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Vercise™ Deep Brain Stimulation Systems for Parkinson's Disease

Clinical Summary

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How to Use This Document

This document provides clinical summary information for the Vercise™, Vercise™ PC, Vercise Gevia™, and Vercise Genus™ Deep Brain Stimulation (DBS) Systems.

Read all information carefully before using the DBS System. For other device-specific information not included in this manual, refer to the appropriate DFU for your Boston Scientific DBS System as listed in your *DBS Reference Guide*.

Guarantees

Boston Scientific Corporation reserves the right to modify, without prior notice, information relating to its products in order to improve their reliability or operating capacity.

Trademarks

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Technical Support

There are no user serviceable parts. If you have a specific question or issue, please contact your sales representative or call (833) DBS-INFO or (833) 327-4636.

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Definition of Terms

Clinical Rating Scales

Global Impression of Change (1): The global impression of change (GIC) is a generic, single-item scale for quantifying one's overall impression of the patient's improvement following therapy. GIC can be patient-reported, clinician-reported or caregiver-reported.

Modified Schwab and England (2): The modified Schwab and England (SE) assessment is a disease-specific single-item scale for quantifying a PD (Parkinson's disease) patient's ability to perform activities of daily living.

Parkinson's Disease Diary (3) (PD diary): A patient-reported motor diary measuring the patient's state in 30 minute interval for 3 consecutive days at home. The patient reports his or her state in one of five categories:

"On without dyskinesia":	Good motor function resulting from therapeutic effects of anti-parkinsonian medication and stimulation but without the drug-induced side effect movements known as dyskinesia.
"On with non-troublesome dyskinesia":	Good motor function from the therapy but with involuntary movements of dyskinesia that are not disturbing to the patient.
"On with troublesome dyskinesia":	Good motor function and relief from PD symptoms but with involuntary movements of dyskinesia that are disturbing to the patient.
"Off":	When medication effect has worn off and the medication is no longer providing clinical benefits including improvement of mobility, lessening of slowness, and improved stiffness.
"Asleep":	Asleep.

39-Item Parkinson's Disease Questionnaire (4): The 39-item Parkinson's Disease Questionnaire (PDQ-39) is a disease-specific patient-reported assessment for measuring the specific impact of PD on a patient's quality of life in the following domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication, and bodily discomfort.

Unified Parkinson's Disease Rating Scale (2) (UPDRS): A standard scale for assessing the current state and progression of Parkinson's Disease (PD). This assessment contains 4 sections: (I) Mentation, Behavior, and Mood, (II) Activities of Daily Living (ADL), (III) Motor Examination, and (IV) Complications of Therapy.

36-Item Short Form Survey (5) (SF-36) v2: A quality of life scale that measures functional health and well-being from patients' own point of view. It is comprised of 36 questions spanning eight health domains that contribute to the scoring of two component summary measures: physical health and mental health.

Symptoms and Side Effects

Bradykinesia: Slowness of movement.

Dysarthria: Poorly articulated or slurred speech.

Dyskinesia: Abnormal involuntary movements, typically non-painful writhing that can be caused by dopaminergic drug therapy.

Dystonia: Abnormal, often painful involuntary muscle contractions of opposing muscles that twist a body part into an uncomfortable, position or posture.

Rigidity: Stiffness or inflexibility of the neck, limbs or joints.

Tremor: Involuntary, regular, sinusoidal, shaking of a limb or the head.

Clinical Study Terms

Meds OFF: A condition/period of assessment where patients have withheld their anti-parkinsonian medications or when they are not medicated as the medications have worn off.

Meds ON: A condition/period of assessment when the patient has taken their anti-parkinsonian medications and the medication has taken effect.

Levodopa equivalent: The conversion in milligrams (mg) to levodopa equivalent dose for non-levodopa medications. For example, 100 mg of standard levodopa = 125 mg of controlled-release levodopa; 10 mg of bromocriptine; 1 mg of pergolide; 1 mg of pramipexole; 3 mg of ropinirole; 4mg/24h of rotigotine; 60-90 mg pirebedil.

Serious adverse event (SAE): Any adverse event that led to death or led to a serious deterioration in the health of the patient that either resulted in:

- a life-threatening illness or injury.
- a permanent impairment of a body structure or a body function.
- in-patient or prolonged hospitalization of existing hospitalization.
- medical/surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

Introduction

The Vercise™ Deep Brain Stimulation (DBS) System includes a Stimulator with DBS Leads for stimulation of the subthalamic nucleus (STN) in the brain. DBS Extensions are used to connect the DBS Leads to the Stimulator implanted near the clavicle. The Vercise DBS System is able to provide precise, independent current steering across each of the eight contacts per DBS Lead.

The Stimulator is controlled by a handheld Remote Control, and can be programmed by a Clinician Programmer using the Bionic Navigator™ Software. Periodically, the rechargeable Stimulator battery must be replenished with a radiofrequency (RF) charging device provided in the Charging Kit.

Indications for Use (Vercise): The Vercise Deep Brain Stimulation (DBS) System is indicated for use in bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.

Indications for Use (Vercise PC, Vercise Gevia, and Vercise Genus): The Vercise PC, Vercise Gevia, and Vercise Genus Deep Brain Stimulation (DBS) Systems are indicated for use in the following:

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.
- Bilateral stimulation of the globus pallidus internus (GPi) as an adjunctive therapy in reducing some of the symptoms of advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.
- Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.
- Bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability.

This Clinical Summary document provides data from two studies: the INTREPID Study, and the VANTAGE Study. The INTREPID Study data has been collected per the pre-specified interim analysis of the ongoing U.S. Clinical Study sponsored by Boston Scientific (May 2013 through December 2016). Additional long-term data from INTREPID is anticipated upon study completion. Safety data from INTREPID includes all available data on 292 consented subjects while effectiveness data is presented for the cohort of 160 randomized subjects per the pre-specified interim analysis. Enrollment for the INTREPID Study is still ongoing. Supplemental safety data from the Boston Scientific VANTAGE Study that was conducted outside the U.S. (OUS) is also provided. This included 40 consented patients.

Appendix A provides a summary of the data supporting the clinical effectiveness of GPi stimulation for Parkinson's disease. The clinically established safety and effectiveness profile of the Medtronic Activa Parkinson's Control Therapy for bilateral GPi stimulation was leveraged based on the technical equivalence of the Boston Scientific systems to the Medtronic Activa Parkinson's Control Therapy system.

Appendix B provides a summary of the data supporting the clinical effectiveness of unilateral thalamic stimulation for the suppression of parkinsonian tremor and essential tremor. The clinically established safety and effectiveness profile of the Medtronic Activa Tremor Control System for unilateral thalamic stimulation was leveraged based on the technical equivalence of the Boston Scientific systems to the Medtronic Activa Tremor Control System.

Appendix C provides a summary of the data supporting the clinical effectiveness of bilateral thalamic stimulation for the suppression of disabling upper extremity tremor in adult essential tremor patients. The clinically established safety and effectiveness profile of the Abbott Brio System for unilateral and bilateral thalamic stimulation was leveraged based on the technical equivalence of the Boston Scientific systems to the Abbott Brio System.

INTREPID Clinical Study

Study Design

INTREPID is a multi-center, prospective, double blind, randomized (3:1) controlled study. The study was designed to evaluate the safety and effectiveness of the Vercise™ Deep Brain Stimulation (DBS) System for bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.

Patients were treated starting in May 2013. The data used in consideration of this PMA reflected data collected through December 31, 2016, and included 292 patients from 23 investigational sites. Safety was evaluated based on all patients enrolled in the study within this timeframe (May 2013-December 2016) while effectiveness was analyzed using the 160 subjects who had been randomized, per the pre-specified interim analysis.

Subjects who passed screening criteria were implanted bilaterally with the Vercise DBS System in the subthalamic nucleus (STN) for the treatment of their Parkinson's disease.

The initial epoch of the study was a period of 12 weeks during which subjects remained blinded to their treatment assignment, and during which a blinded assessor (who was unaware of the subject assignment) completed all study assessments (i.e., a double blind study design). The treating neurologist was responsible for subjects' programming and adjustment of their anti-parkinsonian medications. Subjects were randomized in a 3:1 ratio to either receive Active or Control settings. Subjects in the Active group received therapeutic settings titrated by the treating neurologist to best clinical effect. Subjects in the Control group received sham stimulation where the stimulation was not set to therapeutic levels. At the Week 12 post-randomization visit, all subjects began an open-label period, with a follow up period of up to 5 years. The study design is shown in Figure 1 below.

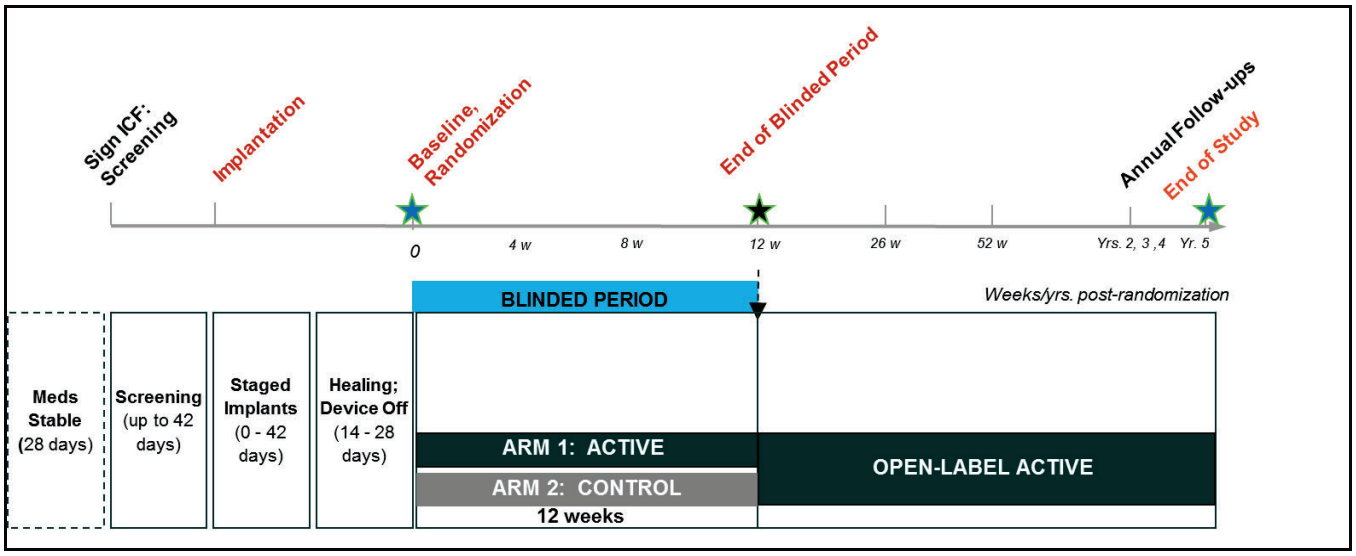


Figure 1. INTREPID Study Schematic

Subjects completed a 3-day Parkinson's Disease (3)(PD) diary to document their PD symptoms prior to each study visit. During specified in-office study visits, subjects completed study assessments in their *stim on/meds off* and *stim on/meds on* condition. A neuropsychological battery of tests was also completed during study screening, Week 12 and Week 52 visits, to evaluate the cognitive and behavioral aspects of the subject prior-to and after receiving their DBS implant.

To obtain a comprehensive overview of subjects' response to treatment in the study, additional assessments were administered including the Unified Parkinson's Disease Rating Scale (2) (UPDRS), 39-Item Parkinson's Disease Questionnaire (4) (PDQ-39), Modified Schwab and England (2) (SE), Treatment Satisfaction, Short Form Survey (5) (SF-36 v2), and Global Impression of Change (assessed by subject and assessor) (1).

During the study, subjects were evaluated without medication (*meds off condition*) and one-hour following intake of their anti-parkinsonian medications (*meds on condition*). The meds *off* and meds *on* condition assessments were completed during screening, and at Baseline, Weeks 12, 26, and 52 visits post-randomization. These were also to be completed at Year 2, 3, 4 and 5 Visits post-randomization.

Safety event rates were monitored for the entire duration of the study by an independent Data and Safety monitoring board (DSMB) comprised of medical and statistical expert reviewers.

Study Inclusion and Exclusion Criteria

Key Inclusion Criteria

- Age at the time of enrollment: 22 - 75 years
- Duration of idiopathic Parkinson's disease (PD): ≥ 5 years of motor symptoms with persistent disabling PD symptoms or drug side effects despite optimal medical therapy; Severity of modified Hoehn and Yahr (6) (H&Y) stage ≥ 2 (*meds off* condition)
- Greater than or equal to 6 hours of poor motor function (OFF time plus ON time with troublesome dyskinesias) per day as assessed by Parkinson's Disease (3) (PD) diary
- Unified Parkinson's Disease Rating Scale – Section III (2) (UPDRS III) score of ≥ 30 in the *meds off* condition and improvement by ≥ 33% following intake of anti-parkinsonian medications
- Dementia Rating Scale – 2 (7) (DRS-2) score ≥ 130 and Beck Depression Inventory II (8) (BDI-II) score < 17 in the *meds on* condition
- Be willing and able to comply with all visits and study related procedures (e.g., using the remote control, charging system and completing the PD Diary (3))
- Able to understand the study requirements and the treatment procedures and provides written informed consent before any study-specific tests or procedures are performed.

Key Exclusion Criteria:

- Any intracranial abnormality or medical condition that would contraindicate Deep Brain Stimulation (DBS) surgery
- Have untreated clinically significant depression per DSM-IV (9) (Diagnostics and Statistical Manual of Mental Disorders) criteria as determined by Beck Depression Inventory II (8) (BDI-II) score ≥ 17. History of suicide attempt or current active suicidal ideation as determined by a positive response to Items 2-5 of suicide ideation sub-scale of the Columbia Suicide Severity Rating Scale (10) (C-SSRS).
- Any current drug or alcohol abuse, per DSM-IV (9) (Diagnostics and Statistical Manual of Mental Disorders) criteria
- Any history of recurrent or unprovoked seizures or hemorrhagic stroke
- Any prior movement disorder treatments that involved intracranial surgery or device implantation.
- Any other active implanted devices including neurostimulators (e.g., cochlear implant, pacemaker) and/or drug delivery pumps, whether turned on or off. Passive implants (e.g., knee prostheses) allowed provided that they do not interfere with the functioning of the Vercise™ System.
- Have any significant medical condition that is likely to interfere with study procedures or likely to confound evaluation of study endpoints
- Any terminal illness with life expectancy of < 1 year
- A female who is breastfeeding or of child-bearing potential with a positive urine pregnancy test or not using adequate contraception
- Any impairment that would limit subject's ability to record PD Diary (3) entries or perform wound care, unless a caregiver is available to assist.

Clinical Endpoints

The primary safety endpoint included the rates of occurrence of the following adverse device effects (ADEs) at 52 weeks post-randomization:

- Cerebrovascular accident (CVA) and subdural hematomas
- Death
- Seizure
- Suicide or suicide attempt
- Pre-specified motor/sensory symptoms:
    - Dystonia;
    - Eye Deviation, Conjugate;
    - Eyelid Apraxia;
    - Muscle Spasm;
    - Postural/Gait Disturbances;
    - Speech Disorders;
    - Swallowing Disorders;
    - Undesired Sensations, Non-target Stimulation Area;
    - Visual Disturbances.
- Pre-specified psychiatric symptoms:
    - Anxiety;
    - Apathy without Mood Disorder;
    - Depression;
    - Emotional Reactivity;
    - Hallucinations;
    - Impulsive Behavior;
    - Mania;
    - Psychosis.

The primary efficacy endpoint for the study was the difference in the mean change from baseline to 12 weeks post-randomization between the Active and Control groups in the mean number of waking hours per day with good symptom control and no troublesome dyskinesia, as measured on the Parkinson's Disease (PD) Diary (3), with no increase in antiparkinsonian medications. The study met success criteria for the primary endpoint based on the pre-specified interim analysis.

The following secondary endpoints were analyzed at 12 weeks post-randomization between the Active and Control groups as compared with Baseline:

- Motor function as assessed by Unified Parkinson's Disease Rating Scale – Section III (2) (UPDRS III) scores in *stim on/meds off* condition and in *stim on/meds on* condition
- Activities of Daily Living (Unified Parkinson's Disease Rating Scale – Section II) (2) (UPDRS II) in *stim on/meds on* condition
- Quality of life as assessed by Parkinson's Disease Questionnaire (4) (PDQ-39), 36-Item Short Form Survey (5) (SF-36) v2 and Modified Schwab and England (2) (SE)
- Treatment Satisfaction
- Global impression of change (1) as assessed by subjects and clinicians.

Pre-Specified Statistical Analysis Plan

The study was designed such that there would be at least 160 randomized subjects, with a maximum of up to 310, at up to 30 US sites. These sample sizes would be based on the outcomes of four pre-specified interim analyses throughout the study. The four interim analyses would be performed as follows:

- For futility after 60 randomized subjects reached the 12 week post-randomization follow-up visit, and
- For effectiveness and futility after 160, 200, and 240 randomized subjects reached the 12 week post-randomization follow-up visit

The adaptive design used the Lan-DeMets group sequential method with the O'Brien-Flemming spending function and Pocock spending function.

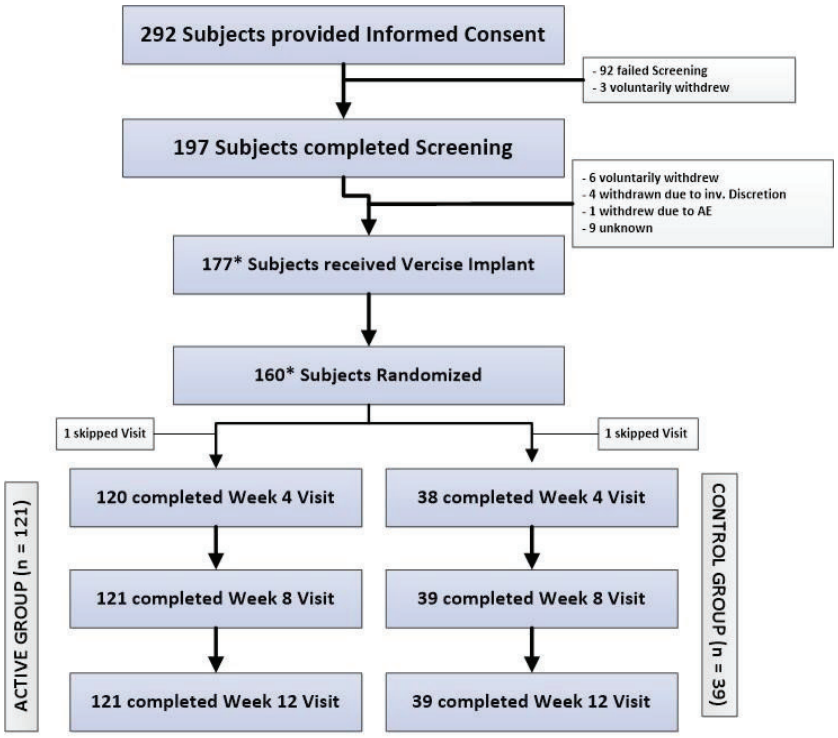
A two group t-test with a one-sided 0.025 significance level (adjusted for the interim analyses) was used to assess the primary endpoint. The Intent-To-Treat (ITT) analysis set was used for the primary analysis. Missing data at 12 week post-randomization were imputed appropriately. The 95% confidence interval (CI) of the treatment effect was reported.

Secondary endpoints were successively analyzed according to a parallel gatekeeping procedure (Benjamini and Hochberg) with five endpoint families using the aforementioned order.

Patient Accountability

Enrollment

A total of 292 subjects provided consent to participate in the study at 23 participating sites in U.S. One hundred and seventy-seven subjects received the Vercise™ Deep Brain Stimulation (DBS) System. The cohort of 160 randomized subjects was identified as the pre-specified interim analysis group. The following flowchart (Figure 2) shows the disposition of subjects in the study.



