Feature-segmentation-based registration for fast and accurate deep brain stimulation targeting

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Abstract. *Objects* Deep brain stimulation (DBS) has turned out to be the surgical technique of choice for the treatment of movement disorders, e.g. Parkinson's disease (PD), the usual target being the subthalamic nucleus (STN). The targeting of such a small structure is crucial for the outcome of the surgery. Unfortunately the STN is in general not easily distinguishable in common medical images. *Material and Methods* Eight bilaterally implanted PD patients were considered (16 STNs). A three-dimensional MR T1-weighted sequence and inversion recovery T2-weighted coronal slices were acquired pre-operatively. We study the influence on the STN location of several surrounding structures through a proposed methodology for the construction of a ground truth and an original validation scheme that allows evaluating performances of different targeting methods. *Results* The inter-expert variability in identifying the STN location is 1.61 ± 0.29 mm and 1.40 ± 0.38 mm for expert 1 and 2 respectively while the best choice of features using segmentation-based registration gives an error of 1.55 ± 0.73 mm. *Conclusions* By registering a binary mask of the third and lateral ventricles of the patient with its corresponding binary mask of the atlas we obtain a fast, automatic and accurate pre-operative targeting comparable to the expert's variability.

Keywords: deep brain stimulation; Parkinson's disease; surgical planning; validation; non-rigid registration; neurosurgery; magnetic resonance imaging

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1. Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus has revealed to be the most effective surgical technique for the treatment of Parkinson's disease (PD) [1]. An accurate pre-operative targeting is a crucial step that influences directly and critically the operating time and, most important, the outcome of the surgery. Unluckily, the STN is not easily targeted because in general it is not clearly distinguishable in common medical imaging modalities. In our state-of-the-art protocol, a typical DBS surgery procedure begins by fixing the stereotactic head frame to the patient's skull, which is used as a coordinate reference system. Next, two kind of images are acquired: MR T1- and MR T2-weighted. The STN targeting is performed on a coronal T2-weighted image acquired perpendicularly to the AC-PC axis and crossing the anterior limit of the Red Nucleus. Although the STN target selection depends on each institution, common methodologies are the use of stereotactic brain atlases [2] and the use of visible surrounding anatomical landmarks [3]. Then, the target coordinates are reported onto the T1 image space where the trajectories are planned. A small hole is drilled into the patient's skull and the electrode is introduced until the pre-operative STN target is reached. This location is only an estimation of the real STN location. Therefore, the surgeons have to adjust the electrode intra-operatively using electrophysiological recordings and from macro stimulation tests. This process can take a lot of time and is painful for the patient whose head frame is attached to the operating table during the surgery.

Taking as starting point previous work [4] [5] we were able to construct a ground truth for the STN location. Then, using the proposed validation scheme, different registration methods can be compared between them and with the experts' ability.

This paper focuses on answering the following main questions: Which feature-structures influence the most the STN location through a registration process? The use of this/these structures alone produces an accurate estimation of the STN target? How well the structures-based registration performs compared to whole-brain non-rigid registration algorithms and atlas-based methods? Is there any subset of structures that produces an error in estimating the STN location comparable to the experts' variability when targeting clearly visible STNs? We demonstrate that such feature-structures exist and that this choice produces an estimation of the target that is more accurate than the estimation produced by the best whole-brain registration algorithm under study. The proposed scheme is easy to implement and it can be fully automatic providing a valuable tool for fast and accurate pre-operative target estimation.

2. Material and Methods

In this study a set of 39 bilaterally implanted parkinsonian patients were considered (78 STNs). Two kinds of images were acquired pre-operatively for each patient: 3D T1-weighted MPRAGE MRI sequence (Siemens Vision®, 1.5T, Erlangen, Germany) TR 9.7 ms, TE 4 ms, number of slices/slice thickness: 164/1.40 mm, FOV 280x280, matrix 256x256, pixel size 1.09x1.09 mm and few coronal slices of an IR T2-weighted, TR 2,560 ms, TE 4 ms, number of slices/slice thickness: 7/3 mm, FOV 300x300, matrix 512x512, pixel size 0.59x0.59 mm.

Taking profit from the fact that in some specific patients the STN is visible in MR T2-weighted images a ground truth is constructed following the protocol described in [5]. Finally 8 patients with clearly visible STNs were selected to take part in this study. Amongst the 8 selected patients, the experts have selected the one with the most clearly visible STN as a reference subject, both for the right and left sides.

