ITERATIVE MULTI-ATLAS BASED SEGMENTATION WITH MULTI-CHANNEL IMAGE REGISTRATION AND JACKKNIFE CONTEXT MODEL

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ABSTRACT

For medical image segmentation, multi-atlas based segmentation methods have attracted great attention recently. Within the multi-atlas segmentation framework, labels of all atlases are propagated to the target image by means of image registration and then fused to achieve segmentation of the target image. While most multi-atlas based segmentation methods focus on developing effective label fusion strategies, few of them make an effort to improve the accuracy of image registration between atlas and target images. Inspired by the idea that the estimated segmentation of the target image can be used to refine the pairwise registration performance, we propose an iterative strategy to improve registration accuracy between the atlas and target images using a multi-channel registration approach. In addition, an overfitting-resistant discriminative learning procedure, referred to as Jackknife Context Model (JCM), is adopted at each iteration to improve accuracy and robustness of label fusion results. Validation experiments on hippocampal segmentation have demonstrated that our method can statistically significantly improve the performance of the state-of-art multi-atlas based methods.

Index Terms— hippocampal segmentation, multi-atlas based segmentation, multi-channel registration, context model

1. INTRODUCTION

Accurate subcortical structure segmentation of the human brain from magnetic resonance (MR) images is important for basic and clinical research of the brain. Manual delineations performed by trained experts were regarded as gold standard traditionally. However, this procedure is time consuming and practically unrealistic for studies with a large number of images. Furthermore, the reproducibility of manual segmentation is relatively poor due to inter-and intra-operator variability. Therefore, it is highly desirable to develop accurate and robust automated segmentation methods.

In medical image segmentation, multi-atlas based strategy has attracted great attention due to its promising performance. Given a set of atlases, pairwise registration is first performed to register each atlas image to the target image space so that its associated atlas label can be propagated to the target image space, and then all the propagated atlas labels are fused to generate segmentation result of the target image. Most existing studies have been focusing on improving label fusion by optimizing the weights for atlas labels, such as majority voting [1, 2], performance based voting [3, 4], local weighted voting [5, 6], and regression based voting [7, 8].

Image registration plays a very important role in multi-atlas based segmentation and its performance hinges on image quality, anatomical variability and the adopted registration algorithm itself. Since improved registration between each atlas and target image will subsequently improve the segmentation performance, we propose an iterative multi-channel image registration strategy to simultaneously improve the registration and segmentation performance. Specifically, we adopt a two-channel registration method with one channel driven by appearance similarity between atlas image and target image while the other channel driven by similarity between atlas label and the estimated target image's label which is computed iteratively. Furthermore, to reduce the computation burden introduced by image registration, an intermediate template space is introduced similar to [9].

To further improve the multi-atlas based segmentation performance, at each iteration of our algorithm a learning based error correction procedure is employed [10, 11]. The philosophy behind this strategy is that the performance of multi-atlas based segmentation methods can be further improved by an error correction classifier which is applied to the multi-atlas based segmentation result. To make the learning based error correction resistant to overfitting, a novel jackknife procedure is used to build an ensemble classifier on atlases, referred to as Jackknife Context Model (JCM). The contributions of this paper can be summarized as:

1) A multi-channel image registration strategy is used to directly improve the registration accuracy.

* Data used in the preparation of this article were obtained from the ADNI database.

2) An overfitting-resistant discriminative learning procedure is designed to reduce systematic segmentation errors.
3) Experimental results demonstrate that the proposed method is statistically significantly better than the state-of-art multi-atlas based methods.

2. METHODS

2.1. Overview

Given a target image to be segmented T^{img} and n atlases $S_1 = \left(S_1^{img}, S_1^{lab}\right), \ldots, S_n = \left(S_n^{img}, S_n^{lab}\right)$, where S_i^{img} is the ith atlas image and S_i^{lab} is its associated label, the multi-atlas based segmentation algorithm typically consists of following steps, as illustrated in the dash line box of Fig. 1. First, based on appearance similarity of the atlas and target images, an image registration algorithm is adopted to estimate n deformation fields $\{U_i, \mathrm{i} = 1, \ldots, \mathrm{n}\}$ which are used to propagate the atlas label information to the target image space; and then a segmentation result T^{lab} of the target image is obtained by fusing n propagated labels $\{S_i^{lab} \circ U_i, i = 1, \ldots, n\}$.

