Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Assistance to Planning in Deep Brain Stimulation: Data Fusion Method for Locating Anatomical Targets in MRI

Alice Villéger*, Lemlih Ouchchane*†, Jean-Jacques Lemaire*†, and Jean-Yves Boire*‡
*ERIM, ESPRI/INSERM, Medicine Faculty of Clermont-Ferrand, Auvergne University, France
Email: alice.villeger@u-clermont1.fr
†Biostatistics Unit, University Hospital of Clermont-Ferrand, France
‡Service of Neurosurgery A, University Hospital of Clermont-Ferrand, France

***Abstract*— Symptoms of Parkinson's disease can be relieved through Deep Brain Stimulation. This neurosurgical technique relies on high precision positioning of electrodes in specific areas of the basal ganglia and the thalamus. In order to identify these anatomical targets, which are located deep within the brain, we developed a semi-automated method of image analysis, based on data fusion. Information provided by both anatomical magnetic resonance images and expert knowledge is managed in a common possibilistic frame, using a fuzzy logic approach. More specifically, a graph-based *virtual atlas* modeling theoretical anatomical knowledge is matched to the image data from each patient, through a research algorithm (or *strategy*) which simultaneously computes an estimation of the location of every structures, thus assisting the neurosurgeon in defining the optimal target. The method was tested on 10 images, with promising results. Location and segmentation results were statistically assessed, opening perspectives for enhancements.**

I. INTRODUCTION

Deep brain stimulation (DBS) is a neurosurgical technique which alleviates movement disorders and is mainly used to treat severe idiopathic Parkinson's disease[1]. It is performed under stereotactic conditions (*i.e.* with a stereotactic frame fixed to the skull) and consists in the implantation of two electrodes (one per hemisphere) into an anatomical target. The electrodes are connected to a neuro-pacemaker placed at the trunk. Various anatomical structures, located in the general area of the central grey nuclei, can be targeted: *e.g.* the subthalamic nucleus (STN), the globus pallidus internus (GPi) and the ventral intermediate nucleus of the thalamus (Vim). The exact location of the optimal target remains unknown, as the biological mechanisms involved in DBS have yet to be fully understood.

Beyond the clinical aspects, the implantation technique itself is still a matter of debate. Two main methods are proposed to define a surgical target. The classical stereotactic approach, historically based on ventriculography and stereotactic atlas [2][3], uses a proportional indirect method, *i.e.* the coordinates of the target are computed relatively to internal landmarks (AC/PC). A more recent approach, called direct targeting, relies on magnetic resonance imaging (MRI), which allows the direct visualization of the target[4].

The clinical protocol routinely applied in our institution is based on direct targeting[5]. The pre-implantation phase starts with the acquisition of tridimensional anatomical data under stereotactic conditions: namely, T_2 weighted MRI sequences resulting in three orthogonal anisotropic images. Using anatomical databases[2][3][6][7] as a reference, the neurosurgeon carries out a visual analysis of the images, in order to estimate the location of anatomical structures of interest, *i.e.* the stereotactic target and its surroundings. The manual labeling of the central grey nuclei area allows to determine an optimal implantation trajectory for the DBS electrodes. At implantation stage, the stereotactic system is used as a fixed referential to insert the electrodes and reach the previously computed coordinates. Since surgery is performed under local anesthesia, the positioning of each electrode along the insertion axis can be optimized according to the clinical effects noticed during acute stimulation tests.

The manual labeling step required at pre-operative stage is relatively time consuming, demands a high level of expertise, and raises reproducibility issues. In order to assist the practitioner in defining an optimal trajectory, we proposed to design a computer process for image analysis, able to automate the extraction of areas of interest (*i.e.* relevant anatomical structures such as the stereotactic targets and their neighbourhood) from MRI. We focused on the STN as this target, which is the reference in DBS for Parkinson's disease, is also difficult to identify due to its small size and its complex anatomical surroundings.

