Clinical Trials Cover Page: Study Protocol and Statistical Analysis Plan

Document Date: 11/5/2021

Multimodal Treatment for Hemiplegic Shoulder Pain

NCT02893267

Date: Friday, November 05, 2021 2:47:55 PM
View: 01-00 Study Information

Print Close

1.0 Study Information:

1.1 * **Short Title:** PNS+PT for HSP

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:**
Multimodal Treatment for Hemiplegic Shoulder Pain

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:**

	Name	CREC Status	CREC Expiration	COI	COI Expire	Management Plan?	Study Roles	Employer Name	Non-Compliance
View	Shannon Hogan	Certified	2/23/2023	no	6/4/2022		Research Support Staff Obtaining Informed Consent	The MetroHealth System	
View	John Chae	Certified	9/1/2022	yes	7/2/2022	yes	Co-investigator	The MetroHealth System	
View	Kristine Hansen	Certified	4/6/2023	no	7/7/2022		Research Support Staff Interviewer (Survey, Focus Group) Study Coordinator Obtaining Informed Consent DRA (only one)	Physical Medicine and Rehabilitation	
View	Amy Friedl	Certified	3/16/2023	no	7/2/2022		Research Support Staff Obtaining Informed Consent	The MetroHealth System	
View	Terri Hisel	Certified	10/18/2022	no	6/5/2022		Research Support Staff	Physical Medicine and Rehabilitation	

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	Nathaniel Makowski	Certified	6/16/2022	no	6/2/2022		Research Support Staff	The MetroHealth System	
View	Victoria Whitehair	Certified	4/11/2022	no	7/2/2022		Research Support Staff	The MetroHealth System	
View	Douglas Gunzler	Certified	12/1/2022	no	7/2/2022		Research Support Staff	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	

1.17

Please attach approval letter/letters.

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:
9/1/2016 — *Anticipated Date Study to Begin (1st Patient)*

Anticipated End Date:
5/31/2021 — *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	4	4	8
Not Hispanic or Latino	44	44	88
Ethnic Category Total of All Subjects	48	48	96

Racial Category

	Females	Males	**Total**
American Indian/Alaska Native	0	0	0

Asian	6	4	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	15	15	30
White	27	29	56
Racial Categories Total of all Subjects	48	48	96

View: CRU 01-02 CRU Resource Needs

2.00 CRU: Resource Needs

Hospital Lab Tests: ◉ **Yes** ○ No

Hospital Lab Tests = CRU draws 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 01-08 Use of CRU Facilities or Equipment Only

8.00 CRU: Use of CRU Facilities or Equipment Only

8.01 Use Of Equipemnt: ○ Yes ◉ **No**

8.02 Use Of Equipment List:

8.03 Use Of Space: ◉ **Yes** ○ No

8.04 Use Of Space Description:
Lab space at Old Brooklyn Health Center routinely will be used.

8.05 Other (Specify):

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:

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?

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

◉ **Yes** ○ No

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?

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

◉ **Yes** ○ No

1.21 What facilities are available to conduct the research? Are they adequate? Please describe.

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

Visits will take place in our labs in PM&R at OBHC.
Some visits may be completed via phone, email or telehealth

Nursing Resources:

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

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

○ Yes ◉ **No**

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
- ☐ 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 deciding if further science review is necessary.

Additional Reasons Why Science Review May Be Required

Investigator-initiated study

4.3 Does this study require review by the Biosafety Committee?

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

No

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+PT NOA	0.01
Summary Statement 1R01HD084564-01A1 2016_04_14 (Scientific Review)	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

Check yes or no.

received?
○ Yes ○ 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 and PT for HSP Grant	

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

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:

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

Name of Site	Address	Telephone Number
There are no items to display		

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

Select yes or no.

○ Yes ○ No

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

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

○ Yes ○ No

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

Attach letter.

Name	Description
There are no items to display	

6.6 Has the external site granted permission for the research to be conducted?

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.

○ Yes ○ No

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?

Please answer yes or no.

◉ **Yes** ○ 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.

Please answer yes or no.

◉ **Yes** ○ **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.

The Shirley Ryan Ability Lab(SRAL) formally Rehabilitation Institute of Chicago (RIC) will serve as a second performance site.

The Investigators and respective project staff will meet or confer at least semi-annually 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.

Carolinas Rehabilitation will serve as a third performance site.

The Investigators and respective project staff will meet or confer at least semi-annually 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.

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:

Country	Address of Research Facility
There are no items to display	

Give country and location.

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.

Hemiplegic shoulder pain (HSP) affects up to 60% of moderate to severely impaired stroke survivors. [12] HSP is associated with poor rehabilitation outcomes, including interference with activities of daily living (ADLs) [13] and poor quality of life (QoL). [14] While many treatments for HSP have been proposed, most do not result in long-term relief of pain.

Our team developed the use of intramuscular peripheral nerve stimulation (PNS) for the treatment of HSP, which involves the temporary placement of a percutaneous intramuscular electrode to stimulate the axillary nerve motor points to the deltoid muscle. [8, 15-22] The deltoid muscle is stimulated for 6 hours per day for 3 weeks, causing comfortable, non-fatiguing contractions. This treatment, which occurs in the community setting, results in pain relief for up to 12 months when compared to treatment with a hemisling. [21] A systematic review of randomized controlled trials (RCT) concluded that intramuscular PNS was the only treatment to provide long-term relief of pain for those with HSP. [23] However, physical therapy (PT), which focuses on correcting biomechanics, is the most commonly prescribed treatment for HSP [24] and is recommended by multiple practice guidelines. [5-7] Prior to acceptance by the clinical community, the superiority of PNS to a course of PT must be demonstrated. We completed a pilot RCT comparing PNS to PT and 67% vs. 25% of participants experienced successful pain relief (i.e., $\geq$ 2-pt or 30% reduction [25]) from PNS and PT, respectively. [8] Thus, the primary objective of this 3 site RCT is to confirm the findings of this preliminary pilot RCT.

Consistent with prior studies, only 2/3 of PNS participants in our preliminary RCT experienced clinically important pain relief. And among these, only a third experienced complete pain relief. Unfortunately, for those with HSP, the altered shoulder biomechanics associated with hemiparesis provides a risk for reinjury even if pain is improved at the end of treatment; this may require co-treatment with PT. There is an opportunity to refine the PNS treatment regimen and thereby increase the magnitude of the response and the number of responders. Consistent with clinical practice, participants in the PT group in our preliminary RCT

experienced an average pain reduction of 33% by the end of treatment. Combining PNS and PT, which may be how PNS is actually implemented in clinical practice, may have a synergistic therapeutic effect. Thus, the second objective of this multisite RCT is to determine if multimodal treatment of HSP with PNS + PT is more efficacious for pain relief than PNS alone or PT alone.

The mechanisms behind PNS and PT for the treatment of HSP are not known. The onset of HSP is associated with the severity of hemiparesis and the resultant biomechanical impairment of the shoulder. [12, 26-28] Our team and others have found that in the chronic stage central mechanisms may also have a role in perpetuating pain, [10, 29-32] as it does in other forms of chronic shoulder pain. [9] Thus, our third objective is to explore mechanisms of PNS and PT for the treatment of HSP. PNS and PT may reduce chronic HSP via central mechanisms, or by improving shoulder biomechanics, or both. These mechanisms will be explored via measures of sensory and pain perception (mechanical pain thresholds, secondary hyperalgesia, and temporal summation) and clinical measures of impairment (shoulder abduction torque, shoulder kinematics, Fugl-Meyer score.)

This pilot-phase II device trial will advance the knowledge about chronic HSP treatment by testing single and multimodal treatments to produce greater pain reduction and increase the number of responders. Information regarding mechanism of action that may lead to future treatment improvements will also be generated. The collaborators involved in this project are leaders in utilizing PNS to reduce pain and disability after stroke and are well positioned to carry out this trial.

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. Compare the efficacy of PNS vs. PT in reducing HSP.
Hypothesis 1. The reduction in HSP and associated improvements in upper limb related ADLs and QoL will be greater with PNS alone versus PT alone.

