

# Electrode Position and the Clinical Outcome after Bilateral Subthalamic Nucleus Stimulation

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We compared the surgical outcome with electrode positions after bilateral subthalamic nucleus (STN) stimulation surgery for Parkinson's disease. Fifty-seven patients treated with bilateral STN stimulations were included in this study. Electrode positions were determined in the fused images of preoperative MRI and postoperative CT taken at six months after surgery. The patients were divided into three groups: group I, both electrodes in the STN; group II, only one electrode in the STN; group III, neither electrode in the STN. Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr stage, and activities of daily living scores significantly improved at 6 and 12 months after STN stimulation in both group I and II. The off-time UPDRS III speech subscore significantly improved ( $1.6 \pm 0.7$  at baseline vs  $1.3 \pm 0.8$  at 6 and 12 months,  $P < 0.01$ ) with least L-dopa equivalent daily dose (LEDD) ( $844.6 \pm 364.1$  mg/day at baseline;  $279.4 \pm 274.6$  mg/day at 6 months; and  $276.0 \pm 301.6$  mg/day at 12 months,  $P < 0.001$ ) at 6 and 12 months after STN deep brain stimulation (DBS) in the group I. Our findings suggest that the better symptom relief including speech with a reduced LEDD is expected in the patients whose electrodes are accurately positioned in both STN.

**Key Words:** Parkinson Disease; Bilateral STN Stimulation; Clinical Outcome; Electrode Position; Fused Images

## INTRODUCTION

The subthalamic nucleus (STN) stimulation has become the preferred treatment for the patients with advanced Parkinson's disease (PD) who have intolerable drug-induced side effects or motor complications following the long-term use of dopaminergic drugs (1, 2). The precise positioning of the electrodes into the STN is important for the good clinical outcome after surgery (2). Many approaches including image fusion of CT-MRI, MRI-MRI, and MRI-brain atlas as well as intraoperative microelectrode recording and stimulation have been practiced for the precise targeting of electrodes (3-7).

However, not all the patients have their electrodes positioned exactly in the STN after surgery. Therefore clinical outcome may differ according to the electrode positions. Possible brain shift due to cerebrospinal fluid (CSF) leakage (8-10), electrode artifacts in the MRI (11), and possible electrode bending during the

surgery may make it difficult to precisely localize the center of the electrodes at a short-term period after surgery (8-11). Thus it is reasonable to estimate the electrode positions at a stable period after surgery. However, little has been written in the literature on the clinical outcome and the electrode position estimated at a stable period after surgery.

Previously we compared the clinical outcomes at 3 and 6 months after bilateral STN stimulation with the electrode positions estimated by the fused images of the pre- and post-operative MRI taken at 6 months by using mutual information technique (12). During the study period we noted that the center of the electrode's MRI artifact in the postoperative MRI was different from the center of electrode estimated by the postoperative CT. Therefore we compared the outcomes at 6 and 12 months after bilateral STN stimulation depending on electrode positions identified in the fused images of the preoperative MRI and the postoperative CT taken at six months after surgery.

## MATERIALS AND METHODS

### Patients

Fifty-seven patients with advanced PD who had been treated with bilateral STN stimulation between March 2005 and October 2006 and followed up more than one-year at the Movement Disorder Center of Seoul National University Hospital (SNUH) were enrolled in this study. The indications of bilateral STN stimulation were advanced PD with at least two cardinal features of parkinsonism, a good response to levodopa, drug-induced side effects such as dyskinesia, or motor fluctuation, and the unsatisfactory management with medication. Patients with severe cognitive impairment, ongoing psychiatric problems, an unsatisfactory general condition for surgery, or an inability to comply with the study protocol, were excluded.

### Clinical evaluation

The patients were evaluated with the use of the Unified Parkinson Disease Rating Scale (UPDRS), Hoehn and Yahr (H&Y) Stage, Schwab and England Activities of Daily Living (SEADL), the Short Form-36 Health Survey (SF-36), and neuropsychological tests (the detailed items were described elsewhere) (13). Evaluations were performed before surgery, at 6 and 12 months after surgery, and then every year. The neurological evaluations were performed by two neurologists. Patients were assessed in two conditions; *off*- (12-hr medication off) and *on*-medication (1 to 3 hr after usual morning dose) conditions. The daily levodopa equivalent dose (LEDD) was computed as described elsewhere (12). The clinical information of the 57 patients is summarized in Table 1.

### Surgical procedure

In all cases, a stereotactic Leksell®-G frame (Elekta Instruments AB, Stockholm, Sweden) was mounted on the head of a patient under local anesthesia. Brain images were acquired on a 1.5-T Signa system (General Electric Medical System, Milwaukee, WI, USA). The STNs were localized by a combination of direct visualization by MRI, microelectrode recording (MER), and stimulation technique as previously described elsewhere (12). The quadripolar chronic electrodes (DBS 3389, Medtronic, Minneapolis, MN, USA) were indwelled under the local anesthesia and the implantable pulse generators (IPG) were then implanted subcutaneously under the general anesthesia in a single session.

Electrical stimulation was started one day after surgery. The stimulation parameters and medications were progressively adjusted using an N'vision® programmer (Medtronic) (12).

### Adjustment after bilateral STN stimulation

An examination of the effectiveness and side effects of the four contacts of the electrodes was performed using an N'vision® programmer (Medtronic) in all patients to select the best contact of

the electrodes and electrical settings for chronic stimulation by neurologists. After turning on the minimal stimulation starting at the lowest level around 1.0 volts, the medication and stimulation parameter were optimized to the demand for the best status of motor functions in harmony with the DBS programming.

### Image fusion of preoperative MRI and postoperative CT

Three-dimensional (3-D) spiral stereotactic CT scans (64-channel Brilliance CT, Philips, Eindhoven, Netherlands) with a 1 mm slice thickness were taken 6 months after bilateral STN stimulation to localize the electrodes by image fusion with preoperative MRI by using mutual information techniques (Fig. 1) (12, 14-18). With CT-MRI image fusion, the electrodes positions were plotted on the human brain atlas of Schaltenbrand and Wahren (19). In brief, the lateral distance from the midline and the antero-posterior distance from the mid-commissural line to each electrode were measured in the reformatted axial images (Fig. 1A). The lateral angles of the electrode trajectory from the midline, and the antero-posterior angle of the electrode trajectory from the line perpendicular to the anterior (AC) - posterior commissural (PC) line and the depth of the electrodes are also measured in the reformatted coronal (Fig. 1B) and sagittal images (Fig. 1C), respectively.

Based on the plotted electrode position on the axial view at the level of 3.5 mm below the AC-PC line, we categorized the electrode positions into three groups: 1) group I, both electrodes in the STN (n = 36); 2) group II, only one electrode in the STN (n = 16); 3) group III, neither electrode in the STN (n = 5) (Fig. 2). The clinical information of the patients in each group is summarized in Table 1.

### Statistical analysis

The primary outcome measures were the total scores and part III scores of the UPDRS; the H&Y stage; the SEADL; the dyskinesia subscores on part IV of the UPDRS; the LEDD; the SF-36; and neuropsychological tests. The secondary measures were the subscores on the part III of the UPDRS. The data for those variables were presented as the mean  $\pm$  standard deviation. Repeated measured ANOVAs were performed to observe the within-factor effect of 3 times measured at the baseline before surgery and 6 and 12 months after surgery and the between-factor effect of 3 groups (group I, II, and III) classified by the electrode positions in STN on the averages of clinical outcomes with scores.

For the baseline characteristics of the 57 patients, one-way ANOVA and chi-square or Fisher's exact test were conducted to find the 3-group differences in the distribution of continuous variables and in the frequency of discrete variables, such as gender. To adjust for multiple comparisons within each outcome, we computed *P* values on Bonferroni correction of each outcome. All statistical analyses were used in SAS version 9.1 (SAS institute, Cary, NC, USA).

