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ORIGINAL ARTICLE

Frame-Based Stereotactic Deep Brain Stimulation for Parkinson's Disease: 12 Months Outcomes for Patients in Cross Hair versus Non-Cross Hair Application Groups

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Background: Because deep brain stimulation (DBS) implantations and other stereotactic and functional surgical procedures require accurate, precise, and safe targeting of the brain structure, the technical aids for preoperative planning, intervention, and postoperative follow-up have become increasingly important. In this paper, we compare the outcomes of advanced Parkinson's disease (PD) patients at our center who received frame-based DBS surgery involving the use of a cross hair with those for patients who received the surgery without the application of the cross hair. A preliminary outcomes analysis is also provided. **Methods and Techniques:** Seventeen patients (10 male and 7 female; mean age: 64.8 ± 9.0 years) with advanced PD underwent frame-based DBS surgery, 8 with noncross hair and 9 with cross hair frame-based stereotaxy. After identifying the coordinates of the subthalamic nuclei, the DBS electrodes were implanted with or without crosshair application and connected to an implanted programmable generator in all patients. Programming started 1 month after the operation, and the patients were followed-upon regularly for at least 6 months. **Results:** After 12 months of follow-up, the patients who received DBS surgery showed improvements in clinical outcome, especially those in the frame-based cross hair group, which resulted in a significantly higher degree of improvement in both the "On" and "Off" states of the postoperative state (cross hair Unified PD Rating Scale [UPDRS] in the "Off" state: Preoperative: 82.3 ± 15.4 vs. postoperative: 37.9 ± 9.4; $P < 0.001$; UPDRS in the "On" state: Preoperative: 47.8 ± 13.6 vs. postoperative "On" state: 28.6 ± 6.0; $P < 0.01$, paired *t*-test). However, improvements were shown only in the "On" state of the noncross hair group (noncross hair group UPDRS in the "Off" state: Preoperative: 71.7 ± 16.6 vs. postoperative 48.9 ± 24.4; $P < 0.05$; "On" state: Preoperative: 55.2 ± 19.1 vs. postoperative: 42.6 ± 27.8; $P > 0.05$, paired *t*-test). **Conclusion:** Targeting accuracy can be increased by detailed preoperative planning and good facilitating equipment. Crosshair application with a frame-based system provides higher accuracy in the postoperative lead position survey and target deviation measurements compared with the preoperative planning image. Furthermore, the outcomes of the DBS group with cross hair application were better than those of the noncross hair application group.

Key words: Frame-based stereotactic, deep brain stimulation, advanced Parkinson's disease

INTRODUCTION

Parkinson's disease (PD) is a common neurodegenerative disease with motor symptoms, including bradykinesia, rigidity, and tremors, which result from the midbrain dopamine degeneration.[1] In addition to the classic motor symptoms, nonmotor symptoms are now widely considered to form part of the overall clinical picture. Cognitive decline is a critical aspect of this disease because it increases the burden on patients and caregivers significantly.[2]

Although medication, in particular levodopa, remains the most effective treatment for PD, the progression of the disease limits the response of the medicine. The fluctuation of the medicine's effect and levodopa-induced dyskinesia still pose significant obstacles to the treatment.[3] Chronic high-frequency stimulation of the ventral intermediate nucleus (VIM) of the thalamus was first described in the early 1990s by Benabid *et al.*[4] Through controlled trials, and large clinical series, the

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benefits and safety of deep brain stimulation (DBS) have been established, and DBS has become a standard treatment for patients in the advanced stages of PD with severe motor complications.[5-8] The stability, reproducibility, and accuracy of frame-based stereotaxy make this procedure an attractive alternative to trajectory-based procedures, wherein real-time feedback is less critical and have provided a reliable method for targeting deep-brain structures accurately.[9] Despite their utility, stereotactic frames have limitations for both the surgical team and the patient, and frames have been supplanted gradually by frameless image-guided surgical systems in most intracranial procedures.[10]

Frame-based surgery still appears to be popular in functional surgery and especially in DBS. The application of the crosshair, which provides anatomical and image guiding, facilitates target localization. Therefore, in this paper, we analyze the preliminary postoperative results of patients following both frame-based with or without crosshair intraoperative correction.

