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Electrophysiology-guided deep brain neurosurgery

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Abstract—. **Since the discovery of x-rays, medical imaging has played a major role in the guidance of surgical procedures. Recent advances in computer technology have only accelerated the rapid development of this field. As interventions become significantly less invasive, the use of pre-operative and intra-operative images to guide surgery has assumed increasing importance. Image-guided techniques have been employed for many years to plan and guide neurosurgical procedures. Amongst the most challenging areas of neurosurgery is the accurate targeting of nuclei within the deep brain for the treatment of Parkinson's and other motor system diseases. Unfortunately, standard CT and MR imaging does not permit the anatomical delineation of the targets, and so additional information, for example atlases and electrophysiological data, must also be employed. Both these forms of data can be mapped, using non rigid image registration techniques, to a standard representation of a brain acquired from MRI. The electrophysiology database can also evolve over time with the incorporation of data acquired from multiple patients operated in the past. Information of this nature can then be incorporated within the patient image, and serve as an invaluable tool in predicting to the surgeon the likely area of the target. This approach can significantly reduce the trauma associated with the insertion of multiple unnecessary electrodes to refine the target location, and speed up the procedure.**

***Keywords*—Brain atlas, electrophysiological database, Parkinson's disease, stereotactic deep-brain neurosurgery.**

INTRODUCTION

Image-guidance is used in surgery in much the same manner as modern navigational technology is employed to guide a pilot of an aircraft at night, through unfamiliar terrain, or through bad weather. In each case, a direct view of the landing site (target) may be unavailable, and so navigation is achieved with respect to a model of the environment, rather than via a direct view. The model is often complemented by real-time information such as weather conditions, altitude, and glide-path. Image-guided surgery employs a similar paradigm, using information acquired from a variety of imaging sources.

I. STEREOTACTIC NEUROSURGERY

What we understand today as image-guided surgery has its roots in stereotactic neurosurgical procedures that were developed in the early 20th century, and have evolved into systems that employ a referencing frame attached rigidly to the patient's skull, along with mechanical devices to guide a probe to deep brain, permitting the position of the target to be described in terms of a frame-based co-ordinate system. However, in spite of the sophistication of today's imaging systems, the brain images that they produce do not provide the necessary tissue discrimination to visualize the targets within the brain that must be treated.

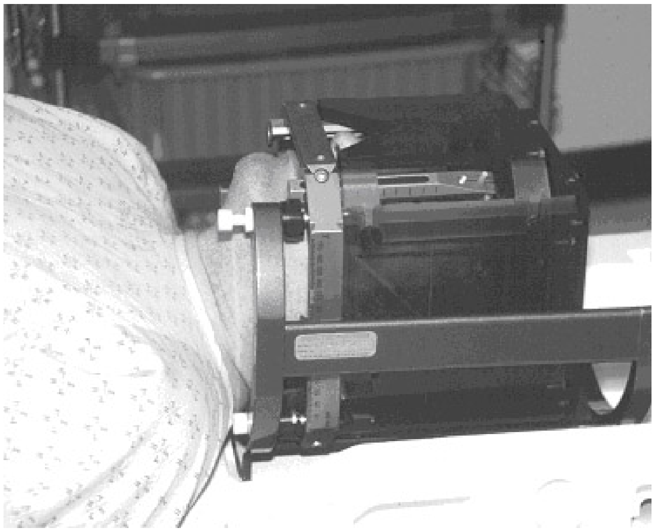


Figure 1. Stereotactic frame attached to patient's head with MRI fiducial marker set attached.

A. Surgical Targets

Continuing advances in the understanding of the neural circuitry in the deep brain has narrowed the surgical focus to functional sub-regions within three key grey matter structures: (1) the thalamus, (2) the globus pallidus internus, and (3) the subthalamic nucleus. Since these regions are not distinguishable in the CT or MR images, thy must generally be identified on the basis of their electrophysiolical behaviour. Once the desired functional sub-region or nucleus is identified within the target structure is located it is either lesioned (radiofrequency thermocoagulation, cryolesioning, or excised) or implanted with a chronic high-frequency deep brain stimulator (dbs) to alter its function.

