COVER PAGE

FAST STUDY (NCT04231409)

Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain (A4070)

This serves as a cover page for the FAST Study – A Sub-study of COMBO Study (NCT03689920)

Version E (Current Version): 31 Jan 2020

Sponsored By

Boston Scientific Neuromodulation Corporation

25155 Rye Canyon Loop

Valencia, CA 91355

United States of America

Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

FAST Study

COMBO Sub-Study

A4070

CLINICAL INVESTIGATION PLAN

NCT03689920

Sponsored By

Boston Scientific Neuromodulation Corporation

25155 Rye Canyon Loop

Valencia, CA 91355

United States of America

[redacted]

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[redacted]

2. Protocol Synopsis

FAST Study A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain	
Primary Objective	To evaluate the effectiveness of Spinal Cord Stimulation (SCS) with **fast-acting subperception (FAST)** as compared to **subperception** SCS in patients with chronic pain when using the Boston Scientific Spectra WaveWriter SCS System.
Secondary Objectives	To determine the impact of Spectra WaveWriter SCS System on global patient outcomes including quality of life, patient preference, etc.
Indication(s) for Use	The Spectra WaveWriter Spinal Cord Stimulator (SCS) System is indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain.
Commercial Device/System	BSC Spectra WaveWriter™ SCS System
Study Design	Prospective, multi-center, parallel-group randomized controlled trial with an adaptive design
Planned Number of Subjects	[redacted]
Planned Number of Sites / Countries	[redacted]

[redacted]

FAST Study **A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
Safety Parameters	Rates of occurrence of all device hardware, device stimulation and procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study.
Primary Effectiveness Endpoint	Proportion of subjects with 50% or greater reduction from Baseline Visit in average overall pain intensity at 3 months post-randomization, with no increase in baseline average daily opioid medications used to treat pain.
Secondary Effectiveness Endpoint	[redacted]
Exploratory Endpoints	[redacted]

[redacted]

FAST Study

A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

[redacted]

[redacted]

FAST Study **A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain**	
	[redacted]
Follow-up Schedule	Study events occur at the following time points: • Screening • Opioid Medication Lock Visit (Up to 35 days following Informed Consent) • Baseline Period (14 days) • Baseline Visit (0 - 7 days post Baseline Period) • Implant Procedures (up to 90 days post Baseline Visit) • Healing Period (0 - 28 days) • Randomization Visit (Day 0) • Programming Lock Visit (70 - 14 days post-randomization Visit) • 3 Month Visit (90 + 14 days post-randomization Visit) • 6-Month Visit (180 ± 30 days post-randomization Visit) • 9-Month Visit (270 ± 30 days post-randomization Visit) • Year 1 Visit (365 ± 30 days post-randomization Visit) • Year 2 Visit (730 ± 30 days post-randomization Visit)
Study Duration	[redacted]
Participant Duration	[redacted]
Inclusion Criteria	IC1. Chronic pain of the trunk and/or limbs for at least 6 months with back pain greater or equal to leg pain.

[redacted]

FAST Study

A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

	[redacted] IC3. No back surgery within 6 months prior to Screening [redacted] IC9. 22 years of age or older when written informed consent is obtained [redacted] IC11. Able to independently read and complete all questionnaires and assessments provided in English [redacted] IC13. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English
Exclusion Criteria	[redacted]

[redacted]

FAST Study

A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

[redacted]

EC7. Any pain-related diagnosis or medical/psychological condition that, in the clinician's best judgment, might confound reporting of study outcomes (e.g. pelvic pain, anginal pain, chronic migraine, brain or spinal cord tumor)

[redacted]

EC15. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to participate in the study

[redacted] Participating (or intends to participate) in another drug or device [redacted]

[redacted]

