Asleep Robot-Assisted Surgery for the Implantation of Subthalamic Electrodes Provides the Same Clinical Improvement and Therapeutic Window as Awake Surgery

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■ OBJECTIVE: **To study the impact of not performing awake clinical evaluation during the robot-assisted implantation of subthalamic nucleus deep brain stimulation (STN-DBS) electrodes on the stimulation parameters and clinical outcomes in patients with Parkinson disease (PD).**

■ METHODS: **A total of 23 patients with PD underwent robot-assisted surgery for the bilateral implantation of STN-DBS electrodes. Thirteen patients received general anesthesia (GA) and a limited intraoperative evaluation (side effects only), and the other 10 patients received local anesthesia (LA) and a full evaluation. The primary endpoint was the therapeutic window (TW), defined as the difference between the mean voltage threshold for motor improvement and the mean voltage threshold for side effects in the active contacts at 12 months after surgery. Motor scores were measured as well.**

■ RESULTS: **The TW was similar in the LA and GA groups, with mean ± standard deviation values of 2.06 ± 0.53 V and 2.28 ± 0.99 V, respectively ($P = 0.32$). In the short term, the Unified Parkinson Disease Rating Scale (UPDRS) III score in the "off-drug, on-stim" condition fell to a similar extent in the LA and GA groups (by 40.3% and 49%, respectively; $P = 0.336$), as did the UPDRS III score in the "on-stim, on-drug" condition (by 57% and 70.7%, respectively; $P = 0.36$).**

■ CONCLUSIONS: **Asleep, robot-assisted implantation of STN-DBS electrodes (with accurate identification of the STN and positioning of the DBS lead) produced the same motor results and TW as awake surgery.**

INTRODUCTION

As one of the most effective treatments for advanced Parkinson disease (PD).[1] subthalamic nucleus deep brain stimulation (STN-DBS) is associated with dramatic reductions in both motor fluctuations and dyskinesia.[2] The implantation of STN-DBS electrodes is usually performed under local anesthesia (LA). This enables intraoperative electrophysiological mapping and awake clinical evaluation, to determine the best target location for the final electrode (i.e., the location with the best motor response and the fewest side effects).[3] After surgery, the electrode contact with the lowest threshold for inducing therapeutic effects and the broadest therapeutic window (TW; defined as the difference between the threshold for beneficial effects and the threshold for stimulation-induced side effects) is selected for chronic STN-DBS.[4] The efficacy of DBS has been shown to be directly related to the electrode's exact position within the STN.[5]

To improve patient comfort and minimize the risk of adverse events (AEs) during prolonged surgery, several centers perform

Key words
- Anesthesia
- Deep brain stimulation
- Parkinson's disease
- Robot-assisted electrode placement
- ROSA robot
- Subthalamic nucleus
- Therapeutic window

Abbreviations and Acronyms
AE: Adverse event
fpCT: Flat-panel computed tomography
GA: General anesthesia
HR-3D SWAN: High-resolution 3-dimensional T2*-weighted angiography
LA: Local anesthesia
LEDD: Levodopa equivalent daily dose
MER: Microelectrode recording
MRI: Magnetic resonance imaging
PD: Parkinson disease
PROIS: Patient-Rated Overall Improvement Score
STN-DBS: Subthalamic nucleus deep brain stimulation
TW: Therapeutic window
UPDRS: Unified Parkinson Disease Rating Scale

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STN-DBS surgery under general anesthesia (GA). This is becoming a valid option,[6,7] particularly for patients who experience severe off-medication symptoms.[8,9] However, some studies have reported that STN-DBS surgery under GA is associated with a smaller reduction in motor signs[8] and an elevated risk of cognitive decline.[7] In contrast, a recent trial of magnetic resonance imaging (MRI)-guided and -verified electrode placement found similar levels of motor improvement and similar or lower frequencies of AEs for GA compared with LA.[10,11] In these studies, the main efficacy criterion for the postoperative outcome was a reduction in the Unified Parkinson Disease Rating Scale (UPDRS) motor score. However, this measurement does not take into account the postoperative outcome as a whole, given that the clinical benefit of STN-DBS can be limited by a low threshold for the occurrence of side effects (i.e., a narrow TW). Thus, the TW is the key factor in DBS programming and overall postoperative outcome. Furthermore, asleep imaging-guided surgery increases patient comfort and might reduce the risk of AEs by shortening the duration of surgery.[11,12] Nonetheless, there is still no strong evidence showing that the therapeutic benefit is the same for asleep surgery (i.e., in the absence of awake clinical testing), mainly because previous studies comparing LA and GA did not consider the TW in their evaluation criteria and did not perform a direct comparison in the same patient population by applying the same inclusion criteria. The use of new technologies, such as the ROSA robot (Medtech, Montpellier, France) increases the accuracy of stereotactic surgery.[13-17] However, the clinical impact of robotic assistance has not been comprehensively evaluated, and whether this technique allows the surgeon to avoid performing awake clinical testing during STN-DBS electrode placement remains to be established.

