30th Annual International IEEE EMBS Conference
Vancouver, British Columbia, Canada, August 20-24, 2008

Non-Rigid Registration Based Segmentation of Brain Subcortical Structures Using a Priori Knowledge

XiangBo Lin, Su Ruan, Frédéric Morain-Nicolier, TianShuang Qiu

Abstract—**Segmentation of the brain internal structures is an important and a challenging task due to their complex shapes, partial volume effects, low contrasts and anatomical variability between subjects. In this paper we propose a new non-rigid registration method that automatically segments the deep brain internal structures from brain MRI images. An atlas of the structures is used as a priori knowledge, which is modeled as a shape representation. By integrating the shape knowledge into a classical intensity based non-rigid registration algorithm, the proposed segmentation method allows to ameliorate the results in the case of low contrast on the boundaries of the structures. The shape model is based on distance representation obtained from the atlas. The segmentation of brain subcortical structures is performed on real MRI images and the obtained results are very encouraging.**

I. Introduction

In recent years, the analysis of anatomical structures and sub-structures from medical images develop rapidly [1], [2] 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 complex shapes, partial volume effects, anatomical variability, and the lack of clearly defined edges. 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 [1]-[8]. However the large amount of data to be analyzed makes manual analysis of these images impractical. Moreover manual segmentation requires a significant time investment and 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.

Manuscript received April 7, 2008. This work was supported in part by the National Natural Science Foundation of China (No.30170259, No.30570475, No. 60372081) and the Youth Foundation of Dalian University of Technology.

XiangBo Lin is with CReSTIC, IUT de Troyes, 9 Rue de Québec, 10026 Troyes CEDEX France and School of Electronic and Information Engineering, Dalian University of Technology, 116023, China. (e-mail: linxbo@dlut.edu.cn)

Su Ruan is with CReSTIC, IUT de Troyes, 9 Rue de Québec, 10026 Troyes CEDEX France (phone: (+33) 3 25 42 71 01, e-mail: su.ruan@univ-reims.fr).

Frédéric Morain-Nicolier is with CReSTIC, IUT de Troyes, 9 Rue de Québec, 10026 Troyes CEDEX France (phone : (+33) 3 25 42 71 01, e-mail: frederic.nicolier@univ-reims.fr).

Tianshuang Qiu is with School of Electronic and Information Engineering, Dalian University of Technology, 116023, China. (phone : (+86) 411 84709573, e-mail: qiutsh@dlut.edu.cn)

A variety of computer-assisted methods has been studied to automatically segment brain internal structures [3]-[9]. We can cite deformable models or active contour evolution based methods [4], [5], [7], 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], [6], [9]. These methods rely on a reference image volume with a corresponding atlas 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 atlas can be projected onto the volume of interest. The segmentation problem is reduced to a registration problem. 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, such as structure shape, relative positions between the structures. This allows helping the segmentation of the anatomical structures which are not clearly defined in the input images (fuzzy contours), such as the caudate nucleus and putamens.

In this paper, a new non-rigid registration method combining both image intensity and structure shape information is proposed to segment the brain MRI internal structures. The main contribution of the proposed method is that *a priori* shape knowledge provided by the atlas is integrated to the intensity based non-rigid registration algorithm efficiently, which makes the segmentation of subcortical structures more accurate and more robust.

II. Methods

A. Intensity Based Non-Rigid Registration

The registration problem can be described as finding an optimal spatial transformation $\boldsymbol{T}^*$ for matching the transformed image to the reference image. In general the optimal transformation is acquired by minimizing the overall cost function E :

$$T^* = \arg\min_{T\in\Gamma}\{E(T)\} = \arg\min_{T\in\Gamma}\{E_{dis}(B, A\circ T) + E_{reg}(T)\} \quad (1)$$

where A and B denote the reference image and the target image respectively. The set Γ is the space of admissible transformations. The first part of E is $E_{dis}(B, A\circ T)$ which denotes the data dissimilarity measure and the second part is $E_{reg}(T)$ which denotes the regularization term to penalize the undesirable transformations. Different features can be used to construct the dissimilarity measure among which the Sum of Squared Differences (SSD) is a simpler one. The formulation of such metric is

$$E_{dis}(B, A\circ T) = E_{SSD}^{intensity}(B, A\circ T) = \frac{1}{2}\| B - A\circ T \|^2 \quad (2)$$

