

Advanced Treatment for Parkinson's Disease

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Boulder
Community
Health 

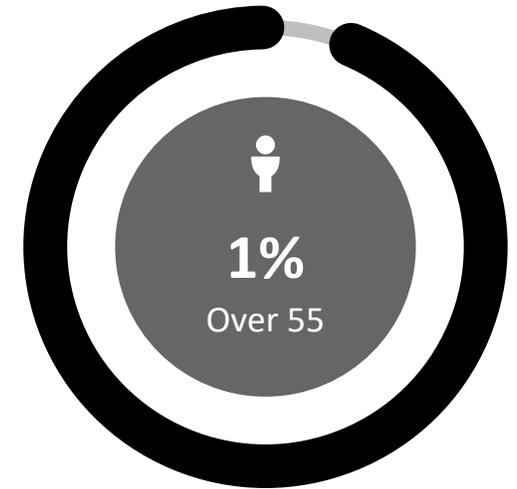
What is Parkinson's Disease?



A progressive, degenerative movement disorder marked by a decrease in dopamine-producing cells in the brain.



Exact cause remains unknown.



Affects 1 million Americans and more than 10 million people worldwide.

1% of people over the age of 55 will be affected with a diagnosis.

Symptoms of Parkinson's Disease

Motor Symptoms

Motor symptoms can make the activities of everyday life challenging.



Rigidity



Speech problems



Tremor



Slowed Movements



Shuffle Steps



Postural instability

Non-Motor Symptoms

Even though Parkinson's disease is a movement disorder, the non-motor symptoms can have just as big an impact on your quality of life.



Decreased sense of smell



Depression or mood problems



Pain



Insomnia



Bladder or bowel dysfunction



Fatigue

Parkinson's disease can be associated with motor and non-motor symptoms.

Treatment Options for Parkinson's Disease



Exercise

The effectiveness of **regular aerobic** exercise is well characterized for both motor and non-motor symptoms.



Medication

Usually the first-line treatment for newly diagnosed patients. **Levodopa (L-DOPA)** is one of the most common medications for newly diagnosed patients.



Ablative surgeries

Pallidotomy and **Thalamotomy** are non-reversible surgeries that use targeted application of heat or ultrasound to ablate tissue causing PD symptoms.



Deep Brain Stimulation

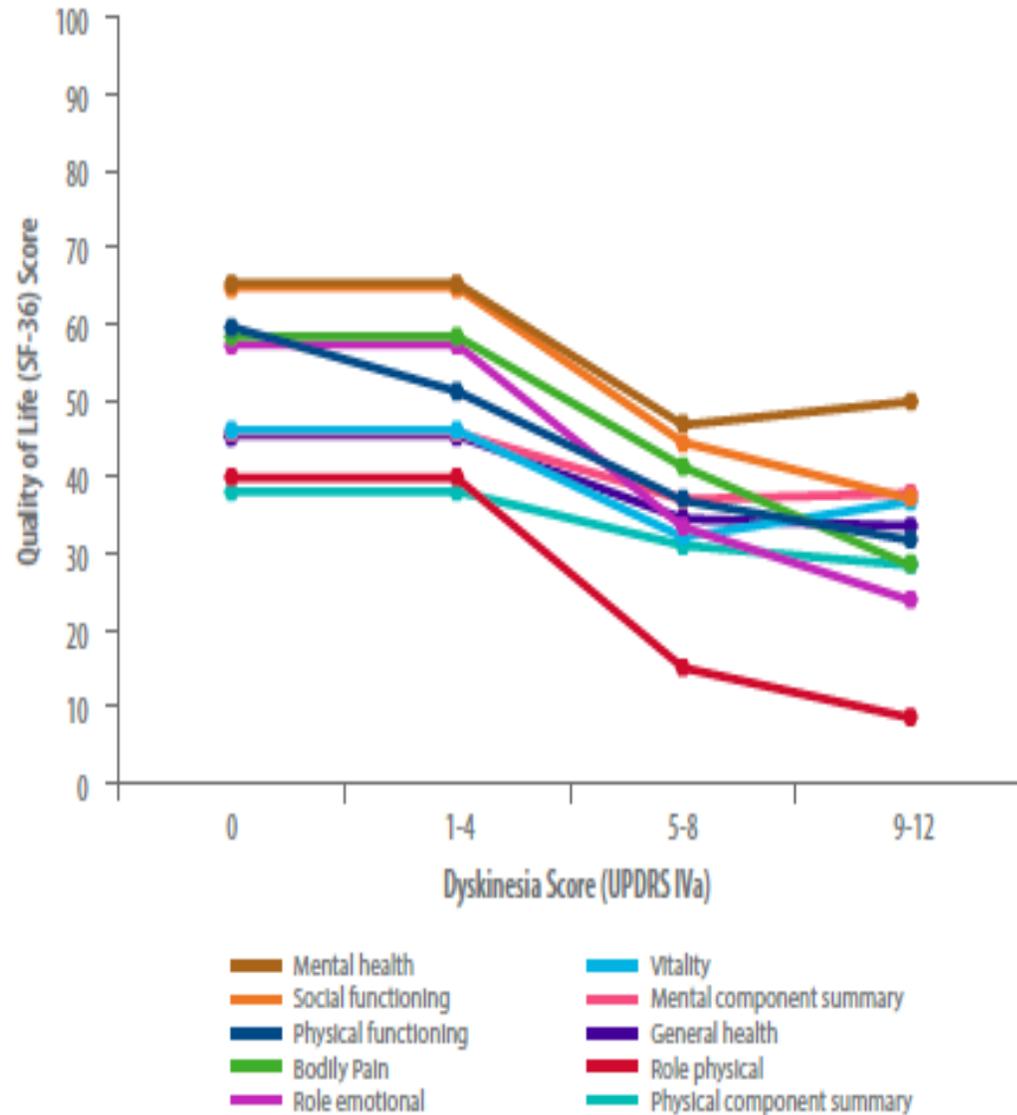
In **Deep Brain Stimulation (DBS)**, a battery-powered device uses electricity to modulate the electrical signaling in the regions of the brain that control movement.



Neurorehabilitation

Rehabilitation therapies such as physiotherapy, occupational therapy, and speech and language therapy are often used in conjunction with the other treatments to assist with motor and non-motor symptoms.

Changes in Quality of Life as Parkinson's Disease Progresses



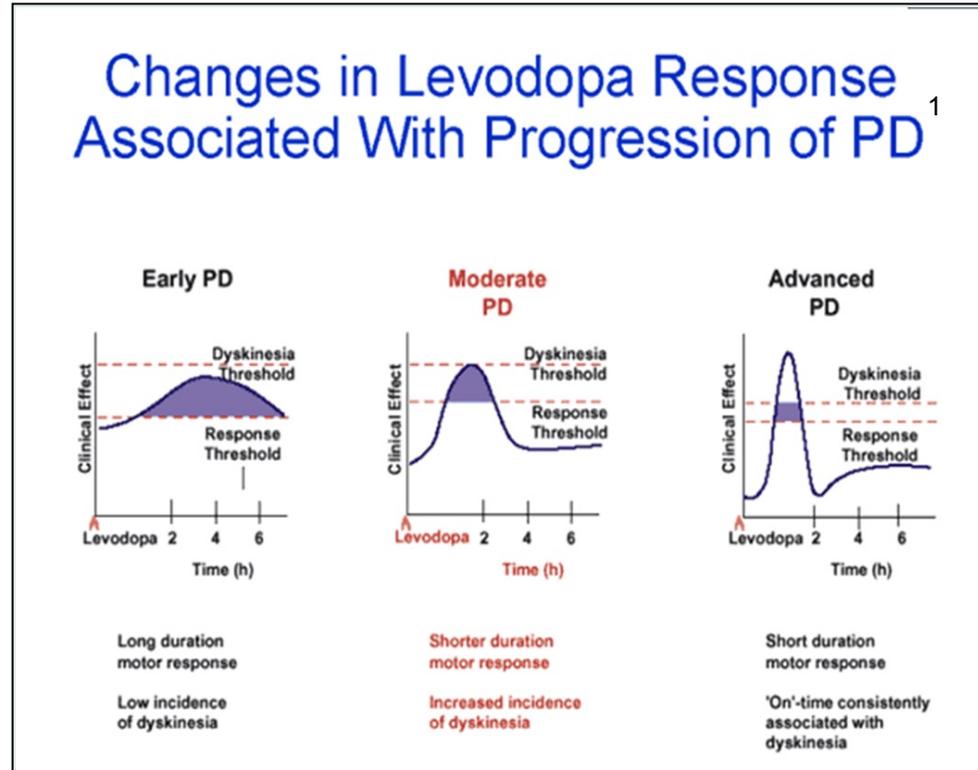
SF-36: 100 = best quality of life, 0 = worst quality of life UPDRS IVa: 0 = no dyskinesia, 12 = worst possible dyskinesia

- PD patients report a significantly worse quality of life compared to the general population.
- Increasing dyskinesia scores on the UPDRS were associated with statistically significant reductions in quality-of-life scores.

*Péchevis M, Clarke CE, Vieregge P, et al.; Trial Study Group; Effects of dyskinesias in Parkinson's disease on quality of life and health-related costs: A prospective European study. *Eur J Neurol.* 2005;12(12):956-963.

Medications initially manage PD well

BUT AS THE DISEASE PROGRESSES.....



- Increasingly troublesome and unpredictable motor fluctuations and dyskinesia begin as early as 2 years following initiation of levodopa therapy.²
- Within 4 to 6 years of initiating levodopa treatment, about 40% of Parkinson's patients experience motor symptoms that impact their quality of life.³

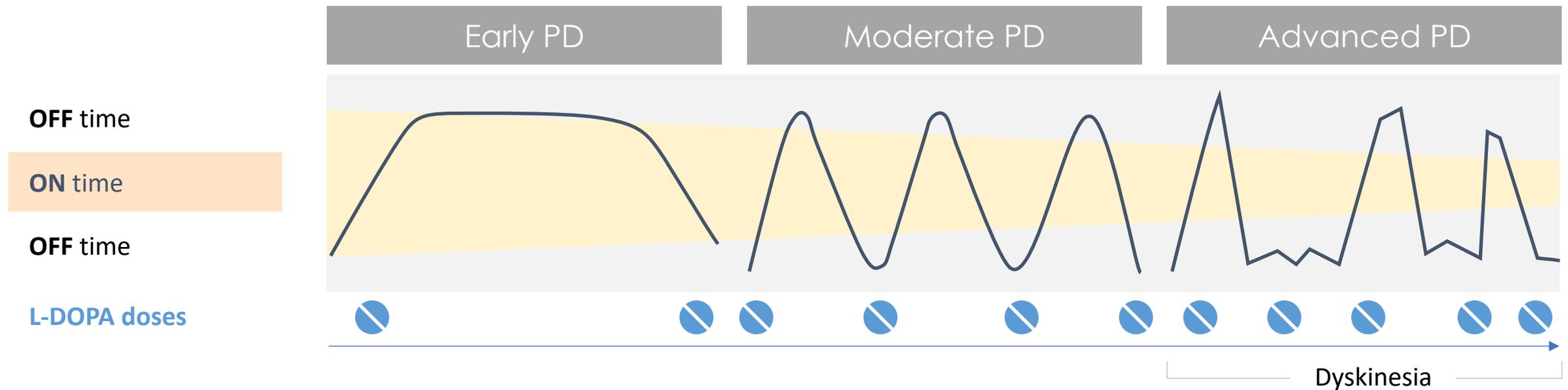
¹http://www.medscape.org/viewarticle/433387_4, New Insights Into the Effective Management of Levodopa-associated Motor Complications, accessed November 29, 2015.