AIM 2. Compare the efficacy of PNS + PT, PNS + ShamPT, and PT + ShamPNS in reducing HSP.
Hypothesis 2. The reduction in HSP and associated improvements in upper limb ADLs, and QoL will be the greatest with PNS + PT, followed by PNS + Sham PT, and finally PT + Sham PNS.

AIM 3. Explore the roles of central and biomechanical mechanisms in pain reduction by PNS and PT.
Hypothesis 3. Improvement in measures of central sensitization (mechanical pain thresholds, secondary hyperalgesia, and temporal summation) will be greatest in those who receive PNS whereas improvements in biomechanics (shoulder abduction torque, shoulder kinematics, and Fugl-Meyer score) will be greatest in those who receive PT; and the PNS+PT group will have improvements in both.

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

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

See attached.

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

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

Name	Description
Background | History	
References | History	

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
Psychological Testing
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)
Use of investigational devices
Psychological testing

8.3 Identify Data Collection types for this study:

Check all that apply.

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.

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

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 to confirm the superiority of PNS over PT in reducing HSP, and to determine if multimodal treatment of HSP with PNS + PT is more efficacious than PNS or PT alone. The standard of care for treating shoulder pain is to try several options, most commonly including medications, injections and therapy. Candidates considering this study likely have tried some treatments but without lasting success. Ninety-six participants will be randomized to receive PNS + PT, PNS + sham-PT, or sham-PNS + PT. The PNS + PT group will receive active PNS therapy for 6 hours per day for 3 weeks along with 8 sessions of PT to improve biomechanics of the affected shoulder. The PNS+ sham-PT group will receive active PNS therapy and sham-PT, consisting of placebo ultrasound, application of inert gel, lower limb strengthening, and walking exercises. The sham-PNS + PT group will receive a percutaneous lead in a similar manner as the active therapy groups, but with sham-stimulation, along with 8 sessions of PT. Measures of pain, pain interference with ADLs, QoL, shoulder biomechanics (shoulder abduction torque, shoulder kinematics, and Fugl-Meyer score), and measures of central sensitization (pain thresholds, secondary hyperalgesia, and temporal summation) will be assessed at baseline and at weeks 4 (end of treatment), 8, 12, 16, 20, 24, and 28.

Baseline Variables and Randomization: Baseline data will be collected so that the balance of covariates across the three groups can be evaluated. Each participant will be characterized with respect to demographics, comorbidities, and medication use. Study outcome measures (see Outcomes Assessment) will be administered to establish baseline levels. Participants are assigned to treatment groups using an adaptive randomization algorithm [90-92] to minimize group imbalances on key patient characteristics: baseline pain (>6 or <=6) [93], duration of pain (>=18 months or <18 months) [15], age (>=55 years or <55 years) and study site. For each assignment, the algorithm calculates the balance of these variables across the groups and makes an assignment that would result in greater balance in the variables across groups.

Percutaneous PNS System: The Sprint PNS System (SPR Therapeutics, Cleveland, OH), also known as the Smartpatch System, will be used to deliver the PNS therapy. The System consists of a small external stimulator, percutaneous 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. The single-channel stimulator outputs a biphasic current waveform with current pulse parameter ranges that are suitable for PNS. These electrodes have been used extensively to deliver percutaneous PNS to shoulder muscles. [16-22, 85, 86]

Lead Placement Procedure:

Active PNS Groups: The procedure will be 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. [16, 19, 71, 86] The introducer loaded with the 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. The subject will be provided the option of subcutaneous lidocaine infiltration prior to placement of the electrode lead.

Sham-PNS Group: In order to facilitate blinding, sham-PNS participants also will receive a percutaneous electrode. The sham-PNS group will not require localization with monopolar needle electrodes.

PNS Treatment Protocol:

Active PNS Groups: After one week for lead stabilization [95], the Sprint PNS System will be programmed for stimulation. Based on over 30-yrs of experience, the Cleveland FES Center established parameters for safe and effective delivery of PNS (pulse frequency = 12 Hz; pulse amplitude = 20 mA; pulse duration = 5-200 usec (set by clinician); duty cycle = 5-sec ramp-up, 10-sec plateau, 5-sec ramp down, 10 sec off; daily dose = 6 hrs/day). [96] These parameters provide strong fused comfortable muscle contraction with minimal fatigue. [16-22, 59, 85, 86, 94, 97, 98] 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. [99] Participants receive 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 PNS; however, the selected duty cycle and daily dose of 6-hrs were used in our prior studies [8, 16-21, 86] and by others with robust results. [85]

Sham-PNS Group: Control participants will not receive active stimulation. The stimulator will be placed in non-stimulation mode by a study team member. In this condition, the stimulator appears to function normally, and the battery will drain, though no stimulation will be 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) due to electrode fragments in this study is 0.1% per electrode. 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 will be trained in the assessment of electrode site and the daily placement of the Sprint Pad. 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 end of treatment. 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 end of treatment, the electrode is removed by gently pulling on the external portion. All participants undergo radiographic surveillance for retained

electrode fragments.

Physical Therapy:

Active PT Groups: The Active PT Groups will receive Shoulder Therapy Treatment. Participants will receive eight 60-minute sessions of outpatient therapy over a 4 week period concurrent with PNS or sham-PNS treatment. Proper Positioning and Handling: Little evidence supports specific positioning or handling of the hemiparetic upper limb to prevent the development or worsening of HSP [5]; however, there is consensus that proper positioning and handling are necessary elements of best practice. [6, 7, 47] Therapists will practice proper positioning and handling of the hemiplegic upper limb and provide training to participants and their caretakers. [100, 101] Based on guidelines and clinical judgement, humeral cuff slings may be issued to reduce the risk of trauma to the hemiparetic upper limb. [6] Chair-bound participants may be provided arm troughs or lap trays as needed. [102] Ambulatory participants may be issued a humeral cuff sling. [103] Therapeutic Positioning and Strengthening Exercises: Therapeutic positioning exercises will be provided by trained therapists, with primary focus on humeral external rotation. [1] Therapists will ensure that the shoulder is moved with appropriate rotation of the scapula and humerus to avoid impingement or damage to the rotator cuff during all ROM. [1, 104] Prior to abduction, the scapula will be rotated upward and the shoulder will be externally rotated to avoid impingement beneath the acromion. [47] Similarly, the subluxed shoulder will be manually reduced prior to any movement to avoid traction damage. [105] Overhead pulleys will not be used. [104] Mirror Therapy: For those with severe hemiplegia, a standardized protocol requiring arm, hand, and fingers will be utilized. [106] Subjects will sit at a table with their affected arm placed in a triangle mirror box so that the mirror image of the unaffected arm appears to be the affected one. Subjects will be asked to move their affected limb as well as possible while watching the reflected image of their unaffected limb. [107] Task-Specific Therapy: High repetitive task-specific therapy will be provided for participants with residual hand function. [1] Sessions will include functional training in basic and instrumental ADLs and active repetitive movement training of the paretic upper limb. The incorporation of the impaired upper limb to carry out specific functional tasks will be emphasized, and traditional compensatory strategies such as singlehanded techniques will be avoided. Home Exercise Program: Except on days they are in outpatient therapy, participants will participate in a daily home exercise program throughout the length of the study. For those without residual motor ability, the home exercise program will exclude ROM exercises for the hemiparetic shoulder due to risk for injury when not conducted with a trained therapist. [5, 6, 47, 108] Exercise will be provided for ROM exercises for the hand, wrist, and elbow. For those with residual shoulder motor ability, active ROM exercises within the limits of pain-free range will be prescribed. Use of these hemiparetic upper limb for functional tasks as much as safely possible will be encouraged for those able. All participants will be provided instructions guiding through a Mental Practice program. [109] Subjects will receive an audio-recorded intervention that begins asking patients to imagine themselves in a warm, relaxing place, and asking them to contract and relax their muscles. This portion is followed by mental practice of internal, cognitive polysensory images related to using the affected arm in one of four functional tasks. The final minutes will allow patients to refocus into the room. Subjects will complete this twice per week. Participants will be asked to self-report compliance with home program at each visit.

