St. Jude Medical Infinity™
Deep Brain Stimulation System

PLATFORM TECHNOLOGY DESIGNED TO CAPTURE AND PROVIDE MEASURABLE THERAPY OUTCOMES FOR MOVEMENT DISORDERS

For the management of movement disorders, the St. Jude Medical Infinity™ Deep Brain Stimulation (DBS) System is a user-friendly platform for both patients and physicians designed to capture and provide measurable therapy outcomes. This system offers the smallest primary cell IPG with a directional lead, providing more programming flexibility and the ability to steer current away from areas generating side effects.

When used to manage symptoms stemming from movement disorders such as Parkinson’s disease and essential tremor (ET), the St. Jude Medical Infinity DBS System is:

- **Clinically proven to minimize disease symptoms and improve quality of life:** The St. Jude Medical Infinity DBS system allows for customizable therapy to fit each patient’s needs while potentially reducing unwanted side effects. In addition, the directional lead is designed to allow targeted control of stimulation.²⁷
- **Upgradeable:** This is the only DBS system on the market that can be upgraded without the need for surgical replacement.⁴
- **Safe and reliable:** Safety profile of the constant-current St. Jude Medical Infinity DBS system is similar to those reported in other DBS studies.²⁹

Parkinson’s disease and ET are chronic, progressive, neurodegenerative diseases characterized by outward symptoms such as tremor/shaking, bradykinesia (slowness of motion), akinesia (muscle rigidity), dystonia (involuntary muscle contracts resulting in slow repetitive movements or abnormal postures) and difficulty walking/shuffling steps.¹⁰ Specifically, Parkinson's disease (PD), the second most common neurodegenerative disorder, is estimated to affect about 0.3% of the entire population and 1% in people over 60 years of age.¹¹ The standard of care for management of the most common movement-related symptoms is typically pharmacological. Levodopa and dopamine agonists can provide adequate symptom control in the first 5-10 years of therapy.¹² The long-term evolution of the disease, however, results in the majority of patients suffering from complications such as fluctuations in the motor state and dyskinesia.¹³ Bilateral DBS of the subthalamic nucleus (STN) is a safe and effective surgical treatment option to address the symptoms of these common movement disorders.¹⁴ This clinical compendium summarizes key studies demonstrating the safety and effectiveness of the DBS therapy and its ability to provide symptom control.
Deep brain stimulation devices come in both voltage-controlled and current-controlled devices. The current applied by constant voltage IPGs is dependent on the tissue impedance that may change over time. In contrast, current-controlled devices deliver constant current by automatically adjusting the voltage in response to changes in impedance.

Constant-current stimulation may provide more accurate control of the spread of the electrical field (and ultimately minimize time-dependent changes in therapeutic efficacy) than voltage-controlled devices because adjustments can be made to account for the potential heterogeneity in tissue impedance. The studies below support the use of constant-current DBS stimulation for the management of movement disorder symptoms and overall quality of life.

SUBTHALAMIC DEEP BRAIN STIMULATION WITH A CONSTANT CURRENT DEVICE IN PARKINSON’S DISEASE: AN OPEN-LABEL RANDOMIZED CONTROLLED TRIAL


SUMMARY

Objective and study design:

- The purpose of this randomized, controlled study across 15 clinical sites was to evaluate the safety and efficacy of bilateral constant-current DBS of the subthalamic nucleus (STN).
  - A total of 136 patients received bilateral implantation in the STN of a constant-current DBS device and randomized to either immediate or three-month delayed DBS after implantation (control group) in a 3:1 ratio.
  - The primary outcome for this study was the change in duration of “on” time without bothersome dyskinesias as recorded in patient diaries, after three months of stimulation and in the medication on condition compared with the control group.
- On medication was defined as roughly 30 minutes after a patient takes anti-parkinsonian medication when both the clinician and the patient indicate that the medication dose is effective.

- Secondary outcome measures included changes in the unified Parkinson’s disease rating scale (UPDRS) part three (motor), part 2 (activities of daily living), and total scores, quality of life, quality of sleep, severity of illness, levodopa equivalent dose, and patient satisfaction. Secondary outcomes were measured at three months, six months and 12 months.

RESULTS

- At three months, both study groups reported an increase in good quality on time from baseline:
  - The mean increase of good quality on time was 4.27 hours in the stimulation group vs. 1.77 hours in the control group (p = 0.003).
- The total UPDRS score (on medication for both groups) significantly improved in both groups, and was significantly greater in the stimulation group (p < 0.0001).
- The responder rate (defined as at least a two-hour increase from baseline in good quality on time) was 72.3% in the stimulation group vs. 38.2% in the control group (p < 0.001).
- After 12 months of stimulation, good quality on time improved by 3.44 hours at six months and by 2.64 hours at 12 months (see Figure 1).