2. Melamed E, Ziv I, Djaldetti R. Management of motor complications in advanced Parkinson's disease. *Mov Disord.* 2007; 22(17):S379-S384.

3. Ahlskog JE, Muenter MD. Frequency of Levodopa-related dyskinesias and motor fluctuations as estimated from the cumulative literature. *Mov Disord.* 2001;16:448-458.

Long-Term Medication Use and Increased Side Effects

ON/OFF fluctuations with levodopa treatment



Long term use of L-DOPA may cause unintended side effects such as **dyskinesia**—rapid, uncontrolled movements

ON/OFF fluctuations are often a catalyst for a switch to another medication

DBS Surgical Techniques and Considerations

THE DBS JOURNEY



**Explore your
options**

01.



**DBS surgery
evaluation**

02.



**Lead implantation
surgery**

03.



**Stimulator
implantation**

04.

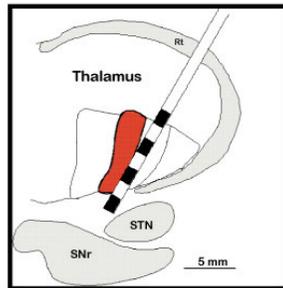


**Programming and
Optimization**

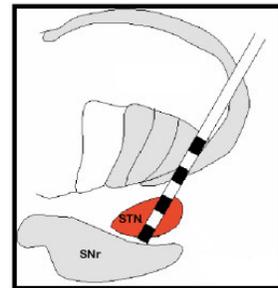
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DBS Therapy

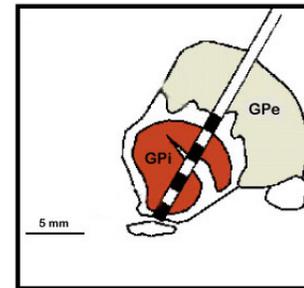
- Also known as deep brain stimulation
- Uses an implanted electrode to deliver high-frequency electrical stimulation to structures involved in the control of movement within either the:



Vim Thalamus:
Essential Tremor*



Subthalamic
Nucleus:
Parkinson's disease



Globus Pallidus
Interna:
Parkinson's disease



- This electrical stimulation overrides abnormal neuronal activity within these brain regions and may bring motor-controlling circuits into a more normal state of function, thereby reducing movement disorder symptoms

Professionals Involved:

- Neurology
- Neuropsychology
- Neurosurgeon
- Rehabilitation
- Psychiatry
- Nursing

Emphasis During Evaluation:

- Confirm diagnosis, optimize medications if needed
- Review potential benefit, risks, safety and alternatives
- Review mood, cognition and social support system
- Establish strengths and weaknesses, treat and optimize physical function
- Long-term care overview

Some Keys to DBS Success for PD Appropriate Patient Selection*

Some Predictors of Potential Benefit:

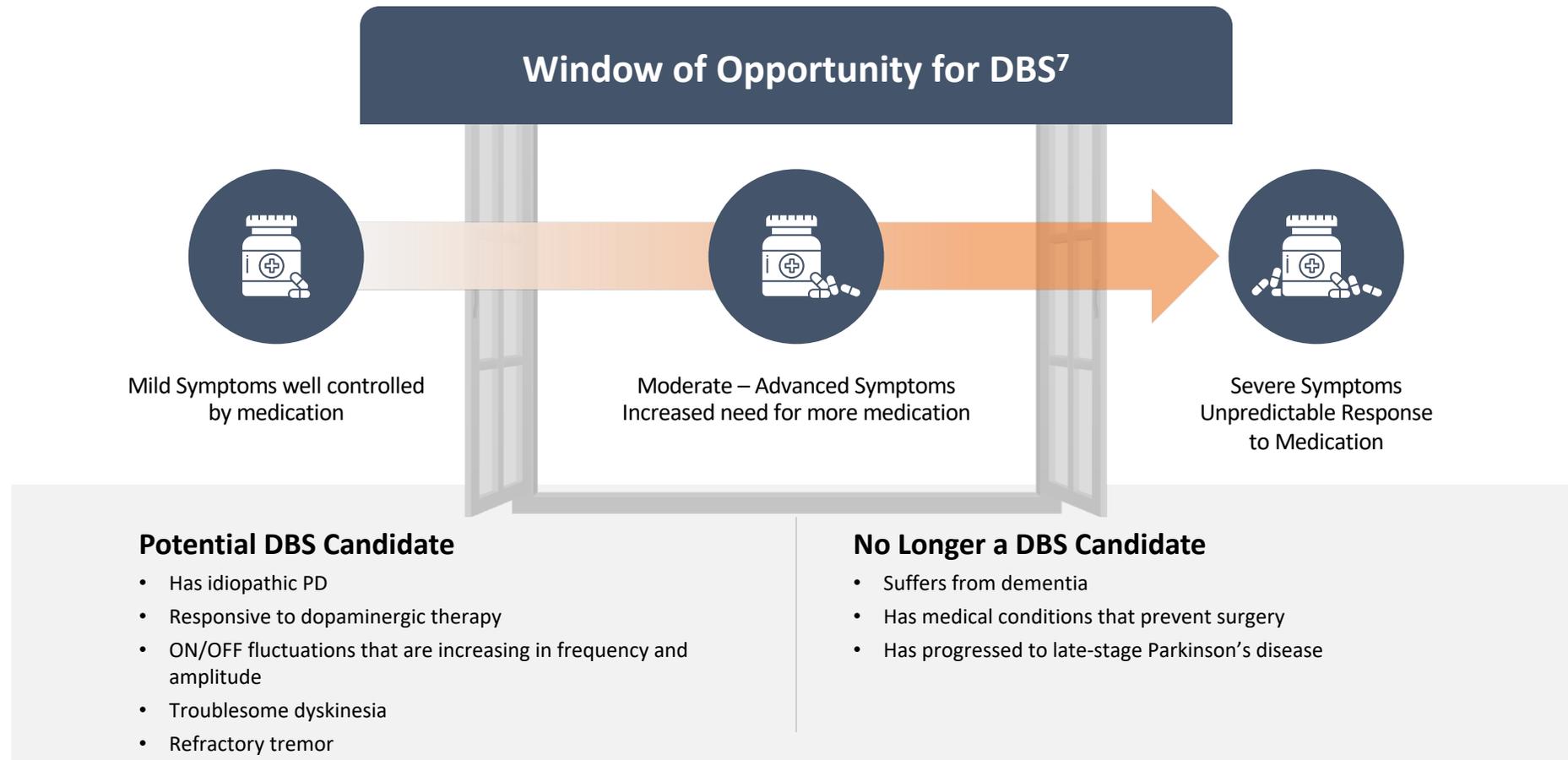
- Response to Dopaminergic Therapy predicts response to DBS
- Pre-operative ON/OFF evaluation: improvement in motor UPDRS¹

Good Outcomes Follow:

- Appropriate patient selection
- Optimal placement of DBS leads
- Optimal post-operative patient management

¹ Charles, P. D., N. Van Blercom, et al. (2002). "Predictors of effective bilateral subthalamic nucleus stimulation for PD." *Neurology* 59(6): 932-4.

When Can a Patient Benefit From DBS?



DBS Patients May Experience a Number of Benefits



Tremor reduction

Depending on its type and location, patients with tremor will typically experience a **70% reduction in tremor events**



Increased mobility

DBS may give you **increased hours of ON time a day**



Medication reduction

You may be able to **reduce the amount of medications you take**



Quality of life

Improvements in quality-of-life metrics frequently reported in DBS patients

Risks and Adverse Events

DBS is generally recognized as a safe and effective therapy, but carries risks such as:

- Infection
- Hemorrhage
- Changes in speech, mood or vision
- Seizures
- Stroke

Goal Oriented Consent

Be sure to discuss:

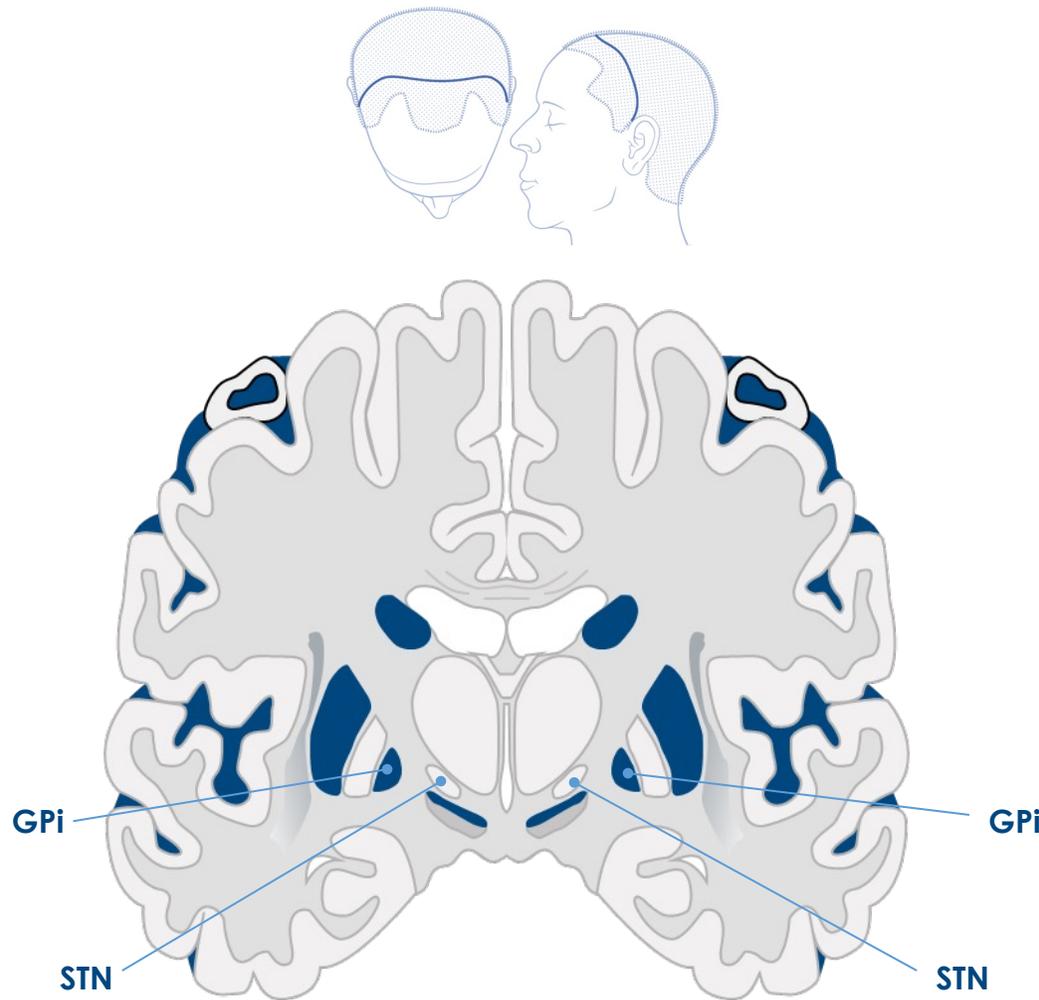
- Goals
- Expectations
- Family and social considerations
- DBS should only be done on the right patient and for the right reasons!!!

