COVER PAGE

Study title:

Objective Assessment of Activity and Sleep Quality In Burst Spinal Cord Stimulation (OASIS)

NCT number:

NCT02950831

Document Date:

05-05-2016

Clinical Investigational Plan

Reference:
SJM-CIP-10133

OASIS

"Objective assessment of Activity and Sleep quality In burst spinal cord Stimulation"

Clinical Investigation Plan (CIP)

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PRINICPAL INVESTIGATOR SIGNATURE PAGE

OASIS

Objective assessment of *A*ctivity and *S*leep quality In burst spinal cord Stimulation

Version A

Reference #: SJM-CIP-10133

I have read and agree to adhere to the clinical investigational plan and all regulatory requirements applicable in conducting this clinical study.

Principal Investigator

Printed name: _____

Signature:_____

Date: _____

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1.0 SYNOPSIS

Title:	Objective assessment of activity and sleep quality in burst SCS
Acronym:	OASIS
Purpose:	The purpose of this study is to assess feasibility of using wearable sensors to capture objective assessments of patient's activity and sleep quality during the spinal cord stimulation (SCS) treatment continuum.
Primary Objective:	To compare objective assessments of activity levels and sleep quality prior to trial, during trial and after permanent implant in failed back surgery syndrome or chronic intractable pain patients who are eligible for a SCS trial
Secondary Objectives:	To compare objective assessments obtained with wearable sensors to subjective assessments of: • Pain; • Quality of life; • Disability obtained using patients questionnaires
Primary Endpoint:	• Change in activity levels and sleep quality between baseline, SCS trial and 1, 2 and 3 months following permanent implant
Secondary Endpoints:	• Compare changes in activity assessed using wearable sensors to changes in visual analog scale (VAS) pain scores, quality of life, and disability scores assessed using patient questionnaires • Compare changes in sleep quality assessed using wearable sensors to changes in visual analog scale (VAS) pain scores, quality of life, and disability scores assessed using patient questionnaires between baseline, SCS trial and 1, 2 and 3 months following permanent implant
Design:	This is a prospective, multicenter, single arm, observational study designed to evaluate feasibility of using wearable sensors to capture objective assessments of patient's activity and sleep quality during SCS treatment continuum. Subjects with a diagnosis of failed back surgery syndrome or chronic intractable trunk and lower limb pain and eligible for a SCS trial will be considered for inclusion in the study. After screening for eligibility using the inclusion/exclusion criteria, baseline evaluation will be performed. Eligible subjects will be provided with wearable sensors in order to record objective activity and sleep quality assessments for 2 weeks and a one-week pain diary to be completed in the last week of the baseline evaluation. Subjects will subsequently be trialed using St. Jude Medical (SJM)

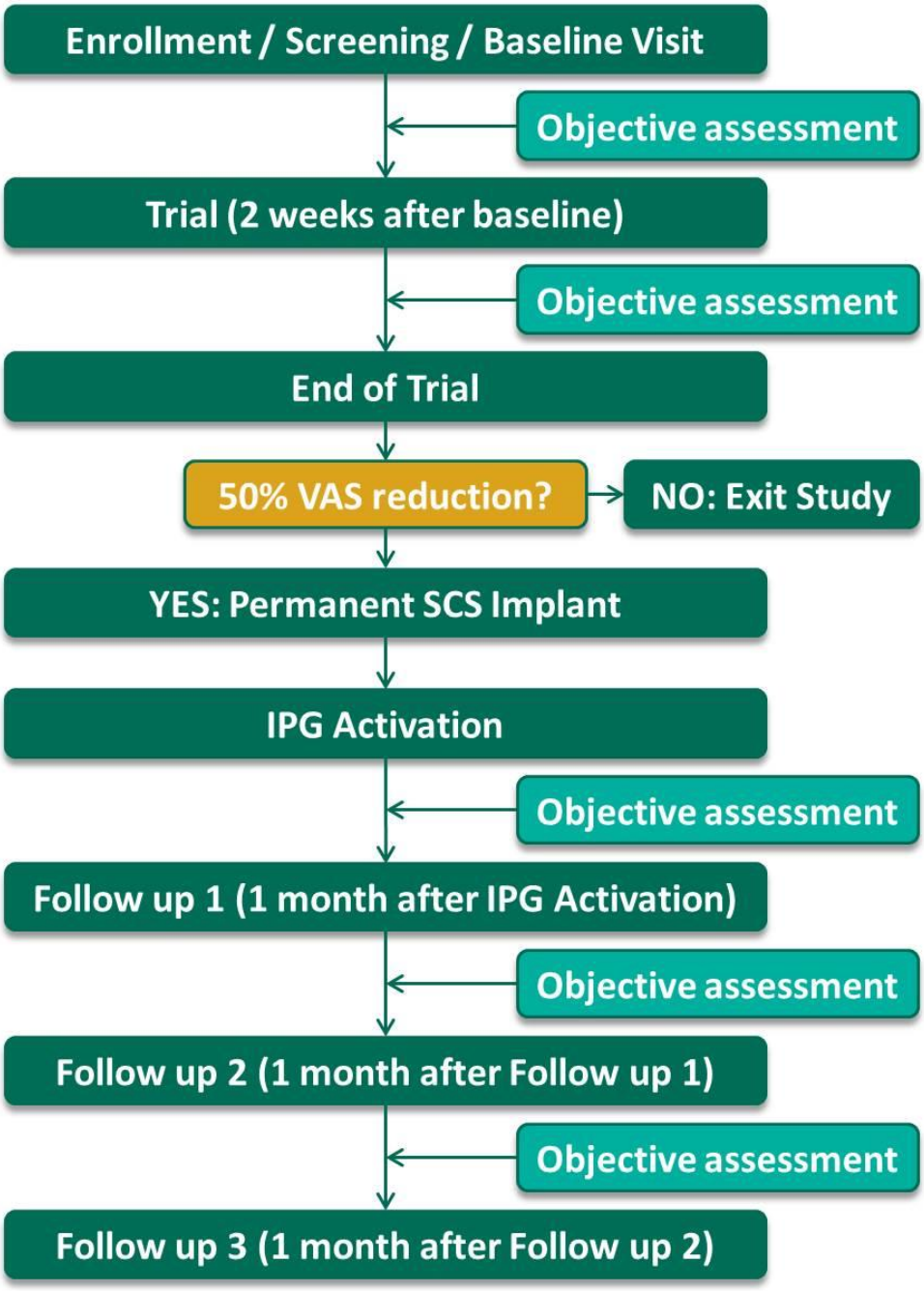
	invisible trial system according to standard clinical procedures. During the trial, objective assessments will be recorded using the wearable sensors and pain will be recorded using a pain diary in the last week of the trial. Subjective assessments will be performed at the end of the trial. Subjects attaining at least 50% low back and lower limbs pain relief (assessed using the VAS questionnaire) will be eligible for permanent implant and further participation in the study. After activation of the permanent implant, subjects will be followed up for 3 months. Objective assessments will be recorded using the wearable sensor throughout the 3 month duration and pain recorded using pain diaries in the week before follow up visits. Subjective assessments will be performed during the 1, 2 and 3 month follow up visits. Subjects w The total duration of the study is expected to be 12 months. The clinical study will be conducted in three centers in the EMEA region Approximately 20 subjects will be enrolled in this study.
Devices used:	• SJM Invisible trial system • SJM SCS leads and extensions • Proclaim, Prodigy or Prodigy MRI™ Implantable Pulse Generator (IPG) • Clinician Programmer • Patient Programmer • Actigraph GT9X link activity monitor
Study Population	A patient becomes a subject once he/she has been fully informed about the study, has agreed to participate, signed & dated the consent. The study population consists of patients with a diagnosis of failed back surgery syndrome or chronic intractable trunk and lower limb pain and who are eligible for a SCS trial. Patients will be considered for enrollment by the Principal Investigator as a candidate for the study at the study site if they meet the inclusion/exclusion criteria requirements, and agree to participate in the study.
Inclusion/Exclusion Criteria	<u>Inclusion Criteria</u> • Subject is able to provide informed consent to participate in the study; • Subject is 18 years of age or older; • Subject has failed to respond to at least 6 months of conventional treatment including pharmacological treatment, physical therapy, epidural injections and/or radiofrequency therapy; • Subjects with the diagnosis of failed back surgery syndrome or

chronic intractable trunk and lower limb pain and are eligible for a SCS trial;
- Subjects have an average trunk pain VAS score of at least 6.0 out of 10.0, and lower limb pain VAS score of at least 6.0 out of 10.0;
- Subject is on stable pain medications, as determined by the Investigator, for at least 28 days prior to enrolling in this study, and is willing to stay on those medications with no dose adjustments until activation of the permanently implanted SCS device;
- Subject's medical record has been evaluated by the Investigator to ensure that the subject is a good candidate for a neurostimulation system;
- Subject is willing to cooperate with the study requirements including compliance with the regimen and completion of all office visits;
- Subject agrees to wear the wearable sensor for the duration of the study;
- Female candidates of child-bearing potential agree to commit to the use of an effective method of contraception (including but not limited to sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, rhythm method, or abstinence) for the duration of the study

