



Sacral Neuromodulation System

Neurostimulator Implant Manual

Model 1101 Neurostimulator

Rx only

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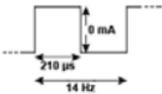
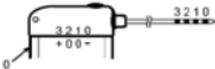
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LABEL SYMBOLS

This section explains the symbols found on the product and packaging.

Symbol	Description
	Axonics Neurostimulator
	Axonics Torque Wrench
	Neurostimulator default waveform with 14 Hz frequency, 0 mA amplitude and 210 μ s pulse width
	Neurostimulator default electrode configuration: Electrode 0: negative (-) Electrode 1: Off (0) Electrode 2: Off (0) Electrode 3: Positive (+) Case: Off (0)
	Product Serial Number

Symbol	Description
	Manufacturer
	Product Model Number
	Manufacturing Date
	Non ionizing electromagnetic radiation
	Conformité Européenne (European Conformity). This symbol means that the device fully complies with AIMD Directive 90/385/EEC (Notified Body reviewed) and RED 2014/53/EU (self-certified)
	Refer to instructions for use (Consult accompanying documents)
	Temperature limitation
	Humidity limitation
	Pressure limitation
	Do not reuse
	Sterilized using Ethylene oxide

Symbol	Description
	Use by
	Do not use if package is damaged
	Do not re-sterilize
	Authorized representative in the European community
	Open here
	For USA audiences only Caution: U.S. Federal law restricts this device for sale by or on the order of a physician
	Warning / Caution
	Product Literature
	Magnetic Resonance (MR) Conditional
IC	Industry Canada certification number

Symbol	Description
	This device complies with all applicable Australian Communications and Media Authority (ACMA) regulatory arrangements and electrical equipment safety requirements
FCC ID	US Federal Communications Commission device identification

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INTRODUCTION

This manual provides information about the Axonics Sacral Neuromodulation (SNM) System Neurostimulator (Model 1101), which is a part of the Axonics SNM System. The Neurostimulator is connected to the Axonics tined lead (Model 1201 or 2201).

DEVICE DESCRIPTION

The Axonics Neurostimulator (**Figure 1**) is part of the Axonics SNM System. The Neurostimulator is a programmable device that is connected to the Axonics tined lead, which conducts stimulation pulses to the sacral nerve.



Figure 1: Axonics Neurostimulator.

Package Contents

The **Neurostimulator** package contains the following:

- Neurostimulator
- Torque wrench
- System registration form
- Patient identification card
- Neurostimulator Implant Manual (this document)

The contents of the inner package are **STERILE**. The contents of the Neurostimulator package are intended for single use only.

System Registration Form and Patient Identification Card

The system registration form registers the device and creates a record of the device in Axonics' implant data system.

The patient identification card is also packaged with this device. The patient should carry the identification card at all times.

AXONICS SNM THERAPY FOR BOWEL CONTROL

INDICATIONS

Axonics SNM therapy for bowel control is indicated for the treatment of chronic fecal incontinence in patients who have failed or are not candidates for more conservative treatments.

CONTRAINDICATIONS

The Axonics SNM System is contraindicated for the following patients

- Patients who have not demonstrated an appropriate response to test stimulation; or
- Patients who are unable to operate the Axonics SNM System.

WARNINGS

Diathermy

Shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (collectively described as diathermy) should not be used on patients implanted with the Axonics SNM System. Diathermy can transmit energy through the implanted system, potentially causing tissue damage at the location of the implanted electrodes, resulting in severe injury.

Magnetic Resonance Imaging (MRI)

The Axonics SNM System is a **MRI** conditional system. Refer to “MRI Guidelines for the Axonics Sacral Neuromodulation System” for more information.

Other Medical Procedures

Medical procedures that may affect the Axonics SNM System and should be avoided include:

- Lithotripsy
- Monopolar electro surgery
- Microwave and Radio-frequency (RF) ablation
- Radiation therapy over the Neurostimulator
- Ultrasound or scanning equipment

Electromagnetic Interference (EMI)

Electromagnetic interference is energy generated by equipment found at home, work, or in public that can interfere with the function of the Axonics SNM System. The Axonics SNM System includes features that provide protection from EMI so that most electrical devices encountered in a normal day are unlikely to affect the operation of the Neurostimulator. While everyday electrical devices are unlikely to affect the Neurostimulator, there are strong sources of EMI that may temporarily affect the operation of your stimulator,

including anti-theft detectors found in stores used to detect stolen merchandise. If patients encounter any of these electrical devices, they should walk as far away from the sides of the anti-theft detector when passing through.

At the Airport, Courthouses, etc.

If patients encounter walkthrough metal detectors or security archways they should walk-through at a normal pace. These detectors should not affect the Stimulator. Hand-held security wands should be passed over the Stimulator quickly and should not affect the stimulator. Full-body security scanners (millimeter wave scanners) are used by the Transportation Security Administration (TSA) and are considered safe in patients that have a stimulator.

Additionally, patients should minimize their exposure by not lingering in the immediate area of the security systems. Some anti-theft detectors may not be visible. If patients feel poorly, they should walk away from the area and anti-theft detectors and security scanners.

Case Damage

The Neurostimulator contains battery chemicals that could cause severe burns if the Neurostimulator case were ruptured or pierced.

Effects on Other Implanted Devices

The effect of the Axonics SNM System on the operation of other implanted devices, such as cardiac devices, other Neurostimulators, and implantable drug pumps, is not known. In particular, if the Axonics device is implanted close to one of these devices, they may have sensing problems and/or inappropriate device responses. Potential interference issues should be investigated before surgery by clinicians involved with both devices. The programming of the devices may need to be optimized to provide maximum benefit from both devices.

Neurostimulator Interaction with Implanted Cardiac Devices

When a patient needs both an Axonics SNM System and an implanted cardiac device (for example, a pacemaker or defibrillator), interactions between the two devices should be discussed by the patients' physicians involved with both devices (such as the cardiologist, electrophysiologist, urologist, and urogynecologist) before surgery. To reduce potential interference, the devices should be implanted on opposite sides of the body and as far away from each other as practical.

The stimulation pulses produced by the Axonics SNM System may interact with cardiac devices that sense cardiac activity, leading to inappropriate behavior of the cardiac device.

Charging Use

If swelling or redness occurs near the Charger attachment site, the patient should contact their clinician before using the Charger again. Swelling or redness may indicate an infection or an allergic reaction to the Charger adhesive.

PRECAUTIONS

Clinician Training

Implanting Clinicians should be trained on the implantation and use of the Axonics SNM System.

Prescribing Clinicians should be experienced in the diagnosis and treatment of fecal incontinence and should be trained on the use of the Axonics SNM System.

Use in Specific Populations

The safety and effectiveness of this therapy has not been established for:

- Pregnant women
- Pediatric use (patients under the age of 18)
- Patients with progressive, systemic neurological diseases
- Bilateral stimulation

Clinician Programming

Parameter Adjustment – The steps below should be taken to prevent sudden stimulation changes that lead to an uncomfortable jolting or shocking feeling:

- Stimulation parameters should be changed in small increments.
- The stimulation amplitude should be allowed to ramp to full amplitude slowly.
- Before disconnecting the stimulation cable or turning the simulation on or off, the stimulation amplitude should be decreased to 0.0 mA.

Sensitivity to Stimulation – Some patients, especially those that are very sensitive to stimulation, may be able to sense the telemetry signals associated with reprogramming.

Programmer Interaction with a Cochlear Implant –

Patients with cochlear implants should keep the external portion of their cochlear implant as far from the Clinician Programmer (CP) or Remote Control as possible to minimize unintended audible clicks or other sounds.

