Segmentation of Brain MRI with Fast and Efficient Registration Algorithm

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Abstract

Currently, one of the best approaches to segmentation of brain MR images into anatomical structures is registration (matching) of the input image with multiple atlases, images with manual segmentation. Final segmentation is obtained by fusing the transformed atlas segmentations. A label in each location is defined by weighted atlas voting. State-of-the-art label fusion algorithm allows getting maximum benefit from the whole atlas set, without choosing the optimal subset. It means that the more atlases are available, the higher is segmentation accuracy. In this case the time needed for registration of each atlas with the input image makes sense. In this work we propose to use a new landmark-based registration algorithm instead of widely used symmetric normalization. We compare segmentation results after both registration algorithms on real brain MR slices from the publicly available database. We demonstrate that the landmark-based registration algorithm, being much faster than symmetric normalization, allows providing comparable overall segmentation accuracy, and for more than a half of anatomical structures the accuracy is even better, especially for structures surrounded by landmarks.

Keywords: *Brain MRI Segmentation, Multi-Atlas Segmentation, Image Registration, Label Fusion*

1. INTRODUCTION

Segmentation of magnetic resonance images (MRI) of human brain into anatomical structures is extremely important and challenging problem. Manual segmentation of the whole brain volume into main structures may require more than a week of the expert's time. So automation of this procedure is really needed. Ideally, automatic algorithms should provide the accuracy comparable with inter-rater variability. If different algorithms demonstrate comparable accuracy, the speed makes sense.

Currently, the best algorithms for segmentation of brain MRI are based on registration, or matching with atlases [6]. An atlas is a pair of MR image and its expert segmentation. Images of different subjects, obtained with the same MRI protocol, look similar. Thus it is possible to find a transformation of one image to the other that approximately matches the images, compensating for global transformations and anatomical differences. Then one can transfer the transformed segmentation from the atlas to the input image in order to obtain the segmentation of the input image.

Recently, it was shown that segmentation based on registration with multiple atlases, demonstrates better accuracy than segmentation after registration with a single atlas [2,12,15]. When a set of MR images of different subjects along with their expert segmentations is available, one can perform a series of transformations of each of these atlases to the input image and obtain a set of potential segmentations of the input image. After that these segmentations can be fused by some algorithm and together give the final segmentation. Using multiple atlases is more reasonable than using a single atlas because it allows taking into account more anatomical variations.

For rough linear registration of images, that is usually done preliminary before more accurate non-linear registration, the FSL FLIRT tool [19] is widely used. As for non-linear registration, according to comparison studies [9,14] the best algorithm is Symmetric Normalization (SyN) [3]. However, it is rather computationally expensive which may be crucial in the case of registration with multiple atlases. Also, this algorithm does not allow to control the accuracy of registration for certain anatomical structures.

In this sense a group of feature-based registration algorithms can be useful. Registration in these algorithms does not seek the best correspondence between all the points of the two images. It just tries to find a transformation that matches a pre-defined set of landmarks, or key points, specifying the most distinguishable and critical anatomical locations. That makes these algorithms more fast and robust for certain anatomical structures. The landmarks can be set manually or detected automatically. Most of automatic algorithms require manually landmarked training bases [10,11]. However, the work [18] describes the approach that makes use of only one manually landmarked image, a template.

The best algorithms for label fusion after registration with multiple atlases perform weighted voting label fusion. It means that the contribution of each atlas to the final label in a certain location is proportional to local similarity of the atlas and the input image [13,17]. In some works the authors propose to use only the most similar atlases from the whole available set [4,16]. In [20] it was shown how to use the whole set of atlases with the maximum gain. The algorithm described in [20] is aimed at minimizing the correlating error of each pair of atlases. Atlas weights for the label fusion are computed in such a way that if both atlases probably propose a wrong label for the current point, their weights will be decreased. The atlases in [20] are registered to the input image by the algorithm SyN [3]. The authors provide segmentation results for one anatomical structure, hippocampus. The algorithm [20] was evaluated for the problem of whole brain segmentation in the work [21].

In this work we also consider whole brain segmentation problem into several dozens of anatomical structures. We try to obtain the best trade-off between speed and accuracy. Thus we propose to use fast landmark-based algorithm [18] for registration of the atlases to the input image, and the best label fusion algorithm [20] for obtaining the final segmentation of the input image. We compare segmentation results of the proposed framework and the similar framework where the algorithm SyN [3] is used for image registration, as it was done in [20]. Speed and accuracy results are presented.

2. METHODS

2.1 Symmetric Diffeomorphic Image Registration

Image registration algorithm [3] is based on a kind of transformation called *diffeomorphism*, differentiable map with differentiable inverse. Shortest paths between elements in the diffeomorphic space are called *geodesics*. The problem of registration of two images, I and J, is formulated in such a way that a geodesic, connecting these images, is required to be symmetric. It means that the path from I to J is the same as the path from J to I.

