Clinical Investigation Plan

Reference:
SJM-CIP-10056: Ver. D [25 JUL 2019]

SCS MRI PMCF

A Post-Market Study Evaluating the Prodigy MRI and Proclaim Elite MR Conditional SCS Systems

Clinical Investigation Plan (CIP)

Sponsor

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PRINCIPAL INVESTIGATOR SIGNATURE PAGE

CIP: SCS MRI PMCF

A Post-Market Study Evaluating the Prodigy MRI and Proclaim Elite MR Conditional SCS Systems
Version D [25 JUL 2019]

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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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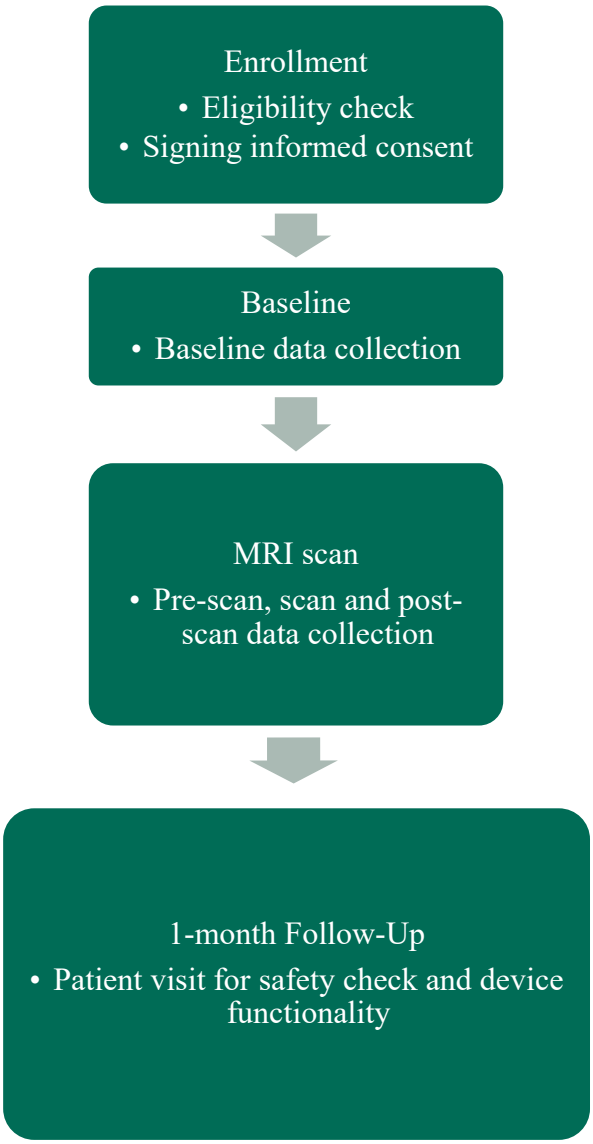
1.0 SYNOPSIS

Title:	A Post-Market Study Evaluating the Prodigy MRI™ and Proclaim Elite™ MR Conditional SCS Systems
Short Title:	SCS MRI PMCF
Purpose:	The purpose of this study is to confirm the safety of the Prodigy MRI and Proclaim Elite MR conditional SCS systems.
Objectives:	The primary objective of this study is to confirm the safety of the Prodigy MRI and Proclaim Elite MR conditional SCS systems.
	The secondary objective of this study is to confirm that the MRI scan does not affect the functionality of the Prodigy MRI or Proclaim Elite MR conditional SCS system.
Endpoints:	The primary endpoint is the rate of MRI scan-related adverse events.
	The secondary endpoints are defined as: • Rate of successful MRI mode 'turn on/off' functionality • Rate of successful 'turn on/off' functionality for the stimulation • Rate of successful adjustments to the program • Rate of successful interrogations and uploads of the IPG parameters
Design:	The study will be performed as an international, multicenter, prospective, and single-arm design. The study will be conducted as a Post Market Clinical Follow Up (PMCF) study and the results will be submitted to the Notified Body: BSI Group (BSI). Enrollment: Subjects who have been implanted with a Prodigy MRI or Proclaim Elite SCS system and are either clinically indicated to receive an MRI scan, or will receive an MRI scan solely for the purposes of this study, will be approached to participate in this study prior to their MRI scan. If the subject matches all of the study eligibility criteria, they will be informed about the study to see if they are interested in participating. After the subject signs the informed consent, the enrollment is complete. Baseline: A baseline evaluation will be performed prior to the MRI scan. MRI scan: Once subject's eligibility for an MRI scan has been confirmed, the MRI scan will be performed according to the SJM IFU for the implanted MR conditional SCS system. Immediate follow-up post-scan: An immediate post-MRI scan follow-up assessment will be performed to determine safety and device functionality. 1-month follow-up: Subject will return to the clinic 1 month after the MRI scan for a safety check and device functionality check.

	The study is complete when data from 46 unique subjects who have undergone an MR scan has been collected.
Devices used:	Prodigy MRI or Proclaim Elite MR conditional SCS systems may be used in this study. See section 5.0 for specific models.
Study Population	The subject population enrolled in this study will be comprised of male and female subjects. Subjects must meet the specific eligibility criteria to participate in the study. Approximately 49 subjects will be enrolled to collect data from 46 subjects. Each subject will be scanned only one time for the purposes of this study.
Inclusion/Exclusion Criteria	Inclusion Criteria • Patient has been implanted with a Prodigy MRI or Proclaim Elite MR conditional SCS system • Patient will receive an MRI scan in compliance with the IFU for the implanted MR conditional SCS system • Patient is ≥ 18 years of age • Patient must be willing and able to comply with study requirements • Patient must indicate his/her understanding of the study and willingness to participate by signing an appropriate Informed Consent Form Exclusion Criteria • Patient has another implanted device (active or passive) that prohibits safe scanning • Patient has previously experienced an MRI scan-related adverse event • Patient is currently enrolled in another Abbott study that collects MRI safety data • Patient is incapacitated, is unable to read or write, or is pregnant or breastfeeding
Data Collection	Data will be collected at Enrollment, Baseline, pre-MRI scan, MRI scan, post-MRI scan, and 1-Month follow-up. • Inclusion/Exclusion Criteria • Demographics • Medical Condition indicated for an MRI scan • Implanted SCS system information • Subject eligibility for MRI scan • MRI scan parameters • Device functionality • Safety events