<u>Exclusion Criteria</u>
- Subject is currently participating in a clinical investigation that includes an active treatment arm;
- Subject has been implanted with or participated in a trial period for a neurostimulation system;
- Subject diagnosed with neurological deficits affecting the lower limbs;
- Subject diagnosed with fibromyalgia or chronic fatigue;
- Subject has an infusion pump;
- Subject has evidence of an active disruptive psychological or psychiatric disorder as determined as per standard of care;
- Subject has a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease or uncontrolled diabetes mellitus;
- Subject has a current diagnosis of a progressive neurological disease as determined by the Investigator;
- Subject is immunocompromised;
- Subjects with concurrent clinically significant or disabling chronic pain problem that requires additional treatment;
- Subject has an existing medical condition that is likely to require repetitive MRI evaluation in the future (i.e. epilepsy, stroke, multiple sclerosis, acoustic neuroma, tumor);
- Subject has history of cancer requiring active treatment in the last 12 months;

	• Subject has an existing medical condition that is likely to require the use of diathermy in the future; • Subject has documented history of allergic response to titanium or silicone; • Subject has a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to baseline data collection; • Female candidates of child bearing potential that are pregnant (confirmed by positive urine/blood pregnancy test)
Data Collection	**Screening visit:** Subjects will be screened as per inclusion/exclusion criteria and will complete questionnaires to collect secondary outcome measures before the SCS trial. Specifically assessments will include: pain as assessed by the VAS, quality of life as assessed by the EQ-5D, and disability as assessed by the Oswestry Disability Index. Subjects will be provided with a wearable accelerometer for a two weeks to collect baseline objective assessment of activity levels and sleep quality as well as a one-week pain diary to be completed in the last week before initiation of the SCS trial. **Trial phase:** Subjects will undergo a SCS trial performed according to standard clinical practice. During the trial period the subjects will continue to wear the wearable accelerometers and will be asked to complete a one-week pain diary during the last week of the trial. During the end of trial visit, subjects will complete questionnaires to collect secondary outcome measures as during the screening visit. Subjects experiencing at least 50% reduction in VAS scores in their primary area of pain will be considered for a permanent SJM SCS neurostimulation implant capable of delivering burst stimulation. **Permanent implant procedure:** Subjects who underwent a successful trial phase will be implanted with an implantable pulse generator following standard surgical procedures. **Follow up visits:** Following permanent implant activation, the subjects will be followed up for 3 months. During the follow up phase of the study, the subjects will continuously wear the wearable sensors and complete one-week pain diaries in the last week before each follow up visit. Follow up assessments will be performed 1, 2 and 3 months post permanent implant. During each of the follow up visits, subjects will complete questionnaires to collect secondary outcome measures as during the screening visit.

1.1 STUDY FLOW CHART



1.2 STUDY CONTACTS

Jeff Kramer
Lalit Venkatesan
Filippo Agnesi

2.0 BACKGROUND AND JUSTIFICATION FOR CLINICAL STUDY

Spinal cord stimulation (SCS) is a well-established therapy for the treatment of chronic, intractable pain. In a systematic meta-analysis of the literature, (Taylor *et al.* 2006) reported that SCS reduces pain, improves quality of life, reduces analgesic use, allows some patients to return to work and may also result in significant cost savings over time, while having minimally significant adverse events in patients with neuropathic back and/or leg pain.

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (derived from Bonica, 1979). It is a complex phenomenon incorporating an affective component meant to orient behavior toward avoidance of painful stimuli. The nature of this emotional experience confines pain measurements to strictly subjective evaluations such as the visual analog scale (VAS) which is currently accepted as the golden standard. While this form of assessment provides viable evaluations, it remains prone to large inter-user variability and is affected from a variety of factors. The perception of, expression of, and reaction to pain are influenced by genetic, developmental, familial, psychological, social and cultural variables. Psychological factors, such as the situational and emotional factors that exist when we experience pain, can profoundly alter the strength of these perceptions. Similarly, attention, understanding, control, expectations, and the aversive significance can affect pain perceptions (McGrath 1994). The use of objective, continuous measurements of pain has the potential to reduce confounding factors in the evaluation of the therapeutic outcome of SCS and to provide feedback to help physicians in the adjustment of pain management strategies.

While considerable efforts toward establishing biomarkers of pain have been performed, no established practical method to objectively measure the sensation of pain has been proposed so far. Nevertheless, studies in the literature suggest that measurements of behaviors affected by pain could be used to indirectly derive information about a person in a painful state. In a nationally representative sample, adults with chronic widespread pain have lower average activity and spend less time engaged in moderate to vigorous activity when compared to those who do not suffer from chronic pain (Dainese *et al.* 2014). In patients with chronic pain, mean and peak activity levels were lower while sedentary time was longer (Wilson *et al.* 2012). Similarly, sleep disturbances are a known comorbidity of chronic pain (Emery *et al.* 2014). SCS has the potential to restore physical activity as shown in animal models (Sato et al. 2014, Gong et al. 2014). Likewise SCS produced improvement in insomnia scores (Ramineni et al 2016)) and sleep quality (Obuchi et al. 2015).
Similar to subjective pain evaluations, scales utilized for subjective assessments of activity and sleep are limited in their reliability. A systematic review of 120 physical activity questionnaires concluded their validity is "moderate at best" (Helmerhorst et al 2012). While sleep questionnaires can have a higher validity (Nascimento-Ferreira et al 2015) a systematic review of the Epworth sleepiness scale does not suggests the use for individual-level comparisons.

Recent advancements in wearable technologies can allow continuous objective assessment of changes in patient activity levels and sleep quality, which could be related to effectiveness of

pain treatment and management. In this study, we aim to evaluate the feasibility of using wearable sensors to record objective assessments of activity and sleep quality over the duration of the SCS treatment continuum. Additionally we also aim to compare these assessments to the commonly used subjective measures in the standard of care in chronic pain patients indicated for a SCS trial. While these objective assessments are not direct measurements of pain, they have the potential to serve as a highly accurate tool to evaluate changes in the quality of life and the level of disability in chronic pain patients.

3.0 RISKS AND BENEFITS OF THE CLINICAL STUDY

The purpose of study is to collect data necessary to evaluate the feasibility of using wearable sensors to capture objective measures of patient's activity and sleep quality during spinal cord stimulation (SCS) treatment continuum using burst stimulation. The study population consists of patients with a diagnosis of failed back surgery syndrome or chronic intractable pain who are eligible for a SCS trial.

The SCS devices used in the study are currently market approved for treatment of chronic trunk and/or limb pain. Objective assessments will be performed using wearable sensors that are commercially available.

We do not foresee any additional risk, beyond those normally associated with SCS therapy.

3.1 DESCRIPTION OF SUBJECT POPULATION

Approximately 20 patients will be enrolled in this study. The study population consists of patients with a diagnosis failed back surgery syndrome or chronic intractable pain who are eligible for a SCS trial. Patients will be considered for enrollment by the Principal Investigator as a candidate for the study at the study site if they meet the inclusion/exclusion criteria requirements, and agree to participate in the study.

3.2 ANTICIPATED CLINICAL BENEFITS

There are no additional clinical benefits associated with the participation in this study beyond those anticipated with standard clinical SCS.

3.3 ANTICIPATED ADVERSE EVENTS AND ADVERSE DEVICE EFFECTS

In addition to those risks commonly associated with surgery, the following risks are associated with implanting or using this neurostimulation system for SCS:

Anticipated adverse events
Undesirable changes in stimulation, which may be related to cellular changes in tissue around the electrodes, changes in electrode position, loose electrical connections, or lead failure
Lead migration, causing changes in stimulation and/or reduced pain relief
Epidural hemorrhage, hematoma, infection, spinal cord compression, or paralysis from placement of a lead in the epidural space
Cerebrospinal fluid (CSF) leakage
Paralysis, weakness, clumsiness, numbness, or pain below the level of the implant
Persistent pain at the electrode or IPG site
Seroma (mass or swelling) at the IPG site

Infection of the lead extension at the exit zone during trial or infection of the IPG site
Allergic or rejection response to implant materials
Implant migration or skin erosion around the implant
Anticipated adverse device effects
Battery failure

These adverse events and adverse device effects are not specific to the study, but related to the approved SCS implant procedure.

