Development and Application of Functional Databases for Planning Deep-Brain Neurosurgical Procedures

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Abstract. This work presents the development and application of a visualization and navigation system for planning deep-brain neurosurgeries. This system, which incorporates a digitized and segmented brain atlas, an electrophysiological database, and collections of final surgical targets of previous patients, provides assistance for non-rigid registration, navigation, and reconstruction of clinical image data. The fusion of standardized anatomical and functional data, once registered to individual patient images, facilitates the delineation of surgical targets. Our preliminary studies compared the target locations identified by a non-expert using this system with those located by an experienced neurosurgeon using regular technique on 8 patients who had undergone subthalamic nucleus (STN) deep-brain stimulations (DBS). The average displacement between the surgical target locations in both groups was 0.58mm±0.49mm, 0.70mm±0.37mm, and 0.69mm±0.34mm in x, y, and z directions respectively, indicating the capability of accurate surgical target initiation of our system, which has also shown promise in planning and guidance for other stereotactic deep-brain neurosurgical procedures.

1 Introduction

Surgical treatments for movement disorders, such as Parkinson's disease and essential tremor, are performed by either creating a small lesion, or placing electrical stimulators at precise locations deep within the brain, using minimally-invasive stereotactic techniques. However localizing the surgical target is challenging due to the incompleteness of the information provided by the regular pre-operative medical images, where neither the motor nuclei of the thalamus, the internal segment of the globus pallidus (GPi), nor the subthalamic nucleus (STN) (the targets for the surgical treatments of Parkinson's disease) can be visualized directly. In clinical practice, additional information from anatomic atlases [1,2] is needed to enhance the accuracy and precision of targeting. Moreover, computerized atlases [3-5] have been implemented to overcome the inherent disadvantages of the printed versions. Digitized atlases can be aligned and fused with individual pre-operative brain images

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to facilitate the identification of the surgical targets. Nevertheless existing anatomical atlases should be employed conservatively for planning stereotactic procedures because of their limitations, such as lack of morphometric information, poor generalization, and insufficient statistical representation of the population.

In addition to the anatomical information derived from pre-operative images and brain atlases, functional information obtained from intra-operative electrophysiological measurements is also required to refine the optimal surgical targets, characterize tissue function, and map somatotopy. Accurate pre-operative surgical target planning can reduce the need for invasive exploration and decrease procedure-related complications. In this case, additional standardized electrophysiological information available prior to surgery may assist the surgical target determination. Previously, researchers have developed electrophysiological atlases [6,8,9] and databases [7] containing data from a series of patients, standardized and normalized to a standard brain template to establish the relationship between functional brain organization and anatomic structures, and to estimate the surgical targets [6-9].

This paper expands that of Finnis *et al.* [7] by adding data of 43 new patients (for a total of 131) and incorporates the database into a comprehensive neurosurgical system. Our work focuses on the integration of a 3D visualization and navigation system for stereotactic functional deep-brain neurosurgery planning and guidance in order to improve target localization accuracy and to minimize electrophysiological exploration and patient trauma. We describe preliminary studies evaluating the effectiveness of this system in surgical targeting for STN deep-brain stimulation (DBS) procedures. This system integrates the electrophysiological database, digitized 3D brain atlases [1], segmented deep-brain nuclei, and surgical targets from previous procedures, along with representations of surgical instruments, into the visualization and navigation system. All the standardized functional and anatomical data in this system, once non-rigidly mapped to a patient brain space, can be an important adjunct for pre-operative surgical target planning and intra-operative surgical guidance.

2 Materials and Methods

2.1 Image Registration

Two registration steps are necessary to implement this procedure. The first rigid-body registration step establishes the transformation between a patient image-space and the stereotactic frame, whereas the second performs the non-rigid mapping of the functional data from each patient brain space to the standard database, and vice versa.

Frame-to-Image: An automatic fiducial localization algorithm registers the image volume to the frame in 1.5s by extracting the ‘Z-bar’ fiducial points from the images with a fiducial localization error of approximate 0.5mm for both MR and CT.

