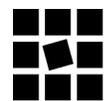


Axium™
Neurostimulator System

CLINICAL IMPLANT
EXPERIENCE SUMMARY



ST. JUDE MEDICAL™

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I. SUMMARY OF PRIMARY CLINICAL STUDY

A. Study Design

Patients in the ACCURATE study were enrolled and randomized between August 23, 2013 and July 28, 2014. The database for this PMA reflected data collected through October 2, 2015 and included 152 patients. There were 22 investigational sites.

The study was a prospective, randomized, controlled, unblinded, multi-centered clinical study comparing the Axium Neurostimulator System (Axium group) to a legally marketed spinal cord stimulation (SCS) system from a single manufacturer (Control group) (i.e., the RestoreSensor® or RestoreUltra® SCS devices manufactured by Medtronic, Inc.). Note that the Control device is approved for use in the treatment of chronic, intractable pain of the trunk and limbs. Note also that The Axium Neurostimulator System group received electrical stimulation at the DRG while the Control group received electrical stimulation at the dorsal column of the spinal cord. Additionally, programming features were selected in the Control devices in order to be as comparable as possible to the Axium Neurostimulator System. For purposes of ensuring comparable features to assess this endpoint, the RestoreSensor Control device had accelerometer feature that can adjust stimulation based on the patient's needs and preferences in different body positions (including stimulation to maintain paresthesia) deactivated. The RestoreUltra device did not have the feature.

Subjects were not blinded as to their device assignment. Subjects were randomized in a 1:1 ratio to the Axium and Control arms. The primary objective of the study was to demonstrate that a composite endpoint of safety and effectiveness of the Axium Neurostimulator System as compared to (i.e., non-inferior or superior) the legally-marketed SCS comparator for the treatment of chronic intractable pain associated with Complex Regional Pain Syndrome (CRPS) and Peripheral Causalgia. Note that although the ACCURATE study enrolled subjects with CRPS and peripheral causalgia, the indications for use utilizes the updated terms of CRPS I and CRPS II. Since the study protocol uses the terms CRPS and peripheral causalgia and not CRPS I and CRPS II, the study summary in this document will use the terms CRPS and peripheral causalgia.

The study included a “Trial Neurostimulator Phase” (3-30 day temporary trial neurostimulation, or TNS Phase), an “Implantable Neurostimulator Phase” (implantable neurostimulator, or INS Phase), and a “Follow-up Phase”. Only subjects who had a $\geq 50\%$ reduction in pain during TNS phase and expressed a desire to have an INS implant moved on to the INS phase. The initial planned sample size was 152 subjects (76 Axium and 76 Controls). An unblinded sample size re-estimation (SSR) based on the “Promising Zone” methods of Mehta and Pocock (2010) was conducted by an independent statistician when 50% of the expected primary endpoint information was available. The SSR found that no sample size increase was needed.

A Data Safety Monitoring Board (DSMB) monitored the study.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the ACCURATE study was limited to patients who met the following inclusion criteria:

- Subject is male or female between the ages of 22 and 75 years.
- Subject is able and willing to comply with the follow-up schedule and protocol.
- Subject has chronic, intractable pain of the lower limb(s) for at least 6 months.
- Subjects are diagnosed with complex regional pain syndrome (CRPS) and/or peripheral causalgia.
- Subjects have a minimum VAS ≥ 60 mm in the area of greatest pain in the lower limb(s).
- Subject has failed to achieve adequate pain relief from at least 2 prior pharmacologic treatments from at least 2 different drug classes.
- Subject has had stable neurologic function in the past 30 days.
- In the opinion of the Investigator, the subject is psychologically appropriate for the implantation of an active implantable medical device.
- Subject is able to provide written informed consent.

Patients were not permitted to enroll in the ACCURATE study if they met any of the following exclusion criteria:

- Back pain is the greatest region of pain as measured on the baseline VAS.
- Female subject of childbearing potential is pregnant/nursing, plans to become pregnant or is unwilling to use approved birth control.
- Subject has exhibited escalating or changing pain condition within the past 30 days as evidenced by Investigator examination.
- Subject is currently involved in medically related litigation, including workers compensation.
- Subject has had corticosteroid therapy at an intended site of stimulation within the past 30 days.
- Subject's pain medication(s) dosage(s) are not stable for at least 30 days.
- Subject has had radiofrequency treatment of an intended target DRG within the past 3 months.
- Subject has previously failed spinal cord stimulation therapy.
- Subject currently has an active implantable device including ICD, pacemaker, spinal cord stimulator or intrathecal drug pump or subject requires magnetic resonance imaging (MRIs) or diathermy.
- Subject has pain only within a cervical or thoracic distribution.
- Subject has cognitive, physical or sensory impairment that, in the opinion of the Investigator, may limit their ability to operate the device.
- Subject currently has an indwelling device that may pose an increased risk of infection.
- Subject currently has an active systemic infection.

- Subject has, in the opinion of the Investigator, a medical comorbidity that contraindicates placement of an active medical device.
- Subject has participated in another clinical investigation within 30 days.
- Subject has a coagulation disorder or uses anticoagulants that, in the opinion of the Investigator, precludes participation.
- Subject has been diagnosed with cancer in the past 2 years.
- Imaging (MRI, CT, x-ray) findings within the last 12 months that, in the Investigator's opinion, contraindicates lead placement.
- Subject is a prisoner.

2. Follow-up Schedule

All subjects had a temporary trial neurostimulator (TNS) for a period of three to 30 days, similar to that used in current clinical practice. If the subject was a treatment success at the end of TNS (i.e. had a $\geq 50\%$ reduction in pain as measured by a 100 mm visual analogue scale and expressed a desire to have a permanent implant), they were scheduled for the fully implantable neurostimulator (INS) procedure.

Post INS placement, subjects were seen for device programming as needed to customize their stimulation parameters. Approximately one week following the INS implant the subjects had a wound check visit. Regularly scheduled study follow-up visits were required at 1-, 3-, 6-, 9-, 12 months, and annually until the study is closed. Primary and secondary endpoints were assessed through the 3 month follow-up visit. Postoperatively, the objective parameters measured during the study included the assessments listed in **Table 1** and **Table 2** below. Adverse events and complications were recorded at all visits.

The key time points are shown below in the tables summarizing safety and effectiveness.

Table 1: ACCURATE Study Visit Schedule (Baseline to 1 Month Post-Implant)

| | Screening/ Baseline | TNS | Post-TNS Placement | End of TNS | INS Implant | Post-INS Placement | 1 Month ± 14 days |
|--|------------------------|-----|-----------------------|------------------------|----------------|-----------------------|----------------------|
| | TNS Phase ¹ | | | INS Phase ¹ | | | |
| Informed Consent | X | | | | | | |
| Inclusion/Exclusion MRI/CT/X-ray | X | | | | | | |
| Baseline Pregnancy Test Medical History/ Physical Exam | X | | | | | | |
| Neurological Exam Medications (all) | | | | | | | |
| Subject Questionnaire Form A: Pain Distribution, Pain (VAS), SF-36, BPI, POMS | X | | | | | | X |
| Pain Diary | X | | | | | | X |
| Procedure Evaluation X-rays/Fluoroscopy | | X | | | X | | |
| Subject Questionnaire Form B: Pain Distribution, Pain (VAS) | | | | X | | | |
| Physical and Neurological Exam | | | | X | | | X |
| Paresthesia Assessment | | | X ² | X | | X ² | X |
| Programming | | | X ³ | X | | X ³ | X |
| Subject Satisfaction | | | | X | | | |
| Pain Medications | | | | X | | | X |
| Telephone Follow-up (prior to visit) | | | | | | | X |
| Adverse Events & Protocol Deviation (if needed) | X | X | X | X | X | X | X |

¹ The post- TNS and post-INS phases do not require unscheduled visits (e.g. Subject Questionnaire B) unless it is determined that more assessments are warranted based on the subjects condition. Only those unscheduled visits that occur after the 1-month visit will be subject to the unscheduled visit requirements. There may be programming forms in the unscheduled interval that are really post-revision/replacement or required to assess an AE in which are not true unscheduled visits (e.g. do not require Subject Questionnaire B).

² The Paresthesia Assessment is only required to be completed once during both the post-TNS and post-INS phase.

³ Multiple programming forms during post-TNS and post-INS phase are allowed

Table 2: ACCURATE Study Visit Schedule (3 Months to Study End)

| | 3 Months ± 14 days | 6 months ± 28 days | 9 months ± 28 days | 12 months ± 28 days | 24 – 60 months ± 90 days | Unscheduled Visits¹ | Revision/ Replace Procedure |
|--|---------------------------------------|---------------------------------------|---------------------------------------|--|---|---|--|
| Physical/Neurological Exam | X | X | X | X | X | | X ³ |
| Pain Medications | X | X | X | X | X | | |
| Subject Questionnaire Form A: Pain Distribution, Pain (VAS), SF-36, BPI, POMS | X | X | X | X | X | | |
| Subject Questionnaire Form B: Pain Distribution, Pain (VAS) | | | | | | X ¹ | |
| Pain Diary | X | X | X | X | | | |
| Telephone Follow-up (prior to visit) | X | X | X | X | | | |
| Paresthesia Assessment | X | X | X | X | X | | |
| Programming | X | X | X | X | X | X | X ³ |
| Subject Satisfaction | X | X | | X | | | |
| Revision/Replacement Procedure: X-rays/Fluoro | | | | | | | X ³ |
| Explant Procedure: X-rays/Fluoro | | | | | | | |
| Study Exit | | | | | X ² | | |
| Adverse Events & Protocol Deviations (if needed) | X | X | X | X | X | X | X |

¹ The post- TNS and post-INS phases do not require unscheduled visits (e.g. Subject Questionnaire B) unless it is determined that more assessments are warranted based on the subjects condition. Only those unscheduled visits that occur after the 1-month visit will be subject to the unscheduled visit requirements. There may be programming forms in the unscheduled interval that are really post-revision/replacement or required to assess an AE in which are not true unscheduled visits (e.g. do not require Subject Questionnaire B).

² The Study Exit form is required at the time of study exit or 60 months as appropriate.

³ Replacement procedures that include external components (TNS, patient programmer, connector cable) do not require pre/post X-rays, physical or neurological exam, or programming. In addition, pre-x-rays were not always attainable (e.g., TNS leads pulled out at subject's home) and were not considered deviations

3. Clinical Endpoints

The primary endpoint was a composite safety and efficacy endpoint, assessed through three months post-implant (including the Trial Stimulation (TNS) and the Implant (INS) phases). Safety and efficacy were determined by the percentage of subjects that were free from a stimulation-induced neurological deficit and achieved at least 50% pain relief in the lower limbs, in the region of greatest baseline pain, in both the TNS and INS phases of the trial. Subjects were required to remain on stable pain medications; as seen in **Table 23**, changes in pain medication were minimal

A stimulation induced neurological deficit was defined as a measurable motor or sensory deficit on the neurological examination, within the appropriate concordant anatomy, that is induced by stimulation and does not persist in the

absence of stimulation within a 24-hour timeframe. Changes in motor and sensory scales were classified into three categories: Change ≤ -2 points (worsening), $-1 \leq \text{Change} \leq +1$ (no clinically meaningful change, and Change $\geq +2$ (improvement). Subjects' pain intensity was measured via a 100 mm visual analogue scale (VAS) with 100 mm representing the "Worst Imaginable Pain" and 0 mm representing "No Pain".

The Statistical Analysis Plan specified the use of the modified-intention-to-treat (MITT) analysis dataset for analyses of primary and secondary endpoints. The MITT analysis data set includes all subjects that were randomized and received a trial neurostimulator. The primary composite endpoint data was also analyzed using the intention-to-treat subjects (ITT) (i.e., all subjects who met the enrollment criteria and received a randomization assignment.) and per-protocol subjects (PP) (i.e., all randomized subjects who have valid data at baseline and the 3-month follow-up, and have no major protocol deviations that would potentially affect study outcomes).

Individual Subject Success

An individual subject was considered a primary composite endpoint success if the subject:

- Experienced at least 50% lower limb pain relief (VAS Score Reduction) in their primary area of pain at the end of the trial phase (TNS), and expressed a desire to go on to INS implant, and
- Received at least 50% lower limb pain relief (VAS Score reduction) in their primary area of pain at the 3-Month visit post implant (INS), and
- Did not experience a stimulation-induced neurological deficit through three months as adjudicated by the Data Safety Monitoring Board (DSMB).

A subject was considered a primary composite endpoint failure if the subject:

- Did not receive at least 50% lower limb pain relief (VAS Score reduction) in their primary area of pain at the end of the trial phase (TNS), or
- Did not receive at least 50% lower limb pain relief (VAS Score reduction) in their primary area of pain at the 3-Month visit post implant (INS), or
- Did receive at least 50% lower limb pain relief (VAS Score reduction) in their primary area of pain at the end of the trial phase (TNS), but chose not to receive the implantable neurostimulator (INS), or
- Experienced a stimulation-induced neurological deficit through three months as adjudicated by the DSMB, or
- Exited the study due to a device- or procedure-related adverse event through three months as adjudicated by the DSMB, or
- Exited the study due to the need for a revision, replacement or explant procedure.

A subject was considered missing for the primary composite endpoint analysis if the subject:

- Exited the study after the initiation of the TNS procedure but prior to INS implant for any reason other than,
 - achieved less than 50% improvement in VAS scores at the End of TNS visit (i.e. primary-endpoint failure), or
 - achieved at least 50% improvement in VAS scores but chose not to move on to INS procedure (i.e. primary-endpoint failure), or
 - had a device- or procedure-related adverse event as adjudicated by the DSMB (i.e. primary-endpoint failure).
- Exited the study after the INS implant for any reason other than a device- or procedure-related adverse event through three months as adjudicated by the DSMB.

Study Success

Study success was defined as the percentage of subjects who met each success criteria in the Axium group and the Control group, using a 10% non-inferiority margin. If non-inferiority was achieved at a one-sided alpha of 0.05, a one-sided superiority test was performed at the significance level of 0.025.

Secondary Endpoints

The following is the study non-powered secondary endpoint:

- Non-Powered

Subjects reported whether or not they felt paresthesia when stimulation was on as a non-powered secondary endpoint. At the 3- month study visit subjects responded “Yes” or “No” to the question “During the past month, did you feel paresthesia in your lower limbs when stimulation was on?” Subjects were categorized into two groups based on their response: Group 1 - Subjects with paresthesia and Group 2 - Subjects without Paresthesia.

At the time of the trial and implant procedures, all subjects were asked to confirm that they were feeling stimulation (i.e. sensation of paresthesia) in the targeted area of pain in order to confirm placement of the implanted leads. Post-procedure, stimulation settings were then programmed based upon physician judgement to optimize the appropriate therapy for each study subject. In addition, all study subjects were able to adjust the intensity level of the therapy, within a physician-prescribed range, with their patient programmers.

Note that the clinical relevance of this result is unknown. The study was a non-inferiority trial, designed to assess device effectiveness in the presence of paresthesia. The instructions for use for the Control device requires the

Control device be programmed for subjects to receive paresthesia. In addition, the number of subjects that did not have paresthesia is very small and this endpoint was not adequately powered to detect the difference in pain relief for subjects who reported feeling versus not feeling paresthesia. A placebo controlled trial would be necessary to rule out the possibility that the effect is greater than placebo.

Tertiary Endpoints

The following are the study Tertiary endpoints:

- SF-36 Quality of Life Questionnaire at 3, 6, and 12-months
- Profile of Mood States (POMS) at 3, 6, and 12-months
- Brief Pain Inventory (BPI) at 3, 6, and 12-months
- Subject Satisfaction at 3, 6, and 12-months:
Subjects completed a satisfaction scale at the End of TNS visit, and at three, six, and 12-months. The first three items below were evaluated on an 11-point numeric scale with 0 indicating “Not Satisfied/Not Likely” and 10 indicating “Very Satisfied/Very Likely.” The last item was measured on a 7- point scale from “Much Worse” to “Much Better.”
 - Please rate your satisfaction with the pain relief provided by the stimulation.
 - Please rate your satisfaction with the therapy in general.
 - Please rate how likely you would be to undergo this therapy again based on your experience thus far.
 - Please rate the change in your pain compared to before the device was implanted.
- Stimulation Specificity at 3-months:
The baseline pain diagrams completed by the subjects were compared to the subjects’ paresthesia maps completed at the end of the follow-up visit. The pain and paresthesia diagram forms had identical diagrams of the human body on which subjects marked where they felt pain and paresthesia coverage. The stimulation specificity endpoint was evaluated at all scheduled visits by determining whether a subject felt paresthesia in anatomical regions that were reported as having no pain at baseline.

B. Accountability of PMA Cohort

The ACCURATE study enrolled and randomized 152 subjects (76 Axium subjects and 76 Control subjects) at 22 investigational sites. As of October 2, 2015, when the database was locked for this report, the average months implanted for subjects that received an INS was 12.6 (\pm 3.5) months in the Axium group, and 12.0 (\pm 2.3) months in the Control group. The cumulative INS months of implanted experience for subjects that received an INS device in the Axium group was 768 months (64

cumulative years), and in the Control group was 649.2 months (54.1 cumulative years).

The Statistical Analysis Plan (SAP) specified the use of the modified-intention-to-treat (MITT) analysis dataset for analyses of primary and secondary endpoints. Missing data sensitivity analyses, Intention-to-treat (ITT) and per-protocol (PP), were conducted to assess the robustness of the primary endpoint analysis.

The MITT analysis data set includes all 146 subjects (73 Axium, 73 Control) that were randomized and received a trial neurostimulator. Six subjects in the ITT analysis data set (3 in the Axium group and 3 in the Control group) were randomized, did not go on to have a TNS procedure, withdrew from the study prior to the TNS procedure, and are not included in the MITT analysis set. One Control subject in the MITT analysis data set had a TNS procedure but withdrew from the study prior to undergoing the end of TNS study visit. Since the subject withdrew due to a device-related adverse event, the subject is counted as a treatment failure. One Axium subject in the MITT data set had an INS procedure but withdrew from the study prior to the 3-month study visit. Since the subject withdrew due to a device-related adverse event, the subject is counted as a treatment failure. Another Axium subject in the MITT data set exited the study prior to their INS procedure due to a device-related adverse event post-TNS procedure. Since this subject withdrew due to a device related adverse event, the subject is counted as a treatment failure.

Seven subjects (four in the Axium group and three in the Control group) in the MITT analysis data set have no evaluable data for the study endpoints and are counted as missing because they withdrew from the study prior to the 3-month study visit, and did not meet any prospectively defined criteria for treatment failure/success at the time of study withdrawal.

The ITT population includes all 152 randomized subjects, 76 subjects in each group. The Per Protocol (PP) analysis set includes all randomized subjects who have valid data at baseline and the 3-month follow-up, and have no major protocol deviations that would potentially affect study outcomes. Major protocol deviations were defined prior to database lock.

The Control group had 16 major protocol deviations in 15 subjects. Twelve deviations were due to noncompliant programming, three deviations were due to performing the neurological examination without stimulation turned on, and one deviation was due to the neurological examination not being done at a follow-up visit. The Axium group had 1 subject with one major protocol deviation due to an incomplete neurological exam at a follow-up visit. These deviations did not change the conclusions drawn from the primary composite endpoint.

See **Figure 1** below for a flow chart describing the subject accountability. Note in **Figure 1**, there are three subjects with missing visits at 12 months. One subject moved to another state. The site is in communication with the individual and the

subject plans to return to the site for another visit at a time that is convenient and has not exited the study. One subject is lost to follow-up. The site has attempted to contact the subject and has sent a certified letter. There has been no response from the subject. One subject missed the 12-month visit but still is enrolled in the study and will be seen at the site as soon as a visit can be scheduled out of window for the 12-month assessment.

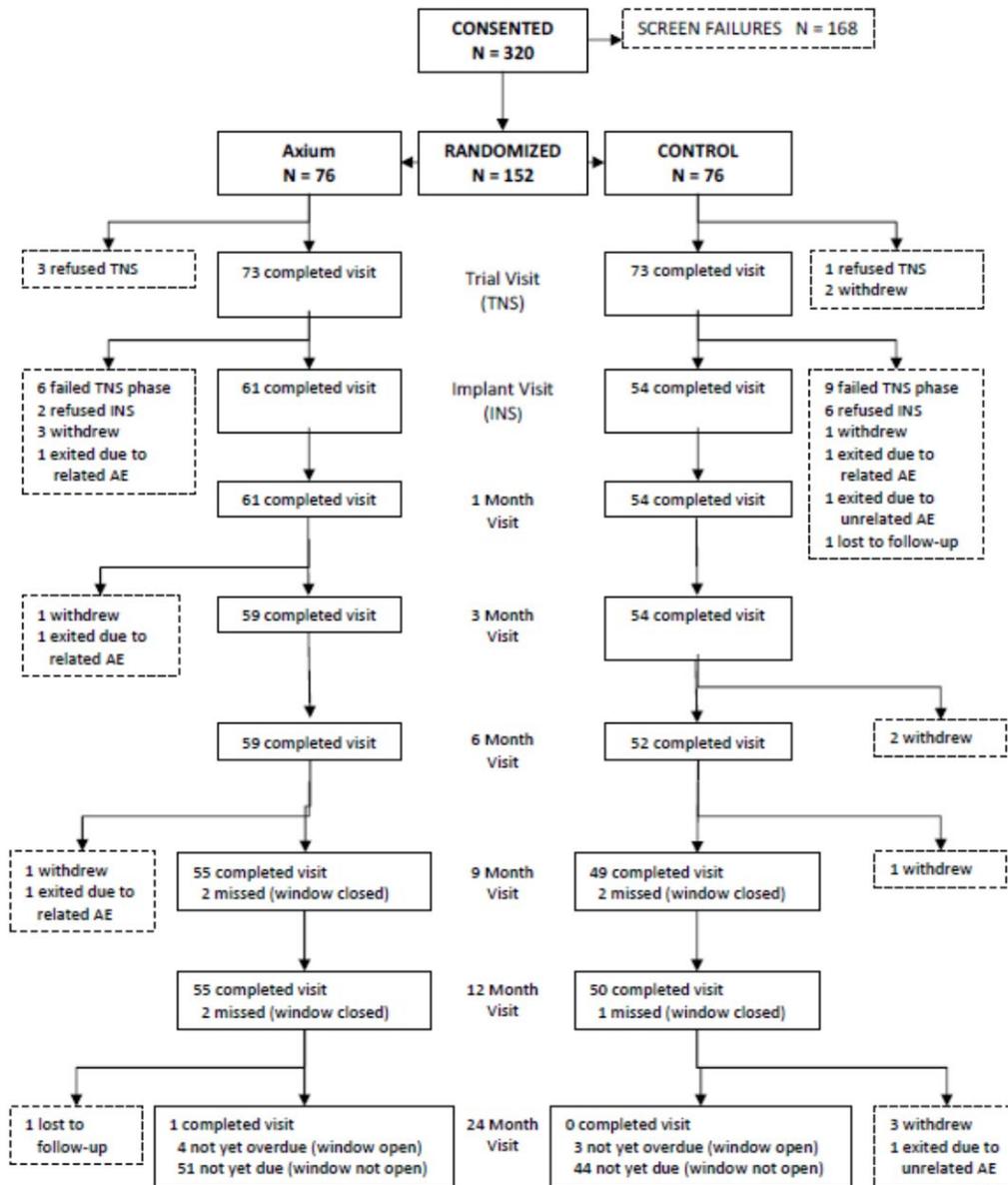


Figure 1: Subject Accountability

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a study of this type performed in the US. **Table 3** presents information on key subject characteristics. No statistically significant differences were found among the baseline characteristics between the Axium group and the Control group. The average age of the subjects in the Axium and Control groups was 52.4 years and 52.5 years, respectively. The distribution of female gender in the Axium and Control groups was 51.3% and 51.3% respectively. Race was predominately white (94.7% and 92.1% Axium and Control, respectively). On average, subjects had an average BMI of 30.5 (Axium) and 28.9 (Control).

The distribution of Complex Regional Pain Syndrome (CRPS) (Axium 57.9% and Control 56.6%) and Peripheral Causalgia (Axium 42.1% and Control 43.4%) was similar between the groups. Subjects' medical history and prior surgeries were comparable for both groups, with average duration of lower extremity pain at 7.5 years (Axium) and 6.8 years (Control).

Table 3: Baseline Demographics and Characteristics

| Baseline Characteristics | Axium N = 76 | Control N = 76 | p-value |
|---|-----------------------------|-----------------------------|----------------------|
| Gender (% Female) | 39/76 (51.3%) | 39/76 (51.3%) | 1.0000 ^{††} |
| Age in Years ± SD (Min., Max.) | 52.4 ± 12.7 (23.9, 75.8) | 52.5 ± 11.5 (25.4, 75.9) | 0.9363 [*] |
| BMI (kg/m²) ± SD (Min., Max.) | 30.5 ± 7.2 (16.9, 54.0) | 28.9 ± 6.0 (17.4, 44.6) | 0.1266 [*] |
| Duration of Lower Limb Pain in years ± SD (Min., Max.) | 7.5 ± 7.5 (1.0, 39.0) | 6.8 ± 7.6 (0.7, 51.0) | 0.5571 ^{**} |
| Primary Diagnosis (n/N (%)) | | | |
| Complex Regional Pain Syndrome | 44/76 (57.9%) | 43/76 (56.6%) | 0.8698 ^{††} |
| Peripheral Causalgia | 32/76 (42.1%) | 33/76 (43.4%) | |

^{*}T-test, ^{**}Wilcoxon test, [†]Fisher exact test, ^{††}Chi-square test

Baseline Lower Limb Pain Medications

Subjects' baseline lower limb pain medications were comparable between the Axium and Control groups (see **Table 4**). Opioids, anticonvulsants and nonsteroidal anti-inflammatory drugs (NSAIDs) were the most frequent medication classes taken by the subjects at the baseline visit. Opioids were taken by 60.5% (Axium) and 67.1% (Control) of subjects. Anticonvulsant medications were taken by 47.4% (Axium) and 46.1% (Control) of subjects. NSAIDs were taken by 48.7% (Axium) and 31.6% (Control) of subjects. There were no statistically significant differences in the use of lower limb pain medications, with the exception of NSAIDs.

Table 4: Baseline Pain Medication Usage for Lower Limb Pain by Medication Class

| | Axium n/N (%) | Control n/N (%) | p-value |
|---|------------------|--------------------|----------------------|
| Analgesics | 5/76 (6.6) | 5/76 (6.6) | 1.0000 ^{††} |
| Anticonvulsants | 36/76 (47.4) | 35/76 (46.1) | 0.8709 ^{††} |
| Antidepressant | 10/76 (13.2) | 11/76 (14.5) | 0.8142 ^{††} |
| Anxiolytics | 2/76 (2.6) | 1/76 (1.3) | 1.0000 [†] |
| Hypnotics | 0/76 (0.0) | 0/76 (0.0) | N/A |
| Muscle Relaxant | 6/76 (7.9) | 5/76 (6.6) | 0.7542 ^{††} |
| NSAIDs (OTC & prescription) | 37/76 (48.7) | 24/76 (31.6) | 0.0315 ^{††} |
| Opioids (incl. synthetic and semisynthetic derivatives) | 46/76 (60.5) | 51/76 (67.1) | 0.3987 ^{††} |
| Sedative | 2/76 (2.6) | 0/76 (0.0) | 0.4967 [†] |
| Local Anesthetic | 10/76 (13.2) | 8/76 (10.5) | 0.6156 ^{††} |
| Other | 2/76 (2.6) | 3/76 (3.9) | 1.0000 [†] |

†Fisher exact test, ††Chi-square test

Lower Limb Pain History

The subjects' lower limb pain history is summarized in **Table 5**. The distribution of Complex Regional Pain Syndrome (CRPS) (Axium 57.9% and Control 56.6%) and Peripheral Causalgia (Axium 42.1% and Control 43.4%) was similar between the groups. All subjects' diagnoses were confirmed by the Medical Monitor during his review.

The diagnostic criteria required for a diagnosis of CRPS were taken from the 1994 consensus statement from the International Association for the Study of Pain (IASP)¹. The CRPS diagnostic criteria were met when the following were present:

- Continuing pain that is disproportionate to any inciting event.
- At least 1 symptom reported in at least 3 of the following categories:
 - Sensory: Hyperesthesia or allodynia.
 - Vasomotor: Temperature asymmetry, skin color changes, skin color asymmetry.
 - Sudomotor/edema: Edema, sweating changes, or sweating asymmetry.
 - Motor/trophic: Decreased range of motion, motor dysfunction (e.g., weakness, tremor, dystonia), or trophic changes (e.g., hair, nail, skin).
- At least 1 sign at time of evaluation in at least 2 of the following categories.
 - Sensory: Evidence of hyperalgesia (to pinprick), allodynia (to light touch, temperature sensation, deep somatic pressure, or joint movement).
 - Vasomotor: Evidence of temperature asymmetry (>1°C), skin color changes or asymmetry.

1 van Eijs F, Stanton-Hicks M, Van Zundert J, Faber CG, Lubenow TR, Mekhail N, van Kleef M, Huygen F. Evidence-based interventional pain medicine according to clinical diagnoses. 16. Complex regional pain syndrome. Pain Pract. 2011 Jan-Feb;11(1):70-87. Epub 2010 Aug 27.

- Sudomotor/edema: Evidence of edema, sweating changes, or sweating symmetry.
- Motor/trophic: Evidence of decreased range of motion, motor dysfunction (e.g., weakness, tremor, dystonia), or trophic changes (e.g., hair, nail, skin).
- No other diagnosis better explaining the signs and symptoms.

For peripheral causalgia, the diagnosis required that the subjects' chronic pain was due to damage to a nerve². The pain was required to be in an anatomical area consistent with the innervation pattern of the damaged nerve (or nerves), and generally, in a hyperalgesic state. In some cases, the nerve damage progressed with secondary changes manifesting themselves. However, this was not a diagnostic requirement. Nerve damage typically resulted from blunt trauma (injury) or other types of injury such as post-surgical nerve cutting or lesioning.

Subjects' average duration of lower extremity pain is 7.5 years (Axium) and 6.8 years (Control). Subjects reported previous attempts to relieve lower extremity pain. Physical therapy, massage therapy, surgery, and injections (epidural steroid injections, sacroiliac joint injections and selective nerve blocks) were most frequently reported.

A primary region of pain targeted for treatment was identified by the investigators for each subject based on their baseline VAS pain assessment. The region with the highest VAS score consistent with the subjects' diagnoses was selected as the primary region of pain. Nine anatomical regions of the lower extremity were defined and subjects rated their pain intensity for each region on the 100mm VAS scale at baseline and at each scheduled visit. The distribution of primary regions of pain was comparable for the Axium and Control groups.

No statistically significant differences were observed in Lower Extremity Pain History indicating similar baseline characteristics; the two groups are balanced based on the randomization scheme.

² Bonica's Management of Pain. [Scott M. Fishman](#) , [Jane C. Ballantyne](#) , [James P. Rathmell](#) (Eds.). Lippincott Williams & Wilkins, 2010.

Table 5: Lower Limb Pain History

| Pain History Parameter | Axium N=76 | Control N=76 |
|--|-----------------------|-------------------------|
| Primary Diagnosis (n/N (%)) | | |
| Complex Regional Pain Syndrome | 44/76 (57.9) | 43/76 (56.6) |
| Peripheral Causalgia | 32/76 (42.1) | 33/76 (43.4) |
| P-value | 0.8698 ^{††} | |
| Duration of CRPS Diagnosis (years) | | |
| N | 43 | 43 |
| Mean (SD) | 1.8 (4.1) | 1.1 (2.1) |
| Median | 0.4 | 0.2 |
| Min. Max. | -0.0, 22.1 | 0.0, 9.9 |
| P-value | 0.5416 ^{**} | |
| Duration of PC Diagnosis (years) | | |
| N | 32 | 33 |
| Mean (SD) | 1.6 (5.1) | 0.8 (2.7) |
| Median | 0.0 | 0.0 |
| Min. Max. | -0.0, 24.8 | -0.0, 11.6 |
| P-value | 0.5401 ^{**} | |
| Duration of Lower Limb Pain (years) | | |
| N | 76 | 76 |
| Mean (SD) | 7.5 (7.5) | 6.8 (7.6) |
| Median | 5.0 | 4.5 |
| Min. Max. | 1.0, 39.0 | 0.7, 51.0 |
| P-value | 0.5571 ^{**} | |
| Primary Region of Pain (n/N (%)) | | |
| Region 2 (right groin) | 4/76 (5.3) | 2/76 (2.6) |
| Region 3 (left groin) | 4/76 (5.3) | 7/76 (9.2) |
| Region 4 (right buttock) | 1/76 (1.3) | 2/76 (2.6) |
| Region 5 (left buttock) | 2/76 (2.6) | 2/76 (2.6) |
| Region 6 (right leg) | 14/76 (18.4) | 16/76 (21.1) |
| Region 7 (left leg) | 8/76 (10.5) | 11/76 (14.5) |
| Region 8 (right foot) | 21/76 (27.6) | 19/76 (25.0) |
| Region 9 (left foot) | 22/76 (28.9) | 17/76 (22.4) |
| P-value (Regions 2-5 vs. Regions 6/7 vs. Regions 8/9) | 0.5228 ^{††} | |
| Previous Attempts to Relieve Lower Limb Pain (not mutually exclusive n/N (%)) | | |
| Massage therapy | 39/76 (51.3) | 33/76 (43.4) |
| Occupational therapy | 18/76 (23.7) | 13/76 (17.1) |
| Physical therapy | 68/76 (89.5) | 63/76 (82.9) |
| Lumbar sympathetic blocks | 33/76 (43.4) | 24/76 (31.6) |
| Facet blocks | 6/76 (7.9) | 5/76 (6.6) |
| Surgery for lower limb pain | 40/76 (52.6) | 40/76 (52.6) |
| Local anesthetic injection | 33/76 (43.4) | 26/76 (34.2) |
| Intradiscal electrothermal therapy (IDET) | 1/76 (1.3) | 1/76 (1.3) |
| Intrathecal injection | 0/76 (0.0) | 3/76 (3.9) |
| Drug pumps (e.g. intrathecal for chronic pain) | 1/76 (1.3) | 0/76 (0.0) |
| TENS unit | 31/76 (40.8) | 31/76 (40.8) |
| Sacroiliac joint injection | 7/76 (9.2) | 9/76 (11.8) |
| Epidural steroid injection | 27/76 (35.5) | 30/76 (39.5) |
| Pulsed or constant radiofrequency near the target DRG | 4/76 (5.3) | 5/76 (6.6) |
| Selective nerve blocks | 27/76 (35.5) | 23/76 (30.3) |
| Other | 38/76 (50.0) | 30/76 (39.5) |

**Wilcoxon test, ††Chi-square test

Implant Characteristics

The following four subgroups were defined: CRPS Type I - Unilateral, CRPS Type I - Bilateral, peripheral causalgia (aka CRPS II) - Unilateral, peripheral causalgia - Bilateral.