**Table 1.** Baseline characteristics of the 57 patients

Parameters	Total (n = 57)	Group I (n = 36)	Group II (n = 16)	Group III (n = 5)	<i>P</i> value <sup>1</sup> (3-group difference)
Gender (number of patients)					
Male	26	15	7	4	0.268
Female	31	21	9	1	
Age (yr)					
Mean ± S.D.	60.1 ± 8.7	60.5 ± 7.8	57.4 ± 10.7	65.2 ± 6.4	0.197
Range	28-72	41-74	28-68	57-73	
Body weight (kg)					
Mean ± S.D.	57.8 ± 10.0	57.6 ± 11.5	56.6 ± 8.1	61.7 ± 6.3	0.627
Symptom duration (yr)					
Mean ± S.D.	12.6 ± 5.1	12.6 ± 4.8	11.4 ± 3.5	16.4 ± 9.3	0.154
Range	5-32	5-27	5-17	8-32	
Duration of medication (yr)					
Mean ± S.D.	11.0 ± 3.8	11.2 ± 4.3	10.1 ± 2.6	12.0 ± 2.4	0.489
Range	4-23	4-23	5-14	9-15	
LEDD (mg/day)*					
Mean ± S.D.	890.8 ± 404.5	844.6 ± 364.1	1038.0 ± 496.6	752.0 ± 276.6	0.207
Total UPDRS score					
On-medication					
Mean ± S.D.	33.5 ± 19.2	32.1 ± 20.7	35.6 ± 19.4	33.5 ± 19.2	0.926
Range	5-91	10-91	11-65	5-91	
Off-medication					
Mean ± S.D.	68.7 ± 19.6	68.9 ± 22.1	67.5 ± 13.3	68.7 ± 19.6	0.990
Range	22-117	33-117	49-84	22-117	
UPDRS part III score					
On-medication					
Mean ± S.D.	21.1 ± 12.8	23.3 ± 15.6	23.5 ± 10.2	21.1 ± 12.8	0.606
Range	2-59	7-59	11-39	2-59	
Off-medication					
Mean ± S.D.	40.1 ± 14.4	40.4 ± 18.2	39.8 ± 8.4	40.1 ± 14.4	0.995
Range	9-78	13-78	28-49	9-78	
Hoehn & Yahr Stage					
On-medication					
Mean ± S.D.	2.4 ± 0.7	2.3 ± 0.7	2.7 ± 0.8	2.4 ± 0.7	0.577
Range	1-4	1-4	2-4	1-4	
Off-medication					
Mean ± S.D.	3.3 ± 0.9	3.2 ± 0.8	3.8 ± 0.4	3.3 ± 0.9	0.390
Range	2-5	2-5	3-4	2-5	
Schwab & England ADL					
On-medication					
Mean ± S.D.	79.7 ± 15.2	83.4 ± 16.4	81.0 ± 11.4	79.7 ± 15.2	0.483
Range	30-100	40-100	70-100	30-100	
Off-medication					
Mean ± S.D.	50.4 ± 20.8	48.4 ± 23.1	44.0 ± 15.2	50.4 ± 20.8	0.659
Range	10-90	10-80	20-60	10-90	
Good awake time (%)					
Mean ± S.D.	57.1 ± 20.1	58.7 ± 20.1	58.1 ± 19.8	42.5 ± 19.2	0.236
Range	16.7-100	25-100	20.8-83.3	16.7-66.7	
Dyskinesia disability					
Mean ± S.D.	2.2 ± 1.4	2.1 ± 1.4	2.3 ± 1.5	3.2 ± 0.8	0.253
Range	0-4	0-4	0-4	2-4	

<sup>1</sup>For gender (discrete scale), the *P* value was estimated by chi-square test; For other variables (continuous scale), the *P* value was estimated by ANOVA (Analysis of Variances).

\*Daily levodopa equivalent dose (LEDD) was calculated for each antiparkinsonian medication by multiplying the total daily dosage of each drug by its potency relative to a standard levodopa preparation assigned at the value of 1. The following conversion factors were used: levodopa controlled release = 0.77, bromocriptine = 10, ropinirole = 20, pramipexole = 100, and pergolide = 100. One patient had a cardiac pacemaker for the sick sinus syndrome prior to STN DBS. Two patients had previous thalamotomy. ADL, Activities of Daily Life; LEDD, Daily levodopa equivalent dose; UPDRS, Unified Parkinson's Disease Rating Scale.

### Ethical statement

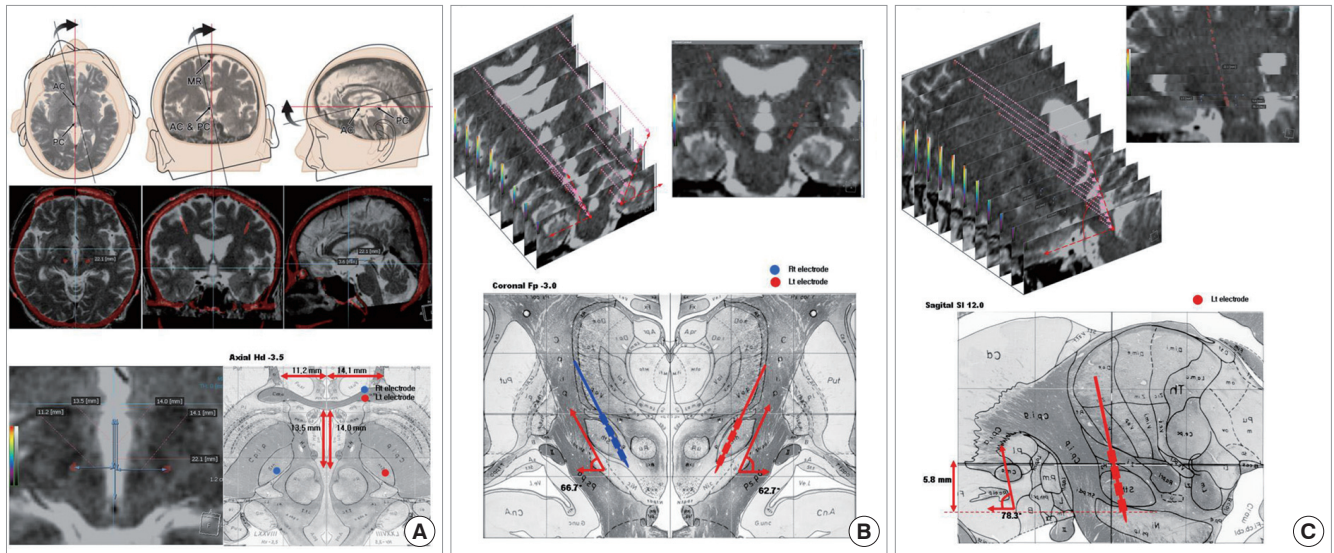
The institutional review board of SNUH approved this study (IRB number:H-0711-023-225). This study is exempted from receiving patient consents due to retrospective review of medical records.

### RESULTS

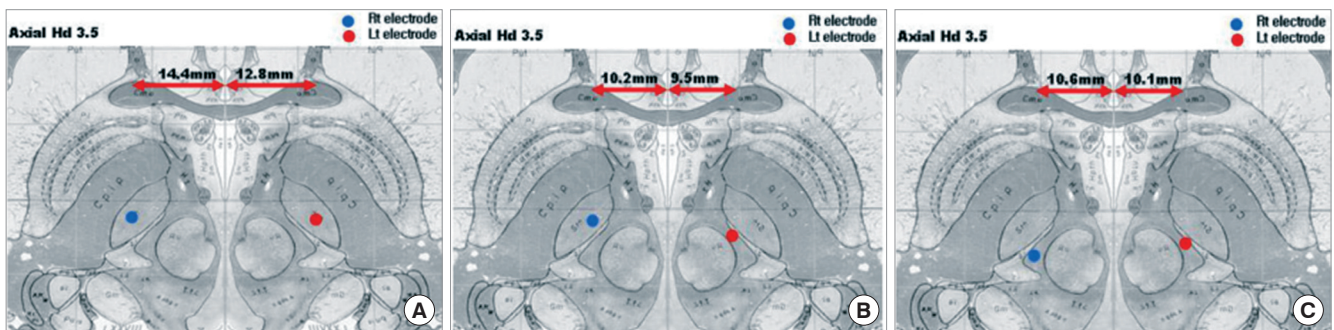
#### Primary outcome after bilateral STN stimulation

The outcomes were compared between preoperative and postoperative status at 6 and 12 months after bilateral STN stimula-





**Fig. 1.** Fused images of the preoperative MRI and postoperative CT. The T2-weighted axial images of brain MRI taken before surgery are fused with 3-D spiral CT scan images at the data set of 1-mm thickness reformatted images, aligned to anterior commissure - posterior commissure (AC-PC) line. The midline of reformatted coronal images also intersect the midsagittal plane for the correction of head-rotation error. The length of AC-PC line and width of the third ventricle are taken into consideration for the proportional localization of the electrodes position in the human brain atlas of Schaltenbrad and Wahren. In the reformatted axial images the lateral distance from the midline and the antero-posterior distance from the mid-commissural line to each electrode are measured (A). In the reformatted coronal images in which the electrode trajectory is best visualized, the lateral angles of the electrode trajectory from the midline are measured for each electrode in every patient (B). In the reformatted sagittal images in which the electrode trajectory is best shown, the antero-posterior angle of the electrode trajectory from the line perpendicular to the AC-PC line and the depth of the electrodes are also measured for each electrode in every patient (C).