Data-to-Database & Database-to-Patient: The rapid 3D non-rigid registration algorithm [10] has been adopted to accommodate the intersubject variability between each patient anatomical brain image and the standard brain template. This algorithm employs a completely unsupervised multi-resolution approach that executes 8 to 12 minutes on a dual PIII 933 MHz machine with an average registration error of 1.04±0.65mm [10].

2.2 Functional Database Construction

Subjects: 131 patients who had undergone a total of 161 surgeries for symptomatic treatment of Parkinson's disease, chronic pain, and essential tremor at London Health Sciences Centre (LHSC), London, Ontario, Canada, have been recruited, for the functional database construction.

MRI data: The pre-operative MRI images of the patients were acquired with a 1.5T GE Signa scanner using a 3D SPGR sequence (TR/TE 8.9/1.9ms, flip angle 20°, NEX 2, voxel size 1.17mm×1.17mm×1mm, in-slice resolution 256×256).

Standard brain template: The CJH-27 dataset [11] was adopted as the standard brain template (the common coordinate system) of the functional database. CJH-27 consists of 27 registered T_1-weighted MRI scans ($20 \times 1mm^3$: TR/TE 18/10ms, flip angle 30°, NEX 1; $7 \times 0.78mm^3$: TR/TE 20/12ms, flip angle 40°, NEX 1) of the same healthy individual averaged into a single volume.

Functional data collection: First of all, the pre-operative brain image of each patient was non-rigidly registered to the CJH-27 template, to establish the 3D transformation and the deformation grid. Then the micro-recording, electrical-stimulation data were coded using a comprehensive coding scheme and intra-operatively entered into single patient brain image space. Finally, the functional data in each patient image space were non-rigidly mapped to the standard brain coordinate according to each 3D non-rigid transformation. The functional data in the population-based database can be applied to the individual brain image using the inverse of the original non-rigid patient-to-database transform.

2.3 Visualization and Navigation System Integration

Electrophysiological Database: Our current electrophysiological database is an expanding version of that reported previously [7]. The functional data in this study were obtained during the procedures performed on the patients, and those relating to a particular firing pattern, a specific body reaction, and certain anatomical regions, can be retrieved and displayed as clusters of spheres in 3D space or density maps on three intersecting orthogonal 2D image planes.

Digitized Brain Atlas and Segmented Deep-brain Nuclei: We non-rigidly mapped a digitized version of Schaltenbrand-Wahren atlas [1] to the standard brain. Deep-brain nuclei were segmented based on the anatomical representation in this atlas, and represented as either 3D objects or triangulated meshes. The centroid of each segmented deep-brain nucleus is shown as a sphere.

Collections of final surgical targets of previous patients: The location of the final target of each surgical procedure was non-rigidly registered to the standard brain coordinate and saved to each categorized database depending on the characteristic of the surgery. Currently we have eight databases containing data from 50 thalamotomy (34 left and 16 right), 59 pallidotomy (30 left and 29 right), 22 thalamus DBS (12 left and 10 right), and 30 STN DBS (18 left and 12 right) procedures. The collection of final targets can be non-rigidly mapped to the pre-operative MR images of individual patients. The center of mass (COM) and the statistical map of a cluster of target locations are used to estimate the initial surgical target of each individual patient.

Representation of surgical instruments: Up to five multiple virtual probes can be manipulated simultaneously or independently to simulate the real surgical procedures. When implemented with the Frame Finder algorithm, this system also provides the simultaneous display of the tip positions of these trajectories in both image space and stereotactic frame space.

Visualization and Navigation Platform: Within this system, coded functional data, plotted directly onto the patient's pre-operative image along a virtual trajectory corresponding to the position and orientation of the physical probe, can be non-rigidly transformed to the standard brain template automatically.

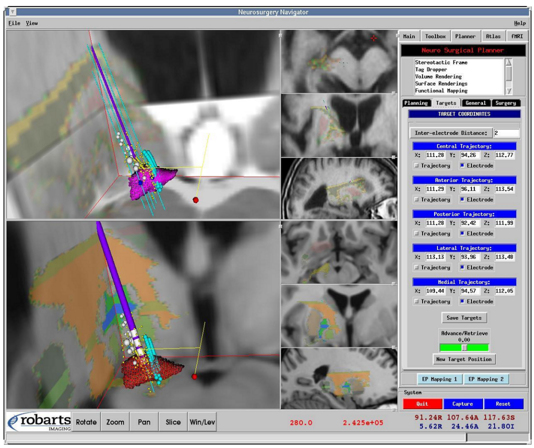

Fig. 1. The primary graphical user interface of the system displays the 3D image volume and 2D slices of a patient (upper) and those of the standard brain template (lower). The digitized atlas is registered and fused with each image. A T2-weighted image is also shown fused with the patient image. The control panel shows the tip locations of the five probes.