1.1 Study flow chart



1.2 Study contacts

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2.0 BACKGROUND AND JUSTIFICATION FOR CLINICAL STUDY

Spinal cord stimulation (SCS) involves the application of electrical stimulation to the large myelinated fibers of the dorsal column via electrical leads placed in the epidural space. SCS is minimally invasive, reversible[1] and has been used successfully to help manage a variety of pain conditions including diabetic neuropathy,[2] failed back surgery syndrome,[3-6] complex regional pain syndrome,[7,8] phantom limb pain,[9] ischemic limb pain,[10] as well as postherpetic neuralgia and acute herpes zoster pain.[11]

A systematic review and meta-analysis of SCS in refractory neuropathic back and leg pain documented 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 with minimal significant adverse events.[12] Because chronic pain patients continue to live normal lives using SCS, they may develop unrelated medical conditions that require medical imaging, such as an MRI, as part of their standard care. An examination of the Truven Health MarketScan Research Database estimates that 82% - 84% of patients eligible for SCS will require an MRI at some point within 5 years of implant.[13]

MRI is a diagnostic method for viewing high quality two and three-dimensional images of the body. MRI systems generate three electromagnetic fields (i.e. a static magnetic field, a time-varying gradient magnetic field, and a radiofrequency field) that are used to produce the image. All three of these fields interact with implanted devices, creating hazards for the device, the subject, or both. Due to these risks, currently marketed implantable generators (IPGs), leads, or accessories may be contraindicated for use in an MRI environment.

Abbott (formerly St. Jude Medical) has developed MR conditional neurostimulation systems designed to mitigate such interactions. These systems provide the option for conditionally safe scanning of subjects when the scan is performed according to approved guidelines. MRI compatible devices improve patient care by reducing limitations that would otherwise prevent patients from taking advantage of this commonly used diagnostic tool.

The devices used in this study have received CE mark and are being implanted in subjects. CE mark was granted based on preclinical device testing. This study will be conducted as a post-market clinical follow up (PMCF) study to collect additional scientific data to support the CE label for Prodigy MRI™ and Proclaim Elite™ systems. Patients with an existing Prodigy MRI or Proclaim Elite MR conditional system who either undergo an MRI scan as standard of care, or agree to an MRI scan for study purposes, will be interviewed before the scan, after the scan, and 30 days later to determine device functioning and record any related adverse events. The rate of MRI scan-related adverse events will be used to evaluate the safety of these MR conditional SCS systems when used in compliance with the approved requirements.

3.0 RISKS AND BENEFITS OF THE CLINICAL STUDY

3.1 Description of subject population

The subject population enrolled in this study will be comprised of male and female subjects who have a previously implanted Prodigy MRI or Proclaim Elite MR conditional SCS system. Subjects must meet the specific eligibility criteria and provide informed consent to participate in the study.

3.2 Anticipated clinical benefits

The primary benefit of the MR conditional SCS systems is that they provide subjects with the option to receive a MRI scan when clinically necessary, while defining the conditions for use that maximize subject safety.

If subjects agree to take part in this study, there may or may not be direct medical benefits to individual subjects. The scientific use of the data collected in this study is to support the CE label of the Prodigy MRI and Proclaim Elite MR conditional SCS systems by confirming they are conditionally safe for MRI scans.

3.3 Potential Adverse Effects

The Prodigy MRI and Proclaim Elite MR conditional SCS systems have been designed to minimize the potential adverse effects that may cause subject harm. The following potential adverse effects may occur in the MRI environment:

- Lead electrode heating resulting in tissue damage or serious subject injury
- IPG heating resulting in tissue damage in the implant pocket or subject discomfort or both
- Induced currents on leads resulting in overstimulation or shocking sensations
- Damage to the IPG or leads causing the system to fail to deliver stimulation or causing the system to deliver overstimulation
- Damage to the functionality or mechanical integrity of the IPG resulting in the inability to communicate with the IPG
- Movement or vibration of the IPG or leads

3.4 Residual risks associated with the study device, as identified in the risk analysis report.

The clinical risks associated with neurostimulation systems for SCS applications are well known. Many of the clinical risks may develop as a consequence of not following the manufacturer recommended guidelines at the time of performing the MRI scans.

Any potential residual risks are considered to be outweighed by the benefits, and the overall residual risk was determined to be acceptable. Clinical evidence demonstrates acceptable safety and performance of the study device.

3.5 Risks associated with participation in the clinical study

The risks involved with this study are comparable to those associated with the implant of any other commercially available MR conditional SCS system.

3.6 Risk-to-benefit rationale

Since no design changes exist between the Prodigy MRI and Proclaim Elite MR conditional SCS systems and the predicate SCS systems, except for implementation of the MRI Mode, the non-MR performance of these products is already well established.

In addition, the clinical evidence demonstrates that the safety and performance of the study device, when used under the conditions and for the purposes intended, as specified by the manufacturer, are in compliance with the Requirements of the AIMD Directive 90/385/EEC, including the Essential Requirements.

Subjects receiving an MRI as standard of care will receive that benefit irrespective of their participation in this study. The MRI scan may not provide additional benefit for subjects who receive a scan without an underlying medical need.

Any undesirable side effects, under normal conditions of use, are considered acceptable risks when weighed against the performance of the device and benefits to the subject.

4.0 STUDY DESIGN

4.1 Purpose

The purpose of this study is to confirm the safety of the Prodigy MRI and Proclaim Elite MR conditional SCS systems.

4.2 Study design and scope

The study will be performed as an international, multicenter, prospective, and single-arm design. The study will be conducted as a Post Market Clinical Follow Up (PMCF) study and the results will be submitted to the Notified Body: BSI Group (BSI).

The study will be conducted in approximately 20 centers in Europe and up to 10 centers in the US.

