

# Deep Brain Stimulation

## Techniques and Practices

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### **The Society for Innovative Neuroscience in Neurosurgery**

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## Preface

This book represents the attempt of a small, passionate group of functional neurosurgeons to describe the rapidly changing practice of deep brain stimulation (DBS) as it pertains to movement disorders and other emerging conditions. The Society for Innovative Neuroscience in Neurosurgery (SINN) was founded in 2014 in Baltimore by members of this group in an effort to improve communication and collaboration within the field of functional neurosurgery. This group has grown over time, and has now adopted an educational role along with a research and clinical practice emphasis.

Within the context of this rapidly growing and technologically dependent field, we present chapter topics covering the basic application of DBS techniques for movement disorders. Over the last 5 years, our field has been transformed by the introduction of intraoperative imaging-guided lead placement techniques (utilizing intraoperative computed tomography or magnetic resonance [MR] imaging) for lead placement in patients under general anesthesia; a discussion of these techniques is included in this book in addition to discussions of standard frame-based techniques. Moreover, the resurgence of lesioning techniques has taken a prominent role in the

treatment of essential tremor in adults and dystonia in children, and we include further discussion of MR-guided focused ultrasound treatment. Importantly, several chapters are included describing the emerging role of DBS for a variety of psychiatric and neurological conditions. Finally, we conclude with practical discussions of intraoperative research implementation, the use of DBS in pediatrics, and some pearls regarding the establishment of a DBS practice for the new surgeon.

It is our hope that this text is useful for neurosurgical residents, functional neurosurgery fellows, and the new DBS practitioners.

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# 1 Introduction to Deep Brain Stimulation: History, Techniques, and Ethical Considerations

Teresa Wojtasiewicz, Nir Lipsman, Jason Gerrard, Travis S. Tierney

## Abstract

Deep brain stimulation (DBS) is a procedure that developed as a result of decades of work in stereotactic guidance, neurophysiology, and neuroanatomy. Now, DBS is a validated, Food and Drug Administration (FDA)-approved treatment for a number of neurological and psychiatric disorders including Parkinson's disease, essential tremor, dystonia, obsessive compulsive disorder, and epilepsy. Further applications remain an area of ongoing investigation. Lesioning is once again regaining interest, particularly with development of minimally invasive techniques such as laser interstitial thermal therapy and transcranial focused ultrasound. There are several methods for lead placement and procedural techniques will continue to evolve with time. A multidisciplinary team is critical for optimal patient evaluation, target selection, and postoperative follow-up. Medical ethics is a key part of the multidisciplinary management, particularly in case of children, patients with psychiatric disorders, and patients who are severely debilitated from their movement disorders.

**Keywords:** deep brain stimulation, functional neurosurgery, ethics

## 1.1 Introduction

Over the past three decades, deep brain stimulation (DBS) has become a widely used treatment for a variety of conditions since Benabid and colleagues first popularized the technique for the treatment of tremor.<sup>1</sup> Even before this, early neuromodulation studies targeted the hypothalamus and somatosensory thalamus, for treatment of pain disorders.<sup>2,3,4</sup> High-frequency stimulation in the thalamus led to discovery that stimulation of the thalamus could reduce tremor.<sup>5,6,7</sup> Further studies showed that modulation or ablation by lesioning had the potential to treat patients with movement disorders.<sup>8,9,10,11</sup> DBS is now a validated, Food and Drug Administration (FDA)-approved treatment for neurological disorders including Parkinson's disease, essential tremor, dystonia, obsessive compulsive disorder, and epilepsy. Additional applications in other conditions remain an area of active investigation. Stereotactic lesioning is regaining additional interest, particularly with development of minimally invasive techniques such as the Gamma Knife and MRI-guided focused ultrasound.<sup>12,13</sup> DBS systems can now be implanted using several different methods, with a range of options of stereotactic frames, image-guided targeting, and intraoperative microelectrode recordings (MERs) and testing. There are now multiple hardware and software options available for use in DBS, including different leads and implanted generators. A multidisciplinary team is critical to decide who is an optimal surgical candidate and what treatment strategy will be most suited for individual patient. Multidisciplinary collaboration maximizes the chance of successful DBS through appropriate

preoperative evaluation of potential surgical candidates and continued postoperative care after DBS hardware placement. Medical ethics is an important part of the multidisciplinary management, particularly in case of children, patients with psychiatric disorders, and patients who are severely debilitated from their movement disorders.

