No

Check yes or no.

19.3 If yes, please explain:

Please explain the risks. Above and beyond universal precautions.

19.4 Will information from the materials be stored in an electronic database?
Yes

Check yes or no.

19.5 If yes, list the database(s) where the information from the materials will be stored and who will have access to them:
urine samples will be collected to confirm eligibility for subjects when necessary. Samples will be taken and tested at Metro using the standard clinical procedures and Metro Lab. Results are made available via EPIC.

List the database(s) and who will have access to them.

19.6 Human Biological Material Destruction: please describe the plan for materials destruction (when, where, how and by whom):
Standard Metro Lab procedure.

Give the destruction plan i.e. shipped back to sponsor for destruction at end of study, incinerated by Browning Ferris 3 months after study ends.

19.7 Storage of Human Biological Materials: please describe where, how and for how long the materials will be stored:
Standard Metro Lab procedure.

Physical storage of materials where will it be, how will it be stored and for how long.

View: 19-01 Use of Human Biological Materials in Research II

19.1 Use of Human Biological Materials In Research II:

19.8 Does this research involve human cell/lines and/or products that are made from human biological materials? ○ Yes ◉ **No**

Check Yes or No.

If yes, please explain:

Please explain.

19.9 Will Human Biological Materials (tissue, blood or salavia) be collected in this study for genetic research?
No

Check Yes or No.

If Yes, please provide additional discussion of the genetic testing components including who will conduct the tests:

19.10 **If yes, can subject(s) decide not to participate in the genetic research and still participate in the study?** — Check Yes or No.

Please submit the appropriate genetic consent/tissue storage form and attached at 17.15
A template for this form can be found on the IRB Home Page. Note: if tissue storage is mandatory for participation in a study the subject consent must be included in the body of the consent form; if it is not mandatory it can be included as a separate page at the end of the consent form.

19.11 **Will NIH Genome-Wide Association Studies (GWAS) be conducted?** ○ Yes ◉ **No** — Check Yes or No.

19.12 **Will you be sending samples/data to the NIH GWAS?** ○ **Yes** ◉ **No** — Check Yes or No.

19.13 **Will you be using sample/data obtained frm the NIH GWAS?** ○ Yes ◉ **No** — Check Yes or No.

19.14 **Please provide justification for using NIH GWAS:** — *Please explain.*

If this is a GWAS study you will need to submit a **Patient Information Sheet (add at 17.16)**. This sheet should summarize the Genetic research component of this study and tell the subjects where their biological materials will be sent, what analysis they will undergo, who will have control of them and for how long and who to contact if they want to withdraw their permission. It must be clear to subjects that these samples will not be housed at MHS nor will the MHS Investigator retain control over them.

View: 20-00 Drug Information I

20.0 Drug Information I:

20.1 *** Does this study involve drugs?** No — If you check no and hit continue you will go to the next page.

If you are doing a drug study you may be required by law to register that study at Clinical Trials.gov Section 113 of the FDA Modernization Act mandates registration with ClinicalTrials.gov of investigational new drug efficacy trials for serious diseases or conditions. For more information click on the link below:
http://prsinfo.clinicaltrials.gov/registering.pdf

If you answer no and hit continue you will go to the next section.

Does this study involve:

Is the study drug(s) FDA approved for this indication? ○ Yes ○ No

Does this study involve use of a Placebo? ○ Yes ○ No

Does this study have a drug washout period? ○ Yes ○ No

Do you have an IND? ○ Yes ○ No

If yes please give the IND: (include a copy of the FDA approval letter at 20.4)

Who is the sponsor or holder of the IND?

Does this study have an IND exemption? (include a copy of the FDA exemption letter at 20.4) ○ Yes ○ No

20.2 **Fill in an entry for all drugs that will be used in the study:** — Please give a complete list.

Drug Name	FDA Approved (yes, no)	IND Number	Supplied By
There are no items to display			

20.3 **Manufacturer (name, address):** — Answer only if produced commercially.

20.4 **Attach a copy of:** — *Attach the IB, 1572 and 1571 here.*
1.) Investigator Brochure and/or Package Insert
2. FDA Form 1571 Investigational new Drug Application Form
3.) FDA Form 1572 Statement of the Investigator Form

4.) FDA Correspondence (i.e. FDA Approval Letter for IND, FDA Exemption letter)

Name	Description
There are no items to display	

View: 21-00 Medical Device Information I rev

21.0 Medical Device Information I:

Definition of a Medical Device:

An instrument, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is

- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in man or other animals.
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

In short any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for *in vitro* diagnosis (IVD) of disease and other medical conditions such as pregnancy.

21.1 **Is this a Medical Device Study?** Yes — Answer yes or no.

If you are doing a device study you may be required by law to register that study at Clinical Trials.gov Section 113 of the FDA Modernization Act mandates registration with ClinicalTrials.gov of investigational new device efficacy trials for serious diseases or conditions. For more information click on the link below:

http://prsinfo.clinicaltrials.gov/registering.pdf

If you answer no and hit continue you will go to the next section.