3 Clinical Application

Usually, the initial pre-operative surgical target is selected by the neurosurgeon using a geometric technique based on measurements relative to the AC-PC positions. For each of the eight STN DBS cases (5 left and 3 right procedures), an experienced stereotactic neurosurgeon performed the pre-surgical planning and targeting using this standard approach, carried out the surgical procedure according to his plan, and refined the surgical target through electrophysiological recording and stimulation. At the same time, one of the authors (TG), a non neurosurgeon familiar with deep brain anatomy, estimated the surgical target location and trajectory orientation for the placement of a DBS electrode independently of the surgeon using the neurosurgical visualization and navigation system integrated with the customized functional and anatomical data. For each case, the pre-operative MR image of each patient was loaded into our system and non-rigidly registered to the standard brain template. Then the 3D transformation and non-rigid displacement grid file generated by registration were applied to map the data in the electrophysiological database, the collection of previous surgical targets, the digitized Schaltenbrand atlas, as well as segmented deep-brain nuclei to the patient brain image. In this preliminary study, the effectiveness of our system for surgical targeting was evaluated by comparing the target locations estimated by the non-expert with those identified by the neurosurgeon.

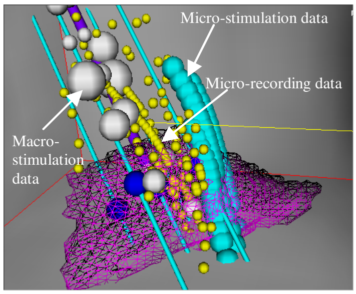

Fig. 2. The magnified version of Fig. 1; Purple lines (central): Central electrodes; Cyan lines (parallel to the central line): surgical trajectories; Yellow spheres (small): micro-recording data; Cyan spheres (medium): micro-stimulation data; White spheres (large): macro-stimulation data; Mesh object: sub-thalamic nucleus (STN); the segmented STN and electro-physiological data are non-rigidly registered from the standard brain space to the patient brain image

4 Results

4.1 Clinical Validation of the Non-rigid Registration Algorithm

Accurate registration plays a critical role in localizing surgical targets with the references of standardized anatomical and functional information. Registering the collection of previous final surgical targets from the standard database to an individual patient image yields a probabilistic estimation of the target location for the patient. To assess our registration algorithm clinically, a cluster of 18 left STN DBS surgical targets contained in the categorized database was non-rigidly transformed to the images of 5 patients who had received similar surgical procedures. That of the 12 right STN DBS targets in another database was mapped to the images of 3 patients undergoing right STN DBS. Table 1 shows the comparison between the center of mass or the most significant position on the probability map of database-initialized locations and the actual surgical targets of the 8 patients. The results demonstrate that the registration algorithm performs well within the homogeneous regions in the deep-brain. Although the average distance between the registered centroid of the collection of previous surgical targets and the target locations of the new patients is 2.19±0.72mm, this technique nevertheless provides a suitable initial estimate of the pre-operative surgical target, which may be further refined with additional functional and anatomical information available on the neurosurgical system.

Table 1. Absolute differences between the database-initialized and the real surgical targets

Difference	*x*	*y*	*z*	*d(x,y,z)*
Avg. (mm)	1.22	1.28	1.08	2.19
Max (mm)	2.09	2.67	2.3	3.6
Min (mm)	0.73	0.83	0.33	1.55
Sd (mm)	0.48	0.59	0.73	0.72

4.2 Application of the Segmented Deep-Brain Nuclei

If the registration is accurate, the atlas-based segmented deep-brain nuclei transformed to a patient brain space should have a high percentage of overlap with the patient's own nuclei. The accuracy of our registration algorithm suggests that the anatomical information provided by a specific segmented nucleus registered to a patient (Fig. 3) should indicate the spatial location of the optimal surgical target within the nucleus. At our institution, the dorsolateral portion of STN is regarded as the most effective stimulation site in STN DBS. Acknowledging the centroid position of the segmented STN and its spatial relationship with respect to the theoretical surgical destination, the neurosurgeon may more confidently localize the surgical target. We compared the centroid of the segmented STN and the real target location for each of the eight patients. Table 2 reports the absolute differences between them. 75 percent of the actual surgical targets are located dorsolateral to the corresponding centroids in our study.

