Postoperative Lead Movement after Deep Brain Stimulation Surgery and the Change of Stimulation Volume

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Keywords

Deep brain stimulation · Displacement · Electric field · Functional neurosurgery · Movement disorder surgery

Abstract

Introduction: Lead movement after deep brain stimulation may occur and influence the affected volume of stimulation. The aim of the study was to investigate differences in lead position between the day after surgery and approximately 1 month postoperatively and also simulate the electric field (EF) around the active contacts in order to investigate the impact of displacement on affected volume. **Methods:** Twenty-three patients with movement disorders underwent deep brain stimulation surgery (37 leads). Computed tomography at the 2 time points were co-fused respectively with the stereotactic images in Surgiplan. The coordinates (x, y, and z) of the lead tips were compared between the 2 dates. Eleven of these patients were selected for the EF simulation in Comsol Multiphysics. Postoperative changes of EF spread in the tissue due to conductivity changes in perielectrode space and due to displacement were evaluated by calculating the coverage coefficient and the Sørensen-Dice coefficient.

Results: There was a significant displacement (mean $\pm$ SD) on the left lead: x (0.44 ± 0.72 , $p < 0.01$), y (0.64 ± 0.54 , $p < 0.001$), and z (0.62 ± 0.71 , $p < 0.001$). On the right lead, corresponding values were: x (-0.11 ± 0.61 , ns), y (0.71 ± 0.54 , $p < 0.001$), and z (0.49 ± 0.81 , $p < 0.05$). The anchoring technique was a statistically significant variable associated with displacement. No correlation was found between bilateral ($n = 14$) versus unilateral deep brain stimulation, gender ($n = 17$ male), age < 60 years ($n = 8$), and calculated air volume. The simulated stimulation volume was reduced after 1 month because of the perielectrode space. When considering perielectrode space and displacement, the volumes calculated the day after surgery and approximately 1 month later were partly overlapped. **Conclusion:** The left lead tip displayed a tendency to move lateral, anterior, and inferior and the right a tendency to move anterior and inferior. The anchoring technique was associated to displacement. New brain territory was affected due to the displacement despite considering the reduced stimulated volume after 1 month. Postoperative changes in perielectrode space and small lead movements are reasons for delaying programming to 4 weeks following surgery.

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Introduction

Deep brain stimulation (DBS) surgery has been proven to be an effective method in the symptomatic treatment of movement disorders such as Parkinson's disease (PD), essential tremor (ET), and dystonia [1–3]. It is also used to explore the therapeutic effect in different neuropsychiatric disorders [3, 4]. The treatment efficacy and absence of adverse effect is highly dependent on the electrode position [2, 5–7]. Previous studies have reported lead displacement that occurs postoperatively [8–11]. The postoperative displacement have been attributed to technical errors, failure of lead fixation, cerebrospinal fluid loss, pneumocephalus, twiddler syndrome, and dystonia [8, 9, 11]. A marginal postoperative movement may affect the clinical outcome after surgery since the target area is small, that is, in the range of millimeters [5, 12]. Therefore, the maintenance of electrode position in the target area is essential for good outcome [13].

Patient-specific simulation of the electric field (EF) surrounding the DBS lead is a method to investigate the affected tissue [14, 15]. The EF can be superimposed on the patient's MR images, thus visualizing the influenced anatomy of the individual patient. Examples of studies where patient-specific simulations have been used are investigation of speech intelligibility in PD [16], delineation of thalamic structures for ET stimulation [17], targeting of the limbic globus pallidus internus (GPi) in Tourette syndrome [18], and variations in lead design [15]. Thus, the impact of a lead displacement can be evaluated using patient-specific simulation.

A notable early clinical symptom relief in some patients is attributed to the microlesion effect from the trauma after lead insertion. This clinical effect is present regardless of stimulation and recedes with time [19, 20]. The trauma of the DBS electrode implantation in the brain will also trigger a small inflammatory response, forming a perielectrode edema. Higher water content in the edematous tissue increases the electric conductivity. With time, the edema recedes and gliosis occurs in the perielectrode space (PES), reducing the electric conductivity. The higher electrical conductivity in the early postoperative stage therefore increases the extension of the EF spread around the electrode compared to the chronic state, that is, a month after implantation [21–23]. Previous simulation studies have also shown that the EF spreads differently depending on the tissue type due to different electric conductivity properties [15]. This is particularly notable in the presence of CSF-filled cysts [24].

