Accuracy of Various Subthalamic Nucleus Targeting Methods and an Appropriated Formula for Thai Patients†

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Objective: *Deep brain stimulation (DBS) of the subthalamic nucleus (STN) has recently been the standard surgical treatment for Parkinson's disease. Besides appropriate selection of patients, precise STN targeting is the most crucial factor for good surgical outcomes. However, there is no single targeting method universally accepted as the most accurate technique. Thus, the authors studied the accuracy of various STN targeting methods and proposed a formula for Thai patients.*

Material and Method: *Sixteen patients with Parkinson's disease who fulfilled the intraoperative criteria of good STN targeting and had significant clinical improvements, without any stimulation-induced adverse effects, were included in the present study. Positions of the STN were determined by four targeting methods, direct targeting by axial T2W MRI, direct targeting by coronal T2W MRI, indirect targeting by anterior commissure-posterior commissure based formula and indirect targeting by adjustable digital Schaltenbrand-Wahren (SW) atlas, were compared with the final lead positions. The final lead positions by the four targeting methods were averaged to get an appropriate AC-PC based formula for Thai patients.*

Results: *The most accurate STN targeting method was axial T2W MRI followed by coronal T2W MRI, AC-PC based formula and the SW atlas, respectively. The averaged final lead positions obtained from the four methods was X = 11.5 $\pm$ 1.0, Y = -3.3 $\pm$ 1.0 and Z = -4.8 $\pm$ 0.42 mm.*

Conclusion: *The direct targeting by axial T2W MRI yielded the highest accuracy and the appropriate STN formula for Thai patients appeared to be X = $\pm$11.5, Y = -3.5 (-3.3) and Z = -5.0 (-4.8) mm.*

Keywords: *Deep brain stimulation, Subthalamic nucleus, Targeting method*

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During the last decade, deep brain stimulation (DBS) of the subthalamic nucleus (STN) has become a standard surgical treatment for Parkinson's disease (PD)(1). Patients with motor fluctuation, dyskinesia or intractable tremor are candidates for the surgery. However, the STN is a small nucleus, being located deeply in the upper brain stem and surrounded by many important structures(2). Therefore, precise STN targeting is of major concern(3).

The most accurate targeting method has remained a subject of controversy(4-9). Indirect targeting method based on cadaveric Schaltenbrand-Wahren (SW) atlas was initially used(10). However, an anatomical deviation of patients' brain from the cadaveric brain makes for an inherent inaccuracy of the technique. Partial compensation for this inaccuracy can be made by using a digital atlas adjusted to match an individual patient's brain(11,12) or by using an anterior commissure-posterior commissure (AC-PC) based formula which is averagely obtained from a large number of DBS of the STN. Nevertheless, all AC-PC based formulas were proposed by the surgery and studies from Europe and North America (Table 1). Differences in cranial morphology between Western and Thai patients may make the proposed formulas inapplicable for Thai patients. Fortunately, the STN is visible on the axial or coronal T2W MRI. This makes it possible to target the STN directly either by axial or by coronal T2W MRI(13-15).

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Table 1. Various proposed AC-PC based formulas for STN targeting

Studies	AC-PC based formulas
Schrader B et al[16]	X: $\pm$12, Y: -3, Z: -3
Benabid AL et al[17]	X: $\pm$10 to 14, Y: 0, Z: 0 to -6
Machado A et al[18]	X: $\pm$11 to 13, Y: -3 to -4, Z: -4 to -5
Starr PA et al[19]	X: $\pm$12, Y: -2 to -3, Z: -4 to -6

Material and Method

Patients

Since 2004, the authors group have performed various operations in more than 150 patients with movement disorders and subthalamic deep brain stimulation (STN-DBS) was the most common procedure. Sixteen patients who had significant clinical improvements without any stimulation-induced adverse effects for at least 2 years and had good follow-up recording, were retrospectively selected for the present study. All patients had to fulfill the authors intraoperative criteria of good STN targeting, namely 1) microelectrode recording which showed STN being at least 4.5 mm in length and containing movement-related cells 2) macrostimulation by using a test electrode and DBS lead (0-, 3+) had a threshold of adverse effects higher than 3.5 mA and 4 V, respectively (pulse width 0.06 msec and frequency 130 Hz) and 3) significant intraoperative clinical improvement.

