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COMPARISON OF TWO TECHNIQUES TO POSTOPERATIVELY LOCALIZE THE ELECTRODE CONTACTS USED FOR SUBTHALAMIC NUCLEUS STIMULATION

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OBJECTIVE: Cerebral ventriculography (Vg) and magnetic resonance imaging (MRI) scanning are routine procedures to determine the implanted electrode placement into the subthalamic nucleus (STN) and are used in several centers that provide deep brain stimulation for Parkinson's disease patients. However, because of image distortion, MRI scan accuracy in determining electrode placement is still matter of debate. The objectives of this study were to verify the expected localization of the electrode contacts within the STN and to compare the stereotactic coordinates of these contacts determined intraoperatively by Vg with those calculated postoperatively by MRI scans. To our knowledge, this is the first study attempting to compare the "gold standard" of stereotactic accuracy (Vg) with the anatomic resolution provided by MRI scans.

METHODS: Images from 18 patients with Parkinson's disease who underwent bilateral operation were used in this study. Among the 36 chronically stimulated contacts, 28 contacts (78%) were localized in the dorsolateral part of the STN. The remaining eight contacts (22%) were located more dorsally in the zona incerta, close to the upper border of the STN.

RESULTS: Significant differences were found between Vg and MRI scans regarding the mediolateral *x* coordinate of the contacts for both left and right electrodes and regarding the right-sided anteroposterior *y* coordinate. No statistical difference was found for the left-sided *y* coordinate and the dorsoventral *z* coordinate for both sides.

CONCLUSION: If we assume that Vg is an imaging gold standard, our results suggest that postoperative MRI scanning may induce a slight image translation compared with Vg. However, MRI scans allowed localization of most of the contacts within the STN.

KEY WORDS: Cerebral ventriculography, Deep brain stimulation, Magnetic resonance imaging, Parkinson's disease, Subthalamic nucleus

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Among surgical treatments for advanced Parkinson's disease (PD), the subthalamic nucleus (STN) has become the preferred target for high-frequency deep brain stimulation (DBS). Stimulation of the STN is able to improve most motor symptoms of PD and consistently reduce the daily dose of dopaminergic drugs (20, 21). Techniques for electrode placement guidance and checking for correct electrode localization varies between centers.

Ventriculography (Vg) used to be the "gold standard" for localization of the target; however, mostly because of its invasiveness (18), Vg is now performed at only a few centers (3, 5, 22, 33). Vg provides an accurate visualization of the anterior commissure (AC) and posterior commissure (PC), as well as the delineation of the third ventricle (V3) without magnetic image distortion. Despite possible image distortion, caused mainly by the orientation of the head in relation to the film and the x-ray source, Vg is of interest for determining localization of the targeted structure (4). Actually, minimal distortion of anatomic structures can be achieved using teleradiographic Vg. This technique remains the most accurate opportunity to check the targeting intraoperatively. Indeed, teleradiographic x-rays obtained

stereotactically during surgery can provide the precise visualization of the electrode implantation, especially when it is performed according to an adequate configuration of the equipment (e.g., a large distance between the x-ray source and the film and the head maintained within the stereotactic frame, which is fixed on the ground). X-rays obtained at the end of surgery provide the precise three-dimensional location of the four contacts of the electrode in relation to the AC and PC but do not show intracerebral structures.

On the other hand, magnetic resonance imaging (MRI) scans are less invasive and allow direct visualization of the targeted structure with a T2-weighted sequence. Compared with Vg, this is of major importance in terms of both surgical constraints and efficacy, which may explain why Vg is performed by so few centers. Postoperatively, MRI scans help to confirm the precise location of the electrode contact that would be used chronically, which is necessary for later adjustment of stimulation parameters. However, the risk of obtaining image distortion with MRI scanning is not negligible. According to the technique used, the electrode artifact can make identification of the structure difficult (14). Moreover, concerns regarding safety should also be stated because, in theory, the presence of a metallic implant causes a potential risk of heating and electrode displacement under a high magnetic field. Risks have been evaluated in phantom studies and, notably, showed that the increase of the electrode's temperature was limited when the wires were placed in a single cable and the leads were twisted around each other (8, 9, 16). However, we do not use this configuration in all cases and have not observed any complications in several hundred patients implanted in the thalamus (ventralis intermediate nucleus), pallidum (globus pallidus internus), or STN. Other experiments using fluoroptic thermometry in models showed a local electrode temperature increase of only 2.3°C (29). Heating of the implanted stimulator during MRI scanning has been observed by some groups (12, 31) but not by others (11, 34). These latter reports highlighted the fact that postoperative MRI scanning is often used routinely to confirm good placement of the electrodes after implantation (11, 34).

In our group, we systematically use both pre- and intraoperative Vg, as well as pre- and postoperative MRI scanning. Therefore, we were able to compare the precision of the two techniques in determining electrode placement. Thus, the aim of this study was twofold: to verify the expected localization of the chronically stimulated electrode contact within the STN area by means of the MRI scans and to compare the stereotactic coordinates of the electrode contacts used for chronic stimulation determined by postoperative MRI scans with those obtained by intraoperative Vg.

PATIENTS AND METHODS

Comparison between MRI scanning and Vg consisted of an analysis of data obtained in 18 PD patients who had electrodes implanted bilaterally into the STN via a previously described surgical procedure (20, 21). At the time of surgery, the mean age of the patients was 50.2 ± 8.6 years and the mean duration of PD was 11.7 ± 5.1 years. The effect of bilateral STN stimulation on the patients' motor disability assessed at 3 months (n = 10) or 1 year (n = 8) postoperatively showed that the global motor score of the Unified PD Rating Scale improved an average of 62% with STN stimulation. Postoperatively, the Unified PD Rating Scale global motor score decreased from 40 ± 14 off L-dopa and off stimulation to 16 ± 9 off L-dopa and on stimulation. Twelve of the patients were previously part of another study; therefore, their clinical evaluation and imaging data were retrospectively analyzed. Six patients were added to the study following the surgical plan.