Table 6 presents the number of Axiom subjects in each subgroup, the number of leads implanted per subject in each sub-group, and the number of subjects in each sub-group with permanent leads at each spinal level.

Table 7 presents the number of Control subjects in each subgroup, the number of leads implanted per subject in each sub-group, and the number of subjects in each sub-group with permanent leads at each spinal level.

Table 6: Leads Implanted in the Axiom Group by Primary Diagnosis and Unilateral/Bilateral Pain

| | Unilateral CRPS n/N (%) | Bilateral CRPS n/N (%) | Unilateral PC n/N (%) | Bilateral PC n/N (%) |
|---|----------------------------|---------------------------|--------------------------|-------------------------|
| Number of Subjects Implanted at INS | 23/61 (37.7) | 11/61 (18.0) | 17/61 (27.9) | 10/61 (16.4) |
| Number of Leads Implanted per Subject | | | | |
| 1 lead | 7/23 (30.4) | 0/11 (0.0) | 6/17 (35.3) | 0/10 (0.0) |
| 2 leads | 15/23 (65.2) | 8/11 (72.7) | 7/17 (41.2) | 8/10 (80.0) |
| 3 leads | 1/23 (4.3) | 1/11 (9.1) | 3/17 (17.6) | 0/10 (0.0) |
| 4 leads | 0/23 (0.0) | 2/11 (18.2) | 1/17 (5.9) | 2/10 (20.0) |
| Level of Lead(s) Implanted Per Subject (not mutually exclusive)* | | | | |
| T10 | 0/23 (0.0) | 0/11 (0.0) | 0/17 (0.0) | 0/10 (0.0) |
| T11 | 1/23 (4.3) | 0/11 (0.0) | 0/17 (0.0) | 0/10 (0.0) |
| T12 | 0/23 (0.0) | 0/11 (0.0) | 3/17 (17.6) | 0/10 (0.0) |
| L1 | 4/23 (17.4) | 2/11 (18.2) | 5/17 (29.4) | 0/10 (0.0) |
| L2 | 4/23 (17.4) | 2/11 (18.2) | 6/17 (35.3) | 3/10 (30.0) |
| L3 | 7/23 (30.4) | 2/11 (18.2) | 3/17 (17.6) | 1/10 (10.0) |
| L4 | 12/23 (52.2) | 5/11 (45.5) | 8/17 (47.1) | 3/10 (30.0) |
| L5 | 12/23 (52.2) | 7/11 (63.6) | 7/17 (41.2) | 6/10 (60.0) |
| S1 | 0/23 (0.0) | 0/11 (0.0) | 1/17 (5.9) | 0/10 (0.0) |
| S2 | 0/23 (0.0) | 0/11 (0.0) | 0/17 (0.0) | 0/10 (0.0) |

* “Not mutually exclusive” refers to the fact that subjects may have up to 4 leads implanted in the Axiom group. Subjects may have one or more leads implanted at one level or at multiple lead levels and are counted in multiple lead level categories. One lead may be implanted per DRG.

Table 7: Leads Implanted in the Control Group by Primary Diagnosis and Unilateral/Bilateral Pain

| | Bilateral CRPS n/N (%) | Bilateral PC n/N (%) | Unilateral CRPS n/N (%) | Unilateral PC n/N (%) |
|---|---------------------------|-------------------------|----------------------------|--------------------------|
| Number of Subjects Implanted at INS | 22/54 (40.7) | 12/54 (22.2) | 11/54 (20.4) | 9/54 (16.7) |
| Number of Leads Implanted per Subject | | | | |
| 1 lead | 1/22 (4.5) | 0/12 (0.0) | 2/11 (18.2) | 1/9 (11.1) |
| 2 leads | 21/22 (95.5) | 12/12 (100.0) | 9/11 (81.8) | 8/9 (88.9) |
| Level of Lead(s) Implanted Per Subject (not mutually exclusive)* | | | | |
| T1 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T2 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T3 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T4 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T5 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T6 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 0/9 (0.0) |
| T7 | 0/22 (0.0) | 0/12 (0.0) | 0/11 (0.0) | 1/9 (11.1) |
| T8 | 0/22 (0.0) | 2/12 (16.7) | 2/11 (18.2) | 0/9 (0.0) |
| T9 | 2/22 (9.1) | 2/12 (16.7) | 3/11 (27.3) | 3/9 (33.3) |
| T10 | 7/22 (31.8) | 3/12 (25.0) | 4/11 (36.4) | 1/9 (11.1) |
| T11 | 8/22 (36.4) | 2/12 (16.7) | 1/11 (9.1) | 1/9 (11.1) |
| T12 | 6/22 (27.3) | 5/12 (41.7) | 4/11 (36.4) | 5/9 (55.6) |

* “Not mutually exclusive” refers to the fact that subjects may have up to 2 leads implanted in the Control group. Subjects may have one or more leads implanted at one level or at multiple lead levels and are counted in multiple lead level categories.

Axium Programming Parameters

Table 8 presents a summary of the average amplitude, frequency and pulse width programmed settings for all Axium subjects over time. The median frequency was 20 Hz at all time points; the median pulse width was 300µs at all time points except 12 months when it was 255µs. The median amplitude varied from 575µA to 687.5µA at the different time points. The median impedance ranged from 1225.5Ω to 1355.0Ω at the different time points.

Table 8: Summary of Axium Programmed Settings Based on Active Leads

| | 1 Month | 3 Month | 6 Month | 9 Month | 12 Month |
|----------------------------------|------------|------------|------------|------------|------------|
| Number of Subjects | 61 | 59 | 59 | 55 | 55 |
| Number of Active Leads | 124 | 118 | 117 | 107 | 110 |
| Frequency/Rate Range (Hz) | | | | | |
| N | 123 | 118 | 117 | 107 | 110 |
| Mean | 22.5 | 20.8 | 20.0 | 19.0 | 19.0 |
| SD | 6.4 | 7.1 | 6.8 | 5.5 | 5.1 |
| Median | 20 | 20 | 20 | 20 | 20 |
| Minimum | 10 | 10 | 10 | 8 | 10 |
| Maximum | 40 | 48 | 48 | 40 | 36 |
| Pulse Width (µs) | | | | | |
| N | 124 | 118 | 117 | 107 | 110 |
| Mean | 312.4 | 308.9 | 315.4 | 295.6 | 289.8 |
| SD | 148.6 | 145.9 | 166.0 | 140.7 | 133.8 |
| Median | 300 | 300 | 300 | 300 | 255 |
| Minimum | 100 | 100 | 60 | 90 | 90 |
| Maximum | 1000 | 1000 | 1000 | 1000 | 1000 |
| Amplitude (µA) | | | | | |
| N | 122 | 118 | 116 | 107 | 107 |
| Mean | 892.3 | 915.4 | 836.4 | 764.6 | 827.4 |
| SD | 703.9 | 822 | 721.9 | 630.9 | 657.1 |
| Median | 687.5 | 675 | 650 | 575 | 650 |
| Minimum | 150 | 75 | 100 | 100 | 75 |
| Maximum | 4400 | 6000 | 4600 | 3950 | 4000 |
| Impedance (Ω) | | | | | |
| N | 116 | 116 | 114 | 107 | 110 |
| Mean | 1321.2 | 1431.7 | 1504.7 | 1583.9 | 1458.9 |
| SD | 527.9 | 571.4 | 700.4 | 792.8 | 714.5 |
| Median | 1225.5 | 1329.5 | 1324.5 | 1355 | 1256.5 |
| Minimum | 645 | 589 | 586 | 572 | 547 |
| Maximum | 5000 | 4795 | 5000 | 5000 | 4962 |

D. Safety and Effectiveness Results

1. Safety Results

As pre-specified in the Statistical Analysis Plan, the study primary composite endpoint data was analyzed using a modified intention to treat (MITT) analysis which included all subjects that were randomized and received a trial neurostimulator. The analysis of safety in the composite endpoint was based on 146 (73 Axium and 73 Control) evaluable subjects at the 3-month time point. The analysis of safety also included the intent-to-treat (ITT) population of 152

subjects (76 Axium and 76 Control) available for the 3 month evaluation and 105 subjects (55 Axium and 50 Control) available at 12 months. None of the study subjects experienced a primary composite endpoint safety event (stimulation induced neurological deficit) through 12 months and up to the date of the database lock.

The overall motor examination results indicate that most of the subjects in both groups experienced no change in their motor examination at three months (96.6% Axium and 100% Control had no change). None of the subjects in the Axium or Control groups experienced a worsening of motor scores. Improvement in the overall motor score occurred in three subjects in the Axium group and none of the subjects in the Control group.

The overall sensory examination results indicate that most of the subjects in both groups experienced no change in their sensory examination at three months (98.3% Axium and 98.1% Control had no change). None of the subjects in the Axium or Control group experienced a worsening of sensory scores. Improvement in sensory scores occurred in one subject in the Axium group, and two subjects in the Control group.

Serious Adverse Events

A total of 21 serious adverse events occurred in 19 subjects, four events in four subjects (Axium 1, Control 3 subjects) during the TNS phase, and 17 events in 15 subjects (Axium 7, Control 8 subjects) in the INS phase. The overall difference in the rate of SAEs between the groups was not statistically different (Axium 10.5%, Control 14.5%, $p=0.6248$); the rate during the TNS phase (Axium 1.3%, Control 3.9%, $p=0.62$), and INS phase (Axium 9.2%, Control 10.5%, $p=1.0$) also were not statistically different. See **Table 9** below. There were no unanticipated AEs or deaths in the study.

Table 9: Percent of Subjects with SAEs

| | Axium N=76 | Control N=76 | P-value |
|----------------------|-----------------------|-------------------------|----------------|
| SAE during TNS Phase | (1/76) 1.3% | (3/76) 3.9% | 0.6200 |
| SAE during INS Phase | (7/76) 9.2% | (8/76) 10.5% | 1.0000 |
| Total | (8/76)10.5% | (11/76) 14.5% | 0.6248 |

Fourteen of the serious adverse events resolved (6 with and 8 without sequelae). In the Control group, there were five unrelated SAEs and one device/procedure related SAE still ongoing at the time of the database lock on Oct. 2, 2015. In the Axium group there was one unrelated SAE still ongoing.

Eighteen of the 21 SAEs were unrelated to the implant procedure, device or stimulation therapy. Two of the SAEs in the Control group were definitely related to the implant procedure and/or device:

- One Control subject had an infection following the TNS procedure that required explantation of the system.
- A second Control subject had an infection following the INS procedure that required explantation of the system.

One Axium subject experienced an episode of atrial fibrillation in the recovery room following the INS implant that was adjudicated as possibly related to a pre-existing condition, the implant procedure or the stimulation therapy.

Table 10 and **Table 11** present the serious adverse events (SAEs) reported for subjects in both the Axium and Control groups through the TNS and INS phases. The total rate of SAEs in the Axium group was not significantly different than the Control group.

Table 10: Distribution of Serious Adverse Events through the TNS Phase

| Subsystem Code/Preferred Code | Axium N=76 | | Control N=76 | |
|--|---------------|-------------------|-----------------|------------------|
| | Events N | Subjects n (%) | Events N | Subject n (%) |
| Total Serious Adverse Events (based on ITT) | 1 | 1 (1.3) | 3 | 3 (3.9) |
| Total Serious Adverse Events (based on At Risk)¹ | 1 | 1 (1.3) | 3 | 3 (3.9) |
| Blood Components / Abnormal Blood Chemistry | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Lower Extremity / Bilateral Lower Leg Pain | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Substance Related Disorders / Overdose | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Wound Issue / Wound Infection | 0 | 0 (0.0) | 1 | 1 (1.3) |

1. Subjects at risk means are all randomized subjects, n=76 in each group

Table 11: Distribution of Serious Adverse Events through the INS Phase

| Subsystem Code/Preferred Code | Axiom N=76 | | Control N=76 | |
|--|---------------|-------------------|-----------------|------------------|
| | Events N | Subjects n (%) | Events N | Subject n (%) |
| Total Serious Adverse Events (based on ITT) | 7 | 7 (9.2) | 10 | 8 (10.5) |
| Total Serious Adverse Events (based on At Risk)¹ | 7 | 7 (11.5) | 10 | 8 (14.8) |
| Degenerative Joint Disease / Arthritis ² | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Bone / Bone Infection ³ | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Cardiac / Arrhythmia and Irregularities | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Injury / ADL ⁴ | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Intestinal / Nausea and/or Vomiting | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Joint or Muscle / Surgery | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Blood Pressure / Hypertension | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Dermatologic ⁵ | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Eyes or Ears or Nose or Throat (EENT) ⁶ | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Infection / Cellulitis | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Infection / Systemic Infection or General or Unknown | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Intestinal / Diverticulitis | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Liver / Cirrhosis or Fatty Liver | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Substance Related Disorders / Substance Dependence or Withdrawal | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Trunk or Ribs / Trunk or Rib Pain | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Wound Issue / Wound Infection | 0 | 0 (0.0) | 1 | 1 (1.3) |

- Subjects at risk means all subjects that underwent an INS procedure, (Axiom n=61, Control n=54).
- One subject reported worsening of left shoulder arthritis. The subject was treated with left shoulder hemiarthroplasty for arthritis, cuff tear and biceps tendonitis. During the surgery a degenerative osteocartilagenous cyst was removed. A second subject had baseline ongoing condition of neck pain with previous cervical radiofrequency thermocoagulation. Three months post INS implant, the subject reported having surgery (ACF and discectomy at C4-5 and C5-6) due to cervical spondylosis with radiculitis.
- Subject reported osteomyelitis of right great toe. The subject's right toe was run over by a cart while working and the right toe started to become red/black. The subject then went to the hospital on and was admitted. The subject presented to the hospital with worsening swelling with a ½ cm diameter deep ulceration and discharge of the right great toe. The subject was started on IV antibiotics (vancomycin) and underwent a great right toe amputation at the MTPJ level.
- The subject reported a chainsaw cutting incident in which he broke his left leg (tibia bone near the knee).
- The subject was noted to have an ulcer of the left plantar foot (neuropathic foot ulcer sub left 1st met heal with a dry neurotic base and large periwound keratosis). The subject has a medical history of diabetes. The subject was treated with an excisional debridement of the ulcer and application of an Aquacel AG dressing.
- The subject reported loss of vision in the right eye. The subject did not receive any treatment from the investigator but it was noted that the subject was being evaluated and treated by an ophthalmologist.

Adverse Events by Relatedness to Implant Procedure, Device or Stimulation Therapy

Adverse events were classified by the DSMB as device-, procedure-, and/or stimulation-related. Note that the categories of device related, procedure related and stimulation related are not mutually exclusive. For some events the DSMB

adjudicated an event as related to multiple categories such as device and procedure related, or device and stimulation related, etc.

As seen in **Table 12**, which represents the ITT population, the rates of device- and stimulation-related events were not statistically different between the groups. However, procedure-related AEs were more frequent in the Axium group (52 events in 35 of 76 subjects (46.1% of subjects)) than the Control group (29 events in 20 of 76 subjects (26.3% of subjects)) (p=0.0177).

Table 12: Definitely Related Adverse Event Rates – ITT Population

| Adverse Event Characteristic | Axium N=76 | | Control N=76 | | P-value |
|---|---------------|-------------------|-----------------|-------------------|---------|
| | Events | Subjects n (%) | Events | Subjects n (%) | |
| Relatedness to Neurostimulator System/ Device | 39 | 28 (36.8%) | 24 | 20 (26.3%) | 0.2217 |
| Relatedness to Implant Procedure | 52 | 35 (46.1%) | 29 | 20 (26.3%) | 0.0177 |
| Relatedness to Stimulation Therapy | 10 | 8 (10.5%) | 10 | 10 (13.2%) | 0.8025 |

In analyzing the procedure-related adverse events the MITT data analysis set (all subjects that had a TNS procedure; Axium = 73 subjects and Control = 73 Subjects) is used since it represents data specifically related to subjects' and physicians experience with Axium device implantation procedures. The number of leads implanted presented in **Table 13** includes the leads implanted during the TNS and INS procedures the subject underwent. For example, if a subject had four DRG leads implanted at TNS, and four DRG leads at INS, the subject would be counted in the table as having eight leads implanted. The subjects excluded from the MITT data analysis set were not exposed to any implant procedure; therefore, the MITT data set is the most relevant for looking at procedure related AEs. As shown in **Table 13**, the number of subjects with procedure related events in the Axium group is associated with the number of leads implanted per subject.

This may be expected since individual needle sticks are required to implant each Axium lead during a procedure (up to four leads), in contrast to the fewer needle sticks typically used to implant one or two leads during a Control procedure. The results show an increasing linear relationship between the number of Axium leads implanted and the number of subjects with procedure-related events, ranging from zero events in two subjects with one lead implanted, to eight events in eight subjects with six leads implanted. There is no apparent increasing linear relationship between the number of leads implanted and the number of Control subjects with procedure-related events.

Table 13: Subjects with Definitely Related Procedure Adverse Events by Leads Implanted

| Number of Leads Implanted | Axium | | Control | |
|---------------------------|----------------------------|--------------------------------------|----------------------------|--------------------------------------|
| | Subjects Implanted n/N (%) | Subjects with Adverse Events n/N (%) | Subjects Implanted n/N (%) | Subjects with Adverse Events n/N (%) |
| 1 lead | 2/73 (2.7) | 0/2 (0.0) | 3/73 (4.1) | 2/3 (66.7) |
| 2 leads | 16/73 (21.9) | 5/16 (31.3) | 20/73 (27.4) | 4/20 (20.0) |
| 3 leads | 10/73 (13.7) | 3/10 (30.0) | 7/73 (9.6) | 3/7 (42.9) |
| 4 leads | 26/73 (35.6) | 13/26 (50.0) | 38/73 (52.1) | 9/38 (23.7) |
| 5 leads | 4/73 (5.5) | 2/4 (50.0) | 2/73 (2.7) | 1/2 (50.0) |
| 6 leads | 9/73 (12.3) | 9/9 (100.0) | 3/73 (4.1) | 1/3 (33.3) |
| 7 leads | 2/73 (2.7) | 0/2 (0.0) | 0/73 (0.0) | -- |
| 8 leads | 4/73 (5.5) | 3/4 (75.0) | 0/73 (0.0) | -- |
| Total | 73/73 (100.0) | 35/73 (47.9) | 73/73 (100.0) | 20/73 (27.4) |

Table 14 presents the distribution and time course of all definitely related adverse events by time course (regardless of seriousness). The most frequently occurring procedure related adverse events in the Axium group were pain at the incision site and post-procedure back pain. The most frequently occurring device related adverse events in Axium subjects were lead migration/loss of stimulation, IPG pocket pain, and lead breakage. The most frequently occurring stimulation related adverse event in the Axium group was over-stimulation.

The most frequently occurring procedure related adverse events in the Control group were pain at the incision site, post-procedure back pain, and wound infection. The most frequently occurring device related adverse events in Control subjects were lead migration/loss of stimulation, IPG pocket pain, and wound infection. The most frequently occurring stimulation related adverse event in the Control group was over-stimulation.

Table 14: Time Course of Definitely Related Adverse Events

| Subsystem Code/Preferred Code | Through TNS Phase | | INS to 30 days | | >30 days to 3 Months | | >3 Months to 6 Months | | >6 Months to 12 Months | | >12 Months | |
|--|-------------------|-----------|----------------|-----------|----------------------|-----------|-----------------------|-----------|------------------------|-----------|------------|-----------|
| | AX | C | AX | C | AX | C | AX | C | AX | C | AX | C |
| Total Adverse Events | 28 | 20 | 22 | 16 | 11 | 10 | 13 | 3 | 9 | 5 | 3 | 0 |
| Subjects At Risk | 76 | 76 | 61 | 54 | 61 | 54 | 59 | 54 | 59 | 52 | 55 | 50 |
| IPG Pocket / IPG Pocket Pain | 0 | 0 | 2 | 0 | 2 | 3 | 4 | 0 | 2 | 1 | 0 | 0 |
| Lead / Migration -Loss of Stimulation | 3 | 5 | 3 | 2 | 0 | 0 | 2 | 0 | 1 | 1 | 0 | 0 |
| Wound Issue / Pain at Incision Site | 0 | 1 | 5 | 2 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lead / Breakage | 0 | 0 | 0 | 0 | 1 | 0 | 3 | 0 | 2 | 0 | 0 | 0 |
| Back / Back Pain | 4 | 4 | 0 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| Side Effect / Procedure Medication | 3 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown device component / Loss Stimulation | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| Stimulation / | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |

| Subsystem Code/Preferred Code | Through TNS Phase | | INS to 30 days | | >30 days to 3 Months | | >3 Months to 6 Months | | >6 Months to 12 Months | | >12 Months | |
|---|----------------------|---|-------------------|---|-------------------------|---|--------------------------|---|---------------------------|---|------------|---|
| | AX | C | AX | C | AX | C | AX | C | AX | C | AX | C |
| Overstimulation | | | | | | | | | | | | |
| Wound Issue / Erythema or Drainage or Inflammation | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Allergic Reaction / Procedure Medications or dressings | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Stimulation / Understimulation | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower Extremity / Unilateral Lower Leg Pain | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Fever / Fever or Pyrexia | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lead / Migration - Observation only | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lead / Severed | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Procedural complications / Dural puncture | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Foot / Foot Pain | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Patient Programmer / Loss of Stimulation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 |
| Back and Lower Extremity / Back Pain and Unilateral Radiation into Upper Leg | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Head and Neck /Headache | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower Extremity/ Unilateral Upper Leg Pain | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sensory Deficit / Sensory Deficit Subjective - Bilateral | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Blood Loss / More than Expected | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Connector cable / Loss of stimulation | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dermatologic | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Fluid Volume Balance / Edema - other | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Head and Neck / Restlessness or Agitation | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INS / Battery depletion | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Joint or Muscle / Pulled or Strained Muscle or Muscle Cramp | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lead / Retained Lead(s) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Lower Extremity / Bilateral Lower Leg Pain | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Reproductive / Vaginal or Yeast Infection | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sensory Deficit / Sensory Deficit Measureable - Unilateral | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Urinary / Urinary Urgency | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Wound Issue / Deep | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |

| Subsystem Code/Preferred Code | Through TNS Phase | | INS to 30 days | | >30 days to 3 Months | | >3 Months to 6 Months | | >6 Months to 12 Months | | >12 Months | |
|--|-------------------|---|----------------|---|----------------------|---|-----------------------|---|------------------------|---|------------|---|
| | AX | C | AX | C | AX | C | AX | C | AX | C | AX | C |
| Wound Issue / Wound Infection | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| Muscle Spasms / Muscle Spasm | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Urinary / Urinary Hesitance | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Knee / Knee Pain | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sensory Deficit / Sensory Deficit Subjective - Unilateral | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Substance Related Disorders / Substance Dependence or Withdrawal | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Wound Issue / Incisional cellulitis | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Axiom Device Complaints

When a site reported a device performance issue, a Complaint was submitted to Spinal Modulation Quality system, and when appropriate, the device component that had the performance issue was returned to SMI for analysis. In addition, all adverse events that were reported by investigators and adjudicated by the DSMB as related to the implant procedure, the device, or stimulation therapy were evaluated for whether a complaint should be reported as well. **Table 15** presents a summary of complaints by complaint category that were reported as of the time of the database lock on Dec 23, 2014. The complaint summary lists all events reported into the SMI quality system as complaints. The events are categorized into five main areas:

- Hardware-related complaints refer to non-procedural events related to the product, including the Clinical and Patient Programmers, stimulators, leads, accessories, and packaging.
- Intra-operative complaints are segmented into two categories:
 - o Events that are probably or likely related to the procedure
 - o Physiological events that occurred during the operative procedure
- Post-operative events occurred after the TNS or INS procedure during normal use of the therapy. The complaints have been segmented into two categories:
 - o Physiological
 - o Device-related

A total of 59 of 73 Axiom subjects experienced a complaint (80.8%). Note that not all complaints were associated with an adverse event. In the trial, 43.8% (67/153) of all Axiom complaints were associated with an adverse event. The most frequently reported device complaints were kinked sheaths (21 events in 19 subjects, 26% of subjects) and connector-cable related events (21 events in 19

subjects, 26% of subjects). Lead migration requiring a replacement procedure occurred in 6.8% of subjects (5/73). Two subjects (2.7%) had lead breakage during an explant procedure that resulted in lead fragments being retained in the body, two subjects had a dural puncture during implant (2.7%), and one subject (1.4%) had a loss of urinary sensation. See **Table 15** below for a summary of complaints associated with the Axium device.

Table 15: Axium Complaints Summary

| Category | Number of Complaints | Number of Subjects with a Complaint | Percentage of Subjects with a Complaint |
|--|----------------------|-------------------------------------|---|
| Hardware-related | 52 | 43 | 58.9% |
| Clinical Programmer | 14 | 11 | 15.1% |
| Impedance Measurement | 4 | 4 | 5.5% |
| Frozen Clinical Programmer Screen | 3 | 3 | 4.1% |
| Communication | 2 | 2 | 2.7% |
| Clinical Programmer Charging | 2 | 2 | 2.7% |
| Misalignment Clinical Programmer Screen | 1 | 1 | 1.4% |
| Programmer Battery | 1 | 1 | 1.4% |
| Clinical Programmer Software Hard Reset | 1 | 1 | 1.4% |
| Patient Programmer | 10 | 9 | 13.7% |
| Patient Programmer Charging | 5 | 5 | 6.8% |
| Frozen Patient Programmer Screen | 3 | 3 | 4.1% |
| Communication | 2 | 2 | 2.7% |
| TNS | 2 | 2 | 2.7% |
| TNS Label Adhesion | 2 | 2 | 2.7% |
| Lead Migration Requiring Revision | 5 | 5 | 6.8% |
| During Trial Phase | 2 | 2 | 2.7% |
| Post-implant (<30 days) | 2 | 2 | 2.7% |
| Post-implant (>30 days) | 1 | 1 | 1.4% |
| Connector Cable | 21 | 19 | 26.0% |
| Connector Cable-Block | 12 | 11 | 14.5% |
| Connector Cable-Hood | 6 | 6 | 8.2% |
| Connector Cable-Damaged | 2 | 2 | 2.7% |
| Connector Cable-Clip | 1 | 1 | 1.4% |
| Intra-operative events (procedural related) | 43 | 41 | 56.2% |
| Kinked Sheath | 21 | 19 | 26.0% |
| Stylet Reinsertion into Lead | 7 | 7 | 9.6% |
| Lead Damaged at Implant | 3 | 3 | 4.1% |
| Lead Fragments | 2 | 2 | 2.7% |
| Dural Puncture | 2 | 2 | 2.7% |
| Lead Movement Without Clinical Effect | 2 | 2 | 2.7% |
| Kinked Lead | 1 | 1 | 1.4% |
| Tyvek tears | 1 | 1 | 1.4% |
| Foot drop | 1 | 1 | 1.4% |
| User product preference | 1 | 1 | 1.4% |
| Sciatica | 1 | 1 | 1.4% |
| Lower Extremity numbness | 1 | 1 | 1.4% |
| Post-operative events (physiological) | 41 | 36 | 49.3% |
| Incisional discomfort after INS | 9 | 7 | 9.6% |
| Post-procedure lower extremity discomfort | 9 | 6 | 7.9% |
| Fever | 3 | 3 | 4.1% |

| Category | Number of Complaints | Number of Subjects with a Complaint | Percentage of Subjects with a Complaint |
|--|----------------------|-------------------------------------|---|
| Incisional Erythema | 3 | 3 | 4.1% |
| Allergic reaction to dressing | 2 | 2 | 2.7% |
| Incisional discomfort after TNS | 2 | 2 | 2.7% |
| Low back pain after TNS | 2 | 2 | 2.7% |
| Nausea after TNS | 1 | 1 | 1.4% |
| Impedance Measurement | 1 | 1 | 1.4% |
| Headache | 1 | 1 | 1.4% |
| Inadequate pain relief/positional changes | 1 | 1 | 1.4% |
| Rash after TNS | 1 | 1 | 1.4% |
| Programming | 1 | 1 | 1.4% |
| Tinea Cruris | 1 | 1 | 1.4% |
| Discomfort at extension connection site | 1 | 1 | 1.4% |
| Discomfort at INS site | 1 | 1 | 1.4% |
| Electrical sensation | 1 | 1 | 1.4% |
| Lesion over INS pocket | 1 | 1 | 1.4% |
| Post-operative events (device related) | 15 | 14 | 19.2% |
| Low Impedance | 4 | 3 | 4.1% |
| INS Replacement | 2 | 2 | 2.7% |
| Lead Movement Requiring Reprogramming | 2 | 2 | 2.7% |
| Lead Fracture | 2 | 2 | 2.7% |
| High Impedance | 1 | 1 | 1.4% |
| Loss of therapy | 1 | 1 | 1.4% |
| Loss of sense of urination | 1 | 1 | 1.4% |
| Pocket stimulation after INS | 1 | 1 | 1.4% |
| Lead Movement Without Clinical Effect | 1 | 1 | 1.4% |
| Intra-operative events (physiological) | 2 | 2 | 2.7% |
| New onset Atrial Fibrillation at INS procedure | 1 | 1 | 1.4% |
| Excess blood loss at INS procedure | 1 | 1 | 1.4% |
| Total Complaints | 153 | | |

All Adverse Events

Investigators reported all adverse events whether or not the event was serious or related to the study devices, implant procedures, or stimulation therapy. **Table 16** presents the distribution of all adjudicated adverse events reported and adjudicated at the time of the database lock. There were 241 adverse events in 62 subjects (81.6%) in the Axium group and 161 adverse events in 55 subjects (72.4%) in the Control group (p=0.2575). There were 24 unadjudicated adverse events in 17 subjects at the time of the database lock. None were reported as serious adverse events by the investigators, and two events of IPG pocket pain were classified as possibly related to the device and/or procedure by the investigators.

Table 16: Distribution of All Adverse Events

| Subsystem Code/Preferred Code | Axium N=76 | | Control N=76 | |
|--|---------------|-------------------|-----------------|-------------------|
| | Events N | Subjects n (%) | Events N | Subjects n (%) |
| Total Adverse Events (based on ITT) | 241 | 62 (81.6) | 161 | 55 (72.4) |
| Total Adverse Events (based on At Risk) | 241 | 62 (81.6) | 161 | 55 (72.4) |
| IPG Pocket / IPG Pocket Pain | 11 | 11 (14.5) | 6 | 5 (6.6) |
| Lead / Migration -Loss of Stimulation | 10 | 9 (11.8) | 9 | 9 (11.8) |
| Dermatologic | 9 | 6 (7.9) | 5 | 5 (6.6) |
| Injury / ADL | 9 | 8 (10.5) | 3 | 3 (3.9) |
| Back / Back Pain | 8 | 8 (10.5) | 10 | 9 (11.8) |
| Wound Issue / Pain at Incision Site | 8 | 7 (9.2) | 6 | 6 (7.9) |
| Eyes or Ears or Nose or Throat (EENT) | 7 | 6 (7.9) | 11 | 8 (10.5) |
| Lead / Breakage | 6 | 5 (6.6) | 0 | 0 (0.0) |
| Side Effect / Procedure Medication | 5 | 3 (3.9) | 5 | 4 (5.3) |
| Injury / Fall or Trip or Slip or Twist | 5 | 5 (6.6) | 4 | 4 (5.3) |
| Sinus / Sinus Infection or Sinusitis | 5 | 5 (6.6) | 4 | 3 (3.9) |
| Foot / Foot Pain | 5 | 5 (6.6) | 3 | 2 (2.6) |
| Lower Extremity / Unilateral Upper Leg Pain | 5 | 5 (6.6) | 3 | 3 (3.9) |
| Intestinal / Nausea and/or Vomiting | 5 | 5 (6.6) | 1 | 1 (1.3) |
| Allergic Reaction / Procedure Medications or dressings | 5 | 4 (5.3) | 0 | 0 (0.0) |
| Unknown device component / Loss of Stimulation | 5 | 5 (6.6) | 0 | 0 (0.0) |
| Stimulation / Overstimulation | 4 | 4 (5.3) | 5 | 5 (6.6) |
| Head and Neck / Headache | 4 | 3 (3.9) | 2 | 2 (2.6) |
| Joint or Muscle / Bursitis | 4 | 4 (5.3) | 1 | 1 (1.3) |
| Knee / Knee Pain | 4 | 4 (5.3) | 1 | 1 (1.3) |
| Upper Respiratory Symptoms / Upper Respiratory Symptoms | 3 | 3 (3.9) | 4 | 4 (5.3) |
| Joint or Muscle / Pulled or Strained Muscle or Muscle Cramp | 3 | 3 (3.9) | 3 | 2 (2.6) |
| Substance Related Disorders / Substance Dependence or Withdrawal | 3 | 3 (3.9) | 3 | 3 (3.9) |
| Lower Extremity / Bilateral Lower Leg Pain | 3 | 3 (3.9) | 2 | 2 (2.6) |
| Wound Issue / Erythema or Drainage or Inflammation | 3 | 3 (3.9) | 2 | 2 (2.6) |
| Degenerative Joint Disease / Arthritis | 3 | 3 (3.9) | 1 | 1 (1.3) |
| Upper Extremity / Upper Extremities Pain | 3 | 3 (3.9) | 1 | 1 (1.3) |
| Urinary / Urinary Tract Infection | 3 | 3 (3.9) | 1 | 1 (1.3) |
| Blood Components / Abnormal Blood Chemistry | 3 | 3 (3.9) | 0 | 0 (0.0) |
| Bone / Bone Fracture | 3 | 3 (3.9) | 0 | 0 (0.0) |
| Fever / Fever or Pyrexia | 3 | 3 (3.9) | 0 | 0 (0.0) |
| Motor Deficit / Motor Deficit Subjective - Unilateral | 3 | 3 (3.9) | 0 | 0 (0.0) |
| Stimulation / Understimulation | 3 | 3 (3.9) | 0 | 0 (0.0) |
| Sensory Deficit / Sensory Deficit Subjective - Unilateral | 2 | 2 (2.6) | 3 | 2 (2.6) |
| Gastric / Gastroenteritis or Stomach Flu | 2 | 2 (2.6) | 2 | 2 (2.6) |
| Lower Extremity / Unilateral Lower Leg | 2 | 2 (2.6) | 2 | 2 (2.6) |

| Subsystem Code/Preferred Code | Axium N=76 | | Control N=76 | |
|--|---------------|-------------------|-----------------|-------------------|
| | Events N | Subjects n (%) | Events N | Subjects n (%) |
| Pain | | | | |
| Lung / Bronchitis | 2 | 2 (2.6) | 2 | 2 (2.6) |
| Back and Lower Extremity / Back Pain and Unilateral Radiation into Lower Leg | 2 | 2 (2.6) | 1 | 1 (1.3) |
| Gastric / Abdominal Pain | 2 | 2 (2.6) | 1 | 1 (1.3) |
| Lung / Respiratory Infection | 2 | 2 (2.6) | 1 | 1 (1.3) |
| Sensory Deficit / Sensory Deficit Subjective - Bilateral | 2 | 2 (2.6) | 1 | 1 (1.3) |
| Trunk or Ribs / Trunk or Rib Pain | 2 | 2 (2.6) | 1 | 1 (1.3) |
| Cardiac / Arrhythmia and Irregularities | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Fluid Volume Balance / Edema - lower extremities | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Intestinal / Constipation | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Intestinal / Diarrhea | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Joint or Muscle / Inflammation of Muscle | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Joint or Muscle / Joint Sprain | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Lead / Migration - Observation only | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Lead / Severed | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Pancreas / Diabetes Mellitus | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Procedural complications / Dural puncture | 2 | 2 (2.6) | 0 | 0 (0.0) |
| Blood Pressure / Hypertension | 1 | 1 (1.3) | 3 | 3 (3.9) |
| Neck or Cervical / Neck or Cervical Pain | 1 | 1 (1.3) | 3 | 3 (3.9) |
| Reflex / Reflex Change or Abnormality | 1 | 1 (1.3) | 3 | 3 (3.9) |
| Back and Lower Extremity / Back Pain and Unilateral Radiation into Upper Leg | 1 | 1 (1.3) | 2 | 2 (2.6) |
| Patient Programmer / Loss of Stimulation | 1 | 1 (1.3) | 2 | 2 (2.6) |
| Foot or Ankle or Toe / Plantar fasciitis | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Hip Joint / Hip Joint Pain and Discomfort | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Infection / Systemic Infection or General or Unknown | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Joint or Muscle / Sacroiliitis | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Liver / Cirrhosis or Fatty Liver | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Lung / COPD (Chronic Obstructive Pulmonary Disease) | 1 | 1 (1.3) | 1 | 1 (1.3) |
| SI Joint / SI Joint Pain and Discomfort | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Sleep Disorders / Insomnia | 1 | 1 (1.3) | 1 | 1 (1.3) |
| Autoimmune Disorder / Celiac disease | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Blood Loss / More than Expected | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Bone / Bone Infection | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Connector cable / Loss of stimulation | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Fluid Volume Balance / Dehydration | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Fluid Volume Balance / Edema - other | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Foot or Ankle or Toe / Foot or Feet Problem - Other | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Gall Bladder / Cholelithiasis or Gallstones | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Gastric / Dyspepsia or Indigestion | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Head and Neck / Restlessness or Agitation | 1 | 1 (1.3) | 0 | 0 (0.0) |
| INS / Battery depletion | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Infection / Viral Infection | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Injury / Motor Vehicle Accident | 1 | 1 (1.3) | 0 | 0 (0.0) |

| Subsystem Code/Preferred Code | Axium N=76 | | Control N=76 | |
|---|---------------|-------------------|-----------------|-------------------|
| | Events N | Subjects n (%) | Events N | Subjects n (%) |
| Intestinal / Irritable Bowel Syndrome | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Joint or Muscle / Surgery | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Lead / Retained Lead(s) | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Lung / Pneumonia | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Prostate / Prostate Cancer | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Psychosocial Disorders / Depressive Disorders | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Reproductive / Vaginal or Yeast Infection | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Sensory Deficit / Sensory Deficit Measureable - Unilateral | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Spine / Degenerative Disc Disease Progression | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Surgery / TURP | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Upper Extremities / Upper Extremity Sensory Deficit - Unilateral | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Urinary / Urinary Urgency | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Whole Body / Chronic Pain Syndrome | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Wound Issue / Deep | 1 | 1 (1.3) | 0 | 0 (0.0) |
| Wound Issue / Wound Infection | 0 | 0 (0.0) | 7 | 5 (6.6) |
| Cardiac / Cardiac Chest Pain | 0 | 0 (0.0) | 3 | 3 (3.9) |
| Muscle Spasms / Muscle Spasm | 0 | 0 (0.0) | 2 | 2 (2.6) |
| Urinary / Urinary Hesitance | 0 | 0 (0.0) | 2 | 1 (1.3) |
| Back and Lower Extremity / Back Pain and Bilateral Radiation into Lower Leg | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Gastric / Acid Reflux | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Head and Neck / Migraine | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Hormones / Decreased Testosterone | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Infection / Cellulitis | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Intestinal / Diverticulitis | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Joint or Muscle / Trigger Finger or Stenosing Tenosynovitis | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Kidney / Kidney Problems - Other | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Lipid Metabolism / Hypercholesterolemia or High Cholesterol or Hyperlipidemia | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Lung / Asthma | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Skin / Melanoma | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Sleep Disorders / Fatigue or Sleepiness or Somnolence | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Substance Related Disorders / Overdose | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Upper Extremities / Carpal tunnel | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Wound Issue / Abscess | 0 | 0 (0.0) | 1 | 1 (1.3) |
| Wound Issue / Incisional cellulitis | 0 | 0 (0.0) | 1 | 1 (1.3) |

Device Replacements, Revisions and Explants through 12 Months

Table 17 summarizes the frequency of replacements of external device components (i.e., TNS, TNS connector cable, and patient programmer) through 12 months.