Methods

Indirect STN targeting by digital SW atlas was done by using Tarairach's grid system to adjust the atlas to match the patients' brain. A target was placed at the level at which an axial cut of the atlas showed the largest red nucleus (the superior-inferior axis; Z), 1 mm behind the anterior border of the largest axial cut of the red nucleus (the anterior-posterior axis; Y) and was not too close to the medial and lateral borders of the STN (the medial-lateral axis; X) (Fig. 1).

Indirect STN targeting by AC-PC based formula was done by placing a target at X = $\pm$12, Y = -2 and Z = -5 mm.

Direct STN targeting by axial T2W MRI was performed by placing a target at the level at which the axial acquisition MRI demonstrated the largest red nucleus (Z), 1 mm behind the anterior border of the largest axial cut of the red nucleus (Y) and was not too close to medial and lateral borders of the STN (X) on the axial T2W MRI (Fig. 2).

Direct STN targeting by coronal T2W MRI was done by using the coronal acquisition MRI to reformat an axial MRI. A target was placed at the level at which the reformatted axial MRI showed the largest

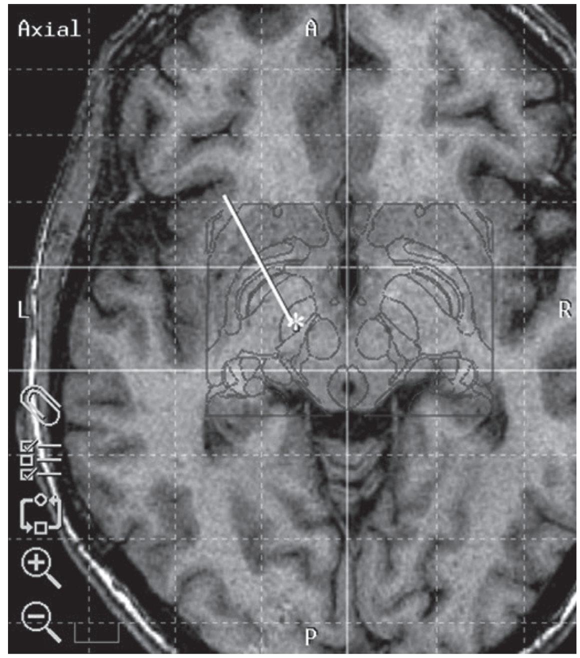

Fig. 1 The STN (*) is targeted by Schaltenbrand-Wahren (SW) atlas

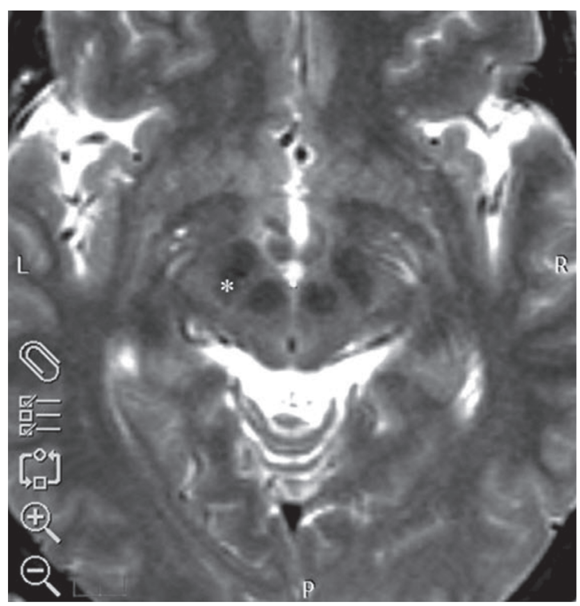

Fig. 2 The STN (*) is targeted by axial T2W MRI

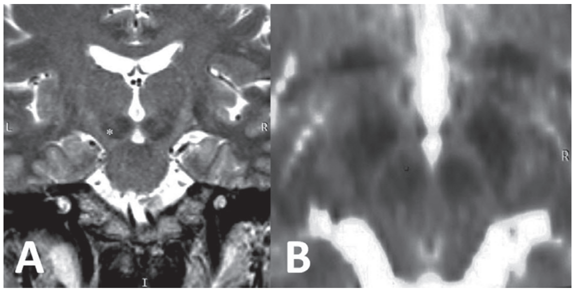

Fig. 3 (A) The STN (*) is targeted by coronal T2W MRI. (B) Reformatted axial image

red nucleus (Z), 1mm behind the anterior border of the largest red nucleus on reformatted axial MRI (Y) and was not too close to the medial and lateral borders of STN on the coronal acquisition MRI (X) (Fig. 3).