Vg Data

The stereotactic system used by our team was based on a modified Cosman-Roberts-Wells solid-state base that maintained the patient's head. A positive-contrast Vg was performed as part of the preoperative procedures, as previously reported (2, 5, 6), to provide precise delineation of the midline passing through the middle of V3 (MLV3) and the line across the posterior border of the AC and the anterior border of the PC (the AC-PC line).Vertical lines passing through the AC (VAC) and PC (VPC) were drawn. This determination was needed preoperatively to calculate the "theoretical target" points according to the points provided by averaging the points of the clinically defined best contacts (3–5) and was useful intraoperatively to calculate the position of the electrode contacts on the final x-rays obtained after electrode fixation and skin suture while the cranium was still fixed in the stereotactic frame. Thus, for each electrode contact, we were able to calculate the mediolateral x coordinate (0 = MLV3), the anteroposterior y coordinate (+, anterior; 0, VPC; −, posterior) and the dorsoventral z coordinate (+, ventral; 0, AC-PC; −, dorsal). The middle of the contact in three dimensions was considered for the calculation. This calculation technique has been reported previously (5).

MRI Scanning Data

At the time of surgery, the patients underwent two MRI scans (1.5 T, Intera; Philips Medical Systems, Eindhoven, The Netherlands) using the Philips quadrature receive-only head coil the week before and the week after electrode implantation. The latter MRI scan was performed before stimulator implantation. All of the implanted electrodes were the same model (3389; Medtronic, Minneapolis, MN).

Preoperative Images

Image acquisition was made stereotactically. T2-weighted coronal images were used to visualize the STN as well as possible on both sides. Two series of a two-dimensional spin-echo T2-weighted (2DT2) sequence, shifted by 2 mm one from the other, were used for the first group of 12 patients, resulting in 4-mm-thick images. A three-dimensional spin-echo T2-weighted (3DT2) sequence was used for the other six patients, resulting in 1-mm-thick images.

Postoperative Images

Images were obtained with the same stereotactic frame used for the acquisition of preoperative images and for surgery. Spin-echo T1-weighted (SET_1) sagittal and coronal images were considered to visualize electrode trajectories and contacts along the leads. This MRI scanning sequence was performed for the entire group of patients for postoperative control of implantation accuracy of the electrodes.

Coordinate Calculation for MRI Scanning Data

We used the same reference axes for calculation of the electrode contact coordinates for MRI scanning determination as those used for Vg (*Fig. 1*). For that purpose, we chose to consider the middle of the hypointense signal as the center of the contacts. Coronal SET_1 images allowed the determination of the mediolateral *x* coordinate of the contacts (*Fig. 2*); MLV3 was the axis reference. The AC-PC line was determined in the sagittal slice passing through the two commissures; VAC and VPC were also drawn (*Fig. 3*). This slice was then superimposed with the slices passing through the left and right electrodes according to the marks of the stereotactic frame, easily visualized in the MRI scans. Thus, determination of the anteroposterior *y* coordinates (0 = VPC) and the dorsoventral *z* coordinates (0 = AC-PC line) of the electrode contacts was possible (*Fig. 4*). Taking the closest preoperative 2DT2 or 3DT2 coronal slice to the *y* coordinate of the stimulated contact electrode, we reported the *x* and *z* coordinates on these images to determine the contacts within the STN area on both sides (*Fig. 4*).

Statistics

To assess potential differences between the two kinds of imaging techniques, measurements of the *x*, *y*, and *z* coordinates of the contacts and the AC-PC lines were compared using Student's *t* tests (two-tailed distribution, two-sample equal variance). Linear regression (Pearson's test) allowed the estimation of a possible correlation between the two measures

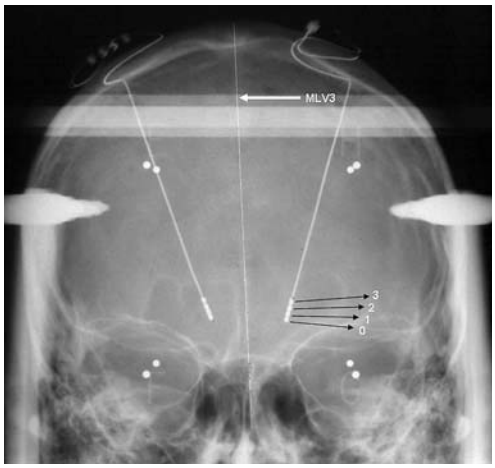

FIGURE 1. *Postoperative teleradiographic Vg for confirmation of the implanted electrode localization within the subthalamic area.* MLV3, *reference axis;* 0, 1, 2, *and* 3, *the four contacts of the implanted electrode.*

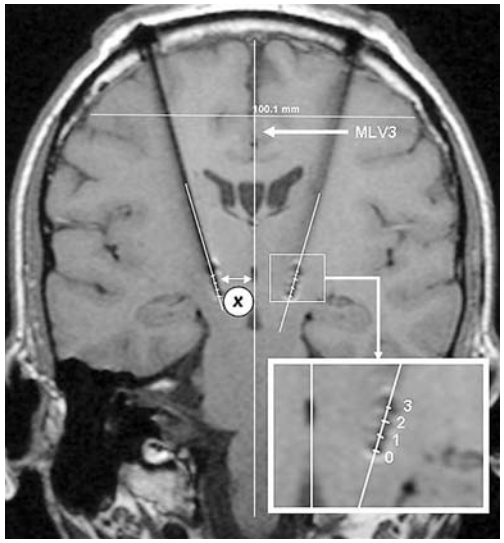

FIGURE 2. *Postoperative frontal spin-echo T1-weighted image for determination of the mediolateral* x *coordinate of the electrode contacts (the image is taken from the same patient as Figure 1).* MLV3, *reference axis;* 0, 1, 2, *and* 3, *the four contacts of the implanted electrode.*

obtained with MRI scanning and Vg. Because of the small number of values for the AC-PC lines (n = 18, one for each patient), the linear regression was only performed for the *x*, *y*, and *z* coordinates of the electrode contacts (four contacts for each of the 18 patients, 72 values for each side of the brain).