II. METHOD

A. General framework

Recognition of brain structures in MRI can be achieved through a data fusion method based on fuzzy logic, where every sources of information (*i.e.* patient data and expert knowledge) are modelized in the same possibilistic frame. Indeed, fuzzy sets and the possibility theory framework appear suitable to account for the inter-individual variability observed in living tissues and anatomical structures. Particularly, encouraging preliminary results were obtained for the segmentation of the subthalamic nuclei[8].

A fuzzy membership map is an image mapping every voxel to a membership degree $\mu \in [0, 1]$, which quantifies how much the voxel belongs to a particular fuzzy set. Fuzzy tissue maps are extracted from the patient's MRI through a clustering step. Prior expert knowledge on the spatial relationships (*e.g.* relative distance or direction) between anatomical structures of interest can also be expressed through fuzzy membership maps.

1-4244-0033-3/06/$20.00 ©2006 IEEE.

The complementary fuzzy maps are then fused, by means of suitable possibilistic operators, in order to achieve a segmentation of the targeted structures. The fusion process relies on the definition of a research route, or *scenario*: a predetermined list of intermediate landmarks, linked by spatial relationships, which are to be segmented successively in order to reach the target.

This method requires the expert to devise a specific single route for each potential target. Furthermore, each intermediate structure has to be segmented accurately: otherwise, errors would be propagated along the research route, down to the final structure. Consequently, additional processings ensuring shape constraints (*e.g.* region growing, fuzzy shape maps, or edge detection) have to be introduced systematically, in order to refine the segmentation obtained by simply fusing the spatial relationships and tissue maps.

B. Toward a global research scheme

It appeared to us the fusion process could instead be guided entirely by a "virtual atlas", *i.e.* a model formalizing expert knowledge by describing every structure in relation to the others within a graph. The use of a relational graph to modelize prior anatomical knowledge has been suggested in other recent works, through either global or progressive approaches[9].

The global approach consists in matching a relational graph, extracted from an anatomical atlas, with a similar graph, extracted from previously segmented patient data. However, the over-segmentation of those images results in a difficult problem of inexact graph-matching. The progressive approach is based on a graph model containing both iconic (*i.e.* extracted from a digital atlas) and symbolic (*i.e.* expressed through linguistic descriptors) knowledge. Yet the associated recognition method still relies on a sequential research route which has to be predefined specifically for each targeted structure.

Instead of relying on predefined research sequences (or *scenario*), we aimed to design a recognition process (or *strategy*) leading to the simultaneous exploration of several research paths, resulting in the progressive segmentation of every structure defined in the model. While a research scenario depends on its target, such strategy, guided solely by prior expert knowledge, depends on the nature of the information contained in the graph-based model.

C. Graph-based model for prior expert knowledge

The expert model is based on a graph, *i.e.* a list of vertices linked by edges. Each vertex represents an anatomical structure of interest and contains relevant information such as tissue composition. Each edge represents a spatial relationship between two structures, such as their relative directions. This generic model leaves much freedom concerning the exact nature of the data it contains: it is possible to add complementary types of information to both the vertices (*e.g.* morphology) or the edges (*e.g.* distance). A specific kind of information such as directions can also be represented relatively to points, or to whole objects, through various models.

These modeling choices partly depend on the available sources of information. Prior knowledge can be provided directly by the expert, expressing qualitative information by means of semantic descriptors (*e.g.* "above" or "anterior to"). Such formal descriptions are often imprecise and unexhaustive, but supposedly reliable and relevant. Conversely, precise quantitative information on every structures and relationships can be extracted from a set of pre-labeled images, but the relevance and statistical representativity of the data remains uncertain.

In our feasibility study, we chose to focus on reliable information which could be obtained either from the expert or from images: tissue composition and relative direction. Actually, direction is a complex information, involving angle and distance relationships, as well as the shape of the objects. We settled for a simple representation method requiring little prior knowledge, and taking little time to compute. Structures are assimilated to their center of gravity, and directional relationships between these single points are defined according to their projections along three orthogonal axis: "above/below", "anterior/posterior" and "left/right".