Programmer Interaction with Flammable Atmospheres –

The CP is not intended to be used in the presence of a flammable gas, and the consequences of using the CP in such an environment is not known.

Programmer Interaction with Other Active Implanted

Devices – When a patient has a Neurostimulator and another active implanted device (for example, a pacemaker, defibrillator, or another neurostimulator), the RF signal used to program any of these devices may reset or reprogram the other devices.

Whenever the settings for these devices are changed, a clinician familiar with each device should check the program settings of each device before the patient is released (or as soon as possible). Patients should contact their physician immediately if they experience symptoms that are likely to be related to the devices or their medical condition.

Telemetry Signal Disruption from EMI –

The Neurostimulator should not be programmed near equipment that may generate electromagnetic interference (EMI) as the equipment may interfere with the CP or Remote Control's ability to communicate with the Neurostimulator. If EMI is suspected to be interrupting programming, the CP or Remote Control and the Neurostimulator should be moved away from the likely source of EMI.

Electromagnetic Interference (EMI)

Patients may encounter additional equipment that generates EMI. This equipment is unlikely to affect the Axonics SNM System if the

patients follows these guidelines:

Bone Growth Stimulators – The external coils of bone growth stimulators should be kept at least 45 cm (18 in) away from the Axonics SNM System. Do not use a bone growth stimulator if it is not working as intended.

Dental Drills and Ultrasonic Probes –The drill or probe should be kept 15 cm (6 in) away from the Neurostimulator. The Neurostimulator should be turned off.

Electrolysis – The electrolysis wand should be kept at least 15 cm (6 in) away from the Neurostimulator. The Neurostimulator should be turned off.

Electromagnetic Field Devices – The following equipment or environments should be avoided or patients should exercise caution around:

- Antenna of citizens band (CB) radio or ham radio
- Electric arc welding equipment
- Electric induction heaters such as those used in industry to bend plastic
- Electric steel furnaces
- High-power amateur transmitters
- High-voltage areas (generally safe if outside the fenced area)
- Linear power amplifiers
- Magnetic degaussing equipment
- Magnets or other equipment that generates strong magnetic fields
- Microwave communication transmitters (generally safe if outside the fenced area)
- Perfusion systems
- Resistance welders
- Television and radio transmitting towers (generally safe if outside the fenced area)

Laser Procedures – The laser should not be directed at the Neurostimulator. The Neurostimulator should be turned off.

Psychotherapeutic Procedures – Equipment used for psychotherapeutic procedures may induce electrical currents which may cause heating at the lead electrodes and could result in tissue

damage. Equipment that generates electromagnetic interference (e.g., electroconvulsive therapy, transcranial magnetic stimulation) during psychotherapeutic procedures have not been established as safe to operate in a patient with a Neurostimulator. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.

Radiation Therapy – Neurostimulator operation may be affected by high-radiation exposure. Sources of high-radiation should not be directed at the Neurostimulator. Neurostimulator damage due to high-radiation exposure may not be immediately evident, and exposure should be limited using appropriate measures, including shielding and adjusting the beam angle to avoid exposure to the Neurostimulator.

Transcutaneous Electrical Nerve Stimulation (TENS) –TENS electrodes should not be placed in locations where the TENS current passes over any component of the Axonics SNM System. Discontinue using TENS if it starts affecting the performance of the Axonics SNM System.

If a patient thinks that an EMI generating equipment or environment is affecting the function of their Axonics SNM System, the patient should:

1. Move away from the equipment or object.
2. Turn off the equipment or object. (if possible)
3. Use the patient Remote Control to adjust stimulation if necessary and to confirm the system is functioning appropriately.

If the patient is unable to eliminate the interference or believes the interference has altered the effectiveness of their therapy, the patient should contact their clinician.

Sources of strong EMI can result in the following:

- **Serious Patient Injury**, resulting from heating of the Neurostimulator and/or leads that causes damage to surrounding tissue.
- **System Damage**, which may require surgical

replacement due to change in symptom control.

- **Operational Changes to the Neurostimulator**, causing it to turn on or off or to reset the settings, resulting in loss of stimulation or return of symptoms, causing a need for reprogramming by the clinician.
- **Unexpected Changes in Stimulation**, leading to a sudden increase or change in stimulation, which may be experienced as a jolting or shocking sensation. While the sensation may be uncomfortable, the device would not be damaged nor would it cause direct injury to the patient. In rare cases, the change in stimulation may cause the patient to fall and be injured.

Patient Activities

Activities Requiring Excessive Twisting or Stretching –

Patient activities that may strain the implanted components of the Axonics SNM System should be avoided. For example, movements that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching may cause migration or breakage of the Axonics SNM leads. Lead breakage or migration may cause loss of stimulation, intermittent stimulation, or stimulation at the fracture site. Additional surgery may be required to replace or reposition the component. Activities that typically involve these movements include gymnastics, mountain biking, and other vigorous sports. Clinicians should ask their patients about the activities in which they participate and inform them of the need for restricted activities.

Component Manipulation by Patient (Twiddler’s Syndrome) – Clinicians should advise patients to refrain from manipulating the Axonics SNM System through the skin. Manipulation may cause device damage, lead migration, skin erosion, or uncomfortable stimulation.

Scuba Diving or Hyperbaric Chambers – Pressures below

10 meters (33 feet) of water (or above 200 kPa) could damage the Axonics SNM System. Diving below 10 meters (33 feet) of water or entering hyperbaric chambers above 200 kPa should be avoided. Patients should discuss the effects of high pressure with their physician before diving or using a hyperbaric chamber.

Skydiving, Skiing, or Hiking in the Mountains – High altitudes should not affect the Neurostimulator. Nevertheless, patients should be cautious with high altitude activities due to the potential for movements that may put stress on the implanted components. For example, the sudden jerk that occurs when a parachute opens while skydiving may cause lead breakage or migration, which may require surgery to replace or remove the lead.

Unexpected Changes in Stimulation – A perceived increase in stimulation may be caused by electromagnetic interference, postural changes, and other activities. Some patients may find this uncomfortable (a jolting or shocking feeling). Before engaging in activities that receiving a jolt would be unsafe for the patient or those around them, patients should lower the stimulation amplitude to the lowest setting and turn off the Neurostimulator. Patients should also discuss these activities with their clinician.

Patient Programming and Remote Control

Patient Access to Remote Control – Patients should carry their Remote Control with them at all times to allow them to adjust the stimulation amplitude and/or turn on/off the Neurostimulator.

Remote Control May Affect Other Implanted Devices – Patients should avoid placing the Remote Control over or near other active implanted medical devices (for example pacemaker, defibrillator and other neurostimulators).

Remote Control Handling – To avoid damaging the Remote

Control, patients should avoid immersing it in liquid and should clean it with damp soft cloth. Patients should avoid dropping the device or mishandling it in any way that may damage it.

Remote Control Use – Patients should avoid operating the Remote Control when near flammable or explosive gases.

Storage and Usage Environment

Component Packaging – Any component that has been compromised in any way should not be implanted. Do not implant the component if any of the following have occurred:

- The storage package or sterile pack has been damaged, pierced, or altered, as sterility cannot be guaranteed, which may lead to infection.
- The component itself shows any signs of damage. The component may not function properly.
- The use-by date has expired. In this case, component sterility cannot be guaranteed and infection may occur.
- The sterile component was dropped onto a non-sterile surface. In this case, the sterility cannot be guaranteed and infection may occur.

