Short communication

Directional DBS leads show large deviations from their intended implantation orientation

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ABSTRACT

Objective: Lead orientation is a new degree of freedom with directional deep brain stimulation (DBS) leads. We investigated how prevalent deviations from the intended implantation direction are in a large patient cohort.
Methods: The Directional Orientation Detection (DiODe) algorithm to determine lead orientation from postoperative CT scans was implemented into the open-source Lead-DBS toolbox. Lead orientation was analyzed in 100 consecutive patients (198 leads). Different anatomical targets and intraoperative setups were compared.
Results: Deviations of up to 90° from the intended implantation direction were observed. Deviations of more than 30° were seen in 42% of the leads and deviations of more than 60° in about 11% of the leads. Deviations were independent from the neuroanatomical target and the stereotactic frame but increased depending on which microdrive was used.
Discussion: Our results indicate that large deviations from the intended implantation direction are a common phenomenon in directional leads. Postoperative determination of lead orientation is thus mandatory for investigating directional DBS.

1. Introduction

Directional leads have been the latest technological advance in deep brain stimulation (DBS) devices and are now used in the treatment of advanced Parkinson's disease, essential tremor, and dystonia. Current directional leads feature two electrode levels with three directional electrode segments each to allow axial stimulation steering (Fig. 1a). First prospective studies with these leads demonstrated an increase in side-effect thresholds [1] and/or a decrease in efficacy thresholds [2] when using directional stimulation. On the other hand, these new stimulation capabilities come with an increase in programming complexity. Detailed knowledge about the lead's position with respect to the surrounding anatomy is an important basis for the clinical interpretation of DBS responses and can guide clinicians in selecting the optimal stimulation parameters. In directional DBS however, the orientation angle of the lead now adds a new degree of freedom which has to be known to relate stimulation parameters to neuroanatomy. While neurosurgeons typically intend the lead to face into a certain direction, it is unclear whether this can be achieved with the current intraoperative techniques. Therefore, a reliable method to determine lead orientation from postoperative imaging is needed. We thus developed and released the Directional Orientation Detection (DiODe) algorithm which calculates the orientation of directional DBS leads based on postoperative CT-scans [3–5]. In this study, we aimed to investigate whether deviations from the intended implantation direction occur by analyzing the orientation of directional DBS leads in a large and

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A

B

Before DiODe, 0°

After DiODe, 68°

2.5 mA, no side effects

3.0 mA, muscle contractions
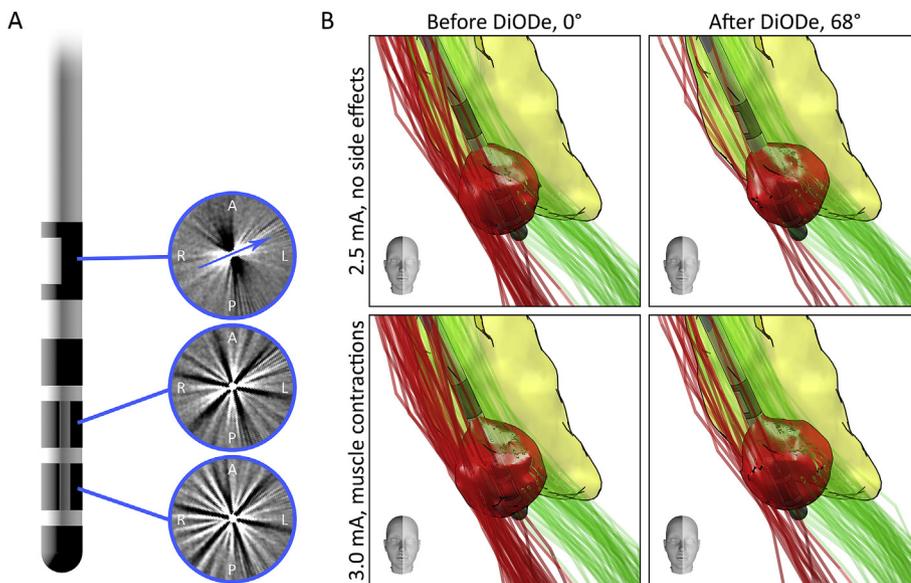
Fig. 1. DiODe.
A) CT artifacts generated by the stereotactic marker and the segmented electrodes. The blue arrow indicates the orientation of the lead. B) Example application in a patient with essential tremor. The right lead is shown from anterior with the intended orientation angle of 0° (left) and with the real orientation angle of 68° (right). VTAs are shown for stimulation on electrode 13 and amplitudes of 2.5 mA (above) and 3.0 mA (below). Fibers activated by stimulation of a connectome (Horn et al., 2014 [3]) based dentato-rubro-thalamic-tract (DRTT) are shown in green, while activated fibers belonging to the cortico-spinal-tract (CST) are shown in red. The premotor thalamus is shown in yellow [12]. At 2.5 mA the patient experienced full tremor control and no observable side-effects, while muscle contractions indicating an affection of the CST began at 3.0 mA. Ignoring the real lead orientation led to widespread activation of the CST in both settings while incorporating the orientation into the analysis only showed CST activation at 3.0 mA, when side-effects were present. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