What Area of the Brain is Stimulated?

The two most common DBS targets in the brain are the Subthalamic Nucleus (STN) or the Globus Pallidus Interna (GPi).

Your doctor will determine which target is best for you.

Stimulation of these regions in the brain can restore your body's ability to control its movements.

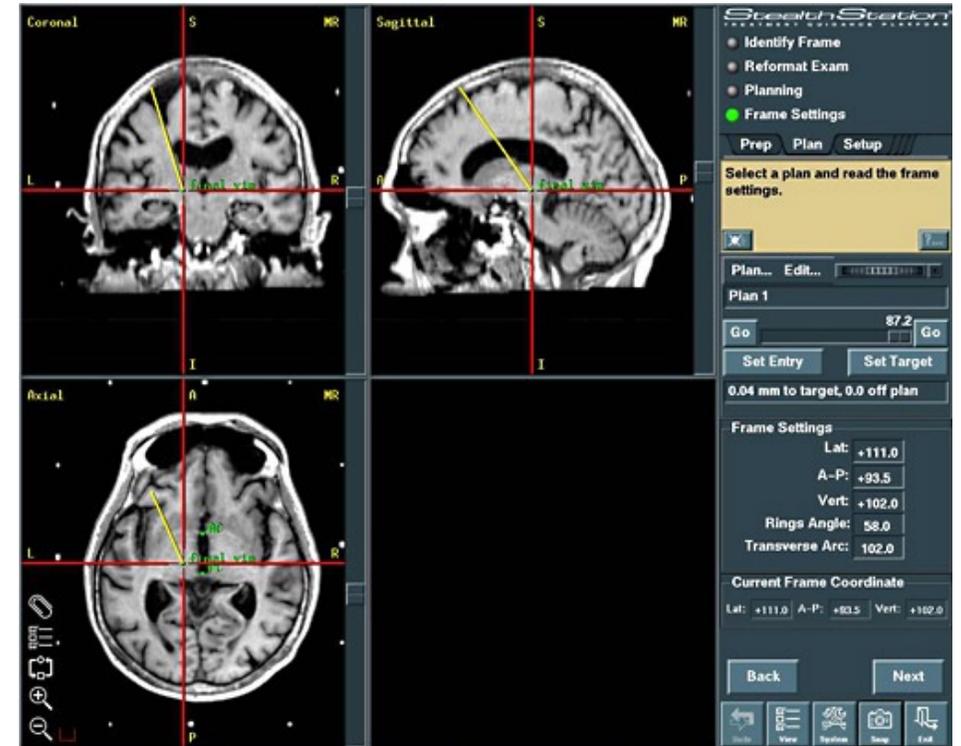


Important Notes:

- These targets are **small**. The STN is roughly the size of an almond.
- You only want to stimulate **a portion** of these structures.
- Making the ability to **precisely control** the stimulation extremely important in this therapy.

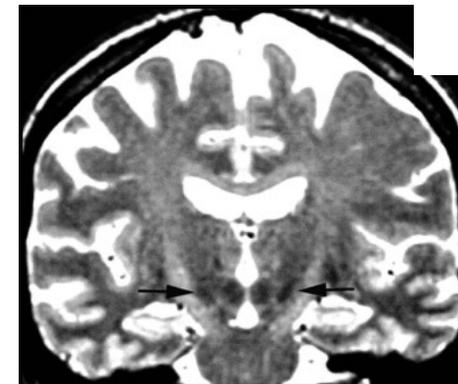
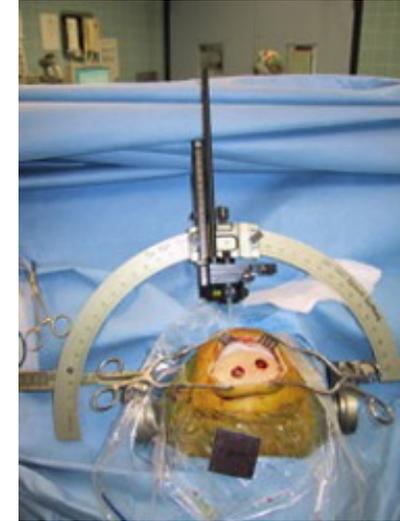
Surgical Technique: Targeting

- Sophisticated imaging and software enables precise targeting for optimal outcomes and minimal risk.
- Microelectrode recording (MER) offers additional levels of verification of lead location.



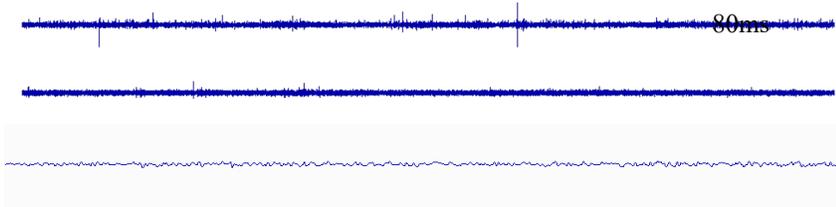
Surgical Technique

- Stereotactic frame placement or frameless stereotaxy
- Targeting
 - Imaging
 - Stereotactic targeting
 - Physiologic targeting (microelectrode recording and stimulation)
- Electrode placement
- Pulse generator implantation

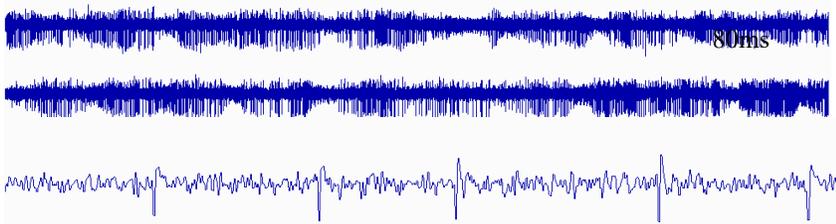


Surgical Technique: Microelectrode Recording

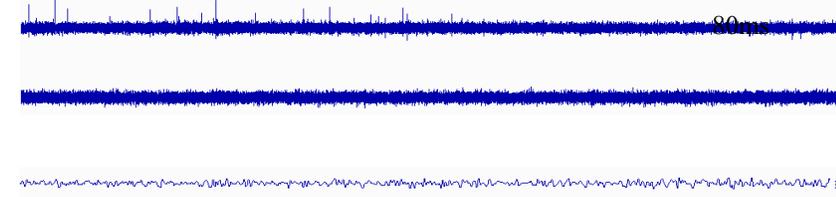
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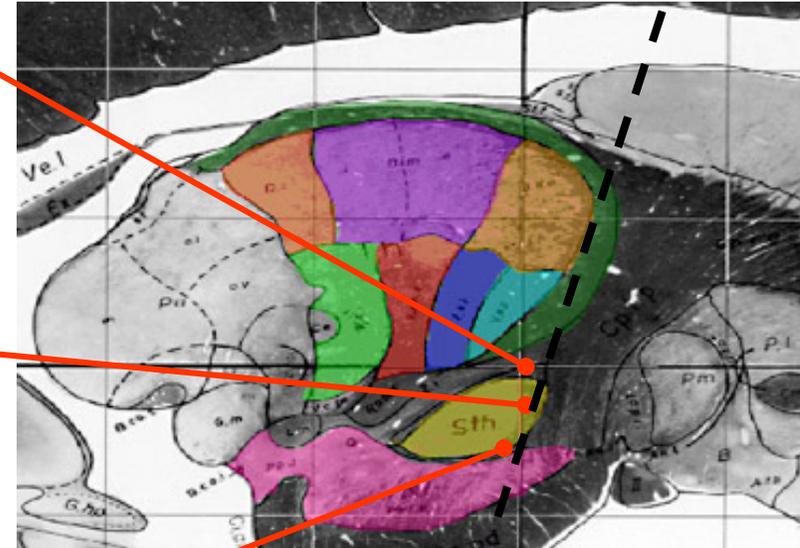
STN



Border/SN



Sagittal Section Through the Thalamus



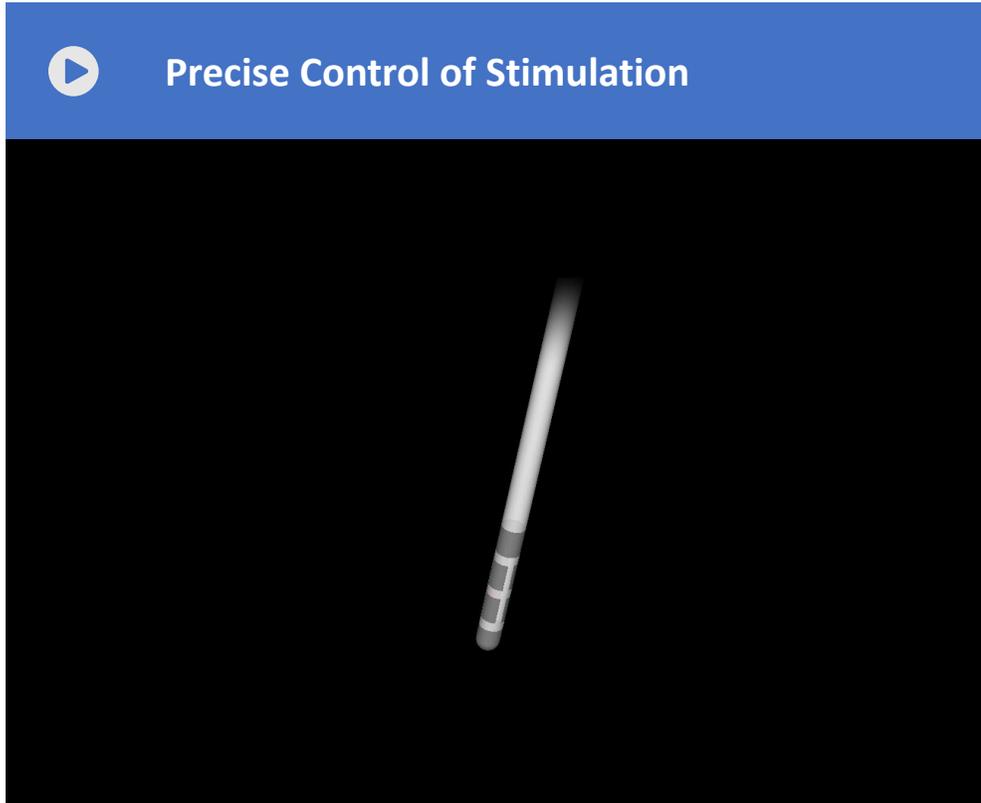
- Programming of neurostimulator and monitoring of side effects
- Initiate post operative therapy
 - Physical therapy
 - Occupational therapy
 - Speech therapy
- Monitoring hardware integrity and battery status

