

A Comprehensive Approach to Deep Brain Stimulation for Movement Disorders

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ABSTRACT

Deep brain stimulation (DBS) is a well-established form of neuromodulation, used primarily for movement disorders such as Parkinson's disease (PD) and Essential Tremor (ET). The selection of patients who will benefit most from DBS depends on a team of clinicians from various disciplines, including neurology, neurosurgery, psychiatry, neuropsychology and rehabilitation specialists. The actual surgical procedure can take many forms. We apply a combination of multidisciplinary, team-based evaluations and intra-operative neurophysiology, test stimulation and imaging to optimize DBS therapy for individual patients.

KEYWORDS: movement disorders, Parkinson's disease, Essential Tremor, Deep Brain Stimulation, neurosurgery

INTRODUCTION

Neurosurgery for movement disorders has evolved dramatically over the past century culminating in the widespread acceptance and use of deep brain stimulation (DBS). While DBS has been and is being tested for a wide variety of neurological and psychiatric conditions (Figure 1), DBS is most widely used to treat the motor symptoms of two common

movement disorders, Parkinson's disease (PD) and Essential Tremor (ET). DBS surgery entails the insertion of electrodes ("wires") into the brain through a small burr-hole and connected subcutaneously to a pacemaker-like battery powered device implanted in the chest wall. The implanted pulse generator battery is then programmed to deliver electrical stimulation to the brain to regularize, or at least limit, abnormal brain activity.

PD affects over 1 million people in the United States (US) and the prevalence is expected to double over the next two decades. The cardinal motor symptoms of PD – bradykinesia, tremor and rigidity – are often adequately treated with medications early in the course of the disease. As the disease progresses, patients develop medication-refractory tremor, motor fluctuations (early "wearing-off" of medication benefit) and dyskinesias, in addition to non-motor symptoms such as mood, cognitive, sleep and autonomic symptoms. The efficacy of DBS for these medication-refractory motor symptoms has been well established through several high-quality, randomized controlled trials.¹⁻³ A meta-analysis of 22 studies demonstrated that subthalamic nucleus (STN) DBS improved motor symptoms (Unified PD rating scale, part 3) by 52%, dyskinesias 69%, off-periods 68%, and activities of daily living by 50%.⁴ GPi DBS is also effective and is often favored for more severe dyskinesias or dystonias, and

may have a slightly lower risk of cognitive- and mood-related adverse effects.⁵⁻⁷ Non-motor symptoms of PD do not directly respond to DBS but can improve indirectly. For example, a patient with difficulty sleeping or depressed mood due to excessive slowness and stiffness may feel improvement in these symptoms after DBS because of improved overall mobility and physical comfort.

In contrast to the resting tremor of PD, ET tremor is typically postural and worsens with movement. Early in the disease, patients with ET often manage their symptoms with behavioral modifications, without medications. Over time, increasing tremor amplitude may lead to difficulty with fine motor tasks, such as handwriting, eating, drinking and dressing. Medications can reduce tremor by about 50%, but benefit wanes over time as the tremor worsens. In these patients, DBS of the ventral-intermediate nucleus of the thalamus can reduce tremor by ~80% (range ~50-100%).^{8,9}

Figure 1. Approved and Experimental Applications of DBS.

Approved	Experimental
Parkinson's Disease	Depression
Essential Tremor	Alzheimer's Disease
Dystonia*	Tourette's Syndrome
Obsessive Compulsive Disorder*	Minimally Conscious State
Epilepsy**	Obesity
	Anorexia
	Autonomic instability due to spinal cord injury
	Neuropathic Pain
	Addiction
	Tinnitus
	Schizophrenia
	Traumatic Brain Injury
	Huntington's Disease

* Approved under FDA Humanitarian Device Exemption (HDE)

** Approved in Europe; USA FDA approval anticipated

DBS for movement disorders should be considered when the quality of life becomes impaired by motor symptoms that are refractory to medical therapy. Patients should generally have preservation of mood and cognitive functions, and should be medically able to undergo surgery.