heterogeneous patient cohort.

2. Methods

2.1. Ethics

Due to the purely retrospective character of this analysis, no approval by the local ethical review board was required. All imaging and clinical data used for this study were gathered as part of routine clinical care and no written informed-consent was needed from patients.

2.2. Clinical data

We retrospectively analyzed data from the first 100 consecutive patients who had been implanted with Cartesia™ directional DBS leads (Boston Scientific, USA) in our center. Patients had been selected for DBS treatment according to our clinical routine. The cohort included different neurological indications and surgical targets (see results). Due to the retrospective nature of our analysis no local ethics approval or written informed consents were obtained.

2.3. Implantation and imaging

All patients received preoperative MRI and CT imaging for stereotactic planning. Two neurosurgeons performed the implantations, using different stereotactic systems (CRW® frame, Integra Life Sciences, USA; RM® frame, Inomed, Germany) respectively. After combined intraoperative microelectrode recording (MER) and macroelectrode stimulation, the final lead was inserted at the supposedly optimal location for clinical effect. The stereotactic marker was implanted to face anteriorly (orientation angle of 0°) which was controlled visually via either intraoperative fluoroscopy (CRW) or intraoperative stereotactic x-ray (RM). After insertion of the final DBS lead, the borehole was closed using bone cement. When the cement had hardened, the stylet inside the DBS lead and the MER system were removed and the lead was fixed to the bone using a microplate (Biomet Microfixation, USA). Afterwards, the tunneling process ensued. During the course of the study, the intraoperatively used microdrives and MER system changed from an ISIS MER system (Inomed, Germany) to a Neuro Omega™ system (AlphaOmega, Israel). Patients received postoperative CT imaging as part of their routine clinical care to exclude perioperative bleeding and to confirm correct lead positioning. CT scanners iCT256

and IQon (Philips, The Netherlands) were used with the following scan parameters: pixel size 0.6 mm (range: 0.4–0.7 mm), slice thickness 0.8 mm (range: 0.6–1.0 mm), spiral pitch factor 0.36 (range: 0.34–0.44), gantry tilt 0°, tube voltage 120 kV, exposure 240 mAs, filter type UB (soft tissue).