Rehab Goals

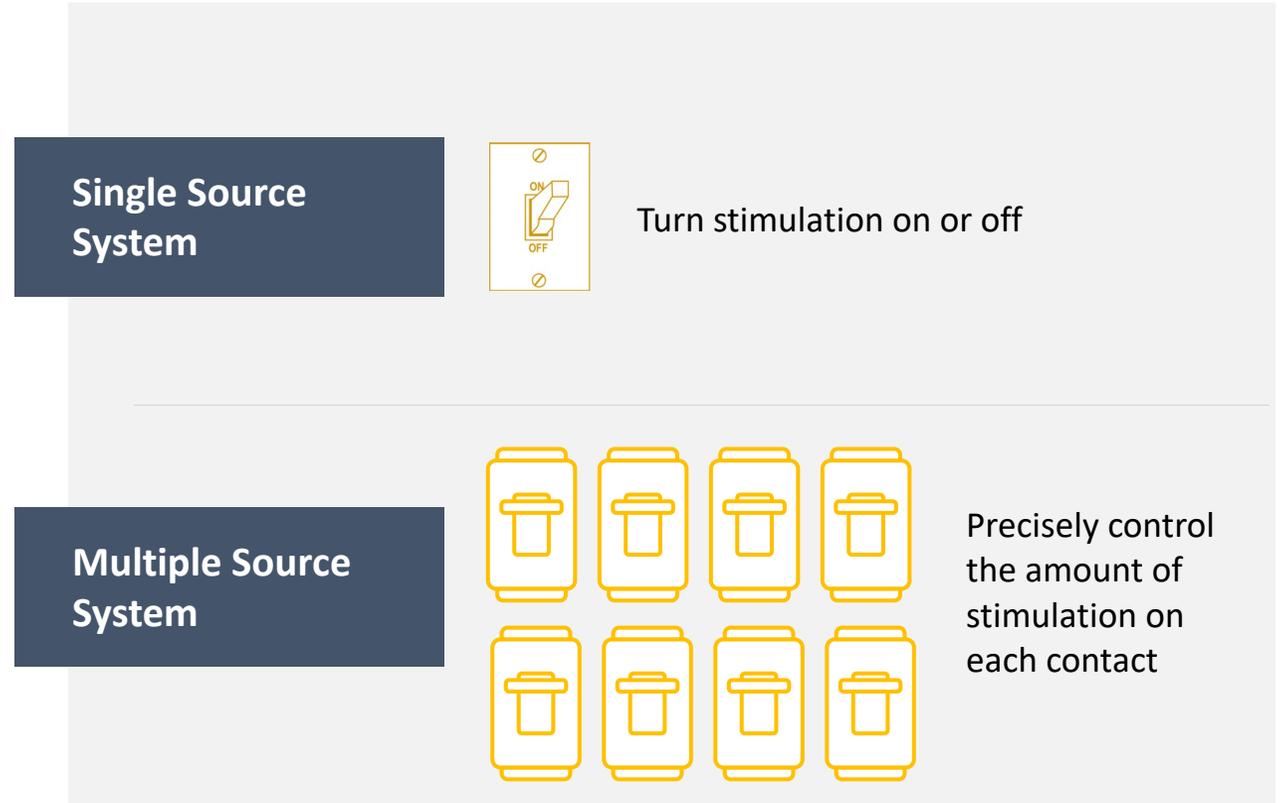
- Functional mobility (gait, transfers)
- Functional ADLs
- Improve posture and balance
- Improve speech/vocalization
- Improve strength and joint mobility
- Prevent aspiration
- Bowel and bladder continence/function
- Safe Environment
- Patient and family education
- Establish home or community exercise program

Programming: Where the rubber hits the road

MICC With Segmented Leads

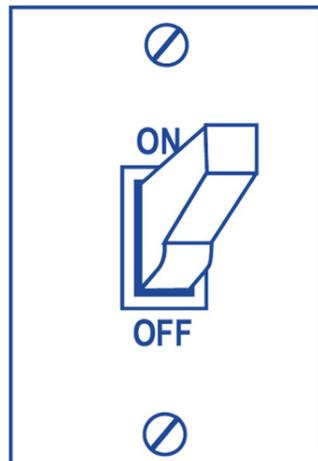


Multiple power sources (MICC) is a unique technology that allows your doctor to precisely control your therapy



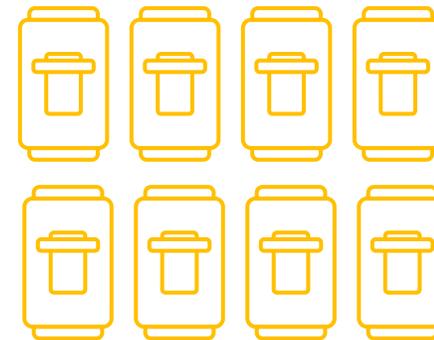
Single Source

Consider a room with multiple lights but just a single light switch. The whole room can either be on or off. This would be an example of a DBS system that uses a single source.



Multiple Power Sources

Now consider a room with multiple lights and each light has its own light switch. In addition to the on/off capability, each light is on a dimmer, giving you the ability to control the exact amount of light you prefer out of each light bulb. In this scenario, this would be a DBS system with multiple sources or MICC.



How Does my Doctor Know Where to Stimulate in my Brain?

THE DBS JOURNEY



Explore your options



DBS surgery
evaluation



Lead implantation
surgery



Stimulator
implantation



**Programming
and Optimization**



Every brain is different, making the programming of your device a very important step in your DBS journey. Traditional programming & optimization of your system can take time and requires patience.

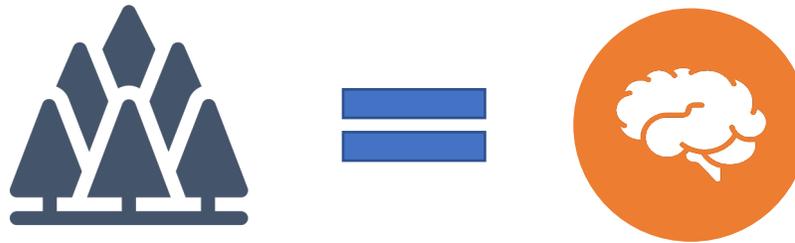
Image Guided Programming was designed to improve the programming process of your system.

How Does my Doctor Know Where to Stimulate in my Brain?

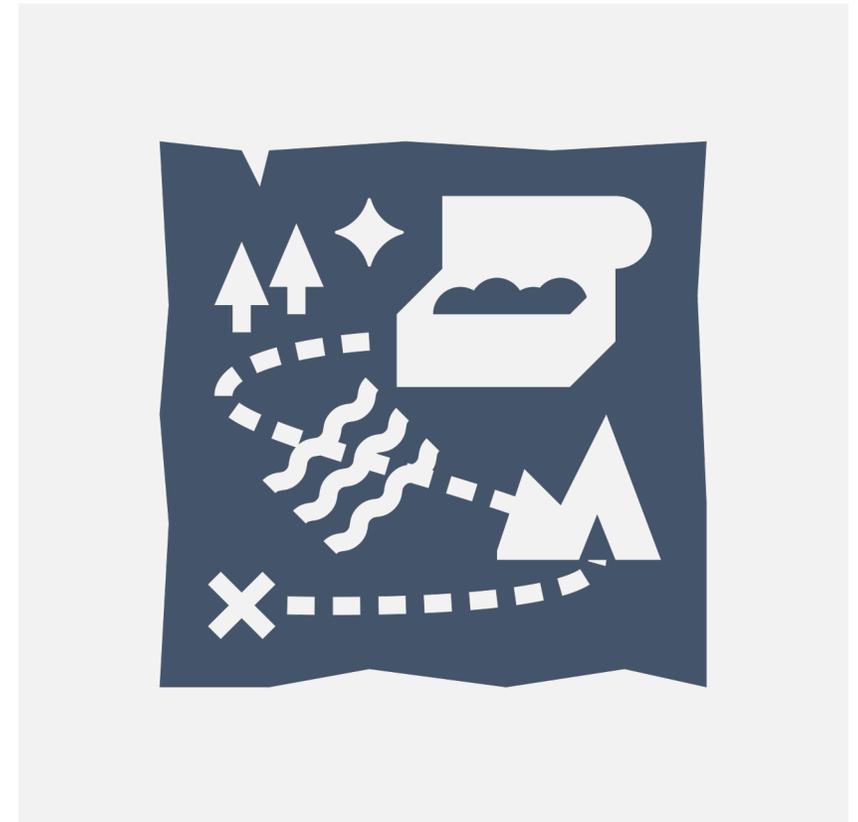
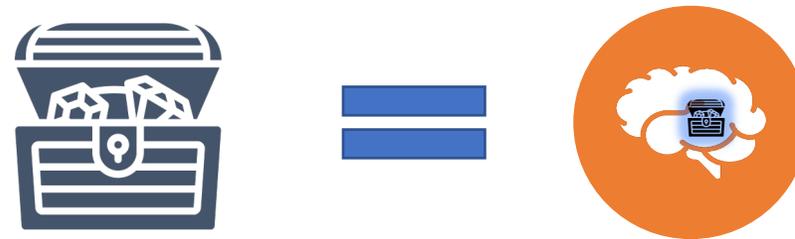
Let's compare DBS programming to a treasure hunt through a forest:



The forest represents your brain.

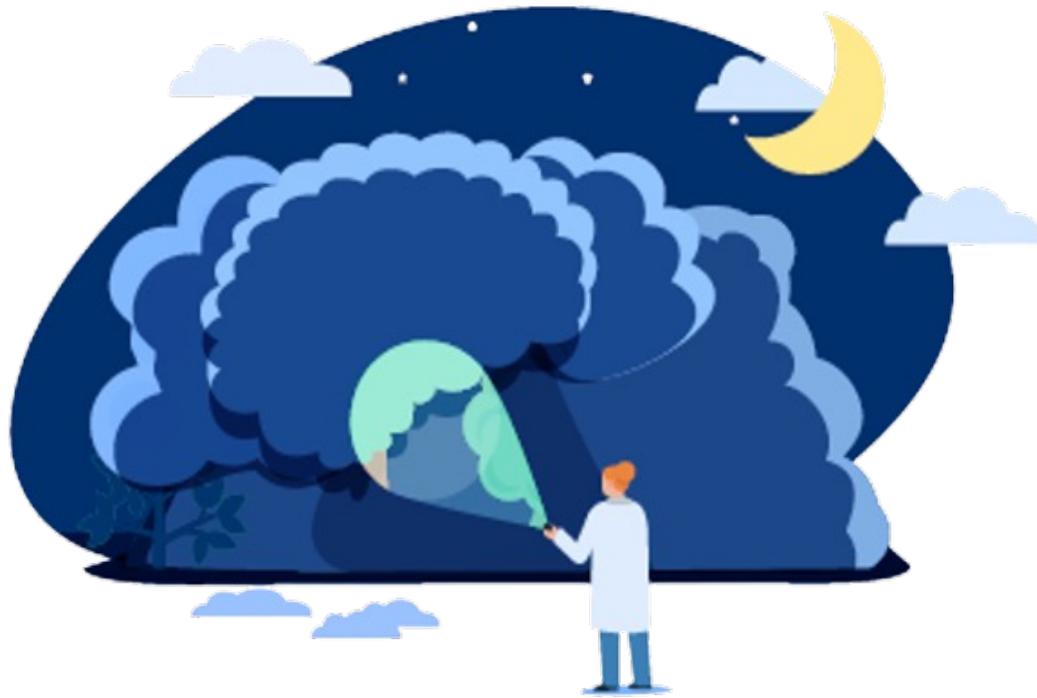


The treasure is the sweet spot within your brain.