The final lead position was demonstrated by image fusion between postoperative cranial CT scan and the preoperative cranial MRI. Targets planned by the four methods were compared with the final lead positions of each method. Deviation of the targets from the final lead positions was analyzed to study the accuracy of each method. The final lead positions from each targeting method were also averaged to get an appropriate formula base on Thai patients.

One-way analysis of variance (ANOVA) and Bonferroni test for Post-HOC comparison were used to analyze the overall targeting methods and between methods respectively. A p-value of less than 0.05 was considered statistical significance different.

Results

Thirty one STNs from 16 patients were analyzed. The mean coordinates of each STN targeting method and mean deviations from the final lead positions are presented in Table 2 and 3. A one-way analysis of variance test (ANOVA) which analyzed accuracy of the four targeting methods revealed that there were statistically significant differences in overall accuracy between some targeting methods (Table 4). The Bonferroni Post-Hoc test showed that the accuracy of direct targeting method, either by axial or by coronal T2W MRI was significantly higher than indirect targeting methods (SW atlas and AC-PC based formula) ($p < 0.05$) (Table 4). The most accurate method was the direct targeting by axial T2W MRI (Table 3) but it was not significantly different from the direct targeting by coronal MRI ($p = 1.00$) (Table 4).

Additionally, analyses of deviation in the medial-lateral axis (X) and anterior-posterior axis (Y) were performed separately (Table 4). The results

Table 2. Comparison between the mean coordinates of each STN targeting method and the mean final lead positions of each methods

Methods	Mean coordinates			Final lead position			ΔX	ΔY	ΔS
	X	Y	Z	X	Y	Z			
Axial T2W	12.5	-3.3	-4.8	11.5	-3.2	-4.8	1.27	0.74	1.67
Coronal T2W	11.9	-3.1	-4.7	11.5	-3.3	-4.7	0.99	1.02	1.71
SW atlas	12.6	-1.0	-4.7	11.5	-3.3	-4.7	1.30	2.40	2.90
AC-PC based formula	12.0	-2.0	-5.0	11.4	-3.5	-5.0	1.07	1.77	2.21

ΔX = deviation in medial-lateral axis, ΔY = deviation in anterior-posterior axis, ΔS = absolute deviation (measured in mm)

Table 3. Deviation in the medial-lateral axis (ΔX), anterior-posterior axis (ΔY) and absolute deviation (ΔS) of each targeting method from the final lead positions

Deviation	Mean deviation ± SD (range) (mm)			
	Axial T2W	Coronal T2W	SW atlas	AC-PC based formula
ΔX	1.27 ± 0.99 (0.0-4.0)	0.99 ± 1.03 (0.0-3.5)	1.30 ± 1.13 (0.0-6.1)	1.07 ± 0.92 (0.2-4.5)
ΔY	0.74 ± 0.82 (0.0-3.0)	1.02 ± 0.95 (0.0-3.0)	2.40 ± 1.23 (0.0-5.0)	1.77 ± 0.97 (0.5-4.0)
ΔS	1.67 ± 0.99 (0.5-4.2)	1.71 ± 1.20 (0.2-5.3)	2.90 ± 1.33 (0.3-6.1)	2.21 ± 1.00 (0.6-4.6)

SD = standard deviation

Table 4. P-values of overall accuracy, accuracy in the medial-lateral axis (X) and accuracy in the anterior-posterior axis (Y) of each targeting method compared with the others