The SSD forms the basis of the intensity-based image registration algorithms and the optimal solution can be obtained by classical optimization algorithms. Among many different intensity based non-rigid image registration algorithms, the Demons algorithm (using SSD metric) [10] and its variants [11]-[13] are proved to be one of the most efficient methods. Demons algorithm belongs to the non-parametric image registration, where a dense displacement vector field u is used to implement the spatial transformation by the iteration procedure $T \leftarrow T + u$. Based on optical flow theory, the displacement vector at each point p is

$$u(p) = -\frac{(A\circ T(p) - B(p))}{(A\circ T(p) - B(p))^2 + \|\nabla B(p)\|^2}\nabla B(p) \quad (3)$$

T is a free form deformation. In order to get a regular displacement field, the regularization term $E_{reg}(T)$ should be added. As is in [10], an ingenious method that alternates between computation of the displacement vector field and their regularization by a simple Gaussian smoothing is designed. So the cost function can be written as

$$E = E_{dis}(B, A\circ T) + E_{reg}(T) = E_{SSD}^{intensity}(B, A\circ T) + E_{reg}(T) \quad (4)$$

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. If the two objects to be matched do not overlap, the Demons algorithm is inefficient [10]. So a fast global registration and an image intensity match procedures should be performed before the Demons non-rigid registration. Here we firstly use the software SPM [14] to do the initialize registration.

B. Combined Intensity with Shape Non-Rigid Registration

It can be seen from the cost function of the Demons non-rigid registration algorithm that only image intensity information is used for matching under the constraint of a smooth deformation field. It is enough in some applications when the multi homologous objects in the two images don't have a large deformation. However it is insufficient in some situations. For example, if only a narrow gap exists between two objects with very similar intensities in the target image, and if one of the corresponding objects in the reference image overlaps with both the two target objects, a split problem will occur. Such situation is not a particular case and is common especially for brain deep gray structures. The final registration result might be good in visual inspection for such cases if we only see image intensities. However if we follow up the displacements of the pixels on the structures, the corresponding pixels after the transformation could not correctly represent the structures. Therefore some complementary information must be taken into account. An atlas of the structures superposed on the reference image, can provide *a priori* knowledge, as about the shapes of the structures, the relative positions between them, and so on. In common sense, homologous subcortical structures among normal subjects would have similar shapes. Therefore adding a shape similarity term in the cost function would be a reasonable strategy. To achieve the goals, an appropriate representation for the shapes of interest is important. Inspired by [15]-[17], we choose the distance transform to represent the shape of interest. The role of distance function in improving registration quality has been mentioned in other early work, such as [18], where a chamfer distance function was used for the improvement of sulcal-based registration.

Let $\Phi:\Omega\rightarrow R^+$ be a distance transform of a shape S, which defines a partition of the image domain Ω. Let ω denote the region that is enclosed by S, and $\Omega-\omega$ denote the background region, the shape representation will be

$$\Phi_S(p) = \begin{cases} 0, & p\in S \\ d(p,S), & p\in\omega \\ -d(p,S), & p\in\Omega-\omega \end{cases} \quad (5)$$

Where $d(p,S)$ refers to the minimum distance between any image point and the shape S. Here simple Euclidean distance is used as the distance metric.

This representation provides supplementary shape information related to the intensity image that can be conveniently used as a new similarity term. It can be easily proved that the gradient of the new shape distance map is continuous and the gradient vector is in the normal direction of the shape. The new added shape similarity term can be considered as

$$E_{SSD}^{shape}(\Phi_S(A), \Phi_S(A\circ T)) = \frac{1}{2}\|\Phi_S(A\circ T) - \Phi_S(A)\|^2 \quad (6)$$

Where $\Phi_S(A)$ is the shape representation of the structure in the atlas on the reference image A and $\Phi_S(A\circ T)$ is the shape representation of the corresponding structure in the deformed atlas after the transformation T. Under the constraint of the shape similarity term, the optimal transform would lead to the final segmented structure shape as closer as that in the atlas. Therefore the above overall cost function can be modified as

$$\begin{aligned} E &= E_{dis}(B, A\circ T) + E_{reg}(T) \\ &= E_{SSD}^{intensity}(B, A\circ T) + E_{SSD}^{shape}(\Phi_S(A), \Phi_S(A\circ T)) + E_{reg}(T) \end{aligned} \quad (7)$$