Table 17: Replacement of External Components

| | Axium | | Control | |
|--|-----------|-----------|----------|----------|
| | TNS | INS | TNS | INS |
| Number of External Component Replacement Procedures | 11 | 11 | 0 | 5 |
| Replacement of External Components | | | | |
| Connector Cable | 10 | 0 | 0 | 0 |
| Patient Programmer | 0 | 11 | 0 | 5 |
| TNS and Patient Programmer | 1 | 0 | 0 | 0 |

A summary of the device replacements, revisions, and explants is presented in **Table 18**. Note that Axium leads are not able to be revised (e.g., same lead moved to an alternate location), but Control leads may be revised. If an Axium lead has an issue, the lead must be replaced with a new lead.

Table 18: Subsequent Replacement, Revision, or Explant Procedures through 12 Months

| | Axium | Control |
|--|-------|---------|
| INS or INS Lead Replacement/Revisions | 8 | 4 |
| TNS Lead Revision | 0 | 1 |
| INS System Replacement/Revision | 5 | 1 |
| TNS System Replacement/Revision | 4 | 3 |
| INS/TNS Lead Addition | 4 | 0 |
| INS System Explant | 5 | 4 |

2. Effectiveness Results

As pre-specified in the Statistical Analysis Plan (SAP), the study primary composite endpoint data was analyzed using a modified intention to treat (MITT) analysis which included all subjects that were randomized and received a trial neurostimulator. The analysis of effectiveness was based on 146 (73 Axium and 73 Control) evaluable subjects at the 3-month time point. Intention-to-treat (ITT) and per-protocol (PP) analyses were also performed.

See **Figure 2** below for a disposition of subjects by analysis data set. One Control subject in the MITT analysis data set had a TNS procedure but withdrew from the study prior to undergoing the end of TNS-study visit. Since the subject withdrew due to a device-related adverse event, the subject is counted as a treatment failure based on the definitions of treatment success and failure, as pre-specified in the SAP. One Axium subject in the MITT data set had an INS procedure but withdrew from the study prior to the 3-month study visit. Since the subject withdrew due to a device-related adverse event, the subject is counted as a treatment failure based on the definitions of treatment success and failure, as pre-specified in the SAP. Another Axium subject in the MITT data set exited the study prior to their INS procedure due to a device-related adverse event post-TNS procedure. Since this subject withdrew due to a device related adverse event, the

subject is counted as a treatment failure based on the definitions of treatment success and failure, as pre-specified in the SAP. Seven subjects (four in the Axium group and three in the Control group) in the MITT analysis data set have no evaluable data for the study endpoints at three months and are counted as missing because they withdrew from the study prior to the 3-month study visit, and did not meet any prospectively defined criteria for treatment failure/success at the time of study withdrawal. Six subjects in the ITT analysis data set (three in the Axium group and three in the Control group), were randomized, did not go on to have a TNS procedure, withdrew from the study prior to the TNS procedure, and are not included in the MITT analysis set.

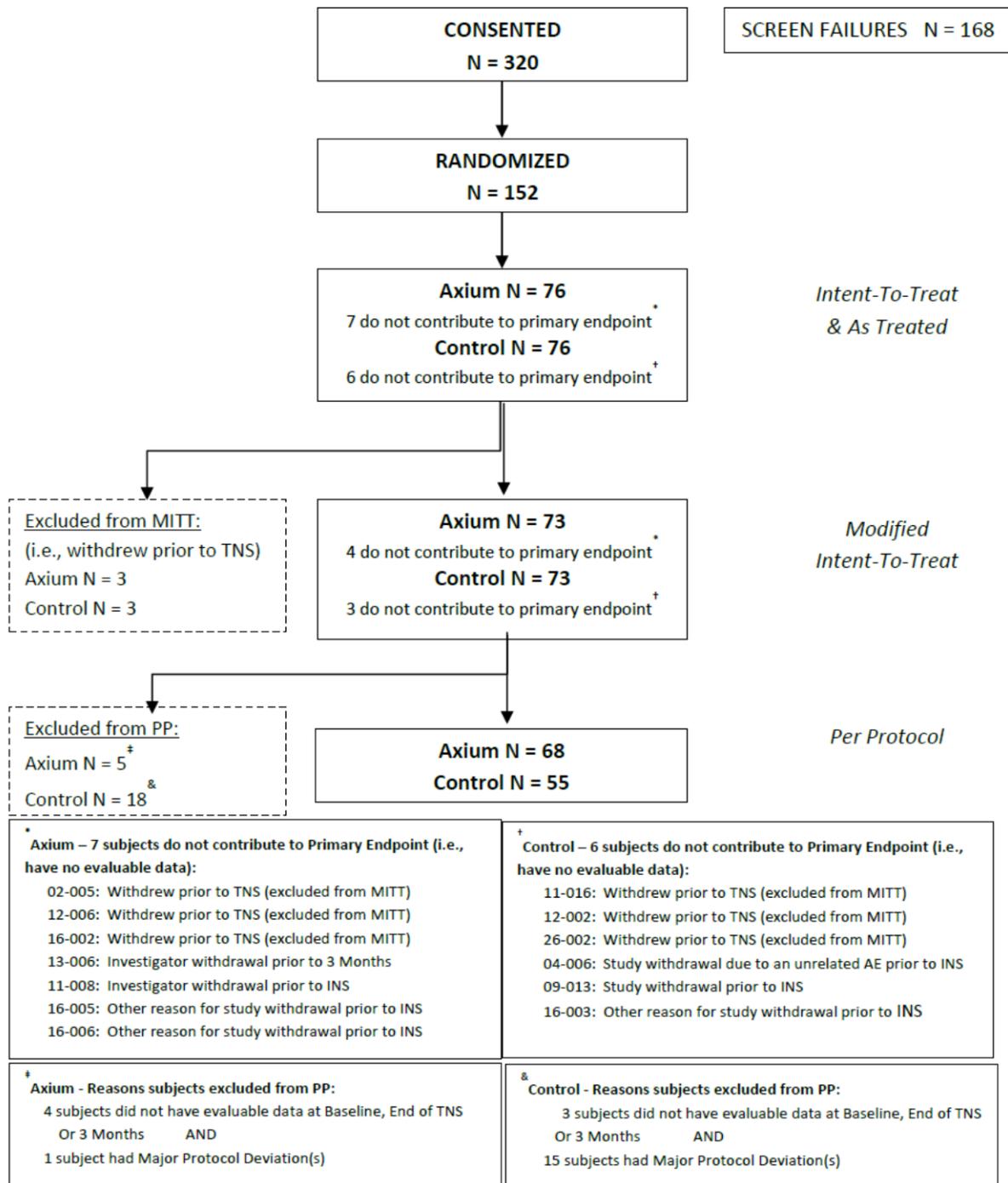


Figure 2: Subject Disposition by Analysis Data Set

Primary Composite Endpoint

The results of the primary endpoint (MITT analysis) are presented in Table 19. As shown in **Table 19**, treatment success in the Axium group at 3 months was 81.2% and treatment success in the Control group was 55.7% at three months. None of the study subjects experienced a primary composite endpoint safety event (stimulation induced neurological deficit). The results demonstrate the non-inferiority ($p < 0.0001$) and superiority ($p = 0.0004$) of Axium therapy over the Control therapy for the primary composite endpoint as defined in the Statistical Analysis Plan.

Table 19: Primary Composite Endpoint Treatment Success through 3 Months

| Primary Endpoint Component | Axium | Control |
|---|--------------------|--------------|
| Number of Subjects - MITT analysis data set | 73 | 73 |
| Number of Subjects-Primary endpoint analysis [†] | 69 | 70 |
| Overall primary endpoint success | | |
| n/N (%) | 56/69 (81.2) | 39/70 (55.7) |
| 95% CI | (69.9, 89.6) | (43.3, 67.6) |
| Success rate difference (%) and 95% CI (Blackwelder) | 25.4 (13.0, 100.0) | |
| P-value (non-inferiority $\delta = 10\%$) | <0.0001 | |
| P-value (superiority) | 0.0004 | |

[†] Subjects excluded since they do not have evaluable data: Axium=4, Control=3. Seven subjects in the MITT analysis have no evaluable data for the study endpoints because they withdrew from the study prior to the 3-month study visit, and did not meet any prospectively defined criteria for treatment failure/success at the time of study withdrawal. Therefore, the number of subjects in the MITT analysis that have evaluable data for the analysis of this endpoint is 69 subjects in the Axium group, and 70 subjects in the Control group.

Figure 3 and **Figure 4** below show the percent improvement at the 3-month follow-up as compared to baseline for the Axium subjects and the Control subjects.

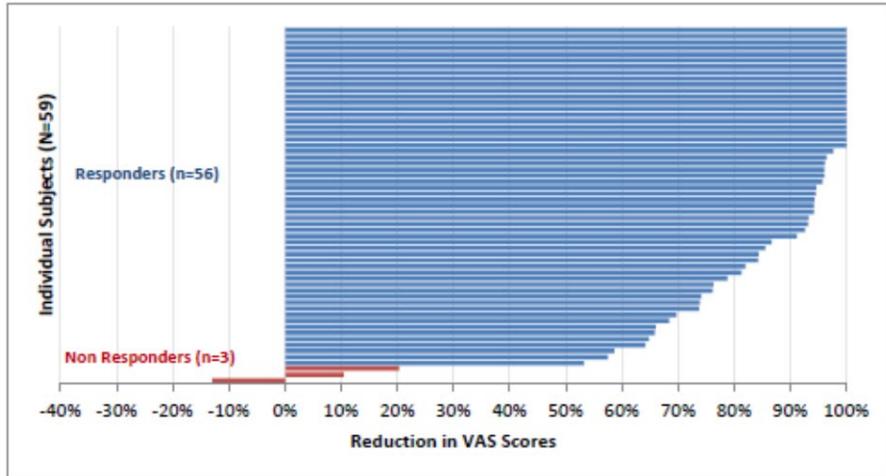


Figure 3: Percent Improvement in Pain from Baseline to 3 Months Post INS Implant Individual Axiom Subjects¹

1. *Note: Fifteen responders decreased their pain medications; three responders increased their pain medications*

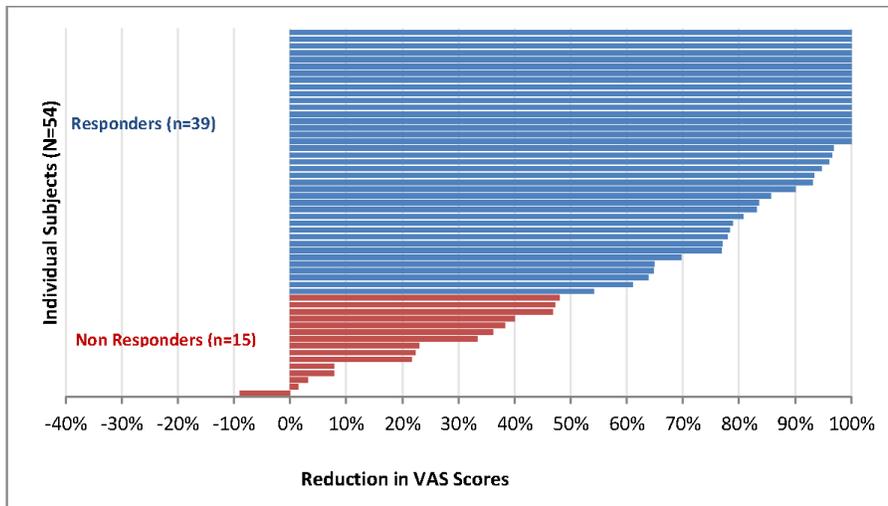


Figure 4: Percent Improvement in Pain from Baseline to 3 Months Post INS Implant Individual Control Subjects¹

1. *Note: Ten responders decreased their pain medications; three responders increased their pain medications.*

Supplemental Effectiveness Analysis - VAS Pain Score

A post-hoc analysis was performed to assess pain relief over time. VAS scores were assessed at each scheduled study visit. Pain level was measured using a 100 mm visual analogue scale (VAS) with 100 mm representing the “Worst Imaginable Pain” and 0 representing “No Pain.” **Figure 5** presents the mean pain ratings with the 95% confidence intervals over time. At baseline, pain scores were equivalent between Axium and Control groups (80.6 and 80.7, respectively). At 3 months and 12-months the Axium group rated their pain as being lower than the Control group (13.1 vs. 23.8 at three months and 15.0 vs. 26.5 at 12 months).

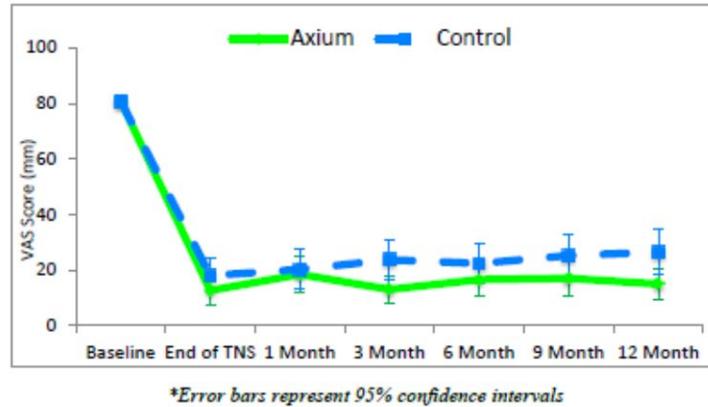


Figure 5: Average Pain Ratings (VAS Scores) over Time

Figure 6 presents average percent pain relief, as measured by the mean percent reduction in VAS scores, over time. The Axium group demonstrated a numerically greater percent reduction than the Control group at the three month interval (84.1% vs. 70.9%) and at 12 months (81.4% vs. 66.5%). These data are complementary to the primary endpoint analyses that demonstrated statistical non-inferiority and superiority in treatment success at 3 months for the Axium group.

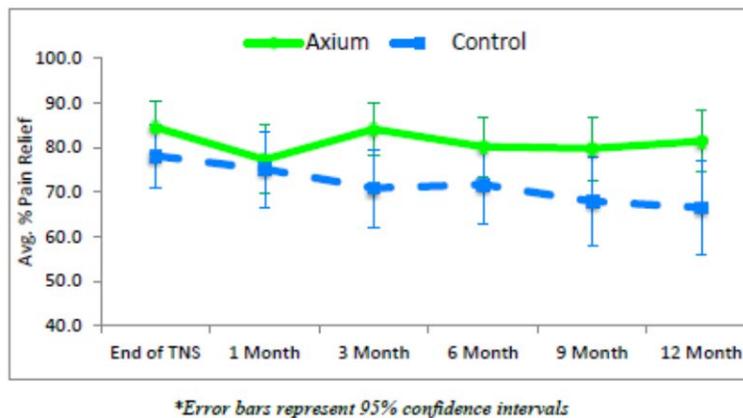


Figure 6: Average Percent Pain Relief (% VAS Reduction) over Time

Pre-specified Primary Composite Endpoint Sensitivity Analyses

All sensitivity analyses, including analyses of the ITT and PP data sets, subjects who received the implantable neurostimulator (INS), and missing data, confirmed the results of the primary analysis. In all cases, non-inferiority and superiority were met, indicating the robustness of the results for the 3- month data. The primary composite endpoint conclusions of non-inferiority ($p \leq 0.0001$) and superiority were met in each sensitivity analysis. See **Figure 7** below.

- Intention-to-Treat (ITT)
The primary non-inferiority ($p < 0.0001$) and superiority ($p = 0.0004$) objectives were met using the intention-to-treat data analysis set (see **Table 20**).

Table 20: Primary Composite Endpoint Success through 3 Months – ITT

| Primary Endpoint Component | Axium | Control |
|---|--------------------|--------------|
| Number of Subjects - ITT analysis data set | 76 | 76 |
| Number of Subjects-Primary endpoint analysis [†] | 69 | 70 |
| Overall primary endpoint success | | |
| n/N (%) | 56/69 (81.2) | 39/70 (55.7) |
| 95% CI | (69.9, 89.6) | (43.3, 67.6) |
| Success rate difference (%) and 95% CI (Blackwelder) | 25.4 (13.0, 100.0) | |
| P-value (non-inferiority $\delta = 10\%$) | <0.0001 | |
| P-value (superiority) | 0.0004 | |

[†] Subjects excluded since they do not have valid data: Axium=7, Control=6

- Per Protocol (PP) Analyses
The primary non-inferiority ($p < 0.0001$) and superiority ($p = 0.0007$) objectives were met using the PP data analysis set (see **Table 21**).

Table 21: Primary Composite Endpoint Success through 3 Months – PP

| Primary Endpoint Component | Axium | Control |
|--|--------------------|--------------|
| Number of Subjects - PP analysis data set | 68 | 55 |
| Overall primary endpoint success | | |
| n/N (%) | 55/68 (80.9) | 30/55 (54.5) |
| 95% CI | (69.5, 89.4) | (40.6, 68.0) |
| Success rate difference (%) and 95% CI (Blackwelder) | 26.3 (12.8, 100.0) | |
| P-value (non-inferiority $\delta = 10\%$) | <0.0001 | |
| P-value (superiority) | 0.0007 | |

- Subjects who Received the Implantable Neurostimulator (INS)
As prespecified in the SAP, since the non-inferiority of the primary endpoint was demonstrated, an analysis of the subset of subjects who received the INS was performed (see **Table 22**).

Table 22: Primary Composite Endpoint Success through 3 Months – INS Subjects Only

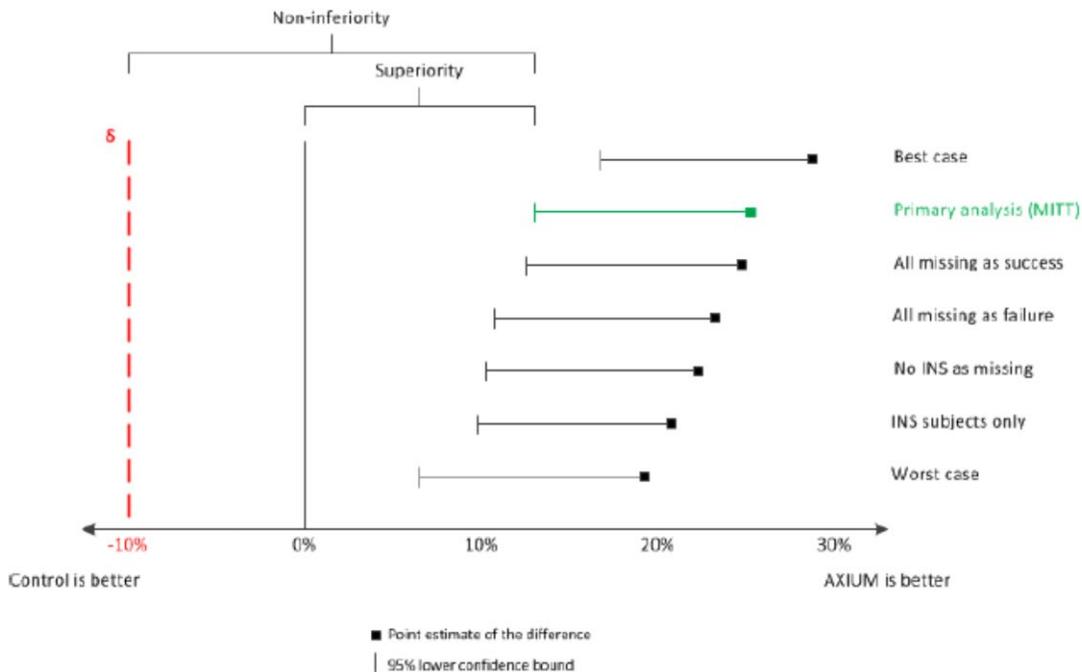
| Primary Endpoint Component | Axium | Control |
|--|-------------------|--------------|
| Number of Subjects – INS Subjects Only | 61 | 54 |
| Number of Subjects – Subjects in the analysis [†] | 60 | 54 |
| Overall primary endpoint success | | |
| n/N (%) | 56/60 (93.3) | 39/54 (72.2) |
| 95% CI | (83.8, 98.2) | (58.4, 83.5) |
| Success rate difference (%) and 95% CI (Blackwelder) | 21.1 (9.8, 100.0) | |
| P-value (non-inferiority $\delta = 10\%$) | <0.0001 | |
| P-value (superiority) | 0.0011 | |

[†]Subjects excluded since they do not have valid data: Axium=1, Control=0

- Missing Data

The sensitivity analyses on the primary composite endpoint to assess the impact of missing data on the results included the following (see **Figure 7**):

- All subjects with missing data counted as failures
- All subjects with missing data counted as successes
- Worst case scenario (including all Control subjects with missing data as successes and all Axium subjects with missing data as failures)
- Best case scenario (including all Control subjects with missing data as failures and all Axium subjects with missing data as successes)
- All subjects with $\geq 50\%$ reduction at end of TNS but chose not to have a TNS treated as missing
- Tipping point analysis – setting all missing values to either success or failure.


Figure 7: Sensitivity Analyses

Additional Sensitivity Analysis - Medication Changes

An additional sensitivity analysis was done to assess the effects of subject's that had medication increases (i.e., increased their maximum daily dose of medication, added adjunctive medications or increased the frequency of adjunctive lower limb pain medications) from baseline through three months post INS implant. These subjects were also identified as having a protocol deviation. There were a total of 12 subjects (4 Axium, 8 Control) that had medication increases. Two of Axium subjects (2/4) and three of the Control subjects (3/8) already were counted as treatment failures for other reasons. The difference in treatment success between the Axium and Control groups met both the non-inferiority ($p < 0.0001$) and superiority hypotheses ($p < 0.0001$). See **Table 23** below.

Table 23: Primary Composite Endpoint Sensitivity Analysis with Subjects with Medication Increases Classified as Treatment Failures

| Primary Endpoint Component | Axium | Control |
|---|---------------------|--------------|
| Number of Subjects – MITT | 73 | 73 |
| Number of Subjects-Primary endpoint analysis [†] | 69 | 71 |
| Overall primary endpoint success | | |
| n/N (%) | 54/69 (78.3) | 35/71 (49.3) |
| 95% CI | (66.7, 87.3) | (37.2, 61.4) |
| Success rate difference (%) and 95% CI (Blackwelder) | 29.0 (16.2, 100.00) | |
| P-value (non-inferiority $\delta = 10\%$) | < 0.0001 | |
| P-value (superiority) | < 0.0001 | |

[†] Subjects excluded since they do not have valid data: Axium=4, Control=2

One Control subject was a missing value in the primary composite endpoint because the subject withdrew prior to the INS implant and did not meet any pre-specified failure criteria (the subject met the success criteria at the end of TNS). However, that subject did have a pain medication increase after randomization and prior to withdrawal from the study. Therefore, since this analysis treats subjects that increased pain medications as treatment failures, the Control group sample size is 71 in this analysis and only two Control subjects do not have evaluable data..

Additional Sensitivity Analysis – Average VAS Scores from Subject Diary Responses

An additional assessment was done to assess the variability in pain severity based on the subjects' VAS ratings done once a day for seven days prior to each scheduled study visit through three months (See **Table 24**).

Table 24: Average VAS Scores Based on Subject Diary Responses – 3 Months

| | Baseline | | 1 Month | | 3 Months | |
|---|-----------|-----------|-----------|-----------|-----------|-----------|
| | Axium | Control | Axium | Control | Axium | Control |
| Number of Subjects | 76 | 76 | 61 | 54 | 59 | 54 |
| Average Pain 'Right Now' Per Subject Diary | | | | | | |
| N | 76 | 76 | 56 | 53 | 54 | 51 |
| Mean | 68.5 | 65.6 | 22.0 | 18.9 | 17.8 | 23.0 |
| SD | 19.3 | 17.5 | 22.2 | 18.4 | 18.4 | 22.0 |
| Median | 73.3 | 65.9 | 13.5 | 10.9 | 13.9 | 14.0 |

| Min | 13.3 | 13.1 | 0.0 | 0.0 | 0.0 | 0.0 |
|--|-------|---------|-------|---------|-------|---------|
| Max | 100.0 | 100.0 | 81.6 | 75.0 | 75.6 | 72.9 |
| Average 'Worst Pain' Per Subject Diary | | | | | | |
| | Axium | Control | Axium | Control | Axium | Control |
| N | 76 | 76 | 56 | 53 | 54 | 51 |
| Mean | 80.8 | 78.6 | 32.3 | 33.1 | 28.6 | 36.8 |
| SD | 13.8 | 13.6 | 25.9 | 24.4 | 24.6 | 27.1 |
| Median | 81.6 | 78.5 | 26.8 | 30.1 | 24.8 | 36.6 |
| Min | 40.4 | 40.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| Max | 100.0 | 100.0 | 87.7 | 89.6 | 96.9 | 100.0 |

Non-powered Secondary Endpoint - Pain Relief for Subjects “With” and “Without” Paresthesia

This non-powered secondary endpoint characterizes pain relief for subjects with and without paresthesia. As shown in **Table 25**, nine subjects in the Axium group and four subjects in the Control group reported a complete absence of paresthesia at three months post implantation. All nine subjects in the Axium group and two of the four subjects in the Control group were treatment successes.

At the time of the trial and implant procedures, all subjects were asked to confirm that they were feeling stimulation (i.e. sensation of paresthesia) in the targeted area of pain in order to confirm placement of the implanted leads. Post-procedure, stimulation settings were then programmed based upon physician judgement to optimize the appropriate therapy for each study subject. In addition, all study subjects were able to adjust the intensity level of the therapy, within a physician-prescribed range, with their patient programmers.

Note that the clinical relevance of this result is unknown. The study was a non-inferiority trial, designed to assess device effectiveness in the presence of paresthesia. The instructions for use for the Control device requires the Control device be programmed for subjects to receive paresthesia. In addition, the number of subjects that did not have paresthesia is very small and this endpoint was not adequately powered to detect the difference in pain relief for subjects who reported feeling versus not feeling paresthesia. A placebo controlled trial would be necessary to rule out the possibility that the effect is greater than placebo.

Table 25: Pain Relief in Axium and Control Subjects Who Did and Did Not Experience Paresthesia at 3 Months

| | Axium | | Control | |
|--|---------------------------|------------------------------|---------------------------|------------------------------|
| | Subjects with Paresthesia | Subjects without Paresthesia | Subjects with Paresthesia | Subjects without Paresthesia |
| Number of Subjects | 49 | 9 | 50 | 4 |
| Percent Pain Relief at 3 Months | | | | |
| N | 49 | 9 | 50 | 4 |
| Mean (SD) | 82.1 (24.3) | 93.6 (13.6) | 71.3 (32.7) | 65.6 (37.3) |

| | Axium | | Control | |
|--------|---------------------------|------------------------------|---------------------------|------------------------------|
| | Subjects with Paresthesia | Subjects without Paresthesia | Subjects with Paresthesia | Subjects without Paresthesia |
| Median | 94.2 | 100.0 | 81.9 | 70.1 |

Tertiary Endpoints

The following tertiary endpoints were evaluated:

- SF-36 Quality of Life Questionnaire at 3, 6, and 12-months

The SF-36 is a self-reported health-related quality of life scale with 36 questions that yield scores on eight dimensions of quality of life including: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. These eight dimensions also are combined to provide two summary scales for physical health (PCS) and mental health (MCS). Improvements on the SF-36 scale are represented by higher scores. **Table 26** presents the mean change from baseline in SF-36 scores to the 3-, 6-, and 12-month follow-up visits with 95% confidence intervals.

Table 26: Change in SF-36 Scores from Baseline through 12 Months

| | Axium | | | Control | | |
|--|---|----------------------|----------------------|---|----------------------|----------------------|
| | Improvement from Baseline Mean (95% CI) | | | Improvement from Baseline Mean (95% CI) | | |
| | 3 Months | 6 Months | 12 Months | 3 Months | 6 Months | 12 Months |
| SF-36 Quality of Life Questionnaire | | | | | | |
| Physical Component Summary (PCS) | 11.8 (9.8, 13.8) | 11.1 (9.1, 13.1) | 11.5 (9.0, 14.1) | 9.4 (6.8, 12.0) | 8.6 (6.3, 11.0) | 8.0 (5.4, 10.6) |
| Mental Component Summary (MCS) | 8.3 (5.4, 11.2) | 6.6 (3.2, 10.0) | 6.2 (2.9, 9.5) | 4.8 (2.0, 7.6) | 4.1 (1.3, 6.9) | 3.6 (0.4, 6.7) |
| Physical Functioning (PF) | 27.1 (21.3, 32.9) | 26.2 (20.1, 32.2) | 26.6 (19.5, 33.8) | 19.5 (12.6, 26.3) | 19.0 (12.1, 25.9) | 17.7 (10.6, 24.7) |
| Role-Physical (RP) | 38.9 (31.9, 46.0) | 33.9 (26.4, 41.4) | 30.4 (22.1, 38.7) | 28.6 (19.8, 37.3) | 28.1 (19.5, 36.7) | 24.6 (15.2, 34.0) |
| Bodily Pain (BP) | 32.7 (26.9, 38.5) | 27.4 (21.6, 33.2) | 27.4 (20.4, 34.3) | 29.0 (22.0, 36.0) | 19.0 (12.1, 25.9) | 23.1 (15.1, 31.1) |
| General Health (GH) | 10.9 (6.2, 15.6) | 11.7 (6.3, 17.1) | 13.0 (7.1, 18.8) | 6.3 (2.2, 10.4) | 2.3 (-2.5, 7.1) | 2.9 (-2.3, 8.1) |
| Vitality (VT) | 21.3 (15.5, 27.2) | 17.5 (12.1, 22.9) | 17.8 (11.1, 24.5) | 14.5 (9.4, 19.6) | 12.0 (6.7, 17.3) | 10.0 (4.0, 16.0) |
| Social Functioning (SF) | 28.9 (20.8, 37.0) | 24.5 (16.5, 32.5) | 23.0 (14.7, 31.3) | 19.8 (12.3, 27.2) | 18.3 (10.6, 26.0) | 13.1 (4.7, 21.5) |
| Role-Emotional (RE) | 17.0 (9.1, 24.9) | 14.7 (5.3, 24.0) | 14.9 (5.6, 24.3) | 15.2 (7.2, 23.2) | 12.6 (4.8, 20.4) | 11.0 (2.0, 20.0) |
| Mental Health (MH) | 15.5 (10.7, 20.3) | 11.9 (6.3, 17.5) | 13.7 (8.2, 19.2) | 8.1 (3.4, 12.8) | 6.7 (1.8, 11.6) | 8.6 (2.9, 14.3) |

- Profile of Mood States (POMS) at 3, 6, and 12-months

The Axium group experienced greater improvement than the Control group in Total Mood Disturbance at three months (19.9 vs.13.1 respectively, 95% CI - 0.2, 13.7) and 12 months post INS implant (18.1 vs. 8.1, 95% CI 2.4, 17.4). **Table 27** shows the improvement in POMS for Axium and Control groups through 12-months. **Table 27** presents the mean improvement and 95% confidence intervals in POMS scores from baseline to three months, six months, and 12 months, for each study group. Note that improvement on the Vigor scale is represented by a decrease in scores, while all other scales represent improvement by an increase in scores.