Accuracy and methods		p-value			
		Axial T2W	Coronal T2W	SW atlas	AC- BC based formula
Overallaccuracy	Axial T2W		1.00	<0.001*	0.002*
	Coronal T2W	1.00		<0.001*	0.022*
	SW atlas	<0.001*	<0.001*		<0.001*
	AC-PC based formula	0.002*	0.022*	<0.001*	
Accuracy in the X axis	Axial T2W		1.00	1.00	1.00
	Coronal T2W	1.00		1.00	1.00
	SW atlas	1.00	1.00		0.723
	AC-PC based formula	1.00	1.00	0.723	
Accuracy inthe Y axis	Axial T2W		1.00	<0.001*	<0.001*
	Coronal T2W	1.00		<0.001*	0.002*
	SW atlas	<0.001*	<0.001*		<0.001*
	AC-PC based formula	<0.001*	0.002*	<0.001*	

* Indicates statistically significant

revealed that the most accurate targeting method on the medial-lateral axis (X) was the direct targeting by coronal T2W MRI (Table 3) but had no statistic significance when compared to the others ($p = 1.00$) (Table 4). In the anterior-posterior axis (Y), the most accurate targeting method was the direct targeting by axial T2W MRI (Table 3), which was significantly more accurate than the targeting by SW atlas or AC-PC based formula ($p < 0.001$) but not significantly better than that by coronal T2W MRI ($p = 1.00$) (Table 4).

Moreover, the 125 final lead positions from each targeting method were averaged and the obtained data suggested that an appropriate coordinate formula for Thai patient was $X = \pm 11.5 \pm 1.0$, $Y = -3.3 \pm 1.0$ and $Z = -4.8 \pm 0.42$ mm from the mid AC-PC plane (Table 5).

Table 5. The final lead positions of each targeting method in the medial-lateral axis (X), anterior-posterior axis (Y) and vertical axis (Z)

Targeting methods	X (mm)	Y (mm)	Z (mm)
Axial T2W	11.5	-3.2	-4.8
Coronal T2W	11.5	-3.3	-4.7
SW Atlas	11.5	-3.3	-4.7
AC-PC based formula	11.4	-3.5	-5.0
Mean	11.5	-3.3	-4.8

Discussion

Using an accurate targeted method can reduce the operative time needed to find an optimal track and reduce brain penetration resulting in decreased brain shift and postoperative complications. Targeting by stereotactic brain atlas has an inherent inaccuracy originating from the difference of patients' brains from cadaveric brains. Earlier experience from thalamotomy and pallidotomy showed that difference in ventricular size was the main cause of the inaccuracy. Fortunately, the STN is located deeply in the upper brain stem, having no ventricle, and therefore is not influenced by the ventricular size. This makes targeting by stereotactic atlas seem to be very promising for STN targeting. However, the present study showed the targeting by stereotactic SW atlas yielding the least accuracy (Table 3, Fig 4B). The major source of inaccuracy occurs from an axis of the brain stem. The cadaveric brain of SW atlas has a mesencephalic angle that is extremely anterior which is probably caused by postmortem processing. This makes targets planned by the SW atlas being excessively anterior in all cases (Table 2, Fig 4B).

The AC-PC based formula of the STN has a wide range of variation (Table 1). There is no single formula accepted as the best. The authors used the formula of $X = \pm 12$, $Y = -2$ and $Z = -5$ mm in the present study as it was considered as the most accurate coordinate from large experience of Medtronic European Group (personal communication). However,

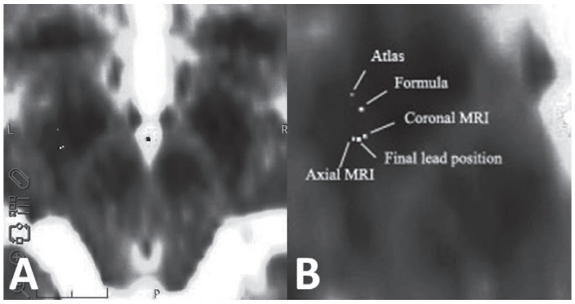

Fig. 4 (A) The positions of the STN planned by the four targeting methods are compared with the final lead positions. (B) Magnification the targets in figure A. The targets planned by axial and coronal T2W MRI are closest to the final lead position

the coordinates were too anterior in most of the presented patients (90.3%) (Table 2, Fig 4B) and the formula may be not appropriate for Thai patients. Based on the data obtained from the present study, the authors proposed an appropriate formula for Thai patients should be X = $\pm$11.5, Y = -3.5 (-3.3) and Z = -5.0 (-4.8) mm (Table 5).