Traditional DBS Programming

With traditional DBS programming your physician is hunting for treasure in the dark with no map.



Dark



NO Map



Challenging



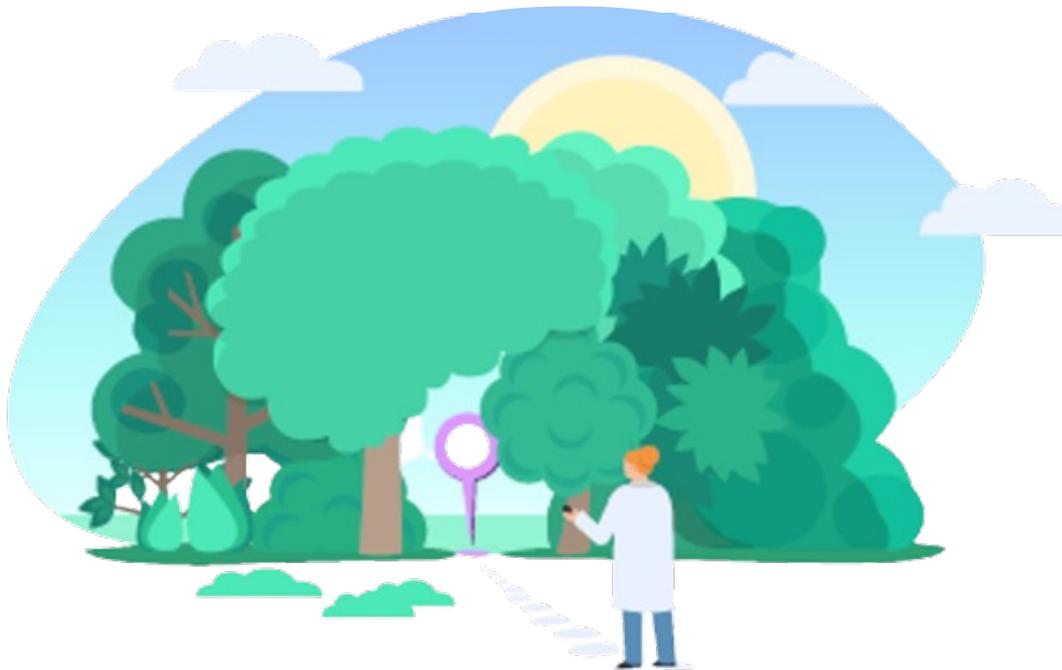
Time Consuming



Because every brain is different, this can be very challenging and time consuming.

Imagine Guided Programming

Image guided programming is a personalized map of your brain that allows your physician to search for the treasure (the DBS sweet spot) in daylight.



Daylight



Map



Designed for
Efficiency



Image Guided Programming (IGP) has shown to reduce initial programming time by 56%*

How Does Imagine Guided Programming Work?

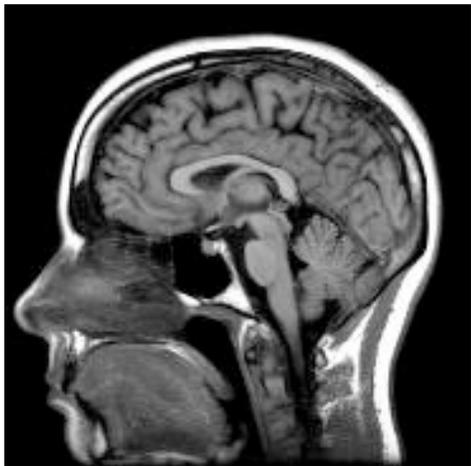
Using your brain images collected during your DBS procedure, Image Guided Programming provides your physician with the ability to see the location of **your** leads within **your** brain **taking the trial and error out** of your DBS programming.



The Map



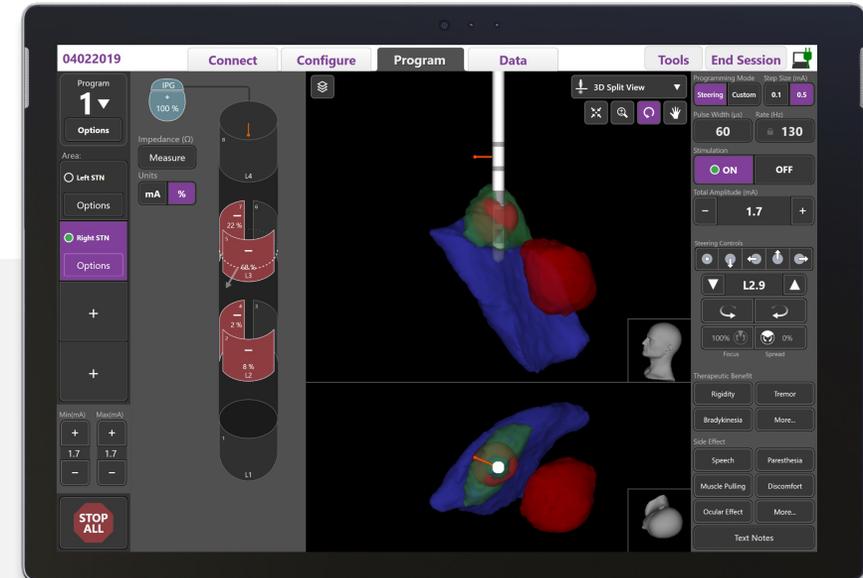
The Treasure



Your Magnetic Resonance Imaging (MRI)



Your Computerized Tomography (CT) scan



Why Do I Want Imagine Guided Programming?

By visualizing the exact location of **your leads** in **your brain**, your physician can take full advantage of all the options the system offers in an efficient manner.



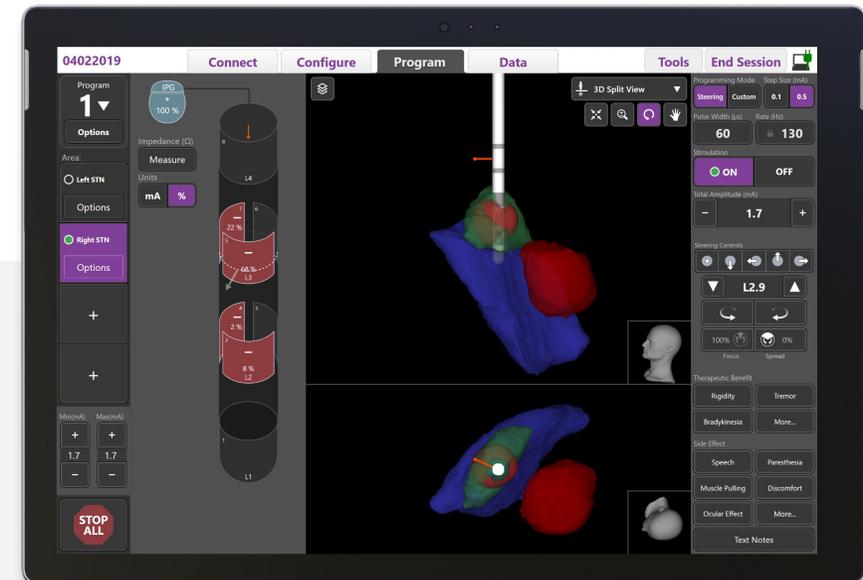
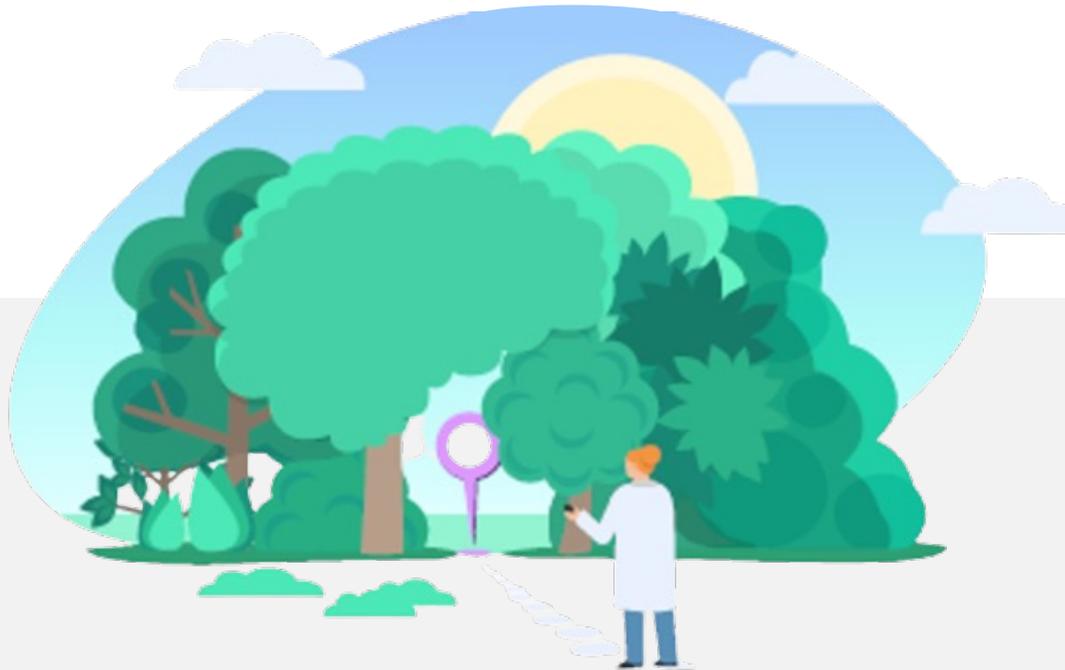
See stimulation



Personalize therapy



In your anatomy



Outcomes Supported With Clinical Data

STUDY DESIGN

FIRST MULTICENTER, PROSPECTIVE, RANDOMISED, SHAM-CONTROLLED, DOUBLE BLIND STUDY

DEVICE



Boston Scientific Vercise™ Deep Brain Stimulation System

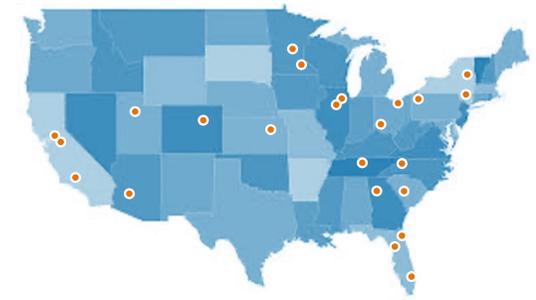
OUTCOMES

Improvement in ON Time

6.0 hours

At 1 year, a 6 ± 3.8 hour increase in ON time without troublesome dyskinesias

SITES & SUBJECTS



23
Sites

160
Randomised Subjects

General DBS Outcomes Data

Level I Clinical Evidence

Primary Clinical Evidence Recent motor complications 4 months to 3 years



The NEW ENGLAND JOURNAL of MEDICINE

Schuepbach WMM, Rau J, Knudsen K, et al.
Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med*. February 14, 2013;368:610-22 7.

