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Article · August 2018

DOI: 10.1049/htl.2018.5075

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Experience-based SEEG planning: from retrospective data to automated electrode trajectories suggestions

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Abstract: StereoElectroEncephaloGraphy (SEEG) is a minimally invasive technique that consists of the insertion of multiple intracranial electrodes to precisely identify the epileptogenic focus. The planning of electrode trajectories is a cumbersome and time consuming task. Current approaches to support the planning focus on electrode trajectory optimization based on geometrical constraints, but are not helpful to produce an initial electrode set to begin with the planning procedure. In this work, we propose a methodology that analyzes retrospective planning data and builds a set of average trajectories, based on the usual practice of a clinical center, that can be mapped to a new patient to initialize planning procedure. In this work, we collected and analyzed the data from 75 anonymized patients, obtaining 30 exploratory patterns and 61 mean trajectories in an average brain space. A preliminary validation on a test set showed that we were able to correctly map 90% of those trajectories and, after optimization, they have comparable or better values than manual trajectories in terms of distance from vessels and insertion angle. Finally, by detecting and analyzing similar plans, we were able to identify 8 planning strategies, which represent the main tailored sets of trajectories that neurosurgeons used to deal with the different patient cases. In this way, we can reduce the amount of information provided by the user to initialize a plan to the selection of a planning strategy, instead of initializing each electrode trajectory or defining multiple constraints for the exploration.

1 Introduction

Drug-resistant focal epilepsy (DRFE) represents a potentially treatable disorder, once the anatomical originating area is defined (so-called Epileptogenic Zone, EZ). When the neuroimaging is poorly supporting the definition of the EZ, an invasive monitoring can be considered. StereoElectroEncefaloGraphy (SEEG) is a percutaneous surgery that allows recording the electrical activity of the brain, through surgically implanted intracranial electrodes. The surgical step of SEEG includes the planning of the electrodes to be placed. Similar to other minimally invasive neurosurgeries, trajectories must avoid vessels, provide a small probe-skull angle at the entry point, and reach the correct targets. Recent research in neurosurgery has been focusing on the optimization of trajectories in order to decrease the planning time and improve the procedure safety and accuracy. In [12], the authors implemented a method for automatic trajectory proposal that computes the risk based on a two step approach which combines a multi-objective optimization and fuzzy logic. Specifically in Deep Brain Stimulation (DBS), in [10] authors improved previous methodologies by optimizing both the trajectory and the stimulation point, by the use of an anatomo-clinical atlas and an estimation of the volume of tissue activated. However, with respect to DBS or general key-hole neurosurgery, which requires accurate targeting of reduced brain zones, SEEG requires a higher number of trajectories aimed to record different cerebral regions. Automated planning in this field has been focusing on the optimization of electrode trajectories based on requirements such as the maximization of the distance from vessels, the minimization of entry angle, increase of GM sampling and conflict avoidance. Optimization approaches usually involve one electrode at a time, except for conflict resolution strategies where the whole set of trajectories is considered. In [5] the authors proposed a method able to optimize the trajectories and maximize the gray matter volume recorded. However their study was limited to three electrodes at a time. Only Sparks et al. [4] propose a method which computes the minimum number of electrodes able to cross all the required regions selected by the surgeon. Nevertheless, this method has the drawback of being very dependent on the atlas used and could lead to solutions that may not be aligned with real clinical decisions. Additionally, as shown in a recent study [9], the planning strategy of different centers may differ due to the hardware used for electrode placement, the imaging protocol and the center experience. Therefore, even if the safety and efficacy requirements are similar, there are no standardized rules that guide all clinical centers and a more tailored approach may provide a better answer to specific center requirements. In Scorza et al. [3], electrodes are manually initialized by surgeons by placing rough entry and target points (respectively EP and TP), while the atlas is only used to maintain the initial anatomical zones during optimization. In this way, the initialization guarantees to respect the clinical practice but requires a manual intervention that may be time consuming.