A diffeomorphism φ of domain Ω for transforming image I is defined by $\varphi I = I \circ \varphi(\mathbf{x}, t=1)$, where t is time and $\mathbf{x}$ is a spacial coordinate. $v(\mathbf{x}, t)$ is a velocity field on Ω, a square-integrable, continuous vector field. We can obtain the correspondence maps by integrating the velocity field:

$$\varphi(\mathbf{x}, t) = \varphi(\mathbf{x}, 0) + \int_0^1 v(\varphi(\mathbf{x}, t), t) dt \,. \tag{1}$$

A diffeomorphism can be split into two parts, φ_1 and φ_2, so that images I and J equally contribute to the path. Optimization problem then is defined as follows:

$$E_{sym}(I, J) = \inf_{\varphi_1} \inf_{\varphi_2} \int_{t=0}^{0.5} \left\{ \|v_1(\mathbf{x}, t)\|_L^2 + \|v_2(\mathbf{x}, t)\|_L^2 \right\} dt + \int_\Omega |I(\varphi_1(0.5)) - J(\varphi_2(0.5))|^2 d\Omega. \tag{2}$$

The second summand in (1) corresponds to cross-correlation metric between images, so the mapping is considered to be optimal when the cross-correlation metric is maximized. The problem is solved by Euler-Lagrange equations.

2.2 Landmark-Based Registration

The algorithm [18], in order to automatically place the landmarks on the images for further registration, requires one manually landmarked image, template T. Let $P^T = \{p_1^T, ..., p_n^T\}$ be a set of manually specified landmarks on T, where $p_i^T = (x, y), i = 1, ..., n$.

The image T along with its landmarks P^T is used for detection of landmarks on each of the images to be registered, I and J. Let's assume that there are two copies of T. First of all, each of the copies is transformed *linearly* in order to roughly match the image I(J). The landmarks' positions are transformed accordingly. Then each landmark p_i^I (p_i^J) on the image I(J) is searched in a square window of the size $2r+1 \times 2r+1$ around the point with the same coordinates as p_i^T . The search is performed only on the edges found by Canny edge detection algorithm [7]. The point $\mathbf{x}$ is considered to be a landmark corresponding to the landmark p_i^T if its SURF descriptor value [5] is the closest to the descriptor value of the landmark p_i^T :

$$p_i^I = \arg\min_{\mathbf{x}^I \in X_s} \left\| D(p_i^T) - D(\mathbf{x}^I) \right\| , \tag{3}$$

where X_s is a search domain.

Also, for correct registration, *quasi-landmarks*, the mid-points of the brain bounding box, are determined automatically both on the input images and the template.

After the set of landmarks is found on both images, I and J, the images can be registered non-linearly by finding such a transformation t of one image that minimizes the distances between corresponding landmarks on two images:

$$t(I) = \arg\min_t \sum_{i=1}^n \left\| p_i^I - p_i^J \right\| . \tag{4}$$

The authors of [18] use thin plate spline transformation [8].

2.3 Segmentation by Joint Label Fusion

The algorithm [20] performs weighted voting label fusion where the atlas weights are computed locally for each point. So, in order to define a label at point x one should compute the following weighted sum for each label $l \in L$:

$$\hat{S}_T^l = \sum_{i=1}^n w_i(x) \cdot S_l^i(x) \,, \tag{5}$$

where $w_i(x)$ is a weight of the i-th atlas at point x, $S_l^i(x)$ is equal to 1 if the i-th has the label l at point x, and 0 otherwise, and n is a number of atlases. Finally, the point x receives the label with the maximum value of (5).

For computation of the vector of weights $\mathbf{w}(x) = [w_1(x), ..., w_n(x)]$ pairwise atlas dependency matrix $M(x)$ is used. The matrix consists of $n \times n$ elements. The element $M_{ij}(x)$ estimates how likely both atlases i and j are to propose wrong labels at x.

$$M_{ij}(x) = p(\delta^i(x)\delta^j(x) = 1 \mid I_t, I_1, ..., I_n) \,, \tag{6}$$

where $\delta^i(x) = 1$ if the i-th atlas proposes the label that differs from the ground truth label at point x, and 0 if the proposed label is correct, I_t is the input (target) image and I_i is the image of the i-th atlas.

If we assume that the matrix M is already computed we can formulate the problem of finding the weights that minimize the expected error of the weighted voting as follows:

$$\mathbf{w}^*(x) = \arg\min_{\mathbf{w}(x)} \mathbf{w}^t(x) M(x) \mathbf{w}(x), \quad \sum_{i=1}^n \mathbf{w}_i(x) = 1. \tag{7}$$

The problem (7) has a closed-form solution:

$$\mathbf{w}(x) = \frac{M^{-1}(x) 1_n}{1_n^t M^{-1}(x) 1_n} \,, \tag{8}$$

where $1_n = [1; ...; 1]$.

The values of dependency matrix can be estimated according to local neighborhood of x. The more similar is local neighborhood of the input image and the i-th atlas, the more probably the i-th atlas will propose the correct label. If we consider a pair of atlases we obtain:

$$M_{ij}(x) = \left(\sum_{y \in N_r(x)} \left| I_t(y) - I_i(y) \right| \cdot \left| I_t(y) - I_j(y) \right| \right)^{\beta}, \tag{9}$$

where r is the radius of the local neighborhood and β is parameter.