The direct targeting by T2W MRI has the advantage of being planned and tailored to an individual patient. Some patients whose brain is extremely different from the general population can be more accurately targeted. Currently, either axial or coronal T2W MRI can be used for direct STN targeting but there is no consensus as to which one has the advantage. The present study showed the STN targeting by axial T2W MRI being the most accurate technique, though it is not statistically significantly different from that by coronal T2W MRI.

One factor that limits the accuracy of MRI is its slice thickness. The accuracy of stereotactic surgery would never go beyond its image slice thickness. Therefore, the thinner MRI slices, the higher stereotactic accuracy will be. For a long pulse sequence spin echo image such as T2W MRI, a very thin MRI slice will produce a too high noise to signal ratio and it may not be practical to have T2W slice thickness less than 2 mm. This value of 2 mm is marked significant for a small target like the STN and makes axial acquisition T2W MRI relatively inaccurate on the superior-inferior axis (Z) and coronal acquisition T2W MRI relatively inaccurate on the anterior-posterior axis (Y). It was confirmed in the present study that axial MRI is more accurate than coronal MRI in the anterior-posterior axis (Y) (Table 3).

During the operation, surgeons can explore the target on the superior-inferior axis (Z) by simply advancing the recording electrode or DBS lead deeper, whereas a new penetrating track is always needed for an exploration of the target on anterior-posterior axis (Y). For this reason, in the authors' opinion, the inaccuracy in the anterior-posterior axis (Y) negatively affects the procedure more than inaccuracy in the superior-inferior axis (Z). Thus the authors prefer the STN targeting by axial T2W MRI over that by coronal T2W MRI.

Conclusion

The most accurate targeting method to locate the STN is the direct targeting by axial T2W MRI, subsequent by using coronal T2W MRI, AC-PC based formula and the SW atlas, respectively. However, if the formula is considered, the appropriate formula for Thai patients appears to be X = $\pm$11.5, Y = -3.5 (-3.3) and Z = -5.0 (-4.8) mm.

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ความแม่นยำของการกำหนดตำแหน่งซับธาลามิคนิวเคลียสด้วยวิธีการต่าง ๆ และพิกัดที่เหมาะสมของซับธาลามิคนิวเคลียสในคนไทย

ศรัณย์ นันทอารี, ดิลก ตันทองทิพย์, บรรพต สิทธินามสุวรรณ, ประจักษ์ ศรีรพีพัฒน์, อัคคพงษ์ นิติสิงห์, ธีรพล วิทธิเวช

วัตถุประสงค์: *การผ่าตัดกระตุ้นสมองส่วนลึกในส่วนซับธาลามิคนิวเคลียส เป็นการผ่าตัดรักษามาตรฐานสำหรับโรคพาร์กินสัน นอกจากการเลือกผู้ป่วยที่เหมาะสมในการผ่าตัดแล้ว การเลือกตำแหน่งซับธาลามิคนิวเคลียสที่ถูกต้องแม่นยำ เป็นปัจจัยที่สำคัญที่สุดเพื่อที่จะได้ผลการผ่าตัดรักษาที่ดี อย่างไรก็ตามยังไม่มีวิธีใดวิธีหนึ่งในการกำหนดตำแหน่งซับธาลามิคนิวเคลียสที่เป็นที่ยอมรับว่าแม่นยำที่สุด ดังนั้นทางคณะผู้นิพนธ์ จึงได้ศึกษาความแม่นยำของการกำหนดตำแหน่งซับธาลามิคนิวเคลียสด้วยวิธีการต่างๆ และวิเคราะห์ตำแหน่งสุดท้ายของขั้วกระตุ้นไฟฟ้าในซับธาลามิคนิวเคลียส และกำหนดเป็นสูตรที่เหมาะสมในการหาตำแหน่งของซับธาลามิคนิวเคลียสในคนไทย*

