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Post-operative deep brain stimulation assessment: Automatic data integration and report generation

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ABSTRACT

Background: The gold standard for post-operative deep brain stimulation (DBS) parameter tuning is a monopolar review of all stimulation contacts, a strategy being challenged by recent developments of more complex electrode leads.
Objective: Providing a method to guide clinicians on DBS assessment and parameter tuning by automatically integrating patient individual data.
Methods: We present a fully automatic method for visualization of individual deep brain structures in relation to a DBS lead by combining precise electrode recovery from post-operative imaging with individual estimates of deep brain morphology utilizing a 7T-MRI deep brain atlas.
Results: The method was evaluated on 20 STN DBS cases. It demonstrated robust automatic creation of 3D-enabled PDF reports visualizing electrode to brain structure relations and proved valuable in detecting miss placed electrodes.
Discussion: Automatic DBS assessment is feasible and can conveniently provide clinicians with relevant information on DBS contact positions in relation to important anatomical structures.

Background

The effectiveness of deep brain stimulation (DBS) is related to the precise placement of electrode leads with respect to specific brain structures. Therapeutic outcome for DBS in Parkinson's disease has been directly linked to precise contact placement within the subthalamic nucleus (STN) [1–3]. In the absence of integrated visual information about the placement of electrode contacts compared to individual deep brain structures of a subject, systematically accessing stimulation effects of all electrode contacts after surgery - the monopolar review strategy [4] - is still the gold standard.

With the introduction of novel lead designs featuring segmented contact areas the number of possible contact combinations increases exponentially. Consequently, there is a need for automatic methods to guide the clinician in post-operative assessment of electrode placement with respect to the patient individual anatomy to enable effective parameter tuning.

Automated segmentation of basal ganglia structures from MRI was reported by Haegelen et al. [5] in 2012. They concluded that a software solution that is usable by clinicians without the aid of engineers is desired in the future.

Recently Wang et al. [6] released a 7 T MR imaging based deep brain structure atlas. The so called Deep7T-atlas consist of unbiased high resolution T1-and T2-weighted average templates with associated labels. The labels include the STN, the substantia nigra (SN), the red nucleus (RN) and the globus pallidus (GP). The atlas proved excellent performance in their initial technical study. Lau et al. [7] suggested to non-linearly transform the high contrast T2 template of this atlas to standard patient imaging data for improved DBS targeting of the STN.

In this report, we introduce DBS auto report (DBSAR), a software method that fully automatically integrates individual neuroanatomical information with highly accurate DBS lead reconstructions.

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Anatomical information is derived by adopting the Deep7T-atlas to the particular subject and automatic lead reconstruction is utilizing the recently introduced PaCER algorithm [8]. In contrast to other approaches DBSAR does not require any user interaction. The output is a report in form of a PDF file encapsulating interactive 3D graphics objects enabling clinical usage with any 3D capable PDF reader (e.g. Adobe Acrobat) and not requiring any additional software on the clinical side.

Material and methods

An overview of the automatic workflow is presented in Fig. 1. The inputs are conventional pre-operative 3D-T1 and T2 MRI and a post-operative CT. By this means the workflow is solely based on wide spread standard modalities in clinical imaging for DBS.

A key point of the processing is that eventually all data are represented in one coordinate space that is related to the native scans of the patient's anatomy by only a rigid transformation. This restriction to rotations and translations guarantees that all geometrical features of the patient are preserved. Thus DBS trajectories can be accurately represented in this space.

Multi-stage atlas registration

To integrate 3D anatomical structure information the Deep7T-atlas is registered to subject space. A key feature of this atlas is that the atlas labels are consistently placed with respect to the respective signal intensities in the atlas template. In example, the labels for the subthalamic nucleus exactly match the hypointens subthalamic region visible in the associated T2 template image of this atlas. This is not the case for many other deep brain structure atlases (cf. [9]) but considered a key feature for meaningful registration-based estimates.

The non-linear atlas-to-subject mapping is based on a multi-stage approach using a chain of registrations with increasing degrees of freedom. In particular: center-of-gravity pre-alignment (three degrees of freedom), rigid registration (six degrees of freedom), affine registration (nine degrees of freedom) and a final diffeomorphic registration (non-linear). The registrations are carried out using the free ANTS software package [10].

