# Analysis of the Electromagnetic Field Generated by Deep Brain Stimulation in Patients with Parkinson's Disease

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***Abstract*— Deep Brain Stimulation (DBS) is a stimulating therapy currently used to treat the motor disabilities that occur as a result of Parkinson's disease (PD). The mechanism of how DBS treats PD is poorly understood. Currently, there is a paucity of data from in-vivo human studies on the electromagnetic field (EMF) generated within neural tissue by DBS. In this study, the EMF generated by DBS was analyzed at different distances from the stimulating electrodes. Our goal was to examine how the EMF strength changed with distance in the human brain. The resulting analysis demonstrated differences of several orders of magnitude across the distances measured. With further study, we aim to connect the EMF effect on neural structures to the efficacy of DBS treatment.**

## I. Introduction

DBS is currently being utilized for the treatment of PD and other movement disorders and is being investigated for the treatment of cognitive and psychiatric disorders [1,2]. The physiological mechanism by which DBS effectively treats patients is poorly understood [2,3]. This is in part due the lack of knowledge of how EMFs interact with the highly complex structure of neural tissue. There is a debate regarding the interaction of DBS with neural tissue behaving as a resistive medium [4] versus that of a more complex resistive-capacitive medium [5]. Further data is required to resolve this issue, and data collected from the human brain would be particularly useful due to the size and structural differences between animal models and humans.

Our goal is to provide empirical data on how EMFs interact with neural tissue and provide insight into how this interaction influences neural physiology. There are multiple mechanisms by which electrical waveforms generated by DBS may propagate through neural tissue. DBS waveform propagation may be mediated through physiological (action potential generation and synaptic transmission) mechanisms. Additionally, DBS induces electromagnetic forces (volume conduction of charge and ephaptic transmission) which may alter neurophysiology in the local region and may also have effects on distant structures.

We are conducting in vivo studies of the electrical waveforms generated by DBS at different locations within the human brain. Our data suggest that electrical shunting through a conductive layer proximal to the DBS electrodes accounts for much of the current flow and thus a large reduction in the EMF experienced by the neural tissue.

## II. Materials & Methods

All procedures were reviewed and approved by the Institutional Review Board (IRB) at St. Joseph's Hospital and patients gave consent for participation in this study.

### A. Subjects

The subjects involved in this experiment were volunteer patients with PD who underwent standard anesthetized DBS implant surgery at Barrow Neurological Institute in St. Joseph's Hospital. Six patients participated in this study. In patients the recording electrode was placed in the STN ipsilateral to the DBS electrodes, and in two patients the recording electrode was placed in the STN contralateral to the DBS electrodes. (Patient 1 – Male, 68 years old, contralateral; Patient 2 – Male, 66 years old, contralateral; Patient 3 – Male, 79 years old, ipsilateral; Patient 4 – Male, 58 years old, ipsilateral; Patient 5 – Male, 72 years old, ipsilateral, Patient 6 – Male, 64 years old, ipsilateral).

### B. Data Collection

*Experimental Configurations*: DBS electrodes were implanted in the STN. After the DBS electrodes were implanted, a microelectrode (Medtronic microtargeting electrode, impedance ~1 MOhm at 1 kHz) was placed in the STN either ipsilateral to the DBS electrodes (2 mm distance from the DBS electrode) or contralateral to the DBS electrodes (~24 mm distance from the DBS electrode [6]) (Fig. 1). DBS was performed using devices from Medtronic (Activa SC) and Boston Scientific (Vercise PC). Electrophysiological recordings were performed on the microelectrode during intra-operative DBS. Data was collected at a sampling frequency of either 24414 Hz (Patients 1 – 5) or 48828 Hz (Patient 6) (Tucker-Davis Technologies, PZ5 Neurodigitizer Amplifier, RZ2 Bioamp Processor).

*Study Protocol*: The studies were performed intra-operatively while the patients were lightly anesthetized with Propofol. Stimulation was delivered with amplitudes of 3V (Patients 1 – 3) or 1.5 mA (Patients 4 – 6), a pulse width of 90 μs and at frequencies of 20/30, 70, 140, and 250 Hz. The order of the four DBS frequencies used was 140, 20/30, 250, and 70 Hz. Due to differences in the DBS hardware specifications, the lowest DBS frequency was 30 Hz in some Patients 1 – 3 and 20 Hz in Patients 4 – 6. DBS was turned on for ~10 seconds followed by off for ~10 seconds. The on/off pattern was repeated 10 times for each frequency and was followed by an approximately three-minute inter-DBS period. This

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protocol yielded four identifiable epochs of DBS for each patient.