Primary Clinical Evidence Longer-standing motor complications

JAMA The Journal of the
American Medical Association



The NEW ENGLAND JOURNAL of MEDICINE

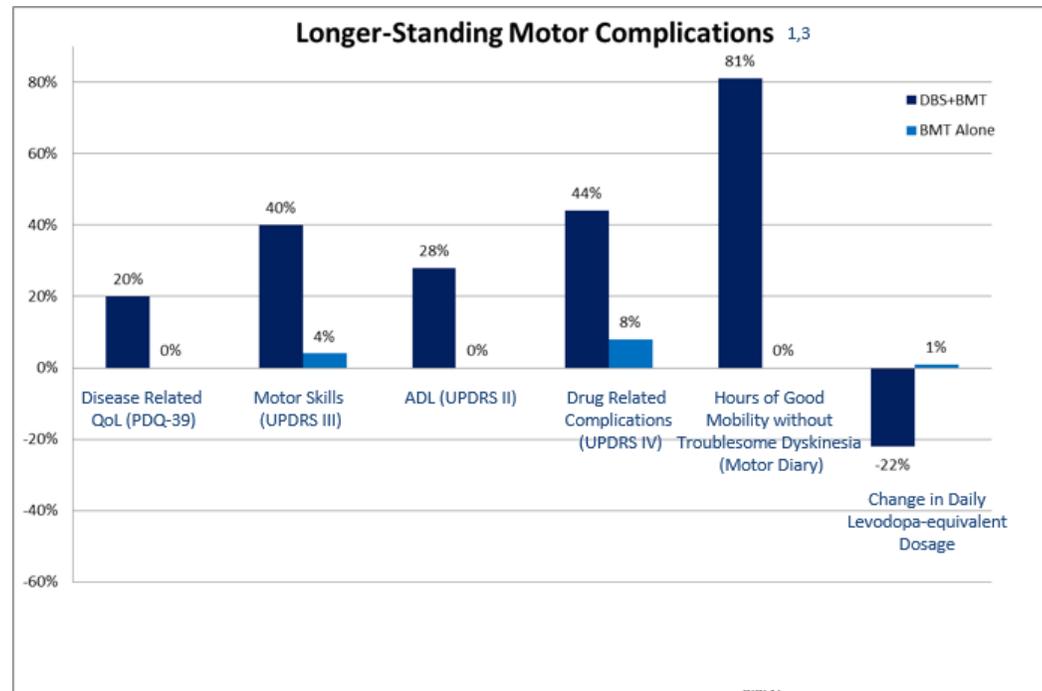
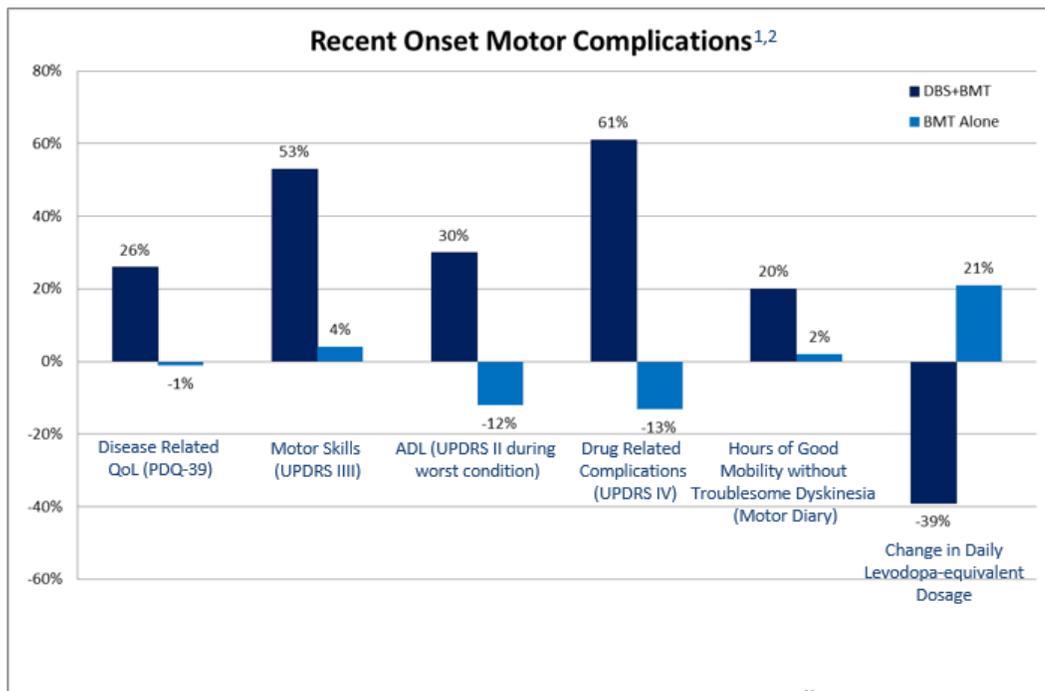
Weaver F, Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. *JAMA*. 2009; 301(1): 63-73.

Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med*. 2010;362(22):2077-2091.

PRIMARY CLINICAL EVIDENCE

RECENT MOTOR COMPLICATIONS 4 MTHS TO 3 YRS

RESULTS: Primary, secondary and medication outcomes¹



Within group change from baseline to 24 months

Within group change from baseline to 6 months

DBS (STN) n=124
BMT alone n=127

DBS (STN and GPi) n=121
BMT alone n=134

¹.Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

².Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. February 14, 2013;368:610-22 7.

³.Weaver F, Follett, K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. JAMA. 2009; 301(1): 63-73.

Article: Schuepbach WMM, et al. Neurostimulation for Parkinson's disease with early motor complications

Study Overview

Inclusion Criteria

- Idiopathic Parkinson's disease (L-DOPA-sensitivity of at least 50%) or classical Parkinsonian tremor
- Age >18 years and \leq 60 years
- Hoehn & Yahr stage \leq 2.5 in the best ON
- Disease duration > 4 years
- Presence of fluctuations and/or dyskinesias for no more than 3 years
- One of the following:
 - **Social and occupational functioning** (measured with a modified SOFAS) due to PD-symptoms despite medical treatment (51-80%), mild-moderate impairment or
 - **Activities of daily living** (UPDRS II > 6) due to PD-symptoms despite medical treatment in the worst condition, mild impairment

Patients were randomized to receive Medtronic neurostimulation (i.e., STN DBS) therapy (n=127) or Best Medical Therapy (BMT) (n=124).

Primary Objective:

The primary outcome was the difference in the mean change in quality of life (QOL), measured by the PDQ-39 summary index at 24 months.

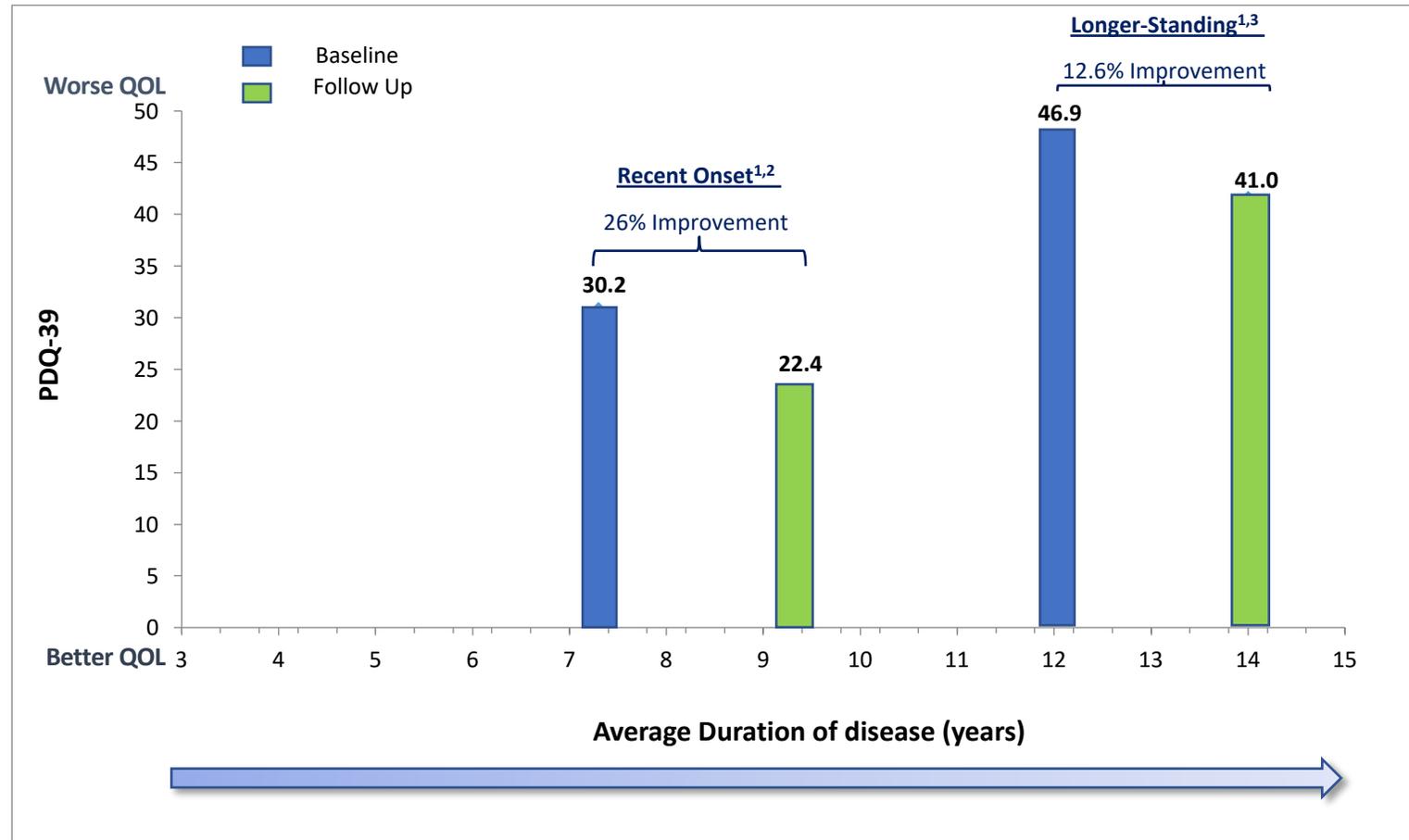
Secondary Objective Endpoints:

- Motor scores (UPDRS III)
- Activities of daily living (UPDRS II)
- Levodopa-induced complications (UPDRS IV)
- Hours of good mobility (motor diary)

Safety endpoints:

- Levodopa equivalent daily dosage
- Cognitive and emotional outcomes

At 24 months post implant, DBS therapy along with PD medication improves quality of life¹. Based on PDQ-39.



Recent Onset of Motor Complications

DBS STN patients showed a statistically significant improvement in QoL of 26%.