METHODS AND TECHNIQUES

We analyzed the postoperative follow-up Unified PD Rating Scale (UPDRS) scores of patients who received bilateral subthalamic nucleus (STN) DBS from 1999 to 2013. Then, we compared the surgical results of patients who underwent frame-based surgery with or without crosshair intraoperative adjustment of the lead, and the approval number of this study from Institutional Review Board (IRB) of Tri-Service General Hospital is (TSGHIRB): 2-102-05-130.

Clinical survey and candidate selection

The criteria for candidate selection for our STN-DBS treatment were:

1. An adequate response to dopaminergic therapy,
2. The presence of On-Off fluctuations,
3. Dyskinesia impairing quality-of-life,
4. Medication-resistant tremors, and
5. Reasonable cognitive function.

Contraindications to surgery included a poor response to dopaminergic therapy, cognitive deterioration, neuroimaging abnormalities, major psychiatric illnesses, and general surgical/anesthetic contraindications.[10] Then, the patients were classified into the cross hair and noncross hair application group according to their admission time (the patient that admitted into the ward before March, 2000 received the surgery with noncross hair application and those admission after March, 2000 received the surgery with cross hair application). The good medication-response of patient is defined as: The difference in UPDRS of preoperative "On and Off" states was more than 30%.

Surgical procedures for frame-based subthalamic nucleus deep brain stimulation implantation

The patients underwent simultaneous bilateral DBS lead and pulse generator implantation on the same day. A standard frame-based procedure described previously[11,12] was applied for the DBS (Kinetra system, Meditronic Inc., Minneapolis, Minnesota, USA). The stereotactic systems that composed a Cartesian coordinate system with x, y, and z coordinates (G frame, Leksell Stereotactic Systems) was used. The base of the frame was placed parallel to a line extending from the lateral canthus/orbital floor to the tragus in order to parallel approximately the anterior commissure-posterior commissure (AC-PC) line. The patients' heads were usually centered in the frame and hence that the midline fell within the center point of the stereotactic space defined by the head-frame system. The frame should not obscure the patient's eyes to avoid difficulty in communicating with the patient and assessing eye movement during surgery.

The pins were inserted under local anesthesia of lidocaine and/or Marcaine after the scalps of patients were shaved and prepared routinely. The anterior pins were placed two finger's breadth above the orbital rim, which is an important step to avoid supraorbital nerve injury. The posterior pins were located properly to avoid penetration of the cerebral venous sinuses.

After the frame had been placed, the patient underwent preoperative magnetic resonance imaging (MRI) to construct the stereotactic imaging database required for DBS implantation. Anatomical targeting of the STN and coordinate calculation were performed based on these imaging modalities, using a commercially available stereotactic software iPlan (BrainLab AG, Munich, Germany). In these initial stages, the DBS operations were performed under an indirect targeting method that is based on a standardized stereotactic atlas and a formula-derived method based on AC and PC landmarks. The coordinates were derived from our neuroradiologist and represent the average values of the coordinates of these best contacts, gathered in a lot of cases. The initial anatomical coordinates for the ventral and sensorimotor STN are usually set at 11-13 mm lateral to the midline, 4-5 mm ventral to the intercommissural plane, and 3-4 mm posterior to the midcommissural point.

Entry points with a safe and optimal trajectory to the STN were set according to the patient's anatomy, and the typical angles of approach are 15-30° from the sagittal plane and 50-70° in the anterior-posterior direction.

Bur holes were performed at the frontal skull region, and the electrodes were inserted according to the set coordination.

The microelectrode was advanced by using hydraulic or electrical microdrive in submillimetric steps, and the cannula was inserted to a predetermined dorsal offset to the chosen anatomical targeting. A Gelfoam or fibrin glue was placed around the cannula in the burr hole, and the dura was opened to provide a seal to minimize cerebrospinal fluid loss and pneumocephalus.

After completing intraoperative physiology, which includes microelectrode recording (MER) and stimulation, when an inserting cannula is used, the chosen electrode is loaded in a manner wherein the first contact is aligned with the tip of the cannula. The tips of the electrode are confirmed by lateral-view fluoroscopy with or without crosshair application. Subsequently, the patients were examined for the baseline tremor, rigidity, and bradykinesia. A microdrive was used to advance the electrode to the desired target or, alternatively, manual advancement was performed on the target. Fluoroscopy with or without the crosshair was used to confirm that the electrodes formed a straight trajectory.