In this work, we propose a new methodology able to analyze retrospective data from successful SEEG implants and extract the most common trajectories used for the exploration of specific brain zones in a given medical center. The main assumption of this work is that, despite SEEG is a patient specific surgery based on individual anatomy and brain activity, it is possible to identify exploration strategies and trajectories that are commonly used to explore multiple brain areas and to provide an adapted model for the center practice. In this way, our system can suggest an initial plan for a new patient, which the neurosurgeon can further adjust manually or be adapted to the specific anatomy thanks to an optimization framework as the ones previously described. As far as we know, this is the first attempt to model SEEG practice combining surgeon knowledge with specific center retrospective data. The final application will provide trajectory suggestions aligned with the clinical experience, and may be a valid assistant especially for junior surgeons. Preliminary experiments show that, after optimization, the initialized trajectories reach similar values in terms of safety that those that have been manually planned by neurosurgeons. Finally, we were able to cluster the trajectories into various planning strategies that have been positively recognized by a surgeon as commonly adopted in the center.

2 Methodology

SEEG is a very tailored surgery, influenced by the specific anatomy and the particular case of each patient. Most of the time, the procedure does not require to reach a precise target. Instead, a set of regions needs to be sufficiently sampled to identify the epileptogenic network. Nevertheless, it is possible to identify exploratory patterns or sets of trajectories aimed to explore the same brain regions in different patients. With the aim of identifying and modeling similar trajectories, the clinical target (target zone between the ones traversed by a single trajectory) needs to be extracted. Actually, the electrode end-point does not necessarily match the clinical target, it can be any of the zones that it crosses, and clinical knowledge is required here to clearly define the target. Hence, we can associate a generic trajectory descriptor $d = [A; B]$, where A and B represent the entry and the clinically relevant target regions, respectively. In this work, retrospective data are collected and analyzed with the aim of modeling the clinical practice of a center and use this knowledge for the initialization of new plans. A plan $p = \{tr_1, \ldots, tr_E\}$ is a set of trajectories aimed to explore a set of brain zones, with E being a variable number of electrodes depending on the case.

2.1 Problem statement

Given the MRI image of a new patient and a planning strategy selected by the surgeon, the goal of the system is to provide a set of trajectories based on surgeons' past experience adapted to current patient specific anatomy. The planning strategy defines a reduced set of trajectories aimed for the exploration of specific brain regions. Those trajectories will be then modified or optimized to adapt them to the specific patient anatomy.

2.2 Solution strategy

The following steps were conducted for the implementation of the proposed system:

- Trajectory descriptor and exploratory patterns: analysis of retrospective cases in subject space, identification of similar trajectories among patients and their normalization on an average brain space.
- Mean trajectories definition (mT): spatial clustering in the average brain space of similar trajectories to produce mean trajectories mT for the exploration of specific brain regions.
- Planning strategies definition (cl): analysis of the spatial relationship between mean trajectories and their clustering, based on the macro-anatomical regions that they explore.
- Plan adaptation: mapping of the selected planning strategy from a common average brain space to the subject space.

Finally, the trajectories obtained may be optimized similarly as described in [3].

2.3 Trajectory descriptor and exploratory patterns

We collected the retrospective data of N patients who successfully underwent SEEG procedure. The inputs for our analysis are an MRI-t1 image and the original trajectories planned by the surgeon in subject space. All data have been processed by the Freesurfer (FS) pipeline [6], which co-registers the patient with the MNI-305 space and labels the different brain zones using a probabilistic atlas segmentation [7]. For each patient, a plan p_j with $j = 1, \ldots, N$ is assigned, where trajectories $tr_{i,j}$ have been manually planned by surgeons and are defined by the entry and target point coordinates. Trajectories were regularly sampled with a method similar to the one described in [8]. For each $tr_{i,j}$, we defined a descriptor $d_{i,j} = [Z^a_{EP}; Z^b_{TP}]$ where Z_{EP} and Z_{TP} are groups containing the labels of the brain zones that are considered as meaningful entry and target zones, respectively ($Z^a_{EP} \in Z_{EP}$ and $Z^b_{TP} \in Z_{TP}$). This definition of Z_{EP} and Z_{TP} resulted from the analysis of the most explored zones in our samples, their anatomical positions, and surgeons suggestions. Finally, sets of similar trajectories $pt_{a,b} = \{tr_{i,j}\}, \forall\, tr_{i.j}\ if\, d_{i,j} = [Z^a_{EP}; Z^b_{TP}]$ were built from all patient data and represent exploratory patterns to explore the regions $[Z^a_{EP}; Z^b_{TP}]$.