This multi-stage-registration pipeline is using both the T1 as well as the T2 modality. T1 imaging, which provides decent delineation of brain boundaries is used for the initial stages thus ensuring a robust alignment. T2 imaging, providing contrast of the STN and SN, is used for the final non-linear stage to yield best accuracy in the region of interest.

Lead and contact detection

Lead reconstruction using the PaCER algorithm is carried out using the native space data of the post-op CT before any transformation. This ensures best signal-to-noise ratio and accuracy. In the data-integration phase, the extracted leads are transformed to match the MRI based imaging applying previously found transformations from CT to MRI data to the lead objects.

Result representation and clinical application

The DBSAR results are converted to a PDF file with embedded 3D objects utilizing the fig2u3d toolbox (https://github.com/johnyf/fig2u3d). This PDF can be displayed using standard office software retaining full 3D rotation capabilities, allowing clinicians to assess electrode placement from arbitrary angles (cf. supplementary example PDF). Additionally, metrics that are very cumbersome to assess manually could be computed automatically. For example distances of the stimulation contacts to the center-of-gravity of the STN or any other labeled brain structures.

Subject data

The method was validated on 20 bilateral STN DBS datasets (40 electrodes) from two centers. The anatomical structures automatically estimated by the atlas registration where manually inspected for each case by assessing the transformed atlas labels overlayed to the pre-OP T2 images.

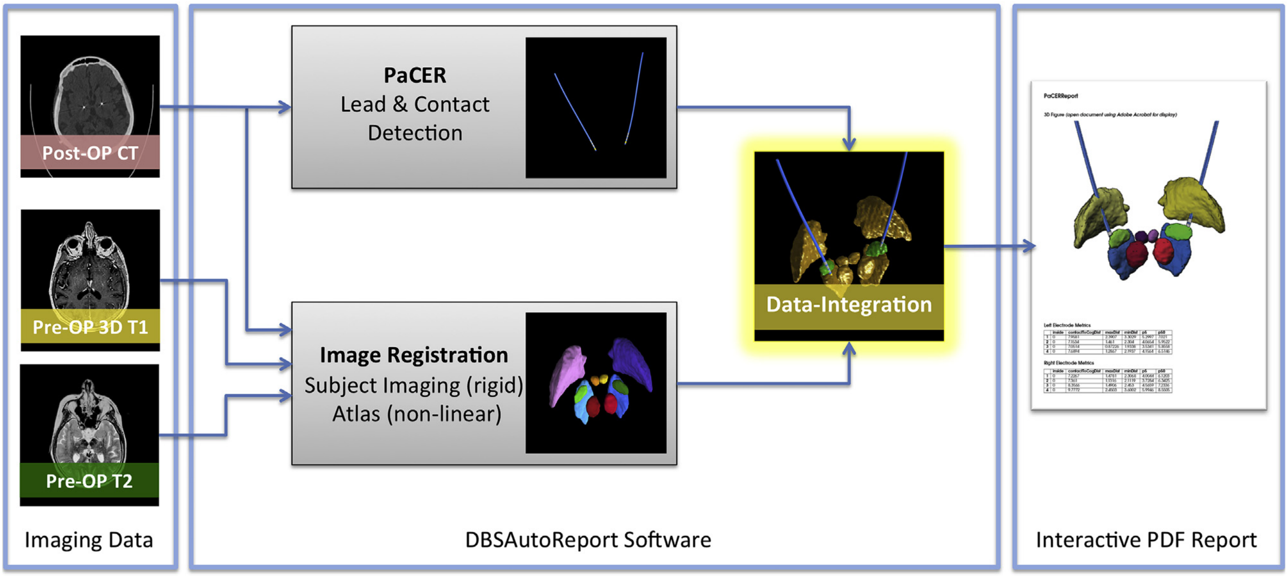

Fig. 1. DBSAR Workflow. The PaCER algorithm is used to extract precise lead and contact locations from post-op CT. Subject image datasets (post-op CT, pre-op T1 and T2 imaging) are aligned using rigid registration followed by a multi-stage multi-modality registration of a 7 T imaging based atlas to the patient space. Finally both DBS leads and anatomical structure information from the atlas are fused in one patient individual space, preserving patient geometry. The result is outputted as a PDF file integrating an interactive 3D rendering of the individual deep brain structures combined with the DBS leads as well as contact to STN metrics (refer to supplementary material for example PDF).