B. Stereotactic Frames

The stereotactic frame forms the reference gold-standard for image-guided neurosurgery. Although there are many different frame designs available [1], they all perform the function of providing a robust rigid reference system that establishes a coordinate system relative to the patient, provides recognizable landmarks in the images, and serves as a stable mounting base and instrument guide (Figure 1).

Stereotactic frames are generally equipped with fiducial markers designed to be imaged by tomographic systems and generally consists of a series of 'Z', 'N' or 'V' bars mounted on the frame. Their configuration is such that when they are intersected by the image slices, their configuration is unique for any slice (Figure 2). If a slice contains at least three sets of markers its oblique position within the volume may be determined unambiguously.

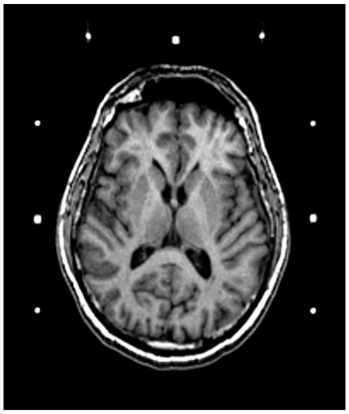


Figure 2. Fiducial markers as they appear in an MR image. The relative positions of these markers uniquely identify the slice within the volume, with respect to the frame, permitting navigation within the brain.

C. Atlases

Current imaging techniques do not provide sufficient information to permit direct delineation of the targets necessary for the surgical treatments of Parkinson's disease. While anatomical atlases have for many years been linearly mapped to patient images to assist in identifying these regions, the intersubject variability and other inherent pitfalls of such approaches limit their ability to localize the surgical target accurately.

In addition, there are several disadvantages associated with standard atlases. When they are constructed, it is not uncommon that several cadaver tissue sections are damaged in the slicing process, sectioned unevenly, or rendered unusable by excessive or uneven shrinkage during histological processing As a result, uneven interslice distances often exist in the final printed atlas. Accordingly, during surgical planning the surgeon must frequently select an atlas plate that most closely approximates the region of brain they wish to target because there is no atlas slice that corresponds directly to the target region. Over the last decade we have used a three-dimensional atlas that may be automatically non-rigidly registered (or warped) to fit the 3-D MRI of an individual patient [2]. To facilitate this matching, the atlas is first registered manually to a standard brain MRI template (the Colin27 brain) [3] that was created by averaging 27 volumes of the same brain together to produce a high resolution, high signal-to noise volume. This volume was matched, using a non-rigid spatial warping algorithm [4], to the patient's MR images. Using the non-rigid registration transform calculated by this operation, the three-dimensional atlas is also mapped to the patient. Using this system, target structures within the atlas that define the lesion site may be visualized in three dimensions along with anatomical landmarks defined by the 3-D MRI, along with models of the recording electrode, the proposed lesion and the probe used to create it.

While such atlases offer a great deal of assistance to the surgeon, it is still necessary to verify that the lesion is being created in exactly the right place through physiological stimulation and recording. Misplacing the position of such a lesion by as little as one or two millimeters could have a disastrous effect on the patient's outcome. The purpose of the atlas therefore, is not so much to guide the surgeon to exactly the right place directly but to make it easier for him to approach the desired region quickly and to verify the target position with a minimum of electro-physiological tests, each of which may require electrodes to be inserted along a new pathway.

