DBS Therapy for Parkinson’s Disease

HELP YOUR PATIENTS

ACHIEVE DAILY VICTORIES

Perry C.
Benefiting from DBS Therapy since 2006
Motor fluctuations and dyskinesias decrease quality of life for people with Parkinson’s disease

- In the United States, there are more than 1 million people living with Parkinson’s disease (PD).
- Levodopa generally provides smooth and stable benefits for up to 5 years after therapy introduction.
- After this period, patients may experience increasingly troublesome and unpredictable motor fluctuations and dyskinesias.

Treating motor fluctuations and dyskinesias requires moving beyond standard dopamine replacement therapy

- The delayed “on,” wearing off, and dose failure of levodopa may be due to its impaired absorption, short half-life, and the loss of striatal dopamine storage capacity.
- When drugs become less reliable, Medtronic DBS Therapy (Deep Brain Stimulation) should be considered to achieve PD treatment goals.

Benefits of Adding Medtronic DBS Therapy

<table>
<thead>
<tr>
<th>Medications Alone</th>
<th>Medtronic DBS Therapy</th>
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<tbody>
<tr>
<td>0 hours of additional “on” time</td>
<td>5.1 hours additional “on” time without troubling dyskinesias*</td>
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<tr>
<td>Unpredictable</td>
<td>More predictable</td>
</tr>
<tr>
<td>Dyskinesias and nonmotor side effects</td>
<td>Medication reduction may lead to fewer drug-induced side effects</td>
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<tr>
<td>Pulsatile delivery</td>
<td>Continuous delivery</td>
</tr>
<tr>
<td>GI absorption required</td>
<td>No GI absorption</td>
</tr>
<tr>
<td>Must cross blood-brain barrier</td>
<td>Targeted and direct</td>
</tr>
<tr>
<td>Dosing compliance challenges</td>
<td>Simplified medication regimen may be possible</td>
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</table>

*Mean results; DBS is adjunctive to medications.

Iris C.
Benefiting from DBS Therapy since 2008
When drugs become less reliable, Medtronic DBS Therapy should be considered

How Medtronic DBS Therapy Works

- One or more leads are implanted to deliver electrical stimulation to parts of the brain involved in movement control, including the globus pallidus or subthalamic nucleus.
- Current delivered by the lead is believed to disrupt and modulate abnormal motor circuit activity in the brain caused by PD, thereby smoothing out motor function. However, the exact mechanism of action isn’t completely understood.

More than 75,000 patients globally have been treated with Medtronic DBS Therapy.

DBS Therapy with Medications Provides an Additional 5.1 Hours of “On” Time to Smooth Out Motor Function Throughout the Day

“Medicine and surgery are not separate disciplines. Surgery is not the failure of neurology, but rather the extension of neurology.”
— George Plotkin, MD, PhD
5.1 hours of additional “on” time without dyskinesias compared to Best Medical Therapy (BMT) alone

![Graph showing 5.1 hours of additional “on” time without dyskinesias for DBS Therapy compared to BMT alone.](#)

- Results from prospective multicenter randomized control trial of patients with advanced PD
- Medications were reduced 25% on average for patients receiving DBS Therapy

In a Separate Clinical Study, Medtronic DBS Therapy Was Shown to Maintain Symptom Improvements After 5 Years

![Graph showing improvement in motor scores after 5 years.](#)

Best Medical Therapy Defined

Patients who received BMT were managed actively by movement disorder neurologists. Patients received state-of-the-art care, including the active management of medications and nonpharmacological therapy (e.g., physical occupational, and speech therapy) as needed to achieve best symptom control.
Proven safety profile

The majority of serious adverse events* with Medtronic DBS Therapy are procedure-related and temporary.4

- Although there was a significantly higher incidence of serious adverse events observed in patients receiving DBS Therapy, 99% of serious adverse events were resolved by 6 months.4
- Improvements in MRI imaging, stereotactic equipment and software, and patient selection have all helped advance DBS Therapy since the FDA first approved it in 1997.