Sham PT Group: The Sham PT Group will receive Stroke Therapy Treatment. Participants randomized to sham-PT will receive eight 60-minute sessions with therapists with the goal of controlling for the effect of regular contact with a therapist and study staff in a therapeutic environment. Therapists will provide sham ultrasound therapy and light application of inert gel to the shoulder for 10 minutes. Pre-Gait Training or Gait Training: Pre-Gait training focuses on trunk and balance control and mastery of specific gait components to walk safely and efficiently. The amount of Pre-Gait Training required before proceeding to Gait Training depends on the individual and will be determined by the therapist. Exercise therapy could include weight shifting exercises, balance training, walking exercises, weight shifts, strengthening exercises, and listening session regarding stroke education, relaxation

and coping. While it is possible that the sham-PT might alter lower limb impairment, it will not affect outcomes related to shoulder function. Aspects of this sham-PT have been used in prior RCTs of shoulder interventions with moderate to high degree of blinding. [110, 111] Participants will be asked to self-report compliance with home program at each visit.

Outcomes Assessment: The primary outcome measure is the worst pain in the prior 7-days (BPI SF-3). Secondary measures include pain interference with ADLs (BPI SF-9); QoL (SF-36); shoulder impairment (isometric voluntary abduction shoulder torque (IVAST), shoulder kinematic analysis, optional Fugl-Meyer Motor Assessment (upper limb)); and measures of central sensitization (mechanical pain thresholds for hyperalgesia, optional pinprick pain thresholds for hyperalgesia, temporal summation of repetitive pin-prick stimuli). Details for each measure are presented below. The outcomes are administered face-to-face in a blinded manner.

Brief Pain Inventory SF-3 (Aims 1 and 2): The BPI has excellent psychometrics [112-118] and is recommended by the IMMPACT group for the assessment of pain in clinical trials. [89] The developers of the BPI recommend BPI SF-3, the "pain worst" rating, as the primary response metric. The question asks participants to rate their worst pain in the 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 order to gain a more comprehensive assessment of participants' pain experience, daily least pain (BPI SF-4), daily average pain (BPI SF-5) and daily present pain (BPI SF-6) after morning ADLs are also collected. To analyze successful treatment, responders will be defined as those who have a clinically meaningful 30% reduction of pain [25] at end of treatment and at the conclusion of the trial. The investigative team has extensive experience with the BPI. [8, 13, 15, 18, 20, 21, 71, 85, 119, 120]

Pain interference with ADLs – BPI SF-9 (Aim 2): BPI SF-9 specifically evaluates the impact of pain on ADL performance within 7 domains of daily activity over a 7-day 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." [121] The BPI SF-9 score is the average of the scores for the 7 domains. Psychometrics have been evaluated as part of the BPI battery. [112-115] BPI SF-9 has been used to evaluate the impact of percutaneous PNS mediated pain reduction on ADLs. [8, 16, 18, 21, 71, 86]

QoL – SF 36 (Aims 1 and 2): SF-36 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. [122] It is the only reliable and valid measure previously used to assess change in QoL associated with the treatment of shoulder pain with PNS. [8, 16, 19, 85]

Isometric Voluntary Abduction Shoulder Torque (IVAST, Aim 3): IVAST is an objective predictor of strength which is an important factor in ability to complete functional tasks in older adults. [123] IVAST will be measured in an established protocol [82] with a Biodex Biomechanical Measurement System (Biodex Medical Systems, Shirley, NY). Participants will be seated and fastened securely with the abduction axis of the shoulder aligned with the rotational axis of the dynamometer. The arm will be attached to the dynamometer by a strap just above the elbow. The arm will be held at 30 degrees of shoulder abduction and neutral rotation. Participants will be asked to abduct their arm in response to an audio tone. The duration of the audio tone randomly varies between 3 and 5 seconds to prevent the anticipation of the start or end of the cue. The average torque during the last second of the audio tone will be calculated and those values will be averaged over three trials, with 1-minute rest between trials. Abduction torque measurement via Biodex shows high intra – and interrater reliability. [124]

Shoulder Kinematic Analysis (Aim 3): An objective measure of glenohumeral and scapular range of motion will be obtained using an optical tracking system (Optotrack Certus, NDI Measurement Science, Ontario, Canada) during the performance of

passive and active pain-free shoulder abduction rotation while seated. Active LED markers will be mounted on the sternum, scapula, upper arm, and forearm. Digitization of bony landmarks on the thorax, scapula, and humerus permit transformation of sensor data into local segment coordinates according to standard protocol. Custom software will be used to extract angular data from the sensors and calculations will be made following the recommendations of the International Society of Biomechanics, Shoulder Group. [125] The extracted angular data includes: 1) peak humeral elevation and 2) Peak scapular tilt. Analysis in post-stroke shoulders is a reliable and valid measure of impairment. [126, 127]

Fugl-Meyer Motor Assessment, upper limb (Aim 3) (optional): If PNS reduces HSP by reducing motor impairment, then Fugl-Meyer Motor Assessment (FMA) scores should improve. The FMA was derived from the Brunnstrom Stages [128] of post-stroke motor recovery. Each test element will be graded on a 3-point ordinal scale and summed to provide a maximum upper limb score of 66. Reliability and validity have been demonstrated. [129-131] The FMA will be administered while the subject was seated.

Mechanical Pain Thresholds for Hyperalgesia (Aim 3): The Pressure Pain Thresholds (PPTs) will be measured with a hand-held Wagner Instruments FPIX Digital dynamometer (Wagner Instruments, Greenwich, CT) with 1 sq-cm rubber tip. The PPT is defined as the amount of force (applied at a rate of 1 kg per second) required to produce a sensation of pain distinct from pressure or discomfort. 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 will be averaged at each site. The reliability and validity of the pressure algometry to evaluate deep somatic tissue sensitivity have been demonstrated [132-134], and the method has been used to evaluate central sensitization in numerous pain conditions [135-145], including chronic shoulder pain. [9, 10]

Pinprick pain thresholds for Hyperalgesia (Aim 3) (optional): Pinprick thresholds will be 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). [146, 147] The stimulators will be applied at a rate of 2 s on, 2 s off in an ascending order until the first percept of sharpness is reached. The final threshold will be the geometric mean of five series of ascending and descending stimuli. Pinprick pain threshold has been used to evaluate central sensitization in numerous conditions [148-151], including chronic shoulder pain. [9, 10]

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). [116] [147]

Other: Five other surveys also are collected once each for either eligibility determination or potential correlative data analysis. These are the Mini Mental State Exam (MMSE), 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.

Concomitant Therapies: Participants may receive additional PT or OT during the treatment period or during follow-up as long as the therapy is not directed at shoulder pain. Subjects may not receive any injections, or any other forms of electrical stimulation, including TENS or surface PNS, to the affected shoulder. Due to ethical considerations, use of non-opioid and opioid analgesics for pain management will be allowed. Participants may adjust dosing of these medications, but it is preferred that they 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 SF-3 and 9. Medication use is monitored via diary.

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*:

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.

The duration of each subject's participation will be ~7 months.

Visit 1 – Consent/Eligibility: Consent form signed; assessed for eligibility per inclusion/exclusion criteria; MMSE administered; BDI, PCS & FABQ administered; medical history, demographics, comorbidities, and medication use recorded; blood drawn for INR (in applicable subjects); pregnancy test (in applicable subjects). (~3.5 hrs)

Visit 2 – Baseline Outcomes Assessment: Study outcome measures (see Outcomes Assessment) administered to establish baseline levels. (~3 hrs)

Visit 3 - 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. Skin checked, subject queried for medication usage. Randomization to treatment group. Subset of study outcome measures (questionnaires only) administered. (~2 hrs)

Visit 4 - PT #1 (1.25 hr)

Visit 5 - PT #2 (1.25 hr)

Note: A 48-72 hour Post-Implant Safety Check (Check the Lead exit site within 48-72 hours of the Implant procedure) can occur during Visit 4 and/or Visit 5. (Add 15 min)

Visit 6 - PT #3 & Start of Stimulation: Collection of parameter data; programming of external stimulator (Sprint Stimulator). Subject given instructions on use of System and care of Lead exit site. Skin checked, subject queried for medication usage and adverse events. Subset of study outcome measures (BPI-SF only) administered. (~2 hrs)

Visit 7 - PT #4 (1 hr)

Visit 8 - PT #5: Subject also queried for medication usage and adverse events. (1.5 hr)

Visit 9 - PT #6 (1 hr)

Visit 10 - PT #7: Subject also queried for medication usage and adverse events. (1.5 hr)

Visit 11 - PT #8 (1 hr)

Visit 12 - EOT Outcomes Assessment & Explant Procedure: Study outcome measures administered (4 weeks post-Implant). PGIC administered. Skin checked, subject queried for medication usage and adverse events. Lead Removed. X-rays performed (may be done as separate clinical visit). (~4 hrs) (Note: This visit optionally could be split into two visits (12A, 12B) based on scheduling and subject tolerance considerations.)

