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ORIGINAL ARTICLE

Application of Preoperative CT/MRI Image Fusion in Target Positioning for Deep Brain Stimulation

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computed tomography; Parkinson's disease; dystonia

Objective To explore the efficacy of target positioning by preoperative CT/MRI image fusion technique in deep brain stimulation.

Methods We retrospectively analyzed the clinical data and images of 79 cases (68 with Parkinson's disease, 11 with dystonia) who received preoperative CT/MRI image fusion in target positioning of subthalamic nucleus in deep brain stimulation. Deviation of implanted electrodes from the target nucleus of each patient were measured. Neurological evaluations of each patient before and after the treatment were performed and compared. Complications of the positioning and treatment were recorded.

Results The mean deviations of the electrodes implanted on X, Y, and Z axis were 0.5 mm, 0.6 mm, and 0.6 mm, respectively. Postoperative neurologic evaluations scores of unified Parkinson's disease rating scale (UPDRS) for Parkinson's disease and Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) for dystonia patients improved significantly compared to the preoperative scores ($P < 0.001$); Complications occurred in 10.1% (8/79) patients, and main side effects were dysarthria and diplopia.

Conclusion Target positioning by preoperative CT/MRI image fusion technique in deep brain stimulation has high accuracy and good clinical outcomes.

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DEEP brain stimulation (DBS) has become an important treatment modality for Parkinson's disease (PD), dystonia, depression and epilepsy due to its safety, efficacy, reversibility

and low incidence of complications.¹⁻³ Accurate preoperative target positioning is a crucial step in DBS.⁴ Previous target positioning mainly relied on magnetic resonance imaging (MRI) alone, which was proved to be relatively accurate.⁵ However, several features of MRI, such as time-consuming, nonlinear distortion artifacts,⁶ and incompatibility of some implants have sabotaged the accuracy of positioning as

well as patient comfort.^{7, 8} Preoperative computed tomography (CT) and MRI fusion take advantages of both the time-saving of CT and the high soft tissue resolution of MRI. Applications of preoperative MRI fused with preoperative CT in target positioning was reported, but the sample sizes were relatively small.⁹⁻¹² In this study, we retrospectively analyzed images and clinical data of 68 patients with PD and 11 patients with dystonia who were treated by DBS of subthalamic nucleus (STN) using target positioning with fusion technique of preoperative MRI and CT scanned after installation of stereotactic head frame. The accuracy of preoperative target positioning and clinical outcomes were studied.

PATIENTS AND METHODS

Patient's selection

Seventy-nine patients who were diagnosed either PD (68 cases) or dystonia (11 cases), hospitalized in the department of neurosurgery, Peking Union Medical College Hospital, went through STN-DBS treatment with targets positioning by preoperative CT-MRI fusion from January 2012 to September 2015 were included in the study. Positioning data on images and clinical data were collected and analyzed retrospectively.

Preoperative MRI scanning

3.0T MRI (GE MR750) scans were performed on the day before surgery. T1 weighed imaging [T1WI, repetition time (TR) 6 ms, echo time (TE) 2.6 ms, field of view (FOV) 24 cm, thickness 2 mm] and T2-weighted imaging (T2WI, TR 8501 ms, TE 87 ms, FOV 24 cm, thickness 2 mm) interval-free scans were performed. Anterior commissure-posterior commissure (AC-PC) plane was chosen as the reference. The axial acquisitions were parallel to the reference plane and coronal acquisitions were perpendicular to the reference plane. The average scan time for each patient was 15 minutes.

Preoperative CT scanning with head frame

On the day of the surgery, patients were examined by CT (GE Discovery CT750 HD) preoperatively, with Leksell™ (G-type, Elekta Inc., Sweden) stereotactic head frame installed under topical anesthesia. During the installation, the reference plane of the head frame was made parallel to AC-PC plane, and the midline of head frame was adjusted identical to the sagittal plane approximately by visual observation. Axial CT images parallel to the AC-PC plane were acquired (FOV 24 cm, thickness 2 mm) from the skull base to the top of head.