3.4 RESIDUAL RISKS ASSOCIATED WITH THE DEVICE UNDER INVESTIGATION, AS IDENTIFIED IN THE RISK ANALYSIS REPORT

There are no residual risks associated with the stimulation protocol under investigation.

3.5 RISKS ASSOCIATED WITH PARTICIPATION IN THE CLINICAL STUDY

There are no risks associated with the participation in the study beyond those associated with to SCS standard of care.

3.6 POSSIBLE INTERACTIONS WITH CONCOMITANT MEDICAL TREATMENTS AND/OR CONCURRENT MEDICAL INTERVENTIONS

There are no possible interactions with concomitant medical treatment and/or concurrent medical intervention beyond those associated with standard medical care using SCS.

3.7 STEPS THAT WILL BE TAKEN TO CONTROL OR MITIGATE THE RISKS

Subjects will be informed concerning the potential risks and benefits associated with participation in the study prior to their enrollment.

3.8 RISK-TO-BENEFIT RATIONALE

The study will use devices currently approved as part of standard pain management care together with commercially available wearable sensors. Establishing feasibility of using wearable sensors to capture objective measures of patient's activity and sleep quality during spinal cord stimulation (SCS) treatment continuum could provide robust outcomes not affected by confounding factors such as subjectivity and emotional state.

3.9 DESCRIPTION OF HISTORY OF MODIFICATIONS OR RECALL IN RELATION TO SAFETY AND CLINICAL PERFORMANCE FOR DEVICE UNDER INVESTIGATION

There have been no modifications or recalls in relation to safety and clinical performance of the devices utilized in this study.

4.0 STUDY DESIGN

4.1 PURPOSE

The purpose of this study is to assess feasibility of using wearable sensors to capture objective measures of patient's activity and sleep quality during spinal cord stimulation (SCS) treatment continuum using burst stimulation.

4.2 STUDY DESIGN AND SCOPE

This is a prospective, multicenter, single arm, observational study designed to compare objective assessment of activity levels and sleep quality prior to trial, during trial and after permanent implant in failed back surgery syndrome or chronic intractable pain patients who are eligible for a SCS trial

Patients with a diagnosis of failed back surgery syndrome or chronic intractable pain who are eligible for a SCS trial and recommended by the principal investigator will be approached to participate in the study. The patient will be informed about the study to determine if he/she is interested in participating. Subjects will be assessed at baseline using questionnaires.

Specifically subjective assessments will include:
- pain level as assessed by the VAS;
- quality of life as assessed by the EQ-5D;
- disability as assessed by the Oswestry Disability Index (ODI).

Subjects will be provided with wearable sensors and to collect baseline objective assessments of activity levels and sleep quality for two weeks. Subjects will also receive a one-week pain diary and will be instructed to complete it in the last week before initiation of the SCS trial.

Subjects will subsequently be trialed using St. Jude Medical (SJM) invisible trial system according to standard clinical procedures. During the trial period subjects will continue to use the wearable sensors; objective assessments will be recorded during the trial while the subjective assessments performed at baseline will be repeated at the end of trial visit.
Subjects obtaining at least 50% low back and lower limbs pain relief (assessed using the VAS questionnaire) will be eligible for permanent implant and further participation in the study.

After activation of the permanent implant, subjects will be followed up for 3 months. Objective assessments will be recorded using the wearable sensor throughout the 3 month duration and subjective assessments will be performed during the 1, 2 and 3 month follow up visits.

The total duration of the study is expected to be 12 months.

The clinical study will be conducted in three centers in the EMEA region.

4.2.1 Number of subjects required to be included in the study

Approximately 20 subjects will be enrolled in the study.

4.2.2 Estimated time needed to enroll this subject population

The study may continue up to 2 years, dependent on the rate of enrollment.

4.3 OBJECTIVES

4.3.1 Primary Objective

To compare objective assessment of activity levels and sleep quality prior to trial, during trial and after permanent implant in failed back surgery syndrome or chronic intractable pain patients who are eligible for a SCS trial.

4.3.2 Secondary Objective

To compare objective assessments obtained with wearable sensors to subjective assessments of:

- Pain;
- Quality of life;
- Disability

obtained using patients questionnaires.

4.4 ENDPOINTS

4.4.1 Primary Endpoint

Change in activity levels and sleep quality between baseline, SCS trial and permanent implant follow up visits.

4.4.2 Secondary Endpoint

- Compare changes in activity assessed using wearable sensors to changes in visual analog scale (VAS) pain scores, quality of life, and disability scores assessed using patient questionnaires
- Compare changes in sleep quality assessed using wearable sensors to changes in visual analog scale (VAS) pain scores, quality of life, and disability scores assessed using patient questionnaires

between baseline, SCS trial and 1, 2 and 3 month visits following permanent implant

4.5 INCLUSION AND EXCLUSION CRITERIA

A subject, who meets all of the inclusion criteria, and none of the exclusion criteria, is eligible to participate in this study.

All subjects enrolled in the clinical study (including those withdrawn from the clinical study or lost to follow-up) will be accounted for and documented, assigning an identification code linked to their names, alternative identification or contact information.

This log will be kept up to date throughout the clinical study by the principal investigator or his/her authorized designee. To ensure subject privacy and confidentiality of data this log must be maintained throughout the clinical study at the clinical site.

To participate in this clinical subject, the subject must meet all of the following inclusion criteria:

4.5.1 Inclusion Criteria

- Subject is able to provide informed consent to participate in the study;
- Subject is 18 years of age or older;
- Subject has failed to respond to at least 6 months of conventional treatment including pharmacological treatment, physical therapy, epidural injections and/or radiofrequency therapy;
- Subjects with the diagnosis of failed back surgery syndrome or chronic intractable trunk and lower limb pain and are eligible for a SCS trial;
- Subjects have an average trunk pain VAS score of at least 6.0 out of 10.0, and lower limb pain VAS score of at least 6.0 out of 10.0
- Subject is on stable pain medications, as determined by the Investigator, for at least 28 days prior to enrolling in this study, and is willing to stay on those medications with no dose adjustments until activation of the permanently implanted SCS device;
- Subject's medical record has been evaluated by the Investigator to ensure that the subject is a good candidate for a neurostimulation system;
- Subject is willing to cooperate with the study requirements including compliance with the regimen and completion of all office visits;
- Subject agrees to wear the wearable sensor for the duration of the study
- Female candidates of child-bearing potential agree to commit to the use of an effective method of contraception (including but not limited to sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, rhythm method, or abstinence) for the duration of the study

Subjects are not eligible for clinical study participation if they meet any of the following exclusion criteria:

4.5.2 Exclusion Criteria

- Subject is currently participating in a clinical investigation that includes an active treatment arm;
- Subject has been implanted with or participated in a trial period for a neurostimulation system;
- Subject diagnosed with neurological deficits affecting the lower limbs;
- Subject diagnosed with fibromyalgia or chronic fatigue;
- Subject has an infusion pump;
- Subject has evidence of an active disruptive psychological or psychiatric disorder as determined as per standard of care;
- Subject has a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease or uncontrolled diabetes mellitus;
- Subject has a current diagnosis of a progressive neurological disease as determined by the Investigator;
- Subject is immunocompromised;
- Subjects with concurrent clinically significant or disabling chronic pain problem that requires additional treatment;
- Subject has an existing medical condition that is likely to require repetitive MRI evaluation in the future (i.e. epilepsy, stroke, multiple sclerosis, acoustic neuroma, tumor);
- Subject has history of cancer requiring active treatment in the last 12 months;
- Subject has an existing medical condition that is likely to require the use of diathermy in the future;
- Subject has documented history of allergic response to titanium or silicone;
- Subject has a documented history of substance abuse (narcotics, alcohol, etc.) or substance dependency in the 6 months prior to baseline data collection;
- Female candidates of child bearing potential that are pregnant (confirmed by positive urine/blood pregnancy test)

4.6 SUBJECT POPULATION

The study population consists of patients with a diagnosis of failed back surgery syndrome or chronic intractable pain patients who are eligible for a SCS trial. Patients will be considered for enrollment by the Principal Investigator as a candidate for the study at the study site if they meet the inclusion/exclusion criteria requirements, and agree to participate in the study.