## 1.2 History of Deep Brain Stimulation

Electricity has been a captivating possibility in treatment of human disorders for centuries, beginning with the earliest descriptions of treatment of pain with torpedo fish in Greek and Egyptian medicine, and investigations of contractions in frog muscle by Galvani.<sup>14,15,16</sup> For thousands of years, many civilizations believed that targeting the brain could treat spiritual and mental ailments. Examples range from the earliest attempts at trepanation to 15th century artistic renditions of extracting "mental stones" from unstable people.<sup>17</sup> Interestingly, attempts at lesions of the brain predated an understanding of functional organization of the brain but electric stimulation was key to this knowledge. Anecdotal studies of pathology, such as the frontal lobe disconnection and behavior changes seen in the case of Phineas Gage, suggested that complex behaviors could be attributed to specific areas of the brain.<sup>17,18</sup> Physicians such as Jean Bouillaud, Simon Aubertin, and Paul Broca observed, from cases of patients with aphasia, that speech could be localized to specific regions of the brain.<sup>19,20</sup> These developments inspired researchers Gustav Fritsch and Eduard Hitzig, who proved localization theory by stimulating the exposed cortical surface in dogs and localizing motor and nonmotor functions of the brain.<sup>21</sup> David Ferrier conducted further experiments in monkeys by localizing hearing, visual attention, and secondary motor areas.<sup>20,22</sup> The first use of neurostimulation in a human patient is attributed to Roberts Barthelow who stimulated the parietal lobes in an awake patient with an erosive basal cell cancer in 1874, producing contralateral movements and, subsequently, seizures.<sup>23</sup> Shortly after that, Sir Victor Horsley, a pioneer in many aspects of neurosurgery, published a case of electric stimulation of an occipital encephalocoele in 1884 and he and other neurosurgeons began using cortical stimulation for functional mapping.<sup>16,24,25</sup> Horsley would also subsequently perform the first movement disorder surgery in 1908, successfully treating a patient with hemiathetosis by resecting the precentral gyrus, which cured the movement disorder but caused hemiplegia.<sup>26</sup>

For the next few decades after Horsley's resection of the precentral gyrus, attempts at treating movement disorders were aimed at interrupting the pyramidal motor tracts, but with a high degree of morbidity and mortality.<sup>15,16</sup> Abnormalities in deep brain structures, including atrophy of basal ganglia, were identified in anatomic studies of patients with movement disorders, but the basal ganglia was thought to be a dangerous

## Introduction to Deep Brain Stimulation: History, Techniques, and Ethical Considerations

target and the physiology of basal ganglia circuits was not yet well understood.<sup>27</sup> Dr. Meyers reported several approaches to the basal ganglia, including sectioning the ansa lenticularis, but these approaches were accompanied by a 12% mortality which he felt was unacceptable.<sup>28</sup> Despite the complications accompanying an open surgical approach, Meyers' contributions definitively demonstrated that basal ganglia lesions could effectively treat tremor *without* causing paralysis or coma. These notions challenged the prevailing dogma of Dandy who believed that encroachment into the basal ganglia always resulted in coma, and previous ideas that only lesions to the pyramidal tract could alleviate tremor. Meyers' important observations set the stage for future stereotactic surgical methods in targeting extrapyramidal subcortical structures for the treatment of refractory movement disorders. Still working with an open approach to the descending tracts, Irving Cooper in 1952 inadvertently encountered and was forced to ligate the anterior choroidal artery while attempting a pedunculotomy.<sup>29</sup> Serendipitously, the resultant choroidal infarct relieved tremor without causing hemiparesis.<sup>29</sup> He was able to reproduce his results with anterior choroidal artery ligation, ascribing the benefit of this procedure to interruption of efferent pathways from the globus pallidus.<sup>30</sup> Despite the well-known introduction of frame-based stereotaxy by Spiegel and Wycis in 1947, Cooper continued to create lesions in the basal ganglia and thalamus with an essentially free-hand method.<sup>31,32</sup> Cooper's approaches were intermittently successful and may have had a lower risk of complications than other prior open approaches. Though his work did little to advance technical refinements in the field of movement disorders surgery, his findings finally reduced further attacks on the descending cortical spinal tracts as a treatment for tremor.