3. RESULTS AND DISCUSSION

For evaluation we used 18 2D slices extracted from each of 18 real T1-weighted MRI volumes of Internet Brain Segmentation Repository (IBSR) [1]. Each slice has 256x256 image resolution. The volumes are manually labeled into several dozens of anatomical structures. We took the slices from the middle of each volume (slice number varies from 49 to 53 in the coronal plane) since they contain the largest subset of the anatomical structures.

For the registration algorithm [18] we used 12 landmarks, as in the original work (Figure 1).

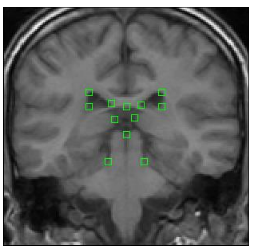

Figure 1: Manually landmarked template.

One of the images was chosen to be a manually landmarked template for detection of landmarks on other images, and therefore it was excluded from further evaluation. Cross-validation was performed on the rest 17 images. Two series of 17 experiments were performed where each of the images was considered to be an input image and the rest 16 images served as atlases. During the first series the algorithm SyN [3] was used for nonlinear registration of 16 atlases to the input image. During the second series the algorithm [18] was used for nonlinear registration. In both series the algorithm [20] was used for label fusion.

Dice score (DS) for each of the anatomical structures and overall Dice score are presented in Table 1.

№	Anatomical Structure	[18]/[3]	DS [18]	DS [3]
	DSC overall	7/10	0,93	0,94
2	Left-Cerebral-White-Matter	3/14	0,74	0,78
3	Left-Cerebral-Cortex	9/8	0,74	0,72
4	Left-Lateral-Ventricle	15/2	0,84	0,73
5	Left-Inf-Lat-Vent	3/0	0,03	0
7	Left-Cerebellum-White-Matter	5/10	0,67	0,70
8	Left-Cerebellum-Cortex	7/8	0,63	0,61
10	Left-Thalamus-Proper	10/7	0,83	0,83
14	3rd-Ventricle	4/0	0,09	0
15	4th-Ventricle	0/8	0	0,20
16	Brain-Stem	4/13	0,87	0,89
17	Left-Hippocampus	7/10	0,60	0,62
24	CSF	7/1	0,27	0,10
41	Right-Cerebral-White-Matter	2/15	0,73	0,78
42	Right-Cerebral-Cortex	8/9	0,75	0,73
43	Right-Lateral-Ventricle	13/4	0,83	0,78
46	Right-Cerebellum-White-Matter	9/5	0,68	0,59
47	Right-Cerebellum-Cortex	6/8	0,63	0,60
49	Right-Thalamus-Proper	11/6	0,84	0,81
53	Right-Hippocampus	10/7	0,58	0,50

Table 2: Evaluation results. First column: the number of the anatomical structure in IBSR. Third column: the number of images on which the algorithm [18] ([3]) showed higher DS for the certain structure. The last two columns: average DS for 17 images.

Linear registration that was performed for each pair of images before nonlinear registration [3] or [18] took ~0,6 s. Registration algorithm [18] was evaluated on PC with Intel Core i5-2410M (2.3 GHz), 4 GB RAM and took ~1,7 s for one pair of images, 0,86 s of which is detection of landmarks and the rest time is thin plate spline transformation. Registration algorithm SyN [3] was evaluated on PC with Intel Core i5-4670 (3.4 GHz), 8GB RAM and took about 13 s for one pair of images. Label fusion algorithm was evaluated on the same PC as SyN and took ~5 s for each of 17 images.

The results examples are presented in Figure 2.

Figure 2: Results example: ground truth; SyN; landmark-based.

So it can be seen that segmentation using registration algorithm [18], being several times faster than segmentation using SyN [3], demonstrates comparable results. In 7 of 17 images the overall DS of segmentation with [18] is higher. For 12 of 20 structures DS with [18] is higher. The superiority of [18] is the most obvious for the structures surrounded by landmarks, such as left and right ventricles (#4 and #43). Also, it can be noticed that the algorithm [18] allows partly capturing structures with a very small presence on the particular slice, such as #5 and #14, while SyN averages them out.

4. CONCLUSION

In this work we explored the problem of brain segmentation by registration with multiple atlases. For registration we proposed to use a fast landmark-based algorithm. We provided comparison of segmentation results using this registration algorithm and the widely used registration algorithm SyN. In both cases we used state-of-the-art label fusion algorithm for combining of segmentations from all the atlases. Although segmentation after registration with the algorithm SyN demonstrates slightly better overall performance than after registration with a new landmark-based registration algorithm, it works much slower and shows worse results for more than a half of anatomical structures. It was shown how landmarks can help to control the registration process and provide much better segmentation accuracy for structures surrounded by them. The landmark-based registration algorithm works many times faster because it does not spend time on finding a dense correspondence between all the pixels of two images, such as SyN. Therefore, it can be concluded that at least in the case of 2D images the landmark-based algorithm can be a good choice for registration of atlases to the input image, especially when segmentation accuracy for certain structures is much more critical than for other structures. Future directions include more sophisticated segmentation algorithms and other types of medical images.

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