4.3 Number of subjects required to be included in the study

Approximately forty-nine (49) subjects will be enrolled in the study. Data from only 1 scan per subject will be collected in the study.

4.4 Estimated time needed to enroll this subject population

The expected enrollment rate for patients requiring MRIs with an eligible MR conditional device is no more than 10 subjects per year. It is unknown how many patients will be interested in receiving an MRI scan for study purposes without an underlying medical need. Therefore, the number of enrollments per year for this group cannot be predicted with precision. However, we estimate that this number will not be less than the 10 subjects per year that are estimated to require an MRI for medical purposes. Therefore, we estimate that enrollment may continue for up to 6 years.

4.5 Objectives

4.5.1 Primary objective

The primary objective of this study is to confirm the safety of the Prodigy MRI and Proclaim Elite MR conditional SCS systems.

4.5.2 Secondary objective

The secondary objective is to confirm that the MRI scan does not affect the functionality of the Prodigy MRI or Proclaim Elite MR conditional SCS system.

4.6 Endpoints

4.6.1 Primary endpoint

The primary endpoint is the rate of MRI scan-related adverse events.

4.6.2 Secondary endpoint

The secondary endpoints are defined as:

- Rate of successful MRI mode 'turn on/off' functionality
- Rate of successful 'turn on/off' functionality for the stimulation
- Rate of successful adjustments to the program
- Rate of successful interrogations and uploads of the IPG parameters

4.7 Inclusion and Exclusion Criteria

A subject, who meets all 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.

4.7.1 Inclusion criteria

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

- Patient has been implanted with a Prodigy MRI or Proclaim Elite MR conditional SCS system
- Patient will receive an MRI scan in compliance with the IFU for the implanted MR conditional SCS system
- Patient is ≥ 18 years of age
- Patient must be willing and able to comply with study requirements
- Patient must indicate his/her understanding of the study and willingness to participate by signing an appropriate Informed Consent Form

4.7.2 Exclusion criteria

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

- Patient has another implanted device (active or passive) that prohibits safe scanning
- Patient has previously experienced an MRI scan-related adverse event
- Patient is currently enrolled in another Abbott study that collects MRI safety data
- Patient is incapacitated, is unable to read or write, or is pregnant or breastfeeding

4.8 Subject Population

The subject population enrolled in this study will be comprised of male and female subjects from the chronic pain population who have a previously implanted Prodigy MRI or Proclaim Elite MR conditional SCS system.

Subjects will either receive an MRI scan as part of standard of care or will receive an MRI scan without an underlying medical necessity solely for the purposes of this study.

Subjects must meet the specific eligibility criteria and provide informed consent to participate in the study.

4.8.1 Subject screening

All subjects presenting at the investigational site can 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. Subjects meeting the inclusion criteria and none of the exclusion criteria will be fully informed about the study and asked to participate in the study.

In case the subject agrees, a duly signed and dated Informed Consent form will be obtained. Once enrolled, the subject is expected to comply with the scheduled visits and required activities according to the protocol.

4.8.2 Point of enrollment

A subject is enrolled in this study only when he/she has provided a written signed and dated Informed Consent form.

4.8.3 Vulnerable population

Not applicable.

4.9 Informed Consent Process

4.9.1 General process

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's IRB/EC. This process will include a verbal discussion with the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate, such as details of clinical investigation procedures, anticipated benefits, and potential risks of clinical investigation participation. Subjects must be informed about their right to withdraw from the clinical investigation at any time and for any reason without sanction, penalty or loss of benefits to which the subject is otherwise entitled. Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. Subjects may be compensated for time and travel directly related to the participation in the clinical investigation. The subject shall be provided with the Informed Consent form written in a language that is understandable to the subject and has been approved by the center's IRB/EC. The subject shall have adequate time to review, ask questions, and consider participation. The Principal Investigator or his/her authorized designee will make efforts to ensure that the subject understands the information provided. If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. The signed original will be filed in the subject's hospital or research charts, and a copy will be provided to the subject.

Failure to obtain informed consent from a subject prior to clinical investigation enrollment should be reported to Sponsor within 5 working days and to the reviewing center's IRB/EC according to the IRB's/ EC's reporting requirements.

If, during the clinical investigation, new information becomes available that can significantly affect a subject's future health and medical care, the Principal Investigator or his/her authorized designee (if applicable) will provide this information to the subject. If relevant, the subject will be asked to confirm their continuing informed consent in writing.

4.9.1.1 Special Circumstances for Informed Consent

Incapacitated individuals, defined as persons who are mentally ill, mentally handicapped, or individuals without legal authority are excluded from the study population. Individuals under the age of 18 or age of legal consent are excluded from the study population. Individuals unable to read or write are excluded from the study population. Pregnant or breastfeeding women are excluded from the study population.

In addition, an authorization for use and disclosure of the subject's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the subject or their legally acceptable representative.

5.0 STUDY DEVICE

5.1 Name of study devices

Any market-released, Prodigy MRI or Proclaim Elite MR conditional SCS system may be used in this study along with its relevant accessories. Table 1 includes a list of all devices included in this study.

Table 1. Study Devices

Device name	Model/Type	Serial/Lot Controlled	Manufacturer	Region/ Country	Investigational or Market Released
Proclaim Elite Implantable Pulse Generator	3660 & 3662	Serialized	St. Jude Medical	Global	Market Released
Prodigy MRI Implantable Pulse Generator	3772	Serialized	St. Jude Medical	Global	Market Released
Octrode™ Lead	3186	Serialized/Lot	St. Jude Medical	Global	Market Released
Penta™ Lead	3228	Serialized/Lot	St. Jude Medical	Global	Market Released
Butterfly Anchor	1105	Lot	St. Jude Medical	Global	Market Released

Device name	Model/Type	Serial/Lot Controlled	Manufacturer	Region/ Country	Investigational or Market Released
Long Anchor	1106	Lot	St. Jude Medical	Global	Market Released
Swift-Lock™ Anchor	1192	Lot	St. Jude Medical	Global	Market Released
Cinch™ Anchor	1194	Lot	St. Jude Medical	Global	Market Released
Prodigy Charging System	3730	Serialized	St. Jude Medical	Global	Market Released
Prodigy Patient Programmer	3856	Serialized	St. Jude Medical	Global	Market Released
Rapid Programmer™ System	3835	Serialized	St. Jude Medical	Global	Market Released
Clinician Programmer	3872	Serialized	St. Jude Medical	Global	Market Released
Patient Controller	3883	Serialized	St. Jude Medical	Global	Market Released

Note: Changes to the lead manufacturing process means that some existing leads may have been lot controlled while others were serialized.

