Implantable Pulse Generator

Prodigy™ IPG
Prodigy MRI™ IPG

Clinician's Manual

Abbott

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Contents

Prescription and Safety Information

Read this section to gather important prescription and safety information.

Intended Use

This rechargeable neurostimulation system is designed to deliver low-intensity electrical impulses to nerve structures. The system is intended to be used with leads and associated extensions that are compatible with the system.

Indications for Use

This neurostimulation system is 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, intractable low back and leg pain, and diabetic peripheral neuropathy of the lower extremities.

Contraindications

This system is contraindicated for patients who are unable to operate the system or who have failed to receive effective pain relief during trial stimulation.

Additional Prescription Information

Refer to the clinician's system reference manual for additional instructions and other important information, including indications for use, contraindications, warnings, precautions, and adverse effects related to the complete neurostimulation system.

MRI Safety Information

Some models of this system are Magnetic Resonance (MR) Conditional, and patients with these devices may be scanned safely with magnetic resonance imaging (MRI) when the conditions for safe scanning are met. For more information about MR Conditional neurostimulation components and systems, including equipment settings, scanning procedures, and a complete listing of conditionally approved components, refer to the MRI procedures clinician's manual for neurostimulation systems (available online at medical.abbott/manuals). For more information about MR Conditional products, visit the Abbott Medical product information page at neuromodulation.abbott/MRI-ready.

Warnings

The following warnings apply to these components.

Poor surgical risks. Neurostimulation should not be used on patients who are poor surgical risks or patients with multiple illnesses or active general infections.

Magnetic resonance imaging (MRI). Some patients may be implanted with the components that make up a Magnetic Resonance (MR) Conditional system, which allows them to receive an MRI scan if all the requirements for the implanted components and for scanning are met. A physician can help determine if a patient is eligible to receive an MRI scan by following the requirements provided by Abbott Medical. Physicians should also discuss any risks of MRI with patients.

Patients without an MR Conditional neurostimulation system should not be subjected to MRI because the electromagnetic field generated by an MRI may forcefully dislodge implanted components, damage the device electronics, and induce voltage through the lead that could jolt or shock the patient.

Diathermy therapy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (all now referred to as diathermy) on patients implanted with a neurostimulation system. Energy from diathermy can be transferred through the implanted system and cause tissue damage at the location of the implanted electrodes, resulting in severe injury or death.

Diathermy is further prohibited because it may also damage the neurostimulation system components. This damage could result in loss of therapy, requiring additional surgery for system implantation and replacement. Injury or damage can occur during diathermy treatment whether the neurostimulation system is turned on or off.

Electrosurgery devices. Electrosurgery devices should not be used in close proximity to an implanted neurostimulation system. Contact between an active electrode and an implanted IPG, lead, or extension can

cause severe injury to the patient. If use of electrocautery is necessary, first turn off the neurostimulation system.

Implanted cardiac systems. Physicians need to be aware of the risk and possible interaction between a neurostimulation system and an implanted cardiac system, such as a pacemaker or defibrillator. Electrical pulses from a neurostimulation system may interact with the sensing operation of an implanted cardiac system, causing the cardiac system to respond inappropriately. To minimize or prevent the implanted cardiac system from sensing the output of the neurostimulation system, (1) maximize the distance between the implanted systems; (2) verify that the neurostimulation system is not interfering with the functions of the implanted cardiac system; and (3) avoid programming either device in a unipolar mode (using the device's can as an anode) or using neurostimulation system settings that interfere with the function of the implantable cardiac system.

Use in patients with diabetes. Surgical complications and adverse effects may be more frequent and severe in patients with diabetes. The following additional considerations should be made for patients with diabetes:

- A pre-operative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease, those with autonomic neuropathy or renal failure, and patients with a Hemoglobin A1C (HbA1c) ≥8% (64 mmol/mol).
- Monitor the patient's blood glucose levels in the perioperative period and instruct the patient to continue to monitor glucose levels as they may fluctuate as a response to surgery or to complications. Implanting physicians or anesthesiologists should consult practice guidelines for the intraoperative management of patients with diabetes.
- Closely monitor patients for signs of infection, delayed wound healing, or cerebrospinal fluid (CSF) leakage as the severity of these complications may be greater in patients with diabetes.

Stimulation modes. The BurstDR™ stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

Device components. The use of components not approved for use by Abbott Medical with this system may result in damage to the system and increased risk to the patient.

Case damage. Do not handle the IPG if the case is pierced or ruptured because severe burns could result from exposure to battery chemicals.

IPG disposal. Return all explanted IPGs to Abbott Medical for safe disposal. IPGs contain lithium ion batteries as well as other potentially hazardous materials. Do not crush, puncture, or burn the IPG because explosion or fire may result.

Product materials. Neurostimulation systems have materials that come in contact or may come in contact with tissue. A physician should determine whether or not a patient may have an allergic reaction to these materials before the system is implanted.

Precautions

The following precautions apply to these components.

General Precautions

Physician training. Implanting physicians should be experienced in the diagnosis and treatment of chronic pain syndromes and have undergone surgical and device implantation training.

Patient selection. It is extremely important to select patients appropriately for neurostimulation. Thorough psychiatric screening should be performed. Patients should not be dependent on drugs and should be able to operate the neurostimulation system.

Infection. Follow proper infection control procedures. Infections related to system implantation might require that the device be explanted.

Implantation of two systems. If two systems are implanted, ensure that at least 20 cm (8 in.) separates the implanted IPGs to minimize the possibility of interference during programming.

Implant heating. While recharging an IPG, patients may perceive an increase in temperature. In patients who have areas of increased sensitivity to heat, consider placing the implant where the patient has normal sensation.

Theft detectors and metal screening devices. Certain types of antitheft devices, such as those used at entrances or exits of department stores, libraries, and other public establishments, and airport security screening devices may affect stimulation. Patients who are implanted with nonadjacent multiple leads and

patients who are sensitive to low stimulation thresholds may experience a momentary increase in their perceived stimulation, which has been described by some patients as uncomfortable or jolting. Patients should use caution when approaching such a device and should request assistance to bypass the device. If they must proceed through the device, patients should turn off the IPG and proceed with caution, being sure to move through the detector quickly.

Mobile phones. The effect of mobile phones on neurostimulation systems is unknown; patients should avoid placing mobile phones directly over the system.

Sterilization and Storage

Single-use, sterile device. The implanted components of this neurostimulation system are intended for a single use only. Sterile components in this kit have been sterilized using ethylene oxide (EtO) gas before shipment and are supplied in sterile packaging to permit direct introduction into the sterile field. Do not resterilize or reimplant an explanted system for any reason.

Storage environment. Store components and their packaging where they will not come in contact with liquids of any kind.

Handling and Implementation

Expiration date. An expiration date (or "use-by" date) is printed on the packaging. Do not use the system if the use-by date has expired.

Care and handling of components. Use extreme care when handling system components prior to implantation. Excessive heat, excessive traction, excessive bending, excessive twisting, or the use of sharp instruments may damage and cause failure of the components.

Package or component damage. Do not implant a device if the sterile package or components show signs of damage, if the sterile seal is ruptured, or if contamination is suspected for any reason. Return any suspect components to Abbott Medical for evaluation.

System testing. To ensure correct operation, the system should always be tested after implantation and before the patient leaves the surgery suite.

Device modification. The equipment is not serviceable by the customer. To prevent injury or damage to the system, do not modify the equipment. If needed, return the equipment to Abbott Medical for service.

Hospital and Medical Environments

High-output ultrasonics and lithotripsy. The use of high-output devices, such as an electrohydraulic lithotriptor, may cause damage to the electronic circuitry of an implanted IPG. If lithotripsy must be used, do not focus the energy near the IPG.

Ultrasonic scanning equipment. The use of ultrasonic scanning equipment may cause mechanical damage to an implanted neurostimulation system if used directly over the implanted system.

External defibrillators. The safety of discharge of an external defibrillator on patients with implanted neurostimulation systems has not been established.

Therapeutic radiation. Therapeutic radiation may damage the electronic circuitry of an implanted neurostimulation system, although no testing has been done and no definite information on radiation effects is available. Sources of therapeutic radiation include therapeutic X-rays, cobalt machines, and linear accelerators. If radiation therapy is required, the area over the implanted IPG should be shielded with lead.

Home and Occupational Environments

Electromagnetic interference (EMI). Certain commercial electrical equipment (for example, arc welders, induction furnaces, and resistance welders), communication equipment (for example, microwave transmitters, linear power amplifiers, and high power amateur transmitters), and high voltage power lines may generate sufficient EMI to interfere with the operation of the neurostimulation system if approached too closely.

Adverse Effects

In addition to those risks commonly associated with surgery, the following risks are associated with implanting or using this IPG:

- Unpleasant sensations or motor disturbances, including involuntary movement, caused by stimulation at high outputs (If either occurs, turn off your IPG immediately.)
- Stimulation in unwanted places

- Paralysis, weakness, clumsiness, numbness, or pain below the level of the implant
- Persistent pain at the IPG site
- Seroma (mass or swelling) at the IPG site
- Allergic or rejection response to implant materials
- Implant migration or skin erosion around the implant
- Battery failure
- Changes in blood glucose levels in response to any adverse effect.

NOTE: Patients with diabetes may have increased risks of infection, problems healing around the surgical site, and complications common to any surgical procedure. The severity of any surgical complication may be greater in patients with diabetes, particularly those with inadequate pre-operative glycemic control. For adverse effects observed in SCS clinical studies, refer to the clinical summaries manual for SCS systems.

Product Description

This IPG is a rechargeable, electronic device designed to be connected to one or more extensions or leads with up to 16 electrodes total. It is powered by a hermetically sealed battery within a titanium case and uses microelectronic circuitry to generate constant-current electrical stimulation. The IPG can deliver stimulation with a single program or with multiple programs. Each program can provide stimulation to a single anatomical area or to multiple areas (called MultiStim™ programs). New features can be introduced to the system via software updates allowing for upgraded technology to be used. A Abbott Medical external programmer may be needed for certain types of software updates to this product.

NOTE: Patients may experience a sensation of tingling, “pins and needles,” prickling, or even burning called paresthesia. Paresthesia may be brief or it may last a long time. Current data shows that most patients using BurstDR™ stimulation therapy do not experience paresthesia.

NOTE: For more information about the neurostimulation system, see the clinician’s programming and reference manual for this system.

Package Contents

In addition to the product documentation, the Prodigy MRI™ IPG kit (Model 3772) and Prodigy™ IPG kit (Model 3799) contain the following items:

- 1 IPG
- 1 pocket sizer
- 1 torque wrench (Model 1101)
- 2 port plugs (Model 1111)
- 1 tunneling tool (Model 1112)

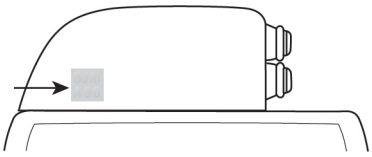
Identifying the IPG

Using standard X-ray procedures, you can view the code that identifies the manufacturer and model number of the IPG in the header of the IPG.

- For the Prodigy MRI™ IPG (Model 3772), the code is SJM N*nn*.
- For the Prodigy™ IPG (Model 3799), the code is SJM Y*nn*.

'SJM' represents Abbott Medical as the manufacturer; 'N' or 'Y' represents Model 3772 or 3799 respectively; and '*nn*' represents the last two digits of the year of manufacture. For example, SJM N15 identifies a Prodigy MRI IPG (Model 3772) manufactured in 2015.

Figure 1. Location of the IPG code



Directions for Use

Read this section carefully for suggested directions for use related to the IPG. For directions for use for other system components not covered in this document, see the clinician's manual for the appropriate device.

NOTE: Well in advance of the surgical procedure, authorize the programmer to the IPG while the IPG is in its sterile packaging to ensure that it is functional.

Creating an IPG Pocket

To create an IPG pocket:

1. Determine the site for the IPG, ensuring that the lead is long enough to reach the pocket and provide a strain relief loop.

   NOTE: The IPG should be located in an area that the patient can easily reach with the programming wand. Common sites for implantation are: along the midaxillary line, in the upper buttock along the posterior axillary line (taking care to avoid the belt line), and in the area over the abdomen just below the lowermost rib. To ensure a flat area is selected, you can mark a flat area prior to the surgical procedure while the patient is in a sitting position.

   CAUTION: Do not place the IPG deeper than 2.25 cm (0.9 in.) because the patient programmer and charger may not communicate efficiently with the IPG and the charger may not charge efficiently.
2. Create the pocket so that the IPG is parallel to the skin surface and no deeper than 2.25 cm (0.9 in.) below the skin surface.
3. Insert and remove the pocket sizer to ensure that the pocket is large enough to accommodate the IPG, allowing enough extra room for a strain relief loop for each lead or extension.

Tunneling to the Pocket

Tunneling is usually done from the lead anchor site directly to the IPG pocket. However, when an extension is used or the IPG pocket is in the abdominal region, tunneling is done from the lead anchor site to a midpoint (where an incision and appropriate dissection have been performed) and then continued to the IPG pocket site.

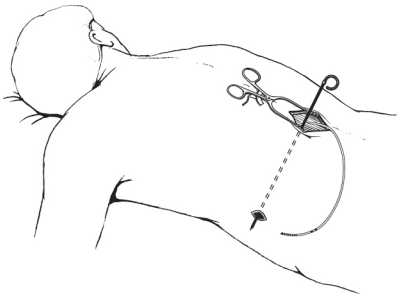
The following steps outline the suggested procedure to tunnel from the lead anchor site to the IPG pocket:

CAUTION: Use extreme care so as not to damage a lead with the sharp point of the tunneling tool.

NOTE: The tunneling tool is malleable and can be bent to conform to the contour of the patient's body.

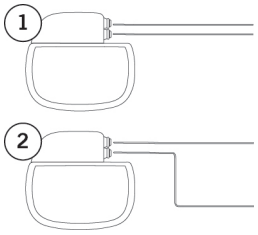
1. With the cannula sleeve in place on the tunneling tool, create a subcutaneous tunnel between the lead anchor site and the IPG pocket.

Figure 2. Suggested tunnel to the IPG pocket



2. Withdraw the tunneling tool from the cannula sleeve, leaving the cannula sleeve in the subcutaneous tunnel.

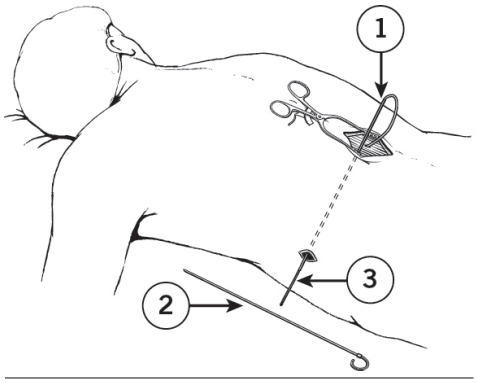
   CAUTION: Multiple leads must be routed adjacent to one another. Patients with nonadjacent leads may experience changes in perceived stimulation from theft detectors and metal screening devices. The correct way to route multiple leads is as follows:



1. Correct
2. Incorrect

3. Carefully pass the end of the lead or leads through the cannula sleeve from the anchor site to the IPG pocket; or, if a two-step tunneling procedure is used, pass the lead or leads from the anchor site to the midway incision site and then to the IPG pocket. Multiple leads may be placed in the same tunnel.

Figure 3. Sequence of tunneling steps



1. Leave cannula sleeve in place
2. Remove tunneling tool
3. Pull lead through cannula sleeve to IPG pocket

4. Withdraw the cannula sleeve from the subcutaneous tunnel by passing it over the lead or leads, taking care not to cause traction on them.

Connecting a Lead or Extension to the IPG

The following steps outline the suggested guidelines to connect a lead or extension to the IPG:

CAUTION: Do not connect a lead or extension with body fluid or saline residue on its contacts because corrosion can occur and cause failure of the system.

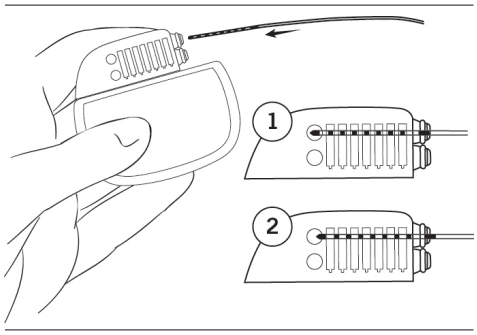
1. If any of the lead or extension contacts came in contact with body fluid or saline, thoroughly clean the contacts with sterile deionized water or sterile water for irrigation and dry them completely.

CAUTION: Observe these cautions when performing the following step:

- **Do not bend the lead sharply or it may be damaged.**
- **Do not loosen the setscrew in the connector more than a quarter turn at a time while trying to insert the lead. Retracting the setscrew too far can cause the setscrew to come loose and make the connector assembly unusable.**

2. Using clean gloves, carefully slide the lead or extension into the IPG header until all of the contact bands are fully inside the connector assembly and hidden from view.

Figure 4. Insert the lead fully into the IPG header

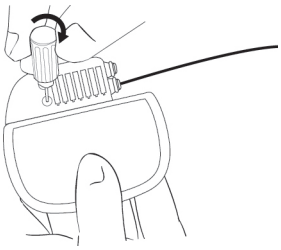


1. Fully inserted
2. Not fully inserted

CAUTION: Use only the torque wrench that is compatible with the IPG or the device may be damaged and rendered unusable.

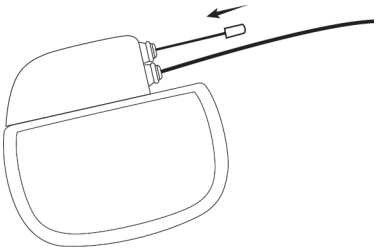
3. Insert the torque wrench through the septum and tighten the setscrew, turning it clockwise until the wrench clicks.

Figure 5. Tighten the setscrew clockwise



4. Remove the torque wrench and check the septum to ensure that it closed. If the septum did not close, gently reseat the septum flaps.
5. If implanting two leads, repeat the previous steps. If implanting a single lead only, insert the header port plug into the unused port, and use the torque wrench to tighten the setscrew until it clicks.

Figure 6. Insert the port plug



Implanting the IPG

The following steps outline the suggested procedure to implant the IPG:

CAUTION: Observe these cautions when performing the following step:

- **Do not implant the IPG face down. Implant it with the label facing toward the skin, or it may not communicate or recharge.**
- **If using more than one IPG, implant them at least 20 cm (8 in) apart. Putting them too close together may interfere with the patient programmer's ability to communicate with each IPG separately.**

1. Place the IPG into the IPG pocket, at a depth not to exceed 2.25 cm (0.9 in), with the label facing the skin surface.

Figure 7. Place the IPG in the pocket

2. Carefully coil any excess lead or extension behind the IPG in loops no smaller than 2.5 cm (1 in) in diameter to provide strain relief for the lead or extension and IPG connection.

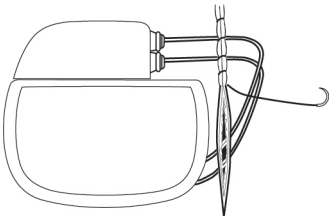
   CAUTION: Do not bring the suture needle in contact with an IPG, lead, or extension, or the component may be damaged.

3. To stabilize the IPG within the pocket, pass a suture through the hole at the top of the IPG header and secure it to connective tissue.
4. Check the entire system by fluoroscopy prior to closing to ensure proper positioning of the lead or leads and that it is straight, with no sharp bends or kinks.
5. Connect the communication wand to the patient programmer, place the wand in a sterile bag, and position the wand over the IPG site.
6. Ensure that the patient programmer achieves effective communication with the IPG and that the system is operational.

   NOTE: IPG output may not be identical to that of the trial stimulator at the same settings.

7. Ensure that the IPG is away from the pocket incision suture line, close the pocket incision, and apply the appropriate dressings.

Figure 8. Close the pocket incision



Replacing the IPG

The following steps outline the suggested procedure to replace an IPG:

1. Turn off the IPG or verify that it is turned off.

   CAUTION: Exercise care when using sharp instruments or electrocautery around leads or extensions, or they may be damaged.
2. Open the IPG implant site per normal surgical procedure.
3. Insert the torque wrench through the septum of the IPG header and loosen the setscrew by turning it counterclockwise.

   CAUTION: When performing the following step, do not bend the lead or extension sharply; or it may be damaged.
4. Gently remove the lead or extension from the IPG header; then clean and dry all connections, ensuring they are free of fluid and tissue.
5. To complete the IPG replacement procedure, see the following sections: “Connecting a Lead or Extension to the IPG” (page 6) and “Implanting the IPG” (page 8).

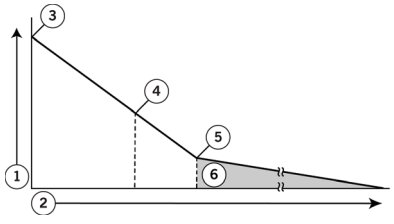
Disposing of Explanted Components

Explanted Abbott Medical components should be returned to Abbott Medical for proper disposal. To return an explanted component, place it in a container or bag marked with a biohazard label and coordinate the return with your Abbott Medical representative or Technical Support.

Maintaining the IPG Battery

The IPG contains a lithium ion battery. The time it takes to recharge a battery depends on these factors: age of the battery, daily usage time, stimulation settings, and length of time since the last recharge. The following graph shows how the rechargeable battery depletes over time.

Figure 9. IPG battery depletion over time



1. Battery capacity
2. Time
3. Battery fully charged
4. Recharge notice
5. Stimulation stops
6. Recharge within 30 to 90 days

If the patient does not recharge the battery, stimulation will eventually stop, and the patient then must recharge the battery to prevent battery damage. After stimulation stops, a new battery can last up to 90 days before it must be recharged, while a ten-year-old battery should be recharged within 30 days.

When the IPG is used at high stimulation parameters for tonic programs or at nominal stimulation parameters for BurstDR™ stimulation programs, battery usage studies demonstrate that the battery should allow at least ten years of practical recharging. In other words, a ten-year-old device will maintain at least 24 hours of continuous therapy between recharges.

Depending on the patient's stimulation parameters, the device will continue to operate for months to years. Patients may experience a significantly longer device life before recharging is determined to be impractical if they use lower stimulation parameters, a frequent recharging protocol, or both. Frequent recharging can reduce charging session times and maximize the IPG's life.

NOTE: The model used to predict device longevity was generated by fitting a mathematical model to three years of real-time cycling data, which was then used to extrapolate device battery capacity at the end of ten years.

Recharging the IPG Battery

For information about the charging system and how to recharge the IPG battery, see the user's guide for the charging system.

WARNING: Do not let an IPG battery remain depleted for an extended period of time. If a depleted battery is not recharged within 30 to 90 days of its full discharge, the charger may not be able to recharge it; and it will have to be surgically replaced to resume therapy.

Preserving the IPG When Not in Use

To preserve the IPG when discontinuing stimulation for an extended period of time, follow these steps:

1. Recharge the battery to its maximum capacity before turning off the IPG.
2. Recharge the battery to its maximum capacity every 3 months while it is not in use.

Technical Support

For technical questions and support for your product, use the following information:

- +1 855 478 5833 (toll-free within North America)
- +1 651 756 5833

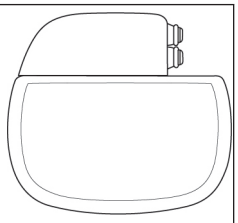
For additional assistance, call your local Abbott Medical representative.

Appendix A: Product Specifications

IPG Specifications

The Prodigy MRI™ IPG (Model 3772) and Prodigy™ IPG (Model 3799) have the following physical specifications.

Table 1. IPG specifications

Model	3772	3799	
MRI status	MR conditional	Untested	
Height	4.8 cm (1.89 in)		
Length	5.3 cm (2.09 in)		
Thickness	0.95 to 1.1 cm (0.37 to 0.43 in)		
Weight	29.0 g (1.0 oz)		
Volume	17.7 cm^3 (1.08 in^3)		
Power source	Rechargeable lithium ion cell		
Storage temperature	-10°C–55°C (14°F–131°F)		
Storage humidity	10%–90% (noncondensing)		
Storage pressure	70–150 kPa (10.2–21.8 psi)		
Connector strength	Exceeds EN45502-1 requirements		

The IPG has the following operating parameters.

Table 2. Operating parameters for the IPG

Parameter	Tonic Range	Tonic Steps	Burst Range*	Burst Steps*
Pulse width	50–500 µs	Alternating 12 and 13 µs (starting with 12 µs)	50–1000 µs	50 µs
Frequency	2–200 Hz	2 Hz	—	—
	200–500 Hz	10 Hz	—	—
	500–1200 Hz	20 Hz	—	—
Burst rate frequency	—	—	10–60 Hz	10 Hz
Intraburst frequency	—	—	250–500 Hz	10 Hz
			500–1000 Hz	20 Hz
Amplitude	0–25.5 mA (max 12 V)	0.1–1.0 mA	0–12.75 mA	0.05–0.50 mA

NOTE: Columns with * represent operating parameters for BurstDR™ stimulation programs on IPGs capable of BurstDR stimulation mode.

NOTE: The number of stim sets in use for a tonic program governs the maximum frequency (1200/number of stim sets).

NOTE: The maximum current depends on the impedance, frequency, and pulse width settings.

Appendix B: Regulatory Statements

This section contains regulatory statements about your product.

Statement of FCC Compliance (FCC ID:PX 2001)

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to part 15 of the FCC rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses, and can radiate radiofrequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
- Consult the dealer or an experienced radio/TV technician for help.

Operation is subject to the following two conditions:

- This device may not cause harmful interference.
- This device must accept any interference received, including interference that may cause undesired operation.

Modifications not expressly approved by the manufacturer could void the user's authority to operate the equipment under FCC rules.

Disposal Guidelines for Battery-Powered Devices

This device contains a battery and a label is affixed to the device in accordance with European Council directives 2002/96/EC and 2006/66/EC. These directives call for separate collection and disposal of electrical and electronic equipment and batteries. Sorting such waste and removing it from other forms of waste

lessens the contribution of potentially toxic substances into municipal disposal systems and into the larger ecosystem. Return the device to Abbott Medical at the end of its operating life.

Appendix C: Symbols and Definitions

The symbols below and harmonized symbols may be found on the product or product label. For harmonized symbols, refer to the Universal Symbols Glossary at medical.abbott/manuals.

Table 3. Symbols and definitions

Symbol	Definition
	Caution
	Consult instructions for use
	Follow instructions for use on this website
	MR Conditional NOTE: Magnetic Resonance (MR) Conditional, an item with demonstrated safety in the MR environment within the defined conditions. At a minimum, address the conditions of the static magnetic field, the switched gradient magnetic field, and the radiofrequency fields. Additional conditions, including specific configurations of the item, may be required.
	MR Unsafe NOTE: Magnetic Resonance (MR) Unsafe, an item poses unacceptable risks to the patient, medical staff, or other persons within an MR environment
	Do not re-use
	Do not resterilize
	Use-by date
	Date of manufacture
	Manufacturing facility
	Temperature limit
	Humidity limitation

Table 3. Symbols and definitions

Symbol	Definition
	Atmospheric pressure limitation
	Do not use if package is damaged
	Catalog number NOTE: This symbol also refers to the model number.
	Manufacturer
	Packaging unit
	Implantable device
	Accessories
	Serial number
	Batch code
	Unique Device Identification
	Prescription use only
	Sterilized using ethylene oxide

Abbott Medical
6901 Preston Road
Plano, Texas 75024 USA
+1 855 478 5833
+1 651 756 5833

Abbott Medical
The Corporate Village
Da Vincilaan 11 Box F1
1935 Zaventem
Belgium
+32 2 774 68 11

2023-01
ARTEN600279432 2

Abbott

Proclaim™ Implantable Pulse Generator

Models 3660, 3661, 3662, 3663, 3665, 3667, 3670, 3671, 3672, 3673

Clinician's System Manual

Abbott

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

WARNING: This product can expose you to chemicals including ethylene oxide, which is known to the State of California to cause cancer and birth defects or other reproductive harm. For more information, go to www.P65Warnings.ca.gov.

™ Indicates a trademark of the Abbott group of companies.

‡ Indicates a third-party trademark, which is property of its respective owner.

Bluetooth and Bluetooth logo are registered trademarks of Bluetooth SIG, Inc.

Pat. http://www.abbott.com/patents

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Contents

Prescription and Safety Information

Read this section to gather important prescription and safety information.

Intended Use

This neurostimulation system is designed to deliver low-intensity electrical impulses to nerve structures. The system is intended to be used with leads and associated extensions that are compatible with the system.

Indications for Use

Refer to the Indications for Use Data Sheet for Abbott Medical spinal cord stimulation systems.

Contraindications

This system is contraindicated for patients who are unable to operate the system or who have failed to receive effective pain relief during trial stimulation.

MRI Safety Information

Some models of this system are Magnetic Resonance (MR) Conditional, and patients with these devices may be scanned safely with magnetic resonance imaging (MRI) when the conditions for safe scanning are met. For more information about MR Conditional neurostimulation components and systems, including equipment settings, scanning procedures, and a complete listing of conditionally approved components, refer to the MRI procedures clinician's manual for neurostimulation systems (available online at medical.abbott/manuals). For more information about MR Conditional products, visit the Abbott Medical product information page at neuromodulation.abbott/MRI-ready.

Warnings

The following warnings apply to this neurostimulation system.

Poor surgical risks. Neurostimulation should not be used on patients who are poor surgical risks or patients with multiple illnesses or active general infections.

Magnetic resonance imaging (MRI). Some patients may be implanted with the components that make up a Magnetic Resonance (MR) Conditional system, which allows them to receive an MRI scan if all the requirements for the implanted components and for scanning are met. A physician can help determine if a patient is eligible to receive an MRI scan by following the requirements provided by Abbott Medical. Physicians should also discuss any risks of MRI with patients.

Patients without an MR Conditional neurostimulation system should not be subjected to MRI because the electromagnetic field generated by an MRI may damage the device electronics and induce voltage through the lead that could jolt or shock the patient.

Diathermy therapy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (all now referred to as diathermy) on patients implanted with a neurostimulation system. Energy from diathermy can be transferred through the implanted system and cause tissue damage at the location of the implanted electrodes, resulting in severe injury or death.

Diathermy is further prohibited because it may also damage the neurostimulation system components. This damage could result in loss of therapy, requiring additional surgery for system implantation and replacement. Injury or damage can occur during diathermy treatment whether the neurostimulation system is turned on or off.

Electrosurgery. To avoid harming the patient or damaging the neurostimulation system, do not use monopolar electrosurgery devices on patients with implanted neurostimulation systems. Before using an electrosurgery device, place the device in Surgery Mode using the patient controller app or clinician programmer app. Confirm the neurostimulation system is functioning correctly after the procedure.

During implant procedures, if electrosurgery devices must be used, take the following actions:

- Use bipolar electrosurgery only.
- Complete any electrosurgery procedures before connecting the leads or extensions to the neurostimulator.
- Keep the current paths from the electrosurgery device as far from the neurostimulation system as possible.

- Set the electrosurgery device to the lowest possible energy setting.
- Confirm that the neurostimulation system is functioning correctly during the implant procedure and before closing the neurostimulator pocket.

Implanted cardiac systems. Physicians need to be aware of the risk and possible interaction between a neurostimulation system and an implanted cardiac system, such as a pacemaker or defibrillator. Electrical pulses from a neurostimulation system may interact with the sensing operation of an implanted cardiac system, causing the cardiac system to respond inappropriately. To minimize or prevent the implanted cardiac system from sensing the output of the neurostimulation system, (1) maximize the distance between the implanted systems; (2) verify that the neurostimulation system is not interfering with the functions of the implanted cardiac system; and (3) avoid programming either device in a unipolar mode (using the device's can as an anode) or using neurostimulation system settings that interfere with the function of the implantable cardiac system.

Other active implanted devices. The neurostimulation system may interfere with the normal operation of another active implanted device, such as a pacemaker, defibrillator, or another type of neurostimulator. Conversely, the other active implanted device may interfere with the operation of the neurostimulation system.