21.2 **Medical Device Generic Name:** — Give generic name.
Peripheral Nerve Stimulator

21.3 **Medical Device Brand Name:** — Give brand name.
The Sprint PNS System

Medicare Code Number:
21.4 **N/A**

As stated in regulations 21 CFR 812.3(m), a device may be considered a, Significant Risk Device, if it meets any of the following criteria and a determination is made by the IRB that the device presents a potential for serious risk to the health, safety or welfare of a subject.

21.5 **Is this device intended as an implant?** No — Check one

21.6 **Is device to be used in supporting or sustaining human life?** No — Check one

21.7 **Is the device for use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health?** — Check one
No

21.8 **Does this device present a potential for serious risk to the health, safety, or welfare of a subject?** — Check one
No

21.9 **If you answered NO to all the above, or if an initial risk assessment has determined that this is a non-significant risk device (21CFR 812.3), attach the appropriate documentation for this justification:** — Attach justification.

Name	Description
There are no items to display	

21.10 **What is the regulatory status of the study device?** — Provide information on the regulatory status of the device.
FDA Cleared via 510(k)

21.11 **What is the long term plan for device management once the study closes?** — Provide information such as how you will communicate important information to subject; plan for
Devices are not retained by subjects beyond the PNS Treatment Phase.

maintenance/repairs; contact information besides the PI.

View: 21-01 Medical Device Information II

21.1 Medical Device Information II:

21.12 What is the FDA Approval date? Please give date.
5/31/2018

21.13 What is the Premarket Approval (PMA)number? Please give number.
N/A

21.14 What is the Premarket Notification (510K) number? Please give number.
K181422

21.15 What is the Investigational Device Exemption (IDE) number? Please give IDE number if applicable.
N/A

Who is the sponsor or holder of the IDE?

21.16 What is the Humanitarian Device Exemption (HDE) number? Please give HDE number if applicable.
N/A

21.17 Has this medical device ever been used in animals? Check one
No

21.18 If yes, please give a brief summary of the results of studies involving animals: Give a brief summary or attach one below at 22.16.

21.19 Please attach supporting documents: Give a brief summary.

Name	Description
K181422 Documentation.pdf | History	
Sprint PNS System Device Description | History	

View: 21-02 Medical Device Information III

21.2 Medical Device Information III:

21.20 Has this medical device ever been used in humans? Yes Check yes or no.

21.21 If yes, please give a brief summary of the results from studies involving humans: Give a brief summary.
Note: The Smartpatch System discussed here has been renamed the Sprint PNS System subsequent to FDA clearance. The Sprint PNS System also is being used in two other current studies of ours at Metro (IRB16-00172 & IRB16-00510).

Principals of SPR Therapeutics (a subsidiary of NDI Medical) and NDI Medical have been involved in the study of peripheral nerve stimulation through percutaneous lead placement for the treatment of post-stroke shoulder pain for more than a decade. Current SPR and NDI staff participated in sponsoring and managing the published studies (led by Dr. John Chae, who continues these studies and is an advisor to SPR) described below. Using the identical Smartpatch Lead and identical stimulus parameters, percutaneous peripheral nerve stimulation for the treatment of post-stroke shoulder pain has been evaluated in multiple studies at Case Western Reserve University by Chae and associates.

Yu, Chae, and colleagues conducted a double-blind crossover trial to determine whether sensation associated with percutaneous electrical stimulation is less painful than sensation associated with surface electrical stimulation. Subjects rated the pain of each treatment modality using a VAS and the Pain Rating Index of the McGill Pain Questionnaire11. The median scores on the VAS and the Pain Rating Index were lower for percutaneous electrical stimulation than for surface electrical stimulation (p=0.007 and p=0.018, respectively), indicating less pain with percutaneous electrical stimulation. In addition, nine out of ten subjects stated that they would prefer to receive percutaneous electrical stimulation over surface electrical stimulation.

A case report of a chronic stroke patient suffering from shoulder subluxation and pain, who was unable to tolerate surface electrical stimulation, suggested initial clinical feasibility of six weeks of percutaneous peripheral nerve stimulation for the treatment of post-stroke shoulder pain. The authors, including current SPR staff, then conducted an exploratory case series in which eight chronic stroke survivors received six weeks of percutaneous electrical stimulation to their posterior deltoid and supraspinatus muscles. Subjects experienced a significant improvement in subluxation and self-reported pain. Furthermore, this study also demonstrated significant improvement in pain related

quality of life based on the pain domain of SF-36.

Yu, Chae and associates, including current SPR and NDI staff, then went on to enroll 61 subjects into a multi-center single-blinded randomized controlled study to assess the safety and effectiveness of percutaneous electrical stimulation for post-stroke shoulder pain. To qualify for participation in the study, subjects had to be more than 12 weeks post stroke and rate their shoulder pain as at least a 2 on the pain intensity question of the Brief Pain Inventory, which is an 11-point numeric rating scale that asks subjects to rate their worst shoulder pain in the last week. Treatment subjects had four percutaneous leads placed in the posterior deltoid, middle deltoid, supraspinatus, and upper trapezius muscles. They were instructed to keep stimulation ON for a total of 6 hours a day during the 6-week treatment period. Control subjects were given a cuff type sling to use whenever the hemiplegic arm was unsupported during the 6-week treatment period and permitted to continue other pain therapies such as PT, OT, and medications.