Preoperative positioning and CT/MRI image fusion

MRI images (including T1WI and T2WI images) and CT images were fused on a workstation using BrainLab iPlan stereotaxy 3.0 software (Brainlab Company, Munich, Germany) and 3 dimensional reconstruction was performed. STN was chosen as the target (Figs. 1A-1C). Target coordinates for surgical procedure were validated by the combination of following 3 methods.¹³ First, AC-PC indirect positioning was performed with the following coordinates: X 12.5-14.0 mm, Y 2.0-3.0 mm and Z 4.0-5.0 mm. X stands for the distance lateral to midline of AC-PC plane defined by images; Y stands for the distance posterior to the midpoint of AC-PC; Z stands for the distance inferior to AC-PC. Second, red nucleus was applied to assist target positioning which was determined as follows: the target lies on the tangent line through the front edge of red nucleus at the axial plane with maximum dimension (Fig. 1D). Finally, positioning of the target was further corrected by direct vision of the neurosurgeon.

Intraoperative microelectrode recording (MER)

During the surgery, the microelectrodes were inserted into the cranial cavity and the brain using micro-thruster toward the target coordinates under the guidance of positioning system. MER was performed with 291A micro-electrodes of Leadpoint system (Medtronic Company, Dublin, Ireland), which was initiated when the electrode was 15 mm away from preoperative target coordinates, advanced continuously till the specific wave form of STN appeared, and did not stop until it disappeared. The length of the nucleus along the axis of insertion was calculated and recorded.

Postoperative target validation of the implanted electrodes

CT scan was performed one week after the surgery without the stereotactic head frame installed to evaluate the actual position of the electrodes. The postoperative CT images were fused with preoperative images at the workstation using BrainLab iPlan stereotaxy 3.0 software (BrainLab Company, Munich, Germany) by the neurosurgeon who performed the preoperative planning (Fig.2). The deviation distance between actual electronic tips and coordinates of target in preoperative planning was then measured and calculated. The coordinate of electrode was defined as (X1, Y1, Z1), and the coordinate of target in preoperative planning was defined as (X2, Y2, Z2). The deviation in X, Y, Z axis was defined as $|X1-X2|$, $|Y1-Y2|$, $|Z1-Z2|$, respectively.