RESULTS

The images of the 18 patients considered for this study allowed measurements on 36 implanted electrodes, correspon-

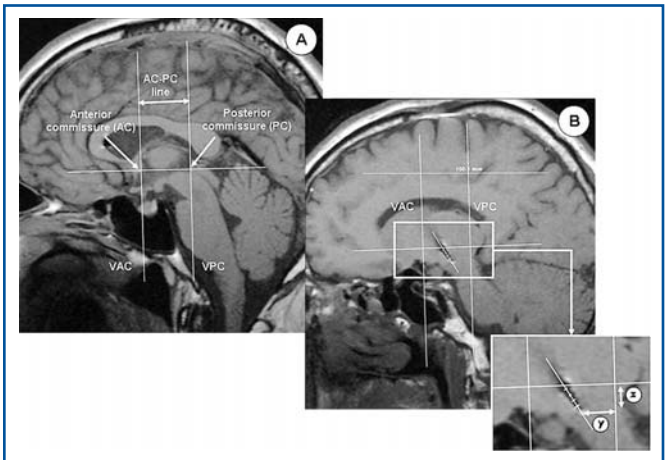

FIGURE 3. *Postoperative sagittal SET_1 MRI scans for measurement of the AC-PC line* (A) *and determination of the anteroposterior* y *and dorsolateral* z *coordinates of the electrode contacts* (B). AC-PC line, *reference axis for* z *coordinate determination;* VAC, *vertical line (orthogonal to the AC-PC line) passing through the AC;* VPC, *vertical line (orthogonal to the AC-PC line) passing through the PC, reference axis for* y *coordinate determination.*

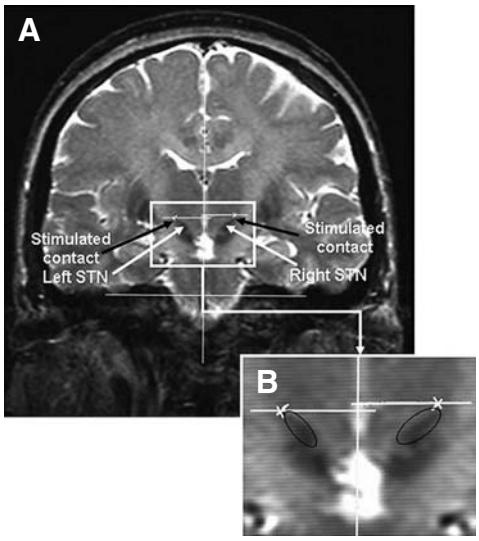

FIGURE 4. *Preoperative frontal T2-weighted MRI scan for localization of the stimulated contacts within the subthalamic area. The STN was estimated as the hypointense signal located lateral to the red nucleus and dorsolateral to the substantia nigra. Taking the closest preoperative 2DT2 or 3DT2 coronal slice to the* y *coordinate of the stimulated contact electrode, the* x *and* z *coordinates were reported in this slice to localize, for both sides, the contacts within the STN area.*

ding to 144 contacts of stimulation. Chronic stimulation for all patients was monopolar, involving one stimulated contact on both the left and right sides of each patient's brain.

MRI Scanning Localization of the Contacts

Among the 36 contacts chronically used for bilateral stimulation of the STN, all but eight contacts (four each in the left and right sides) were localized in the dorsolateral part of the hypointense signal, referred to as the STN shape by reporting the contact coordinates measured on the postoperative SET_1 images on the preoperative 2DT2 and 3DT2 images. The other eight contacts were localized just above the nucleus in the zona incerta or even reaching the ventral border of the thalamus (*Fig. 4*).

Comparison of the AC-PC Lines

The mean value of the AC-PC lines obtained was 24.96 ± 1.76 mm with sagittal SET_1 and 25.38 ± 1.63 mm with Vg; no significant difference was found for either measure. The mean subtraction between SET_1 and Vg values (SET_1 − Vg) was −0.42 ± 0.87 mm (range, −2.1–1.3 mm). Of the 18 AC-PC lines, 12 presented a negative deviation between the values measured with SET_1 and Vg, reflecting a more frequent underestimation of the measurement using the sagittal SET_1 images.

Despite the fact that MRI-related distortion is known to be less on axial than on coronal or sagittal slices, we measured the AC-PC lines with the sagittal images to follow our methodological plan. Considering these slices allowed us to visualize the contacts along the electrodes, which would not be possible on axial slices. A recent study reported measures of the AC-PC lines using axial MRI scans and compared the values with Vg data (7). In this case, the AC-PC distances measured on MRI scans were significantly larger than those measured on Vg images, which is the opposite of what we observed. The AC convexity orientated posteriorly on axial slices might be a possible explanation of an overestimation of the AC-PC distance that may not be fully parallel with the AC-PC line. On the other hand, the AC convexity is orientated anteriorly on sagittal slices. If the image taken into account is not fully parallel with the AC-PC line, a kind of "partial volume" would appear, leading to an underestimation of the AC-PC measure.

Comparison of the Contact Electrode Coordinates

Stereotactic *x*, *y*, and *z* coordinates of the stimulated electrode contacts measured with SET_1-MRI scans and Vg images are shown in *Tables 1* and *2*, respectively. For all coordinates, linear regression analysis showed strong correlations between SET_1 and Vg measurements: all r^2 coefficients reached values greater than 0.75.

Mediolateral x *Coordinate*

Significant differences were found between both measures (SET_1 versus Vg) for the *x* coordinate of both the left ($P = 0.02$) and right ($P = 0.03$) sides. The mean subtraction between both measures (SET_1 − Vg) was −0.59 ± 0.67 mm for the left side (range, −2.6–0.61 mm; 60 out of 72 were negative values) and 0.46 ± 0.66 mm for the right side (range, −1.05–1.66 mm; 56 out of 72 were positive values). The *x* coordinate contact localization seemed to be translated to the right when measured using SET_1 images.

Anteroposterior y *Coordinate*

A significant difference between both measures (SET_1 versus Vg) was found for the right side ($P = 0.038$) but not for the left side ($P = 0.68$). The mean subtraction between both measures (SET_1 − Vg) was 0.13 ± 1.01 mm for the left side (range, −2.66–2.69 mm; 44 out of 72 were positive values) and 0.60 ± 0.84 mm for the right side (range, −1.06–2.19 mm; 55 out of 72 were positive values). For the *y* coordinate of the contacts, a trend toward an anterior translation seemed probable if using MRI scan measurements.