The aim of the present study was to investigate postoperative lead displacement after approximately 1 month and to study possible contributing factors such as age, diagnosis, bilateral/unilateral implantation, postoperative air volume, and lead anchoring. Postoperative changes of the EF spread in the tissue due to displacement and changes in PES conductivity were evaluated at the 2 time points, directly after (acute) and 1 month post-implantation (chronic) in order to investigate their impact on stimulated surrounding volume.

Material and Methods

Patients

Twenty-three patients (17 male and 6 female, mean $\pm$ SD age 61 $\pm$ 10 years) were operated with DBS at the Department of Neurosurgery, Linköping University Hospital, between January 2014 and February 2016. The population included 11 ET, 10 PD, 1 Parkinson tremor, and 1 patient with Dystonia. A total of 37 leads were implanted, 14 bilateral, and 9 unilateral. All unilateral leads were placed on the left side. Targets for DBS treatment were zona incerta ($n = 11$), ventral intermediate nucleus of the thalamus ($n = 8$), subthalamic nucleus ($n = 16$), and GPi ($n = 2$). Bilateral implantations were counted as 2 leads for target numbers. The study was approved by the local Ethics Committee (2012/434-31) and all patients gave their informed written consent to participate in the study.

Surgery

Prior to surgery, the stereotactic frame (Leksell Stereotactic System, Elekta Instruments AB, Stockholm, Sweden [LSS]) was mounted on the head. Surgery was performed during general anesthesia using direct visualization of targets (subthalamic nucleus, zona incerta, and GPi) with SurgiPlan (Elekta Instruments AB, Stockholm, Sweden). Coordinates from the Schaltenbrand-Wahren human brain atlas was utilized for indirect targeting of ventral intermediate nucleus of the thalamus. The DBS surgery was performed for all patients in 1 stage. The head elevation was approximately 20–30° in a semirecumbent position. Burr holes were made at the level of the coronal suture 2–3 cm lateral from the midline. Tisseel glue (Baxter Medical AB, Sweden) was placed in the burr hole after opening the dura to minimize the CSF loss and air entry. Under fluoroscopic visualization (Philips BV Pulsera, Philips Medical Systems, Best, The Netherlands) the quadripolar DBS electrode lead 3389 (Medtronic, Minneapolis, MN, USA) was implanted. The left lead was always implanted first. The leads were secured in the burr hole by using either the anchoring cover that is boxed with the lead, standard anchoring ($n = 24$) (Medtronic, Minneapolis, MN, USA), Stimloc™ Burr Hole Cover ($n = 9$) (Medtronic, Minneapolis, MN, USA) or with the anchoring device from Guardian™ Burr Hole Cover ($n = 4$) (St. Jude Medical Inc., Little Canada, MN, USA). The extension kit 37086 (Medtronic, Minneapolis, MN, USA) and the implantable pulse generator were subcutaneously placed in the same procedure. Activa PC 37601 (Medtronic, Minneapolis, MN, USA) was used for bilateral stimulation and Activa SC 37603 (Medtronic, Minneapolis, MN, USA) for unilateral stimulation. The surgical procedure is described in previous studies [25, 26] and usually took 4–5 h.

Imaging

Preoperative MRI examination using axial slices, $0.49 \times 0.49 \times 2$ mm, on either a 3 T (Ingenia, Philips Healthcare, Best, The Netherlands) or a 1.5 T (Achieva, Philips Healthcare, Best, The Netherlands) system was performed. MRI were either with LSS ($n = 16$ [3 T: $n = 13$, 1.5 T: $n = 3$]) or frameless ($n = 7$). In patients examined with frameless preoperative MR a 3D CT imaging with voxel size $0.55 \times 0.55 \times 1$ mm, with the use of a 128-slice CT scanner (Somatom Definition AS, Siemens, Forchheim, Germany) was done with LSS. The stereotactic CT with frame was co-registered to the frameless MRI before planning of targets and trajectories in SurgiPlan. The day after surgery and after 33 ± 6 days (mean $\pm$ SD), a postoperative high definition CT was taken using the same CT scan protocol as previously described.