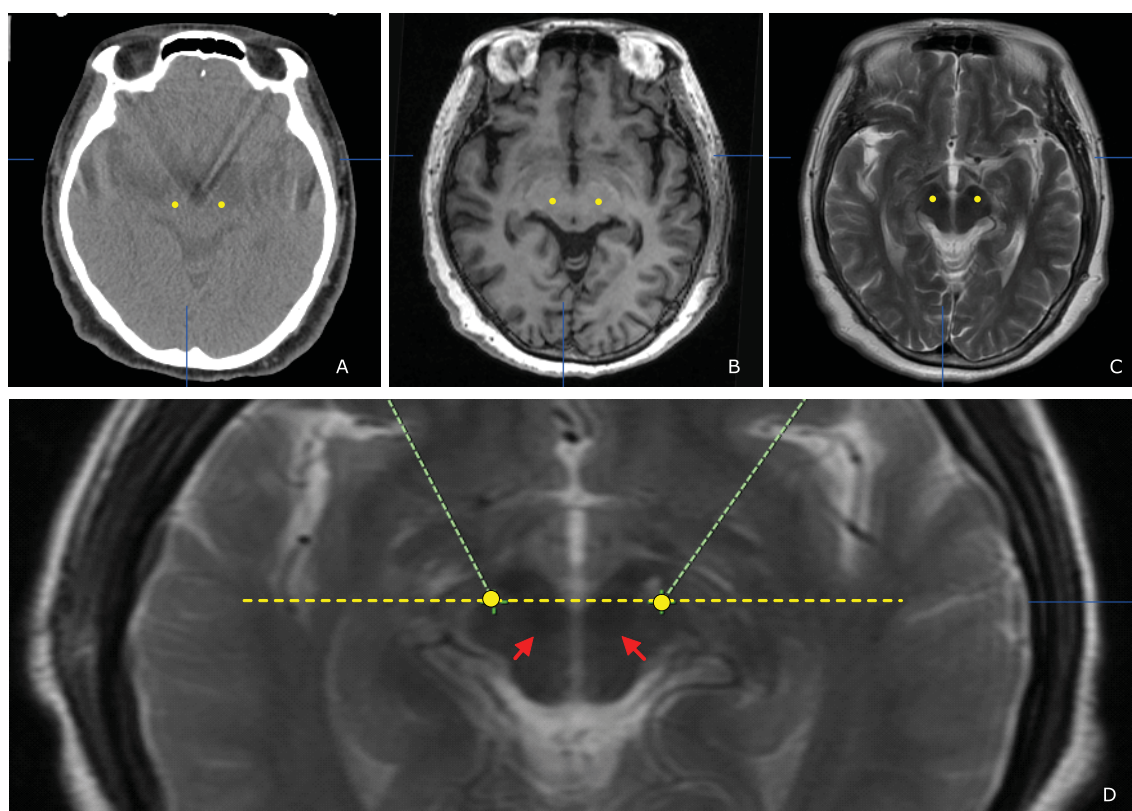


Figure 1. Preoperative positioning with MRI and CT fusion technique.

The locations of target nucleus (yellow dots) were recognized by the system on CT image (A), T1WI MRI image (B), and T2WI MRI image (C). Determination of target nucleus location in the reference of the position of red nucleus (D): The target nucleus (yellow dots) lies on the tangent line (yellow line) through the front edge of the red nucleus (red arrows) at the maximum axial dimension. The green dotted lines indicate the trajectories towards the targets.

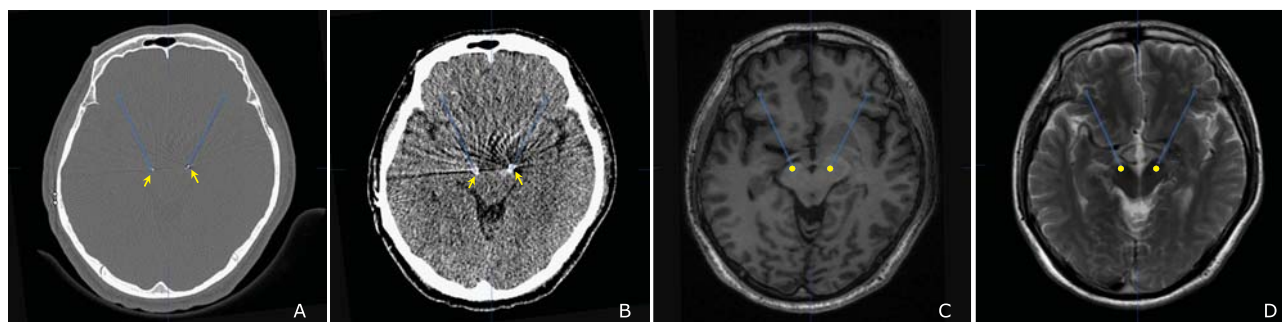


Figure 2. Postoperative CT fusion with preoperative MRI.

Tips of electrodes shown on post-operative CT image as high density ovoid spots with artifacts (yellow arrows) on both bone window (A) and soft tissue window (B) of CT images, where the coordinates of spots center were acquired. The locations of targets nucleus (yellow spots at the end of trajectory lines in blue) were recognized on preoperative T1WI (C) and T2WI (D) by system. The deviations were 0.24 mm, 0.24 mm and 0.31 mm (X, Y and Z) for the left and 0.37 mm, 0.43 mm and 0.42 mm (X,Y and Z) for the right, which were calculated by difference of coordination between actual electrodes and retrieved targets on preoperative images.

Postoperative programming of stimulation

To minimize micro-lesion effects caused by focal edema after the surgery which might affect the stimulation outcomes,

pulse generators were turned on one to two weeks after the surgery. Postoperative programming was performed and adjusted parameters were recorded. The stimulators were

kept on continuously after postoperative programming.