Usage Environment:

The following lists the appropriate temperature, humidity, and pressure usage conditions for use of the Neurostimulator:

- Temperature: 20 °C to 45 °C
- Pressure: The Neurostimulator should function at up to 10 m (33 feet) underwater (200 kPa) and at altitudes up to 3000 m (10,000 feet) associated with activities like hiking and skydiving (as low as 70 kPa)

Shipping and Storage Environment:

The following lists the appropriate temperature, humidity, and pressure conditions for shipping and storing the Neurostimulator:

- Temperature (short term: 3 days): -10 °C to 55 °C
- Temperature (long term): 20 °C to 30 °C
- Humidity (short term: 3 days): 15% to 95%
- Humidity (long term): 30% to 85%
- Pressure (short term): 57 kPa to 106 kPa
- Pressure (long term): 70 kPa to 106 kPa

If the Neurostimulator is exposed to extreme temperatures, it may be permanently damaged and should not be used, even if it has returned to a temperature that is within the specified operating range.

Sterilization

The contents of this package have been sterilized using ethylene oxide. This device is for single use only and should not be re-sterilized.

System Implant

Compatibility – For proper therapy, use only Axonics SNM components. The use of non-Axonics components with the Axonics SNM System may result in damage to Axonics components, loss of stimulation, or patient injury. Use of non-Axonics components voids Axonics warranty coverage.

Component Failures – The components of the Axonics SNM System may fail at any time. Such failures, such as electrical shorts, open circuits, and insulation breaches are unpredictable. Also, the Neurostimulator battery will eventually fail to recharge. The rechargeable Neurostimulator battery should provide at least 15 years of

service and with repeated charging the battery will lose its ability to recharge to its full capacity. This may result in the Neurostimulator requiring more frequent recharging. When stimulator can no longer be maintained with regular charging, the Neurostimulator may need to be replaced.

Component Handling – The components of the Axonics SNM System must be handled with extreme care. They may be damaged by excessive force or sharp instruments, which can lead to intermittent stimulation or loss of stimulation altogether and may require surgery to replace. Do not use saline or other ionic fluids at connections, which could result in a short circuit.

POTENTIAL ADVERSE EVENTS SUMMARY

Implantation and use of the Axonics SNM System incurs risk beyond those normally associated with surgery, some of which may necessitate surgical intervention. These risks include, but are not limited to the following:

- Adverse change in voiding function (bowel and/or bladder)
- Allergic or immune system response to the implanted materials that could result in device rejections
- Change in sensation or magnitude of stimulation which has been described as uncomfortable (jolting or shocking) by some patients
- Device fracture/failure
- Device migration
- Electrical shock
- Infection

- Pain or irritation at Neurostimulator and/or lead site
- Seroma, hemorrhage, and/or hematoma
- Suspected lead or Neurostimulator migration or erosion
- Suspected nerve injury (including numbness)
- Suspected technical device malfunction
- Transient electric shock or tingling
- Unintended nerve activation
- Heating or burn at Neurostimulator site
- Lack of efficacy
- Reoperation/Revision
- Undesirable change in pelvic function

INDIVIDUALIZATION OF TREATMENT

The patient should be fully informed about the risks and benefits of SNM therapy, including risks of the surgical procedure, follow-up responsibilities, and self-care requirements. In order to achieve optimal benefits from the therapy, the Axonics SNM System requires a long-term commitment to post-surgical management.

Patient Selection – Patients should be carefully selected to ensure they meet the following criteria:

- The patient is an appropriate surgical candidate with special consideration for the lead length, implant depth, and ability to successfully implant the lead and route the lead to the Neurostimulator.
- The patient can properly operate the Axonics SNM System, including the ability to use the Remote Control, to detect alignment of the Charger, and to understand when charging is complete.
- Trial Stimulation: The patient has undergone a trial stimulation with either a temporary lead for up to 7 days, or a permanent lead for up to 14 days, and he/she experienced a 50% reduction in fecal incontinence episodes.
- The patient does not have a history of sensitivity to stimulation.

SUMMARY OF CLINICAL EVALUATION

The safety and effectiveness of the Axonics Sacral Neuromodulation (SNM) System for fecal control was based on a systematic review of published clinical studies that evaluated the safety and/or effectiveness of the Interstim fully implantable SNM system and on a study of the Axonics SNM System. The Axonics SNM System is similar in design, technology, performance, indications for use, output characteristics, and patient population to the SNM systems evaluated in these studies. The literature review strategy was conducted according to the guidelines and methods suggested by Egger, Smith and Altman in their book “Systematic Reviews in Health Care.”¹

The result of the systematic review and meta-analysis included 5 articles including 5 unique studies, representing a total of 430 implanted patients implanted with SNM systems. The data consisted of a systematic literature review of clinical research, a qualitative evaluation of the peer-reviewed published clinical research, and a quantitative meta-analysis of safety and efficacy using relevant clinical studies.

Additionally, safety data for the Axonics SNM System was reviewed from the ARTISAN-SNM study, which was an investigational device exemption (IDE) pivotal study in which 129 patients with urinary urgency incontinence (UUI) were treated with the Axonics SNM System.

Objective of Studies

Based on nonclinical studies that demonstrated that the Axonics neurostimulator has comparable output characteristics to the Interstim system reported in the

¹Egger M, Smith GD, Altman DG (2007). Systematic Reviews in Health Care. Meta-Analysis. Second Edition. BMJ Books. ISBN: 978-0-727-91488-0

literature, the primary objective was to use published clinical literature to provide clinical evidence of the safety and effectiveness of the device for the improvement of fecal incontinence symptoms.

Effectiveness of the subject device was evaluated by one of the following endpoints (obtained from the literature specific to the improvement of fecal incontinence with the use of SNM systems):

- Patients obtained at least a 50% reduction in the number of bowel episodes (i.e., Responder rate)
- Patients obtained an absolute decrease in the number of FI episodes per week.
- Patients obtained an improvement in their St. Mark's score as compared to baseline (scored from 0 (completely continent) to 16 (completely incontinent))
- Patients obtained an improvement in their Wexner score as compared to baseline (the Wexner score ranges from 0 – 20 and considers the type and frequency of incontinence and the extent to which it alters the patient's life).
- The change from baseline in the Fecal Incontinence Quality of Life (FIQL) questionnaire and the Fecal Incontinence Severity Index (FISI) were also evaluated

Safety was demonstrated by a review of the following sources, which totaled 459 patients:

- Review of incidence of complications of the InterStim System from literature for the fecal incontinence indication
- Review of all Adverse Events (AE) from the ARTISAN-SNM study, the IDE pivotal study for the Axonics SNM System, which was conducted in 15 US clinical sites

and 5 sites in Western Europe under G170100. The study enrolled 153 patients, of which 129 were implanted with the Axonics SNM System

Summary of Literature Search Strategy

The objective of the literature review was to systematically identify, select, collate and review relevant studies to support the marketing application of the Axonics SNM System. A summary of the literature search strategy and inclusion/exclusion criteria is provided below.

The scientific literature database, Medline/PubMed, was used by Axonics and duplicated by FDA to perform a search for published data relevant to the clinical evaluation of the Axonics SNM System. The search was conducted for literature published through January 15, 2019.

All articles from the published literature were triaged for inclusion based on their suitability prior to full review. Studies were selected for inclusion in this review if the methods section clearly indicated the equivalent neurostimulation system (InterStim) was used in the treatment of urinary and/or bowel dysfunction. These studies were initially selected by Axonics based on the studied endpoints and the safety and efficacy criteria selected. Systematic meta-analysis reviews, randomized clinical trials and prospective clinical studies were included by Axonics because, these were deemed “to be of the highest data quality” by Axonics. However, FDA excluded the meta-analyses, because their inclusion/exclusion criteria were different, allowing for differences in the study population and smaller sample sizes, as well as, to avoid duplication, because some of the articles included in the meta-analyses were already included as primary studies in this systematic literature review. Individual cohort studies published less than 15 years ago were included, or if the cohort studies were published over 15 years ago and had more than 100 patients, the studies were also included in this search.