4.6.1 Subject Screening

Patients who are recommended by the Investigator as a candidate for the study will be fully informed about the study and asked to participate in the study. In case the patient agrees, a duly signed and dated Patient Informed Consent will be obtained. Subjects will be screened by a member of the investigational team previously trained on the CIP and delegated to do so.

Subjects who do not meet the inclusion/exclusion criteria will not be eligible to participate in this study.

4.6.2 Point of Enrollment

Subjects are considered enrolled in the study from the moment the subject has provided written Patient Informed Consent. (Refer to section 4.7 for the Informed Consent Process).

4.7 INFORMED CONSENT PROCESS

4.7.1 General process

Prior to enrolling in the clinical study and conducting study-specific procedures, all subjects will be consented, as required by applicable regulations and the center's IRB/EC. Informed consent must be obtained from each subject prior to any study related procedures. The consent form must be signed and dated by the subject and by the person obtaining the consent.

The principal investigator or his/her authorized designee will conduct the Informed Consent Process. This process will include a verbal discussion with the subject on all aspects of the clinical study that are relevant to the subject's decision to participate in the clinical study.

The subject shall be provided with the informed consent form that is written in a language that is understandable to the subject and has been approved by the center's IRB/EC. Failure to obtain informed consent from a subject prior to study enrollment should be reported to St. Jude Medical within 5 working days and to the reviewing center's IRB/EC/ consistent with the center's IRB/EC reporting requirements.

5.0 DEVICE UNDER INVESTIGATION AND CONTROL/COMPARATORS (IF APPLICABLE)

5.1 DEVICE DESCRIPTION

In this study, the SJM Invisible trial system and the Proclaim, Prodigy or the Prodigy MRI neurostimulation system will be used. The SCS system consists of the following devices

Table 1: Description of Proposed Devices

Device Component	Model/Type	Investigational or Market Released
SJM Invisible trial external pulse generator (EPG)	3599 (Base), 3032 (Header)	Released
SJM Invisible trial Clinician Programmer	3870, 3872	Released
SJM Invisible trial Patient Controller	3871, 3873	Released
SJM Percutaneous trial lead	31XX	Released
SJM Lead extension	33XX	Released
SJM Prodigy internal pulse generator (IPG)	3799	Released
SJM Prodigy MRI IPG	3772	Released
SJM Prodigy Charger	3730	Released
SJM Prodigy Patient Programmer	3856	Released
SJM Rapid Programmer programming device	3835	Released
SJM Proclaim IPG	3660, 3662	Released
SJM Clinician Programmer App	3874	Released
SJM Patient Controller App	3875	Released
SJM Octrode™ lead	318X	Released
SJM Cinch™ Lead Anchor	1194	Released
SJM Swift-Lock™ Anchor	1192	Released
Actigraph wearable sensor	GT9X link activity monitor	Released

- **SJM Invisible trial external pulse generator (EPG):** a 16 channels, software controlled, battery powered, external stimulator that generates the electrical pulses to be used during the trial phase of the study
- **SJM Invisible trial Clinician Programmer:** software compatible with iOS™ App 8.1 or later to be used on iPad mini™; enables the clinician to program the SJM Invisible trial EPG

- **SJM Invisible trial Patient Controller:** software compatible with iOS™ App 8.1 or later to be used on iPad touch™; enables patient-controlled therapy adjustment of the SJM Invisible trial EPG
- **SJM Percutaneous trial lead:** sterile stimulating electrode placed in the epidural space of the spinal cord and connected to the EPG
- **SJM Lead extension:** sterile extension that connects the pulse generator to the stimulating electrode
- **SJM Prodigy:** a 16 channels, software controlled, rechargeable battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses.
- **SJM Prodigy MRI:** a 16 channels, software controlled, rechargeable battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses.
- **SJM Prodigy Charger:** The IPG Charging System provides the capability to recharge the IPG battery while stimulation is either on or off. The charging system has several main parts: AC line cord, AC power supply, power cable, and charger antenna. The charger transmits RF energy through the antenna to the IPG battery to recharge it.
- **SJM Patient Programmer:** the patient programmer allows subjects to adjust stimulation intensity and to select a different stimulation programs in the Prodigy MRI IPG.
- **SJM Rapid Programmer:** the rapid programmer enables the clinician to program the Prodigy IPG.
- **SJM Proclaim internal pulse generator (IPG):** a 16 channels, software controlled, battery powered, internal stimulator to be used during the follow up phase of the study that generates the electrical pulses
- **SJM Clinician Programmer App:** software compatible with iOS™ App 8.3 or later to be used on iPad mini™; enables the clinician to program the Proclaim IPG
- **SJM Patient Controller App: :** software compatible with iOS™ App 8.1 or later to be used on iPad touch™; enables patient-controlled therapy adjustment of the Proclaim IPG
- **SJM Octrode™ lead:** sterile stimulating electrode that placed in the epidural space of the spinal cord and connected to the Proclaim IPG
- **SJM Cinch™ Lead Anchor:** securing device designed to reduce lead migration and breakage
- **SJM Swift-Lock™ Anchor:** securing device designed to reduce lead migration and breakage
- Actigraph GT9X link activity monitor: wrist worn watch containing a gyroscope, magnetometers and 3-axis accelerometer designed for objective assessment of activity and sleep quality

5.2 DEVICE ACCOUNTABILITY (if applicable)

Device accountability is not required in post market studies.

6.0 PROCEDURES

6.1 STUDY FLOW CHART

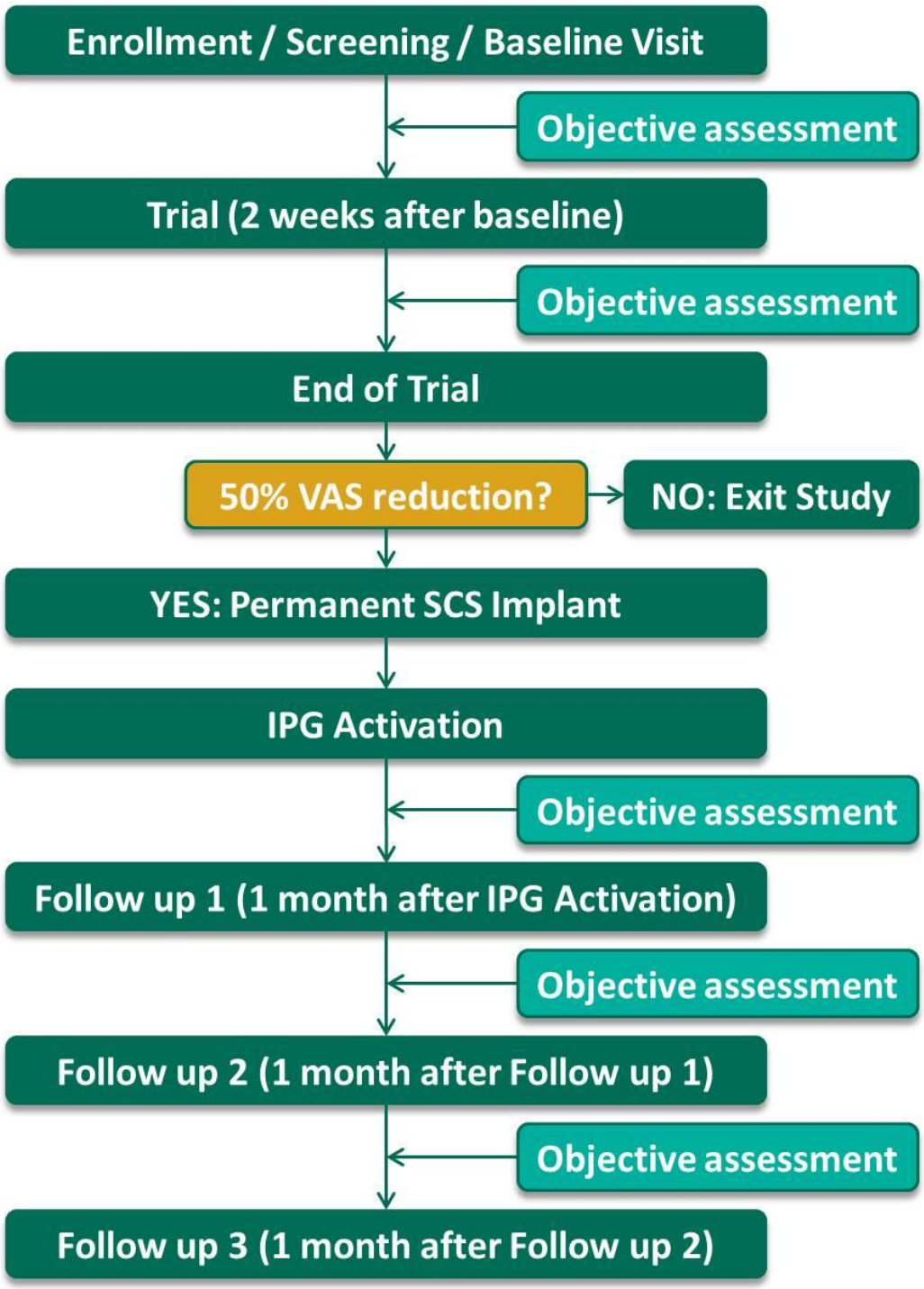


Figure 2: Study Flow Chart

6.2 PROCEDURES

The clinical study will be conducted in accordance with the CIP. All parties participating in the conduct of the clinical study will be qualified by education, training, or experience to perform their tasks and this training will be documented appropriately.