Dorsoventral z *Coordinate*

No statistical differences were found between *z* coordinates evaluated with both measures (SET_1 versus Vg) for both the left ($P = 0.49$) and right ($P = 0.63$) sides. The mean subtraction between both measures (SET_1 − Vg) was 0.28 ± 0.78 mm for the left side (range, −2.13–1.85 mm; 46 out of 72 were positive values) and 0.20 ± 0.86 mm for the right side (range, −1.38–3.39 mm; 41 out of 72 were positive values).

DISCUSSION

The present study confirms that the effective and chronic contacts stimulated for STN DBS are mostly located in the dorsolateral part of the STN, which corresponds to the sensorimo-

TABLE 1. Coordinates x, y, and z of the electrode contacts measured by means of T1-weighted postoperative magnetic resonance imaging scans (mm radio)[a]

Patient no.	Left implantation				Right implantation			
	Contact	x	y	z	Contact	x	y	z
1	0	9.5	8.6	−5.8	0	10.8	9.0	−5.9
	1	10.0	9.5	−3.9	1	11.1	9.9	−4.0
	2	**10.5**	**10.8**	**−1.9**	**2**	**11.5**	**11.4**	**−2.0**
	3	11.1	12.0	+0.8	3	11.9	12.6	+0.2
2	0	12.0	7.5	−5.9	0	10.0	9.3	−5.9
	1	13.0	8.9	−4.1	1	10.8	10.5	−4.0
	2	**14.0**	**10.7**	**−2.0**	2	11.4	11.8	−2.1
	3	14.5	12.2	0	**3**	**11.8**	**12.9**	**−0.2**
3	0	11.9	10.0	−5.5	0	11.0	10.1	−6.9
	1	12.1	10.8	−3.5	1	11.5	11.1	−4.9
	2	12.4	11.6	−1.5	2	12.0	12.1	−3.1
	3	**12.7**	**12.1**	**+0.5**	**3**	**12.6**	**13.1**	**−1.1**
4	0	10.0	7.0	−5.9	0	10.9	7.5	−3.8
	1	10.4	8.8	−3.6	1	11.2	8.6	−2.0
	2	**11.0**	**10.1**	**−1.5**	**2**	**11.5**	**9.7**	**−0.8**
	3	11.5	11.5	+0.9	3	11.8	10.8	+1.3
5	0	12.0	9.2	−3.2	0	12.3	9.0	−6.3
	1	12.3	10.4	−1.4	1	13.0	10.0	−4.2
	2	12.6	11.9	+0.5	2	13.4	11.0	−2.0
	3	**13.0**	**13.0**	**+2.5**	**3**	**13.7**	**12.2**	**0**
6	0	11.8	12.3	−4.5	0	12.8	12.5	−5.0
	1	12.2	13.0	−2.5	1	13.3	13.5	−3.0
	2	**12.5**	**14.2**	**−0.5**	2	14.1	13.8	−1.0
	3	12.8	15.3	+1.5	**3**	**15.0**	**16.0**	**+1.0**
7	0	13.8	7.2	−5.8	0	14.0	9.1	−5.8
	1	14.3	8.8	−3.8	1	14.6	10.5	−4.2
	2	**14.8**	**10.0**	**−1.8**	**2**	**15.2**	**12.1**	**−2.2**
	3	15.3	11.0	0	3	15.8	13.5	−0.8
8	0	11.5	11.6	−4.9	0	12.8	9.9	−4.7
	1	**12.0**	**12.5**	**−3.0**	1	13.0	10.6	−2.5
	2	12.5	13.1	−.0	**2**	**13.5**	**11.8**	**−0.5**
	3	12.9	15.1	−0.5	3	13.8	12.7	+1.5
9	0	12.0	8.5	−6.8	0	12.0	7.7	−5.0
	1	12.5	9.5	−4.8	**1**	**12.3**	**8.7**	**−3.0**
	2	**13.0**	**10.5**	**−2.8**	2	12.6	9.7	−1.0
	3	13.5	11.5	−0.8	3	13.0	10.7	+1.0
10	0	10.5	9.1	−3.9	0	13.0	8.0	−4.4
	1	11.2	10.1	−2.3	1	13.4	9.2	−2.8
	2	**11.5**	**11.1**	**−0.9**	**2**	**13.8**	**10.5**	**−1.0**
	3	12.0	12.4	+1.0	3	14.0	12.0	+1.2
11	0	9.8	8.0	−7.1	0	12.5	9.0	−7.6
	1	10.1	9.0	−5.2	1	12.8	10.0	−5.9
	2	**10.3**	**10.3**	**−3.0**	**2**	**13.2**	**11.7**	**−3.5**
	3	11.8	11.0	−0.8	3	13.6	12.4	−1.0
12	0	10.8	7.3	−4.3	0	11.0	8.8	−7.2
	1	11.2	8.5	−2.5	1	11.6	9.9	−6.2
	2	**11.8**	**9.5**	**−0.8**	**2**	**12.4**	**10.8**	**−4.2**
	3	12.2	10.5	+1.7	3	13.3	11.5	−1.9
13	0	8.5	9.7	−7.1	0	11.0	10.0	−6.9
	1	9.0	10.7	−5.5	1	11.5	11.0	−4.9
	2	**9.5**	**11.8**	**−3.5**	2	12.0	12.0	−2.9
	3	10.0	12.8	−1.2	**3**	**12.5**	**13.0**	**−0.7**
14	0	10.5	7.8	−7.0	0	12.1	7.5	−7.5
	1	11.0	8.8	−5.0	1	12.8	8.5	−5.8
	2	11.3	10.0	−2.8	2	13.0	9.5	−3.9
	3	**12.0**	**11.2**	**−0.2**	**3**	**13.2**	**11.0**	**−1.5**
15	0	10.5	6.7	−7.4	0	9.5	9.5	−5.9
	1	11.0	7.8	−5.3	1	10.0	10.5	−3.1
	2	11.5	9.0	−3.1	2	10.8	11.5	−2.3
	3	**12.0**	**10.5**	**−0.9**	**3**	**11.2**	**12.5**	**−0.6**
16	0	8.2	7.8	−7.0	0	11.1	9.5	−7.0
	1	9.1	8.8	−5.0	1	11.9	10.5	−5.0
	2	10.0	9.8	−3.0	**2**	**12.4**	**11.5**	**−3.0**
	3	**10.9**	**10.8**	**−1.0**	3	12.9	12.5	−1.0
17	0	11.0	12.0	−6.5	0	11.5	9.8	−6.4
	1	11.5	13.2	−5.0	1	12.0	11.2	−4.5
	2	12.0	14.0	−3.0	2	12.8	12.4	−2.4
	3	**12.5**	**15.5**	**−1.0**	**3**	**13.5**	**13.3**	**−0.8**
18	0	12.5	9.8	−7.2	0	11.0	10.6	−6.2
	1	13.5	10.9	−5.2	1	11.5	11.8	−4.2
	2	14.2	11.9	−3.2	**2**	**12.0**	**13.2**	**−2.2**
	3	**14.9**	**12.9**	**−1.2**	3	12.5	14.8	−0.4