Evaluation of the treatment effect

The "off-drug" state of patients with PD before and six months after surgery were evaluated using Unified Parkinson's disease rating scale (UPDRS).¹⁴ Daily dose of Levodopa intake for the treatment of PD were also recorded. Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) movement scoring system¹⁵ was used for evaluation of patients with dystonia. Complications were recorded if occurred. Each complication was classified into one of three categories: surgery-related, hardware-related or stimulation-related.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 19 software (IBM Corporation, Somers, New York). Qualitative variables were interpreted by count and frequency, and quantitative variables were interpreted by mean value $\pm$ standard deviation. *T*-test was used in comparison of neurologic evaluations scores before and after treatment. For all statistical tests, *P* values less than 0.05 were considered significant.

RESULTS

Baseline characteristics

Seventy-nine patients included 44 males and 35 females. The mean age was 61 ± 10.7 years old. Disease durations ranged from 3 to 20 years with an average of 5.5 ± 2.3 years.

A total of 156 stimulation electrodes were placed into 79 patients. Considering the number of MER needle tracks was 175, each stimulation electrode was placed with an average of 1.12 MER. The average length of STN along the axis of MER by

calculation was 5.5 ± 0.6 mm. For postoperative programming, adjusted parameters were as follows: frequency 130 Hz-160 Hz, pulse width 60 μ s-90 μ s, and voltage 2.0 V-3.5 V.

Deviation of electrodes

The deviation distances of the leads are shown in Table 1. The mean deviation lay between 0.5 and 0.6 mm for each axis. The minimum deviation was 0.1 mm for each axis. The maximum deviation lay between 1.2 and 1.4 mm for each axis.

Neurologic evaluations

Preoperative and postoperative neurologic evaluations for patients are summarized and listed in Table 2. For 68 patients with PD, both UPDRS motor score and life score were significantly lower at the 6-months postoperative follow-up than in the preoperative evaluation. Levodopa dose was also significantly decreased at the 6-months follow-up after surgery. The BFMDRS motor scores were also significantly lowered for 11 patients with dystonia.

Complications

Complications were reported in 10.1% (8/79) patients in total. No hardware-related complications were observed. As for surgery-related complications, wound infections occurred in 2.5% (2/79) patients. Both cured by debridement and flap transfer treatment. Stimulation-related complications occurred in 7.6% (6/79) patients: 1 case suffered from euphoric symptoms, 2 cases suffered from diplopia and dysarthria occurred in 3 cases. All stimulation-related complications mentioned above disappeared after reprogramming the stimulation parameters.

Table 1. Deviations of electrodes calculated by fusion of preoperative and postoperative images (mm)

Axis	Mean	Standard deviation	Minimum	Maximum
X (lateral)	0.5	0.3	0.1	1.4
Y (anteroposterior)	0.5	0.2	0.1	1.3
Z (vertical)	0.6	0.3	0.1	1.2

Table 2. Preoperative and postoperative neurologic evaluations for patients with PD and dystonia[§]

Groups	<i>n</i>	Items	Pre-operation	Post-operation	<i>P</i> value
PD	68	UPDRS motor score	56.0 ± 7.6	23.0 ± 2.9	<0.001
		UPDRS life score	25.5 ± 6.8	6.4 ± 3.4	<0.001
		Levodopa dose (mg/d)	1067 ± 356	434.0 ± 269	<0.001
Dystonia	11	BFMDRS motor score	23.0 ± 5.8	6.4 ± 2.4	<0.001

§: Plus-minus values are means $\pm$ SD.

PD: Parkinson's disease; UPDRS: Unified Parkinson's disease rating scale; BFMDRS: Burke-Fahn-Marsden Dystonia Rating Scale.

DISCUSSION

Accuracy of target positioning

Our study showed that the average deviation of preoperative positioning by MRI/CT image fusing was 0.5-0.6 mm on each axis. It is acceptable regarding the length of STN (5.5 mm on average). The accuracy in our study was also comparable with previous studies using either MRI¹⁶⁻¹⁹ or stereotactic CT alone²⁰ for preoperative targeting (Table 3). So far there was no study comparing accuracy of target positioning by preoperative CT/MRI fusion and by pre-operative MRI alone. Chen *et al*⁹ reported a significantly longer STN length recorded along the axis in MER in the CT/MRI fusion group than the MRI group. Considering that the STN was ovoid in shape, the longer the axes of nucleus MER recorded, the closer the electrode was to the center of STN. This result support the point that target positioning by CT/MRI fusion might have higher accuracy than MRI positioning alone.