*As of Dec 31st 2016. Only those subjects included in the analysis are included

Figure 2. INTREPID Study Disposition

Study Population Demographics and Baseline Characteristics

One hundred sixteen of 160 subjects (72.5%) were male. The mean age of subjects at the time of consent was 59.9 ± 7.95 years. 43.1% (69/160) of subjects were younger than 60 years of age and 10.6% (17/160) of subjects were over the age of 70.

Subjects' medical history revealed that two subjects had a prior intracranial surgery - one had a temporal lobe biopsy and the other had surgical repair of a Chiari malformation. Four subjects had a history of major depressive disorder and two had a diagnosis of dopamine dysregulation syndrome. In the last four weeks prior to screening, 30% (48/160) reported anxiety and 17.5% (28/160) reported restless legs syndrome.

Subjects were diagnosed with bilateral idiopathic Parkinson's disease (3) (PD) with disease duration of 10.1 ± 3.61 years and mean severity of modified Hoehn and Yahr (6) (H&Y) score of 2.8 ± 0.73. Subjects' mean Unified Parkinson's Disease Rating Scale – Section III (2) (UDPRS III) Scores in *meds off* condition was 43.4 ± 9.6. Following intake of anti-parkinsonian medications, mean UPDRS III (2) scores improved by 57.5% (18.5 ± 8.26) in *meds on* condition.

Subjects completed a 3-day diary (3) in which they reported their PD symptoms in 30 minute increments. Subjects reported poor motor function with regard to the time spent ON with troublesome dyskinesias and OFF as summarized in Table 1 below. Subjects also demonstrated a poor quality of life as reported by scores in 39-Item Parkinson 's Disease Questionnaire (4) (PDQ-39), Modified Schwab and England (2) (SE), Modified Hoehn and Yahr (6) (H&Y) and EuroQol-5D-5L (11) (EQ-5D-5L) scores.

Table 1: INTREPID Study Clinical Characteristics

	All Randomized Subjects
	Mean (SD) N
Parkinson's Disease Duration	10.1 (3.61) 160
Parkinson's Disease Diary (hours/day)	
Asleep	7.20 (1.47) 158
OFF Time	6.92 (2.99) 158
ON without dyskinesia	4.65 (2.67) 150
ON with non-troublesome dyskinesia	3.65 (1.90) 120
ON with troublesome dyskinesia	4.35 (2.63) 105
UPDRS III Scores	
UPDRS-III score (meds off condition)	43.4 (9.60) 153
UPDRS-III score (meds on condition)	18.5 (8.26) 157

Safety Results

The analysis of the INTREPID safety data was based on a total of 292 consented (enrolled) subjects. Of these 292 subjects, 177 subjects received the Vercise System. Safety data for all the consented (enrolled) subjects (n = 292) is presented in this section (Table 2). Additionally, the safety data on the interim analysis cohort (n = 160) up to Week 12 post randomization (end of blinded period) is presented in Table 3. Please note that the VANTAGE Study (see below) also includes supplemental safety data on the 40 patients implanted with the Vercise System.

The primary safety endpoint of the study included the rates of occurrence of pre-specified adverse device effects (ADEs) at 52 weeks post-randomization. Additional safety parameters evaluated in the study included the rates of occurrence of all serious adverse events (SAEs) and all adverse device effects (ADEs), including serious adverse device effects (SADEs) and unanticipated adverse device effects (UADEs) at 5 years post-randomization (available upon study completion).

Safety event rates were monitored for the entire duration of the study by an independent Data and Safety monitoring board (DSMB) comprised of medical and statistical expert reviewers.

All Adverse Events

A total of 788 adverse events in 143 subjects were reported in the study for all consented (enrolled) subjects as of December 31, 2016. Of 788 events, 74 events were considered Serious Adverse Events (SAE) and 714 events were considered non-serious adverse events. There were no unanticipated adverse events.

All adverse events related to hardware, stimulation or procedure are summarized in Table 2 below. Of 788 events, a total of 65 events were reported as related to hardware, 157 related to stimulation and 128 related to procedure.

Table 2: All Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Events	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Abnormal behavior	0 (0.0%)	2 (0.7%)	0 (0.0%)
Adverse drug reaction	0 (0.0%)	0 (0.0%)	1 (0.3%)
Affect lability	0 (0.0%)	2 (0.7%)	1 (0.3%)
Aggression	0 (0.0%)	1 (0.3%)	0 (0.0%)
Agitation	1 (0.3%)	3 (1.0%)	0 (0.0%)
Agitation postoperative	0 (0.0%)	0 (0.0%)	1 (0.3%)
Amnesia	1 (0.3%)	0 (0.0%)	2 (0.7%)
Anxiety	0 (0.0%)	1 (0.3%)	1 (0.3%)
Apathy	1 (0.3%)	2 (0.7%)	1 (0.3%)
Aphasia	0 (0.0%)	1 (0.3%)	1 (0.3%)
Apraxia	0 (0.0%)	4 (1.4%)	0 (0.0%)
Arthralgia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Asthenia	0 (0.0%)	1 (0.3%)	0 (0.0%)
Balance disorder	1 (0.3%)	12 (3.4%)	1 (0.3%)
Blepharospasm	0 (0.0%)	1 (0.3%)	1 (0.3%)
Burning sensation	1 (0.3%)	0 (0.0%)	0 (0.0%)

Table 2: All Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Events	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Cerebral hemorrhage	1 (0.3%)	0 (0.0%)	3 (1.0%)
Cervicobrachial syndrome	0 (0.0%)	1 (0.3%)	0 (0.0%)
Chest discomfort	0 (0.0%)	1 (0.3%)	0 (0.0%)
Cognitive disorder	3 (1.0%)	2 (0.7%)	3 (1.0%)
Complex partial seizures	1 (0.3%)	0 (0.0%)	1 (0.3%)
Confusion postoperative	2 (0.7%)	0 (0.0%)	3 (1.0%)
Confusional state	0 (0.0%)	0 (0.0%)	6 (2.1%)
Convulsion	1 (0.3%)	0 (0.0%)	2 (0.7%)
Depressed mood	0 (0.0%)	1 (0.3%)	0 (0.0%)
Depression	2 (0.7%)	2 (0.7%)	4 (1.4%)
Device related infection	4 (1.4%)	0 (0.0%)	4 (1.4%)
Diplopia	0 (0.0%)	2 (0.7%)	0 (0.0%)
Dizziness	0 (0.0%)	2 (0.7%)	0 (0.0%)
Dysarthria	0 (0.0%)	7 (1.7%)	1 (0.3%)
Dysgeusia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Dyskinesia	0 (0.0%)	33 (10.3%)	1 (0.3%)
Dysphagia	0 (0.0%)	6 (1.7%)	1 (0.3%)
Dysphonia	0 (0.0%)	2 (0.7%)	0 (0.0%)
Dyspnoea	0 (0.0%)	1 (0.3%)	0 (0.0%)
Dystonia	0 (0.0%)	4 (1.4%)	0 (0.0%)
Ecchymosis	1 (0.3%)	0 (0.0%)	1 (0.3%)
Electrocardiogram change	0 (0.0%)	0 (0.0%)	1 (0.3%)
Emotional disorder	0 (0.0%)	1 (0.3%)	0 (0.0%)
Encephalitic infection	1 (0.3%)	0 (0.0%)	1 (0.3%)
Epicondylitis	0 (0.0%)	1 (0.3%)	0 (0.0%)
Fall	0 (0.0%)	9 (2.7%)	4 (0.3%)
Fatigue	0 (0.0%)	1 (0.3%)	0 (0.0%)
Freezing phenomenon	0 (0.0%)	0 (0.0%)	1 (0.3%)
Gait disturbance	0 (0.0%)	4 (1.4%)	1 (0.3%)
Hematoma	0 (0.0%)	0 (0.0%)	1 (0.3%)
Hallucination, auditory	0 (0.0%)	0 (0.0%)	1 (0.3%)
Hallucination, visual	0 (0.0%)	0 (0.0%)	1 (0.3%)
Headache	1 (0.3%)	1 (0.3%)	4 (1.0%)
Hiccups	0 (0.0%)	1 (0.3%)	1 (0.3%)

Table 2: All Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Events	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Hypersensitivity	0 (0.0%)	0 (0.0%)	1 (0.3%)
Hypoaesthesia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Hypomania	0 (0.0%)	3 (1.0%)	0 (0.0%)
Hypotension	0 (0.0%)	0 (0.0%)	1 (0.3%)
Hypoventilation	0 (0.0%)	0 (0.0%)	1 (0.3%)
Impaired healing	1 (0.3%)	0 (0.0%)	1 (0.3%)
Implant site cellulitis	0 (0.0%)	0 (0.0%)	1 (0.3%)
Implant site erythema	2 (0.7%)	0 (0.0%)	1 (0.3%)
Implant site hemorrhage	1 (0.3%)	0 (0.0%)	1 (0.3%)
Implant site hypersensitivity	1 (0.3%)	0 (0.0%)	0 (0.0%)
Implant site infection	4 (1.4%)	0 (0.0%)	3 (1.0%)
Implant site edema	15 (4.8%)	0 (0.0%)	13 (4.1%)
Implant site pain	3 (1.0%)	0 (0.0%)	1 (0.3%)
Implant site paresthesia	1 (0.3%)	0 (0.0%)	1 (0.3%)
Implant site reaction	1 (0.3%)	0 (0.0%)	2 (0.7%)
Impulsive behavior	0 (0.0%)	4 (1.4%)	2 (0.7%)
Insomnia	0 (0.0%)	1 (0.3%)	0 (0.0%)
Intracranial hypotension	1 (0.3%)	0 (0.0%)	1 (0.3%)
Irritability	1 (0.3%)	0 (0.0%)	1 (0.3%)
Mania	0 (0.0%)	2 (0.7%)	0 (0.0%)
Medical device pain	1 (0.3%)	0 (0.0%)	1 (0.3%)
Memory impairment	0 (0.0%)	0 (0.0%)	1 (0.3%)
Mental status changes	1 (0.3%)	0 (0.0%)	2 (0.7%)
Musculoskeletal pain	0 (0.0%)	2 (0.7%)	0 (0.0%)
Musculoskeletal stiffness	0 (0.0%)	1 (0.3%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	1 (0.3%)
Nausea	0 (0.0%)	0 (0.0%)	1 (0.3%)
Neck pain	1 (0.3%)	1 (0.3%)	1 (0.3%)
Oesophageal obstruction	0 (0.0%)	1 (0.3%)	0 (0.0%)
Oropharyngeal discomfort	0 (0.0%)	1 (0.3%)	0 (0.0%)
Pain in extremity	0 (0.0%)	1 (0.3%)	0 (0.0%)
Paresthesia	0 (0.0%)	1 (0.3%)	0 (0.0%)
Paranoia	0 (0.0%)	2 (0.7%)	0 (0.0%)
Parkinson's disease	1 (0.3%)	2 (0.7%)	1 (0.3%)

Table 2: All Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Events	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Parosmia	0 (0.0%)	1 (0.3%)	0 (0.0%)
Photophobia	0 (0.0%)	1 (0.3%)	0 (0.0%)
Photosensitivity reaction	0 (0.0%)	1 (0.3%)	0 (0.0%)
Pneumocephalus	3 (0.7%)	0 (0.0%)	5 (1.4%)
Postoperative fever	0 (0.0%)	0 (0.0%)	2 (0.7%)
Procedural vomiting	0 (0.0%)	0 (0.0%)	1 (0.3%)
Psychotic disorder	0 (0.0%)	1 (0.3%)	0 (0.0%)
Pyrexia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Respiratory disorder	0 (0.0%)	1 (0.3%)	0 (0.0%)
Road traffic accident	0 (0.0%)	1 (0.3%)	0 (0.0%)
Salivary hypersecretion	0 (0.0%)	2 (0.7%)	0 (0.0%)
Sleep disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)
Somnolence	0 (0.0%)	0 (0.0%)	2 (0.7%)
Speech disorder	0 (0.0%)	1 (0.3%)	0 (0.0%)
Staphylococcal skin infection	1 (0.3%)	0 (0.0%)	1 (0.3%)
Stitch abscess	0 (0.0%)	0 (0.0%)	1 (0.3%)
Subdural hemorrhage	0 (0.0%)	0 (0.0%)	1 (0.3%)
Suicidal ideation	0 (0.0%)	2 (0.7%)	0 (0.0%)
Suicide attempt	0 (0.0%)	1 (0.3%)	1 (0.3%)
Supraventricular tachycardia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Suture related complication	0 (0.0%)	0 (0.0%)	2 (0.3%)
Thrombophlebitis superficial	0 (0.0%)	0 (0.0%)	1 (0.3%)
Tremor	2 (0.7%)	5 (1.0%)	3 (1.0%)
Urinary tract infection	0 (0.0%)	0 (0.0%)	1 (0.3%)
Venous injury	0 (0.0%)	0 (0.0%)	1 (0.3%)
Vomiting	0 (0.0%)	0 (0.0%)	1 (0.3%)
Weight decreased	0 (0.0%)	1 (0.3%)	0 (0.0%)
Weight increased	0 (0.0%)	5 (1.7%)	0 (0.0%)
Wound dehiscence	2 (0.7%)	0 (0.0%)	3 (1.0%)
Wound hemorrhage	0 (0.0%)	0 (0.0%)	1 (0.3%)
Wound infection	0 (0.0%)	0 (0.0%)	1 (0.3%)
TOTALS	**65 (20.70%)**	**157 (48.80%)**	**128 (39.10%)**

Incidence = Number of subjects with events divided by all consented subjects (n = 292)

Adverse Events up to 12 Weeks Post Randomization

In the cohort of 160 randomized subjects, a total of 362 events in 111 subjects were reported from time of consent to 12 weeks post randomization.

Of 362 adverse events, 283 events occurred in 86 subjects in the Active Group and 79 events occurred in 25 subjects in the Control Group. Table 3 summarizes only those events related to procedure, stimulation, or hardware, based on their treatment assignment.

Table 3: Adverse Events related to hardware, stimulation or procedure up to 12 weeks post randomization based on treatment assignment

	Related to Hardware		Related to Stimulation		Related to Procedure	
	Number of Events (Incidence)		Number of Events (Incidence)		Number of Events (Incidence)	
Event	Active	Control	Active	Control	Active	Control
Abnormal behavior	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adverse drug reaction	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Aggression	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Agitation	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Agitation postoperative	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Amnesia	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Anxiety	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Aphasia	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Apraxia	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Arthralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Asthenia	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Balance disorder	1 (0.8%)	0 (0.0%)	6 (5.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Blepharospasm	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Burning sensation	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cerebral hemorrhage	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Chest discomfort	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cognitive disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Confusion postoperative	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)
Confusional state	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.1%)	1 (2.6%)
Convulsion	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Depressed mood	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)
Depression	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	1 (2.6%)
Device related infection	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)
Diplopia	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysarthria	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Dyskinesia	0 (0.0%)	0 (0.0%)	22 (16.5%)	1 (2.6%)	0 (0.0%)	0 (0.0%)
Dysphagia	0 (0.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	1 (0.8%)	0 (0.0%)

Table 3: Adverse Events related to hardware, stimulation or procedure up to 12 weeks post randomization based on treatment assignment

	Related to Hardware		Related to Stimulation		Related to Procedure	
	Number of Events (Incidence)		Number of Events (Incidence)		Number of Events (Incidence)	
Dysphonia	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyspnoea	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dystonia	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Electrocardiogram change	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Fall	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	4 (0.8%)	0 (0.0%)
Freezing phenomenon	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Gait disturbance	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hematoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hallucination, auditory	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hallucination, visual	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Headache	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (2.6%)
Hiccups	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hypersensitivity	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Hypoaesthesia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Hypomania	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypotension	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hypoventilation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Impaired healing	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Implant site erythema	1 (0.8%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Implant site infection	2 (1.7%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	1 (2.6%)
Implant site edema	8 (5.8%)	2 (5.1%)	0 (0.0%)	0 (0.0%)	5 (3.3%)	3 (7.7%)
Implant site pain	1 (0.8%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Implant site paresthesia	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Implant site reaction	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Impulsive behavior	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Insomnia	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Intracranial hypotension	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Mania	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Memory impairment	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Mental status changes	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.1%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Nausea	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Neck pain	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Oropharyngeal discomfort	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3: Adverse Events related to hardware, stimulation or procedure up to 12 weeks post randomization based on treatment assignment

	Related to Hardware		Related to Stimulation		Related to Procedure	
	Number of Events (Incidence)		Number of Events (Incidence)		Number of Events (Incidence)	
Paranoia	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Parkinson's disease	0 (0.0%)	1 (2.6%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pneumocephalus	3 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.3%)	0 (0.0%)
Postoperative fever	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Procedural vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Pyrexia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Somnolence	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (2.6%)
Staphylococcal skin infection	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Stitch abscess	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Supraventricular tachycardia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Tremor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	1 (2.6%)
Urinary tract infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Venous injury	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Weight increased	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Wound dehiscence	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (2.6%)
Wound haemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
TOTALS	**29 (22.20%)**	**11 (28.50%)**	**67 (53.60%)**	**2 (5.20%)**	**76 (58.20%)**	**22 (54.40%)**

Serious Adverse Events

Among all the consented (enrolled) subjects (n = 292), a total of 74 Serious Adverse Events (SAE) were reported in 46 subjects. All serious adverse events related to hardware, stimulation or procedure are summarized in Table 4 below. Of 74 Serious Adverse Events, 19 were related to hardware, 2 related to stimulation, and 31 related to procedure.

Infection has been the most commonly reported serious adverse event associated with device-hardware/procedure (8 events, representing 2.7% of subjects). There were three events (each) of device-hardware/procedure-related serious adverse events of peri-operative intracranial hemorrhage (representing 1% of subjects) and seizure (representing 1% of subjects). Stimulation-related serious adverse events include one event of mania and one event of a failed suicide attempt.

Table 4: Serious Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Event	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Aphasia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Cerebral hemorrhage	0 (0.0%)	0 (0.0%)	1 (0.3%)
Complex partial seizures	1 (0.3%)	0 (0.0%)	1 (0.3%)
Confusion postoperative	1 (0.3%)	0 (0.0%)	2 (0.7%)
Confusional state	0 (0.0%)	0 (0.0%)	1 (0.3%)
Convulsion	1 (0.3%)	0 (0.0%)	2 (0.7%)
Device related infection	4 (1.4%)	0 (0.0%)	4 (1.4%)
Encephalitic infection	1 (0.3%)	0 (0.0%)	1 (0.3%)
Hypoventilation	0 (0.0%)	0 (0.0%)	1 (0.3%)
Implant site hemorrhage	1 (0.3%)	0 (0.0%)	1 (0.3%)
Implant site infection	1 (0.3%)	0 (0.0%)	1 (0.3%)
Implant site edema	5 (1.7%)	0 (0.0%)	5 (1.7%)
Intracranial hypotension	1 (0.3%)	0 (0.0%)	1 (0.3%)
Mania	0 (0.0%)	1 (0.3%)	0 (0.0%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	1 (0.3%)
Pneumocephalus	1 (0.3%)	0 (0.0%)	1 (0.3%)
Pyrexia	0 (0.0%)	0 (0.0%)	1 (0.3%)
Staphylococcal skin infection	1 (0.3%)	0 (0.0%)	1 (0.3%)
Subdural hemorrhage	0 (0.0%)	0 (0.0%)	1 (0.3%)
Suicide attempt	0 (0.0%)	1 (0.3%)	1 (0.3%)
Wound dehiscence	1 (0.3%)	0 (0.0%)	1 (0.3%)
Wound hemorrhage	0 (0.0%)	0 (0.0%)	1 (0.3%)
Wound infection	0 (0.0%)	0 (0.0%)	1 (0.3%)
TOTALS	**19 (6.10%)**	**2 (0.60%)**	**31 (9.90%)**

Incidence = Number of subjects with events divided by all consented subjects (n = 292)

In the cohort of 160 randomized subjects, a total of 26 serious adverse events in 20 subjects were reported. Of those, 21 serious adverse events in 16 subjects were in the active group and 5 serious adverse events in 4 subjects were in the control group was reported.