Surgical risks include:
- Infection
- Cerebral hemorrhage

Hardware related risks include:
- Lead fractures

Stimulation related side effects include:
- Paresthesia
- Speech
- Dystonia

Additional risks and side effects:
- Speech may get worse after DBS Therapy, requiring speech therapy.
- Some risks associated with DBS Therapy may be due to improved function and greater activity.5

Unlike thalamotomy:
- DBS Therapy preserves brain structures for future therapies and treatments.
- DBS Therapy is safely performed bilaterally.4

* A serious adverse event was defined according to FDA regulations as any event that: results in death, is life-threatening, results in prolonged or new hospitalization, results in disability or congenital anomaly/birth defect, or requires medical or surgical intervention to prevent one of the above outcomes.

Note: Adverse events vary depending on implanting centers. Consult with the implanting center you refer patients to in order to determine risks and adverse events.
In order to obtain maximum benefits from DBS Therapy, patients with idiopathic Parkinson’s disease must be referred at the optimal time, or during a “window of opportunity” when the therapy may be most effective.

Window of Opportunity

Patient is experiencing troubling motor symptoms not effectively controlled by medications.

- “On” time characterized by disabling dyskinesias (or other nonmotor side effects)
  OR
- “Off” time characterized by disabling tremor, rigidity, or akinesia Bradykinesia
  OR
- Unpredictable “on/off” motor fluctuations
  OR
- Medication-resistant tremor

DBS Therapy Exclusion Criteria

- No longer responsive to dopaminergic medication
- Severely disabled even in the best “on” state
- Medical conditions that prevent surgery
  - Onset of frank dementia

According to the American Academy of Neurology (AAN), “10% to 20% of people with PD may be eligible for surgical treatments.”
When is Medtronic DBS Therapy appropriate?

DBS Therapy should be considered when the patient, despite optimal medical therapy, reaches a stage where the daily burden of PD begins to cause significant interference with:

- Daily function
- Occupational activities
- Important leisure time pursuits
- Basic activities of daily living

Medtronic DBS Patient Referral Advisor

The Patient Referral Advisor is a software tool that creates a patient “appropriateness” profile for DBS Therapy based on 5 absolute criteria and 7 relative criteria.

To download the Patient Referral Advisor software visit: www.medtronic.com/dbsreferraladvisor.

Discuss each patient’s goals and expectations to determine whether DBS Therapy is right for him or her. It’s important to set realistic goals about the benefits of Medtronic DBS Therapy.
Patient management

Establish a partnership with your Medtronic DBS Therapy implant center to manage postimplant patient care, which involves programming and medical management.

- **Initial Device Programming**—Identifying and programming optimal stimulation parameters during the first several months
- **Maintenance Device Programming**—Titrating stimulation as needed over time

Patient programming is reimbursed.

Innovative programming software

Medtronic has developed technology to make device programming easier, including:

- A step-by-step process that provides a systematic approach to programming
- The ability to capture, store and sort patient data in the device
- Features that maximize therapeutic response and device longevity

Medtronic provides comprehensive education, training, and clinical and technical support to help manage patients with DBS Therapy.
Present and future neuromodulation therapies

A paradigm shift

- Today, more than 500,000 patients globally have received Medtronic neuromodulation devices.9
- The future of neurology will include the integration of device-based neuromodulation treatment into the management of the most common neurological disorders.

DBS Therapy continues to be the fastest growing treatment option for people suffering from movement disorders.