Interference with other devices. Some of this system's electronic equipment, such as the programmer and controller, can radiate radiofrequency (RF) energy that may interfere with other electronic devices, including other active implanted devices. Avoid placing equipment components directly over other electronic devices. To correct the effect of interference with other devices, turn off the equipment or increase the distance between the equipment and the device being affected.

Operation of machines, equipment, and vehicles. Patients using therapy that generates paresthesia should turn off stimulation before operating motorized vehicles, such as automobiles, or potentially dangerous machinery and equipment because sudden stimulation changes may distract them from properly operating it. However, current data shows that most patients using BurstDR™ stimulation therapy do not experience paresthesia. For patients who do not feel paresthesia, sudden stimulation changes are less likely to occur and distract them while operating motorized vehicles, machinery, or equipment.

Explosive and flammable gases. Do not use a clinician programmer or patient controller in an environment where explosive or flammable gas fumes or vapors are present, including hyperbaric chambers. The operation of these devices could cause them to ignite, causing severe burns, injury, or death.

Keep the device dry. Programmer and controller devices are not waterproof. Keep them dry to avoid damage. Advise patients to not use their device when engaging in activities that might cause it to get wet, such as swimming or bathing.

Pediatric use. Safety and effectiveness of neurostimulation for pediatric use have not been established.

Pregnancy and nursing. Safety and effectiveness of neurostimulation for use during pregnancy and nursing have not been established.

Use in patients with diabetes. Surgical complications and adverse effects may be more frequent and severe in patients with diabetes. The following additional considerations should be made for patients with diabetes:

- A pre-operative risk assessment should be performed for patients with diabetes who are at high risk for ischemic heart disease, those with autonomic neuropathy or renal failure, and patients with a Hemoglobin A1C (HbA1c) ≥8% (64 mmol/mol).
- Monitor the patient's blood glucose levels in the perioperative period and instruct the patient to continue to monitor glucose levels as they may fluctuate as a response to surgery or to complications. Implanting physicians or anesthesiologists should consult practice guidelines for the intraoperative management of patients with diabetes.
- Closely monitor patients for signs of infection, delayed wound healing, or cerebrospinal fluid (CSF) leakage as the severity of these complications may be greater in patients with diabetes.

Stimulation modes. The BurstDR™ stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

Device components. The use of components not approved for use by Abbott Medical with this system may result in damage to the system and increased risk to the patient.

Device modification. The equipment is not serviceable by the customer. To prevent injury or damage to the system, do not modify the equipment. If needed, return the equipment to Abbott Medical for service.

Application modification. To prevent unintended stimulation, do not modify the operating system or application in any way. Do not use the application if the operating system is compromised (that is, jailbroken).

Case damage. Do not handle the IPG if the case is pierced or ruptured because severe burns could result from exposure to battery chemicals.

IPG disposal. Return all explanted IPGs to Abbott Medical for safe disposal. IPGs contain batteries as well as other potentially hazardous materials. Do not crush, puncture, or burn the IPG because explosion or fire may result.

Product materials. Neurostimulation systems have materials that come in contact or may come in contact with tissue. A physician should determine whether or not a patient may have an allergic reaction to these materials before the system is implanted.

Precautions

The following precautions apply to this neurostimulation system.

General Precautions

Clinician training. Implanting physicians should be experienced in the diagnosis and treatment of chronic pain syndromes and have undergone surgical and device implantation training.

Patient selection. It is extremely important to select patients appropriately for neurostimulation. Thorough psychiatric screening should be performed. Patients should not be dependent on drugs and should be able to operate the neurostimulation system.

Infection. Follow proper infection control procedures. Infections related to system implantation might require that the device be explanted.

Implantation of two systems. If two systems are implanted, ensure that at least 20 cm (8 in.) separates the implanted IPGs to minimize unintended interaction with other system components.

Implantation of multiple leads. If multiple leads are implanted, leads and extensions should be routed in close proximity. Nonadjacent leads can possibly create a conduit for stray electromagnetic energy that could cause the patient unwanted stimulation.

High stimulation outputs. Stimulation at high outputs may cause unpleasant sensations or motor disturbances, or render the patient incapable of controlling the stimulator. If unpleasant sensations occur, the device should be turned off immediately.

Electromagnetic interference (EMI). Some equipment in home, work, medical, and public environments can generate EMI that is strong enough to interfere with the operation of a neurostimulation system or damage system components. Patients should avoid getting too close to these types of EMI sources, which include the following examples: commercial electrical equipment (such as arc welders and induction furnaces), communication equipment (such as microwave transmitters and high-power amateur transmitters), high-voltage power lines, radiofrequency identification (RFID) devices, and some medical procedures (such as therapeutic radiation and electromagnetic lithotripsy).

Lead movement. Patients should be instructed to avoid bending, twisting, stretching, and lifting objects over 2 kg (5 lb) for six to eight weeks after implantation of a neurostimulation system. Extension of the upper torso or neck may cause lead movement and alter the stimulation field (especially with leads in the cervical area), resulting in overstimulation or ineffective stimulation.

Patient training. Instruct patients to use their neurostimulation system only after an authorized clinician has programmed the device and has trained the patient how to control stimulation and safely use the system.

Programmer use. Allow only authorized use of the clinician programmer to avoid any programming changes that may injure a patient.

Sterilization and Storage

Single-use, sterile device. The implanted components of this neurostimulation system are intended for a single use only. Sterile components in this kit have been sterilized using ethylene oxide (EtO) gas before shipment and are supplied in sterile packaging to permit direct introduction into the sterile field. Do not resterilize or reimplant an explanted system for any reason.

Storage environment. Store components and their packaging where they will not come in contact with liquids of any kind.

Handling and Implementation

Expiration date. An expiration date (or "use-by" date) is printed on the packaging. Do not use the system if the use-by date has expired.

Handle the device with care. The clinician programmer and patient controller are sensitive electronic devices that can be damaged by rough handling, such as dropping them on the ground.

Care and handling of components. Use extreme care when handling system components prior to implantation. Excessive heat, excessive traction, excessive bending, excessive twisting, or the use of sharp instruments may damage and cause failure of the components.

Package or component damage. Do not implant a device if the sterile package or components show signs of damage, if the sterile seal is ruptured, or if contamination is suspected for any reason. Return any suspect components to Abbott Medical for evaluation.

Exposure to body fluids or saline. Prior to connection, exposure of the metal contacts, such as those on the connection end of a lead or extension, to body fluids or saline can lead to corrosion. If such exposure occurs, clean the affected parts with sterile, deionized water or sterile water for irrigation, and dry them completely prior to lead connection and implantation.

System testing. To ensure correct operation, always test the system during the implant procedure, before closing the neurostimulator pocket, and before the patient leaves the surgery suite.

Hospital and Medical Environments

High-output ultrasonics and lithotripsy. The use of high-output devices, such as an electrohydraulic lithotriptor, may cause damage to the electronic circuitry of an implanted IPG. If lithotripsy must be used, do not focus the energy near the IPG.

Ultrasonic scanning equipment. The use of ultrasonic scanning equipment may cause mechanical damage to an implanted neurostimulation system if used directly over the implanted system.

External defibrillators. The safety of discharge of an external defibrillator on patients with implanted neurostimulation systems has not been established.

Therapeutic radiation. Therapeutic radiation may damage the electronic circuitry of an implanted neurostimulation system, although no testing has been done and no definite information on radiation effects is available. Sources of therapeutic radiation include therapeutic X-rays, cobalt machines, and linear accelerators. If radiation therapy is required, the area over the implanted IPG should be shielded with lead. Damage to the system may not be immediately detectable.

Home and Occupational Environments

Security, antitheft, and radiofrequency identification (RFID) devices. Some antitheft devices, such as those used at entrances or exits of department stores, libraries, and other public places, and airport security screening devices may affect stimulation. Additionally, RFID devices, which are often used to read identification badges, as well as some tag deactivation devices, such as those used at payment counters at stores and loan desks at libraries, may also affect stimulation. Patients who are implanted with nonadjacent multiple leads and patients who are sensitive to low stimulation thresholds may experience a momentary increase in their perceived stimulation, which some patients have described as uncomfortable or jolting. Patients should cautiously approach such devices and should request help to bypass them. If they must go through a gate or doorway containing this type of device, patients should turn off their IPG and proceed with caution, being sure to move through the device quickly.

Scuba diving or hyperbaric chambers. Patients should not dive below 30 m (100 ft) of water or enter hyperbaric chambers above 4.0 atmospheres absolute (ATA). Pressures below 30 m (100 ft) of water (or above 4.0 ATA) could damage the neurostimulation system. Before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their physician.

Wireless use restrictions. In some environments, the use of wireless functions (for example, Bluetooth® wireless technology) may be restricted. Such restrictions may apply aboard airplanes, near explosives, or in hazardous locations. If you are unsure of the policy that applies to the use of this device, please ask for authorization to use it before turning it on.

Consumer goods and electronic devices. Magnetic interference with consumer goods or electronic devices that contain magnets, such as mobile phones and smart watches, may unintentionally cause the neurostimulation system to turn on or turn off or affect communication between the device and generator; however, it will not change the prescribed programmed parameters. Patients should be advised to keep their mobile phones and smart watches at least 15 cm (6 in.) away from the generator and avoid placing any

smart device in a pocket near the generator. If a patient is concerned about a smart device interacting with their neurostimulation system, consider disabling magnet mode. For more information about setting the magnet mode, refer to the clinician programmer manual or contact Technical Support.

Adverse Effects

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

- Unpleasant sensations or motor disturbances, including involuntary movement, caused by stimulation at high outputs (If either occurs, turn off stimulation 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 (such as radicular stimulation of the chest wall)
- 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 migration or skin erosion around the implant
- Battery failure
- Changes in blood glucose levels in response to any adverse effect

  NOTE: Patients with diabetes may have increased risks of infection, problems healing around the surgical site, and complications common to any surgical procedure. The severity of any surgical complication may be greater in patients with diabetes, particularly those with inadequate pre-operative glycemic control. For adverse effects observed in SCS clinical studies, refer to the clinical summaries manual for SCS systems.

Safety and Effectiveness Studies

For information that supports the clinical use of this neurostimulation system, refer to the clinical summaries manual for spinal cord stimulation (SCS) systems (available online at medical.abbott/manuals). This neurostimulation system is similar in technology and intended use to the systems reported in the literature and clinical studies. Therefore, the literature and clinical studies represent the safety and effectiveness of this neurostimulation system.

System Overview

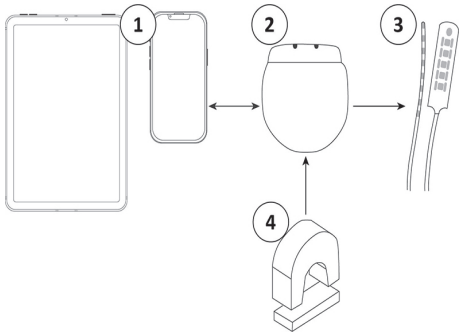
This neurostimulation system is designed to deliver electrical stimulation to nerve structures. The neurostimulation system includes the following main components:

- Implantable pulse generator (IPG)
- Leads
- Clinician programmer
- Patient controller
- Patient magnet

The IPG delivers electrical pulses through the leads to electrodes near selected nerve fibers in order to provide therapeutic stimulation. The patient magnet can turn the IPG on and off if the physician enabled this functionality. Physicians use the clinician programmer to create and modify programs for a patient. Patients use the patient controller to control their prescribed programs.

The following image shows how the major system components are intended to interact.

Figure 1. Interaction among main system components



1. Clinician programmer or patient controller
2. IPG
3. Leads
4. Patient magnet

NOTE: This manual provides instructions for implanting the IPG. For instructions for using other components, see the applicable manuals for those components.

Product Description

This implantable pulse generator (IPG) is an electronic device designed to be connected to one or more extensions or leads with up to 16 electrodes total. It is powered by a hermetically sealed battery within a titanium case and uses microelectronic circuitry to generate constant-current electrical stimulation. The IPG can deliver stimulation with a single program or with multiple programs. Each program can provide stimulation to a single anatomical area or to multiple areas. The IPG communicates wirelessly with system programmers and controllers, and IPGs are available in small and large sizes to accommodate different power needs.

Some models support additional functions:

- **Upgradeability.** Models can receive software upgrades after implantation to provide patients with additional features as approved by the respective regulatory agencies. To upgrade features on the IPG, a system programmer is needed.
- **Compatible header.** Models with a compatible header are designed to allow the IPG to connect to leads or extensions from another manufacturer that meet the compatibility guidelines (referred to as “IPGs with compatible headers”).

For more information about which models provide these additional functions, as well as other IPG specifications, see the appropriate appendix in this manual.

NOTE:

- For more information about the neurostimulation system, see the clinician’s programming manual for this system.
- In this document, the term “clinician programmer” refers to the NeuroSphere™ Clinician Programmer device, “patient controller” refers to the NeuroSphere™ Patient Controller device, “clinician programmer app” refers to the NeuroSphere™ Clinician Programmer software application (app), and “patient controller app” refers to the NeuroSphere™ Patient Controller app.

Package Contents

In addition to the product documentation, the IPG kit contains the following items:

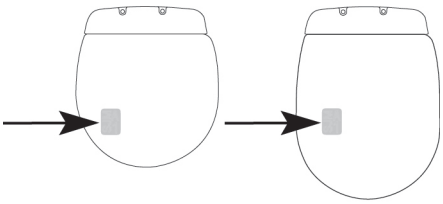
- 1 IPG (see the appendix in this manual for model numbers)
- 1 pocket sizer
- 1 torque wrench (Model 1101)
- 2 port plugs (Model 1111)

Identifying the IPG

Before implanting the IPG, you can view the model number engraved on the IPG. After implantation, you can identify the IPG using a radiopaque identification tag that you can view with standard X-ray procedures. The tag, which is located in the lower left corner of the IPG when the logo side of the IPG is facing toward you, contains a code in the following format: SJM*LN*. 'SJM' designates Abbott Medical as the manufacturer; *'LN'* is a letter and a number combination that identifies the model family (see the following figure).

For the Proclaim™ IPG, the code is SJM A1. To determine the exact model IPG that is implanted, use the clinician programmer app to communicate with the IPG and view IPG information. See the clinician's manual for the clinician programmer for instructions.

Figure 2. Location of the IPG code on a small IPG (left) and large IPG (right)



Directions for Use

Read this section carefully for suggested directions for use related to the IPG. For directions for use for other system components not covered in this document, see the clinician's manual for the appropriate device.

NOTE: Before the surgical procedure, set up communication between the clinician programmer and the IPG while the IPG is in its sterile packaging to ensure that it is functional. If the IPG has never established communication with a programmer, you must first activate the IPG for communication ("wake up" the IPG) by holding a magnet over the IPG for 10 seconds.

Creating an IPG Pocket

The following steps outline the suggested procedure to create an IPG pocket:

1. Determine the site for the IPG, ensuring that the lead is long enough to reach the pocket and provide a strain relief loop.

   CAUTION: Do not place the IPG deeper than 4.0 cm (1.57 in.) because the clinician programmer may not communicate effectively with the IPG.

   NOTE: Common sites for IPG implantation are along the midaxillary line, in the upper buttock along the posterior axillary line (taking care to avoid the belt line), and in the area over the abdomen just below the lowermost rib. To ensure a flat area is selected, you can mark a flat area prior to the surgical procedure while the patient is in a sitting position.

2. Create the pocket so that the IPG is parallel to the skin surface and no deeper than 4.0 cm (1.57 in.) below the skin surface.
3. Insert and remove the pocket sizer to ensure that the pocket is large enough to accommodate the IPG, allowing enough extra room for a strain relief loop for each lead or extension.

Connecting a Lead or Extension to the IPG

The following steps outline the suggested guidelines to connect a lead or extension to the IPG:

WARNING: To avoid harming the patient or damaging the neurostimulation system, ensure that any electrosurgery procedures are completed before connecting the leads or extensions to the IPG.

CAUTION: Do not connect a lead or extension with body fluid or saline residue on its contacts because corrosion can occur and cause failure of the system.

1. If any of the lead or extension contacts came in contact with body fluid or saline, thoroughly clean the contacts with sterile deionized water or sterile water for irrigation and dry them completely.

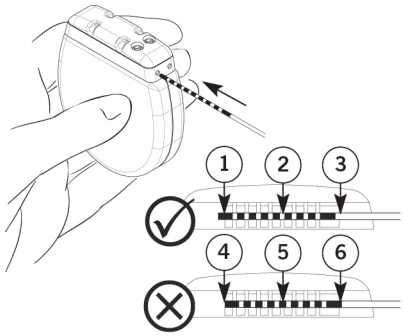
2. To help ensure that the lead or extension can be fully inserted into the IPG header, insert the torque wrench through the septum on the IPG header, turn the torque wrench clockwise to tighten the setscrew until the torque wrench clicks, and then loosen the setscrew again by turning the wrench counterclockwise about 2.5 times.

CAUTION:

- **Use only the torque wrench included in the extension, IPG, or torque wrench kit. If you need to loosen the setscrew, turn the setscrew (in quarter turns counterclockwise) just enough to insert or remove the lead or extension from the IPG header. Retracting the setscrew too far may cause it to come loose and fail to secure the lead or extension to the IPG.**
- **To avoid sharply bending and damaging the lead or extension when performing the following step, insert the lead or extension parallel with the header port. Additionally, try grasping the lead or extension about 5 mm at a time from the opening of the header port while inserting.**

3. Using clean gloves, carefully slide the proximal end of the lead or extension into the IPG header until it stops. Confirm that the lead or extension is correctly inserted by following these visual indicators and referring to the corresponding figures that follow:
   - For IPGs that connect to Abbott Medical leads or extensions, the first contact band (at the tip) of the lead or extension extends slightly past the first header contact and is visible, the windows between each of the header contacts are clear, and the ninth contact band of the lead or extension is not visible.
   - For IPGs with compatible headers, the windows between each of the header contacts are clear and none of the contact bands are visible.

Figure 3. Correct versus incorrect insertion of the lead or extension (IPGs with Abbott Medical leads or extensions)



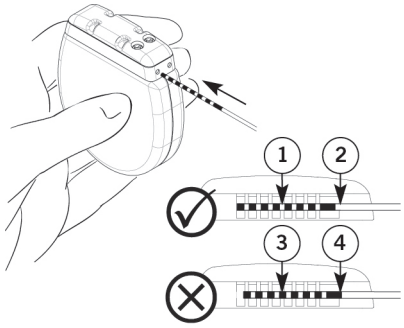
Fully inserted

1. First contact band (tip) is visible past the first header contact
2. Window between each header contact is clear
3. Ninth contact band is not visible

Not fully inserted

4. First contact band (tip) is not visible past the first header contact
5. Window between each header contact is partially blocked by contact band
6. Ninth contact band is visible

Figure 4. Correct versus incorrect insertion of the lead or extension (IPGs with compatible header)



Fully inserted

1. Window between each header contact is clear
2. Eighth contact band is not visible

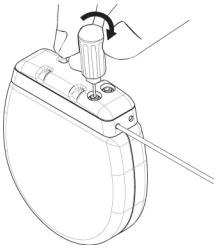
Not fully inserted

3. Window between each header contact is partially blocked by contact band
4. Eighth contact band is visible

4. Use the clinician programmer app to communicate with the IPG, and test the impedance to ensure that the lead or extension is fully inserted. See the clinician's manual for the clinician programmer app for instructions.
5. Insert the torque wrench through the septum and tighten the setscrew, turning it clockwise until the torque wrench clicks.

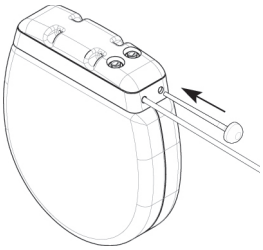
   NOTE: After removing the torque wrench, check the septum to ensure it has closed. If the septum did not close, gently reseat the septum flaps.

Figure 5. Tighten the setscrew clockwise



6. If implanting two leads, repeat the previous steps. If implanting a single lead only, insert the header port plug into the unused port, and use the torque wrench to tighten the setscrew until the torque wrench clicks.

Figure 6. Insert the port plug



Implanting the IPG

The following steps outline the suggested procedure to implant the IPG:

1. Place the IPG into the IPG pocket with the logo side facing the skin surface and at a depth not to exceed 4.0 cm (1.57 in.).

   NOTE: By implanting the IPG with the logo side facing the skin surface, you enhance the IPG's ability to detect a magnet.

2. Carefully coil any excess lead or extension behind the IPG in loops no smaller than 2.5 cm (1 in.) in diameter to provide strain relief for the lead or extension and IPG connection.

   CAUTION: Do not bring the suture needle in contact with an IPG, lead, or extension, or the component may be damaged.
3. To stabilize the IPG within the pocket, pass suture through the holes at the top of the IPG header and secure it to connective tissue.
4. Check the entire system by fluoroscopy before closing to ensure proper positioning of the lead or leads and that it is straight, with no sharp bends or kinks.
5. Use the clinician programmer app to communicate with the IPG and perform intraoperative testing to confirm that the system is operational. See the clinician's manual of the clinician programmer app for instructions.

   NOTE: IPG output may not be identical to that of the trial stimulator at the same settings.

6. Ensure that the IPG is away from the pocket incision suture line, close the pocket incision, and apply the appropriate dressings.

Replacing the IPG

The following steps outline the suggested procedure to replace an IPG:

1. Turn off stimulation or verify that it is turned off.

   CAUTION: Exercise care when using sharp instruments or electrocautery around leads or extensions, or they may be damaged.
2. Open the IPG implant site per normal surgical procedure.
3. Insert the torque wrench through the septum of the IPG header and loosen the setscrew by turning it counterclockwise.

   CAUTION: When performing the following step, do not bend the lead or extension sharply; or it may be damaged.
4. Gently remove the lead or extension from the IPG header; then clean and dry all connections, ensuring they are free of fluid and tissue.
5. To complete the IPG replacement procedure, see the following sections: “Connecting a Lead or Extension to the IPG” (page 7) and “Implanting the IPG” (page 9).

Disposing of Explanted Components

Explanted Abbott Medical components should be returned to Abbott Medical for proper disposal. To return an explanted component, place it in a container or bag marked with a biohazard label and coordinate the return with your Abbott Medical representative or Technical Support.

Checking the Status of the IPG Battery

The IPG contains a nonrechargeable battery. The amount of time that the battery will provide active stimulation depends on the patient’s stimulation settings and daily usage time. To check the status of the IPG battery, use the clinician programmer app or patient controller app. For more information about this function, refer to the clinician’s programming manual and the user’s guide for the patient controller app. For information about estimating longevity of the IPG battery, see the appropriate appendix in this manual.

NOTE: IPG battery status is available one day after first using the clinician programmer app to program the IPG.

The following list provides general information about the battery status:

- A low-battery warning will appear on the clinician programmer app or patient controller app when the battery is approaching its end of service.
- Stimulation will automatically stop when the battery cannot support stimulation.

Technical Support

For technical questions and support for your product, use the following information:

- +1 855 478 5833 (toll-free within North America)
- +1 651 756 5833

For additional assistance, call your local Abbott Medical representative.

Appendix A: Product Specifications

NOTE: Not all models are available in all countries. Contact your local representative for more information.

Storage Specifications

Store the components in this kit according to the following conditions.

Table 1. Storage conditions for components

Temperature	-20°C–60°C (-4°F–140°F)

Product Materials

The following components are intended to come into contact with tissue.

Table 2. Product materials for IPG kit

Component	Material
IPG	Titanium, silicone rubber
Pocket sizer	Polybutylene terephthalate
Port plug	Polysulfone
NOTE: These components are not made with natural rubber latex.	

IPG Specifications

The Proclaim™ IPGs have the following physical specifications.

Table 3. IPG specifications

			MRI Status	Upgradeable Features, Burst Capable	FlexBurst360 ™ Capable	Compatible Header
Model	3660	3662	MR Conditional	Yes	No	No
	3661	3663	MR Unsafe	Yes	No	Yes
	3665	3667	MR Unsafe	No	No	No
	3670	3672	MR Conditional	Yes	Yes	No
	3671	3673	MR Unsafe	Yes	Yes	Yes
Height	5.55 cm (2.19 in.)	6.68 cm (2.63 in.)				
Length	4.95 cm (1.95 in.)	5.02 cm (1.98 in.)				
Thickness	1.34 cm (0.53 in.)	1.35 cm (0.53 in.)				
Weight	48.9 g (1.7 oz)	58.3 g (2.1 oz)				
Volume	30.4 cm^3 (1.9 $in.^3$)	38.6 cm^3 (2.4 $in.^3$)				
Power source	Carbon monofluoride/silver vanadium oxide cell					
Connector strength	10 N (Models 3660, 3662, 3665, 3667, 3670, 3672) 5 N (Models 3661, 3663, 3671, 3673)					
Program storage capacity	15 programs					

The IPG has the following operating parameters.

Table 4. Operating parameters for the IPG

Parameter	Tonic Range	Tonic Steps	Burst Range*	Burst Steps*
Pulse width	20–1000 µs	10 µs (20–500 µs range) 50 µs (500–1000 µs range)	50–1000 µs	50 µs
Frequency	2–200 Hz	2 Hz	—	—
	200–500 Hz	10 Hz	—	—
	500–1200 Hz	20 Hz	—	—
Burst rate frequency	—	—	10–60 Hz	10 Hz
Intraburst frequency	—	—	250–500 Hz	10 Hz
			500–1000 Hz	20 Hz
Amplitude	0–25.5 mA	0.1–1.0 mA	0–12.75 mA	0.05–0.50 mA
	0–12.75 mA	0.05–0.50 mA		

NOTE:

- Columns with * represent operating parameters for BurstDR™ stimulation programs on IPGs capable of BurstDR stimulation mode.
- For each tonic program, you have the option to select the amplitude range. For information on setting the amplitude range, see the clinician's programming manual for this system.
- The number of areas in use for a tonic program governs the maximum frequency (1200/number of areas). The number of areas in use for a burst program governs the maximum burst rate frequency (60/number of areas).
- The maximum current depends on the impedance, frequency, and pulse width settings.

Compatibility Guidelines for IPGs with Compatible Headers

IPGs with compatible headers are compatible with the following Medtronic‡ leads and extensions available before May 5, 2015.

Table 5. Compatible Medtronic leads and extensions

Device	Model
Permanent lead	3776-45, 3776-60, 3776-75, 3876-45, 3876-60, 3876-75, 3777-45, 3777-60, 3777-75, 3877-45, 3877-60, 3877-75, 3778-45, 3778-60, 3778-75, 3878-45, 3878-60, 3878-75, 39286-30, 39286-65, 39565-30, 39565-65
Extension	3708120, 3708140, 3708160, 3708220, 3708240, 3708260, 3708320, 3708340, 3708360, 3876, 3877, 3878

WARNING: The use of Medtronic leads or extensions other than those specified in this table may increase risk to the patient, including the potential for tissue damage.

Appendix B: System Components and Accessories

The Proclaim™ neurostimulation system includes the following components.

NOTE:

- Not all models are available in all countries. Contact your local representative for more information.
- Model 3661, 3663, 3671, and 3673 IPGs are compatible only with the leads and extensions listed in “Compatibility Guidelines for IPGs with Compatible Headers” (page 12). They are not compatible with Abbott Medical leads and extensions.

IPGs

3660 Proclaim™ XR 5 implantable pulse generator
3661 Proclaim™ 5 implantable pulse generator
3662 Proclaim™ XR 7 implantable pulse generator
3663 Proclaim™ 7 implantable pulse generator
3665 Proclaim™ 5 implantable pulse generator
3667 Proclaim™ 7 implantable pulse generator
3670 Proclaim™ Plus 5 implantable pulse generator
3671 Proclaim™ Plus 5 implantable pulse generator
3672 Proclaim™ Plus 7 implantable pulse generator
3673 Proclaim™ Plus 7 implantable pulse generator

IPG Accessories

1101 Torque wrench
1111 Port plug

Programmers and Controllers

3874 NeuroSphere™ Clinician Programmer App
3875 NeuroSphere™ Patient Controller App

Programmer and Controller Accessories

1210 Patient magnet
3884 SCS patient manual and magnet

Leads and Extensions

3100-series percutaneous leads
3200-series paddle leads
3300-series extensions

Lead and Extension Accessories

1100-series stylets
1102 Guide wire for percutaneous leads
1103 Introde-AK™ lead introducer
1105 Lead anchor, butterfly
1106 Lead anchor, long
1109 Strain relief
1112 Tunneling tool, 12 in.
1114 Epidural needle, 14 gauge, 4 in. (10 cm)
1116 Epidural needle, 14 gauge, 6 in. (15 cm)
1120 Tunneling tool, 20 in.
1192 Swift-Lock™ anchor
1194 Cinch™ anchor
1701 SCS accessory kit
1803 Lead and extension insertion tool

Adapters

2311 8-channel adapter, M, 10 cm
2316 8-channel adapter, M, 60 cm

Trial System

3599 Abbott Medical External Pulse Generator

Trial System Accessories

1203 Cleaning cloths
1212 Coin cell batteries
1213 Pouch with adhesive (5)
1214 Pouch without adhesive and belt (5)
1216 EPG header cap
1218 Carrying case
1917 Battery door
3013 Multilead trial cable
3032 External pulse generator, 2-port header

Appendix C: Battery Longevity Information

The longevity of the IPG battery depends on the following factors:

- Programmed settings for each area
- Program impedance
- Hours of stimulation per day
- Shelf life of the device between the dates of manufacture and implant
- Duration of communication sessions between the IPG and the patient controller or clinician programmer

  NOTE: An “Area” refers to a combination of selected stimulation parameters. For tonic stimulation, stimulation parameters for each area include electrode configuration, amplitude, frequency and pulse width. For BurstDR™ stimulation, stimulation parameters for each area include electrode configuration, amplitude, pulse width, burst frequency, intra-burst rate and number of pulses.

To estimate battery longevity manually, perform the following steps. For additional help with estimating battery longevity, contact Technical Support.

1. Locate the energy factor for the desired stimulation parameters according to the lead impedance in the tables in one of the following sections:
   - For IPGs using tonic stimulation parameters, see “Energy Factors for Tonic Stimulation Parameters” (page 15).
   - For IPGs using BurstDR™ stimulation parameters, see “Energy Factors for BurstDR™ Stimulation Parameters” (page 19).

     NOTE: If the desired parameters do not appear in the tables, estimate the energy factor by choosing a value between the listed energy factors for the closest parameters.

2. For IPGs using multiple areas, perform one of the following options:
   - For tonic stimulation programs, determine the energy factor for each area from the previous step, and add each of these values together.
   - For BurstDR stimulation programs with equivalent parameters for each area, find the tables with the equivalent number of areas and burst frequency and determine the energy factor.
   - For BurstDR stimulation programs with different parameters for each area, find the tables with the equivalent number of areas and burst frequency. Then, determine the energy factor for each area’s parameters and average the energy factor values.
3. Use the figures in “Battery Longevity Graphs” (page 32) to determine the estimated battery longevity by finding the energy factor from the previous steps on the curve for the appropriate model IPG.

Energy Factors for Tonic Stimulation Parameters

The following tables show energy factors according to various stimulation parameters for tonic programs.

NOTE: Energy factors are for IPGs that provide 12 hours of daily stimulation. For an IPG that is providing 24 hours of daily stimulation, double the energy factor shown in the table.