2.4 Mean trajectory definition

Once similar trajectories have been grouped in subject space, their coordinates were transformed to the MNI-305 space by using the registration matrix provided by the FS pipeline. Since we based our analysis on an anatomical atlas, we must assume that, due to their size, some regions are explored with several electrodes for higher coverage. Therefore, for a given plan p_j we may find a variable number of trajectories $tr_{i,j}$ with the same descriptor $pt_{a,b}$. To keep the spatial relationship between those trajectories, we used a k-means algorithm to automatically cluster entry and target coordinates into $U_{a,b}$ groups and generate a set of mean trajectories $mT^u_{a,b}$, where $u = 1, \ldots U_{a,b}$. The number of groups $U_{a,b}$ is defined as the maximum number of trajectories aimed to explore the same regions a and b in a single plan among all plans p_j, $j = 1, \ldots, N$. To avoid an erroneous definition of groups due to particular cases, an $mT^u_{a,b}$ is considered significant only if contains at least 5% of trajectories described by $pt_{a,b}$. Otherwise the maximum number of clusters $U_{a,b}$ is decreased by 1 and the k-means algorithm applied iteratively. Figure 1 shows an example of the procedure for trajectories commonly used to explore the insular region. Finally we obtained a set of mean trajectories $mT = \{mT^u_{a,b}\}$ where $a \in Z_{EP}, b \in Z_{TP}$ and $u = 1, \ldots, U_{a,b}$, composed by couples of mean entry and target coordinates and their standard deviations.

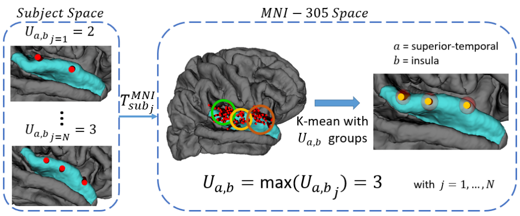

Fig. 1: Mean trajectories for a single pattern $pt_{a,b}$ obtained with K-means algorithm: insular exploration (region b) are usually performed from the superior-temporal (region a), with a maximum of 3 electrodes in the same plan $U_{a,b} = 3$.

2.5 Planning strategies

To find a high-level feature describing a precise planning strategy, the different plans were compared and clustered. Since we defined a set of mean trajectories mT from manually planned trajectories $tr_{i,j}$, we can define and assign to each plan p_j a new binary descriptor f_j of fixed length $\#(mT)$, which contains only boolean values and represent the presence or absence of a mean trajectory mT_y, with $y = 1, \ldots, \#(mT)$ in a plan p_j. Since the plans can be hierarchically connected (e.g. one can be the composition of others), we opted for a hierarchical clustering method which operates on the basis of an empirical coefficient of similarity (the Jaccard distance) computed over the descriptors f_j (figure 2).

By the analysis of the generated dendogram, we grouped the plans into G clusters by the selection of a cut-threshold. Finally, for each group $g \in G$, we defined a new binary descriptor cl_g of length $\#(mT)$ and we set $cl^y_g = True$ if at least $\#(f^y_j = True) >= 2$,

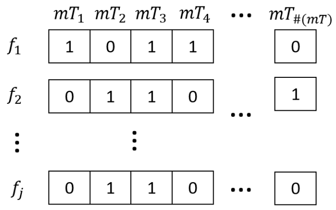

Fig. 2: Binary vector representation f_j for each plan p_j, representing the presence or absence of a mean trajectory. The Jaccard distance is computed to measure the dissimilarity between binary vectors.

$\forall\, f_j$ in g. The new descriptor cl_g codifies a set of mean trajectories to explore macro-regions of the brain and represents a planning strategy.