After correct placement was confirmed, and trial stimulation was found to be successful, a pulse generator implantation procedure, similar to the procedure used to implant a pacemaker, was performed in the subclavicular space. The patient was placed in a supine position, with the head turned to the opposite side of the intended site of implantable pulse generator (IPG) implantation. Preoperative antibiotics were again administered 30 min prior to making the incision. Then a subcutaneous pocket was created for the IPG, which is connected to the DBS lead that was tunneled previously to the parietal/occipital region. The most common location for IPG placement is the infraclavicular region, and it is marked typically 2 cm below the clavicle and 4 cm away from the midline or 2 cm away from the lateral manubrial border. Stimulation parameters (frequency, amplitude, pulse widths, etc.) vary, based on the disorder being treated, patient response, and the presence of side effects.

Postoperative follow-up

Testing and DBS electrode programming was performed 1 month after surgery, and patient follow-ups took place every 1-2 months for the first 6 months and every 3-4 months thereafter. For PD patients, testing was performed in the Off-medication and On-DBS conditions, and assessment was executed using the UPDRS. At each follow-up, stimulation parameters were adjusted to achieve optimal symptom relief and diminish side effects.

Statistical analysis

Data collected include the patients' age, sex, levodopa dosage, and UPDRS-II and-III scores. Pre- and post-operative data were compared statistically using a paired *t*-test. Statistical analyses were performed on the clinical-rating scores and the levodopa dosage pre- and post-DBS. Difference-of-outcome scales were analyzed using an unpaired *t*-test. In the analysis, the assumption of normality was made and confirmed with a normal probability plot.

RESULTS

The patients were followed-up 1 year after the STN-DBS, and the original preoperative and postoperative outcomes of each patient are listed in Table 1. The general characteristics of the patients are listed in Table 2. The duration of the disease range from 6 to 20 years, with a mean of 10.4 ± 3.5 years, and the dosage of the medication leveodopa ranged from 750 to 1500 mg/day, with a mean dosage of 1105.4 ± 285.5 mg. The first patient that received the device implant without the crosshair did not show improvement, as a result, of the treatment, but the patient's motor symptoms were shown to have been exacerbated at the postoperative following-up. This may have been caused by the insufficient accuracy of the lead. Patient number 6, who also received the procedure without the crosshair application, demonstrated spontaneous intracerebral hemorrhage (ICH) after surgery, and she died from cerebrovascular failure 2 weeks later.

The primary results of the UPDRS are listed in Table 3. No significant differences are shown in the results of Part I of the cognitive survey within the 12 months period following the operation between the crosshair and noncross hair groups. Neurocognitive function may be affected by the procedure, especially in cognitively impaired patients.

Regarding the scores for Part II, quality-of-life showed that the outcome tends to improve more in the cross hair group, though no statistical significance was shown [Figure 1a, one-way ANOVA with F = 2.38, followed by Bonferroni's *post-hoc* test, $P = 0.08$ in the noncross hair difference vs. cross hair difference].

A comparison of the UPDRS scores showed only significant changes in the total scores of On state for the noncross hair group [Figure 2a, $P < 0.05$ at the Off state, $P > 0.05$ at the On state, paired *t*-test], but significant improvements in both the Off and On states [Figure 2b, $P < 0.001$ at the Off state and $P < 0.01$ at the On state, paired *t*-test]. The motor score showed significant improvements in both noncross hair and cross hair application groups [Figure 2c, $P < 0.05$, paired *t*-test], but improvements in the cross hair group were more notable [Figure 2d, $P < 0.001$ at the Off state and $P < 0.01$ at the On state, paired *t*-test]. The motor score improved significantly in both the Off and On states.

Improvements in the UPDRS scores in the good medication-response group, wherein the difference in UPDRS

Table 1. The original records of the patients

Case Number	Age/Sex	Improvement (%) Off	Improvement (%) On	Pre-OP UPDRS Off	Post-OP UPDRS Off	Pre-OP UPDRS On	Post-OP UPDRS On	Cross Hair application
1	78/M	-37	-100	78	105	52	104	−
2	67/F	47	30	108	57	77	54	−
3	75/M	61	0.1	70	27	17	16	−
4	57/M	41	38	51	30	45	28	−
5	58/M	19	39	68	55	66	40	−
6	57/F			70	Expired due to ICH	66		−
7	70/F	33	35	69	46	68	44	−
8	61/F	47	47	53	28	38	20	−
9	61/M	45	49	78	43	68	35	+
10	68/M	62	44	90	34	39	22	+
11	79/M	51	38	78	38	45	28	+
12	52/M	42	18	65	38	45	37	+
13	61/M	62	36	100	38	44	28	+
14	46/M	52	10	60	29	29	26	+
15	67/M	71	65	85	25	63	22	+
16	68/F	30	31	103	55	72	38	+
17	76/M	40	38	77	46	45	28	+