Table 6. Energy factors for various tonic stimulation parameters (350-ohm impedance)

		Pulse Width (µs)			
Amplitude (mA)	**Frequency (Hz)**	**100**	**200**	**300**	**500**
1	**30**	13	14	14	15
	60	18	19	20	23
	90	22	24	26	29
2	**30**	15	17	20	24
	60	21	26	30	40
	90	27	34	41	54
3	**30**	16	19	23	30
	60	24	30	37	51
	90	30	41	51	71
4	**30**	17	22	26	47
	60	26	35	44	85
	90	34	47	61	122
5	**30**	21	30	38	55
	60	34	51	68	102
	90	46	71	97	148
6	**30**	23	33	43	81
	60	37	58	78	152
	90	51	81	112	223
7	**30**	29	44	60	92
	60	49	80	112	175
	90	68	115	162	257
8	**30**	31	49	67	125
	60	53	89	125	242
	90	74	129	183	359
9	**30**	33	64	89	139
	60	58	118	169	271
	90	81	173	249	401
10	**30**	41	69	97	182
	60	73	130	186	355
	90	105	190	274	528

Table 7. Energy factors for various tonic stimulation parameters (500-ohm impedance)

Amplitude (mA)	Frequency (Hz)	Pulse Width (µs) 100	200	300	500
1	30	13	14	14	15
	60	18	19	20	23
	90	22	24	26	29
2	30	15	17	20	24
	60	21	26	30	40
	90	27	34	41	54
3	30	16	19	23	38
	60	24	30	37	68
	90	30	41	51	97
4	30	19	26	33	47
	60	31	44	58	85
	90	41	61	82	122
5	30	24	35	47	69
	60	40	62	85	130
	90	54	88	122	190
6	30	26	40	54	81
	60	44	71	98	152
	90	61	102	142	274
7	30	33	52	72	111
	60	57	96	135	214
	90	80	139	198	317
8	30	35	58	94	148
	60	62	107	180	288
	90	88	156	264	426
9	30	43	74	104	190
	60	78	139	200	372
	90	112	203	294	554
10	30	53	92	131	210
	60	96	175	254	412
	90	140	258	376	613

Table 8. Energy factors for various tonic stimulation parameters (700-ohm impedance)

Amplitude (mA)	Frequency (Hz)	Pulse Width (µs) 100	200	300	500
1	30	13	14	16	18
	60	18	19	24	28
	90	22	24	31	38
2	30	15	17	20	24
	60	21	26	30	40
	90	27	34	41	54
3	30	18	23	28	38
	60	27	37	48	68
	90	36	51	66	97
4	30	22	31	40	58
	60	35	53	71	107
	90	47	75	102	156
5	30	24	41	55	83
	60	40	73	102	158
	90	54	105	148	232
6	30	30	47	63	114
	60	51	85	119	220
	90	71	122	173	325
7	30	37	60	84	151
	60	65	112	159	294
	90	92	163	234	436
8	30	45	76	108	197
	60	81	144	207	382
	90	116	211	305	566
9	30	58	98	139	220
	60	103	184	265	427
	90	147	269	390	710
10	30	62	119	169	271
	60	112	225	326	529
	90	160	330	482	871

Table 9. Energy factors for various tonic stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Frequency (Hz)	Pulse Width (μs) 100	200	300	500
1	30	14	15	16	18
	60	19	21	24	28
	90	24	27	31	38
2	30	16	20	23	30
	60	24	31	37	51
	90	31	41	51	72
3	30	20	26	33	47
	60	31	44	58	85
	90	41	61	81	122
4	30	24	35	47	69
	60	40	62	85	130
	90	54	88	122	190
5	30	30	47	64	98
	60	51	85	119	186
	90	72	122	173	275
6	30	37	60	84	131
	60	65	112	160	292
	90	92	163	234	431
7	30	49	80	112	195
	60	85	148	211	377
	90	120	215	345	558
8	30	58	98	139	243
	60	103	184	293	473
	90	148	269	432	702
9	30	68	119	185	297
	60	124	225	358	580
	90	178	362	529	939
10	30	80	153	221	356
	60	147	293	429	699
	90	213	433	635	1126

Energy Factors for BurstDR™ Stimulation Parameters

The following tables show energy factors according to various stimulation parameters for BurstDR™ stimulation programs. There are unique sets of tables for various numbers of BurstDR™ stimulation areas and frequency combination.

NOTE:

- Energy factors represent IPGs that provide 24 hours of daily stimulation using default values for the number of pulses, Intra-burst Rate, and Pulse Width settings.
- In neurostimulation therapy, “dose” refers to the delivery of a quantity of energy to tissue. A difference in “dose” in this context does not imply differences in expected effectiveness response as it would with a drug. There is no demonstrated difference in safety or effectiveness among these doses.

One BurstDR™ Stimulation Area with Frequency of 40 Hz

Table 10. Energy factors for one BurstDR stimulation area at 40 Hz for various BurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	47	31	25	23	16	13	7	77
0.4	71	43	34	28	20	17	10	89
0.6	93	53	41	34	24	20	12	104
0.8	117	65	49	40	29	25	13	118
1.0	146	76	56	46	34	28	16	134
1.2	175	106	84	73	50	42	24	240
1.4	202	121	95	82	56	48	26	270
1.6	230	135	106	91	63	55	29	301
1.8	247	151	120	100	70	60	33	330
2.0	279	163	133	110	76	65	35	361

Table 11. Energy factors for one BurstDR stimulation area at 40 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	46	32	25	23	15	13	7	76
0.4	71	44	34	29	19	18	9	91
0.6	95	56	41	34	24	20	12	105
0.8	121	67	49	41	28	25	14	120
1.0	151	93	73	64	43	37	21	211
1.2	174	108	84	73	50	43	23	240
1.4	203	122	96	82	57	48	26	271
1.6	225	137	106	93	64	55	29	301
1.8	264	160	129	111	70	59	32	330
2.0	297	196	168	146	97	83	45	512

Table 12. Energy factors for one BurstDR stimulation area at 40 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	49	32	26	23	15	13	8	73
0.4	72	43	34	29	20	17	10	90
0.6	94	53	41	35	24	21	12	101
0.8	125	79	62	54	37	31	17	180
1.0	153	95	74	64	43	37	20	208
1.2	177	108	85	73	50	42	23	239
1.4	209	129	103	90	57	48	27	273
1.6	239	159	132	115	80	68	36	417
1.8	271	179	149	132	88	75	41	465
2.0	299	195	164	146	97	83	44	509

Table 13. Energy factors for one BurstDR stimulation area at 40 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	48	32	26	23	15	13	7	77
0.4	71	43	34	29	20	17	10	93
0.6	100	64	51	45	30	26	15	152
0.8	126	78	62	56	37	31	17	182
1.0	151	96	73	64	44	37	20	212
1.2	184	127	106	94	62	53	29	333
1.4	215	145	119	107	72	61	33	378
1.6	241	163	134	120	80	68	37	422
1.8	281	208	183	160	106	92	49	556
2.0	312	228	197	182	117	100	54	607

Two BurstDR™ Stimulation Areas each with Frequency of 20 Hz

Table 14. Energy factors for two BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	58	41	31	25	20	18	10	79
0.4	92	62	43	34	30	25	14	—
0.6	128	83	56	42	38	33	17	—
0.8	162	105	69	50	47	40	21	—
1.0	197	127	83	59	55	47	25	—
1.2	232	158	110	86	75	64	34	—
1.4	267	179	125	97	85	73	39	—
1.6	304	202	142	109	95	82	44	—
1.8	338	226	156	120	106	91	49	—
2.0	371	249	172	132	116	100	54	363

Table 15. Energy factors for two BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	58	40	31	26	21	18	10	79
0.4	93	62	44	34	29	26	13	—
0.6	127	83	57	42	38	33	17	—
0.8	161	105	69	51	46	40	21	—
1.0	196	136	95	74	64	56	29	—
1.2	232	157	110	86	75	65	34	—
1.4	268	180	125	98	85	73	39	—
1.6	303	203	140	109	95	83	44	—
1.8	338	227	156	121	106	91	49	—
2.0	370	263	197	163	133	115	61	511

Table 16. Energy factors for two BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	57	41	30	25	21	18	9	79
0.4	93	62	44	34	29	26	14	—
0.6	128	83	57	42	38	33	18	—
0.8	162	111	79	63	53	46	25	—
1.0	196	134	95	75	64	55	29	—
1.2	231	156	110	86	74	64	34	—
1.4	267	181	125	98	85	73	39	—
1.6	302	215	162	134	110	94	51	—
1.8	337	240	180	149	122	105	56	—
2.0	373	266	198	163	134	115	62	512

Table 17. Energy factors for two BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	57	40	30	25	21	18	10	78
0.4	94	63	43	34	29	25	14	—
0.6	127	88	64	51	43	37	20	—
0.8	161	111	79	63	54	47	25	—
1.0	196	134	95	75	63	56	30	—
1.2	233	166	126	104	85	73	39	—
1.4	268	191	144	120	97	84	45	—
1.6	301	216	162	135	109	94	50	—
1.8	338	252	203	177	137	117	63	—
2.0	371	278	222	194	150	130	69	661

Two BurstDR™ Stimulation Areas each with Frequency of 30 Hz

Table 18. Energy factors for two BurstDR stimulation areas each at 30 Hz for various BurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	78	45	38	32	25	21	12	107
0.4	126	68	51	42	34	30	16	—
0.6	177	90	64	53	44	38	20	—
0.8	226	112	78	62	53	45	25	—
1.0	275	134	93	72	63	54	29	—
1.2	326	177	134	111	90	77	42	—
1.4	378	202	153	127	103	88	48	—
1.6	428	229	172	141	116	100	53	—
1.8	477	254	190	157	128	111	59	—
2.0	480	280	209	172	141	121	65	533

Table 19. Energy factors for two BurstDR stimulation areas each at 30 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	78	47	37	32	26	23	12	107
0.4	117	69	50	42	35	31	16	—
0.6	176	91	65	51	44	38	20	—
0.8	226	113	78	61	53	46	25	—
1.0	277	153	116	97	78	68	36	—
1.2	327	178	134	112	90	79	42	—
1.4	377	203	154	126	103	89	47	—
1.6	428	231	171	142	115	100	53	—
1.8	440	289	231	203	155	134	72	—
2.0	531	318	254	223	171	148	79	757

Table 20. Energy factors for two BurstDR stimulation areas each at 30 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	78	47	37	32	24	22	11	107
0.4	128	69	52	41	34	30	16	—
0.6	161	90	64	52	43	37	20	—
0.8	229	128	99	82	65	57	30	—
1.0	253	151	116	96	78	68	36	—
1.2	326	179	134	112	91	79	42	—
1.4	379	232	185	163	125	108	58	—
1.6	430	260	209	183	140	121	65	—
1.8	481	289	232	203	156	135	72	—
2.0	531	328	270	243	185	157	83	867

Table 21. Energy factors for two BurstDR stimulation areas each at 30 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	73	47	37	32	25	22	11	107
0.4	117	69	51	42	34	30	16	—
0.6	179	102	78	67	53	46	24	—
0.8	209	127	97	82	66	56	30	—
1.0	278	151	116	97	78	68	36	—
1.2	304	200	163	143	109	95	50	—
1.4	381	231	185	163	125	108	57	—
1.6	405	290	245	223	165	143	75	—
1.8	484	322	273	249	184	159	85	—
2.0	536	354	301	274	203	175	93	981

Three BurstDR™ Stimulation Areas each with Frequency of 20 Hz

Table 22. Energy factors for three BurstDR stimulation areas each at 20 Hz for variousBurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	81	58	43	35	29	25	13	107
0.4	134	89	61	47	42	36	19	—
0.6	188	122	82	60	54	47	25	—
0.8	239	155	101	72	68	58	31	—
1.0	290	186	120	85	81	70	37	—
1.2	344	232	162	125	109	94	51	—
1.4	394	267	185	143	125	108	57	—
1.6	447	302	208	160	141	121	65	—
1.8	503	337	231	178	157	135	72	—
2.0	553	370	254	195	171	148	79	533

Table 23. Energy factors for three BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	82	57	42	35	30	26	13	107
0.4	133	90	62	48	42	36	19	—
0.6	187	122	81	60	55	47	25	—
0.8	237	154	101	72	69	59	31	—
1.0	291	199	138	108	94	81	43	—
1.2	342	234	162	126	110	94	51	—
1.4	393	267	185	143	126	108	58	—
1.6	448	302	208	160	140	122	65	—
1.8	501	356	266	220	180	155	83	—
2.0	551	393	293	242	197	169	91	757

Table 24. Energy factors for three BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	81	57	43	34	29	25	13	107
0.4	135	90	62	47	42	37	19	—
0.6	187	122	81	59	55	47	25	—
0.8	239	163	115	91	79	68	36	—
1.0	292	198	139	109	93	81	43	—
1.2	342	232	163	126	110	94	50	—
1.4	393	283	210	176	143	124	66	—
1.6	446	321	240	198	161	139	74	—
1.8	498	358	266	221	180	155	83	—
2.0	554	396	302	263	203	174	94	866

Table 25. Energy factors for three BurstDR stimulation areas each at 20 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	81	58	42	35	28	25	13	107
0.4	135	89	62	47	41	36	19	—
0.6	187	129	93	74	63	53	29	—
0.8	237	163	117	91	78	67	36	—
1.0	289	197	139	109	94	81	43	—
1.2	344	246	185	154	125	107	58	—
1.4	396	283	212	176	142	123	66	—
1.6	447	338	269	235	181	156	83	—
1.8	500	376	300	262	202	173	93	—
2.0	550	414	332	289	223	192	103	981

Four BurstDR™ Stimulation Areas each with Frequency of 10 Hz

Table 26. Energy factors for four BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	59	52	42	31	28	24	13	79
0.4	92	83	66	45	44	38	21	—
0.6	128	115	89	59	59	51	28	—
0.8	162	148	113	72	76	65	36	—
1.0	197	177	135	86	92	79	43	—
1.2	233	212	165	114	112	96	52	—
1.4	267	243	190	130	128	111	60	—
1.6	304	274	215	147	145	125	68	—
1.8	338	308	239	163	162	139	75	—
2.0	371	336	264	179	178	153	82	363

Table 27. Energy factors for four BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	58	51	42	31	28	25	13	79
0.4	93	83	65	44	44	38	21	—
0.6	128	115	89	58	59	51	28	—
0.8	163	147	113	72	75	66	36	—
1.0	197	179	141	98	95	81	44	—
1.2	234	210	166	115	112	96	51	—
1.4	267	243	190	130	128	110	60	—
1.6	303	274	215	147	145	126	67	—
1.8	338	307	239	163	162	139	75	—
2.0	371	337	275	203	184	159	85	512

Table 28. Energy factors for four BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	58	52	42	31	28	24	13	79
0.4	93	83	65	45	44	38	20	—
0.6	128	115	89	59	60	51	28	—
0.8	162	146	116	82	78	68	36	—
1.0	197	179	141	98	95	82	44	—
1.2	231	211	166	114	112	95	52	—
1.4	267	243	191	130	128	110	60	—
1.6	302	276	223	166	151	130	70	—
1.8	339	309	249	184	168	145	78	—
2.0	371	339	274	202	185	159	86	514

Table 29. Energy factors for four BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	57	51	41	31	28	24	13	79
0.4	93	83	65	45	44	38	20	—
0.6	128	116	91	65	62	54	29	—
0.8	163	146	116	82	79	68	36	—
1.0	196	180	141	98	95	82	44	—
1.2	232	211	172	128	116	100	54	—
1.4	266	242	197	147	134	115	62	—
1.6	303	275	224	166	151	130	70	—
1.8	338	305	257	205	174	150	81	—
2.0	373	339	284	226	192	165	89	661

Six BurstDR™ Stimulation Areas each with Frequency of 10 Hz

Table 30. Energy factors for six BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (350-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	82	73	59	43	40	34	18	108
0.4	134	120	95	63	63	55	30	—
0.6	189	168	130	85	87	75	40	—
0.8	240	216	165	106	112	95	52	—
1.0	291	263	200	126	136	116	63	—
1.2	344	312	244	168	165	142	76	—
1.4	397	357	282	192	189	163	88	—
1.6	451	406	319	217	216	185	99	—
1.8	504	454	355	242	240	208	112	—
2.0	551	500	393	265	264	227	123	534

Table 31. Energy factors for six BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (500-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	82	72	60	43	39	34	18	108
0.4	134	122	94	64	65	55	30	—
0.6	189	170	129	85	88	75	41	—
0.8	240	215	165	105	112	96	52	—
1.0	292	264	208	144	140	120	65	—
1.2	346	311	245	168	165	142	77	—
1.4	399	359	282	192	191	164	88	—
1.6	450	408	319	217	215	185	100	—
1.8	503	454	370	273	249	215	115	—
2.0	552	505	408	301	275	236	127	758

Table 32. Energy factors for six BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (700-ohm impedance)

Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	83	73	59	43	39	34	18	107
0.4	135	120	95	64	65	55	29	—
0.6	188	169	129	85	88	76	41	—
0.8	241	216	171	119	115	99	54	—
1.0	291	265	208	145	140	121	65	—
1.2	343	312	245	168	165	143	77	—
1.4	395	362	292	217	198	171	91	—
1.6	453	408	332	246	224	192	104	—
1.8	504	453	370	274	250	214	115	—
2.0	552	502	410	305	277	238	127	831

Table 33. Energy factors for six BurstDR stimulation areas each at 10 Hz for various BurstDR stimulation parameters (1000-ohm impedance)

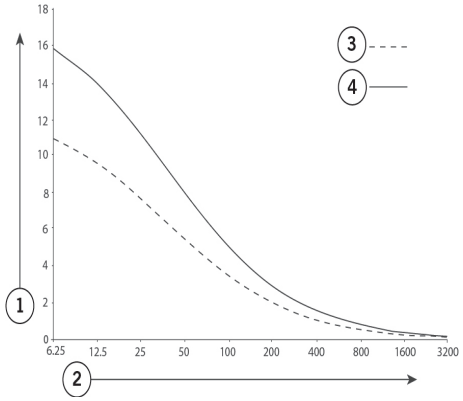
Amplitude (mA)	Intermittent Dosage (On Time/Off Time)							Continuous Dosage
	5 s/ 15 s	15 s/ 45 s	30 s/ 90 s	60 s/ 180 s	30 s/ 150 s	30 s/ 180 s	30 s/ 360 s	
0.2	82	73	59	43	40	34	18	108
0.4	133	120	94	64	63	55	30	—
0.6	187	168	134	95	90	78	42	—
0.8	240	218	172	120	115	100	54	—
1.0	292	264	208	144	140	121	65	—
1.2	343	312	255	189	172	147	79	—
1.4	397	360	293	218	197	170	92	—
1.6	449	409	344	274	232	200	107	—
1.8	503	455	384	305	258	223	119	—
2.0	552	503	424	336	284	246	132	982

Battery Longevity Graphs

The first figure shows the estimated battery longevity of a newly implanted IPG. The second figure shows the estimated longevity of an IPG battery after the low-battery warning, also called an elective replacement indicator (ERI). The ERI first appears on the clinician programmer app or patient controller app when the battery is approaching its end of service.

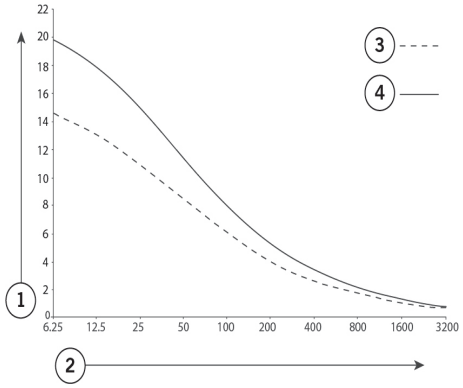
NOTE: The following figures show estimated battery longevity, and several factors may affect the actual longevity. This neurostimulation system allows you to monitor IPG battery status and usually first displays the ERI at least 3 months before the IPG needs to be replaced. The ERI may first appear when less than 3 months remain of the battery's life if a patient's system uses high settings.

Figure 7. Estimated battery longevity by energy factor for Proclaim™ IPGs (from time of implant)



1. Estimated battery longevity (years)
2. Energy factor
3. Models 3660, 3661, 3665, 3670, 3671
4. Models 3662, 3663, 3667, 3672, 3673

Figure 8. Estimated battery longevity by energy factor for Proclaim IPGs (from time of ERI)



1. Estimated battery longevity (months)
2. Energy factor
3. Models 3660, 3661, 3665, 3670, 3671
4. Models 3662, 3663, 3667, 3672, 3673

Appendix D: Regulatory Statements

This section contains regulatory statements about your product.

Disposal Guidelines for Battery-Powered Devices

This device contains a battery and a label is affixed to the device in accordance with European Council directives 2002/96/EC and 2006/66/EC. These directives call for separate collection and disposal of electrical and electronic equipment and batteries. Sorting such waste and removing it from other forms of waste lessens the contribution of potentially toxic substances into municipal disposal systems and into the larger ecosystem. Return the device to Abbott Medical at the end of its operating life.

Statement of FCC Compliance

This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to part 15 of the FCC rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses, and can radiate radiofrequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures:

- Reorient or relocate the receiving antenna.
- Increase the separation between the equipment and receiver.
- Connect the equipment into an outlet on a circuit different from that to which the receiver is connected.
- Consult the dealer or an experienced radio/TV technician for help.

Operation is subject to the following two conditions:

- This device may not cause harmful interference.
- This device must accept any interference received, including interference that may cause undesired operation.

Modifications not expressly approved by the manufacturer could void the user's authority to operate the equipment under FCC rules.

Identification Information for Product Registration

This device has a label that contains, among other information, a product identifier in the following format:

Table 34. Registration identification information

Identifier Type	Registration Identifier
FCC registration number	RIASJMRFC

Wireless Technology Information

The following table summarizes the technical details of the Bluetooth® Low Energy (LE) wireless technology as it is implemented in the device.

Table 35. Bluetooth Low Energy (LE) wireless technology information

Antenna type	Embedded patch antenna in header
Antenna dimensions	8.1 mm x 5.1 mm x 4.9 mm
Modulation	GFSK
Magnetic field strength (at 2 m distance)	16.3 µA/m
Electric field strength (at 2 m distance)	6.1 mV/m

Table 35. Bluetooth Low Energy (LE) wireless technology information

Output power (EIRP*)	1 mW (0 dBm) typical, 10 mW (+10 dBm) maximum
Range	1–2 m typical
Center frequency	2.44 GHz
Channel	40 logical channels
Bandwidth	2 MHz per channel
Data flow	Bi-directional
Protocol	Bluetooth LE wireless technology

*EIRP = Equivalent isotropically radiated power

Radio Transmitter, Cables, Transducers

The device contains a radio transmitter/receiver with the following parameters.

Radio transmitter parameters:

- Frequency (range): 2.4000 to 2.4835 GHz
- Bandwidth (-15 dB): 2.398 to 2.4855 GHz
- Channel: 40 logical channels using AFH
- Modulation: GFSK
- Radiated output power: 10 mW (+10 dBm) maximum
- Magnetic field strength (at 2 m distance): 16.3 µA/m
- Duty cycle: Variable, but low (<5%)
- Semi-duplex capability

The radio receiver in the device is using the same frequency and bandwidth as the transmitter.

Cables and transducers:

Cables and transducers are not used during normal use of the device nor while programming the device.

Quality of Service for Wireless Technology

Bluetooth® Low Energy (LE) wireless technology enables communication between the generator and the clinician programmer or patient controller. The requirements for the quality of service (QoS) vary depending on the use environment (operating room, recovery room, and home environment).

After the clinician programmer or patient controller is paired with a generator, the Bluetooth® wireless technology symbol is visible on the clinician programmer or patient controller in the upper right corner of the screen. When the Bluetooth wireless connection is not active, the symbol is grayed out.

The quality of service (QoS) should allow wireless data to be transferred at a net rate of 2.5 kB/sec. Each connection interval includes a semi-duplex transmission with a required acknowledge, a transmission latency in each direction (2x), and a receive-to-transmit mode (RX-to-TX) time. Data is resent if not sent successfully. Each key press may transmit up to 4 data packets with up to 20 bytes per packet, depending on the number of packets that need to be transmitted (that is, if there is only one packet to transmit, only one packet will be transmitted). If the interference is high (that is, the bit error rate exceeds 0.1%), the user may experience what appears to be a slow connection, difficulty pairing devices, and a need to decrease the distance between connected devices. For information on how to improve connection issues, please refer to “Troubleshooting for Wireless and Coexistence Issues” (page 35).

Wireless Security Measures

The wireless signals are secured through device system design that includes the following:

- The generator will encrypt its wireless communication.
- Only one patient controller or clinician programmer may communicate with the generator at the same time.
- A unique key for each unit that is checked during each transmission.
- Built-in pairing that specifies valid and legitimate pairing among units.
- Proprietary authentication in addition to the pairing procedure specified in Bluetooth® Low Energy (LE) wireless technology, which includes an element of proximity.
- A proprietary algorithm that detects and prevents an unauthorized user from attempting to pair with the generator.

Troubleshooting for Wireless and Coexistence Issues

If you experience issues with the wireless communication between the generator and the clinician programmer or patient controller, try the following:

- Decrease the distance between the devices.
- Move the devices so they share line of sight.
- Move the devices away from other devices that may be causing interference.
- Close the clinician programmer or patient controller app, and turn the clinician programmer or patient controller off and on.
- Wait a few minutes and try connecting again.
- Do not operate other wireless devices (such as laptop, tablet, mobile phone, or cordless phone) at the same time.

  NOTE: Wireless communication equipment (such as wireless home network devices, mobile and cordless telephones, and tablets) can affect the device.

Appendix E: Symbols and Definitions

The symbols below and harmonized symbols may be found on the product or product label. For harmonized symbols, refer to the Universal Symbols Glossary at medical.abbott/manuals.

Table 36. Symbols and definitions

Symbol	Definition
	Caution
	Consult instructions for use
	Follow instructions for use on this website
	MR Conditional NOTE: Magnetic Resonance (MR) Conditional, an item with demonstrated safety in the MR environment within the defined conditions. At a minimum, address the conditions of the static magnetic field, the switched gradient magnetic field, and the radiofrequency fields. Additional conditions, including specific configurations of the item, may be required.
	MR Unsafe

Table 36. Symbols and definitions

Symbol	Definition
	NOTE: Magnetic Resonance (MR) Unsafe, an item poses unacceptable risks to the patient, medical staff, or other persons within an MR environment
	Non-ionizing electromagnetic radiation
	Do not re-use
	Do not resterilize
	Use-by date
	Date of manufacture
	Manufacturing facility
	Temperature limit
	Humidity limitation
	Atmospheric pressure limitation
	Do not use if package is damaged
	Catalog number NOTE: This symbol also refers to the model number.
	Manufacturer
	Packaging unit
	Implantable device
	Accessories
	Serial number

Table 36. Symbols and definitions

Symbol	Definition
LOT	Batch code
UDI	Unique Device Identification
℞ ONLY	Prescription use only
STERILE EO	Sterilized using ethylene oxide
EC REP	Authorized representative in the European Community
CE 2797	European conformity, affixed according to the relevant provisions of AIMD directive 90/385/EEC and RE directive 2014/53/EU Annex II. Hereby, Abbott Medical declares that this device complies with the essential requirements and other relevant provisions of these directives. The full text of the European Union RE directive 2014/53/EU declaration of conformity is available at the following internet address: www.neuromodulation.abbott/euconformity.
	Australian Communications and Media Authority (ACMA) and New Zealand Radio Spectrum Management (RSM) Regulatory Compliance Mark (RCM)
	This equipment is certified for type certification pursuant of Article 38-24 of the Japan Radio Law

Abbott Medical
6901 Preston Road
Plano, Texas 75024 USA
+1 855 478 5833
+1 651 756 5833

Abbott Medical
The Corporate Village
Da Vincilaan 11 Box F1
1935 Zaventem
Belgium
+32 2 774 68 11

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Clinical Summaries
Spinal Cord Stimulation Systems

Clinician's Manual

Abbott

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.
™ Indicates a trademark of the Abbott group of companies.
‡ Indicates a third-party trademark, which is property of its respective owner.
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Contents

Clinical Studies

This manual contains summaries of clinical studies conducted with Abbott Medical spinal cord stimulation (SCS) systems. The clinical studies were conducted to assess safety and effectiveness of SCS systems and will also apply to additional neurostimulation systems that are similar in technology and intended use.

The studies in this manual support the clinical use of the neurostimulation systems identified in the following table. Refer to the clinician's system reference manual for instructions and other important information, including indications for use, contraindications, warnings, precautions, and adverse effects related to the complete neurostimulation system.

Table 1. Summaries of clinical studies for supported SCS systems and leads

Clinical Summary	Supported SCS Systems	Leads
Genesis™ (IPG) Neurostimulation System for SCS	▪ Proclaim™ SCS system ▪ Eterna™ SCS system ▪ Prodigy™ SCS system ▪ Prodigy MRI™ SCS system ▪ Prot g ™ SCS system ▪ Prot g MRI™ SCS system ▪ Abbott Medical Invisible Trial System*	▪ Trial leads ▪ Percutaneous leads ▪ Paddle leads
BurstDR™ Stimulation	▪ Proclaim™ SCS system ▪ Eterna™ SCS system ▪ Prodigy™ SCS system ▪ Prodigy MRI™ SCS system ▪ Prot g ™ SCS system ▪ Prot g MRI™ SCS system ▪ Abbott Medical Invisible Trial System*	▪ Trial leads ▪ Percutaneous leads ▪ Paddle leads
Anatomical Lead Placement	▪ Proclaim™ SCS system ▪ Eterna™ SCS system ▪ Prodigy™ SCS system ▪ Prodigy MRI™ SCS system ▪ Abbott Medical Invisible Trial System*	▪ Trial leads ▪ Percutaneous leads
Diabetic Peripheral Neuropathy	▪ Proclaim™ SCS system ▪ Prodigy™ SCS system ▪ Prodigy MRI™ SCS system ▪ Abbott Medical Invisible Trial System*	▪ Trial leads ▪ Percutaneous leads ▪ Paddle leads

* The invisible trial system consists of the external pulse generator, the trial clinician programmer, and the trial patient controller.

Clinical Summary for the Genesis™ (IPG) Neurostimulation System for SCS

The safety and effectiveness of the Genesis™ (IPG) neurostimulation system was determined based on available published clinical studies for similar totally implanted SCS systems. The IPG device is similar to the SCS systems reported in published literature in intended use, target patient population, technology, device design, and output characteristics. Therefore, the clinical data from the published literature described below represents evidence supporting the safety and effectiveness of the Genesis (IPG) neurostimulation system for use 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. The studies in this clinical summary support the SCS systems listed in “Clinical Studies” (page 1).

Efficacy Evaluation

Three clinical literature studies were used to assess the safety and effectiveness of the Genesis™ (IPG) neurostimulation system (Ohnmeiss et al. 1996, Villavicencio et al. 2000, Hassenbusch SJ et al. 1995). The studies included a total of 116 patients that were implanted with an SCS system. A total of approximately 3166 device months of experience was considered in the retrospective clinical evaluation. All three studies

examined the effectiveness of SCS on patients with chronic pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome or intractable low back and leg pain. In all studies, an identified totally implantable spinal cord stimulator was used in association with a quadripolar percutaneous epidural lead or a quadripolar lead. These studies provide the same diagnostic or therapeutic intervention for the same disease/conditions and patient population as the Genesis (IPG) neurostimulation system.

The prospective study by Ohnmeiss et al. 1996 examined the long-term effectiveness of SCS in patients with intractable leg pain. Forty patients were implanted with SCS systems and evaluated at 6 weeks, 12 months, and 24 months follow-up. Outcome measures included the VAS, pain drawings, medication use, SIP, isometric lower extremity testing, and patient questionnaires. An intent to treat analysis was performed. After patients had SCS for 24 months, leg pain, pain when walking, standing pain, pain's effect on overall lifestyle, and the total analog scale scores were significantly improved from baseline. In this study, SCS was effective in improving intractable leg pain.

In addition, three patients from this study had their stimulators repositioned due to pain at the original location. Three patients had reoperations to adjust lead position; one patient required two reoperations, one to have the device removed due to infection and later to have a new device implanted. A diabetic patient had skin problems, which required device removal; a new device was later implanted. Two patients had the device removed due to unsatisfactory pain relief.