**Fig. 2.** Plotting of electrode positions in the human brain atlas. With the information from the fused images of preoperative MRI and postoperative CT taken at 6 months after surgery as shown in Fig. 1, the electrode positions are plotted on the human brain atlas of Schaltenbrand and Wahren in each patient. Representative illustration of the electrode positions (A-C) are plotted in the axial, sagittal, and coronal planes. Based on the axial view at the level of 3.5 mm below the AC-PC line in the atlas, electrode positions (in blue and red colors) are categorized into three groups: 1) group I, both electrodes in the STN ( $n = 36$ ) (A); 2) group II, only one electrode in the STN ( $n = 16$ ) (B); 3) group III, neither electrode in the STN ( $n = 5$ ) (C).

tion (Table 2). Significant improvement in off-time scores of total UPDRS, UPDRS III, H&Y scores, SEADL, and dyskinesia disability with decreased LEDD was observed at 6 and 12 months after surgery in the group I and II or as a whole group. The LEDD tended to be low in the patients of group I at 6 and 12 months after surgery ( $844.6 \pm 364.1$  at baseline;  $279.4 \pm 274.6$  at 6 months; and  $276.0 \pm 301.6$  at 12 months;  $P$ -interaction = 0.023).

Regarding the eight sub-scales of the SF-36, the scores of bodily pain and summary scores of physical health improved at 6 and 12 months after surgery in the patients as a whole group. From the neuropsychological evaluation, the verbal memory test using Rey-Kim memory battery showed the decline in rec-

ognition at 6-month follow up in the patients as a whole group ( $P = 0.002$ ), whereas nonverbal memory showed no meaningful change. In frontal lobe function tests, the Stroop test (Stroop-a,  $P = 0.006$ ; Stroop-b,  $P = 0.004$ ; Stroop-c,  $P = 0.034$ ) and the fluency test ( $P = 0.013$ ) tended to aggravate at 6 and 12 months after the surgery, especially in the group III ( $P = 0.046$  for Stroop-a;  $P = 0.053$  for fluency), but lacked statistical significance after a Bonferroni correction. Other tests including Boston Naming test, Grooved Pegboard test, Mini-Mental state examination, Trail-Making test, Beck Depression Inventory, and Wisconsin Card Sorting test, did not show significant changes.

The average stimulation parameters of the patients as a whole

**Table 2.** The clinical outcomes of 57 patients after bilateral subthalamic nucleus stimulation

	Medi- cation	Total subjects				Subjects according to each group						
		Baseline	6 months <sup>1</sup>	12 months <sup>1</sup>	<i>P</i> value <sup>2</sup>	Group	Baseline	6 months <sup>1</sup>	12 months <sup>1</sup>	<i>P</i> value <sup>2</sup> for within- factor	<i>P</i> value <sup>3</sup> for group- factor	<i>P</i> value <sup>4</sup> for interac- tion
Total UPDRS	On	33.5 ± 19.2	29.3 ± 13.7	29.4 ± 14.0	0.079	I	33.9 ± 19.1	28.3 ± 14.8	28.1 ± 14.6	0.717	0.421	0.840
						II	32.1 ± 20.7	30.4 ± 10.9	29.8 ± 11.9			
						III	35.6 ± 19.4	32.9 ± 15.0	37.0 ± 15.6			
	Off	68.7 ± 19.6 <sup>†</sup>	46.7 ± 18.3	42.6 ± 17.0	< 0.001*	I	68.8 ± 19.7 <sup>†</sup>	44.4 ± 18.7	39.5 ± 17.9			
						II	68.9 ± 22.1 <sup>†</sup>	50.5 ± 18.0	43.4 ± 12.0			
						III	67.5 ± 13.3	51.2 ± 17.4	62.5 ± 11.2 <sup>†</sup>			
UPDRS III	On	21.1 ± 12.8 <sup>†</sup>	16.0 ± 9.2	16.1 ± 8.2	0.003*	I	19.8 ± 11.9	16.2 ± 9.9	15.3 ± 9.2	0.016*	0.578	0.601
						II	23.3 ± 15.6	15.4 ± 7.9	16.4 ± 5.4			
						III	23.5 ± 10.2	16.9 ± 8.3 <sup>†</sup>	20.6 ± 7.2			
	Off	40.1 ± 14.4 <sup>†</sup>	23.7 ± 12.4	21.3 ± 9.3	< 0.001*	I	40.0 ± 13.6 <sup>†</sup>	23.1 ± 12.9	20.1 ± 10.0			
						II	40.4 ± 18.2 <sup>†</sup>	24.1 ± 11.7	21.6 ± 7.2			
						III	39.8 ± 8.4	26.4 ± 13.3	28.5 ± 8.1			
Hoehn & Yahr Stage	On	2.4 ± 0.7	2.3 ± 0.7	2.4 ± 0.7	0.815	I	2.4 ± 0.7	2.3 ± 0.6	2.3 ± 0.7	0.431	0.146	0.522
						II	2.4 ± 0.7	2.2 ± 0.7	2.3 ± 0.4			
						III	2.7 ± 0.8	2.6 ± 1.1	3.1 ± 0.5 <sup>†</sup>			
	Off	3.3 ± 0.9 <sup>†</sup>	2.6 ± 0.7	2.6 ± 0.6	< 0.001*	I	3.3 ± 0.9 <sup>†</sup>	2.6 ± 0.7	2.5 ± 0.5			
						II	3.3 ± 0.9 <sup>†</sup>	2.5 ± 0.7	2.5 ± 0.5			
						III	3.8 ± 0.4	3.1 ± 1.1	3.3 ± 1.0 <sup>†</sup>			
Schwab & England ADL	On	79.7 ± 15.2	82.0 ± 15.3	83.0 ± 13.5	0.325	I	77.9 ± 15.2 <sup>†</sup>	84.4 ± 11.3	84.4 ± 11.1	0.769	0.320	0.036*
						II	83.8 ± 16.0	78.7 ± 16.4	84.4 ± 8.9			
						III	81.0 ± 11.4	74.0 ± 31.3	68.0 ± 29.5 <sup>†</sup>			
	Off	50.4 ± 20.8 <sup>†</sup>	66.4 ± 18.6	71.2 ± 18.7	< 0.001*	I	52.1 ± 20.7 <sup>†</sup>	68.3 ± 16.6	73.9 ± 18.9			
						II	45.6 ± 25.2 <sup>†</sup>	64.7 ± 21.3	72.5 ± 12.4			
						III	40.0 ± 15.2	58.0 ± 24.9	48.0 ± 21.9 <sup>†</sup>			
Dyskinesia disability		2.2 ± 1.4 <sup>†</sup>	0.8 ± 1.2	1.0 ± 1.4	< 0.001*	I	2.1 ± 1.4 <sup>†</sup>	0.8 ± 1.2	0.9 ± 1.3	< 0.001*	0.306	0.718
					II	2.3 ± 1.5 <sup>†</sup>	0.5 ± 1.2	1.1 ± 1.5				
					III	3.2 ± 0.8	1.2 ± 1.8	1.4 ± 1.9				
LEDD (mg/day)		890.8 ± 404.5 <sup>†</sup>	344.3 ± 317.8	340.0 ± 322.6	< 0.001*	I	844.6 ± 364.1 <sup>†</sup>	279.4 ± 274.6	276.0 ± 301.6	< 0.001*	0.149	0.023*
					II	1038.0 ± 496.6 <sup>†</sup>	373.5 ± 269.8	396.1 ± 241.1				
					III	750.0 ± 276.6	724.0 ± 502.9 <sup>†</sup>	691.3 ± 574.0 <sup>†</sup>				