D. Electrophysiological Atlases

Due to the limitations described above, superposition of digitized anatomical atlases over patient brain images can provide only an approximation of target loci regardless of the atlas-to-patient registration technique employed. To refine the atlas-approximated target into a final target, multiple exploratory trajectories with a recording and/or stimulating electrode are performed within and adjacent to the intended target to characterize tissue function and to map somatotopy. Physical responses elicited by the patient, verbal descriptions of stimulation induced phenomena, and microelectrode recording data obtained during exploration help the surgeon to mentally reconstruct the somatotopic organization contained within the target structure and to establish functional borders. Comparison of the patient functional organization with that contained in the literature allows estimation of probe tip position within the target and is used to plan subsequent trajectories until the ideal target loci are determined. targeting accuracy.

E. Electrophysiological Databases

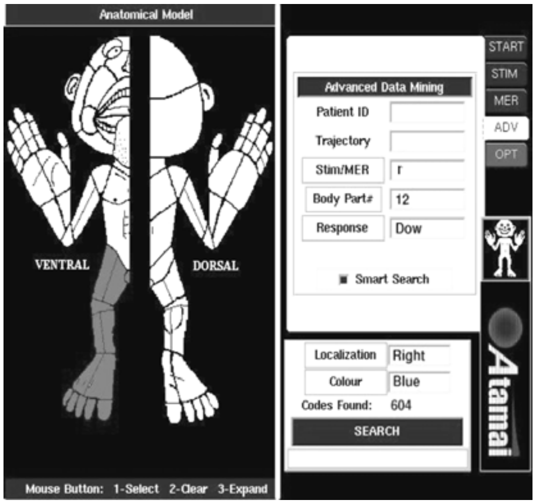
In attempts to increase the accuracy of approaching the surgical target, numerous authors have compiled and analyzed the functional information described above from subcortical structures of many individuals acquired during stereotaxy [5;6]. The electrophysiologic data may be standardized using alphanumeric codes and normalized to an anatomical atlas to create composite functional maps.

While current electrophysiological atlases provide an approximation of functional organization within some subcortical structures, they are of limited use as a source of surgical guidance. The poor clustering of population data results primarily from the inability of linear registration to accommodate inter-patient anatomical variability.

These limitations are addressed via a database of deep-brain electrophysiology containing functional data from multiple procedures on approximately 100 prior patients [7]. The anatomical variability between patients is accounted for using a nonlinear registration algorithm that non-rigidly registers the deep brain anatomy as observed in a patient MRI to that of the reference MRI, and enters the electrophysiological data into the reference MRI space using the resulting "warp" transform. This system also employs a comprehensive coding protocol for describing observed response, coupled to an interactive graphical user interface (GUI). In addition, the database is easily accessible through a flexible search engine that permits searches of varying specificity, and the search results may be displayed as autonomous three-dimensional objects or as cluster probability maps that can be nonlinearly registered to the MR images of individual patients.

II. SURGICAL PLANNING SYSTEM

A. Graphical User Interface



Patient ID:
Trajectory:
Stim/MER: r
Body Part#: 12
Response: Dow
Localization: Right
Colour: Blue
Codes Found: 604

Figure 3. Graphical user interface used to enter new data in patient image-space and searching database contents. The user may indicate the receptive/projected field for any response on the interactive homunculus model on the left. front surface of leg and foot shown selected here.

A key component of the electrophysiological database is its user interface that both facilitates the consistent entry of data from patients during surgical procedures, as well as the retrieval of any selected atlas data during a surgical procedure, for inclusion within the planning and/or guidance environment (Figure 3). By clicking onto a particular body part and entering a minimum of text, the recorded data are accurately tagged with respect to position and function. Similarly, when the database has been registered to an individual patient, retrieval of the necessary information is again achieved by indicating the body part(s) related to the nucleus in the brain being targeted, and all of the appropriate data points are immediately retrieved for display in the surgical planning workstation (Figure 4).

