Deep Brain Stimulation : Applications and Challenges

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***Abstract*—** Deep Brain Stimulation (DBS) is widely used for the treatment of movement disorder. It is being explored in the new application areas. Since DBS deals with the internal portion of the brain it offers several challenges. It is difficult to understand the exact mechanism of DBS. This therapy is patient dependent and procedures may change drastically from patient to patient. In this paper DBS is discussed and its potential applications are explored. There are many challenges/restrictions while using this technique. Some major challenges are analyzed for better understanding of DBS.

Keywords-*DBS; neuromodulation; brain mapping; ultra microelectrode;Implantable medical devices*

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I. INTRODUCTION

Deep Brain Stimulation (DBS) is a well-established neurosurgical technique to treat movement disorder. Food and Drug Administration (FDA) approved this technique for essential tremor in 1997, Parkinson Disease (PD) in 2002[1, 2]. In this technique DBS electrode is implanted inside the brain at suitable place [Figure 1]. The DBS electrode is made of specialized metal e.g. Platinum-Iridium microelectrode. This electrode is energized by a battery and programmer device. The battery provides continuous power to the system and programmer provides prescribed electrical stimulus signals to the target area of the brain via DBS microelectrode. DBS electrode are placed in the area of the subthalamic nucleus (STN) to treat PD. For essential tremor it is placed at globus pallidus. A successful implant at STN will remove all the symptoms of PD [1].

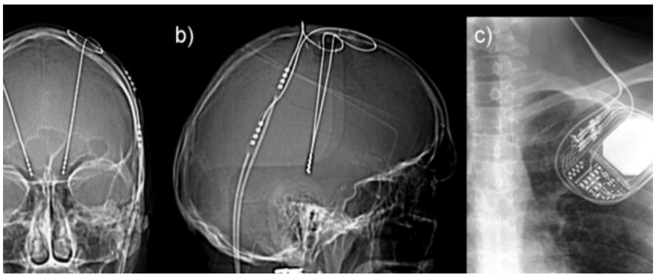

Figure 1. DBS electrode inside the brain (Courtesy of Patric Blomstedt, University Hospital, Umea)

In DBS therapy, electrical signals are used. Therefore, study on electrical interaction with brain tissue is needed. It is also required to know the effect of stimulation parameters on DBS therapy. The major restriction is the understanding of DBS mechanism. It is still not clearly understood. Since DBS is developed and used without much clinical analysis, therefore, many effects need to be simulated in the laboratory before actual implementation. The other major concern is that the DBS situation changes from patient to patient. Each patient is chosen differently and stimulation parameters need to be adjusted accordingly. The clinical results obtained cannot be applied directly in actual treatment because conditions are quite different in both cases. The benefit of DBS is highly dependent on the distribution of the electric fields generated by electrical stimulation. Therefore, detailed knowledge of the electric field developed inside the brain is crucial. It is difficult to measure the distribution of the electric field in vivo. Alternatively, computational models are investigated with finite element model. The brain stimulation can be applied in a brain network located in cortical or subcortical layers. In deep nuclei groups or in a combination of both. The domain of DBS is operative neuromodulation [3]

2. APPLICATIONS FOR DBS

DBS has got wide applications in several fields and more opportunities are being investigated by researchers.

(1) Movement disorder treatment:

As discussed earlier, the major successful area of application is the treatment of PD. A neuromicroelectrode (NME) is implanted inside the brain and electrical pulses are provided from a device. This device is placed in the upper part of the chest of the patient and is connected with the NME through internal wire. As a therapy, stimulation parameters are set according to the patient**.** [1, 4, 5, 6, 7].The earlier work on movement disorder treatment was carried out in 1939[8].
A typical NME is described in Figure 2.

Figure 2 The quadripolar electrodes (leads) used for deep brain stimulation. (The contact is 1.5mm long and 1.27 mm diameter. The left microelectrode is Model 3387 and right model is 3389) Courtesy Medtronic, Inc.

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These electrodes have contacts as shown. These are responsible for the electrical interaction between the stimulated signals and the brain tissues.
DBS therapy is also used in the treatment of tremors and dystonia. These diseases have shown improvement upon DBS treatment.

(2) DBS Neuropsychiatry:

Neuropsychiatric conditions involve mood, memory, personality and behavior. DBS is used to treat such patients by targeting the ventral capsule/ventral striatum (VC/VS).
FDA approved DBS for obsessive-compulsive disorder (OCD) in 2009[9, 10, 11]. There are limited number of patients undergoing DBS treatment for OCD but it has shown improvement in such patients. DBS has shown encouraging results in treating depression. For OCD treatment STN and inferior thalamic peduncle is targeted

(3) DBS for trauma and acquired Injury: [12, 15]

Traumatic brain injury is a serious medical condition and it has affected the lives of millions of people. Moreover, disabilities caused by spinal cord injury is another kind of misery. The applications of DBS for traumatic brain relies on restoring function in the damaged brain by modulating behavior of circuits to compensate the altered behavior of the circuit following the traumatic incident.