FAST Study

A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain

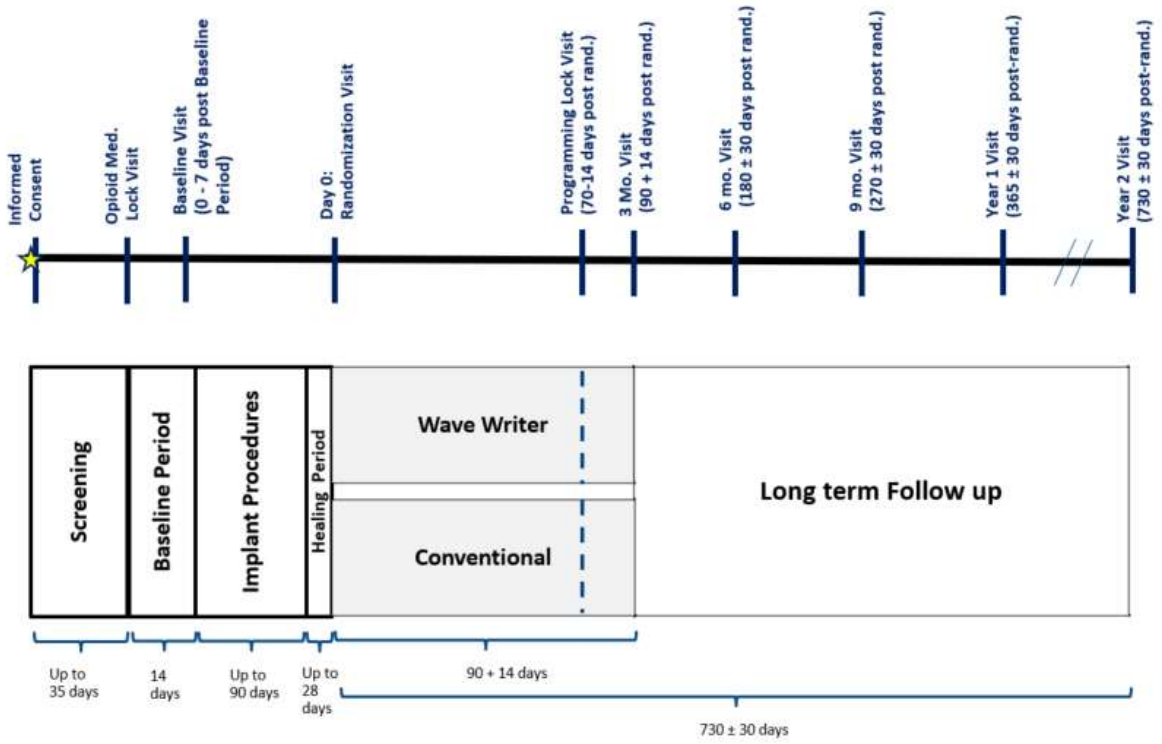
	[redacted] EC23. [redacted]
Statistical Methods	
Primary Statistical Hypothesis	The primary statistical hypothesis in this study is that the proportion of subjects with 50% or greater reduction from Baseline Visit in average daily overall pain intensity at 3 months post randomization in the FAST group is non-inferior compared to the Control (i.e. subperception) group $H_0: \pi_t - \pi_c \leq -0.20$ $H_1: \pi_t - \pi_c > -0.20$ Where π_t and π_c are the proportion of subjects with 50% or greater reduction from Baseline in average daily overall pain intensity at 3 months post randomization with no increase in baseline average daily opioid pain medications using FAST and subperception settings, respectively. The study's non-inferiority margin is 0.20.
Statistical Test Method	[redacted]

[redacted]

FAST Study A Study to Demonstrate the Value of Fast-Acting Subperception (FAST) using the Spectra WaveWriter™ Spinal Cord Stimulator System in the Treatment of Chronic Pain	
Sample Size Parameters	[redacted]
Interim Analysis	[redacted]

[redacted]

STUDY SCHEMATIC



[redacted]

4. Introduction

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

5. Commercial Device Description (part of Standard of Care)

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

6. Study Objectives and Endpoints

6.1. *Primary Objective*

The primary objective of this study is to evaluate the effectiveness of Spinal Cord Stimulation (SCS) with fast-acting subperception (FAST) as compared to subperception SCS in patients with chronic pain when using the Boston Scientific Spectra WaveWriter SCS System.

6.2. *Secondary Objective*

The secondary objective of this study is to determine the impact of Spectra WaveWriter SCS System on global patient outcomes including quality of life, patient preference, etc.