The deviations can be attributed to two factors. Firstly, STN displacement caused by intraoperative brain shift results in deviations.^{21, 22} Previous studies have shown that electrodes shifted more in the anteroposterior direction¹⁷ and vertical direction,¹⁹ where head positioning and intraoperative cerebrospinal fluid (CSF) leakage were considered the main reasons. To minimize the effect of intraoperative brain shift, measures should be taken to reduce CSF leakage. It was suggested not take postoperative CT scan soon after the surgery in order to allow CSF to compensate.¹⁷ Secondly, the electrodes might slowly shift away from their initial position after implantation surgery, which cause the deviations too.

Advantages of preoperative CT/MRI fusion compared with MRI alone

Previous preoperative target positioning was mainly performed by MRI alone. Patients had MRI scan after installation of stereotactic head frame, and an experienced clinician performed delineation on MRI images. There are several drawbacks in target positioning by preoperative headframe-bound MRI. First, MRI is time-consuming, which is hard for patients with movement disorders to keep from moving during the exam. This is more significant for PD patients because most of them are in the "off-drug" state with prominent tremor, which is likely to cause movement artifacts and further sabotage quality of MRI. Second, headframe-bound MRI is not compatible to certain coils of MRI scanner, which limits the application of MRI. On the contrary, CT scan is time-saving, not as sensitive to the movements as MRI, and has good delineation of implanted electrodes. However, it is of low contrast resolution on soft tissues to recognize neural nucleus.²³ Accordingly, preoperative CT/MRI fusion take advantages of high soft tissue resolution of MRI^{9, 24, 25} as well as the time-saving feature of CT.

Preoperative target positioning by CT/MRI fusion has other advantages compared with target positioning by MRI alone. First, the former allows patients to receive MRI scan in "on-drug" state without stereotactic head frame, which improve patient compliance and comfort, enabling a more dedicate MRI scan preoperatively. On the other hand, CT scan greatly reduces the preparation time for operation and enhance comfort level of patient during procedures of the treatment.

Table 3. Deviations of electrodes from previous studies using either MRI or CT alone in preoperative target positioning

Studies	Sample size	Modalities for positioning		Deviation (mm)
		Pre-operation	Post-operation	
Barnaure <i>et al</i> ¹⁶	23	Headframe-bound MRI	CT	0.17-0.97
Shin <i>et al</i> ¹⁷	16	Headframe-bound MRI	CT	0.39±0.76 (rostral) 0.27±0.74 (caudal)
O'Gorman <i>et al</i> ¹⁸	20	Headframe-bound MRI	CT	0.5 (lateral) 0.5 (anteroposterior) 1.0 (vertical)
Hamid <i>et al</i> ¹⁹	27	Headframe-bound MRI	MRI	0.48 (lateral) 0.69 (anteroposterior) 2.9 (vertical)
Ferroli <i>et al</i> ²⁰	10	Stereotactic CT	MRI	0.65±0.27 (lateral) 0.61±0.22 (anteroposterior) 0.82±0.31 (vertical)

Clinical outcomes

In our study, incidence of complications was relatively low, and there was no hardware-related complications occurred, indicating the safety of the positioning procedures. Moreover, clinical symptom evaluation of patients showed significant improvements at the post-operative 6-month follow-up compared to the pre-operative evaluations. Although we did not make direct connections between targeting accuracy and clinical outcomes, it is reasonable to believe that more precise positioning of electrodes is related to less complications and side effects. Studies have shown that stimulation on different functional domains of STN could further improve specific symptoms.^{26, 27} The development of high-accuracy preoperative target positioning technique will enhance the application of sub-nucleus level stimulation, bringing about a better clinical outcome.

To sum up, this retrospective study on the patients of PD and dystonia showed that preoperative CT/MRI fusion technique can achieve accurate target positioning of STN stimulation with small deviations and good clinical outcomes.

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