Definition of Final Lead Position

In order to define the final position of the leads, the 2 postoperative CT images were co-registered in SurgiPlan respectively with the MR or CT images preoperatively taken with the stereotactic frame and aligned to the AC-PC-line. The lead tip, center of the bottom edge of contact 0, was used as the reference point. Each electrode was visualized with appropriate windowing by adjusting the level in SurgiPlan. The Leksell coordinates (x, y, z) of the lead tip on the 2 postoperative images were defined. Lead movement was measured by comparing the coordinates on the distal contact between the CT images taken at the 2 postoperative time points, acute and chronic. The displacement in millimeter was defined as the coordinate at the chronic time point minus the coordinate at the acute time point giving a displacement in x, y , and z directions. Eleven of these patients were selected for the EF simulation part. These patients fulfilled technical requirement of a high quality preoperative 3 T MRI with frame and active electrode settings after at least 1 month. There were 2 additional patients with 3 T MRI and frame. One had suboptimal image quality for simulation and 1 patient suffered from an early infection and the DBS system was removed before starting. These 2 patients were therefore excluded for the EF simulation part. In the simulation group the coordinates of the lead 10 mm above AC-PC was also noted for the 2 postoperative time points. This gave 2 positions per time point, the tip and 10 mm above AC-PC along the lead. These coordinates were used to place the DBS lead in a patient-specific brain model [15, 27].

Patient-Specific Simulation of Electric Field

Models of the Medtronic 3389 lead were made in Comsol Multiphysics 5.2 (Comsol AB, Sweden). The electric field magnitude EF was calculated from the equation for steady currents with the electric conductivity taken from tissue classification with in-house software ELMA [15, 27, 28] of the T2-weighted preoperative 3 T MRI. The tissue was classified into gray matter, white matter, blood, or CSF, and their conductivities were assigned from tabulated values [29, 30]. The negative contacts were assigned the electric potential used for the individual patients while the surrounding surfaces were set to ground for monopolar stimulation. For bipolar stimulation, the positive contacts were assigned to ground instead.

Brain models were made for the acute and chronic stages with and without inclusion of the PES. For the latter case a PES of $250 \mu\text{m}$ [22] was assumed to have an electric conductivity of 0.14 S/m in the acute phase and 0.05 S/m in the chronic phase based on model adaptations [23] to impedance measurements by Codrin

Table 1. Stimulation parameters of the patients with EF simulations

Parameter	Mean $\pm$ SD	Range
Voltage	$2.2 \pm 1 \text{ V}$	$0.2\text{--}3.8 \text{ V}$
Pulse frequency	$133 \pm 8 \text{ Hz}$	$130\text{--}160 \text{ Hz}$
Pulse width	$66 \pm 14 \mu\text{s}$	$60\text{--}100 \mu\text{s}$
Contacts	1.7 ± 0.8	1–3
Monopolar/bipolar	15/3	
Bilateral/unilateral	7/4	

EF, electric field.

Fig. 1. Sagittal plane of a skull. Demonstrating the postoperative air located in the frontal subdural space anterior to the electrode.

Lungu et al. [31]. Within the PES, conductivity values of the PES replaced the tissue classification conductivity from the tabulated values. The electrodes were aligned by the 2 coordinates along the lead, the tip and 10 mm above AC-PC, at the 2 time points respectively. Simulations were done using the latest clinical settings, all in the chronic stage. For detailed description of modeling and simulation see Åström et al. [14], Alonso et al. [15], and Johansson et al. [23].

The threshold electric field magnitude EF_t required for stimulation of the axons in the surrounding tissue of the lead was assumed to be 0.2 V/mm for the 9 patients with the pulse width of $60 \mu\text{s}$. This threshold has been used in several previous studies [15–17]. Increasing the pulse width lowers the EF_t and consequently also the voltage required for clinical effect. For the 2 patients with larger than $60 \mu\text{s}$ pulse width, we used 0.17 V/mm for the pulse width of $90 \mu\text{s}$ and 0.16 V/mm for the pulse width of $100 \mu\text{s}$ respectively according to strength-duration measurements by Mario Rizzone et al. [32]. These values have been found to be consistent with experimental estimation of the stimulation spatial extent by Alexis Kuncel et al. [33]. The stimulation parameters for the simulated patients are presented in Table 1. For details, see reference [23, 34].