Subjects were assessed at baseline, at 3-weeks, at EOT, and at 3-, 6-, and 12-months post-EOT. The primary outcome measure was the same as in the present study (BPI pain intensity). However, these data were collected on the BPI form rather than a subject diary. Secondary measures included the same Pain Interference Question of the BPI (BPI 9) as is planned for use in the present study and a variety of physical functioning assessments, including pain-free passive external rotation range of motion (ROM) of the glenohumeral joint.

The group receiving electrical stimulation demonstrated a significantly higher success rate (as measured by a minimum 2-point reduction on the scale) than the control group (84% vs. 31%, p=.001 at the end of treatment; and 63% vs. 21%, p=.001 for all follow-up visits). In addition, 34% (11 subjects) of the group receiving electrical stimulation were pain free (reported "0", indicating no pain) at the EOT compared to only 3.4% (one subject) in the control group.

The 32 subjects randomized to the treatment group each had four percutaneous leads placed that were identical to the Smartpatch Lead. The lead placement procedure was well tolerated. All leads remained intact and free of infection during the 7-week indwelling period. Of the 128 leads placed in this study, the tips of five leads (3.9%) among four subjects (12.5%) broke during removal, none of which resulted in an adverse event. Granuloma formation defined as localized tissue inflammation exhibited by redness, swelling, or pain at the lead exit site was noted for five leads (3.9%) in two subjects (6.3%). All granulomas resolved after lead removal with no further intervention required.

The authors concluded that percutaneous electrical stimulation is safe and effective in reducing post-stroke shoulder pain, with sustained pain reduction in a cohort of subjects to at least 12 months after the end of treatment. Placement of leads in proximity to peripheral nerves within target muscles bypasses cutaneous pain receptors, which minimizes the discomfort of stimulation and ensures stable electrode placement. Further, once placed, skilled personnel are not needed on a daily basis to place electrodes to ensure effective positioning.

In an IRB approved Non Significant Risk (NSR) study, eight chronic stroke survivors with post-stroke shoulder pain, five with subluxation and three without, received three weeks of peripheral nerve electrical stimulation, 6-hrs daily via a single Smartpatch Lead placed between the motor points of the middle and posterior deltoids, which produced strong contractions of both muscles. The primary outcome measure was pain intensity (BPI 3) on the short form of the BPI. Longitudinal analysis demonstrated that participants experienced significant reduction in pain intensity. Participants also experienced significant reduction in pain interference with daily activities based on BPI 9 ($F=5.9$, $p<0.01$), and significant improvement in QoL based on the bodily pain component of the SF-36 ($F=12.8$, $p<0.001$). All 8 participants exhibited significant pain reduction at EOT. This study indicated that the three-week, single-lead approach produced pain relief comparable to the more complex six week, 4-lead approach. The three participants without subluxation all exhibited substantial pain reduction, which reinforced that pain reduction is not mediated by improvements in subluxation and that subluxation is the not a necessary inclusion criterion.

Additional testing was conducted in 5 subjects to validate the design of the Smartpatch Stimulator and other external components. This design validation of a non-stimulating Smartpatch System provided evidence that the Smartpatch System meets user needs regarding usability and comfort. Physical aspects of system usage, such as making cable connections, attachment between Stimulator and Pad, and attachment to the skin, were reported as easy and acceptable. Software aspects of the Smartpatch Stimulator usage, such as starting and stopping stimulation, identifying the battery level, and adjusting

stimulus intensity were all reported as easy and acceptable.

Furthermore, a stimulating Smartpatch System has been used by 3 subjects to date in an ongoing IDE study being conducted under G090085. In this protocol, the system is used in the Trial Stage for determining eligibility for our implantable system. All three subjects completed the Trial Stage and were able to use the Smartpatch components successfully to deliver their stimulation therapy. Subjects completed satisfaction surveys upon completion of Smartpatch System use. All three subjects reported that it was easy to understand how to use the Smartpatch System and that the System was easy to operate. Two subjects reported that the pad wasn't sticky enough, sometimes causing them to use more than one Pad per day. Subjects in the proposed study will be given more guidance on the proper preparation of the skin to ensure pad adhesion. The subjects reported that the covering bandages used were of an acceptable adhesion and size, but two subjects reported that the Lead Connector Tapes were difficult to use. All three subjects reported that the system as comfortable, "not at all" bothersome to wear, and that they were comfortable going out in public with the system on. The subjects reported that they were satisfied with their experience in the study, felt that the study had a positive impact on their lives, and would recommend participation in the study to a friend.

21.22 Please list all research personnel authorized to use the study device:

List all research personnel authorized to use study device.

Name	Employer	Department	Employer Name
John Chae	Metro	PM&R	The MetroHealth System
Travis Cleland	MetroHealth	Physical Medicine and Rehabilitation	The MetroHealth System
Amy Friedl	MetroHealth	PM & R	The MetroHealth System
Kristine Hansen	MHS	Physical Medicine and Rehabilitation	Physical Medicine and Rehabilitation
Terri Hisel	MHS	PM&R Research	Physical Medicine and Rehabilitation
Shannon Hogan	MetroHealth	PM & R	The MetroHealth System
Chong Kim	metrohealth	PMR	The MetroHealth System
Victoria Whitehair	The MetroHealth System	PM&R	The MetroHealth System
Richard Wilson	Metro	PM&R	The MetroHealth System

21.23 How will this medical device be used in research?

Give a brief description.