D. Research strategy

We designed a simple automated fusion algorithm which uses the information contained in the virtual atlas to guide the whole segmentation process. This particular method takes advantage of a specific property of our model: directional relationships between lined up points translate into partial order relations, allowing us to sort structures along each main axis.

The very first step consists in a tissue classification[10] of the patient's MRI. Each structure's membership map is then initialized with the fuzzy map of the tissue it belongs to. Throughout the whole process, these membership maps are used to estimate a structure's location by computing its center of gravity.

The next step of the algorithm consists in roughly separating structures belonging to the same tissue class. Spatial relationships are propagated from the most central structures toward the most outer ones, then back from the border toward the center.

The final step consists in an iterative refinement of that first solution, in order to ensure that every spatial constraint is respected: every relationship in the model is propagated iteratively until convergence toward a stable solution is achieved. The fuzzy membership map obtained for every structure can be interpreted as crisp segmentation results, once a defuzzification threshold (set to 0.5 by default) has been applied: membership degrees are set to 1 when above the threshold, and set to 0 when below.

Propagating a relationship from a S_1 structure toward a S_2 structure means redefining the membership map of the S_2 structure by fusing it with the directional map obtained from the S_1 structure. But there is no unique method for computing a fuzzy directional map, even from a single point.

TABLE I

STRUCTURES OF INTEREST

#	Structure	Tissue
1	Lateral Ventricle	CSF
2	Third Ventricle	CSF
3	Thalamus	GM
4	Caudate Nucleus	GM
5	Pyramidal Tract	WM
6	Lenticular Nucleus	GM
7	STN + Substentia Nigra	GM

We used a simple function projecting coordinates along the direction axis, then setting the membership degree to 1 when the directional constraint was respected (for instance, $y_1 > y_2$ when the models said "S_1 is above S_2"), or to 0 when it was not.

III. RESULTS

A. Test protocol

First preliminary tests were performed on simulated data, *i.e.* randomly generated 3D images on which structures were represented by spheres of various random radius. Right after the first step of the algorithm, each structure was already correctly identified: the computed center of gravity was located within the corresponding sphere, though small segmentation errors could occur in case of close structures.

More realistic tests were performed afterward on a sample of ten images from parkinsonian patients. The MRI sets were composed of $512\times512\times24$ voxels of $0.52\times0.52\times2\text{mm}^3$. An appropriate coronal slice containing the STN was selected for each patient and pre-labeled by the expert for further comparison. We used a 2D anatomical model containing seven structures of interest. Every structure was allocated to a specific tissue class among the three taken into account, *i.e.* cerebrospinal fluid (CSF), white matter (WM) and grey matter (GM). Direction relationships were defined based on directional invariants extracted from the pre-labeled images (table I and fig. 1) and validated by the expert.

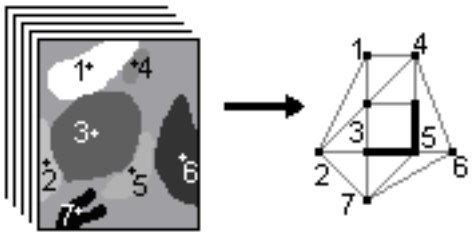

Fig. 1. Anatomical model

A rectangular Region of Interest (ROI) containing every structure defined in the model was defined manually in order to constrain the fusion algorithm to that particular region. This was the only non-automated step of the process. Preliminary tissue clustering was performed on each slice, resulting in four tissue maps: CSF, WM, GM and background. The first three tissue maps were then used to initialize the fusion algorithm. For each image, the final step of the fusion algorithm converged after two or three iterations. The whole process (tissue clustering and fusion algorithm) took about 30 seconds. Fig. 2 and 3 illustrate results obtained for one patient.

The expert assessed the location results as satisfactory. Every structure, except for the CN, was correctly located: when compared with the expert's labeled image, the computed center of gravity was always located within the corresponding structure. However, the membership maps contain holes and unconnected parts, and some of them tend to differ significantly from the expert's labeling: small structures such as the STN/SN group tend to be overestimated, at the expense of larger structures such as the thalamus, which seems underestimated.