2.6 Clinical scenario and validation

To construct our model we used 75 anonymized patient data provided by Niguarda Hospital (Milan, Italy), for a total of 1100 trajectories. For each patient, MR images were acquired using the hospital system $1.5T$ (Intera Achieva, Philips Medical System, The Netherlands, T1 3D FFE sagittal images, $0.90mm \times 1.07mm \times 0.90mm$ voxel dimensions, without any inter-slice gap, then reconstructed and reformatted on the axial plane with $560 \times 560 \times 220$ matrix, $0.45mm \times 0.45mm \times 0.9mm$ voxel dimensions). The FS pipeline was used to obtain the cortical reconstructed surface and the probabilistic atlas segmentations (the Desikan-Killiany atlas, with 75 labels per hemisphere, was used in this study). The pipeline also provides the affine registration matrix used to map patients and trajectories from the subject space to the average space (MNI-305). As a preliminary validation of our method, we used a test set composed by 10 patients that were not included to build our model. For each patient's plan, we identified the manually planned trajectories corresponding to mean trajectories mT_y and mapped them to the subject's space generating and initialized plan (IP). Hence, we computed the euclidean distances $d_{ep}^{\alpha,\beta}$ and $d_{tp}^{\alpha,\beta}$ between entry and target point coordinates respectively, where α, β are two corresponding trajectories between the mapped mean trajectories and those planned by the surgeon. We considered that a trajectory has been correctly mapped when $d_{ep}^{\alpha,\beta} \leq 2\sigma(mT_y^{ep})$ and $d_{tp}^{\alpha,\beta} \leq 2\sigma(mT_y^{tp})$. The value of σ varies based on the trajectories used to define the average mT_y. This metric provides a measure of the generalizability of trajectories mT. However, the mapped mean trajectories may not comply with clinical criteria (e.g. safe distance to vessels), and therefore they need to be optimized to produce valid initial plans and adapt to the specific patient anatomy. For the optimization we used the method presented in [3], and verified the compliance in terms of distance from vessels and insertion angle. We evaluated initial quantitative values comparing manual planned (MP) trajectories, the corresponding initialized trajectories (IP), and their optimized solution OMP and OIP respectively. Finally, the groups obtained by the hierarchical clustering have been presented and qualitatively evaluated by a surgeon. Results are reported in the following section.

3 Results

3.1 Exploratory patterns and mean trajectories

The analysis of the planned trajectories based on the Desikan-Killiany atlas reduced the possible target regions used to classify the trajectories. We did not take into account the white matter, while other structures such as ventricles, brain stem or cerebellum, where automatically excluded since they were classified as outliers. Following the clinician's advice, electrodes crossing the *insula* and ending in the *putamen* were included in the Insular pattern. In the same way, we consider as a single target point the *hippocampus* and the *para-hippocampus*, since it is not possible to explore the last without crossing the *hippocampus*, and on the other side by prolonging the trajectory we easily reach the *para-hippocampus*, increasing the recorded information. Finally, since our data had poor representation of occipital trajectories, we joined the occipital zones of *lingual cortex*, *cuneus*, *pre-cuneus* and *pericalcarine*, assuming that the spatial distribution of those were more important than the specific description pattern in terms of entry and target zones.

By grouping the trajectories with the reduced descriptors presented in section 2.3, we found 30 exploratory patterns $pt_{a,b}$, for a total of 61 mean trajectories mT that represent the mean coordinates of the most representative trajectories in our data. Figure 3 shows the mean trajectories in the average space.

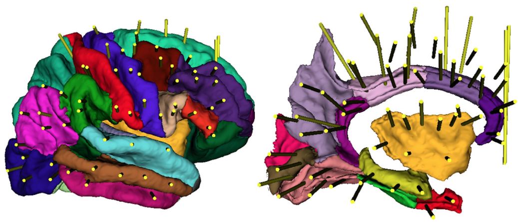

Fig. 3: A sagittal view of the mean trajectories computed in the average space: dimensions have been enlarged for visualization purposes.

To test the viability of our method, we mapped the recognized trajectories on 10 patients that were not included in the initial database as explained in section 2.6, for a total of 95 initialized trajectories. By computing the initial euclidean distance with their corresponding manually planned trajectories at EP and TP in subject space, we found that the 90% of the initialized ones satisfy the criteria presented in 2.6. Finally, to test the viability of our initialization method, we compared the values of distance from vessels at the entry points, distance from vessels in the second tract and insertion angle before and after the optimization for both groups (MP and IP). The results are shown in image 4.