The objective of the present study was to evaluate whether a robot-assisted procedure under GA and in the absence of awake clinical testing could provide the same degree of clinical improvement and the same TW as conventional STN-DBS electrode placement and testing under LA.

METHODS

Patients and Clinical Assessment

Twenty-three consecutive patients (14 men and 9 women) were included in this retrospective study after the completion of a 1-year observation period. All but 1 of the first 11 patients underwent surgery under LA (a patient with a respiratory disorder received GA), and all of the last 12 patients received GA.

Patients were evaluated within 12 months of surgery. The presurgery UPDRS part III motor score had been assessed in the "worst off-medication" condition and then in the "best on-medication" condition after the administration of a single suprathreshold dose of levodopa (as defined by the Core Assessment Program for Surgical Interventional Therapies in Parkinson's Disease).[18] The UPDRS part IV score provided an overall evaluation of motor complications. Levodopa-induced dyskinesia (UPDRS part IVa score) and motor fluctuations (UPDRS part IVb score) were rated for all patients. During the postsurgery follow-up, each patient was evaluated according to the UPDRS III under 4 different conditions: on-stimulation/worst off-medication, off-stimulation/worst off-medication, off-stimulation/best on-medication, and on-stimulation/best on-medication. The off-stimulation condition was defined as a return to the patient's "worst off" status after turning the stimulation off (for at least 1 hour in general). The levodopa equivalent daily dose (LEDD; as defined by Tomlinson et al.[19]) was noted, and each patient was asked to estimate the overall percentage improvement in his or her status at 1 year relative to baseline; this parameter is referred to below as the Patient-Rated Overall Improvement Score (PROIS). Cognitive function at 1 year was evaluated on the Mattis Dementia Rating Scale. Patients were also assessed for mood using either the Montgomery and Asberg Depression Scale or the Beck Depression Inventory. Apathy was rated according to the Lille Apathy Rating Scale or the Starkstein Apathy Scale. All AEs were recorded and classified into 1 of 2 categories (events associated with surgery or with the implanted device or stimulation).

In accordance with the tenets of the Declaration of Helsinki, all patients provided written informed consent. The study's objectives and procedures were approved by the local Institutional Review Board.

Surgical Procedure and Intraoperative Assessment

Our surgical procedure has been described in detail elsewhere.[14,20] All patients underwent T2 spin-echo MRI or high-resolution, 3-dimensional T2*-weighted angiography (HR-3D SWAN) for direct identification of the STN. Intraoperative microelectrode recording (MER) of the STN was performed in all cases. During MER, the robot and all other electrical devices were switched off. In the GA group, the depth of anesthesia was monitored as described by Fluchere et al.[10] In the LA group, 5 microelectrodes were always used for MER. In the GA group, we initially used 3 microelectrodes and then just 2. We progressively abandoned MER for more lateral/median or posterior trajectories, as a previous study had shown no significant differences between the anatomic and electrophysiological data when HR-3D SWAN sequences were used.[20] All surgical procedures were performed with a ROSA robot (Medtech, Montpellier, France) coupled to a flat-panel computed tomography (fpCT) device (O-arm Surgical Imaging System; Medtronic, Minneapolis, Minnesota, USA).

In the LA group, awake clinical testing after craniotomy was performed using the 2 or 3 electrodes that were the most electrophysiologically relevant, that is, those providing a typical electrical pattern for the STN (a sudden increase in background noise level and an increase in the discharge rate, characterized by rhythmic bursts of activity with a burst frequency of 5–20 Hz). The voltage was increased stepwise, to evaluate the effects on akinesia, tremor, and hypertonia. All side effects (and dyskinesia in particular) were documented. In the GA group, patients remained under anesthesia during MER and clinical testing. Only side effects were documented, with particular attention given to oculomotor side effects (eye deviation) and electrical effects that spread to the corticospinal tract (e.g., tonic contraction of one part of the contralateral hemibody).

After the microelectrodes were removed, the quadripolar STN-DBS electrodes (model 3389; Medtronic) were implanted bilaterally. In the LA group, the electrode in the STN with the best TW was chosen as the active electrode. In the GA group, the active