Percutaneous IM PNS System: The Sprint PNS System (SPR Therapeutics, Cleveland, OH) is used to deliver the IM PNS. The System consists of a small external stimulator, percutaneous IM lead, and pad. The external stimulator "snaps" on to the pad. The pad has an embedded power source for the System but also serves as the anode. The pad is replaced regularly based on treatment parameters, allowing the investigative team to prescribe the total dosage based upon the number of pads. The single-channel stimulator outputs a biphasic current waveform with current pulse parameter ranges that are suitable for IM PNS. The IM electrode, originally developed at the Cleveland FES Center, has a coiled helical configuration wound from a 7-strand type-316LVM stainless-steel wire insulated with a poly-fluorocarbon, similar to Teflon®. These electrodes have been used extensively to deliver percutaneous IM PNS to shoulder muscles. [19, 36, 37, 39-42, 62, 75]

Lead Placement Procedure:

IM PNS Group: The procedure is performed under a sterile condition. The location and depth of the electrode implant site are determined by monopolar needle stimulation with demonstration of strong contraction of both the middle and posterior deltoid muscles. [18, 19, 39, 42] The introducer loaded with the IM lead is inserted perpendicular to the skin surface and advanced to the depth (3-4 cm) defined by the monopolar test stimulation. The introducer is then withdrawn with the electrode retained in the muscle by a barb at its tip.

Control Group: In order to facilitate blinding, control participants receive an IM electrode placed between the middle and posterior deltoid muscles similar to the IM PNS group. The only difference is that the monopolar electrodes are not used to guide IM electrode implantation so that no electrical stimulation is ever provided.

PNS Treatment Protocol:

IM PNS Group: After one week for lead stabilization [87] the Sprint System is programmed for stimulation. Based on over 30-yrs of experience, the Cleveland FES Center established parameters for safe and effective delivery of IM PNS (pulse frequency = 12 Hz; amplitude (0.2-30 mA) and pulse duration (10-200 μsecs) (set by clinician); duty cycle = 2-sec ramp-up, 16-sec

plateau, 2-sec ramp down, 10 sec off; daily dose = 6 hrs/day). [88] These parameters provide strong fused comfortable muscle contraction with minimal fatigue. [19, 36, 37, 39-42, 61, 62, 75, 89-91] Stimulation frequency is fixed. The pulse duration and amplitude are set to produce strong, comfortable contraction of both the middle and posterior deltoids. A balanced biphasic waveform allows an equal amount of current to flow in either phase, creating a safe net zero charge. [92] Participants receive a total of 6 hrs of stimulation per day in their home. The stimulator keeps an electronic log for compliance monitoring. There are no formal dose response studies to provide guidance on the optimal dose of IM PNS; however, the selected duty cycle and daily dose of 6-hrs were used in our prior studies [19, 36, 37, 39-42] and by others with robust results. [75]

Control Group: Control participants will receive an identical stimulator that will be placed in sham-stimulation mode by the nurse coordinator. The stimulator appears to function identically to that used in the active stimulation group and the battery drains with use, although no stimulation is delivered. All participants are queried at their final visit to determine the success of blinding. The implanted electrode poses minimal risk to control participants. The probability of serious adverse event (e.g. infection) for IM electrodes is 0.0006 per electrode. [41] The implantation of electrodes is no more painful than subcutaneous infiltration of lidocaine.

Electrode and Electrode Site Surveillance and Electrode Removal: All caregivers and participants are trained in the assessment of electrode site and the daily placement of the Sprint device. The caregiver conducts daily inspections to detect complications. The nurse coordinator inspects the site for infection and performs motor/sensory threshold testing for lead migration and lead integrity, respectively, at the following times: within 48-72 hrs of lead placement, at the beginning of PNS treatment, and at the EOT. Inspection and testing of motor/sensory thresholds and impedance may also occur anytime during the 3-wk PNS treatment period as deemed necessary. At the EOT, the electrode is removed by gently pulling on the external portion. All participants undergo radiographic surveillance for retained electrode fragments.

21.24 **Please list all possible complications:** List all complications.

Complications are addressed in the Risks for the Study (duplicated from 10.5):
1) Risks associated with needle insertion for Lead placement
Tissue damage, such as puncturing a blood vessel, irritating a nerve, or temporary bruising or pain at the insertion site may occur when the needle is placed.
• The risks of bruising and pain are common.
• The risks of puncturing a blood vessel or irritating a nerve are uncommon.
• It is possible, but rare, that you could feel dizzy or faint during the procedure.
To reduce this risk, the needles will be placed carefully by a trained doctor. In addition, local anesthesia (numbing medication) will be used to reduce the risk of pain. If you have a history of fainting, the procedure will be done with you lying down on your side.

It is possible that it may take more than one try to place the Lead (wire) in your shoulder. If this happens, you will have a needle placed in your shoulder more than once.