Longer-Standing Motor Complications

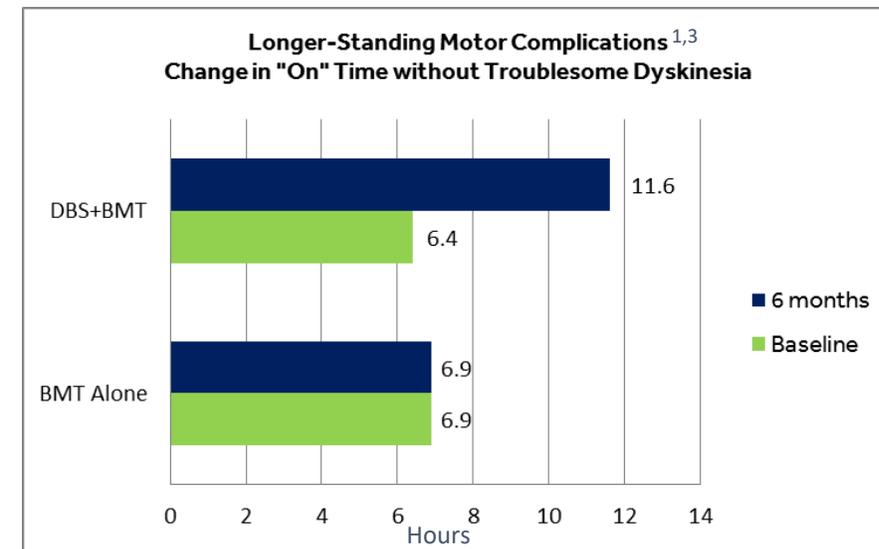
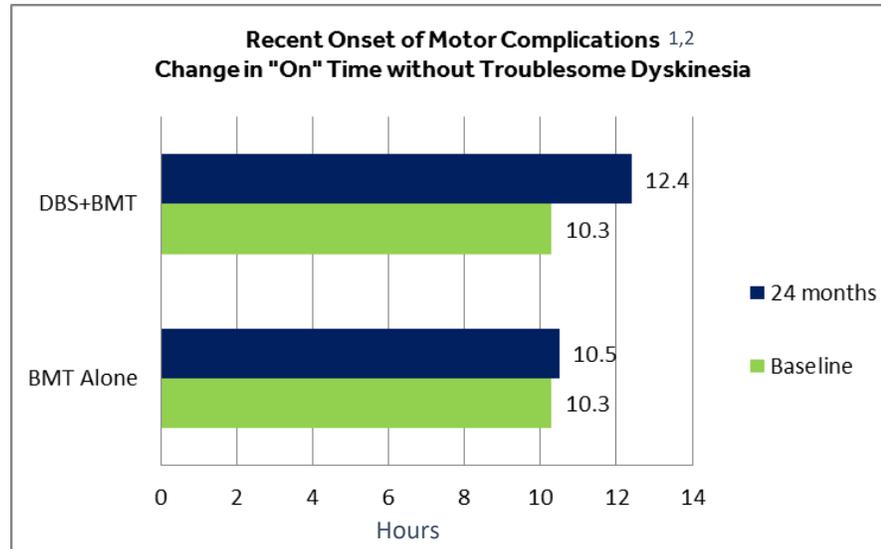
DBS STN patients improved by 12.6% and GPi patients improved by 12.5% vs baseline.

¹.Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

².Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med.* February 14, 2013;368:610-22 7.

³.Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med.* 2010;362(22):2077-2091.

DBS Therapy provided additional hours of “on” time without troublesome dyskinesia each day¹. Motor diary.



- “On” time without troublesome dyskinesias at baseline was 10.3 hours.^{1,2}
- DBS (STN) patients achieved a 20% significant improvement (2.1 hours from baseline) compared to 2% (0.2 hours) with BMT alone at 24 months follow up.^{1,2}

- “On” time without troublesome dyskinesias at baseline was only 6.4 hours.^{1,3}
- DBS patients (STN and GPi) gained up to 5.2 hours each day compared to 0 hours with BMT at 6 months follow-up.^{1,3}
- DBS Therapy had a sustained improvement to 24 months with a 5-hour gain for STN and a 5.2-hour gain for GPi.^{1,4}

73% of patients in a study identified troublesome dyskinesia as a reason for receiving DBS Therapy.⁵

¹Medtronic DBS Therapy for Parkinson’s Disease and Essential Tremor Clinical Summary, November 1, 2015

²Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson’s disease with early motor complications. *N Engl J Med.* February 14, 2013;368:610-22 7.

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⁴Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson’s disease. *N Engl J Med.* 2010;362(22):2077-2091.

⁵Williams A, Gill S, Varma T et al. Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson’s disease (PD SURG trial): a randomized, open-label trial. *Lancet Neurol.* 2010;9:581-591.

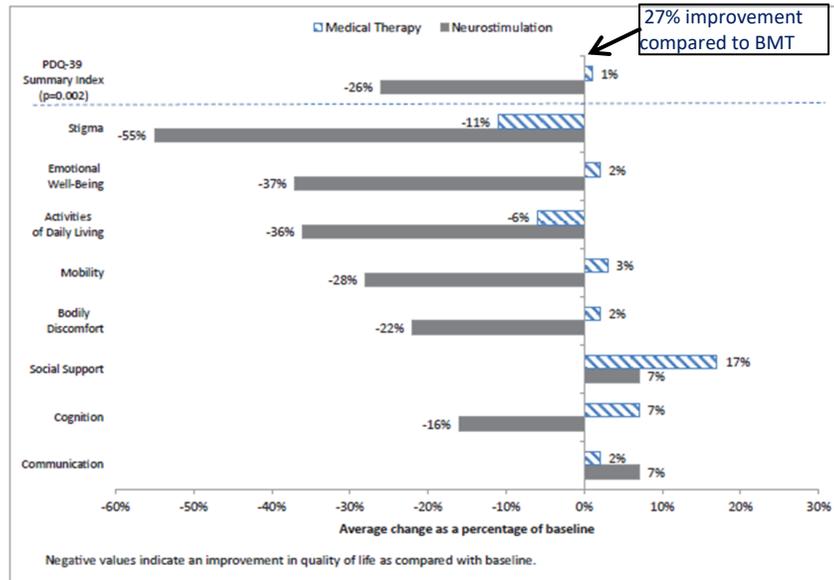
DBS Therapy reduces time spent in the “off” state. Motor diary.

- DBS Therapy (STN) provided a 39% significant reduction in “off” time (-1.9 hours from baseline) compared to 2% (-0.1 hours) with BMT alone at 24 months, in the study of those with recent-onset of motor complications.
- DBS Therapy (STN and GPi) reduced “off” time by 2.9 hours/day (-49.9%) compared to 0.1 hour/day (-1.3%) reduction with BMT alone ($p < 0.001$) at 6 months, in the study of those with longer-standing motor complications.

DBS Therapy improves quality of life

Recent Onset Motor Complications

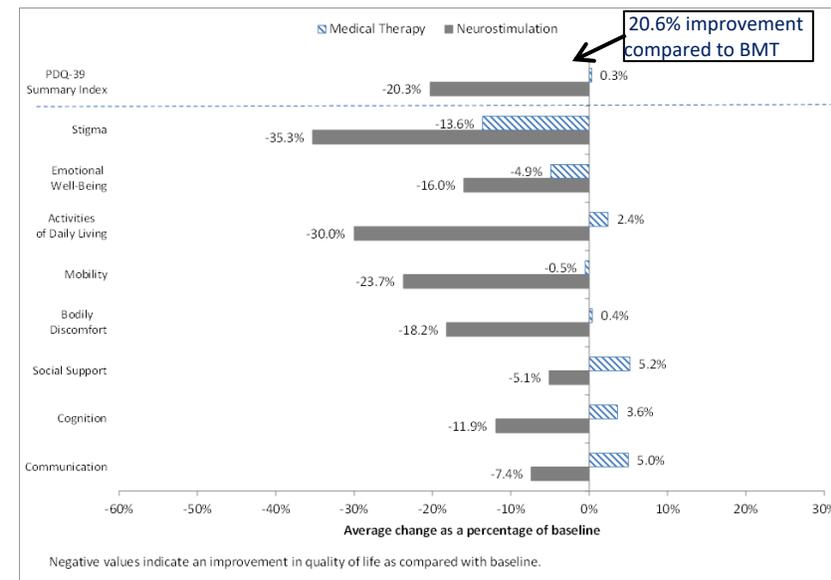
Quality of Life – PDQ-39
24 month, DBS+BMT vs BMT alone



- DBS improved PD-related QoL factors by 27% over BMT alone at 24 months follow up.

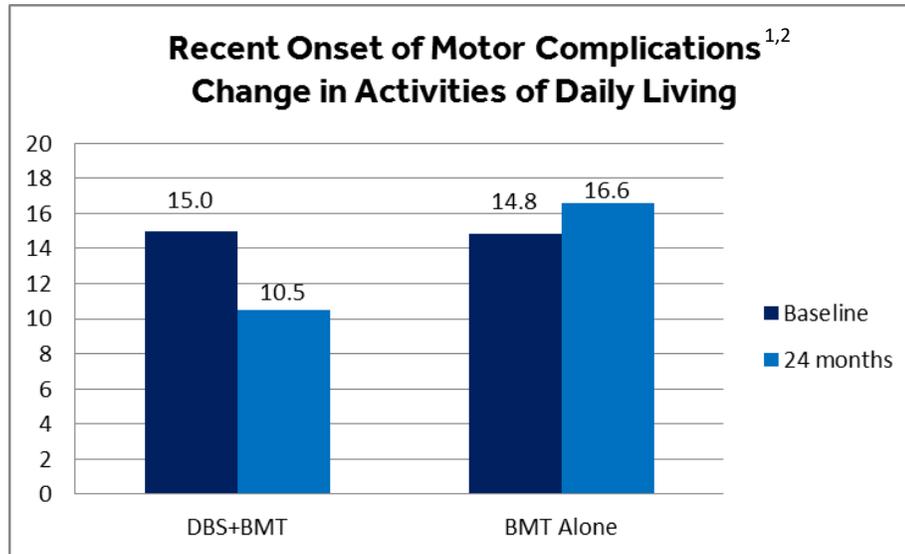
Longer-Standing Motor Complications

Quality of Life- PDQ-39
6 month, DBS+BMT vs BMT alone

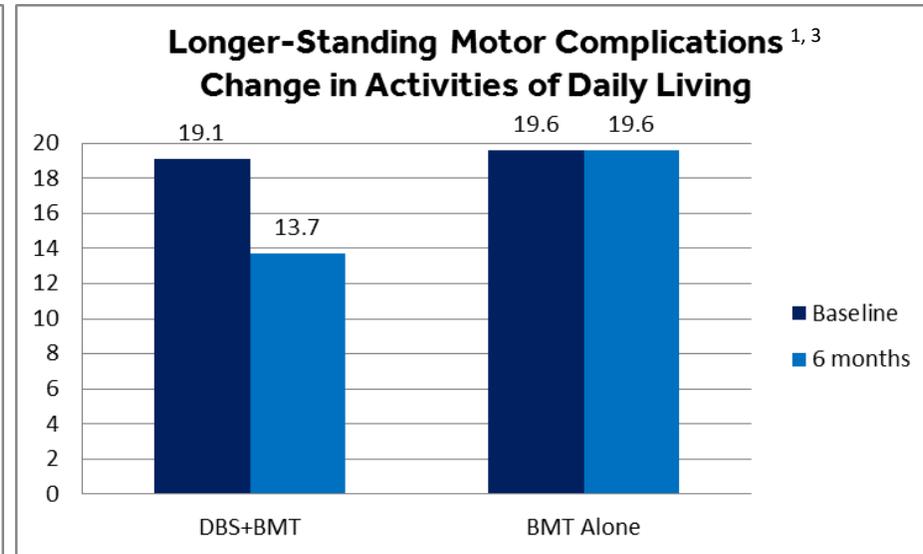


- DBS improved PD-related QoL factors by 20.6% over BMT alone at 6 months follow up.