[a] Contacts in bold are those used for chronic stimulation.

TABLE 2. Coordinates x, y, and z of the electrode contacts measured by means of the postoperative ventriculographies (mm radio)[a]

Patient no.	Left implantation				Right implantation			
	Contact	x	y	z	Contact	x	y	z
1	0	9.90	10.21	−5.12	0	9.94	9.28	−6.03
	1	10.43	10.89	−3.20	1	10.46	10.21	−3.89
	2	**10.97**	**11.58**	**−1.28**	**2**	**10.98**	**11.14**	**−1.75**
	3	11.50	12.26	0.64	3	11.50	12.07	0.40
2	0	13.75	7.70	−6.26	0	11.05	8.69	−6.69
	1	14.23	8.86	−4.33	1	11.58	9.83	−4.75
	2	**14.70**	**10.01**	**−2.41**	2	12.11	10.98	−2.81
	3	15.18	11.17	−0.48	**3**	**12.64**	**12.12**	**−0.87**
3	0	11.29	8.25	−6.83	0	10.71	8.39	−7.86
	1	11.97	9.28	−4.53	1	11.24	9.48	−5.44
	2	12.65	10.30	−2.23	2	11.77	10.57	−3.02
	3	**13.33**	**11.33**	**0.07**	**3**	**12.30**	**11.66**	**−0.60**
4	0	10.65	8.56	−7.19	0	9.97	8.56	−7.19
	1	11.14	9.52	−4.98	1	10.45	9.52	−4.98
	2	**11.62**	**10.47**	**−2.76**	**2**	**10.92**	**10.47**	**−2.76**
	3	12.11	11.43	−0.55	3	11.40	11.43	−0.55
5	0	11.67	8.42	−4.32	0	12.59	8.77	−4.92
	1	12.20	9.60	−2.59	1	13.13	9.83	−3.00
	2	12.73	10.78	−0.85	2	13.67	10.89	−1.09
	3	**13.26**	**11.96**	**0.88**	**3**	**14.21**	**11.95**	**0.83**
6	0	13.39	11.74	−5.71	0	11.25	12.87	−5.27
	1	13.87	12.82	−3.73	1	11.95	13.86	−3.34
	2	**14.34**	**13.91**	**−1.75**	2	12.65	14.86	−1.41
	3	14.82	14.99	0.24	**3**	**13.35**	**15.85**	**0.52**
7	0	13.92	7.36	−6.49	0	13.29	8.55	−6.92
	1	14.46	8.62	−4.56	1	13.91	9.79	−4.90
	2	**14.99**	**9.88**	**−2.62**	**2**	**14.54**	**11.03**	**−2.88**
	3	15.53	11.14	−0.69	3	15.16	12.27	−0.86
8	0	11.78	9.90	−4.64	0	12.48	9.01	−3.91
	1	**12.24**	**10.74**	**−2.55**	1	12.86	9.80	−1.93
	2	12.70	11.57	−0.46	**2**	**13.24**	**10.60**	**0.05**
	3	13.16	12.41	1.63	3	13.62	11.39	2.03
9	0	12.40	8.39	−6.12	0	11.69	7.81	−5.78
	1	12.84	9.40	−4.15	**1**	**12.19**	**8.91**	**−3.87**
	2	**13.29**	**10.42**	**−2.19**	2	12.69	10.00	−1.95
	3	13.73	11.43	−0.22	3	13.19	11.10	−0.04
10	0	10.82	8.94	−5.75	0	13.08	6.97	−5.26
	1	11.20	10.03	−3.72	1	13.57	8.28	−3.20
	2	**11.57**	**11.11**	**−1.68**	**2**	**14.07**	**9.60**	**−1.13**
	3	11.95	12.20	0.35	3	14.56	10.91	0.93
11	0	12.06	6.54	−6.42	0	10.87	8.33	−6.67
	1	12.52	7.92	−4.59	1	11.31	9.56	−4.72
	2	**12.97**	**9.31**	**−2.76**	**2**	**11.75**	**10.80**	**−2.76**
	3	13.43	10.69	−0.93	3	12.19	12.03	−0.81
12	0	11.30	7.36	−5.24	0	10.91	9.59	−7.92
	1	12.06	8.26	−3.11	1	11.52	10.48	−5.82
	2	**12.82**	**9.15**	**−0.97**	**2**	**12.14**	**11.38**	**−3.71**
	3	13.58	10.05	1.16	3	12.75	12.27	−1.61
13	0	8.84	10.23	−7.07	0	9.34	9.54	−6.81
	1	9.36	11.14	−5.08	1	9.88	10.43	−4.87
	2	**9.87**	**12.05**	**−3.09**	2	10.43	11.31	−2.94
	3	10.39	12.96	−1.11	**3**	**10.97**	**12.20**	**−1.00**
14	0	10.80	8.55	−7.07	0	11.69	7.22	−7.07
	1	11.18	9.52	−5.15	1	12.11	8.19	−5.15
	2	11.55	10.50	−3.24	2	12.53	9.17	−3.24
	3	**11.93**	**11.47**	**−1.32**	**3**	**12.95**	**10.14**	**−1.32**
15	0	10.80	9.36	−6.65	0	9.17	7.61	−6.67
	1	11.13	10.36	−4.68	1	9.68	8.66	−4.69
	2	11.47	11.37	−2.71	2	10.20	9.72	−2.72
	3	**11.80**	**12.37**	**−0.74**	**3**	**10.71**	**10.77**	**−0.74**
16	0	9.49	6.74	−7.42	0	10.09	7.36	−7.18
	1	10.09	7.70	−5.34	1	10.61	8.42	−4.87
	2	10.70	8.67	−3.26	**2**	**11.12**	**9.47**	**−2.55**
	3	**11.30**	**9.63**	**−1.18**	3	11.64	10.53	−0.24
17	0	12.06	11.98	−7.03	0	11.05	9.59	−6.89
	1	12.65	12.88	−5.02	1	11.78	10.51	−4.92
	2	13.23	13.77	−3.00	2	12.51	11.43	−2.95
	3	**13.82**	**14.67**	**−0.99**	**3**	**13.24**	**12.35**	**−0.98**
18	0	12.75	10.42	−6.31	0	10.66	10.03	−5.82
	1	13.45	11.35	−4.44	1	11.34	10.89	−4.07
	2	14.14	12.29	−2.57	**2**	**12.02**	**11.75**	**−2.31**
	3	**14.84**	**13.22**	**−0.70**	3	12.70	12.61	−0.56