Medtronic neuromodulation therapies

<table>
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<tr>
<th>PRESENT</th>
<th>FUTURE</th>
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<tr>
<td>Parkinson’s Disease</td>
<td>Intracerebroventricular (ICV) Applications</td>
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<tr>
<td>Essential Tremor</td>
<td>Depression</td>
</tr>
<tr>
<td>Dystonia*</td>
<td>Chronic Migraine (ONS)</td>
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<tr>
<td>Obsessive-Compulsive Disorder*</td>
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<tr>
<td>Chronic Pain (Opioid)</td>
<td>Chronic Pain (Nonopiod)</td>
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<tr>
<td>Malignant Pain</td>
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<tr>
<td>Chronic Pain</td>
<td></td>
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<tr>
<td>Spasticity</td>
<td></td>
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<tr>
<td>Urinary Incontinence and Retention</td>
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*Humanitarian Device:
The effectiveness of this device for the treatment of dystonia or obsessive-compulsive disorder has not been demonstrated.
Medtronic: The leader in DBS Therapy

Medtronic is committed to advancing the science of neuromodulation through:

Product innovation
• Providing new products such as Activa® PC—the next generation primary cell neurostimulator—and Activa® RC—the first rechargeable neurostimulator for DBS Therapy
• New programming platform provides step-by-step guidance and advanced device programming options

Education
• Customized courses for clinicians designed to make DBS Therapy successful in your practice

Procedure support
• Medtronic Procedure Solutions provides a complete system to plan, record, place and manage with success

Innovative clinical research
• Medtronic has sponsored numerous studies to evaluate the safety and efficacy of DBS for current and future indications

Indications for DBS Therapy

Parkinson’s Disease

Essential Tremor
• AAN Guidelines concluded that unilateral deep brain stimulation resulted in a significant (60% to 90%) reduction of contralateral limb tremor.8
• DBS Therapy improves activities of daily living in patients with ET.4

Dystonia
• Approved in 2003 under Humanitarian Device Exemption (HDE) for the treatment of dystonia.*

Obsessive-Compulsive Disorder
• Approved in 2009 under HDE for the treatment of obsessive-compulsive disorder.*

* Humanitarian Device: The effectiveness of this device for the treatment of dystonia or obsessive-compulsive disorder has not been demonstrated.

Kristin E.
Benefiting from DBS Therapy since 2003
Medtronic DBS Therapy for Parkinson’s Disease, Tremor and Dystonia: Patients should always discuss the potential risks and benefits with a physician.

Indications:

Medtronic DBS Therapy for Parkinson’s Disease: Bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson’s Disease is indicated for adjunctive therapy in patients with moderate to severe, motor symptoms of advanced Parkinson’s disease that are not adequately controlled with medications.

Medtronic DBS Therapy for Tremor: Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Tremor is indicated for patients who have experienced a return or worsening of symptoms of tremor, including unilateral or bilateral tremor or a combination of tremor and rigidity.

Contraindications:

Contraindications: Patients who will be exposed to MRI using a full body radio-frequency (RF) coil or a head transmit coil that extends over the chest area, patients who are unable to properly operate the neurostimulator, or for Parkinson’s disease and Essential Tremor, patients for whom test stimulation is unsuccessful. Also, diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy) is contraindicated because diathermy's energy can be transferred through the implanted system (or any of the separate implanted components), which can cause neurostimulation system or tissue damage and can result in severe injury or death. Transcranial Magnetic Stimulation (TMS) is contraindicated for patients with an implanted DBS System.

Humanitarian Device (Humanitarian Device): Authorized by Federal Law for the use in the management of chronic, intractable (drug refractory) tertiary dystonia, including generalized and segmental dystonia, hemidystonia, and cervical dystonia (torticollis), for individuals 7 years of age and older. The effectiveness of this device for this use has not been demonstrated. USA Rx only. Rev 07/11

Reclai™ Deep Brain Stimulation Therapy for Obsessive-Compulsive Disorder: Product labeling must be reviewed prior to use for detailed disclosure of risks. Contraindications: Patients who will be exposed to MRI using a full body radio-frequency (RF) coil or a head transmit coil that extends over the chest area, and for patients who are unable to properly operate the neurostimulator. Also, diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy) is contraindicated because diathermy's energy can be transferred through the implanted system (or any of the separate implanted components), which can cause tissue damage and can result in severe injury or death. Diathermy can damage parts of the neurostimulation system. Transcranial Magnetic Stimulation (TMS) is contraindicated for patients with an implanted DBS System.