The following registration methods have been tested through the validation scheme proposed in [4][5] using the whole MR T1-weighted images: *AC-PC Atlas-based targeting*: This method locates the STN following the Schaltenbrand-Wahren atlas [2].

Affine registration: A 12 degrees of freedom (translation, rotation, scaling and shearing) algorithm based on the work of Maes et al. [6]. *Demons algorithm*: It is an independent implementation of the intensity-based algorithm developed by Thirion [7]. *B-splines algorithm*: It is a mutual-information-based free-form deformation algorithm similar to the method proposed by Rueckert [8].

In this work the structures that surround the STN have been considered. We have chosen 4 easy-segmentable structures: lateral (right and left) ventricles, third ventricle and interpeduncular cistern, we denote L, T and C respectively (see figure 1).

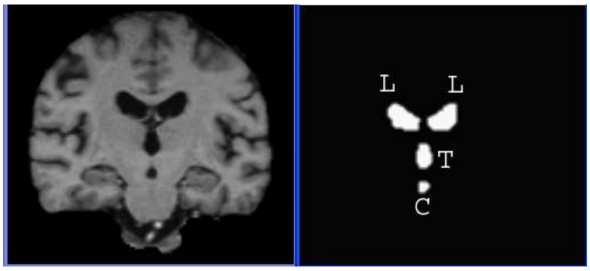

Fig. 1. Segmented structures used for feature-based registration: lateral ventricles (L), third ventricle (T) and interpeduncular cistern (C) (coronal view).

The segmentation has been done using a semi-automatic thresholding method but can be easily transformed in fully automatic using shape a priori knowledge [9]. In this case each segmented structure or a subset of them (binary mask) of the atlas is registered with the corresponding binary mask of all the patients using a tandem of affine-demons non-rigid registration. First an affine registration using whole-brain images is performed to cope with global misalignment (as for the above B-splines or demons methods). Then, demons registration is applied between the binary masks of the structures considered both for the atlas and the patient under study. By registering a binary mask that is located in a small region of interest compared to the whole brain, the registration process is speeded up hugely.

3. Results

The intra-expert variability computed as the Euclidean distance from each expert targeting to the centroid of the cloud of targeted points for a given STN is (mean and unbiased standard deviation): 1.06 ± 0.61 mm and 0.80 ± 0.52 mm for expert 1 and 2 respectively, showing a high expert repeatability. The estimation errors have been computed as the Euclidean distance from the estimated target given by each method to the ground truth. The inter-expert variability has been computed as the Euclidean distance from the expert targeting to the ground truth. The statistics, mean and unbiased standard deviation, of the errors committed when applying each of the methods and the expert variability are shown in table 1 (ordered by decreasing mean error).

Table 1
Statistics of the estimation errors committed with whole-image registration, atlas-based method, segmented-structures-based registration and inter-expert variability.

Methods, Features and Experts	Mean ± Std (in mm)
Affine	2.42 ± 0.84
C	2.00 ± 0.72
AC-PC	1.96 ± 0.90
T	1.80 ± 0.69
Demons	1.77 ± 0.65
T-C	1.74 ± 0.71
B-Splines	1.72 ± 0.48
L	1.70 ± 0.80
L-C	1.67 ± 0.72
Expert 1	1.61 ± 0.29
L-T	1.58 ± 0.71
L-T-C	1.55 ± 0.73
Expert 2	1.40 ± 0.38

In order to compare the results, a one-way analysis of variance (ANOVA) statistical test of the hypothesis that the errors and the expert variability come from distributions with equal means has been performed at a 5% significance level. In figure 3, a statistical box plot generated by this test is shown as well as the result of a multi-comparison test of the means. We can see from this statistical test all-at-the-same-time, that if we use the segmented lateral and third ventricles, we obtain a mean error that is statistically different from the affine registration method while it is not statistically different from the experts. In figure 5 we show the coronal, axial and sagital projections of each estimated STN (in red) onto the reference subject (in black) using a L-T segmentation-based method.