วัสดุและวิธีการ: *ประชากรที่ศึกษาได้แก่ผู้ป่วยโรคพาร์กินสันจำนวน 16 คน ที่ได้รับการผ่าตัดฝังอุปกรณ์กระตุ้นสมองส่วนซับธาลามิคนิวเคลียสด้วยไฟฟ้า โดยในผู้ป่วยทุกรายได้ตำแหน่งของซับธาลามิคนิวเคลียสที่เหมาะสมในขณะผ่าตัด และมีอาการดีขึ้นขณะผ่าตัดอย่างมีนัยสำคัญโดยปราศจากภาวะแทรกซ้อนจากการกระตุ้นด้วยไฟฟ้า การกำหนดตำแหน่งของซับธาลามิคนิวเคลียสในการศึกษานี้แบ่งออกได้เป็นสี่วิธี ได้แก่ วิธีการกำหนดตำแหน่งโดยตรงในภาพทีทูของการตรวจแม่เหล็กไฟฟ้าสมองตามแนวแอ็คเซียล, วิธีการกำหนดตำแหน่งโดยตรงในภาพทีทูของการตรวจแม่เหล็กไฟฟ้าสมองตามแนวโคโรนัล, วิธีการกำหนดตำแหน่งทางอ้อมโดยใช้สูตรที่อาศัยแอนทีเรียคอมมิสเชอร์และโพสทีเรียคอมมิสเชอร์, และวิธีการกำหนดตำแหน่งทางอ้อมโดยใช้แผนที่นิวเคลียสในสมองตำแหน่งของซับธาลามิคนิวเคลียสที่กำหนดได้จากวิธีการต่างๆ จะถูกนำไปเปรียบเทียบกับตำแหน่งสุดท้ายของขั้วกระตุ้นไฟฟ้าในซับธาลามิคนิวเคลียส และตำแหน่งสุดท้ายของขั้วกระตุ้นไฟฟ้าในซับธาลามิคนิวเคลียสจะถูกไปคำนวณหาสูตรที่เหมาะสมในการหาตำแหน่งของซับธาลามิคนิวเคลียส โดยอาศัยแอนทีเรียคอมมิสเชอร์และโพสทีเรียคอมมิสเชอร์ในคนไทย*

ผลการศึกษา: *วิธีการที่มีความแม่นยำสูงที่สุดในการกำหนดตำแหน่งของซับธาลามิคนิวเคลียส คือการกำหนดตำแหน่งโดยตรงในภาพทีทูของการตรวจแม่เหล็กไฟฟ้าสมองตามแนวแอ็คเซียล, รองลงมาคือวิธีการกำหนดตำแหน่งโดยตรงในภาพทีทูของการตรวจแม่เหล็กไฟฟ้าสมองตามแนวโคโรนัล, วิธีการกำหนดตำแหน่งทางอ้อมโดยใช้สูตรที่อาศัยแอนทีเรียคอมมิสเชอร์ และโพสทีเรียคอมมิสเชอร์, วิธีการกำหนดตำแหน่งทางอ้อมโดยใช้แผนที่นิวเคลียสในสมองตามลำดับ, ค่าเฉลี่ยของตำแหน่งซับธาลามิคนิวเคลียสในระนาบสามมิติ ที่ได้จากตำแหน่งสุดท้ายของขั้วกระตุ้นไฟฟ้าในซับธาลามิคนิวเคลียสคือ* $X = 11.5 \pm 1.0$ *มิลลิเมตร,* $Y = -3.3 \pm 1.0$ *มิลลิเมตร และ* $Z = -4.8 \pm 0.42$ *มิลลิเมตร*

สรุป: *วิธีการกำหนดตำแหน่งโดยตรงของซับธาลามิคนิวเคลียสในภาพทีทูของการตรวจแม่เหล็กไฟฟ้าสมองตามแนวแอ็คเซียลมีความแม่นยำสูงที่สุด และสูตรที่เหมาะสมของตำแหน่งของซับธาลามิคนิวเคลียสในคนไทยคือ* $X = \pm 11.5$ *มิลลิเมตร,* $Y = -3.5\ (-3.3)$ *มิลลิเมตรและ* $Z = -5.0\ (-4.8)$ *มิลลิเมตร*