Figure 1: Duration of good quality on time per treatment group over the 12-month study. The stimulation group started stimulation within seven days of device implant. The control group started stimulation after the three-month visit.
• The off-medication, on-stimulation total UPDRS scores improved by 19.4 points at six months and 17.1 points at 12 months compared with off-medication, off-stimulation.

• DBS improved not only motor function and motor complications, but also depressive symptoms at three months.

• Results were sustained through the 12 month follow-up.

**TWELVE-MONTH NEUROPSYCHOLOGICAL OUTCOME OF BILATERAL STN DBS IN PARKINSON’S DISEASE: A DELAYED ACTIVATION ARM CONTROLLED, RANDOMIZED STUDY**

Troster AI, et al. *Movement Disorder Society, 2011*

**SUMMARY:**

• The purpose of this study was to evaluate the short-term neuropsychological safety effects of bilateral subthalamic nucleus (STN) DBS.

• A total of 136 PD patients were randomized in a 3:1 ratio to either receive immediate stimulation following implantation (stimulation group) or a three-month delayed activation following implantation (control group).

  – At the 12-month follow-up, patients had been stimulated for either nine months or 12 months, depending on which group they were randomized to.

• A battery of neuropsychological tests were administered, including Dementia Rating Scale-2, Wechsler Abbreviated Scale of Intelligence (WASI), Hopkins Verbal Learning Test – Revised, Hamilton Depression Inventory-Self Report (HDI), Delis-Kaplan Executive Function System (D-KEFS), and Frontal Systems Behavior Scale-Self Rating (FrSBe).

• At 12 months, patients had significant improvements from baseline in memory and depression, but were worse in fluency and processing speed. The authors stated that these results are consistent with other studies.

**KEY TAKEAWAYS:**

• This was the first study to evaluate neuropsychological effects of STN DBS in a delayed activation group.

• Results were consistent with other studies, showing that at 12 months, patients had significant improvements from baseline in memory and depression, but were worse in fluency and processing speed.
Traditionally, DBS has been delivered through cylindrical electrodes at fixed sizes. However, to effectively target small anatomical structures with deep brain stimulation, precise stimulation is required for successful therapy while avoiding unwanted side effects.

A previous study has shown that the average therapeutic window for a similar directional lead is 41.3% wider than a conventional DBS lead (p = 0.037). In addition, the study showed that the current threshold needed to produce a meaningful therapeutic effect was 43% lower with a directional lead as compared to a conventional lead (p = 0.002). The modeling studies outlined below support the use of a new electrode design in deep brain stimulation.

### Evaluation of Electrode Design on Activation Volumes Produced During Deep Brain Stimulation


**Summary:**
- The objective of this modeling study was to evaluate the effects of electrode size and shape on the volume of tissue activated (VTA), which is a prediction of activated brain tissue in the region surrounding the DBS electrode.
- Three-dimensional finite element models of the electrodes and surrounding medium were created to calculate electric fields produced during DBS, and multi-compartmental models of myelinated axons were used to predict the neural response.
- Volume and dimensions of VTA were measured for three different types of electrodes: baseline electrode (1.27 mm diameter, 1.5 mm height), a cylindrical electrode with a larger diameter (1.41 mm diameter, 1.5 mm height), and a cylindrical electrode with larger diameter and a conductive tip (ActiveTip™ electrode, 1.41 mm diameter, 3 mm overall length).
- Results showed that all electrodes produced comparable volumes of tissue activation across the entire range of stimulus electrodes.
- Increasing the electrode diameter alone had little effect on the height or width of the VTA.
- The volume differences between voltage settings and current-based stimulation settings were different and need further evaluation.

### Key Takeaways:
- 3-D finite element models of the electrodes and surrounding tissue medium, and multi-compartmental models of myelinated axons to predict neural response, may estimate the volume of tissue activated and be predictive of brain tissue activation surrounding DBS electrodes.
- Computer modeling results in this study suggest that alternative electrode designs are capable of producing comparable volumes of tissue activation across a large range of stimulus amplitudes.

### Comparison of Neural Activation Between Standard Cylindrical and Novel Segmented Electrode Designs


**Summary:**
- In this study, computational models were used to evaluate whether DBS leads with segmented contacts could provide directional control of neural activation as compared to conventional cylindrical contacts.
- A schematic of the directional DBS lead is shown in Figure 3 below. In this novel electrode design, there are four “rows” of electrodes, two are standard cylindrical contacts and two are divided into thirds. Each contact has an arc length of 1.1 mm and all electrode contacts are 1.5 mm long.

![Directional DBS lead](image)

**Figure 3:** Directional DBS lead.
When all segments around the circumference of the lead were simultaneously activated, the VTAs produced were comparable between the segmented electrodes and the standard cylindrical electrodes.

Both types of leads produced VTAs that were roughly spherical, however when individual segmented contacts were activated in the directional lead, the VTA was displaced on the side of the lead.

Additionally, results showed it was possible to steer the activation volume around the directional lead, creating preferential activation on one side. See Figure 4 for more details.