4. Discussion and Conclusions

Many important conclusions can be extracted from this study. Amongst the non-rigid registration methods applied to the whole brain and the atlas-based targeting, the B-splines algorithm has shown an extremely good performance. Nevertheless, the use of segmented structures has revealed the possibility of improving this performance. Specifically, the registration of a binary mask of the lateral and third ventricles produces estimation errors that are statistically different from an affine registration but comparable to the expert's ability. From the statistical tests we can reject the use of the interpeduncular cistern with the lateral and third ventricles given that the results do not improve significantly. The fact of using these structures allows us to register only the region of interest, resulting in faster algorithms but at the same time providing an accurate targeting. On the other hand, the method can easily become fully automatic by including shape a priori knowledge in the segmentation step. Although the choice of the STN of reference can influence the results, we have tested the feature-segmentation-based method using a leave-one-out technique (all the patients are considered once as the reference) and the results, numerically and statistically, were similar.

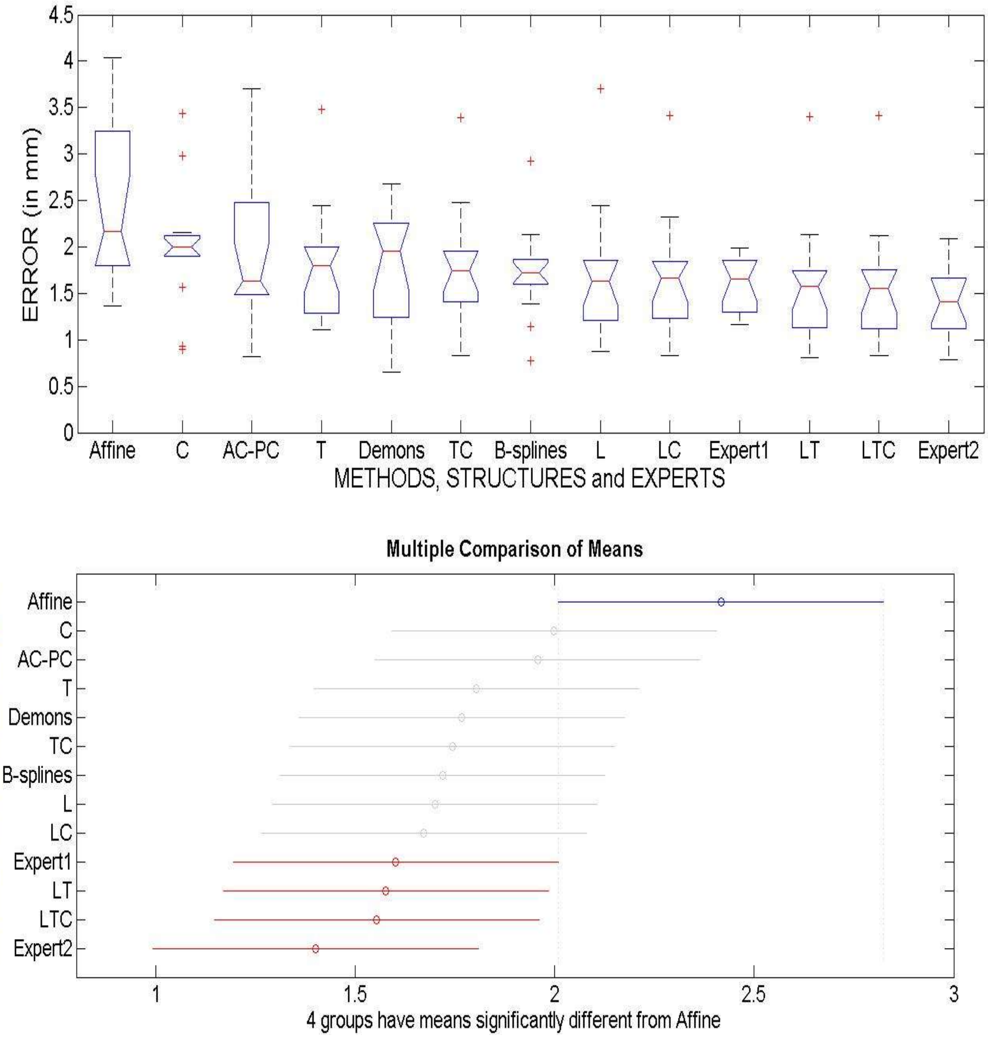

Fig. 3. Statistical tests of the errors committed using different atlas-based, segmentation-based and automatic registration algorithms versus expert's variability (using the *anova1* and *multcompare* functions of MATLAB®).