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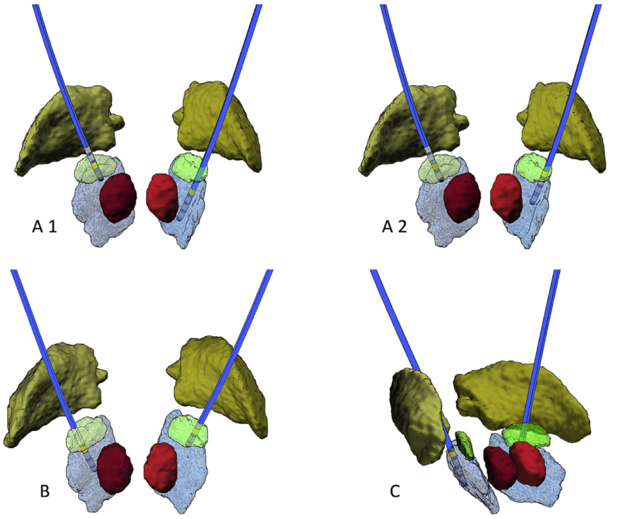

Fig. 2. Example of DBSAR electrode and brain structure visualizations for three cases with sub-optimal electrode placement. STN displayed in green, SN in blue, RN in red, GP in yellow. Contacts highlighted in yellow are predicted as closest to the center-of-gravity of the STN. A1 and A2 show a case with the right lead placed to deep before and after minor lead revision. B shows a case with a sub-optimal placement on the left side. C demonstrates a case with placement of the left electrode in the anterio-lateral substantia nigra. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Results

Automatic electrode lead reconstruction as well as atlas registration was successful in all 20 datasets evaluated. Automatically estimated brain structures demonstrated a qualitatively excellent alignment with T2 hypointens STN regions in manual comparisons (cf. supplementary Figure). For 12 datasets manual 3D segmentations of the STN from T2 imaging were available for comparisons. The mean dice-agreement computed to 0.66 ± 0.05 which is superior to inter-rater agreements reported for manual raters in the literature (0.55 ± 0.08 [5]). In general relatively low dice-kappa agreements are to expect for the STN due to its small volume (cf. [6]).

Clinical potential

The proposed method offers considerable potential for more efficient DBS programming. However, larger clinical studies out of scope of this report are needed to prove this. A field where 3D visualization of DBS lead and individual anatomy might be instantly helpful is the assessment in cases of sub-optimally placed leads. To demonstrate this clinical potential three DBS cases with known sub-optimal electrode placement were selected and assessed using DBSAR in a post-hoc analysis.

DBSAR visualizations of the three cases are shown in Fig. 2. In (A1) the automatic reconstruction revealed a DBS lead placed significantly to deep, a second reconstruction (A2) after minor electrode revision (pull without trajectory change) demonstrates the effect of the revision. The DBSAR report suggest the most proximal contact as best after revision. Indeed this contact turned out to be most effective in monopolar review. In Case (B), the second most proximal contact was chosen as stimulation contact for the well placed right lead by monopolar review, which is congruent to the prediction by DBSAR. The left electrode is predicted as slightly misplaced by DBSAR, with only the most proximal contact close to the STN. Again this contact was found most effective by the gold standard method too.

Case (C) demonstrates a case that exhibited psychiatric side effects when enabling stimulation on the left electrode. No effective contact could be found for the left lead in this case. DBSAR consistently reports a placement outside the STN with all electrode contacts located in the anterior-lateral part of the substantia nigra.

Discussion

We introduced a method to automatically integrate neuroanatomical data on electrode location and deep brain structure morphology solely based on freely available tools. Evaluation on 20 datasets from two centers demonstrated that automatic application without any user interaction is possible on clinical imaging data. The output is a 3D enabled PDF file, which was deemed as very efficiently usable by clinicians. While the used electrode extraction method was previously shown to be very accurate, the accuracy of the atlas based individual deep brain structure estimation is more difficult to assess. The underlying ground truth is unknown and to some extend open to debate due do very large variability between human raters [5]. However, the method already proved useful in the rapid identification of electrodes placed sub-optimal demonstrating congruent results to conventional monopolar review.

Future clinical studies will evaluate the predictive power of the presented method on clinical outcome to enable objective judgment. Future methodological improvements might integrate subregions of the STN, e.g. the sensorimotor region. The greatest potential for improvement is expected when applying DBSAR for the analysis of cases implanted with novel segmented leads.

The straightforward integration of recent algorithms to recover segmented contacts (for example as in Ref. [11]) thus constitutes the next step for the near future.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.brs.2018.01.031.

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