Phone Call - 1 week Post-Explant Safety Check: Subject queried on condition of Lead exit site. (15 min)

Visit 13 - 8-wk Outcomes Assessment: Subset of study outcome measures

(questionnaires only) administered (8 weeks post-Implant (4 weeks post-EOT)). Subject queried for medication usage. (~1 hr)

Visit 14 - 12-wk Outcomes Assessment: Subset of study outcome measures (questionnaires only) administered (12 weeks post-Implant (8 weeks post-EOT)). Subject queried for medication usage. (~1 hr)

Visit 15 - 16-wk Outcomes Assessment: Study outcome measures administered (16 weeks post-Implant (12 weeks post-EOT)). Subject queried for medication usage. (~3 hrs)

Visit 16 - 20-wk Outcomes Assessment: Subset of study outcome measures (questionnaires only) administered (20 weeks post-Implant (16 weeks post-EOT)). Subject queried for medication usage. (~1 hr)

Visit 17 - 24-wk Outcomes Assessment: Subset of study outcome measures (questionnaires only) administered (24 weeks post-Implant (20 weeks post-EOT)). Subject queried for medication usage. (~1 hr)

Visit 18 - 28-wk Outcomes Assessment: Study outcome measures administered (28 weeks post-Implant (24 weeks post-EOT)). Subject queried for medication usage. (~3 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 and additional 48-72 hour safety check. Other visits may be repeated as appropriate.

*Any visit may be completed via telephone, telehealth or email as determined by the principle investigator in case of immediate hazard to the subject
*Visits 13,14,16,17: These visits include questionnaires only and can be completed via telephone, telehealth or email at the discretion of the Research coordinator or PI

8.7 Please attach study design/subject visit schedule here:

Name	Description
PNS+PT Visit Schedule Table (06-14-2017) | History	

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

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 localized to the glenohumeral joint, subacromial area or deltoid insertion associated with: a) rest; b) passive abduction or external rotation range of motion (ROM); c) active abduction ROM; or, d) manual palpation;
• shoulder pain onset or worsening after the most recent stroke;
• weakness of shoulder abductors (≤4/5 on MRC if isolated movement is present);
• ≥ 21-yrs old; < 90-yrs old;
• time of stroke ≥ 3-mo;
• duration of HSP ≥3-mo;
• HSP with moderate to severe pain (BPI SF-3 ≥ 4);
• cognitive and communication ability to fulfill study requirements (cognitive ability based upon a score of ≥24 on the Mini Mental Status Exam (MMSE));
• availability of reliable adult who can assist with study procedures if necessary;
• willing and able to report shoulder pain and other conditions and complete study visits throughout the 7 month study period.

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

Please list exclusion criteria.

• joint or overlying skin infection or history of recurrent skin infections;
• insensate skin;
• need to take > 1 opioid and > 1 nonopioid analgesic medication for HSP;
• regular intake of pain medications for another chronic pain;
• botox injection or subacromial steroid injections to the shoulder within the past

12 wks;
• receiving OT or PT for HSP;
• bleeding disorder or INR > 3.0;
• sensitivity to skin surface electrodes and/or medical-grade adhesives, gels, tapes;
• medical instability;
• pregnancy;
• uncontrolled seizures (>1/mo for 6-mo);
• history of cardiac arrhythmia with hemodynamic instability;
• history of lidocaine allergy;
• history of Parkinson's disease, SCI, TBI, MS, or ipsilateral UE lower motor neuron lesion;
• history of complex regional pain syndrome, myofacial pain syndrome, other pain conditions (investigator discretion);
• cardiac pacemaker or other implanted electronic device;
• history of valvular heart disease (artificial valves, requiring antibiotics for procedures, etc.);
• severely impaired communication;
• history of compromised immune system (i.e., recently or actively taking immunosuppressive therapies, AIDS) congenital immunodeficiency, or any other cause for compromised immune system with which participation would pose excessive risk.

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;
• completion of the Brief Pain Inventory Short Form (to confirm baseline degree of pain of ≥ 4);
• bloodwork (to confirm suitable coagulation levels in patients on anticoagulants) or pregnancy urine or serum test in applicable female subjects;
• physical examination of shoulder.

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 with chronic post-stroke shoulder pain etiologies and 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.
• Collection of bloodwork (standard): The blood test (INR score) is standard for patients taking anticoagulants. This test will be collected in applicable subjects at Visit 1. 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 (experimental): The placement of the lead during the lead implant procedure and the use of stimulation during the treatment phase are experimental. Local anesthetic will be used.
• X-rays (standard): One 2-view (AP/Lateral and Scapular Y) shoulder x-ray 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 treatment phase for the active PT groups. For the sham PT group (experimental), sham ultrasound therapy and light application of inert gel to the shoulder will be utilized, but standard PT not expected to affect outcomes related to shoulder function will be utilized as well. There are 8 PT Visits.
• Collection of surveys and questionnaires - BPI, SF-36 (standard): These surveys are used for research, but are commonly used in pain patients. These surveys will be collected as defined elsewhere in this protocol for 9 Outcomes Assessments Visits; the BPI additionally is collected at the Start of Stimulation Visit. The Mini Mental Status Exam (MMSE, also standard) will be collected at Visit 1. The BDI and PCS (also standard) are used for research, but are commonly used in pain patients. They will be collected at Visit 1. The FABQ (experimental) will be collected at Visit 1. The PGIC (experimental) will be collected at Visit 12.
• Fugl-Meyer Motor Assessment (upper limb): The FMA (standard) will be used as defined elsewhere in this protocol for 4 Outcomes Assessments Visits.
• Other outcomes measures (experimental): Isometric voluntary abduction shoulder torque (IVAST), shoulder kinematic analysis, and measures of central sensitization (mechanical pain thresholds for hyperalgesia, pinprick pain thresholds for hyperalgesia, temporal summation of repetitive pin-prick 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 for 4 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?

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.***
See attachments below.

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

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
Data Analysis (inc. Sample Size Calculation under Expectations and Analysis, Aim 1) | History	
Outcomes Measures | History	
Revised Sample Size Wilson PNS+PT R01 (2016_10_12) | 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:** **1) Risks associated with needle insertion for Sprint MicroLead placement** **There are minor risks associated with inserting a Lead through the skin with a needle. These risks are similar to the risks of any needle injection including the possibilities of puncturing a blood vessel, irritating a nerve, and temporary bruising or pain at the insertion site. The risks of puncturing a blood vessel and irritating a nerve are uncommon, but the risks of temporary bruising and pain at the insertion site are common.** **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.** **To minimize the risks associated with percutaneously placing fine wire leads, only appropriately trained physician investigators will perform the procedure. In addition, the risk of excessive bleeding will be reduced by excluding candidates who are taking warfarin with an INR > 3.0 and by placing manual pressure on the implantation site until hemostasis is achieved. Finally, the risk of discomfort during the procedure will be reduced by the use of an appropriate amount of local anesthetic.** **It is possible that, in some cases, multiple attempts may be required to achieve appropriate placement of the Lead during the procedure. Each additional attempt at Lead placement carries the same risks as the initial attempt described in this section.** **2) Risk of skin irritation, infection, or inflammation at the Sprint MicroLead exit site** **There are risks of leaving a Sprint MicroLead in place for 4 weeks, including skin irritation, infection, and granuloma formation (mild tissue inflammation) at the Lead exit site. Symptoms include redness, swelling, or pain. The risk of skin irritation is common while the risks of infection and granuloma formation are rare.** **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**	Select all that apply.