Table 5 summarizes only those serious adverse events related to hardware, stimulation or procedure up to Week 12 post randomization based on treatment assignment.

Table 5: Serious Adverse Events related to hardware, stimulation or procedure up to 12 weeks post randomization based on treatment assignment

	Related to Hardware		**Related to Stimulation**		**Related to Procedure**	
	Number of Events (Incidence)		Number of Events (Incidence)		Number of Events (Incidence)	
Event	Active	Control	Active	Control	Active	Control
Aphasia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Confusion postoperative	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)
Confusional state	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Convulsion	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Device related infection	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)
Hypoventilation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Implant site edema	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Implant site infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Intracranial hypotension	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Pneumocephalus	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Pyrexia	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Staphylococcal skin infection	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
Wound hemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
TOTALS	**5 (4.10%)**	**4 (10.40%)**	**0 (0.00%)**	**0 (0.00%)**	**13 (10.60%)**	**4 (10.40%)**

Incidence = Number of subjects with events divided by number of subjects in each group (Active = 121 subjects, Control = 39 subjects)

Deaths

Two deaths were reported. One subject died as a result of accidental physical trauma which was determined to be unrelated to the study device and/or implant procedure. The other cause of death is unknown; additional information is not available, and the relationship of the death to the device or stimulation is not known.

Efficacy Results

Primary Endpoint

The study efficacy results are based on a cohort of 160 randomized subjects who completed their Week 12 post randomization. Please note that though the total number of randomized subjects is 160, the total number of subjects available for analysis is 156 (118 active and 38 control). This is because four subjects (3 in treatment group and 1 in the control group) did not have baseline scores.

Based on the results of a pre-specified interim analysis, the study successfully met its primary endpoint with statistically significant improvement ($p < 0.001$) in mean change in waking hours per day with good symptom control and no troublesome dyskinesia, with no increase in antiparkinsonian medications (i.e., Levodopa Equivalent Dosage (LED)), from baseline to 12 weeks post-randomization in the Active (3.74 ± 4.79 hours) compared to the Control group (0.72 ± 3.56 hours) as shown in Table 6.

Table 6: Mean change in waking hours per day with good symptom control and no troublesome dyskinesia, with no increase in antiparkinsonian medications (LED), from baseline to 12 weeks post-randomization

	Active Group	Control Group
	Mean (SD) N [95% CI]	Mean (SD) N [95% CI]
Baseline	7.78 (3.65) 118 [7.1 - 8.4]	8.08 (2.92) 38 [7.1 - 9.0]
12 weeks post-randomization	12.37 (3.56) 118 [11.7 - 13.0]	8.96 (3.94) 38 [7.7 - 10.3]
Change from baseline to 12 weeks post-randomization	3.74 (4.79) 118 [2.9 - 4.6]	0.72 (3.56) 38 [-0.5 - 1.9]
Difference in change from baseline to 12 weeks post-randomization between Active and Control groups	3.03 (4.52) [1.4 - 4.7]	
p-value	<0.001	

Post-hoc analysis was performed to report the improvement in mean change in waking hours per day with good symptom control and no troublesome dyskinesias from Baseline to 12 weeks post-randomization, without requirement in the anti-parkinsonian medication (as included in the primary endpoint). An improvement of 4.6 ± 4.81 hours in the Active group compared to 0.88 ± 3.57 hours in the Control group was noted.

Secondary Endpoints

For the following secondary endpoints the sample size is reported as a single "n" out of the 160 (active and control) pre-specified interim analysis cohort. These analyses are reported using the available data only; this is acceptable because the missing data rate for this study is sufficiently low (~5%).

Unified Parkinson's disease Rating Scale – Section III (UPDRS III)

UPDRS III is the motor sub-section of the Unified Parkinson's disease Rating Scale (2) (UPDRS) and is used to evaluate overall motor disability, including the classic symptoms of Parkinson's Disease (PD).

This questionnaire was administered in the *meds off* and *meds on* condition.

Meds off condition

This section summarizes the results in the *meds off* condition. Subjects withheld their anti-parkinsonian medications for at least 12 hours (or overnight) prior to study visit.

A 12.0 ± 11.4 (n = 115) point improvement in the UPDRS III scores in the *stim on/meds off* condition was reported in the Active group compared to a 1.19 ± 8.96 (n = 37) in the Control group as illustrated in Figure 3 below. A difference of 10.83 ± 10.88 ($p < 0.001$)[1] points between both the group was found.

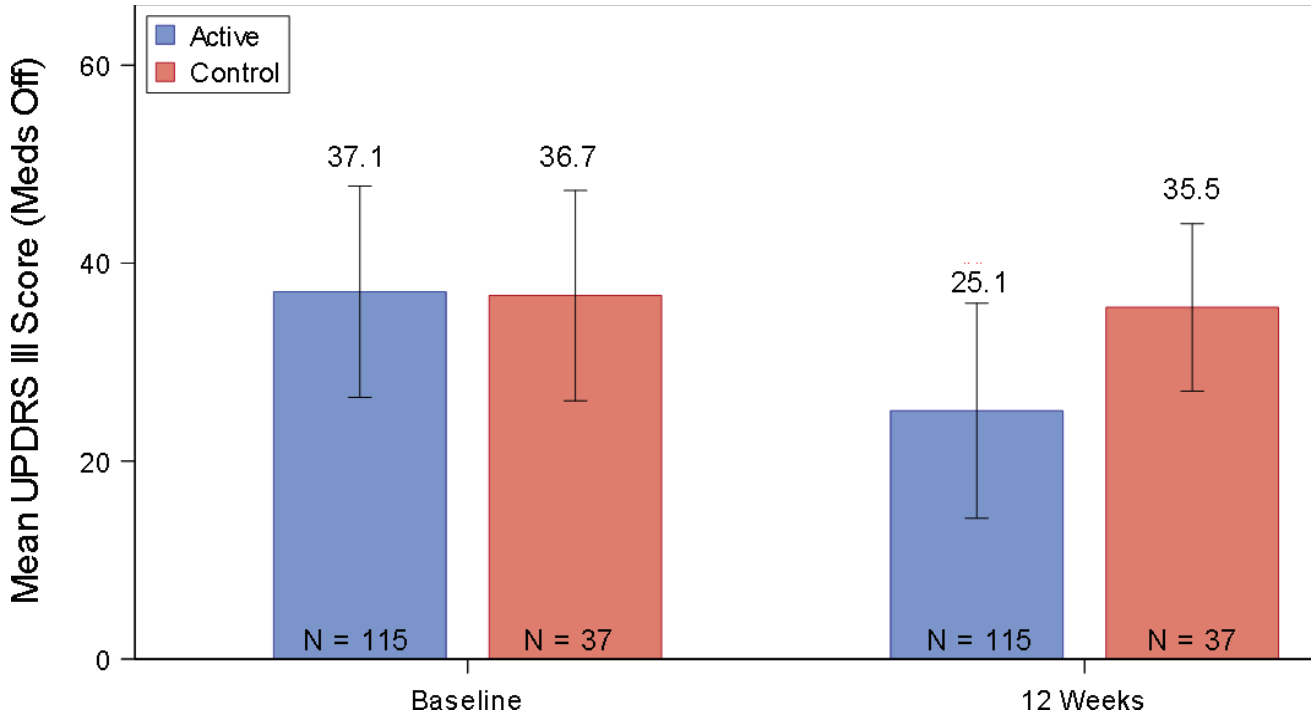


Figure 3. Difference between the Active and Control groups in the mean change in UPDRS-III Score from baseline *meds off* to 12 weeks post-randomization *stim on/meds off*.

At 12 weeks post-randomization, subjects in the Active group demonstrated over twice the improvement for clinical significance. Subjects in the Control group showed almost no change.

1 Not adjusted for multiplicity

Meds on condition

In the *meds on* condition subjects took their usual anti-parkinsonian medications and assessments were performed at 1 hour (± 10 minutes) post-dosing. (Note that it is possible that subjects may not have reached their Best *meds on* condition but instead be at a partial meds on condition at 1 hour post-dosing.) All *meds on* assessments were completed without any additional intervention (i.e., additional medication given or longer wait to get to Best *meds on* condition).

A larger improvement in UPDRS III scores in *stim on/meds on* condition at Week 12 post-randomization was noted in the Active group (5.06 ± 8.72, n = 114) compared to the Control group (2.84 ± 11.20, n = 37) as shown in Figure 4. However, this difference between the two groups was not statistically significant.

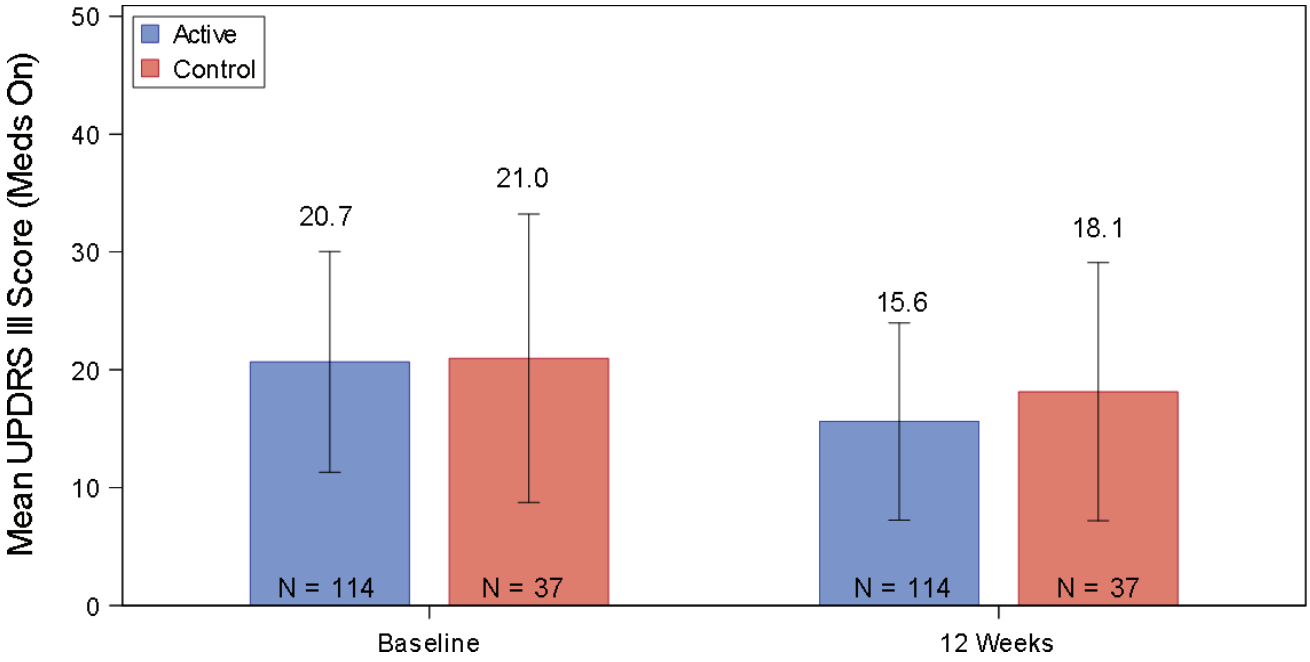


Figure 4. Difference between the Active and Control groups in the mean change in UPDRS-III scores from baseline *meds on* to 12 weeks *stim on/meds on* post-randomization.

39-Item Parkinson's Disease Questionnaire (PDQ-39)

The impact of treatment on subjects' quality of life was evaluated using 39-Item Parkinson's Disease Questionnaire (4) (PDQ-39), a 39-Item questionnaire designed to measure the specific impact of Parkinson's disease on quality of life. The questionnaire measures the impact on health-related quality of life along 8 dimensions including mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication and bodily discomfort (higher scores indicate worsening of quality of life).

This questionnaire was administered in the *meds on* condition.

A 7.79 ± 12.55 (n = 115) point improvement (22%) in the Active group and a 2.56 ± 13.81 (n = 37) worsening (23%) in Control group was noted in the PDQ-39 summary index score as illustrated in Figure 5 below.

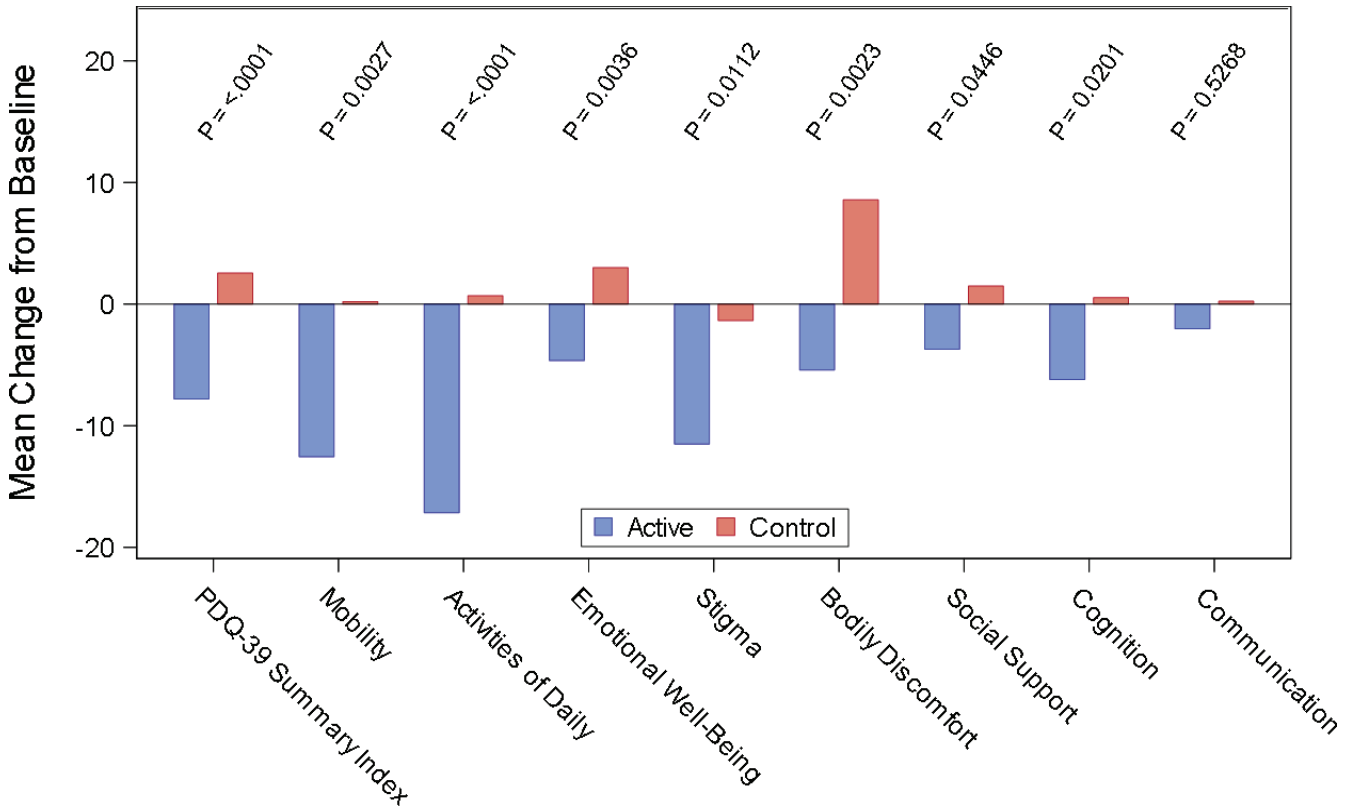


Figure 5. Difference between the Active and Control groups in mean change in PDQ-39 score from baseline to 12 weeks post-randomization. P value from two sample test (Not adjusted for multiplicity).

As illustrated in Figure 5 several sub-domains of the PDQ Questionnaire - mobility, ADL, stigma and cognition showed improvement in the Active group at Week 12 post-randomization.

Modified Schwab and England (SE)

Modified Schwab and England (2) (SE) is a single-item scale to quantify a PD patients' ability to perform activities of daily living. Scores range from 0% (completely bed-ridden) to 100% (completely independent) with higher scores indicating better function.

This questionnaire was administered in the *meds on* condition.

As shown in Figure 6, a 5.70 ± 14.26 (n = 114) point improvement in SE scores in the Active group as compared to a 1.89 ± 7.76 (n = 37) point worsening in SE scores in the Control group was reported.

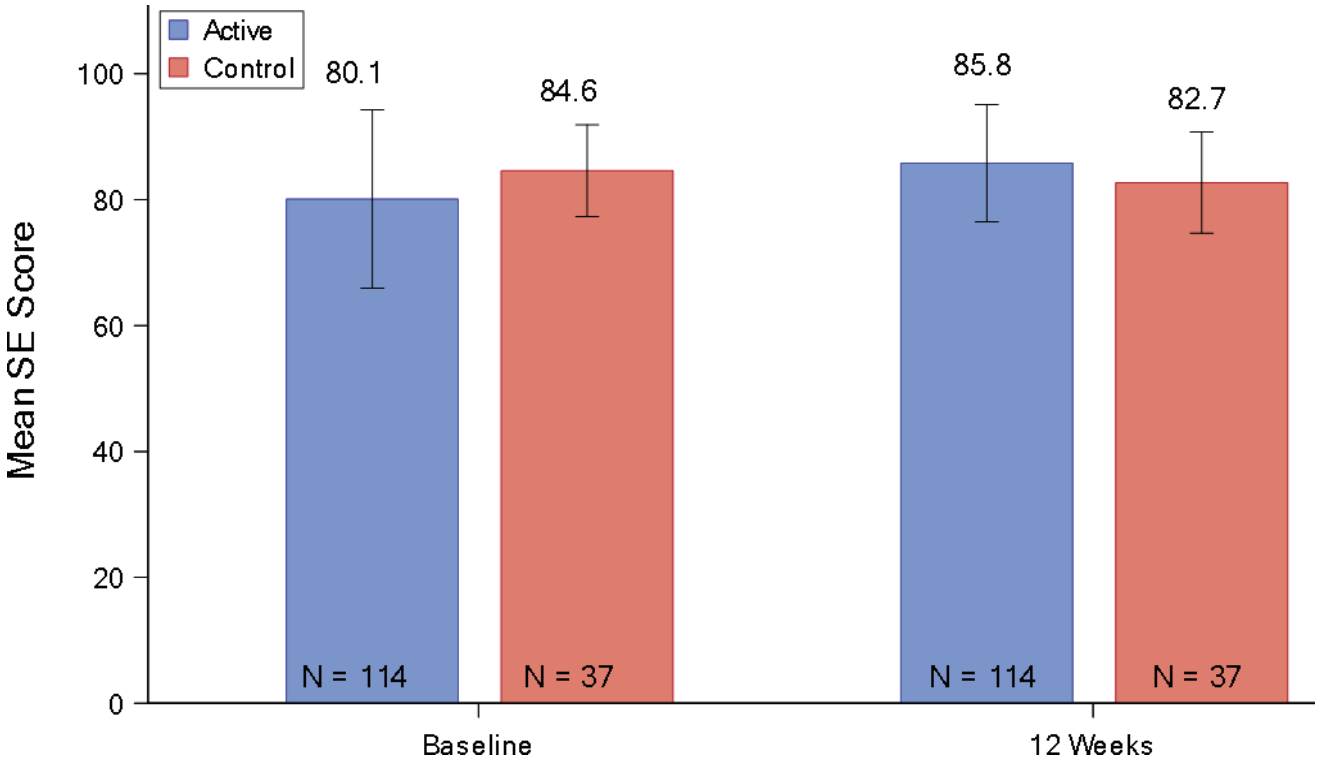


Figure 6. Difference between the Active and Control groups in the mean change in SE scores from baseline to 12 weeks post-randomization.