THE COMPREHENSIVE FAST-TRACK PRE-OPERATIVE EVALUATION

Even though quality of life in many domains improves with DBS, some areas may worsen. A 4-year follow up study of STN vs. globus pallidus interna (GPi) DBS showed increased risk of speech, gait, cognitive and mood adverse effects, and up to 30% of patients undergoing DBS may have negative outcomes due to inappropriate screening.¹⁰ However, comprehensive and thorough pre-operative screening can detect problems and stratify the risk of post-operative worsening based on baseline functioning. To achieve this, our institution utilizes a unique, multi-disciplinary, pre-operative DBS clinic in which patients are evaluated by neurology, neurosurgery, psychiatry, neuropsychology and rehabilitation services (physical therapy, speech therapy and swallowing assessment); these are typically conducted at a single, convenient location in a one-day visit.

- Neurology – confirm diagnosis; ensure medical optimization; assess severity of disease and appropriateness for surgical intervention; identify motor symptom(s) to be treated by surgery; discuss unilateral vs. bilateral; discuss target selection; discuss risks/benefits;
- Neurosurgery – discuss surgical options; discuss surgery-related risks; assess overall medical condition to undergo surgery; discuss contraindications for surgery;
- Psychiatry – screen for mood and behavioral problems; ensure chronic, underlying mood issues are adequately treated; discuss risk of mood and behavioral problems with DBS;
- Neuropsychology – conduct a thorough assessment of cognitive functions; compare baseline performance to peers; discuss risk of cognitive decline after DBS;
- Physical therapy – assess baseline gait and balance; make recommendations to optimize gait before DBS; discuss risk of worsening after DBS;
- Speech therapy – assess baseline speech function; make recommendations to optimize speech before DBS; discuss risk of worsening after DBS;
- Swallowing assessment – assess baseline swallowing function; make recommendations to optimize swallowing function before DBS; discuss risk of worsening after DBS.

The multidisciplinary team discusses the candidacy of each patient in a meeting at the conclusion of the clinic. The patient is rated on a scale of low, medium or high risk by each specialist based on their evaluations, and the final recommendation is communicated to the patient.

DBS SURGERY: BENEFITS, RISKS AND OPTIONS

The primary goals of DBS surgery are safety and accuracy. The risk profile of DBS surgery has been extensively studied.¹¹⁻¹³ Some risks, such as hemorrhage, are significant and potentially life threatening, but are fortunately rare. Other risks include seizure, hardware infection, discomfort, hardware failure and suboptimal electrode placement (**Figure 2**). This last risk is minimized by careful design and meticulous execution of the surgical procedure. There are many different ways to “do” DBS surgery. Individual surgeons often develop customized, stereotyped workflow preferences to promote reproducibly good results.

DBS is currently approved by the FDA to be implanted while the patient is awake in order to confirm neurologic benefit without intolerable side effects. Nonetheless, there is a growing utilization of asleep procedures for the implantation of DBS as an off-label approach. But even within these categories of “awake” vs. “asleep” there are many different ways in which surgeons can perform the procedure.

The main technical goal is accurate placement of electrodes within a target, typically with about 1mm precision. Classically, this is achieved with the use of a stereotactic frame affixed to the head while a scan (MRI or CT) is obtained. The target location is then computed with respect to the frame coordinates, and these x, y and z values are manually dialed into an arc attached to the frame. More recently, some centers including ours, have switched to using a different system consisting of a patient-customized 3D-printed stereotactic platform (FHC Inc, Bowdoin, ME). Here, temporary skull screw fiducial markers are implanted a week prior to electrode implantation. These then serve as the reference coordinate system for selecting targets and trajectories by co-registering a CT scan showing these fiducials with a “clean” pre-operative MRI. Computer assisted design (CAD) software then designs a frame specifically for that patient and the planned trajectories. While adding an extra step, this approach reduces the potential for human or mechanical error (because the targets and trajectories need not be manually transferred to a mechanical frame, which itself would have moving parts and mechanical backlash). It also may increase patient comfort during awake procedures,

Figure 2. Major Surgical Complications of DBS.

These data are summarized from Zrinzo et al., and Boviatsis et al.^{12,13}

Complication	Incidence: Mean (range)
Radiographic Hemorrhage	6.5% (0-34.4%)
Symptomatic Hemorrhage	2.6% (0-8.9%)
Infection	5.4% (0 - 15.2%)
Electrode Breakage	4.2% (0 - 15.2%)
Electrode Misplacement	5.4% (0 - 18.8%)

because it does not apply intense pressure to the skull as does a classical stereotactic frame.