6.3. *Primary Endpoint*

The primary endpoint is the proportion of subjects with 50% or greater reduction from the Baseline Visit in average overall pain intensity at 3 months post randomization, with no increase in baseline average daily opioid medications used to treat pain.

6.4. *Secondary Endpoints*

[redacted]

[redacted]

6.6. *Safety Parameters*

Safety parameters include the rates of occurrence of all device hardware, device stimulation and procedure related non-serious adverse events, all serious adverse events, and unanticipated adverse events through the end of the study.

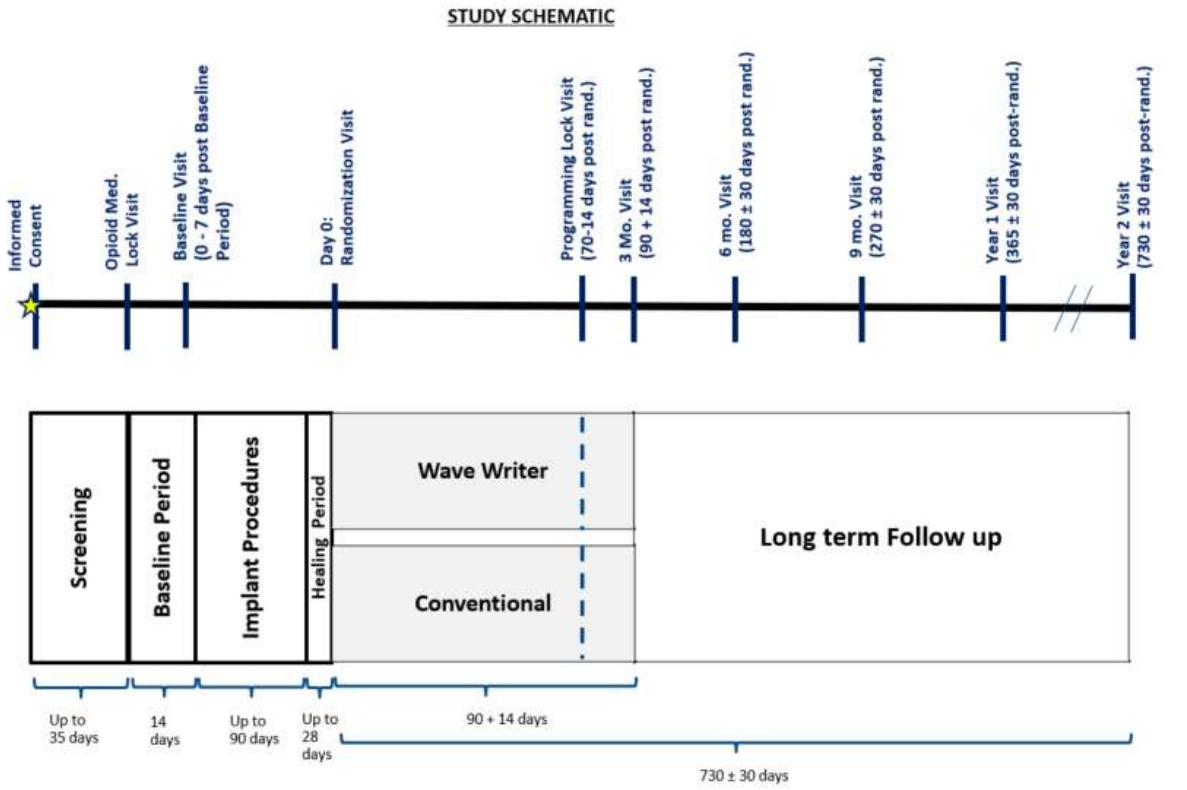
7. Study Design

The study is a prospective, multi-center, parallel group randomized controlled trial with an adaptive design. All participants will receive the Spectra WaveWriter Spinal Cord Stimulator (SCS) system and followed per the study schedule as shown in study schematic Figure 7.1-1.