2) Risk of skin irritation, infection, or inflammation at the Lead exit site
Skin irritation, infection, or granuloma formation (mild tissue inflammation) may occur at the Lead exit site.
• Skin irritation is common.
• Infection and granuloma are rare.
Symptoms include redness, swelling, or pain. To reduce this risk, you should keep your shoulder clean and dry. After the Lead has been placed (Visit 3), it is important that the exit site remain clean and dry and be monitored as long as the Lead remains in place. You should notify the study staff if you see changes in skin color or have any discomfort where the Lead exits your skin.

To minimize the risk of infection:
To minimize the risk of infection, you must follow the specific instructions for the care of the electrode site.
• After electrode placement, the transparent dressing should be changed 3 days after the placement procedure or if the dressing becomes wet. This initial dressing will also be changed by study staff one week after the placement procedure.
• To minimize the risk of infection after this period, you should keep the electrode exit site clean and dry, and look for changes in skin color or sensitivity.
• You will be asked to change the dressing every 2-3 days or if the dressing becomes wet.

• If an infection occurs, it must be treated promptly. Untreated or delayed treatment of infection is very dangerous and could lead to severe complications including kidney failure, heart attack, stroke, blood clots or death. One participant who developed an infection did not follow the specific instructions for the care of the electrode site and did not come in for his scheduled follow-up appointment after the implantation. The participant was hospitalized, but subsequently died during the hospitalization. The cause of death is thought to be a heart attack,

but the exact cause and its relationship to the infection are not known.

3) Risk of the Lead breaking beneath the skin

There is a possibility that the Lead may break beneath your skin either during stimulation or during the procedure to pull the Lead out at the end of the treatment period. This risk is uncommon. When a Lead breaks, one or more Lead pieces could stay in your body. An x-ray will be taken to see if any pieces remain in your body. Dr. Wilson will use his judgment to decide if the Lead pieces should be removed.

4) Risk of tissue infection from a piece of the Lead remaining in your shoulder

An infection or granuloma can happen during the study (as mentioned above) or after the study if a piece of the Lead stays in your body. This risk is uncommon. Symptoms of an infection or granuloma include swelling, pain, or fever. If this happens, Dr. Wilson, or an appropriately qualified doctor, will remove the piece of Lead and/or give you the necessary treatment (such as antibiotics) for this infection.

5) Risks of removing pieces of the Lead from your body

If Lead pieces need to be removed, Dr. Wilson will make a small cut in your skin and pull out the Lead pieces, which are usually right under the skin. The risks of doing so include discomfort during the procedure and skin irritation or infection where the pieces were removed. Call the study staff if you see any signs of redness, swelling, or pain. This risk is rare.

6) Risk of the Lead moving from its original position or coming out

It is possible that the Lead may move from its original location or come out during the treatment period. This risk is rare.

• If the Lead moves from its original position slightly and the stimulation is still comfortable, nothing will be done.

• If the Lead has moved a lot or come out of your shoulder, you may be asked if you are interested in having another Lead placed in your shoulder. Whether or not you get another Lead will depend upon your length of time in the treatment period, whether or not your shoulder is healthy enough to have another Lead placed, and if you agree to it.

• The risk of the Lead moving from its original location is that you could feel discomfort from the stimulation or “pins and needles”.

If your Lead comes out or moves from its original location and you decide to have another Lead placed, you would again be exposed to the same risks of placing the original Lead.

7) Risk of skin irritation under the Sprint Pad, or bandages

The skin under the Sprint Pad, or bandages can get irritated. Skin irritation is common. Symptoms include redness and itching. To reduce this risk, medical grade tapes and bandages will be used. The Sprint Pad, and bandages should not be applied to unhealthy skin (such as skin that has scars or recent surgical incisions) to avoid irritation. If there is irritation, the Sprint Pad, or bandages will be moved slightly to a different area of your shoulder, or different bandages will be used.

8) Risk of the Sprint Stimulator working incorrectly

There is a small chance that the Sprint Stimulator may stop working correctly. It is very unlikely that this will be harmful to you. This risk is rare. If there is a problem with the Sprint Stimulator, electrical stimulation will turn off automatically. You should call the study staff if the Sprint Stimulator shows an error message or you can’t turn the stimulation on.

9) Risks for pregnant women

The effects on the developing child of using electrical stimulation during pregnancy and the risk of birth defects are unknown. Therefore, women who are pregnant may not participate in this study. Women should not become pregnant while participating in this study. If you are a woman of childbearing age and potential, you should use birth control during the treatment phase of the study. Your doctor can discuss birth control methods with you. If you become pregnant during the study, notify the study staff immediately. Electrical stimulation will be turned off, the Lead will be removed, and you will be withdrawn from the study.

10) Risk of discomfort due to electrical stimulation

• The small amounts of electricity delivered to your shoulder muscle could feel like a tingling or vibrating sensation.

• You could also feel pain or discomfort if the level of stimulation is too high or if your muscle becomes tired from stimulation (known as muscle fatigue).

This risk is uncommon. The study staff will carefully choose a level of stimulation that is comfortable for you during set up of the system.

• You may also feel a tingling sensation under the Sprint Pad.