The literature search strategy from Axonics, and duplicated by FDA, consisted of the following three primary steps. FDA added one more step to select only randomized clinical trials and prospective cohort studies with clearly defined study design:

- The Medline database was searched for indexed articles using 21 MeSH terms (Medical Subject Headings, National Library of Medicine) and broad relevant terms for pelvic neurostimulation systems and treatment of fecal and urinary incontinence. After eliminating duplicates, there were 923 articles.
- The abstract of each article was reviewed and categorized according to the same rigorous inclusion/exclusion criteria used by Axonics. Exclusions eliminated 896 articles resulting in the selection of 27 articles for full review.

Exclusions included: N<100 pts non-randomized (42 articles), N<100 pts, >15 years (83 articles), > 10 years, non-randomized (1 article), animal data (3), technical note/clinician technique (66 articles), case report/series (38 articles), cost assessment (20 articles), disease state (17 articles), dissimilar medical area (7 articles), dissimilar patient population (64 articles), dissimilar device [e.g., tibial] (151 articles), dissimilar indication (53 articles), excluded study type (e.g., bench, retrospective study) (123 articles), intra-device comparison, (2 articles), medicinal substance (16 articles), no abstract (53 articles), No author (4 articles), no clinical data (98 articles), no device evaluation/no device identification (32 articles), patient care management (30 articles) and articles that only included patient physiology/anatomy/demographics (54 articles). Of note, the exclusion numbers above add to 957, because some excluded articles fit in more than one

category.

- Three additional articles were selected from other sources including 2 articles identified from meta-analysis reviews and one more that was found by cross reference (it was cited in the most current study publication). This step brought the review to a total of 30 articles for full assessment.
- An additional selection step was made by FDA to include only the randomized clinical trials and prospective cohort studies in which the study design was clearly stated and unequivocal. In this last step, 25 articles including meta-analyses and cohort studies with unclear study design were excluded. This resulted in 5 articles for inclusion in this review. Out of these 5 articles:
 - a. Four of the 5 studies had safety endpoints appropriate for the assessment of safety.
 - b. All 5 were appropriate for the evaluation of effectiveness due to their endpoints to assess improvements in FI.

Evaluation of Safety

FDA evaluated the safety of the Axonics SNM System based on two sources of data, namely the published articles on the use of the InterStim System for fecal incontinence and a review of any AE from the ARTISAN-SNM study (the IDE study for the Axonics SNM System). The ARTISAN-SNM study was conducted in 15 US clinical sites under G170100 and evaluated 129 implanted patients. Taking these two sources of data together, there were 459 implanted patients evaluated for AEs.

Literature Source Evaluation of Safety

The literature provided strong evidence to support a low serious AE (SAE) rate for the use of the InterStim System in

330 patients treated with the device to treat fecal incontinence.

All AEs and SAEs reported per article are provided in **Table 1**.

Table 1: Adverse Events Reported in the Literature for the InterStim System.

Article Reference	Follow up duration	Adverse Events	SAE
Hull, 2013 (120 subjects)	5 years	<ul style="list-style-type: none"> • Pain at implant site (32.5%) • Paresthesia (19.2%) • Change in sensation of stimulation (11.7%) • Infection, implant site (10%) • Urinary incontinence (8.3%) • Battery depletion (6.7%) • Diarrhea (6.7%) • Pain, extremity (5.8%) • Change in stimulation, undesirable (5.8%) • Pain, buttock (5.0%) • Migration, Implant (2.5%) • Other (58.3%) 	<ul style="list-style-type: none"> • Pain at implant site (9%) • Infection, implant site (3.3%) • Battery depletion (0.8%) § • Other (9.2%)

Article Reference	Follow up duration	Adverse Events	SAE
Patton, 2016 (127 subjects)	2.7 years	<ul style="list-style-type: none"> • Lead migration (13%) • Explantations (11%) • Infection, wound (6%) • Infection, implant (4%) • Reoperation (4%) • Neurostimulator revision (4%) • Pain, Neurostimulator site (3%) • Hematoma (2%) 	<ul style="list-style-type: none"> • NR ‡
Tjandra, 2008 (53 subjects)	12 months	<ul style="list-style-type: none"> • Uncomfortable sensation (9%) • Pain at implant site (6%) • Seroma (2%) 	<ul style="list-style-type: none"> • NR ‡
Rydningen, 2017 (30 subjects)	6 months	<ul style="list-style-type: none"> • Pain at Neurostimulator (NR ‡) • Neurostimulator revision (NR ‡) 	<ul style="list-style-type: none"> • NR ‡

§ One event of battery depletion occurred which was considered serious because of the patient being admitted to hospital for > 24 hrs; however, no complications occurred during or after the battery replacement.

‡ NR: Rates are not reported by author or not relevant since the sample size is too small (N<30) to have a meaningful rate associated with it.

As shown above, Hull, et al (2013) followed patients up to 5 years. This publication was the results of Medtronic's s post-approval study as required by FDA at the time of approval of a Premarket Approval (PMA) to help assure continued safety and effectiveness of the approved device. Post-approval

studies (PAS) are conditions of device approval.

More information on the PAS for P080025 can be found on FDA's website:

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=415338&c_id=398

The initial enrollment across 16 institutions included a total of 285 patients with a minimum of 2 episodes of fecal incontinence (FI) per week for a duration of longer than 6 months (1 year after vaginal childbirth), had failed or were not candidates for more conservative medical treatments and were 18 years of age or older.

In this study, 120 patients were implanted and over the study duration these patients experienced 218 total device-related AEs. The most common device-related AEs included implant site pain (n = 53), paresthesia (n = 30), change in sensation of stimulation (n = 21), implant site infection (n = 12) and urinary incontinence (n = 10). The majority of these events (80%) were successfully treated non-invasively with medication, other medical therapy, reprogramming, or no intervention.

In addition, 47 (39.2%) patients had at least 1 device revision, replacement, and/or explant during the study. There was a total of 10 device revisions in 10 patients (9 neurostimulators and 1 lead), 40 device replacements in 29 patients (neurostimulator, lead, extension, or a combination thereof), and 22 system explants in 22 of the 120 implanted patients. The most common reason for a surgical revision was device migration (n = 8), the most common reason for a device replacement was battery depletion (n= 12), and the most common reason for a system explant was lack of efficacy (n = 11).

Patton, et al (2016), conducted a prospective, non-randomized study in 127 patients with fecal incontinence (without rectal prolapse) who had failed conservative therapies. In this study complications occurred in all 127

subjects. Deep wound infection required surgery in 5 patients (4%), superficial wound infections were treated with antibiotics in 7 patients (6%), rotation of the neurostimulator required repositioning in 5 patients (4%) and pain over the neurostimulator occurred in 4 patients (3%). The implant was explanted permanently in 14 subjects due to infection (n = 3), hematoma (n = 2), pain over the neurostimulator (n = 4), no clinical benefit (n = 4) and in 2 patients who required magnetic resonance imaging (MRI) (subsequently reimplanted in one). Lead migration requiring replacement occurred in 17 patients (13%).

Tjandra et al (2008), conducted a RCT in 120 patients with severe FI with 12 months follow-up. This study compared the effect of SNM with optimal medical therapy in patients with severe FI. Full assessment included endoanal ultrasound, anorectal physiology, 2-week bowel diary, and FI quality of life index. There were no septic complications. The study reported adverse events as minor and included pain at implant site especially in slimmer patients (6%), seroma (2%) which resolved after percutaneous aspiration, and excessive tingling in the vaginal region (9%). There were no septic complications requiring explantation. There were no adverse events associated with urinary or sexual function..