Even if the mapped trajectories (IP) could not be considered safe in terms of indexes, the optimization performed provides a better solution (OIP group) with respect to the manually planned (MP) trajectories and a comparable solution with respect to the optimized ones (OMP), making this a valid method to initialize an optimization strategy provided by an automated planner. No statistical difference has been found between the indexes of the two groups OMP and OIP after optimization.

3.2 Planning clustering and strategies definition

The hierarchical clustering method applied and the cutting-threshold chosen led to 8 different clusters composed by similar plans. The cut-threshold has been chosen empirically, in order to balance the number of groups and its components.

Therefore, for each cluster obtained we selected those trajectories which appear in at least two plans and generate the planning strategies cl_g. The clusters were evaluated by a neurosurgeon, who recognized the main trends in the trajectories proposed. Therefore, we were able to name each cluster, as reported in figure 6.

Since SEEG is a patient-specific procedure, the clusters obtained do not completely match with actual patient plans. Additionally, some of the clusters (e.g. *Fronto-central*) result to be over-populated, since we preferred a reduced number of clusters with more trajectories rather than more groups to be combined. From a usability

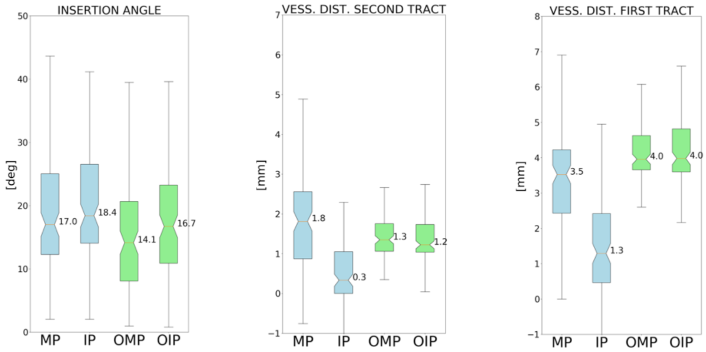

Fig. 4: Comparison of quantitative indexes between Manual Planning (MP), Initialized Planning (IP) trajectories and their optimized versions (OMP and OIP). The mean values of insertion angle and distance from vessels (first and second tract as reported in [3]) present no statistical difference between OIP and OMP

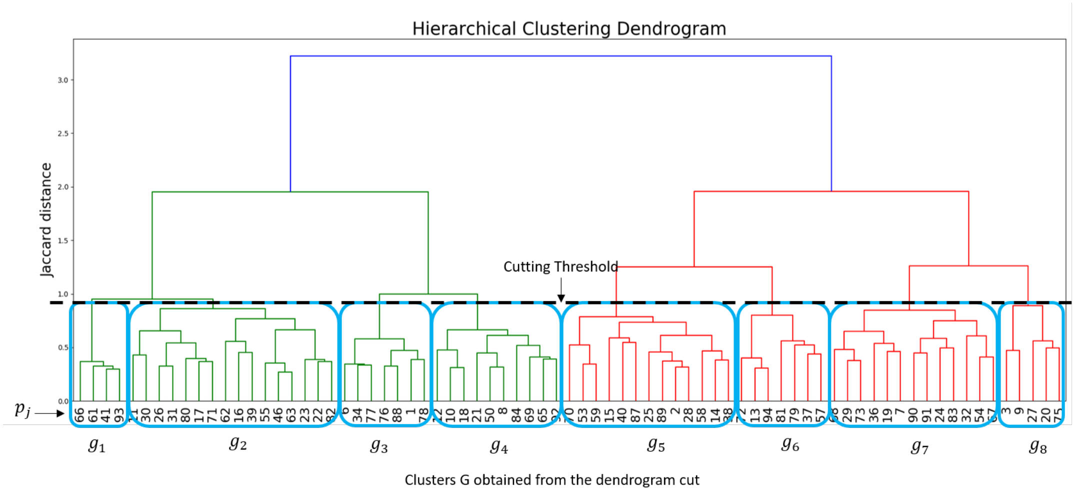

Fig. 5: Dendrogram obtained by the hierarchical clustering performed using the Jaccard distance. The cutting threshold defined 8 groups.