Table 27: Change from Baseline in POMS Brief Score through 12 Months

| | Axium | | | Control | | |
|--------------------------------------|---|----------------------|----------------------|---|----------------------|----------------------|
| | Improvement from Baseline Mean (95% CI) | | | Improvement from Baseline Mean (95% CI) | | |
| | 3 Months | 6 Months | 12 Months | 3 Months | 6 Months | 12 Months |
| Profile of Mood States (POMS) | | | | | | |
| Total Mood Disturbance | 19.9 (14.3, 25.5) | 18.1 (12.3, 23.9) | 18.1 (12.8, 23.4) | 13.1 (8.9, 23.9) | 11.8 (7.2, 16.4) | 8.1 (2.7, 13.5) |
| Tension | 3.5 (2.5, 4.4) | 3.1 (1.9, 4.3) | 3.2 (2.2, 4.3) | 3.1 (0.9, 2.9) | 1.4 (0.2, 2.6) | 1.5 (0.5, 2.5) |
| Depression | 3.7 (2.4, 5.0) | 3.4 (2.1, 4.7) | 3.5 (2.2, 4.8) | 2.0 (0.8, 3.2) | 1.6 (0.6, 2.6) | 0.8 (-0.5, 2.1) |
| Anger | 3.3 (2.0, 4.6) | 3.3 (2.1, 4.5) | 2.3 (0.9, 3.7) | 2.0 (0.9, 3.1) | 1.8 (0.8, 2.8) | 1.2 (0.2, 2.2) |
| Vigor | -3.7 (-2.3, -5.1) | -2.7 (-4.2, -1.2) | -3.1 (-1.9, -4.4) | -2.6 (-3.7, -1.5) | -3.3 (-4.7, -1.9) | -2.1 (-3.5, -0.6) |
| Fatigue | 4.9 (3.3, 6.5) | 4.5 (2.9, 6.1) | 4.7 (3.1, 6.3) | 3.5 (2.4, 4.6) | 3.3 (2.1, 4.5) | 2.7 (1.2, 4.2) |
| Confusion | 0.8 (0.0, 1.6) | 1.0 (0.2, 1.8) | 1.3 (0.5, 2.1) | 1.1 (0.3, 1.9) | 0.5 (-0.4, 1.4) | -0.2 (-1.1, 0.7) |

- Brief Pain Inventory (BPI) at 3, 6, and 12-month

Table 28 depicts the change from baseline in the BPI through 12-months.

Table 28: Change from Baseline in Brief Pain Inventory through 12 Months

| | Axium | | | Control | | |
|-----------------------------------|---|-------------------|-------------------|---|-------------------|-------------------|
| | Improvement from Baseline Mean (95% CI) | | | Improvement from Baseline Mean (95% CI) | | |
| | 3 Months | 6 Months | 12 Months | 3 Months | 6 Months | 12 Months |
| Brief Pain Inventory (BPI) | | | | | | |
| Severity | 4.2 (3.6, 4.9) | 3.8 (3.2, 4.4) | 3.8 (3.0, 4.5) | 3.8 (3.2, 4.4) | 3.6 (3.0, 4.2) | 3.3 (2.5, 4.1) |
| Interference | 4.2 (3.5, 4.9) | 3.8 (3.1, 4.5) | 3.9 (3.1, 4.6) | 3.8 (3.1, 4.5) | 3.1 (2.4, 3.8) | 2.6 (1.9, 3.3) |
| Activity | 4.5 | 4.1 | 4.1 | 3.4 | 2.8 | 2.9 |

| | Axium | | | Control | | |
|------------------|---|-------------------|-------------------|---|-------------------|-------------------|
| | Improvement from Baseline Mean (95% CI) | | | Improvement from Baseline Mean (95% CI) | | |
| | 3 Months | 6 Months | 12 Months | 3 Months | 6 Months | 12 Months |
| | (3.8, 5.1) | (3.4, 4.8) | (3.4, 4.9) | (2.6, 4.2) | (2.6, 4.2) | (2.1, 3.7) |
| Affective | 3.8 (3.0, 4.6) | 3.5 (2.7, 4.3) | 3.5 (2.7, 4.3) | 2.5 (1.8, 3.2) | 2.6 (1.8, 3.4) | 2.2 (1.4, 3.0) |

- Subject Satisfaction at 3, 6, and 12-months
At 3, 6, and 12-months post INS implant, subjects rated their satisfaction with the degree of pain relief they received, the therapy in general, and the likelihood that they would undergo therapy again. Subjects in both groups reported a high degree of satisfaction. See **Table 29** below for results.

Table 29: Subject Satisfaction through 12 Months

| | Axium | | | Control | | |
|---|----------|----------|-----------|----------|----------|-----------|
| | 3 Months | 6 Months | 12 Months | 3 Months | 6 Months | 12 Months |
| Subject Satisfaction | | | | | | |
| How likely you would undergo the therapy again¹ | 9.0 | 8.7 | 8.9 | 9.1 | 8.7 | 8.5 |
| Change in your pain as compared to before the device was implanted² | | | | | | |
| Much Worse | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.1 |
| Worse | 0.0 | 1.7 | 1.8 | 1.9 | 0.0 | 0.0 |
| A Little Worse | 1.7 | 0.0 | 0.0 | 1.9 | 1.9 | 0.0 |
| No change | 0.0 | 5.1 | 3.6 | 3.7 | 5.8 | 4.2 |
| A Little Better | 6.8 | 6.8 | 3.6 | 11.1 | 9.6 | 12.5 |
| Better | 27.1 | 20.3 | 25.5 | 14.8 | 19.2 | 20.8 |
| Much Better | 64.4 | 66.1 | 65.5 | 66.7 | 63.5 | 60.4 |

¹ Scale 0-10 [0=Not Likely, 10=Very Likely]; the mean ratings are displayed.

² The percent of subjects that selected each response option is displayed

- Stimulation Specificity at 3 and 12-months
In the ACCURATE study, the stimulation specificity endpoint was evaluated at three months per the SAP and post-hoc at 12 months by determining whether a subject felt paresthesia in anatomical regions that were reported as having no pain at baseline. Subjects in the Control group were 2.3 times more likely to report feeling paresthesia in one or more non-painful areas when compared to subjects in the Axium group (35.2% vs.15.3%) at three months. At 12 months post INS implant, subjects in the Control group were 7.1 times more likely to report feeling paresthesia in one or more non-painful areas as subjects in the Axium group (38.8% vs. 5.5%). Therefore, this endpoint shows that paresthesias in the Control group were more likely to be experienced in non-painful regions, as compared to the Axium group.

Results Over Time

This section provides the results of additional endpoints (assessments performed through one year). Since a multiplicity adjustment procedure was not pre-specified for these endpoints, the results are presented with 95% CIs instead of p-values.

- Primary Composite Endpoint – 12 Months (MITT)

Results for 12 months show that the Axium group continued to show a greater treatment success (74.2%) when compared to the Control group (53.%). See **Table 30** below.

Table 30: Primary Composite Endpoint Treatment Success through 12 Months – MITT

| Primary Endpoint Component | Axium | Control |
|--|-------------------|--------------|
| Overall Treatment Success at 12-Months | | |
| n/N (%) | 49/66 (74.2) | 35/66 (53.0) |
| 95% CI | (62.0, 84.2) | (40.3, 65.4) |
| Success rate difference (%) and 95% CI (Blackwelder) | 21.2 (7.8, 100.0) | |

- *Pain Relief for Subjects “With” and “Without” Paresthesia Through 12-Months*

A post-hoc analysis was performed to characterize pain relief for subjects with and without paresthesia through 12-months. At twelve months, 19 subjects in the Axium group and six subjects in the Control group reported a complete absence of paresthesia. Of the 19 subjects in the Axium group, 17 were treatment successes and three of the six subjects in the Control group were treatment successes (See **Table 31**).

At the time of the trial and implant procedures, all subjects were asked to confirm that they were feeling stimulation (i.e. sensation of paresthesia) in the targeted area of pain in order to confirm placement of the implanted leads. Post-procedure, stimulation settings were then programmed based upon physician judgement to optimize the appropriate therapy for each study subject. In addition, all study subjects were able to adjust the intensity level of the therapy, within a physician-prescribed range, with their patient programmers.

Note that the clinical relevance of this result is unknown. The study was a non-inferiority trial, designed to assess device effectiveness in the presence of paresthesia. The instructions for use for the Control device requires the Control device be programmed for subjects to receive paresthesia. In addition, the number of subjects that did not have paresthesia is very small and this endpoint was not adequately powered to detect the difference in pain relief for subjects who reported feeling versus not feeling paresthesia. A placebo controlled trial would be necessary to rule out the possibility that the effect is greater than placebo. However, the results show that pain relief can be experienced without feeling paresthesia, at least in some subjects.

Table 31: Pain Relief for Subjects with and without Paresthesia – 12 Months

| | Axium | | Control | |
|--|---------------------------|------------------------------|---------------------------|------------------------------|
| | Subjects with Paresthesia | Subjects without Paresthesia | Subjects with Paresthesia | Subjects without Paresthesia |
| Number of Subjects | 35 | 19 | 43 | 6 |
| Percent Pain Relief at 3 Months | | | | |
| N | 35 | 19 | 43 | 6 |
| Mean (SD) | 81.4 (22.8) | 86.0 (25.3) | 70.2 (34.9) | 48.1 (50.8) |
| Median | 89.1 | 100.0 | 83 | 51.2 |

Responder Rates Over Time – INS Subjects Only

Responders are defined as subjects who achieve 50% or greater pain relief compared to baseline (as measured by the change in VAS scores). By definition, these analyses include only subjects who received an INS implant. **Table 32** presents the $\geq 50\%$ improvement responder rates over time. As this table demonstrates, the Axium group had a numerically higher percent of subjects that had $\geq 50\%$ improvement in VAS scores at every time point. At three months post INS implant, 94.9% of subjects in the Axium group had $\geq 50\%$ improvement in VAS scores, and 72.2% of subjects in the Control group improved by $\geq 50\%$. At 12 months post INS implant, 89.1% of subjects in the Axium group had $\geq 50\%$ improvement in VAS scores, and 70% of subjects in the Control group improved by $\geq 50\%$. Figure 8 presents the distribution of responder rates at three months post INS implant.

Table 32: Responder Rates over Time (INS Only Subjects)

| | BL | | 1 Month | | 3 Month | | 6 Month | | 9 Month | | 12 Month | |
|--|-----------|-----------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| | AX | C | AX | C | AX | C | AX | C | AX | C | AX | C |
| Number of Subjects | 76 | 76 | 61 | 54 | 59 | 54 | 59 | 52 | 55 | 49 | 55 | 50 |
| Responder rate $\geq 50\%$ Improvement | | | 50/61 (82.0) | 41/54 (75.9) | 56/59 (94.9) | 39/54 (72.2) | 51/59 (86.4) | 41/52 (78.8) | 46/55 (83.6) | 34/49 (69.4) | 49/55 (89.1) | 35/50 (70.0) |

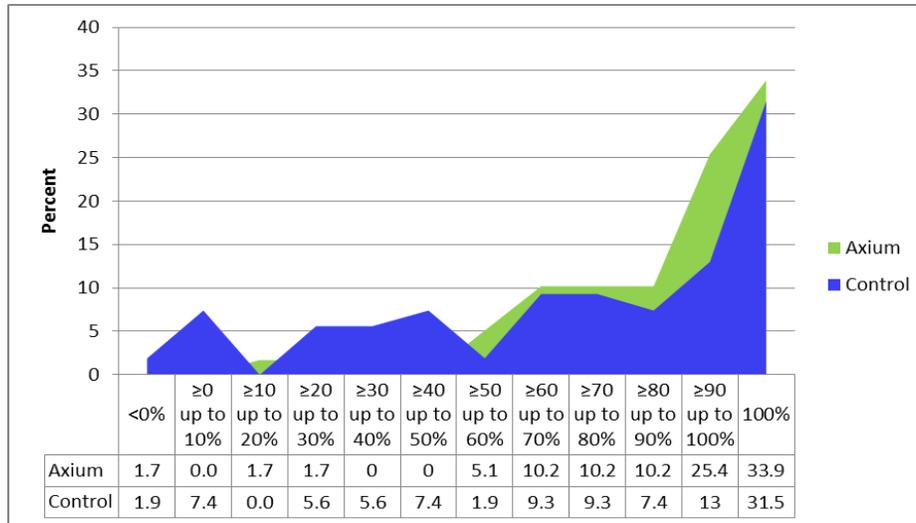


Figure 8. Distribution of Percent Improvement in VAS Scores

3. Subgroup Analyses

As prespecified in the SAP, the primary composite endpoint was analyzed by age, gender and primary diagnosis (MITT). Results are summarized below.

- Age
The primary non-inferiority endpoint was met both in subjects ≤ 53 years and > 53 years. The median age was selected as the cut point for the age analysis. The primary composite endpoint conclusion of superiority was met for subjects ≤ 53 years. There was a trend for superiority for subjects > 53 years of age.
- Gender
The primary non-inferiority endpoints were met both in male and female subjects. The primary superiority endpoint also was met for female subjects.
- Diagnosis
The primary non-inferiority endpoints were met both for subjects diagnosed with CRPS and subjects diagnosed with Peripheral Causalgia. The primary superiority endpoint also was met for subjects diagnosed with CRPS and subjects diagnosed with Peripheral Causalgia.

II. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Effectiveness for the Axium Neurostimulator System was based on a non-inferiority pivotal study. A total of 152 subjects were enrolled and randomized

1:1 with 76 subjects in the Axium group and 76 subjects in the Control group (a commercially available SCS system). Baseline assessments demonstrated a well-matched population with no statistical differences on demographic, lower extremity pain history and primary diagnosis. Of the 152 subjects randomized, 113 subjects (all subjects expected) completed the three month primary composite endpoint. A total of 105 subjects (105/108 = 97.2%) of expected subjects completed the post-INS 12-month follow-up visit.

The primary objective of the study was to demonstrate safety and effectiveness with a composite endpoint at 3 months with two components defined as 1) a $\geq 50\%$ pain relief (as measured by VAS scores), and 2) the absence of any stimulation-induced neurological deficit. If a subject met this endpoint they were considered to be a treatment success for the ascertainment of the primary endpoint. The Axium group had a greater number of subjects achieving success (81.2%) as compared to the Control (55.7%). Using a predefined MITT analysis, the Axium group achieved statistical non-inferiority ($p < 0.0001$) and superiority ($p = 0.0004$) in treatment success compared to the Control. Similar results were found in the ITT and PP analyses and at the 12-month follow-up. Secondary and tertiary endpoints were considered hypothesis generating and were not considered in the evaluation of effectiveness.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as data collected in a clinical study conducted to support PMA approval as described above. The Axium group demonstrated a comparable safety profile to the Control in the following:

- In the pre-specified safety component of the primary composite endpoint there were no subjects in the Axium or the Control group who experienced stimulation induced neurological deficit.
- The overall difference in the rate of SAEs between the groups was similar and not clinically or statistically different (Axium 10.5%, Control 14.5%, $p = 0.6248$); the rate during the TNS phase (Axium 1.3%, Control 3.9%, $p = 0.62$), and INS phase (Axium 9.2%, Control 10.5%, $p = 1.0$).
- There were no unanticipated safety events and no deaths in the trial.

Additionally, there were 241 adverse events in 62 subjects (81.6%) in the Axium group, and 161 adverse events in 55 subjects (72.4%) in the Control group ($p = 0.2575$).

There were differences between the Axium and Control groups in the number of subjects with procedure related events in the Axium group (35/76, 46.1%) was statistically significantly greater ($p = 0.0177$) than that in the Control group (20/76,

26.3%) and appears to be associated with the number of leads implanted per subject. The results show an increasing linear relationship between the number of Axium leads implanted and the number of subjects with procedure-related events, ranging from zero events in two subjects with one lead implanted, to eight events in eight subjects with six leads implanted. This may be expected since individual needle sticks are required to implant each Axium lead during a procedure (up to four leads), in contrast to the fewer needle sticks typically used to implant one or two leads during a Control procedure. There is no apparent increasing linear relationship between the number of leads implanted and the number of Control subjects with procedure-related events.

C. **Benefit-Risk Conclusions**

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The study met its primary endpoint which was to demonstrate non-inferiority/superiority as compared to a legally marketed Control spinal cord stimulation system using a composite endpoint with two components defined as 1) a $\geq 50\%$ pain relief (as measured by VAS scores) and 2) no stimulation-induced neurological deficit. Results were consistent at 12-months.

Additional factors to be considered in determining probable risks and benefits for the Axium Neurostimulation System included the following:

- Durability of the benefit, majority of test subjects having persistent reduction in pain at 12 months compared to control subjects (74.2% vs. 53%, $p < 0.0001$).
- Comparable total, device-related, stimulation-related, and serious adverse event rates between the test and the control groups.
- Higher incidence of procedure-related adverse events with mitigation in the form of a mandatory Axium Implantable Neurostimulator System training program prior to actual patient implantation.
- Lack of a commercially-available DRG stimulator in the U.S. market.
- Challenging disease process in the form of lower extremity pain in CRPS I and II with few medical, interventional pain, and surgical therapies that have demonstrated limited efficacy.

The following limitations were considered when determining probable risks and benefits for the Axium Neurostimulator System:

- The non-inferiority design of the clinical study did not blind subjects as to which device they had implanted. This may have resulted in investigator and patient bias and 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 response may be long lasting.

- The primary endpoint was pain in the area of greatest pain. This endpoint was chosen due to the dermatomal coverage of the targeted DRG. The Axium device is limited to lower limb pain while the Control device is indicated for the trunk and/or limbs. Additionally, pain during activity, worst pain, and specific attributes of neuropathic pain (i.e., dermatome, response to temperature, palpation, quality, etc.) were not assessed.
- The primary endpoint was based on an in-clinic evaluation rather than a patient pain diary and thus, day-to-day variation in pain was not assessed.
- The purpose of the study was to study device effect on pain and all secondary and tertiary endpoints not specifically related to pain should be interpreted as hypothesis generating only.
- The Control group subjects received either the RestoreSensor or RestoreUltra SCS devices manufactured by Medtronic, Inc. and for purposes of ensuring comparable features to assess this endpoint, the RestoreSensor Control device had accelerometer feature that can adjust stimulation based on the patient's needs and preferences in different body positions (including stimulation to maintain paresthesia) deactivated. The RestoreUltra device does not have the feature.
- Pain medications were kept stable through the three month assessment. However, changes in pain medication may have affected pain assessments following 3 months.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results from the clinical study support a reasonable assurance of the safety and efficacy of the Axium Neurostimulator System, as well its long-term performance, when used in a manner consistent with its labeling and intended use. The evidence supporting the safety and effectiveness of the Axium Neurostimulator System is on a non-inferiority pivotal study. The results from comprehensive pre-clinical testing show that the Axium Neurostimulator System performs as intended. The analyses also support a clinical benefit to risk determination that is favorable.



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ST. JUDE MEDICAL™

2016-02
LP0872 Rev B

Axium™ Neurostimulator System

PHYSICIAN IMPLANT MANUAL

Proposition 65, a State of California voter initiative, requires the following notice:

WARNING: This product and its packaging have been sterilized with ethylene oxide. This packaging may expose you to ethylene oxide, a chemical known to the state of California to cause cancer or birth defects or other reproductive harm.

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**Caution: Federal law restricts this device to sale by or
on the order of a licensed healthcare practitioner.**

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Explanation of Symbols on Product or Package Labeling

| | | | |
|---|--|---|--|
|  | Model Number |  | Manufacturer |
|  | Lot Number |  | Manufacturing Date |
|  | Consult Instructions for Use |  | Warning |
|  | Read the Manual |  | Contents of Package are Non-Sterile |
|  | Do Not Resterilize |  | Keep Dry |
|  | Single Use Only |  | Storage Temperature |
|  | Sterilized by Ethylene Oxide Gas |  | Store between 10% and 90% humidity - Sterile Components |
|  | Use by YYYY-MM-DD |  | Store between 0% and 93% humidity -TNS and Programmers |
|  | Open Sterile Pouch by Peeling Pouch Corner |  | The device is a radio transmitter |
|  | Open Sterile Tray by Peeling Tray Corner |  | Magnet - Shows the location of the Programmer Magnet |
|  | Do not use if package is damaged |  | Not waterproof - Applies to the Programmer when it is not in its carrying case |
|  | Turns the Programmer ON and OFF. Turns the stimulation OFF on the TNS. |  | Limited waterproof - Applies to the TNS. Applies to the Programmer in its carrying case |
|  | Caution |  | Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner. |
|  | Serial Number |  | Quantity |

| | | | |
|---|-----------|--|---------------------------------|
|  | MR Unsafe |  | Electrical Safety Certification |
|---|-----------|--|---------------------------------|

Introduction

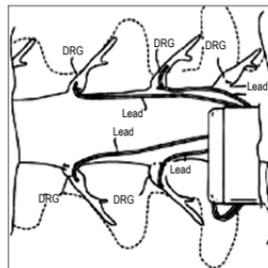
This manual describes the Axiom Neurostimulator System, including instructions for implantation. For detailed operation and clinical programming instructions, refer to the Clinical Programmer Manual.

System Overview

The Axiom Neurostimulator System consists of an Implantable Neurostimulator (INS) device, Trial Neurostimulator (TNS) device, a Clinical Programmer, a Patient Programmer, one or more leads which may be used in combination with a lead extension and the accessories and tools used for implanting the system.

The TNS or INS is connected to leads placed within the epidural space near the dorsal root ganglion (DRG). Up to four leads may be placed and connected to the neurostimulator to provide stimulation.

Patients who are indicated for the Axiom Implantable Neurostimulator (INS) System will first undergo a temporary trial period using an external Trial Neurostimulator (TNS) connected to implanted leads. If both the clinician and patient believe that sufficient pain relief was achieved, then the patient will be scheduled for an implant, in which the INS will be implanted.



NOTE: In this manual, the general abbreviation “NS” is used for information which applies to both TNS and INS. In all other cases, the specific abbreviations “TNS” or “INS” are used.

System Description

The Axiom Neurostimulator System consists of the following components:

| Component Model Number | Package Contents | Associated Instructions for Use |
|-------------------------------|-----------------------|---------------------------------|
| Trial Neurostimulator MN10100 | Trial Neurostimulator | Trial Neurostimulator Manual |

| Component Model Number | Package Contents | Associated Instructions for Use |
|---|---|---------------------------------|
| Implantable Neurostimulator MN10200 | Implantable Neurostimulator Lead Port Plugs (3) Torque Wrench Medical Alert Card | Physician Implant Manual |
| Trial Lead Kit (length in cm specified by -XX) MN10350-XX MN10350-XXA | Trial Lead / Trial Lead, SlimTip 22 cm Small Curve Delivery Sheath 22 cm Big Curve Delivery Sheath Guidewire Complex Curve Stylet 4.5” 14G Delivery Needle Soft Tissue Anchor (2) Straight Stylet (SlimTip lead kits only) | Physician Implant Manual |
| Implant Lead Kit (length in cm specified by -XX) MN10450-XX MN10450-XXA | Implant Lead / Implant Lead, SlimTip 22 cm Small Curve Delivery Sheath 22 cm Big Curve Delivery Sheath Guidewire Complex Curve Stylet 4.5” 14G Delivery Needle Soft Tissue Anchor (2) Straight Stylet (SlimTip lead kits only) | Physician Implant Manual |
| Connector Cable Kit MN11350 | Connector Cable | Physician Implant Manual |
| Tunneling Tool Kit 30 cm / 51 cm MN11900 MN12200 | Tunneling Tool 30 cm / 51 cm Straw Trocar Tip Pencil Tip INS Sizer Port Plugs (3) Torque Wrench Hex Key Sterile Magnet Sleeve | Physician Implant Manual |

| Component Model Number | Package Contents | Associated Instructions for Use |
|---|--|---------------------------------|
| Clinical Programmer MN10700 | Clinical Programmer External Magnet Programmer Charger Carrying Case | Clinical Programmer Manual |
| Patient Programmer MN10600-02 | Patient Programmer External Magnet Programmer Charger Carrying Case Medical Alert Card | Patient Programmer Manual |
| Lead Accessories Kit MN12050 | 4.5" 14G Delivery Needle 6.0" 14G Delivery Needle Soft Tissue Anchor Complex Curve Stylet 30 cm Big Curve Delivery Sheath 30 cm Small Curve Delivery Sheath | Physician Implant Manual |
| 22 cm Small Curve Delivery Sheath Kit MN12150 | 22 cm Small Curve Delivery Sheaths (2) | Physician Implant Manual |
| 22 cm Big Curve Delivery Sheath Kit MN13650 | 22 cm Big Curve Delivery Sheaths (2) | Physician Implant Manual |
| 22 cm Axium Small Curve Delivery Sheath MN13850 | 22 cm Axium Small Curve Delivery Sheath (1) | Physician Implant Manual |
| 22 cm Axium Big Curve Delivery Sheath MN13950 | 22 cm Axium Big Curve Delivery Sheath (1) | Physician Implant Manual |
| Lead Extension Kit (length in cm specified by -XX) MN10550-XX | Lead Extension 50 cm Torque Wrench | Physician Implant Manual |

| Component Model Number | Package Contents | Associated Instructions for Use |
|--|-----------------------------------|---------------------------------|
| Auxiliary Magnet Kit MN23300 | Auxiliary Magnet | Ancillary Manual |
| Clinical Programmer Charger Kit MN23400 | Clinical Programmer Charger | Ancillary Manual |
| Patient Programmer Charger Kit MN23400-U | Patient Programmer Charger | Ancillary Manual |
| Clinical Programmer Carrying Case MN13500 | Clinical Programmer Carrying Case | Ancillary Manual |
| Patient Programmer Carrying Case MN13500-S | Patient Programmer Carrying Case | Ancillary Manual |
| Curved Needle MN14000 | 4.5" 14G Curved Delivery Needle | Physician Implant Manual |

Trial Neurostimulator (TNS)

The external TNS device connects to the Trial Lead(s) or Lead Extensions and is worn by the patient for up to 30 days during the trial period. The TNS device has a belt clip for the patient's convenience.



Implantable Neurostimulator (INS)

The Axium Implantable Neurostimulator (INS) is a non-rechargeable, 4-channel electronic device. It uses microelectronic circuitry, powered by a hermetically sealed battery, to generate a pulsed waveform to stimulate neural tissue. The electronic circuitry and battery are housed in a hermetically sealed titanium case.

Each neurostimulator has a unique internal identifier that allows the physician to identify the type of device through an X-ray. The radiopaque identifier inside the case allows identification of both the device manufacturer and model number using standard x-ray equipment. For the Axium Neurostimulator, the code is SM001, which identifies Spinal Modulation as the manufacturer. The INS is packaged in a sealed inner tray within a sealed outer tray.



Implant Leads / Trial Leads / Lead Extension

The Lead Kits contain the Leads and the individual delivery devices that are required for their placement.

- **Implant / Trial Leads:** The Leads are designed for percutaneous introduction into the body using a special needle and a set of custom delivery tools provided in their respective kits. The Trial and Implant leads are designed with identical technical and performance characteristics in order to help ensure that the therapy experienced during the Trial phase is as close as possible to that experienced during the Implant phase. Each Lead is fitted with four cylindrical electrodes spaced at equal intervals, which are intended to provide stimulation at the target dorsal root ganglion (DRG).
- **Lead Extension:** The Lead Extension consists of a silicone port header that accepts the Axiom Trial Lead and Implant Lead. It is intended to extend the length of the lead and provide a connection between the lead and the Connector Cable or the lead and the Implantable Neurostimulator. The Lead Extension is intended for chronic implantation as a component of the Axiom Neurostimulator System.

Connector Cable Kit

The Connector Cable connects the Leads or Lead Extension to the external TNS.

- **Connector Cable:** The Connector Cable is packaged separately from the Lead and Lead Extension Kit. The Connector Cable includes a connector and two extension cables for use as needed.

Lead Accessories

- **Small / Big Curve Delivery Sheath:** The Delivery Sheaths are intended to allow passage of the lead percutaneously into the epidural space. The labeled length of the sheath is the distance from the hub to the pre-shaped tip and the length of the curve at the tip is approximately 2 mm for the Small Curve and approximately 8 mm for the Big Curve.
- **Axiom Small / Big Curve Delivery Sheath:** Axiom Delivery Sheaths are also intended to allow passage of leads percutaneously into the epidural space. Axiom sheaths are internally reinforced with thin stainless steel braiding.
- **Complex Curve / Straight Stylet:** The Complex Curve and Straight stylets assist in steering and positioning the lead within the epidural space.
- **14G Delivery Needles:** The Delivery Needle is intended to access the epidural space, providing a conduit for lead, guidewire and delivery sheath placement. It is available as a straight needle or a curved needle. The Axiom Curved Needle is available in a separate package and is uniquely identified by the colored hub. The 14 Ga Delivery Needle is only available in the Implant Lead, Trial Lead, and Lead Accessories Kits.

- **Guidewire:** The Guidewire is intended to verify that the needle is in the epidural space after using a loss of resistance technique. It also provides stability to the sheath before front-loading the SlimTip lead.
- **Soft Tissue Anchor:** The Soft Tissue Anchors are intended to anchor the Lead in the soft tissue or on the skin surface proximal to the distal contacts of the Lead.

Implantation Tools

- **Tunneling Tool:** The tunneling tool is used to provide a conduit for the Trial Lead, Implant Lead, or Lead Extension to the INS or away from the midline of the spine. It is packaged with 2 exchangeable tips: a blunt pencil tip and a sharp trocar tip. A straw is slid over the tunneling tool and when the steel handle is removed, the straw provides the conduit for tunneling.
- **INS Sizer:** The INS Sizer is approximately the same size as the INS and allows the physician to properly size the INS pocket.
- **Port Plugs:** The port plugs are used to fill unused ports in the INS. They are packaged with the INS, but spare port plugs are also packaged with the Tunneling Tool Kits for the convenience of the physician.

Additional Accessories

- **Sterile Magnet Sleeve:** The magnet is placed in the sterile sleeve to allow it to be used during the implantation of the INS.
- **Medical Alert Card:** Identifies the patient as a user of the Neurostimulator System.
- **Programmer Charger:** To be used with the Clinical or Patient Programmers to charge the battery or allow use of the Programmers while plugged into standard electrical outlets.
- **Programmer Carrying Case:** Protects the Programmers from water.
- **Auxiliary Magnet:** Allows the user to turn the NS off or activates RF to allow the user to communicate with the NS.
- **Hex Key:** Allows the user to release a set screw in the INS header or Lead Extension header that has been unscrewed too far. The Hex Key is not to be used to tighten the set screw against the lead.

Clinical Programmer and Patient Programmer

The Clinical Programmer is used to program the stimulation parameters for both the TNS and the INS. The instructions for programming the TNS and INS devices are the same. The Clinical Programmer is used by the physician or clinical staff. The Patient Programmer allows the patient to adjust the stimulation settings of the TNS and INS devices within limits preset by the clinician. The Patient Programmer also allows the patient to turn stimulation off, if necessary.

NOTE: For detailed information and instructions related to the Clinical and Patient Programmers and the Trial Neurostimulator, refer to the respective user manuals.

Indications for Use

The Axiom Neurostimulator System is indicated for spinal column stimulation via epidural and intra-spinal lead access to the dorsal root ganglion as an aid in the management of moderate to severe chronic intractable* pain of the lower limbs in adult patients with Complex Regional Pain Syndrome (CRPS) types I and II.**

*Study subjects from the ACCURATE clinical study had failed to achieve adequate pain relief from at least 2 prior pharmacologic treatments from at least 2 different drug classes and continued their pharmacologic therapy during the clinical study.

**Please note that in 1994, a consensus group of pain medicine experts gathered by the International Association for the Study of Pain (IASP) reviewed diagnostic criteria and agreed to rename reflex sympathetic dystrophy (RSD) and causalgia, as complex regional pain syndrome (CRPS) types I and II, respectively.

Contraindications

Patients contraindicated for the Axiom Neurostimulator System are those who:

- Are unable to operate the system
- Are poor surgical risks

Patients who failed to receive effective pain relief during trial stimulation are contraindicated to proceed to the INS procedure.

Safety Information

General Warnings

The following warnings apply to the use of the Axiom Neurostimulator System:

- **Other Active Implantable Devices** - The Axiom system may interfere with other implanted stimulators, such as cardiac pacemakers and defibrillators which have sensing features, and may result in sensing problems or inappropriate responses. The effect of other implanted devices, including deep brain stimulators, peripheral nerve stimulators, implanted drug delivery pumps, and cochlear implants on the Axiom system are unknown.
- **External Defibrillators** – Safety for use of external defibrillator discharges on a patient receiving neurostimulation has not been established. External defibrillation can cause induced currents in the lead-extension portion of the neurostimulation system. After defibrillation confirm the neurostimulation system is still working.
- **Magnetic Resonance Imaging** – The Axiom System is MRI unsafe. The patient should be advised to not undergo any elective magnetic resonance imaging (MRI) with the entire system, or (in the case of removal of the implanted generator) leads or lead fragments in place. Use of MRI in the vicinity of the lead(s) may result in forceful dislodgment of the lead(s), or damage to the neurostimulator. If a voltage is induced through the lead, it may cause uncomfortable (“jolting” or “shocking”) levels of stimulation or injury to the patient. MRI may cause heating at the lead tip and unintended stimulation could result in tissue damage.
- **Computed Tomography (CT)** – If the patient requires a CT scan, all stimulation should be turned OFF prior to the procedure. If stimulation is not turned off, the patient may experience a momentary increase in stimulation, which may be uncomfortable. Before beginning a CT scan, the operator should use CT scout views to determine if implanted or externally worn electronic medical devices are present and if so, their location relative to the programmed scan range.

For CT procedures in which the medical device is in or immediately adjacent to the programmed scan range, the operator should:

- Determine the device type;
- If practical, try to move external devices out of the scan range;
- Ask patients with neurostimulators to shut off the device temporarily while the scan is performed.
- Minimize x-ray exposure to the implanted or externally worn electronic medical device by:
 - Using the lowest possible x-ray tube current consistent with obtaining the required image quality; and
 - Making sure that the x-ray beam does not dwell over the device for more than a few seconds;

Important note: For CT procedures that require scanning over the medical device continuously for more than a few seconds, as with CT perfusion or interventional exams, attending staff should be ready to take emergency measures to treat adverse reactions if they occur.

