Segmentation of Brain Internal Structures Automatically Using Non-Rigid Registration with Simultaneous Intensity and Geometric Match

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Abstract

Segmentation of the brain internal structures is an important and a challenging task due to their small size, partial volume effects, and anatomical variability. In this paper we propose a method that segments automatically the deep brain internal structures from brain MRI images. It uses a combination of local affine transformation and optical flow based non-rigid registration, which has the advantages of modifying the larger geometric deformation and intensity differences simultaneously. Meanwhile the residual subtle differences decrease due to the high degree of freedom. Both simulated data and real data are used to validate the proposed method and the results are encouraging. It can be concluded that the image gray level of the corresponding structures plays an important role in registration based segmentation using intensity metric.

***Key words**: Non-rigid registration; Brain structures segmentation; MRI*

1. Introduction

In recent years, the analysis of anatomical structures from medical images develops rapidly [1-3] due to the widespread research on brain functions and brain disorders. Brain internal structures play a central role in the intellectual capabilities of the human brain. Additionally, these structures are also relevant to a set of clinical conditions, such as Parkinson's and Creutzfeldt-Jakob diseases. However, segmenting these structures remains a challenging task due to their small size, partial volume effects, anatomical variability, and the lack of clearly defined edges [4]. Concerning about the reliability and the flexibility, manual delineation is still the main choice in clinical medicine at present despite the fact that many fully automatic and semiautomatic segmentation methods have been proposed in the literatures [2, 5-14]. However the large amount of data to be analyzed makes manual analysis of these images impractical. Moreover manual segmentation is prone to errors associated with inter-observer and intro-observer variability. Therefore it is necessary to find accurate automatic segmentation methods close to manual delineation.

A variety of computer-assisted methods has been studied to automatically segment brain internal structures [5]. We can cite deformable models or active contour evolution based methods [6-9, 13], which can be good solutions to the problem because of their abilities to capture the information of the shapes or structures of interest. However the initialization of these methods prior to deformation remains difficult. Another crucial technology is image registration [1, 2, 10-12]. These methods rely on a reference image volume in which structures of interest have been carefully segmented by experts. To segment a new image volume, a transformation that registers the reference volume to the target volume is computed, which gives a spatial correspondence between the two image volumes. Then regions labeled in the reference volume can be projected onto the volume of interest. The key of this approach is to design a method being capable of computing the transformation in a reliable and accurate way. These methods take advantage of the prior knowledge, which is explicitly provided by the atlas (segmented reference volume), such as structure shape, relative positions between the structures. This allows helping the segmentation of the anatomical structures without clearly defined contours.

The adopted method in this paper, Demons registration [15], belongs to intensity based non-rigid

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registration algorithm. It has high ability to model local deformation and has been used in medical image registration [15-18] successfully. However the requirements of intensity correspondence and small initial deformation between homologous structures put some limitations on it. In general global rigid or affine transformation and simple histogram match were often used to solve the problem [1, 19-22], but they were not ideal solutions. Therefore, we propose to implement the preprocess using a local affine transformation methods, which has the advantages of modifying the larger geometric deformation and intensity differences simultaneously [23]. Then the Demons registration with higher degree of freedom is used to cope with the residual subtle differences.

2. Methods

The designed model of the local affine transformation to get the intensity match and the rough spatial match is

$$\begin{aligned} & m_7 f(x, y, t) + m_8 \\ & = f(m_1 x + m_2 y + m_5, m_3 x + m_4 y + m_6, t-1) \end{aligned} \tag{1}$$

Where the position parameters $m_i, i = 1, \cdots, 6$ reflect the spatial deformation, the brightness and contrast parameters m_7, m_8 reflect the intensity variation between the two images, and a temporal parameter t is used to distinguish the two images. The model parameters will be acquired after the error function

$$E(\overline{\boldsymbol{m}}) = \sum_{x,y \in \omega} [k - \vec{\boldsymbol{c}}^T \vec{\boldsymbol{m}}]^2$$

is minimized.

($k = f_t - f + x f_x + y f_y$, $\vec{\boldsymbol{c}} = [x f_x \; y f_x \; x f_y \; y f_y \; f_x \; f_y \; f \; -1]^T$, ω denotes a small spatial neighborhood).