Rydningen et al (2017), was a single-blinded RCT for FI. Fifty-eight (58) women were randomly assigned to SNM (n = 30) or Permacol (n = 28) (a bulking agent). After SNM, nine (9) patients (35%) reported adverse events at 6 months, which included one (1) patient reporting pain related to the neurostimulator and one (1) describing pain in her leg. Five (5) women reported a deterioration of urinary function, which resolved after resetting the neurostimulator. Two (2) women were referred to specialists for further investigation after 6 months because of deterioration of urinary function. The IPG was reset during follow-up in 17 (57%) patients, including an adjustment of the amplitude and readjustment because of pain (n = 1) or deterioration of urinary function (n = 7).

Axonics Clinical Data Evaluation of Safety

The ARTISAN-SNM Study was a single arm, prospective, multicenter, unblinded, pivotal study with the primary objective of evaluating the safety and effectiveness of the Axonics SNM System for the treatment of Urinary Urgency Incontinence (UUI), a subtype of overactive bladder (OAB). The study was conducted in 15 US Centers (97 patients implanted) and 5 Centers in Western Europe (32 patients implanted).

In this study, patients were tested intraoperatively for responses suggestive of lead placement near the target sacral nerve, and were then implanted with the permanent implant rather than undergoing the typical SNM trial period (with external stimulator and percutaneous lead). FDA utilized the outcomes of this study for their evaluation of the safety of the Axonics SNM System at 6 months post-implantation and therapy activation. In McCrery et al (2019), additional study design details are provided.

The primary safety endpoint was the rate of AEs reported in the study.

A total of 181 AEs were reported among 80 subjects across the entire study experience. Out of 181 AEs, 180 AEs occurred in implanted subjects, and one (1) AE occurred in a subject that was enrolled in the study but not implanted. Of the 180 AEs, 7 were SAEs and no SAEs were procedure-related or device-related. Out of the 173 non-serious AEs, 13 were related to device, and 15 were related to procedure (as shown in the tables below). One (1) death occurred from complications following multiple perforated diverticulum of the large intestine. The death was not related to device or procedure. None of the reported AEs were unanticipated.

The total number and percentage of AEs by event category, seriousness, and relatedness to device or procedure is presented in **Table 2** and **Table 3**.

Table 2: Device Related AEs and SAEs Reported in the ARTISAN-SNM Study.

AE Type	Device Related		Serious Device Related	
	Events (n)	Subjects (n/N) (%)	Events (n)	Subjects (n/N) (%)
Proctalgia	1	1 (0.8)	0	0 (0.0)
Pain	1	1 (0.8)	0	0 (0.0)
Medical device discomfort	1	1 (0.8)	0	0 (0.0)
Implant site pain	2	2 (1.6)	0	0 (0.0)
Incision site infection	1	1 (0.8)	0	0 (0.0)
Pain at extremity	2	2 (1.6)	0	0 (0.0)
Groin Pain	1	1 (0.8)	0	0 (0.0)
Dysaesthesia	1	1 (0.8)	0	0 (0.0)
Lead dislodgement	1	1 (0.8)	0	0 (0.0)
Vulvovaginal pain	1	1 (0.8)	0	0 (0.0)
Vulvovaginal discomfort	1	1 (0.8)	0	0 (0.0)
Total	13	13 (10.1)	0	0 (0.0)

Table 3: Procedure Related AEs and SAEs Reported in the ARTISAN-SNM Study.

AE Type	Procedure Related		Serious Procedure Related	
	Events (n)	Subjects (n/N) (%)	Events (n)	Subjects (n/N) (%)
Vomiting	1	1 (0.8)	0	0 (0.0)
Implant site pain	1	1 (0.8)	0	0 (0.0)
Hypersensitivity	1	1 (0.8)	0	0 (0.0)
Allergy to chemicals	1	1 (0.8)	0	0 (0.0)
Incision site infection	1	1 (0.8)	0	0 (0.0)
Fungal infection	1	1 (0.8)	0	0 (0.0)
Procedural pain	4	4 (3.1)	0	0 (0.0)
Incision site pain	1	1 (0.8)	0	0 (0.0)
Paraesthesia	1	1 (0.8)	0	0 (0.0)
Keloid scar	1	1 (0.8)	0	0 (0.0)
Dermatitis papillaris capillitii	1	1 (0.8)	0	0 (0.0)
Suture insertion	1	1 (0.8)	0	0 (0.0)
Total	15	13 (10.1)	0	0 (0.0)

Note: A total of 15 events occurred in a total of 13 subjects.

The most common device related AEs were implant site pain (n=2), extremity pain (n=2) and vulvovaginal pain/discomfort (n=2). No other device related AE occurred more than once. The most common procedure-related AE was procedural pain (n=4). No other procedure-related AE occurred more than once.

There were no device or procedure-related SAEs.

The time course and resolution status of device-related and procedure-related adverse events (AEs) from the Artisan-SNM study are provided in Tables below. All AEs and their resolution status are reported as of the data lock date of 18 January 2019. Tables 4 and 5 provide summarized information.

Device-related adverse events

Table 4: Summary and time-course device-related adverse events

Number of implanted subjects = 129							
AE Type	Implant to 2 Weeks	2 weeks to 1 Month	1 Month to 3 Months	3 Months to 6 Months	6 Months to 12 Months	Beyond 12 Months	Status Resolved*/ Ongoing
Total events	1	4	2	3	3	0	13/0
Proctalgia	0	0	0	1	0	0	1/0
Pain	0	1	0	0	0	0	1/0
Medical device discomfort	0	0	0	0	1	0	1/0
Implant site pain	1	0	1	0	0	0	1*/0
Incision site infection	0	1	0	0	0	0	1/0
Pain in extremity	0	1	0	1	0	0	1/0
Groin pain	0	0	1	0	0	0	1/0
Dysaesthesia	0	0	0	0	1	0	1/0
Lead dislodgement	0	1	0	0	0	0	1/0
Vulvovaginal pain	0	0	0	0	1	0	1/0
Vulvovaginal discomfort	0	0	0	1	0	0	1/0

** Includes events that were resolved with sequelae*

Procedure-related adverse events

Table 5: Summary and time-course of procedure-related adverse events

Number of implanted subjects = 129							
AE Type	Implant to 2 Weeks	2 weeks to 1 Month	1 Month to 3 Months	3 Months to 6 Months	6 Months to 12 Months	Beyond 12 Months	Status Resolved */ Ongoing
Total events	10	3	1	1	0	0	13/2
Vomiting	1	0	0	0	0	0	1/0
Implant site pain	1	0	0	0	0	0	1*/0
Hypersensitivity	0	1	0	0	0	0	1/0
Allergy to chemicals	1	0	0	0	0	0	1/0
Incision site infection	0	1	0	0	0	0	1/0
Fungal infection	0	1	0	0	0	0	1/0
Procedural pain	4	0	0	0	0	0	3/1
Incision site pain	1	0	0	0	0	0	1/0
Paraesthesia	0	0	1	0	0	0	0/1
Keloid scar	0	0	0	1	0	0	1*/0
Dermatitis papillaris capillitii	1	0	0	0	0	0	1*/0
Suture insertion	1	0	0	0	0	0	1/0

* Includes events that were resolved with sequelae

Evaluation of Effectiveness

The analysis of effectiveness for the treatment of fecal incontinence was based on a review of the same four (4) articles discussed above for safety, but with the addition of a study by Melenhorst et al. The five (5) studies encompassed 430 subjects. The ARTISAN study was not used in the assessment of effectiveness because its primary objective was to treat urinary urgency incontinence, not fecal incontinence.

Key effectiveness outcomes are presented in **Table 4**.

Table 5: Effectiveness Outcomes Reported in the Literature for the InterStim System.