5.2 Indication for Use

The Prodigy MRI and Proclaim Elite SCS systems are indicated as an aid in the management of chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome and intractable low back and leg pain.

5.3 Description of the study devices

Please refer to the country- and device-specific IFU for additional information regarding the devices used in this clinical investigation.

The Proclaim Elite system is MR conditional for scans of the head, extremities (upper except shoulder, lower except hip), or any other body part. The Prodigy MRI system is only MR conditional for scans of the head and extremities (upper except shoulder, lower except hip). Scan requirements for each system (Proclaim Elite and Prodigy MRI)/lead (Octrode and Penta) combination are provided in the MRI Procedure Information Manual.

Clinically relevant MRI safety criteria identified by St. Jude Medical (now Abbott) are unchanged between the Prodigy MRI and Proclaim Elite systems. Additional Proof of Safety testing has demonstrated that the Proclaim Elite device satisfies these same criteria when used with a body RF

transmit coil under the specified scan conditions. Therefore, data gathered on Proclaim Elite and Prodigy MRI will be evaluated as a single group.

5.4 MRI Procedure Information Manual

To ensure the MR Conditional requirements are met, the healthcare providers involved in MRI scanning of the Prodigy MRI and Proclaim SCS systems will need to take multiple actions. To ensure subject and device safety during the MRI procedure, a recommended procedural workflow has been developed in the MRI Procedure Information manual. To collect impedance check data in this study, this clinical investigation plan adds the requirement of having a Clinician Programmer (for Proclaim devices) or a Rapid Programmer (for Prodigy devices) present at every MRI scan.

The MRI Procedure Information manual allows for the determination of whether conditions have been satisfied by the SCS system and the MR environment to qualify for an MRI scan. This labeling allows radiologists and MR technologists to identify MR conditional components and assess whether their MRI equipment can safely scan a subject implanted with an Abbott (formerly St. Jude Medical) MR conditional SCS system. Guidance is also provided to the physician and subject on how to prepare for an MRI scan.

Additionally, a Subject Identification (ID) Card is provided to all subjects as labeling that allows for identification of their implanted neurostimulation system in support of determining if the subject has an MR conditional system.

Additional resources (including the MRI Procedure Information manual) for ensuring that the MRI scan complies with the MRI conditional labeling can be obtained from the Sponsor or found on the following websites:

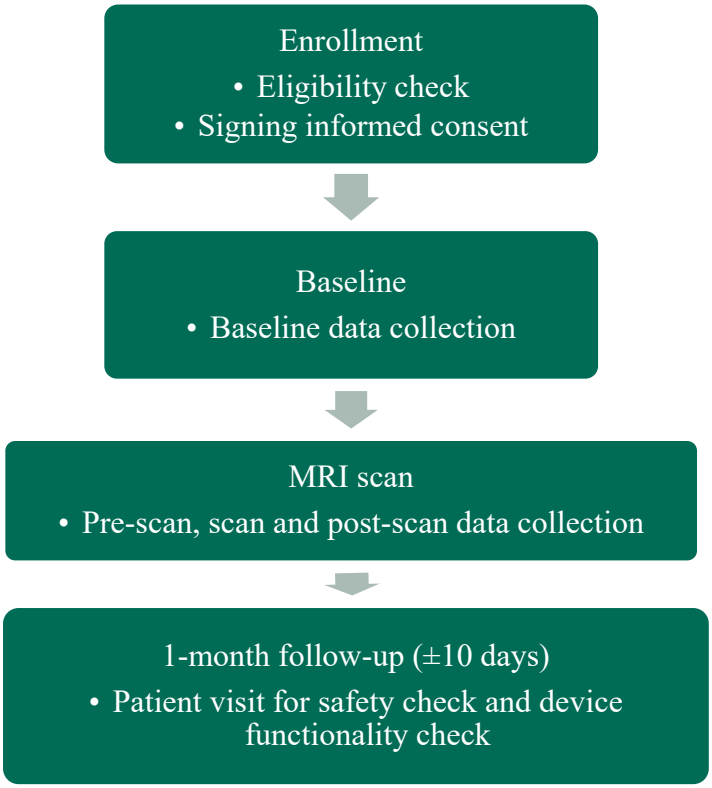
- https://www.sjm.com/en/professionals/resources-and-reimbursement/technical-resources/mri-ready-resources
- https://manuals.sjm.com/

5.5 Device handling & storage

The Sponsor requires all products to be stored according to the appropriate labeling and IFU as per standard practice at each center.

6.0 PROCEDURES

6.1 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 Abbott receives written approval from the IRB/EC and relevant regulatory authorities and all required documents have been collected from the site(s).

Table 2: List of all study specific activities/procedures

Visit / Study Activity	Enrollment (in clinic, prior to MRI scan)	Baseline (in clinic, prior to MRI scan)	MRI scan (in clinic, pre-, during, and post-scan	1 Month follow up (in clinic, 1 months ± 10 days since MRI scan)	Unscheduled	Additional surgery
Informed Consent Process	X					

Visit / Study Activity	Enrollment (in clinic, prior to MRI scan)	Baseline (in clinic, prior to MRI scan)	MRI scan (in clinic, pre-, during, and post-scan	1 Month follow up (in clinic, 1 months ± 10 days since MRI scan)	Unscheduled	Additional surgery
Inclusion/Exclusion Criteria Check	X					
Demographics Collection		X				
Collection of Medical Condition indicated for MRI scan		X				
Subject eligibility for MRI scan Check			X (pre-scan)			
Lead and IPG data Collection		X				X
Programming Functionality			X (pre- and post-scan)	X	X	
Device Functionality Check			X (pre-and post-scan)			
MRI Scan			X			
MRI Scan Parameters Collection			X			
Determine Reason for the Visit and Action Taken					X	X
Adverse Events Check		(X)	(X)	(X)	(X)	(X)
Protocol Deviation	(X)	(X)	(X)	(X)	(X)	(X)

(X) if applicable

Informed Consent Procedure and Inclusion/Exclusion Criteria:
Subject's eligibility criteria and Informed Consent Procedure is performed at the Enrollment visit.