All data was expressed as a mean ± standard deviation. \**P* < 0.05. The bold-faced *P* values were statistically significant (*P* < 0.005) after Bonferroni multiple comparison correction of 10 clinical outcomes; <sup>†</sup>significant different group among three groups or three repeated measured outcomes in the repeated measures ANOVA. <sup>1</sup>, with DBS stimulation; <sup>2</sup>, *P* value for within-factor of three repeated measured outcomes at the baseline and 6 and 12 months after bilateral STN stimulation; <sup>3</sup>, *P* value for between-group-factor of three groups: I (both electrodes in the STN), II (only 1 electrode in the STN) and III (neither electrode in the STN); <sup>4</sup>, *P* value for interaction between the within-factor and between-group-factor. Abbreviations as Table 1.

group are 2.6 V (± 0.6 V) in amplitude, 60.6 μsec (± 4.4 μsec) in pulse width, and 139.1 Hz (± 15.7 Hz) in frequency. The average stimulation parameters of the patients in group I are 2.6 V (± 0.6 V) in amplitude, 60.5 μsec (± 3.8 μsec) in pulse width, and 137.6 Hz (± 15.2 Hz) in frequency. The average stimulation parameters of the patients in group II are 2.6 V (± 0.6 V) in amplitude, 61.3 μsec (± 6.1 μsec) in pulse width, and 142.0 Hz (± 17.0 Hz) in frequency. The average stimulation parameters of the patients in group III are 2.2 V (± 0.9 V) in amplitude, 60.0 μsec (± 6.0 μsec) in pulse width, and 140.5 Hz (± 16.2 Hz) in frequency.

#### UPDRS part III subscores after bilateral STN stimulation

The subscores of UPDRS III were compared between preoperative and postoperative status at 6 and 12 months after bilateral STN stimulation (Table 3). The off- and on-time tremor and rigidity, the off-time bradykinesia, the off-time gait and postural stability subscores significantly improved at 6 months and 12 months after surgery in the group I and II or as a whole group.

The off-time UPDRS III speech subscore significantly improved at 6 and 12 months after STN DBS in the group I (1.6 ± 0.7 at baseline vs 1.3 ± 0.8 at 6 and 12 months; *P* < 0.01 by paired t-tests) (*P*-interaction = 0.008). But no significant improvement was observed in other groups. We further confirmed the speech improvement by comparing the sum of the speech subscores of UPDRS-II and UPDRS-III between preoperative and postoperative status at 12 month after STN DBS in three groups (*P* for trend = 0.003) (Table 4).

#### Outcomes of 13 patients with nil LEDD after bilateral STN stimulation

Among 57 patients, the LEDD of 13 patients was zero at their last follow up. Their preoperative characteristics were not different from the other patients. Their total UPDRS scores, H&Y Stage, SEADL, and dyskinesia disability scores dramatically improved at 12 months after STN DBS (Table 5). Their off-time UPDRS part III subscores including speech were significantly improved at

**Table 3.** UPDRS-III subscores of 57 patients after bilateral subthalamic nucleus stimulation

	Medication	Total subjects				Subjects according to each group (group 1, n = 36; group 2, n = 16; group 3, n = 5)						
		Baseline	6 months <sup>1</sup>	12 months <sup>1</sup>	P value <sup>2</sup>	Group	Baseline	6 months <sup>1</sup>	12 months <sup>1</sup>	P value <sup>2</sup> for group-factor	P value <sup>3</sup> for group-factor	P value <sup>4</sup> for group-factor
Speech	On	1.2 ± 0.7	1.2 ± 0.8	1.3 ± 0.9	0.772	I	1.2 ± 0.8	1.1 ± 0.8	1.2 ± 0.9	0.103	0.171	0.060
						II	1.3 ± 0.6	1.4 ± 0.8	1.4 ± 0.8			
						III	1.1 ± 0.9	1.9 ± 1.1 <sup>†</sup>	1.9 ± 1.1			
	Off	1.5 ± 0.7	1.4 ± 0.8	1.4 ± 0.8	0.119	I	1.6 ± 0.7 <sup>‡</sup>	1.3 ± 0.8 <sup>‡</sup>	1.3 ± 0.8 <sup>‡</sup>	0.388	0.402	0.008*
						II	1.5 ± 0.5	1.6 ± 0.6	1.4 ± 0.7			
						III	1.3 ± 0.9	2.1 ± 0.7 <sup>†</sup>	1.9 ± 1.1			
Tremor	On	2.4 ± 2.9 <sup>†</sup>	0.5 ± 1.4	0.3 ± 0.9	< 0.001*	I	2.0 ± 3.0 <sup>†</sup>	0.6 ± 1.6	0.4 ± 1.0	< 0.001*	0.888	0.385
						II	2.8 ± 2.8 <sup>†</sup>	0.3 ± 0.6	0.3 ± 0.7			
						III	3.0 ± 2.8 <sup>†</sup>	0.2 ± 0.4	0.2 ± 0.5			
	Off	6.2 ± 5.2 <sup>†</sup>	1.6 ± 2.8	0.7 ± 1.7	< 0.001*	I	5.6 ± 5.1 <sup>†</sup>	1.4 ± 2.2	0.5 ± 1.5	< 0.001*	0.230	0.583
						II	7.3 ± 5.6 <sup>†</sup>	2.5 ± 4.0	1.3 ± 2.4			
						III	7.2 ± 4.5 <sup>†</sup>	0.4 ± 0.9	0.3 ± 0.7			
Rigidity	On	4.1 ± 3.6 <sup>†</sup>	2.7 ± 3.4	2.5 ± 2.7	0.004*	I	3.4 ± 3.3	2.7 ± 3.6	2.0 ± 2.6	0.007*	0.275	0.481
						II	5.2 ± 4.4	2.7 ± 2.9	3.3 ± 2.8			
						III	5.5 ± 2.5	2.6 ± 4.0	3.2 ± 3.7			
	Off	7.9 ± 3.9 <sup>†</sup>	4.3 ± 3.9	3.5 ± 3.3	< 0.001*	I	7.4 ± 3.9 <sup>†</sup>	4.2 ± 4.0	3.2 ± 3.4	< 0.001*	0.526	0.772
						II	9.2 ± 4.3 <sup>†</sup>	4.2 ± 3.6	3.8 ± 3.2			
						III	8.2 ± 2.5	5.0 ± 4.7	4.8 ± 3.0			
Bradykinesia	On	7.7 ± 5.3	6.6 ± 5.3	6.7 ± 4.4	0.222	I	7.8 ± 5.2	7.8 ± 5.2	6.7 ± 4.9	0.394	0.965	0.606
						II	7.9 ± 6.2	5.7 ± 4.7	6.3 ± 3.6			
						III	6.5 ± 3.4	5.8 ± 3.9	8.2 ± 3.0			
	Off	13.2 ± 6.6 <sup>†</sup>	9.0 ± 5.9	8.9 ± 4.7	< 0.001*	I	14.3 ± 6.4 <sup>†</sup>	9.3 ± 6.2	8.8 ± 5.3	0.006*	0.744	0.211
						II	11.5 ± 7.3	8.3 ± 5.8	8.6 ± 4.0			
						III	10.9 ± 4.8	9.1 ± 5.0	11.3 ± 2.8			
Gait	On	0.8 ± 0.7	0.9 ± 0.7	1.0 ± 0.7	0.104	I	0.7 ± 0.6	0.8 ± 0.7	0.9 ± 0.7	0.053	0.436	0.556
						II	0.9 ± 0.9	1.0 ± 0.8	1.1 ± 0.7			
						III	0.8 ± 0.8	0.9 ± 0.7 <sup>†</sup>	1.5 ± 0.7 <sup>†</sup>			
	Off	1.9 ± 0.9 <sup>†</sup>	1.3 ± 0.8	1.3 ± 0.9	< 0.001*	I	1.9 ± 1.0 <sup>†</sup>	1.3 ± 0.8	1.2 ± 0.7	0.019*	0.547	0.287
						II	1.8 ± 0.8	1.4 ± 0.7	1.4 ± 0.9			
						III	1.9 ± 0.7	1.4 ± 1.7	2.1 ± 1.2 <sup>†</sup>			
Postural stability	On	1.1 ± 0.8 <sup>†</sup>	0.7 ± 0.8	0.8 ± 0.8	0.007*	I	1.1 ± 0.8 <sup>†</sup>	0.7 ± 0.8	0.8 ± 0.8	0.116	0.105	0.648
						II	1.1 ± 0.9	0.7 ± 0.7	0.6 ± 0.8			
						III	1.5 ± 0.7 <sup>†</sup>	1.2 ± 0.8	1.6 ± 0.6 <sup>†</sup>			
	Off	1.8 ± 0.9 <sup>†</sup>	1.2 ± 0.9	1.1 ± 0.9	< 0.001*	I	1.8 ± 1.0 <sup>†</sup>	1.2 ± 0.9	1.0 ± 0.8	0.001*	0.173	0.241
						II	1.8 ± 0.8 <sup>†</sup>	1.1 ± 0.8	0.9 ± 0.8			
						III	2.0 ± 0.7	1.6 ± 0.9	2.1 ± 0.5 <sup>†</sup>			