UPDRS = unified Parkinson's Disease Rating Scale; ICH = intracerebral hemorrhage

Table 2. Characteristics of patients undergoing STN-DBS surgery (n = 17)

Characteristics	
Age (years) at surgery	
Range	46~79
Mean+/- SD	64.8+/- 9.0
Sex	
Males	10
Females	7
Duration of PD (years)	
Rage	6~20
Mean+/-SD	10.4+/-3.5
Levodopa dose (mg/day)	
Rage	750~1500
Mean_/-SD	1105.4+/- 285.5
Side of STN stimualtion	
Bilateral	17
Unilateral	0

*Levodopa equivalent dose, calculated using the following accepted equivalents: 100 mg levodopa = 125 mg controlled-release levodopa = 1 mg; pergolide = 1.5 mg. Pramipexole, which were based on the statement of a previous study.[9] STN = subthalamic nucleus; DBS = deep brain stimulation; SD = standard deviation; PD = parkinson's disease

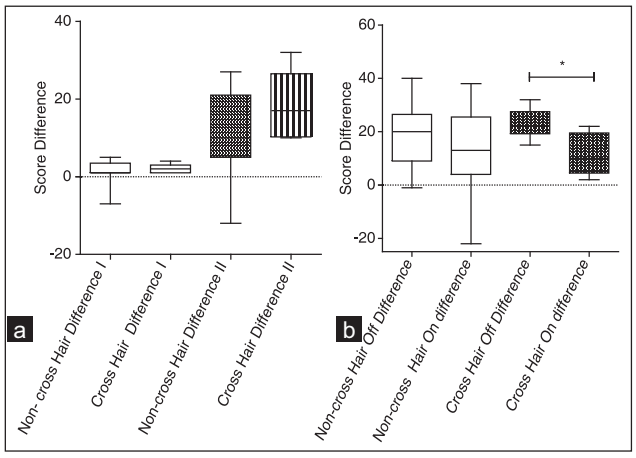

Figure 1. The effect of the application of cross hairs on the outcome of patients: (a) The analysis of differences in pre- and post-operation scores for Part I and Part II of the Unified Parkinson's Disease Rating Scale (UPDRS) indicate a higher increase for the cross hair group in Part II, although no statistical significance was found. (Part I difference for noncross hair vs. cross hair; P = 0.3; Part II difference for noncross hair vs. cross hair; P = 0.37, unpaired t-test) (b) The difference in Part III motor scores of the UPDRS in each group with and without medication. Significant improvements can be found between the Off and On states of good medication-response patient group (*P < 0.05, unpaired t-test)

scores between preoperative "On and Off" states was higher than 30%, were more obvious. Improvements in the UPDRS