This is not expected to be uncomfortable. If stimulation is painful, you should turn off the stimulation and notify the study staff.

If the Lead starts to come out of your body, you may feel electrical stimulation near your skin

surface, which could feel like “pins and needles” and may be uncomfortable. If you think your Lead has started to come out, you should turn off the Sprint Stimulator and notify the study staff.

11) Risks associated with Diathermy
Tissue damage can happen if you receive diathermy, a form of short-wave or microwave therapy that may be used to apply deep therapeutic heat for the treatment of selected medical conditions such as relief of pain, muscle spasms, and joint contractures. Diathermy over or near the Lead may heat it and hurt the tissue. You must not receive diathermy during the study. You also must not receive diathermy after the study if a piece of the Lead remains in your shoulder. This risk is rare.

12) Risks associated with MRI
If you have an MRI procedure while the Lead, or a piece of the Lead, is in your body, you could have tissue damage. You can tell that you might be having tissue damage because you might feel warming, burning, or muscle contraction. To minimize this risk, you should always tell study staff before you schedule an MRI. Study doctor, or an appropriately qualified doctor, will remove the Lead and may remove any remaining pieces of the Lead. During the treatment period, you should carry this consent with you to show to medical staff to explain that you have a metal Lead in your shoulder if you need an emergency MRI. This risk is rare.

13) Risk of allergic reaction to anesthetic (numbing) medication and/or risk of accidental injection of anesthetic into a vein
• There is a risk that you might have an allergic reaction to the local anesthetic used just before the Lead is inserted. You could feel itching, have problems breathing, or get a swollen tongue (common signs of an allergic reaction).
If you were to have an allergic reaction, it would probably happen while you were still at MetroHealth. If you feel these things after you leave, notify the study staff right away. This risk is rare.
• There is also a risk that the numbing medication (anesthetic) could be accidentally administered into a blood vessel. If this happens, it could affect your heart, blood vessels, and/or nerves. This could cause your heart and/or breathing to stop.
This risk is rare. Your doctor is trained on how to administer the numbing medication correctly.

14) Risk of worsening of pain symptoms
Your shoulder pain may get worse during this study. The risk of your pain getting worse is uncommon.

15) Risks of Therapy and performing shoulder exercises
Your shoulder pain may be worse during therapy or during home exercises. This risk is common. All exercises will be done under the supervision of a trained therapist during Therapy Visits and you will be trained to perform home exercises as safely as possible.

16) Risks of Outcomes Assessments
• The questionnaires present no risks other than a rare risk of psychological harm since answering some of the questions may make you feel uncomfortable or uneasy. You have the right to review these surveys before you begin participating in the study and you may skip any questions that you do not wish to answer.
• The assessments of range of motion, strength and functional ability may be uncomfortable.
• The assessments of your sensitivity to pain are uncomfortable and may cause brief skin irritation. This risk is common.

17) Risk of MRI visit(MetroHealth only)
For the MRI visits, there are no expected risks associated with the MRI itself. However, these visits will be treated like any clinically-prescribed MRI visit. The usual common concerns associated with MRI will be explained at each visit. Because the MRI machine acts like a large magnet, it could move metallic objects in the MRI room during your examination that could possibly harm you. Precautions have been taken to minimize such an event from happening.

For example, loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you cannot have an MRI. Body piercing jewelry must be removed for scanning. Some tattoos could experience localized heating, although patients having tattoos are routinely scanned without problems. Cold compresses could be applied if heating were to occur.
Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia [being closed in a small space] and by the loud banging noise during the test. Temporary hearing loss has been reported from this loud noise. This noise will be diminished by the headphones you will be asked to wear to follow verbal commands. If you

would also like to wear earplugs, they will be provided as long as you can still hear commands through the headphones. At times during the test, you may be asked to not swallow for a while, which can be uncomfortable.

The MRI scan being done is designed to answer research questions, not to examine your shoulder medically. This MRI scan is not a substitute for one a doctor would order. However, if we believe that we have found a medical problem in your MRI scan, we will refer you to your primary care physician for further assessment. Since it is possible that an MRI abnormality could be suspected during this study, it is possible that you could experience worry or anxiety regardless of whether the abnormality was later confirmed.

18) Other
Since you will not know which treatment group you are in, there is a rare risk of psychological harm.

Lastly, there may be risks and discomforts that are not yet known.

When PHI is involved there is the rare risk of a privacy breach.

There may be other risks as yet unknown

21.25 **Please list all precautions, warnings, and contraindications:**
Detailed precautions, warnings, and contraindications are detailed in the manuals attached at 27.1.

List all precautions, warnings and contraindications.

View: 21-03 Medical Device IV

21.03 Medical Device IV

INVESTIGATOR'S RESPONSIBILITY FOR CONTROL OF THE INVESTIGATIONAL DEVICES:
To protect the rights, safety and welfare of research participants the investigator must ensure control and accountability of all devices used in conjunction with clinical research protocols. To make certain that investigational devices are used only on research participant's who have signed the informed consent form specific for the device and IDE number.

Please check these boxes

21.26 ☑ The device will not be used on a research participant until FDA(when FDA regulated investigational device is being studied) and IRB approval has been obtained and the research participant has signed an informed consent document.