The prospective study by Villavicencio et al. 2000 included 41 patients with pain of various etiologies. The majority of the patients, 24 (59%), had failed back surgery syndrome (FBSS), 7 (17%) had complex regional pain syndrome (CRPS I and II), 4 (10%) had neuropathic pain syndrome, and 6 (15%) were diagnosed as stroke or other. Patients underwent an initial trial period for SCS with temporary leads. If the trial resulted in greater than 50% reduction in the patient's pain, as measured by the VAS, the patient was implanted with a SCS system. In the study, 27 of 41 (66%) patients had permanent implants. All patients were examined after 6 weeks. Pain measurements were assessed at 3–6 month intervals for the first year and annually thereafter. The median long-term follow-up was 34 months. A total of 24 of 27 (89%) patients reported greater than 50 % reduction in pain. Since the majority of the patients were treated for FBSS, this article supports the use of SCS for the treatment of FBSS.

In this study, one patient required a revision because of electrode fracture. One patient required removal of the system due to local infection. One patient required replacement of the IPG due to mechanical failure. Overall, 16 of 27 (59%) patients required a total of 36 repositioning procedures.

A retrospective analysis by Hassenbusch SJ et al. 1995 included patients with chronic lower body pain, predominately neuropathic pain and pain either midline lower back and/or unilateral or bilateral leg pain treated over a 5-year period. The study was a comparison of SCS to spinal infusion of opioids. For patients with radicular pain involving one leg with or without unilateral buttock pain, a trial of SCS was recommended first. For patients with midline back pain and/or bilateral leg pain, a trial of long-term spinal infusion was recommended first. If the patients failed screening with either of these modalities, the other was then tested. If the treatment reduced the pain by 50%, the systems were internalized. A retrospective analysis of patients with unilateral leg and/or buttock pain treated initially with SCS and bilateral leg or mainly low back pain treated initially with spinal infusions of opioids was then done.

In this study, 42 patients were screened; 26 (62%) patients received spinal stimulation; 16 (38%) received opioids via a spinal infusion pump. A total of 5 patients did not receive adequate pain relief with SCS; 3 (7%) of these patients underwent trial spinal infusions and had effective pain relief. There were 4 (10%) patients that underwent a trial of spinal infusion of opioid but did not receive adequate pain relief; these patients were not tested with SCS. Pain severity was rated using a verbal digital pain scale: "On a scale of 0 to 10 where 0 is no pain and 10 is the worst pain you could ever imagine, what is your pain now?" (Hassenbusch SJ et al. 1995) 16 of 26 patients (62%) had greater than 50% pain relief with SCS. A total of 2 of 16 (13%) patients had greater than 50% pain relief with opioids. Mean follow-up was 2.1±0.3 years. This analysis supports the use of SCS for intractable low back and leg pain.

In this study, 7 (17%) patients suffered complications after implantation of the device; 5 (12%) patients required repositioning of catheter type electrodes and 2 patients required revision of the stimulator generator.

Safety Evaluation

Sixteen studies were identified based on the detailed inclusion/exclusion criteria to demonstrate the safety of the Genesis™ (IPG) neurostimulation system (all references in the bibliography were used). The studies included a total of 1253 patients.

The following table depicts the number of patients, the number of events observed, and the percentage of occurrences of each event compared to the total number of patients. It should be noted that several studies include both IPG and RF systems. The clinical experience reported in the literature on RF systems is relevant to determining the safety of totally implantable IPG systems.

Table 2. Summary of risks identified in the retrospective clinical studies

Risks	Number of Patients	Number of Events	Percent of Patients
Lead migration	1059	144	13.6
Infection	1253	37	3.0
Epidural hemorrhage	1253	0	0
Seroma	1253	0	0
Hematoma	1253	5	0.4
Paralysis	1253	1	0.1
CSF leak	1253	6	0.5
Over/under stim	1059	27	2.6
Intermittent stim	1059	0	0
Pain over implant	1059	12	1.1
Allergic reaction	1059	2	0.2
Skin erosion	1059	1	0.1
Lead breakage	1059	182	17.2
Hardware malfunction	1059	32	3.0
Loose connection	1059	10	1.0
Battery failure	911	17	1.9
Other	1059	24	2.3

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Clinical Summary for BurstDR™ Stimulation

Abbott Medical performed a clinical study to establish reasonable assurance of safety and effectiveness of BurstDR™ stimulation for the treatment of chronic, intractable pain of the trunk and/or limbs. The clinical study supports the SCS systems listed in "Clinical Studies" (page 1). The following sections present information and results for the SUNBURST™ study.

SUNBURST™ Study Design

Subjects began to enroll in the study in January 2014, and treatment has continued through the time of this report. This report includes the data collected through February 2016, accounting for 173 subjects at a total of 20 investigational sites.

The study was a prospective, multicenter, randomized, open-label, crossover study that compared two different stimulation modes:

- Arm 1: tonic-then-burst stimulation (tonic/burst)
- Arm 2: burst-then-tonic stimulation (burst/tonic)

Subjects with chronic intractable pain of the trunk and/or limbs were informed about the study to determine if they were interested in participating. After subjects signed an informed consent agreement, they were screened according to the inclusion and exclusion criteria and underwent a baseline evaluation. Those subjects who met the criteria to participate were scheduled to receive a commercially available Abbott Medical trial neurostimulation system for spinal cord stimulation (SCS). Subjects underwent a trial period using tonic stimulation, and those subjects who completed the trial successfully were scheduled to receive a Prodigy™ neurostimulation system, which is capable of delivering both stimulation modes.

Subjects were implanted with the permanent Prodigy neurostimulation system, and the device remained off during a recovery period. After the recovery period, subjects were randomized to receive either burst stimulation or tonic stimulation. The implanted system was then activated and programmed accordingly. Depending on randomization, a subject experienced either tonic stimulation or burst stimulation first for a total of 12 weeks. At the week-12 visit, the subject was then crossed over to the alternate stimulation mode for another 12 weeks. Subjects reported to the office at 6, 12, 18, and 24 weeks after randomization and activation. After the primary endpoint at the week-24 visit, all subjects were programmed to tonic or burst stimulation based on what the subject and physician preferred, and they continued to attend follow-up visits every 6 months for 2 years or until the study closed, whichever occurred first.

The purpose of the clinical study was to collect the data needed to demonstrate the safety and effectiveness of a neurostimulation system that is capable of both tonic and burst stimulation modes.

SUNBURST™ Study Clinical Inclusion and Exclusion Criteria

Enrollment in the SUNBURST™ study was limited to subjects who met the following selection criteria.

Inclusion Criteria

Subjects were limited to those who met all of the following criteria:

- Subject signed an informed consent to participate in the study.
- Subject was at least 22 years old.
- Subject had chronic intractable pain of the truck and/or limbs.
- Subject scored a baseline average of 60 or higher for average daily overall pain on the visual analog scale (VAS) 7-day pain diary.
- Subject tried "best" medical therapy, but failed at least three documented, medically supervised treatments (including, but not limited to, physical therapy and acupuncture) and failed medication treatment from at least two different classes.
- Subject's pain-related medication regimen was stable 4 weeks before the screening evaluation.
- The Investigator evaluated the subject's medical record to ensure that the subject was a good candidate for a neurostimulation system.
- A psychologist or psychiatrist evaluated the subject and found him or her to be a suitable SCS candidate.
- Subject agreed not to increase the number of or dosage of pain-related medications from activation through the week-24 follow-up visit.

- Subject was willing to cooperate with the study requirements such as complying with the treatment regimen and completing all office visits.
- Subject was female candidate of childbearing potential who agreed to commit to using effective contraception (including, but not limited to, sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, the rhythm method, or abstinence) throughout the study.

Exclusion Criteria

Subjects were excluded if they met any of the following criteria:

- Subject was participating in a clinical investigation that included an active treatment arm.
- Subject had previously been implanted with a neurostimulation system or participated in a trial period for a neurostimulation system.
- Subject had an overall Beck Depression Inventory‡-II (BDI‡-II) score greater than 24 or had a score of 3 at the screening visit on question 9, which relates to having suicidal thoughts or wishes. (Beck Depression Inventory and BDI are trademarks of NCS Pearson, Inc.)
- Subject was receiving, applying for, or considering seeking workers compensation or was involved in disability litigation.
- Subject had an infusion pump or any implantable neurostimulator device.
- Subject had a concurrent, clinically significant or disabling chronic pain problem that required additional treatment.
- Subject had an existing medical condition, such as epilepsy, stroke, multiple sclerosis, acoustic neuroma, or a tumor, that was likely to require repetitive evaluations using magnetic resonance imaging (MRI).
- Subject had a history of cancer requiring active treatment in the last 6 months.
- Subject had an existing medical condition that was likely to require the use of diathermy.
- Subject had pain that originated from peripheral vascular disease.
- Subject had an impaired immune system (immunocompromised).
- Subject had a documented history of an allergic response to titanium or silicone.
- Subject had a documented history of substance abuse (with substances such as narcotics or alcohol) or substance dependency within 6 months of the collection of baseline data.
- Subject was a female of childbearing potential who was pregnant (confirmed by a positive urine or blood pregnancy test).

SUNBURST™ Study Follow-Up Schedule

Subjects who met the aforementioned criteria for participation underwent a conventional SCS trial using tonic stimulation. Subjects with an unsuccessful SCS trial exited the study following a safety assessment 2 weeks after the trial. The subjects who remained in the study were implanted with a permanent system, and then they returned to the office after a recovery period of 2 to 3 weeks (2 weeks minimum) for randomization and system activation. After randomization and activation, subjects returned to the office for follow-up at 6 and 12 weeks. During the week-12 visit, subjects crossed over to the alternative stimulation mode. Subjects continued to report to the office at 18 and 24 weeks for follow-up. After the week-24 visit, subjects continued to attend follow-up visits every 6 months for 2 years or until the study closed, whichever occurred first.

Clinical Endpoints

The primary effectiveness endpoint was a non-inferiority test comparing the change in the VAS pain diary score during tonic stimulation with the change in VAS pain diary score during burst stimulation.

The secondary endpoints that were assessed included

- Determining superiority of burst stimulation compared to tonic stimulation using VAS pain diary scores for average daily overall pain (after non-inferiority was demonstrated)
- Comparing the responder rate, which is defined by a 30% decrease in the VAS pain diary scores for average daily overall pain
- Comparing the percentage of paresthesia coverage

The following descriptive endpoints and additional data were assessed:

- Demographics, including gender, age, height, weight, ethnicity, and marital status
- Pain history, including primary diagnosis, pain duration, pain etiology, and prior treatments
- Adverse events
- Summary of adverse events related to tonic and burst stimulation
- Surgery and device information
- Programming and stimulation mode data
- Recharging data
- Comparison of the responder rate, which is defined by a 50% decrease in the VAS pain diary scores for average daily overall pain
- Average daily trunk pain and average daily limb pain as assessed by the VAS
- Comparison of VAS pain diary scores for worst daily overall pain
- Patient satisfaction with the device
- Stimulation mode preference (tonic or burst)
- Patient Global Impression of Change (PGIC)
- Comparison of the quality of life in physical and mental components of Short Form 36 (SF-36)
- Comparison of function in the Oswestry Disability Index (ODI), version 2.1a
- Pain quality as assessed by the Short-Form McGill Pain Questionnaire (SF-MPQ-2)
- Pain catastrophizing as assessed by the Pain Catastrophizing Scale (PCS)
- Depression as assessed by the BDI‡-II clinical assessment
- Medication usage

Primary Statistical Analysis Plan

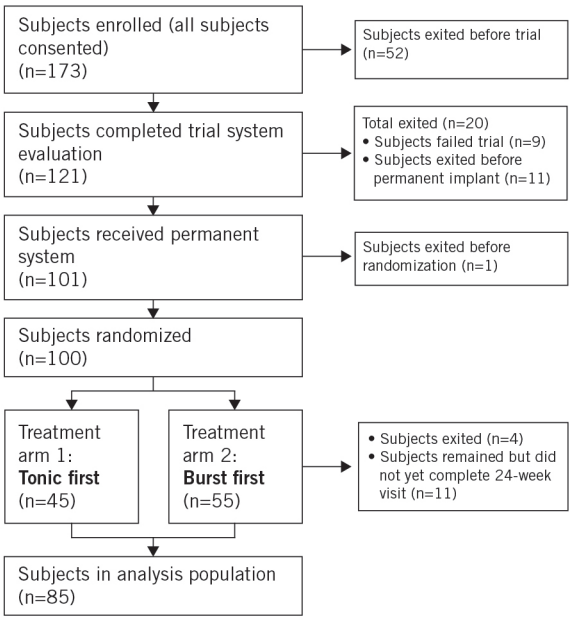
To analyze the primary endpoint—evaluating non-inferiority of burst stimulation to tonic stimulation in overall VAS scores—the non-inferiority margin was set to 7.5 mm for the overall VAS score on a scale of 0 to 100. The standard deviation of the difference between the VAS scores for tonic and burst stimulation was assumed to be 18.4 points. Setting the Type I error rate to 0.05, a minimum sample size of 76 subjects was required to achieve 80% power to demonstrate non-inferiority of burst stimulation to tonic stimulation.

The secondary endpoints were tested if the primary endpoint was met. Each secondary endpoint was tested at a 5% significance level. Statistical tests were not performed for descriptive endpoints and additional data.

Accountability of Subject Cohort

A total of 173 subjects consented and enrolled at 20 investigational sites. Of the 141 subjects completing the baseline evaluation, 121 underwent an evaluation using an SCS trial system with tonic stimulation. After the SCS trial evaluation, 101 subjects met the standard criteria for success and were implanted with the Prodigy™ neurostimulation system. Of these 101 subjects, 100 were randomized and activated. The final subject was randomized in August 2015. A total of 96 subjects completed the week-24 follow-up visit for the primary endpoint. The following figure summarizes the accounting for study subjects.

Figure 1. Subject accounting



SUNBURST™ Study Demographics and Pain Baseline Characteristics

A total of 141 subjects had a baseline visit in this study, 100 of whom were randomized (45 to receive tonic stimulation then burst stimulation [tonic/burst] and 55 to receive burst stimulation then tonic stimulation [burst/tonic]). The following tables show subject demographics and primary diagnosis. Pain duration, origin, and prior treatments are also shown, respectively.

Table 3. Demographics and primary diagnosis

Variable	Subjects with Baseline Visit (N=141)	Randomization		
		Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)	*p*-value
Age				
Mean ±SD	59.1±13.5 (141)	58.8±13.6 (45)	60.4±13.4 (55)	0.562[t]
Minimum, Median, Maximum	25.0, 60.0, 88.0	27.0, 62.0, 88.0	25.0, 61.0, 84.0	
Gender, n/N (%)				
Female	85/141 (60.3%)	26/45 (57.8%)	31/55 (56.4%)	0.887[c]
Male	56/141 (39.7%)	19/45 (42.2%)	24/55 (43.6%)	
Weight (lb)				
Mean ±SD	191.7±48.0 (141)	189.0±42.8 (45)	195.31±47.1 (55)	0.509[t]
Minimum, Median, Maximum	85.0, 190.0, 350.0	85.0, 184.0, 340.0	113.0, 193.0, 289.0	

Table 3. Demographics and primary diagnosis

Variable	Subjects with Baseline Visit (N=141)	Randomization		
		Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)	*p*-value
Height (in.)				
Mean ±SD	66.7±4.4 (141)	66.2±4.4 (45)	66.8±4.4 (55)	0.502[t]
Minimum, Median, Maximum	55.0, 66.0, 79.1	57.0, 66.1, 73.0	55.0, 66.0, 76.0	
Race, n/N (%)				
Black or African American	3/141 (2.1%)	0/45 (0.0%)	1/55 (1.8%)	1.000[f]
White	136/141 (96.5%)	45/45 (100.0%)	54/55 (98.2%)	
Other	2/141 (1.4%)	0/45 (0.0%)	0/55 (0.0%)	
Ethnicity, n/N (%)				
Hispanic or Latino	2/141 (1.4%)	0/45 (0.0%)	0/55 (0.0%)	—
Non-Hispanic or Non-Latino	139/141 (98.6%)	45/45 (100.0%)	55/55 (100.0%)	
Marital Status, n/N (%)				
Married	107/141 (75.9%)	39/45 (86.7%)	41/55 (74.5%)	0.479[f]
Separated/divorced	13/141 (9.2%)	2/45 (4.4%)	4/55 (7.3%)	
Single	8/141 (5.7%)	2/45 (4.4%)	3/55 (5.5%)	
Widowed	13/141 (9.2%)	2/45 (4.4%)	7/55 (12.7%)	
Diagnosis, n/N (%)				
Arachnoiditis	1/141 (0.7%)	1/45 (2.2%)	0/55 (0.0%)	0.189[f]
CRPS I/CRPS II	2/141 (1.4%)	0/45 (0.0%)	2/55 (3.6%)	
Degenerative spine disease	7/141 (5.0%)	1/45 (2.2%)	2/55 (3.6%)	
Failed back surgery syndrome (FBSS)	59/141 (41.8%)	15/45 (33.3%)	27/55 (49.1%)	
Neuritis/neuropathy/ neuralgia	3/141 (2.1%)	0/45 (0.0%)	2/55 (3.6%)	
Postoperative chronic pain	5/141 (3.5%)	1/45 (2.2%)	2/55 (3.6%)	
Radiculopathies	52/141 (36.9%)	21/45 (46.7%)	17/55 (30.9%)	
Chronic pain (non-postoperative)	12/141 (8.5%)	6/45 (13.3%)	3/55 (5.5%)	

[t] Two-sample t-test

[c] Chi-square test

[f] Fisher's exact test

Table 4. Pain duration and origin

Pain History	Subjects with Baseline Visit (N=141)	Randomization		
		Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)	*p*-value
How long has the subject experienced chronic pain (years)?				
Mean ±SD	12.8±10.9 (141)	11.1±9.5 (45)	15.1±12.1 (55)	0.075[w]
Minimum, Median, Maximum	0.8, 10.0, 60.0	0.8, 9.0, 50.0	1.3, 10.0, 60.0	
How did the subject's pain start?				
Accident	31/141 (22.0%)	12/45 (26.7%)	12/55 (21.8%)	0.605[f]
Medical condition	9/141 (6.4%)	0/45 (0.0%)	3/55 (5.5%)	
Motor vehicle accident	5/141 (3.5%)	2/45 (4.4%)	3/55 (5.5%)	
Surgery	13/141 (9.2%)	3/45 (6.7%)	7/55 (12.7%)	
Other	11/141 (7.8%)	5/45 (11.1%)	4/55 (7.3%)	
Unknown	72/141 (51.1%)	23/45 (51.1%)	26/55 (47.3%)	

[w] Wilcoxon rank-sum test

[f] Fisher's exact test

Table 5. Pain treatment history

Pain History	Subjects with Baseline Visit (N=141)	Randomization		
		Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)	*p*-value
Non-Invasive Interventions				
Oral medications	137/141 (97.2%)	43/45 (95.6%)	54/55 (98.2%)	0.587[f]
Physical therapy	129/141 (91.5%)	41/45 (91.1%)	51/55 (92.7%)	1.000[f]
Transcutaneous electrical nerve stimulation (TENS)	89/141 (63.1%)	35/45 (77.8%)	29/55 (52.7%)	0.009[c]
Acupuncture	37/141 (26.2%)	7/45 (15.6%)	17/55 (30.9%)	0.074[c]
Acupressure	11/141 (7.8%)	3/45 (6.7%)	5/55 (9.1%)	0.727[f]
Physiological interventions	18/141 (12.8%)	7/45 (15.6%)	4/55 (7.3%)	0.214[f]
Other	55/141 (39.0%)	19/45 (42.2%)	23/55 (41.8%)	0.968[c]
At least on non-invasive intervention	141/141 (100.0%)	45/45 (100.0%)	55/55 (100.0%)	—
Invasive Nonsurgical Interventions				
Steroid injections (epidural, facet [zygapophysial] injections, etc.)	130/141 (92.2%)	43/45 (95.6%)	51/55 (92.7%)	0.688[f]

Table 5. Pain treatment history

Pain History	Subjects with Baseline Visit (N=141)	Randomization		
		Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)	*p*-value
Therapeutic intradiscal injections	7/141 (5.0%)	4/45 (8.9%)	1/55 (1.8%)	0.171[f]
Intrathecal therapy	2/141 (1.4%)	0/45 (0.0%)	1/55 (1.8%)	1.000[f]
Therapeutic medial branch block	33/141 (23.4%)	8/45 (17.8%)	12/55 (21.8%)	0.615[c]
Botulinum toxin	3/141 (2.1%)	0/45 (0.0%)	3/55 (5.5%)	0.250[f]
Radiofrequency denervation	33/141 (23.4%)	10/45 (22.2%)	9/55 (16.4%)	0.458[c]
Intradiscal electrothermal therapy (IDET)	0/141 (0.0%)	0/45 (0.0%)	0/55 (0.0%)	—
Percutaneous intradiscal radiofrequency thermocoagulation	0/141 (0.0%)	0/45 (0.0%)	0/55 (0.0%)	—
Local anesthetic injections (tender or trigger-point injections)	28/141 (19.9%)	7/45 (15.6%)	10/55 (18.2%)	0.728[c]
Other	30/141 (21.3%)	9/45 (20.0%)	13/55 (23.6%)	0.662[c]
At least one nonsurgical intervention	138/141 (97.9%)	45/45 (100.0%)	54/55 (98.2%)	1.000[f]
Surgical Interventions				
Laminectomy	54/141 (38.3%)	16/45 (35.6%)	23/55 (41.8%)	0.523[c]
Facetectomy	3/141 (2.1%)	1/45 (2.2%)	2/55 (3.6%)	1.000[f]
Foraminotomy	1/141 (0.7%)	1/45 (2.2%)	0/55 (0.0%)	0.450[f]
Laminoplasty	0/141 (0.0%)	0/45 (0.0%)	0/55 (0.0%)	—
Fusion and vertebral disc replacement	56/141 (39.7%)	18/45 (40.0%)	22/55 (40.0%)	1.000[c]
Discectomy (open, microdiscectomy, laser, coblation nucleoplasty, etc.)	24/141 (17.0%)	11/45 (24.4%)	6/55 (10.9%)	0.073[c]
Other	26/141 (18.4%)	6/45 (13.3%)	13/55 (23.6%)	0.191[c]
At least one surgical intervention	102/141 (72.3%)	32/45 (71.1%)	38/55 (69.1%)	0.826[c]

[c] Chi-square test

[f] Fisher's exact test

SUNBURST™ Study Safety Results

The analysis of safety was based on the report of adverse events. Serious adverse events (SAEs) were reported after enrollment through study activation. After activation, all adverse events (AEs) were reported

whether or not they were considered device- or procedure-related. No unanticipated adverse device affects (UADEs) were reported during the study. Both study-related and non-study related adverse events were collected and monitored through long-term study visits up to 24 months or until study completion.

A total of 158 AEs were reported during the study, 97 (59.5%) of which were considered to be non-study related. Twenty-one (21) events were considered SAEs and were reported in a total of 16 subjects (9.2%). Of all SAEs reported, only two were considered study-related in a total of 2 subjects (1.2%). The following table summarizes all the adverse events.

Table 6. Summary of all AEs

AE Description	Number of Events	Number of Subjects	Percent of Subjects (n/N**)
SAEs			
Study-related	2	2	1.2% (2/173)
Non-study related	19	15	8.7% (15/173)
SAE subtotal	**21**	**16***	**9.2% (16/173)**
Non-SAEs			
Study-related	62	31	17.9% (31/173)
Non-study related	75	44	25.4% (44/173)
Non-SAE subtotal	**137**	**58***	**33.5% (58/173)**
All AEs total	**158**	**67***	**38.7% (67/173)**

* Some subjects experienced more than one event; therefore, the number of subjects experiencing an event is not equal to the number of events in the neighboring column.

** Subjects at risk out of subjects enrolled in study

Two (1.2% of total number of subjects at risk) SAEs were reported that were categorized as study-related. No study-related SAEs occurred following device activation. The following table summarizes the SAEs that occurred before stimulation began.

Table 7. Summary of study-related SAEs

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N*)
Enrollment to activation			
Persistent pain and/or numbness	1	1	0.58% (1/173)
Unsuccessful lead placement	1	1	0.58% (1/173)
Total	**2**	**2**	**1.16% (2/173)**

* Subjects at risk out of subjects enrolled in study

The following table shows SAEs that were unrelated to the study. Nineteen (19) events were reported in 15 subjects (8.7%). Thirteen (13) SAEs were reported following device activation.

Table 8. Summary of non-study related SAEs

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N)
Enrollment to activation			
Abdominal pain	1	1	0.58% (1/173)[a]

Table 8. Summary of non-study related SAEs

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N)
Bowel obstruction	1	1	0.58% (1/173)[a]
Femur fracture	1	1	0.58% (1/173)[a]
Hip pain/replacement	1	1	0.58% (1/173)[a]
Low potassium levels	1	1	0.58% (1/173)[a]
Persistent pain and/or numbness	1	1	0.58% (1/173)[a]
Following activation			
Bladder tumor	1	1	1.04% (1/96)[b]
Broken femur	1	1	1.04% (1/96)[b]
Cancerous tumor on vocal chords	1	1	1.00% (1/100)[c]
Death[d]	1	1	1.04% (1/96)[b]
Infection	1	1	1.00% (1/100)[c]
Loss of speech and memory, and headache	1	1	1.00% (1/100)[c]
Myocardial infarction	1	1	1.04% (1/96)[b]
Scheduled right total-knee arthroplasty	1	1	1.00% (1/100)[c]
Seizure	1	1	1.04% (1/96)[b]
Shortness of breath	1	1	1.00% (1/100)[c]
Somnolence (sleepiness)	1	1	1.00% (1/100)[c]
Temporary paralysis	1	1	1.00% (1/100)[c]
Withdrawal symptoms from tapering off of oxymorphone*	1	1	1.00% (1/100)[c]
Total	**19**	**15****	**8.67% (15/173)**

* The generic name of the medication, oxymorphone, is used instead of the brand name.

** Some subjects experienced more than one event; therefore, the number of subjects experiencing an event is not equal to the number of events in the neighboring column.

[a] Subjects at risk out of all subjects enrolled in study

[b] Subjects at risk out of subjects who completed the week-24 visit

[c] Subjects at risk out of all subjects who had the implanted system activated

[d] Subject died of natural causes at home. No autopsy was performed.

The following table identifies all 62 non-serious AEs that were study-related.

Table 9. Summary of study-related, non-serious AEs (following activation)

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N)
Charger stopped working	1	1	1.00% (1/100)[c]
Device pocket heating while charging	1	1	1.00% (1/100)[c]
Diminished or loss of stimulation*	9	7[a]	7.00% (7/100)[c]
Diminished or loss of symptom relief*	23	14[a]	14.00% (14/100)[c]
Increased pain	1	1	1.00% (1/100)[c]
Infection	2	2	2.00% (2/100)[c]
Local skin erosion	1	1	1.00% (1/100)[c]
Persistent pain and/or numbness	6	6	6.00% (6/100)[c]
Postoperative low back pain	1	1	1.00% (1/100)[c]
Seroma at the implant site	1	1	1.00% (1/100)[c]
Stimulation in wrong place**	6	4[a]	4.00% (4/100)[c]
Unpleasant sensations**	7	6[a]	6.00% (6/100)[c]
Weakness	3	3	3.00% (3/100)[c]
Total	**62**	**31**[b]	**31.00% (31/100)**

* Undesirable changes in stimulation

** Unintended effects of stimulation

[a] Some subjects experienced more than one event.

[b] The total number of subjects who experienced at least one event listed from the previous rows.

[c] Subjects at risk out of subjects who had the implanted system activated.

The following table identifies non-serious study-related AEs. Of all the stimulation-related non-serious AEs, 13 occurred with burst stimulation and 16 occurred with tonic stimulation. Fewer non-serious AEs were noted for burst stimulation mode than tonic stimulation mode.

Table 10. Summary of stimulation-related, non-serious AEs (activation to 24 weeks)

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N)
Burst stimulation-related			
Diminished or loss of stimulation*	4	3[a]	3.00% (3/100)[c]
Diminished or loss of symptom relief*	5	5	5.00% (5/100)[c]

Table 10. Summary of stimulation-related, non-serious AEs (activation to 24 weeks)

Event Description	Number of Events	Number of Subjects	Percent of Subjects (n/N)
Unpleasant sensations**	4	4	4.00% (4/100)[c]
Tonic stimulation-related			
Diminished or loss of stimulation*	2	2	2.06% (2/97)[d]
Diminished or loss of symptom relief*	8	6[a]	6.19% (6/97)[d]
Stimulation in wrong place**	5	4[a]	4.12% (4/97)[d]
Unpleasant sensations**	1	1	1.03% (1/97)[d]
Total	**29**	**16**[b]	**16.00% (16/100)**

* Undesirable changes in stimulation
** Unintended effects of stimulation

[a] Some subjects experienced more than one event; therefore, the number of subjects experiencing an event is not equal to the number of events in the neighboring column.

[b] The total number of subjects who experienced at least one event listed from the previous rows.

[c] Subjects at risk out of the 55 subjects from the burst/tonic arm, as well as the 45 subjects from the tonic/burst arm who completed the week-12 visit (when they crossed over to burst stimulation).

[d] Subjects at risk out of the 45 subjects from the tonic/burst arm, as well as the 52 subjects from the burst/tonic arm who completed the week-12 visit (when they crossed over to tonic stimulation).

Device and Device Usage Data

Surgery and device data were collected for the 100 subjects that were randomized and received a permanent implant. As shown in the following tables, randomization groups showed a similar number of implanted leads and similar IPG placement.

Table 11. Summary of surgery and device information for all randomized subjects (N=100)

Surgery	Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)
Number of leads implanted		
Mean ±SD (N)	1.8±0.7 (45)	1.7±0.8 (55)
Minimum, Median, Maximum	1.0, 2.0, 4.0	1.0, 2.0, 4.0
1 lead	16/45 (35.6%)	22/55 (40.0%)
2 leads	26/45 (57.8%)	27/55 (49.1%)
3 leads	1/45 (2.2%)	4/55 (7.3%)
4 leads	2/45 (4.4%)	2/55 (3.6%)
IPG placement side		
Left	39/45 (86.7%)	44/55 (80.0%)
Right	6/45 (13.3%)	11/55 (20.0%)
IPG anatomic location		

Table 11. Summary of surgery and device information for all randomized subjects (N=100)

Surgery	Arm 1: Tonic/Burst (N=45)	Arm 2: Burst/Tonic (N=55)
Abdomen	1/45 (2.2%)	2/55 (3.6%)
Lower axilla	0/45 (0.0%)	1/55 (1.8%)
Upper buttock	35/45 (77.8%)	38/55 (69.1%)
Other	9/45 (20.0%)	13/55 (23.6%)
Missing	0/45 (0.0%)	1/55 (1.8%)

Programming and stimulation mode data were collected at follow-up visits including unscheduled programming visits. The following table shows a summary of the burst stimulation settings through 24 weeks. The 100 randomized subjects underwent 350 programming sessions, and the programmed parameters were within the ranges recommended in the protocol (pulse width of 1000 µs, burst rate of 40 Hz, intra-burst frequency of 500 Hz, and burst train of 5 pulses).

Table 12. Summary of burst stimulation settings for all randomized subjects (N=100)

Number of Programming Sessions	Burst Rate		Intra-Burst Rate	Burst Train	
	40 Hz	20 Hz	500 Hz	5 pulses	Missing
351	350 (99.7%)	1 (0.3%)	351 (100.0%)	350 (99.7%)	1 (0.3%)
	Pulse Width (µs)	Amplitude			
		Minimum	Target	Maximum	
Mean ±SD (N)	994.8±68.6 (348)	0.5±0.6 (343)	1.6±1.0 (347)	2.7±0.8 (346)	
Minimum	0	0	0	1	
Maximum	1000	2	5	5	

Recharging data were collected at follow-up visits including unscheduled programming visits. The following table shows a summary of recharging information through 24 weeks. Recharging instructions for routine care of a typical neurostimulation system (using tonic stimulation) were given at the discretion of the investigator; thus, no differences in recharging for tonic and burst stimulation were expected.