This difference in quality of life as measured by SE scores between Active and Control groups was statistically significant ($p < 0.01$)[2].

2 Not adjusted for multiplicity

Clinical Global Impression of Change (CGI-C) as assessed by physician

Physicians (blinded assessor) were asked to report their impression of change (1) in subjects' symptoms in a manner similar to what was done by subjects' themselves at Week 12 post-randomization. The responses are illustrated in Figure 7 below.

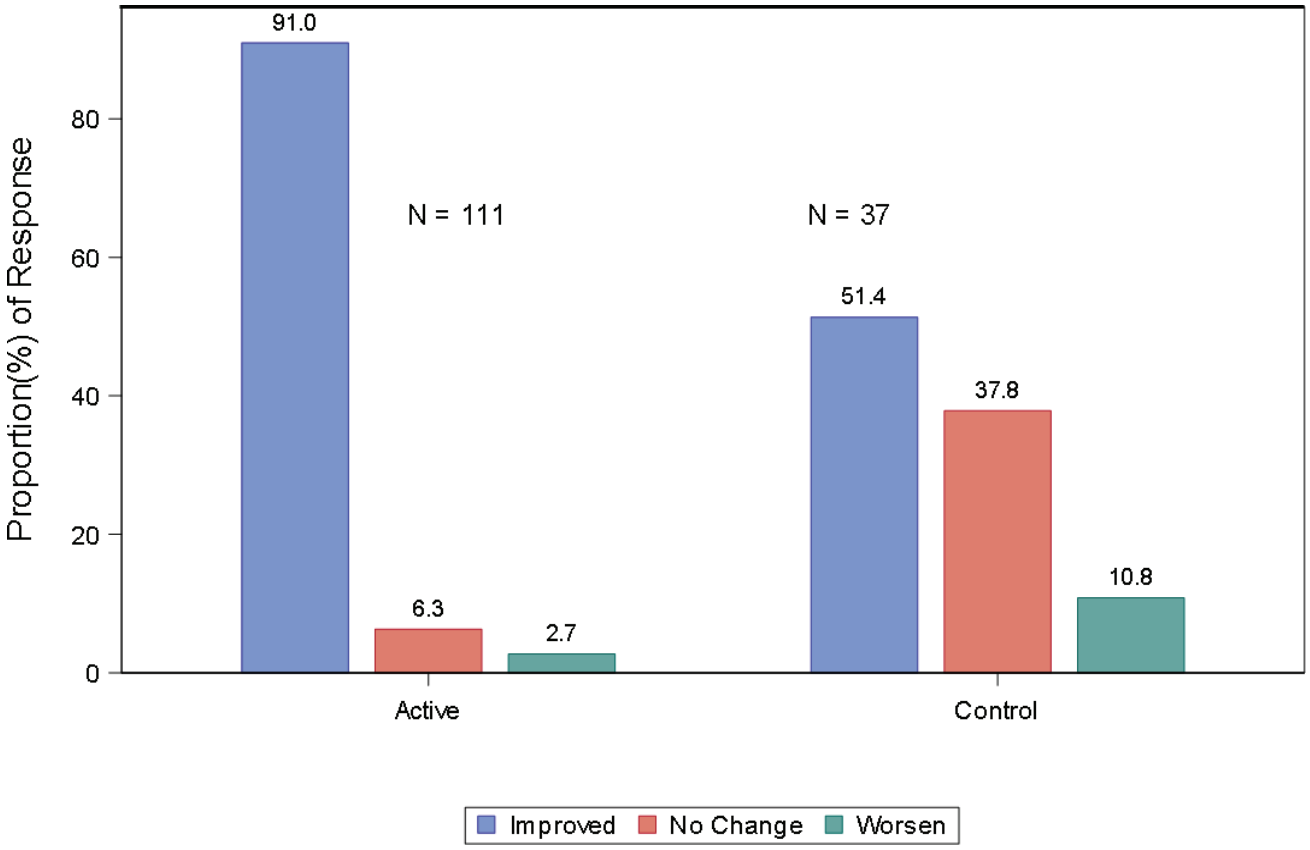


Figure 7. Difference between the Active and Control groups in the mean CGI-C, as assessed by the physician, at Week 12 post-randomization.

At Week 12 post-randomization, in the opinion of the blinded assessor (clinician), 91.0% of subjects in the Active group improved following DBS. A significant percentage of these subjects were in the "very much improved" and "much improved" category.

For those subjects in the Control group, the assessor reported 37.8% of subjects had no change in their PD symptoms. It was also interesting to note that they reported 51.4% of subjects showed improvement at 12 weeks as well.

A statistically significant ($p < 0.0001$)[3] difference between the Active and Control groups was observed.

3 Not adjusted for multiplicity

Clinical Global Impression of change as assessed by subjects

Subjects were asked to report their impression of change in their symptoms at Week 12 post-randomization as compared with Baseline using a questionnaire with a seven-point scale (ranging from “marked worsening” to “very much improved”). This questionnaire was administered in the *meds on* condition.

The results are illustrated in Figure 8 below.

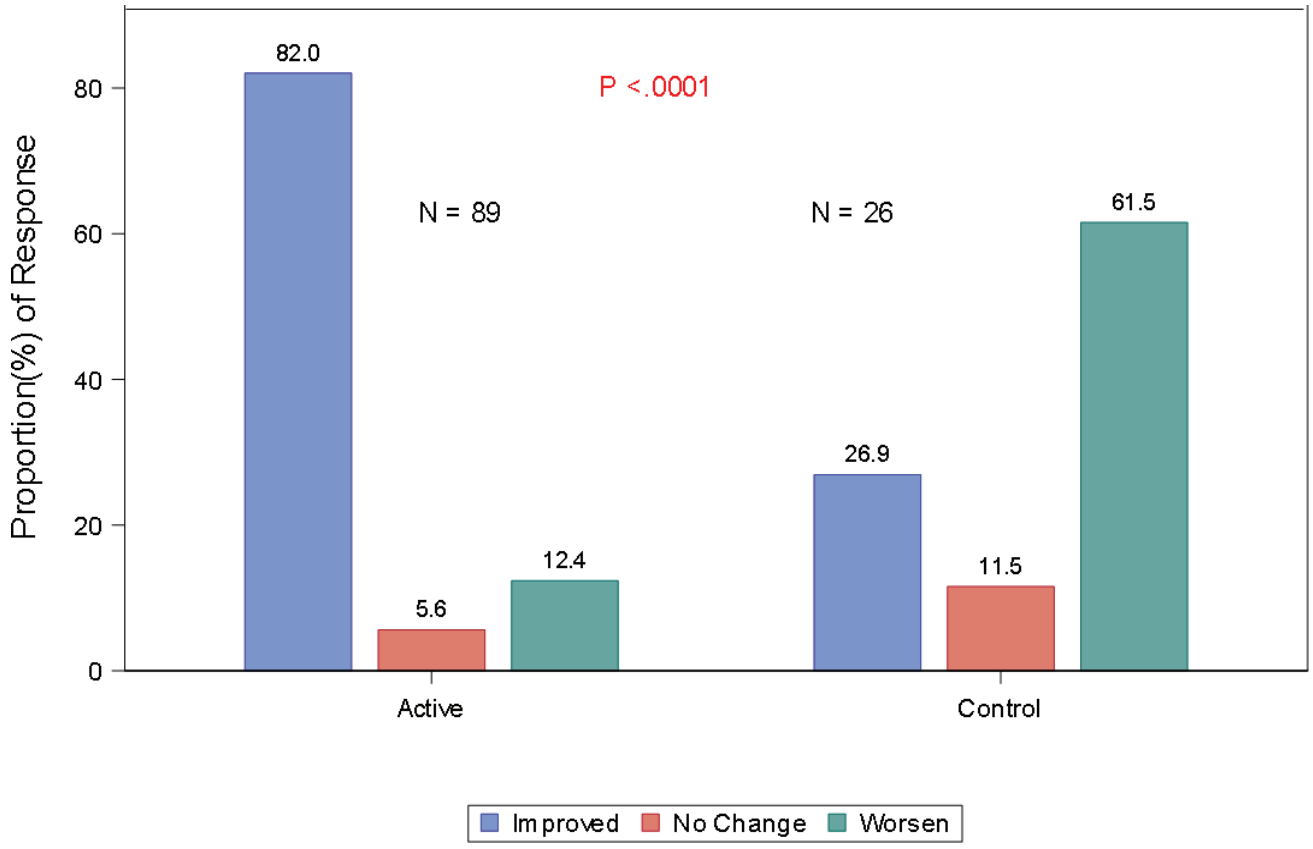


Figure 8. Difference between the Active and Control groups in the mean CGI-C, as assessed by the subject, at Week 12 post-randomization. P value from Fisher’s Exact test.

At Week 12 post-randomization, 82.0% of Active subjects reported an improvement in their PD symptoms compared to 26.9% in the Control group. In the Control group, while 26.9% reported improved, a majority (61.5%) reported worsened disease state at 12 weeks.

A statistically significant ($p < 0.0001$)[4] difference between the Active and Control groups was reported.

4 Not adjusted for multiplicity

Treatment Satisfaction score

Subjects' satisfaction with treatment was assessed where they rated their overall satisfaction with the device and their willingness to recommend the therapy. They were also asked if they would be willing to repeat the treatment process again.

The responses of subjects in the Active and Control groups are summarized in Table 7 below.

Table 7: Treatment Satisfaction Score at 12 weeks post-randomization

	Active Group	Control Group
Overall Satisfaction	%(n/N)	%(n/N)
Extremely Dissatisfied	3.4% (4 / 116)	11.1% (4 / 36)
Very Dissatisfied	3.4% (4 / 116)	13.9% (5 / 36)
Dissatisfied	1.7% (2 / 116)	16.7% (6 / 36)
Somewhat Satisfied	5.2% (6 / 116)	13.9% (5 / 36)
Satisfied	16.4% (19 / 116)	16.7% (6 / 36)
Very Satisfied	28.4% (33 / 116)	22.2% (8 / 36)
Extremely Satisfied	41.4% (48 / 116)	5.6% (2 / 36)
Willingness to go through treatment process again		
Yes	90.5% (105 / 116)	80.6% (29 / 36)
No	9.5% (11 / 116)	19.4% (7 / 36)
Would recommend therapy to a friend with Parkinson's disease		
Yes	91.4% (106 / 116)	83.3% (30 / 36)
No	8.6% (10 / 116)	16.7% (6 / 36)

91.4% of subjects in the Active group and 58.4% in the Control group reported being overall satisfied (varying degrees) with their treatment.

Over 90% of subjects in the Active group were willing to go through the treatment process again and would also recommend the therapy to a friend with Parkinson's disease. A similar trend was observed in the Control group as well.

A statistically significant ($p < 0.0001$)[5] difference in treatment satisfaction score for both the groups was reported.

5 Not adjusted for multiplicity

Unified Parkinson's Disease Rating Scale – Section II (UPDRS II) (Activities of Daily Living)

Unified Parkinson's Disease Rating Scale – Section II (2) (UPDRS II) is a sub-section of the UPDRS Scale and focuses on subjects' activities of daily living such as speech, salivation, swallowing, handwriting, cutting food and handling utensils, dressing, etc. UPDRS II was administered in the *meds off* and *meds on* condition during the study.

This section describes the results in the *meds on* condition. Details on how the *meds on* condition was achieved are summarized earlier in this section. A 1.74 ± 5.90 (n = 115) in the Active group versus a 0.06 ± 5.25 (n = 36) point improvement in the Control group in UPDRS II scores in the *stim on/meds on* condition was reported at Week 12 post-randomization as shown in Figure 9 below.

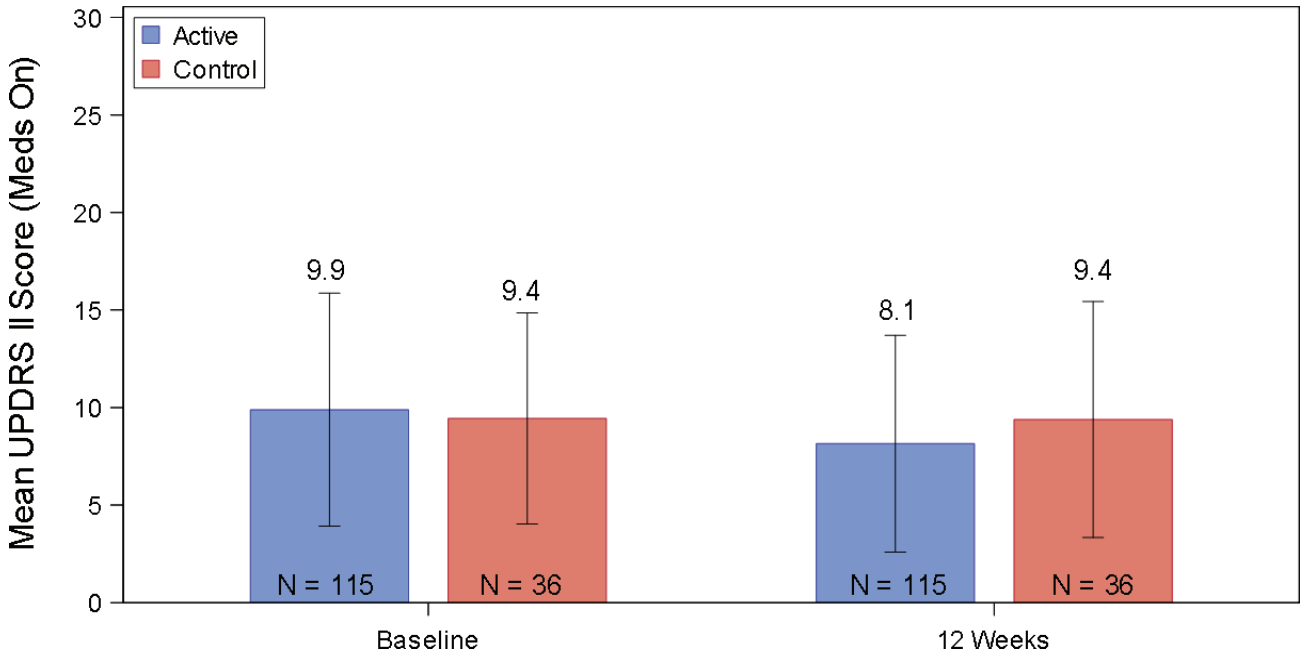


Figure 9. Difference between the Active and Control groups in the mean change in UPDRS-II scores from baseline *meds on* to 12 weeks *stim on/meds on* post-randomization.

The change in UPDRS II scores in *meds on* condition was not statistically significant.

36-Item Short Form Survey (SF-36 v2) (Quality of Life)

36-Item Short Form Survey (5) (SF-36v2) is a quality of life scale that measures subjects' functional health and well-being from their own point of view. It is comprised of several questions spanning eight health domains which contribute to the scoring of two component summary measures: physical health and mental health.

Subjects in the Active group noted an improvement of 3.35 ± 7.90 points compared to a slight worsening (-0.23 ± 6.79) in the Control group in the physical health domain. In the mental health domain, both groups showed small improvements as shown in Table 8 below. The difference between the two groups is not statistically significant.

Table 8: Mean change in the SF-36v2 score from baseline to 12 weeks post-randomization for Active and Control groups

	SF-36v2 Physical (PCS) Mean (SD) N [95% CI]		SF-36v2 Mental (MCS) Mean (SD) N [95% CI]	
	Active Group	Control Group	Active Group	Control Group
Baseline	39.77 (7.64) 114 [38.3 - 41.2]	39.55 (6.52) 36 [37.3 - 41.8]	49.97 (8.23) 113 [48.4 - 51.5]	50.33 (8.44) 36 [47.5 - 53.2]
12 weeks post-randomization	43.12 (7.95) 114 [41.6 - 44.6]	39.32 (8.37) 36 [36.5 - 42.1]	51.18 (9.04) 113 [49.5 - 52.9]	52.01 (9.82) 36 [48.7 - 55.3]
Change from baseline to 12 weeks post-randomization	3.35 (7.90) 114 [1.9 - 4.8]	-0.23 (6.79) 36 [-2.5 - 2.1]	1.21 (9.53) 113 [-0.6 - 3.0]	1.68 (8.16) 36 [-1.1 - 4.4]
Difference in change between Active and Control groups	3.58 (7.65) [0.7 - 6.5]		-0.47 (9.22) [-4.0 - 3.0]	
p-value	0.0591			

PCS = Physical Component Summary score.

MCS = Mental Component Summary score.

p-value is from a two-sided two-group paired Hotelling's T-square test using the 2x1 vector of PCS and MCS difference in change between Active and Control groups. Not adjusted for multiplicity.

Conclusions from INTREPID Clinical Study

The INTREPID Study was designed to evaluate the safety and effectiveness of the Boston Scientific Vercise™ Deep Brain Stimulation (DBS) System for bilateral stimulation of the subthalamic nucleus (STN) in the treatment of patients with advanced, levodopa-responsive bilateral Parkinson's disease (PD), which is not adequately controlled with medication.

Of the 292 subjects who provided consent to participate in the study, 177 subjects were implanted bilaterally in the STN with the Vercise DBS System. This document provides the effectiveness data for 160 randomized subjects that completed their Week 12 post-randomization visit as of December 31, 2016 and safety data for 292 enrolled subjects.

The primary endpoint of the study was the difference in change from Baseline to Week 12 post-randomization visit between the Active and Control groups in subjects' ON time with no increase in antiparkinsonian medications. ON time included "ON time" as well as "ON time with non-troublesome dyskinesias" as measured on the Parkinson's Disease (PD) diary (3). This validated measure was utilized for the primary endpoint as the PD diary allowed for subjects' to assess their own health status without any bias from study investigators or their interpretation. The PD diary collects subjects' PD symptoms/health status in 30 minute increments during their awake hours – this allows for a deeper understanding of their disease state including fluctuations and impact to their daily routine. In addition to ON time, the primary endpoint also included a requirement that subjects must have no increase in their antiparkinsonian medications during the blinded period as calculated via levodopa equivalents. This was included to isolate the benefits of DBS for the treatment of PD. This additional criterion is stringent and further added to the scientific rigor of the INTREPID Study. Other randomized controlled trials including Okun 2012 (12), Weaver 2009 (13), Deuschl 2006 (14) did not have this additional criterion.

Though the study is still ongoing, per the scheduled interim analysis, the study successfully met its primary endpoint with statistically significant improvement ($p < 0.001$) in mean change in waking hours per day with good symptom control and no troublesome dyskinesia, with no increase in antiparkinsonian medications (LED), from baseline to 12 weeks post-randomization in the Active (3.74 ± 4.79 hours) compared to the Control group (0.72 ± 3.56 hours). Post-hoc analysis showed that this improvement increased when the analysis was performed with no requirement in medication (as included in the primary endpoint). An improvement of 4.6 ± 4.81 hours in the Active group compared to 0.88 ± 3.57 hours in the Control group was noted.

In addition to their ON time (good symptom control and no troublesome dyskinesia), subjects in the Active group also noted a significant improvement in their OFF time when the medication is no longer effective and subjects' symptoms return.

The primary endpoint result was also supported by several secondary endpoints including improvement in Unified Parkinson's Disease Rating Scale – Section III (2) (UPDRS III) scores, quality of life such as 39-Item Parkinson's Disease Questionnaire (4) (PDQ-39), Modified Schwab and England (2) (SE) scores. The overall change in subjects' disease state during the study follow-up as compare to Baseline was evaluated by the subjects and physicians to provide different perspectives. In the Active group, 82.0% of subjects reported varying degrees of improvement as compared to Baseline, which was supported by physician response of 91.0%, who similarly reported varying degrees of improvement in their subjects.

91.4% of subjects in the Active group reported being overall satisfied with their treatment. A similar trend was observed when subjects were asked if they would recommend the therapy or be willing to repeat the treatment again. This is indicative of the overall impact that DBS with the Vercise System had on subjects' PD state and their overall quality of life.