2.4. Orientation detection from postoperative CT

The DiODe algorithm is based on previous works from our center and the detailed methodology is explained elsewhere [4,5]. In short DiODe inspects the artifacts generated by the Cartesia leads (Fig. 1a) in postoperative CT scans to determine the orientation of the lead. In a first step, the orientation of the artifact generated by the stereotactic marker is analyzed. Afterwards the characteristic streak artifacts generated by the directional electrode segments are used to calculate a more accurate estimation. The original user-supervised algorithm, which was implemented in IDL (Exelis Visual Information Solution, USA), has been extensively validated in both geometrical and anthropomorphic phantoms [4,5]. It yielded accurate and robust results, as long as the polar angle between the lead and the CT scanner axis remained below 60°. We now provide an adaptation of DiODe implemented in Matlab (The MathWorks, USA) and fully integrated into the open-source Lead-DBS toolbox (www.lead-dbs.org) [3]. Lead-DBS enables the user to a) conduct coregistration of preoperative and postoperative imaging, b) to normalize images to different atlas spaces, and c) to reconstruct lead trajectories. Based on these trajectories DiODe automatically extracts the relevant artifacts and calculates the orientation angles in a matter of seconds (*automatic* workflow). The user is then required to visually inspect and confirm the results or, if deemed necessary, to use a *manual refine* workflow to improve results by respecifying the CT slices where the artifacts are most visible, respecifying the centers of the artifacts within the slices, and/or by choosing a different solution for the symmetric marker artifact. The results are automatically propagated from the CT space into both the patient MRI and the atlas space. The Matlab implementation of DiODe was extensively validated against the previously published version (see Data Supplement). The *automatic* workflow yielded accurate results for polar angles < 40° while the *manual refine* workflow was accurate for polar angles < 55°.

2.5. Image analysis in Lead-DBS

Preoperative MRI and postoperative CT images were coregistered linearly using Advanced Normalization Tools (ANTs) in all patients [6]. Images were then normalized to standard stereotactic space (MNI ICBM 2009b, asymmetric) using nonlinear ANTs with subcortical refine [6–8]. Lead trajectories were identified using the PaCER algorithm [9]. Afterwards the DiODe algorithm was used to determine the orientation angles. In a first step, only the *automatic* workflow was used. In a second step, results were inspected and, if warranted, improved via the *manual refine* workflow. Both workflows were used for validation (see Data Supplement).

2.6. Analysis of deviations

The final orientation results after manual refinement were used to investigate deviations from the intended implantation orientation (anterior, 0°) with respect to the patient's coordinate system defined by the line connecting anterior commissure (AC) and posterior commissure (PC). The prevalence of deviations was explored using histograms. To test whether there was a systematic deviation from 0° we used one-sample Wilcoxon signed-rank test with a significance threshold of $p < 0.05$. We also investigated differences in deviations for different anatomical targets using the nonparametric Kruskal-Wallis test and post-hoc Wilcoxon rank-sum test with significance thresholds of $p < 0.05$, Bonferroni-corrected for multiple comparisons. Additionally, we compared our different intraoperative setups (CRW-frame, intraoperative fluoroscopy versus RM frame, intraoperative stereotactic x-ray) and the two MER-systems (AlphaOmega versus Inomed) to see whether deviations differed between approaches (Wilcoxon rank-sum test, $p < 0.05$). Furthermore differences in variance were analyzed using the Brown-Forsythe test ($p < 0.05$).

3. Results

3.1. Data

One-hundred patients receiving a total of 198 directional leads were analyzed. Surgical targets were the subthalamic nucleus (STN) in 101 leads, the ventral intermediate nucleus and the posterior subthalamic area (VIM/PSA) in 69 leads, and the internal part of the globus pallidus (GPI) in 28 leads. The CRW frame was used in 98 leads while the RM frame was used in 100 leads. The Inomed system was used in 115 leads, while the AlphaOmega system was used in 83 leads.

3.2. Prevalence of deviations

Large deviations ranging from $-89.1°$ to $88.1°$ with respect to the desired implantation direction of 0° were observed in our cohort as can be seen in Fig. 2. Deviations of more than 30° occurred in 82 leads (41%) and deviations of more than 60° in 23 leads (11%). The median deviation was $-4.3°$ (interquartile range: $-26.7°–21.5°$) and did not differ from 0° ($p = 0.22$), indicating that leads did not systematically deviate into one direction. No differences in deviations ($p = 0.73$) or differences in variances ($p = 0.26$) were observed for the different anatomical targets STN, PSA/VIM, and GPI. Also there was no difference regarding deviation ($p = 0.46$) and variance ($p = 0.53$) between the two different intraoperative setups (frame, surgeon, intraoperative imaging). While deviations did not differ when comparing the two MER-systems (Inomed versus AlphaOmega, $p = 0.59$) variance was significantly increased by a factor of 2.24 when using the AlphaOmega system ($p < 0.0001$, Fig. 2).