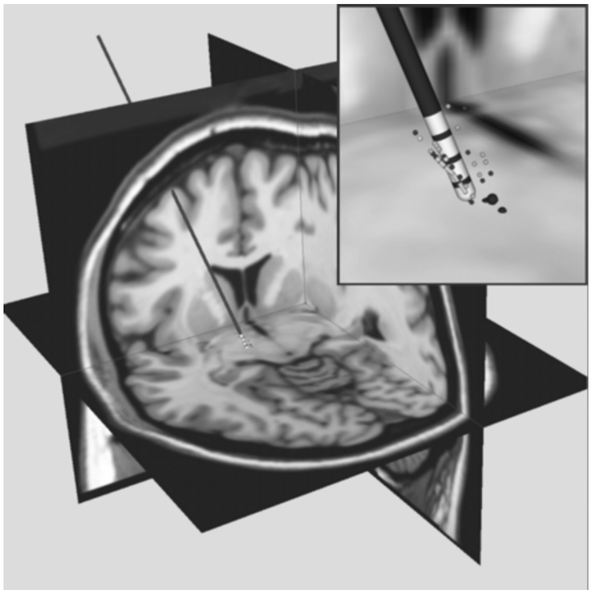


Figure 4. Brain MRI and model of deep brain stimulator with tip inserted into the deep brain *Inset:* Results of a search for functional data characteristic of those acquired during previous procedures related to the Sub-thalamic nucleus.

B. Apply Database to Patient

After a patient's MR image volume has been obtained, the reference MR image is non-rigidly registered to it, which at the same time registers the entire electrophysiology database to the new patient. Then, using the user interface (Figure 3), data from previous cases that are relevant to the current procedure may be recalled and placed within in the new patient's image (Figure 4). This procedure allows the surgeon to immediately determine where, in previous patients, EP data had been obtained. The non-rigid registration procedure allows this information to be immediately related to the new patient, informing the surgeon where best to make the initial exploratory measurement.

C. Planning and Navigating

This system can interactively display the 3D image volumes and 2D image planes of both an individual patient brain image and the standard brain template. Digitized versions of standard atlases (that have also been non-rigidly registered to the patient), along with any segmented anatomical landmarks, representations of instruments and other relevant information, may be incorporated into the display. The instrument coordinates (relative to the stereotactic frame) may be entered manually, or automatically if the instrument is tracked during the procedure. Under such image guidance, the surgeon may therefore place the exploratory or ablative probe (accessed via a small twist-drill hole in the skull), close to the desired target point within the deep brain. He of course does not rely solely on the information provided by the pre-operative data, but confirms the suitability of a particular target through confirmatory electrical stimulations (while observing the reaction of the patient), or through the recording of activity in response to tactile or motor stimulus of the patient. It should be noted that the patient is conscious throughout these procedures.

III. DISCUSSION

Previously, databases of electrophysiology integrated into stereotactic planning systems were restricted to a 2D displays and relied upon digitized atlases of anatomy to provide a common coordinate space. The work described here represents the first truly three-dimensional collection of subcortical electroanatomic observations that can be non-rigidly registered to a patient MRI.

When database contents are selectively displayed within this system, delineation of functional borders within otherwise homogeneously appearing anatomy is possible, somatotopic organization may be visualized, and areas of high probability for tremor activity can be identified.

The interactive GUI is a key element of this project. First, it facilitates rapid, detailed coding of patient data that will not impede the normal flow of the surgical procedure if used intra-operatively; it is sufficiently generic to allow expansion of the database to include other procedures and anatomy; and it vastly simplifies the integration of surgical data from multiple institutions. This system is now being employed in conjunction surgical procedures, and we have demonstrated that its use can allow targets to be rapidly localized and also dramatically reduce the number of exploratory pathways that must be used to determine the final site of the lesion.

This application focuses on neurosurgery. Nevertheless it illustrates the value of integrating pre-operative images, atlases, and functional data into an image-guide surgery environment Similar approaches, along with dynamic image modeling, will become increasingly important in the development of minimally-invasive image-guided surgery and therapy.

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