There were no unanticipated adverse events and the overall incidence of device/procedure-related serious adverse events (SAEs) was comparable to published reports. The adverse event and safety profiles were similar to those seen in other recent studies of DBS Systems.

Results of this prospective, multi-center, double-blinded randomized controlled trial designed to evaluate the Vercise DBS System for bilateral stimulation of the subthalamic nucleus in the treatment of Parkinson's disease demonstrated that its benefits outweigh the associated risks. Furthermore, the safety and effectiveness of the Vercise System were established.

VANTAGE Clinical Study

Study Design

VANTAGE is a multi-center, prospective, open-label, single-arm study of the safety and efficacy of the Vercise DBS System for bilateral stimulation of the subthalamic nucleus (STN) in the treatment of moderate to severe idiopathic Parkinson's Disease (PD). Six (6) sites participated in this study from Austria, France, Germany, Italy, Spain and the U.K. Enrollment was completed between November 2010 and December 2012. The study population included male and female patients, ages 21 to 75, diagnosed with idiopathic PD as determined by clinical presence of at least 2 of the 3 cardinal features (resting tremor, rigidity, and bradykinesia) and good levodopa response. Subjects were required to have a PD symptom severity level based on the following criteria:

- Modified Hoehn and Yahr (6) stage ≥ 2
- Unified Parkinson's Disease Rating Scale (2) (UPDRS) motor exam of ≥ 30 in the "Meds Off" condition
- Motor complications that cannot be controlled with pharmacologic therapy.

During the first 52 weeks post-implant, there were 2 pre-implant visits and 3 evaluation follow-up visits at 12, 26, and 52 weeks post-implant. Following DBS implant, clinicians monitored anti-parkinsonian medication dosages.

To obtain a comprehensive picture of patients improvement in the study, data collected at study visits (baseline and follow-up) included a 3-day motor diary recorded at home prior to the visit, the Unified Parkinson's Disease Rating Scale (2) (UPDRS), 39-Item Parkinson's Disease Questionnaire (4) (PDQ-39), 36-Item Short Form Survey (5) (SF-36 v2), and Global Impression of Change (1). At each visit, patients were evaluated without medication (Meds Off) and with medication (Meds ON). At follow-up visits post-implant, patients were evaluated with the DBS device turned on (Stim On).

Patient Accountability

A total of 40 patients were implanted in the study with the Vercise Deep Brain Stimulation (DBS) System. The majority of study patients were male (27/40; 67.5%). The mean age of study patients was 60.2 years (± 7.82) and the mean duration of Parkinson's Disease (PD) symptoms was 11.7 years (± 4.57).

Of the 40 patients implanted with the Vercise DBS System, 39 completed the 52 weeks of follow-up. 1 patient (2.5%) terminated prior to the 26 Week Visit due to death following pneumonia, not related to the study device or procedure.

Safety Results

All Adverse Events

During the 52 weeks post-implant period, a total of 125 adverse events (AEs) were reported in 37 implanted patients. Out of 125 adverse events, 107 were non-serious and 18 were serious adverse events. All adverse event relationships were assessed and reported by the investigators. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA).

All adverse events reported by study site personnel as related to hardware, stimulation or procedure is summarized in Table 9 below. Of the 125 events, 6 events were considered related to hardware, 17 events were related to stimulation and 12 events were related to procedure.

Table 9: All Adverse Events related to Hardware, Stimulation or Procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Preferred Term	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Anxiety	0 (0.0%)	1 (2.5%)	0 (0.0%)
Apathy	0 (0.0%)	3 (7.5%)	2 (5.0%)
Confusional state	0 (0.0%)	1 (2.5%)	0 (0.0%)
Device migration	0 (0.0%)	0 (0.0%)	1 (2.5%)
Diplopia	0 (0.0%)	1 (2.5%)	0 (0.0%)
Dysarthria	0 (0.0%)	1 (2.5%)	1 (2.5%)
Dystonia	0 (0.0%)	2 (2.5%)	0 (0.0%)
Fall	0 (0.0%)	1 (2.5%)	0 (0.0%)
Gait disturbance	0 (0.0%)	1 (2.5%)	0 (0.0%)
Hallucination, auditory	0 (0.0%)	0 (0.0%)	1 (2.5%)
Hypoaesthesia	0 (0.0%)	1 (2.5%)	0 (0.0%)
Implant site haematoma	0 (0.0%)	0 (0.0%)	1 (2.5%)
Implant site infection	0 (0.0%)	0 (0.0%)	1 (2.5%)
Incision site infection	1 (2.5%)	0 (0.0%)	1 (2.5%)
Laboratory test abnormal	0 (0.0%)	0 (0.0%)	1 (2.5%)
Localised infection	1 (2.5%)	0 (0.0%)	0 (0.0%)
Movement disorder	0 (0.0%)	1 (2.5%)	0 (0.0%)
Neck pain	1 (2.5%	0 (0.0%)	0 (0.0%)
Parkinson's disease	1 (2.5%)	1 (2.5%)	0 (0.0%)
Postoperative wound infection	0 (0.0%)	0 (0.0%)	1 (2.5%)
Respiratory depression	0 (0.0%)	0 (0.0%)	1 (2.5%)
Speech disorder	0 (0.0%)	2 (5.0%)	1 (2.5%)
Staphylococcal infection	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tremor	1 (2.5%)	0 (0.0%)	0 (0.0%)
Weight increased	0 (0.0%)	1 (2.5%)	0 (0.0%)
TOTALS	**6 (12.5%)**	**17 (40.0%)**	**12 (30.0%)**

Incidence = Number of subjects with events divided by all implanted subjects (n = 40)

Serious Adverse Events

A total of 18 Serious Adverse Events (SAE) were reported in 10 subjects. All serious adverse events related to hardware, stimulation or procedure is summarized in Table 10 below. Of 18 Serious Adverse Events, 2 were related to hardware and 3 were related to procedure. There were no serious adverse events related to stimulation.

Table 10: Serious Adverse Events related to hardware, stimulation or procedure

	Related to Hardware	Related to Stimulation	Related to Procedure
Preferred Term	Number of Events (Incidence)	Number of Events (Incidence)	Number of Events (Incidence)
Device migration	0 (0.0%)	0 (0.0%)	1 (2.5%)
Implant site infection	0 (0.0%)	0 (0.0%)	1 (2.5%)
Localised infection	1 (2.5%)	0 (0.0%)	0 (0.0%)
Respiratory depression	0 (0.0%)	0 (0.0%)	1 (2.5%)
Staphylococcal infection	1 (2.5%)	0 (0.0%)	0 (0.0%)
TOTALS	**2 (5.0%)**	**0 (0.0%)**	**3 (7.5%)**

Incidence = Number of subjects with events divided by all implanted subjects (n = 40)

Two serious adverse events of infection reported as related to the study device occurred in 1 patient. These events included an initial infection of the patient's scalp treated with antibiotics and recurrent scalp infection (due to staphylococcus), also treated with antibiotics. Both infections have resolved without residual effects. In addition, there were 3 SAEs which were considered related to the study-procedure. The procedure related events include one event of implant site infection in the vicinity of the Implantable Pulse Generator (IPG) pocket (treated with antibiotics and surgical revision of the pocket area); one event of IPG migration (treated with surgical repositioning of the IPG); and one event of respiratory depression occurring during the implant procedure as a result of poor body positioning (treated with repositioning of the patient). All 3 procedure-related SAEs resolved without residual effects.

Of the 16 serious adverse events which were not device or hardware-related, 14 have resolved with/without residual effects; 2 are presently not resolved. These include individual reports of lumbago and neoplasm. One SAE of pneumonia resulted in death.

Conclusion from VANTAGE Clinical Study

The safety profile in VANTAGE Study was similar to those seen in the INTREPID Study and other recent studies of Deep Brain Stimulation (DBS). The most frequent device and/or procedure-related adverse events included infection, device migration and respiratory depression. All serious adverse events (SAEs) related to either a device or procedure resolved without residual effects. There were no unanticipated adverse events and the overall incidence of device and procedure-related SAEs is comparable to published reports. The VANTAGE Study data further supports the results from the INTREPID Study in demonstrating the safety of the Vercise DBS System.

Appendix A: Summary of Clinical Effectiveness of GPi Stimulation for Parkinson's Disease

In lieu of providing a clinical data set for Vercise PC and Vercise Gevia DBS Systems, Boston Scientific provided a technological comparison (including a comparison of the technology, surgical procedures, and instructions for use) of Vercise PC and Vercise Gevia DBS Systems to the Medtronic Activa Parkinson's Control Therapy which was approved under P960009/S007 for GPi stimulation. The purpose of the technological comparison was to establish sufficient similarity of the two DBS devices such that FDA could apply Section 216 of the Food and Drug Modernization Act (FDAMA), i.e., the "six-year rule," to assess the effectiveness profile of Vercise PC and Vercise Gevia DBS Systems.

According to FDA's "Guidance on Section 216 of the Food and Drug Modernization Act of 1997" available at: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073709.pdf, FDA may choose to utilize the publicly available detailed SSED of a previously approved device to support approval of a PMA for a new device if the applicant provides "a detailed justification of how the information in the earlier SSED applies to the applicant's device" and if the applicant is able "to describe how the devices are similar enough to allow for the data from the earlier device to apply to the new device."

Technical Comparison

For the purposes of establishing sufficient similarity of Vercise PC/Vercise Gevia DBS Systems and the Medtronic Activa Parkinson's Control Therapy, Boston Scientific provided a technical comparison of the two devices. Deep brain stimulation (DBS) systems work by sending electrical stimulation from an implanted neurostimulator to leads in the brain where the current is dispersed through electrodes into the brain tissue in order to activate neurons in specific brain regions. The clinical response of stimulation varies depending on the brain target and the orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. By comparing the Volume of Tissue Activation (VTA) of the Vercise PC and Vercise Gevia DBS Systems to the Medtronic Activa Parkinson's Control Therapy, it was determined that the Vercise PC and Vercise Gevia DBS Systems stimulate, and thus activate, neurons with volume of brain tissue equivalent to that which was shown to be safe and effective for the Medtronic Activa Parkinson's Control Therapy approved in P960009/S007.

VTA modeling has been used to estimate the degree of neuronal activation and by extension the degree of stimulation efficacy [15]. The modeled Boston Scientific 8-contact Standard and Directional DBS leads were able to achieve a comparable VTA volume and shape when compared the Medtronic leads. In all the modeled scenarios, the percent deviation of the VTAs of the Boston Scientific leads from the VTA of the Medtronic lead ranged between 4.34% (meaning greater coverage for Boston Scientific leads) and -3.26%. The results show that parameters of the Vercise PC and Vercise Gevia DBS Systems can be varied to achieve a VTA comparable to that achieved by the Medtronic Activa Parkinson's Control Therapy approved in P960009/S007; the range of deviation is acceptable. These results also demonstrate that a desired VTA can be achieved by adjusting stimulation parameters on any of the lead models (Boston Scientific 8-contact Standard and Directional DBS leads, Medtronic lead models 3387 and 3389).

The clinical response to stimulation varies depending on the brain target and the position and orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. Parameters can be adjusted to achieve a desired VTA, with shaping customized on a patient by patient basis.

The Vercise PC and Vercise Gevia DBS Systems demonstrated the capability to replicate at least the same output as the Medtronic Activa Parkinson's Control Therapy System indicating it can provide at least a comparable level of efficacy. Though the waveforms of Vercise PC/Gevia and Soletra differ in their method of charge balancing they both have the capability to inhibit and excite action potentials. The degree of neuronal activation with DBS is proportional to the amount

of charge delivered. The intensity of the charge delivered (charge density) also has implications for clinical safety. For parameters that differ between the devices, the Vercise PC and Vercise Gevia DBS Systems ensure safety by providing a charge density limit and preventing charge imbalance conditions.

The Boston Scientific INTREPID Parkinson's study of STN stimulation provides further assurance of the safety of the additional parameters provided by the Boston Scientifc DBS devices. The study was used to support the safety of DBS at therapeutic levels for Parkinson's disease. Although patients in the study were implanted in the STN, both STN and GPi are grey matter nuclei that can be stimulated to treat some of the symptoms of Parkinson's disease.

The Vercise PC and Vercise Gevia DBS System and the Medtronic Activa Parkinson's Control Therapy System leads and extensions are clinically equivalent. Although there are differences in some physical aspects, those differences have been demonstrated not to impact the safe and effective delivery of the stimulation to the targeted location. A comparison of accessories establishes that there are no differences that impact the safety and effectiveness of the respective systems during use for a GPi target location. The instructions for use are equivalent regarding implant procedures, stimulation related device programming and other instructions for use. The devices also have comparable labeling for contraindications, warnings, precautions, and adverse events.

Effectiveness Conclusions

Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC and Vercise Gevia DBS Systems with regard to its technological characteristics as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Parkinson's Control Therapy approved under P960009/S007 is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC and Vercise Gevia DBS Systems for GPi stimulation. As detailed in the SSED for the Medtronic Activa Parkinson's Control Therapy, prospective open label studies of the Medtronic Activa Parkinson's Control Therapy demonstrated that "On" time improved between pre-implant and 12 months by an average of 6.7 hours for the subset of GPi patients whose data were verified against medical records. Additionally, for the subset of patients whose data were verified against medical records, for the GPi and STN, symptoms of Parkinson's disease (UPDRS TME scores) improved for 56/117 patients while ON medication and symptoms of Parkinson's disease (UPDRS TME scores) improved for 102/117 patients while OFF medication.

Safety Conclusions

Boston Scientific performed a multi-center, prospective, double-blind, randomized, controlled study (INTREPID Study) that was design to evaluate the safety and effectiveness of the Vercise DBS System for bilateral stimulation of the STN as an adjunctive therapy for improving dyskinesia and other symptoms in adults with advanced, levodopa-responsive bilateral Parkinson's disease which is not adequately controlled with medication. This study was used to support approval of the Vercise DBS System under P150031. Additional details of this study is provided in the SSED for P150031 that is available on the CDRH website. The Vercise PC and Vercise Gevia DBS Systems were approved under P150031/S001 based on a similarity of technological characteristics to the Vercise DBS System. Although the data were used to support the safety of DBS at the STN, findings have applicability to the safety of stimulation at the GPi of similarity of the technological characteristics. Location of the stimulation is different, but stimulation related adverse effects can be resolved at either of the grey matter locations by adjustments to stimulation parameters.

The INTREPID safety data was based on a total of 292 consented (enrolled) subjects. Of these 292 subjects, 177 subjects received the Vercise System. In the INTREPID Study, a total of 788 adverse events in 143 subjects were reported at the time of the data snapshot. Of these, 74 events were reported as serious adverse events. Infection has been the most commonly reported serious adverse event associated with device-hardware/procedure (8 events, representing 2.7% of subjects). There were three events (each) of device-hardware/procedure-related serious adverse events of peri-operative intracranial hemorrhage (representing 1% of subjects) and seizure (representing 1% of subjects). These events are comparable to published reports. The nature and incidence rate of the reported adverse events in the study was anticipated.

Boston Scientific also provided adequate evidence of the sufficient similarity of the Vercise PC and Vercise Gevia DBS Systems with regard to its technological characteristics. Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Parkinson's Control Therapy approved under P960009/S007 is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC and Vercise Gevia DBS Systems for GPi stimulation.

As detailed in the SSED for the Medtronic Activa Parkinson's Control Therapy all 160 enrolled patients (both the STN and GPi) were evaluated for the occurrence of adverse events. One or more adverse events occurred in one hundred and fifty-four enrolled patients (154/160, 96.3%). Table 3 of the SSED lists adverse events for all patients reported during the clinical investigation by major category and subcategories. Over the entire study duration, 12/160 patients (7.5%) had intracranial hemorrhage; 17/160 patients (10.6%) had device-related infection; 16 patients (10.0%) had paresis/asthenia; and 13/160 patients (8.1%) had hemiplegia/hemiparesis. In addition to the adverse events collected through the 12 months of study follow-up, Medtronic has provided adverse event information for 100 patients at 2 years (60 STN and 40 GPi), 82 patients at 3 years (47 STN and 35 GPi), 38 patients at 4 years (17 STN and 21 GPi), and 16 patients at 5 years (4 STN and 12 GPi). FDA review of the safety data concluded that the probable benefits to health outweigh the probable risks.

Overall Conclusions

The data in this application and its applicability to the Vercise PC and Vercise Gevia DBS Systems for GPi stimulation support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

With regard to reasonable assurance of the effectiveness of the Vercise PC and Vercise Gevia DBS Systems, Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC and Vercise Gevia DBS Systems and the Medtronic Activa Parkinson's Control Therapy with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Parkinson's Control Therapy is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC and Vercise Gevia DBS Systems.

With regard to reasonable assurance of the safety of the Vercise PC and Vercise Gevia DBS Systems, Boston Scientific also provided adequate evidence of the sufficient similarity to the Vercise DBS System approved under P150031. Although the data were used to support the safety of DBS at the STN, the findings have applicability to the safety of stimulation at the GPi because of the similarity of the technological characteristics, although the location of the stimulation is different. Boston Scientific also provided adequate evidence of the sufficient similarity of the Vercise PC and Vercise Gevia DBS Systems and the Medtronic Activa Parkinson's Control Therapy with regard to technological characteristics. Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Parkinson's Control is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC and Vercise Gevia DBS Systems for GPi stimulation.

In conclusion, given the available information identified above and its applicability to the Vercise PC and Vercise Gevia DBS Systems, the data supports that the probable benefits for the Vercise PC and Vercise Gevia DBS Systems outweigh its probable risks for GPi stimulation.

Appendix B: Summary of Clinical Effectiveness of Unilateral Thalamic Stimulation for the Suppression of Essential Tremor and Parkinsonian Tremor

In lieu of providing a clinical data set for Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, Boston Scientific provided a technological comparison (including a comparison of the technology, surgical procedures, and instructions for use) of Vercise PC/Gevia/Genus DBS Systems to the Medtronic Activa Tremor Control System which was approved under P960009 for unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) for the suppression of parkinsonian tremor and essential tremor in the upper extremity. The purpose of the technological comparison was to establish sufficient similarity of the Boston Scientific and Medtronic DBS devices such that FDA could apply Section 216 of the Food and Drug Modernization Act (FDAMA), i.e., the "six-year rule," to assess the effectiveness profile of Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

According to FDA's "Guidance on Section 216 of the Food and Drug Modernization Act of 1997" available at: https://www.fda.gov/media/71743/download"https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073709.pdf, FDA may choose to utilize the publicly available detailed Summary of Safety and Effectiveness Data (SSED) of a previously approved device to support approval of a PMA for a new device if the applicant provides "a detailed justification of how the information in the earlier SSED applies to the applicant's device" and if the applicant is able "to describe how the devices are similar enough to allow for the data from the earlier device to apply to the new device."

Technical Comparison

For the purposes of establishing sufficient similarity of Vercise PC/Gevia/Genus DBS Systems and the Medtronic Activa Tremor Control System, Boston Scientific provided a technical comparison of the devices. Deep brain stimulation (DBS) systems work by sending electrical stimulation from an implanted neurostimulator to leads in the brain where the current is dispersed through electrodes into the brain tissue in order to activate neurons in specific brain regions. The clinical response of stimulation varies depending on the brain target and the orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. By comparing the Volume of Tissue Activation (VTA) of the Vercise PC/Gevia/Genus DBS Systems to the Medtronic Activa Tremor Control System, it was determined that the Vercise PC/Gevia/Genus DBS Systems stimulate, and thus activate, neurons with volume of brain tissue equivalent to that which was shown to be safe and effective for the Medtronic Activa Tremor Control System approved in P960009.