The clinical study will not commence until St. Jude Medical receives written approval from the EC and relevant regulatory authorities and all required documents have been collected from the site(s).

Table 1: List of all study specific activities/procedures

Visit / Study Activity	Enrollment	Baseline	SCS Trial	End of Trial	SCS Implant Procedure	Activation	Follow up Visits*
Informed Consent Process	X						
Inclusion/Exclusion Criteria Screening	X						
VAS assessment		X		X			X
EQ-5D questionnaire		X		X			X
ODI questionnaire		X		X			X
Provide wearable sensor		X					
Provide pain diary		X	X			X	X
Collect wearable sensor data			X	X			X
Collect pain diary			X	X			X
Trial system implant			X				
Permanent lead implant					X		
IPG implant					X		
IPG Programming						X	

*Follow up visit assessments will be performed after activation visit at weeks 4 (28±7 days), 8 (56±7 days) and 12 (84±7 days).

6.3 ENROLLMENT

The following enrollment activities are performed after the subject has been screened and must occur before any study procedure/visit.

- The principal or delegated study personnel are responsible for screening all potential subjects to determine subject eligibility for the study
- Record enrollment information (name of the study, date of consent and Inclusion/exclusion information) in the hospital records and complete and submit the Enrollment form in a timely manner (recommended within 5 days)
- Notification of enrollment to the sponsor will take place only when the sponsor receives the enrollment form

NOTE: As soon as the subject signs the Patient Informed Consent, adverse events need to be reported according to the guidelines mentioned in section 8.2.

If a subject does not meet all inclusion criteria or meets any of the exclusion criteria, the subject cannot participate in the study and cannot be enrolled.

In case the subject was already consented to participate in the study, but does not meet inclusion/exclusion criteria, the following actions will be taken.

If study procedure/device implant has not occurred:

- Document enrollment information (name of the study, date of consent and inclusion/exclusion) in the hospital records; complete the Enrollment and Withdrawal Forms. The form must be authorized / approved by the principal or delegated investigator.
  - Inform the subject about the withdrawal.
  - The EC/IRB and CA should be notified appropriately about any deviations with regards to obtaining the informed consent.

If study procedure/device implant has occurred:

- Document enrollment information (name of the study, date of consent and inclusion/exclusion) in the hospital records; complete the Enrollment and Withdrawal Forms. The form must be authorized / approved by the principal or delegated investigator.
  - Complete study deviation for inclusion/exclusion not met
  - The EC/IRB and CA should be notified appropriately about any deviations with regards to obtaining the informed consent.

The following activities and assessments will be performed during screening:

Timing of visit	Activities at visit	Case Report Form
Screening	• Subject is screened for inclusion/exclusion criteria • Subject signs informed consent	• Enrollment Form • Inclusion/Exclusion Form

6.4 BASELINE VISIT

Baseline visit activities can occur at the same visit of enrollment after the informed consent has been obtained.
Subjects will complete the questionnaires to assess:

- pain level as assessed by the VAS;
- quality of life as assessed by the EQ-5D;
- disability as assessed by the ODI

Subjects will be provided with the wearable sensor and will be instructed on the correct usage. Subjects will also be provided with a one-week pain diary and instructed to complete it on the last week before initiation of the SCS trial.

The following activities and assessments will be performed during baseline visit:

Timing of visit	Activities at visit	Case Report Form
Screening	• Subject assess pre-trial pain levels, quality of life and, disability,Provide wearable sensor • Provide one-week pain diary	• VAS Form • EQ-5D Form • ODI From

6.5 SCS Trial

Subjects will report for SCS trial system implant. Pain diaries will be collected. Subjects will be provided with a new one-week pain diary and instructed to complete it in the last week before the "end of trial" visit. Data stored in the wearable sensors will be downloaded and stored securely in a computer such that can be traced to the subject ID and study visit. Wearable sensor memory will be wiped clean and devices prepared for the next acquisition period.

Subject will be implanted according to standard of care with a SJM invisible trial system.
EPG will be programmed using burst stimulation according to standard programming techniques.

The following activities and assessments will be performed during SCS trial:

Timing of visit	Activities at visit	Case Report Form
SCS Trial	• SCS trial lead implant • EPG programming • Collect pain diary • Collect wearable sensor baseline data • Provide pain diary	• VAS Pain Diary Form

6.6 END OF TRIAL VISIT

During the End of Trial visit, subjects will complete the same questionnaires completed during the baseline visit. Pain diaries will be collected. Data stored in the wearable sensors will be downloaded and stored securely in a computer such that can be traced to the subject ID and study visit. Wearable sensor memory will be wiped clean and devices prepared for the next acquisition period. Subjects will be instructed not to wear the wearable sensor until the activation visit.

If the VAS score is >50% of the VAS collected during the screening visit the subject will exit the study. Subjects whose VAS score at the end of the trial is ≤50% of the VAS collected during the screening visit will be considered for permanent lead and IPG implantation.

The following activities and assessments will be performed during end of trial visit:

Timing of visit	Activities at visit	Case Report Form
End of Trial	• Subject assess during-trial pain levels, quality of life and disability • Collect pain diary	• VAS Form • EQ-5D Form • ODI From

	• Collect wearable sensor SCS trial data	• VAS Pain Diary Form

6.7 PERMANENT IMPLANT

Permanent implant will be performed according to standard clinical practice

The following activities and assessments will be performed during SCS implant:

Timing of visit	Activities at visit	Case Report Form
SCS Implant	• SCS permanent lead implant • IPG implant	

6.8 ACTIVATION VISIT

IPG will be programmed using burst stimulation according to standard programming techniques. Subjects will be provided with a new one-week pain diary and instructed to complete it in the last week before the first "follow up" visit. Subjects will be instructed to start wearing the wearable sensor again.

The following activities and assessments will be performed during activation visit:

Timing of visit	Activities at visit	Case Report Form
Activation	• IPG programming • Provide pain diary	

6.9 SCHEDULED FOLLOW-UPS

Subjects will be followed up for 3 months at one-month intervals. During each visit, subjects will complete the same questionnaires completed during the baseline visit. Pain diaries will be collected. Subjects will be provided with a new one-week pain diary and instructed to complete it in the last week before the next "follow up" visit. Data stored in the wearable sensors will be downloaded and stored securely in a computer such that can be traced to the subject ID and study visit. Wearable sensor memory will be wiped clean and devices prepared for the next acquisition period.

The following activities and assessments will be performed during follow up visits:

Timing of visit	Activities at visit	Case Report Form
Follow up	• Subject assess during-trial pain levels, quality of life and disability • Collect pain diary • Collect wearable sensor SCS trial data	• VAS Form • EQ-5D Form • ODI From • VAS Pain Diary Form

6.10 UNSCHEDULED VISITS

An Unscheduled Visit is defined as any visit where an active study subject returns to the participating study site for medical care outside of a specified study visit. Unscheduled visits may include subjects returning to the office for an adverse event.

The visit should be documented by completing the Unscheduled Visit Form and any other applicable forms (Adverse Event, Deviation, Death and/or Withdrawal Form.

6.11 DESCRIPTION OF ACTIVITIES PERFORMED BY SPONSOR REPRESENTATIVES

Trained sponsor personnel may perform certain activities to ensure compliance to the clinical investigational plan and may provide technical expertise.