[a] Contacts in bold are those used for chronic stimulation.

tor area of the nucleus (23) and, more rarely, just above it. In fact, all patients whose images have been considered in this study showed a beneficial and significant effect of STN stimulation in global motor disability. Our study compared the gold standard for stereotactic accuracy (Vg) with the gold standard for anatomic resolution (MRI scanning). The results showed few differences between MRI scanning and Vg measurement of stereotactic coordinates and suggest that MRI scanning induces a probable right anterolateral translation of the images compared with Vg.

MRI Scanning and DBS: Anatomy and STN Stimulation Effects

Visualization of the STN on the T2-weighted images was performed after a previous report that highlighted the landmarks of the STN on such images (1). As recently proposed, the STN was estimated as the hypointense signal located lateral to the red nucleus and dorsolateral to the substantia nigra, reflecting the presence of iron and corresponding to the STN (10). As pointed out by the authors of that study, it seems that the hypointensity more likely reflects the anterior half of the STN than the posterior part of the nucleus, which was not visible in most patients in their study (10). Regarding the four patients for whom the stimulated contacts have been localized outside the STN, the distance between the upper border of the STN and the contacts was often less than 3 mm, which leads to an acceptable spatial error regarding the millimetric anatomic resolution of MRI scanning, especially considering that a contact is a not a virtual point but a cylinder 1.5 mm high and 1.27 mm wide, and to a careful interpretation of the localization considering the partial visualization of the STN. Thus, it is reasonable to imagine that the contacts we found outside of the STN might, in fact, be located in the upper border of the nucleus or at least sufficiently close to consider that the effect induced by its stimulation belongs by diffusion to the upper part of the STN.

Indeed, another study has reported that the size, position, and shape of the STN are highly variable (30). If direct visualization of the STN with preoperative MRI scanning is largely used to guide the surgical act, postoperative MRI scanning as a contact electrode localization procedure has, during the past few years, led to various investigations; the aims of these studies were both to test somatotopy in subcortical structures (37) and to correlate therapeutic effects of DBS with contact electrode localization (13, 15, 36).

Precision of MRI Scanning: A Question Still Debated

On MRI scans, we observed a translation of the electrode shape for the *x* coordinate on frontal images; the translation was directed toward the right of the image (the right side of the brain) along the phase-encoding gradient. For the *y* coordinate on sagittal images, significantly for the right electrode, the translation was also directed toward the right side of the image (the anterior part of the brain) along the phase-encoding gradient. This was probably caused by the MRI scanning sequence, which led to a systematic modified estimation of the electrode and reference lines shape. We may hypothesize that the MRI scanning translation reflected an artifact associated with the phase-encoding gradient. Therefore, confirmation of this point is still needed and could be achieved with in vitro measurements and phantom studies, particularly to understand the reason why only a right *y* shift was observed. We cannot exclude that measuring errors and the statistical significance level we considered contributed to this unilateral shift. Moreover, it should be also noticed that, according to the MRI scanning sequence protocol followed by our MRI scanning group, preoperative T1-weighted images were obtained parallel to the AC-PC line; whereas T1-weighted images parallel to both the electrode trajectories and the AC-PC line were obtained postoperatively. We did use the postoperative T1-weighted images parallel to the electrode trajectories to locate the electrode contacts and do not think that measurement accuracy would have been considerably altered. However, this may contribute to errors of measurement.

Even if deviations between both measures (SET_1 versus Vg) were generally less than 3 mm, a considerable variability of the values must be acknowledged, as shown by the high degree of standard deviation. Errors inherent to the Vg measurements must also be taken into account in the interpretation of our findings. This fact again questions the measurements made with MRI scans compared with Vg; a larger series of patients is required to draw robust conclusions. A previous comparison between anatomic (MRI scanning) and electrophysiological (intraoperative microrecording) of STN localization for DBS has concluded that MRI scan targeting is less accurate (38). MRI scan targeting of deep brain structures is widely used in several centers (1, 13, 14, 17, 19, 24–28, 32, 35) and can provide visualization of the STN area and implanted electrodes with minimum artifacts (15). However, Vg is still performed for targeting subcortical nuclei by a few centers (3, 5, 22, 33). The number of centers using Vg and those using MRI scanning alone reflects motivations other than the precision of the targeting and the invasiveness of the procedure; it also takes into account several parameters, including the availability of the x-ray equipment in the operating room, the increased time of surgery, or the legal situation in countries with a high rate of medical trials. In the present study, we have reached the conclusion that few differences can be pointed out between the two anatomic imaging methods when comparing the localization of the electrode contacts postoperatively. Our results suggest a translation of the electrode location induced by MRI scanning, which is not crucial for electrode contact localization postoperatively. This latter point seems to be confirmed by the comparison between in vitro and in vivo measurements of artifact dimensions (27).