Air Volume Calculation

All the patients were considered for volume analysis. As the volume always was zero in the nonoperated side, the air was only calculated in the hemisphere where the lead was implanted. The air volumes on the left side and right side were categorized separately and in total. The air locations were first identified in the Sante DICOM Viewer program (Santesoft Ltd., Nicosia, Cyprus)

Fig. 2. The common volume of 2 volumes used for D_C and C_C . Red is the acute volume, blue is the chronic volume. Example is given in the axial plane, showing anterior and lateral movement. **a** The 2 volumes show a complete overlap, D_C and $C_C = 1$. **b** The 2 volumes are completely separated, D_C and $C_C = 0$. **c** A typical presentation in our series. The 2 volumes are partly overlapped, $1 > D_C$ and $C_C > 0$. D_C , Sørensen-Dice coefficient; C_C , coverage coefficient.

by a neurosurgeon. The images were then imported to MATLAB® (2015b, MathWorks™, Inc., Natick, MA, USA) for rendering a 3D image, and the air volumes were segmented using the *im2bw* and *graythreshold* functions (intensity based). Positions of the segmented air volumes in MATLAB® were compared to the previously identified air by the neurosurgeon in order to exclude from the image the segmented structures that were not air. Region properties of the air volumes were then extracted and thereby number of pixels in the region multiplied by the pixel size in the 3 dimensions was used as air volume (mL). An example of 1 air volume is visualized in Figure 1.

Statistics

The displacements in x , y , and z for each side were checked for normal distribution (normplot, MATLAB, Mathworks, USA) and tested for statistical significance by paired, double-sided t tests (t test, MATLAB Mathworks, USA). Values of $p < 0.05$ were considered statistically significant. Unpaired, double-sided t tests (t test, Excel, Microsoft, USA) were performed to see whether the displacements on the left side were related to bilateral ($n = 14$) versus unilateral DBS, gender ($n = 17$ male), diagnosis ET versus PD or age < 60 years ($n = 8$).

Volumes, V , within the pulse width-dependent activation threshold EF_t were exported as binary matrices with voxel sizes of $0.1 \times 0.1 \times 0.1$ mm for calculation of the simulated volume, coverage coefficient, C_C and the Sørensen-Dice coefficient, D_C [35, 36] between the acute and chronic simulations for each patient. The simulated volumes did not have a normal distribution and the paired Wilcoxon's signed rank test was used instead (signrank, MATLAB, Mathworks, USA) to compare simulated acute and chronic volumes when considering PES and not. In this study, C_C describes the common acute and chronic volume divided by the chronic volume. D_C describes the common acute and chronic volume divided by the acute and chronic volume (Fig. 2). C_C assumes 1 if the chronic volume is completely covered by the acute volume. D_C value of 1 means that the acute and chronic simulations have equal volume and position. Both C_C and D_C is 0 if there is no overlap between the 2 volumes (Fig. 2). Paired, double-sided t tests

Table 2. Effects on left electrode displacement

Parameter	p value from t test	Difference, mm
Double ($n = 14$) vs. single-sided ($n = 9$) implantation		
x	ns	0.05
y	ns	0.02
z	ns	-0.04
Age < 60 years ($n = 8$) vs. ≥ 60 years ($n = 15$)		
x	ns	0.11
y	ns	0.37
z	ns	-0.23
Gender man ($n = 17$) vs. woman ($n = 6$)		
x	ns	0.32
y	ns	0.19
z	ns	-0.13
ET ($n = 11$) vs. PD ($n = 10$)		
x	ns	-0.41
y	ns	-0.21
z	ns	-0.16
Standard anchoring ($n = 14$) vs. Stimloc™ + Guardian™ ($n = 9$)		
x	ns	-0.01
y	ns	0.16
z	< 0.05	0.63

ET, essential tremor; PD, Parkinson's disease.

were done to compare the C_C value between acute and chronic assuming displacement versus no displacement, both for the simulations with PES and for the simulations without. The same t test was performed when evaluating D_C . Air volume was split in volumes for the left and the right brain hemisphere. Correlation between air volume and displacement was tested for x , y , and z in each side (corrcoef, Matlab, Mathworks, USA).

Results

Displacements

The lead displacement tendencies were statistically significant on group level (Fig. 3). On average after approximately 1 month, the leads moved anterior (y) and inferior (z). The left side movements were (mean $\pm$ SD) y (0.64 ± 0.54 , $p < 0.001$) and z (0.62 ± 0.71 , $p < 0.001$) and corresponding values on the right side were y (0.71 ± 0.54 , $p < 0.001$) and z (0.49 ± 0.81 , $p < 0.05$). On the left side there was also a tendency for lateral displacement x , (0.44 ± 0.72 , $p < 0.01$), while it was not significant on the right side x (-0.11 ± 0.61 , ns). The statistically significant contributing factor to the displacement was the anchoring technique and it reduced displacement in the z direction (Table 2).