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 48-72 hour 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

There is a possibility of a Lead breaking beneath the skin either during the course of the study or during the procedure to remove Lead. This risk is uncommon. However, when a Lead breaks, one or more Lead fragments usually remain in the body. The Investigator will use clinical judgment to determine if the removal of such fragments is necessary. Visual inspection of the Lead after it has been removed as well as x-rays will be used to determine if any Lead fragments remain. The risk associated with the x-rays is no greater than that associated with conventional clinical x-rays. If the Investigator determines a Lead fragment has been retained in the body, he/she will determine what is medically required to further evaluate and treat this retained fragment. Typically, no treatment is required unless there are further sequelae, such as an infection or granuloma, associated with the fragment.

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 4 weeks.

4) Risk of infection associated with retained Sprint MicroLead fragments

A Lead fragment could result in the formation of a granuloma or infection. Although the occurrence of a fragment-related infection or granuloma is uncommon an infection may require removal of the Lead fragment and/or treatment with antibiotics. 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

It is possible that a Lead fragment or fragments may be retained in the body following removal of the Sprint MicroLead. If the Investigator determines that a lead fragment has been retained, the Investigator will instruct the subject and his/her caregiver to carefully inspect the Sprint MicroLead exit site and the surrounding skin in the weeks subsequent to Lead 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.

The risks associated with the Lead fragment removal procedure include discomfort during the procedure and skin irritation or infection in the area of the retained fragment. These risks are rare. The risk of infection is mitigated by instructing the subject and/or his caregiver to carefully monitor the site and immediately report any signs of infection.

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. This risk is rare. If lead migration occurs, it is possible that the subject may experience discomfort during stimulation (described further below under "risk of discomfort with electrical stimulation"). If the Lead has migrated substantially or has come out, it may be necessary to place another Lead. 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, and collecting an additional INR blood sample for subjects who are taking warfarin.

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

It is possible that the skin could become irritated under the Sprint Pad. Additionally, there may be skin irritation in the area surrounding the Lead insertion site, where an adhesive bandage is taped to the skin. This risk is common; however, the bandages can be changed to prevent the irritation from returning.

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

Intramuscular electrical stimulation may be perceived by the subject as a tingling or vibrating sensation, which may feel uncomfortable or painful. The risk of discomfort due to stimulation is uncommon. At high stimulation intensities, shoulder pain may worsen.

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

There is a risk of tissue damage if a subject undergoes diathermy. Shortwave or microwave diathermy is a 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 can cause excessive heating of any implanted metal part (including Leads), resulting in serious injury. The risk of tissue damage associated with diathermy is rare.

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

Tissue damage may occur if a subject undergoes an MRI procedure while the Sprint MicroLead, or a fragment of the Sprint MicroLead, is in the body. The risk of tissue damage associated with MRI use is rare.

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

There is a risk that the subject may have an allergic reaction to the local anesthetic used during the treatment phase prior to insertion of the Sprint MicroLead. If the subject were to have an allergic reaction, it would usually

happen while the subject was still in the clinic. If a subject complains of itching, difficulty breathing, lightheadedness and dizziness, or a swollen tongue (common signs of an allergic reaction), appropriate medical treatment will be administered. The risk of allergic reaction to local anesthetics is rare. In addition, there is a risk of adverse central nervous system and/or cardiovascular effects (including a rare risk that the subject's heart can stop beating or that they could stop breathing) if the local anesthetic is administered improperly.

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.

14) Risk associated with venipuncture (if applicable)

The risks of drawing blood from a vein include discomfort at the site of puncture, possible bruising and swelling around the puncture site, an infection, and faintness from the procedure. The risks of discomfort, bruising, and swelling around the puncture site are common while the risks of infection and fainting are rare. Blood sample collections are only required in subjects taking warfarin.

Subjects taking warfarin are at greater risk for developing bruises following venipuncture. However, the risk of discomfort and bruising at that puncture site will be reduced by applying gentle pressure following venipuncture as is the standard practice for collection of blood samples. The rare risk of infection due to venipuncture will be reduced by using proper blood collection technique including wiping the puncture site with an appropriate cleansing solution.

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.

15) 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.

16) 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.

17) Risks of Outcomes Assessments

The questionnaires and Fugl-Meyer Assessment present no risks. The assessments of shoulder torque and kinematics may be slightly uncomfortable. The measures of central sensitization (mechanical pain thresholds for hyperalgesia, pinprick pain thresholds for hyperalgesia, temporal summation of repetitive pin-prick stimuli) may be slightly uncomfortable and may cause brief skin irritation.

18) Other

When using a sham group there is always the rare risk of psychological harm. Some of the survey questions present a rare risk of psychological harm.

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.

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

A text box is provided for further explanation.

10.9 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. In addition, the risk of excessive bleeding will be reduced by excluding candidates who are taking warfarin with an INR > 3.0 and by placing manual pressure on the implantation site until hemostasis is achieved. 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 48-72 hour 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 4 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, and collecting an additional INR blood sample for subjects who are taking warfarin.

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.

14) Risk associated with venipuncture (if applicable)

Subjects taking warfarin are at greater risk for developing bruises following venipuncture. However, the risk of discomfort and bruising at that puncture site will be reduced by applying gentle pressure following venipuncture as is the standard practice for collection of blood samples. The rare risk of infection due to venipuncture will be reduced by using proper blood collection technique including wiping the puncture site with an appropriate cleansing solution.

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.

15) 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.

16) 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.

17) 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.

18) 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 chronic HSP, 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):**
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 stroke physicians. Additionally, potential participants may be recruited from the Greater Cleveland area (as allowed for in the Recruitment section).

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.

11.2 **Anticipated number of subjects (all sites): [enter a number]**
96

Anticipated number of subjects to be enrolled at MHS: [enter a number]
96

Anticipated number of potential subjects to be approached: [enter a number]
400

11.3 **If this is a multi-site study, how many sites will there be? [enter a number]**
3

How many total sites?

11.4 **Subject Characteristics:**
Subject Population Categories
Outpatients
Patients with the "disease in question"

Check all that apply

11.5 **Subject Source:**
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)

Check all that apply

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:**
Subject Age Range
18 - 64
65 - 89

Check all that apply.

12.2 *** Will the study enroll vulnerable subject groups?**
Yes

Check yes or 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
Poor / Uninsured
Elderly
Minorities
Cognitively Impaired

12.4 If you selected "other" above please describe: *Please describe other.*

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. *Please enter a detailed plan.*

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
Advertisements-Newspapers/Magazines, Television, Radio
Notices/Posters/Flyers
Letters
Research Match

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.

Subjects will be recruited from the outpatient stroke and brain injury rehabilitation programs 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 Department of PM&R, and many will already be Dr. Wilson's or Dr. Chae's patients.

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, Orthopaedics, 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
• Stroke 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 Website Stroke Research Information Page. Basic study and contact information will be displayed on a webpage associated with the MHS website. Developed in cooperation with Metro Communications.
• 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.
• Stroke 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.

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. 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.

No

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.

Transportation may be arranged for the study participant and covered by the study budget. Alternatively, subjects who are able to drive may receive reimbursement for parking.

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

Attach copies of all recruitment and advertising materials.

Name	Version
PNS PT study information sheet(tracked).docx | History	0.01
PNS+PT Brochure (11-Sept-2018) | History	0.06

Name	Version
PNS+PT for HSP Appointment Reminder | History	0.01
PNS+PT for HSP Consent Cover Form Letter | History	0.04
PNS+PT for HSP Evaluation Cover Form Letter | History	0.08
PNS+PT for HSP Evaluation Cover Form Letter- Tracked.doc | History	0.03
Poster - PMR Research (5 versions with varying logos, Sep 2017) | History	0.03
Poster - Shoulder Pain (5 versions with varying logos, Sep 2017) | History	0.03
Research Ad(newsletter) | History	0.01
ResearchMatch Study Contact Message | History	0.01
Shoulder Pain Studies Recruitment Video (21-Jun-2017) | History	0.02
Shoulder Pain Study Flyer | History	0.01
Splash Clinical -- MetroHealth Campus_Stroke Study_Marketing Materials_10.3.17 | History	0.01
Stroke Research Ad 5.0 for Craigslist (24-Jul-2013) | History	0.02
Stroke Research Ad 6.0 (01-Aug-19) | History	0.03
Stroke Research Metro In-House Messaging 5.0 (24-Jul-2013) | History	0.02
Study Information Sheet | History	0.03

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 first stroke 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.