All data was expressed as a mean ± standard deviation. \**P* < 0.05. The bold-faced p-values were statistically significant (*P* < 0.004) after Bonferroni multiple comparison correction of 12 UPDRS III subscores. <sup>†</sup>significant different group among three groups or three repeated measured outcomes in the repeated measures ANOVA with post-hoc tests. <sup>‡</sup>The speech subscore at 6 months or at 12 months was significantly lower than that at baseline (paired t-test, *P* < 0.001 for 6 months vs baseline; *P* < 0.001 for 12 months vs baseline). <sup>1</sup>, with DBS stimulation; <sup>2</sup>, *P* value for within-factor of three repeated measured outcomes at the baseline and 6 months and 12 months after bilateral STN stimulation; <sup>3</sup>, *P* value for between-group-factor of three groups: I (both electrodes in the STN), II (only 1 electrode in the STN) and III (neither electrode in the STN); <sup>4</sup>, *P* value for interaction between the within-factor and between-group-factor effects.

**Table 4.** Speech outcomes of 57 patients after bilateral subthalamic nucleus stimulation

	Group I	Group II	Group III	Total
Aggravated	13 (36%)	11 (69%)	5 (100%)	28 (49%)
Stationary	5 (14%)	1 (6%)	0	7 (12%)
Improved	18 (50%)	4 (25%)	0	22 (39%)
Total	36	16	5	57

Mantel-Haenszel chi-square test for trend, chi-square value = 8.819 (degree of freedom = 1), *P* value = 0.003. Three groups were classified by the fused images of preoperative MRI and postoperative CT scans taken six months after surgery: group I, both electrodes in the STN; group II, only 1 electrode in the STN; group III; neither electrode in the STN. The assessment of speech improvement was based on the summation of the speech subscores of UPDRS part II and part III. All patients were evaluated at 12 months after bilateral STN stimulation.

12 months after surgery (Table 6). Looking into their electrode position, all patients have both electrodes mostly positioned into middle one third of the STN on axial view at the level of 3.5 mm below the AC-PC line (Fig. 3A). The x, y, z coordinates of the active contacts referenced to the AC-PC midpoint in these patients are depicted in Fig. 3B. The mean (SD) x, y, z coordinates of active contacts were 12.6 (1.5), -1.2 (1.0), and 3.6 (0.9) on the left electrodes and 12.0 (1.8), -0.5 (0.9), and 3.7 (1.1) on the right electrodes.

**Complications**

Thirteen (22.8%) of 57 patients had complications after surgery.

**Table 5.** Clinical outcomes of nil-LEDD patients after bilateral subthalamic nucleus stimulation

	Medication	Group <sup>†</sup>	Baseline	On-DBS stimulation		Off-DBS stimulation		Baseline vs On-DBS stimulation			Baseline vs Off-DBS stimulation			
				6 months	12 months	6 months	12 months	P value <sup>1</sup> for within-factor	P value <sup>2</sup> for group-factor	P value <sup>3</sup> for interaction	P value <sup>1</sup> for within-factor	P value <sup>2</sup> for group-factor	P value <sup>3</sup> for interaction	
Total UPDRS	On	nil-LEDD	42.8 ±	29.6 ±	32.9 ±				0.016*	0.171	0.105			
		Others	24.5	15.4	13.8									
			30.9 ±	29.2 ±	28.3 ±									
	Off	nil-LEDD	74.3 ±	42.7 ±	39.1 ±				< 0.001*	0.853	0.051			
		Others	25.3 <sup>†</sup>	18.4	18.6									
			67.0 ±	47.9 ±	43.6 ±									
UPDRS III	On	nil-LEDD	21.5 ±	16.8 ±	16.6 ±	29.4 ±	33.8 ±	0.017*	0.798	0.961	< 0.001*	0.553	0.346	
		Others	17.1	10.5	10.9	12.0	17.2							
			20.9 ±	15.8 ±	15.9 ±	29.6 ±	27.8 ±							
	Off	nil-LEDD	41.9 ±	21.6 ±	19.2 ±	35.3 ±	37.0 ±	< 0.001*	0.724	0.364	0.012*	0.702	0.679	
		Others	18.3 <sup>†</sup>	12.7	11.0	15.5	17.2							
			39.5 ±	24.3 ±	21.9 ±	35.8 ±	34.1 ±							
Hoehn & Yahr Stage	On	nil-LEDD	2.2 ±	2.3 ±	2.4 ±	3.2 ±	3.1 ±	0.884	0.778	0.354	< 0.001*	0.346	0.062	
		Others	0.8	0.6	0.6	1.1	1.2							
			2.4 ±	2.3 ±	2.3 ±	2.8 ±	2.7 ±							
	Off	nil-LEDD	3.1 ±	2.6 ±	2.4 ±	3.5 ±	3.2 ±	< 0.001*	0.320	0.410	0.177	0.704	0.038	
		Others	1.1	0.7	0.6	1.2	1.2							
			3.4 ±	2.6 ±	2.6 ±	3.1 ±	2.9 ±							
Schwab & England ADL	On	nil-LEDD	70.8 ±	80.8 ±	80.8 ±			0.072	0.128	0.122				
		Others	19.8	13.2	11.9									
			82.4 ±	82.3 ±	83.6 ±									
	Off	nil-LEDD	51.7 ±	66.5 ±	77.7 ±			< 0.001*	0.343	0.565				
		Others	24.4 <sup>†</sup>	19.0	15.4									
			50.0 ±	66.5 ±	69.3 ±									
Dyskinesia disability	nil-LEDD	1.9 ±	0.5 ±	0.6 ±			< 0.001*	0.172	0.903					
	Others	1.7 <sup>†</sup>	1.1	1.3										
		2.3 ±	0.8 ±	1.1 ±										
LEDD (mg/day)	nil-LEDD	860.3 ±	106.9 ±	66.9 ±			< 0.001*	0.011*	0.023*					
	Others	448.4	174.8	130.9										
		899.8 ±	416.1 ±	422.5 ±										
		395.8	317.5	318.3										

All data was expressed as a mean ± standard deviation. \* $P < 0.05$ . The bold-faced  $P$  values were statistically significant after Bonferroni multiple comparison correction ( $P < 0.005$  for comparison between Baseline and On-DBS stimulation for 10 clinical outcomes;  $P < 0.01$  for comparison between Baseline and Off-DBS stimulation for 4 clinical outcomes); <sup>†</sup>13 patients are in nil-LEDD and 44 patients are in the other group. <sup>1</sup>,  $P$  value for within-factor of three repeated measured outcomes at the baseline and 6 months and 12 months after bilateral STN stimulation; <sup>2</sup>,  $P$  value for between-group-factor of three groups: I (both electrodes in the STN), II (only 1 electrode in the STN) and III (neither electrode in the STN); <sup>3</sup>,  $P$  value for interaction between the within-factor and between-group-factor. Abbreviations as Table 1.