4. Discussion

This is the first study investigating the orientation of directional DBS leads in patients. In this large cohort of 100 patients, deviations of up to 90° from the intended implantation direction could be observed. In more than 10% of the leads the deviation was more than 60°. This was independent from the surgical target and the intraoperative setting comprising of stereotactic frame, neurosurgeon, and intraoperative imaging modality. However, the variance increased depending on the intraoperatively used MER-system. The prevalence and amount of deviations might sound surprising at first, but many factors may impede the accurate placement of the lead into a predefined direction. First and foremost, while the depth of the lead can be adjusted using a microdrive, the orientation of the lead has to be adjusted manually. Considering the small diameter of the lead, a manual correction by 10° for example would require the neurosurgeon to turn the lead by just 0.1 mm, which is almost impossible to achieve by hand. Furthermore, while the neurosurgeon intends to position the lead into a certain direction with respect to the patient's neuroanatomy, the neuroanatomic frame of reference is elusive in most intraoperative settings. Instead the neurosurgeon has to use detached landmarks to guide manual rotation (e.g. skull features). Finally, the lead in itself is not stiff but susceptible to internal torsion [10], some of which may occur during or even after lead fixation. Concluding that accurate manual orientation of directional DBS leads is not possible in a relevant amount of cases, a reliable way to determine the lead orientation postoperatively gains even more importance. The difference in results between the two MER-systems used in this study most likely occurred due to differences in the respective handling of the DBS lead before it is inserted into the drive. While the Inomed system relies on a simple plastic stopper provided by the lead manufacturer to indicate the lead's length and the directionality, the AlphaOmega system provides a specialized lead holder into which the lead is inserted. This holder makes it more difficult to maintain the correct orientation of the lead and also increases the difficulty of post-hoc corrections in orientation.

A few other approaches have been proposed to determine the orientation of directional leads from intraoperative stereotactic x-ray, rotational fluoroscopy, or flat-panel CT [4,10,11]. The approach used in this study has the advantage, that postoperative CT imaging is already part of the routine care in many centers to verify lead location and to exclude intracerebral hemorrhage. Second, other methods relied on subjective user assessment [10,11]. While those methods are accurate and show high inter-rater reliability, we think that an automatic approach is less cumbersome and increases comparability. Our algorithm is able to provide accurate results in a few seconds and even the manual refine workflow takes less than a minute – much less than user-dependent approaches. Third, our algorithm in combination with Lead-DBS automatically translates the lead's orientation into a variety of neuroanatomical spaces. This allows users to investigate lead orientation in relation to individual anatomy, neuroanatomical atlases, tractography and connectomes, and to use simulated stimulation volumes (VTAs) to investigate the origins of directional DBS effects (Fig. 1b). So far, no information is available regarding the stability of orientation angles over time. This might be a problem, especially when relying on immediate postoperative imaging which may include brainshift due to CSF drainage, edema, or pneumocephalus. Consecutively, one could argue for postponing the postoperative imaging by at least several days and to gather longitudinal data for further investigations.