Table 13. Summary of IPG recharging for all available subjects

IPG Recharging		Burst	Tonic
Week 6			
Recharged	Yes	51/52 (98.08%)	44/45 (97.78%)
Frequency	Daily	4/51 (7.84%)	3/44 (6.82%)
	2–3 times a week	15/51 (29.4%)	13/44 (29.5%)
	Weekly	28/51 (54.9%)	23/44 (52.3%)
	Every other week	3/51 (5.88%)	3/44 (6.82%)
	Once a month or less often	1/51 (1.96%)	2/44 (4.55%)
Reason	Battery heats up	1/51 (1.96%)	0/44 (0.0%)
	Low battery message	3/51 (5.88%)	5/44 (11.4%)
	Normal routine	43/51 (84.3%)	39/44 (88.6%)

Table 13. Summary of IPG recharging for all available subjects

IPG Recharging		Burst	Tonic
	Recommended time frame	4/51 (7.84%)	0/44 (0.0%)
Week 12			
Recharged	Yes	52/52 (100.00%)	45/45 (100.00%)
Frequency	Daily	7/52 (13.5%)	1/45 (2.22%)
	2–3 times a week	16/52 (30.8%)	11/45 (24.4%)
	Weekly	23/52 (44.2%)	29/45 (64.4%)
	Every other week	5/52 (9.62%)	2/45 (4.44%)
	Once a month or less often	1/52 (1.92%)	2/45 (4.44%)
Reason	Low battery message	4/52 (7.69%)	1/45 (2.22%)
	Normal routine	46/52 (88.5%)	41/45 (91.1%)
	Recommended time frame	2/52 (3.85%)	2/45 (4.44%)
	Thought it was needed	0/52 (0.0%)	1/45 (2.22%)
Unscheduled before week 12			
Recharged	Yes	15/18 (83.33%)	22/28 (78.57%)
Frequency	Daily	1/15 (6.67%)	0/22 (0.0%)
	2–3 times a week	4/15 (26.7%)	3/22 (13.6%)
	Weekly	8/15 (53.3%)	17/22 (77.3%)
	Every other week	1/15 (6.67%)	2/22 (9.09%)
	Once a month or less often	1/15 (6.67%)	0/22 (0.0%)
Reason	Low battery message	3/15 (20.0%)	4/22 (18.2%)
	Normal routine	10/15 (66.7%)	15/22 (68.2%)
	Patient checks battery and charges when less than 50% depleted	1/15 (6.67%)	0/22 (0.0%)
	Recommended time frame	1/15 (6.67%)	3/22 (13.6%)
Week 18			
Recharged	Yes	44/44 (100.00%)	51/51 (100.00%)
Frequency	Daily	1/44 (2.27%)	3/51 (5.88%)
	2–3 times a week	10/44 (22.7%)	11/51 (21.6%)
	Weekly	28/44 (63.6%)	29/51 (56.9%)
	Every other week	5/44 (11.4%)	6/51 (11.8%)

Table 13. Summary of IPG recharging for all available subjects

IPG Recharging		Burst	Tonic
	Once a month or less often	0/44 (0.0%)	2/51 (3.92%)
Reason	Low battery message	0/44 (0.0%)	3/51 (5.88%)
	Normal routine	44/44 (100%)	45/51 (88.2%)
	Recommended time frame	0/44 (0.0%)	3/51 (5.88%)
Week 24			
Recharged	Yes	45/45 (100.00%)	50/51 (98.04%)
Frequency	Daily	3/45 (6.67%)	2/50 (4.00%)
	2–3 times a week	13/45 (28.9%)	8/50 (16.0%)
	Weekly	25/45 (55.6%)	32/50 (64.0%)
	Every other week	4/45 (8.89%)	7/50 (14.0%)
	Once a month or less often	0/45 (0.0%)	1/50 (2.00%)
Reason	Battery heats up	1/45 (2.22%)	0/50 (0.0%)
	Charged daily due to time it took (1.5 hours daily or more than 3 hours if patient waited)	1/45 (2.22%)	0/50 (0.0%)
	Low battery message	1/45 (2.22%)	3/50 (6.00%)
	Normal routine	42/45 (93.3%)	46/50 (92.0%)
	Recommended time frame	0/45 (0.0%)	1/50 (2.00%)
Unscheduled between weeks 12 and 24			
Recharged	Yes	11/11 (100.00%)	7/7 (100.00%)
Frequency	2–3 times a week	0/11 (0.0%)	3/7 (42.9%)
	Weekly	10/11 (90.9%)	4/7 (57.1%)
	Once a month or less often	1/11 (9.09%)	0/7 (0.0%)
Reason	Normal routine	10/11 (90.9%)	7/7 (100.00%)
	Recommended time frame	1/11 (9.09%)	0/7 (0.0%)

SUNBURST™ Study Results

This section provides results from the SUNBURST™ study.

Primary Effectiveness

The analysis of effectiveness was an intention-to-treat analysis based on the randomization population of 100 subjects.

Statistical methods were used to impute VAS scores for the following subjects and reasons:

- Six (6) subjects increased pain medication in during the 12 weeks following device activation (2 while using tonic and 4 while using burst) and 15 subjects increased pain medication in between weeks 12 and 24 (5 while using burst and 10 while using tonic), and their overall VAS score at the trial baseline was used to impute their overall VAS score for the week-12 or week-24 visit as appropriate per the protocol.
- Four (4) subjects withdrew from the study before week 24, and their overall VAS score was imputed using the hot deck method, which replaces missing values of a visit for a non-respondent with observed values during the same visit from a respondent who shares similar characteristics observed by both cases.
- Three (3) subjects underwent an invasive procedure for a new clinically significant or disabling chronic pain problem, and their overall VAS score was imputed using the hot deck method or the last observation carried forward (LOCF) method, which replaces missing values by using the last value observed for the score.

The following table shows the results of testing the primary endpoint. In both randomization groups, burst stimulation scored lower overall than tonic stimulation on the VAS by 3.6 in the tonic/burst group and 6.5 in the burst/tonic group. The estimated difference in the overall VAS score between burst and tonic stimulation was -5.1, and the 95% upper confidence bound (UCB) for the mean difference between burst and tonic stimulation was -1.14, which is less than the non-inferiority margin of 7.5. Additionally, the ***p***-value for the test of the non-inferiority hypothesis was <0.001. Therefore, the primary endpoint was met, and it is concluded that burst stimulation is non-inferior to tonic stimulation.

Table 14. Primary endpoint (overall VAS score)

Randomization	**Arm 1: tonic/burst**	**Arm 2: burst/tonic**	**Pooled**
Burst			
Mean ±SD (N)	42.7±26.1 (45)	44.2±25.3 (55)	43.5±25.6 (100)
Minimum, Median, Maximum	0.9, 41.1, 100.0	0.0, 45.1, 98.1	–
Tonic			
Mean ±SD (N)	46.3±22.8 (45)	50.0±24.8 (55)	48.7±23.9 (100)
Minimum, Median, Maximum	1.0, 49.3, 88.1	0.0, 49.3, 98.7	–
Burst-Tonic			
Mean ±SD (N)	-3.6±26.3 (45)	-6.5±21.0 (55)	–
Minimum, Median, Maximum	-64.6, -3.7, 79.0	-70.4, -2.6, 48.4	–
Burst-Tonic Average ± Pooled SD Across Arms		-5.1±11.8	
95% UCB on Difference (Burst-Tonic)		-1.14[t]	
Non-Inferiority Margin		7.5	
***p*-value for Non-Inferiority Test**		<0.001[t]	

Table 14. Primary endpoint (overall VAS score)

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Endpoint Met?		Yes	

[t] 95% UCB and ***p*-**value for non-inferiority are based on a t-distribution with n_1+n_2-2 degrees of freedom, where n_1 and n_2 are the number of subjects in each arm.

In addition to demonstrating non-inferiority, superiority was also shown. The following table contains the results of testing the superiority hypothesis for burst over tonic stimulation. The difference in the overall VAS score between burst and tonic stimulation is -5 points, with a 95% UCB of -1.14, which is less than 0 and results in a rejection of the hypothesis that burst stimulation is not superior to tonic stimulation (***p***=0.017). Therefore, the results demonstrate that burst stimulation is superior to tonic stimulation.

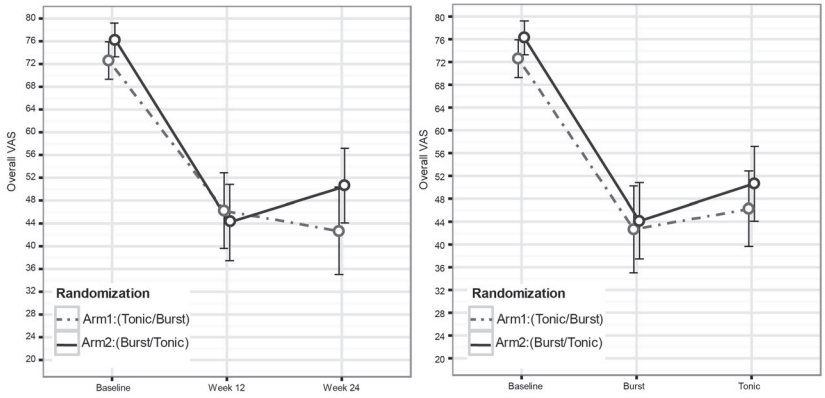
Table 15. Superiority of overall VAS score with burst over tonic

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Burst			
Mean ±SD (N)	42.7±26.1 (45)	44.2±25.3 (55)	43.5±25.6 (100)
Minimum, Median, Maximum	0.9, 41.1, 100.0	0.0, 45.1, 98.1	–
Tonic			
Mean ±SD (N)	46.3±22.8 (45)	50.7±24.8 (55)	48.7±23.9 (100)
Minimum, Median, Maximum	1.0, 49.3, 88.1	0.0, 49.3, 98.7	–
Burst-Tonic			
Mean ±SD (N)	-3.6±26.3 (45)	-6.5±21.0 (55)	–
Minimum, Median, Maximum	-64.6, -3.7, 79.0	-70.4, -2.6, 48.4	–
Burst-Tonic Average ± Pooled SD Across Arms		-5.1±11.8	
95% UCB on Difference (Burst Tonic)		-1.14[t]	
Superiority Margin		0	
***p*-value for Superiority Test**		0.017[t]	
Endpoint Met?		Yes	

[t] 95% UCB and ***p*-**value for superiority are based on a t-distribution with n_1+n_2-2 degrees of freedom, where n_1 and n_2 are the number of subjects in each arm.

The following figure presents the overall VAS scores by visit and by stimulation mode. The graph on the left shows that both randomization groups had high overall VAS scores at baseline and, at week 12, both stimulation modes reduced the overall VAS score as expected since all subjects were known responders to tonic stimulation during the stimulation trial period). The graph on the right shows these same data by stimulation method. The figure shows a large reduction in overall VAS score from baseline with burst stimulation and less reduction in VAS during tonic stimulation.

Figure 2. Main overall VAS score with 95% CI by visit (left) and by stimulation mode (right)



Secondary Effectiveness

The following table compares responder rates for burst stimulation versus tonic stimulation, where "responder rate" is defined as a decrease in the overall daily VAS score from baseline by at least 30%. A total of 69 subjects (69%) responded to tonic stimulation, burst stimulation, or both. Responder rates are 60.0% with burst stimulation and 51.0% with tonic stimulation. A cross-tabulation of responders for burst stimulation versus tonic stimulation shows numerically more subjects whose VAS score decreased by at least 30% with burst stimulation than with tonic stimulation (18 versus 9). However, this difference was not statistically significant (***p***=0.083).

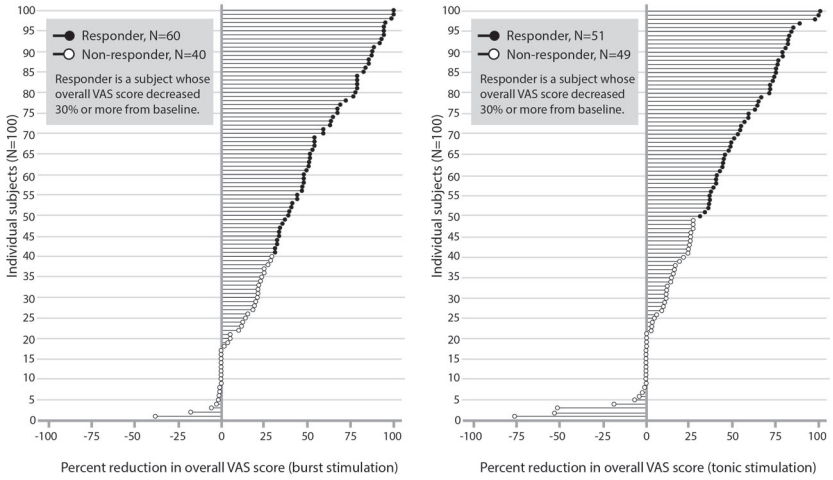
Table 16. Responder rates (decrease of ≥30**%** from baseline) for overall daily VAS score

Overall Responder Rate			
Percent of burst subjects (n/N)		60.0% (60/100)	
Percent of tonic subjects (n/N)		51.0% (51/100)	
Cross-Tabulation of Responders by Stimulation Mode			
Stimulation mode		**Tonic**	
Burst	**Responder**	No	Yes
	No	31/100 (31.0%)	9/100 (9.0%)
	Yes	18/100 (18.0%)	42/100 (42.0%)
***p*-value (Burst vs. Tonic)**			
0.083[m]			

[m] McNemar's test

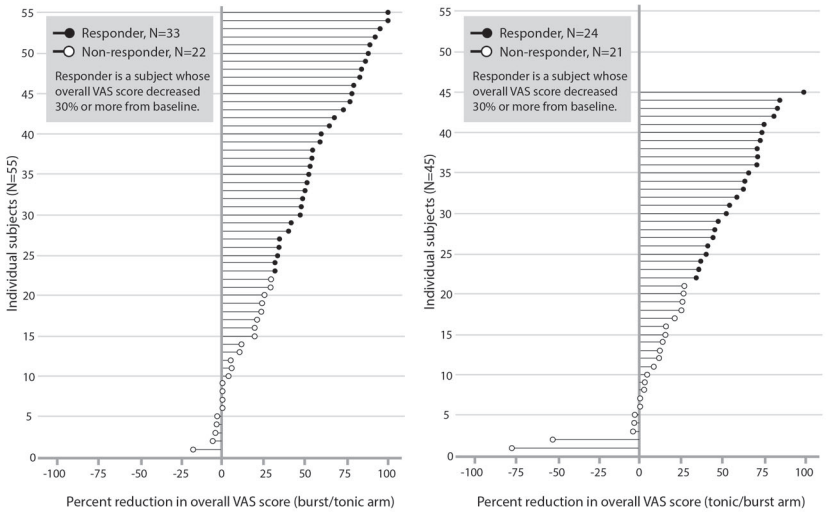
The following figure shows the percentage of pain relief for burst stimulation (left graph) and tonic stimulation (right graph) in individual subjects overall from baseline through week 24. For this figure, the responder rate was defined as a 30% or more reduction in the overall VAS score.

Figure 3. Percentage reduction (≥30% responder rate) in overall VAS score from baseline by stimulation mode



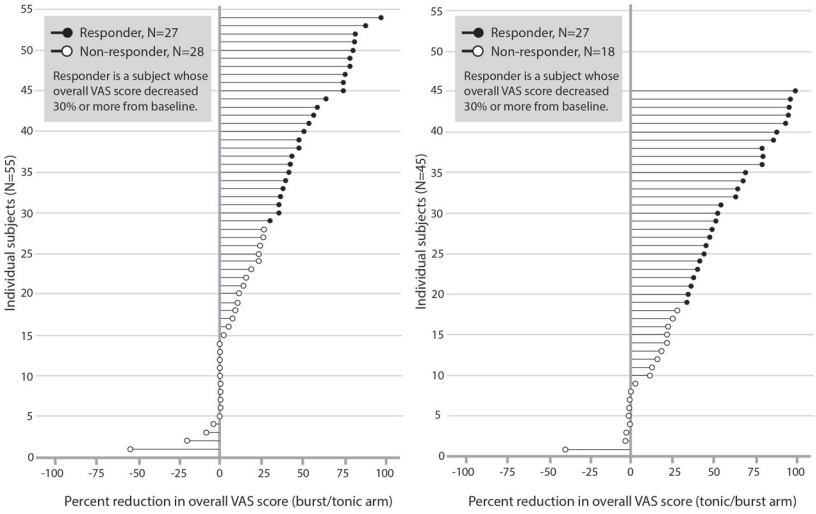
The following figure shows the percentage of pain relief from burst stimulation (left graph) and tonic stimulation (right graph) in the individual subjects for week 12, using a responder rate definition of 30%.

Figure 4. Percentage reduction (≥30% responder rate) in overall VAS score at week 12 from baseline



The following figure shows the percentage of pain relief from tonic stimulation (left graph) and burst stimulation (right graph) in the individual subjects for week 24, using a responder rate definition of 30%.

Figure 5. Percentage reduction (≥30% responder rate) in overall VAS score at week 24 from baseline



Data for paresthesia coverage at both 12 and 24 weeks were available for 73 subjects. More than half of the subjects (45 out of 73 [61.6%]) were paresthesia-free using burst stimulation, while only 2 subjects (2.7%) were paresthesia-free using tonic stimulation. In addition, 89.0% of subjects (65/73) experienced a reduction in paresthesia or no paresthesia with burst stimulation compared to tonic stimulation. The following table summarizes these results.

Table 17. Summary of paresthesia mapping with burst and tonic stimulation

Cross-Tabulation of Paresthesia by Stimulation Mode				
Stimulation mode		**Tonic**		
	Paresthesia	No	Yes	Overall
Burst	No	2/73 (2.7%)	45/73 (61.6%)	47/73 (64.4%)
	Yes	0/73 (0.0%)	26/73(35.6%)	26/73 (35.6%)
	Overall	2/73 (2.7%)	71/73 (97.3%)	
Subjects with Reduction of Paresthesia				
Reduction of 100% (No paresthesia)			45/73 (61.6%)	
Reduction of 1%–99%			20/73 (27.4%)	
No Reduction			8/73 (11.0%)	

The mean percentage of paresthesia coverage for burst is significantly lower than that for tonic. The following table summarizes the results of the test of the hypothesis of equality between burst and tonic stimulation. On average, subjects reported only 4.5% of the mapped body segments had paresthesia with burst stimulation compared to 22.7% with tonic stimulation. This difference represents an 80.2% relative reduction in paresthesia coverage with burst stimulation over tonic stimulation.

Table 18. Percentage of paresthesia coverage

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Burst			
Mean ±SD (N)	3.9±6.6 (37)	5.0±10.5 (36)	4.5±8.7 (73)
Minimum, Median, Maximum	0.0, 0.0, 23.4	0.0, 0.0, 51.1	–
Tonic			
Mean ±SD (N)	20.1±14.3 (37)	25.3±18.1 (36)	22.7±16.3 (73)
Minimum, Median, Maximum	0.0, 17.0, 59.6	0.0, 20.2, 66.0	–
Burst-Tonic			
Mean ±SD (N)	-16.2±14.5 (37)	-20.3±19.5 (36)	–
Minimum, Median, Maximum	-57.4, -12.8, 8.5	-61.7, -18.1, 12.8	–
Burst-Tonic Average ± Pooled SD Across Arms		-18.2±8.6	
95% CI		22.2, -14.2	

Additional Nonpowered Effectiveness

The following data consist of descriptive secondary and additional endpoints that were predetermined within the clinical study protocol. See “Clinical Endpoints” (page 6), “Clinical Endpoints” (page 39), “Clinical Endpoints” (page 49). Additional descriptive (nonpowered) data have also been provided.

Pain Measures

The FDA requested analyses to be performed on overall pain, trunk and limb VAS pain measures from baseline to 12 weeks. Because the study had a crossover design in which subjects were randomized to receive either tonic stimulation or burst stimulation from activation to 12 weeks, these analyses were performed to evaluate study treatment to exclude the possibility of an unequal carryover effect that would influence the results. Within the crossover design of this study, analyses of the data from baseline to 24 weeks would not provide the same meaningful evaluation of the study treatment.

As shown in the following table, the average changes in overall VAS score from baseline to week 12 were -32.1 and -26.4 for burst and tonic stimulation, respectively. The difference was -5.8 with a 95% UCB for a mean difference of 2.9, which is less than the non-inferiority margin of 7.5. Therefore, despite the smaller sample size, the primary endpoint of non-inferiority was met.

Table 19. Change in overall VAS score from baseline to week 12

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic
Stimulation	Tonic	Burst
VAS at Baseline		
Mean ±SD (N)	72.7±11.4 (45)	76.3±11.3 (55)
Minimum, Maximum	44.4, 90.3	43.9, 98.9
VAS at Week 12		
Mean ±SD (N)	46.3±22.8 (45)	44.2±25.3 (55)
Minimum, Maximum	1.0, 88.1	0.0, 98.1
Burst-Tonic		

Table 19. Change in overall VAS score from baseline to week 12

Randomization	**Arm 1: tonic/burst**	**Arm 2: burst/tonic**
Mean ±SD (N)	-26.4±24.9 (45)	-32.1±26.7 (55)
Minimum, Maximum	87.4, 34.0	87.7, 15.0
Burst-Tonic	-5.8±25.9	
95% UCB on Difference (Burst-Tonic)	2.9	
Non-Inferiority Margin	7.5	
***p*-value for Non-Inferiority Test**	0.006	
***p*-value for Superiority Test**	0.136	

The following table shows a cross-tabulation of responder rates (≥50% decrease in overall VAS score from baseline) with burst and tonic stimulation. A total of 49 subjects (49%) responded to tonic stimulation, burst stimulation, or both. The overall VAS scores decreased by at least 50% for more subjects with burst stimulation than with tonic stimulation (17 versus 10).

Table 20. Responder rates (decrease of ≥50**%** from baseline) for overall daily VAS score

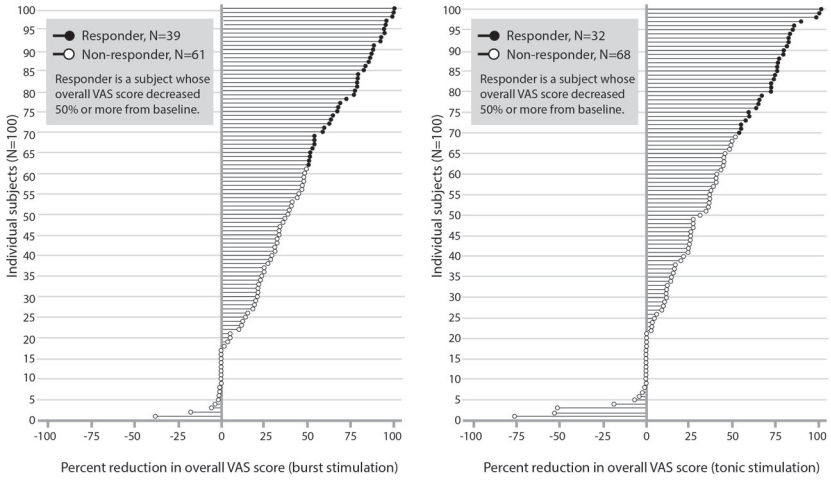
Overall Responder Rate			
Burst subjects (n/N)	39/100 (39.0%)		
Tonic subjects (n/N)	32/100 (32.0%)		
Difference in responder rate with 95% CI* (Burst-Tonic)	7.0% (-1.0%, 19.0%)		
Cross-Tabulation of Responders by Stimulation Mode			
Stimulation mode		**Tonic**	
Burst	**Responder****	No	Yes
	No	51/100 (51.0%)	10/100 (10.0%)
	Yes	17/100 (17.0%)	22/100 (22.0%)

* 95% CI was calculated using asymptotic method without continuity correction. (May and Johnson, 1997; Newcombe, 1998)

** Responder is defined as a subject whose overall VAS score decreased 50% or more from baseline.

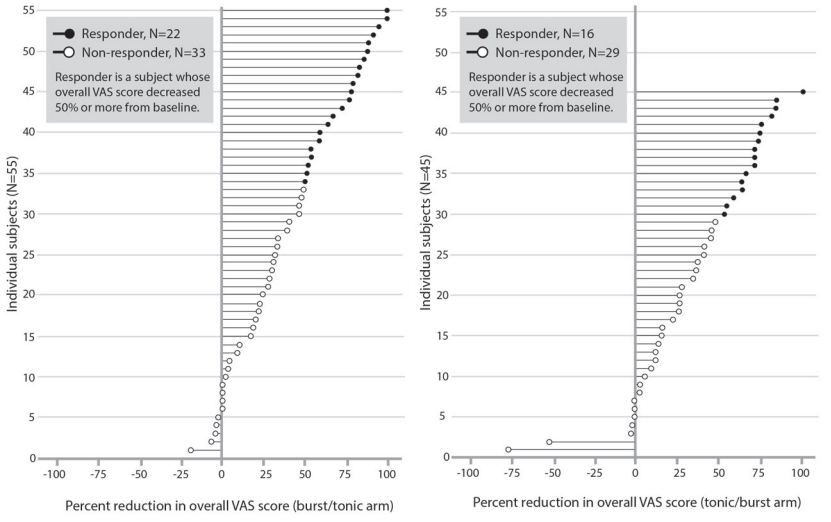
The following figure shows the percentage of pain relief for burst stimulation (left graph) and tonic stimulation (right graph) in individual subjects overall from baseline through week 24. For this figure, the responder rate was defined as a 50% or more reduction in the overall VAS score.

Figure 6. Percentage reduction (≥50% responder rate) in overall VAS score from baseline by stimulation mode



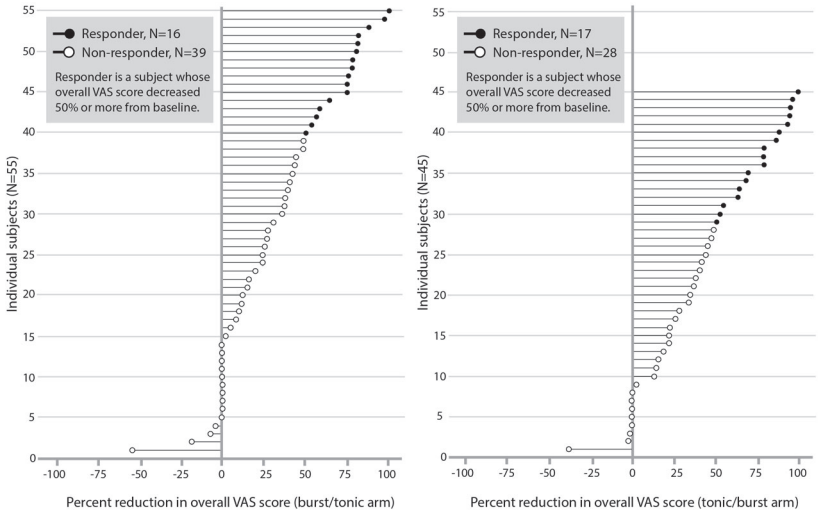
The following figure shows the percentage of pain relief from burst stimulation (left graph) and tonic stimulation (right graph) in the individual subjects at week 12, using a responder rate definition of 50%.

Figure 7. Percentage reduction (≥50% responder rate) in overall VAS score at week 12 from baseline



The following figure shows the percentage of pain relief from burst stimulation (left graph) and tonic stimulation (right graph) in the individual subjects at week 12, using a responder rate definition of 50%.

Figure 8. Percentage reduction (≥50% responder rate) in overall VAS score at week 24 from baseline



The following table summarizes the proportion of subjects with a decrease in overall VAS score by <30%, ≥ 30% and <50%, and ≥50% under each stimulation mode. Overall, more subjects experienced a reduction in overall VAS score of ≥50% while using burst stimulation than while using tonic stimulation (39 versus 32) and fewer subjects experienced reduction in overall VAS score by <30% while using burst stimulation (40 versus 49).

Table 21. Summary of decrease in overall VAS score from baseline by three categories

Decrease in Overall VAS From Baseline	Burst	Tonic
Arm 1: Tonic/Burst		
<30%	18/45 (40.0%)	21/45 (46.7%)
≥30%, <50%	10/45 (22.2%)	8/45 (17.8%)
≥50%	17/45 (37.8%)	16/45 (35.6%)
Arm 2: Burst/Tonic		
<30%	22/55 (40.0%)	28/55 (50.9%)
≥30%, <50%	11/55 (20.0%)	11/55 (20.0%)
≥50%	22/55 (40.0%)	16/55 (29.1%)
All Subjects		
<30%	40/100 (40.0%)	49/100 (49.0%)
≥30%, <50%	21/100 (21.0%)	19/100 (19.0%)
≥50%	39/100 (39.0%)	32/100 (32.0%)

The following two tables summarize trunk VAS scores for the randomization subject population and only from baseline to 12 weeks. The complete data show that trunk VAS scores for burst stimulation were lower than those during tonic stimulation by 5.7. Average changes for trunk VAS scores for baseline to week 12 are also lower for burst stimulation by 8.9.

Table 22. Summary of trunk VAS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Burst			
Mean ±SD (N)	39.7±25.3 (45)	41.8±25.8 (55)	40.9±25.5 (100)
Minimum, Median, Maximum	0.6, 38.0, 85.4	0.0, 40.6, 99.0	–
Tonic			
Mean ±SD (N)	44.2±21.9 (45)	48.8±25.6 (55)	46.7±24.0 (100)
Minimum, Median, Maximum	0.6, 48.9, 84.0	0.0, 51.1, 86.7	–
Burst-Tonic			
Mean ±SD (N)	-4.5±22.0 (45)	-7.0±23.1 (55)	–
Minimum, Median, Maximum	-49.6, -3.7, 57.9	-75.7, -2.3, 36.4	–
Burst-Tonic Average ± Pooled SD Across Arms		-5.7±11.3	
95% CI		-10.3, -1.2	

Table 23. Change in trunk VAS score from baseline to week 12

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic
Stimulation	**Tonic**	**Burst**
VAS at Baseline		
Mean ±SD (N)	70.4±17.2 (45)	77.0±11.6 (55)
Minimum, Maximum	19.3, 98.3	42.6, 97.1
VAS at Week 12		
Mean ±SD (N)	44.2±21.9 (45)	41.8± 25.8 (55)
Minimum, Maximum	0.6, 84.0	0.0, 99.0
Burst-Tonic		
Mean ±SD (N)	26.3±23.4 (45)	35.2±27.0 (55)
Minimum, Maximum	87.0, 36.4	83.7, 7.3
Burst-Tonic	-8.9±25.4	
95% CI	-19.2, 1.2	

The following two tables summarize limb VAS scores for the randomization subject population and only from baseline to 12 weeks. The complete data show that limb VAS scores for burst stimulation were lower than those during tonic stimulation by 4.7. Average changes for limb VAS scores for baseline to week 12 are also lower for burst stimulation by 5.8.

Table 24. Summary of limb VAS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Burst			

Table 24. Summary of limb VAS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Mean ±SD (N)	37.2±27.8 (44)	35.9±27.1 (54)	36.5±27.3 (98)
Minimum, Median, Maximum	0.7, 38.2, 100.0	0.0, 30.0, 98.9	–
Tonic			
Mean ±SD (N)	37.2±24.2 (44)	45.2±27.3 (54)	41.6±26.1 (98)
Minimum, Median, Maximum	0.7, 36.2, 82.6	0.0, 43.6, 99.0	–
Burst-Tonic			
Mean ±SD (N)	-0.0±22.2 (44)	-9.3±22.9 (54)	–
Minimum, Median, Maximum	-44.0, -0.1, 82.0	-69.3, -5.2, 40.1	–
Burst-Tonic Average ± Pooled SD Across Arms		-4.7±11.3	
95% CI		-9.2, -0.1	

NOTE: This analysis includes only subjects who reported limb pain at baseline.

Table 25. Change in limb VAS score from baseline to week 12

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic
Stimulation	**Tonic**	**Burst**
VAS at Baseline		
Mean ±SD (N)	68.1±21.0 (44)	72.5±21.6 (54)
Minimum, Maximum	0.4, 93.0	2.1, 98.3
VAS at Week 12		
Mean ±SD (N)	37.2±24.2 (44)	35.9±27.1 (54)
Minimum, Maximum	0.7, 82.6	0.0, 98.9
Burst-Tonic		
Mean ±SD (N)	30.9±25.1 (44)	36.6±29.7 (54)
Minimum, Maximum	88.0, 13.3	89.1, 16.1
Burst-Tonic	-5.8±27.7	
95% CI	-16.9, 5.4	

The following table summarizes worst VAS scores for the randomization subject population. The data shows that burst stimulation worst VAS scores were lower than those during tonic stimulation by 4.1 points.