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant <i># subjects at follow up (% of subjects receiving permanent implant)</i>	Effectiveness Endpoint (Responder ₅₀ Rate, St. Mark's score, FI episodes or other)
Hull, 2013	133	120 (90%)	5 years 72 subjects (60%)	Responder ₅₀ Rate: 89% (64/72 subjects), Mean number of FI episodes per week: Baseline: 9.1 5 years: 1.7 36% (26/72) were totally continent

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant <i># subjects at follow up (% of subjects receiving permanent implant)</i>	Effectiveness Endpoint (Responder ₅₀ Rate, St. Mark's score, FI episodes or other)
Patton, 2016	166	127; 112 after test stimulation (68%); 15 implants without trial	2.7 years <i>91 subjects (72%)</i>	St. Mark's score: baseline: 14.4 (95% CI: 13.44, 15.33) follow-up: 10.3 (95% CI: 9.2, 11.44)
Melenhorst, 2007	134	100 (75%)	25.5 months <i>33 subjects (33%)</i>	Mean number of FI episodes per 3 weeks: baseline: 31.3 3 years: 4.5 Mean number incontinent days per 3 weeks: baseline: 12.7 3 years: 3.3

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant <i># subjects at follow up (% of subjects receiving permanent implant)</i>	Effectiveness Endpoint (Responder ₅₀ Rate, St. Mark's score, FI episodes or other)
Tjandra, 2008	60	53 (88%)	12 months <i>53 subjects (100%)</i>	<p>Mean number of FI episodes per week: baseline: 9.5 ± 12.8 (SD) 12 months: 3.1 ± 10.1 (SD)</p> <p>Mean number incontinent days per week: baseline: 3.3 ± 2.4 (SD) 12 months: 1 ± 1.7 (SD)</p> <p>Wexner Score: baseline: 16. ±1.3 12 months: 1.2 ± 1.8</p> <p>47% (25/53) were totally continent</p>

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant <i># subjects at follow up (% of subjects receiving permanent implant)</i>	Effectiveness Endpoint (Responder ₅₀ Rate, St. Mark's score, FI episodes or other)
Rydninge n, 2017	N/A	30 (N/A)	6 months 30 subjects (100%)	St. Mark's score: Baseline: 19.0 ± 2.5 (SD) 6 months: 7.7 ± 5.5 (SD)

In the Hull, et al study, a total of 133 patients met all the inclusion and exclusion criteria and underwent test stimulation for a period of 10 to 14 days to determine the effectiveness of the therapy. There were 120 patients who achieved a $\geq 50\%$ improvement in incontinent bowel episodes (met Responder₅₀ Rate) and subsequently underwent implantation with the approved SNM device. Patients had a follow-up of up to 5 years. The results are reported as the proportion of patients that had a minimum of a 50% reduction of fecal incontinence episodes (Responder₅₀ Rate). The change from baseline in the Fecal Incontinence Quality of Life (FIQL) questionnaire and the Fecal Incontinence Severity Index (FISI) were also evaluated.

Of the 120 subjects receiving permanent implants in the Hull study, 5 year responder rates were available for 72 subjects (60%). Among these subjects, 89% (64/72) had at least a 50% improvement from baseline in weekly incontinent episodes and 36% (26/72) of patients at 5 years post-implantation had achieved total continence. The average number of weekly incontinent episodes decreased

from 9.1 at baseline to 1.7 at 5 years. In addition, improvements in all four (4) scales of the FIQOL from baseline to 5 years post-implantation were statistically significant. With the use of the patient weighting for scores, the mean FISI decreased from 37.95 at baseline to 28.33 at the 5-year follow-up.

In the Patton, et al study, the investigators evaluated the improvement in the St. Mark's score, which is a patient scoring of fecal incontinence from 0 (completely continent) to 16 (completely incontinent). An initial enrollment of 166 subjects underwent trial testing of which 112 progressed to a permanent SNM implant. An additional 15 subjects received an implant without the testing phase, giving a total of 127 subjects of which 109 subjects were available for follow-up and 91 were included in the analysis (18 did not respond to a survey). The mean follow-up was 2.7 years. Continence improved from a baseline St. Mark's mean score of 14.4 (95% CI: 13.44, 15.33) to a follow-up mean score of 10.3 (95% CI: 9.2, 11.44).

In the Mellenhorst, et al. study, of 134 subjects with at least one (1) episode of FI per week, there were 100 subjects that received a permanent implant. The mean number of FI episodes per 3 weeks decreased from 31.3 episodes at baseline to 4.5 episodes at 3 years. The mean number of FI days per 3 weeks decreased from 12.7 at baseline to 3.3 at 3 years. There were 21 subjects that were considered to be late failures based on the relapse of symptoms to < 50% improvement from baseline symptoms, implementation of another therapy for FI and patient dissatisfaction.

In the Tjandra, et.al study, the absolute decrease in the number of FI episodes was evaluated in 120 subjects (minimum Wexner incontinence score of > 12, mean of 16)

that were randomized to SNM or control group having optimal medical therapy (pelvic floor exercises, bulking agents, and dietary control). During the test period for the SNM cohort, incontinence episodes improved by more than 50% in 54 of 60 patients (90%). Full systems were implanted in 53 of these 54 patients, who were then followed for 12 months. Subjects that received SNM had a decrease of the mean incontinence episodes per week from 9.5 to 3.1 and a mean decrease in incontinent days per week from 3.3 to 1 at 12 months. Complete continence was accomplished in 25 SNM patients (47.2%). The mean Wexner score at baseline was 16 at baseline, and 1.2 at 12 months. There was also improvement in FIQL index in all 4 domains (lifestyle, coping/behavior, depression/self-perception and embarrassment) as compared to the control subject cohort. There was no improvement in the FIQL in the 60 control subjects.

In the Rydningen, et al study, the effectiveness of InterStim was evaluated in comparison to submucosal injection of collagen (Permacol) among 58 female patients (30 SNM and 28 Permacol) with FI. Both patient groups had a baseline St. Mark's score > 8 and $\geq 50\%$ improvement with a test period evaluation. The reduction in the St. Mark's score between baseline and 6 months was 11.2 (SD 5.3) in the SNM group versus 2.3 (SD 5.0) in the Permacol group, resulting in a treatment difference of 8.9 (95% CI: 6.1–11.7), in favor of SNM. SNM was also superior to Permacol regarding the four (4) domains of the FIQL.

Conclusions

The body of published clinical literature concerning SNM is significant enough to conduct an adequate assessment of the risks and benefits of the technology. The results of this clinical evaluation demonstrated robust clinical outcomes for the use of fully implantable SNM systems in the treatment of FI in patients where surgical interventional measures are clinically indicated.

Based on a thorough review, it can be concluded that:

Adequate evidence exists to support the use of SNM systems in patients with fecal incontinence

The safety profile is well documented in clinical studies. Rates of AEs are low to moderate and generally minor

The clinical literature concerning the use of comparable SNM systems is relevant to the Axonics SNM System in the following ways:

Results of the clinical literature evaluation indicate that the use of SNM has been shown to be a safe and effective option for treatment of fecal incontinence, in patients who have failed or could not tolerate more conservative treatments.

The characteristics of the Axonics SNM System are represented in whole, or in part, by the technologic characteristics of the equivalent SNM systems which have been studied in the aforementioned clinical literature. The use aspects of these systems are well-known and understood by the intended clinician population and there is no evidence to suggest that the Axonics SNM System would produce anything less than comparable clinical results.

The percutaneous surgical technique used with the Axonics SNM System is consistent with standard SNM practices. Moreover, it is not anticipated that the Axonics SNM System would have new procedure-related complications

The ARTISAN-SNM study provides evidence that the Axonics SNM System can be used to provide SNM therapy to patients with FI with a comparable safety profile to the clinical literature.