Warnings/precautions/adverse events:

There is a potential risk of tissue damage using stimulation parameter settings of high amplitudes and wide pulse widths. Extreme care should be used with lead implantation in patients with a heightened risk of intracranial hemorrhage. The lead-extension connector should not be placed in the soft tissues of the neck due to an increased incidence of lead fracture. Theft detectors and security screening devices may cause stimulation to switch ON or OFF, and may cause some patients to experience a momentary increase in perceived stimulation. Although some MRI procedures can be performed safely with an implanted DBS System, clinicians should carefully weigh the decision to use MRI in patients with an implanted DBS System. MRI can cause induced voltages in the neurostimulator and/or lead possibly causing uncomfortable jolting, or shocking levels of stimulation.

The DBS System may be affected or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/ defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy. Safety and effectiveness has not been established for patients with neurologic disease other than Parkinson’s disease or Essential Tremor, previous surgical ablation procedures, dementia, coagulopathies, or moderate to severe depression; or for patients who are pregnant, under 18 years, over 75 years of age (Parkinson’s Control Therapy) or over 80 years of age (Tremor Control Therapy). For patients with Dystonia, age of implant is suggested to be that at which brain growth is approximately 90% complete or above. Depression, suicidal ideations and suicide have been reported in patients receiving Medtronic DBS Therapy for Movement Disorders, although no direct cause and effect relationship has been established.

Abrupt cessation of stimulation should be avoided as it may cause a return of disease symptoms, in some cases with an intensity greater than was experienced prior to system implant (“rebound” effect). Adverse events related to the therapy, device, or procedure can include: stimulation not effective, neurological disorders, pain, dyskinesia, dystonia, speech disorders including dysarthria, infection, paresthesia, intracranial hemorrhage, electromagnetic interference, cardiovascular events, visual disturbances, sensory disturbances, device migration, paresis/asthenia, abnormal gait, incoordination, headaches, leed repositioning, thinking abnormal, device explant, hemplegia, lead fracture, seizures, respiratory events, and shocking or jolting stimulation.

Medtronic DBS Therapy for Dystonia: Bilateral or primary stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Dystonia is indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and segmental dystonia, hemidystonia, and cervical dystonia (torticollis), for individuals 7 years of age and older.

Contraindications: Contraindications include patients who will be exposed to MRI using a full body radio-frequency (RF) coil or a head transmit coil that extends over the chest area, patients who are unable to properly operate the neurostimulator. Also, diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy) is contraindicated because diathermy’s energy can be transferred through the implanted system (or any of the separate implanted components), which can cause neurostimulation system or tissue damage and can result in severe injury or death. Transcranial Magnetic Stimulation (TMS) is contraindicated for patients with an implanted DBS System.

Humanitarian Device (Dystonia): Authorized by Federal Law for the use in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and segmental dystonia, hemidystonia, and cervical dystonia (torticollis), for individuals 7 years of age and older. The effectiveness of this device for this use has not been demonstrated. USA Rx only. Rev 07/11

Medtronic DBS Therapy for Parkinson’s Disease, Tremor and Dystonia: Patients should always discuss the potential risks and benefits with a physician.

References:

Ensure that Medtronic DBS Therapy is a successful part of your practice

**Step 1.** Partner with your local implanting team.
- Establish referral processes and communications.
- Establish postimplant patient management roles.

**Step 2.** Identify appropriate patients.
- Attend a Medtronic education program to learn more about appropriate patient selection.
- Use the DBS Therapy Patient Referral Advisor to confirm appropriateness for patient referral.

**Step 3.** Discuss DBS Therapy with patients and their caregivers.
- Discuss patients’ goals with them.
- Educate patients about the benefits and risks of DBS Therapy.
- Set appropriate expectations.

**Step 4.** Refer appropriate patients for DBS Therapy.

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