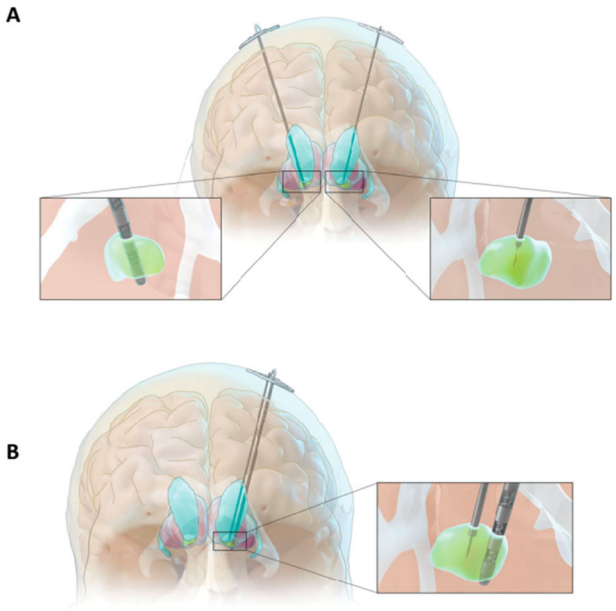


Figure 1. Relative positions of the DBS electrodes and the microelectrode placement. In the contralateral configuration the DBS electrodes and the microelectrode were located in the different right and left STNs at a distance of approximately 24 mm. The lower insets show the DBS electrodes in the right STN and the microelectrode in the left STN (A). In the ipsilateral configuration the DBS electrodes and the microelectrode were located in the same STN at a distance of approximately 2 mm. The lower inset shows the DBS electrodes and the microelectrode in the left STN (B).

### C. *Data Analysis*

Neural recordings were imported into Matlab for analysis (MathWorks, Inc., Natick, MA). The raw data were high pass filtered using a third-order elliptical filter with a cutoff frequency of 250 Hz and 60 dB of stop-band attenuation. The data were truncated to just the data containing the DBS epochs in order to remove large artifacts caused by movement of the electrode during insertion and removal. The start and end times of each DBS frequency epoch were determined by visual inspection of the data for each patient. A voltage threshold for detecting the occurrence of DBS waveforms was also determined by visual inspection of the data for each patient.

Data snippets, the data ±1 millisecond around all DBS waveforms that crossed the amplitude thresholds, were collected for each patient and each DBS frequency epoch. From this data, the mean DBS waveforms and their standard deviations were calculated for each patient and each DBS frequency epoch. The maximum voltage amplitude of individual DBS waveforms was also measured for each patient and each DBS frequency epoch.

A nonparametric statistical test (Wilcoxon rank sum test, $\alpha = 0.001$) was used to identify significance differences between test groups.

## III. Results

### A. *Contralateral vs. Ipsilateral*

We compared the data recorded from the microelectrode placed ipsilateral to the DBS electrodes with the data recorded on the microelectrode placed contralateral to the DBS electrodes. With ipsilateral electrode placement within the STN on the same side of the brain, the DBS electrodes and the recording micro-electrode are separated by ~2 mm. With contralateral electrode placement within the STNs on opposite sides of the brain, the DBS electrodes and the recording micro-electrode are separated by ~24 mm.