After CT scanning directly over the implanted or externally worn electronic medical device:

- Have the patient turn the device back on if it had been turned off prior to scanning.
- Have the patient check the device for proper functioning, even if the device was turned off. Advise patients to contact their healthcare provider as soon as possible if they suspect their device is not functioning properly after a CT scan.
- Advise patients to contact their healthcare provider as soon as possible if they suspect their device is not functioning properly after a CT scan.
- **Ultrasonic Scanning** – Ultrasonic equipment may cause mechanical damage to the lead if used directly over the site.
- **Electrosurgery Devices** – Electrosurgery devices should not be used in close proximity to implanted lead(s). Contact between an active lead and the electrosurgical pencil can cause direct stimulation of the contacted nerve and can cause severe injury to the patient. Electrosurgery devices may also damage the lead and cause a loss of stimulation. Do not apply electrocautery directly to the INS as this can damage the INS or cause interference while communicating with the INS. The INS may be damaged, the output may be temporarily changed or suppressed, or stimulation may stop if exposed to electrosurgical devices.
- **Electrocautery** - If electrocautery is used, follow these steps:
 - Turn off the INS before the procedure.
 - Use the equipment as far away from the INS as possible.
 - Keep fields, such as current, radiation, or high-output ultrasonic beams, away from the INS.
 - Equipment should be set to the lowest energy setting possible.
 - After the therapy or procedure, check to see that the INS is functioning properly by gradually increasing stimulation to the desired level.
 - If the patient suspects that the device is not functioning properly after the use of these therapies or procedures, advise the patient to contact his or her healthcare provider.
- **Radiofrequency or microwave ablation** – Safety has not been established for radiofrequency (RF) or microwave ablation in patients who have an implanted neurostimulation system. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.
- **Pediatric Use** – The safety and effectiveness of the Axium Neurostimulator System has not been established for pediatric use.
- **Pregnancy** – The safety and effectiveness of this therapy has not been established for pregnancy, nursing, the unborn fetus, or delivery.
- **Implantation at Vertebral Levels above T10** – The safety and efficacy of implantation of leads implanted above the T10 vertebral level has not been evaluated.

- **Number of Leads Implanted** – The safety and efficacy of the implantation of greater than 4 leads has not been evaluated.
- **Back Pain** - The safety and efficacy for the treatment of patients who have back pain as the greatest region of pain has not been evaluated.
- **Non-Emergency Procedures** – The patient must be advised that they must not have non-emergency procedures while they are undergoing trial stimulation.
- **Emergency Procedures** – The patient should be instructed to designate a representative (family member or close friend) to notify any emergency medical personnel of their neurostimulator implant, if emergency care is required. Each patient will be provided with a Medical Alert Card to carry with them that will inform emergency medical personnel of the patient's implant. The patient should be advised to use caution when undergoing any procedure that could include RF or microwave ablation, defibrillation or cardio version.
- **Routine Medical Procedures** – The patient should be instructed to not to undergo dental procedures, diathermy, electrolysis, diagnostic ultrasound, static field therapeutic magnets, diagnostic X-ray, and high output ultrasonic lithotripsy. These procedures may provide interference that can affect TNS or INS device operation or use or damage components of the system that may cause patient harm. If the patient with an INS or TNS device is subsequently given any medical treatment in which an electrical current is passed through his/her body from an external source, either the device should first be deactivated, or care should be taken to monitor the functioning of the neurostimulator during the initial stages of treatment.
- **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 removal and replacement. Injury or damage can occur during diathermy treatment whether the neurostimulation system is turned on or off. All patients are advised to inform their health care professionals that they should not be exposed to diathermy treatment.
- **Explosive or Flammable Gases** – Do not use the patient programmer or clinical programmer to communicate with the INS or TNS in an environment where explosive or flammable gas fumes or vapors are present. The operation of the programmer could cause them to ignite, causing severe burns, injury, or death.
- **Case Damage** – If the INS case is pierced or ruptured, an explosion can occur from the battery chemicals, which can lead to severe burns or even death.
- **Device Components** – The use of non-Spinal Modulation components with the system may result in damage to the system and increased risk of harm to the patient.

- **Component Disposal** – Dispose of leads and neurostimulators per local requirements. Do not crush, puncture, or burn the Neurostimulator because explosion or fire may result.
- **Exposure to Fluids** – Exposure of the external TNS or the Connector Cable to water, body fluids, saline, or cleaning agents can cause corrosion and affect stimulation. If this occurs, dry all components thoroughly prior to lead connection. Do not immerse the external TNS or Connector Cable in fluids.
- **Manipulation of the Trial Lead/Extension and the INS** –
 - The patient must be instructed to not remove their Trial Lead(s) or Connector Cable. Manipulation of the components may result in an undesired outcome, such as the patient developing an infection, getting undesirable stimulation, or accidentally turning their stimulation off.
 - The patient must be instructed to not rub or exert pressure on the implantable neurostimulator through the skin as this may cause: lead dislodgement leading to stimulation at the implant site, device inversion leading to the inability to communicate with the device, or skin erosion that can lead to another surgical procedure or possible infection.
- The patient must be instructed to always wear the TNS on the outside of clothing to avoid skin irritation.
- **Physician Training** – Physicians must be experienced in the diagnosis and treatment of chronic pain syndromes and have completed the Axiom Implantable Neurostimulator training program.

Warnings - For Use in Home or Work Environments

- **Equipment Operation** – Advise all patients who feel uncomfortable paresthesia during postural changes that they should not operate potentially dangerous equipment, such as power tools, automobiles, or other motor vehicles. These patients should not climb ladders or participate in activities where postural change or abrupt movement could alter the perception of stimulation intensity and cause patients to fall or lose control of equipment or vehicles or injure others.
- **Patient Activity** – Patients should be advised to limit their activities to low or moderate levels during their trial stimulation period and the first six weeks of implantation of the INS. Failure to do so may result in migration of the leads causing loss of stimulation therapy, muscle stimulation or painful stimulation thereby requiring reoperation to reposition. The patient may be advised to turn off their device if stimulation becomes uncomfortable.
- **Theft Detectors and Metal Screening Devices** – Certain types of anti-theft devices, such as those used at entrances/exits of department stores, libraries, and other public establishments, and/or airport security screening devices may affect stimulation. It is possible that patients who are implanted with non-adjacent multiple leads and/or 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. It is recommended that patients use caution when approaching such a device and that they request assistance to bypass the device. If they must proceed through the device, patients should turn off the NS and proceed with

caution, being sure to move through the detector quickly.

- **Restricted Areas** – The patient should be warned to seek medical guidance before entering environments which could adversely affect the operation of the implanted device, including areas protected by a warning notice preventing entry by patients fitted with a pacemaker.
- **Patient Activities Related to Lead Movement** – The patient should be instructed to avoid excessive bending, twisting, and stretching, and operating the neurostimulator while lifting objects over 2 kg (5 lbs) for a minimum of 6 weeks after implantation. These activities may cause lead movement, which can result in understimulation or overstimulation. Excessive lead migration may require reoperation to replace the leads.
- **Scuba Diving and Hyperbaric Chambers** – The patient should be instructed to avoid scuba diving and entering hyperbaric chambers above 150 kPa. These activities may damage the Axiom System.
- **Therapeutic Radiation** – Therapeutic radiation may damage the electronic circuitry of an implanted neurostimulation system, although no testing has been performed and no definite information on radiation effects is available. Sources of therapeutic radiation include x-rays, cobalt machines, and linear accelerators. If radiation therapy is required, the area over the implanted INS should be shielded with lead.
- **Electromagnetic Interference (EMI)** – Electromagnetic interference is a field of energy generated by equipment found in the home, work, medical or public environments that is strong enough to interfere with neurostimulator function. Most electrical devices and magnets encountered in a normal day are unlikely to affect the operation of a neurostimulator. Patients should keep away from areas of EMI and turn off the stimulator if they are in such an area. Sources of strong electromagnetic interference can result in the following:
 - Operational changes to the neurostimulator, causing it to turn on or off (particularly in neurostimulators enabled for magnet use), or to reset to power-on- reset (POR) settings, resulting in loss of stimulation, return of symptoms, and in the case of POR, requiring reprogramming by a clinician.
 - Unexpected changes in stimulation, causing a momentary increase in stimulation or intermittent stimulation, which some patients have described as a jolting or shocking sensation. Although the unexpected change in stimulation may feel uncomfortable, it does not damage the device or injure the patient directly. In rare cases, as a result of the unexpected change in stimulation, patients have fallen down and been injured.

Sources of potentially strong EMI include the following:

- Microwave transmitters
- Communication equipment such as microwave transmitters, linear power amplifiers, and high voltage power lines and power generators
- Electric arc welding equipment
- Large, magnetized stereo speakers
- Radio frequency identification devices (RFID)
- Antenna of citizens band (CB) or ham radio

- Electric steel furnaces
- Dental drills and ultrasonic probes
- Electrolysis

Warnings for the Lead Implant Procedure

- The placement of the leads involves some risk, as with any surgical procedure. Conscious sedation can cause side effects such as systemic toxicity, or cardiovascular or pulmonary problems. Use caution when sedating the patient. The patient must be awake and conversant during portions of the procedure to minimize the likelihood of nerve damage.
- As with any spinal epidural procedure, potential risks of serious injury to the patient, although extremely rare, include epidural hemorrhage, hematoma, infection, spinal cord or nerve compression, and/or paralysis.
- Always be aware of the needle tip position. Use caution when positioning the needle to avoid unintended injury to surrounding anatomical structures.
- When using a contralateral approach, advance the needle slowly into the epidural space and take caution as it enters. The needle will be inserted at a steeper angle than in an antegrade approach and there is a greater chance of dural puncture that will lead to a cerebrospinal fluid leak.
- Use fluoroscopy and extreme care when inserting, advancing, or manipulating the guidewire or lead in the epidural space to minimize the risk of a dural tear.
- Dural puncture can occur if needle or guidewire is advanced aggressively once loss of resistance is achieved. Advance the needle and/or guidewire slowly.
- Insertion of a sheath without the lead may result in dural puncture. Securing the lead with the lead stabilizer will mitigate this risk.
- If the sheath needs to be retracted from the epidural space, verify that the steering wing is no more than 90 degrees rotated away from the mark on the needle. Failure to do so may result in damage to the sheath. Before reinserting the sheath, verify there is no damage to the sheath.
- Do not pull the standard Implant Lead through the sheath as this can cause separation of the ball-tip from the lead. With the SlimTip Implant Lead, it may be removed through the sheath as the ball-tip is small enough to allow passage back and forth through the sheath.
- If the sheath is not responding to rotation, do not rotate the steering wing out of plane from the curve of the sheath more than 90 degrees. The tip of the sheath may whip around and could cause harm to the patient.
- If the lead is unable to deploy out of the sheath, inject sterile water or saline slowly to release tissue that may have entered between the sheath and the lead. Do not use excessive pressure when injecting through the sheath.

- Do not use excessive force to push the lead or sheath into the neural foramen as this may result in permanent or transient nerve damage. The patient should be awake and conversant during this part of the procedure, so they can provide feedback to the physician.
- Failure to provide strain relief may result in lead migration requiring a revision procedure.
- If the sheath has been kinked during delivery, slowly retract through the needle with the curve facing the same direction as the bevel. Failure to do so can damage or cut the lead or sheath. If resistance is encountered, pull the needle out of the epidural space and then remove the sheath.
- Do not suture directly onto the lead, as there is a risk of damaging the lead. Failure to secure the lead to the skin, or other tissue, may result in lead migration and/or motor activation or painful stimulation.
- Failure to appropriately anchor may result in lead migration and/or motor activation or painful stimulation.
- Use extreme care when using sharp instruments or electrocautery around the lead to avoid damaging the lead.
- Use extreme care when removing the lead stylet, the delivery sheath, and the needle, to ensure that the distal tip of the lead remains in the desired location. Removing each item in slow movements, while holding the remaining components in place, will assist this process.

Warnings During Intraoperative Testing

- Maintain adequate slack in the cable. If there is not enough slack and the cable is pulled, the lead may be dislodged and will need to be replaced. This will extend the procedure.
- As described in the Clinical Programmer User Manual, always turn the external TNS amplitude to 0 μ A when repositioning a lead, changing the selected electrode combination, or attaching the Connector Cable to the external TNS. When restarting stimulation, increase the amplitude SLOWLY until the desired paresthesia is achieved. Failure to do so may result in uncomfortable motor activation or painful stimulation.
- Once the clinical programmer ENABLE function is ON for a specific therapy target, any parameter change will be immediately active.

Warnings While Removing the Lead

- If resistance is met while removing leads from the epidural space, do not use excessive force to extract. Always perform removal with the patient conscious and able to give feedback.
- Always remove the Trial Leads before implanting the Implant Leads, as there is a risk of infection that may cause death if the leads are not removed. Always practice proper sterile practices when implanting leads and the implantable neurostimulator.
- Do not remove a lead quickly, as this may result in lead breakage and unintentional lead fragments being left in the patient. Spinal Modulation recommends pulling slowly at a rate of approximately 1cm/second while holding the lead between the thumb and forefinger.

- Take proper precautions when handling removed Trial Lead components. Treat all used Trial Leads and delivery components as a “biohazard.”

Warning While Removing the INS

- Do not crush, puncture, or burn the INS because it may explode or catch on fire.

Warnings for Your Patient

- Do not use your Programmer or the Stimulator until your doctor has trained you.
- The safety and effectiveness of this therapy has not been established for pregnancy, nursing, the unborn fetus, or delivery.
- The safety and effectiveness of the Axium Neurostimulator System has not been established for pediatric use.
- Do not use your Programmer until your doctor has set up your Stimulator.
- Before having a CT scan, tell your doctor that you have an implanted device. All stimulation for your device should be turned OFF before the procedure. After the scan, your doctor should turn it back on and make sure the system is working properly.
- Do not remove your leads or Connector Cable by yourself. This may cause serious injury and could cause an infection.
- Do not open or modify the Programmer or TNS. Keep them closed to protect them. Modifications to the device may cause improper operation.
- Do not transport the Programmer outside of its carrying case. Operate it only in a moisture-free environment. The Programmer may malfunction if it becomes wet.
- Power generators, arc welders and large magnetized speakers may cause interference. Do not stand near these or similar devices.
- Be aware of where you place your Charger. Pets, children or you can become entangled in the cord, which could cause a fall or strangulation.
- If contact with the Stimulator System causes a rash, report this to your doctor. If your throat or tongue starts to swell, get emergency aid immediately.
- Please contact your doctor if you experience unusual pain or discomfort during stimulation, the implant site is swollen, reddened, tender, or painful.

Precautions

The following precautions apply to the use of the Axium Neurostimulator System:

- **Patient Selection** – It is extremely important to select patients appropriately for neurostimulation and that thorough psychiatric screening be performed. Patients should not be dependent on drugs and should be able to operate the spinal cord stimulator system.
- **Infection** – It is important to 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 15 cm (6 in) separates the implanted INSs to minimize the possibility of interference during programming.
- **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 may render the patient incapable of controlling the patient programmer. If unpleasant sensations occur, the device should be turned off immediately.
- **Stimulation Parameters** – Patients should be cautioned that stimulation parameters must be determined under the supervision of a physician and that they should not adjust stimulation parameters within prescribed programs unless ordered to do so by a physician.
- **Overprogramming** – Excessive communication with the device can shorten the life of the INS. The patient should be warned to communicate with the device only when necessary.
- **TNS Device Care** – The patient must be instructed to not spill fluids on, to wash or otherwise get their TNS device wet. The patient must not shower or bathe with it (sponge baths are acceptable as long as the TNS device does not get wet). The patient must be instructed not to drop or mishandle their TNS device. Physical damage to the unit may impair its function. The patient must be instructed to not open the TNS case.
- **TNS Device Failure** – Device failure, although unlikely, is possible due to random component failure. If the TNS device stops working, the patient should contact their physician.
- **TNS Device Disposal** – The patient is to be instructed that they must return their TNS device and Patient Programmer to their physician after the trial period. The patient must be instructed to not discard or burn their TNS device. Fire may cause the internal battery to explode.
- **TNS Battery Replacement** – It is unlikely that the battery will need replacement in the short time that the patient has their TNS device. However, if the TNS device does not function the patient must not try to open the TNS case. The internal battery must be replaced by Spinal Modulation personnel only. The patient should be advised to contact their physician during regular business hours.

- **Material Sensitivity** – Hypersensitivity (redness in the area of skin contact) can happen if the patient has an allergic reaction to the materials. If this occurs, the patient should be instructed to contact their physician during regular business hours.
- **Transcranial Magnetic Stimulation (TMS) and Electroconvulsive Therapy (ECT)** – Safety has not been established for TMS or ECT in patients who have an implanted neurostimulation system. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.
- **Transcutaneous Electrical Nerve Stimulation** – Do not place transcutaneous electrical nerve stimulation (TENS) electrodes so that the TENS current passes over any part of the neurostimulation system. If patients feel that the TENS may be interfering with the implanted neurostimulator, patients should discontinue using the TENS until they talk with their doctor.
- **Long-Term Effectiveness of DRG Stimulation** – The long-term effectiveness of DRG stimulation has been documented. Not all patients realize long-term benefits from DRG stimulation. Stimulation effectiveness has been established for one year.
- **Cell Phones** - While interference with cell phones is not anticipated, cell phone technology continues to change, and interaction with an neurostimulation system is possible. Advise patients to contact your office if they have a concern about cell phone interaction with their neurostimulator system.

Precautions During Lead Implant

- When handling the lead, do not bend the lead sharply as this may cause lead damage.
- Use caution when attaching the soft tissue anchor because damage to the anchor or lead can occur and result in failure of the system.
- Failure to push the short end of the soft tissue anchor into the ligament or fascia may result in lead migration and a procedure to revise the lead location.
- Use extreme care to not damage the lead with the sharp point of the tunneling tool.
- Leads or Extensions should be routed adjacent to one another to prevent changes in perceived stimulation from theft detectors and metal screening detectors.

Precautions During INS Implant

- Before implantation, do not use chemicals or any cleaning agents to wipe the INS. This may cause irritation or inflammation at the implant site.
- Use only the torque wrench provided by Spinal Modulation or the device or lead may be damaged and unusable. Tighten until a click is heard or the lead may make intermittent contact with the stimulator.
- Do not implant the INS deeper than 2.0 cm, as the programmer will not be able to communicate with the INS.

- Do not connect a lead to the INS with body fluid on its contacts because corrosion can occur and cause failure of the system.
- If there is a need to communicate with the INS prior to implantation, do not put the INS on a stainless steel table, as communication may be difficult. This may prolong the procedure.
- Insert the lead slowly into the header to prevent damage to the INS. If the lead needs to be retracted, retract the lead slowly.
- Do not implant the INS face down. Always implant with the label facing up. Failure to do so will prevent communication with the programmer and/or magnet.
- Coiling the lead on the top surface of the INS (closest to the skin) will interfere with the ability of the programmer to communicate with the device.
- Do not bring the suture needle in contact with the INS or lead while sewing the INS into the pocket or closing the pocket. The components may be damaged if this occurs.

Precaution During Intraoperative Testing

- Put the Trial Stimulator in standby mode or reduce amplitude of leads to zero before plugging in the cable. Failure to do so may result in delivering an uncomfortable stimulation to the patient.

Precautions During the Implant Procedure

- Do not bend, kink, or stretch the lead body, sheaths, or other components as this may result in damage to the component and poor function.
- Do not insert the sheath into the epidural space without the lead or guidewire inserted, as this may cause injury to the dura. The standard Implant Lead cannot be loaded into the sheath after the sheath is in the body. The SlimTip Lead, however, can be loaded after the sheath has been initially placed in the body.
- When inserting the lead/sheath assembly through the needle into the epidural space, tighten the lead stabilizer to prevent lead migration out of the sheath. Failure to do so may cause harm to the patient such as damage to the dura.
- Do not bend the sheath without the lead inside the sheath, as this will permanently kink it and make it difficult to deploy the lead.
- Do not use surgical instruments to handle the lead. The force of the instruments may damage the lead or lead stylet.
- Do not bend, kink or use surgical instruments on the stylet, as this may damage it. Use care when reinserting a stylet. Too much pressure on the stylet could damage the lead, resulting in intermittent or loss of stimulation.

Remove the stylet from the lead only when satisfied with lead placement. If the stylet is removed from the lead, it may be difficult to reinsert it.

- Do not over manipulate the sheath and lead system as this may result in trauma within the epidural space.
- Do not use saline or other ionic fluids at or near any of the electrical connections, as this could result in short circuits.
- Before opening any sterile package, verify the kit model number, that the kit is within its expiration (use-by) date and that the packaging has not been damaged or compromised in any way. If the packaging has been compromised or the device is beyond its expiration date, do not use the device as it may be compromised and could cause harm to the patient.
- Carefully inspect the lead (in the sterile field) for damage after removing it from the sterile package. Damage to the lead body can cause improper function and stimulation or stimulation to areas other than the intended target.
- If the operating field is bloody, wipe gloves, lead, stylet, and sheath before handling the lead. Failure to do so may result in difficulty delivering the lead.
- The leads, accessories, and neurostimulator are only compatible with the Spinal Modulation components. Use of other manufacturer's components may result in unexpected device performance and increased risk of injury to the patient.

Precautions When using the Clinical and Patient Programmers

- Do not drop or mishandle the programmer. Physical damage may impair its function.
- Do not spill fluids on or wash the programmers. Excessive moisture may impair function. If cleaning is necessary, remove soil with a soft damp cloth.
- Do not use abrasive or caustic cleaning products on the programmers.
- Do not attempt to open the case for the programmers. Attempts to open a case may expose the programmer to elements that alter its function.
- The programmers have an internal magnet. Keep the programmers away from any credit cards, hard drives, or magnetic storage devices as it may demagnetize them.
- Do not operate the programmers outside the specified temperature range of 5°C to 40°C (41°F to 104°F). Rapid temperature changes may affect proper device operation.
- Do not store the programmers outside the specified temperature range of -10°C to 50°C (14°F to 122°F).
- Do not leave the programmers in a car or other places where temperatures can exceed 50°C (122°F).
- Do not burn or otherwise dispose of the programmers. Fire may cause the internal battery to explode.

- Do not allow unauthorized use of the programmers to avoid injury to patients.
- The NS device can only be programmed using Spinal Modulation's Clinical or Patient Programmer. Do not try to use any other manufacturer's device to program them.
- Do not use the programmers or NS in the presence of explosive or flammable gases as this may cause serious injury.
- Do not use the Programmer Charger if the power cord is damaged, excessively worn or frayed. This may cause injury or damage the Programmer.
- Frequent programming of the implanted device will cause the battery to deplete faster. Avoid unnecessary programming.

Precautions While Removing Lead

- Always perform removal with the patient conscious and able to give feedback.
- If resistance is met while removing leads from the epidural space, do not use excessive force to extract. If the lead cannot be easily removed, seek surgical advice regarding lead removal.

Sterilization Information

Single-use, sterile device – The sterile components of the Axiom Neurostimulator System are provided sterile in a double pouch or tray assembly and are intended for single use only. An expiration date (or "use-before" date) is marked on the label of each package. Use proper sterile techniques to open the packaging.

 **WARNING:** Do not resterilize or reuse any devices for any reason because of risk of infection to the patient and malfunction of the devices.

Sterilization – The sterile components of the Axiom Neurostimulator System have been sterilized using ethylene oxide (EO) gas.

Storage Conditions

Store all sterile product including the INS, Leads, and Lead Accessories Kits as follows:

Storage Temperature – Store components between 14°F (-10°C) and 122°F (50°C). Temperatures outside this range may damage the components. If a temperature deviation has occurred, do not use the product.

Storage Humidity – Store components between 10% and 90% humidity.

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

Product Materials

Portions of the Axium Neurostimulator System will come in contact with bodily tissues.

⚠ WARNING: Neurostimulation systems have materials that 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.

The following materials are implanted and come in contact with tissue:

| | |
|------------------|---|
| Platinum iridium | Stainless Steel |
| Polyurethane | MP35N (nickel-cobalt-chromium-molybdenum alloy) |
| Titanium | PEEK (polyether ether ketone) |
| Epotek | PFA (perfluoroalkoxy copolymer resin) |
| Silicone rubber | PMMA [poly(methyl methacrylate)] |

Adverse Events

The implantation of a neurostimulation system involves risk. In addition to those risks commonly associated with surgery, the following risks are also associated with implantation and use of the Axium Neurostimulator System:

- Pain (where the needle has been inserted)
- Pain (caused by understimulation due to lead migration)
- Pain over the implantable neurostimulator site
- Escalating pain
- Bleeding (where the needle has been inserted)
- Headache
- Infection
- Localized collection of serous (clear) fluid at injection site
- Discomfort during the treatment
- Allergic or rejection response to implant materials
- Constant pain at the lead site
- Stimulation of the chest wall

- Lead migration (movement) and/or local skin breakage
- Weakness
- Clumsiness
- Numbness
- Temporary muscle activation
- Cerebral Spinal Fluid (CSF) leakage
- Tissue damage
- Nerve damage
- Spinal cord compression
- Paralysis
- Hematoma
- Swelling
- Seroma
- Sensory loss
- Skin erosion around the INS or leads
- Battery failure and/or battery leakage
- Lead breakage requiring replacement of the lead
- Hardware malfunction requiring replacement of the neurostimulator
- Pain from a non-injurious stimulus to the skin (allodynia)
- An exaggerated sense of pain (hyperesthesia)
- Change in stimulation, possibly related to tissue changes around the electrodes, shifts in electrode position, loose electrical connections, lead or extension fractures, which has been described by some patients as uncomfortable stimulation (jolting or shocking sensation).
- Formation of reactive tissue in the epidural space around the lead can result in delayed spinal cord compression and paralysis, requiring surgical intervention. Time to onset can range from weeks to many years after implant.

Additional risks to the patients, as a result of the placement and stimulation of the lead in the area of the DRG, include pain due to setting the stimulation parameters too high. This may occur once the lead is in place and is connected to the neurostimulator and activated. The neurostimulator is controlled by a trained operator and the starting point for the stimulation will be set to the lowest available settings. Additionally, all patients will be awake and conversant during the procedure to minimize the impact.

Implanting the Neurostimulator System

Selection of Neurostimulator Trial Approach

There are two suggested approaches for a neurostimulation trial:

- A. Percutaneous Lead Trial** - A trial is done using a Trial Lead which exits the skin at the needle entry site and which is completely removed after the trial period. In a second procedure, the system is implanted, including the Implant Leads.
- B. Implanted Lead + Percutaneous Extension Trial** - A trial is done with an Implant Lead sutured to the soft tissue just above the spinous process, using the soft tissue anchor to protect the lead. An extension is tunneled away from the needle insertion site where it exits the skin. In a second procedure only the Lead Extension is removed and the Lead or a new Lead Extension is tunneled to a pocket, the INS is implanted in the pocket, and the Lead or Lead Extension is connected to the INS.

Preparing the Patient and Devices for Use

Leads are designed for placement in the epidural space. Each Lead is accompanied by accessories designed to aid the clinician in positioning the tip of the Lead near the target DRG.

- To perform a Percutaneous Lead trial, use the temporary Trial Lead Kit.
- To perform an Implant Lead trial, use the Implant Lead Kit.

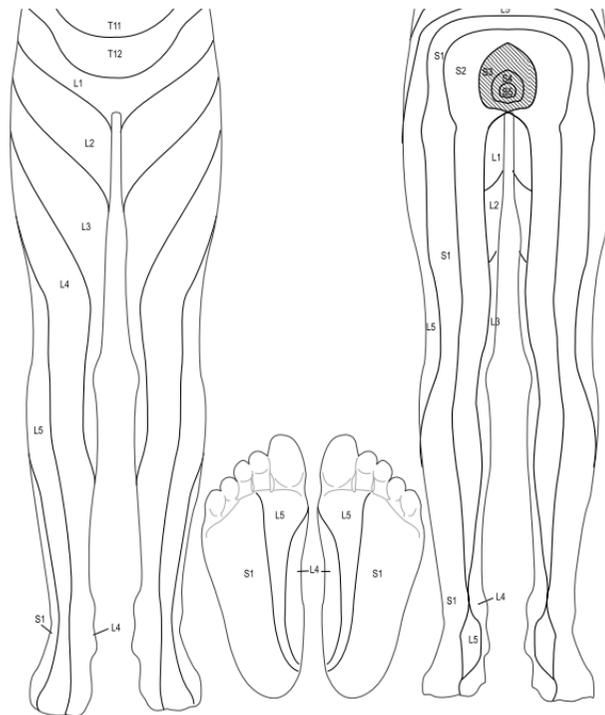
⚠ WARNING: The temporarily placed Trial Leads are intended for use up to 30 days. Use of these devices must be performed in accordance with the instructions provided in this manual.

Using standard sterile technique, perform the appropriate skin prepping, draping and injection of local anesthetic to perform the epidural approaches for percutaneous lead placement.

⚠ WARNING: The placement of the leads involves some risk, as with any surgical procedure. Conscious sedation can cause side effects such as systemic toxicity, or cardiovascular or pulmonary problems. Use caution when **sedating** the patient. The patient must be awake and conversant during portions of the procedure to minimize the likelihood of nerve damage.

Placing the Lead

Lead placement should always be done under fluoroscopic guidance. The appropriate vertebral level for needle entry should be identified and marked. Use a dermatomal map to identify the correct level to place the leads. One example is the following:

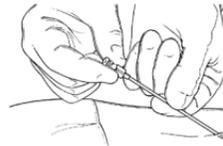


⚠ WARNING: As with any spinal epidural procedure, potential risks of serious injury to the patient, although extremely rare, include epidural hemorrhage, hematoma, infection, spinal cord or nerve compression, and/or paralysis.

⚠ WARNING: Always be aware of the needle tip position. Use caution when positioning the needle to avoid unintended injury to surrounding anatomical structures.

1. Determine the length of the lead required to extend from the target foraminal level to the Neurostimulator implantation site.
2. Choose an approach:

- **Antegrade Approach:** Under fluoroscopic guidance, use a contralateral or ipsilateral approach, with the bevel of the needle facing toward the target level, to insert the Delivery Needle into the epidural space at the appropriate angle until you encounter resistance from the ligamentum flavum. Start by inserting the needle into the interlaminar space at the appropriate level, based on the patient's anatomy. The needle angle should be shallow to ensure a smoother delivery.



Example of Needle Angle

- **Contralateral Approach:** Under fluoroscopic guidance, use a contralateral approach with the bevel of the needle facing toward the target level to insert the 14G delivery needle into the epidural space.

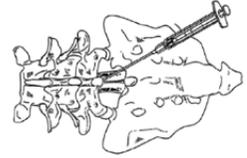
- **WARNING:** When using a contralateral approach, advance the needle slowly into the epidural space and take caution as it enters. The needle will be inserted at a steeper angle than in an antegrade approach and there is a greater chance of dural puncture that will lead to a cerebrospinal fluid leak.



Examples of Angles of Approach

3. Confirm entry into the epidural space using standard methods, such as a loss of resistance technique.
4. Once loss of resistance is achieved, the clinician may verify complete insertion into the epidural space using fluoroscopic guidance and/or inserting the guidewire through the needle. If resistance is discovered during guidewire insertion, either pull the needle out and repeat Steps 1-3 using a more acute angle or advance the needle further and reconfirm placement using the guidewire.

- **WARNING:** Use fluoroscopy and extreme care when inserting, advancing, or manipulating the guidewire or lead in the epidural space to minimize the risk of a dural tear.



- **WARNING:** Dural puncture can occur if needle or guidewire is advanced aggressively once loss of resistance is achieved. Advance the needle and/or guidewire slowly.

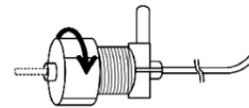
5. Remove the guidewire (if used) after confirmation of access to the epidural space.
6. Before insertion into the needle, push the lead outside the sheath and verify that the stylet is pushed fully distal within the lead.

NOTE: Failure to ensure the stylet is completely inserted may make delivery of the lead more difficult.

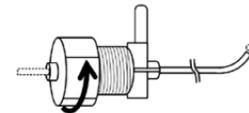
7. Before insertion into the needle, pull back on the lead so that the ball-tip end is protruding slightly from the Delivery Sheath tip and tighten down the lead stabilizer until the lead does not slide within the sheath. One way to ensure this placement is to line up the marker band of the sheath with the distal electrode.

- **WARNING:** Insertion of a sheath without the lead may result in dural puncture. Securing the lead with the lead stabilizer will mitigate this risk.

NOTE: Use of the delivery sheath is necessary for successful placement of the Lead.

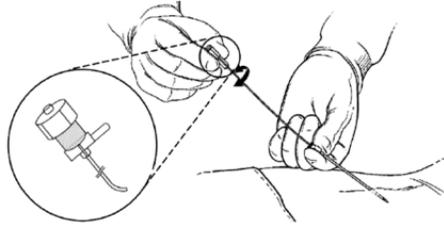


Tightening the Lead Stabilizer



Loosening the Lead Stabilizer

- Note that the steering wing on the sheath lines up with the bend in the sheath.

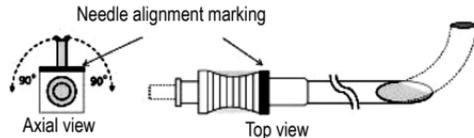


- Before inserting the sheath into the needle, verify that the lead is loaded. The Implant Lead cannot be loaded into the sheath after the sheath is in the body. The SlimTip Lead, however, can be loaded after the sheath has been initially placed in the body.
- Insert the sheath, lead, and stylet through the needle and advance through the epidural space to the target foraminal opening.

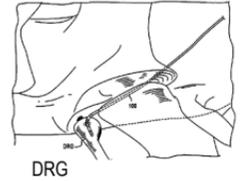
WARNING: If the sheath needs to be retracted from the epidural space, verify that the steering wing is no more than 90 degrees rotated away from the mark on the needle. Failure to do so may result in damage to the sheath. Before reinserting the sheath, verify there is no damage to the sheath.

WARNING: Do not pull the standard Implant Lead through the sheath as this can cause separation of the ball-tip from the lead. With the SlimTip Implant Lead, it may be removed through the sheath as the ball-tip is small enough to allow passage back and forth through the sheath.

WARNING: If the sheath is not responding to rotation, do not rotate the steering wing out of plane from the curve of the sheath more than 90 degrees. The tip of the sheath may whip around and could cause harm to the patient.



- With the distal end of the sheath in or at the target foramen, loosen the lead stabilizer, and advance the lead so that it moves into the foramen. Confirm placement of the lead on the dorsal side of the foramen using a lateral fluoroscopic view. Verify that the electrodes extend out of the sheath. If the electrodes remain within the sheath, stimulation will not be possible because of high impedance readings.

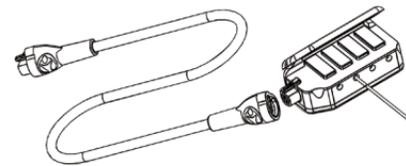


WARNING: If the lead is unable to deploy out of the sheath, inject sterile water or saline slowly to release tissue that may have entered between the sheath and the lead. Do not use excessive pressure when injecting through the sheath.