7.1. *Scale and Duration*

[redacted]

Figure 7.1-1: FAST Study Design



7.2. *Treatment Assignment*

All enrolled subjects who pass eligibility criteria will receive a trial. Subjects with a positive trial will proceed to receive permanent implant. Following permanent implant, all subjects' device will be randomized in a 1:1 ratio to either receive:

- WaveWriter Settings: Fast-acting subperception (FAST)
- Conventional Settings: Subperception

7.3. *Justification for the Study Design*

The study is a prospective, multi-center, parallel group randomized controlled trial with an adaptive design. The study is designed to demonstrate the value of fast-acting subperception for sustained clinically significant pain relief in patients with chronic pain when using the Boston Scientific Spectra WaveWriter SCS System. Additionally, the impact of the Spectra WaveWriter SCS System on global patient outcomes, quality of life and patient preference will also be evaluated.

A prospective study design will eliminate the bias associated with case selection in a retrospective review and will ensure that identical procedures are followed for data capture and review.

[redacted]

A multi-center design will minimize the impact on treatment outcome that may potentially result from differences in patient selection, regional differences in the patient demographic, and differences in investigator technique and patient management.

The study design includes two groups (arms) – WaveWriter group and Conventional group. The WaveWriter group will receive fast-acting subperception (FAST) as available in the WaveWriter SCS System while the conventional group will receive subperception programming. The Conventional group will serve as a control in this study. Randomization (1:1) will minimize selection bias and impact of demographic variables.

The primary endpoint is the proportion of subjects with 50% or greater reduction (responder rate) from the Baseline Visit in average overall pain intensity at 3 months post-randomization, with no increase in baseline average daily opioid medications used to treat pain. A 3-month endpoint was chosen as 3 months provides adequate time for a subject to have their programming parameters optimized.

8. Subject Selection

8.1. *Study Population and Eligibility*

Study candidates will be drawn from the population of patient's resident in pain management or surgical medical practices. The study eligibility criteria are listed below.

8.2. *Inclusion Criteria*

Subjects who meet all of the following criteria (see Table 8.2-1) may be given consideration for inclusion in this clinical investigation, provided no exclusion criterion (see Section 8.3-1) is met.

[redacted]

Table 8.2-1: Inclusion Criteria

Clinical Inclusion Criteria	IC1. Chronic pain of the trunk and/or limbs for at least 6 months with back pain greater or equal to leg pain. [redacted] IC9. 22 years of age or older when written informed consent is obtained [redacted] IC11. Able to independently read and complete all questionnaires and assessments provided in English [redacted] IC13. Subject signed a valid, IRB-approved informed consent form (ICF) provided in English

8.3. *Exclusion Criteria*

Subjects who meet any one of the following criteria cannot be included in this study or will be excluded from this clinical study.

Table 8.3- 1 Exclusion Criteria

[redacted]

Clinical Exclusion Criteria	[redacted] Average leg pain intensity is greater than average low back pain [redacted] EC7. Any pain-related diagnosis or medical/psychological condition that, in the clinician's best judgment, might confound reporting of study outcomes (e.g. pelvic pain, anginal pain, chronic migraine, brain or spinal cord tumor) EC15. Significant cognitive impairment at Screening that, in the opinion of the Investigator, would reasonably be expected to impair the study candidate's ability to participate in the study EC16. Participating (or intends to participate) in another drug or device clinical trial that may influence the data that will be collected for this study EC18. A female who is breastfeeding EC19. A female of childbearing potential planning to get pregnant during the course of the study or not using adequate contraception

[redacted]

	[redacted] EC23. [redacted]

9. Subject Accountability

9.1. *Point of Enrollment*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

9.2. *Withdrawal*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

9.3. *Subject Status and Classification*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

9.4. *Enrollment Controls*

[redacted].

The study will implement a formal *Enrollment Communication Plan*. The plan will outline the specific activities, as well as the nature and timing of communications to investigators in order to minimize the risk of enrollment beyond the protocol-specified enrollment caps determined by the statistical analysis plan.

9.5. *End-of-Study Action Plan*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

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10. Study Methods

10.1. *Data Collection*

The data collection schedule is shown in table below.