21.27 ☑ The informed consent document will inform the research participants that their names and information will be shared with the device company for tracking purposes.

21.28 ☑ The investigation will be conducted in accordance with the signed agreement with the sponsor, the investigational plan, and all applicable laws and regulations.

21.29 ☑ The device will be used only in accordance with the MHS IRB approved protocol.

21.30 ☑ The Investigator is thoroughly familiar with the appropriate use of the investigational device, as described in the protocol, in the product information, and in other information sources provided by the sponsor.

21.31 ☑ All persons assisting with the trial are adequately informed about the protocol and the investigational product(s).

21.32 ☑ Devices will be properly maintained and cleaned.

21.33 ☑ Research participants will receive adequate instructions about the investigational device to assure their safe participation in a research study.

21.34 **Any investigational devices used in conjunction with an investigational protocol must be kept in a locked and secured area. Access to investigational devices must be limited to personnel designated by the Principal Investigator. Please describe How you will secure the investigational devices to be used in this study and who will have access to them.**
Device accountability will be maintained by the Investigator and his study staff. All devices that are not deployed will be secured by the research staff in their offices and/or labs. Dr. Wilson and Krissy Hansen/Study staff will have primary responsibility for device accountability, but the other staff listed in this protocol will share responsibility.

21.35 **Attach copies of device logs, see examples of logs on the IRB Home Page in the IRB Guidelines Section under MHS Medical Device Guidelines :**

Name	Version
PNS for SIS Device Inventory Log | History	0.03

View: 22-00 Clinical Trials Registration

22.0 Clinical Trials Registration:

Note: Phase 2 - 4 trials of drugs and biologics (controlled clinical investigations other than Phase 1 investigations of a product subject to FDA regulation) AND trials of devices (controlled trials with health outcomes, other than small feasibility studies and pediatric post-marketing surveillance) must be registered per the Food and Drug Administration Act of 2007; NIH encourages registration of all trials, regardless of whether required under applicable law.

How are study protocols submitted to ClinicalTrials.gov?
The FDA Guidance Document (March 2002) (http://www.fda.gov/cder/guidance/4856fnl.htm) describes the submission criteria. The NLM has developed the Protocol Registration System (PRS), a Web-based tool for submitting information to ClinicalTrials.gov. Study sponsors or their representatives may register online to apply for a PRS account (http://prsinfo.clinicaltrials.gov/).

22.1 Has this trial been registered on www.clinicaltrials.gov?
◉ **Yes** ○ No

Web link to clinical trails website.

22.2 If **Yes**, who registered the trial?(i.e. sponsor, investigator)
Investigator

Please respond

22.3 Please provide ClinicalTrials.gov Identifier (i.e. NCT00391872)

NCT03752619

The sponsor can provide you with this information or you can look it up on the website.

22.4 If **No**, are there plans to register the study? ○ Yes ○ No

If you answer No you must provide an reason why this study will not be registered.

22.5 If the answer to 22.4 is **No**, provide and explanation:

Provide a response if the answer to 22.4 is No.

View: 23-00 Interview/Focus Groups

23.0 Interview/Focus Groups:

23.1 Does this study involve Interviews/Focus Groups? No

Answer yes or no.

If you answer no and hit continue you will go to the next page.

23.2 Attach copies of any scripts/or questions that will be used to guide the interview focus/groups:

Attach scripts or questions.

Name	Version
There are no items to display	

23.3 Idendtify all Staff conducting interviews on page 1 question 1.4 by selecting the correct role.

23.4 Is there any specific training or qualifications needed to conduct the interviews/focus groups?

Describe training and/or qualifications.

View: 24-00 Psychological Testing

24.0 Psychological Testing:

24.1 Does this study involve Psychological testing? No

Answer yes or no.

If you answer no and hit continue you will go to the next page.

24.2 First Please list all Psychological Tests that will be given:

First please list the test(s)/measures to be used.

24.3 Attach copies of all psychological test(s)/measures that will be used for this study:

Second attach copies of all test(s)/measures.

Name	Version
There are no items to display	

24.4 Is there any necessary training or licenses required of those administering the psychological testing?

Describe any training or licenses required to administer test(s).

Idendtify all Staff Administering tests on page 1 question 1.4 by selecting the correct role.

View: 25-00 Surveys/Questionnaires

25.0 Surveys/Questionnaires:

25.1 Does this study involve Surveys/Questionnaires? Yes

Answer yes or no.

If you answer no and hit continue you will go to the next section.

25.2 Please attach all questionnaires and/or surveys to be used in this study:

Attach survey(s)/questionnaire(s).

Name	Version
BDI-2 | History	0.01
BPI-SF_English-LastWeek | History	0.01
FABQ | History	0.01
PCS- Pain Catastrophizing Scale | History	0.01
PGIC Questionnaire (Shoulder Studies, Feb-2017) | History	0.01
SF-12v2 health survey | History	0.01
Shoulder Pain and Disability Index (SPADI) | History	0.01

25.3 Idendtify all Staff conducting Surveys on page 1 question 1.4 by selecting the correct role.

View: 26-00 Deception

26.0 Deception:

Deception is a research methodology. When deception is used in research the subject is not told, or is misled, about the true purpose of the research, such as in certain studies of group processes, contextual influences on cognition, etc.