Table 26. Summary of worst VAS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Burst			
Mean ±SD (N)	52.2±27.9 (45)	52.3±26.9 (55)	52.3±27.2 (100)

Table 26. Summary of worst VAS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Minimum, Median, Maximum	0.4, 54.4, 100.0	0.0, 50.1, 97.7	–
Tonic			
Mean ±SD (N)	54.3±24.4 (45)	58.5±26.1 (55)	56.6±25.3 (100)
Minimum, Median, Maximum	0.8, 54.1, 99.0	0.0, 63.3, 99.3	–
Burst-Tonic			
Mean ±SD (N)	-2.1±25.8 (45)	-6.2±22.8 (55)	–
Minimum, Median, Maximum	-57.0, -0.4, 83.1	-70.1, -2.4, 54.6	–
Burst-Tonic Average ± Pooled SD Across Arms		-4.1±12.1	
95% CI		-9.0, 0.7	

Device Satisfaction and Stimulation Preference

At each follow-up visit, subjects specified their overall level of satisfaction with the device, and they specified their preference with the stimulation mode at the week-24 visit. The following tables show that most subjects were satisfied with the device therapy during both stimulation modes (78.1%), few subjects were dissatisfied with the device (4.2%), and a similar number of subjects had opposite responses for burst and tonic. These data are reflected more clearly in the summary of stimulation preference, which shows that more than two-thirds of subjects (70.8%) preferred burst stimulation over tonic stimulation. While most subjects preferred burst stimulation, 18 subjects (18.8%) still preferred tonic stimulation. This is important to note because the investigational device is capable of both stimulation modes.

Table 27. Subject satisfaction summary at week 24

Satisfaction Level		Burst	Tonic
Burst subjects (n/N)		85/96 (88.5%)	82/96 (85.4%)
Tonic subjects (n/N)		11/96 (11.5%)	14/96 (14.6%)
Difference in satisfaction rate (burst-tonic)		3.1%	
95% CI of difference in satisfaction rate (lower bound, upper bound)		-5.3%, -11.5%	
Cross-Tabulation of Satisfaction Level by Stimulation Mode			
Stimulation mode		**Tonic**	
Burst	**Satisfaction Level**	Dissatisfied*	Satisfied**
	Dissatisfied*	4/96 (4.2%)	7/96 (7.3%)
	Satisfied**	10/96 (10.4%)	75/96 (78.1%)

* Dissatisfied is a combination of “very dissatisfied,” “dissatisfied,” and “neither satisfied nor dissatisfied.”

** Satisfied is a combination of “satisfied and very satisfied.”

Table 28. Summary of subject stimulation preferences at week 24

	Stimulation Preference			
	Burst Stimulation	Tonic Stimulation	No Preference	95% CI*
Arm 1: Tonic/Burst	37/45 (82.2%)	3/45 (6.7%)	5/45 (11.1%)	–
Arm 2: Burst/Tonic	31/51 (60.8%)	15/51 (29.4%)	5/51 (9.8%)	–
All Subjects	68/96 (70.8%)	18/96 (18.8%)	10/96 (10.4%)	60.7%, 97.7%

* 95% CI of proportion of subjects preferring burst stimulation

Psychosocial Health and Physical Function Measures

The PGIC questionnaire was completed at the week-12 and week-24 visits and was used to evaluate the subject's impression of change since beginning the study treatment. The following table shows the summary of responses to this questionnaire pooled across the two arms. Overall, the proportion of subjects whose global impression was moderately better, better, or a great deal better was comparable between the two stimulation modes (72/97 for burst versus 71/96 for tonic).

Table 29. Summary of PGIC questionnaire

PGIC	Burst	Tonic
No change (or condition has got worse)	6/97 (6.2%)	1/96 (1.0%)
Almost the same, hardly any change at all	7/97 (7.2%)	11/96 (11.5%)
A little better, but no noticeable change	7/97 (7.2%)	3/96 (3.1%)
Somewhat better, but the change has not made any real difference	5/97 (5.2%)	10/96 (10.4%)
Moderately better, and a slight but noticeable change	20/97 (20.6%)	16/96 (16.7%)
Better, and a definite improvement that has made a real and worthwhile difference	35/97 (36.1%)	43/96 (44.8%)
A great deal better, and a considerable improvement that has made all the difference	17/97 (17.5%)	12/96 (12.5%)

The following table presents the physical and mental component scores for the SF-36 quality of life survey. Burst stimulation had higher pooled scores than tonic stimulation with a difference of 0.4 for the physical component score and 0.7 for the mental component score. It is important to note that baseline scores for the mental component of the SF-36 (48.7) are near the normative mean (50.0) for this subscale (Ware, 2000), indicating that the subject's quality of life based on mental health was about the same as the general population (Bell, 2015; Verkerk, 2015) and were not representative of chronic pain patients (Elliott et al, 2003).

Table 30. Components of SF-36 quality of life physical and mental scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Physical Component Scores			
Baseline			
Mean ±SD (N)	29.0±6.5 (42)	28.3±8.3 (47)	28.6±7.5 (89)
Minimum, Median, Maximum	16.2, 27.7, 45.6	12.9, 27.7, 49.3	–
Burst			
Mean ±SD (N)	37.3±8.4 (42)	35.3±8.3 (47)	36.2±8.4 (89)

Table 30. Components of SF-36 quality of life physical and mental scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Minimum, Median, Maximum	23.2, 37.8, 53.6	20.7, 34.8, 51.2	–
Tonic			
Mean ±SD (N)	36.1±8.0 (42)	35.6±10.1 (47)	35.8±9.2 (89)
Minimum, Median, Maximum	22.3, 36.1, 55.6	18.9, 34.4, 64.6	–
Burst-Tonic			
Mean ±SD (N)	1.1±7.3 (42)	-0.3±7.0 (47)	–
Minimum, Median, Maximum	-15.4, 2.1, 19.1	-17.8, 0.6, 19.5	–
Burst-Tonic Average ± Pooled SD Across Arms		0.4±3.6	
95% CI		-1.1, -1.9	
Mental Component Scores			
Baseline			
Mean ±SD (N)	47.1±12.9 (42)	50.2±11.6 (47)	48.7±12.3 (89)
Minimum, Median, Maximum	18.6, 48.4, 71.4	24.5, 54.4, 69.5	–
Burst			
Mean ±SD (N)	50.2±12.6 (42)	52.3±9.6 (47)	51.3±11.1 (89)
Minimum, Median, Maximum	16.1, 50.9, 72.5	31.2, 56.2, 68.6	–
Tonic			
Mean ±SD (N)	49.1±11.9 (42)	52.0±9.8 (47)	50.6±10.9 (89)
Minimum, Median, Maximum	19.3, 49.6, 67.7	25.6, 53.5, 64.2	–
Burst-Tonic			
Mean ±SD (N)	1.1±8.4 (42)	-0.3±7.9 (47)	–
Minimum, Median, Maximum	-26.5, 1.5, 21.3	-20.1, -0.3, 19.3	–
Burst-Tonic Average ± Pooled SD Across Arms		0.7±4.1	
95% CI		-1.0, 2.5	

The following table shows a summary of ODI scores. Subjects experienced a reduction in ODI scores from baseline during both stimulation modes. However, neither burst nor tonic stimulation produced clinically meaningful changes on the ODI. One reason for this observation may be the relatively low baseline scores observed in this population. The baseline score for the ODI was 49.1, which is less than what is typical for chronic pain patients. Typical scores are in the 61- to 80-point range (Kumar, 2007). Thus, in light of the low baseline ODI scores, a significant improvement would not necessarily be expected.

Table 31. Summary of ODI scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Baseline			
Mean ±SD (N)	48.9±11.3 (45)	49.2±10.6 (50)	49.1±10.9 (95)
Minimum, Median, Maximum	24.0, 50.0, 80.0	17.8, 50.0, 72.0	–
Burst			
Mean ±SD (N)	33.4±16.9 (45)	37.5±15.6 (50)	35.6±16.3 (95)
Minimum, Median, Maximum	0.0, 32.0, 80.0	4.0, 41.0, 70.0	–
Tonic			
Mean ±SD (N)	34.4±15.3 (45)	36.5±14.3 (50)	35.5±14.8 (95)
Minimum, Median, Maximum	0.0, 34.0, 74.0	0.0, 37.9, 72.0	–
Burst-Tonic			
Mean ±SD (N)	-1.0±12.5 (45)	1.0±11.8 (50)	–
Minimum, Median, Maximum	28.0, -2.0, 40.0	24.0, 2.0, 44.0	–
Burst-Tonic Average ± Pooled SD Across Arms		0.0±6.1	
95% CI		-2.5, 2.5	

The Short Form McGill Pain Questionnaire (SF MPQ-2) assesses pain quality and the intensity or severity of those qualities. The following table shows a summary of the mean SF MPQ-2 score. Both burst and tonic stimulation show improvement from baseline scores.

Table 32. Summary of SF MPQ-2 scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Baseline			
Mean ±SD (N)	4.5±1.8 (44)	4.6±1.2 (51)	4.5±1.5 (95)
Minimum, Median, Maximum	0.5, 4.4, 7.7	1.5, 4.5, 7.4	–
Burst			
Mean ±SD (N)	2.0±2.0 (44)	2.2±1.4 (51)	2.1±1.7 (95)
Minimum, Median, Maximum	0.0, 1.3, 8.0	0.0, 2.2, 5.3	–
Tonic			
Mean ±SD (N)	2.2±1.8 (44)	2.4±1.7 (51)	2.3±1.8 (95)
Minimum, Median, Maximum	0.0, 1.7, 8.5	0.0, 2.4, 8.0	–
Burst-Tonic			
Mean ±SD (N)	-0.2±1.6 (44)	-0.2±1.2 (51)	–

Table 32. Summary of SF MPQ-2 scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Minimum, Median, Maximum	4.3, -0.1, 5.3	-3.0, -0.2, 2.0	–
Burst-Tonic Average ± Pooled SD Across Arms		-0.2±0.7	
95% CI		-0.5, 0.1	

The PCS measures negative thoughts and feelings associated with pain. The following table shows the overall PCS scores. Both burst and tonic stimulation reduced the PCS score; however, neither produced clinically meaningful changes on the PCS. Again, the reason for this observation may be the relatively low baseline scores observed in the study population. The average baseline PCS score of 20.4 was well below what is considered to reflect a clinically relevant level of pain catastrophizing, which is a score that is more than 30 (Sullivan, 2009).

Table 33. Summary of PCS scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Baseline			
Mean ±SD (N)	21.0±11.9 (45)	20.0±11.8 (51)	20.4±11.8 (96)
Minimum, Median, Maximum	1.0, 20.0, 47.0	0.0, 20.0, 44.0	–
Burst			
Mean ±SD (N)	10.3±11.1 (45)	14.6±10.9 (51)	12.6±11.1 (96)
Minimum, Median, Maximum	0.0, 8.0, 50.0	0.0, 15.0, 52.0	–
Tonic			
Mean ±SD (N)	12.5±11.2 (45)	11.5±11.6 (51)	12.0±11.4 (96)
Minimum, Median, Maximum	0.0, 12.0, 43.0	0.0, 9.0, 45.0	–
Burst-Tonic			
Mean ±SD (N)	-2.2±10.3 (45)	3.1±11.8 (51)	–
Minimum, Median, Maximum	-24.0, 0.0, 31.0	-22.0, 2.0, 52.0	–
Burst-Tonic Average ± Pooled SD Across Arms		0.5±5.6	
95%CI		-1.8, 2.7	

The BDI‡-II was completed at baseline, week 12, and week 24. Higher scores indicate higher levels of depression symptoms. Subjects with moderate to severe depression symptoms, with a score of 24 or more at baseline, were not eligible to continue in the study. The mean baseline score (10.1) indicates the subject population had minimal depression symptoms. The minimal depression symptoms that were observed at baseline continued to be observed under both stimulation modes at follow-up. The BDI-II scores may have remained the same because those subjects with clinically significant depression symptoms were excluded from the study. Further, an improvement from minimal depression symptoms would not necessarily be expected. The following table shows a summary of BDI-II scores.

Table 34. Summary of BDI-II scores

Randomization	Arm 1: tonic/burst	Arm 2: burst/tonic	Pooled
Baseline			
Mean ±SD (N)	10.5±6.6 (45)	9.8±5.5 (51)	10.1±6.0 (96)
Minimum, Median, Maximum	0.0, 9.0, 24.0	0.0, 9.0, 23.0	–
Burst			
Mean ±SD (N)	9.0±9.4 (45)	8.9±5.7 (51)	8.9±7.6 (96)
Minimum, Median, Maximum	0.0, 7.0, 50.0	0.0, 9.0, 24.0	–
Tonic			
Mean ±SD (N)	9.8±7.6 (45)	9.5±6.5 (51)	9.6±7.0 (96)
Minimum, Median, Maximum	0.0, 9.0, 35.0	0.0, 9.0, 27.0	–
Burst-Tonic			
Mean ±SD (N)	-0.8±6.1 (45)	-0.5±5.0 (51)	–
Minimum, Median, Maximum	-12.0, -2.0, 17.0	-18.0, -1.0, 13.0	–
Burst-Tonic Average ± Pooled SD Across Arms		-0.7±2.8	
95% CI		-1.8, 0.4	

Pain Medication

In the first 12 weeks, 6 subjects (2 using tonic stimulation, 4 using burst stimulation) increased pain medication. Between weeks 12 and 24, 15 subjects (5 using burst stimulation, 10 using tonic stimulation) increased pain medication. Altogether, 12 tonic stimulation subjects and 9 burst stimulation subjects increased pain medication. More subjects decreased pain medication during the study than increased it, and more subjects decreased medication while receiving burst stimulation (31 subjects) than while receiving tonic stimulation (27 subjects). The following table shows a summary of medication changes from activation for each stimulation mode.

Table 35. Summary of medication changes from activation

Medication Change	Burst	Tonic
Decreased	31/96 (32.3%)	27/96 (28.1%)
Increased	9/96 (9.4%)	12/96 (12.5%)
No change	56/96 (58.3%)	57/96 (59.4%)

Summary of Supplemental Clinical Information

This pivotal, prospective, multicenter, randomized, crossover study assessed the safety and effectiveness of a neurostimulation system which enables the use of both tonic and burst stimulation modes. Twenty (20) experienced pain centers in the United States participated in the study. One hundred seventy three (173) subjects were enrolled across the 20 sites, and all were diagnosed with chronic, intractable pain of the trunk and/or limbs; had an average overall VAS pain score of at least 60 on a 0-to-100 scale; and had attempted and previously failed at least 3 medically supervised treatments.

Conclusions Drawn from the Study

This section provides study conclusions based on stimulation effectiveness, safety, and risks and benefits, as well as overall conclusions.

Effectiveness Conclusions

This section provides conclusions on stimulation effectiveness.

- **Pain measures.** The primary effectiveness endpoint of non-inferiority was met (43.5 versus 48.7, ***p***< 0.001), and burst stimulation was found to be superior to tonic stimulation (***p***=0.017). Differences in VAS scores for burst stimulation and tonic stimulation from baseline were assessed for carryover effect, with no statistical difference (***p***=0.883). Burst stimulation was preferred by over two-thirds of subjects (70.8 %) who had responded to tonic stimulation during an SCS trial period.

  The mean VAS scores for trunk and limb pain were lower with burst stimulation than with tonic stimulation (40.9 versus 46.7 for trunk and 36.5 versus 41.6 for limb, respectively). The percentage of subjects reporting at least a 30% decrease in VAS pain diary scores for the average overall pain was higher with burst stimulation than with tonic stimulation (60.0% compared to 51.0%). A higher percentage was also observed in subjects reporting at least a 50% decrease in VAS pain diary scores (39.0% compared to 32.0%).

- **Paresthesia.** More than half of subjects (61.6%) reported no paresthesia during burst stimulation while 97.3% of subjects reported paresthesia during tonic stimulation. When compared to tonic stimulation, burst stimulation was associated with a reduction of paresthesia or no paresthesia, representing a relative reduction of 80.2% in average paresthesia from tonic stimulation to burst stimulation.

  Programming parameters for tonic stimulation are based on long-term experience and subject-optimization needs, while burst programming parameters for pulse width and frequency were selected from feasibility studies and did not allow subject-specific customization except for amplitude adjustment. Future studies that optimize burst programming may show additional reduction in paresthesia.

- **Pain medication.** The use of pain medications decreased more often during burst stimulation (32.3%) than during tonic stimulation (28.1%). In addition, the use of pain medications increased less often during burst stimulation (9.4%) than during tonic stimulation (12.5%).

- **Psychosocial measures.** Based on the study exclusion criteria, only subjects with a BDI‡-II score of less than 24 could be enrolled. The exclusion of subjects with a BDI-II score of 24 or more most likely contributed to the observed low baseline scores for the other psychosocial measures, as depression has been shown to be directly related to quality of life, disability, and catastrophizing (Brenes, 2007; Currie & Wang, 2004; Richardson et al., 2009; Tennen et al., 2006). Other pain studies that have shown clinically significant changes for these domains have generally included such patients.

  The baseline scores for the SF-36 physical component (28.6), ODI (49.1), and PCS (20.4) in the study population were also below clinically relevant levels of impairment typically seen in SCS candidates in quality of life, disability (Kumar et al., 2007), and catastrophizing (Sullivan, 2009), respectively. Neither burst stimulation nor tonic stimulation produced clinically meaningful changes for any of these psychosocial measures. Based on the baseline scores, an improvement of the scores would not be expected.

Safety Conclusions

No device- or stimulation-related SAEs or any events categorized as unanticipated adverse device effects (UADEs) were reported during the study. Fewer stimulation-related events occurred during burst stimulation than tonic stimulation (13 events in 11 subjects and 16 events in 10 subjects, respectively).

Benefit-Risk Conclusions

The probable benefits of the device are based on this clinical study for burst stimulation. Effectiveness was demonstrated by the primary and powered secondary study endpoints. Burst stimulation was also shown to be safe as described in the safety conclusions.

- **Limitations.** The open label crossover design did not blind subjects as to whether they were receiving burst or tonic stimulation. The only randomized variable was the order in which a subject would experience each stimulation mode—burst stimulation first or tonic stimulation first. Blinding the stimulation mode was not feasible because subjects may have experienced different sensations with each mode. Since the mode was not blinded, investigator and subject bias may have affected the results for both tonic and burst stimulation modes.

  In addition, the study design did not allow an assessment of the placebo response. Placebo response is well known in pain studies due to the subjective nature of the pain assessment, and the duration of the placebo response may be long lasting. Finally, subjects in the study were required to maintain stable doses of their adjunctive pain medications. However, some subjects in both groups required additional pain medications; these subjects were considered non-responders for the stimulation mode in which they increased their medications and were accounted for in the statistical plan.

  Subjects had to complete a successful SCS trial using tonic stimulation before being implanted with a permanent system and the success of tonic stimulation during the trial period may have resulted in investigator and subject bias. Additionally, a washout phase was not included before switching between stimulation modes.

Overall Conclusions

The nonclinical laboratory testing performed on the SCS leads, SCS extensions, IPG, charger, patient programmer, and accessories demonstrates that the individual components, as well as the combined system, are reliable and that the probable health benefits from using the device outweigh any probable injury or illness from such use.

Further, the nonclinical laboratory studies that Abbott Medical conducted, when combined with the clinical experience, provide assurance that a Prodigy™ neurostimulation system using burst stimulation is safe and effective when treating chronic pain. The clinical experience also shows that burst stimulation is superior to tonic stimulation in reducing overall pain and provides additional advantages over tonic stimulation including patient preference and reduced paresthesia.

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Clinical Summary for Anatomical Lead Placement

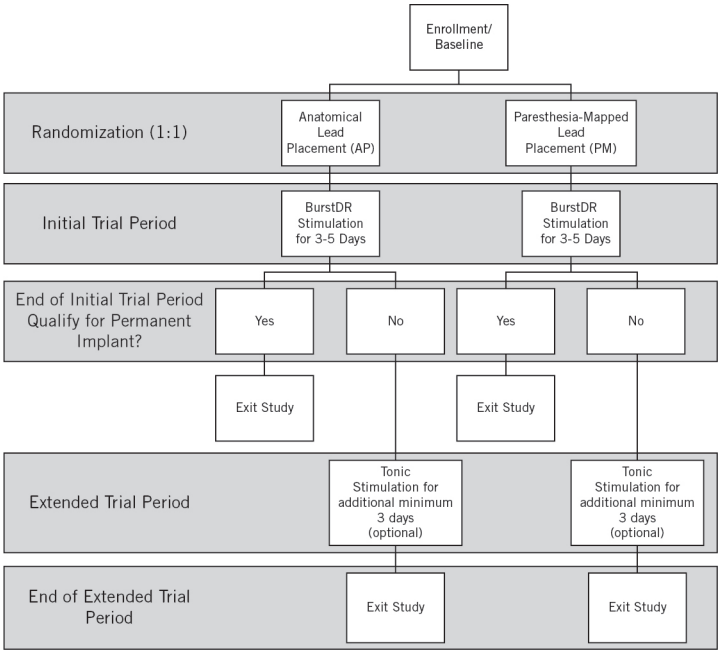
Abbott Medical conducted two clinical studies to compare effectiveness of BurstDR™ spinal cord stimulation (SCS) using traditional paresthesia-mapped lead placement or anatomical lead placement. DELIVERY evaluated the trial success rate for anatomical lead placement compared to traditional paresthesia-mapped lead placement in patients with chronic, intractable pain of the trunk and/or lower limbs. CRISP was performed to evaluate trial pain relief and outcomes up to one year after permanent implant from anatomically placed and paresthesia-mapped leads in patients with failed back surgery syndrome and predominant low back pain. The clinical studies support the SCS systems listed in “Clinical Studies” (page 1). The following sections present information and results for the two studies.

DELIVERY Study

Study Design

DELIVERY was a multicenter, randomized, controlled, single-blind, clinical study. The purpose was to compare trial success rate between anatomical lead placement (AP) and paresthesia-mapped (PM) lead placement techniques with the St. Jude Medical™ Invisible Trial System using BurstDR™ stimulation. Enrollment in the DELIVERY study (NCT03277378 on clinicaltrials.gov) began September 22, 2017 and ended August 23, 2018. A total of 288 subjects were enrolled at 23 sites in the United States, Europe, and Australia. The following figure shows the flow of study design.

Figure 9. DELIVERY study design flow



Patients who met the inclusion/exclusion criteria of the study signed the informed consent and were enrolled in the study. The enrolled subjects underwent baseline assessment prior to the trial. The subjects were blinded to treatment group and randomized in a 1:1 ratio. Trial procedures were as follows:

- AP group: When using one lead, the tip was placed at the superior endplate of T9. When using two leads, one lead was placed at the mid-body of T8 and the second was placed at the superior endplate of T9. Lead position was confirmed using fluoroscopy. This was followed by BurstDR stimulation during an initial trial evaluation period.

- PM group: The implanting physician confirmed coverage of the patient's primary pain location using intraoperative testing. This was followed by BurstDR stimulation during an initial trial evaluation period.

Subjects who successfully completed the trial exited the clinical study and continued treatment per the physician's standard of care. Any subject who did not qualify for a permanent system implant after the initial trial evaluation period was offered to participate in an extended trial evaluation period, at physician discretion, during which they were programmed with tonic stimulation. These subjects were followed through the completion of the extended trial period and exited the clinical study at the end of this period.

Clinical Inclusion and Exclusion Criteria

Inclusion Criteria

Subjects were limited to those who met all of the following criteria:

- Subject signed an informed consent to participate in the study.
- Subject was at least 18 years old.
- Subject had chronic, intractable pain of the trunk and/or lower limbs.
- Subject indicated for SCS therapy in accordance with the approved labelling.
- Indication of subject's pain profile to appropriate lead placement at one or more levels from T7 to T10 to achieve pain coverage.
- Subject scored a baseline of 6 or higher on the numeric rating scale (NRS) over the past 24 hours for "average overall pain" specific to the area(s) of chronic pain that could be treated with spinal cord stimulation.
- The Investigator evaluated the subject's medical record to ensure that the subject was a good candidate for implantation of a spinal cord stimulation system according to the system's Instructions for Use.
- Subject was willing to cooperate with the study requirements such as complying with the treatment regimen and completing all office visits.

Exclusion Criteria

Subjects were excluded if they met any of the following criteria:

- Subject had a spinal cord stimulation system currently implanted.
- Subject had previously failed a spinal cord stimulation therapy (either trial system evaluation or permanent system implant).
- Subject had a primary diagnosis of peripheral vascular disease, angina pectoris, or chronic migraine.
- Subject was scheduled to undergo an on-the-table trial evaluation (all-in-one procedure).
- Subject was scheduled to be implanted with one or more surgical paddle trial leads.
- Subject was participating in a clinical investigation that included an active treatment arm.
- Subject was unable to read and/or write.

Clinical Endpoints

The primary endpoint was the trial success rate for permanent system implant at the end of the trial evaluation period, defined by a composite where a subject met all the following conditions:

- Subject with >50% patient-reported pain relief (PRP) at the end of the trial evaluation.
- Trial evaluation period lasted a minimum of 3 days.
- Physician recommended subject for permanent system implant.
- Subject was willing to pursue a permanent system implant.

Subjects did not qualify for permanent system implant if there was <50% PRP at the end of a trial that lasted at least 5 days.

The secondary endpoint was the rate of physician preference for anatomical placement versus paresthesia-mapped placement at the end of the study. There were also descriptive endpoints reported using summary statistics:

- Overall procedure time (in-room to out-room), implant procedure time (needle-in to needle-out), and total time of intraoperative fluoroscopy exposure for each randomized group and stratified by number of leads and lead type (permanent lead or temporary lead).

- Programming time required for each randomized group.
- Change from pre-implant NRS in each randomized group to end of initial trial evaluation period and to the end of the extended trial evaluation period, as applicable.
- Number of subjects in each randomized group who have affirmative assessment for each of the independent criteria required for trial success.
- Proportion of subjects in each randomized group who do not qualify for permanent implant, but proceed with permanent implant per physician discretion.
- Time from trial system implant to >50% PRP measured by the number of days (also known as "wash-in period").
- Rate of serious adverse device effects (SADE) in each group.
- Number and proportion of meaningful lead migrations during the initial trial evaluation periods by treatment group. A meaningful lead migration is defined as a lead migration resulting in the inability to program for therapeutic response.
- Number and proportion of meaningful lead migrations during the initial trial evaluation period in subjects who have a temporary trial lead implant compared to subjects who have a permanent trial lead implant.
- Clinician assessment of anesthesia related difficulty (assessed primarily in the procedure room for the trial) on a 5-point Likert scale for each randomized group.
- Clinician assessment of lead placement difficulty on a 5-point Likert scale for each randomized group.
- Clinician affinity for lead placement technique at the end of the trial implant procedure.
- Trial success rate at the end of extended trial period.

Statistical Plan

The primary objective was to evaluate non-inferiority of trial success rate for anatomical lead placement, compared to paresthesia-mapped lead placement, at the end of the initial trial evaluation period. The non-inferiority margin was set at 15% with a significance level of 5%. The analysis required the 95% lower confidence bound on the difference of trial success rates using the Farrington-Manning method to exceed -15%.

The secondary objective was to demonstrate physician preference for anatomical placement over paresthesia-mapped placement. The analysis required the 95% lower confidence bound on the percentage of physicians who preferred anatomical placement over paresthesia-mapped placement to exceed 60%, using the Clopper-Pearson exact method.

Study Results

Demographics and Baseline Assessments

Between September 2017 and August 2018, 288 subjects at 23 investigational sites were enrolled; 18 subjects were withdrawn before randomization as shown in the following table. The average age of the randomized subjects was 63 ±14 years and 61% of the subjects were female. Subjects experienced pain for an average of 11.5 ±11.5 years at the time of study enrollment. Demographics and baseline characteristics were statistically comparable between the two randomized arms (all p >0.05). Many randomized subjects had a pain diagnosis of either radiculopathy (49.1%) or post laminectomy syndrome commonly known as failed back surgery syndrome (40.2%). In the sites located outside of the United States (OUS), the predominant pain diagnosis among the subjects was failed back surgery syndrome (68.6%).

Table 36. Demographics and baseline characteristics

Variable	All Randomized Subjects	Anatomical Lead Placement	Paresthesia-Mapped Lead Placement
Age (years)	**(N=270)**	**(N=135)**	**(N=135)**
Mean ±SD	62.8±13.5	61.8±13.2	63.9±13.8
Range (Min, Max)	(25, 89)	(31, 86)	(25, 89)
Gender, n (%)	**(N=270)**	**(N=135)**	**(N=135)**

Table 36. Demographics and baseline characteristics

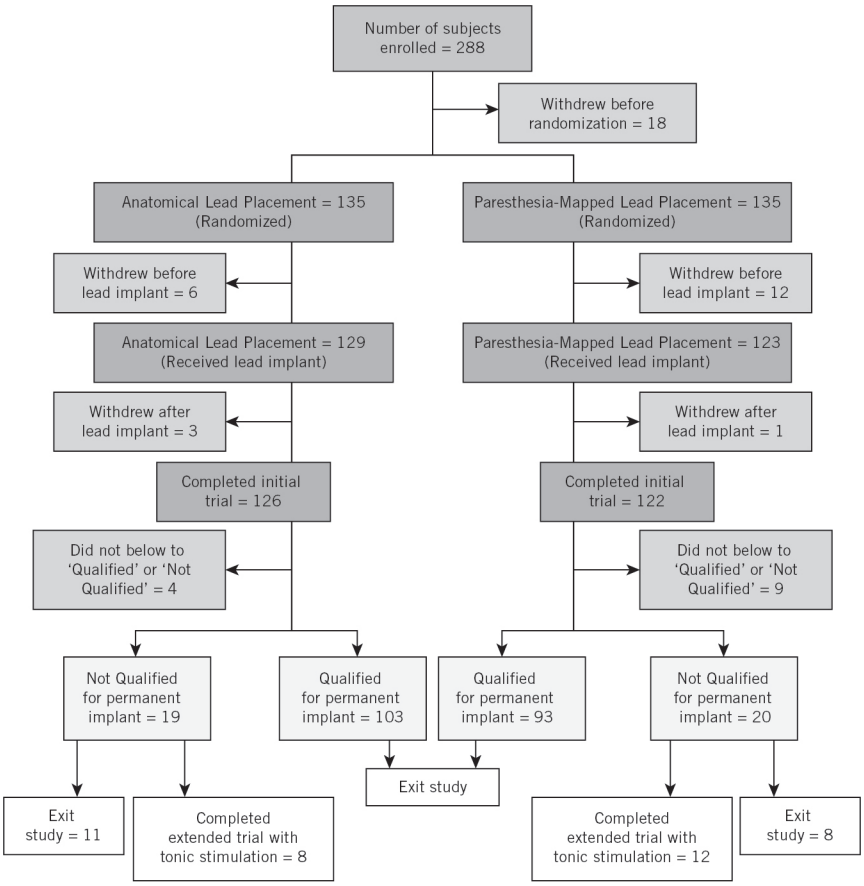
Variable	All Randomized Subjects	Anatomical Lead Placement	Paresthesia-Mapped Lead Placement
Female	165 (61.1%)	78 (57.8%)	87 (64.4%)
Male	105 (38.9%)	57 (42.2%)	48 (35.6%)
Race, US and Australia Only, n (%)	**(N=232)**	**(N=116)**	**(N=116)**
Black or African American	8 (3.4%)	5 (4.3%)	3 (2.6%)
Native Hawaiian or Other Pacific Islander	2 (0.9%)	1 (0.9%)	1 (0.9%)
White	201 (86.6%)	103 (88.8%)	98 (84.5%)
Other	21 (9.1%)	7 (6.0%)	14 (12.1%)
Years of having chronic pain	**(N=270)**	**(N=135)**	**(N=135)**
Mean ±SD	11.46±11.48	12.23±11.83	10.69±11.11
Range (Min, Max)	(0.08, 60.00)	(0.33, 58.08)	(0.08, 60.00)
Pain Primary Diagnosis, US Patients, n (%)	**(N=218)**	**(N=109)**	**(N=109)**
Chronic pain due to trauma	23 (10.6%)	16 (14.7%)	7 (6.4%)
Chronic pain syndrome	119 (54.6%)	53 (48.6%)	66 (60.6%)
Other chronic post procedural pain	32 (14.7%)	17 (15.6%)	15 (13.8%)
Other chronic pain	44 (20.2%)	23 (21.1%)	21 (19.3%)
Pain Secondary Diagnosis, US Patients, n (%)*	**(N=214)**	**(N=106)**	**(N=108)**
None	2 (0.9%)	1 (0.9%)	1 (0.9%)
Causalgia	6 (2.8%)	3 (2.8%)	3 (2.8%)
Post-laminectomy syndrome	86 (40.2%)	44 (41.5%)	42 (38.9%)
Lumbosacral plexus disorders	1 (0.5%)	0 (0.0%)	1 (0.9%)
Radiculopathy	105 (49.1%)	52 (49.1%)	53 (49.1%)
Intervertebral disc disorder with/without radiculopathy	20 (9.3%)	8 (7.5%)	12 (11.1%)
Complex regional pain syndrome	5 (2.3%)	3 (2.8%)	2 (1.9%)
Other	45 (21.0%)	22 (20.8%)	23 (21.3%)

Table 36. Demographics and baseline characteristics

Variable	All Randomized Subjects	Anatomical Lead Placement	Paresthesia-Mapped Lead Placement
Pain Diagnosis, Non-US Patients, n (%)*	**(N=51)**	**(N=26)**	**(N=25)**
Failed back surgery syndrome	35 (68.6%)	18 (69.2%)	17 (68.0%)
Causalgia	1 (2.0%)	0 (0.0%)	1 (4.0%)
Post-laminectomy syndrome	3 (5.9%)	1 (3.8%)	2 (8.0%)
Radiculopathy	7 (13.7%)	5 (19.2%)	2 (8.0%)
Lumbosacral plexus disorders	1 (2.0%)	0 (0.0%)	1 (4.0%)
Complex regional pain syndrome	1 (2.0%)	1 (3.8%)	0 (0.0%)
Other	3 (5.9%)	1 (3.8%)	2 (8.0%)

*Subjects may have more than one diagnosis.