Table 10.1-1: Data Collection Schedule

	Screening	Opioid Medication Lock Visit Up to 35 days following informed consent	Baseline Period 14 days post-Medication Lock	Baseline Visit (0 - 7 days post Baseline Period)	Implant Procedures *(Trial and Permanent)* Up to 90 days post-Baseline Visit		Randomization/ Activation Visit Day 0	Programming Lock Visit 70 - 14 days	3-Month Visit 90 + 14 days post randomization	6-Month Visit 180 ± 30 days post randomization	9-Month Visit 270 ± 30 days post randomization	1-Year Visit 365 ± 30 days post randomization	2-Year Visit *End of Study* 730 ± 30 days post randomization	Unscheduled Visit
Informed Consent (ICF)	X													
Inclusion/Exclusion Criteria Evaluation	←	—	—	→										
Demography				X										
Medical History				X										
Beck Depression Inventory (BDI-II)				X					X			X	X	
Oswestry Disability Index (ODI v2.1a)				X					X	X	X	X	X	
Short Form Health Survey 36 item (SF-36v2)				X					X	X	X	X	X	
EQ-5D-5L				X					X	X	X	X	X	
Pain Intensity (NRS)				X					X	X	X	X	X	
Pain Intensity (VRS)				X					X	X	X	X	X	
Pittsburgh Sleep Quality Index (PSQI)				X					X	X	X	X	X	
Procedure Information					X†									X**
End of Trial Assessment					X									
Programming Parameters* **					X		X	X	X	X	X	X	X	X
Activation Questionnaire							X							
Clinician Global Impression of Change (CGI-C)									X	X	X	X	X	
Patient Global Impression of Change (PGI-C)									X	X	X	X	X	
Percent Pain Relief (PPR)									X	X	X	X	X	
Preference Questionnaire										X	X	X	X	
Treatment Satisfaction Questionnaire (TSQM-9m)									X	X	X	X	X	
Concomitant Medications (opioid pain medications)		X		X	X		X	X	X	X	X	X	X	X
Adverse Events (AE)	X	X	X	X	X		X	X	X	X	X	X	X	X
		←	—	—	—	Opioid Medications Locked								

Healing Period (0-28 days)

** For unscheduled visits where procedures are performed.

*** Only when device programming is performed.

† The device will remain off after permanent implant until the Activation Visit

10.2. *Study Candidate Screening*

Subjects' eligibility for the study will be assessed based on study Inclusion and Exclusion criteria listed in Sections 9.2 and 9.3, respectively. Subjects who have provided informed consent and who have been determined to not meet all eligibility requirements will be withdrawn.

10.3. *Informed Consent*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

10.3.1. Screening Period

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

10.4. *Opioid Medication Lock Visit (Up to 35 days following informed consent)*

The Opioid Medication Lock Visit will occur within 35 days following informed consent. However, this visit may occur on the same day as that of the Informed consent as well following completion of consent.

At this visit, the subject's opioid pain medications will be locked, with no increase in type/dose/route/frequency, until the 3-Month post-randomization Visit.

At this visit (or during the screening period), the investigator will convert the subject's opioid medication prescriptions from PRN to a fixed dose, as needed.

10.5. *Baseline Period (14 days)*

The Baseline Period will last for 14 consecutive days following the Opioid Medication Lock Visit. At the end of the Baseline Period, subjects will return to the clinic for their Baseline Visit.

Subjects are to not make any increases to their opioid pain medications during this period.

10.6. *Baseline Visit (0 – 7 days post Baseline Period)*

At the Baseline Visit, subjects will return to the clinic to complete remaining screening requirements. Any adverse since the last study visit will be collected.

The following assessments, as outlined in Table 11.1-1, will be conducted:

- Demographics

- Medical history
- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index (ODIv2.1a)
- Short Form Health Survey 36 (SF-36v2)
- EQ-5D 5-Level
- Pain Intensity: VRS
- Pain Intensity: NRS
- Pittsburg Sleep Quality Index (PSQI)

Subjects that meet all study criteria will be scheduled for the device implant procedures (trial and permanent implant of the SCS system). If a subject fails to meet all the eligibility criteria, they will be withdrawn from the study.

End of Visit Information:

- Subjects should be reminded not to make any increases to their opioid medications.

10.7. *Implant Procedures (Up to 90 days following the Baseline Visit)*

Subjects will have up to 90 days following the Baseline Visit to receive their Spectra WaveWriter System. Subjects will undergo a trial procedure per standard of care. Following a successful trial, i.e. at least 50% pain reduction in their overall pain as compared with Baseline, the subject will proceed to permanent implantation. Subjects with an unsuccessful implant procedure will be followed for 2 weeks for procedure related adverse events then withdrawn from the study. Acute opioid pain medications may be taken.