Since the segmentation performance hinges on the propagated label information, improved image registration will certainly improve the segmentation performance. To improve the registration between the target image and each atlas, shape information might be helpful to increase the registration robustness and accuracy. In addition, A recent study has demonstrated that systematic segmentation error of automatic algorithms can be reduced by a learning based error correction procedure [10]. Such a procedure might be helpful in the multi-atlas based image segmentation.

Based on above considerations, an improved multi-atlas based image segmentation algorithm is proposed, consisting of three iterative steps as illustrated in Fig. 1.

1. Given an intermediate segmentation result $\hat{T}^{lab-ec}$ of the target image T^{img} generated by error correction, the deformation fields $\{\hat{U}_i, i = 1, \ldots, n\}$ are computed using a fast multi-channel **pairwise registration** strategy in which the image registration is driven by an appearance similarity term and a shape similarity term. The first term is defined by image similarity between the atlas and target images, while the second term is defined by similarity between the atlas label and the intermediate segmentation result $\hat{T}^{lab}$. At the first iteration, the image registration is performed based on image appearance similarity.
2. The label information of atlases is transferred to the target image space based on the computed deformation fields $\{\hat{U}_i, i = 1, \ldots, n\}$. The generated propagated labels $\{S_i^{lab} \circ \hat{U}_i, i = 1, \ldots, n\}$ are then fused using a selected **label fusion** strategy to compute a segmentation result $\hat{T}^{lab-lf}$ of the target image T^{img}.
3. Using the segmentation result $\hat{T}^{lab-lf}$ estimated in step 2 as context information, an error correction strategy is used to further improve the results by an overfitting-resistant discriminative learning method, referred as to as Jackknife Context Model (JCM). Particularly, an ensemble classifier built on atlas information is used to perform the error correction.

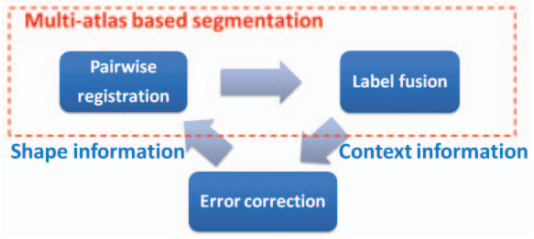


Fig.1. Diagram showing the framework of our proposed method.

2.2. Fast multi-channel pairwise registration

The pairwise registration procedure is illustrated by the flow chart in Fig. 2. Given a target image T^{img}, its intermediate segmentation result $\hat{T}^{lab-ec}$ produced by the error correction step and n atlases $S_i, i = 1 \ldots N$, the ith atlas is registered to the target image space by minimizing

$$E(U_i) = w_1 CC\left(T^{img}, S_i^{img} \circ U_i\right) + w_2 \left\| \hat{T}^{lab-ec} - S_i^{lab} \circ U_i \right\|^2 + Reg(U_i), \quad (1)$$

where U_i is the deformation field, the first term measures the cross correlation of image intensities between the target image and the transformed atlas image, the second term measures the similarity between the intermediate segmentation result and the transformed atlas label, w_i weights the two terms, and $Reg(U_i)$ is a regularization term to make the deformation field to be diffeomorphic. The two channel image registration is performed using the Multivariate Symmetric Normalization (MVSyN) algorithm implemented in ANTS [12].

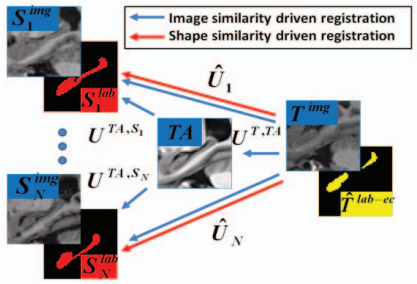


Fig.2. Schematic diagram of image registration, showing the deformations between target, intermediate template and atlas images in the multi-channel pairwise registration.

To reduce the computation burden of image registration, an intermediate template TA is introduced to provide initialization for the computation of deformation fields. The

template *TA* is generated from the atlases using a groupwise registration strategy, and the deformation field U^{TA,S_i} from the template *TA* to each atlas S_i is pre-computed. Given a target image, the deformation field $U^{T,TA}$ between the template *TA* and target image *T* is computed first, and then the deformation field $\widehat{U}_i$ is initialized by concatenating U^{TA,S_i} with $U^{T,TA}$.