Lesioning for psychiatric conditions also blossomed in the early to mid 20th century. Developments in neuroanatomy showed function could be localized to certain areas and anecdotal evidence of patients with frontal lobe damage and behavior changes led to a perception that psychopathology could be localized to the frontal lobes.<sup>17</sup> A few early attempts at frontal lobe resection, such as Gottlieb Burckhardt's report of six patients published in 1891 and Lodovico Puusepp's report of three patients he operated on in 1910, had high rates of mortality and low rates of success in alleviation of symptoms and did not inspire enthusiasm for psychosurgery.<sup>17,33,34</sup> The era of psychosurgery would begin in earnest when, at the Second International Neurologic Congress in London in 1935, John Fulton and Carlyle Jacobsen presented results of chimpanzee experiments showing that frontal lobe resection reduced "frustration behavior" associated with not receiving an anticipated reward.<sup>35</sup> The audience for this meeting included Walter Freeman and Antonio Egas Moniz, who were keen to clinically translate these results. Moniz, in collaboration with Almeida Lima, successfully performed the first frontal lobotomies to treat patients with psychosis, first with alcohol injections and subsequently with a new instrument—the leukotome.<sup>36</sup> Soon after, Walter Freeman and James Watts would replicate Moniz' lobotomy technique, finding that it was successful in treating psychosis and other disorders including depression.<sup>37,38</sup> Freeman and Watts refined Moniz' technique and produced a calibrated instrument—the precision leukotome—and reported initial positive results; though 14% of patients had a poor

outcome and there were high rates of uncontrolled bleeding, seizures, and the apathetic "frontal lobe syndrome."<sup>38</sup> Freeman, enthusiastic about these results, modified a transorbital technique developed by Amaro Fiamberti, which he could perform without assistance from a neurosurgeon or anesthesiologist in patients rendered unconscious from an electroshock treatment.<sup>39</sup> These techniques were admonished by the academic medical establishment, including his former collaborator Watts, but Freeman ignored this criticism and began performing his transorbital leukotomies with portable machines around the United States in various settings, including offices, asylums, and motels.<sup>40</sup> His procedural complications, seemingly indiscriminate patient selection, lack of sterility, and inability to recognize his own limitations began to attract significant negative attention from the medical community and general population.<sup>17,41</sup> Ultimately, the development of chlorpromazine and other antipsychotics brought an end to transorbital leukotomies.<sup>17</sup> Though the legacy of frontal lobotomy would permanently mar psychosurgery, many of Freeman's contemporaries recognized that more precise frontal lobe resection could alleviate psychiatric symptoms, including John Fulton who remarked, "Why not use a shotgun?" in describing the crude Freeman lobotomy and William Scoville who developed a method of cortical undercutting.<sup>42,43</sup> Stereotaxy would allow a much higher level of precision in treating targets for psychiatric surgery.