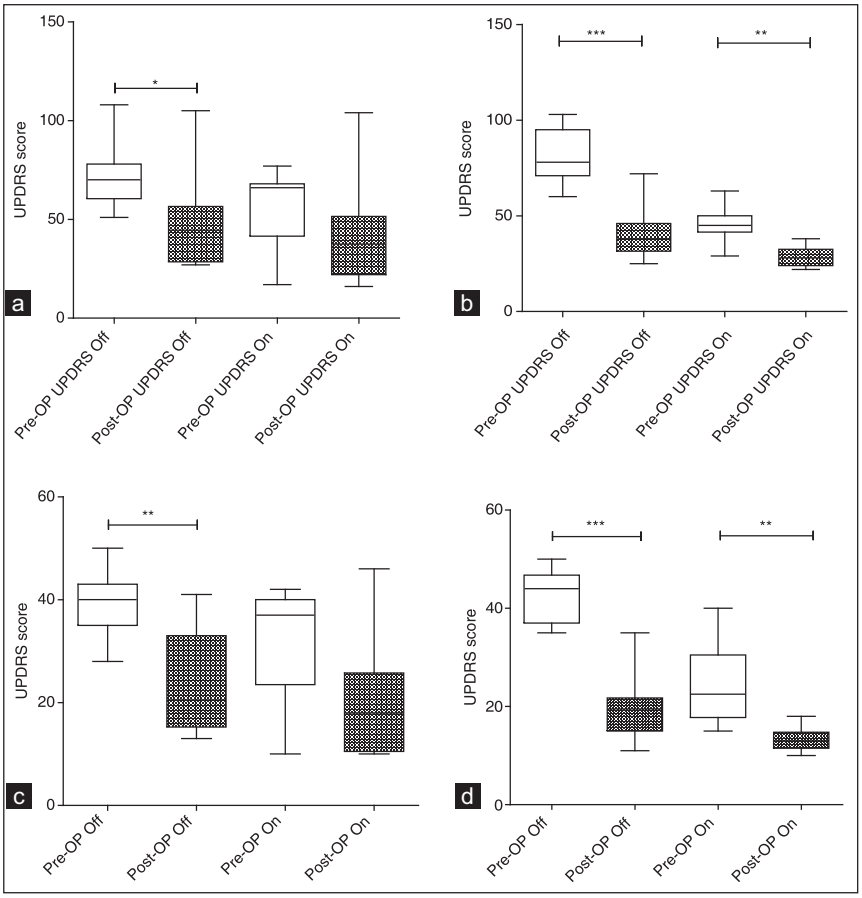

Figure 2. (a) The change in Unified Parkinson's Disease Rating Scale (UPDRS) scores between preoperative and 12 months postoperative follow-up in noncross hair subthalamic nucleus deep brain stimulation group are shown, which indicate that significant change are found only at the Off state. (b) The change in UPDRS scores in the cross hair group revealed more significant decreases in both postoperative Off and On states. The analyzed data in Part III (motor score) of the UPDRS demonstrated significant decreases in the Off state in the noncross hair application group (c) and significant decreases in either the Off or On state of the cross hair application group (d). (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, paired *t*-test)

scores were significant in the Off state [Figure 3a, *$P > 0.05$, unpaired *t*-test] but not in the On state [Figure 3b, $P > 0.05$ unpaired *t*-test].

Regarding adverse events in our study group, one patient (1/17; 5.9%) died due to postoperative ICH. Surgical-site infection (2/17; 11.8%) and surgical-site pain occurred in two of the patients (2/17; 11.8%) that underwent DBS in this study.

DISCUSSION

Technological advances have made it possible to implant neuro stimulation devices with or without stereotactic surgery to treat a wide range of neurological symptoms as well as to provide relief to patients by means of cochlear implants, cortical and deep brain stimulators, and systems for spinal cord, vagus, and gastric nerve stimulation.[13] DBS of the globus pallidus interna (GPi) or STN has become an accepted treatment for advanced PD when symptoms can no longer be managed adequately through medication.[14] Moreover, DBS of the STN has been shown to improve consistently bradykinesia, rigidity, tremors, postural control, and gait.[15-18] The outcome data of the patients who received frame-based DBS in this study have demonstrated this phenomenon.

The placement of the electrodes is a crucial procedure in DBS implantation, and it poses a challenge to neurosurgeons. Achieving optimal results, and minimal side effects depend on a high degree of precision and accuracy in electrode positioning, which requires anatomically reliable preoperative target planning, intraoperative anatomical localization device support, and physiologically intraoperative MER. Concerning the imaging modalities, the AC-PC were used as references for atlas-based targeting, and this AC-PC line was previously identified by MRI.[11] The sequence used depends on the chosen target structure: T1[19] or proton density imaging[20] is used

Table 3. Primary outcome and motor scores for UPDRS in both groups at 12 months follow-up

Outcome	Non-crosshair baseline	Non-cross hair 24 months	Cross hair baseline	Cross hair 24 months	Non- cross hair vs. cross hair difference (95% CI)	*P* values
Score on UPDRS						
I (mentation, behavior, and mood, Range, 0-16)	5.6+/- 3.0	5.0+/-5.1	6.8+/-2.4	4.6+/-2.1	-0.9 (-4.895 to 3.090)	0.22
II (activities of daily living, range 0-52)	26.0+/-8.3	17.0+/-10.0	32.5+/-8.8	13.9+/-6.4	-7.7 (-20.60 to 5.131)	0.08
III (motor score, without medication)	39.7+/-6.4	23.5+/-10.1	42.8+/-5.3	19.8+/-7.2	-4.2 (-20.49 to 12.04)	0.73
III (motor score, with medication)	31.1+/-10.9	20.7+/-12.0	24.4+/-8.2	13.3+/-2.4	1.8 (-14.49 to 18.04)	0.3

