Abstract
Deep brain stimulation (DBS) in the subthalamic nucleus (STN) region reduces the motor symptoms of Parkinson’s disease (PD). In our previous study, we identified an optimal locus of stimulation to provide maximal motor symptomatic relief in a mathematically defined and atlas-independent manner. In the present study, we identified the optimal site of stimulation for the cardinal motor symptoms of PD: bradykinesia, rigidity, and tremor. In 46 patients treated with STN DBS for PD, we mapped active electrode position to Unified Parkinson’s Disease Rating Scale (UPDRS) improvement. We then applied a novel computational electrical field model of neuronal activation to provide a prediction of optimal lead location for each of the cardinal motor symptoms of PD across patients. Using our outcomes analysis and our electrophysiological model, we identified the optimal locus of stimulation for the individual motor symptoms (bradykinesia, rigidity, and tremor) and the overall stimulation site in PD patients to be in a region dorsal, posterior, and lateral to the anatomical midpoint of the STN. Our findings also suggest that it may be beneficial to target leads more anterior, yet still posterior, relative to the STN midpoint for the overall and rigidity sites, than is current practice.

Electrode Implantation Procedure

Clinical Outcomes Data and Optimal DBS Electrode Location

Figure 2 A, B. The average position for the high improvement-to-voltage ratio is 0.24 mm posterior, 0.11 mm lateral, and 1.87 mm dorsal to the STN midpoint. The average position for the low improvement-to-voltage ratio is 1.41 mm posterior, 0.03 mm lateral, and 1.87 mm dorsal to the STN midpoint. These data are have excluded the medically-refractory patients; however, the results between the two groups was not statistically significant. Additionally, the individual motor symptoms sites were not significantly different from the overall optimal site nor from one another (bradykinesia: 0.56 mm posterior, 0.12 mm lateral, 1.95 mm dorsal; rigidity: 0.03 mm posterior, 0.09 mm lateral, 1.95 mm dorsal; tremor: 0.59 mm posterior, 0.14 mm lateral, 1.79 mm dorsal; graphs not shown). The more anterior leads in the high improvement-to-voltage ratio were statistically significant compared to the posterior leads for the overall and rigidity sites ($p = 0.0154$ and, $p = 0.001$ respectively; Student’s T-test).

Probabilistic Model of Optimal Site Location

Figure 3 A heat map generated from our probabilistic model of neuronal activation showing the optimal site of stimulation for the most optimal outcomes in motor symptoms for Parkinsonian Patients. Our probabilistic model identified an optimal site at 0.17 mm lateral, 0.26 mm posterior, and 2.25 mm dorsal to the STN midpoint. The individual motor symptoms had optimal sites that were not significantly different from the overall site nor from one another (bradykinesia: 0.08 mm lateral, 0.81 mm posterior, 1.87 mm dorsal; rigidity: 0.08 mm lateral, 0.66 mm posterior, 1.83 mm dorsal; tremor: 0.03 mm lateral, 0.84 mm posterior, 1.81 mm dorsal; graphs not shown). This is represented in the above heat map (the most red area) with respect to the STN (the oblong shape penetrating the heat map).

Conclusions
• Our clinical outcomes and imaging data identified an optimal site for overall symptomatic improvement as well as for bradykinesia, rigidity, and tremor in a location lateral, posterior, and dorsal relative to the STN midpoint.
• Our probabilistic model also identified an optimal site that is posterior, lateral, and dorsal relative to the STN midpoint for the same motor symptoms.
• For both models, the individual motor symptoms were not significantly different from one another or from the overall optimal site.
• The optimal sites of DBS for PD patients that decreases motor UPDRS scores and also improves bradykinesia, rigidity, and tremor are located in the same region, suggesting that these motor symptoms share a common pathway within this area in the brain.

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