10.8. *Healing Period (0 - 28 days following Implant Procedures)*

The subject's device will remain inactivated (device OFF) for up to 28 days following the permanent implantation procedure to allow for healing. Acute opioid pain medications may be taken during this period. No additional scheduled assessments will be completed during this period.

For those subjects receiving the surgical (paddle) lead, it is recommended that their device remain inactivated (device OFF) as part of healing for 21-28 days.

10.9. *Randomization Visit (Day 0)*

At the Randomization Visit, subjects will be randomized in a 1:1 ratio to either receive

- WaveWriter Settings: Fast-acting subperception
- Conventional Settings: Subperception

Subjects will receive their assigned treatment settings up to 3 Mo. Visit. Any protocol required adverse events since the last study visit will be collected.

The Activation Questionnaire must be completed prior to and post-activation to document pain scores, time taken, etc.

Subjects must stop taking acute opioid pain medications, as applicable, and are not to increase their opioid pain medications up to the 3-Month Visit.

Information regarding programming parameters will be collected. To aid in programming it is recommended that thoracic and/or lumbar imaging is obtained at this visit or up to 7 days prior to the visit to show the position(s) of the study device lead(s). In the event of suspected lead migration, imaging may be performed to document lead positions.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Subjects should be reminded not to make any increase in their opioid pain medications.

10.10. *Programming Lock Visit (Day 70 - 14 days post randomization Visit)*

At the Programming Lock Visit, subjects will return to the clinic to have their programs locked. Any protocol required adverse events since the last study visit will be collected.

No further changes to the subject's programs (for e.g. electrode configuration) will be allowed except to resolve a device and/or stimulation-related AE.

Information regarding programming parameters and device information may be collected.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Subjects should be reminded not to make any increase in their opioid medications.

10.11. *3-Month Visit (90 + 14 days post randomization Visit)*

During the 3-Month Visit, subjects will return to the clinic for study evaluations and programming. Any protocol required adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)

- EQ-5D 5-Level
- Pain Intensity: VRS
- Pain Intensity: NRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Pittsburg Sleep Quality Index (PSQI)
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will be programmed as needed and programming information may be collected. At this visit, all subjects may receive programming as available on the device with no restrictions. .

- In the event of suspected lead migration or to aid programming the subject's device, imaging may be performed to document lead position.
- Any additional instructions related to charging of the device and/or use of Remote Control may be provided.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Subjects' opioid medications are no longer locked and can be changed, if needed for the remainder of the study

10.12. *6-Month Visit (180 ± 30 days post randomization Visit)*

During the 6-Month Visit, subjects will return to the clinic for study evaluations and programming. Any protocol required adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)

- Percent Pain Relief (PPR)
- Pittsburg Sleep Quality Index (PSQI)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will be programmed as needed and programming information may be collected.

- In the event of suspected lead migration or to aid programming the subject's device, imaging may be performed to document lead position.
- Any additional instructions related to charging of the device and/or use of Remote Control may be provided.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.
- Changes to opioid pain medications are allowed up to End of Study Visit.

10.13. *9-Month Visit (270 ± 30 days post randomization Visit)*

During the 9-Month Visit, subjects will return to the clinic for study evaluations and programming. Any protocol required adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Pittsburg Sleep Quality Index (PSQI)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will be programmed as needed and programming information may be collected.

- In the event of suspected lead migration or to aid programming the subject's device, imaging may be performed to document lead position.
- Any additional instructions related to charging of the device and/or use of Remote Control may be provided.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.

10.14. *Year 1 and Year 2 Visit (365 ± 30 days post randomization Visit and 730 ± 30 days post-randomization Visit))*

During the 1 and 2 Year Visits, subjects will return to the clinic for study evaluations and programming. Any protocol required adverse events since their last study visit will be collected.