VTA modeling has been used to estimate the degree of neuronal activation and by extension the degree of stimulation efficacy [15]. The modeled Boston Scientific 8-contact Standard and Directional DBS leads were able to achieve a comparable VTA volume and shape when compared to the Medtronic leads. In all the modeled scenarios, the percent deviation of the VTAs of the Boston Scientific leads from the VTA of the Medtronic lead ranged between 0.61% (meaning greater coverage for Boston Scientific leads) and -3.26%. The results show that parameters of the Vercise PC/Gevia/Genus DBS Systems can be varied to achieve a VTA comparable to that achieved by the Medtronic Activa Tremor Control System approved in P960009; the range of deviation is acceptable. These results also demonstrate that a desired VTA can be achieved by adjusting stimulation parameters on any of the lead models (Boston Scientific 8-contact Standard and Directional DBS leads, Medtronic lead model 3387).

The clinical response to stimulation varies depending on the brain target and the position and orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. Parameters can be adjusted to achieve a desired VTA, with shaping customized on a patient by patient basis.

The Vercise PC/Gevia/Genus DBS Systems demonstrated the capability to replicate at least the same output as the Medtronic Activa Tremor Control System, indicating it can provide at least a comparable level of efficacy. Though the waveforms of Vercise PC/Gevia/Genus pulse generators and the Medtronic Model 7424 Itrell II pulse generators differ in their method of charge balancing, they both have the capability to inhibit and excite action potentials. The degree of neuronal activation with DBS is proportional to the amount of charge delivered. The intensity of the charge delivered (charge density) also has implications for clinical safety. For parameters that differ between the devices, the Vercise PC/Gevia/Genus DBS Systems ensure safety by providing a charge density limit and preventing charge imbalance conditions.

The Boston Scientific INTREPID Parkinson's study of STN stimulation provides further assurance of the safety of the additional parameters provided by the Boston Scientific DBS devices. The study was used to support the safety of DBS at therapeutic levels for Parkinson's disease. Although patients in the study were implanted in the STN, both STN and VIM are grey matter nuclei that can be stimulated to treat some of the symptoms of Parkinson's disease.

The Vercise PC/Gevia/Genus DBS System and the Medtronic Activa Tremor Control System leads and extensions are clinically equivalent. Although there are differences in some physical aspects, those differences have been demonstrated not to impact the safe and effective delivery of the stimulation to the targeted location. A comparison of accessories establishes that there are no differences that impact the safety and effectiveness of the respective systems during use for a VIM target location. The instructions for use are equivalent regarding implant procedures, stimulation related device programming and other instructions. The devices also have comparable labeling for contraindications, warnings, precautions, and adverse events.

Effectiveness Conclusions

Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC/Gevia/Genus DBS Systems to the Medtronic Activa Tremor Control with regard to its technological characteristics as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System approved under P960009 is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC/Gevia/Genus DBS Systems for thalamic stimulation for the suppression of parkinsonian tremor and essential tremor. As detailed in the SSED for the Medtronic Activa Tremor Control System, in the prospective US Tremor Study of the Medtronic Activa Tremor Control System, activities of daily living showed statistically significant improvement in both essential tremor and Parkinson's disease patients. For the prospective European Tremor Study, activities of daily living and other functional improvements were statistically significant in both essential tremor and Parkinson's disease patients.

Safety Conclusions

Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC/Gevia/Genus DBS Systems with regard to its technological characteristics. Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System approved under P960009 is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC, Vercise Gevia, and Vercise Genus DBS Systems for thalamic stimulation for the suppression of parkinsonian tremor and essential tremor.

As detailed in the SSED for the Medtronic Activa Tremor Control System, the frequency of adverse events reported in the US and European Tremor Trials did not differ markedly from the frequencies reported for DBS in the European Basic Study and DBS for Pain Study that were performed to generate a safety profile for the Activa System.

Boston Scientific also performed a multi-center, prospective, double-blind, randomized, controlled study (INTREPID Study) that was designed to evaluate the safety and effectiveness of the Vercise DBS System for bilateral stimulation of the STN as an adjunctive therapy for improving dyskinesia and other symptoms in adults with advanced, levodopa-responsive bilateral Parkinson's disease which is not adequately controlled with medication. This study was used to support approval of the Vercise DBS System under P150031. The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems were approved under

P150031/S001 and P150031/S034 based on a similarity of technological characteristics to the Vercise DBS System. Although the data were used to support the safety of DBS at the STN, findings have applicability to the safety of stimulation at the VIM because of similarity of the technological characteristics. Location of the stimulation is different, but stimulation related adverse effects can be resolved at either of the grey matter locations by adjustments to stimulation parameters.

Overall Conclusions

The data and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for thalamic stimulation for the suppression of parkinsonian tremor and essential tremor support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

With regard to reasonable assurance of the effectiveness of the Vercise PC/Gevia/Genus DBS Systems, Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC/Gevia/Genus DBS Systems and the Medtronic Activa Tremor Control System with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

With regard to reasonable assurance of the safety of the Vercise PC/Gevia/Genus DBS Systems, Boston Scientific also provided adequate evidence of the sufficient similarity to the Vercise DBS System approved under P150031. Although the data were used to support the safety of DBS at the STN, the findings have applicability to the safety of stimulation at the VIM because of the similarity of the technological characteristics, although the location of the stimulation is different. Boston Scientific also provided adequate evidence of the sufficient similarity of the Vercise PC/Gevia/Genus DBS Systems and the Medtronic Activa Tremor Control System with regard to technological characteristics. Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Medtronic Activa Tremor Control System is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC/Gevia/Genus DBS Systems for thalamic stimulation for the suppression of parkinsonian tremor and essential tremor.

In conclusion, given the available information identified above and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the data supports that the probable benefits for these DBS Systems outweigh its probable risks for thalamic stimulation for the suppression of parkinsonian tremor and essential tremor.

Appendix C: Summary of Clinical Effectiveness of Bilateral Thalamic Stimulation for the Suppression of Essential Tremor

In lieu of providing a clinical data set for treatment of essential tremor with the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, Boston Scientific provided a technological comparison (including a comparison of the technology, and instructions for use) of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Abbott Brio Neurostimulation System which was approved under P140009 for the suppression of disabling upper extremity tremor in adult essential tremor patients. The purpose of the technological comparison was to establish sufficient similarity of the Boston Scientific and Abbott DBS devices such that FDA could apply Section 216 of the Food and Drug Modernization Act (FDAMA), i.e., the "six-year rule," to assess the effectiveness profile of Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

According to FDA's "Guidance on Section 216 of the Food and Drug Modernization Act of 1997" available at: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073709.pdf, FDA may choose to utilize the publicly available detailed SSED of a previously approved device to support approval of a PMA for a new device if the applicant provides "a detailed justification of how the information in the earlier SSED applies to the applicant's device" and if the applicant is able "to describe how the devices are similar enough to allow for the data from the earlier device to apply to the new device."

Technological Comparison

For the purposes of establishing sufficient similarity of the Vercise PC/Vercise Gevia/Vercise Genus DBS Systems and the Abbott Brio Neurostimulation System, Boston Scientific provided a technical comparison of the devices. Deep brain stimulation (DBS) systems work by sending electrical stimulation from an implanted neurostimulator to leads in the brain where the current is dispersed through electrodes into the brain tissue in order to activate neurons in specific brain regions. The clinical response of stimulation varies depending on the brain target and the orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. By comparing the VTA of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Abbott Libra and Brio Neurostimulation Systems, it was determined that the Vercise DBS Systems stimulate, and thus activate, neurons with volume of brain tissue equivalent to that which was shown to be safe and effective for the Abbott Brio Neurostimulation System approved in P140009.

VTA modeling has been used to estimate the degree of neuronal activation and by extension the degree of stimulation efficacy [15]. The modeled Boston Scientific leads were able to achieve a comparable VTA volume and shape when compared the Abbott lead. In all the scenarios above the percent deviation of the VTAs of the Boston Scientific leads from the VTA of the Abbott lead ranged between 3.14% (meaning greater coverage for Boston Scientific leads) and -6.21%. The results show that parameters of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems can be varied to achieve a VTA comparable to that achieved by the Abbott Libra and Brio Neurostimulation Systems (latter approved in P140009); the range of deviation is acceptable. These results also demonstrate that a desired VTA can be achieved by adjusting stimulation parameters on any of the lead models (Boston Scientific lead models DB-2201 and DB-2202, Abbott lead model families of 6142 and 6146).

The clinical response to stimulation varies depending on the brain target and the position and orientation of the DBS lead within the target. As part of DBS programming, the clinician can adjust the combination of parameters, including amplitude, pulse width, frequency and electrode configuration, to tailor the stimulation field to the needs of each patient. Parameters can be adjusted to achieve a desired VTA, with shaping customized on a patient by patient basis.

The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems demonstrated the capability to replicate at least the same output as the Abbott Libra and Brio Neurostimulation Systems indicating it can provide at least a comparable level of efficacy. The degree of neuronal activation with DBS is proportional to the amount of charge delivered. The intensity of the charge delivered (charge density) also has implications for clinical safety. For parameters that differ between the devices,

the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems ensure safety by providing a charge density limit and preventing charge imbalance conditions.

The Boston Scientific INTREPID Parkinson's study of STN stimulation provides further assurance of the safety of the additional parameters provided by the Vercise PC, Vercise Gevia and Vercise Genus devices. The study was used to support the safety of DBS at therapeutic levels for Parkinson's disease. Although patients in the study were implanted in the STN, both STN and VIM are grey matter nuclei that can be stimulated to treat some of the symptoms of Parkinson's disease.

The Vercise PC, Vercise Gevia and Vercise Genus DBS System and the Abbott Neurostimulation System Leads and Extensions are clinically equivalent. Although there are differences in some physical aspects of the Leads, those differences have been demonstrated not to impact the safe and efficacious delivery of the stimulation to the targeted location. A comparison of accessories establishes that there are no differences that impact the safety and effectiveness of the respective systems during use for a VIM target location. The instructions for use are equivalent regarding implant procedures, stimulation related device programming and other instructions. The devices also have comparable labeling for contraindications, warnings, precautions, and adverse events.

Effectiveness Conclusions

Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Abbott Brio Neurostimulation System with regard to its technological characteristics as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Abbott Brio Neurostimulation System approved under P140009, in support of the reasonable assurance of its effectiveness, is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for bilateral stimulation of the VIM for treatment of essential tremor.

As detailed in the SSED for the Abbott Brio Neurostimulation System, effectiveness for the essential tremor indication was based on 127 patients implanted at 12 U.S. sites. The primary effectiveness endpoint was based on the postural tremor score of the target limb between stimulation On and stimulation Off, at the Day 180 visit, as measured by the blinded reviewer. The primary endpoint was successful, with the stimulation On performing significantly better in their postural or kinetic tremor reduction than stimulation Off at Day 180. In addition, the secondary endpoint of non- target and bilateral side CRST scores showed tremor reduction at Day 180 compared to baseline.

The secondary analyses supported the primary effectiveness endpoint. The CRST which assessed the patients' total motor, handwriting and pouring score demonstrated that stimulation improved all outcomes. In addition, the QUEST and the SF-36 showed improvement.

The results of the clinical study demonstrate a clinically meaningful reduction in tremor with the Brio Neurostimulation System in essential tremor patients with unilateral or bilateral disabling medication-refractory upper extremity tremor.

Safety Conclusions

Boston Scientific provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems to the Abbott Brio Neurostimulation System with regard to its technological characteristics, as described in Section IX(B). Therefore, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Abbott Brio Neurostimulation System approved under P140009 is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for bilateral stimulation of the VIM for treatment of essential tremor.

As detailed in the SSED for the Abbott Brio Neurostimulation System, the primary safety endpoint which was a comparison of the rate of device-related or procedure related adverse events within 6 months post-implant compared to a historical control rate of 38.1%. was met. Forty patients (31.5%) had a device or procedure-related adverse event that occurred within 180 days of the initial implant. The one-sided 95% upper confidence bound on this proportion was 38.9%, which is less than 10 percentage points more than the comparator rate of 38.1%.

A total of 34 serious adverse events occurred in 29 patients during the study. These included 8 infections, 3 intracranial hemorrhages, 2 paresis, 1 seizure, 1 stroke and 3 deaths. Two of the 2 deaths were related to cardiac events and the cause of

the other death was unknown.

A total of 327 adverse events in 127 (100%) subjects occurred during the study. The most common adverse events were headache, dysarthria, and jolting or shocking sensations. No unanticipated adverse events occurred during the study.

Boston Scientific also performed a multi-center, prospective, double-blind, randomized, controlled study (INTREPID Study) that was design to evaluate the safety and effectiveness of the Vercise DBS System for bilateral stimulation of the STN as an adjunctive therapy for improving dyskinesia and other symptoms in adults with advanced, levodopa-responsive bilateral Parkinson's disease which is not adequately controlled with medication. This study was used to support approval of the Vercise DBS System under P150031. The Vercise PC, Vercise Gevia and Vercise Genus DBS Systems were approved under P150031/S001 and P150031/S034 based on a similarity of technological characteristics to the Vercise DBS System. Although the data were used to support the safety of DBS at the STN, findings have applicability to the safety of stimulation at the VIM because of similarity of the technological characteristics. Location of the stimulation is different, but stimulation related adverse effects can be resolved at either of the grey matter locations by adjustments to stimulation parameters.

Overall Conclusions

The data and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems for treatment of essential tremor support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

With regard to reasonable assurance of effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, Boston scientific provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems and the Abbott Brio Neurostimulation System with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Abbott Brio Neurostimulation System is directly applicable towards establishing reasonable assurance of the effectiveness of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

With regard to reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, Boston Scientific also provided adequate evidence of sufficient similarity to the Vercise DBS System approved under P150031. Although the data were used to support the safety of DBS at the STN, the findings have applicability to the safety of stimulation at the VIM because of the similarity of the technological characteristics, although the location of the stimulation is different. Boston scientific also provided adequate evidence of the sufficient similarity of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems and the Abbott Brio Neurostimulation System with regard to technological characteristics. Because of this, FDA was able to apply Section 216 of the FDAMA and confirm that the evidence presented in the SSED for the Abbott Brio Neurostimulation System is directly applicable towards establishing reasonable assurance of the safety of the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems.

In conclusion, given the available information identified above and its applicability to the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems, the data support that for the requested indications for use the probable benefits for the Vercise PC, Vercise Gevia and Vercise Genus DBS Systems outweigh its probable risks.

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Information for Prescribers

℞ ONLY CAUTION: Federal law restricts this device to sale, distribution and use by or on the order of a physician.

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How to Use this Manual

This manual provides information about the Boston Scientific Deep Brain Stimulation (DBS) System. Throughout this manual, the name “Boston Scientific DBS System” refers to the following: Vercise Genus™, Vercise Gevia™, and Vercise™ PC Deep Brain Stimulation Systems.

Read all instructions carefully before using the DBS System. For other device-specific information not included in this manual, refer to the appropriate DFU for your Boston Scientific DBS System as listed in your *DBS Reference Guide*.

Guarantees

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For device warranty information, visit www.bostonscientific.com/warranty.

Technical Support

There are no user serviceable parts. If you have a specific question or issue, please contact your sales representative or call (833) DBS-INFO or (833) 327-4636.

Registration Information

Device registration information must be provided to Boston Scientific following device implantation. The purpose of this registration is to maintain traceability of all products and to secure warranty rights. It also allows the institution involved in the evaluation or replacement of a specific implanted DBS Lead, accessory, or device to gain quick access to pertinent data from the manufacturer.

To complete device registration, follow the instructions provided by your local sales representative or fill out the registration form included in the package contents. A device registration form is included with each Boston Scientific DBS Lead, DBS Extension, and some DBS Stimulators. Return one copy to the Boston Scientific Customer Service Department, keep one copy for patient records, provide one copy to the patient, and save one copy for the physician.

Boston Scientific Neuromodulation Corporation
Attention: Customer Service Department
25155 Rye Canyon Loop
Valencia, CA 91355, USA

Patient Identification Card

Ensure that the patient receives a completed Temporary Identification Card after their surgery. Permanent ID cards will be mailed directly to the patient following patient registration.

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Device Description

The Boston Scientific Deep Brain Stimulation (DBS) System provides a reversible therapy where structures in the brain are stimulated with small electrical pulses. A Boston Scientific DBS System utilizes current steering (also known as multiple independent current control or MICC) across eight or sixteen Contacts per DBS Lead to provide precise positioning of stimulation. The implantable components of the Boston Scientific DBS System include the following:

- An Implantable Pulse Generator (IPG) that is either rechargeable or non-rechargeable.
  - The IPG is also referred to as a Stimulator.
- Leads that deliver electrical pulses to the brain.
- Lead Extensions that connect the Leads to the IPG.
- A Lead Boot to protect the proximal end of the Lead between surgeries.
- Sutures Sleeves to protect the Lead and/or to anchor the Leads and Lead Extensions.
- Port Plugs for unused IPG or Lead Extension ports.
- The Boston Scientific SureTek™ Burr Hole Cover that may be used to anchor the Leads.

The non-implantable components of the Boston Scientific DBS System include the following:

- An External Trial Stimulator (ETS) and OR Cables that may be used for intraoperative testing.
- A Clinician Programmer (CP) that is used to set and adjust stimulation parameters.
  - A Pairing Magnet is used to facilitate first-time pairing between a Vercise Genus IPG and CP and/or Remote Control.
  - A Programming Wand is used to connect the CP to Vercise Gevia and Vercise PC IPGs.
- A Tunneling Tool that is used to create a subcutaneous tunnel for the Leads and Lead Extensions.
- External patient devices, such as the Remote Control that is used to communicate with the IPG, and a Charging System to recharge the battery of rechargeable IPGs.
  - The Charging System is only applicable for rechargeable IPGs.

Note: *The DBS System components were not made with natural latex.*

Intended Use / Indications for Use

The Boston Scientific DBS System is indicated for use in the following:

- Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms of moderate to advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.
- Bilateral stimulation of the internal globus pallidus (GPi) as an adjunctive therapy in reducing some of the symptoms of advanced levodopa-responsive Parkinson's disease (PD) that are not adequately controlled with medication.
- Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.
- Bilateral stimulation of the ventral intermediate nucleus (VIM) of the thalamus for the suppression of disabling upper extremity tremor in adult essential tremor patients whose tremor is not adequately controlled by medications and where the tremor constitutes a significant functional disability

Safety Information

Contraindications

The Boston Scientific DBS System, or any of its components, is contraindicated for the following:

Diathermy: Shortwave, microwave, and/or therapeutic ultrasound diathermy should not be used on patients implanted with the Boston Scientific DBS System, or any of the system components. The energy generated by diathermy can be transferred to the Boston Scientific DBS System, causing tissue damage in the brain resulting in severe injury or death.

Electroconvulsive Therapy (ECT) and Transcranial Magnetic Stimulation (TMS): The safety of these therapies in patients implanted with the Boston Scientific DBS System has not been established. It is possible that the energy generated by these therapies can be transferred to the Boston Scientific DBS System, causing tissue damage that may result in severe patient injury or death.

Magnetic Resonance Imaging (MRI) (Vercise PC Only): Patients implanted with the full Vercise PC DBS System (DBS Leads, Lead Extensions, and Stimulator) should not be subjected to MRI. MRI exposure may result in the following:

- Dislodgement of implanted components.
- Heating of the Contacts or other system components, causing permanent tissue lesioning.
- Damage to the Stimulator's electronics.
- Current induction through the DBS Leads and Vercise PC DBS System causing unpredictable levels of stimulation.
- Distortion of the diagnostic image.
- Personal injury or death.

Note: *The Vercise DBS Lead-Only System (before Stimulator is implanted), the Vercise Gevia System, and the Vercise Genus System are MR Conditional. An MRI examination can be conducted safely when all the instructions in the supplemental manual ImageReady™ MRI Guidelines for Boston Scientific DBS Systems are followed.*

For the latest version of the manual, go to http://www.bostonscientific.com/manuals.

Patient Incapability: Patients who are unable to properly operate the Remote Control and Charging System (when applicable) should not be implanted with the Boston Scientific DBS System.