Sponsor personnel may:

- Provide technical support to the Investigators during trial

Sponsor personnel will not:

- Perform the informed consent process
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject without the approval and presence of a health care practitioner
- Independently collect clinical investigational data

6.12 SUBJECT STUDY COMPLETION

When the subject's participation in the clinical study has been completed the subject will return to the medical care as per physician's recommendation.

6.13 ANY KNOWN OR FORSEEABLE FACTORS THAT MAY COMPROMISE THE OUTCOME OF THE CLINICAL STUDY OR THE INTERPRETATION OF THE RESULTS

All foreseeable factors that may compromise the outcome have been taken into account by clinical study design and well-defined subject selection criteria.
Patient recruitment and retention will be monitored throughout the study and include (but are not limited to) the following activities: evaluation of the site and investigators, training of site personnel, developing site support materials, providing patient visit calendars.

6.14 CRITERIA AND PROCEDURES FOR SUBJECT WITHDRAWAL OR DISCONTINUATION

Each subject should remain in the study until completion of the required follow up period; however, a subject's participation in the study may be discontinued at any time. Should this occur, the reason for discontinuation must be documented in the withdrawal form.

Subjects must be informed about their right to withdraw from the study at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled and withdrawal from the study will not jeopardize their future medical care or relationship with the investigator. Subjects will be asked to specify the reason for the termination, but have the right not to answer.

The investigator may decide to withdraw a subject from the study at any time with reasonable rationale. The subject's future care will not be influenced by a decision, voluntary or otherwise, to withdraw from the study. All reasonable efforts should be made to retain the subject in the clinical study until completion of the study.

Reasons for subject's withdrawal include, but are not limited to:

- Subject refuses to continue participating in the study
- Subject does not meet the inclusion/exclusion criteria and does not require additional follow-up for safety reasons.
- Subject is deceased (cause must be documented)
- Subject's non-compliance
- Subject's participation is terminated by the PI or investigator, although the subject consented, since participation is no longer medically appropriate
- Subject is 'lost to follow up': Subject does not adhere to the scheduled follow up visits but has not explicitly requested to be withdrawn from the clinical study. (This does not apply to missed visits). Site personnel should at all times make all reasonable efforts to locate and communicate with the subject in order to achieve subject compliance to the scheduled follow up visits:
  1. A subject will be considered 'Lost to Follow Up' after a minimum of 2 phone calls of a physician or delegate at the investigational site to the subject or contact. These 2 phone calls need to be documented in the subject's hospital records.
  2. If these attempts are unsuccessful, a letter should be sent to the subject's last known address or general practitioner (GP) and a copy of this letter should be maintained in the subject's hospital records.

Note: If a subject misses one or more of the scheduled follow up visits (inclusive of the assigned visit windows), this will be considered as a missed visit. The subject may therefore still return for subsequent visits and will not be excluded from the study.

If a subject withdraws from the clinical study, the site will record the subject's reasons for withdrawal, on a Withdrawal CRF.

When subject withdrawal from the clinical study is due to an adverse event the subject will be followed until resolution of that adverse event or determination that the subject's condition is stable. The status of the subject's condition should be documented at the time of withdrawal.

The third follow up visit will be the final study visit. The subject will complete the questionnaires as in the previous follow up visit, return the last pain diary, return the wearable sensor and will exit the study.

7.0 COMPLIANCE TO CIP

7.1 STATEMENTS OF COMPLIANCE

The study will be performed in accordance with the most current versions of the World Medical Association (WMA) Declaration of Helsinki, ISO14155 and any regional and/or national regulations and will be compliant to this International Standard and any regional and national regulations, as appropriate.

- The investigator will not start enrolling subjects or requesting informed consent from any subject prior to obtaining IRB/EC approval and Competent Authority approval, if applicable, and authorization from the sponsor in writing for the study.

In case additional requirements are imposed by the IRB/EC or Competent Authority, those requirements will be followed, if appropriate. If any action is taken by an IRB/EC, and regulatory requirements with respect to the study, that information will be forwarded to St. Jude Medical.

As sponsor, St. Jude Medical has taken up general liability insurance in accordance with the requirements of the applicable local laws. Appropriate country representative will be utilized to understand the requirements for the type of insurance that will be provided for subjects, such information will be incorporated into the informed consent, as applicable

If required, additional subject coverage or a study specific insurance will be provided by the Sponsor as well.

7.2 ADHERENCE TO THE CLINICAL INVESTIGATION PLAN

A deviation is defined as an event where the clinical investigator, site personnel, sponsor or sponsor representative did not conduct the clinical study according to the Clinical Investigational Plan, IRB/EC requirements or the Investigator Agreement. The investigator is not allowed to deviate from the CIP, except as specified under emergency circumstances.

In some cases, failure to comply with the CIP may be considered failure to protect the rights, safety and well-being of subjects, since the non-compliance exposes subjects to unreasonable risks. For example, failure to adhere to the inclusion/exclusion criteria: these criteria are specifically defined by the Sponsor to exclude subjects for whom the device is not beneficial and the use involves unreasonable risks. This may be considered failure to protect the rights, safety and well-being of the enrolled subject. Similarly, failure to perform safety assessments intended to detect adverse events may be considered failure to protect the rights, safety and well-being of the enrolled subject. Investigators should seek minimization of such risks by adhering to the CIP.

Simultaneously, in the event that adhering to the CIP might expose the subject to unreasonable risks, the investigator is also required to protect the rights, safety and well-being of the subject by intentionally deviating from the requirements of the CIP, so that subjects are not exposed to unreasonable risks.

It is the responsibility of the investigator to provide adequate medical care to a subject enrolled in a study.

Regulations require that the PI maintain accurate, complete, and current records, including documents showing the date of and reason for every deviation from the Clinical Investigational Plan. Relevant information for each deviation will be documented on a Deviation Case Report Form. The site will submit the CRF to St. Jude Medical.

Regulations require Investigators obtain approval from St. Jude Medical and the IRB/EC [as required] before initiating changes in or deviations from the protocol, except when necessary to protect the life or physical well-being of a subject in an emergency. Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of human subjects may proceed without prior approval of

the sponsor and the EC. Such deviations shall be documented and reported to the sponsor and the EC as soon as possible, but no later than 5 working days.
Prior approval must be requested when the PI anticipates, contemplates, or makes a conscious decision to depart from the CIP, except when unforeseen circumstances are beyond the investigator's control (e.g. a subject who fails to attend a scheduled follow-up visit, a subject is too ill to perform a CIP-required test, etc.). All deviations, including those beyond the investigator's control, must be reported on a CRF.

To obtain approval, the Principal Investigator may call or email and discuss the potential deviation with St. Jude Medical or designee prior to initiating any changes.

All deviations must be reported to appropriate regulatory authorities in specified timelines (if appropriate).

Investigators or the designee must notify St. Jude Medical, Inc. as soon as possible and complete the Deviation CRF.

The Investigator is required to adhere to local regulatory requirements for reporting deviations to IRB/EC.

7.3 REPEATED AND SERIOUS NON-COMPLIANCE

In the event of repeated non-compliance or a one-time serious non-compliance, as determined by the Sponsor, a Clinical Research Associate or clinical representative will attempt to secure compliance by one or more of the following actions:

- Visiting the investigator
- Contacting the investigator by telephone
- Contacting the investigator in writing
- Retraining of the investigator

If an investigator is found to be repeatedly non-compliant with the signed agreement, the CIP or any other conditions of the clinical study, the Sponsor will either secure compliance or, at its sole discretion, terminate the investigator's participation in the clinical study.

8.0 ADVERSE EVENT, ADVERSE DEVICE EFFECT, DEVICE DEFICIENCY

8.1 DEFINITIONS

8.1.1 Medical device

Any instrument, apparatus, implement, machine, appliance, implant, software, material or other similar or related article

- Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of
  - Diagnosis, prevention, monitoring, treatments or alleviation of disease,
  - Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury,

- Investigation, replacement, modification, or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
- Control of conception,
- Disinfection of medical devices and

- Which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means

8.1.2 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device under study.

This definition includes events related to the investigational medical device or the comparator.
This definition includes events related to the procedures involved.

8.1.3 Serious Adverse Event (SAE)

An adverse event that led to:

- Death
- A serious deterioration in the health of the subject, that either resulted in:
  - A life-threatening illness or injury OR
  - A permanent impairment to a body structure or a body function OR
  - An in-patient or prolonged hospitalization OR
  - A medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body OR
  - A malignant tumor
- Fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition, or a procedure required by the CIP is not considered a serious adverse event.