Transient confusion and abulia was the most common (7.0%) followed by transient dysarthria (5.3%). Two patients (3.5%) had wound infection, one in the scalp and the other in the left subclavicular area which was well controlled with antibiotic therapy. Intracerebral hematomas were found in two patients (3.5%) on immediate postoperative CT scans, which were asymptomatic. Other complications were seizure (1.8%), transient hypophonia (1.8%), transient restless leg syndrome (1.8%) and permanent personality change (1.8%).

## DISCUSSION

Most studies in the literature correlated the clinical improvement with the localization of the electrodes determined by the fused images of preoperative and postoperative brain CT or MRI taken at the immediate postoperative period (5, 15, 20-26). But the immediate postoperative imaging make it difficult to precisely localize the center of electrodes in relation to the STN because of brain shift due to CSF leakage at the immediate postoperative period or the electrode artifacts caused by the elec-



**Table 6.** UPDRS-III subscores of nil-LEDD patients after bilateral subthalamic nucleus stimulation

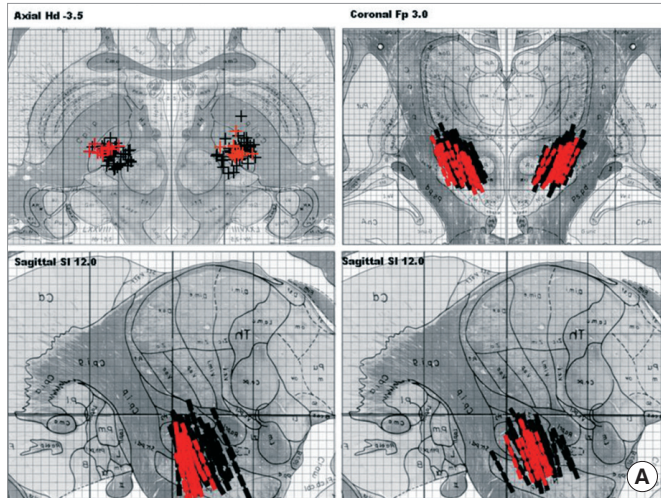
	Medication	Group <sup>†</sup>	Baseline	On -DBS stimulation		Off -DBS stimulation		Baseline vs On -DBS stimulation			Baseline vs Off -DBS stimulation		
				6 months	12 months	6 months	12 months	<i>P</i> value <sup>1</sup> for within-factor	<i>P</i> value <sup>2</sup> for group-factor	<i>P</i> value <sup>3</sup> for interaction	<i>P</i> value <sup>1</sup> for within-factor	<i>P</i> value <sup>2</sup> for group-factor	<i>P</i> value <sup>3</sup> for interaction
Speech	On	nil-LEDD	1.3 ± 0.6	1.0 ± 0.5	1.0 ± 0.6	1.2 ± 0.4	1.3 ± 0.7	0.460	0.326	0.086	0.818	0.811	0.310
		Others	1.2 ± 0.8	1.3 ± 0.9	1.4 ± 1.0	1.5 ± 0.8	1.3 ± 0.9						
	Off	nil-LEDD	1.7 ± 0.6 <sup>†</sup>	1.1 ± 0.5	1.4 ± 0.7	1.3 ± 0.4	1.4 ± 0.7	<b>0.003*</b>	0.317	0.007*	0.313	0.605	0.050
		Others	1.5 ± 0.7	1.5 ± 0.8	1.4 ± 0.8	1.6 ± 0.8	1.5 ± 0.8						
Tremor	On	nil-LEDD	2.7 ± 4.1	1.0 ± 2.4	0.4 ± 0.9	1.8 ± 3.7	2.8 ± 4.0	< 0.001*	0.363	0.721	0.598	0.677	0.542
		Others	2.3 ± 2.5 <sup>†</sup>	0.3 ± 0.8	0.3 ± 0.9	2.1 ± 3.5	1.9 ± 3.1						
	Off	nil-LEDD	5.7 ± 5.1 <sup>†</sup>	1.6 ± 2.9	0.5 ± 1.0	2.9 ± 4.3	3.2 ± 3.9	< 0.001*	0.657	0.721	< 0.001*	0.863	0.498
		Others	6.4 ± 5.2 <sup>†</sup>	1.6 ± 2.7	0.7 ± 1.9	3.3 ± 4.0	2.5 ± 3.7						
Rigidity	On	nil-LEDD	3.9 ± 4.4	3.2 ± 2.6	3.0 ± 3.5	6.1 ± 3.9	7.3 ± 4.2	0.058	0.647	0.633	0.001*	0.693	0.510
		Others	4.2 ± 3.4 <sup>†</sup>	2.6 ± 3.6	2.3 ± 2.5	5.9 ± 4.5	6.1 ± 3.9						
	Off	nil-LEDD	8.0 ± 4.2 <sup>†</sup>	3.8 ± 2.9	3.7 ± 3.6	7.5 ± 3.7	7.9 ± 4.4	< 0.001*	0.963	0.816	0.592	0.644	0.890
		Others	7.9 ± 3.9 <sup>†</sup>	4.4 ± 4.1	3.4 ± 3.2	7.0 ± 4.5	7.2 ± 4.1						
Bradykinesia	On	nil-LEDD	8.7 ± 6.9	7.2 ± 5.7	6.8 ± 5.0	12.7 ± 6.0	13.0 ± 7.8	0.235	0.582	0.781	< 0.001*	0.388	0.911
		Others	7.4 ± 4.8	6.4 ± 5.2	6.7 ± 4.3	11.6 ± 7.1	11.0 ± 5.4						
	Off	nil-LEDD	15.3 ± 9.0 <sup>†</sup>	9.0 ± 6.5	8.2 ± 5.2	13.9 ± 6.3	14.3 ± 5.2	< 0.001*	0.732	0.124	0.966	0.505	0.408
		Others	12.6 ± 5.7 <sup>†</sup>	9.0 ± 5.8	9.1 ± 4.7	13.6 ± 7.2	13.5 ± 5.4						
Gait	On	nil-LEDD	0.7 ± 0.8	0.7 ± 0.6	1.1 ± 0.7	1.7 ± 1.2	2.0 ± 1.2	0.059	0.668	0.264	< 0.001*	0.418	0.208
		Others	0.8 ± 0.7	1.0 ± 0.7	1.0 ± 0.8	1.6 ± 1.0	1.5 ± 0.8						
	Off	nil-LEDD	1.9 ± 1.3 <sup>†</sup>	1.0 ± 0.7	1.2 ± 0.8	2.0 ± 1.2	2.2 ± 1.1	< 0.001*	0.406	0.255	0.806	0.434	0.503
		Others	1.9 ± 0.8 <sup>†</sup>	1.4 ± 0.8	1.4 ± 0.9	1.9 ± 1.0	1.8 ± 0.9						
Postural stability	On	nil-LEDD	0.8 ± 0.9	0.7 ± 0.8	0.9 ± 0.9	1.2 ± 0.8	1.5 ± 1.1	0.158	0.627	0.195	0.283	0.913	0.053
		Others	1.2 ± 0.8 <sup>†</sup>	0.7 ± 0.8	0.8 ± 0.8	1.2 ± 1.0	1.1 ± 0.9						
	Off	nil-LEDD	1.6 ± 1.4	1.2 ± 0.9	0.9 ± 0.9	1.7 ± 1.1	1.6 ± 1.2	< 0.001*	0.538	0.546	0.162	0.816	0.121
		Others	1.9 ± 0.7	1.2 ± 0.9	1.1 ± 0.9	1.5 ± 1.0	1.4 ± 0.9						