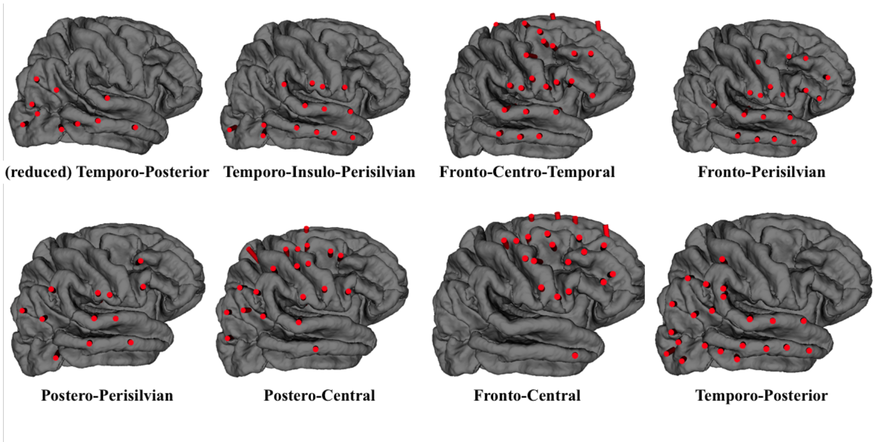

Fig. 6: Lateral view of the 8 clusters obtained, with the labels defined according to the surgeon suggestions

point of view, we considered that removing trajectories from a suggested strategy would be more easy for the surgeon in order to adapt the plan for a specific patient than to combine different cluster and then refine the plan. However, they seem to be a good representation of the planning strategies adopted in the center to explore specific macro-areas of the brain. Notice that the results have been obtained from a reduced set of data, with unbalanced distribution of plans. However, the system was able to group the plans into clinically meaningful clusters, that can be used as an initial starting point for a new patient planning. By the use of those clusters, the clinician should only remove or add few specific trajectories, while the rest would be directly mapped to the patient anatomy. Nonetheless, the use of a cluster is not mandatory, since there may be specific patients where the direct choice of single trajectories from the mT set would provide a faster initialization.

4 Conclusion

In this work, we presented a new methodology that merges clinical knowledge with the analysis of retrospective data of a given clinical center. The approach presented has been able to identify and model the most used trajectories, and define specific planning strategies by clustering similar plans. To the best of our knowledge, this is the first application that provides a trajectory initialization method adapted to a single center strategy based on its retrospective data analysis. The final application allows to easily visualize and select the most common trajectories, and cluster electrodes commonly used for a specific exploration. Preliminary results show that mean trajectories can be successfully mapped to patient plans that were not included to build our model, and provide a meaningful initialization for an automated planner as the work presented in [3]. The cluster obtained have been positively recognized by surgeons as exploratory strategies used in their center and we were able to map 90% of the trajectories. Finally, those initialized trajectories have been correctly optimized by the automated planner, adapting to the subject anatomy and reaching quantitative results comparable or superior than manually planned trajectories, in terms of safety. An extended validation with surgeons is still needed to assess the viability of those trajectories. Current limitations of this approach are represented by the need of FS pipeline and of a large amount of data. Since the trajectories extracted represent the most common trajectories used in the center, a new patient plan would be unlikely initialized completely by a chosen set and surgeons will still have to manually plan few trajectories depending on specific patient requirements (e.g. lesions). Nonetheless, the method presented provides a model of the clinical practice mostly based on the data provided by the center. The database constructed for this work will store new patient information and their planned trajectories, allowing our model to continuously adapt while new patients are added. To improve our model, especially regarding the planning strategies proposed, Diffusion Weighted Imaging (DWI) and tractography may be used to identify specific brain networks and generate more specific electrode clusters to map them. Similarly, in the future, we would like to include other functional imaging techniques as functional-MRI and/or EEG-signals. Future work will be focused on the generalization of this methodology and to provide a more complete validation.

Acknowledgment

This research is a part of the SINAPSIS Project funded by ELKARTEK 2017 by the industry department of the Basque Country.

Conflict of Interest

Dr. Rizzi is a paid medical advisor of WISE Srl since February 2018.

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