Figure 10. DELIVERY study disposition of subjects



Procedural Results

Operative conditions and patient preparation were performed according to routine practice for each participating investigator. Implanters used either one or two trial or permanent leads at their discretion. Since most of the participating study sites were in the US, a majority of subjects were implanted with two trial leads. Implantation of permanent leads during the SCS trial procedure is sometimes done outside the US. The following table shows the number of leads implanted per subject.

Table 37. Number of leads implanted per subject (N=252)

Number of Leads Implanted	Trial Leads Implanted n (%)	Permanent Leads Implanted n (%)
2	203 (80.6%)	6 (2.4%)
1	24 (9.5%)	19 (7.5%)

Primary Effectiveness

Trial success was achieved in 84% (103/122) of patients undergoing AP lead placement and in 82% (93/113) of patients with PM lead placement. The estimated difference between the trial success rates for the AP and PM groups was 2.1%, and the 95% lower confidence bound of -6.1% was above the pre-specified non-

inferiority margin of -15%. Therefore, the primary endpoint indicating non-inferiority of AP lead placement compared to PM lead placement was satisfied ($p < 0.001$).

Secondary Effectiveness

Physicians who performed both techniques preferred anatomical lead placement in 70% of cases, compared to paresthesia-mapped placement for 30% of cases. The 95% lower confidence bound was 49.2%, but did not exceed the pre-specified performance goal of 60%.

Descriptive Endpoint Results

- The study noted differences in lead placement and total procedure times for anatomical placement compared to paresthesia-mapped placement in 203 subjects who received two trial leads.
  - Average lead placement time (needle-in to needle-out) was reduced by 31% for AP (14 ±9 minutes) compared with PM technique (21 ±11 minutes).
  - Average total procedure time (room-in to room-out) was reduced by 12% for AP (40 ±12 minutes) compared with PM technique (46 ±14 minutes).
- In 24 subjects who received a single trial lead:
  - Average lead placement time was reduced by 19% for AP (21 ±15 minutes) compared with PM technique (26 ±15 minutes).
  - Average total procedure time was reduced by 10% for AP (45 ±14 minutes) compared with PM technique (50 ±18 minutes).
- There were 25 cases with leads placed that would remain in for permanent implant, including 6 using two leads and 1 using a single lead. Average lead placement time for a single lead was 12 ±9 minutes for AP placement compared to a PM placement of 23 ±12 minutes. For implants with two leads, average lead placement time was 19 ±5 minutes for AP placement compared to 27 ±7 minutes for PM placement.
- Programming time for anatomical lead placement was 5.0 ±6.4 minutes, compared to 6.0 ±6.0 minutes for paresthesia-mapped lead placement.
- Decrease in mean NRS pain score was similar between groups (53.2% for AP and 53.8% for PM) at the end of initial trial evaluation period, and after extended trial evaluation period.
- The wash-in period to reach 50% patient-reported pain relief was 3.0 ±2.0 days for AP, compared to 3.3 ±2.8 days for PM placement.
- Both groups had one meaningful lead migration resulting in inability to program for therapeutic response during the initial evaluation period.
- No differences were observed between groups in anesthesia-related difficulty or lead placement difficulty.
- Compared to usual clinical practice, 35.7% of clinicians declared the highest affinity, for anatomical lead placement, meaning it was “very much” liked. Clinicians rated paresthesia-mapped lead placement “very much” liked 8.9% of the time compared to usual practice. Paresthesia-mapped lead placement was considered a usual practice for clinicians in 82.1% of trial procedures, and anatomical lead placement was already considered a usual practice 45.7% of the time.

Adverse Events

A total of 13 adverse events were reported during the study. There were two serious device-related adverse effects (SADEs), ten adverse device effects (ADEs), and one non-device related serious adverse event (SAE). The following table summarizes adverse events.

Table 38. Adverse events for each group, as reported by site investigators

Event Type	Number of Events	Anatomical Lead Placement	Paresthesia-Mapped Lead Placement
SADE	2	1	1
ADE	10	4	6
SAE	1	1	0

Table 38. Adverse events for each group, as reported by site investigators

Event Type	Number of Events	Anatomical Lead Placement	Paresthesia-Mapped Lead Placement
Total	**13**	**6**	**7**

One non-device-related SAE occurred in the AP group undergoing permanent lead implant in which a patient was hospitalized for stroke.

Two device- or procedure-related serious adverse events were reported. There was one spinal cord compression in the AP group, and one occurrence of stimulation in unwanted places in the PM group, as shown in the following table.

Table 39. Summary of serious adverse device effects (SADEs)

Event Description	Related to	Subjects with Events n (%)	Number of Events
Spinal cord compression	Procedure, Lead	1 (0.3%)	1
Stimulation in unwanted places	Procedure	1 (0.3%)	1

Ten non-serious adverse device effects were reported at the time of study close-out, as shown in the following table.

Table 40. Summary of adverse device effects (ADEs)

Event Description	Related to	Subjects with Events n (%)	Number of Events
Cerebrospinal fluid leakage	Procedure	1 (0.3%)	1
Hematoma	Procedure	1 (0.3%)	1
Lead migration, causing changes in stimulation or reduced pain relief	Leads (4), Procedure (1)	4 (1.4%)	4
New leg pain on walking instead of original dysaesthetic sensation	Procedure, EPG, Lead, Accessory	1 (0.3%)	1
Persistent pain at the lead site	Procedure (2)	2 (0.7%)	2
Unpleasant sensations or motor disturbances	Procedure	1 (0.3%)	1

There were no deaths reported in the study. The AEs reported in this study were anticipated for the study population and are considered acceptable.

Conclusions Drawn from the Study

Effectiveness

Leads placed using an anatomical approach resulted in equivalent SCS trial success when compared with leads placed using paresthesia mapping. Physicians who performed both implant techniques preferred AP over PM placement by 70% to 30%, although the difference did not reach statistical significance. When two trial leads were used, average lead placement time (needle-in to needle-out) was reduced by 31% for AP compared with PM technique. Furthermore, average total procedure time (room-in to room-out) was reduced by 12% for AP compared with PM technique. Anatomical placement technique resulted in a less complex procedure and more predictable lead placements.

Safety

No deaths were reported during the study. There were similar rates of AEs between the two groups.

Study Limitations

The study was designed to collect data during the initial trial period only. However, CRISP was a prospective, multicenter, randomized, double-blinded, crossover study that collected data up to one year after permanent implant.

Benefit-Risk Conclusions

This clinical study established non-inferiority of the trial success rate for anatomical placement of leads compared with paresthesia-mapped placement. An acceptable rate of events occurred in the DELIVERY study.

Overall Conclusions

When using BurstDR™ stimulation, the anatomical placement of leads during the trial phase is a viable alternative to paresthesia-mapped lead placement.

CRISP Study

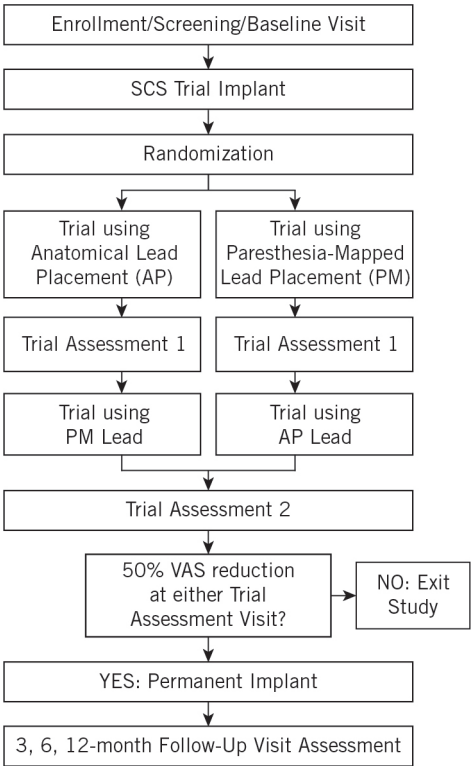
Study Design

The study was a prospective, multicenter, randomized, double-blinded, crossover feasibility study that consisted of two phases: spinal cord stimulation (SCS) trial and permanent implant follow-up. Subjects were evaluated at SCS trial followed by evaluation at 3, 6, and 12 months post-permanent implantation.

Subjects began to enroll in the study on October 28, 2016 with the study enrollment completing on June 5, 2018. All follow-up visits were completed on August 19, 2019. The study included a total of 60 subjects at two investigational sites in Europe (NCT02986074 on clinicaltrials.gov).

The study compared the therapeutic efficacy of the conventional, paresthesia mapping-based BurstDR™ stimulation implantation strategy to a more novel, anatomical approach. The following figure shows the flow of study design.

Figure 11. CRISP study design flow



Subjects with failed back surgery syndrome (FBSS) with predominant low back pain were informed about the study to determine if they were interested in participating. After subjects signed an informed consent agreement, they were screened according to the inclusion and exclusion criteria and underwent a baseline evaluation to collect primary and secondary outcome measures prior to the SCS trial. Subjects scored pain ratings using visual analog scale (VAS), quality of life using EuroQol-5D instrument (EQ-5D), and functionality using Oswestry disability index (ODI) during the course of the study. Those subjects who met the criteria to participate were scheduled to receive a St. Jude Medical™ Invisible Trial System for spinal cord stimulation (SCS). During the trial implant, two SCS leads were implanted using standard surgical techniques. One lead was implanted using paresthesia mapping to maximize the overlap between painful regions and evoked paresthesia according to standard clinical practice. A second lead was implanted using a novel anatomical

approach. Under fluoroscopic guidance, the lead was positioned above the anatomical midline such that it extends over the T9-T10 junction.

Subjects underwent BurstDR stimulation therapy using both leads. Subjects were randomized 1:1 to decide which lead they would evaluate first (lead placed using paresthesia mapping first and then lead placed by anatomical approach or vice versa) and were blinded to the randomization order. The SCS trial consisted of two phases and lasted for a total of 4 weeks. During the first trial phase, BurstDR stimulation was delivered for two weeks using the first lead in the randomization sequence. Subjects were then crossed over to the second trial phase during which BurstDR stimulation was delivered for an additional two weeks using the second lead in the randomization sequence. If the VAS score during either of the two trial assessments is reduced by at least 50% compared to the baseline score, the subject was considered for permanent SCS implant.

Subjects who underwent a successful trial (≥50% overall pain relief) were implanted with a Proclaim™, Prodigy™, or Prodigy MRI™ neurostimulation system. The lead that was activated depended on the subject's preference following the trial. For subjects without a preference, the lead placed using the anatomical technique was activated. Subjects were followed for 12 months to assess the long-term treatment outcome.

Clinical Inclusion and Exclusion Criteria

Inclusion Criteria

Subjects were limited to those who met all of the following criteria:

- Subject signed an informed consent to participate in the study.
- Subject was at least 18 years old.
- Subject had failed to respond to at least 6 months of conventional treatment including pharmacological treatment, physical therapy, epidural injections and/or radiofrequency therapy as per NICE Tag 0159.
- Subject with failed back surgery syndrome (FBSS) had predominant low back pain.
- Subject scored a baseline of at least 6.0 out of 10.0 for low back and pain intensity on the visual analog scale (VAS).
- Subject's pain-related medication regimen with a total opioid equivalent of 120 mg/day or less was stable for at least 28 days before enrolling in the study, and was willing to stay on the medication with no dose adjustments until activation of the permanently implanted SCS device.
- The Investigator evaluated the subject's medical record to ensure that the subject was a good candidate for a neurostimulation system.
- Subject was willing to cooperate with the study requirements such as complying with the treatment regimen and completing all office visits.
- Subject was female candidate of childbearing potential who agreed to commit to using effective contraception (including, but not limited to, sterilization, barrier devices, oral contraceptives, intrauterine devices (IUDs), condoms, the rhythm method, or abstinence) throughout the study.

Exclusion Criteria

Subjects were excluded if they met any of the following criteria:

- Subject had significant scoliosis even if surgically corrected.
- Subject was participating in a clinical investigation that included an active treatment arm.
- Subject had previously been implanted with a neurostimulation system or participated in a trial period for a neurostimulation system.
- Subject had an infusion pump.
- Subject had evidence of standard care for an active disruptive psychological or psychiatric disorder.
- Subject had a current diagnosis of a coagulation disorder, bleeding diathesis, progressive peripheral vascular disease, or uncontrolled diabetes mellitus.
- The Investigator determined the subject had a current diagnosis of a progressive neurological disease.
- Subject had an existing medical condition, such as epilepsy, stroke, multiple sclerosis, acoustic neuroma, or a tumor, that was likely to require repetitive evaluations using magnetic resonance imaging (MRI).
- Subject had a history of cancer requiring active treatment in the last 12 months.
- Subject had an existing medical condition that was likely to require the use of diathermy.

- Subject had an impaired immune system (immunocompromised).
- Subject had a documented history of an allergic response to titanium or silicone.
- Subject had a documented history of substance abuse (with substances such as narcotics or alcohol) or substance dependency within 6 months of the collection of baseline data.
- Subject was a female of childbearing potential who was pregnant (confirmed by a positive urine or blood pregnancy test).

Follow-up Schedule

Subjects were followed through 12 months post-permanent implant with follow-up visits at 3, 6, and 12 months. Subjects who did not pass the stimulation trial (with <50% pain relief or did not express a desire for the permanent implant) were exited from the study.

Clinical Endpoints

The primary effectiveness endpoint was evaluating the change in pain intensity between baseline and trial using the VAS assessment. The first SCS trial assessment was up to 2 weeks after electrodes implantation, and the second SCS trial assessment was up to 2 weeks after the first trial assessment.

The secondary endpoints that were assessed included:

- Comparing the subject preference between the two lead implantation techniques during the SCS trial.
- Evaluating changes in lower back and lower limbs pain between baseline and 3, 6, and 12 months after permanent implant (VAS assessments).
- Evaluating changes in quality of life assessed using the EuroQol (EQ-5D) questionnaire, and disability assessed using the Oswestry Disability Index (ODI) between baseline, trial assessments, and at 3, 6, and 12 months after permanent implant.
- Evaluating subject satisfaction at 3, 6, and 12 months after permanent implant.

This study did not have any descriptive endpoints.

Primary Statistical Analysis Plan

The primary analysis assessed improvements in pain intensity, using VAS, was conducted using repeated measures ANOVA (RMANOVA). Post-hoc Tukey's pairwise comparisons followed to determine specific differences between follow-up visits. Secondary analyses assessed improvements in quality of life, disability, and satisfaction was conducted using repeated measures ANOVA (RMANOVA).

Study Results

Demographics and Pain Baseline Characteristics

The following table shows subject demographics and baseline characteristics of the CRISP study.

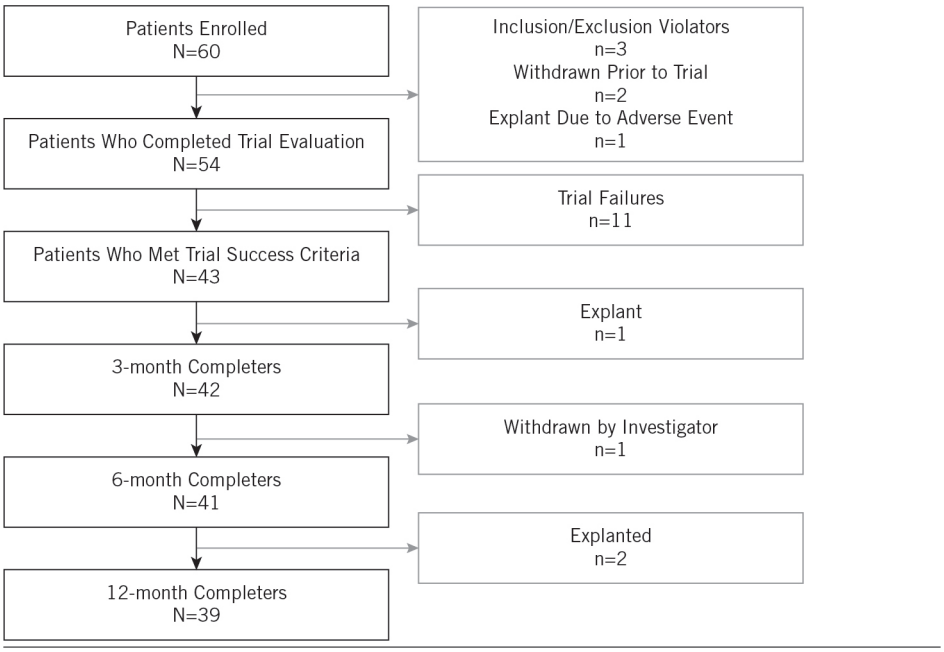
Table 41. Demographics and baseline characteristics

Variable	Subjects Starting Trial (N=60)
Age	
Mean ±SD	51.6±12.1
Gender, n (%)	
Female	34 (56.7%)
Male	26 (43.3%)

Disposition of Subjects

A total of 60 subjects were enrolled in this study, 54 of whom completed the trial phase, and 43 subjects continued into the follow-up after a successful trial completion. The following figure shows the disposition of all subjects.

Figure 12. CRISP study disposition of subjects



Procedural Results

Forty three (43) out of the 54 subjects who underwent the trial received at least 50% reduction in pain and continued to the follow-up phase of the study. Twenty one (21) subjects (48.8%) preferred the lead placed through paresthesia mapping, and 21 subjects (48.8%) preferred the lead placed using anatomical positioning. One subject (2.4%) had no preference, so the anatomical lead was activated for the follow up phase as per protocol.

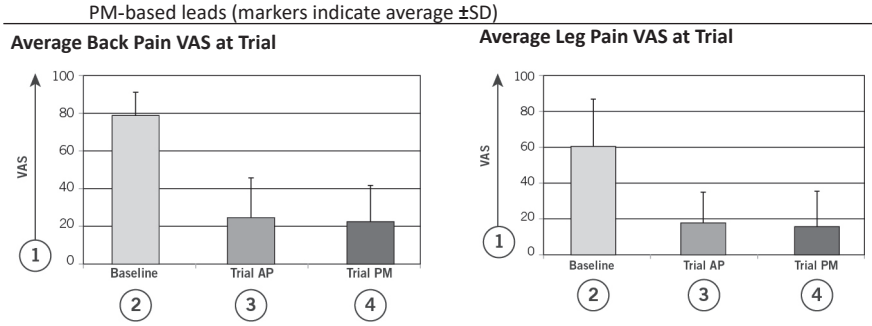
Primary Effectiveness

The primary effectiveness endpoint was the change in pain intensity, as assessed by VAS, between baseline and end of trial. During the trial, all subjects underwent testing with both implantation strategies: the anatomically implanted lead and the paresthesia implanted lead in a cross over design. The study demonstrated a significant improvement (p <0.001) in the average back and leg pain scores (VAS) from the baseline to the end of the trial period in both AP and PM lead activation, as shown in the following table and figure. No significant difference was observed in pain scores (Back pain, p=0.85; Leg pain, p=0.91) between the AP and PM lead.

Table 42. Average pain scores of subjects at the baseline and end of trial period for AP and PM-based leads (n=43)

Evaluated Parameters	Baseline	Anatomical Placement	Paresthesia Mapping
Back average VAS score in mm ±SD; number of subjects (n)	78.9±12.5	24.6±21.3	22.5±19.2
Leg average VAS score in mm ±SD; number of subjects (n)	60.4±26.9	17.7±17.5	15.7±19.5

Figure 13. Average back and leg pain scores of subjects at the baseline and end of trial period for AP and PM-based leads (markers indicate average ±SD)



1. Average VAS score
2. Baseline
3. Trial anatomical placement (AP)
4. Trial paresthesia mapping (PM)

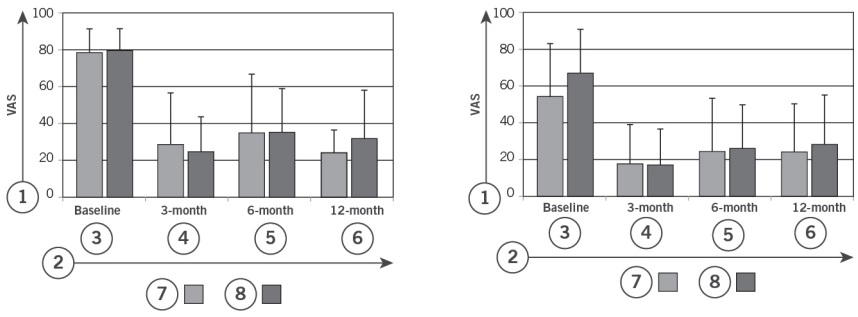
Secondary Effectiveness

The study demonstrated a significant improvement (***p*** <0.0001) in the average back and the average leg pain scores (VAS) from the baseline to follow-up at 3, 6, and 12 months respectively in both AP and PM lead groups, as shown in the following table and figure. No significant difference was observed in pain scores (back pain; leg pain) between the AP and PM lead groups at all time points considered for the study. The following table summarizes the follow-up assessments of pain intensity by back and leg average VAS score.

Table 43. Average pain scores at the baseline and follow-up for AP and PM-based lead groups

Evaluated Parameters	Follow-up Visit	Anatomical Placement	Paresthesia Mapping
Back average VAS score in mm ±SD; number of subjects (n)	Baseline	78.4±13.1; n=22	79.4±12.0; n=21
	3 month	28.5±28.1; n=21	24.6±19.0; n=20
	6 month	34.8±32; n=19	35.2±23.7; n=19
	12 month	24.0±24.5; n=19	31.8±26.4; n=20
Leg average VAS score in mm ±SD; number of subjects (n)	Baseline	54.2±28.7; n=22	66.9±23.8; n=21
	3 month	17.6±21.6; n=19	17.0±19.5; n=21
	6 month	24.3±29.1; n=18	26.0±23.8; n=19
	12 month	24.2±26.3; n=19	28.2±26.7; n=20

Figure 14. Average back and leg pain scores of subjects at the baseline and follow-up visits for AP and PM-based leads (markers indicate average ±SD)



1. Average VAS score
2. Follow-up visit
3. Baseline
4. 3 month
5. 6 month
6. 12 month
7. Anatomical placement
8. Paresthesia mapping

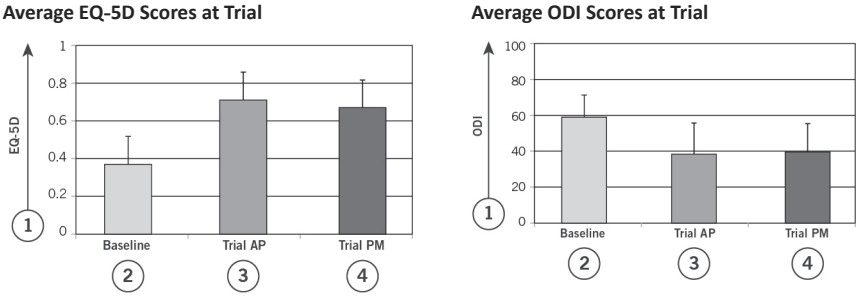
Quality of Life and Functionality Assessments – SCS Trial Results

The average EQ-5D score and ODI score significantly improved (***p*** <0.001) from baseline to the end of trial period in both AP and PM lead activation, as shown in the following table and figure. No significant difference was observed in the quality of life and disability scores between the AP and PM lead.

Table 44. Average pain scores of subjects at the baseline and end of trial period for AP and PM-based leads

Evaluated Parameters	Baseline	Anatomical Placement	Paresthesia Mapping
Average EQ-5D score; number of subjects (n)	0.4±0.1; n=43	0.7±0.2; n=42	0.7±0.2; n=43
Average ODI score; number of subjects (n)	59.0±12.3; n=43	38.4±17.5; n=43	39.6±16.1; n=43

Figure 15. Average quality of life (left) and functionality assessment (right) scores of subjects at the baseline and end of trial period for AP and PM-based leads (markers indicate average ±SD)



1. Average score
2. Baseline
3. Trial anatomical placement (AP)
4. Trial paresthesia mapping (PM)

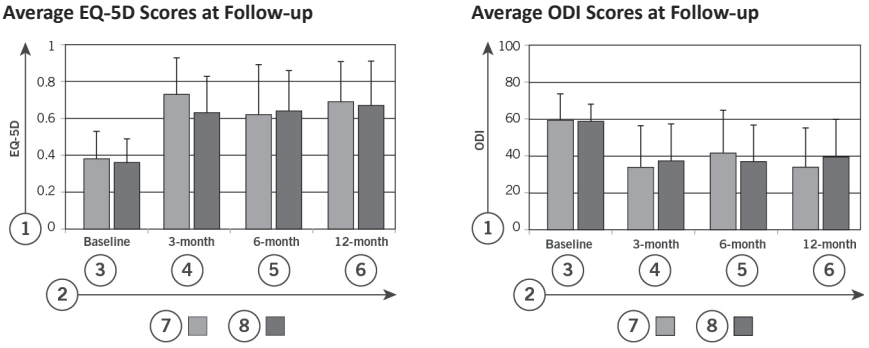
Quality of Life and Functionality Assessments – Follow-up Results

The study demonstrated significant improvement (***p*** <0.0001) in the average quality of life (assessed by EQ-5D) in the average functionality scores (assessed by ODI) from baseline to follow-up at 3, 6, and 12 months, respectively in both AP and PM lead groups, as shown in the following table and figure. No significant difference was observed in quality of life (***p***=0.58) and in disability (***p***=0.66) between the AP and PM lead groups at all time points considered for the study.

Table 45. Average quality of life and disability scores at the baseline and follow-up for AP and PM-based lead groups

Evaluated Parameters	Follow-up Visit	Anatomical Placement	Paresthesia Mapping
EQ-5D score ±SD; number of subjects (n)	Baseline	0.4±0.2; n=22	0.4±0.1; n=21
	3 month	0.7±0.2; n=20	0.6±0.2; n=19
	6 month	0.6±0.3; n=19	0.6±0.2; n=21
	12 month	0.7±0.2; n=19	0.7±0.2; n=20
ODI score ±SD; number of subjects (n)	Baseline	59.4±14.5; n=22	58.7±9.7; n=21
	3 month	33.8±22.6; n=21	37.3±20.5; n=21
	6 month	41.5±23.5; n=19	36.9±20.2; n=21
	12 month	33.9±21.5; n=19	39.4±20.8; n=20

Figure 16. Average quality of life (left) and functionality assessment (right) scores of subjects at the baseline and end of trial period for AP and PM-based leads (markers indicate average ±SD)



1. Average score
2. Follow-up visit
3. Baseline
4. 3 month
5. 6 month
6. 12 month
7. Anatomical placement
8. Paresthesia mapping

Satisfaction Assessment

At the 12 month follow-up, 94% of the patients who used AP leads and 85% of the patients who used PM lead were reported to be either satisfied or very satisfied, as shown in the following table.

Table 46. Subject satisfaction scores for AP and PM-based lead groups during follow-up

Subject Satisfaction	Follow-up Visit	Anatomical Placement	Paresthesia Mapping
Very Dissatisfied	3 month	–	–
	6 month	5.9%	–
	12 month	–	–
Dissatisfied	3 month	–	–
	6 month	5.9%	9.5%
	12 month	5.6%	5%
Neither Satisfied or Dissatisfied	3 month	19.1%	5%
	6 month	23.5%	14.3%
	12 month	–	10%
Satisfied	3 month	33.3%	40%
	6 month	23.5%	23.8%
	12 month	50%	20%
Very Satisfied	3 month	46.6%	55%
	6 month	41.2%	52.4%
	12 month	44.4%	65%

Adverse Events

A total of 58 adverse events were reported in 24 subjects during the study. Of these, 40 were classified as serious or non-serious adverse events. These are summarized below.

There were 6 serious adverse device effects reported in 5 subjects, as shown in the following table.

Table 47. Summary of serious adverse device effects (SADEs)

Event Description	Related to	Subjects with Events	Number of Events
Difficulty with urination and unable to weight bear on the right leg associated with pre-existing cauda equina	Device	1	1
Worsening of right leg pain after implant	Device, Procedure	1	1
Photophobia	Procedure	1	1
Explant due to suspicion of infection	Device	1	1
Right leg numbness	Procedure	1	1

Table 47. Summary of serious adverse device effects (SADEs)

Event Description	Related to	Subjects with Events	Number of Events
Wound exploration due to weeping wound at the IPG site	Device	1	1
Total		**5***	**6**

* Some subjects experienced more than one event.

There was 1 serious adverse event in 1 subject classified by investigators as not related to a device or procedure, as shown in the following table.

Table 48. Summary of serious adverse events (SAEs)

Event Description	Subjects with Events	Number of Events
Acute abdominal pain due to gall stones	1	1

A total of 26 non-serious adverse device effects were reported in a total of 15 subjects, as shown in the following table.

Table 49. Summary of non-serious adverse device effects (ADEs)

Adverse Device Event	Subjects with Events	Number of Events
IPG unpairing	2	2
Increase in pain due to lead migration	1	1
Suspect infection	1	1
Numbness in leg on change of program	1	1
Ache at base of skull when lying down	1	1
Pain at IPG site	2	2
Tremor and weakness	1	1
Worsening of back pain symptoms	1	1
Short IPG battery life span	1	1
Rib pain	1	1
Anchor revision due to pain at the anchor site	1	1
Irritation around surgery site	1	2
Skin suture remains in-situ	1	1
Knee pain	1	1
Leg cramps	1	1
Leakage at wound site/IPG scar	1	2
Tingling in right leg	1	1
Bleeding from back wound	1	1
Headache	3	3
Lead explanted due to light growth of bacillus cereus on lead exit	1	1

Table 49. Summary of non-serious adverse device effects (ADEs)

Adverse Device Event	Subjects with Events	Number of Events
Total	**15***	**26**

* Some subjects experienced more than one event.