Like original Demons registration algorithm, the optimal solution can be obtained by the alternating strategy. First the displacement vector related to the intensity and the shape at the point p of interest is computed:

$$\boldsymbol{u}_{intensity}(\boldsymbol{p}) = -\frac{(A \circ \boldsymbol{T}(\boldsymbol{p}) - B(\boldsymbol{p}))}{(A \circ \boldsymbol{T}(\boldsymbol{p}) - B(\boldsymbol{p}))^2 + \|\nabla B(\boldsymbol{p})\|^2}\nabla B(\boldsymbol{p}) \tag{8}$$

$$\boldsymbol{u}_{shape}(\boldsymbol{p}) = -\frac{(\Phi_S(A \circ \boldsymbol{T}(\boldsymbol{p})) - \Phi_S(A(\boldsymbol{p})))}{(\Phi_S(A \circ \boldsymbol{T}(\boldsymbol{p})) - \Phi_S(A(\boldsymbol{p})))^2 + \|\nabla \Phi_S(A(\boldsymbol{p}))\|^2}\nabla \Phi_S(A(\boldsymbol{p}))$$

The combined displacement vector is:

$$\boldsymbol{u}(\boldsymbol{p}) = \alpha \boldsymbol{u}_{intensity}(\boldsymbol{p}) + \beta \boldsymbol{u}_{shape}(\boldsymbol{p}) \tag{9}$$

Here the parameters α and β are used to balance the contribution of the intensity metric and the shape metric.

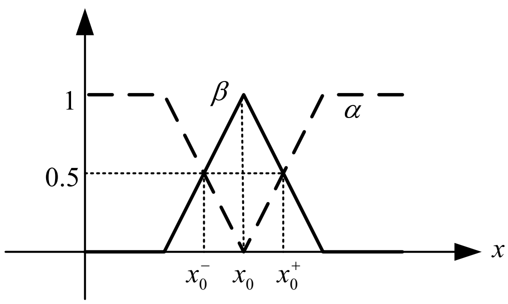

Fig. 1. The function of the balance parameters. The solid line denotes β function and the dotted line denotes α function.

A simple piecewise linear function is used to adaptively adjust the weights of the parameters, which are depicted in Fig. 1. The symbols used in Fig.1is as follows:

- x : The intensity I of the target image in the region of interest.
- $x_0 = mean(I_{structure})$: The average intensity of the structure region enclosed by the boundary of the deformed atlas structure.
- $x_0^- = x_0 - \lambda\sigma_{structure}$ and $x_0^+ = x_0 + \lambda\sigma_{structure}$: Key intensity value where the intensity metric and the shape metric have the same importance. Herein $\sigma_{structure}$ denotes the intensity standard deviation of the structure region enclosed by the boundary of the deformed atlas structure. λ is an empirical parameter to control the dynamic intensity range in which the shape metric is more or less important than the intensity metric according to the intensity value near to or far from the intensity mean x_0.
- β : Weight of the shape metric.
- α : Weight of the intensity metric, with $\alpha + \beta = 1$.

C. Summary of the Segmentation Framework Based on Non-Rigid Registration with the Prior Shape Knowledge

In summary, our overall segmentation framework based on the intensity based non- rigid registration with the *a priori* shape knowledge is as follows:

1. Given a reference image $\boldsymbol{A}$ with the superposed subcortical structures (the atlas) and the target image B, a histogram match and a global registration by SPM[14] is first carried out.
2. Perform the intensity based Demons non-rigid registration between the global transformed reference image $\boldsymbol{A}$ and the target image $\boldsymbol{B}$. A local match of the corresponding structures will be obtained after this step.
3. Perform independently the non-rigid registration combining both intensity and shape for each structure of interest to refine the structure match. Furthermore this refinement allows resolving the narrow gap problem existing between two objects with very similar intensities.
4. Transform the atlas using the obtained deformation fields from step1, 2 and 3. Then the final segmentation of the structures of interest has been acquired.

III. Experiments and Results

The reference image used in the experiment is the one from the Surgical Planning Laboratory of Harvard Medical School [19]. 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 the same as the reference.