Poor Surgical Candidates: The Boston Scientific DBS System is not recommended for patients who are poor surgical candidates.

Unsuccessful Test Stimulation: The Boston Scientific DBS System should not be used in patients who experience unsuccessful test stimulation.

Warnings

Automobiles and Equipment: Patients should operate automobiles, other motorized vehicles, or potentially dangerous machinery/equipment with caution after receiving the Boston Scientific DBS System. Patients should avoid performing activities that would be dangerous if treated symptoms were to return, or in which stimulation changes could occur.

Charge Density: High levels of stimulation may damage brain tissue. To maintain safe limits, the DBS programming software will display a message when the stimulation level selected would exceed the safe limit, and programming of these settings will be prevented.

Patients may be granted the ability to change stimulation amplitude with the Remote Control within clinician-defined limits. The software prevents patient-controlled amplitude from exceeding the limit.

DBS Extension Connector: Implanting the DBS Lead Extension Connector in the soft tissue of the neck may increase the chance of DBS Lead breakage. Boston Scientific recommends placing the DBS Lead Extension Connector behind the ear such that glasses or headgear do not interfere with the implanted DBS System.

Electromagnetic Interference: Strong electromagnetic fields can potentially turn stimulation off, cause temporary unpredictable changes in stimulation, or interfere with Remote Control communication. If an electromagnetic field is strong enough to turn stimulation off, this will be temporary and stimulation may automatically return once the electromagnetic field is removed. Patients should be advised to avoid or exercise care around the following:

- Theft detectors, tag deactivators and RFID devices, such as those used at department stores, libraries, and other public establishments. Patients should proceed with caution, ensuring that they move through the center of the detector as quickly as possible. Interference from these devices should not cause damage to the implanted device.
- Security screeners, such as those used in Airport Security or at entrances to government buildings, including hand-held scanners. Patients should request assistance to bypass the security screener and advise the security staff that they have an implanted medical device. If patients must pass through the security screener, they should move through the security screener quickly and stay as far as allowed from the screener. Interference from these devices should not cause damage to the implanted device.
- Power lines or power generators.
- Electric steel furnaces and arc welders.
- Large magnetized stereo speakers.
- Strong magnets.
- Automobiles or other motorized vehicles using a LoJack system or other anti-theft systems that can broadcast a radio frequency (RF) signal. The high energy fields produced by these systems may interfere with the operation of the Remote Control and its ability to control stimulation.
- For DBS devices not using Bluetooth technology for communication, other sources of electromagnetic disturbance, such as RF transmitters at television or radio broadcast stations, Amateur Radio or Citizens Band radio transceivers, or Family Radio Service band transceivers.

- For DBS devices using Bluetooth technology for communication, other sources of electromagnetic disturbance, such as Wi-Fi routers, cordless phones, Bluetooth wireless streaming devices, baby monitors, and microwave ovens.

Note: *When in close proximity to them, equipment that generates strong electromagnetic fields might cause unintended stimulation or interfere with wireless communication even if they comply with International Special Committee on Radio Interference (CISPR) requirements.*

Heat Due to Charging: Patients should not charge while sleeping. This may result in a burn. The Charger may become warm while charging the Stimulator. The Charger should be handled with care. Failure to use the Charging Collar, Charging Belt, or an Adhesive Patch while charging, as directed, may result in a burn. If the patient experiences pain or discomfort, they should stop charging and contact their healthcare provider.

Intracranial Hemorrhage: Special precautions should be taken for patients who are prone to hemorrhage, including patients with coagulopathy, high blood pressure, or those who are using prescribed anticoagulants. Microelectrode penetration and DBS Lead insertion can put patients who have a likelihood of intracranial hemorrhages at greater risk.

Magnetic Resonance Imaging (MRI): The Vercise Genus and Vercise Gevia DBS Systems are “MR Conditional.” This means that an MRI examination can be conducted safely using a 1.5 Tesla horizontal closed bore MRI system when all instructions and safety information in the supplemental manual *ImageReady™ MRI Guidelines for Boston Scientific DBS Systems* are followed.

The *ImageReady™ MRI Guidelines for Boston Scientific DBS Systems* manual appears on the Boston Scientific website www.bostonscientific.com/manuals or may be provided in your region. It is important to read the information in this supplemental manual in its entirety before conducting or recommending an MRI examination on a patient with a Boston Scientific DBS System.

External Devices: The external/non-implantable components of the Boston Scientific DBS System (External Trial Stimulator, ETS Adapter, OR Cables, Remote Control, Charging System, Clinician Programmer, and accessories) are MR Unsafe. They must not be taken into any MR environment such as the MRI scanner room.

Other Active Implantable Devices: Concurrent use of Stimulators such as the Boston Scientific DBS Stimulator and other active implantable devices, such as pacemakers, cardioverter defibrillators, or medication delivery pumps may result in interference with the operation of the devices. If the patient requires concomitant implantable active devices, careful programming of each system is necessary.

Pregnancy: It is unknown whether this device may cause complications with pregnancy and/or hurt an unborn baby.

Stimulator Damage: Chemical burns may result if the Stimulator housing is ruptured or pierced, exposing the patient’s tissue to battery chemicals. Do not implant the Stimulator if the housing is damaged.

Suicide: New onset or worsening depression which may be temporary or permanent is a risk that has been reported with DBS therapy. Suicidal ideation, suicide attempts, and suicide are events that have also been reported. Therefore, physicians should consider the following:

- Preoperatively, assess patients for the risks of depression and suicide. This assessment should consider both the risk of depression and suicide as well as the potential clinical benefits of DBS therapy for the condition being treated.
- Postoperatively, actively monitor patients for new or worsening symptoms of depression, suicidal thoughts or behaviors, or changes in mood or impulse control.
- If a patient experiences new or worsening depression or suicidal ideation, manage these symptoms appropriately.
- Educate patients and caregivers about these potential risks prior to implantation, and be sure that they know about the importance of ongoing support and follow-up, including when to contact their health care provider.

Therapeutic Ultrasound: Implanted components of the Boston Scientific DBS System should not be exposed to therapeutic levels of ultrasound energy. The implanted device may concentrate the ultrasound field and may cause patient harm.

Unauthorized Modification: Unauthorized modification to the medical devices is prohibited. The integrity of the DBS System could be compromised and harm or injury to the patient could occur.

Precautions

Physician training is required for usage of the Boston Scientific DBS System. The implanting physician should be experienced in the subspecialty of Stereotactic and Functional Neurosurgery. The following is a list of precautions that should be taken when implanting or using the DBS Stimulator.

Bathing: Patients should exercise reasonable caution when bathing.

Cell Phones and Other Portable RF Communication Devices: While interference caused by cell phones is not anticipated, the full effects of interaction with cell phones are unknown at this time. Patients should be instructed that portable RF communications equipment (for example, mobile phones) should be kept a minimum distance of 6 inches (15 cm) from the area of the implanted device. If interference does occur, move the cell phone away from the implanted Stimulator or turn off the cell phone. If there is a concern or a problem is encountered, patients should contact their healthcare provider.

Cleaning the Charging Belt or Charging Collar: Do not machine wash the Charging Belt or Charging Collar.

Cleaning the Remote Control, External Trial Stimulator, Charger, Base Station, Power Supply, and Programming Wand: Do not use abrasive cleansers for cleaning. Do not clean any of the accessories while they are directly or indirectly connected to a power outlet.

As an operator of the external devices, perform only the following maintenance tasks on the external devices:

- Changing the battery
- Charging the battery
- Cleaning

Ensure that the devices are not in use while performing service and maintenance tasks.

Component Removal, Disposal, and Return: Any explanted components should be returned to Boston Scientific. The Stimulator should be explanted in the case of cremation and returned to Boston Scientific. Cremation may cause the Stimulator battery to explode.

The Remote Control or Charger should not be disposed of in fire, as these devices contain batteries which may explode causing injury when exposed to fire. Used batteries should be disposed of in accordance with local laws and regulations.

Dispose of non-implantable components and packaging in accordance with hospital, administrative, and/or local government policy.

Components: The use of components other than those approved and/or supplied by Boston Scientific and intended for use with the Boston Scientific DBS System may damage the DBS System, diminish the effectiveness of therapy, and/or put the patient at unknown risk.

Connections: Before inserting any DBS Lead or DBS Lead Extension into any Connector or Header ports, including the Stimulator Header, DBS Lead Extension Connectors, and OR Cable Assembly, always wipe the DBS Lead with a sterile, dry cotton sponge. Contamination inside the Connector or Header ports may be difficult to remove and can cause high impedances, preventing electrical connectivity which may compromise the integrity of the stimulation circuit.

Device Failure: Implants can fail at any time due to random component failure, loss of battery functionality, or DBS Lead breakage. Stopping brain stimulation suddenly can cause serious reactions to develop. If the Stimulator stops working, patients should be instructed to turn off the Stimulator and contact their healthcare provider immediately so that the system can be evaluated and appropriate medical care can be given to manage the return of symptoms.

Environmental Precautions: Patients should avoid activities that could potentially involve large amounts of electromagnetic interference. Devices that contain permanent magnets, such as speakers, should not be placed near the Stimulator because they may cause the DBS System to turn on or off.

Excess DBS Extension: Coil excess DBS Lead Extension around or below the Stimulator. Excess wire on top of the Stimulator may increase the potential for communication interference, tissue erosion, or damage during Stimulator replacement surgery.

Inspect Packaging Before Use: Check the expiration date on the package before opening the sterile package and using the contents. Do not use the contents if the current date is past the expiration date, if the package is opened or damaged, or if contamination is suspected because of a defective sterile package seal.

- Inspect the seal integrity of the outer tray before use.
- Open the inner tray in the sterile field.
- If the Stimulator was dropped, do not implant it in a patient. The dropped Stimulator may have lost sterility, experienced a loss of hermeticity, or been otherwise damaged. Replace the dropped Stimulator with a new, sterile Stimulator prior to implantation. Return the damaged Stimulator to Boston Scientific.
- Do not use any component that shows signs of damage.
- Do not use if “Use By” date has expired.

Massage Therapy: Patients should avoid receiving massage therapy near the implanted system components. If a patient does receive massage therapy, the patient should inform the masseuse that they have an implanted device and show him/her where the Stimulator, DBS Lead Extensions, and DBS Leads are located. The patient should advise the masseuse to avoid these areas and proceed with caution.

Medical Devices/Therapies: The following medical therapies or procedures may turn stimulation off, cause permanent damage to the Stimulator, or may cause injury to the patient. If any of the procedures below is required by medical necessity, the procedure(s) should be performed as far from the implanted components as possible. Stimulator function should be confirmed after the procedure. Ultimately, however, the Stimulator may require explantation because of damage to the device or patient harm.

- Diagnostic ultrasonic scanning is unlikely to damage the Stimulator if stimulation is turned off. Testing has been completed to applicable standards.
- Electrocautery – Electrocautery can transfer destructive current into the DBS Leads and/or Stimulator. See additional instructions below. Bipolar or monopolar electrocautery may be used. Electrocautery probes must be kept a minimum of 1 inch away from the implanted device.
- External Defibrillation – Safe usage of external defibrillation has not been established in DBS patients. Defibrillation of the patient is unlikely to permanently damage the implanted device if stimulation is turned off and the defibrillator electrode does not come into contact with any component of the implantable device. Testing has been completed to applicable standards.
- Lithotripsy – High frequency signals directed near the Stimulator may damage circuitry. See additional instructions below.
- Radiation Therapy – Lead shielding should be used over the Stimulator to prevent damage from high radiation. Any damage to the device by radiation may not be immediately detectable.
- X-ray and CT scans may damage the Stimulator if stimulation is on. X-ray and CT scans are unlikely to damage the Stimulator if stimulation is turned off.

If the patient is required to undergo lithotripsy, electrocautery, external defibrillation, radiation energy, ultrasonic scanning, X-ray, or CT scan, observe the following:

- Turn off stimulation at least five minutes before the procedure application.
- All equipment, including probes, ground plates and paddles, must be used as far away from the Stimulator as possible and oriented such that energy is not directed through or across the Stimulator, Leads, or Lead Extensions.
- Every effort should be taken to keep fields, including current, radiation, or high-output ultrasonic beams, away from the Stimulator.
- Equipment should be set to the lowest energy setting clinically indicated.
- Confirm the system is functioning properly following the procedure. Turn stimulation on and observe for the return of therapy to confirm functionality.

Operating Temperature: The operating temperature of the External Trial Stimulator, Remote Control, and Programming Wand is 5 °C to 40 °C (41 °F to 104 °F). For proper operation, do not use the Charging System if the ambient temperature is above 35 °C (95 °F).

Other Models of External Devices: Only the Remote Control, Charging System (as applicable), and Clinician Programmer that were provided with the Boston Scientific DBS System should be used with the Boston Scientific DBS System. Other models of these devices will not function with the Boston Scientific DBS System.

Patient Activities Requiring Coordination: Loss of coordination is a potential side effect of DBS therapy. Patients should exercise reasonable caution when participating in activities requiring coordination, including those that they were able to perform prior to receiving DBS therapy (e.g., swimming).

Patient Activity Following Surgery: During the two weeks following surgery, it is important for the patient to exercise extreme care so that appropriate healing will secure the implanted components. During this period, the patient should not attempt to move heavy objects. Instruct the patient to restrict head movements, including extension or flexion of the neck and rotation of the head, until healing is complete.

Setscrews: Before tightening Setscrews, always test impedance to confirm electrical connectivity. Tightening a Setscrew onto a Lead Contact may damage the Contact and may result in the need to replace the DBS Lead or DBS Lead Extension.

Single Use Only, Do Not Resterilize: For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

Sterilization: Contents of the surgical kits are supplied sterile using an ethylene oxide process. Do not use if sterile barrier is damaged. If damage is found, call Boston Scientific Technical Support and return the damaged part to Boston Scientific.

Stimulator Orientation: Orient the Stimulator parallel to the skin surface. Suboptimal placement of the Stimulator may result in a revision surgery. Patients should avoid touching the Stimulator site or incisions. If patients notice a change in the appearance of the skin at the Stimulator location, such as the skin becoming thin over time, they should contact their healthcare provider.

In order to ensure effective device communications, including device programming, and proper charging, perform the following:

- For rechargeable IPGs, orient the Stimulator parallel to the skin surface and at a depth less than 2 cm and greater than 0.5 cm below the skin.
- For non-rechargeable Vercise Genus IPGs, orient the Stimulator parallel to the skin surface and at a depth less than 2.5 cm below the skin to ensure effective device communication.
- For the non-rechargeable Vercise PC IPG (DB-1140-S), orient the Stimulator parallel to the skin surface. There is no depth restriction for the Vercise PC IPG.
- The etched writing “This Side Up” must be facing out of the pocket toward the patient’s skin.

Suboptimal placement of the Stimulator may result in the inability to communicate with the device or inability to recharge and may require a revision surgery.

Patients should be instructed not to change the orientation of or turn over the Stimulator. If the Stimulator flips over in the body, then it cannot communicate or be charged. If stimulation cannot be turned on after charging, the Stimulator may have changed orientation or rotated; patients should contact their healthcare provider to arrange an evaluation of the system.

Storage, Handling, and Transport: Store implanted components, such as the Stimulator, Leads, and Lead Extensions, between 0 °C to 45 °C (32 °F to 113 °F) in an area where they are not exposed to liquids or excessive moisture. Temperatures outside of the stated range can cause damage. If stored in conditions beyond the required storage temperature, do not use the components and return to Boston Scientific.

The non-rechargeable Stimulator will enter storage mode if its temperature falls below 5 °C. When the Stimulator is in storage mode, it will not connect to a Remote Control or Clinician Programmer. To exit storage mode, increase the Stimulator temperature above 8 °C.

Store external components like the Remote Control, External Trial Stimulator, ETS Adapter, OR Cable and Extension (DB-4100-A and SC-4100-A), and Charging System between -20 °C to 60 °C (-4 °F to 140 °F). Store the Push-Button OR Cables (DB-4120-08 and DB-4120-16) between 0 °C to 45 °C (32 °F to 113 °F). Do not expose the external components to excessively hot or cold conditions. Do not leave the devices in your car or outdoors for extended periods of time. The sensitive electronics can be damaged by temperature extremes, particularly high heat.

Handle the system components and accessories with care. Do not drop them or submerge them in water. Avoid all sources of water that could come into contact with the devices. Although reliability testing has been performed to ensure quality manufacturing and performance, dropping the devices on hard surfaces or in water, or other rough handling, can permanently damage the components. Keep the Remote Control and Charger away from pets, pests, and children to avoid damage to the devices.

Care must be taken to avoid damaging the DBS Lead with sharp instruments or excessive force during surgery. The following guidelines will help to ensure the longevity of components:

- Do not sharply bend or kink the DBS Lead or Lead Extension.
- Do not tie Suture(s) directly to the DBS Lead or Lead Extension body.
- Avoid pulling an implanted DBS Lead taut; stress relief loops may help to minimize tension on the DBS Lead.
- Avoid handling the DBS Lead with sharp instruments; use only rubber-tipped forceps.
- Take care when using sharp instruments, such as hemostats or scalpels, to prevent damaging the DBS Lead.

Surgical Tape: If tape is used to temporarily secure the DBS Lead during surgery, caution should be used to ensure the Lead is not cut or damaged when removing the tape.

Sutures: Do not apply Sutures tightly around the DBS Leads, as this may damage the insulation of the DBS Lead and may result in DBS Lead failure.

Tissue Reaction: Temporarily, there may be some pain in the area of the Stimulator as the incisions heal. If there is excessive redness around the wound area, it should be checked for infection. In rare cases, adverse tissue reaction to implanted materials can occur.

Adverse Events

The following is a list of known risks with the use of deep brain stimulation. There may be risks that are unknown. Note that some of these symptoms may be resolved or reduced by current steering, changing stimulation parameters, or by changing the position of the Lead during surgery.

If any of these events occur, patients should inform their healthcare provider as soon as possible.

Risks Associated With Surgical Procedure and Post-Operative Period

- Allergic reaction to anesthesia or antibiotics including anaphylaxis
- Blood clot formation in the extremities (e.g., in the veins of the legs)
- Blood clot or air forming in or traveling through the blood stream, which can block blood flow to parts of the lungs or other tissue that could be life-threatening
- Brain contusion (bruising)
- Brain or cerebral spinal fluid (CSF) fluid infection or inflammation
- CSF leaking outside the skull or collecting inside the skull abnormally
- Confusion or problems with attention, thinking, or memory (acute or chronic)
- Death
- Fibrosis (thickened skin and scarring) around the Lead Extension (including tightening, tethering, and bowstringing)
- Hemiparesis (muscular weakness or partial paralysis on one side of the body)
- Hemiballism (uncontrollable involuntary movements of a limb or limbs on one or both sides of the body)
- Intracranial hemorrhage (which can lead to stroke, paralysis, or death)
- Intraparenchymal cyst
- Infection
- Injury to areas next to the implant, such as blood vessels, nerves, the chest wall, and the brain
- Injury to the nerves in the armpit (brachial plexus) leading to pain or weakness of the arm or hand
- Neurosurgery/anesthesia risks, including unsuccessful implant and pneumonia
- Pain at the surgical site(s), headache or discomfort
- Seizures
- Speech or language difficulties
- Subcutaneous hemorrhage or seroma (blood or fluid collection under the skin, including the skin over the skull)
- Stroke resulting in temporary or permanent problems
- Swelling or bruising of the muscles or skin in the area of the Lead or of the IPG implant

Possible Side-Effects of Stimulation

- Confusion or problems with attention, thinking, or memory
- Gait difficulty (trouble walking) and falls
- New onset or worsening depression, which may be temporary or permanent, and suicidal ideations, suicide attempts, and suicide

- Pain, headache or discomfort
- Pneumonia from difficulty with swallowing or from inhaling fluid
- Psychiatric disturbances such as anxiety, depression, lessened interest or emotion, hypersexuality, aggression, mania or hypomania, psychosis, emotional sensitivity, sleep problems, suicide, or suicidal thoughts or attempts
- Seizures
- Sensory changes
- Speech or language problems
- Swallowing difficulty
- Systemic effects such as rapid heart beat, sweating, fever, dizziness, changes in kidney function, difficulty passing urine, sexual effects, nausea, difficulty having bowel movements, bloating
- Weakness, muscle spasms, shaking, restlessness, or problems with movement
- Undesirable sensations (e.g., tingling)
- Visual problems, eyelid or eye movement difficulties or other eye-related symptoms
- Weight changes

Device-Related Risks

- Allergic or immune system response to implanted materials
- Failure or malfunction of any part of the device, including but not limited to: Battery leakage, battery failure, Lead or Extension breakage, hardware malfunctions, loose connections, electrical shorts or open circuits, and Lead insulation breaches, whether or not these problems require device removal and/or replacement
- Implant site complications such as pain, poor healing, redness, warmth, swelling or wound reopening
- Implanted device components (Stimulator, Lead, or Extension) may move from original implanted location or wear through the skin, which may lead to the need for additional surgery
- Infection
- Interference from external electromagnetic sources
- Loss of adequate stimulation
- Pain, headache or discomfort
- Skin irritation or burns at the Stimulator site
- Stiffness in muscles or joints
- Worsening of disease symptoms, potentially caused by loss of stimulation, medication changes, surgery, or illness. In rare cases worsening can become a life-threatening crisis associated with varied symptoms such as mental status changes, fever, and muscle rigidity
- Swelling, including fluid collecting around the device

Service and Maintenance

External Trial Stimulator (ETS) Maintenance

The ETS may be used to conduct intraoperative stimulation testing during the Lead implantation procedure. Refer to the DFU listed in your *DBS Reference Guide* for detailed procedure and guidelines for intraoperative testing.