CONCLUSION

Our findings confirm the fact that, in our measurements (i.e., using our specific teleradiographic Vg and MRI scanning equipment), the electrode presence does not create insurmount-

able MRI distortion that could impede confirmation of correct implantation. However, this postoperative image analysis can only reflect the preoperative targeting efficiency for which further information is still needed. Another important issue is to preoperatively compare the accuracy of targeting using Vg and MRI scanning that provides direct visualization of the STN using T2-weighted sequences in a randomized trial.

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COMMENTS

Pinto et al. discuss topics that are extremely relevant for all surgeons involved in subthalamic nucleus (STN) stimulation for advanced Parkinson disease and other abnormal movement diseases. It is also of great relevance for the youngest generation of surgeons who never used stereotactic ventriculography (VG). The authors suggest that magnetic resonance imaging (MRI) targets may be affected by certain errors which affect the anterior commissure and posterior commissure (AC-PC) based targeting procedure versus ventriculography. In our opinion, this is true for not only STN targeting but also for all deep brain stimulation (DBS) targets. Target calculations on any of the neuroradiological images are only part of the first step of the entire DBS surgical procedure. In our opinion, the most important task is the preoperative neurophysiological assessment and macrostimulation with the definitive electrode to check for the definitive implant site. Another relevant topic in this article concerns the feasibility of magnetic resonance in patients with brain electrode. The authors put forth a straightforward and precise viewpoint in a highly vague and debated subject that has been further complicated by the recently emphasized alarms by the Medtronic factory, and the connected medico-legally issue.

Finally, we cannot avoid briefly addressing our own experience with more than 400 implants. AC-PC recognition on computed tomography (CT) is not affected by any of the errors the authors demonstrated in the MRI. Target recognition should be used to provide the first target to be refined. In our opinion, the CT-MRI image fusion should only be used to verify the target calculation. When a target far below the intercommissural plane is chosen, a third point, such as the interpeduncolar nucleus, should be used to better correct the individual anatomical variability. In the past, our group has dealt with problems of recognizing the position of the stimulating electrodes in operated patients. We conclude that the electrode position should be obtained by merging the postoperative CT with the preoperative MRI (1). What can be learned from this article is of remarkable interest for all surgeons involved in DBS.

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This article compares DBS electrode locations measured by two methods: intraoperative VG and postoperative MRI. The author's ability to perform spatially accurate ventriculography is enhanced by using an operating room specifically designed for this purpose. They found a small, yet significant, difference between the measured coordinates in the right to left direction only, which in their study, was in the phase-encoding direction. There was a small rightward deviation in MR coordinates compared to ventriculographic coordinates. Overall, however, the study is noteworthy for the lack of evidence for severe image distortion in MRI, and it validates the use of MRI for the measurement of DBS electrode position. Because their results are not necessarily able to be completely generalized, other MRI units and other pulse sequences may be subject to different distortion effects. Although a receive-only headcoil was used, it is also noteworthy that adverse effects were not seen using MRI. Current manufacturer recommendations should use a transmit-receive type of headcoil, which would avoid the use of the body transmit coil.

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This article compares VG and MRI in 18 patients with respect to location of the DBS electrode contact used for chronic STN stimulation. Of the total 36 contacts, 78% were in the dorso-lateral part of the STN, and the remaining 22% were only dorsal to that in the zona incerta. It was found that MRI may induce a slight image translation compared to VG. The significant differences between VG and MRI concerned the right-sided y-coordinate and the x-coordinate on both the left and right sides. The authors should be commended on a very meticulous study, given the method they chose to address this issue.

The authors stated several times that VG constitutes the "the stereotactic accuracy gold standard," and further stated, "If we assume that VG is an imaging gold standard, our results suggest that postoperative MRI may induce a slight image translation compared to VG." In my opinion, VG may be the gold standard method to visualize the third ventricle; however, it may not be the gold standard to visualize brain structures that are readily visualized in individual patients by modern MRI machines using appropriate sequences, such as proton density sequences to visualize the pallidum and its subdivisions (1), or T2-weighted sequences to visualize the STN (2).

The issue is to audit the accuracy of the stereotactic MRI procedure, including the eventual distortion of the MRI and the errors resulting from a combination of a particular stereotactic frame and MRI. For example, frames at the very periphery of the scan with fiducials that are far away from the head may induce larger calculation inaccuracies on MRI than frames with fiducials closer to the head (3). In addition, even when using teleradiography, misalignment of the head within the frame, or misalignment of the frame's base ring in relation to x-ray source and/or x-ray film may also provoke non-negligible distortions.

Further, the authors used sagittal MRI scans to measure the length of the AC-PC, despite the fact that axial scans would be more accurate to use, as acknowledged by the authors. Because the authors wanted to conform to VG, in which axial scans are impossible, they used the less accurate sagittal MRI scans for their measurement of AC-PC length. This creates an unfair comparison that will be detrimental to MRI as a method, especially when the MRI scans were 4 mm thick in 12 out of the 18 patients. Despite these disadvantages, this article contains meticulous measurements of electrode contact positions with interesting results. There were a few patients in whom the active contact was at or above the AC-PC level, or by definition, in the ventral thalamus. This could be attributed to either a miscalculation of the real contact position as a result of the imaging method used, or a *de facto* thalamic (i.e., neither subthalamic or zona incerta (ZI) stimulation). In this respect, it is interesting to note that in three of the five published autopsy reports of STN DBS, the DBS electrode was not in the sensorimotor part of the STN,

despite microelectrode recording in two of these three cases (4, 5, 6).

The authors mention that even though contacts located at or above the AC-PC level were used, the positive effect must have been mediated by a current diffusion from these dorsally located contacts to the zona incerta or the upper part of STN. If this is true, it is unclear why more ventral contacts located within the ZI or the dorsolateral STN were not used right away. I agree with the authors' conclusion that an "important issue would be to compare preoperatively, in a randomized trial, the accuracy of targeting using VG and MRI that provides direct visualization of the STN using T2- weighted sequences." For a fair comparison, one needs to use the best that the MRI has to offer by avoiding sagittal pictures, 4 mm-thick scans, and stereotactic frames with fiducials that are far away from the patient's head.