The development of stereotactic frames allowed more precise and safe neurosurgical procedures that had the potential to treat neurological diseases. Sir Victor Horsley collaborated with Robert Clarke to develop the first stereotactic frame (► Fig. 1.1a). This frame was used in animal experiments to successfully insert a probe.<sup>44,45</sup> This initial frame was based on a three-dimensional (3D) Cartesian coordinate system and included a needle holder to insert into a specified structure, which would allow entry to a specified target with minimal injury to surrounding tissue.<sup>44,45</sup> However, the Horsley-Clarke frame relied on external cerebral landmarks, which was not reliable and it was not used in human subjects.<sup>44,45</sup> Spiegel and Wycis addressed this problem by creating a similar frame at Thomas Jefferson Hospital in Philadelphia (► Fig. 1.1b). Together with stereoencephalographic methods, they used their frame to perform true stereotactic approaches to thalamotomy, pallidotomy, ablation of the Gasserian ganglion, and ablation of the spinothalamic tract.<sup>46</sup> After viewing the Spiegel-Wycis frame, Lars Leksell created a novel frame with an arc center target and published his results in 1951 (► Fig. 1.1c).<sup>44,47</sup> The Leksell frame had ring and arc angle that could be used to easily create trajectories to a target from virtually any point on the skull.<sup>44,47</sup> Leksell, like the Wycis and Spiegel group, used his stereotactic methods to perform anterior capsulotomies and treated patients with obsessive compulsive disorder.<sup>48</sup> The advent of stereotaxy allowed neurosurgeons to safely target deep regions of the brain for stimulation and other treatment modalities, including capsulotomies, cingulotomies, subcaudate tractotomies, and limbic leukotomies.<sup>49</sup> In the 1960s and 1970s, as lobotomy was beginning to fall out of favor, several other groups attempted to perform stereotactic lesioning procedures to treat psychiatric illness. The anterior capsule, first targeted by Talairach and colleagues and later refined by Leksell and others, could be ablated with an approximate efficacy of 50 to 70% in treating obsessive compulsive disorder.<sup>50,51</sup> Anterior cingulotomy could also be

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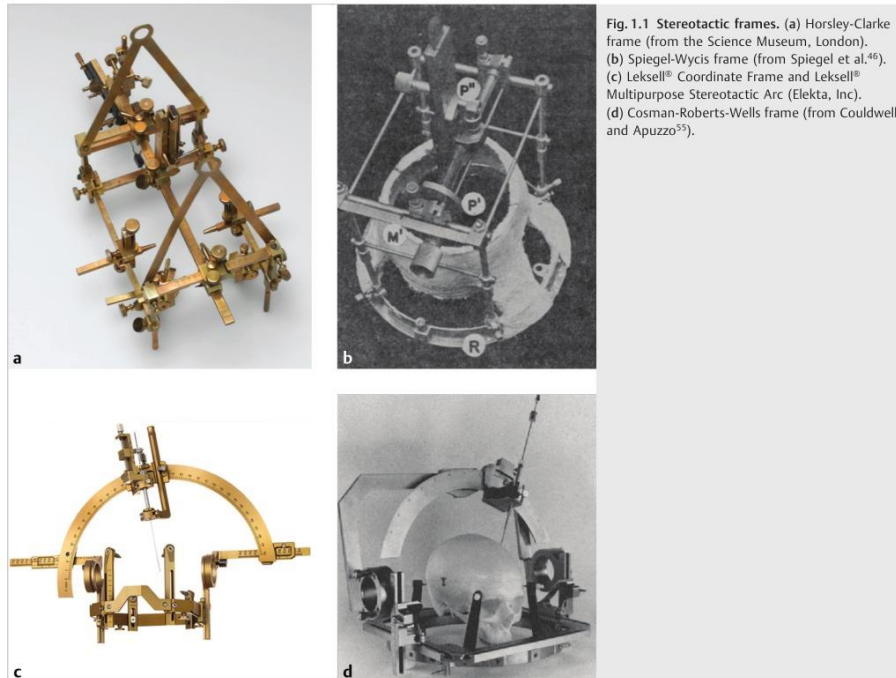


Fig. 1.1 Stereotactic frames. (a) Horsley-Clarke frame (from the Science Museum, London). (b) Spiegel-Wycis frame (from Spiegel et al.<sup>46</sup>). (c) Leksell® Coordinate Frame and Leksell® Multipurpose Stereotactic Arc (Elekta, Inc). (d) Cosman-Roberts-Wells frame (from Couldwell and Apuzzo<sup>53</sup>).