The following assessments will be completed as summarized in Table 11.1-1:

- Beck Depression Inventory (BDI-II)
- Oswestry Disability Index version 2.1a (ODI v2.1a)
- Short Form Health Survey 36 items (SF-36 v2)
- EQ-5D 5-Level
- Pain Intensity: NRS
- Pain Intensity: VRS
- Clinical Global Impression of Change (CGI-C)
- Patient Global Impression of Change (PGI-C)
- Percent Pain Relief (PPR)
- Pittsburg Sleep Quality Index (PSQI)
- Preference Questionnaire
- Treatment Satisfaction Questionnaire for Medication - modified (TSQM-9m)

Following completion of assessments, subjects' device will be programmed as needed and programming information may be collected.

- In the event of suspected lead migration or to aid programming the subject's device, imaging may be performed to document lead position.
- Any additional instructions related to charging of the device and/or use of Remote Control may be provided.

End of Visit Information:

- Subjects will receive instructions on the use of the device including the Remote Control and charging system, as needed.
- Subjects are to contact the site in an event that any additional intervention is warranted, to report a complaint and/or a suspected adverse event, reprogramming, etc.

The 2 Year Visit is the End of Study Visit and End of Study Action Plan (ESAP) will be followed as described in Section 10.5.

10.15. *Unscheduled Visit*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

10.15.1. Revision or Replacement of Leads, Extensions and/or IPGs

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

10.15.2. Interventional Pain Procedures

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

10.16. *Medication Requirements*

Opioid Medication Lock Period (Medication Lock visit to 3-Month Visit):

Investigators/Subjects will not be allowed to increase opioid pain medications from the Medication Lock visit until completion of the 3-Month Visit.

The use of acute opioid pain medication for procedural discomfort is allowed during the Procedures and Healing Period and in the event of the revision or replacement of leads, extensions and/or IPG, per site's routine care.

Opioid Medication Open Period (3-Month Visit to End of Study visit)

Investigators/Subjects may change opioid pain medications during the pain medication open period, from the 3-Month Visit to the End of Study Visit as needed.

10.17. *Study Completion*

All randomized subjects permanently implanted will be followed through completion of the 2-Year Visit or study withdrawal. The End of Study Action Plan defines the actions to be taken when the subject reaches the end of their study participation.

10.18. *Source Documents*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

11. Statistical Considerations

11.1. *Endpoints*

11.1.1. Primary Endpoint

The primary endpoint for this study is the proportion of subjects with 50% or greater reduction from Baseline Visit in average overall pain intensity at 3 months post randomization with no increase in baseline average opioid medications used to treat pain.

[redacted]

11.1.1.1. Hypotheses

The primary statistical hypothesis in this study is that the proportion of subjects with 50% or greater reduction from Baseline Visit in average daily overall pain intensity at 3 months post randomization in the FAST group is non-inferior compared to the Control (i.e. subperception) group

$$H_0: \pi_t - \pi_c \leq -0.20$$

$$H_1: \pi_t - \pi_c > -0.20$$

Where π_t and π_c are the proportion of subjects with 50% or greater reduction from Baseline in average daily overall pain intensity at 3 months post randomization with no increase in baseline average daily opioid pain medications using FAST and subperception settings, respectively. The study's non-inferiority margin is 0.20.

11.1.1.2. Sample Size

[redacted]

11.2. *General Statistical Methods*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

12. Data Management

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

12.1. *Data Collection, Processing, and Review*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document

12.2. *Study Assessments*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

12.2.1. Activation Questionnaire

The Activation Questionnaire is administered by site personnel at the activation/randomization visit and will collect information related to subject's overall improvement in pain scores, time taken to achieve pain relief, etc.

12.3. *Data Retention*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document

13. Deviations

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

14. Compliance

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

15. Monitoring

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.
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16. Potential Risks and Benefits

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

17. Safety Reporting

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

18. Informed Consent

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

19. Committees

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

19.1. *Safety Monitoring Process*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

20. Suspension or Termination

20.1 This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

21. Publication Policy

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

22. Bibliography

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

23. Abbreviations and Definitions

23.1. *Abbreviations*

This is an appendix to the COMBO Study and only contains information that is unique to this sub-study.

Information that is common to both is not repeated in this document.

New abbreviations shown below.

Table 23.1-1: Abbreviations

Abbreviation/Acronym	Term
FAST	Fast Acting Subperception

23.2. *Definitions*

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