The main contribution of the proposed non-rigid registration algorithm is that a simple shape similarity metric is integrated to the intensity based classic Demons registration algorithm. It overcomes the inference induced by the neighboring gray structures with similar intensities as much as possible by penalizing the shape dissimilarity between two homologous structures. It is to be noted that the combined intensity and shape non-rigid registration is performed only on structure of interest and the adjustment is carried out one structure after another. The transform of each structure should influence other regions as little as possible. Therefore a region of interest selection must be done before refinement. Because the target structures, the subcortical gray structures, are relatively very small and often are neighboring, we use the maximum distance value inside the shape as the threshold of the region of interest. Points that are farther away than the threshold point are not considered. The selection of the parameter λ is to be mentioned. It can be seen from the Fig.1 that the parameters. α and β vary with intensities of structures. Only parameter λ is constant and can be determined empirically. However its value is not arbitrary but is easy to find a convenient one. Because a good intensity match has been obtained after Demons registration, more weightiness should be given to the shape metric. So a larger parameter λ should be better. We set it to be 0.7 in our experiments for all structures.

The experiment results are depicted in Fig. 2. It can be seen from Fig. 2(d) that the segmentation of the left putamen is a local optimum (the part enclosed by a black circle). The left putamen is close to the cortex gray matter with a narrow white matter gap between them. They have similar intensities and at the meanwhile both of them partly overlap with the putamen in the reference image. There are more possibilities to stick into the local optimum if only intensity metric is used. Fig.2 (b) is an example of the shape representation based on Euclidean distance for the left putamen, where the distance map of the left atlas putamen is superimposed by its boundary. Fig.2 (e) is the distance map of the deformed putamen based on formula (3) superimposed by its boundary. It can be seen that the shape match between the left atlas putamen and its deformed version is not very good. Under the joint constrains of both the intensity and the shape with formula (9), the reference shape and the target shape will match as much as possible. Therefore, using the proposed method with the integrated shape metric, a better segmentation is obtained, which is showed in Fig. 2(f).

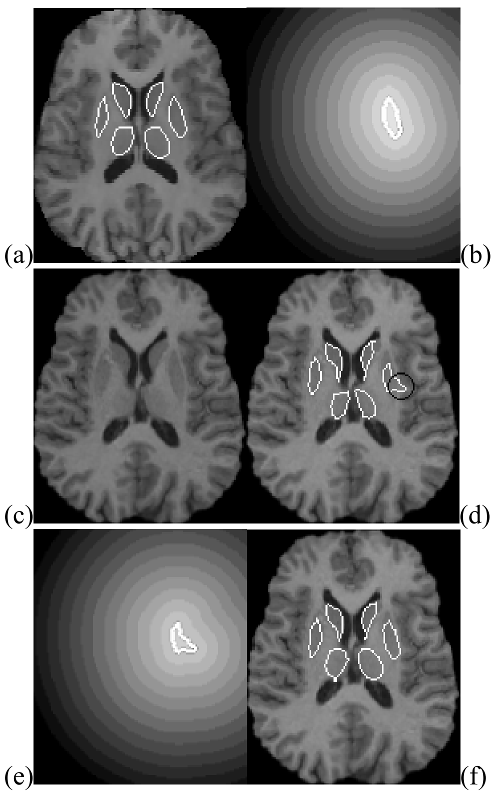

Fig.2 Segmentation results: comparison between Demons non-rigid registration and the proposed method. (a) the reference image superimposed by the atlas of subcortical structures (b) the shape representation of the left putamen in the atlas superposed by the structure's boundary (c) the target image (d) segmentation based on Demons non-rigid registration (e) the shape representation of the deformed left putamen superposed by the structure's boundary (f) the segmentation based on the proposed method.

IV. CONCLUSION

In this paper, a combined intensity and shape non-rigid registration algorithm is proposed. It is derived by integrating simple shape information into a classical intensity based non-rigid registration algorithm. The new added shape metric in the overall cost function provides a remedy to the common used SSD intensity metric. Furthermore it has a simple form, is easy to understand and fully automatic. The choice of the parameters is discussed and a solution is proposed. It is effective to prevent the solutions from local optimum in case of a narrow gap problem occurring or fuzzy boundaries. However, it should be noted that a drawback of the proposed method is its slow speed caused mainly by the re-iteration of the registration process for each structure at a time. Further research will be aimed on testing the algorithm on a large database, performing a more comprehensive evaluation of the proposed method and designing an effective range competitive strategy to adjust all the structures in one time.

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