UPDRS = unified parkinson's disease rating scale; CI = confidence interval

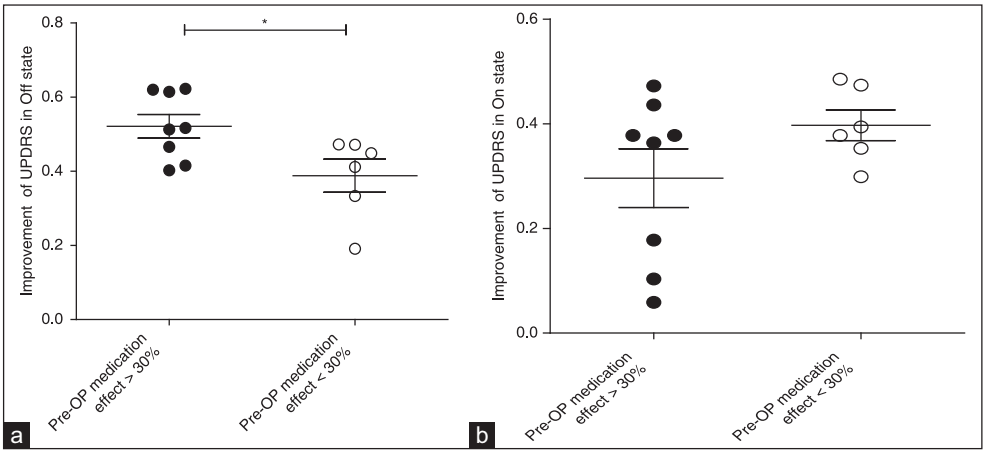

Figure 3. The improvement of the Unified Parkinson's Disease Rating Scale (UPDRS) in good medication-response group (the difference in UPDRS of preoperative "On and Off" states was more than 30 %): (a) Significant improvement (*$P < 0.05$, unpaired *t*-test) could be found in the Off state of the good medication-response group but not in the On state (b, $P > 0.05$ unpaired *t*- test)

especially for targeting the GPi; T2 imaging is used for STN targeting;[11,21,22] inversion recovery images are also beneficial for the direct targeting of Gpi and STN.[23] In our study, better outcomes over 12 months in the cross hair application group were shown, compared to the noncross hair application group. Significant improvements in UPDRS scores can be obtained at either the Off or On state in the cross hair application group [Figure 2]. This result is compatible to the one in a previous report, and it indicates that the cross hair application provides more precise target localization and benefit of outcome.

The accuracy of stereotactic frames and frameless systems has been well studied using phantoms. There was no significant difference between the accuracy of frameless navigation and that of the stereotactic frame as cited in the literature.[24-27] In Holloway *et al.*, study, they found that he center of the error ellipsoid in the frameless group was not only closer to zero but also better centered around zero than that for the frame-based data, and the error was greatest in the z plane: 1.7 mm for the frame-based system and 2 mm for the frameless system; while the difference in the x and y planes was 1.4-1.6 mm for both systems.[28] Furthermore, in the Leksell frame-based system, mean deviation of 3.15 mm from the expected target location was found, and there was a mean vector error of 2.9 mm (ranges: 0.1-6.44 mm) for VIM, 2.3 mm (ranges: 0-7.61 mm) for STN, and 2.2 mm (ranges: 0.03-4.5 mm) for GPi targets. However, the clinical accuracy of frameless systems using skin fiducial markers has the additional error introduced by mobile or nonfixed marks and the accuracy data reflect this result.[28]

On the other hand, in frameless system, the mean registration error reported when using the Frame Link software after patient registration with skull fiducial markers was 0.6-0.2 mm, while the mean registration error using skin fiducial markers, by manually, is generally in the range of 1.5-2 mm. There was no correlation between the mean registration error and the deviation of the DBS lead from its expected location, as well as an underestimation of the total localization error by the mean registration error, .[28] In Tai *et al.*, study, they also documented that either a frame-based system or frameless system could offer adequate accuracy for DBS targeting, and both systems resulted in similar clinical outcomes 1 year after DBS therapy.[29]

Based on the UPDRS, we reanalyzed the outcomes of the patients after DBS implantation. Short-term outcomes during

12 months of follow-up show improvements in patients after the DBS had turned on initially. Off medication motor symptoms appeared to improve most significantly in both the crosshair and noncross hair application groups [Figure 2]. Average improvements ranged between 40% and 60% on the standardized UPDRS.[17,18,30,31]