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

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

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?**
Data will be maintained by the study coordinator in REDCAP. Data will be deindentified and labeled with each subject's ID. The Subject ID Log which provides a link between the subject ID and patient name will be kept on Redcap, 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):**

Add data collection forms and CRFs.

Name	Version
PNS+PT Adverse Event | History	0.01
PNS+PT Assessment CRFs (23-Feb-2017) | History	0.03
PNS+PT Medication Diary | History	0.01
PNS+PT Study Termination (16-Nov-2016) | History	0.02
PNS+PT Survey Outcomes Visits (16-Nov-2016) | History	0.02
PNS+PT Treatment Binder CRFs (07-Jun-2017) | History	0.04
PNS+PT Unscheduled Study Visit (16-Nov-2016) | History	0.02
REDCAP Data Collection Forms(all forms) | History	0.01

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.** 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. The Subject ID log will be stored on Metro Redcap. 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: OBC 2 Main SM2-057. Also, the PI's office is OBC 2 Main. These records with PHI are kept in locked cabinets in these rooms.	State the exact physical location of paper files and the network drive for electronic files.
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?** Non-Metro staff who will have access to at least some PHI as well as deidentified data include the following study staff: Nathan Makowski (Post-Doctoral Research Staff). 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).	Give name and title exclude study staff who are MHS employees.

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?**
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:

Check the MHS Record retention policy for guidance.

You must have a plan for data destruction.

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. The Subject ID log will be stored on 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: OBC 2Main SM2-057. Also, the PI's office OBC 2Main. 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).

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

If necessary, FDA is authorized to review information.

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 of the patients? ○ Yes ◉ **No** — Check yes or 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 department 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.

Candidates who agree to an Eligibility visit will be asked to sign a Consent and HIPAA Authorization.

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
Nathaniel Makowski	Case Western Reserve University	Physical Medicine and Rehabilitation	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:

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

Name	Version
There are no items to display	

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 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

Check one, please read carefully if you are not receiving data or sending 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 the letter "M". Thus, the enrolled subjects would be numbered M-01, M-02, etc. (At SRAL, numbers will be preceded by the letter "R". Thus, the enrolled subjects would be numbered R-01, R-02, etc.) "CR" will be use for Carolinas Rehabilitation

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.

Note: practicably does not mean it would be inconvenient.

This research study involves no more than minimal risk:

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

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.

Check yes or no.

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.
○ 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 our Metro clinical staff listed on the study (physicians, nurses, therapists, coordinator). Physicians may cite the study during a clinical visit if the patient seems appropriate. Clinical Staff(Coordinator) 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. In addition, after consent, only subjects that obtain a score of ≥24 on the Mini Mental Status Examination will be enrolled as it is used to determine the subject's cognitive ability to understand the study requirements.

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. Cognitive function is assessed as described in the inclusion criteria. 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** Attach a plan for consenting subjects. This must give detail

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.*

about the consent process.

Name	Description
Informed Consent Process (01-09-2009) | 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
PNS+PT in HSP Consent and HIPAA 2.4	0.18
PNS+PT in HSP Consent and HIPAA 2.4 (tracked)	0.14
PNS+PT in HSP HIPAA Alternative Means 1.3 (30-Jul-2019)	0.04
PNS+PT in HSP HIPAA Alternative Means 1.3 (30-Jul-2019, highlighted)	0.02
PNS+PT in HSP Video-Photo Consent 1.0 (16-May-2016)	0.01

17.16 Will non-English speaking subjects be enrolled?

Check one

○ Yes ◉ No Clear

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

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

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
Psychological Testing
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)
Use of investigational devices
Psychological testing

****

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
Elderly Population
Psychologically or neurologically impaired population

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, 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	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 is being used in accordance with its labeling. 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: Study Coordinator

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:
A DSMB has been established consisting of 5 members. Jayme Knutson PhD is ideally suited to serve as the DSMB Chair based on his years of experience with FES research and technology, and with the stroke subject population with whom we work.

Chair:
Jayme S. Knutson, PhD
Associate Director of Regulatory Affairs, Cleveland FES Center
Assistant Professor, Department of Physical Medicine & Rehabilitation, School of Medicine,
Case Western Reserve University, Cleveland, OH
Senior Staff Scientist, Department Physical Medicine & Rehabilitation,
MetroHealth Medical Center, Cleveland, OH
Director of Research, MetroHealth Rehabilitation Institute of Ohio
MetroHealth Medical Center
4229 Pearl Rd.
Cleveland, OH 44109
jsk12@case.edu
216-957-3557

Statistics/Clinician:
Douglas Einstadter, MD, MPH
Professor of Medicine, Epidemiology and Biostatistics
Member, Center for Health Care Research and Policy
Staff Physician, Department of Medicine
MetroHealth Medical Center
2500 MetroHealth Dr.
Cleveland, OH 44109
deinstatadter@metrohealth.org
216-778-3901

Clinician:
Prathap Jayaram, MD; Clinician
Director of Regenerative Sports Medicine
Assistant Professor of Physical Medicine & Rehabilitation
Assistant Professor of Sports Medicine
Assistant Professor of Orthopedic Surgery

Baylor College of Medicine
7200 Cambridge St
Houston, TX 77030
prathap.jayaram@bcm.edu
786-427-9174

Clinician:
Christina Oleson, MD
MetroHealth Rehabilitation Institute
MetroHealth Medical Center
4229 Pearl Rd.
Cleveland, OH 44109
coleson@metrohealth.org
216-957-3556

Ethicist:
Nicole Deming JD, MA
Assistant Dean, Faculty Affairs and Human Resources
Case Western Reserve University
10900 Euclid Ave
Cleveland, OH 44106
nicole.deming@case.edu
216-368-2821

The DSMB will convene regularly to review and monitor the progress of the study with respect to enrollment, drop-outs, outcomes and safety.

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 Sprint MicroLead placement

There are minor risks associated with inserting a Lead through the skin with a needle. These risks are similar to the risks of any needle injection including the possibilities of puncturing a blood vessel, irritating a nerve, and temporary bruising or pain at the insertion site. The risks of puncturing a blood vessel and irritating a nerve are uncommon, but the risks of temporary bruising and pain at the insertion site are common.

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.

To minimize the risks associated with percutaneously placing fine wire leads, only appropriately trained physician investigators will perform the procedure. In addition, the risk of excessive bleeding will be reduced by excluding candidates who are taking warfarin with an INR > 3.0 and by placing manual pressure on the implantation site until hemostasis is achieved. Finally, the risk of discomfort during the procedure will be reduced by the use of an appropriate amount of local anesthetic.

It is possible that, in some cases, multiple attempts may be required to achieve appropriate placement of the Lead during the procedure. Each additional attempt at Lead placement carries the same risks as the initial attempt described in this section.

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

There are risks of leaving a Sprint MicroLead in place for 4 weeks, including skin irritation, infection, and granuloma formation (mild tissue inflammation) at the Lead exit site. Symptoms include redness, swelling, or pain. The risk of skin irritation is common while the risks of infection and granuloma formation are rare.

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 48-72 hour 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

There is a possibility of a Lead breaking beneath the skin either during the course of the study or during the procedure to remove Lead. This risk is uncommon. However, when a Lead breaks, one or more Lead fragments usually remain in the body. The Investigator will use clinical judgment to determine if the removal of such fragments is necessary. Visual inspection of the Lead after it has been removed as well as x-rays will be used to determine if any Lead fragments remain. The risk associated with the x-rays is no greater than that associated with conventional clinical x-rays. If the Investigator determines a Lead fragment has been retained in the body, he/she will determine what is medically required to further evaluate and treat this retained fragment. Typically, no treatment is required unless there are further sequelae, such as an infection or granuloma, associated with the fragment.