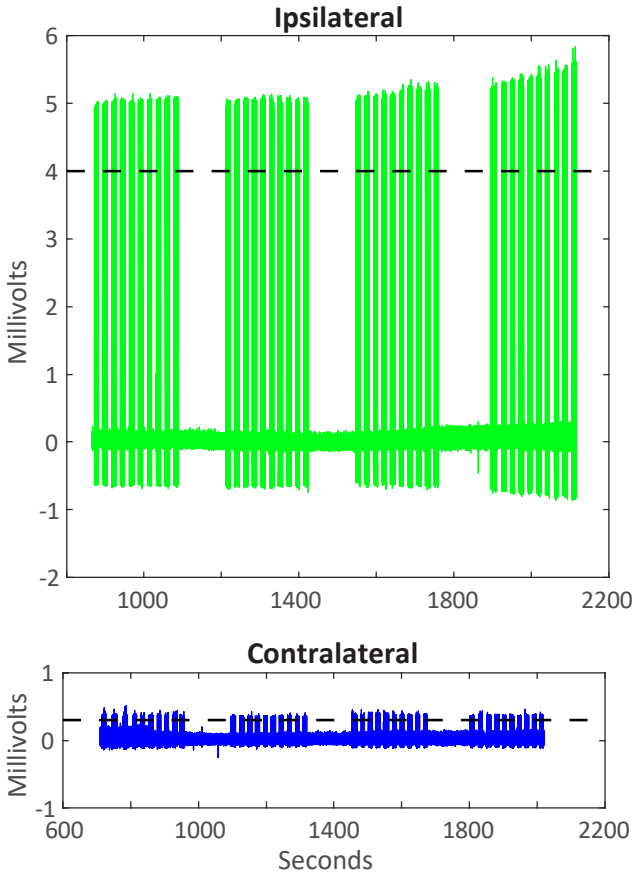


Figure 2. Electrophysiological recordings from microelectrodes placed in the STN ipsilateral and contralateral to the DBS electrodes. The electrophysiological data across all DBS epochs for an example ipsilateral configuration (Patient 3) and an example contralateral configuration (Patient 1) are shown. The dashed black lines indicate respective threshold amplitudes used for DBS waveform detection. The threshold used for the ipsilateral configuration was 4.0 mV, while the threshold used for the contralateral configurations was 0.3 mV.

The DBS waveforms showed a large decrease in amplitude when comparing the ipsilateral and contralateral electrophysiological recordings (Fig. 2). The thresholds used to detect DBS waveforms were set at 4.0, 5.0, and 3.0 mV for ipsilateral patients 3, 4, and 5 respectively. The Thresholds used to detect DBS waveforms were set at 0.3 and 0.2 mV for contralateral Patients 1 and 2 respectively.

We further quantified this decrease in DBS waveform amplitude by examining the peak amplitudes of all DBS

waveforms. The mean DBS waveforms for contralateral Patient 1 and ipsilateral Patient 3 exhibited a difference of approximately an order of magnitude (Fig. 3A). The mean peak DBS waveform amplitudes for ipsilateral Patients 3, 4, and 5 were 4.85, 7.04, and 4.77 mV. The mean peak DBS waveform amplitudes for contralateral Patients 1 and 2 were 0.34 and 0.27 mV. When compared with the DBS voltage of 3.0 V input into the brain there is an attenuation of approximately three orders of magnitude at 2 mm distance and four orders of magnitude at 24 mm distances (Fig. 3B).

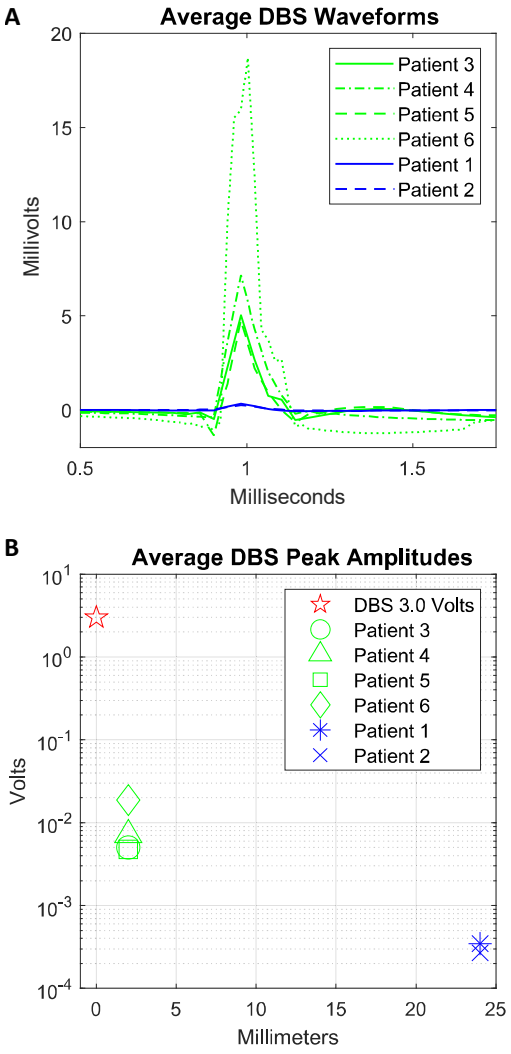


Figure 3. Average DBS waveforms and peak amplitudes. The mean DBS waveform across all DBS epochs for all ipsilateral patients (green) and all contralateral patients (blue) are shown (A). The average DBS peak voltage amplitudes across all DBS epochs for all patients are plotted against the distance of the microelectrode from the DBS electrodes. The 3 V DBS input is also shown (B).

### *B. Micro-Motion of Tissue & Electrodes*

Gradual changes in the DBS waveform amplitudes were observed in the time-voltage plots of the electrophysiological data (Fig. 1A). The changes in DBS waveform amplitude were readily apparent in ipsilateral recording configurations (Patients 3 – 6) but less obvious when recording contralaterally to the DBS electrodes (Patient 1 – 2, Fig. 1B). We compared the DBS waveform amplitude distributions for the first and last DBS epochs (Fig. 4A). The DBS waveform amplitudes for the first and last DBS epochs were not normally distributed (one-sample Kolmogorov-Smirnov test, $p < 0.001$). The change in DBS peak amplitudes from the first to the last DBS epoch was significant (Wilcoxon Ranksum test, $p < 0.001$) for all ipsilateral patients (Fig. 4B).