All data was expressed as a mean ± standard deviation. <sup>†</sup>13 patients are in nil-LEDD and 44 patients are in the other group. \**P* < 0.05. The bold-faced *p*-values were statistically significant (*P* < 0.004) after Bonferroni multiple comparison correction of 12 UPDRS III subscores. <sup>1</sup>, *P* value for within-factor of three repeated measured outcomes at the baseline and 6 months and 24 months after bilateral STN stimulation; <sup>2</sup>, *P* value for between-group-factor of three groups: I (both electrodes in the STN), II (only 1 electrode in the STN) and III (neither electrode in the STN); <sup>3</sup>, *P* value for interaction between the within-factor and between-group-factor. Abbreviations as Table 1.

trode-induced magnetic inhomogeneity (8, 9-11). Miyagi et al. confirmed the significant contralateral brain shift in the unilateral procedure and posterior shift in the bilateral procedure by comparing the three-dimensional coordinated of the AC and

PC on MRIs before and after implantation of the electrodes (10). Khan et al. (9) reported a shift of deep brain structures up to 4 mm after the surgery. Halpern et al. (8) reported posterior shift of the deep brains structures had impacted the number of mi-



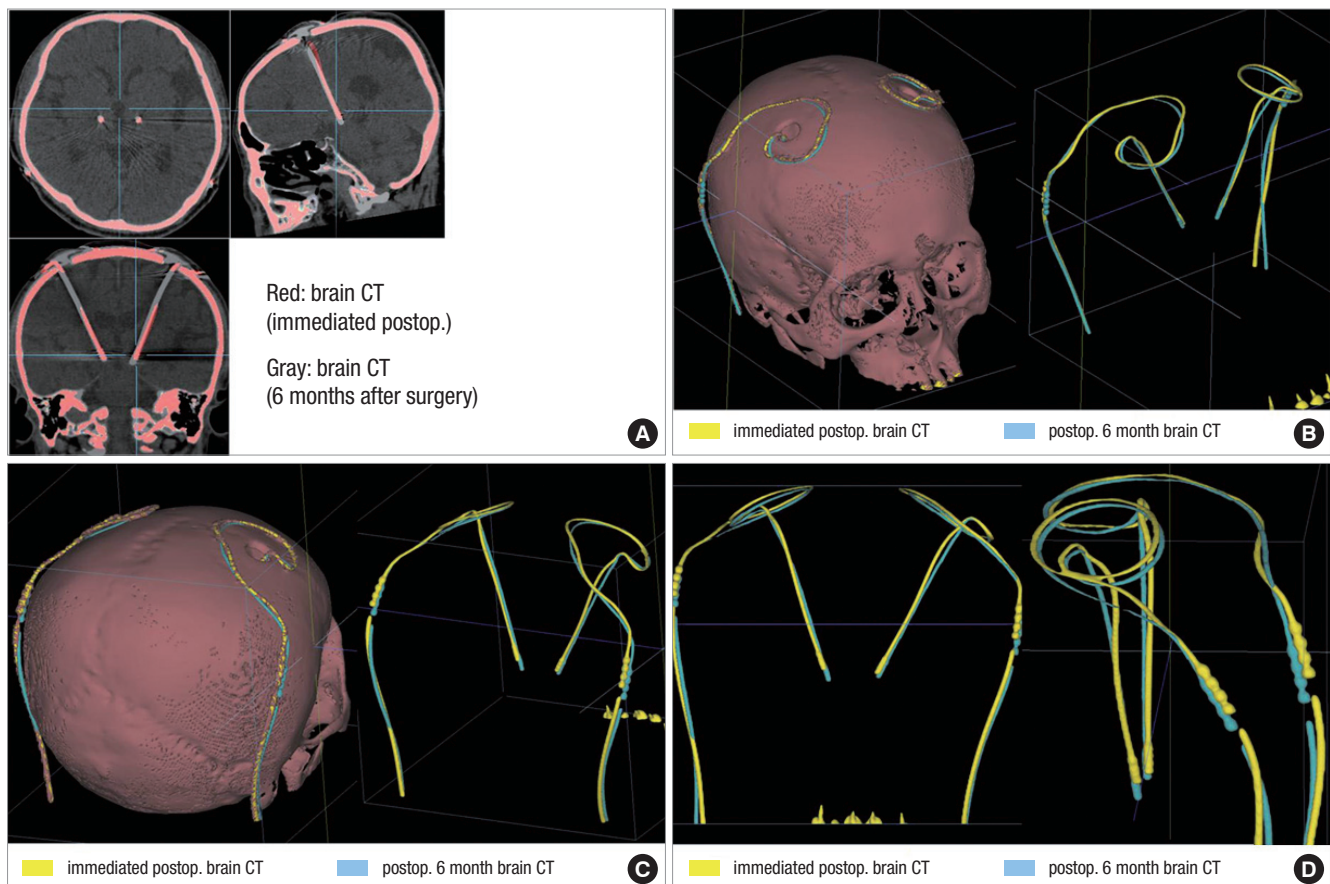


**The x, y, z coordinates of the active contacts in 13 patients with nil-LEDD**

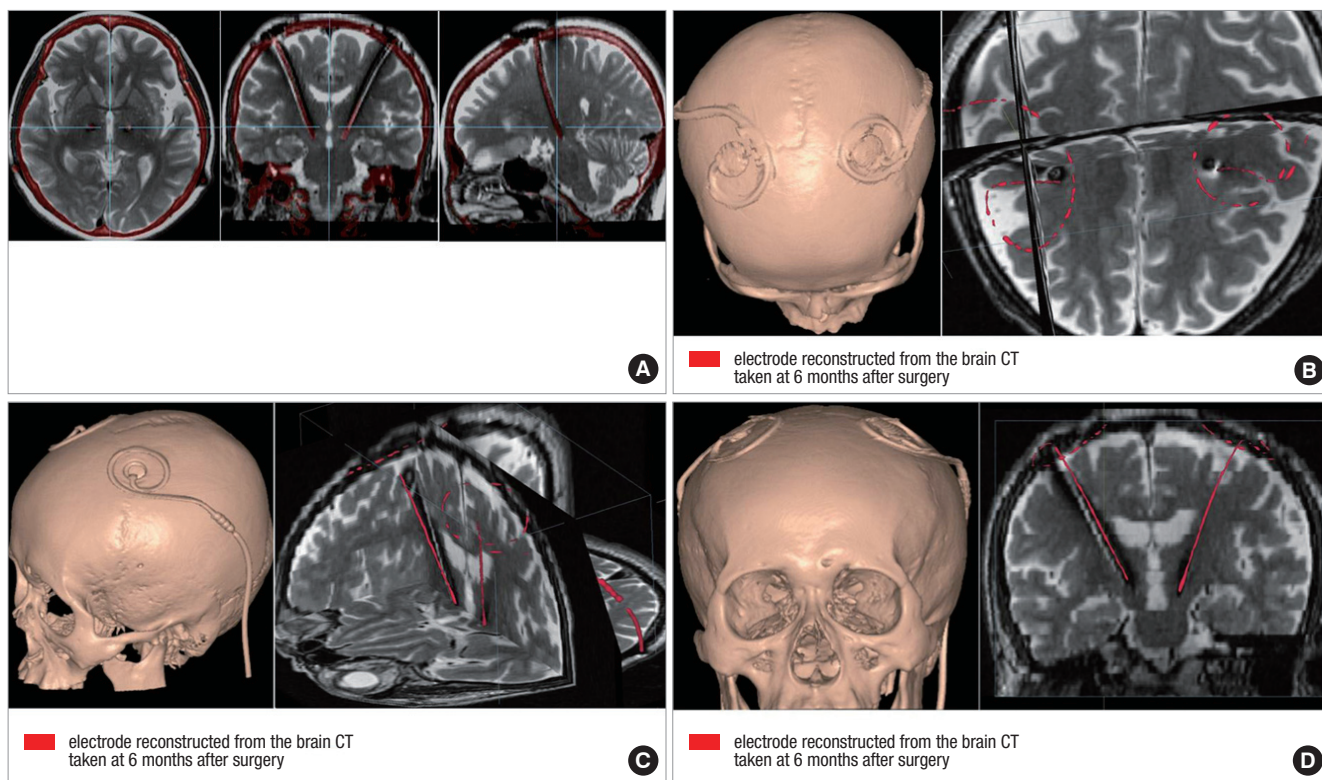
Electrode		x	y	z
Left	mean	12.6	-1.2	3.6
	SD	1.5	1.0	0.9
Right	mean	12.0	-0.5	3.7
	SD	1.8	0.9	1.1