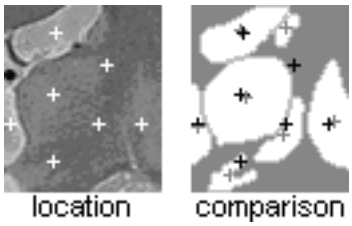

Fig. 2. Location results

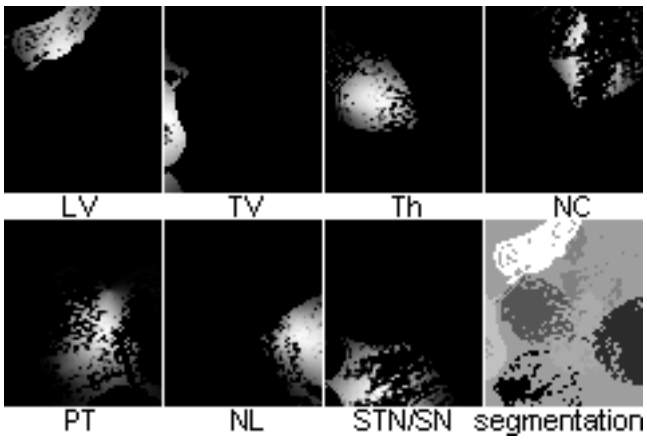

Fig. 3. Segmentation results

B. Statistical analysis

For every structure, over the ten patients, results have been statistically analysed in term of location and segmentation, by comparing them with the results obtained with the reference method, *i.e.* expert labeling. Location results (the coordinates of the center of gravity) were assessed using intraclass correlation coefficients (ICC) between the computed values and the reference values, while segmentation results were assessed using the Tanimoto coefficient[11]:

$$TC(S_{result}, S_{reference}) = \frac{|S_{result} \cap S_{reference}|}{|S_{result} \cup S_{reference}|}$$

The impact of the defuzzification threshold has also been studied.

The statistical analysis confirmed our first visual estimations. The ICC, with an average value of 89%, showed almost perfect concordance for the location of most structures (usually above 90%, sometimes 80%), the only notable exception being the abscissa of the caudate nucleus (54%). On the other hand, the TC, with an average value of 35%, emphasized the mediocre overall quality of the segmentation, which would differ greatly among structures (from 13% for the caudate nuclei to 65% for the lateral ventricule).

Our tests also revealed some structures exhibited significantly different reactions to the setting of the threshold parameter. Two groups could be distinguished: the LV, Thalamus, LN, and PT (or "large structures"), on the one hand, and the TV, CN, and STN/SN (or "small structures"), on the other hand. The large structures reacted favorably to a very low threshold value, while the small structures required a higher one.

IV. DISCUSSION AND PERSPECTIVES

The statistical concordance of the location results is encouraging, especially considering the mediocre quality of the segmentation itself: it proves the structures do not have to be perfectly segmented in order to be properly located. The inaccuracies observed in the segmentation are not surprising: holes and unconnected parts were to be expected since the model did not define any morphologic constraints. Nevertheless, naturally connected structures belonging to the same tissue class, such as the lateral ventricle and the third ventricle, could still be correctly set apart. This result demonstrates that directional relationships alone can be powerful tools, when used concurrently, for guiding the identification and segmentation of anatomical structures. In order to refine the initial segmentation, the current results may be used to initialize a method of competitive region growing or edge detection. Preliminary tests involving connected component labeling have already shown promising results.

Errors in the segmentation seem mostly due to a size difference between the various structures. As the simple model used in this preliminary study represents structures by their center of gravity, with no complementary information on their relative size, all the resulting segmented structures tend to be roughly of the same size. Consequently, large structures are often underestimated while small structure are overestimated. This is why we chose to consider the subthalamic nucleus and substantia nigra (which are both relatively small, and very close) as a single structure. This result emphasizes the need for a multiscale approach. The scale of the model could be adjusted to take into account different layers of details: a set of small neighboring structures could be gathered to define a super-vertex, while a single huge structure could be split into several sub-vertices. The resulting inclusion relationships between these new vertices could be expressed quite easily by simply adding corresponding inclusion edges to the graph. The inclusion edges would form a tree between the various layers of detail, resulting in a multiscale atlas. Of course the whole process would have to be adjusted to factor in the various scales. For instance, the fusion algorithm could be used successively for each layer.