Although no significant perioperative differences in Part II of the outcome scale in our series are shown [Figure 1a], multiple studies demonstrated significant quality-of-life improvements in not only those measures related to motor benefits, but also in mental, emotional, social, cognitive, and communicative aspects of life.[32-34] These benefits have also been shown to be associated with quality-of-life improvements in the patients' caregivers as well.[33] Furthermore, nonmotor improvement in constipation, sleep quality, sensory complaints, bladder symptoms, and urodynamics, as a result, of STN-DBS have also been reported.[35-38]

The prognostic factors for STN-DBS benefit were different for short- and long-term follow-ups. Good prognostic factors for long-term STN-DBS for PD patients were good cognitive function and tremor dominance. Poor prognostic factors were related to older age and nondopaminergic-responsive axial disability.[39] In our study, we found that patients who respond well to levodopa can benefit from DBS implantation, which revealed in the off state difference shown on Figure 3a. STN-DBS alone improved motor scores and daily-life activities scores significantly, and anti-PD drugs were significantly reduced are indicated previously.[40] Our data showed that significant difference between post-DBS motor score at medication On state and Off state only revealed in those patient had good responses to the medication (>30%) [Figure 1b].

The dose of levodopa is also markedly reduced with an associated reduction in levodopa-induced dyskinesias (Kumar *et al.*, 1998; Limousin *et al.*, 1998; Moro *et al.*, 1999; Fraix *et al.*, 2000; Houeto *et al.*, 2000; Volkmann *et al.*, 2001; Kleiner-Fisman *et al.*, 2003; Krause *et al.*, 2004b). Molinuevo *et al.* have even shown that complete withdrawal of levodopa is feasible with bilateral STN-DBS.

Regarding the adverse events, one patient (1/17; 5.9%) in our study group died, as a result, of postoperative ICH. Surgical site infection (2/17; 11.8%) and surgical site pain occurred in only two patients (2/17; 11.8%) who underwent DBS in our study.

Severe intraoperative adverse events have been reported, including vasovagal response (0.8%), hypotension (0.3%), and seizures (0.3%). The most common and serious adverse event related to surgery was intracranial hemorrhaging, which has been reported in 3.9% of patients.[7] Postoperative imaging confirmed asymptomatic ICH (0.5%), asymptomatic intraventricular hemorrhage (3.4%), symptomatic ICH (1.1%), and ischemic infarction (0.4%), associated with hemiparesis and/or decreased consciousness (1.7%). Hardware-related complications (1.7-2.6%) requiring surgical revision include wound infections, lead malposition and/or migration, component fracture, component malfunction, and loss of effect.[41] The most frequent adverse events related to the effect of DBS that have been reported are falls, gait disturbance, dyskinesia, motor dysfunction, balance disorder, depression, and dystonia (9% patients for each event).

The cross hair application can provide more precise target localization to compensate the mechanical draft of the lead tip. Dementia, cognitive deficits, and psychosis (not drug-induced) are not improved by DBS. When patients are not able to see experienced doctors who can effectively manage and deal with postoperative problems, they are not appropriate candidates.

Finally, most centers using MER also perform intraoperative stimulation along the trajectory using microelectrodes stimulating in the microampere range[42-44] or the milliampere range, using, for example, RF- or DBS stimulation electrodes.[45,46] In general, this is performed at the same measurement points as those for MER to evaluate the clinical effects with increasing stimulation current and to determine symptom reduction, the clinical therapeutic and side effect thresholds at each measurement point. In this study, intraoperative correction can also be provided by cross hairs in frame-based surgery, and functional improvement is significant after cross hairs were applied in the initial development stage at our center.

CONCLUSION

Deep brain stimulation surgery using frame-based stereotaxy as a treatment for advanced PD can result in positive clinical outcomes for motor symptoms as evidenced by the significant improvements in UPDRS scores at mean follow-up. In this retrospective study, DBS with cross hair intraoperative application was shown to be more effective than the one with noncross hair application in alleviating disability in patients who suffer from moderate-to-severe PD with motor complications, who are responsive to levodopa, and who have no significant cognitive impairments. The improvements in the clinical outcome of PD in the UPDRS may have resulted from higher accuracy in the lead insertion when cross hairs are applied. In addition, a good response to medication was also positively related to the post-DBS outcome.

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DISCLOSURE

The authors have no financial conflicts of interest.

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