Demographics:
Subject's year of birth, weight, height, and sex will be collected at the Baseline visit.

Medical Condition indicated for MRI Scan:
Subject's medical condition requiring a MRI scan will be collected at the Baseline visit.

Subject's eligibility for MRI scan:
Subject's eligibility for MRI scan will be checked BEFORE the scan will be done.

Lead, Extension, Anchor and IPG Data:
At Baseline, and in case of additional surgery, information of the implanted leads and IPG (model number, serial/lot number, and positions), presence and type of any anchors used, as well as the presence of lead extensions, will be collected.

Programming Functionality:

Information regarding the ability to re-program will be collected at pre- and post-scan, during the 1-month follow up visit and at unscheduled visits.

Device Functionality:
Data regarding the device functionality, including impedance check, will be collected pre-and post-scan.

MRI Scan:
MRI scan will be conducted in compliance with the SJM Instructions for Use (IFU) for the implanted MR conditional SCS system and the MRI Procedure Information manual.

MRI Scan Parameters:
MRI scan parameters will be documented post-scan.

Reason for the Visit and Action taken:
Information regarding the reason for the visit, as well the action taken, will be collected in case of unscheduled visit or additional surgery.

Adverse Events Check: Serious adverse events (SAEs) and/or MRI scan-related adverse events will be checked at all visits except enrollment.

6.3 Enrollment visit

(In clinic, prior to performing MRI scan)

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

- The principal or delegated Investigator is responsible for screening all potential subjects to determine subject eligibility for the study
- If a subject meets all inclusion criteria and does not meet any of the exclusion criteria, he/she is eligible for the study
- The subject is enrolled in the study when the subject signed the EC approved consent form

Enrollment information (name of the study, date of consent and inclusion/exclusion information) will be recorded in the hospital records the Enrollment form will be completed, preferably within 5 days after enrollment.

As soon as the subject signs the Informed Consent Form, AEs need to be reported according to the guidelines mentioned in this CIP.

In case the subject was consented to participate in the study, but does not meet inclusion/exclusion criteria, and did not receive a MRI scan, the subject should be withdrawn and a Withdrawal form must be completed. The subject will resume his/her regular standard of care with his/her physician.

In case the subject was consented to participate in the study and did receive a MRI scan, but does not meet inclusion/exclusion criteria, it will be considered a protocol violation. A protocol deviation form needs to be completed and the Sponsor must be informed. The EC and Competent Authority

(CA), if applicable, should be notified appropriately about any deviations with regards to the violation of inclusion/exclusion criteria.

6.4 Baseline visit

(In clinic, prior to performing MRI scan)
The baseline visit may be conducted on the same day as -but prior to- the MRI scan.

The following information will be collected at the baseline visit:

- Demographics
- Medical condition indicated for an MRI scan
- Lead and IPG data
- AE and/or protocol deviation (if applicable)

6.5 MRI scan

(In clinic)
There is no minimum required time gap between implantation of the neurostimulator and the MRI scan. This will be determined by the physician's standard of care.

6.5.1 Pre-scan

- Subject eligibility for MRI scan
- Device functionality, including impedance check
- Programming functionality
- AE and/or protocol deviation (if applicable)

MRI scan will be performed. Ensure to follow the instructions as mentioned in the MRI Procedure manual.

6.5.2 Post-scan

- MRI scan information
- DICOM image files (deidentified) if available
- Device functionality
- Programming functionality
- AE and/or protocol deviation (if applicable)

6.6 1-Month follow-up visit

(In clinic, 1 month ± 10 days since MRI scan)

The following information will be collected at the 1-month follow-up visit:

- Programming functionality
- AE and/or protocol deviation (if applicable)

6.7 Unscheduled visit

Subjects may be asked or need to return to the clinic to assess various program parameters and stimulation coverage or undergo additional surgery. If this occurs, the following information will be recorded:

- Reason for visit

- Action taken
- Programming functionality (if applicable)
- AE and/or protocol deviation (if applicable)
- Additional surgery information (if applicable)

6.8 Additional surgery

Subjects may be asked to return to the clinic for an additional surgery to revise, replace, reposition, or explant the leads or IPG. If this occurs, the following information will be recorded:

- Reason for surgery
- Action performed
- Lead and IPG data (if applicable)
- AE and/or protocol deviation (if applicable)

6.9 Health care economic data

Not applicable.

6.10 Description of activities performed by Sponsor Representatives

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

Sponsor personnel may:

- Provide technical support to the Investigators during MRI scan, additional surgery, and programming

Sponsor personnel will not:

- Perform the informed consent process
- Practice medicine
- 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

6.11 Subject study completion

When the subject's participation in the clinical study has been completed (at 1-Month Follow-Up), the subject will return to the medical care as per physician's recommendation.

6.12 Any known or foreseeable factors that may compromise the outcome

All foreseeable factors that may compromise the outcome of the clinical study or the interpretation of the results have been accounted for by clinical study design and well-defined subject selection criteria.

Subject recruitment and retention will be mastered 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 subject visit calendars.

A Clinical Events Committee (CEC) will be formed as best practice to ensure that the primary outcome is as free from bias as possible. The CEC will review and adjudicate reportable adverse events as defined in the CEC charter for seriousness, device-relatedness, and MRI-relatedness.

6.13 Description of the methods that will be used to address potentially confounding factors

Stratified analysis will be used to diagnose the potential confounding factors, and multiple regression will be used to adjust the outcome of the primary endpoint in case confounding factors are identified. The factors of interest can be, but are not limited to:

- Subject baseline characteristics
- Use of other medical devices

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 that 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 make all reasonable efforts to locate and communicate with the subject to achieve subject compliance to the scheduled follow up visits:
    - 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.
    - 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.