After preprocess, a rough match is acquired. Then subtle differences are corrected using the Demons registration algorithm. The main idea of the Demons registration algorithm is to consider the non-rigid registration as a diffusion process. Although the behavior of the Demons can be designed in different ways, implementation method based on the optical flow theory is used for most medical image analysis. The assumption in optical flow field is intensity preservation in image moving process, that is

$$I(x(t), y(t), t) = \text{const} \tag{2}$$

Differentiating I with respect t results in a velocity vector

$$\vec{\boldsymbol{v}} = \frac{(m-s)\nabla s}{\| \nabla s \|^2 + (m-s)^2} \tag{3}$$

Where $(m-s)^2$ is an added term to keep the stability. When $\vec{\boldsymbol{v}}$ is obtained, the atlas can be registered to the input image. More details about the local affine registration algorithm and the Demons algorithm can be found in [23] and [15].

The two assumptions of the Demons registration algorithm using optical equation are as follows: small deformation and intensity conservation between the reference image and the floating image. However it is hard to satisfy the assumptions in real image registration, especially in atlas-based registration, because the brain morphology and the intensities of any input image will be different comparing to the reference image. Fortunately the adopted local affine transformation is more effective to deal with larger deformation and can modify simultaneously the geometric shape and brightness/contrast differences despite its limited ability in registering subtle deformation due to the necessary size of the sub-regions. It shows that it is reasonable to combine the two registration algorithm to complete the segmentation task. After local affine transformation with adaptively intensity correction, the shape differences and the intensity variations between the reference image and the floating image will be small enough to satisfy the assumption of Demons algorithm. This enables the Demons registration algorithm more effectively to deal with subtle local differences.

3. Experiments and Results

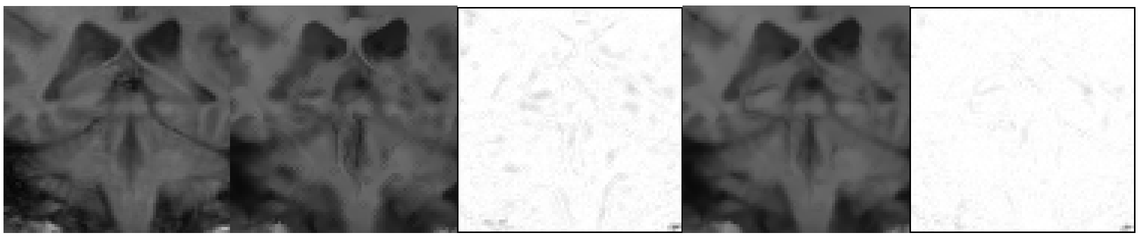
3.1. Materials

The reference image used in the experiment is the one from the Surgical Planning Laboratory of Harvard Medical School [24]. It consists of 256×256×160 voxels with a spatial resolution of 0.9375mm×0.9375mm×1.5 mm. The test images were imaged with 1.5T GE scanner, and Axial 3D IR T1-weighted (TI/TR/TE: 600/10/2) acquired using a fast gradient echo with inversion recovery sequence. Each dataset (volume) consists of 256×256×124 voxels, and the resolution of each voxel is 0.9375mm×0.9375mm×1.5 mm. Both larger intensity difference between the reference image and the test image due to different scan equipment and the individual morphology differences between subjects can be observed, that makes the registration difficult.

Two experiments were carried out to get the quantitative assessment of the performance of the segmentation method. The first was synthetic deformation experiment, in which the SPL [24] standard reference image and the corresponding atlas were deformed using an analytic harmonic deformation approach [25]. Then the reference image was registered to the deformed image to get the deformation field. Finally the acquired segmentation result using the deformation field was compared with the real segmentation, the deformed atlas. Ten volumes were used in this experiment. The second experiment consists of a performance comparison between the automatic segmentation and expert segmentation using ten real data.

3.2. Results

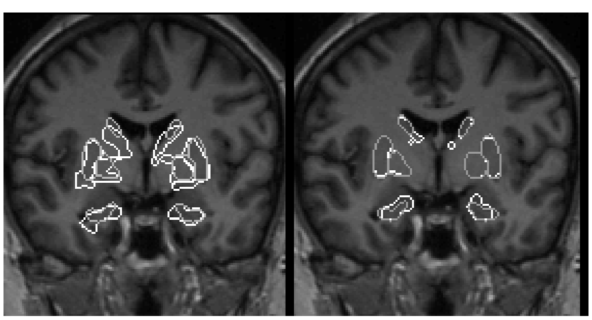
3.2.1. Visual inspection and comparison. Figure 1 shows the registration performances before and after correcting subtle local differences using Demons registration. It can be seen that the difference is larger when only using local elastic registration (Figure 1(c)). After subtle local difference correction using Demons registration, the difference decreases.