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The authors present their comparison of the location of DBS electrode contacts in the subthalamic nucleus as determined by intraoperative VG versus postoperative MRI. They conclude that the " . . . electrode presence does not create insurmountable MRI distortion that could impede confirmation of correct implantation." This seems to be somewhat at odds to their finding of significant differences between the two methods in certain electrode coordinates, if 1 to 2 mm accuracy is being sought. Currently, intraoperative VG is infrequently performed. Dr. Benabid and colleagues have one of the few outstanding facilities in which to perform stereotactic functional neurosurgery with stereotactic teleradiographic VG that has very high precision. This is a valuable tool in their trajectory planning and confirmation, and this study clearly requires special resources. The ventriculogram has been called the "gold standard" for stereotactic localization; however, others consider it the "old standard" with MRI as a replacement. This study explores those assumptions.

The strength of the study will stand or fall with the strength of the statistics. An overall Euclidean error would have been more useful than individual coordinates. Nevertheless, comparisons of the x, y, or z coordinates of 144 contacts, as localized by intraoperative VG or postoperative MRI, provided powerful correlations with r2 equal to or greater than 0.75. These are very strong correlations; however, it is assumed that each contact is an independent variable. They are not. Most statisticians would have severely restricted this type of evaluation because each set of four contacts are physically linked together, and as such, represent not only independent variables, but dependent variables dramatically reducing the N. If dropped to 36 active electrodes, the statistics become far more interesting and more variable. In addition, some statistician purists would say there is still linked data because the patient's side-to-side contacts (i.e., left to right) are not truly independent variables, but dependent variables related to the patient's anatomy, measuring devices, etc. Having shown clear differences in side-to-side active lead locations in most of the patients (63.7% asymmetry as studied by Benabid et al.), one can argue that the two sides are not dependent. However, the errors that affect the VG on the right or the left side should be the same in one patient, and potentially different in another patient. While these errors may be very small, those affecting the MRI are potentially large.

In terms of MRI measurement, the side-to-side errors are clearly subject to the same forces. Moreover, the MRI was acquired in an irregular manner. Twelve of the patients had 2-dimensional spin-echo T2-weighted sequences that were 4 mm thick, whereas six patients had 3-dimensional spin-echo T2-weighted sequences 1 mm thick. The accuracy of the MRI will depend on the sequencing, the phase shift, the slice thickness, the angulation of the sections, partial volume effects, and the distortion caused by air, plastic, metal, and blood. The theoretical accuracy of localization should be close to the resolution limit because of voxel volume. However, geometric and intensity distortions owing to the presence of metallic implants in MRI impede the full exploitation of this imaging modality. Metallic implants in MRI cause spin-echo images to be distorted in the slice and frequency-encoding directions that can potentially be corrected (1). The best sequence to diminish distortion in the presence of a metal prosthesis may be 3-dimensional spin-echo (2). T2-weighted acquisitions have been shown to have greater frequency-encoded directional problems. The errors found in this study would be consistent with errors in the frequency-encoding direction. If they all go in the same direction, even small errors tend to be additive. Altering the direction of frequency-encoding direction could help resolve some of these issues.

Another possibility is that the VG affects the measurements. As the calvarium is penetrated, there are pressure changes that occur within the cerebrospinal fluid spaces (3, 4). When the VG is performed, there is a sudden channel between the ventricles and the subarachnoid spaces of the lateral hemisphere that did not previously exist. It is presumed that this immediately closes and the pressure changes resolve. However, as anyone who has seen such a procedure intraoperatively during a craniotomy can attest, this is not necessarily the case. A freshly created ventricular tract can easily allow egress of CSF fluid by pulsations or valsalva maneuvers. Although this should equilibrate, the equilibration could result in decreased intracranial pressure (ICP) and result in brain movement. As pressure within the third ventricle is diminished, the AC-PC distance and lateral wall should decrease. The result could effect both x and y. In their previous study (5), there was a clear difference in the AC-PC length when measured by VG versus that of preoperative MRI. In this current study, this difference was identified in the postoperative (post-VG) MRI. Although the difference in the parameters of MRIs performed preoperatively versus postoperatively may account for this difference, it is also possible that the VG could account for this difference. Therefore, it is quite possible that the MRI measurements before VG are precise but the dynamics have changed post-VG. This is a question that needs to be resolved.

It is also unclear why the right-sided y-coordinates on the active contacts were not significantly different in the frequency-encoding direction. While this unilateral shift could represent unique random

measuring errors that reach the statistically significant level, it is also possible that if the left side is always completed first, then the right side may be affected by shifts unrelated to the left side. Furthermore, if there is going to be a brain shift in the supine position with patients in this study, it will be posterior. Such changes may occur acutely, but with time, the posterior shift is more exaggerated as a result of valsalva maneuvers. If the patient is aligned perfectly, this might only effect the y-direction. Alternatively, after many hours of probing, stimulating, testing, and lead placement, edema and swelling on the initial side may result in distortion that could affect the second side. We are suggesting the possibility of very small and possibly occasional shifts. Again, it is the additive effect of small errors in the same direction.

Other types of localization studies are not immune to cerebrospinal fluid shifts as an approach to target through the ventricle, which could have the same effect as VG. Therefore, if the VG was not done, it does not mean there have not been pressure changes within the ventricle and the potential for shifts. Finally, there is the assumption that once placed intraoperatively, the leads will remain exactly where they were placed postoperatively. There is clearly the potential for shifts with or without VG before and after lead placement. Depending on how much shift occurs, its direction and resolution, the ultimate postoperative location could vary. In the supine position with the posterior shift occurring before placement of the lead, the lead could appear to be placed more posterior, yet the resolution of the shift may end up more anterior. The potential shift in a head up position is even more complex. The end results are distortions and errors in the methods of localization, potentials for unaccounted distortions, and limited ability to account for all the potential errors. Therefore, while some think the active leads are in STN, others think they are above STN, and others, as myself, are unclear exactly where these leads end up because we do not feel that there is enough accuracy and precision within the measurement devices to be sure whether or not a 1.5 lead is completely inside or outside of an amorphous STN border. Current spread may make the point mute (6). The authors will hopefully continue to investigate this problem.

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