(4) DBS for Obesity and habitual disorder: [13, 14, 15]

For addiction and eating disorders "Limbic" circuits have been targeted to apply DBS. The reward circuit inside the brain is supported by lateral hypothalamus and ventromedial hypothalamus and therefore is the main target for DBS for addiction and eating habits [16]. Case studies have shown improvement of addiction in heroin addiction [17] and alcohol or smoking addiction. Improvement in eating disorder are reported due to DBS therapy [18]. In the patients having traumatic brain injury but some consciousness, DBS of the anterior interlaminar thalamic nuclei and paralaminar regions of the association nuclei is targeted [19].

(5) Other applications [20, 21, 22]

DBS electrodes (or modified accordingly) can be used for brain monitoring and recording. We call such electrodes as recording electrodes in the literature. Microelectromechanical Systems (MEMS) are used to design and fabricate such microelectrodes. Companies are working on microelectrodes to communicate and control common functions literally thought this technique [23, 24]. A Utah-style electrode array is implanted in the brain to monitor signals and record them and use to move cursor on the computer screen; to know the wished of the patient. The ultimate goal should be to enable the control of actual or prosthetic limbs [25, 26].
The latest development in the field of brain microelectrode development is to microfabricate electrode arrays that can be placed directly on the brain. Such microelectrodes are fabricated on silk-like substrate that conforms to the surface of the brain and dissolves over time. At the end only microelectrode is left. Such microelectrodes can offer therapies to those patients who suffer from intractable neurological conditions. Such techniques are being developed Tufts University, University of Illinois- Urbana, and the University of Pennsylvania.

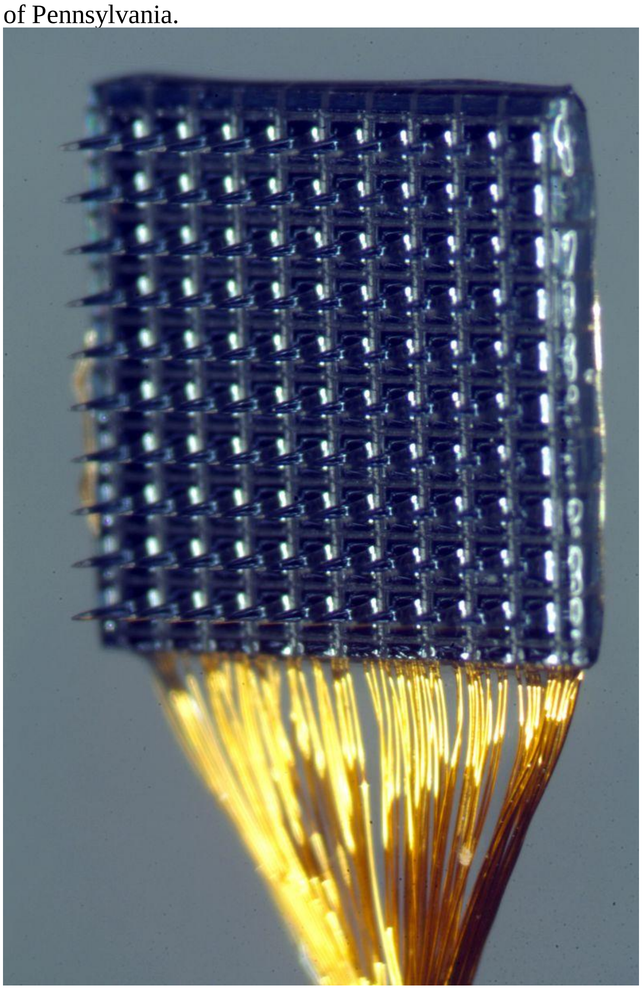

Figure 3. A Utah-style MEMS electrode array used in the Brain gate system [1]

3. CHALLENGES FOR DBS

DBS have several complications associated with it. These complications can be classified into three categories.

(1) Pertaining to Surgical Procedures: This category includes infections and other surgical procedure related causes. The most paramount complication being the internal hemorrhage because it may be fatal for the patient [27]. The main risk factor is hypertension and old age of the patient. However, DBS is more beneficial for such patients. To minimize such risk enhanced magnetic resonance imaging (MRI) is recommended. It is also recommended to navigate the electrode trajectory from surface of the cortex to the target sites. The blood pressure of the patient should be kept normal while operation. The frequency of the use of microelectrode technique in DBS surgery should be minimized. It is recommended to use semi-microelectrodes for unit recording as their tips are not sharp. A dull-point catheter is used to make an electrode root above the target [28].

(2) Pertaining to DBS accessories and machinery: In this category we include machinery breakdown, electrode breakage,

skin erosion over the implantable pulse generator or electric wires, and related infections. It also includes complications related to electromagnetic fields surrounding patients. It is reported in literature that DBS failure due to machine related incidence accounts for 4-9.7 %. [29]

These failures are breakage of the electrode or extension cords, mechanical failure of programmer, and migration of the intracranial electrode. [30] It has been noticed that the most frequent place for breakage of the electrode or extension cord is the connection area of the intracranial electrode and the extension cord, and there is a tendency for breakage due to twisting force at these points.