8.1.4 Adverse Device Effect (ADE)

An adverse event related to the use of an investigational medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

This definition includes any event resulting from the use error or from intentional misuse of the investigational medical device.

8.1.5 Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

1. **Unanticipated Serious Adverse Device Effect (USADE) [applicable to studies following ISO 14155]**

A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

2. **UADE [applicable to investigational studies following FDA regulations]**

As defined in 21 CFR §812.3, unanticipated adverse device effects (UADE) are defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

If an unanticipated adverse device effect occurs, the investigator must notify St. Jude Medical and the IRB/MEC immediately, but no later than 10 working days of the investigator's knowledge of the event, as required by 21 CFR §812.150. St. Jude Medical will take any steps necessary to investigate the event, and will be responsible for notifying FDA and all other participating IRBs/MECs and investigators.

3. **Anticipated Serious Adverse Device Effect (ASADE)**

A serious adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

8.2 PROCEDURE FOR ASSESSING, RECORDING, AND REPORTING ADVERSE EVENTS, DEVICE DEFICIENCIES/COMPLAINTS, ADVERSE DEVICE EFFECTS, SERIOUS ADVERSE EVENTS, AND SERIOUS ADVERSE DEVICE EFFECTS:

Safety surveillance within this study and the safety reporting both performed by the investigator, starts as soon as the subject is enrolled in this study (date of signature of the informed consent). The safety surveillance and the safety reporting will continue until the last investigational visit has been performed, the subject is deceased, the subject/investigator concludes his participation into the study or the subject/investigator withdraws the subject from the study, except as otherwise specified in the CIP.

All adverse event data including deaths and device deficiency data (if applicable) will be collected throughout the clinical study and will be reported to the Sponsor on a dedicated case report form or through the EDC system. The Investigator will record all adverse events and device deficiencies on the appropriate case report forms.

Records relating to the subject's subsequent medical course must be maintained and submitted (as applicable) to the Sponsor until the event has subsided or, in case of permanent impairment, until the event stabilizes and the overall clinical outcome has been ascertained. Adverse events will be monitored until they are adequately resolved. The status of the subject's condition should be documented at each visit.

The investigator will report the event to the IRB/EC per their reporting requirements.

Reportable events to sponsor are considered:

- All Adverse Device Effects
- All Serious Adverse Events (whether or not the event is considered device or procedure related and regardless the randomization group)
- (if applicable) device deficiencies, that could have led to a serious adverse device effect
  - if either suitable action had not been taken;
  - if intervention had not been made or
  - if circumstances had been less fortunate

All above events will be reported to the Sponsor, as soon as possible, but no later than 72 hours of first learning of the event.

The Sponsor will ensure that all events and device deficiencies are reported to the relevant authorities as per regulations.

Additional information may be requested, when required, by the Sponsor in order to support the reporting of AEs to regulatory authorities.

The investigator must notify the IRB/EC, if appropriate, in accordance with national and local laws and regulations, of the AEs reported to the Sponsor.

All adverse events will be reported as per applicable regulatory requirements.

8.3 SUBJECT DEATH

8.3.1 Procedure for recording and reporting subject death

All subject deaths are to be documented and reported to the sponsor within 72 hours after becoming aware of the event.
All subjects' deaths should be documented using the "Death Form" and a "Withdrawal Form".

8.4 DEVICE DEFICIENCY (DD)

- A Device Deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.
-
- Device deficiencies include malfunctions, use errors and inadequate labeling.
-

St. Jude Medical will appropriately manage all device deficiencies related to the identity, quality, durability, reliability, safety or performance of an investigational medical device. All device deficiencies will be documented throughout the clinical study.

NOTE: Device deficiencies that occur in investigational products must be captured on case report forms that include user error information.

Device deficiencies in St. Jude Medical market-released products must be reported per St. Jude Medical product surveillance process.

9.0 DATA MANAGEMENT

Overall, the Sponsor will be responsible for the data handling.

The sponsor and/or its affiliates will be responsible for compiling and submitting all required reports to governmental agencies.

Data will be analyzed by the Sponsor and may be transferred to the Sponsor's locations outside of Europe and/or any other worldwide regulatory authority in support of a market-approval application.

St. Jude Medical respects and protects personally identifiable information that we collect or maintain. As part of our commitment, St. Jude Medical is certified to the U.S. - European Union Framework and U.S. – Swiss Safe Harbor Framework Agreements regarding human resources and subject clinical trial personal information. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data. Confidentiality of data will be observed by all parties involved at all times throughout the clinical study. All data will be secured against unauthorized access.

During this study the following documents will be produced:

- Patient's ICF
- Enrollment clinical report form
- Inclusion/Exclusion clinical report form
- VAS clinical report form
- EQ-5D clinical report form
- ODI clinical report form

The ICF, VAS, EQ-5D and ODI clinical report forms will be translated in the language of the country or countries where the study will be conducted.

The Principal Investigator or institution will provide direct access to source data during and after the clinical study for monitoring, audits, IRB/EC review and regulatory authority inspections. As required, the Principal Investigator or institution will obtain permission for direct access to source documents from the subject, hospital administration and national regulatory authorities before starting the clinical study.

9.1 DATA MANAGEMENT PLAN

Data are captured on paper CRFs which are verified and signed by the Principal Investigator or his/her designee. Paper CRFs will be electronically sent to SJM and then captured in a validated electronic database management system hosted by St. Jude Medical.

All CRF received data for the study will be entered by trained and qualified St. Jude Medical personnel. An electronic audit trail will be used to track any subsequent changes of the entered data.

9.2 DOCUMENT AND DATA CONTROL

9.2.1 Traceability of documents and data

The investigator will ensure accuracy, completeness, legibility and timeliness of the data reported to the sponsor on the CRFs and in all required reports.

9.2.2 Recording data

Source documents will be created and maintained by the investigational site team throughout the clinical study.

The data reported on the CRFs will be derived from, and be consistent with, these source documents, and any discrepancies will be explained in writing.

The following data can be recorded directly in the CRFs:

- Pain VAS scores
- EQ-5D scores
- ODI scores

The CRFs will be signed and dated by the authorized site personnel. Any change or correction to data reported on a paper CRF will be dated, initialed and explained if necessary, and will not obscure the original entry.

10.0 MONITORING

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential protocol deviations that may be indicative of site non-compliance. On site monitoring may occur at the discretion of the sponsor.

11.0 REGULATORY INSPECTIONS

- The investigator and/or delegate should contact St. Jude Medical immediately upon notification of a governmental agency inspection at the site. A clinical monitor or designee will assist the investigator and/or delegate in preparing for the audit.
-
- An investigator who has authority to grant access will permit authorized governmental agency employees, at reasonable times and in reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are used or where records or results are kept).
-
- An investigator, or any person acting on behalf of such a person with respect to the study, will permit authorized governmental agency employees, at reasonable times and in reasonable manner, to inspect and copy all records relating to the study.
-
- An investigator will permit authorized governmental agency employees to inspect and copy records that identify subjects, upon notice that governmental agency has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator, to the Sponsor or IRB/EC have not been submitted or are incomplete, inaccurate, false or misleading.

12.0 STATISTICAL CONSIDERATIONS

12.1 STATISTICAL DESIGN, HYPOTHESES, METHOD AND ANALYTICAL PROCEDURES

This study is a prospective, single arm, open label observational study. The analysis will be conducted under the null hypothesis that SCS treatment will increase the activity level and sleep quality in the subjects. Data collected from wearable sensors will be compared between the baseline, trial and follow up periods using a repeated measurement ANOVA analysis followed by post-hoc testing.

12.2 SAMPLE SIZE

We will enroll approximately 20 subjects in three study centers in the EU. This study is a feasibility trial, the sample power cannot be calculated because the effect size is not known. The sample size was selected to obtain early evidence and estimates of the effect size.

13.0 DOCUMENT RETENTION

The principal investigator (PI) will maintain all clinical study documents from prior, during and (as specified) after the clinical study on file at the site for a minimum of 15 years after the termination of this study, or longer as per local laws, or when it is no longer needed to support a marketing application, whichever is later.

The PI must contact the sponsor prior to destroying or archiving off-site any records and reports pertaining to this study to ensure that they no longer need to be retained on-site.

All original subject files must be stored for the longest possible time permitted by the regulations at the hospital, research institute, or practice in question. If archiving can no longer be maintained at the site, the investigator will notify the sponsor.

All data and documents will be made available on request of the relevant authorities in case of an audit.