SD=standard deviation; LEDD=L-dopa equivalent daily dose (B)

**Fig. 3.** Electrode positions of 13 patients without medication after surgery. (A) The location of the electrodes are plotted based on the fused images of the 13 patients showing significant clinical improvement in UPDRS part III including speech with nil LEDD (in red color) and of the remaining 44 patients (in black color) at the last follow-up period of more than one year after surgery. Most electrodes of these 13 patients are positioned in the middle one third of the subthalamic nucleus in the axial view at the level of 3.5 mm below the AC-PC line (upper left), and also positioned in the subthalamic nucleus in the coronal view at the level of 3.0 mm posterior to midcommissural point (upper right) and in the sagittal view at the level of 12 mm lateral to the midline (lower). (B) The x, y, z coordinates of the active contacts referenced to the AC-PC midpoints in the 13 patients with nil LEDD.



**Fig. 4.** Fused images of two brain CT scans taken after surgery. The fused images obtained from the CT scans taken at the immediate postoperative day and six months after surgery are aligned along the AC-PC line at the level of AC and PC in axial, sagittal, and coronal plane. The red represents the electrode extracted from the images of brain CT taken immediately after surgery and the gray represents the electrode extracted from the images of the brain CT taken at six months after surgery. The red and the gray electrodes do not fit into each other with significant discrepancy of their position in the axial and coronal planes (A). With the adjustment of window level and width of the fused images, only the shadow of both electrodes is extracted in 3-D reconstructive rendering image of right superior oblique view (B), right posterior oblique view (C), and AP and lateral view (D). The yellow represents the electrode extracted from the images of brain CT taken immediately after surgery and the sky-blue represents the electrode extracted from the images of the brain CT taken at six months after surgery. Significant discrepancy of the electrode position between the two CT scans is remarkable.



**Fig. 5.** Fused images of brain CT and MRI taken after surgery. Fused images of the brain CT and the brain MRI both taken at 6 months after bilateral subthalamic stimulation are illustrated. The fused images obtained from the brain MRI and the brain CT taken at 6 months after bilateral subthalamic stimulation are aligned along the AC-PC line at the level of AC and PC in axial, sagittal, and coronal plane. The red represents the electrode extracted from the images of brain CT taken at six months after surgery and the gray represents the electrode extracted from the images of the brain MRI taken at six months after surgery. The center of red and gray one representing the center of electrodes extracted from brain CT and brain MRI do not fit into each other with significant discrepancy of their position in the axial, coronal, and sagittal plane of the fused images (A). With the adjustment of window level and width of the fused images, only the electrodes in red color are superimposed in 3-D reconstructive rendering brain MR images of superior anterior view (B), left anterior superior oblique view (C), and anterior posterior view (D). The discrepancy of the electrode position extracted from brain CT and the center of electrode artifact from brain MRI taken at 6 months after surgery is remarkable in all three axial, sagittal, and coronal planes.

croelectrode tracks to optimize STN targeting.

Kim et al. (27) found that there was a significant discrepancy in the implanted electrode positions between the immediate postoperative period and six months after DBS surgery in 53 patients with Parkinson's disease. The considerable discrepancy of electrode position between the immediate postoperative CT scan and the brain CT taken at 6 months after surgery makes it difficult to precisely localize the center of the electrode with the fused images of preoperative MRI and the immediate postoperative CT scans (Fig. 4).

Martinez-Santesteban et al. (11) found that image artifacts in 2.0 Tesla MRI produced by microelectrodes were highly dependent not only on the magnetic susceptibility of the materials used but also on the size, shape and orientation of the electrodes with respect to main magnetic field. Lee et al. (28) compared the X-, Y-, Z- coordinates of the center of the electrodes estimated by MRI and CT in 61 patients who had taken both MRI and CT at least six months after bilateral STN DBS to validate the accuracy of MRI in electrode localization in comparison with CT scan. They found that the electrode location evaluated by postoperative MRI had significant discrepancy with the location estimat-

ed by brain CT scan. The artifacts caused by the electrode interference of local magnetic field makes it difficult to precisely localize the center of the electrodes in MRI (Fig. 5).

As in the previous studies (12), we observed that the improvement of symptoms, the LEDD, the neuropsychological changes other than speech and stimulation side effects did not vary significantly between the patients of group I and group II in this series. Although the number of the patients was too small to get a statistical significance, there was a good deal of symptomatic improvements after surgery even in the patients of group III. This suggested that there is a significant target volume in the region of the STN that provides equivalent clinical efficacy, which is comparable with the report that McClelland et al. (26) had described. They suggested that a DBS electrode placed anywhere within 6-mm-diameter cylinder centered at the presumed middle of the STN might result in similar clinical efficacy.

In this study the best symptom relief including speech with a reduced LEDD was observed in the patients whose electrodes were accurately positioned in both STN. There are debates regarding the surgical outcome of speech after bilateral STN stimulation (1, 29, 30). In this study, patients of group II or III had



speech deterioration after bilateral STN stimulation more commonly than those of group I. Such speech deterioration was reversible when turning off the stimulation. The patients whose electrodes were positioned medial to the STN experienced speech deterioration more frequently.

The average LEDD at 6 and 12 months after STN stimulation was lower in the group I than in the group II or III in this study. The LEDD was zero at their last follow up in a subgroup of 13 (36%) patients in 36 patients of group I. This subgroup of 13 patients had significant clinical improvement in sub-scores of UPDRS part III including speech at the last follow-up more than one year after surgery. These 13 patients had their stimulation electrodes mostly positioned within the middle one third of both STN on the axial view at 3.5 mm from the AC-PC line (Fig. 3).

This study has several limitations. First, we categorized the electrode positions into three groups based on the plotted electrode position on the axial view at the level of 3.5 mm below the AC-PC line in the human brain atlas of Schaltenbrand and Wahren (19). We assumed that the patient's brain would conform to the atlas with adjustment of the length of AC-PC line and size of the third ventricle. However, there might be a discrepancy between the real location of the electrodes in the individual brain and the location of the electrodes plotted in the human brain atlas confirmed to the patients. Second, we did not take the depth and trajectory of the electrodes into consideration to assess the thorough information of all four contacts in relation of the STN. We need further studies to assess four contacts of DBS electrodes in relation to the STN to recognize the best anatomical structures such as dorsal STN or zona incerta for the modulation of each specific motor symptom. Third, it needs further long-term follow-up in the estimation of clinical outcome in correlation with electrode positions identified on the CT-MR fused images.

So far little has been reported in the literature regarding the clinical outcome up to one year according to the electrode positions estimated at a stable period after bilateral STN stimulation as in this study. The patients of group I, especially whose electrodes were located in the middle one third of both STN at 3.5 mm below the anterior-posterior commissural line, had better outcome in speech with least LEDD than two other groups. Our findings suggest that the better symptom relief including speech with a reduced LEDD is expected in the patients whose electrodes are accurately positioned in both STN.

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## AUTHOR SUMMARY

### Electrode Position and the Clinical Outcome after Bilateral Subthalamic Nucleus Stimulation

Sun Ha Paek, Jee-Young Lee, Han-Joon Kim, Daehee Kang, Yong Hoon Lim, Mi Ryoung Kim, Cheolyoung Kim, Beom Seok Jeon and Dong Gyu Kim

We prospectively compared the clinical outcome of the advanced Parkinson's disease (PD) after bilateral STN stimulation according to electrode positions that were identified in the fused images of the preoperative MRI and the postoperative CT. We found that electrode position in the middle one third of both STN leads to the best outcome. It is suggested that documenting the electrode position at a stable period after bilateral STN stimulation is necessary for the prediction of symptomatic improvement, reprogramming, and possible repositioning of electrodes.