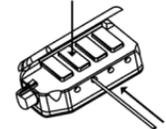
WARNING: Do not use excessive force to push the lead or sheath into the neural foramen as this may result in permanent or transient nerve damage. The patient should be awake and conversant during this part of the procedure, so they can provide feedback to the physician.

Intraoperative Testing

- Connect the head to the cable. Press and hold the cable button down to release the locking mechanism and slide the proximal end of the leads into the head. Release the cable button to lock the lead into place. Verify that the lead comes to a stop before releasing the button. This will ensure that the electrical contacts are in the appropriate position.



Push cable button down



Insert lead

- Put the TNS in standby mode or turn the amplitude of each lead set to zero.

PRECAUTION: Put the Trial Stimulator in standby mode or reduce amplitude of leads to zero before plugging in the cable. Failure to do so may result in delivering an uncomfortable stimulation to the patient.

3. Pass the proximal end of the Connector Cable off the sterile field and connect to the TNS.

NOTE: Refer to the *Trial Neurostimulator User Manual and Clinical Programmer User Manual* for specific instructions on the operation of these devices.

WARNING: Maintain adequate slack in the cable. If there is not enough slack and the cable is pulled, the lead may be dislodged and will need to be replaced. This will extend the procedure.

4. Using the TNS, test the various electrode configurations used to obtain appropriate paresthesia or pain relief.
5. Turn off the Trial Neurostimulator and disconnect the lead from the connector cable.

NOTE: Up to four leads may be placed in one patient. Refer to "Placing the Lead" to position subsequent leads.

PRECAUTION: As described in the Clinical Programmer User Manual, always turn the external TNS amplitude to 0 μ A when repositioning a lead, changing the selected electrode combination, or attaching the Connector Cable to the external TNS. When restarting stimulation, increase the amplitude SLOWLY until the desired paresthesia is achieved. Failure to do so may result in uncomfortable motor activation or painful stimulation.

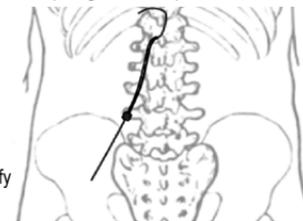
Removing the Delivery System Components - Percutaneous Lead Trial

1. Before removing the delivery system components, advance the lead further into the epidural space to create a strain relief.
2. Slowly remove the delivery sheath by first pulling back the sheath near the needle. Always hold forward pressure on the Lead while retracting the delivery sheath to prevent lead movement.
3. Retract the stylet into the needle, so that it is retracted beyond the tip of the sheath.
4. Turn the sheath away from the opening of the foramen and push out the lead. To provide strain relief, create an S-curve with the lead in the epidural space.

WARNING: Failure to provide strain relief may result in lead migration requiring a revision procedure.

5. Remove the sheath completely while holding forward pressure on the lead.

WARNING: When removing the sheath, verify that the steering wing is no more than 90 degrees rotated away from the mark on the needle. Failure to do so may result in damage to the sheath. Before reinserting sheath, verify there is no damage to the bend of the sheath.



6. Remove the needle following the same procedure. It is recommended that the desired paresthesia be re-tested after the removal of the delivery system components but before the complete removal of the stylet. With the external TNS amplitude set to 0 μ A, reconnect the Connector Cable as described before.

WARNING: If the sheath has been kinked during delivery, slowly retract through the needle with the curve facing the same direction as the bevel. Failure to do so can damage or cut the lead or sheath. If resistance is encountered, pull the needle out of the epidural space and then remove the sheath.

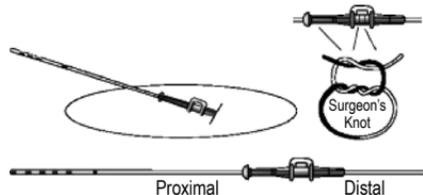
WARNING: Do not use excessive force if the lead needs to be removed. Excessive force may cause lead breakage.

7. Record the lead position with both an A/P and lateral fluoroscopic view for comparison of the position at time of closure to ensure that the lead has not moved. Remove the stylet by holding forward pressure on the lead while retracting the stylet.

WARNING: Use extreme care when removing the lead stylet, the delivery sheath, and the needle, to ensure that the distal tip of the lead remains in the desired location. Removing each item in slow movements, while holding the remaining components in place, will assist this process.

Lead Anchoring - Percutaneous Lead Trial

1. After placing a Trial Lead in its final position, it should be secured using a lead anchor on the skin.



Depiction of Anchoring Technique

2. Carefully, slide the lead anchor over the proximal end of the Trial Lead and advance it to the puncture site. The short end of the suture anchor must be facing towards the incision.
3. Apply sutures around the anchor and cinch onto the Trial Lead as shown. One option would be to apply at least two ties to the main body and one tie to the leg. Physicians may apply their own technique based on patient anatomy, physical activity and other factors.

WARNING: Do not suture directly onto the lead, as there is a risk of damaging the lead. Failure to secure the lead to the skin, or other tissue, may result in lead migration and/or motor activation or painful stimulation.

WARNING: Failure to appropriately anchor may result in lead migration and/or motor activation or painful stimulation.

4. Apply an antibacterial agent to the puncture site, if desired.
5. Reconnect the connector cable to the leads and coil any excess Trial Lead length around the distal end of the Connector Cable, fold a gauze pad around the block, and apply a large adhesive patch over the area containing the Trial Lead(s), puncture site and Connector Cable.
6. Verify the connection of the Connector Cable to the Trial Leads and the external TNS prior to discharge of the patient.

Neurostimulation Trial - Percutaneous Lead Trial

Using the Clinical Programmer, program the TNS with the neurostimulation trial parameters.

NOTE: Refer to the Trial Neurostimulator User Manual and Clinical Programmer User Manual for specific instructions on the programming of these devices.

Removing Trial Lead - Percutaneous Lead Trial

WARNING: Always remove the Trial Leads before implanting the Implant Leads, as there is a risk of infection that may cause death if the leads are not removed. Always practice proper sterile practices when implanting leads and the implantable neurostimulator.

To remove the Trial Lead(s) from a patient:

1. Disconnect the Connector Cable connection for each Trial Lead.
2. Remove any sutures or anchor securing each Trial Lead to the patient's skin.
3. Slowly apply light tension to each Trial Lead and verify that the lead is retracting from the patient.

WARNING: Do not remove a Trial Lead quickly, as this may result in lead breakage and unintentional lead fragments being left in the patient. Spinal Modulation recommends pulling slowly at a rate of approximately 1cm/second while holding the lead between the thumb and forefinger.

WARNING: Take proper precautions when handling removed Trial Lead components. Treat all used Trial Leads and delivery components as a "biohazard."

Removing the Delivery System Components - Implant Lead Trial Only

These instructions pertain only after placing Implant Leads during the trial procedure. After placing a lead in its final position, using the techniques described above, it should be secured using a lead anchor to the supraspinous ligament or fascia and then connected to the externalized lead extensions.

WARNING: Do not suture directly onto the lead, as there is a risk of damaging the lead. Failure to secure the lead may result in lead migration and uncomfortable motor stimulation or painful stimulation.

WARNING: Use extreme care when using sharp instruments or electrocautery around the lead to avoid damaging the lead.

3. Leaving the needle in place, prepare the anchor site by making an approximately 3 - 7 cm longitudinal incision, centered on the needle to the depth of the supraspinous ligament.
4. Establish hemostasis and use retractors for good visualization.
5. Slowly remove the delivery sheath by first pulling back the sheath near the needle. Always hold forward pressure on the Lead while retracting the delivery sheath to prevent movement.
6. Retract the stylet into the needle so that it is retracted beyond the tip of the sheath.
7. Turn the sheath away from the opening of the foramen. To provide strain relief, create an S-curve with the lead in the epidural space.

WARNING: Failure to provide strain relief may result in lead migration requiring a revision procedure.

8. Remove the sheath completely while holding forward pressure on the lead.

WARNING: When removing the sheath, verify that the steering wing is no more than 90 degrees rotated away from the mark on the needle. Failure to do so may result in damage to the sheath.

WARNING: If the sheath has been kinked during delivery, slowly retract through the needle with the curve facing the same direction as the bevel. If resistance is encountered, pull out the needle and then proceed to remove the sheath. Failure to do so can damage or cut the lead or sheath.

9. Remove the needle following the same procedure.
10. It is recommended that the desired paresthesia be re-tested after the removal of the delivery system components, but before the complete removal of the stylet. With the TNS amplitude set to 0 μ A, reconnect the Connector Cable as described before.

WARNING: Do not use excessive force if the lead needs to be removed. Excessive force may cause lead breakage.

11. Record the lead position with both an A/P and lateral fluoroscopic view for comparison of the position at time of closure to ensure that the lead has not moved. Remove the stylet by holding forward pressure on the lead while retracting the stylet.

WARNING: Use extreme care when removing the lead stylet, the delivery sheath, and the needle, to ensure that the distal tip of the lead remains in the desired location. Removing each item in slow movements, while holding the remaining components in place, will assist this process.

Lead Anchoring

After placing a lead in its final position, it should be secured using a soft tissue anchor and then connected to externalized extensions.

WARNING: Do not suture directly onto the lead, as there is a risk of damaging the lead. Failure to secure the lead to the skin, or other tissue, may result in lead migration and uncomfortable muscle stimulation.

WARNING: Use extreme care when using sharp instruments or electrocautery around the lead to avoid damaging the lead.

1. Soak the anchor in sterile water (not saline) to lubricate it.
2. Place the anchor on the lead and slide it down as close as possible to where the lead emerges from the vertebral column. Be careful not to move the lead.

NOTE: *If implanting multiple leads, tag the leads with suture (ligature) so that their position can be identified later.*

PRECAUTION: Observe these cautions when attaching the soft tissue anchor because damage to the anchor or lead can occur and result in failure of the system:

- Do not use polypropylene or monofilament suture.
 - Do not place sutures directly on the lead.
 - Avoid sharp bends or kinking on the lead.
3. Apply sutures around the anchor and cinch onto the Lead as shown. One option would be to apply at least two ties to the main body and one tie to the leg. Physicians may apply their own technique based on patient anatomy, physical activity and other factors.

PRECAUTION: Failure to push the short end of the soft tissue anchor into the ligament or fascia may result in lead migration and a procedure to revise the lead location.

4. It is recommended that the lead position is verified under fluoroscopy and desired paresthesia be re-tested after fixation. With the external TNS amplitude set to 0 μ A, reconnect the Connector Cable as described before.

Percutaneous Extension Tunneling - Implant Trial Lead Only

1. Identify the tunneling route between the lead incision and the extension exit site.
2. Administer anesthetic at the exit site and along the tunneling route.
3. Assemble the tunneling tool packaged with the lead by slipping the passing straw over the tunneling rod, then attaching the tunneling tip.
4. Bend the tunneling tool as necessary to conform to the patient's contour along the tunneling route.
5. Make a stab wound at the exit site.
6. Begin at the exit site and tunnel subcutaneously to the lead incision.
7. Guide the tunneling tool subcutaneously along the tunneling route by pushing the skin over the advancing tool tip until the tip and approximately 1 cm of the passing straw are exposed at the lead incision.
8. Withdraw the tunneling tool leaving the passing straw in place in the tunnel.
9. Gently insert the proximal end of the extension through the passing straw to the exit site.
10. Slide the passing straw over the extension and out of the skin exit site, leaving the extension in place.
11. If not done previously, use blunt dissection to form a subcutaneous pocket off the lead incision for the lead-extension connection.
12. Wipe the lead and extension connector junction with sterile gauze. If necessary, moisten the gauze with sterile water or a nonionic antibiotic solution.
13. Dry all connections. Fluid in the connection may result in stimulation at the connection site, intermittent stimulation, or loss of stimulation.
14. Hold the extension connector straight while firmly, but gently, inserting the lead into the connector one or two contacts at a time until each lead contact is aligned under each extension connector contact. During insertion, some resistance is typical because the internal seals provide electrical isolation.
15. Verify that the mark on the lead aligns with the end of the extension connector. This will verify that the lead is fully inserted.

NOTE: If it is difficult to insert the lead, the set screw may be unscrewed with the Torque Wrench just enough to allow the lead to pass. If the set screw is fully unscrewed, the Torque Wrench may not be able to tighten it again.

- If this occurs, use the Hex Key included in the Tunneling Tool Kit to release the set screw. Insert the Hex Key into the set screw and release it by turning the key only part of a turn clockwise.
 - Once the set screw is released, remove the Hex Key. Do not use the Hex Key to tighten the screw against the lead as it may be overtightened and may damage the lead or the screw head.
16. Use the torque wrench supplied in the package to tighten the set screw. Tighten until a click is heard. Using minimal force, and while securely holding the lead to prevent dislodgement, pull on the connection to ensure that it is secure.
- ⚠ PRECAUTION:** Use only the Torque Wrench provided by Spinal Modulation or the device or lead may be damaged and unusable.
17. Using minimal force, pull the extension from the skin exit site, feeding the lead-extension connection into the lead-extension connection pocket.
 18. In order to aid in identification of each lead after the trial period, tie a suture lightly to the lead and another one to the lead extension. Use different color suture and numbers of suture to identify the leads. This will aid in identification during the implant procedure.
 19. Create strain relief loops by coiling excess lead proximal to the soft tissue anchor in loops. Insert the lead into the pocket, under the connection, leaving as much slack as possible in the lead between the anchor and the lead-extension connection.
 20. Close the incision and dress the incision site.
 21. At the exit site, coil any excess extension around the distal end of the Connector Cable, fold a gauze pad around the block, and apply a large adhesive patch over the area containing exit puncture, excess extension, and Connector Cable.

Removing Lead Extension - Implant Trial Lead Only

1. Remove the bandage near the exit point of the lead extension.
2. Pull the lead extension lightly out of the incision and cut the lead extension.

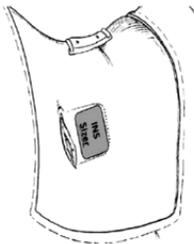
3. Expose the lead-extension to lead connection.
4. While maintaining lead position, carefully remove the lead-extension connections from the incision.
5. Disconnect the lead from the extension.
6. Cut the extension near the lead-extension connector.
7. Discard the lead-extension connector.
8. Preserving sterility, pull the extension out through the skin exit site.
9. Discard the extension.
10. If multiple extensions are implanted, repeat the removal steps for the other extensions.

Creating the INS Pocket - Implant

Once the leads have been anchored, a Neurostimulator pocket should be created and the lead tunneled for connection to the INS.

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

1. Determine the site for the INS. This should be done before implanting the lead to verify there is enough length to reach the INS pocket and provide strain relief in the pocket, near the anchor, and in the epidural space.



NOTE: *The INS should be located in an area that the patient can easily reach with the magnet and/or programmer:*

- *In the upper buttocks along the posterior axillary line (avoiding the belt line)*
 - *Just over the abdomen below the lowest rib*
2. Administer local anesthetic at the neurostimulator pocket site.
 3. Use blunt dissection to create a pocket so that the INS is parallel to the skin surface and no deeper than 2.0 cm below the skin surface. Use electrocautery to maintain hemostasis.
 4. (Optional) Insert the INS sizer to ensure the pocket is large enough to accommodate the INS, allowing extra room for a strain relief loop with each lead.

⚠ PRECAUTION: Do not implant the INS deeper than 2.0 cm, as the programmer will not be able to communicate with the INS.

⚠ WARNING: Do not apply electrocautery directly to the INS as this can damage the INS or cause interference while communicating with the INS.

Lead or Extension Tunneling

Tunnel the leads from the anchor site to the INS pocket. When tunneling to the abdomen, tunnel to a midpoint and then continue to INS site.

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

⚠ WARNING: Use extreme care to not damage the lead with the sharp point of the tunneling tool.

1. Identify the tunneling route between the lead incision and the neurostimulator pocket.
2. Administer local anesthetic along the tunneling route. Additional sedation may be administered at the discretion of the physician.
3. Bend the tunneling tool as necessary to conform to the patient's contour along the tunneling route.
4. With the straw in place on the tunneling tool, tunnel from the INS pocket to the lead anchor site.
5. Withdraw the tunneling tool from the straw, leaving the straw in the subcutaneous tunnel.

⚠ PRECAUTION: Leads or Extensions should be routed adjacent to one another to prevent changes in perceived stimulation from theft detectors and metal screening detectors.

6. Pass the end of the Leads or Extensions through the straw from the anchor site to the INS pocket or to the midpoint if tunneling to the abdomen. At each incision point, leave a strain relief loop in place to minimize the chances of lead migration.
7. Remove the straw from the tunnel by passing it over the leads, taking care not to cause traction on them and disturb the lead position.

Connecting Lead to Extension

If an extension is used to connect the Lead to the INS, refer to the section “Percutaneous Extension Tunneling” for instructions on how to connect the Extension to the Lead.

Connecting the INS

The following steps outline the guidelines to connecting a Lead or Extension to the INS:

⚠ PRECAUTION: Do not connect a lead with body fluid on its contacts because corrosion can occur and cause failure of the system.

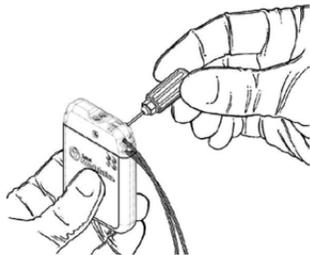
⚠ PRECAUTION: If there is a need to communicate with the INS prior to implantation, do not put the INS on a stainless steel table, as communication may be difficult. This may prolong the procedure.

1. If the lead contacts came in contact with body fluids or saline, thoroughly clean with sterile deionized water or sterile water for irrigation and then dry them completely.
2. Using clean gloves, carefully slide the lead or extension into the INS header until the depth marker aligns with the edge of the header.

NOTE: *If it is difficult to insert the lead, the set screw may be unscrewed with the Torque Wrench just enough to allow the lead to pass. If the set screw is fully unscrewed, the Torque Wrench may not be able to tighten it again.*

- *If this occurs, use the Hex Key included in the Tunneling Tool Kit to release the set screw. Insert the Hex Key into the set screw and release it by turning the key only part of a turn clockwise.*

- *Once the set screw is released, remove the Hex Key. Do not use the Hex Key to tighten the screw against the lead as it may be overtightened and may damage the lead or the screw head.*



⚠ PRECAUTION: Use only the torque wrench provided by Spinal Modulation or the device or lead may be damaged and unusable. Tighten until a click is heard or the lead may make intermittent contact with the stimulator.

3. Insert the torque wrench through the seal plug and tighten the set screw by turning it clockwise, until the wrench clicks.

4. Carefully remove the torque wrench and verify that the septum over the set screw is closed. Reseat the flaps if it is not closed.
5. If implanting less than 4 leads, insert the port plugs in each of the vacant header ports. Use the torque wrench to tighten the set screw on the port plug until it clicks.

⚠ PRECAUTION: Insert the lead slowly into the header to prevent damage to the INS. If the lead needs to be retracted, retract the lead slowly.

Implanting the INS

The following steps outline the procedure for implanting the INS:

⚠ PRECAUTION: Do not implant the INS face down. Always implant with the label facing up. Failure to do so will prevent communication with the programmer and/or magnet.



⚠ PRECAUTION: If using more than one INS, implant them at least 15 cm apart. Putting them too close together may interfere with the programmer’s ability to communicate with each one separately.

1. Place the INS into the pocket at a depth no greater than 2 cm from the skin surface, with the label facing the skin surface.
2. Carefully coil excess lead behind the INS or around the INS in loops to provide strain relief for the lead and the INS connection.

⚠ PRECAUTION: Coiling the lead on the top surface of the INS (closest to the skin) will interfere with the ability of the programmer to communicate with the device.

⚠ PRECAUTION: Do not bring the suture needle in contact with the INS or lead while sewing the INS into the pocket or closing the pocket. The components may be damaged if this occurs.

- To stabilize the INS within the pocket, pass a suture through the two suture holes in the INS and secure it to connective tissue.
- Check the entire system by fluoroscopy prior to closing to ensure proper positioning of the leads. Verify that the leads have no sharp bends or kinks.
- Place the magnet into a sterile bag and wave over the INS.

Magnet Activation Target

Magnet must be within 3.5 cm of INS surface to activate communication.



- Slowly awaken the patient and test for stimulation perception and thereby verifying the system is operational.

NOTE: *The INS output may not be identical to the Trial Neurostimulator output. When restarting stimulation, increase amplitude SLOWLY until the desired paresthesia is achieved. Failure to do so may result in uncomfortable motor activation or painful stimulation. Always start stimulating from a setting lower than that used to stimulate with the Trial Neurostimulator.*

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

Checking System Integrity

- Place the magnet in a sterile pouch and wave it over the device to start programmer communication.
- Using the Clinical Programmer in the non-sterile field, program the basic stimulation parameters, check the battery status, and check the electrode impedances to ensure there is no short or open circuit.
- Once the system's function is verified, turn the Neurostimulator off.

Completing the Procedure

Follow standard procedure for wound closure and bandaging.

Replacing an INS

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

- Turn off the INS and verify that it has been turned off.

WARNING: Exercise care when using sharp instruments or electrocautery around leads or they might be damaged.

- Open the INS implant site per normal surgical procedures.
- Remove the suture from the INS header, without damaging the lead, and carefully remove the INS from the pocket.
- Clean the INS header and the lead with sterile water and then wipe with a surgical sponge.
- Insert the torque wrench through the septum of the INS header and loosen the set screw by turning it counterclockwise.

PRECAUTION: When performing the following steps, do not bend the lead sharply as this may cause lead damage.

- Gently remove the lead from the INS header; then clean and dry all connections on the lead, ensuring they are free from fluid and tissue.

PRECAUTION: If resistance is met while removing leads from the epidural space, do not use excessive force to extract. Always perform removal with the patient conscious and able to give feedback.

WARNING: Do not remove a lead quickly, as this may result in lead breakage and unintentional lead fragments being left in the patient.

WARNING: Take proper precautions when handling removed lead components. Treat all used leads and delivery components as a "biohazard".

- If you need to replace a lead, see "Revising or Removing a Lead".
- To complete the INS replacement procedure, see "Connecting the INS".
- To complete lead placement, see "Placing The Lead".

Disposing of an Explanted Device

Dispose of INS per local waste disposal requirements.

1. Decontaminate the explanted device.
2. Place it in a container with a biohazard label.
3. If you wish to return it to Spinal Modulation, contact your Spinal Modulation representative for device return.

WARNING: Do not crush, puncture, or burn the INS because it may explode or catch on fire.

Revising or Removing a Lead

1. Place the patient in a flexed position–

Put the patient in the prone position by bolstering with pillows or bend the table into an inverted “V”. This will put the patient in flexion and may help release tension on the lead.

PRECAUTION: Always perform removal with the patient conscious and able to give feedback.

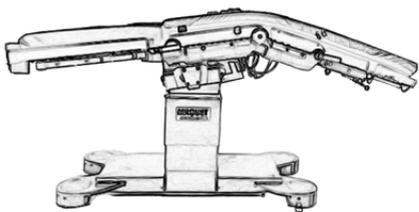


Table in “inverted V” position.



2. Disconnect the lead from the extension or INS.

WARNING: Exercise care when using sharp instruments or electrocautery around leads, or they may be damaged.

Lead Extension – If the lead is connected to an extension and not directly to the INS:

- a. Using standard surgical technique, make an incision above the location of the suture anchor.
- b. Carefully cut the sutures from the suture anchor.

INS – If the lead is connected directly to the INS without an extension:

- a. Open the INS implant site using standard surgical procedure.
- b. Remove the suture from the INS header, without damaging the lead, and carefully remove the INS from the pocket.

PRECAUTION: Do not bend the lead sharply as this may cause lead damage.

- c. Clean the INS header and the lead with sterile water, and then wipe with a surgical sponge.
 - d. Insert the torque wrench through the septum of the INS header, and loosen the set screw by turning it counterclockwise.
 - e. Gently remove the lead from the INS header.
 - f. Make an incision above the location of the suture anchor.
 - g. Carefully cut the sutures from the suture anchor.
3. Slowly slide the lead out of the epidural space.

When removing the lead, use live fluoroscopy to monitor the position of the lead during extraction.

NOTE: Spinal Modulation recommends pulling slowly at a rate of approximately 1cm/second while holding the lead between the thumb and forefinger.

WARNING: Do not remove a lead quickly, as this may result in lead breakage and unintentional lead fragments being left in the patient.

PRECAUTION: If resistance is met while removing leads from the epidural space, do not use excessive force to extract. If the lead cannot be easily removed, seek surgical advice regarding lead removal.

WARNING: Take proper precautions when handling removed lead components. Treat all used leads and delivery components as a “biohazard”.

4. To complete the procedure, see Implanting an INS.

Appendix A: Trial Lead Kit / Implant Lead Kit

How Supplied

The components of the Axium Lead Kits are provided sterile in a double pouch assembly and are intended for single use only.

WARNING: Do not resterilize the Lead Kits or any other sterile components as it will create a risk of infection or malfunction of the device.

Storage Temperature - Store the Lead Kits and Lead Accessories Kit between 14°F (-10°C) and 122°F (50°C). Temperatures outside this range may damage the components. If a temperature deviation has occurred, do not use the product.

Sterilization - The Lead Kits, Lead Extension Kit, and all Lead Kit Accessories have been sterilized using ethylene oxide (EO) gas.

Package Contents

| | | | |
|-----|--|-----|--------------------------|
| (1) | Trial / Implant Lead 50 cm / 90 cm | (1) | Complex Curve Stylet |
| (1) | 22 cm Small Curve Delivery Sheath | (1) | 4.5" 14 Gauge Needle |
| (1) | 22 cm Big Curve Delivery Sheath | (2) | Soft Tissue Anchors |
| (1) | Guidewire | (1) | Physician Implant Manual |
| (1) | Straight Stylet (SlimTip lead kits only) | | |

Device Specifications

The Lead has four electrodes on the distal end and the proximal end fits into a four conductor connector on the Connector Cable, Lead Extension or into the INS ports.



Lead showing four proximal electrical connectors and four radiopaque electrodes

The approximate measurements for a Lead are presented below:

| | |
|---|--------------------------------|
| Proximal Electrical Connector | Quadrapolar, in-line |
| Center to Center Connector Spacing | 3.3 mm (0.130") |
| Diameter..... | 1.0 mm (0.040") |
| Length | 50 cm (20") or 90 cm (35") |
| Number of Electrodes | 4 |
| Electrode Shape..... | Cylindrical |
| Electrode Length..... | 1.25 mm (0.050") |
| Edge to Edge Spacing | 5 mm (0.200") |
| Center to Center Spacing..... | 6.25 mm (0.250") |
| Array Length..... | 20 mm (0.790") |
| Ball Tip Diameter..... | 1.0 - 1.5 mm (0.040" - 0.060") |
| Stylet Wire Diameter | 0.25 mm (0.010") |
| DC Lead Impedance (50cm / 90cm / Extension) | <20Ω / <35Ω / <60Ω |

Appendix B: Trial Neurostimulator

Device Description

See the Trial Neurostimulator Manual for the full description of the device. The external Trial Neurostimulator (TNS) provides energy and controls electrical signals delivered to the Leads. The TNS device is intended to be connected to the Leads and worn by the patient for up to 30 days during the study period. The device is intended to be connected to the Axiom Connector Cable. It is not compatible with other cables from other manufacturers. The external TNS device has a belt clip that can be used or the patient may choose to use a flexible, elastic bandage to secure their TNS device during the trial period. The patient should be advised not to allow the TNS to make direct contact with skin.



Package Contents

- (1) Trial Neurostimulator
- (1) TNS Manual

Device Specifications

| Specifications | Range | Step Size | Default Value |
|---|-------------------------|---|-------------------|
| Pulse Amplitude - PA (μA) (Depending on measured impedance) | 0 – 6000 μA | 25 μA @ 0-2000 μA 50 μA @ 2000-6000 μA | 0 μA |
| Maximum Pulse Amplitude - Max (μA) Programmable by Patient | Same as PA | Same as PA | 0 μA |
| Pulse Width – PW (μs) | 40 – 1000 μs | 10 μs | 300 μs |
| Pulse Frequency - PF (Hz) | 4 – 80 Hz | 2 Hz | 20 Hz |

Handling

Storage Conditions: -10°C - 50°C

Humidity Range: 0 – 93%

Cleaning Instructions for Healthcare Professional: For disinfecting the TNS surfaces after gross filth and heavy soil loads have been removed, spray Cavicide or equivalent onto a paper towel, and then wipe the surface of the TNS with the wet paper towel. Allow the surface to remain damp for 2 minutes. Dry the surface using a dry paper towel. Do not immerse the TNS in liquid. Advise the patient not to clean the TNS with excessive liquid. A damp cloth may be used to wipe the TNS, if necessary.

WARNING: Always wear the TNS on the outside of clothing to avoid skin irritation.

Appendix C: Implantable Neurostimulator

How Supplied

The Axiom Implantable Neurostimulator is provided sterile in a double tray assembly and is intended for single use only.

WARNING: Do not resterilize the INS as it will create a risk of infection or malfunction of the device.



Device Description

The Implantable Neurostimulator is a four channel neurostimulator that is only compatible with Axiom Leads and Lead Extensions. Four ports allow for simultaneous stimulation of up to four leads. An antenna in the header allows wireless communication with the Axiom Clinical Programmer or Patient Programmer.

Package Contents

- (1) Implantable Neurostimulator
- (1) Torque Wrench
- (1) Physician Implant Manual
- (3) Lead Port Plugs
- (1) Medical Alert Card

Device Specifications

Output of the INS is equivalent to the output of the TNS. The device is programmed in current, impedance is measured by the device, and the appropriate output voltage matches the impedance and current programmed.

| Specifications | Range | Step Size | Default Value |
|---|-------------------------|---|-------------------|
| Pulse Amplitude - PA (μA) (Depending on measured impedance) | 0 – 6000 μA | 25 μA @ 0-2000 μA 50 μA @ 2000-6000 μA | 0 μA |
| Maximum Pulse Amplitude - Max (μA) Programmable by Patient | Same as PA | Same as PA | 0 μA |
| Pulse Width – PW (μs) | 40 – 1000 μs | 10 μs | 300 μs |
| Pulse Frequency - PF (Hz) | 4 – 80 Hz | 2 Hz | 20 Hz |

| | |
|-------------------------------------|--|
| Therapy Accuracy | 10% over the range of 1000 to 6000 μA |
| Impedance Measurement Accuracy..... | 10% over the range of 400 to 2500 Ohms |
| Height..... | 6.52 cm (2.57 in) |
| Width..... | 4.77 cm (1.88 in) |
| Thickness..... | 1.10 cm (0.43 in) |
| Volume..... | 31 cm^3 (1.89 in^3) |
| Maximum Connector Strength | 10N |
| Number of Channels | 4 |
| Power Source..... | CFx, lithium - carbon monofluoride |

Handling

Storage Conditions: -10°C - 50°C (14°F - 122°F)

Storage Humidity Range: 10 – 90%

Handling: Before implantation, only wipe with sterile water and do not use any cleaning agents.



PRECAUTION: Before implantation, do not use chemicals or any cleaning agents to wipe the INS. This may cause irritation or inflammation at the implant site.

Device Longevity

Programmed settings impact the longevity of the implanted device. With 2 leads at 1600 ohms impedance programmed at nominal stimulation settings of 800 μA amplitude, 300 μsec pulse width, 20 Hz frequency, the battery may be expected to last 3.3 years. These nominal settings represent average settings seen in world-wide use of the Axium system. Higher stimulation settings, especially pulse amplitude and frequency, result in greater energy usage and therefore reduce the estimated battery longevity.

The system has two warnings about battery life – ERI which is Elective Replacement Indication when the battery is low but stimulation is still available, and EOS which is End of Service when stimulation has been permanently turned off. At nominal settings, there is a 1 month period between ERI and EOS. Depending on specific settings, the duration may range between 20 and 35 days.

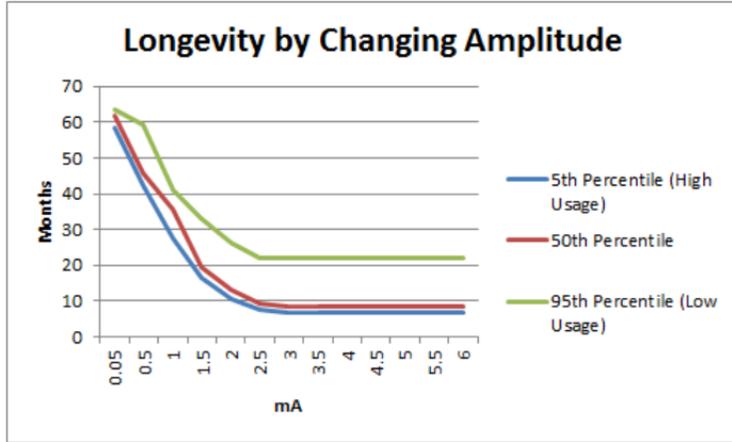
The table below includes patient settings used in the US ACCURATE Clinical Study. The 5th percentile, 50th percentile, and 95th percentile patients were selected based on estimated longevity. The Low Settings example shows the effect of reducing amplitude and frequency.

| Patient Settings used in the US ACCURATE Clinical Study | | | | | | |
|---|-----------------------------|---------------------------------|----------------|------------------|-------|-----------------------------|
| Patient | Amplitude (μA) | Pulse Width (μsec) | Frequency (Hz) | Impedance (ohms) | Leads | Estimated Longevity (Years) |
| 5th Percentile | 2750 | 410 | 20 | 1609 | 2 | 0.9 |
| | 1350 | 300 | 34 | 1796 | | |
| 50th Percentile | 675 | 1000 | 16 | 1727 | 1 | 3.5 |
| 95th Percentile | 500 | 160 | 20 | 1886 | 1 | 4.9 |
| Low Settings | 650 | 110 | 10 | 1140 | 2 | 5.0 |
| | 350 | 230 | 10 | 1968 | | |

The number of leads is not directly proportional to longevity, but on average the longevity decreases as multiple leads are added. The summation of energy delivered through the leads is the primary factor for longevity. Note that both the 0.9 year and the 5.0 year patients have two leads, but the 0.9 year patient is programmed with higher energy settings of 2.75 mA amplitude and 34 Hz frequency compared to the 5.0 year patient's lower energy settings of 350 μA amplitude and 10 Hz frequency.