Concluding, we demonstrate that large deviations from the intended implantation direction are seen in a significant proportion of patients. To address this we provide a freely-available algorithm which can reliably detect the orientation of directional DBS leads from postoperative CT with only minimal user-intervention.
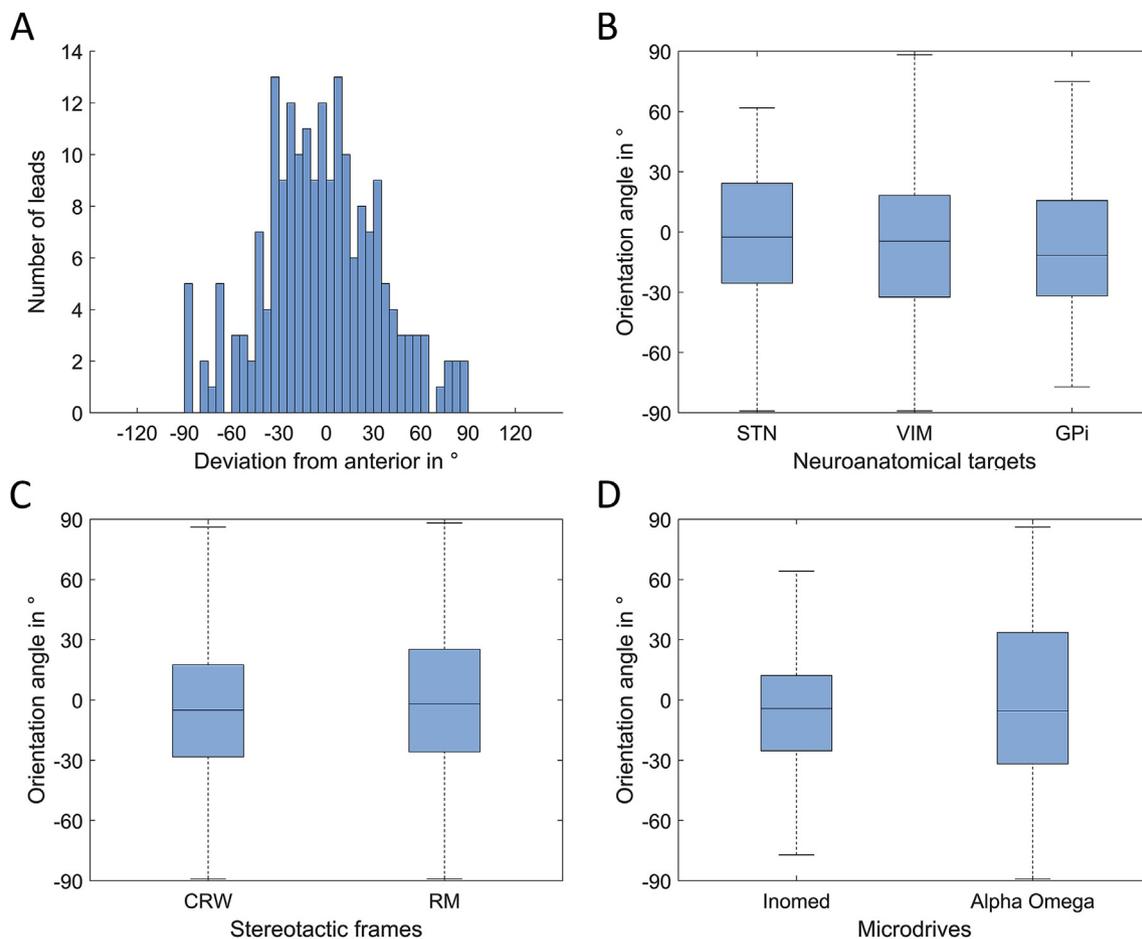
Fig. 2. Results.

A) Histogram of orientation angles with respect to the intended orientation (anterior, 0°). B) Boxplot depicting the orientation of leads implanted into the STN, the VIM, and the GPI. C) Boxplot depicting the orientation of leads implanted using either the CRW or the RM stereotactic frame. D) Boxplot depicting the orientation of leads implanted using either the Inomed or the AlphaOmega microdrive. Variance was increased with the AlphaOmega compared to the Inomed system (p < 0.0001).

Full disclosures

Contributions

TAD – Study conception, development of methods, data & statistical analysis, drafting of the manuscript.

MH – Study conception, development of methods, data analysis, critical revision of the manuscript.

HA – Study conception, development of methods, data analysis, critical revision of the manuscript.

AH – Development of methods, critical revision of the manuscript.

JNPS – Development of methods, critical revision of the manuscript.

JB – Development of methods, critical revision of the manuscript.

JW – Data acquisition, critical revision of the manuscript.

HSD – Data acquisition, critical revision of the manuscript.

MTB – Data acquisition, critical revision of the manuscript.

VVV – Study conception, data acquisition, critical revision of the manuscript.

HT – Study conception, development of methods, data acquisition & analysis, drafting of the manuscript.

All Authors gave final approval of this manuscript to be submitted.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.08.017.

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