To minimize mechanical complications, the angles and positions of the electrodes, the extension cords should be monitored carefully.

The other major effect is caused by electromagnetic fields on DBS system. The patient should be aware of the surroundings of the machines generating electromagnetic waves in their daily life. It is suggested by Medtronic, Inc. manual of DBS to keep phones at least 10 cm away from the programmer.

The DBS patient should be careful while undergoing magnetic resonance imaging. There is debate about the MRI sequence permissible after DBS implantation. Few patients have shown neurological deficits due to MRI session. [31, 32].

Skin erosion above the DBS system and infection of the DBS system is reported and it ranges between 2.9 to 7.7% [33]. The patients, age under 58 and over 65, patients with diabetes, thin scalp are more susceptible to skin infection. Patient management and precautions on handling the DBS should be made. It is recommended to use crescent incisions, instead of linear incisions, which cross over the burr hole, or intracranial electrodes. It is also recommended to place the stimulating electrode, extension wires, and connectors under or around the skin incision should be avoided [34]. For thin scalp patient, one scheme is to drill out skull to make a space for connector placement, although this may be difficult. The other recommended scheme is to place the connectors at patient’s neck area where it is supported by soft tissue rather than any hard bone. It is recommended to place electrodes and connecting wires be placed as deep as possible under the scalp.

(3) DBS and neuron interaction related:

This complication is related to electrical stimulation of targeted neuronal structures or the neuronal circuits themselves and the stimulation of the surrounding structures of the targeted area by spreading current. When stimulating electrodes are placed near untargeted neural fibers pathway, these untargeted neurons are also excited. The current spread to the internal capsule of ventral caudal thalamic nucleus, causes rigidity or dysarthria. Additionally, when current spreads to the optic tract underlying the internal globus pallidus (GPi), can cause scintillation. Recently, these complexities have concerned related with cognitive and psychiatric symptoms and the suicide risk accompanying STN-DBS surgery [35]. There are reports indicating a decline in verbal fluency after STN-DBS. In a report where comparison between STN-DBS and GPi-DBS is made, has shown the decreased verbal fluency in both groups. However, STN-DBS group showed greater cognitive decline as compared to the GPi-DBS group [36]. There are several reports on psychiatric symptoms, but without any typical trends. The prominent psychiatric symptom in patients with PD is the emergence of depression, which is related to suicidal risks [35]. Some other psychiatric symptoms are mood changes, depression, and apathy after DBS, especially STN-DBS surgeries. In other report, symptoms that suggest dopamine dysregulation symptoms, such as excessive gambling or shopping, has been discussed [37].

DBS patients have shown a tendency towards suicide. There are three risk factors involved (1) relative younger age, (2) early onset of PD, and (3) a preoperative suicide attempt. There are several reports showing suicide attempt ranging between 0.45 to 5% [38].

The mechanisms underlying the development of psychiatric symptoms after DBS surgery are unclear. Therefore, methods to avoid these complications also remain under development. The topography within the STN is divide into three parts: (1) lateral upper STN –motor related part, (2) lateral lower STN-association-related, (3) medial part- limbic related [39]. It has been found that the most effective for the treatment of PD is the upper dorsal part of the STN [40]. The medial STN is stimulated to treat intractable OCD [41]. The acute depression after electrical stimulation of STN, may be the result of stimulation of substantia nigra pars reticulate (SNr) [42]. To avoid/minimize psychiatric symptoms after STN-DBS treatment following guidelines may be adopted:

(1) To determine the exact location of the motor area: It is necessary to avoid the electrical stimulation to the medical limbic part of STN. The goal is to stimulate dorsolateral part of the STN.

(2) To avoid micro-lesioning of the SNr: To achieve this use a unit recording technique to search for the precise ventral border of the STN.

It is also suggested to pay substantial attention to the suicide risks tendency among DBS patients by psychiatrists and psychologists’ consultations.

4. CONCLUSION

The brain stimulation is a delicate area of research with many promising applications. The patients should be aware of the treatment along with the risks associated with it. The major problem with this therapy is higher treatment cost, which acts a hindrance for many patients living in developed countries. In this paper the technique for brain stimulation was based on electrical properties of the microelectrode. It is expected that feedback based DBS will help the patients in a more acceptable manner. New microelectrodes based on optical properties of light will offer several advantages over electrical microelectrodes. The suicidal tendency of the patients after the implantation is a serious area of research, however it may not be related with the DBS treatment as such. But certainly the advantages offered by DBS could not encourage the patient to avoid suicidal tendency in some OCD cases.

This paper gives a view of the DBS technology and its applications. Some major challenges are also discussed with the help of literature and cases available. The ethical aspect of such therapy is still under discussion and new finding are coming. It is hope that the more awareness about this technique with lower cost has immense potential to treat many diseases.

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