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 4 weeks.

4) Risk of infection associated with retained Sprint MicroLead fragments

A Lead fragment could result in the formation of a granuloma or infection. Although the occurrence of a fragment-related infection or granuloma is uncommon an infection may require removal of the Lead fragment and/or treatment with antibiotics. 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

It is possible that a Lead fragment or fragments may be retained in the body following removal of the Sprint MicroLead. If the Investigator determines that a lead fragment has been retained, the Investigator will instruct the subject and his/her caregiver to carefully inspect the Sprint MicroLead exit site and the surrounding skin in the weeks subsequent to Lead 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.

The risks associated with the Lead fragment removal procedure include discomfort during the procedure and skin irritation or infection in the area of the retained fragment. These risks are rare. The risk of infection is mitigated by instructing the subject and/or his caregiver to carefully monitor the site and immediately report any signs of infection.

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. This risk is rare. If lead migration occurs, it is possible that the subject may experience discomfort during stimulation (described further below under “risk of discomfort with electrical stimulation”). If the Lead has migrated substantially or has come out, it may be necessary to place another Lead. 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, and collecting an additional INR blood sample for subjects who are taking warfarin.

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

It is possible that the skin could become irritated under the Sprint Pad. Additionally, there may be skin irritation in the area surrounding the Lead insertion site, where an adhesive bandage is taped to the skin. This risk is common; however, the bandages can be changed to prevent the irritation from returning.

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

Intramuscular electrical stimulation may be perceived by the subject as a tingling or vibrating sensation, which may feel uncomfortable or painful. The risk of discomfort due to stimulation is uncommon. At high stimulation intensities, shoulder pain may worsen.

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

There is a risk of tissue damage if a subject undergoes diathermy. Shortwave or microwave diathermy is a 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 can cause excessive heating of any implanted metal part (including Leads), resulting in serious injury. The risk of tissue damage associated with diathermy is rare.

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

Tissue damage may occur if a subject undergoes an MRI procedure while the Sprint MicroLead, or a fragment of the Sprint MicroLead, is in the body. The risk of tissue damage associated with MRI use is rare.

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

There is a risk that the subject may have an allergic reaction to the local anesthetic used during the treatment phase prior to insertion of the Sprint MicroLead. If the subject were to have an allergic reaction, it would usually happen while the subject was still in the clinic. If a subject complains of itching, difficulty breathing, lightheadedness and dizziness, or a swollen tongue (common signs of an allergic reaction), appropriate medical treatment will be administered. The risk of allergic reaction to local anesthetics is rare. In addition, there is a risk of adverse central nervous system and/or cardiovascular effects (including a rare risk that the subject's heart can stop beating or that they could stop breathing) if the local anesthetic is administered improperly.

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.

14) Risk associated with venipuncture (if applicable)

The risks of drawing blood from a vein include discomfort at the site of puncture, possible bruising and swelling around the puncture site, an infection, and faintness from the procedure. The risks of discomfort, bruising, and swelling around the puncture site are common while the risks of infection and fainting are rare. Blood sample collections are only required in subjects taking warfarin.

Subjects taking warfarin are at greater risk for developing bruises following venipuncture. However, the risk of discomfort and bruising at that puncture site will be reduced by applying gentle pressure following venipuncture as is the standard practice for collection of blood samples. The rare risk of infection due to venipuncture will be reduced by using proper blood collection technique including wiping the puncture site with an appropriate cleansing solution.

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.

15) 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.

16) 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.

17) Risks of Outcomes Assessments

The questionnaires and Fugl-Meyer Assessment present no risks. The assessments of shoulder torque and kinematics may be slightly uncomfortable. The measures of central sensitization (mechanical pain thresholds for hyperalgesia, pinprick pain thresholds for hyperalgesia, temporal summation of repetitive pin-prick stimuli) may be slightly uncomfortable and may cause brief skin irritation.

18) Other

When using a sham group there is always the rare risk of psychological harm. Some of the survey questions present a rare risk of psychological harm.

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 Executive Committee (PI and Site PI) and respective project staff meet at least quarterly (including remotely) to review all adverse events and study data collected since the previous meeting. The Executive Committee reviews all adverse events to determine a course of action.

The Data and Safety Monitoring Board will convene semi-annuall to review and monitor the progress of the study with respect to enrollment, drop-outs, outcomes and safety.(per DSMB report attached)

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? Yes

Children? No

Decisionally Impaired Subjects? No

Pregnant Women and/or Fetuses? No

Will you be enrolling Prisoners? No

Other Populations being studied:

Vulnerable Populations
Poor / Uninsured
Elderly
Minorities
Cognitively Impaired

**** 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.

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

Name	Version
PM&R Research Team Routine Study Safety Review Procedure	0.01
Wilson - DSMB Charter Version 3 - PNS+PT in HSP 2018-Mar 8 APPROVED	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:
Blood/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?** Check Yes or No.
○ Yes ◉ **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: *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) and used in accordance with its labeling (thus exempt from IDE regulation).

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 maintenance/repairs; contact information besides the PI.
Devices are not retained by subjects beyond the Treatment Phase.

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
K170902 Documentation | History	
Sprint PNS System Device Description | History	
Updated 510K letter | 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.

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
Kristine Hansen	MHS	Physical Medicine and Rehabilitation	Physical Medicine and Rehabilitation
Richard Wilson	Metro	PM&R	The MetroHealth System

21.23 How will this medical device be used in research?

Give a brief description.

Percutaneous PNS System: The Sprint PNS System (SPR Therapeutics, Cleveland, OH) will be used to deliver the PNS therapy. The System consists of a small external stimulator, percutaneous lead, hand held wireless remote and pad. The external stimulator "snaps" on to the pad. 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 PNS. These electrodes have been used extensively to deliver percutaneous PNS to shoulder muscles. [16-22, 85, 86]

Lead Placement Procedure:

Active PNS Groups: The procedure will be 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. [16, 19, 71, 86] The introducer loaded with the 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. The subject will be provided the option of subcutaneous lidocaine infiltration prior to placement of the electrode lead.

Sham-PNS Group: In order to facilitate blinding, sham-PNS participants will receive a percutaneous electrode between the middle and posteriod deltoid muscles. The sham-PNS group will not require localization with monopolar needle electrodes. The introducer will be advanced 3-4 cm from the skin surface.

PNS Treatment Protocol:

Active PNS Groups: After one week for lead stabilization [95], the Sprint PNS System will be programmed for stimulation. Based on over 30-yrs of experience, the Cleveland FES Center established parameters for safe and effective delivery of PNS (pulse frequency = 12 Hz; pulse amplitude = 20 mA; pulse duration = 5-200 usec (set by clinician); duty cycle = 5-sec ramp-up, 10-sec plateau, 5-sec ramp down, 10 sec off; daily dose = 6 hrs/day). [96] These parameters provide strong fused comfortable muscle contraction with minimal fatigue. [16-22, 59, 85, 86, 94, 97, 98] 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. [99] Participants receive two 3-hr sessions 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 PNS; however, the selected duty cycle and daily dose of 6-hrs were used in our prior studies [8, 16-21, 86] and by others with robust results. [85]

Sham-PNS Group: Control participants will not receive active stimulation. The stimulator will be placed in non-stimulation mode by a study team member. In this condition, the stimulator appears to function normally, and the battery will drain, though no stimulation will be 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)

due to electrode fragments in this study is 0.1% per electrode. 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 will be trained in the assessment of electrode site and the daily placement of the Sprint Pad. 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 end of treatment. 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 end of treatment, 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 Sprint MicroLead placement

There are minor risks associated with inserting a Lead through the skin with a needle. These risks are similar to the risks of any needle injection including the possibilities of puncturing a blood vessel, irritating a nerve, and temporary bruising or pain at the insertion site. The risks of puncturing a blood vessel and irritating a nerve are uncommon, but the risks of temporary bruising and pain at the insertion site are common.

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.