DBS THERAPY IMPROVES ACTIVITIES OF DAILY LIVING.¹ UPDRS II



DBS Therapy (STN) improved ADLs by 30% compared to a 12% decline in those receiving BMT alone at 24 months.



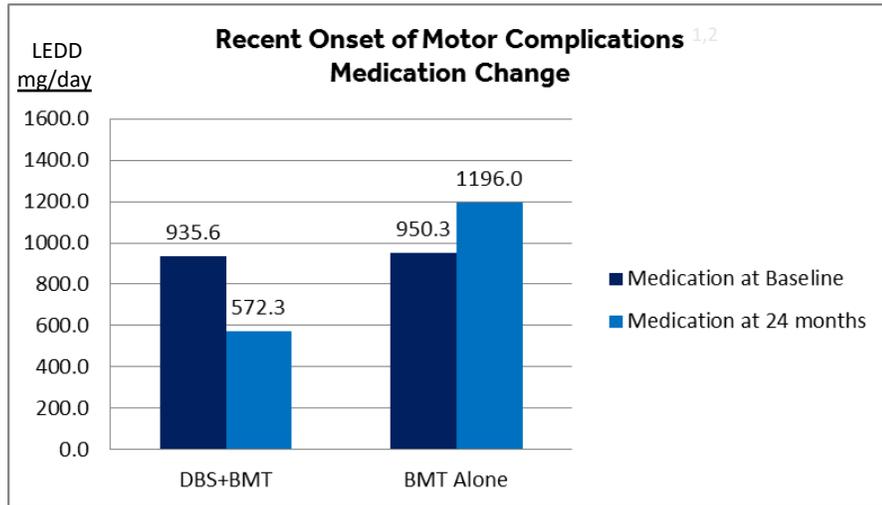
DBS Therapy (STN and GPi) improved ADL's by 28.2% compared to no improvement with BMT alone at 6 months.

¹.Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

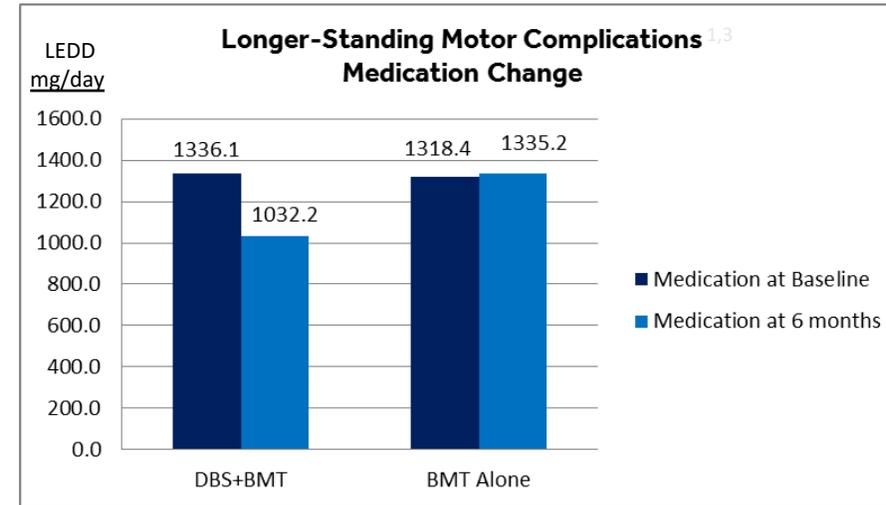
².Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. February 14, 2013;368:610-22 7.

³.Weaver F, Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. JAMA. 2009; 301(1): 63-73.

DBS Therapy significantly reduces dopaminergic medication used for treatment of PD.¹



DBS showed a 39% statistically significant reduction (STN) in medication versus a 21% statistically significant increase in dosage in the BMT alone* group at 24 months.



DBS showed a 22% significant reduction (STN and Gpi) in medication versus a 1.3% increase in dosage in the BMT alone* at 6 months.

- Medication was reduced by 33.6% with STN and by 16.7% with Gpi at 24 months

*A reduction in medication would not be expected in the group taking medication alone.

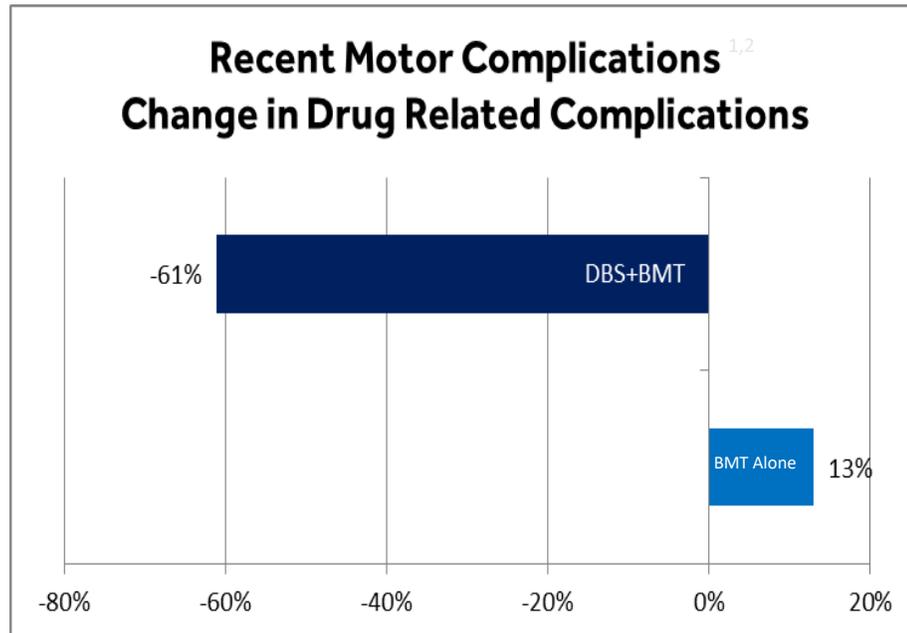
¹ Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

² Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med.* February 14, 2013;368:610-22 7.

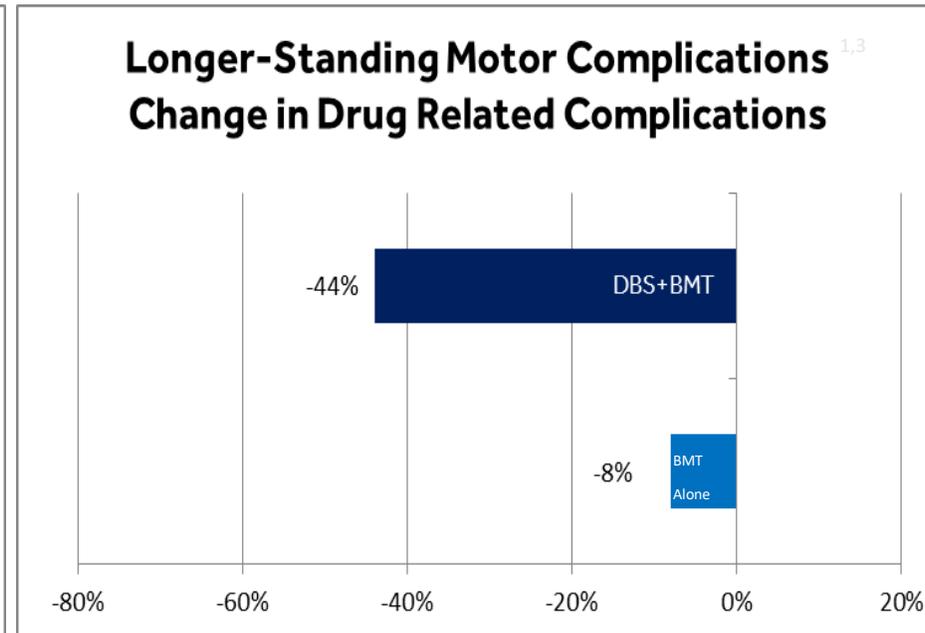
³ Weaver F, Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. *JAMA.* 2009; 301(1): 63-73.

⁴ Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med.* 2010;362(22):2077-2091.

DBS Therapy reduced drug-related complications¹. UPDRS IV



DBS showed a 61% statistically significant reduction (STN) compared to a 13% significant worsening in BMT alone in drug-related complications at 24 months.



DBS had a 44% reduction (STN and GPi) and BMT had an 8% reduction in drug-related complications at 6 months.

- These reductions were sustained in the DBS groups to 24 months: GPi and STN patients had a 46% and 51% improvement, respectively.⁴

¹.Medtronic DBS Therapy for Parkinson's Disease and Essential Tremor Clinical Summary, November 1, 2015

².Schuepbach WMM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med.* February 14, 2013;368:610-22 7.

³.Weaver F, Follett K, Stern M, et al. Bilateral deep brain stimulation vs. best medical therapy for patients with advanced Parkinson's disease: a randomized controlled trial. *JAMA.* 2009; 301(1): 63-73.

⁴.Follett KA, Weaver FM, Stern M, et al. Pallidal versus subthalamic deep-brain stimulation for Parkinson's disease. *N Engl J Med.* 2010;362(22):2077-2091.

In Summary, When to Consider DBS Therapy

- ✓ Diagnosis of PD for 4 years
- ✓ Levodopa responsive or tremor refractory
- ✓ Not adequately controlled with medication
- ✓ And motor complications (dyskinesias and/or motor fluctuations) for a minimum of 4 months (recent onset) or longer standing

REFERENCES

Jerrold L Vitek, et. al., Subthalamic nucleus deep brain stimulation with a multiple independent constant current-controlled device in Parkinson's disease (INTREPID): a multicenter, double-blind, randomized, sham-controlled study, *The Lancet Neurology*, Volume 19, Issue 6, 2020, Pages 491-501

Cusso *et al.* (2016). "The impact of physical activity on non-motor symptoms in Parkinson's disease: A systematic review." *Frontiers in Medicine*. 3: 1-9.

Timmerman *et al.* (2105). Multiple-source current steering in subthalamic nucleus deep brain stimulation for Parkinson's disease (the VANTAGE study): a non-randomized, prospective, multi-centre, open label study. *Lancet Neurology*. 14: 693 – 701.

<https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/diagnosis-treatment/drc-20376062> | Accessed February 2021

<https://www.michaeljfox.org/news/deep-brain-stimulation> | Accessed February 2021

<https://www.apdaparkinson.org/what-is-parkinsons> | Accessed February 2021

http://www.pdf.org/parkinson_statistics | Accessed February 2021

<http://movementdisorders.ufhealth.org/for-patients/deep-brain-stimulation-information/who-is-a-candidate-for-dbs> | Accessed February 2021

Questions



Advanced Treatment for Parkinson's Disease

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