Fig. 3. The boxplot (Matlab, Mathworks, USA) shows median values (red line), 25 and 75 percentiles (box), total range without outliers (dashed whiskers) and outliers (crosses). Directions of electrode movement in x (medial-lateral, depending on the side), y (anterior-posterior), z (inferior-superior) for left side (**a**) and right side (**b**). The lead displacement was statistically significant in the direction anterior and inferior on both sides. The left side also showed a lateral displacement.

Fig. 4. The images display EF change due to lead movement and electric conductivity changes in the PES. Red is the acute volume, and blue is the chronic volume. The STN, axial view (**a**), coronal view (**b**). The GPi, axial view (**c**), coronal view (**d**). EF, electric field; PES, perielectrode space; STN, subthalamic nucleus; GPi, globus pallidus internus.

Air Volume

The median and range of the air volumes on the left and right side were 0.19 (0–8.76) and 0.18 (0–2.01) cm^3 , respectively. The median and range of air volume for all 37 leads was 0.19 (0–8.76) cm^3 . There was no statistically significant correlation between calculated air volume and lead movement in any direction (x , y , and z) for either hemisphere.

Electric Field Simulations

An example of change in EF due to lead movement and electric conductivity changes in the PES can be seen in Figure 4. The image shows the cumulative effect of both the typical electrode displacement (anterior and inferior) and the reduction of electric spread as the edema recedes with time and is replaced by gliosis. Thus, even though the EF shrinks, the displacement causes previ-

Table 3. Acute and chronic stimulation volumes

Parameter	With PES	Without PES
Acute postoperative volume, mm ³ , median (25–75 percentiles)	162 (76–190)	130 (57–173)
Chronic volume assuming displacement, mm ³ , median (25–75 percentiles)	87 (46–113)	143 (56–177)
<i>p</i> value, volume difference acute – chronic	<0.001	ns
<i>C_C</i> between acute and chronic assuming displacement, mean ± SD	0.72±0.18	0.61±0.17
<i>C_C</i> between acute and chronic, assuming no displacement	1	1
<i>p</i> value, <i>C_C</i> difference, displacement – no displacement	<0.001	<0.001
<i>D_C</i> between acute and chronic assuming displacement, mean ± SD	0.54±0.14	0.61±0.17
<i>D_C</i> between acute and chronic, assuming no displacement, mean ± SD	0.74±0.06	1
<i>p</i> value, <i>D_C</i> difference, displacement – no displacement	<0.001	<0.001

PES, perielectrode space; *D_C*, Sørensen-Dice coefficient; *C_C*, coverage coefficient. *n* = 17, bilateral: 6, unilateral: 5.

ously unaffected tissue to be affected. Results of the simulations are summarized in Table 3 together with statistical comparisons. The PES reduced the volume from 191 ± 174 mm³ in the acute stage to 111 ± 101 mm³ in the chronic stage. This change was statistically significant at $p < 0.001$. The *C_C* when considering PES and when not considering PES between acute and chronic assuming displacement was 0.72 ± 0.18 and 0.61 ± 0.17 respectively. The impact of displacement on *C_C* was statistically significant both with and without PES at $p < 0.001$. The *D_C* when considering PES and without PES between acute and chronic assuming displacement was 0.54 ± 0.14 and 0.61 ± 0.17 . The *D_C* when considering PES between acute and chronic assuming no displacement was 0.74 ± 0.06 . The impact of displacement on *D_C* was statistically significant both with and without PES at $p < 0.001$.

Discussion

The left lead tip displayed a tendency to move lateral, anterior, and inferior and the right a tendency to move anterior and inferior after 1 month. This small displacement was affected by the anchoring technique with Guardian and Stimlock covers on average giving a smaller displacement than the standard boxed cover. The PES changes with time and reduces the stimulation volume in the chronic stage compared to the acute. Despite this volume reduction, the electrode displacement gives a part of the stimulation volume in the chronic case that was not included in the acute phase, thus affecting new brain territory.