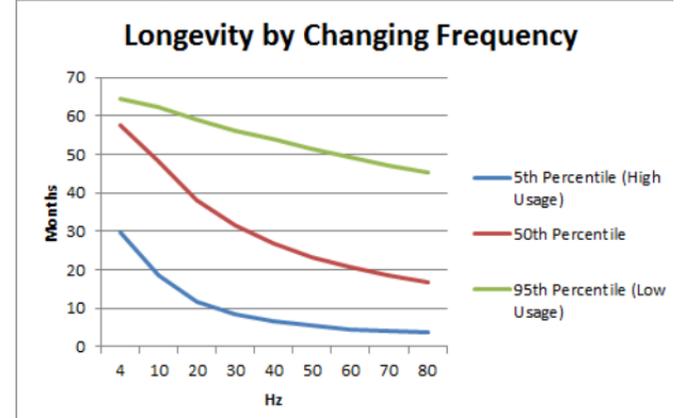
Impact of programmed amplitude on battery longevity

Modifying programmed amplitude can impact the longevity of an implanted device. The graph below depicts expected battery longevity for the percentile patients listed above. The patient's pulse width and frequency settings are kept fixed, and the Amplitude setting is varied across the X-axis for all leads. Longevity ranges from 5.3 years to 7 months, depending on the programmed amplitudes for the leads. Note: When the INS reaches maximum output, the expected longevity plateaus.



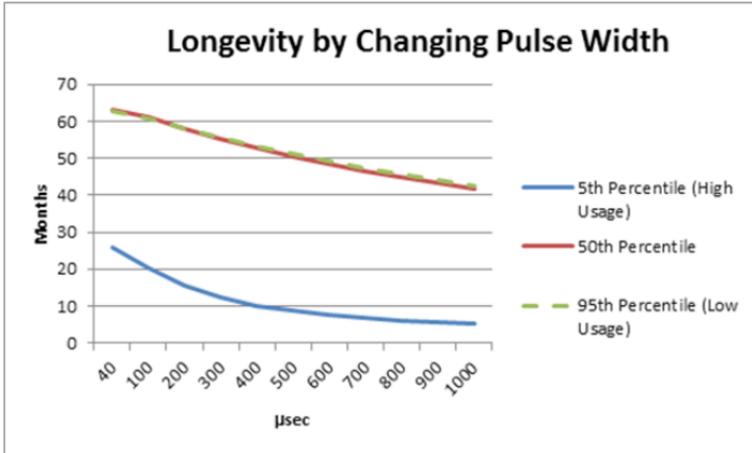
Impact of programmed frequency on battery longevity

Modifying programmed frequency can also impact the longevity of an implanted device. The graph below depicts expected battery longevity for the chosen percentile patients above. The patient's pulse width and amplitude settings are kept fixed, and the Frequency setting is varied across the X-axis for all leads. Longevity ranges from 5.4 years to 4 months, depending on the programmed frequencies for the leads.



Impact of programmed pulse width on battery longevity

Modifying programmed pulse width can impact the longevity of an implanted device. The graph below depicts expected battery longevity for the selected percentile patients. The patient's amplitude and frequency settings are kept fixed, and the Pulse Width setting is varied across the X-axis for all leads. Longevity ranges from 5.3 years to 5 months, depending on the programmed pulse widths for the leads. Note: The amplitude and frequency settings are very similar for the 50th and 95th percentile patients, so the lines overlap each other.



Manufacturer Statements

RF Operating Frequencies: Nearby equipment emitting strong magnetic fields can interfere with RF communication, even if the other equipment complies with CISPR emission requirements. The operating characteristics are as follows:

MICS/MedRadio band: 402-405 MHz

The effective radiated power is below the limits as specified in:

Europe: EN ETSI 301 839-2

USA FCC 47 CFR Part 95; 95.601-95.673 Subpart E, 95.1201-95.1219

FCC ID: Y8L-MN0200

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.

**Manufacturer:**

Spinal Modulation
1135 O'Brien Drive
Menlo Park, CA 94025
United States
+1.650.543.6800

Axiom™
Neurostimulator System

CLINICAL PROGRAMMER
USER MANUAL
MODEL MN10700



ST. JUDE MEDICAL™



Caution: Federal law restricts this device to sale by
or on the order of a licensed healthcare practitioner.

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Explanation of Symbols on Product or Package Labeling

| | | | |
|--|-------------------------------------|---|--|
|  | Model Number |  | Not waterproof. Applies to the Programmer when it is not in its carrying case. |
|  | Serial Number |  | Limited waterproof. Applies to the TNS. Applies to the Programmer in its carrying case. |
|  | Read the Manual |  | Turns the Programmer ON and OFF. Turns stimulation OFF on the TNS. |
|  | Consult the Manual |  | Keep Dry |
|  | Contents of Package are Non-Sterile |  | Store between -10°C and 50°C (14°F and 122°F) |
|  | Manufacturing Date |  | Store between 0 and 93% humidity |
|  | Manufacturer |  | The device is a radio transmitter |
|  | Caution |  | Warning. Pay attention. |
|  | Protected against Electric Shock |  | Magnet. Shows the location of the Programmer magnet. |
|  | Quantity |  | Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner. |
|  | Do not use if package is damaged. |  | MR Unsafe |
|  | Electrical Safety Certification | | |

Introduction

The Clinical Programmer is part of the Spinal Modulation Axium Neurostimulator System. It is intended to be used by the clinician or a Spinal Modulation representative to query and program the Neurostimulator (NS), to retrieve data from the NS and to allow for adjustment of the patient's therapy. This User Manual gives detailed instructions on how to use the Clinical Programmer safely, how to recharge it and how to use it to set up the patient's pain management therapy.

Description

Patients who are indicated for the Axium Neurostimulator System system will first undergo a trial period using an external Trial Neurostimulator connected to leads placed within the epidural space near the dorsal root ganglion (DRG). Up to four leads may be placed and connected to the Neurostimulator.

Although the leads and Stimulator hardware used differ, the Programmer hardware and instructions for programming the TNS and INS devices are the same.

NOTE: *In this manual the general abbreviation "NS" is used for information which applies to both TNS and INS. In all other cases the specific abbreviations "TNS" or "INS" are used.*

For specific description of the TNS and INS system components and implant procedures, refer to the relevant labeling.

Two Programmers are available to interact with the NS device.

1. The Clinical Programmer described in this user manual is used to program the stimulation parameters for the NS, as determined by the physician. The NS delivers the programmed stimulation parameters (energy) to the implanted Leads.
2. The Patient Programmer allows the patient to adjust the stimulation settings of the NS devices within limits preset by the physician. The Patient Programmer also allows the patient to turn stimulation off, if necessary. For further information and instructions related to the Patient Programmer, refer to the respective user manual.

Indications for Use

The Axium Neurostimulator System is indicated for spinal column stimulation via epidural and intra-spinal lead access to the dorsal root ganglion as an aid in the management of moderate to severe chronic intractable* pain of the lower limbs in adult patients with Complex Regional Pain Syndrome (CRPS) types I and II.**

*Study subjects from the ACCURATE clinical study had failed to achieve adequate pain relief from at least 2 prior pharmacologic treatments from at least 2 different drug classes and continued their pharmacologic therapy during the clinical study.

**Please note that in 1994, a consensus group of pain medicine experts gathered by

the International Association for the Study of Pain (IASP) reviewed diagnostic criteria and agreed to rename reflex sympathetic dystrophy (RSD) and causalgia, as complex regional pain syndrome (CRPS) types I and II, respectively

Contraindications

Patients contraindicated for the Axium Neurostimulator System are those who:

- Are unable to operate the system
- Are poor surgical risks

Patients who fail to receive effective pain relief during trial stimulation are contraindicated to proceed to the INS procedure.

Warnings, Precautions and Adverse Events

Refer to the Physician Implant Manual for a complete list of warnings, precautions and adverse events for the Axium Neurostimulator System.

Warnings

The Warnings listed below pertain to the Clinical Programmer only:

- The physician must be trained by Spinal Modulation personnel before using the Clinical Programmer. The Clinical Programmer must be used and maintained in accordance with the information in this manual.
- Do not use the Clinical Programmer with an NS device that appears to be faulty or fails to properly communicate.
- Improper use of the Clinical Programmer may cause irreversible injury to the patient. All patients are to be awake and conversant during the procedure to minimize the likelihood of any nerve damage.
- Always set the NS device amplitude to 0 μ A when repositioning a lead or attaching the Connector Cable to the external TNS. When restarting stimulation, increase the NS amplitude slowly until the desired paresthesia is achieved.

Procedural Warning

- Once the ENABLE function is ON for a specific therapy target, any parameter change will be immediately active.

Precautions

The following precautions should be taken to avoid damage to the Clinical Programmer and to ensure proper function:

- Do not drop or mishandle the Clinical Programmer. Physical damage to the Clinical Programmer may impair its function.
- Do not spill fluids on or wash the Clinical Programmer. Excessive moisture may impair its function. If cleaning is necessary, remove soil with a soft damp cloth.
- Do not use abrasive or caustic cleaning products on the Clinical Programmer.
- Do not attempt to open the case for the Clinical Programmer. Attempts to open the case may expose the Clinical Programmer to elements that alter its function.

- The Clinical Programmer has an internal magnet. Keep the Clinical Programmer away from any credit cards, hard drives, or magnetic storage devices as it may demagnetize them.
- Do not operate the Clinical Programmer outside the specified temperature range of 5°C to 40°C (41°F to 104°F). Rapid temperature changes may affect proper device operation.
- Do not store the Clinical Programmer outside the specified temperature range of -10°C to 50°C (14°F to 122°F).
- Do not leave the Clinical Programmer in a car or other places where temperatures can exceed 50°C (122°F).
- Do not burn or otherwise dispose of the Clinical Programmer. Fire may cause the internal battery to explode.
- Do not allow unauthorized use of the Clinical Programmer to avoid injury to patients.
- The NS device can only be programmed using Spinal Modulation's Clinical or Patient Programmer. Do not try to use any other manufacturer's device to program it.
- Do not use the Clinical Programmer or NS in the presence of explosive or flammable gases as this may cause serious injury.
- Do not use the Programmer Charger if the power cord is damaged, excessively worn or frayed. This may cause injury or damage the Programmer.
- Frequent programming of the implanted device will cause the battery to deplete faster. Avoid unnecessary programming.
- If there is any concern regarding the proper function of the Spinal Modulation NS System, please contact your Spinal Modulation representative.

RF OPERATING FREQUENCIES

Nearby equipment emitting strong magnetic fields can interfere with RF communication, even if the other equipment complies with CISPR emission requirements. The operating characteristics are as follows:

MedRadio/MICS band: 402-405 MHz

The effective radiated power is below the limits as specified in

Europe: EN ETSI 301 839-2

USA FCC 47 CFR Part 95; 95.601-95.673 Subpart E, 95.1201-95.1219

FCC ID: Y8L-MN0700

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.

Clinical Programmer System Overview

The Axiom Clinical Programmer allows you to establish two-way communication with the patient's NS device for querying and programming.

It is a portable, hand-held device that can be plugged into a power outlet or be powered by an internal battery. The battery is rechargeable using the power supply provided and a power outlet.

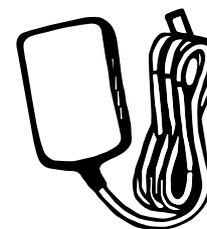
The Clinical Programmer System includes:

- Clinical Programmer with Stylus
- Programmer Charger
- External Auxiliary Magnet
- Programmer Carrying Case
- Clinical Programmer User Manual (this document)

Clinical Programmer Features



Stylus



Programmer Charger



Clinical Programmer

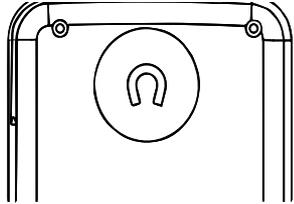
With the Clinical Programmer, you can:

- Turn OFF all stimulation.
- Turn stimulation ON for up to four leads and measure lead impedance.
- Change stimulation settings for each lead.
- Configure Patient Controlled Therapy settings for each lead.
- Enter patient and lead identification information, clinician and clinic name and contact information, and clinician's notes.
- Create and name groups of stimulation sets with each group containing up to four leads with different settings on each lead.
- Perform a real time trial (test) to assess the patient stimulation response for each lead.
- Acquire identification, diagnostic, and historic information about the NS device.

Magnet

A magnet is built into the Clinical Programmer. It is located on the back side of the Programmer underneath the indent with the magnet symbol (shown below).

The NS system has the capability of detecting the presence of a magnet. The magnet puts the NS device in communication mode, allowing it to connect to the Programmer. An alternate function of the magnet is that by holding the magnet over the device long enough, all stimulation therapy will be switched off. (Refer to the “Workspace - Profile>System” section for more information).



⚠ PRECAUTION: Keep the Programmer magnet away from credit cards. It may erase the magnetic strip and render the card useless.

Charging the Clinical Programmer Battery

You will need the Programmer Charger provided to charge the battery in the Clinical Programmer. It takes approximately 2–4 hours to fully charge the battery. The battery charge level is indicated in the “Programmer Status Bar” at the bottom of the screen.

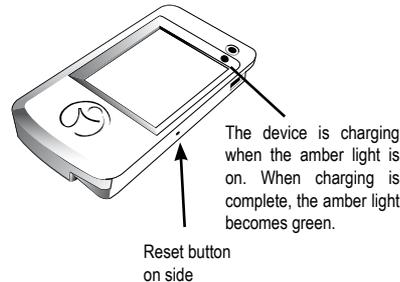
1. Connect the power supply to a power outlet.

Input: 100-240 VAC, 50-60 Hz, 0.6A

Output: 5V --- 3.0A

2. Connect the Charger to the Programmer.

3. When the battery is charging, the battery icon on the screen contains “AC”. When the charging is complete, the indicator light turns green.



When the Clinical Programmer is connected to a power outlet as described above, it is being powered by the outlet and will not use battery power. The battery can be expected to last at least 500 discharge cycles with normal use. Connect the Clinical Programmer to the Charger and attach to an outlet regularly to keep it charged.

Programmer Power Up

Turn the Clinical Programmer ON by pressing the “” button. The Main Menu will be displayed.

NOTE: If the Clinical Programmer screen does not turn on, follow the instructions for charging the battery, and try again.

Main Menu

The Main Menu displays three primary functions:

- **Demo:** Puts the system into a stand-alone demo mode allowing you to use all Programmer functions without it being connected to an NS.
- **Programmer Setup:** Allows you to set the Clinical Programmer date and time, activate the FCE Workspace on the Programmer, and set and modify the Programmer password.
- **Connect to Stimulator:** Opens a screen that allows you to communicate with the NS device.

The Main Menu identifies the device as the Spinal Modulation Clinical Programmer. Furthermore, Programmer’s Serial Number, Software Version, and Manufacturing date are displayed.

At the bottom of the Main Menu, the status bar displays the Programmer – NS connection status, the battery charge level and the time. Refer to the section on the Programmer Status Bar in this User Manual.

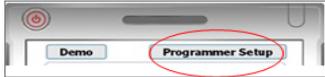


Demo



Select “Demo” on the Main Menu to initiate Demo mode. Buttons will be purple to indicate that the Programmer is operating in Demo mode. No NS device is needed for this mode —just the Programmer. The Programmer will have simulated NS data on it and will simulate the RF communication with the NS.

Programmer Setup



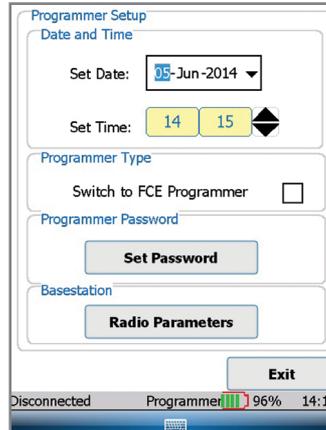
Select “Programmer Setup” on the Main Menu to get the setup screen.

To change the date, select the drop down arrow on the right side of the “Set Date” box. A calendar will appear and you can set the month, day and year using your stylus.

To change the time (24 hour format), first select the hour or minute field that you would like to change.

To change the selected field, use the “Up” or “Down” arrows to increase, decrease or toggle the setting.

NOTE: Establishing a connection updates the NS device’s clock to the newly set time.



Switch to FCE Programmer

By checking this box the Clinical Programmer will get additional functionality, which should only be used by Spinal Modulation’s Field Clinical Engineers and Staff.

Set Password

A password may be set to limit access to the Programmer. The password is for the Programmer itself and is not associated with any NS.

Establishing Communication with the NS Device

To change the patient’s stimulation settings, you must first establish communication between the Clinical Programmer and the patient’s NS device.



1. Make sure that the Clinical Programmer is turned on, and the Main Menu screen is displayed.
2. Press “Connect to Stimulator” on the Main Menu.
3. Select the text box next to “Stimulator SN.”

4. Enter the serial number using the pop-up keyboard.

If the serial number format is valid for an NS device, the “Connect” button will be enabled.

5. Press the “Connect” button.

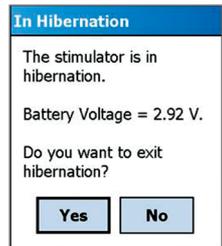
After pressing the “Connect” button, the “Cancel” button becomes enabled. If the Cancel button is pressed, the telemetry connection is cancelled.

6. Move the Clinical Programmer magnet over the NS device in a circular motion to connect. The indicator status bar on the bottom left of the screen will display “Connected” if the connection attempt is successful. If the Programmer could not communicate with the NS device, an error message will appear and “Disconnected” will be displayed in the status bar.

NOTE: If after two minutes the Clinical Programmer has failed to communicate with the NS device, the Programmer will automatically cancel the connection attempt. Try to communicate with the NS device by again pressing the “Connect” button, and begin moving the Clinical Programmer magnet symbol over the NS device in a circular fashion.

When a successful connection is established, the Programmer chimes, and the NS device will be queried.

NOTE: If the ‘In Hibernation’ message is displayed, select ‘Yes’ to exit Hibernation. Hibernation is a low-power state that the NS is in prior to first use.



7. For the duration of the programming session, keep the Clinical Programmer near the NS device. Moving the Programmer too far away may cause the telemetry connection to be lost.

Back to Main Menu

Located at the bottom right side of the Programmer Connect window, the “Exit” button is used to return to the Main Menu.

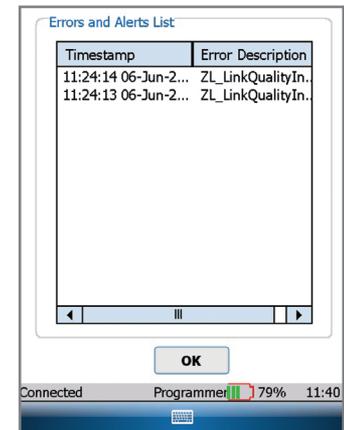
Navigation and Screen Elements

Neurostimulator Dashboard



Once the selected NS device is connected to the Clinical Programmer, the NS Dashboard is displayed in the screen’s header providing:

- **Patient ID:** The patient’s ID Number



- **Stimulator Serial Number:** The NS device's serial number
- **Alerts Button:** The button turns orange when any of the NS System Alerts become active. When the "Alerts" button is orange, press the button to display a window showing details of all the System Alerts. An example of the screenshot is shown to the right.

Programmer Status Bar



Located at the bottom of the Clinical Programmer screen, the Programmer Status Bar displays:

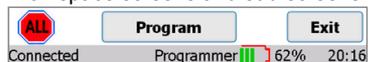
- **Programmer-Stimulator Connection Status:** Displays the status of the communication between the Clinical Programmer and the NS device: "Connecting" is displayed when establishing a connection. "Connected" is displayed when there is communication between the Clinical Programmer and the NS device. "Disconnected" is displayed when there is no communication between the Clinical Programmer and the NS device.
- **Programmer Battery Level:** Displays the Clinical Programmer battery charge level. It is recommended that the Programmer be plugged in and charging when not in use. Plug in and charge the Programmer before reaching 30% remaining life.
- **Programmer Clock:** Displays the time. See User Manual section on Change the Date and Time.

Workspace Navigation



Once the NS is connected, tabs are displayed for the systems' four main workspaces ("Profile", "Stim", "Group" and "Utility"). The Workspaces are used to view and program the NS therapy settings and to obtain diagnostic information. A record of the programmed settings and diagnostic information is generated after every session. A fifth Workspace labeled "FCE" will only appear when FCE mode is ON.

Workspace screens and sub-screens are navigated by selecting the labeled tabs.



Located at the bottom of each of the Workspaces are the "ALL", "Program" and "Exit" buttons.

- **Exit button:** is used to close the current window, end the patient therapy session, and return to the Main Menu.
- **Program button:** programs all changes made within the current Workspace.
- **ALL button:** turns all stimulation off.

NOTE: Returning to the Main Menu or turning off the Programmer will not change any of the programmed NS settings.

When programming is complete, select the "Exit" button to conserve power.

Temporary and Permanent Programming

Whenever a change is made to a parameter value or other data field while the NS is within telemetry range, this value immediately becomes temporarily active. The corresponding value or data selection appears in a red bold underlined font.

NOTE: The "temporarily active" state does not apply to the Group workspace.

Temporary programmed values or text data can be **permanently programmed** by pressing the program button. The font color changes from red to black.

NOTE: When leaving a Workspace while values are temporarily active you will be prompted to either program these values permanently or cancel the pending changes.

Parameters can be temporarily active on multiple tabs of the same Workspace.

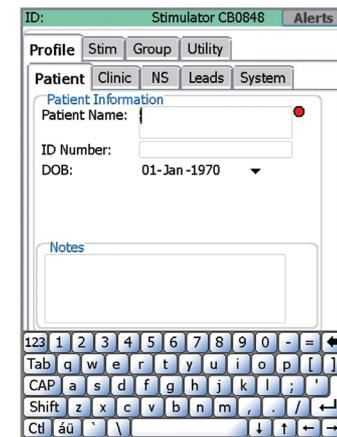
More on Editing Text Fields

NOTE: Selecting a text field will pop up a keyboard at the bottom of the screen. To close the keyboard after modifying the entry, press the keyboard key centered in the blue bar at the bottom of the screen.

While text fields are **being edited**, they appear in a black bold font (no underline). At the same time to the right of the text field a red dot indicates that editing is in progress.

Once editing for a field is complete, tap the red dot to make the change temporarily active. The red dot disappears and the font changes from black bold to red bold underlined.

Only upon pressing the programming button does the change become **permanently programmed** and the font color changes from red to black.



Using the Workspaces

Profile Workspace

Press the "Profile" tab to access the Profile Workspace. The Profile Workspace is divided into five tabs ("Patient", "Clinic", "NS", "Leads" and "System") which are used to:

- Enter patient information
- Enter clinician contact information
- Enter NS device information
- Enter lead identification information
- Change basic system parameters

Patient Information Tab [Profile>Patient]

Enter or modify the patient information in the fields provided:

- **Patient Name:** Enter the patient's name using the on-screen keyboard.
- **ID:** Enter the patient's unique identification using the on-screen keyboard.
- **Date of Birth:** Enter the patient's date of birth using the drop-down calendar.
- **Notes:** Enter notes if needed.

Profile | Stim | Group | Utility
Patient | Clinic | NS | Leads | System
Patient Information
Patient Name: **Bob Johnson**
ID Number: **JO52122**
DOB: 24-Feb-1952
Notes
Left unilateral leg pain
ALL | Program | Exit
Connected Programmer 80% 11:38

NOTE: Pressing the "äü" button near the space bar allows the use of accented characters.

Clinic Information Tab [Profile>Clinic]

Enter or modify the physician and clinic information in the text fields provided:

- **Physician Name**
- **Clinic Name**
- **Clinic After Hours Contact Phone Number**
- **Clinic Phone Number**
- **Clinic Email**
- **Clinic Address**

ID: JO52122 Stimulator CB0848 Alerts
Profile | Stim | Group | Utility
Patient | Clinic | NS | Leads | System
Clinic Information
Physician Name: **Dr. Smith**
Clinic Name: **ABC Pain Clinic**
After Hrs Contact: **650-543-6800**
Phone: **650-543-6800**
Email: **info@spinalmodulation.com**
Address: **1135 O'Brien Dr,
Menlo Park, CA 94025**
ALL | Program | Exit
Connected Programmer 93% 14:26

Stimulator Information Tab [Profile>NS]

The NS tab provides a summary of information related to the NS.

- **Date of Implant:** Enter the Stimulator date of use using the drop-down calendar.
- **Implant Battery Voltage:** The current battery voltage is automatically displayed here.
- **History:** Shows recent programming history at the start of follow-up.

NOTE: The battery information pertains to an INS and does not pertain to the TNS.

ID: JO52122 Stimulator CB0848 Alerts
Profile | Stim | Group | Utility
Patient | Clinic | NS | Leads | System
Stimulator Information
Implant Date: 05-Jun-2014
Stimulator FW Version: 5.1.0.1
Stimulator Battery
Stimulator Voltage: 2.80 V
History
Last Patient Program: 01-Jan-1970
Last Clinic Program: 05-Jun-2014
ALL | Program | Exit
Connected Programmer 93% 14:27

Leads Information Tab [Profile>Leads]

Lead 1 through **Lead 4** are the default labels used to identify the implanted leads in the "Stim" Workspace. It is recommended that these names be changed into something more meaningful, for example the body region it covers.

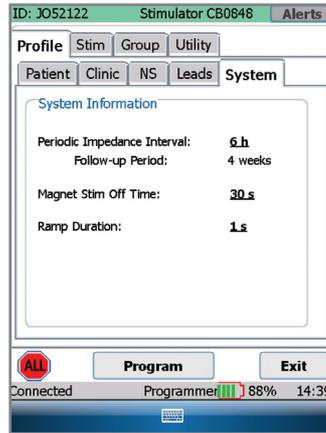
- **Target Name:** for each of the implanted leads, enter the body region covered (text field).
For each of the leads enter the Lot and Model number:
- **Lot #:** Enter the Lot number found on the lead packaging.
- **Model #:** Enter the lead Model number.

ID: JO52122 Stimulator CB0777 Alerts
Profile | Stim | Group | Utility
Patient | Clinic | NS | Leads | System
Lead Information
Lead # Lot # Model # Target Name
1 100001 MN10450 L Foot
2 100001 MN10450 L Leg
3 0 =
4 0 =
ALL | Program | Exit
Connected Programmer 90% 15:26

System Information Tab [Profile>System]

From the system tab the following system parameters can be managed:

- **Periodic Impedance Interval:** Set the frequency with which you want the system to measure lead impedance.
- **Follow-up Period:** A calculated field which displays the recommended follow-up time based on the programmed settings. It is an indicator of when the NS will run out of memory and will begin to overwrite old data.
- **Ramp Duration:** Ramp duration is how long it takes for the NS to reach the requested amplitude. If set to 8 seconds, the NS will take 8 seconds to get from 0 to the requested amplitude when a lead is switched from not enabled to enabled. Ramping also occurs when the step between the current amplitude and the next amplitude is greater than 100 mV.
- **Magnet Stim Off Time:** Allows you to control how long it takes before a magnet held over the device switches off delivered therapy.



Stim Workspace

Press the “Stim” tab to access the Stimulation Settings Workspace. The Stimulation Settings Workspace is divided into five tabs which are used to:

- Activate (turn on) up to four leads
- Adjust electrode configurations
- Measure impedance
- Set nominal values to begin stimulation
- Perform trial mapping
- Confirm the response and sensation of specific body regions to be stimulated

Stim Tabs [Stim>Target Name]

The Stim tabs are the main tabs from which therapy is controlled and programmed. This can be done either temporarily (testing) or permanently.

- **Select Group:** Select the group for which you want to change the stimulation settings.

NOTE: In the Group Workspace, up to four different groups can be defined, each with their own stimulation parameters. A group can be linked for example to a specific activity or posture. Refer to the Group Workspace section in this manual for more information.

- **Select the Tab:** To adapt stimulation parameters, choose the desired target labeled tab (The sample screen shows “L Foot” as the target.)

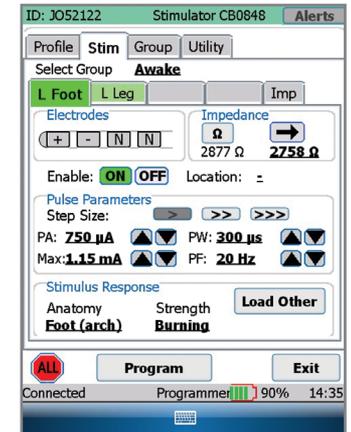
NOTE: There are up to four tabs that can be labeled with the body region in which stimulation with the corresponding lead is targeting (defined in Profile>Leads). For each body region (lead) stimulation can be adjusted independently.

- **Electrode Configuration:** Each lead has four electrodes each of which can be programmed with a positive or negative polarity, or be programmed as neutral (off). There must be at least one positive and one negative electrode before the Clinical Programmer allows the amplitude to be adjusted and for the lead to be enabled.

1. Select one of the four electrodes by clicking on it using the stylus. Clicking once will turn the electrode positive (“+”), clicking it twice will turn it negative (“-”) and clicking it three times will turn it Neutral (“N”) again. To exit from the electrode editing mode, click on the neighboring Impedance box.
2. Continue by setting each of the implanted leads with at least one positive and one negative electrode for each body region to be treated.

- **Impedance:** Press the “Instant Impedance” button (“Ω”) to measure the lead’s impedance. Once pressed, the impedance value will be displayed underneath the button. If you want the NS to use this Instant Impedance value for therapy delivery, press the “Transfer Instant Impedance” button (“→”).

NOTE: The patient may feel the effect of the impedance measurement. Alert the patient to the possible stimulation.



A transferred impedance value is required before other stimulation parameters can be selected.

- **Enable:** Select “ON” to enable the lead so that it provides stimulation therapy to the patient. Select “OFF” if the lead is not being used.
 - When Enable is ON, the “ON” button will turn the color green.
 - When Enable is OFF, the “OFF” button will turn the color black.
 - The button border is red if the activation state is different from the programmed value.

WARNING: Once Enable is ON for this target, any parameter change will be immediately active.

NOTE: When the lead electrode configuration changes, the lead is disabled and the amplitude is automatically changed to zero. The lead electrode configuration must be valid prior to activating the lead. A valid lead configuration must include at least one positive and one negative electrode. Lead “Enable” must be “ON” before the amplitude can be increased from 0 μA .

- **Location:** Enter the spinal level where stimulation therapy is delivered by this lead
- **Pulse Parameters:** To select and change pulse parameters, first press the desired increment level: Fine(>), Medium(>>), Coarse(>>>).
 - Amplitudes below 2.0 mA (>: 25 μA , >>: 50 μA , >>>: 200 μA)
 - Amplitudes above 2.0 mA (>: 50 μA , >>: 100 μA , >>>: 400 μA)
 - Pulse Width (>: 10 μs , >>: 40 μs , >>>: 100 μs)
 - Frequency (>: 2 Hz, >>: 4 Hz, >>>: 10 Hz)
 - The UP (\wedge) and Down (\vee) buttons next to the specific pulse parameter will allow the user to change the setting at the desired increments.

The following table lists the pulse parameters, their range, increments and default value:

| Specifications | Range | Step Size | Default Value |
|---|-------------------------|---|-------------------|
| Pulse Amplitude - PA (μA) (Depending on measured impedance) | 0 – 6000 μA | 25 μA : 0-2000 μA 50 μA : 2000-6000 μA | 0 μA |
| Maximum Pulse Amplitude - Max (μA) Programmable by Patient | Same as PA | Same as PA | 0 μA |
| Pulse Width – PW (μs) | 40 – 1000 μs | 10 μs | 300 μs |
| Pulse Frequency - PF (Hz) | 4 – 80 Hz | 2 Hz | 20 Hz |

- **Maximum Amplitude:** Enter the maximum stimulation amplitude, from the clinically set amplitude up to 6.0 mA, that the patient is allowed to set for each lead.

WARNING: Unless the stimulation settings are known for a specific patient, start with a Pulse Amplitude of 0 μA .

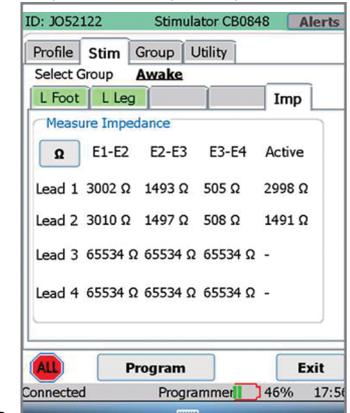
- **Stimulus Response:** Allows you to assign a descriptor to a set of programmed pulse parameters. The descriptor is composed of a body region where the sensation is felt and a description of the sensation. (E.g. Lower Back & Massaging → Lower Back Massaging). **A Stimulus Response must be selected in order to program the set of pulse parameters.** The Load Other button pulls down a drop-down menu and allows the user to load another Stimulus Response that has been previously saved for that lead.

NOTE: When restarting stimulation, increase the amplitude slowly until paresthesia is achieved.

Impedance Tabs [Stim>Impedance]

The **Impedance Button (Ω)** initiates impedance measurements between adjacent electrode couples in all of the configured leads and displays on the Imp screen.

NOTE: 65534 Ω indicates an open or missing lead.



Group Workspace

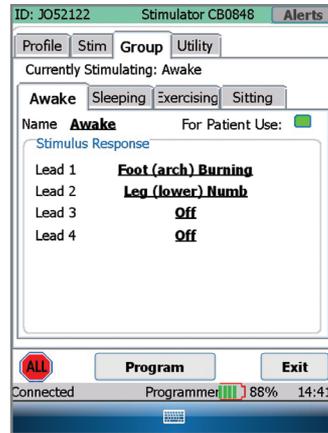
Press the “Group” tab to access Group Workspace.

The Group Workspace is divided into four tabs (Groups) by default named “Awake”, “Sleeping”, “Exercising” and “Sitting”. Each tab summarizes Group specific settings for each of the implanted leads. These Groups can be easily programmed as needed by the patient using the Patient Programmer.

Group Tabs [Group>Group Name]

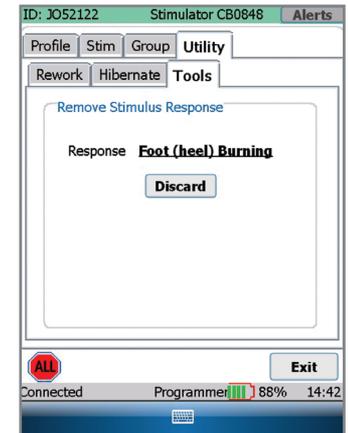
Each Group can be configured by selecting the desired tab.

- **Name:** The Group can be renamed here (free-form text entry)
- **For Patient Use:** The Group will be displayed on the Patient Programmer only if this box is checked. Note that the currently active Group must be checked/enabled.
- **Lead 1 through Lead 4:** The Stimulus Response for each Lead within a Group can be changed here. Stimulus Responses that have been previously saved for that Lead will be shown in the drop-down menu.



Discard

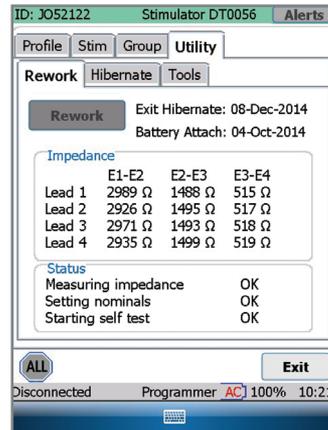
When you are close to using all 12 Stimulation Responses, the Discard button may be used to delete any unused Stimulation Responses.