In an awake procedure, microelectrode recordings are typically used to map the target region using a combination of neurophysiological patterns and neuronal responses to interactive patient testing. Once the target has been characterized, the permanent DBS electrode lead is placed according to those findings and test stimulation is delivered. Because the patient is awake, neurologic benefit with no or minimal side effects can be assessed. If these results are satisfactory, the lead is locked in-place. If results are suboptimal, a different location can be assessed for lead implantation.

Awake procedures are feasible because only the skin perceives pain (although some patients will report brief discomfort upon passing through the dura); generous infusion of local anesthetic typically eliminates most discomfort. PD patients, because they are off medications for neurologic assessment during the procedure, typically experience discomfort mostly due to the primary disease symptoms, such as rigidity and dystonia.

The need for empirical assessment of lead placement derives from two main factors: first, once the skull is opened for insertion of electrodes, there may be an egress of cerebrospinal fluid (CSF) and an ingress of air. Good surgical technique aims to minimize these factors but even a slight change in skull contents can cause brain shift of a magnitude which, although small in absolute terms, may diminish surgical accuracy in a clinically meaningful way.^{14,15} Second, there is debate in the field over the question of whether the visually identified “optimal” target on imaging is truly the best target for that individual patient, both in terms of maximizing benefit and minimizing side effects. Therefore, empirical assessment of potential targets adds a level of certainty that is otherwise unavailable.

The first factor, brain shift, can be addressed by the use of intra-operative imaging. Indeed, asleep procedures typically use this as the primary method of achieving accurate electrode placement. Many major academic centers now have intra-operative MRI suites which allow visual confirmation of targeting during the electrode implantation procedure. However, many centers use intra-operative CT imaging; the brain tissue resolution of CT, especially intra-operative CT, is less than that of MRI, and so these CT scans are often co-registered with pre-operative MRI. Because most co-registration algorithms are “rigid” (in the sense that they cannot account for brain movement with respect to the skull), brain shift is potentially a limitation with this approach. Yet even procedures performed with intra-operative MRI cannot address the second factor, that is, whether the visually identified target truly represents the optimal brain circuit for patient-specific neuromodulation. So far, several studies have compared results of awake vs. asleep DBS and, according to the fairly course measures used, there do not seem to be major differences.¹⁶⁻¹⁸ However, one study has observed

that thresholds to motor side effects may not be predictable based upon the imaging alone,¹⁹ and so clinical assessment of these side effects in an awake patient may in some cases yield a larger available dynamic range of stimulation and thus potentially more optimal results.

Most centers implant the battery in a delayed fashion, typically one week later. In the case of awake DBS surgery, this allows continuous neurological monitoring of the patient without a period of general anesthesia for battery implantation.

DBS SURGERY AT RHODE ISLAND HOSPITAL

Our preference is to perform DBS as an awake procedure in order to maximize the possibility of obtaining optimal results for each individual patient. We typically perform microelectrode recordings along three tracks on each side, aligned according to the dimension of highest anatomical-radiographic uncertainty about the target. The best track in terms of neurophysiological patterns and responses is selected first for test stimulation using the permanent DBS electrode. If results are good, the electrode is locked in-place at that location; otherwise additional locations are tested in order of the quality of their neurophysiological signals. In addition, we perform most of our procedures with the aid of an intra-operative CT scanner. This adds an extra level of safety and certainty regarding our targeting, should there be any question about the signals we are observing or about the patient’s condition.

Many of our procedures are performed as a collaboration between our lead movement disorders neurologist and functional neurosurgeon. Both have extensive experience interpreting neurophysiological signals and assessing clinical responses. This team-based approach affords an added level of confidence about the quality of these procedures and the ultimate clinical benefit.

CONCLUSION

DBS is potentially a valuable therapy for patients whose movement disorders are poorly managed on medications alone. Comprehensive, multidisciplinary evaluation of patients pre-operatively maximizes good outcomes by screening out those who are more likely to decline after surgery. The surgery itself can be performed using a variety of approaches, but ultimately, surgical safety and precision are the main goals. Throughout this process, a team-based approach works to ensure the best course of treatment for each patient.

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