Note on Limitation of the Data

The effectiveness of SNM therapy and the Axonics SNM System is based on published studies from medical journals

and results from an open label study sponsored by Axonics. In these studies, patients were aware they were receiving sacral neuromodulation therapy and the studies did not assess whether or not there was a significant placebo response. This may result in an overestimation of therapy results.

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PATIENT COUNSELING INFORMATION

Clinicians should provide the following:

- Information about the components of the Axonics SNM System.
- Instructions for using the Remote Control and Charging System.

Also, the clinician should provide each patient with a copy of the Axonics SNM System Patient Therapy Guide and, in particular, review the following sections with him/her:

- Getting the Axonics SNM System
- Living with the Axonics SNM System

Clinicians should also instruct their patients as follows:

- Patients should tell their healthcare professionals, including their primary doctor and dentist, that they have an implanted neuromodulation system. Patients should bring their Patient Therapy Guide to all medical and dental appointments in the event that their healthcare professional has any questions regarding any precautions to take to avoid potential device problems.
- Patients should always carry their Remote Control to allow them to change the stimulation amplitude and/or turn the Neurostimulator on or off.
- Patients should always bring their Remote Control to appointments related to their Axonics SNM System, including all programming sessions.
- Patients should contact their physician if they have any unusual signs or symptoms.

COMPONENT DISPOSAL

The following steps should be taken when the Axonics SNM System is explanted (for example, due to replacement, cessation of therapy, or after patient death) or when disposing of accessories:

- If possible, the explanted component should be returned to Axonics along with completed paperwork for analysis and disposal.
- The device should not be autoclaved or exposed to ultrasonic cleaners to allow it to be analyzed by Axonics.
- Any components not returned to Axonics should be disposed of according to local regulations. Any potentially contaminated materials should be treated as biohazardous waste.

Note that in some countries, explanting a battery-operated implantable device is mandatory.



Cautions:

- Components that are explanted or that have come into contact with bodily fluids should be handled with appropriate biohazard controls. Such components should only be returned to Axonics in packaging supplied by Axonics.
- The Neurostimulator may explode if subjected to high temperatures; therefore the Neurostimulator should not be incinerated and should be explanted before patient cremation.
- Implantable devices should not be reused after exposure to body tissues or fluids because the sterility and functionality of these devices cannot be assured.

SPECIFICATIONS

Table 5 shows the Neurostimulator physical specifications. For detailed descriptions and specifications for other components and accessories, refer to the product literature packaged with those devices.

Table 6: Neurostimulator Specifications.

Physical Attributes	Height	42 mm
	Length	22 mm
	Thickness	6 mm
	Weight	11 grams
	Volume	5.5 cc
	Radiopaque identifier	AXA
	Stimulation Characteristics	Frequency
Pulse Width		60-450 μ s
Amplitude		0-12.5 mA
Minimum Amplitude Step Size		0.05 mA
Ramping		0-30 s
Stimulation Mode		Continuous or Cycling
Mode of Operation		Current-Controlled
Power Source	Battery	Rechargeable
	Power Source	50 mAh (3.6V)
	Battery life	15 years (open-ended)*

Note: All dimensions are approximate.

*Battery life estimated at nominal and worst case stimulation settings.

Nominal: 1 mA, 14 Hz, 210 μ s, continuous stimulation, impedance = 1,600 Ohms.

Worst case: 4 mA, 14 Hz, 210 μ s, continuous stimulation, impedance = 1,600 Ohms.

Table 6 shows the materials used in the Neurostimulator kit components that come in contact with human tissue.

Table 7: Human-Contact Materials.

Device	Component	Material
Neurostimulator	Neurostimulator case	Titanium-Ceramic
	Neurostimulator header	Epoxy
	Septum and strain relief	Silicone
	Setscrew	Titanium
	Adhesive	Silicone
Torque wrench	Torque wrench handle	Polyetherimide
	Torque wrench shaft	Stainless steel

Note: The Neurostimulator case, which contains the electronics and power source, is hermetically sealed.

X-RAY IDENTIFICATION

The radiopaque marker allows physicians to identify the manufacturer and model number under standard x-ray procedures. For the Axonics Neurostimulator, the designated code is AXA, which appears as light characters on a black background (**Figure 2**).

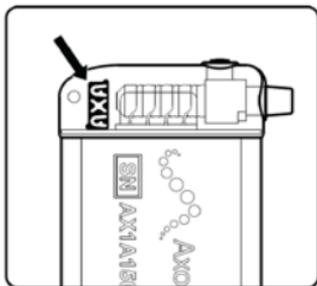


Figure 2: The Axonics Neurostimulator radiopaque marker, “AXA”.

NEUROSTIMULATOR IMPLANT PROCEDURE

The following section describes the procedure for implanting the Axonics Neurostimulator. This procedure should be performed when an Axonics tined lead has already been implanted.

Procedure Supplies

In addition to the general surgical tools required by the physician, the following supplies are needed for the preparation, implantation, programming, and Remote Control pairing of the Neurostimulator:

- Axonics Neurostimulator
- Axonics Charging System
- Axonics Clinician Programmer (CP)
- Axonics Remote Control



Caution: The user should avoid damaging the Neurostimulator and be especially cautious using sharp instruments as damage to the Neurostimulator may require a surgical replacement.

Neurostimulator Preparation

Use the Charger to activate the Neurostimulator. Before opening the sterile Neurostimulator package, the Clinician Programmer (CP) should be used to communicate with the Neurostimulator to verify the ability to communicate and to check battery status. If the Neurostimulator battery is low, the device should be charged through the box before implantation by using the Charger. Refer to the CP and Charging System Manuals for further instructions.

Creating the Neurostimulator Pocket

1. The Neurostimulator will be placed in a subcutaneous pocket at the anterior surface of the muscle in the upper buttock area. Create a small incision, slightly larger than the smaller dimension of the Neurostimulator, and then bluntly dissect a subcutaneous pocket.

Notes:

- The Neurostimulator should be placed no deeper than 3.0 cm (about 1 in) below the skin and should be parallel to the skin. If the Neurostimulator is too deep or is not parallel to the skin, charging and/or programming the device may be unsuccessful.
 - The Neurostimulator should be implanted horizontally (**Figure 3**) with the ceramic side farthest from the patient's midline to facilitate charging and programming.
 - For a patient with another neurostimulator already implanted, the neurostimulators should be placed as far away as practical and separated by a minimum of 20 cm (8 in).
-



Cautions:

- The Neurostimulator implant site should be irrigated with antibiotic solution, and it is recommended that IV antibiotics be administered perioperatively. Do not soak the Neurostimulator in antibiotic solution as this may affect lead connections.
 - The Neurostimulator has been sterilized. The Neurostimulator should not be placed on any non-sterile surface. The Neurostimulator should not be placed on skin. An infection may require surgical removal of the implanted system.
-

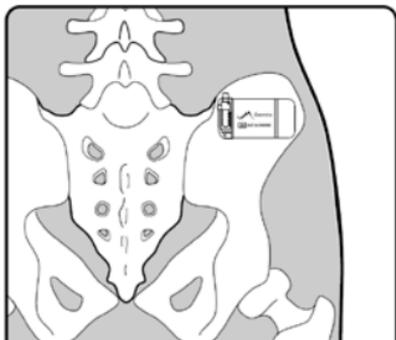


Figure 3: Axonics Neurostimulator Implantation Position.

2. Use the tunneling tool to create a tunnel from the lead incision site to the neurostimulator pocket. Refer to the Tined Lead Manual for detailed tunneling and lead implant instructions.

Connecting the Lead to the Neurostimulator

1. The components should be wiped and dried to remove any fluids before making the connections. If necessary, use sterile water or a non-ionic antibiotic solution, then wipe dry.