Rework

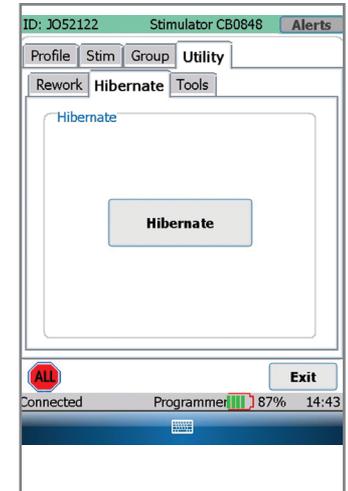
The Rework screen is used to rework a TNS between patient trials. The Rework button performs the following actions:

- Measures detected impedances. Impedances will display as 65k if no load is detected.
- Sets nominal values on the TNS. This will remove all settings from the previous patient.
- Performs a self-test on the TNS.



Hibernate

Hibernate mode is used to conserve battery life of the INS while on the shelf.



Battery Longevity

Programmed settings impact the longevity of the implanted device. With 2 leads at 1600 ohms impedance programmed at nominal stimulation settings of 800 μA amplitude, 300 μsec pulse width, 20 Hz frequency, the battery may be expected to last 3.3 years. These nominal settings represent average settings seen in world-wide use of the Axium system. Higher stimulation settings, especially pulse amplitude and frequency, result in greater energy usage and therefore reduce the estimated battery longevity.

The system has two warnings about battery life – ERI which is Elective Replacement Indication when the battery is low but stimulation is still available, and EOS which is End of Service when stimulation has been permanently turned off. At nominal settings, there is a 1 month period between ERI and EOS. Depending on specific settings, the duration may range between 20 and 35 days.

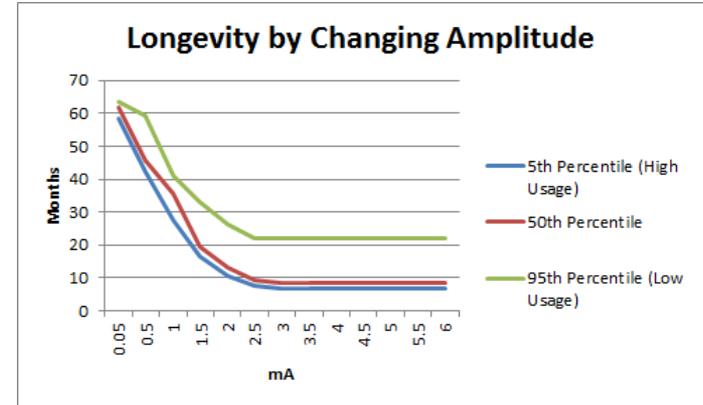
The table below includes patient settings used in the US ACCURATE Clinical Study. The 5th percentile, 50th percentile, and 95th percentile patients were selected based on estimated longevity. The Low Settings example shows the effect of reducing amplitude and frequency.

| Patient Settings used in the US ACCURATE Clinical Study | | | | | | |
|---|-----------------------------|---------------------------------|----------------|------------------|-------|-----------------------------|
| Patient | Amplitude (μA) | Pulse Width (μsec) | Frequency (Hz) | Impedance (ohms) | Leads | Estimated Longevity (Years) |
| 5th Percentile | 2750 | 410 | 20 | 1609 | 2 | 0.9 |
| | 1350 | 300 | 34 | 1796 | | |
| 50th Percentile | 675 | 1000 | 16 | 1727 | 1 | 3.5 |
| 95th Percentile | 500 | 160 | 20 | 1886 | 1 | 4.9 |
| Low Settings | 650 | 110 | 10 | 1140 | 2 | 5.0 |
| | 350 | 230 | 10 | 1968 | | |

The number of leads is not directly proportional to longevity, but on average the longevity decreases as multiple leads are added. The summation of energy delivered through the leads is the primary factor for longevity. Note that both the 0.9 year and the 5.0 year patients have two leads, but the 0.9 year patient is programmed with higher energy settings of 2.75 mA amplitude and 34 Hz frequency compared to the 5.0 year patient's lower energy settings of 350 μA amplitude and 10 Hz frequency.

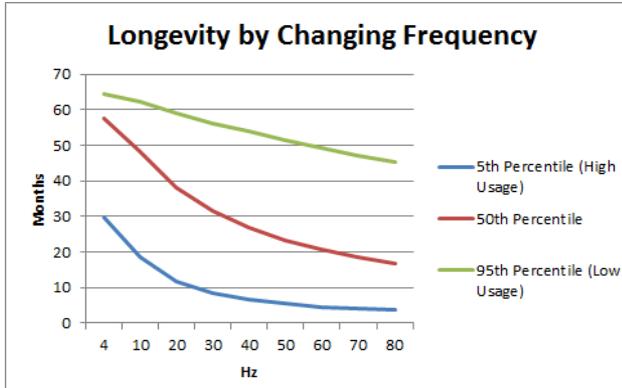
Impact of programmed amplitude on battery longevity

Modifying programmed amplitude can impact the longevity of an implanted device. The graph below depicts expected battery longevity for the selected percentile patients. The patient's pulse width and frequency settings are kept fixed, and the Amplitude setting is varied across the X-axis for all leads. Longevity ranges from 5.3 years to 7 months, depending on the programmed amplitudes for the leads. Note: When the INS reaches maximum output, the expected longevity plateaus.



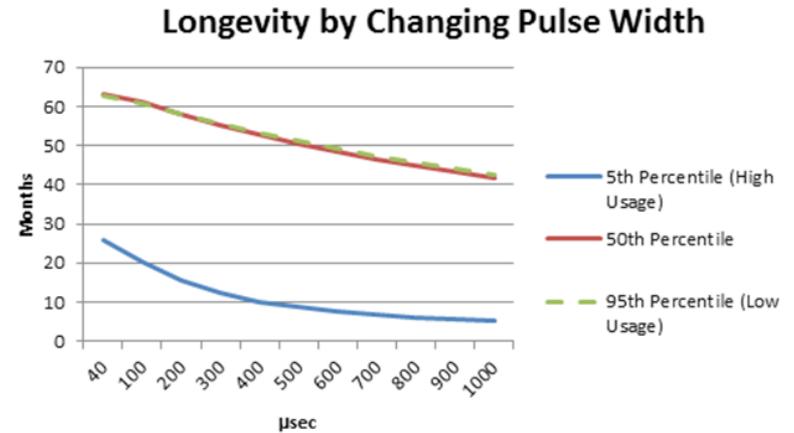
Impact of programmed frequency on battery longevity

Modifying programmed frequency can also impact the longevity of an implanted device. The graph below depicts expected battery longevity for the selected percentile patients. The patient's pulse width and amplitude settings are kept fixed, and the Frequency setting is varied across the X-axis for all leads. Longevity ranges from 5.4 years to 4 months, depending on the programmed frequencies for the leads.



Impact of programmed pulse width on battery longevity

Modifying programmed pulse width can impact the longevity of an implanted device. The graph below depicts expected battery longevity for the selected percentile patients. The patient's amplitude and frequency settings are kept fixed, and the Pulse Width setting is varied across the X-axis for all leads. Longevity ranges from 5.3 years to 5 months, depending on the programmed pulse widths for the leads. Note: The amplitude and frequency settings are very similar for the 50th and 95th percentile patients, so the lines overlap each other.



Guidance and Manufacturer's Declarations

| GUIDANCE AND MANUFACTURER'S DECLARATION <i>Electromagnetic Emissions</i> | | |
|---|------------|---|
| The Spinal Modulation Neurostimulator System is intended for use in the electromagnetic environment specified below. The customer or the user of the Spinal Modulation Neurostimulator System should assure that it is used in such an environment. | | |
| Emissions test | Compliance | Electromagnetic Environment – Guidance |
| RF Emissions 1 | Group 2 | The Spinal Modulation Neurostimulator System must emit electromagnetic energy in order to perform its intended function. Nearby electronic equipment may be affected. |
| RF emissions CISPR 11 | Class B | |
| Harmonic emissions IEC 61000-3-2 | Class B | |
| Voltage fluctuations/ flicker emissions IEC 61000-3-3 | Complies | |
| | | The Spinal Modulation Neurostimulator System is suitable for use in all establishments, including domestic establishments and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes. |
| CISPR 14-1 | Complies | The Clinical Programmer is not intended to be connected to other equipment except the Programmer Charger. |

| GUIDANCE AND MANUFACTURER'S DECLARATION <i>Electromagnetic Emissions</i> | | | |
|---|--|------------------------------|---|
| The Spinal Modulation Neurostimulator System is intended for use in the electromagnetic environment specified below. The customer or the user of the Spinal Modulation Neurostimulator System should assure that it is used in such an environment. | | | |
| Immunity | IEC 60601 Test Level | Compliance Level | Electromagnetic Environment Guidance |
| Electrostatic discharge (ESD) | IEC 61000-4-2 | ± 6 kV contact ± 8 kV air | Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%. |
| Electrical fast transient/burst IEC 61000-4-4 | ± 2 kV for power supply lines ± 1 kV for input/output lines | Pass | Mains power quality should be that of a typical commercial or home environment |
| Surge IEC 61000-4-5 | ± 1 kV line(s) to line(s) ± 2 kV line(s) to earth | | Mains power quality should be that of a typical commercial or home environment |

| | | | |
|--|---|--|--|
| Voltage dips, short interruptions and voltage variations on power supply | input lines IEC 61000-4-11 <5% UT (>95% dip in UT) for 0.5 cycle 40% UT (60% dip in UT) for 5 cycles 70% UT (30% dip in UT) for 25 cycles <5% UT (>95% dip in UT) for 5 s NOTE UT is the a.c. mains voltage prior to application of the test level. | | Mains power quality should be that of a typical commercial or home environment |
| Power frequency (50/60 Hz) magnetic field IEC 61000-4-8 | 3 A/m | | Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial, hospital, or home environment. |

| GUIDANCE AND MANUFACTURER'S DECLARATION <i>Electromagnetic Immunity</i> | | | |
|---|-----------------------------|------------------|--|
| The Spinal Modulation Neurostimulator System is intended for use in the electromagnetic environment specified below. The customer or the user of the Spinal Modulation Neurostimulator System should assure that it is used in such an environment. | | | |
| Immunity Test | IEC 60601 Test Level | Compliance Level | Electromagnetic Environment Guidance |
| Conducted RF IEC 61000-4-6 | 3 Vrms 150 kHz to 80 MHz | 3 V | Portable and mobile RF communications equipment should be used no closer to any part of Spinal Modulation Neurostimulator System, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. The recommended separation distance is a minimum of 0.2 meter for transmitters of 80 MHz to 2.5 GHz Interference may occur in the vicinity of equipment marked with the following symbol:  |
| Radiated RF IEC 61000-4-3 | 3 V/m 80 MHz to 2.5 GHz | 3 V/m | |
| NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies. | | | |
| NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people. | | | |

Recommended separation distances between portable and mobile RF communications equipment and the Spinal Modulation Neurostimulator System

The Spinal Modulation Neurostimulator System is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the Spinal Modulation Neurostimulator System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the System.

| Rated maximum output power of transmitter (W) | Separation distance according to frequency of transmitter (m) | | |
|---|---|-------------------|--------------------|
| | 150 kHz to 80 MHz | 80 MHz to 800 MHz | 800 MHz to 2.5 GHz |
| 0.01 | 0.12m | 0.12m | 0.23m |
| 0.1 | 0.37m | 0.37m | 0.74m |
| 1 | 1.17m | 1.17m | 2.33m |
| 10 | 3.70m | 3.70m | 7.37m |
| 100 | 11.70m | 11.70m | 23.30m |

NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Appendix I: Programmable Parameters and Values

| Parameter | Programmable Values | Default |
|-------------------------|---|-------------|
| Pulse Amplitude | 0 – 6000 μ A 0-2000 μ A (25 μ A increments) 2000-6000 μ A (50 μ A increments) | 0 μ A |
| Maximum Pulse Amplitude | Same as Pulse Amplitude | 0 μ A |
| Pulse Width | 40 – 1000 μ s (10 μ s increments) | 300 μ s |
| Pulse Frequency | 4 – 80 Hz (2 Hz increments) | 20 Hz |

| Data Field | Selectable Values |
|-----------------------------|--|
| Periodic Impedance Interval | Off; 30 s; 1 min; 5 min; 20 min; 30 min; 1 h; 6h; 12 h; 1 days; 3 days; 7 days; 10 days; 30 days |
| Lead Model Number | MN10350, MN10450 |
| Stimulus Response Anatomy | Off; Lower Back; Back & Leg; Thigh; Knee; Lower Leg; Ankle; Foot (top); Foot (bottom); Toes; Hip; Groin |
| Stimulus Response Sensation | Off; Burning; Buzzing; Cold; Comforting; Cramping; Heavy; Massaging; Numb; Other; Pain; Paresthesia; Pressure; Relief; Soothing; Spasm; Tapping; Tingling; Vibrating; Warm |
| Spine Location | L T10; R T10; L T11; R T11; L T12; R T12; L L1; R L1; L L2; R L2; L L3; R L3; L L4; R L4; L L5; R L5; L S1; R S1; L S2; R S2 |
| Magnet Turnoff Time | Off; 1 s; 2 s; 3 s; 4 s; 5 s; 6 s; 7 s; 8 s; 9 s; 10 s; 15 s; 20 s; 25 s; 30 s; 40 s; 50 s; 1 min; 70 s; 80 s; 90 s; 100 s; 110 s; 2 min |
| Ramp Duration | 1 s; 2 s; 3 s; 4 s; 5 s; 6 s; 7 s; 8 s |

Appendix II: Troubleshooting

Pop-up Messages

| Pop-up Messages | Condition | Buttons | Resolution |
|---|---|---------------------------|---|
| All stimulation has been turned OFF. | All stimulation turned off due to data corruption. | “OK” | Contact your Spinal Modulation Representative. |
| Changes since last programming were lost due to loss of connection with the stimulator. Please reconnect to stimulator. | Communication was lost prior to programming attempt. | “OK” | Reconnect to Stimulator and re-enter program changes. |
| Communication is poor. | All RF channels have noise levels above the noise threshold. | “OK” | Hold the Programmer closer to the Stimulator, turn off other equipment in the area, or move to another area in the building, etc. |
| Connection with stimulator was lost. Please reconnect. | Dropped RF connection. | “OK” | |
| Do you want to program changes? | A new Workspace or Exit button was selected without saving (programming) changes. | “Yes” “No” “Cancel” | |
| Invalid FCE password. Please try again. | Invalid FCE password was entered. | “OK” | Only Spinal Modulation representatives should access the FCE mode. |
| Lead N detected a Current Too High condition. | During an impedance measurement, the measured current was too high. | “OK” | Repeat measurement. If problem reoccurs, contact your Spinal Modulation representative. |

| Pop-up Messages | Condition | Buttons | Resolution |
|---|---|---------|--|
| Lead N impedance of NNN Ω is out of range. | Lead impedance is out of range | "OK" | Repeat measurement or accept as is. |
| Maximum stimulation output has been reached. | Maximum stimulation output has been reached (4.6V). | "OK" | Investigate lead integrity. |
| Please specify a Stimulus Response before programming | Attempt to program a set of pulse parameters without a Stimulus Response Name. | "OK" | Select stimulus response. |
| Programmer battery is low. Please recharge. | Programmer battery reaches 30%. | "OK" | Recharge as soon as possible. |
| Programmer is booting after a reset. When you click OK the Programmer will switch off. Press the Power button to restart. | Hardware reset Button on the Programmer was pressed, Programmer detected an error or the Programmer is launched for the first time. | "OK" | Press Power button  |
| Programmer storage space is low. Please contact your Spinal Modulation representative for maintenance. | Programmer storage is nearing full capacity (log files are stored on the Programmer with each significant operation such as programming). Message is displayed and file logging should continue. Normal operation continues after user acknowledgement. | "OK" | Contact your Spinal Modulation Representative. |
| Stimulation for one or more leads has been turned OFF. | One or more leads turned off due to Low Impedance. | "OK" | Perform impedance measurement and re-enable if within range. Otherwise, investigate lead integrity. |
| Stimulation has been turned OFF due to a magnet. | Stimulation can be turned off by applying a magnet for the duration specified by the Magnet Turnoff Time programmable parameter. | "OK" | |
| Stimulation has been turned OFF. | Stimulation can be turned off, either by the "All Stim OFF" software button on the Programmer, or the Off switch on the TNS. | "OK" | |
| Stimulator battery has reached End of Service (EOS). Stimulation has been turned OFF permanently. | Battery has reached EOS voltage. Stimulation is disabled in order to preserve power for RF communication. | "OK" | Schedule replacement of the Stimulator. |
| Stimulator battery has reached the Elective Replacement Indicator (ERI). | Battery has reached ERI voltage. | "OK" | Schedule replacement of the Stimulator. |

| Pop-up Messages | Condition | Buttons | Resolution |
|---|--|---------|---|
| The stimulator has been set to default values. | The Programmer has encountered an NS with unreadable or invalid data. Parameters have been set and programmed to default values. | "OK" | Setup device parameters as desired. |
| The stimulator is in Upgrade Mode. Please reconnect with programmer in FCE mode or contact your Spinal Modulation representative. | NS in Boot mode. All stimulation is disabled. | "OK" | Contact your Spinal Modulation Representative. |
| The stimulator has unreadable data. Please reconnect with programmer in FCE mode or contact your Spinal Modulation representative. | NS has unreadable data (such as Trim data). | "OK" | Contact your Spinal Modulation Representative. |
| Unable to connect to stimulator. Make sure the programmer is close to the stimulator and try again. | Cannot connect to the NS. | "OK" | Move the Programmer above the Stimulator in circular motions. |
| The file "CProgrammerMobile" cannot be opened. Either it is not signed with a trusted certificate, or one of its components cannot be found. If the problem persists, try reinstalling this file. | Programmer cannot operate due to file corruption. | "OK" | Contact your Spinal Modulation Representative. |
| All other messages | | "OK" | <ul style="list-style-type: none"> • Attempt to perform the actions again if possible. • Contact your Spinal Modulation Representative. |

Error messages may contain additional troubleshooting information such as "Code P-162, Key: *NsNotProgrammed*". This is an aid for Spinal Modulation engineers to debug errors.

When you receive such error codes, please take note of the error code and contact your SMI representative.

Troubleshooting Other Issues

| Condition | Resolution |
|---|---|
| The Programmer is unresponsive (frozen screen, unable to power on, etc.). | Press the reset button on the side of the Programmer. Note: this will not change the Stimulator or Programmer settings. |

| Condition | Resolution |
|---|---|
| Impedance measurements may timeout when <u>all</u> measured leads are below 8Hz. | Increase Pulse Frequency to 8Hz to measure impedance and then return to desired Pulse Frequency. |
| Depending on NS programmed settings, stimulation amplitude may slightly dip during periodic impedance (nominally every 6 hours) and may be noticeable to the patient. | Increasing the stimulation amplitude may decrease the dip in amplitude. Also, the Periodic Impedance interval can be adjusted for less frequent occurrence. |
| Lead Disabled message (due to impedance) is always shown on Connection. | The message can only be cleared when a valid impedance measurement occurs on the lead that was disabled. If it cannot be cleared, contact your Spinal Modulation representative. |
| NS Battery voltage is displayed as 65.00 V. | This is the initial NS battery measurement value. A valid value will automatically replace it when the next periodic battery measurement occurs. |
| Keyboard is stuck on display. | Try to navigate to another screen. If the keyboard remains stuck, press the reset button on the side of the Programmer. This will not change the Stimulator or Programmer settings. |
| Data fields on non-therapy screens (such as Date of Birth) may display incorrectly. This is a display issue that does not impact therapy. | Reprogram the data. |
| Basestation Firmware version on the Clinical Programmer start-up screen shows as "FV". | Connect to an NS device then press the Reset button. This will not change the Stimulator or Programmer settings. |

| Condition | Resolution |
|---|--|
| A spinning icon is displayed on the Alerts screen, possibly blocking full view of the alerts. | Navigate away and then return to the Alerts screen. |
| Spine location setting may change after an NS reset. | Reprogram Spine location. |
| When the Pulse Frequency is programmed for less than 8 Hz, it may take up to twice as long for the programmed Ramp Duration to reach the desired Amplitude. | Decrease the programmed Ramp Duration or increase the programmed Pulse Frequency. |
| Following a magnet reset, another magnet reset is not possible until the NS is programmed with a Clinical Programmer. | Use the Clinical Programmer to re-program the NS after a magnet reset. If unsuccessful, contact your Spinal Modulation representative. |



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Axium™
Neurostimulator System

TRIAL NEUROSTIMULATOR
PHYSICIAN MANUAL
MODEL MN10100

R_{ONLY}

Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.



ST. JUDE MEDICAL

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Explanation of Symbols on Product or Package Labeling

| | | | |
|---|--|---|-----------------------------------|
|  | Model Number |  | Serial Number |
|  | Read the Instructions for Use |  | Consult the Instructions for Use |
|  | Contents of Package are Non-Sterile |  | Protected against Electric Shock |
|  | Manufacturing Date |  | Manufacturer |
|  | Turns off all stimulation on the TNS |  | The device is a radio transmitter |
|  | Limited waterproof |  | Keep Dry |
|  | Store between 0 and 93% humidity |  | Do not use if package is damaged |
|  | MR Unsafe |  | Quantity |
|  | Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner. | | |
|  | Storage Temperature: Store the TNS between -10°C and 50°C (14°F and 122°F) | | |
|  | Electrical Safety Certification | | |

Glossary

Lead – Surgical wire: takes electrical signals from the neurostimulator to the stimulation area.

NS – Neurostimulator: stimulator device that creates electrical signals to stimulate the neural structures. Refers to either the Trial Neurostimulator or the Implantable Neurostimulator.

TNS – Trial Neurostimulator: external NS that attaches to the Connector Cable which is connected to leads.

INS – Implantable Neurostimulator: NS implanted in the back or abdomen and directly connected to the leads.

Connector Cable – Connects the implanted leads to the TNS.

Patient Programmer – Portable, hand-held device: allows the patient to modify the stimulation settings on the NS.

Clinical Programmer – Portable, hand-held device: used by the clinician to program the NS device.

Computer Tomography (CT) Imaging – Computerized X-ray imaging: produces electronic images of tissues and organs.

Diathermy – High energy heat: used to cut or cauterize during surgery, or a type of therapy.

DRG Stimulation – Electrical pulses applied to the dorsal root ganglion in order to block pain signals to the brain.

Electromagnetic Interference (EMI) – Electrical signals that interfere with the device function.

Magnetic Resonance Imaging (MRI) – Medical imaging: produces electronic images of tissues and organs.

Paresthesia – Tingling sensation felt during therapy delivery: produced by spinal cord stimulation.

Precaution – Situations the patient should be aware of in order to avoid uncomfortable stimulation and possible damage to the TNS device.

Program – Instructions or changes to stimulation settings that are programmed into the Programmer and transmitted to the NS device.

Stimulation – A pain therapy reference to small electrical pulses felt as a tingling sensation that replaces pain signals.

Stimulation Level – Measure of stimulation: can be increased or decreased within a range specified by the clinician.

Warning – Potentially serious hazard to be aware of in order to avoid situations that could cause injury or death.

Introduction

This manual describes the care and use of the Spinal Modulation Axiom™ Trial Neurostimulator.

Description

The Trial Neurostimulator (TNS) is an external NS which attaches to the Connector Cable and delivers energy to the leads. The TNS has a female locking connector that attaches to the Connector Cable, a Stimulation OFF button that disables stimulation, and a clip for the patient to use to attach the TNS to their belt or waistband.

The output ranges for the system are:

| Parameter | Range |
|------------------|-----------|
| Frequency (Hz) | 4 – 80 |
| Pulse Width (µs) | 40 – 1000 |
| Amplitude (µA) | 0 – 6000 |

The Clinical and Patient Programmers are used to communicate with the Trial Neurostimulator.

- The Clinical Programmer is used by the physician or clinical staff to program the stimulation parameters in the TNS. The TNS device delivers the programmed stimulation parameters (energy) to the Leads.
- The Patient Programmer allows the patient to adjust the stimulation level within limits preset by the physician. It also allows the patient to turn stimulation off, if necessary.

The Clinical and Patient Programmers are portable, hand-held devices powered by internal rechargeable batteries. Chargers provided with the Programmers are used for recharging and also allow the Programmers to be used while plugged in. Both Programmers contain an internal magnet to initiate communication with the TNS device. Both Programmers also come with a Programmer Carrying Case and should be kept in the case when not in use.

Indications for Use

The Axium Neurostimulator System is indicated for spinal column stimulation via epidural and intra-spinal lead access to the dorsal root ganglion as an aid in the management of moderate to severe chronic intractable* pain of the lower limbs in adult patients with Complex Regional Pain Syndrome (CRPS) types I and II.**

*Study subjects from the ACCURATE clinical study had failed to achieve adequate pain relief from at least 2 prior pharmacologic treatments from at least 2 different drug classes and continued their pharmacologic therapy during the clinical study.

**Please note that in 1994, a consensus group of pain medicine experts gathered by the International Association for the Study of Pain (IASP) reviewed diagnostic criteria and agreed to rename reflex sympathetic dystrophy (RSD) and causalgia, as complex regional pain syndrome (CRPS) types I and II, respectively.

Contraindications

Patients contraindicated for the Axium Neurostimulator System are those who:

- Are unable to operate the system
- Are poor surgical risks

Patients who fail to receive effective pain relief during trial stimulation are contraindicated to proceed to the INS procedure.

Warnings

Following is a partial list of warnings for the use of the Axiom Neurostimulator System. Refer to the Physician Implant Manual for a complete list of warnings and precautions.

- The patient should be trained by their doctor before using the Patient Programmer and the NS device.
- The patient must not use their Patient Programmer until their doctor has set up the NS System.
- The Axiom System is MRI unsafe. The patient should be advised to not undergo any elective magnetic resonance imaging (MRI) with the entire system, or (in the case of removal of the implanted generator) leads or lead fragments in place. Use of MRI in the vicinity of the lead(s) may result in forceful dislodgment of the lead(s), or damage to the Neurostimulator. If a voltage is induced through the lead, it may cause uncomfortable (“jolting” or “shocking”) levels of stimulation or injury to the patient. MRI may cause heating at the lead tip and unintended stimulation could result in tissue damage.
- CT Scans – If the patient requires a CT scan, all stimulation should be turned OFF prior to the procedure. If stimulation is not turned off, the patient may experience a momentary increase in stimulation, which may be uncomfortable. After the procedure, stimulation should be turned back on and the system should be checked

for proper function.

- The patient must not undergo any diathermy (high energy heat) procedures. Diathermy could injure the patient or damage the NS device.
- The patient must not remove the leads or Connector Cable from their body. Removal of the leads or Connector Cable may result in serious injury or development of an infection.
- Changes in body position can affect the amount of stimulation felt, causing increased feelings of pain or uncomfortable stimulation. The patient should use the Patient Programmer to adjust stimulation levels or to turn stimulation off, if needed.
- Pediatric Use – The safety and effectiveness of the Axiom Neurostimulator System has not been established for pediatric use.
- Pregnancy – The safety and effectiveness of this therapy has not been established for pregnancy, nursing, the unborn fetus, or delivery.
- Under certain conditions, strong electromagnetic fields may affect the NS device, possibly affecting the level of stimulation and causing discomfort. The patient should avoid theft detection devices at store and library exits and security screeners at airports. The patient must not stand near the screening equipment.
- Other equipment that may cause interference includes but is not limited to: power generators, arc welders and large magnetized speakers.

Precautions - Device

The following precautions should be taken to avoid damage to and ensure proper function of the Patient Programmer and TNS device.

- The patient should not drop or mishandle the Patient Programmer or TNS device. Physical damage to the units may impair their function.
- The patient should not wash or get the Patient Programmer or TNS device wet.
- The patient should not use abrasive or caustic cleaning products on the Patient Programmer or TNS device.
- The patient should not shower or bathe with the TNS device. A sponge bath is acceptable as long as the TNS device does not get wet.
- To avoid potential skin irritation, the patient should only wear the TNS on the outside of clothing or on a belt.
- The patient should not open the cases of the Patient Programmer or TNS device. Attempts to open the cases may expose the units to elements that alter their function.
- The patient should not place the Patient Programmer close to credit cards or other cards with magnetic strips, as the Patient Programmer contains a magnet and may demagnetize the cards. Also, the patient should keep the Patient Programmer away from computer hard drives or magnetic storage devices.

- The patient should not operate the Patient Programmer or TNS device outside the specified temperature range of 5°C to 40°C (41°F - 104°F). Rapid temperature changes may affect proper device operation.
- The patient should not store the Patient Programmer outside the specified temperature range of -10°C to 50°C (14°F - 122°F).
- The patient should not leave the Patient Programmer in a car or other places where temperatures can reach 50°C (122°F).
- Failure of the NS System, although unlikely, is possible due to random component failure. If an unexpected change in performance occurs and troubleshooting is unsuccessful, the patient should turn stimulation OFF and contact the physician.
- The Patient Programmer and the TNS device must be returned to the physician at the end of the trial period. The patient must not discard or burn the TNS device or Patient Programmer. Fire may cause its internal battery to explode.
- The patient should not try to replace the TNS device battery, even if the TNS device does not appear to be functioning. The internal battery for the TNS device must be replaced by Spinal Modulation personnel only.
- The NS device can only be programmed using Spinal Modulation's Patient Programmer. The patient should not attempt to use any other manufacturer's device to program it.
- The patient should not allow unauthorized use of their Patient Programmer. This

may cause unwanted changes in the programming.

- The patient should not use the Patient Programmer or NS in the presence of explosive or flammable gases as this may cause serious injury.

Precautions - Therapy

The patient should be instructed to take the following precautions to maintain appropriate therapy:

- Follow proper wound care techniques as instructed by their physician.
- Do not rub or exert pressure at the implant site as it may cause dislodgement of the leads or skin erosion.
- Avoid excessive bending, twisting and stretching, and do not lift objects over five pounds. These activities may result in lead movement producing either understimulation or overstimulation.
- Avoid driving a car or operating other potentially dangerous machinery while stimulation is turned on. If sudden changes in stimulation were to occur, the patient may be distracted from vehicle or device operation.
- The NS System may affect the operation of other implantable devices such as

pacemakers or implantable cardiac defibrillators. The physician should be aware of any other implantable devices the patient may have or is scheduled to get.

- The patient's other healthcare providers should be aware of their NS. They should not undergo any elective medical procedures during the trial stimulation period. Some medical devices or therapies, such as those listed below, may produce interference with the TNS System:
 - Electrocautery – Electric probe: to cauterize blood vessels and stop bleeding during surgery.
 - Lithotripsy – High-output shock waves: to break up gallstones and kidney stones.
 - Therapeutic Radiation – Ionizing radiation: to destroy cancer cells.
 - High-output ultrasound – High frequency sound waves: to treat bone and muscle injuries, or to stimulate muscle or improve blood flow.
 - RF Ablation – Radio frequency energy: causes controlled tissue damage.
 - Microwave Ablation – High speed alternating electric field: causes controlled tissue damage.
 - Dental procedures, electrolysis, static field therapeutic magnets and diagnostic X-ray.
- The patient should designate a representative (family member or friend) to notify emergency medical personnel of their trial stimulator, in case they require emergency care. The patient will be provided with a Medical Alert Card to carry with them that will inform emergency medical personnel that they have an NS.

If there is any concern regarding the proper function of the NS System, the patient should contact their physician during normal business hours.

TNS Device Overview

The Trial Neurostimulator device connects to the Trial or Implant Leads through the Connector Cable and is worn by the patient for up to 30 days during the trial period. The TNS may be expected to have an operating life of two years. The TNS device has a clip that the patient can use to secure the TNS device to a belt or clothing during their trial period.



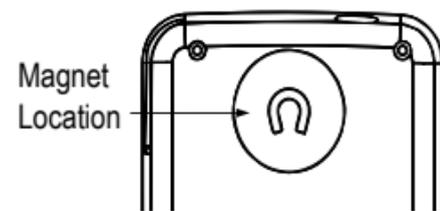
The TNS device must be programmed by the physician or company representative using a Clinical Programmer in order for it to provide stimulation to the leads. The TNS device will periodically check for communication from the Patient Programmer. The location and level of stimulation can be selected and adjusted or may be turned OFF. For detailed instructions on the use of the Patient Programmer, see the Patient Programmer Manual.

Stimulation OFF Switch

The TNS device has a red button  located on the top of the device. Pressing this button for more than two seconds will turn OFF stimulation on all leads. Stimulation may be turned back ON by using the Programmer.

Magnet Activation

Move the magnet located in the Programmer in a circular motion over the top of the TNS in order to initiate communication between the TNS and the Patient Programmer or Clinical Programmer.



TNS Device Care

The patient must be instructed to not pour water over or immerse their TNS device. A damp cloth may be used to wipe the TNS, if necessary.

RF OPERATING FREQUENCIES

Nearby equipment emitting strong magnetic fields can interfere with RF communication, even if the other equipment complies with CISPR emission requirements. The operating characteristics are as follows:

MedRadio/MICS band: 402-405 MHz

The effective radiated power is below the limits as specified in

Europe: EN ETSI 301 839-2

USA FCC 47 CFR Part 95; 95.601-95.673 Subpart E, 95.1201-95.1219

FCC ID: Y8L-MN0100

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.

Appendix 1: Troubleshooting

| Issue | Potential Solutions |
|---|---|
| Unable to connect to the TNS using the Programmer | <ul style="list-style-type: none">• Verify that the back side of the Programmer and the magnet label was put over the “label” side of the TNS. This is the side without the belt clip. Press “Connect” again. It should not take more than 30 seconds to connect.• The Programmer may be too far away from the TNS; bring the Programmer closer to the TNS and wait for connection. You may have to activate the switch in the TNS using the magnet.• Verify that the patient has put the magnet of the Programmer over the correct side of the TNS. The patient may need to use the stand alone magnet to activate the TNS instead.• Move to another location as there may be interference in your current location and reconnect.• The Programmer battery may be low. Charge the Programmer and then attempt to reconnect.• The battery of the TNS may need to be replaced. Contact your Spinal Modulation representative. |

| Issue | Potential Solutions |
|------------------------------------|---|
| Understimulation or no stimulation | <ul style="list-style-type: none"> • Verify that the connection of the Connector Cable to the TNS has not come loose. Before reconnecting the cable, the patient should connect to the stimulator and turn the stimulation levels down on each lead. • The Stimulation OFF button may have been pressed. Connect to the stimulator and re-enable each lead to turn stimulation on. • The patient may have activated a new Group. The patient should reconnect to the stimulator and adjust the Group or stimulation levels on each lead appropriately. • The magnet may have been held in place too long over the switch and turned stimulation OFF. The patient should reconnect to the device and turn each lead back on individually. • If the leads cannot be re-enabled, the physician should be contacted. |

| Issue | Potential Solutions |
|-----------------|---|
| Overstimulation | <ul style="list-style-type: none"> • Postural changes can affect stimulation. Before lying down or standing up, the patient may need to adjust the stimulation levels. • Stimulation levels can change due to interference from anti-theft devices, high power lines and large magnetized speakers. If this occurs, the patient should be instructed to use the Patient Programmer to adjust their stimulation setting. |



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