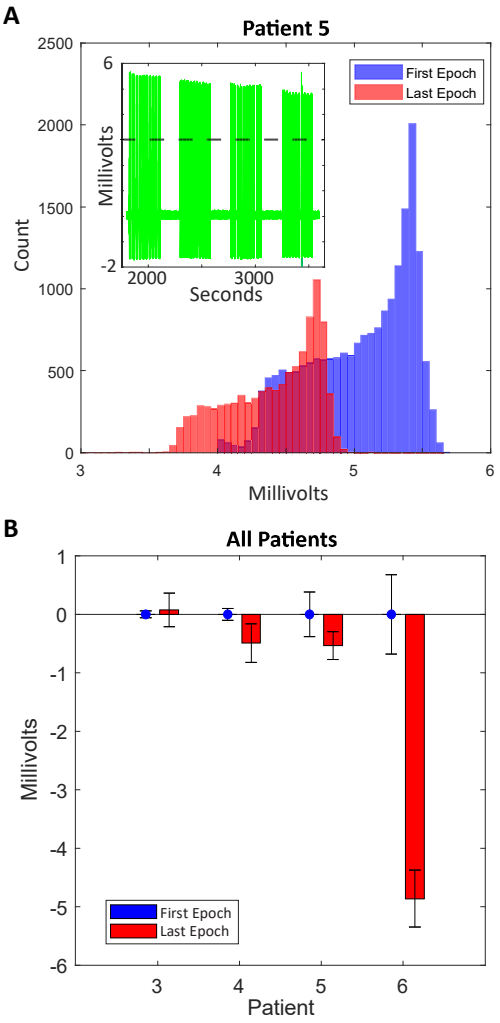


Figure 4. Changes in DBS waveform peak amplitudes over time. The electrophysiological data across all DBS epochs for an example ipsilateral configuration (Patient 5) are shown. The dashed black lines indicate the threshold used for DBS waveform detection (A, inset). The distributions of DBS waveform peak amplitudes from the first and last DBS epochs are shown (A). The mean and standard deviations of the DBS waveform peaks amplitudes for the first and last DBS epochs are shown for all ipsilateral patients (B). The mean peak amplitude for the first epoch was subtracted from the the data to emphasize the change in peak amplitudes regardless of the overall amplitude of the waveforms.

## IV. Discussion & Conclusion

### *A. Contralateral versus Ipsilateral*

In this study we elucidate the change in the amplitude of waveforms generated by DBS at different distances from the DBS electrodes. When comparing the DBS input voltage of 3 V to peaks of the waveforms generate by DBS at 2 mm

distance from the DBS electrodes, there was an amplitude reduction of approximately three orders of magnitude, i.e., 2.99 V. With the acute stimulation and recording paradigm used during this study it is unlikely that this large reduction in voltage is caused by any changes to the neural tissue, e.g., gliosis. It is likely that much of the observed attenuation of the DBS waveform amplitude is due to shunting between the anodic and cathodic electrodes through a thin layer of CSF surrounding the DBS lead [7]. The attenuation of DBS waveform amplitude at 24 mm distance observed between the ipsilaterally and contralaterally placed micro-electrode represents a more robust assessment of the influence of neural tissue on DBS. Within neural tissue the DBS waveform was attenuated by a much smaller factor, i.e., 0.606 mV. These results suggest that only a small fraction of the DBS voltage is injected into neural tissue.

### *B. First Epoch versus Last Epoch*

Significant changes in the amplitudes of DBS waveforms were observed overtime. In most patients (Patients 4 – 6) decreases in DBS waveform amplitudes were observed, however in one patient (Patient 3) an increase in amplitude was observed. Additionally, the distributions of DBS waveforms amplitudes were significantly non-normal. These finding demonstrate a non-stationary process influencing the DBS waveform amplitudes. Insertion of the DBS electrodes and the micro-electrode cause minor compression of the neural tissue. The DBS electrode is compliant and moves with the neural tissue, while the micro-electrode is ridged and fixed to the stereotaxic frame. We suggest that the observed non-stationary process is micro-scale changes in distance between the DBS electrodes and the micro-electrode cause by decompression of the neural tissue. The mean change in DBS waveform amplitude from the first to last DBS epoch was 1.5 mV. Assuming the change in distance is ~100 μM, then these findings suggest that small changes in distance result in amplitude changes of several percent.

In future work we plan on making measurements at multiple distances simultaneously and at very high sampling rates. This empirical data can serve as validation for computational modeling of DBS. Through the biophysical understanding of how DBS interacts with neural tissue and circuitry we hope to facilitate its application to other neurological disorders.

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