(a) (b) (c) (d) (e)

Fig. 1. Comparison of the pure local elastic registration and the proposed method. (a) Internal region of reference image. (b) Result of local elastic registration. (c)Differences between (a) and (b). (d) Result of the proposed method. (e) Differences between (a) and (d).

Figure 2 shows a comparison between the Demons algorithm with global affine transform and histogram match and the Demons algorithm with the proposed preprocess method. Visual inspection of the segmentation results was performed by comparing "gold standard (gray)" and automatic (white) segmentation on caudate, putamen, pallidus and hippocampus. It can be clearly seen that better segmentation results are obtained with the proposed method.



(a) (b)

Fig. 2. Comparison of "gold standard (gray)" and automatic (white) segmentation on caudate, putamen, pallidus and hippocampus (a) using Demons algorithm with global affine transform and histogram match (b) using Demons algorithm with the proposed preprocess method.

3.2.2. Quantitative evaluation.

validation criteria. To validate the results quantitatively, the criteria widely used in atlas-based segmentation [1-3, 13, 16], a kappa statistic based similarity index (KI) is adopted in this paper. The KI value measures the overlap ratio between the segmented structure and the ground truth, which is defined as $\mathrm{KI}=2\mathrm{TP}/(2\mathrm{TP}+\mathrm{FN}+\mathrm{FP})$. The definitions of the parameters are as follows: $\mathrm{TP} = G \cap E$ is the number of true positive; $\mathrm{FP} = \overline{G} \cap E$ is the number of false positive and $\mathrm{FN} = G \cap \overline{E}$ is the number of false negative. Where G is the ground truth segmentation of a given structure, E is the estimated segmentation of the same structure, and $\overline{A}$ denotes the complement of a set A.

validation using synthetic deformation. It is hard to obtain real MRI images of the human brain with known segmentation results of the internal structures. Therefore, a quantitative assessment of the performance of the segmentation method requires the use of simulated data with known segmentation as the gold standard. The synthetic images came from the deformed SPL reference image, which was deformed using an analytic harmonic deformation approach [25].

Table 1 shows the segmentation results on simulated data. It can be seen that there were great differences in cross correlation between the deformed images and the original reference image by the synthetic deformation. However the mean KI ± *standard deviation* for the four structures for ten cases was 0.9902 ± 0.0085 which was perfect results regardless how low the cross correlation was before registration between the reference image and the floating image. It showed that high registration quality could lead to high segmentation results.

validation with expert delineation. Although validation with simulated data is a common method for its known segmentation, it is not sufficient to validate the approach. One drawback is that the deformation is not representative of the real inter-subject variability, and the other is that it doesn't consider the noise and artifact in real MRI images. So additional testing with real data must also be completed to demonstrate the ability of the algorithm to work under real-world conditions. For this reason, several real MRI datasets from different subjects were also used to test the performance of the approach. Table 2 shows the segmentation result using real brain MRI data. For caudate, the best overlap ratio was 0.8186 and the worst was 0.6686, and the mean±standard deviation was 0.7656±0.0517 for ten cases. For putamen, the best overlap ratio was 0.8606 and the worst was 0.4981, and the mean±standard deviation was 0.7065 ±0.0873. And for hippocampus, the best overlap ratio was 0.8636 and the worst was 0.6592, and the mean± standard deviation was 0.7749±0.0564. Comparison to the three structures, segmentation result for the pallidus was not very well. The reason may be due to its small size, which is easy to be influenced by the noise and artifact.