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

No additional follow–up will be required or data recorded from subjects once withdrawn from the clinical investigation.

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, and any regional and/or national regulations as appropriate.

The current version of the harmonized ISO14155 shall be used as a guideline.

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 Abbott.

As sponsor, Abbott has taken up general liability insurance in accordance with the requirements of the applicable local laws.

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 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 an investigation.

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 Abbott.

Regulations require Investigators obtain approval from Abbott 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.

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 Abbott or designee prior to initiating any changes.

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

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 investigation.

8.0 ADVERSE EVENT, ADVERSE DEVICE EFFECT

8.1 Definitions

8.1.1 Medical device

Any instrument, apparatus, 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
- 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)

An adverse event (AE) is 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 medical device under study.

Note 1: This definition includes events related to the medical device under study.
Note 2: This definition includes events related to the procedures involved.
Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

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-subject 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
- Fetal distress, fetal death, or a congenital abnormality or birth defect
- Malignant tumor

Note: 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 a study device.

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

This definition includes any event resulting from the use error or from intentional misuse of the study 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.

8.1.5.1 Unanticipated Serious Adverse Device Effect (USADE)

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.

8.1.6 Device relationship

Determination of whether there is a reasonable possibility that a study device caused or contributed to an AE will be determined by the Investigator and recorded on the appropriate CRF. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

8.2 Procedure for assessing, recording and reporting AEs, ADEs, SADEs:

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 study visit has been performed, the subject is deceased, the subject/Investigator concludes his participation in the study or the subject/Investigator withdraws the subject from the study.

Records related 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.

Adverse event data will be collected throughout the clinical study and will be reported to the Sponsor on a dedicated case report form.

Reportable events to sponsor are considered:

1. All Serious Adverse Events
2. All procedure- (e.g., MRI scan) or device-related Adverse Events (whether or not the event is considered serious).

<u>SAE Reporting</u>

The investigator should report all SAEs to the Sponsor as soon as possible but no later than outlined below.

Clinical Site	Reporting timelines

All Sites	SAEs must be reported to the Sponsor no later than 3 calendar days from the day the site personnel became aware of the event or as per the investigative site's local requirements, if the requirement is more stringent than those outlined.

The date the site staff became aware the event met the criteria of an SAE must be recorded in the source document. The Investigator will further report the SAE to the local IRB/EC according to the institution's IRB/EC reporting requirements.

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

Foreseeable Adverse Effects

In addition to the adverse events commonly associated with surgery, the following adverse effects are associated with implanting or using the neurostimulation for SCS.

List of foreseeable adverse effects:

- Unpleasant sensations or motor disturbances, including involuntary movement, caused by stimulation at high outputs (if either occurs, turn off the IPG immediately)
- 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
- Stimulation in unwanted places
- Lead migration, causing changes in stimulation 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
- Allergic or rejection response to implant materials
- Implant (IPG) migration or skin erosion around the implant
- Battery failure or battery leakage

Changes in stimulation parameters may occur due to the failure of, or changes in, components over time, which results in:

- Understimulation
- Return of underlying symptoms
- Overstimulation
- Premature battery depletion
- The need to explant the device

The following potential adverse effects may occur in the MRI environment:

- Lead electrode heating resulting in tissue damage or serious subject injury
- IPG heating resulting in tissue damage in the implant pocket, or subject discomfort, or both
- Induced currents on leads resulting in overstimulation or shocking sensations
- Damage to the IPG or leads causing the system to fail deliver stimulation or causing the system to deliver overstimulation
- Damage to the functionality or mechanical integrity of the IPG resulting in the inability to communicate with the IPG

- Movement or vibration of the IPG or leads

In addition, subjects may experience unavoidable events related to the MRI scan. An unavoidable event is an event related to the MRI scan that may occur for a projected duration in any subject. Unavoidable events are expected to occur with any MRI scan and are not reportable unless the condition worsens or continues beyond the timeframe listed below. Unavoidable events do not need to be reported on an Adverse Event form if they are resolved within the time frame specified.

Table 3. List of unavoidable MRI-related events

Event	Timeframe
Claustrophobia	During MRI scan
Mild diaphoresis	During and < 1-hour post MRI scan
Sensation of bodily warmth	During and < 1-hour post MRI scan
Sensation of warmth at device pocket not arising to the level of discomfort	During and < 1-hour post MRI scan
Hearing Impairment	< 24 hours post MRI scan
Body Stiffness related to immobility	< 48 hours post MRI scan

8.2.1 Procedure for recording and reporting subject death

All subject deaths that occur during this study must be reported to Abbott within 3 calendar days of the site being notified (refer to Section 8.2). Notification of a death should include a detailed statement of the pertinent events and be signed by the investigator in addition to the completion of the appropriate forms (Death form and Withdrawal form) and submitted to Abbott using the paper CRFs in this study. It is the Investigator's responsibility to notify the IRB/EC per the IRB/EC policy.

8.3 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.

Device deficiencies are not collected in this study. While some device functionality information will be collected as secondary endpoints (Section 4.6.2), the device deficiency reporting instructions below should be followed for all device deficiencies identified during this study.

If the device deficiency does not involve an AE, the Investigator must notify the Abbott Post Market Surveillance Department by submitting the complaint information via email to CCoordinators@sjm.com or by phone +1 972.309.8000 as soon as possible after becoming aware of the complaint.

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.

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 Protection of personally identifiable information

The Sponsor respects and protects personally identifiable information collected or maintained for this clinical investigation.

The Sponsor implements technical and physical access controls to ensure that Personal Information is accessible only to and processed only on a 'need to know' basis, including periodic review of access rights, and revocation of access when an individual's employment is terminated or the individual transitions to a role that does not require access to Personal Information, and appropriate restrictions on physical access to premises, facilities, equipment, and records containing Personal Information.