The method should also be evaluated on real 3D images. Actually, preliminary tests have already been performed, showing results similar to those observed on the 2D ROI, but which could not be formally assessed as the expert had not yet labelized the area. Moreover, the low depth resolution of the images used in the clinical protocol is a source of imprecision in the location along the z axis. This is why we are currently working on a process for fusing the complementary information provided by the three complementary perpendicular anisotropic images, into a single isotropic image.

Concerning the future clinical validation of the process, we obtained a high-resolution *post mortem* MRI (4.7 Tesla) from a histologic slice[7]. This data will be used as a reference for evaluating segmentation results computed from a standard MRI acquired from the same individual. The neurosurgical department of our institution has also granted us access to a large database of patients who have already been treated through DBS and can be studied *a posteriori*.

Once perfected and validated, our method should relieve the physician from the time-consuming process of manual labeling, providing him with useful assistance for the positioning of electrodes. By precisely identifying the optimal area for DBS, it could lead to a better understanding of the clinical phenomena involved. In the long run, the approach might also be extended to guide robotic surgery.

REFERENCES

[1] B. L. Walter and J. L. Vitek, Surgical treatment for Parkinsons disease, *Lancet Neurol.*, vol. 3, 2004, pp. 719-728

[2] J. Talairach, M. David, P. Tournoux, H. Corredor and T. Kvasina, *Atlas d'anatomie stéréotaxique*, Masson et Cie, Paris; 1957

[3] G. Schaltenbrand and P. Bailey, *Introduction to stereotaxis with an atlas of the human brain*, Volume II, Georg Thieme Verlag, New York, NY, Stuttgart; 1959

[4] J.-J. Lemaire, F. Durif, J.-Y. Boire, B. Debilly, B. Irthum and J. Chazal, "Direct Stereotactic MRI Location in the Globus Pallidus for Chronic Stimulation in Parkinson's Disease", *in Acta Neurochirurgica*, vol. 141, 1999, pp. 759-766

[5] F. Caire, P. Derost, J. Coste, J.-M. Bonny, and F. Durif, E. Frenoux, A. Villéger and J.-J. Lemaire, Stimulation sous-thalamique dans la maladie de Parkinson sévre : étude de la localisation des contacts effectifs, *Neurochirurgie*, 2005

[6] A. Parent, "Basal ganglia", *in Carpenter's human neuroanatomy*, Williams and Wilkins, Baltimore; 1996

[7] J.-J. Lemaire, F. Caire, J.-M. Bonny, J.L. Kemeny, A. Villéger, J. Chazal, "Contribution of 4.7 Tesla MRI in the analysis of the MRI anatomy of the human subthalamic area", *in Acta Neurochirurgica*, vol. 8, 2004, pp. 906-907

[8] V. Barra, J.-J. Lemaire, F. Durif and J.-Y. Boire, "Segmentation of the subthalamic nucleus in MR images using information fusion a preliminary study for a computer-aided surgery of Parkinsons disease", *in MICCAI*, 2001

[9] I. Bloch, O. Colliot, O. Camara and T. Géraud, Fusion of spatial relationships for guiding recognition, example of brain structure recognition in 3D MRI, *Pattern Recognition Letters*, vol. 26, 2005, pp. 449-457

[10] V. Barra and J.-Y. Boire, Tissue Characterization on MR images of the Brain by Possibilistic Clustering on a 3D Wavelet Representation, *Journal of Magnetic Resonance Imaging*, vol. 11, 2000, pp. 267–278

[11] T.T. Tanimoto, *IBM Internal Report*, 1957