26.1 Does this study involve the use of deception as a study design method for the research? No

Deception is defined as intentionally misleading or withholding information about the nature of the experiment.

If you checked no then hit the continue button and you will be taken to the next page.

26.2 Describe in detail the nature of the deception and explain why this is necessary for the research:

Please describe the nature of the deception.

26.3 State how, when and by whom the research subjects will be debriefed:

Briefly describe your plan to debrief subjects.

View: 27-00 Additional Documents

27.0 Additional Documents:

27.1 Are there any additional study documents you wish to attach to this application?

Attach any additional study documents i.e protocols supplied by sponsor.

Name	Version
Bandage Change Instructions | History	0.02
Electrode Fragment Information Sheet 4.0 | History	0.01
Electrode Fragment Wallet Card | History	0.02
Human Investigation Consent Addendum letter(X-ray risk).docx | History	0.01
Instructions for Care of Electrode Exit Site 1st 48 hrs | History	0.03
IRB Local Context Intake_Relying site(UTSW)_02March2020.pdf | History	0.01
PNS For SIS - Posture exercises.pdf | History	0.01
PNS for SIS - SIS Treatment Exercise Program.pdf | History	0.01
PNS for SIS prone shoulder exercises.pdf | History	0.01
PNS for SIS Subject Schedule.docx | History	0.01
Sprint Clinician - Sham mode | History	0.01
Sprint Clinician Manual | History	0.02
Sprint Patient Manual | History	0.02
Sprint Stimulator Subject Set up | History	0.01
UTSW - Instructions for Care of Electrode Exit Site 1st 48 hrsv1.1.docx | History	0.03
UTSW - Overall PI Lead Study Team Checklist.pdf | History	0.01
UTSW Local Context Language-02-21-20.pdf | History	0.01
UTSW sIRB Communications Plan.pdf | History	0.01

View: The End

To Finalize this application you must do two things:

1.) As a final step you should click on Hide/Show Errors on the top of this page. If there are any required fields in the Application you have omitted they will show up in red. If you click on each item you will be taken to that page of the application so you can complete the question.

Note: Unless all named Co-investigators have agreed to participate you will not be able to submit your study. Co-Investigators have to press the Co-Investigators agree to participate button. You can send them an email message tellng them to do this by pressing

Notify Co-Investigators of Need to Agree to Participate. The minute you have selected your Co-Investigators you can press this button it is not advisable to wait until you have completed the application as it may hold up your submission.

When all error messages are gone then...

2.) Click Finish

Please click on the "Finish" button to finalize and exit the Study application. Doing so will **NOT** submit the application for review.

3.) The PI must press the Submit Study button (when they are ready to submit to the IRB)

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must push **" Submit Study"** in the blue area on the left hand side of the page under **My Activities**. Only the PI will have this button it will not be visible to any other study team members.

You can track the ongoing status of your submission by logging into the study workspace. On the top left hand side of the page in the light blue area there will be a box labeled with the **Current State** of your study.

Please contact the IRB with any questions or concerns. When calling the IRB Office Please direct your questions to the IRB staff named as the "Owner" of your study.

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Terri Hisel

Study Role:
Name
Research Support Staff
Interviewer (Survey, Focus Group)

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Douglas Gunzler

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** David DiLorenzo

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Steven Lewis

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** John Chae

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Chong Kim

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Victoria Whitehair

Study Role:
Name
Co-investigator

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Kristine Hansen

Study Role:
Name
Study Coordinator
Research Support Staff
Interviewer (Survey, Focus Group)
eIRB Notification Recipient

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Amy Friedl

Study Role:
Name
Research Support Staff
Interviewer (Survey, Focus Group)
Obtaining Informed Consent

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Shannon Hogan

Study Role:
Name
Research Support Staff
Obtaining Informed Consent

View: CRU DSMP Data Collection Simple View
Name: Chart Review, interview, questionnaire
Level of Risk: Minimal and Low Risk Studies
Type: Data Collection
View: Create CRU Procedure Risk

CRU Procedure Risk:	
Procedure	Risk
* Outcomes Assessments (questionnaires, tests of arm and shoulder movement & strength, pain thresholds)	* Name ○ Minimal or Low ◉ Moderate ○ High

View: Create CRU Procedure Risk

CRU Procedure Risk:	
Procedure	Risk
* Percutaneous electrode implant procedure/short term implant and e-stim	* Name ○ Minimal or Low ◉ Moderate ○ High

View: Create CRU Procedure Risk

CRU Procedure Risk:	
Procedure	Risk
* Percutaneous electrode removal	*

				Name Minimal or Low Moderate High

View: Create CRU Procedure Risk

	CRU Procedure Risk:			
		Procedure		Risk
		* Physical Therapy		* Name Minimal or Low Moderate High

View: Create CRU Procedure Risk

	CRU Procedure Risk:			
		Procedure		Risk
		* Venipuncture		* Name Minimal or Low Moderate High

View: Create CRU Procedure Risk

	CRU Procedure Risk:			
		Procedure		Risk
		* X-Ray & Ultrasound		* Name Minimal or Low Moderate High