2.3. Label fusion

The purpose of label fusion is to estimate label $\hat{T}^{lab-lf}$ of the target image by fusing propagated atlas labels $\{S_i^{lab} \circ \widehat{U}_i, i = 1 \dots n\}$. For similarity, we donate $\bar{S}_i^{lab}$ and $\bar{S}_i^{img}$ as the *i*th atlas's label and image which have been transformed to the target image space using $\widehat{U}_i$. Applying a fusion strategy to the propagated atlases' labels, we can get a segmentation probability map of the target image. It is worth noting that any label fusion strategy can be adopted in our method. Specifically, two strategies, namely majority voting [1] and local weighted label fusion [5], are used in this paper to demonstrate the proposed method's performance. Majority voting is used as the baseline method, while local weighted label fusion has been demonstrated effective [5, 6].

2.4. Error correction using Jackknife Context Model

To improve the segmentation result of label fusion at each iteration, an ensemble error correction classifier is built on available atlases using a jackknife procedure to achieve overfitting resistance. Given *n* atlases, the ensemble classifier is built by three steps, as summarized in Algorithm. 1.

Step 1. The multi-atlas based segmentation algorithm is applied to each of the atlas image with the remaining *n*-1 atlases used as atlas information, generating *n* segmented atlas images from which image features will be extracted to build the error correction classifier.

Step 2. Instead of training a single error correction classifier based on all atlas information [10, 11], *n* classifiers are trained by putting one atlas aside and using the remaining atlases as training data. A total of 2000 features are extracted for both image and fusion based segmentation result of each atlas, including intensity, gradients, curvatures, and various Haar filter based features. Using atlases' labels as the classification information, we utilize the Adaboost with decision stumps as weak learners to train classifiers. These *n* classifiers are subsequently combined using an average strategy to generate an ensemble classifier.

Step 3. Once the error correction classifier is built, we apply it to the target image and its fusion based segmentation result. It is worth noting that at the first iteration, as no estimated segmentation result is available for the atlases and target image, only the image similarity is used to drive the registration. The algorithm is iterated until the segmentation result remaining stable.

Algorithm 1: Jackknife Context Model(JCM)

Input: The target image T^{img}, its associated fusion based segmentation $\hat{T}^{lab-lf(t)}$, *n* atlases used as training data $S_i = (S_i^{img}, S_i^{lab}), i = 1 \dots n$, and their estimated segmentations $\{S_i^{lab-ec(t-1)}\}, i = 1 \dots n$ which are computed at last iteration *t-1*.

Step 1

- **For each of the training data $S_i, i = 1 \dots n$**
  1) *n-1* deformation field $\{U_i^{j(t)}, j \in 1 \dots n, j \neq i\}$ is computed using multi-channel pair-wise registration (Eqn. 1) by treating all other data $\{S_j | j \in 1 \dots n, j \neq i\}$ as atlases. At the first iteration, as no estimated segmentation of S_i is available, only the image similarity is used to drive the registration.
  2) Propagate *n-1* atlases' label information to the space of S_i and fuse them to generate segmentation result $S_i^{lab-lf(t)}$ using the selected fusion strategy described in subsection 2.3.
- **End for**

Step 2

- **For each of the training data $S_i, i = 1 \dots n$**
  1) Using all the other data $\{S_j | j \in 1 \dots N, j \neq i\}$ as training subjects, a total of 2000 features are extracted for both image and fusion based segmentation result of each subject, including intensity, gradients, curvatures, and various Haar filter based features. The subjects' labels are treated as the classification information
  2) Adaboost with decision stumps as weak learners is used to train a classifier H_i. Each classifier H_i contains 500 weak classifiers.
  3) Compute segmentation S_i^{lab-ec} for subject S_i by applying H_i.
- **End for**
- An ensemble classifier $H = \frac{1}{N}\sum_{i=1}^{N} H_i$ is generated by an averaging strategy.

Step 3

- Error correction based segmentation $\hat{T}^{lab-ec(t)}$ of the target image is generated by applying *H* to the image and its fusion based segmentation result.