Table 1. Segmentation results on simulated data

cross correlation		KI							
		Caudate		Putamen		Pallidus		Hippocampus	
before	*after*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*
0.5700	1	0.9800	0.9697	0.9868	0.9809	0.9756	0.9688	0.9762	0.9756
0.6339	1	0.9735	0.9806	0.9912	0.982	0.9968	0.9933	0.9922	0.995
0.6583	1	0.9830	0.9789	0.9960	0.9803	0.9913	0.9966	0.9941	0.9928
0.7173	1	0.9734	0.9732	0.9873	0.9849	0.9778	0.996	0.9867	0.9871
0.7499	1	0.9898	0.9823	0.9886	0.9878	0.9863	0.9885	0.9902	0.9875
0.7573	1	0.9801	0.9925	0.9944	0.9865	0.9924	0.9955	0.9889	0.9921
0.8238	1	0.9924	0.989	0.9923	0.9894	0.9928	0.9921	0.9965	1
0.9421	1	0.9895	0.9963	0.981	1	1	1	1	1
0.9555	1	1	0.9925	1	0.992	1	1	1	1
0.9738	1	1	1	1	0.9974	1	1	1	1

Table 2. Segmentation results on real data

cross correlation		KI							
		Caudate		Putamen		Pallidus		Hippocampus	
before	*after*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*
0.6248	0.979	0.8186	0.6988	0.7251	0.695	0.5354	0.3981	0.8636	0.7410
0.6128	0.967	0.7244	0.8046	0.7447	0.8606	0.4889	0.2994	0.7351	0.7722
0.5987	0.98	0.8089	0.6686	0.6402	0.6596	0.3626	0.0244	0.8075	0.6592
0.6177	0.975	0.8164	0.7772	0.7216	0.824	0.3846	0.0092	0.8555	0.8207
0.6012	0.98	0.7893	0.6942	0.7433	0.4981	0.6627	0.1176	0.8155	0.7359
0.6278	0.979	0.8024	0.7413	0.6291	0.6759	0.2857	0.2431	0.7543	0.7807
0.6459	0.966	0.7181	0.7063	0.679	0.7614	0.314	0.0632	0.7502	0.6621
0.5887	0.982	0.7685	0.8173	0.6912	0.8376	0.25	0.2922	0.7630	0.8026
0.5816	0.978	0.8184	0.7114	0.7342	0.5534	0.3576	0.0153	0.8299	0.7427
0.5832	0.979	0.8139	0.8129	0.7444	0.7125	0.356	0.1705	0.8431	0.7639

4. Discussion

Two validation methods were used in this paper to evaluate the segmentation ability of the proposed non-rigid registration approach. The first was on the simulated data with known segmentation acquired from the synthetic deformation, while the second was on real data with the expert delineation. Each validation method show their advantages and disadvantages. Validation on simulated data makes it possible generate known reference segmentation, thus the accuracy of the estimated solution can be evaluated. However there exist two main drawbacks. One is that the deformation is not representative of the real inter-subject variability and the other is that it doesn't consider the noise and artifact in real MRI images. The second validation method is obviously in line with the actual situation. The main drawback of this validation is that the segmentation map, provided by an expert, cannot be considered as a perfect ground truth. So it can be seen that the first validation method has true reference segmentation but is not representative of the real situation, while the second validation method reflects the real situation but has no completely true reference segmentation. From the two experiment results, a phenomenon was also worthy of paying attention to. The segmentation result is very nice on simulated data in all cases and in all the four structures. While the segmentation result on real data is relatively not good enough on real data. It is possible that using expert segmentation as gold standard may have influence on the result, but it should not be the main reason. The actual reason should be due to the data differences. As it can be seen there are two main differences between the two data. One is that the deformation in simulated data couldn't reflect the real shape difference in different subjects while the real data could. However both the deformation are nonlinear, they should have the same characteristic. Thus it should not be the main reason. The other difference is that for simulated data, the homologous structures in reference image and floating image have the similar intensity. But for real data, these are not true because of the noise and interference introduced by the scanning procedure. This should be a serious problem for intensity based registration. The obtained better results using the proposed method have provided some evidences. Therefore, improving image quality and intensity correspondence of homologous structures should be a promising strategy for structure segmentation based on intensity based non-rigid registration.

5. Conclusion

A combination of local affine transformation and Demons free-form transformation is used to segment automatically the brain internal structures in this paper. The segmentation results on both the simulated data and the real data are encouraging. It indicates that the proposed method could be a solution for segmenting brain internal structures which lack clearly defined intensity boundaries from human MRI images. Compared to global affine transform and simple histogram match, the selected local affine transform with intensity correction simultaneously provide a better initial conditions to the Demons registration algorithm. Furthermore, the results on the simulated data are superior to that on the real data due to the nice intensity correspondence between the homologous structures. It can be concluded that the image gray level of the corresponding structures plays an important role in registration based segmentation using intensity metric.

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