used to interrupt limbic projections with reasonable efficacy in a variety of conditions including obsessive compulsive disorder, anxiety, depression, and bipolar disorder.<sup>49</sup> Studies suggest a reasonable, i.e., 33 to 60% efficacy and a low risk of complications in patients with medically refractory disease with anterior capsulotomy.<sup>49</sup> Subcaudate tractotomy, first introduced by Geoffrey Knight in 1964, targeted anterior white matter tracts connecting the orbitofrontal and limbic regions. The procedure was used for obsessive compulsive disorder, anxiety, depression, and bipolar disorder with 40 to 60% efficacy, comparable to cingulotomy, with a similarly low rate of complications<sup>52,53</sup> A combination of anterior cingulotomy and subcaudate tractotomy lesions called the limbic leucotomy was also used for obsessive compulsive disorder and depression with reasonable efficacy and a low incidence of side effects.<sup>54</sup> The ablation procedures made possible with stereotactic surgery would lay a foundation to perform DBS for treatment of psychiatric illness. Both movement disorder surgery and psychosurgery led to the development of DBS.

Though the birth of modern DBS is typically attributed to Benabid's 1987 paper on thalamic stimulation, neurosurgeons had been using acute stimulation long before that.<sup>1,15</sup> DBS gained acceptance in the 1950s, after the rise of stereotaxy. In the 1940s and early 1950s, many surgeons, including Spiegel

and Wycis, would stimulate stereotactic trajectories before ablation as a method of ensuring safety.<sup>15</sup> Soon, electrode stimulation began to be used for psychiatric indications, starting with Dr. Pool's studies of hypothalamic stimulation and continuing to Robert Heath's cerebellar stimulation for psychosis.<sup>2,56,57</sup> Although enthusiasm for movement disorder and psychiatric surgery diminished in the 1970s after the introduction of levodopa<sup>58</sup> and chlorpromazine, respectively, investigation into ablation and neurostimulation for these neurological disorders continued at select centers. DBS was also investigated for use in other conditions, such as chronic pain disorders.<sup>2,3,4</sup> Attempts at stimulation for pain in the somatosensory thalamus then led to the discovery that thalamic stimulation could reduce tremor.<sup>5,6,7</sup> In 1987, Dr. Benabid and his group showed that thalamic DBS could alleviate medication-refractory tremor symptoms in Parkinson's disease patients. Subsequent investigation proved the safety and efficacy of thalamic DBS for tremor and led to FDA approval of thalamic DBS in 1997 for essential tremor.<sup>8,9,10</sup> Randomized-controlled and large prospective trials confirmed the efficacy of thalamic DBS in essential tremor.<sup>59,60,61</sup> Over the next several years, other DBS targets would be established for movement disorders, including the globus pallidus interna (GPi)<sup>1,62</sup> and subthalamic nucleus (STN).<sup>9,63</sup> The FDA approved both GPi and STN DBS in Parkinson's disease in 2002.

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Subsequently randomized-controlled trials verified that DBS in the GPI and STN were effective in Parkinson's disease.<sup>64,65,66,67</sup>

### 1.3 Ablative Procedures

Ablative procedures started to fall out of favor when DBS was introduced, but lesioning has remained an option for certain patients. Lars Leksell's initial use of the Leksell frame included radiosurgical pallidotomies and thalamotomies,<sup>68,69</sup> and stereotactic radiosurgery continues to be used for these purposes.<sup>70,71,72</sup> Lesioning has regained some interest in psychiatric treatment, despite its negative association with earlier psychiatric ablative procedures.<sup>73</sup> Stereotactic radiosurgery can be used for focused ablation of structures including the anterior cingulate, substantia innominata, and the anterior limb of the internal capsule, and it may alleviate symptoms of obsessive compulsive disorder, anxiety, and depression.<sup>74</sup> Laser interstitial therapy (LITT), in which a laser fiber is passed through a burr hole and an ablation trajectory can be defined, has also been used anecdotally for pallidotomy.<sup>75</sup> Finally, MRI-guided focused ultrasound for unilateral thalamotomy has been shown to be effective in treatment of essential tremor<sup>12</sup> and tremor-dominant Parkinson's disease<sup>13</sup> with low complication rates.<sup>76</sup> Though there is no current procedure that can supplant DBS, these new applications and methods of DBS will continue to be an active area of investigation.