Caution: Failure to completely dry the components could lead to undesired stimulation, intermittent stimulation, or loss of therapy.

2. Ensure that the Neurostimulator connector block is dry and clean.

3. Use the torque wrench to turn the setscrew counterclockwise to back up the setscrew. Do not remove the setscrew from the connector block (**Figure 4**).

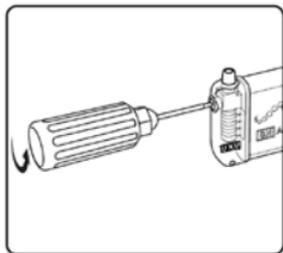


Figure 4: Use the Torque Wrench to Turn the Setscrew Counterclockwise to **Back up** the Neurostimulator Setscrew and Allow for Insertion of the Lead.

4. Insert the lead into the Neurostimulator connector block until fully seated and the lead cannot be inserted further. Marker D on the lead should be inside the Neurostimulator strain relief (**Figure 5**). The retention sleeve on the tined lead should be positioned under the Neurostimulator setscrew.

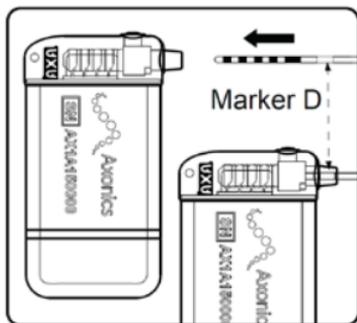


Figure 5: Insert Lead Fully into the Neurostimulator Connector Block.



Cautions:

- Avoid pulling the lead body taut when implanted.
 - Do not attempt to insert the lead into the Neurostimulator if the setscrew is not sufficiently retracted as doing so may cause damage to the lead and/or cause the lead to not seat fully into the connector block.
 - Ensure that the setscrew tightens on the retention sleeve, not an electrode. Tightening the setscrew onto the contact could damage the contact, leading to lack of therapy.
-

5. Fully insert the torque wrench into the hole of the Neurostimulator connector block. Tighten the setscrew by turning the torque wrench clockwise until it clicks (**Figure 6**).

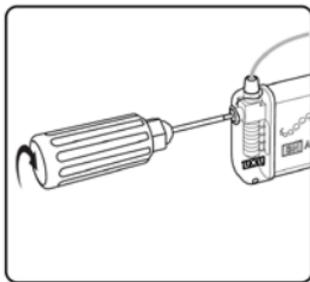


Figure 6: Secure the Lead by Tightening the Setscrew Clockwise onto the Retention Sleeve.



Cautions:

- Ensure that the torque wrench is fully inserted into the setscrew. Otherwise the setscrew may be damaged, which can result in intermittent or loss of stimulation.
 - The torque wrench is designed for single use only and cannot be assured to work appropriately if used for multiple surgeries. Discard the torque wrench after use.
-

Implanting the Neurostimulator

1. Place the Neurostimulator into the subcutaneous pocket. Ensure that the ceramic side is placed away from the patient's midline to ensure good communication with the Remote Control and ease of

recharging (**Figure 3**). The etched writing can face either towards or away from the muscle tissue. Ensure that the lead curves gently away from the Neurostimulator with no sharp bends.

Note: The Neurostimulator should be placed no deeper than 3.0 cm (about 1 in) below the skin and should be parallel to the skin. If the Neurostimulator is too deep or is not parallel to the skin, telemetry and/or charging may be unsuccessful.



Caution: Do not coil excess length in front of Neurostimulator. Wrap excess length around the perimeter of the Neurostimulator (**Figure 7**) or place under the Neurostimulator to minimize interference with telemetry during programming.

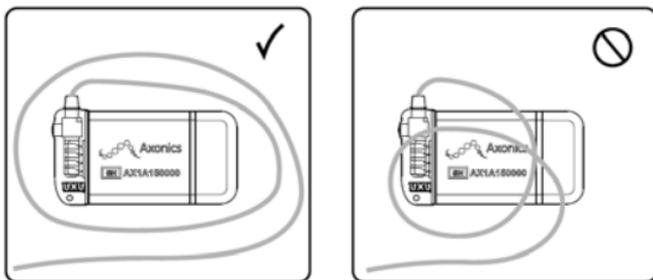


Figure 7: Wrap Excess Lead Around or Under, but not on Top of, the Neurostimulator.

2. Use the Clinician Programmer to check the impedances and ensure good function and connectivity of the system.

Notes:

- The Neurostimulator should be in the subcutaneous pocket during system interrogation to ensure proper

readings.

- Refer to the Clinician Programming Manual for detailed instruction on checking the system integrity and impedances.
3. Use the suture hole in the header to secure the Neurostimulator to the muscle fascia with non-absorbable silk

Completing the Implant Procedure

1. Close and dress all incisions.
2. Program the patient's Neurostimulator and Remote Control. Refer to the Clinician Programming Manual for more detailed instruction.
3. Give a Remote Control and patient ID card to the patient.



Caution: The patient must carry the Remote Control at all times to be able to adjust or turn off the Neurostimulator.

4. Complete the system registration paperwork and return to Axonics.
5. Schedule the patient's follow-up visits at regular intervals to ensure that the stimulation is programmed optimally.

Post-Surgery Treatment

Administer prophylactic antibiotics for 24 hours.

Replacing the Neurostimulator

1. Carefully open the implant site and remove the Neurostimulator from the subcutaneous pocket. Avoid

cutting the tined lead to preserve for connection with the new Neurostimulator.

2. Clean the Neurostimulator connector block and lead with sterile water. Wipe both dry with sterile gauze.
3. Use the torque wrench to loosen the setscrew in the Neurostimulator connector block by turning it counterclockwise (**Figure 5**).
4. Gently remove the lead from the Neurostimulator.



Caution: Replace any device that shows signs of damage, pitting, or corrosion.

5. Set aside the explanted components, which should be returned to Axonics.
6. Connect the lead and replacement Neurostimulator according to the steps above.

Return explanted devices to Axonics using materials provided.

WIRELESS COMMUNICATION

Model: 1101

IC: 20225-X

FCC ID: 2AEEGX

FCC Compliance

This device complies with part 15 of the FCC Rules. Operation is subject to the following two conditions:

- (1) This device may not cause harmful interference, and
- (2) This device must accept any interference received, including interference that may cause undesired operation

This transmitter is authorized by rule under the Medical Device Radio communication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150–406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation.

This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radio Communication Service. Analog and digital voice communications are prohibited. Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

IC Compliance

This device complies with Industry Canada license-exempt RSS standard(s). Operation is subject to the following two conditions: (1) this device may not cause interference, and (2)

this device must accept any interference, including interference that may cause undesired operation of this device.

FCC and IC Compliance

This device may not interfere with stations operating in the 400.150–406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

Note: Changes and modifications to the Neurostimulator are not authorized by Axonics could void FCC and IC certification and negate the user’s authority to use the product.

Quality of Wireless Service: This device operates in the 402-405 MHz frequency and the maximum effective radiated power of the Neurostimulator communication is below the limit of 25 μ W ERP/EIRP as specified in EU: EN ETSI 301-839 and USA: FCC 47 CFR Part 95; Subpart I. The Remote Control, Clinician Programmer, or Charger have to be within 1 meter from the implant for successful communication.

Wireless Security: The Neurostimulator can only communicate with a single Remote Control that is paired to it using the Clinician Programmer. Any Axonics Clinician Programmer or Charger can communicate with a Neurostimulator. Additional mechanisms exist to ensure the integrity of radio data.

CUSTOMER SERVICE

For questions regarding the Axonics SNM System, call our Customer Support Center toll-free at +1-877-929-6642.

Additional information and product manuals can be found at our website: www.axonics.com



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