To minimize the risks associated with percutaneously placing fine wire leads, only appropriately trained physician investigators will perform the procedure. In addition, the risk of excessive bleeding will be reduced by excluding candidates who are taking warfarin with an INR > 3.0 and by placing manual pressure on the implantation site until hemostasis is achieved. Finally, the risk of discomfort during the procedure will be reduced by the use of an appropriate amount of local anesthetic.

It is possible that, in some cases, multiple attempts may be required to achieve appropriate placement of the Lead during the procedure. Each additional attempt at Lead placement carries the same risks as the initial attempt described in this section.

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

There are risks of leaving a Sprint MicroLead in place for 4 weeks, including skin irritation, infection, and granuloma formation (mild tissue inflammation) at the Lead exit site. Symptoms include redness, swelling, or pain. The risk of skin irritation is common while the risks of infection and granuloma formation are rare.

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 48-72 hour 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

There is a possibility of a Lead breaking beneath the skin either during the course of the study or during the procedure to remove Lead. This risk is uncommon. However, when a Lead breaks, one or more Lead fragments usually remain in the body. The Investigator will use clinical judgment to determine if the removal of such fragments is necessary. Visual inspection of the Lead after it has been removed as well as x-rays will be used to determine if any Lead fragments remain. The risk associated with the x-rays is no greater than that associated with conventional clinical x-rays. If the Investigator determines a Lead fragment has been retained in the body, he/she will determine what is medically required to further evaluate and treat this retained fragment. Typically, no treatment is required unless there are further sequelae, such as an infection or granuloma, associated with the fragment.

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 4 weeks.

4) Risk of infection associated with retained Sprint MicroLead fragments

A Lead fragment could result in the formation of a granuloma or infection. Although the occurrence of a fragment-related infection or granuloma is uncommon an infection may require removal of the Lead fragment and/or treatment with antibiotics. 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

It is possible that a Lead fragment or fragments may be retained in the body following removal of the Sprint MicroLead. If the Investigator determines that a lead fragment has been retained, the Investigator will instruct the subject and his/her caregiver to carefully inspect the Sprint MicroLead exit site and the surrounding skin in the weeks subsequent to Lead 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.

The risks associated with the Lead fragment removal procedure include discomfort during the procedure and skin irritation or infection in the area of the retained fragment. These risks are rare. The risk of infection is mitigated by instructing the subject and/or his caregiver to carefully monitor the site and immediately report any signs of infection.

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. This risk is rare. If lead migration occurs, it is possible that the subject may

experience discomfort during stimulation (described further below under “risk of discomfort with electrical stimulation”). If the Lead has migrated substantially or has come out, it may be necessary to place another Lead. 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, and collecting an additional INR blood sample for subjects who are taking warfarin.

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

It is possible that the skin could become irritated under the Sprint Pad. Additionally, there may be skin irritation in the area surrounding the Lead insertion site, where an adhesive bandage is taped to the skin. This risk is common; however, the bandages can be changed to prevent the irritation from returning.

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

Intramuscular electrical stimulation may be perceived by the subject as a tingling or vibrating sensation, which may feel uncomfortable or painful. The risk of discomfort due to stimulation is uncommon. At high stimulation intensities, shoulder pain may worsen.

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

There is a risk of tissue damage if a subject undergoes diathermy. Shortwave or microwave diathermy is a 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 can cause excessive heating of any implanted metal part (including Leads), resulting in serious injury. The risk of tissue damage associated with diathermy is rare.

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

Tissue damage may occur if a subject undergoes an MRI procedure while the Sprint MicroLead, or a fragment of the Sprint MicroLead, is in the body. The risk of tissue damage associated with MRI use is rare.

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

There is a risk that the subject may have an allergic reaction to the local anesthetic used during the treatment phase prior to insertion of the Sprint MicroLead. If the subject were to have an allergic reaction, it would usually happen while the subject was still in the clinic. If a subject complains of itching, difficulty breathing, lightheadedness and dizziness, or a swollen tongue (common signs of an allergic reaction), appropriate medical treatment will be administered. The risk of allergic reaction to local anesthetics is rare. In addition, there is a risk of adverse central nervous system and/or cardiovascular effects (including a rare risk that the subject's heart can stop beating or that they could stop breathing) if the local anesthetic is administered improperly.

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.

14) Risk associated with venipuncture (if applicable)

The risks of drawing blood from a vein include discomfort at the site of puncture, possible bruising and swelling around the puncture site, an infection, and faintness from the procedure. The risks of discomfort, bruising, and swelling around the puncture site are common while the risks of infection and fainting are rare. Blood sample collections are only required in subjects taking warfarin.

Subjects taking warfarin are at greater risk for developing bruises following venipuncture. However, the risk of discomfort and bruising at that puncture site will be reduced by applying gentle pressure following venipuncture as is the standard practice for collection of blood samples. The rare risk of infection due to venipuncture will be reduced by using proper blood collection technique including wiping the puncture site with an appropriate cleansing solution.

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.

15) 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.

16) 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.

17) Risks of Outcomes Assessments

The questionnaires and Fugl-Meyer Assessment present no risks. The assessments of shoulder torque and kinematics may be slightly uncomfortable. The measures of central sensitization (mechanical pain thresholds for hyperalgesia, pinprick pain thresholds for hyperalgesia, temporal summation of repetitive pin-prick stimuli) may be slightly uncomfortable and may cause brief skin irritation.

18) Other

When using a sham group there is always the rare risk of psychological harm. Some of the survey questions present a rare risk of psychological harm.

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, PT 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+PT Device Inventory Logv3 (11-Nov-2017) | History	0.04

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)

NCT02893267

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? Yes

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:
Mini Mental State Exam (MMSE)

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
MMSE | History	0.02

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).

No for MMSE.

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	0.02
BPI-SF Last Week | History	0.02
FABQ | History	0.01
PCS- Pain Catastrophizing Scale | History	0.01
PGIC (Shoulder Studies, Feb-2017) | History	0.01
SF-36 | History	0.02

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?

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

No

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	0.01
Electrode Fragment Information Sheet 4.0 | History	0.02
Electrode Fragment Wallet Card 2.0 | History	0.03
Instructions for Care of Electrode Exit Site 1st 48 hrs | History	0.03
Instructions for Care of Electrode Exit Site 1st 48 hrs(with Mark up).docx | History	0.04
PNS PT group assignment letter(tracked) | History	0.01
PNS+PT Group Assignment Letter | History	0.03

Name	Version
PNS+PT Other Therapy Diary (during treatment) | History	0.01
PNS+PT Other Therapy Diary (outcomes visits) | History	0.01
PNS+PT Phone Log | History	0.01
PNS+PT Screening Form | History	0.01
PNS+PT Subject Schedule | History	0.02
PNS+PT Subject Scheduletrackchange.docx | History	0.01
Quickstart guide: Sprint Clinician Sham Mode: Non-Contracting PNS | History	0.03
Sprint Clinician Manual Version 2 | History	0.03
Sprint Patient Manual Version 2 | History	0.03
Sprint Stimulator Set up for subject | 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:** Shannon Hogan

Study Role:
Name
Research Support Staff
Obtaining Informed Consent

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:** Kristine Hansen

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

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

Study Role:
Name
Research Support Staff
Obtaining Informed Consent

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

Study Role:
Name
Research Support Staff

View: CCF Key Personnel Questions View
*** Name of Key Personnel Working on Study:** Nathaniel Makowski

Study Role:
Name
Research Support Staff

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

Study Role:
Name
Research Support Staff

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

Study Role:
Name
Research Support Staff

View: CRU DSMP Data Collection Simple View
Name: Chart Review, interview, questionnaire
Level of Risk: Minimal and Low Risk Studies
Type: Data Collection
View: CRU DSMP Data Collection Simple View
Name: Elderly Population
Level of Risk: Moderate Risk Studies
Type: Study Population
View: CRU DSMP Data Collection Simple View
Name: Psychologically or neurologically impaired population
Level of Risk: Moderate Risk Studies
Type: Study Population
View: Create CRU Procedure Risk

	CRU Procedure Risk:		
	Procedure		Risk

* Outcomes Assessments (questionnaires, tests of arm and shoulder movement, 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

				Name High

View: Create CRU Procedure Risk

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