The Sponsor requires the investigational sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the patient's medical condition, treatment, dates of treatment, etc. The Sponsor discloses as part of the clinical investigation informed consent process that some Sponsor representatives still may see Personal Information at the participating sites for technical support of the participating physicians on the device implant or procedures, monitoring and quality control purposes. Confidentiality of Personal Information will be observed by all parties involved at all times throughout the clinical investigation. The privacy of each subject and confidentiality of his/her information will be preserved in reports and when publishing any data.

The Sponsor data management systems and processes were designed, developed, and tested according to industry standards to appropriately safeguard Confidential Information (including any Personal Information) against unauthorized access and/or interference by third parties, intrusion, theft, destruction, loss or alteration. Clinical Investigation data are encrypted in transit and at rest.

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

9.2 Data management plan

A detailed Data Management Plan will be established to ensure consistency of the data. This document will include procedures used for data review, database cleaning, and issuing and resolving data queries. If appropriate, the DMP may be updated throughout the study duration. All revisions will be tracked and document controlled.

CRF data will be captured in a validated electronic database management Oracle Clinical system hosted by Abbott.

Only authorized site personnel will be permitted to enter the data on paper CRFs provided by Abbott.

9.3 Document and data control

9.3.1 Traceability of documents and data

The Investigator shall ensure accuracy, completeness, legibility, and timeliness of the data reported to the sponsor on the CRFs and in all required reports. Where copies of the original source document as well as printouts of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document.

9.3.2 Recording data

Source documents shall be created and maintained by the investigation site team throughout the clinical study. The data reported on the CRFs shall be derived from, and be consistent with, these source documents, and any discrepancies shall be explained in writing.

The CRFs shall be validated by the Principal Investigator or designee. In case of modifications after the validation, the CRFs should be re-approved by the Investigator or designee.

10.0 MONITORING

It is the responsibility of Abbott, as the sponsor of the study, to ensure the study is conducted, recorded, and reported according to the approved protocol, subsequent amendment(s), applicable regulations, and guidance documents. Monitoring will be conducted according to the Abbott Clinical Monitoring standard operating procedure.

Prior to beginning the study, Abbott will contact the Investigator or designee to discuss the study and data requirements. An Abbott monitor will periodically review the subject records and associated source documents.

The Investigator shall make subject and study records available to the clinical monitor for monitoring.

11.0 REGULATORY INSPECTIONS

The Investigator and/or delegate should contact Abbott 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 is a prospective, multicenter, and single arm study.

- Analysis for primary endpoint

The primary endpoint is the event rate of MRI scan-related adverse events. The hypothesis is formally expressed as:
H_0: MRI scan-related adverse event rate $\geq$ 10%
H_1: MRI scan-related adverse event rate < 10%

MRI-scan related adverse event rate will be summarized as the proportion of subjects who have of MRI-scan related events. The primary endpoint will be tested at the 5% significance level. The null hypothesis will be rejected if the 95% UCB for MRI scan-related adverse event rate is less than 0.10. Confidence intervals will be calculated based on the Clopper-Pearson exact method for binomial proportion.

The performance goal of 10% is based on performance goals used by historical MRI safety studies.[14-17]

- Analysis for secondary endpoint

The success of each of secondary endpoint will be summarized as the number of success and its percentage, together with its 95% confidence interval estimated using Clopper-Pearson exact method for binomial distribution.

12.2 Sample size

The sample size estimation is based on the study design, the purpose of the study, and the primary endpoint, namely the MRI scan-related adverse event rate.

The performance goal for MRI scan-related adverse event rate is 10%. Assuming using MRI conditional SCS systems, the MRI scan-related adverse event rate would achieve 1%. A sample size of 46 scans will be able to provide 80% power at one-sided significant level of 5% for this endpoint. Data from only 1 scan per subject will be collected in the study, so a total of 46 subjects will be enrolled and scanned. Assuming the dropout rate between the enrollment and the MRI scan-visit is about 5%, the total expected sample size is 49 (46/0.95). The sample size was calculated using SAS version 9.3.

12.3 Pass/fail criteria to be applied to the results of the clinical study

Not applicable

12.4 The provision for an interim analysis

Not applicable

12.5 Criteria for the termination of the clinical study on statistical grounds

Not applicable

12.6 Procedures for reporting any deviation(s) from the original statistical plan

Any deviations from the statistical analysis plan will be documented.

12.7 The specification of subgroups for analysis

Not applicable

12.8 Procedures that take into account all the data

All subjects who have signed an Informed Consent will be considered enrolled in the clinical investigation (refer to Section 4.8.2). However, it is anticipated that there will be subjects who are enrolled in the study but will not be included in the primary endpoint analysis, such as:

- Subjects who are enrolled but do not meet baseline inclusion or meet exclusion criteria before the MRI scan; these are considered as screen failures
- Subjects who are enrolled but do not receive a MRI scan

12.9 The treatment of missing, unused or spurious data, including drop-outs and withdrawals

No imputation technique will be used, unless specified in the guidelines of the questionnaire data.

12.10 The exclusion of particular information for the testing of the hypothesis

Not applicable

12.11 The minimum and maximum number of subjects to be included for each center

This study is expected to enroll 49 subjects who are previously implanted with a Proclaim Elite or Prodigy MRI neurostimulator at up to 30 centers. From a statistical perspective, there is no expectation for heterogeneity across centers, therefore the minimum number of subjects required from enrolling centers is 1 and the maximum number of subjects is 49.

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, 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 clinical study

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
- 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 Abbott 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

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 routine care.

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, Abbott may suspend the clinical study as appropriate while the risk is assessed. Abbott will terminate the clinical study if an unacceptable risk is confirmed.

Abbott 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 Abbott will keep each other informed of any communication received from IRB/EC or regulatory authority.

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

If suspension or premature termination occurs, Abbott 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.
When Abbott concludes an analysis of the reasons for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, Abbott 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.

15.1.1 Study conclusion

The study will be concluded when:

- All sites are closed AND
- The final report generated by Abbott has been provided to sites or Abbott has provided formal documentation of study closure.

16.0 PUBLICATION POLICY

The results of the clinical study will be submitted, whether positive or negative 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.

For more information on publication guidelines, please refer to the International Committee of Medical Journal Editors (ICMJE) on www.icmje.org.