**Figure 4.** VTAs (red) are shown relative to the thalamus (yellow) and subthalamic nucleus (green) as directional contacts are selectively activated. Changing active contacts can preferentially steer activation around the directional DBS lead.

At common stimulation settings (2.5 mA, 60 μsec, 130 Hz):
- Activation of a single directional lead electrode generated VTAs that were 60% larger than the standard cylindrical electrode contact.
- Activation of two directional lead contacts generated VTAs that were 46% larger.
- Activation of three directional lead contacts generated VTAs that were 36% larger.

Results in this study suggest that more precise activation of target regions during DBS is possible, at potentially a better power efficiency.

**KEY TAKEAWAYS:**
- Results in this study confirm the ability to steer current toward regions of the brain during DBS that may help mediate therapeutic effects while potentially avoiding regions of stimulation-induced side effects.
- At the same stimulation settings, directional lead contacts generated larger VTAs than the standard cylindrical lead contacts, suggesting a better power efficiency for the segmented contacts.

**EFFECTS OF STIMULATION LOCATION ON MOTOR OUTCOMES DURING CURRENT-CONTROLLED DEEP BRAIN STIMULATION FOR PARKINSON’S DISEASE**


**SUMMARY:**
- In this sub-study of the constant-current RCT, computational models were used to quantify the effects of stimulation location on outcomes in 60 patients.
- The study used previously published methods to create patient-specific computation models of DBS. The volume of tissue activated (VTA) was determined for each patient, and from the VTAs, a probabilistic stimulation atlas of outcomes was constructed. See Figure 5 below.

**Figure 5.** Stimulation atlas of outcomes was constructed for each patient.

- At common stimulation settings (2.5 mA, 60 μsec, 130 Hz):
  - Activation of a single directional lead electrode generated VTAs that were 60% larger than the standard cylindrical electrode contact.
  - Activation of two directional lead contacts generated VTAs that were 46% larger.
  - Activation of three directional lead contacts generated VTAs that were 36% larger.

Results in this study suggest that more precise activation of target regions during DBS is possible, at potentially a better power efficiency.
• All patients had a pre-operative MRI which was fused to a post-operative CT acquired at least 12 months post-operatively.

• All patients were implanted with bilateral DBS leads; electrode contacts were either 0.5 mm or 1.5 mm contact spacing.

• DBS lead locations for 60 patients among eight surgical sites were registered to an atlas brain. The sum of all VTAs encompassed a region including the STN and portions of the thalamus. See Figure 6 below.

• Results showed that an overall improvement in UPDRS scores could be achieved from stimulating a large region around the STN. See Figure 7 below.

• A cluster analysis revealed subregions around the STN where stimulation led to statistically significant improvements in tremor, rigidity and bradykinesia. See Figure 8 below.

**Figure 6.** Left: DBS lead locations for 60 bilateral patients. Right: The sum of all VTAs (gray) encompassed a region including the STN (green) and portions of the thalamus (yellow).

**Figure 7.** Size and color of spheres indicate post-pre DBS change in raw scores for UPDRS behavior, motor and total score. Red indicates worsening (i.e., higher score), blue indicates improvement (i.e., lower score). Note that in some cases such as tremor, distinct clusters were identified for both improvement and worsening of a single symptom.

**Figure 8.** Size and color of spheres indicate post-pre DBS change in raw scores for UPDRS behavior, motor and total score. Red indicates worsening (i.e., higher score), blue indicates improvement (i.e., lower score). Note that in some cases such as tremor, distinct clusters were identified for both improvement and worsening of a single symptom.

**KEY TAKEAWAYS:**

• Results from this computational analysis suggest that stimulation location is a significant predictor of motor outcomes during DBS, supporting the possibility of using DBS lead location and stimulation parameters to predict DBS outcomes.

• Further studies are needed to confirm these preliminary findings.
REFERENCES


8. St. Jude Medical Infinity™ IPG First and Only Related Claims Memo, Zinc # SJM-INF-0815-0008.


Brief Summary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

Intended Use: This rechargeable neurostimulation system is intended to deliver electrical stimulation to targets in the brain. The system is intended to be used with leads and associated extensions that are compatible with the system. Indications for Use: The St. Jude Medical Infinity™ deep brain stimulation system is indicated for the following conditions: Bilateral stimulation of the subthalamic nucleus (STN) as an adjunctive therapy to reduce some of the symptoms of advanced levodopa-responsive Parkinson's disease that are not adequately controlled by medications. Unilateral or 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. Contraindications: This system is contraindicated for patients who meet the following criteria: are unable to operate the system have unsuccessful test stimulation. The following procedures are contraindicated for patients with a deep brain stimulation system. Advise patients to inform their healthcare professional that they cannot undergo the following procedures: Diathermy (short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy) Electroshock therapy and transcranial magnetic stimulation (TMS).