Displacement

Our experience is that if the DBS is initiated in the acute phase directly after surgery, the setting and chosen contact need to be changed within a short period. A lower voltage is needed for both clinical effect and to avoid side effects in the acute stage. This can partially be due to the microlesioning effect from the DBS lead itself which can be seen in up to 50% of the patients [19, 20]. However, this observation can also be explained by postoperative lead displacement and changes of the electric conductivity. To our knowledge this study is the first to investigate postoperative lead displacement in addition to changes of the influence from PES and thus alteration of the electric conductivity after DBS. The lead displacement tendencies in our study after 1 month were small but statistically significant on group level (Fig. 3).

Co-fusion error, imaging resolution limitations, and brain pulsations could result in measured nonzero displacement values even if the electrode position is unchanged between the 2 points. The same method was utilized when analyzing the lead position at the 2 time points by using the identical imaging technique and protocol for co-fusion postoperatively. Any bias error in the coordinate estimation should thus be the same for the 2 time points and we should only have a variance error from the intrinsic imaging errors. When calculating absolute values, these random measurement errors may contribute to an overestimation of an average measured displacement. A previous study reported absolute confusion errors of about 0.5 mm which is in the range of the measured displacement in this study [37]. We, therefore, considered the displacement direction instead of investigating absolute values. By keeping the direction the intrinsic errors should only add to the variability of the displacement and

any remaining significant difference in the t test should be due to a real displacement on an average group level.

The lead tip displayed bilaterally a tendency to move anterior and inferior in the anatomy after approximately 1 month. A lateral displacement was seen for the left leads but not for the right. This discrepancy may be explained by that the lateral displacement is the smallest measured value and the right-side leads are fewer in number. Also, the p value of the lateral displacement is, even though significant, weaker than the rest of the directions on the left side and therefore has the biggest risk of being a false positive value. In addition, it can be noted that the implantation of the lead was performed first on the left side for all bilateral surgeries and it cannot be discounted that this might affect the lateral displacement. Van den Munckhof et al. [9] and Sillay et al. [38] described an anterior and rostral movement. Kim et al. [8] suggest that the electrode position is stabilized 1 month after surgery and that the lead tip moves anterior and inferior with a measured discrepancy in accordance with our data. Considering that the target area is a few mm in size [13] and the quadripolar DBS lead consists of four 1.5-mm contacts and three 0.5-mm interspaces, even a small displacement can theoretically have a clinical impact regardless of the direction of displacement. Further supporting this statement is that the side effects depend on the structures surrounding the target affected by the EF [2].

Brain Shift

Several studies discuss the role of brain shift on the electrode location. The direction of brain shift is hypothesized to move the brain laterally and caudally [38]. Van den Munckhof et al. [9] and Bentley et al. [10] describes that the shift is less in the deeper parts of the brain compared to the more superficial. When the brain shift resides, the brain tissue around the electrode contact can theoretically move with the electrode. Subsequently, the lead tip remains in the same anatomical position, but a new stereotactical position can be registered. Our data suggest that the displacement in itself represents an actual change in affected structures since the direction of displacement is inferior in addition to anterior and not superior as would be expected if the electrode followed the brain shift.

Previous studies have attributed displacement to technical errors, dystonia, twiddler syndrome, cerebrospinal fluid loss, pneumocephalus, and failure of lead fixation, [8, 9, 11]. We perform DBS surgery in 1 stage and thus the technical errors leading to dorsal migration of the lead associated with 2 stage implantation was not seen as de-

scribed by Morishita et al. [11]. The single patient with dystonia displayed a higher displacement than average. Twiddler syndrome was not seen during the period of this study.

Correlation between Air and Lead Displacement

Correlation between intracranial air (ICA) and lead displacement has previously been reported by van den Munckhof et al. [9] with a mean air volume to 17 cm³ with a max of 88 cm³. They showed that the ICA was correlated to an upward movement of the lead. Kim et al. [8] associated pneumocephalus to a difference in the y coordinate of the lead tip coordinate with an estimated mean ICA of 11.9 cm³ with a max of 76 cm³. Bentley et al. [10] found that ICA was correlated to movement of the proximal part of the lead but not to the distal contact. Sillay et al. [38] had relatively lower ICA in comparison to the above mentioned studies and did not establish a correlation between pneumocephalus and displacement. The lesser air volume in our study may explain why no correlation was seen between ICA and lead movement in any direction (x , y , and z) for either hemisphere.