1. Left Connector
2. Right Connector
3. Stimulator Light
4. Stimulation ON/OFF
5. Battery Indicator Light

Figure 1. External Trial Stimulator

To turn stimulation on and off on the ETS, press and release the ON/OFF button on the ETS (Figure 1). When the stimulation is on, the Stim Indicator Light will blink green. The ETS runs on two AA batteries that are provided with every ETS kit. When the batteries need replacement, the Battery Indicator Light will change from a flashing green to a flashing yellow.

Ensure that stimulation is off (the indicator light is not blinking) before opening the ETS battery compartment.

To install new batteries in the ETS:

1. Confirm that stimulation is OFF by confirming that the stimulation indicator light is not blinking.
2. On the rear of the ETS, push in slightly and slide down the battery compartment cover.
3. Remove the old batteries.
4. Place two new AA batteries in the slots matching the positive (+) and negative (-) markings in the compartment.
5. Align the battery compartment cover on the case and slide the cover into position until is snaps closed.
6. Both the Battery Indicator light and the Stim On indicator lights will emit an amber glow for 15 seconds after which the Battery Indicator light blinks green.

Cleaning the Charging System

The components of the Charging System (Charger, Base Station, and Power Supply) can be cleaned using alcohol or a mild detergent applied with a cloth or tissue. Residue from soapy detergents should be removed with a damp cloth. Do not use abrasive cleansers for cleaning. Do not clean any of the accessories while they are directly or indirectly connected to a power outlet.

Hand wash the Charging Belt or Charging Collar with mild soap and warm water. Do not machine wash the Charging Belt or Charging Collar. Let the Charging Belt or Charging Collar air dry. Be sure to remove the Charger and Counterweight from the Charging Collar before washing the Charging Collar. Be sure to remove the Charger from the Charging Belt before washing the Charging Belt.

Cleaning the Remote Control

The components of the Remote Control can be cleaned using alcohol or a mild detergent applied with a cloth or tissue. Residue from soapy detergents should be removed with a damp cloth. Do not use abrasive cleansers for cleaning. Do not clean while directly or indirectly connected to a power outlet.

Cleaning the Programming Wand

The components of the Programming Wand can be cleaned using alcohol or a mild detergent applied with a cloth or tissue. Residue from soapy detergents should be removed with a damp cloth. Do not use abrasive cleansers for cleaning. Do not clean while directly or indirectly connected to a power outlet.

Electromagnetic Compatibility

EN 60601-1-2 Classification Information

- Internally Powered Equipment
- Continuous Operation
- Ordinary Equipment
- Class II

Table 1: Guidance and Manufacturer's Declaration Electromagnetic Emissions

The Boston Scientific DBS System is intended for use in electromagnetic environment specified below. The customer or the user of the Boston Scientific DBS System should ensure that it is used in such an environment.

Emissions Test	Compliance	Electromagnetic Environment – Guidance
RF emissions CISPR 11	Group 1	The Boston Scientific DBS System uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The Boston Scientific DBS 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.
Harmonic emissions IEC 61000-3-2	Class B	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

Table 2: Guidance and Manufacturer's Declaration Electromagnetic Immunity

The Boston Scientific DBS System is intended for use in the electromagnetic environment specified below. The customer or the user of the Boston Scientific DBS System should assure that it is used in such an environment.

Immunity Test	IEC 60601-1-2 Test Level	Compliance Level	Electromagnetic Environment – Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	Air: ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV Contact: ± 8 kV	Air: Remote Control and Charger: ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV ETS and Wand: ± 2 kV, ± 4 kV, ± 8 kV, ± 15 kV[1] Contact: Remote Control, Charger, and ETS 3: ± 8 kV ETS 2 and Wand: ± 6 kV	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30 %. ***Note:*** *Applies to external electrical components.*
Electrical fast transient/ burst IEC 61000-4-4 (Programming Wand only)	± 2 kV for power supply lines ± 1 kV for input/output lines	± 2 kV for power supply lines ± 1 kV for input/output lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5 (Programming Wand only)	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	± 1 kV line(s) to line(s) ± 2 kV line(s) to earth	Mains power quality should be that of a typical commercial or hospital environment.

1 ± 15 kV compliance level applies to Vercise ETS 3 only.

Table 2 (Continued): Guidance and Manufacturer's Declaration Electromagnetic Immunity			
Immunity Test	**IEC 60601-1-2 Test Level**	**Compliance Level**	**Electromagnetic Environment – Guidance**
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11 (Programming Wand only)	<5 % U_T (>95 % dip in U_T) for 0,5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70 % U_T (30 % dip in U_T) for 25 cycles <5 % U_T (>95 % dip in U_T) for 5 s	<5 % U_T (>95 % dip in U_T) for 0,5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70 % U_T (30 % dip in U_T) for 25 cycles <5 % U_T (>95 % dip in U_T) for 5 s	Mains power quality should be that of a typical commercial or hospital environment. If the user of the Boston Scientific DBS System requires continued operation during power mains interruptions, it is recommended that the Boston Scientific DBS System be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment. Magnetic fields from common appliances are not expected to affect the device.
Note: *UT is the a.c. mains voltage prior to application of the test level.* ***Note:*** *The Charger is used with rechargeable DBS Systems only.* ***Note:*** *The Programming Wand is used with Vercise PC and Vercise Gevia DBS Systems only.*			

Table 3: Guidance and Manufacturer's Declaration Electromagnetic Immunity

The Boston Scientific DBS System is intended for use in the electromagnetic environment specified below. The customer or the user of the Boston Scientific DBS System should assure that it is used in such an environment.

Immunity Test	IEC 60601-1-2 Test Level	Compliance Level	Electromagnetic Environment - Guidance
Conducted RF IEC 61000-4-6 (ETS only)	3 Vrms 150 kHz to 80 MHz	3 Vrms 150 kHz to 80 MHz 6 Vrms in ISM and amateur radio bands between 150 kHz and 80 MHz	Professional healthcare facility environment and home healthcare environment.
Radiated RF IEC 61000-4-3	10 V/m 80 MHz to 2,7 GHz	10 V/m 80 MHz to 2,7 GHz	Professional healthcare facility environment and home healthcare environment. Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey[a], should be less than the compliance level in each frequency range. Interference may occur in the vicinity of equipment marked with the symbol shown below: 

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

a Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Boston Scientific DBS System is used exceeds the applicable RF compliance level above, the Boston Scientific DBS System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the Boston Scientific DBS System.

Table 4: Immunity Testing RFID Readers

The external electrical components of the Boston Scientific DBS System have been tested for immunity to interference from RFID readers per the following specifications.

RFID Spec Per AIM 7351731	Frequency	Test Level (RMS)
ISO 14223	134.2 kHz	65 A/m
ISO/IEC 14443-3 (Type A)	13.56 MHz	7.5 A/m
ISO/IEC 14443-4 (Type B)	13.56 MHz	7.5 A/m
ISOAEC 15693 (ISO 18000-3 Mode 1)	13.56 MHz	5 A/m
ISO 18000-3 Mode 3	13.56 MHz	12 A/m
ISO/IEC 18000-7	433 MHz	3 V/m
ISO/IEC 18000-63 Type C	860-960 MHz	54 V/m
ISO/IEC 18000-4 Mode 1	2.45 GHz	54 V/m

Table 5: Manufacturer's Declaration Proximity Fields

The Boston Scientific DBS System is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The users of the Boston Scientific DBS System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the Boston Scientific DBS System as recommended below, according to the maximum output power of the communications equipment.

Proximity Test	IEC 60601-1-2 Test Level	Compliance Level	Electromagnetic Environment Guide
IEC 61000-4-3	385 MHz: 27 V/m @ 18 Hz pulse modulation	27 V/m	Recommended separation distance d = 30 cm
	450 MHz: 28 V/m @ FM modulation	28 V/m	
	710 MHz, 745 MHz, 780 MHz: 9 V/m @ 217 Hz pulse modulation	9 V/m	
	1720 MHz, 1845 MHz, 1970 MHz: 28 V/m @ 217 Hz pulse modulation	28 V/m	
IEC 61000-4-3	1720 MHz, 1845 MHz, 1970 MHz: 28 V/m @ 217 Hz pulse modulation	28 V/m	Recommended separation distance d = 30 cm
	2450 MHz: 28 V/m @ 217 Hz pulse modulation	28 V/m	
	5240 MHz, 5500 MHz, 5785 MHz: 9 V/m @ 217 Hz pulse modulation	9 V/m	

Note: *For the frequency bands in this table, use the specified recommended separation distance. The recommended minimum separation distance of 30 cm between portable and mobile RF communications equipment (transmitters) and the Boston Scientific DBS System apply to all other frequencies within the specified ranges.*

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

Essential Performance

External Trial Stimulator

The stimulation pulse shall meet the requirements for charge balance and amplitude while stimulation is on.

Other External Devices

Failure of the external electrical components will not result in an unacceptable risk to the user.

Telemetry Information

Vercise PC and Vercise Gevia DBS Systems

The following parameters describe the wireless communication link between the Stimulator and Remote Control:

- Frequency Band: 119 kHz to 131 kHz
- Modulation Type: FSK
- Effective Radiated Power: 0.05 mW (-13 dBm) maximum
- Magnetic Field Strength (at 3 m distance): 46 µA/m

Vercise Genus DBS System

The following parameters describe the wireless communication link between the Remote Control or Clinician Programmer and the Implantable Pulse Generator or External Trial Stimulator:

- Frequency Band: 2.402 GHz to 2.480 GHz
- Modulation Type: GFSK
- Maximum Radiated Power: 5 dBm
- Protocol: Bluetooth Low Energy technology

Quality of Wireless Service

Vercise PC and Vercise Gevia DBS Systems

The Vercise PC and Vercise Gevia DBS Systems use a Half-Duplex, direct point-to-point, primary-secondary communication system with the characteristics listed in Table 6:

Table 6: Quality of Wireless Service of the Configure Tab (Vercise PC and Vercise Gevia)

Boston Scientific Stimulator Type	Typical Range	
	Between the Remote Control and Stimulator	Between the Wand and Stimulator
Non-Rechargeable Stimulator	22 in (55.8 cm)	18 in (45.7 cm)
Rechargeable Stimulator	36 in (91.4 cm)	33 in (83.8 cm)

Vercise Genus DBS System

The Vercise Genus DBS System uses a Half-Duplex, direct point-to-point, primary-secondary communication system based on Bluetooth Low Energy technology with the typical communication ranges listed in Table 7:

Table 7: Quality of Wireless Service of the Configure Tab (Vercise Genus)

Typical Range			
Between the Remote Control and Implanted Stimulator (IPG)	Between the Remote Control and External Trial Stimulator (ETS)	Between the Clinician Programmer and Implanted Stimulator (IPG)	Between the Clinician Programmer and External Trial Stimulator (ETS)
9.8 ft (3 m)	19.6 ft (6 m)	9.8 ft (3 m)	19.6 ft (6 m)

Data will be resent if not successfully received on supported devices. Sources of in-band high interference may result in slow connection, difficulty when pairing devices, or both. If you experience any of these, you may need to decrease the distance between the communicating devices. For information on how to improve connection issues, see the *"Troubleshooting Wireless Coexistence Issues"* section of this manual.

Timing for Vercise PC and Vercise Gevia DBS Systems

Once a command is initiated by the user, the system will respond in less than 1.5 seconds.

Timing for Vercise Genus DBS System

When a user initiates a communication session, the system will typically respond in 1 to 6 seconds. The typical data throughput during an active programming session will be more than 10 kbps.

Troubleshooting Wireless Coexistence Issues

Other wireless and RF technology based equipment operating in close proximity to a similar frequency band may degrade the range and responsiveness of the Boston Scientific DBS System. If you experience issues with the wireless communication behavior between the Remote Control/Clinician Programmer and Stimulator, try the following steps to correct the behavior:

For Vercise PC and Vercise Gevia DBS Systems

- Decrease the distance between the two devices if possible.
- Change the orientation of the communicating device.
- Move the communicating devices away from other equipment or devices that may cause interference, such as television and computer monitors, short range RFID electronic tracking systems such as badge scanners and parking lot scanners, power adapters, and wireless chargers.

For Vercise Genus DBS System

- Decrease the distance between the two devices if possible.
- Ensure there are no objects between the communicating devices.
- Move the communicating devices away from other equipment or devices that may cause interference, such as Wi-Fi routers, cordless phones, Bluetooth wireless streaming devices, baby monitors, and microwave ovens.

Wireless Security

Vercise PC and Vercise Gevia DBS Systems

The Vercise PC and Vercise Gevia DBS Systems have a short range inductively coupled telemetry system. A Remote Control (or Wand) has to be linked with a Stimulator to allow communication. The Stimulator will not respond to any unlinked device. There are additional mechanisms that ensure the integrity of the communicated data.

Vercise Genus DBS System

The Vercise Genus DBS System utilizes Bluetooth Low Energy for communication. The Vercise Genus DBS System supported devices implement the following Bluetooth Low Energy security features:

- LE Privacy
- LE Secure Connections

Additionally, the Vercise Genus DBS System implements proprietary authentication and encryption that supports:

- Authenticated pairing sequences that are initiated by the healthcare provider.
- Establishing a bonded connection only after successfully completing the authentication sequence.
- Creating a validated and encrypted communication link during each connection with a previously paired device.

The additional application level authentication and encryption ensures that communication with the Stimulator is only accomplished by authorized Boston Scientific devices.

Clinician Programmer Security

The Clinician Programmer (CP) is a hardened computer with the following security controls:

- Access to the CP is restricted to authorized users and the CP screen locks out if there is no activity and may only be unlocked with a password to prevent unauthorized access.
- The CP Platform enforces a password lockout duration after a predefined number of unsuccessful login attempts.
- Only authorized incoming connections are allowed.
- The encrypted file system restricts access of the data in the file system to authorized users only.
- Non-whitelisted applications cannot be installed.
- All BSN applications are code signed so that any compromise to their integrity via USB or other data channels may be detected and prevented from execution.
- User actions and login attempts are logged by the Windows Event Log.
- The CP logs and notifies the user upon detection of malicious software.

Boston Scientific has developed a process to receive potential product security vulnerabilities from external sources in order to validate their existence and determine how to best respond to improve product security and safety. Please refer to the following webpage to report potential product security vulnerabilities to the Boston Scientific Product Security team: https://www.bostonscientific.com/en-US/customer-service/product-security/responsible-disclosure.html

FCC Compliance

The following is federal government communications regulation information about the Boston Scientific DBS System.

This device complies with part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) This device must accept any interference received including interference that may cause undesired operation.

The Boston Scientific DBS System components should only be serviced by Boston Scientific. Do not attempt to open or repair any of the components.

Changes or modifications to this product not authorized by Boston Scientific Corporation could void the FCC Certification and negate your authority to operate this product.

FCC ID

Vercise PC and Vercise Gevia IPG

FCC ID: Q4D-SC1132

Vercise Genus Rechargeable IPG

FCC ID: Q4D-SC1232

Vercise Genus Non-Rechargeable IPG

FCC ID: Q4D-SC1432

Rechargeable Stimulator Battery

Stimulator Battery

The rechargeable Stimulator battery should provide at least five years of service. In many cases, the Stimulator battery should provide at least 15 years of service. Battery life is dependent on the stimulation settings and conditions.

Recharge Estimate

Boston Scientific recommends any recharge schedule that fits the patient's schedule and lifestyle while maintaining sufficient charge to maintain stimulation. Patients should expect a daily recharging time of 5 to 30 minutes per day or a periodic recharging time of 30 minutes to 4 hours every 1 to 2 weeks, but their recharge routine may vary depending on their stimulation parameters. High power users will require more frequent charging. Developing a patient's recharge routine involves finding the right balance among the following:

- How much power is required for the patient to experience effective therapy
- How often the patient wants to recharge
- How long the patient wants to recharge
- How the patient would like to manage their personal schedule

After years of service, the Stimulator may require shorter intervals between charges. The Stimulator will need replacement when stimulation no longer can be maintained with routine charging.

The Clinician Programmer will provide a recharging estimate based on 24 hours per day of stimulation at the programmed settings. If fully charging the Stimulator, patients should be instructed to charge until the Charger emits the end of charge double beep.

Note: *For instructions on charging the Stimulator, refer to the appropriate Charging Handbook for your DBS System as listed in your DBS Reference Guide. For instructions on checking the Stimulator battery status, refer to the appropriate Remote Control DFU for your DBS System as listed in your DBS Reference Guide.*

Non-Rechargeable Stimulator Battery

Stimulator Battery

The longevity of the non-rechargeable Stimulator battery depends on the following factors:

- Programmed parameters
- System impedance
- Hours per day of stimulation
- Changes to stimulation made by the patient

For additional information on estimating the longevity of the non-rechargeable battery, refer to the appropriate *Programming Manual* as listed in your *DBS Reference Guide.*

Elective Replacement

When the implanted non-rechargeable Stimulator is nearing the end of its battery life, the Stimulator will enter the Elective Replacement mode. The Elective Replacement Indicator (ERI) will appear on the Remote Control and Clinician Programmer. Stimulation is still being provided during this ERI period. Changes made to the stimulation will not be saved, and stimulation will not be available soon. Patients should be advised to contact their healthcare provider to report this message screen. The Stimulator must be replaced to continue receiving stimulation. Batteries that have lasted 12 months or more without entering ERI mode will have a minimum of 4 weeks between entering ERI mode and reaching End of Battery Life. Surgery is required to replace the implanted non-rechargeable Stimulator, although Leads may stay in place while the Stimulator is exchanged.

End of Service

End of Battery Life

When the Stimulator battery is fully depleted, the End of Service (EOS) indicator will be displayed on the Remote Control and Clinician Programmer. Stimulation will not be available. Surgery is required to replace the implanted non-rechargeable Stimulator to continue providing stimulation.

End of Programmed Service (Vercise PC Only)

The non-rechargeable Stimulator software has been programmed to end service after a defined period. When the Stimulator is within approximately 180 days of the end of its programmed period, the Remote Control and Clinician Programmer will display a message indicating the number of service days available. Refer to the *Remote Control DFU* listed in your *DBS Reference Guide* for description of the End of Service messages displayed.

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Boston Scientific

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