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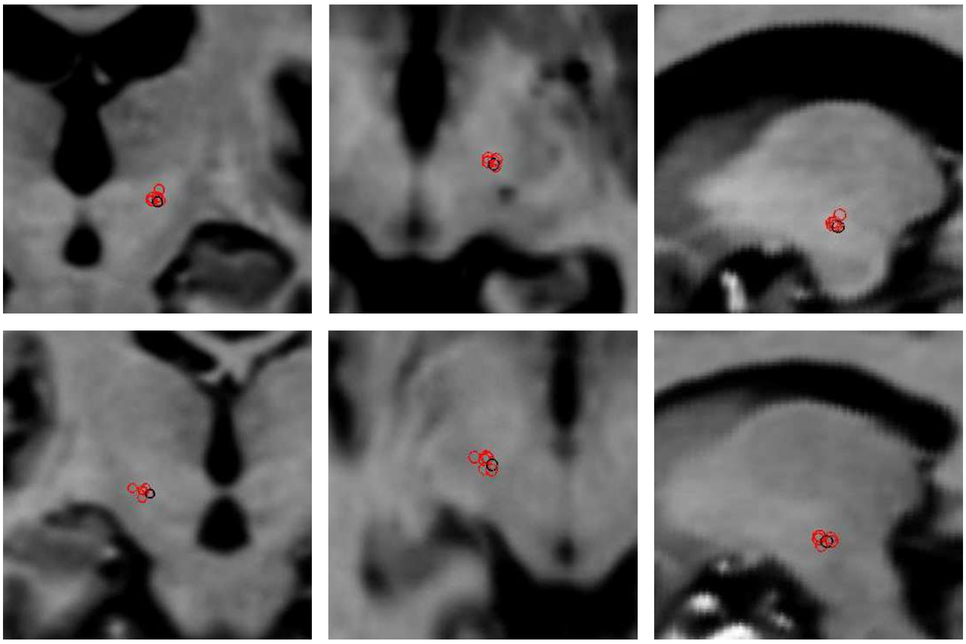

Fig. 4. STN estimation (in red) using a tandem of affine-demons registration of the segmented lateral and third ventricles. In black the atlas. Each point represented by a circle of radius 1 mm.

References

[1] A.L. Benabid, A. Koudsie, A. Benazzouz, et al.: Subthalamic stimulation for Parkinson's disease. Archives of Medical Research 31 (2000) 282-289

[2] G. Schaltenbrand, W. Wahren: Atlas for Stereotaxy of the Human Brain. 2 edn. Thieme (1977)

[3] C. Pollo, R. Meuli, P. Maeder, F. Vingerhoets, J. Ghika, J.-G. Villemure: Subthalamic nucleus deep brain stimulation for Parkinson's disease: Magnetic resonance imaging targeting using visible anatomical landmarks. In: Proceedings of the Meeting of the American Society for Stereotactic and Functional Surgery 80 (2003) 1-4

[4] F. J. Sanchez Castro, C. Pollo, O. Cuisenaire et al.: Validation of Experts versus Atlas-Based and Automatic Registration Methods for Subthalamic Nucleus Targeting on MRI. International Journal of Computer Assisted Radiology and Surgery, 2006 [In Press]

[5] F. J. Sanchez Castro, C. Pollo, R. Meuli et al.: Cross Validation of Experts versus Registration Methods for Target Localization in Deep Brain Stimulation. Proc. of the 8th Int. Conference in Medical Image Computing and Computer-Assisted Intervention MICCAI, Palm Springs, USA. LNCS 3749 (2005) 417-424

[6] F. Maes, A. Collignon, D. Vandermeulen, G. Marchal, P. Suetens: Multimodality image registration by maximization of mutual information. IEEE Transactions on Medical Imaging 16 (1997) 187-198

[7] J.P. Thirion: Image matching as a diffusion process: an analogy with Maxwell's demons. Medical Image Analysis 2 (1998) 243-260

[8] D. Rueckert, L.I. Sonoda, C. Hayes, D.L.G. Hill, M.O. Leach, D.J. Hawkes: Nonrigid registration using free-form deformations: Application to breast MR images. IEEE Transactions on Medical Imaging 18 (1999) 712-721

[9] X. Bresson, P. Vandergheynst, J-Ph. Thiran: A Variational Model for Object Segmentation Using Boundary Information and Shape Prior Driven by the Mumford-Shah Functional. International Journal of Computer Vision, 2005, [In Press]