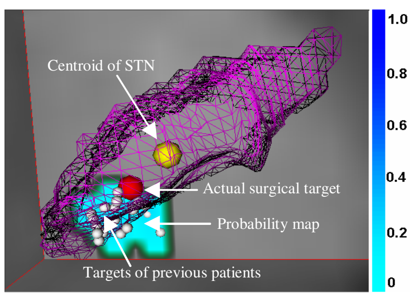

Fig. 3. Mesh object: STN; Yellow sphere: the centroid of STN; White spheres: surgical targets of previous patients; Colour-coded map: the probability map of a collection of left STN DBS targets; Red sphere: the actual surgical target

Table 2. Absolute differences between the centroids of the segmented STN and the real targets

Difference	*x*	*y*	*z*	*d(x,y,z)*
Avg. (mm)	1.41	1.99	0.89	2.84
Max (mm)	2.24	3.23	1.41	3.52
Min (mm)	0.32	0.01	0.23	1.24
Sd (mm)	0.73	1.15	0.58	0.85

4.3 Effectiveness in Surgical Targeting

We evaluated the effectiveness of our neurosurgical visualization and navigation system in surgical targeting on eight STN DBS patients. The average distance between the non-expert-planned surgical targets and the expert-localized ones was 0.58±0.49mm, 0.70±0.37mm, and 0.69±0.34mm in x, y, and z directions respectively. In addition, the surgical sites determined with the combined information from both electrophysiological database and the anatomical resources were closer to the final surgical targets chosen by the neurosurgeon than those defined either by regular image-based techniques, or by the mapping of a cluster of surgical targets on the pre-operative images. Practically, these residuals indicate that an initial estimation of target location, made on the basis of this software, is typically within 1.7mm of the real surgical target. Therefore, the final surgical target can be reached by slightly refining the initiation of the target position estimated using this system with greatly reduced electrophysiological exploration.

Table 3. Absolute differences between the system estimated and the real surgical targets

Difference	*x*	*y*	*z*	*d(x,y,z)*
Avg. (mm)	0.58	0.70	0.69	1.67
Max (mm)	1.28	1.35	1.27	2.75
Min (mm)	0.06	0.30	0.2	0.65
Sd (mm)	0.49	0.37	0.34	0.70

5 Discussion

This visualization and navigation system has been used both pre- and intra-operatively for planning the surgical trajectories, plotting and analyzing functional data in patient pre-operative image space during eight separate surgeries. Even without considering the possibility of brain movement/shift, this system has been proved helpful in facilitating the identification of surgical loci for STN DBS. The visualization capabilities, designed for presentation of all the relevant functional and anatomical data along with multiple virtual surgical instruments, have made simulating real surgical procedures feasible. In conjunction with the function of automatic calculation of frame-to-MRI transforms, the intra-operatively acquired data can be saved in a text file whose header contains the code describing the physical information of the patient and specifications of the probes used during the procedure. Meanwhile, the homologous data in the standard brain space can be stored in the functional database. This initial pilot study, involving only one non-expert and one neurosurgeon, yielded promising results that need to be further validated on more subjects and a study of inter and intra "non-expert" variability for the application of our system to deep-brain neurosurgical procedures. While only a single neurosurgeon was involved in this work to date, we hope to address this problem through a multi-centre study in the future. Despite the difficulty and complexity of the accurate STN segmentation on the patient image files, comparing overlapping ratio between the registered segmented STN of each patient and that of the standard brain atlas could also provide valuable measurements for the validation of the registration algorithm. Although the system has reached a stage of development where prediction of surgical targets is possible, further clinical evaluation is required for thorough validation and application of this system in stereotactic deep-brain neurosurgical procedures.

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