Output: One error correction based segmentation $\hat{T}^{lab-ec(t)}$ of the target image and segmentations $\{S_i^{lab-ec(t-1)}\}, i = 1 \dots n$ of the atlases for next iteration.

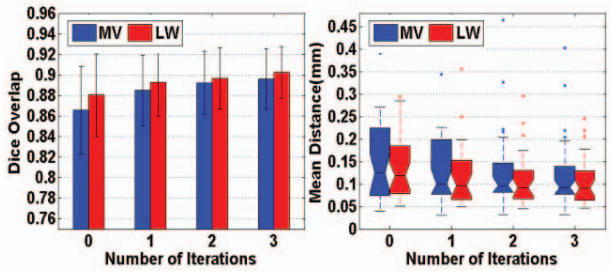


Fig.3. Dice overlap (left) and Mean distance (right) computed between results from automated segmentation methods and the manual segmentation at different iterations. MV: majority voting, LW: local weighted label fusion.

3. EXPERIMENTAL RESULTS

The proposed algorithm is validated on a data set of 30 subjects with 3.0T MRI images obtained from ADNI database (www.loni.ucla.edu/ADNI). These subjects are

equally distributed in 3 diagnostic groups, i.e., 10 patients of Alzheimer's disease (AD), 10 subjects of mild cognitive impairment (MCI), and 10 cognitively normal people (CN). These images were manually segmented by experts.

A 3-fold cross-validation is used to test the performance of our method. It is worth noting that any label fusion strategies of the multi-atlas based segmentation can be employed in our framework. In this paper, we choose majority voting (MV) and local weighted label fusion (LW) [5] for validation. Dice overlap index $2V(A \cap B)/(V(A)+V(B))$) and Mean distance $mean_{a\in A}(min_{b\in B}(d(a,b)))$ are used to test each method's performance, where A is the manual segmentation result, B is the output of automatic image segmentation methods, $V(X)$ is the volume of segmentation X and $d(a,b)$ is the Euclidian distance between a and b.

Fig.3 shows the quantitative measures of the hippocampal segmentation performance for multi-atlas based segmentation and our proposed method at different iterations. The iteration 0 represents the multi-atlas based segmentation, two different label fusion strategies, majority voting [1] and local weighted label fusion [5], are used respectively to test the effectiveness of our method.

As shown in Fig. 3, the results have demonstrated that statistical significant improvement can be achieved by the proposed method. Specifically, for majority voting, the Dice index is improved from 0.866 to 0.896 ($p<4.2e-6$), while the Mean distance is reduced from 0.168 to 0.128 ($p< 9.8e-031$), for local weighted label fusion, the Dice index is improved from 0.880 to 0.902 ($p<2.8e-5$), while the Mean distance is reduced from 0.135 to 0.107($p<3.7e-3$). The p-value is computed based on Student's one tailed paired t-test.

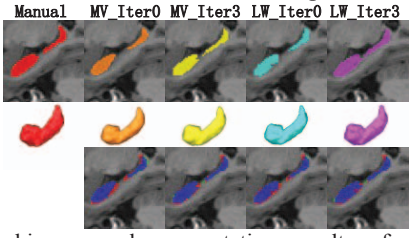


Fig.4. The hippocampal segmentation results of a randomly selected subject generated by different methods. The first row shows the segmentation results produced by manual segmentation and the automatic methods, the second row demonstrates the corresponding surface rendering results, and the difference between results of the manual segmentation and the automatic segmentation is showed in the third row (Red: Manual Segmentations, Green: Automated Segmentations, Blue: Overlap between Manual and Automated Segmentations).

To demonstrate the effectiveness of our proposed method, segmentation results of one subject for visual inspection are shown in Fig.4.

4. CONCLUSION

In this paper, we proposed an iterative framework combing multi-channel registration, label fusion and error correction together for subcortical structure segmentation. Compared to traditional multi-atlas based segmentation, a multi-channel registration strategy is used to explicitly improve the registration robustness and accuracy by introducing a shape similarity term. In addition, a learning based error correction procedure resistant to overfitting is used to reduce the systematic segmentation errors. The segmentation results of hippocampal on a dataset with mixed diagnostic groups have demonstrated that the proposed method can statistically significantly improve the performance of existing multi-atlas based segmentation methods.

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