This study will be posted on ClinicalTrials.gov and results will be posted on ClinicalTrials.gov as required.

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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
EC	Ethics Committee
GP	General Practitioner
IB	Investigator Brochure
ICMJE	International Committee of Medical Journal Editors
IFU	Instructions for Use
IRB	Institutional Review Board
ISB	Investigator Site Binder
ISO	International Organization for Standardization
MP	Monitoring Plan
NA	Not Applicable
PI	Principal Investigator
PMCF	Post Market Clinical Follow Up
RDC	Remote Data Capture
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SJM	St. Jude Medical
US	United States
USADE	Unanticipated Serious Adverse Device Effect
WMA	World Medical Association

APPENDIX B: CIP REVISION HISTORY

Revision History				
Amendment Number	Version	Date	Rationale	Details
Not Applicable. Internal Document.	1.0	26 MAY2015	This version of the CIP was submitted to TÜV.	NA
Not Applicable. Internal Document.	1.1	13 AUG2015	Additional internal comments:	-Battery recharging data added as an option at unscheduled and additional surgery visits. -MRI Scan Form was removed as this is not applicable. -Clinical Coordinating Investigator signatory has been removed since there will not be a CCI assigned to the study.
Not Applicable. Internal Document.	2.0	14 SEP 2015	-Additional internal comments on spelling. -Data will be collected via paper CRF -Sample Size was recalculated	Spelling corrections have been made. References to eCRF and EDC have been removed. Sample size has been updated.
Not Applicable Internal Document	3.0	15 JAN2015	Additional internal comments on study activities and data points.	Study activities and data points have been revised to align with the objectives and endpoints of the study.
Not applicable	4.0	18 FEB2016	The word 'interventional' was replaced by 'observational'. Section 9.0 Data Management has been updated.	The procedures and tests applied in this study would have been applied as standard of care for subjects that are clinically indicated to undergo a MRI scan and being followed up. Reference to the EU-US Swiss Safe Harbor framework has been removed since it is no longer valid. Most current verbiage was added.
1	D	27 FEB 2019	Enrollment criteria now allow subjects to receive an MRI scan solely for research purposes to increase enrollment rate.	Requirement that MRI be conducted as standard of care has been removed. Population now allows MRI scans as standard of care or for the sole purpose of this study.

				Estimated time to enroll patients has been updated from 10 to 6 years.
			This study will support MRI labeling for Proclaim as well as Prodigy devices.	Proclaim Elite devices have been added to the list of devices included in this study and the study title has been updated. The inclusion criteria have been updated to clarify which devices are eligible.
			Unification of CIP across study regions.	Additional relevant clarifications have been made throughout the document
			Abbott/St. Jude Medical integration has modified some clinical study-related templates/practices.	Addition of "malignant tumor" as a possible SAE. References to St. Jude Medical have been changed to Abbott where appropriate. Table of devices has been expanded with additional details. Clarified Abbott post-market surveillance policy regarding device deficiencies. A clinical events committee has been added to reduce bias. Section 8.2.1 clarifies how the relationship between adverse events and medical devices should be decided. Section 5.0 has been split into multiple sub-sections. Guidance for SAE reporting has been updated.

			Data collection has been revised.	Deidentified DICOM image files have been added to data collection at the MRI scan visit. The image tags will serve a source for scan details that are otherwise difficult to capture.
			Clarification.	Background and rationale was expanded with appropriate citations. References to neurostimulation systems have been replaced with SCS or device names where appropriate to clarify the scope of this study. Added a list of unavoidable MRI events that are not reportable unless condition worsens or duration exceeds expected timeframe. Highlighted MRI-related adverse events in the list of reportable events. Added citations for 10% safety performance goal. Section 9.1 has been added to expand the description of personal information protection. Various typos and grammatical errors have been corrected. Version identifier has been changed to “D” for consistency with document control processes.
			Notified Body has been updated.	References to TUV have been replaced by BSI after project transfer completed in December 2018.

2	D	25 JUL 2019	US sites are now allowed in the study to increase enrollment and to increase Abbott's ability to evaluate Proclaim devices (more commonly used at US sites).	Section 4.2 now clarifies that the study will be conducted in up to 10 sites in the US, in addition to the approximately 20 sites in Europe. Similarly, Section 12.11 is updated to indicate that subjects will be enrolled at up to 30 centers.
			Enrollment rate was adjusted following the addition of US sites. The estimated time needed to enroll this subject population remains the same in current update (6 years) because enrollment in previous protocol update (March 2019) did not reflect the situation in the field.	Section 4.4 was updated to indicate that, with the addition of US sites, Abbott expects enrollment rate for patients requiring MRIs with an eligible MR conditional device to be no more than 10 subjects per year.
			Reporting subject death to applicable committee according to geographic location.	In case of death, the investigator will need to notify the IRB (for US sites) or EC (for EU sites) per IRB/EC policy. EC has been added to this version of the protocol (Section 8.2.1).
			Update of informed consent language according to the latest Abbott standard and in view of adding US sites to the study.	Informed consent section (Section 4.9.1) has been updated. Special Circumstances for Informed Consent (Section 4.9.1.1) has been updated with US HIPAA compliant statement.
			Device functionality check further specified. Wording added that supplements MRI Procedure Information Manual to allow	Section 6.2 and Section 6.5.1 has been updated to specify that data collection regarding device functionality includes impedance check, performed before the MRI scan. This can only be done when

			impedance check at every MRI scan.	the Clinician Programmer (for Proclaim devices) or Rapid Programmer (for Prodigy devices) is present. This requirement at every MRI scan has been added to the section describing the MRI Procedure Information Manual (Section 5.4).

Appendix C: Declaration of Helsinki

The most current version of the document will be followed.

Appendix D: Questionnaires

The questionnaire used in this study will be kept under a separate cover and is available upon request.

Appendix E: Device Manual

The manuals for the devices used in this study will be kept under a separate cover and are available upon request.

Appendix F: 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 G: Sample Informed Consent

The sample informed consent will be kept under a separate cover and is available upon request.

Appendix H: Case Report Forms

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