The sponsor will archive and retain all essential clinical study documents from prior, during and (as specified) after the clinical study as per requirements.

14.0 AMENDMENTS TO CLINICAL INVESTIGATIONAL PLAN

Study related documents such as, the Investigator Brochure (IB), Report of Prior Investigations (RPI) CIP, CRFs, Informed Consent form and other subject information, or other clinical study documents will be amended as needed throughout the clinical study, and a justification statement will be included with each amended section of a document. Proposed amendments to the CIP will be agreed upon between the Sponsor and the coordinating investigator (if applicable).

The amendments to the CIP and the subject's Informed Consent will be notified to, or approved by, the IRB/EC and regulatory authorities, if required. The version number and date of amendments will be documented.

The amendment will identify the changes made, the reason for the changes and if it is mandatory or optional to implement the amendment.

Any amendment affecting the subject requires that the subject be informed of the changes and a new consent be signed and dated by the investigator at the subject's next follow up.

Changes to, or formal clarifications of, the CIP will be documented in writing and provided to the investigators. This information will be incorporated when an amendment occurs.

15.0 INVESTIGATION SUSPENSION OR TERMINATION

15.1 PREMATURE TERMINATION OF THE WHOLE CLINICAL STUDY OR OF THE CLINICAL STUDY IN ONE OR MORE INVESTIGATIONAL SITES

The Sponsor reserves the right to stop the study at any stage, with appropriate written notice to the investigator.

Possible reasons for early termination of the study by the sponsor, either at local, national or international level, may include, but are not limited to:

- The device / therapy fails to perform as intended
- Occurrence of USADE which cannot be prevented in future cases
- Sponsor's decision
- Recommendation from DSMB to Steering committee and Sponsor
- Request from Regulatory bodies
- Request of Ethics Committee(s)
- Concern for subject safety and welfare
- Failure to secure subject Informed Consent prior to any investigational activity
- Failure to report unanticipated adverse device effects within 72 hours to St. Jude Medical and the EC
- Repeated non-compliance with this CIP or the Clinical Trial Agreement
- Inability to successfully implement this CIP
- Violation of the Declaration of Helsinki 2008 (refer to Appendix C)
- Violation of applicable national or local laws and regulations
- Falsification of data, or any other breach of ethics or scientific principles
- Loss of or unaccounted use of investigational device inventory

The study will be terminated according to applicable regulations.

The investigator may also discontinue participation in the clinical study with appropriate written notice to the Sponsor.

Should either of these events occur, the investigator will return all documents to the sponsor; provide a written statement as to why the premature termination has taken place and notify the IRB/EC and/or the Competent Authority (if applicable). Follow-up for all enrolled subjects will be as per CIP requirements.

A Principal Investigator, IRB/EC or regulatory authority may suspend or prematurely terminate participation in a clinical study at the investigational sites for which they are responsible.

If suspicion of an unacceptable risk to subjects arises during the clinical study or when so instructed by the IRB/EC or regulatory authority, St. Jude Medical may suspend the clinical study as appropriate while the risk is assessed. St. Jude Medical will terminate the clinical study if an unacceptable risk is confirmed.

St. Jude Medical will consider terminating or suspending the participation of a particular investigational site or investigator in the clinical study if monitoring or auditing identifies serious or repeated deviations on the part of an investigator.

If suspension or premature termination occurs, the terminating party will justify its decision in writing and promptly inform the other parties with whom they are in direct communication. The Principal Investigator and St. Jude Medical will keep each other informed of any communication received from IRB/EC or regulatory authority.

If for any reason St. Jude Medical suspends or prematurely terminates the study at an individual investigational site, St. Jude Medical will inform the responsible regulatory authority, as appropriate, and ensure that the IRB/EC are notified, either by the Principal Investigator or by St. Jude Medical. If the suspension or premature termination was in the interest of safety, St. Jude Medical will inform all other Principal Investigators.

If suspension or premature termination occurs, St. Jude Medical will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following up the subjects enrolled in the clinical study, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site, if appropriate.

15.2 RESUMING THE STUDY AFTER TEMPORARY SUSPENSION

When St. Jude Medical concludes an analysis of the reasons for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, St. Jude Medical will inform the Principal Investigators, IRB/EC, or regulatory authority, where appropriate, of the rationale, providing them with the relevant data supporting this decision.

Concurrence will be obtained before the clinical study resumes from the IRB/EC or regulatory authority where appropriate.

If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

15.3 STUDY CONCLUSION

The study will be concluded when:

- All sites are closed AND
- The Final report generated by St. Jude Medical has been provided to sites or St. Jude Medical has provided formal documentation of study closure

16.0 PUBLICATION POLICY

The results of the clinical study may be submitted for publication.

A 'Publication Agreement' will be signed between the Principal Investigator and the Sponsor either as a separate Publication Agreement or within the Clinical Trial Agreement.

17.0 BIBLIOGRAPHY

Bonica JJ. The need of a taxonomy. Pain. 1979;6(3):247–8

Dansie EJ, Turk DC, Martin KR, Van Domelen DR, Patel KV. Association of chronic widespread pain with objectively measured physical activity in adults: findings from the National Health and Nutrition Examination survey. J Pain. 2014 May;15(5):507-15

Emery PC, Wilson KG, Kowal J. Major depressive disorder and sleep disturbance in patients with chronic pain. Pain Res Manag. 2014 Jan-Feb;19(1):35-41.

Gong W, Johanek LM, Sluka KA. Spinal cord stimulation reduces mechanical hyperalgesia and restores physical activity levels in animals with noninflammatory muscle pain in a frequency-dependent manner. Anesth Analg. 2014 Jul;119(1):186-95.

McGrath PA. Psychological aspects of pain perception. Arch Oral Biol. 1994;39 Suppl:55S-62S.

Nascimento-Ferreira MV, Collese TS, de Moraes AC, Rendo-Urteaga T, Moreno LA, Carvalho HB. Validity and reliability of sleep time questionnaires in children and adolescents: A systematic review and meta-analysis. Sleep Med Rev. 2015 Dec 6;30:85-96

Obuchi M, Sumitani M, Shin M, Ishii K, Kogure T, Miyauchi S, Yamada Y. Spinal cord stimulation ameliorates neuropathic pain-related sleep disorders: a case series. Neuromodulation. 2015 pr;18(3):191-3;

Ramineni T, Prusik J, Patel S, Lange S, Haller J, Fama C, Argoff C, Pilitsis J. The Impact of Spinal Cord Stimulation on Sleep Patterns. Neuromodulation. 2016 Feb 5.

Sato KL, Johanek LM, Sanada LS, Sluka KA. Spinal cord stimulation (SCS) improves decreased physical activity induced by nerve injury. Behav Neurosci. 2014 Oct;128(5):625-32.

Wilson AC, Palermo TM. Physical activity and function in adolescents with chronic pain: a controlled study using actigraphy. J Pain. 2012 Feb;13(2):121-30.

APPENDIX A: ABBREVIATIONS

Abbreviation	Term
ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
CA	Competent Authority
CIP	Clinical Investigational Plan
CRF	Case Report Form
DD	Device Deficiency
DMP	Data Management Plan
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EMEA	Europe, Middle East, Africa
EPG	External Pulse Generator
EQ-5D	European Quality of life questionnaire 5 dimensions
GP	General Practitioner
IB	Investigator Brochure
ICMJE	International Committee of Medical Journal Editors
IPG	Implantable Pulse Generator
IRB	Institutional Review Board
ISB	Investigator Site Binder
ISO	International Organization for Standardization
MP	Monitoring Plan
NA	Not Applicable
ODI	Oswestry Disability Index
PI	Principal Investigator
POA	Power of Attorney
RDC	Remote Data Capture
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SC	Steering Committee
SJM	St. Jude Medical
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analog Scale
WMA	World Medical Association

APPENDIX B: CIP REVISION HISTORY

Revision History				
Amendment Number	Version	Date	Rationale	Details
Not Applicable	VA	ddMMMyyyy	First release of CIP	NA

Appendix C: DECLARATION OF HELSINKI

The most current version of the document will be followed.

Appendix D: LIST OF CLINICAL INVESTIGATION SITES AND IRB/EC

A list of Clinical Investigational sites and IRB/EC will be kept under a separate cover and is available upon request.

Appendix E: SAMPLE INFORMED CONSENT

Study specific informed consent will be kept under a separate cover and is available upon request.

Appendix F: CASE REPORT FORMS

Case report forms will be kept under a separate cover and are available upon request.