### 1.4 Operative Techniques

DBS can be successfully performed in many different ways, with several options for targeting and hardware placement. Between centers, there is significant heterogeneity in how the procedure is performed, with differences in many elements of surgery including preoperative target and trajectory planning, frame usage, incision and burr hole planning, intraoperative clinical and stimulation testing, and postoperative imaging for confirmation.<sup>77</sup> The majority of surgeons perform DBS as a staged procedure with electrode placement and extension cabling/pulse generator implantation as separate procedures.<sup>77</sup> The rationale for staging may be related to the duration of the procedure, the need for different anesthesia techniques and patient positioning, and a concern for increased risk of infection. At the present time, both staged and single-operation DBS are appropriate techniques.<sup>77,78</sup> As the companies that offer DBS devices compete with each other, more hardware choices are available and will continue to develop. Directional leads with segmented contacts can be programmed to "steer" current to avoid delivering current to unwanted structures, such as the internal capsule, while maintaining current delivery to therapeutic targets.<sup>79,80</sup> Rechargeable implanted pulse generators are now available which last longer before needing replacement and may be a good option for patients who are willing to recharge their devices.<sup>81,82</sup>

#### 1.4.1 Frame-based versus Frameless Approaches

Accurate targeting is critical to successful DBS. DBS can be performed with frame-based approaches and there are several

frames available including the Leksell (► Fig. 1.1c) and Cosman-Roberts-Wells (CRW) frames (► Fig. 1.1d). It has been shown that DBS can also be safely and accurately performed with frameless technology, and there are several options available including NexFrame and StarFix. The procedures and technology for frameless DBS will be discussed at length in other sections in this text. Experimental studies with skull models suggested frameless technology could exceed the accuracy of frame-based approaches (with a mean of 1.25 mm of localization error for frameless techniques, compared to 1.8 mm for CRW and 1.7 mm error for Leksell frames).<sup>83,84,85</sup> However, some studies of frameless technology in patients have shown that frameless technology may not be as accurate as frame-based approaches, though the outcomes for patients appear comparable.<sup>86,87</sup> Nowadays, surgical robot assistance may offer another accurate technique in stereotactic cranial procedures and may be useful for electrode placement in DBS.<sup>88,89</sup>

#### 1.4.2 Microelectrode Recording and Intraoperative Monitoring

Another topic of debate is whether DBS performed with MER and intraoperative testing ("awake") or DBS performed solely with anatomic/image-guided targeting ("asleep") is more accurate and effective. There is some controversy regarding whether MER is an indispensable tool for accurate lead placement or current image-guided techniques are sufficiently accurate.<sup>90,91,92</sup> Studies have shown that MER frequently provides data that leads to a revision in the final lead location, suggesting that the information gathered by MER is vital to accurate lead placement.<sup>93,94,95</sup> There is no consensus of whether the revisions in lead location suggested by MER lead to improved outcomes and studies of DBS without MER indicate good results.<sup>96,97</sup> In addition, the proponents of direct image guidance techniques suggest that the corrections made with intraoperative recordings are done at the time of image-based target selection, which often varies somewhat from the indirect coordinates. A recent meta-analysis showed that MER and awake surgery is associated with more lead passes and a higher rate of complications, but a lower rate of stimulation-induced side effects.<sup>98</sup> The overall motor outcomes appear comparable with both "awake" and "asleep" procedures, though there is some suggestion that patients may improve more quickly after "awake" procedures.<sup>98</sup> Patients seem to have a preference for DBS performed under general anesthesia.<sup>99</sup> Some patients are either unwilling or unable to tolerate being awake and participating in testing during a long procedure so further improvement in accuracy of asleep procedures, such as robotic guidance, will be of great benefit.<sup>100</sup>

#### 1.4.3 Description of Surgical Procedure

As described above, there are various methods of performing DBS, with new technology providing additional options that may make surgery more comfortable, convenient, safer, and more accurate. We will describe the surgical procedure for frame-based DBS, using MER and intraoperative stimulation. For other excellent reviews of surgical techniques, please see (Kramer et al)<sup>101</sup> and (Machado et al).<sup>102</sup> Other sections in this textbook will detail alternatives, including frameless stereotaxy and magnetic resonance imaging/computed