Anchoring Technique

The only statistically significant variable found to be associated with displacement was the anchoring technique. Usage of StimlocTM or GuardianTM reduced displacement in the inferior direction compared to using the standard anchoring cover that is boxed with the lead. This finding is supported by Contarino et al. [39] who correlated the anchoring technique to postoperative displacement after minimizing CSF leakage. No association was found between displacement and any of the other investigated factors: bilateral versus unilateral DBS, gender, and age <60 years or ET versus PD (Table 2). The results for the left side are presented in the case of bilateral placement since it would otherwise count as 2 independent observations for 1 patient when regarding the different factors.

Perielectrode Space

Evidence for increased conductivity from edema surrounding the electrode in the acute phase of DBS and reduced conductivity from gliosis in the chronic phase comes from impedance measurements over the first 20 weeks after implantation [31]. The edema surrounding the electrode is evident only in the acute phase after DBS implantation and has a higher conductivity compared to the gliosis-influenced chronic phase when using the same programming setting. The higher electric conductivity of

the initial edema makes the EF spread further compared to the later gliosis formation, reducing the coverage of the initially affected volume. The simulated volume becomes smaller as the edema is replaced with gliosis which has lower electric conductivity. The conductivity properties will also be different if the lead has moved since the brain is heterogenic. This explains the small difference in volume also seen when not considering PES in the acute versus chronic phase since the lead movement was also considered when calculating the chronic volume. The edema, the gliosis, and the movement all can affect the size of the EF volume. However, the volume difference is only statistically significant in our study when including the effect of edema and gliosis in the PES (Table 3).

We show that even a small lead movement after DBS can be a factor to consider before starting the stimulation. The EF in the chronic stage is significantly lesser than the volume in the acute stage when considering PES. Therefore, the displaced chronic field may or may not be engulfed by the larger acute EF because of the size difference. Since the C_C is <1 , the smaller chronic EF are partially situated outside the larger acute volumes (Fig. 2). The measured displacement indicates that new brain territory might be affected even when considering PES and this may be clinically important (Fig. 4). A C_C value of 0.72 ± 0.18 when considering PES corresponds to that 28% of the chronic volume is not overlapped by the acute volume. D_C considers both size and position. D_C without PES assuming displacement (0.61 ± 0.17) is smaller than D_C with PES assuming no displacement (0.74 ± 0.06). Thus, our data suggests that the displacement has a greater impact on D_C than the PES (Table 3). It should be noted that the decrease in D_C due to displacement may be overestimated because of the previously mentioned limited image resolution. With this mentioned, our data suggests that the displacement has a greater impact on D_C than the PES (Table 3).

Conclusion

A programming setting that provides adequate symptom relief and avoids side effects is the goal after a properly placed electrode. Optimal programming is dependent on the final electrode location and brain structures stimulated. Using the Guardian™ and Stimlock™ as anchoring device seems better in reducing displacement in our series. Settings can change due to displacement and changes of PES. In some departments early postoperative programming to determine the amplitude threshold for

clinical benefits and to determine side effects for each of the electrode contacts is performed direct postoperatively during the hospitalization period. The results in this study, however, suggest possible benefits with delayed programming at 4 weeks, in a more chronic state. New brain territory was affected due to the small displacement despite considering the reduced stimulated volume after 1 month. At this time the perielectrode edematic space has receded and the electrode is presumably fixated to its final position thus enhancing the possibilities for an optimal review of the contacts. This suggests that the patient comfort can be improved by providing a more correct and representative programming setting after 1 month compared to the acute phase. It also implies a cost beneficial aspect. Reducing excessive programming decreases the number of clinical visits to the hospital. The clinical implication by delaying the programming suggested by this paper can improve the treatment with DBS.

Acknowledgement

We would like to thank Neda Haj-Hosseini, PhD, Department of Biomedical Engineering, Linköping University for the air volume calculations.

Statement of Ethics

The study was approved by the local Ethics Committee (2012/434-31) and all patients gave their informed written consent to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare. K.W. has shares in FluoLink AB, Sweden. K.W. has shares in FluoLink AB, Sweden.

Funding Sources

The study was supported by the Swedish Research Council (2016-03,564), Swedish Foundation for Strategic Research (BD15-0032) and by ALF Grants Region Östergötland (LIO-698041).

Author Contributions

N.G. performed the image analysis and the statistics. J.D.J. performed the FEM simulations and the statistics. N.G., J.D.J., K.W., and P.Z. all contributed to the study design and writing.

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