A total of 7 non-serious adverse events were reported in a total of 5 subjects, as described in the following table. Although formal event adjudication was not performed, several events related to lead explant, wound site, and pain would likely be considered device-related.

Table 50. Summary of non-serious adverse events

Adverse Event	Subjects with Events	Number of Events
Diarrhea	1	1
Vomiting	1	1
Pain due to falling	2	2
Swelling on right side of face, leg, and ankle	1	1
Complains of palpitation	1	1
Acquired shingles	1	1
Total	**5***	**7**

* Some subjects experienced more than one event.

There were no unanticipated serious adverse device effects. There were no deaths reported in the study. There were no device deficiencies reported in the study.

Conclusions Drawn from the Study

Effectiveness

There were similar results using BurstDR™ stimulation from trial leads implanted with paresthesia-mapping and anatomical placement. Back and leg pain scores, quality of life and disability measures improved, and there were no statistical differences between the lead groups. At the end of the trial, there was an even distribution of preferences for the leads. No order effect was observed.

The study demonstrated equivalent long-term clinical outcomes with BurstDR SCS treatment regardless of lead placement method. Back and leg pain scores, quality of life and disability measures improved from baseline to 3-, 6-, and 12-month follow-up for leads positioned through paresthesia-mapping as well anatomical placement. There were no statistical differences between the lead groups.

Safety

No deaths or any events categorized as unanticipated serious adverse or device effects were reported during the study. A total of 58 adverse events were reported in 24 subjects during the study. Of these, 40 were classified as serious or non-serious adverse events.

Study Limitations

This study has a limited size, and may lack statistical power to detect differences in pain rating between the groups. However, the even split in blinded subjects' preferences at the end of the trial suggest that both implant techniques provide equivalent therapeutic outcomes that are sustained over 12 months.

Paresthesia mapping typically involves the use of two leads to improve pain-paresthesia overlap. However, this study had used only one lead for mapping. While the use of a single lead could have resulted in sub-optimal paresthesia coverage, the long-term results have demonstrated clinically and statistically significant improvement from baseline with both approaches. Moreover, as BurstDR stimulation is programmed at amplitudes that do not evoke sensory percepts, optimal pain-paresthesia overlap may not be necessary to produce effective pain relief with this waveform.

Benefit-Risk Conclusions

This clinical study demonstrated equivalent outcomes with BurstDR™ stimulation delivered through the positioning of leads using paresthesia mapping and anatomical placement in both trial phase and long-term follow-up.

Overall Conclusions

The study reported equivalent long-term clinical outcomes with BurstDR™ stimulation treatment regardless of the lead placement method. Implanting physicians could employ either of the lead placement methods based on the specific circumstances and patient characteristics. Anatomical placement of lead does not require paresthesia or require patient input or feedback for effective stimulation. This placement may bypass the need to reduce sedation or analgesia during the procedure, contributing to the reduction of patient discomfort and stress.

Clinical Summary for Diabetic Peripheral Neuropathy

Diabetic peripheral neuropathy (DPN) pain is often associated with a history of poorly controlled diabetes that presents as pain in the extremities. It will typically begin in the toes and progress upward to the foot and legs. The pain is described as uncomfortable “tingling,” “shooting,” or “burning” pain.

The recommended primary course of treatment for DPN is for patients to improve their glycemic control through diet, exercise, and medical management. If those approaches are unsuccessful, secondary treatments include medications for neuropathic pain, topical treatments, physical therapy, and noninvasive neuromodulation. Patients may benefit from invasive neuromodulation approaches if they are refractory to those more conservative measures.

Review Design and Methodology

The safety and effectiveness of the Abbott implantable neurostimulation system to treat DPN was based on clinical safety outcome data from a systematic review of published scientific literature reporting on the use of any commercially available spinal cord stimulation (SCS) systems for the treatment of chronic intractable pain in a diabetic population and Medicare claims data collected from patients implanted with Abbott SCS devices.

The systematic review of published literature was conducted by searching EMBASE and PubMed for terms relating to SCS and for the term diabetes. Two reviewers independently screened 503 search results, ultimately selecting 103 publications for full text review. In addition, a retrospective real world evidence (RWE) study was conducted based on Medicare claims data to provide supplementary safety information on the use of SCS for DPN.

The analysis included patients implanted with an Abbott SCS system between January 1, 2014 and September 30, 2020, identified in the Medicare databases and categorized into two cohorts based on Medicare claims diagnosis codes: 1) DPN patients with a primary diagnosis of DPN or a secondary diagnosis of DPN and a primary being chronic pain and 2) non-DPN patients without any DPN diagnosis on the implant date or any evidence of a diagnosis in the year prior to implant. The incidence rate and cumulative incidence of common safety events up to 12 months following implantation were compared between the two cohorts to determine whether patients with DPN, who are implanted with SCS exhibited an increased risk of particular safety events when compared to the general population of SCS patients. For both cohorts, the incidence of safety events potentially associated with device related surgeries (i.e., device removal, reimplant, or revision) following implantation were also evaluated.

Safety

Safety objective: Identify risks relevant to SCS to which diabetic patients are predisposed and to characterize the safety profile of SCS to treat DPN.

The safety profile of Abbott SCS systems to treat DPN was characterized through analysis of data from the published scientific literature and Medicare claims data relevant to the use of Abbott SCS devices. The analysis characterized the overall safety profile by common adverse events, as well as specifically examining the risks to which the diabetic population are predisposed such as inherent surgical complications that may occur more frequently or have greater impact in these patients.

Effectiveness

Effectiveness objective: Characterize the clinical benefits related to pain relief for SCS used to treat DPN, when compared to the standard-of-care.

The effectiveness of Abbott SCS systems to treat DPN was demonstrated through analysis of clinical study results from the systematic review of published scientific literature. Effectiveness was demonstrated by the probability of treatment success. The probability of treatment success (responder rate or proportion of successfully treated subjects) was defined by a specified percent reduction in pain rating or Patient Global Impression of Change (PGIC) rating.

Review Results

Safety

Literature Search Results

Selection criteria were 1) treatment with SCS and 2) a distinctly identifiable diabetic population with either (a) an analysis of the impact of a diabetic state on a safety related outcome, or (b) a comprehensive listing of adverse events. After full text review of 103 publications, 22 publications on 16 studies were included for analysis. Three studies resulted in multiple publications; safety information was extracted from the publication with the longest follow-up from each study that included comprehensive adverse event information.

Real World Evidence Evaluation of Medicare Claims Data

Available data on 36,004 patients (DPN: 507 and non-DPN: 35,497) implanted with Abbott SCS systems were included in the safety analysis. Incidence rates and cumulative incidence up to 12 months following implantation for a total of 23 common safety events were calculated. The safety events were identified from International Statistical Classification of Diseases and Related Health Problems (ICD) 9 and ICD 10 diagnosis codes that are used by the Center for Medicare and Medicaid Services (CMS) for diagnostic, billing, and reporting purposes. A systematic review of ICD-9 and ICD-10 codes was conducted to identify diagnostic codes that are either associated with known SCS risks (e.g., infection and CSF leak) or are specific to nervous system implants or neurostimulators for the spinal cord. These safety events include device related events (e.g., lead migration, stimulator failure), negative device or procedure effects (e.g., infections, thrombosis, and hemorrhages that are specific to an implanted nervous system device), and general adverse events that are not specific to the device (e.g., CSF leak, infection due to any cause).

The results indicate low incidences of device or procedure related safety events in DPN patients implanted with SCS, including incidence rates of 2.6% for device specific infections (compared to 1.8% for non-DPN patients), 2.2% for lead migration (compared to 2.9% for non-DPN patients), 7.5% for lead failure (compared to 8.6% for non-DPN patients), and 4.9% for stimulation issues that require adjustment of the stimulation settings (compared to 3.4% for non-DPN patients). Furthermore, there was no statistically reliable evidence of a difference between DPN and non-DPN patients in the incidence and cumulative incidence rates for any safety events that were specific to the device or procedure. The incidence and cumulative incidence rates for safety events that are associated with device related surgical procedures (i.e., revision, replacement, or removal) were also not significantly different between DPN and non-DPN patients. This suggests that the use of SCS in this patient population does not lead to increased risk of device related safety events or safety events that may be associated with a device related surgery following initial implantation.

Common Adverse Events

Studies which included detailed adverse event information were pooled to assess common adverse event occurrences. The table below presents study data grouped by reports of common patient cohorts and by populations defined specifically by DPN or by those reporting on patients with diabetes mellitus (DM) in general. Studies that did not include AE information specific to the diabetic or DPN population were not included in this table.

Table 51. Common Adverse Events

		Adverse Event Counts (%)							
		Sample size	**Infection**	**Lead migration**	**Lead failure**	**Device site swelling or pain**	**Hematoma, Erosion, Wound dehiscence**	**CSF leak, Dural tear**	**Uncomfortable stimulation, Stimulation issues**
DPN	DPN SCS RWE study on Abbott devices[a]	n^{i} = 507	13 (2.6)[b]	11 (2.2)[c]	38 (7.5)[d]	<11 (0.2 –2.0)[e]			25 (4.9)f
	Petersen (2021) Petersen (2022)	$n^{t,i}$ = 104	8 (7.7)	1 (1.0)		2 (1.9)	4 (3.8)		1 (1.0)
	Pluijms (2012) Slangen (2013, 2014) van Beek (2015, 2018)	$n^{t,i}$ =49	2 (4.1)	5 (10.2)	4 (8.2)	10 (20.4)		1 (2.0)[h]	9 (18.4)
	Galan (2020)	$n^{t,i}$ =9				1 (11.1)[i]	1(11.1)		
	de Vos (2014)	$n^{t,i}$ =40	3 (7.5)[g]	1 (2.5)		2 (5)			2 (5)
	de Vos (2009)	$n^{t,i}$ = 11	1 (9.1)		2 (18.2)				
	Tesfaye (1996) Daousi (2005)	$n^{t,i}$ =10	2 (20)	2 (20)	1 (10)		1(10)		
DM	Falowski (2019)	$n^{t,i}$ =1663	59 (3.5)						
	Hoelzer (2017)	$n^{t,i}$ =452	9 (2.0)						
	Mekhail (2011)	$n^{t,i}$ = 56	5 (8.9)						
	Petrakis (1999)	$n^{t,i}$ = 64	2 (3.1)	2 (3.1)					
	Range		2.0–20%	1.0–20%	7.5–18.2%	0.2–20.4%	3.8–11.1%	2.0%	1.0–18.4%

DPN: Diabetic peripheral neuropathy

DM: Diabetes mellitus

n^{i} Sample size reflects patients with DPN who were implanted with a permanent implantable pulse generator (IPG).

n[t,i] Sample size reflects subjects exposed to either the trial stimulation or permanent IPG implant as described in the individual publications.

[a] Incidence rates at 12 month post-implant based on Abbott real world evidence study of Medicare claims based on Medicare ICD-9 and ICD-10 diagnosis codes.

[b] Based on diagnosis codes that are specific to an implanted nervous system device, infection related to an implanted neurostimulator lead and infection related to an implanted neurostimulator IPG.

[c] Based on diagnosis codes that are specific to displacement of implanted nervous system lead.

[d] Based on diagnosis codes that are for mechanical breakdown of implanted nervous system lead and other mechanical complication of implanted nervous system lead.

[e] Based on diagnosis codes that are for pain due to implanted nervous system device.

[f] Based on diagnosis codes that are for encounters for adjustment and management of neurostimulator.

[g] Two patients with infection also had fluctuations in their blood glucose levels.

[h] CSF leak reported in one subject during aborted trial lead placement and reported in Slangen (2014).

[i] Based on report of implant site seroma.

Three publications reported sub-analyses on the impact of diabetes on a specific safety related outcome (without detailed adverse event information).

- TenVaarwerk et al. (1999)[1] was a retrospective, multicenter study of patients with angina pectoris treated with spinal cord stimulation to evaluate risk factors associated with morbidity and mortality in SCS. Insulin dependent diabetes was reported as the only important risk factor between survivors and non-survivors (p=0.05). Additionally, a multivariate analysis showed that diabetes was significantly correlated with mortality (p=0.01).
- Bir et al. (2016)[2] was a retrospective study of SCS in patients with chronic back pain to evaluate potential predictors of SCS revisions. The authors conducted an analysis of the effect of diabetes on revision free survival (RFS). RFS in patients with diabetes was 35 months, and in patients without diabetes it was 43 months; however, this difference was not statistically significant (log-rank, p=0.98).
- Antonovich et al. (2021)[3] was a single center, retrospective analysis of SCS re-operation rates for specific lead types (paddle vs. percutaneous). Of the study participants, 22.34% had diabetes, and patient data was collected over a 10 year period. The authors evaluated whether or not there was an association between diabetes and lead type and time to re-operation but found none (p=0.197).

Published literature describing treatment of DPN with SCS and published clinical practice guidelines on perioperative care of diabetic patients provide information on specific inherent risks that may be of concern for diabetic patients when it comes to the delivery and management of SCS therapy.

Infection

Data on device or procedure related infections in DPN and diabetic patients reported in the literature indicate an infection rate ranging from 2–20%. The incidence of infection is comparable to overall rates of infection associated with SCS of 4.89% (range: 2.5% to 10%) as reported in a systematic literature review by Eldabe et al. (2016)[4]. In the literature, infections were either resolved using solely antibiotics or through removal of the infected components of the SCS system, followed by administration of antibiotics. Data from the RWE study suggest that in general patients diagnosed with DPN have higher risk of infection at 12 months following implantation and higher cumulative incidence of infection during the 12 month period following implantation than subjects who were not diagnosed with DPN. However, these infections are not necessarily device or procedure related.

The results of the RWE study indicate that the incidence of device specific infections is 2.6%. The device specific infection rate falls within the 2–20% incidence range reported in the literature. Additionally, device specific infections and infections that may be associated with device related surgical procedures (i.e., revision, replacement, or removal) were not significantly different between DPN and non-DPN patients (device related infections: risk difference of 0.7%, 95% CI: -0.6% to 2.1%; infections associated with device related surgical procedures post implant: risk difference of 1.0%, 95% CI: -0.7% to 2.7%). This suggests that while DPN subjects have elevated all-cause infection rates, device specific infection and infections that may be associated with device related post-implant surgeries are not significantly different among patients with DPN as compared to non-DPN patients implanted with SCS. This finding is consistent with the results of

three large retrospective studies on SCS, which also reported no significant difference in the rate of device specific infection for patients with diabetes[5, 6, 7].

Data from the RWE study, however, suggest that patients diagnosed with DPN in general have a higher risk of infection at 12 months following implantation and higher cumulative incidence of infection during the 12 month period following implantation than subjects who were not diagnosed with DPN. Therefore, the various sources of evidence are consistent and show DPN subjects in general do not have a higher risk of device or procedure related infections. The data also suggests that diabetic patients have an increased risk of all-cause infection; however, this risk can be appropriately communicated through device labeling and clinical guidelines.

The only complications as a result of infections explicitly mentioned in the literature include device explantation, abscess formation, and changes in glucose level stability. Another infection related complication that is of note is an increased risk of blood glucose fluctuations. This risk is highlighted by de Vos et al. (2014)[8] in which two subjects experienced fluctuations in blood glucose levels in response to an infection. Although the study did not attribute these infections to the device, the impact of blood glucose fluctuations in diabetic patients that may arise from device related infections can lead to increased morbidity and mortality in this patient population.

Hematoma, Erosion, Wound Dehiscence

Based on the literature, the incidence rate of hematoma, erosion, and wound dehiscence ranged from 3.8% to 11.1%. Diabetes is known to be a potential risk factor for hematoma, erosion, and wound dehiscence, which can lead to infection. However, these rates may be underreported due to greater attention to infections that may result from this adverse event.

Cardiovascular Events

Several reports of subject or patient death attributed to myocardial infarction (n=4) or heart failure (n=1) were included in the available data on SCS to treat DPN[9, 10]. While none were reported to be related to SCS procedures or therapy, patients with poorly controlled diabetes may have an elevated risk for cardiovascular events in the perioperative period. In an analysis of outcomes in patients undergoing elective orthopedic surgery (Marchant et al., 2009)[11], patients with poor glycemic control showed a nonsignificant trend towards greater odds of myocardial infarction and significantly greater odds of stroke (odds ratio 3.42 CI: 1.87–6.25; p<0.001).

Dural Puncture and CSF Leak

Only one of the studies reviewed in the literature reported CSF leak. Specifically, Slangen et al. (2014) reported one death due to subdural hematoma after dural puncture during the trial. A review of the literature was conducted to identify publications that reported CSF leak in patients with diabetes. Specifically data from craniotomy procedures in Ha et al. (2016)[12] and Hutter et al. (2014)[13] suggest that diabetes may be a risk factor for CSF leaks. However, the more invasive nature of craniotomy procedures described in Hutter et al. and Ha et al. limits the translation of this concern to SCS procedures.

Wang et al. (2014)[14] also reported a 1.57-fold higher incidence of subdural hematoma in general (rates were not specific to SCS procedures) in diabetic patients than in non-diabetic patients (2.04 vs. 1.30 per 1000 person-years), with an adjusted hazard ratio of 1.63 [95% confidence interval (CI) 1.43–1.85].

It should be noted that although CSF leak was evaluated in the RWE study, results of the study were not included in the previous table since the common adverse events presented in the table are device or procedure related. The CSF leak safety event that was evaluated in the RWE study included all diagnosis codes that were related to CSF leak without regard to device or procedure causality. This approach was taken to induce a level of conservativeness in the incidence rate associated with this serious adverse event.

Out of the 507 DPN patients, there were fewer than 11 patients that were identified with CSF leaks from the medical claims data. Due to confidentiality concerns and per CMS cell suppression policy[15], we are unable to report on patient data that have fewer than 11 subjects. As such, CSF leak in the DPN patients may have occurred in one subject or in 10 subjects; this range corresponds to an incidence rate ranging from 0.2–2%. Additionally, there was no statistically reliable evidence of a difference in the incidence in CSF leak between DPN and non-DPN subjects implanted with an SCS system (risk difference=0.0% to 1.8%, 95% CI: -0.4, 3.0%).

Glycemic Control

de Vos et al. (2014)[1] reported 2 subjects experiencing fluctuations in blood glucose levels following infections. While these were assessed by authors as unrelated to SCS, the physiologic stress of surgery or any adverse event may impact glycemic control.

Effectiveness

Literature Search Results

Selection criteria were 1) treatment of DPN with SCS systems delivering therapy at frequencies of 0 to 1200 Hz, and 2) a distinctly identifiable DPN population with quantifiable effectiveness data on pain related outcomes including the proportion of patients assessed as treatment success (responder rate), the magnitude of pain relief, or improvements in quality of life. After full text review, 14 publications on 8 studies were included for analysis. Three studies produced multiple publications, and one publication combined 2 separately studied cohorts.

Noncomparative Studies

Ten publications include data from 6 single-arm studies that evaluated the use of SCS to treat DPN[16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26]. SCS trial success rates ranged from 73% to 93%. The proportion of subjects assessed as successfully treated ranged from 55% to 100% with average pain relief ranging from 41% to 80% (up to 12 months). Successful treatment during long term follow-up ranged from 40% to 77% (24 months to 7.5 years).

Comparative Studies

Two randomized controlled trials (RCT) investigated the use of SCS to treat DPN; results from these studies were described in 5 publications[27, 28, 29, 30, 31]. The following table presents a comparison of the two initial studies that reported on the primary outcomes.

Table 52. Details of publications describing randomized studies on DPN

	Publication	
	Slangen et al., 2014[32]	**de Vos et al., 2014[33]**
Sponsor	Maastricht University Medical Center (NCT01162993)	Medisch Spectrum Twente (ISRCTN03269533)
Population	Diabetic patients with moderate to severe DPN in the lower limbs, who were refractory to conventional medical treatments for more than 12 months; NPRS pain rating ≥5, 18 and 80 years of age	Patients with DPN in the lower extremities for more than 1 year and refractory to conventional treatments; VAS pain rating ≥50 mm ≥ 18 years of age
Design-allocation	Open Label, Randomized, Parallel assignment (3:2)	Open Label, Randomized, Parallel assignment (2:1)
Comparator	Best medical treatment (BMT)	Best conventional medical practice (BCMP)
Sample size (countries)	36 from 2 centers (NL)	60 from 7 centers (NL, BE, DK, DE)
Primary endpoint	≥50% pain reduction during daytime or nighttime or a score of ≥6 on a 7-point Likert scale of the PGIC scale for pain and sleep	Treatment success at 6 months ≥50% pain reduction

Table 52. Details of publications describing randomized studies on DPN

	Publication	
	Slangen et al., 2014[32]	**de Vos et al., 2014[33]**
Publication date	Nov 2014	Nov 2014

The demographic characteristics for subjects participating in both studies were comparable for most categories. Fewer Type I diabetic subjects were included in Slangen et al. though in both studies the majority of subjects were diagnosed as Type II diabetics. Subject demographics for each study are presented in the following table.

Table 53. Comparison of study demographics

Demographic	**Slangen et al.[21]**	**de Vos et al.[24]**
Age (years)	56.9	59.0
Duration of diabetes mellitus (years)	12.7	16.3
Duration of pain (years)	5.5	7.0
Male	67%	63%
Female	33%	37%
Type I	11%	25%
Type II	89%	75%

Primary pain related outcome measures between the two trials were compared to determine if the trials demonstrated similar effectiveness levels within the two similar populations; the subject measure averages are shown in the following table. Pain related outcomes were similar between studies with slightly greater reductions in pain reported by de Vos et al. Control groups from both studies did not achieve any notable reduction in average pain; however, one subject in the control arm reported treatment success.

Table 54. Comparison of pain measure (95% CI)

	Pain Rating[a]			
	Slangen et al.[21]		**de Vos et al.[24]**	
	SCS (n=22)	**Control (n=14)**	**SCS (n=40)**	**Control (n=20)**
Baseline	7.1 (6.3–7.9)	6.5 (5.5–7.5)	7.3 (6.8–7.8)	6.7 (5.9–7.5)
6 month	4[d] (2.6–5.4)	6.5 (5.4–7.6)	3.1 (2.2–4.0)	6.7 (5.7–7.7)
Pain relief[b]	44%	0%	58%	0%
Responder rate[c]	59% (36%–79%)	7% (0%–34%)	63% (46%–77%)	5% (0%–25%)

[a] VAS (0–100 mm) and NRS (0–10) were normalized to a 0–10 scale.

[b] 95% CI not provided due to required distributional assumptions.

[c] Study design defined successful pain relief by different measures.

[d] N=19 subjects with available data for pain scores at 6 months.

Combined Data from Comparative Studies

Because the two RCTs had highly similar trial designs, and patient populations and both compared SCS to conventional medical management with primary endpoints at 6 months, data from both studies were pooled and are presented in the following table. Average values were weighted by the number of subjects in the respective SCS and control treatment groups for each study.

Table 55. Combined subject measures (95% CI)

Measure	SCS (n=62)	Control (n=34)
Age (years)	57.7	59.1
Duration of DM (years)	14.8	15.2
Duration of pain (years)	6.6	6.1
Male	65%	65%
Female	35%	35%
Type I	21%	18%
Type II	79%	82%
Average baseline pain rating	7.2 (6.5–10)	6.6 (5.7–9.6)
Average 6 month pain rating	3.4 (2.1–4.4)	6.6 (5.6–9.5)
Average pain reduction[a]	53%	0%
Responder rate per protocol[b,c]	61% (48%–73%)	6% (0%–20%)
Responder rate ≥50% reduction in pain[c]	55% (42%–68%)	3% (0%–15%)
Responder rate per protocol as-treated[d]	70% (56%–82%)	6% (0%–20%)
Responder rate ≥50% reduction in pain as-treated[d]	63% (49%–76%)	3% (0%–15%)

[a] 95% CI not provided due to required distributional assumptions.

[b] Each study design defined successful pain relief by different measures.

[c] Analysis of all randomized subjects in an intent-to-treat approach.

[d] Including only subjects who received an SCS system implant.

Meta-analysis for Comparative Studies

A meta-analysis of responder rate (≥50% pain relief) from the two RCTs was performed. A random effects analysis of heterogeneity between studies supported homogenization (Cochran's Q=0.113, p-value=0.737; Higgin's I^2 test=0.0%). The confidence intervals of these studies overlap, and the estimate of odds ratios are consistent, demonstrating subjects treated with SCS for DPN are more likely to achieve ≥50% pain relief at 6 months. The overall mean logOR is 3.21 (95% CI 1.68 to 4.73), corresponding to an odds ratio of 24.8 in favor of treatment success with SCS treatment of DPN.

A second analysis based on a fixed effects model on the risk differences was performed. Similar to the random effects analysis, there is no statistically reliable evidence of heterogeneity between the studies I^2=0.0%, and Q=0.129 (p=0.719). The fixed effects model estimates a group difference of 55.3% with a 95% CI from 40.8% to 69.9%. The data pooled from both studies showed that the binomial responder rates (defined as ≥50% reduction in pain at 6 months) for all subjects randomized to receive SCS treatment was 62.9% and supports probability of treatment success.

Long Term Effectiveness

Van Beek et al. (2018)[34] published long term follow-up results for subjects from the studies reported by Pluijms et al. (2012)[35] and Slangen et al. (2014)[36]. Forty-eight subjects (40 with permanent implant) were included in the analysis for follow-up to 5 years. Treatment success was defined as ≥50% pain relief in day or nighttime pain or a PGIC rating of “much improved” or “very much improved”. Treatment success was observed in 86%, 71%, 77%, 67%, and 55% at 1 (n=36), 2 (n=35), 3 (n=34), 4 (n=30), and 5 (n=22) years, respectively. A Michigan Diabetic Neuropathy Score (0 to 3 scale) of 3 at baseline was associated with treatment failure during the 5 year follow-up (hazard ratio 3.9; p-value=0.014). This suggests patients with severe neuropathy may be less likely to experience treatment success.

Summary of Articles with Meta-analyses

There were 6 meta-analyses[37, 38, 39, 40, 41, 42], which included reviews of 77 publications, covering a range of study types from randomized controlled trials to case series. There is significant overlap in studies that were included in each publication, and many of the articles cited were included in the previous discussions of results for the safety and efficacy literature search; therefore, only high level conclusions were pulled from the analyses.

The adverse events identified in these meta-analyses included infections, meningitis, hematoma, lead migration or failure, and IPG failure requiring revision. Other adverse events mentioned in Hou et al. (2016) included dizziness, headache, or a sensation of heaviness or warmth in the legs. One death from subdural hematoma was originally reported in Slangen et al., 2014. Two meta-analyses reported infection rates of 4% (Raghu et al., 2021) and 14% for infections requiring antibiotics (Pluijms et al., 2011).

From an effectiveness perspective, these meta-analyses provide reasonable evidence of the effectiveness for the use of SCS in DPN. As reviewed in Raghu et al., 2021 and Duarte et al., 2021, two RCTs demonstrated that SCS provided superior treatment over best medical therapy at 6 months follow-up with continued significant improvement compared to baseline for many years. Xu et al., 2022 and D'Souza et al., 2022 concluded that the studies reviewed provided moderate to strong support of SCS to treat refractory DPN. Pluijms et. al., 2011 compared long term effectiveness across multiple studies and determined that SCS provided continued pain relief at 7 years in DPN patients. At this point, 57% of patients (4 of 7) achieved ≥50% pain relief, and 30% reported stoppage of analgesic use. Based on the collected information in the meta-analyses, there is general support on the use of SCS for DPN.

Overall Conclusions

Safety

The clinical evidence supporting the safety of Abbott implantable SCS systems to treat DPN includes a systematic literature review of published scientific articles reporting SCS as treatment for chronic intractable pain in patients with diabetes in general, and Medicare claims data on patients treated with SCS for DPN. Safety data from 730 subjects treated with SCS for their DPN was included. An additional 2235 patients were included across 4 studies that reported on diabetic patients treated with SCS.

The rates of common adverse events in the DPN population were similar to that of the general SCS population. The literature highlighted some inherent risks that are associated with spinal cord stimulation in DPN subjects, including but not limited to infection, delayed wound healing, cardiovascular events, dural puncture and subsequent subdural hematoma, and fluctuations in glycemic control. These events can be mitigated through appropriate patient selection, or with the use of appropriate surgical techniques and procedures.

Device labeling has been updated to provide information on warnings, advice on appropriate selection of patients healthy enough to receive SCS, and steps to take to avoid or reduce the impact of complications with SCS for patients with DPN. Refer to the system related clinician manuals for safety information specifically addressing the diabetic population. Underlying health conditions related to diabetes or other diseases may disqualify some patients from receiving SCS.

Published literature describing SCS as treatment for DPN and published clinical practice guidelines on perioperative care of diabetic patients provide information on specific inherent risks for the diabetic patient in the delivery and management of SCS therapy. These inherent risks include, but are not limited to delayed wound healing, cardiovascular events, dural puncture and subsequent subdural hematoma, and fluctuations in glycemic control. These events may be avoided by appropriate patient selection, or by the use of appropriate surgical techniques and procedures. There were an additional 5 meta-analyses that independently reviewed safety information and determined that risks of SCS in the diabetic population were similar to conclusions from previously published studies.

Effectiveness

A total of 14 publications from 8 studies (several publications reported alternative analyses or long term follow-up) described effectiveness outcomes associated with SCS to treat DPN. Four prospective studies without a comparator included a total of 84 subjects. Two retrospective studies contained data on 68 patients with diabetic neuropathy, and 2 RCTs comparing SCS to the standard-of-care included a total of 96 subjects.

Two independent RCTs evaluating SCS to treat DPN compared to standard-of-care included a total of 62 subjects in the treatment group and 34 subjects in the control group. At the 6 month primary endpoint,

the outcomes for subjects randomized to receive SCS treatment were consistent between both studies with treatment success rates of 59% and 63%, and an average pain relief of 44% and 58% in Slangen et al. (2014) and de Vos et al. (2014), respectively. The overall mean logOR is 3.21 (95% CI 1.68 to 4.73), corresponding to an odds ratio of 24.8 is in favor of treatment success with SCS treatment for DPN. The data pooled from both studies showed that the binomial responder rates (defined as ≥50% reduction in pain at 6 months) for all subjects randomized to receive SCS treatment was 62.9% and supports probability of treatment success.

Long term efficacy data on subjects treated with SCS to treat DPN from one nonrandomized study and one RCT, reflecting outcomes after 5 years of treatment showed a sustained pain relief at clinically meaningful levels. There were an additional 6 meta-analyses that independently reviewed effectiveness from previously published studies and determined that there was sufficiently strong evidence to support the use of SCS to treat DPN.

Limitations

Limitations of the available data include lack of a placebo control in the 2 randomized studies, no impact of medication use on criteria for treatment success, and the open-label design of long term follow-up reports. Studies without a placebo control arm are unable to measure the contribution of the placebo effect to the overall outcomes reported by subjects. While study data may reflect an average reduction in medication use, an individual patient's treatment success with SCS could be attributed to changes in pain medication. Data from open-label studies or long term, non-randomized follow-up may result in an overestimation of the treatment effect.

A limitation of data on the safety and effectiveness of SCS to treat DPN based on published literature and claims data is the lack of access to primary source data on patient-reported outcomes such as pain scores and detailed adverse event descriptions. In the absence of primary source data, analyses of associated variables (for example, diabetes type, baseline pain scores, or relevant pre-enrollment diagnoses) are not possible. While some published reports of studies of SCS to treat DPN provide covariate analyses, data included in these publications do not allow for verification of the analyses. Variation in diagnosis descriptions and criteria for inclusion of adverse events reported in publications limits the resolution of safety information that can be extracted from the published literature.

NOTE: The BurstDR™ stimulation mode has not been evaluated for effectiveness in the diabetic peripheral neuropathy (DPN) population.

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Abbott Medical
6901 Preston Road
Plano, Texas 75024 USA
+1 855 478 5833
+1 651 756 5833

Abbott Medical
The Corporate Village
Da Vincilaan 11 Box F1
1935 Zaventem
Belgium
+32 2 774 68 11

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