RABBIT: Rapid Alignment of Brains by Building Intermediate Templates

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ABSTRACT

This paper proposes a brain image registration algorithm, called RABBIT, which achieves fast and accurate image registration by using an intermediate template generated by a statistical shape deformation model during the image registration procedure. The statistical brain shape deformation information is learned by means of principal component analysis (PCA) from a set of training brain deformations, each of them linking a selected template to an individual brain sample. Using the statistical deformation information, the template image can be registered to a new individual image by optimizing a statistical deformation model with a small number of parameters, thus generating an intermediate template very close to the individual brain image. The remaining shape difference between the intermediate template and the individual brain is then minimized by a general registration algorithm, such as HAMMER. With the help of the intermediate template, the registration between the template and individual brain images can be achieved fast and with similar registration accuracy as HAMMER. The effectiveness of the RABBIT has been evaluated by using both simulated atrophy data and real brain images. The experimental results show that RABBIT can achieve over five times speedup, compared to HAMMER, without losing any registration accuracy or statistical power in detecting brain atrophy.

Keywords: Statistical deformation model, principal component analysis, intermediate template, fast image registration

1. INTRODUCTION

The explosive growth of medical imaging has highlighted the need for highly automated, accurate, and robust tools for analysis of medical imagery. Image registration has attracted particular scientific interest, since it is necessary for integration and comparison of data from individuals or groups, as well as for the development of statistical atlases that encode anatomical and functional variability within a group of individuals. A plethora of image registration methods have been developed and used extensively [1]. Generally, image registration is formulated as a problem of minimizing an energy function that evaluates both image similarity and deformation smoothness. The smoothness of estimated deformations is particularly measured by Laplacian term, elastic energy, viscous fluid, biomechanical model or statistical constraints learned from the training samples [2-8]. In elastic image registration, the parameters needed to represent the deformation field are often in thousands when the deformation field is modeled by a linear combination of basis functions, or even in the magnitude of the number of voxels of images under registration when PDE methods are used. These high dimensional image registrations are typically solved by using aggressive, iterative “local search” techniques, which are prone to local minima if good initializations cannot be provided due to the high dimensionality of parameters.

In general, registration algorithms estimate shape deformation field (**f**) between a template (**A**) and an individual subject (**S**) (c.f. Fig. 1) from zero deformations. This generally needs a long time to complete and can potentially result in a noisy shape deformation due to the ambiguity in estimating large complex deformations. For fast estimation of shape deformation **f**, we present a PCA-based technique to capture the statistics of shape deformations between the template and individual samples [9, 10], and use the learned shape deformation statistics to rapidly estimate a shape deformation (e.g., $\mathbf{h}_1$) for a new subject **S** and warp the template **A** close to this new subject **S**. Thus, the remaining small deformation $\mathbf{h}_2$ between the warped template **B**, called as intermediate template in this paper, and the new subject **S** can be easily estimated by using a conventional registration algorithm such as HAMMER [2]. Accordingly, the registration can be performed fast and can achieve similar registration accuracy as HAMMER does.

The proposed method, RABBIT, consists of four main steps. First, a PCA-based technique is used to build a statistical model of shape deformations, based on a set of sample shape deformations estimated between the template and

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individual brain samples using a conventional registration algorithm such as HAMMER. In general, a small number of leading eigenvectors can capture a majority of variations of shape deformations. Therefore, a deformation field can be represented by a linear model with a small number of parameters. Second, for a new subject, its initial deformation parameters are estimated by maximizing its similarity with pre-placed templates generated by uniformly sampling the statistical shape deformation model. Third, by using Powell's optimization, we can optimize the deformation parameters in PCA space, to make the warped template as close as possible to the new subject. The warped template is called as individualized intermediate template for this new subject, and it is close to the new subject. Finally, to further improve the registration, we use a conventional registration algorithm, namely HAMMER, to register the intermediate template to the new subject. Thus, by combining the deformation field from the template to the intermediate template in the PCA space and the deformation field estimated from the intermediate template to the subject, we can obtain a complete deformation field from the template to the subject.

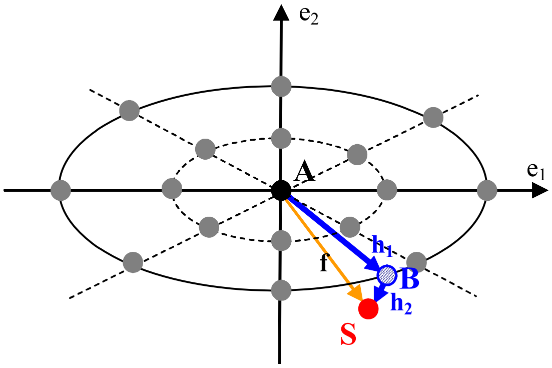


Fig. 1. Schematic explanation on the proposed fast image registration algorithm. The black point indicates the location of atlas **A**. The two axes denotes two main eigen directions of brain deformations learned from a number of brain samples. The grey points denote the pre-placed intermediate atlases, used to fast estimate the initial deformation paramters for a new subject (**S**). Here, the red point **S** denotes the location of the linearly aligned image of a new subject. Using Powell's optimization, the deformation paramters can be further refined for the subject **S**, e.g., $\mathbf{h}_1$, which can be used to create an individualized intermediate template **B** for the new subject **S**. Since the remaining deformation $\mathbf{h}_2$ from **B** to **S** is small, it can be estimated relatively easily and fast by a conventional registration algorithm.

RABBIT has been applied to the spatial normalization of both simulated and real MR brain images. The registration performance has been quantitatively and qualitatively compared with HAMMER. The experimental results show that these two algorithms have similar statistical power in detecting brain atrophy, but RABBIT is much faster than HAMMER. The experiment to generate an average brain image from a set of individual brain images also qualitatively demonstrates that these two algorithms can achieve similar image registration performance.

2. METHOD

2.1 Statistical Model of Shape Deformation

To elastically register a template with an image, we need to estimate a dense deformation field to establish spatial correspondence between the template and the image under registration. In the case of 3D image registration, the deformation field that warps a template ***T*** to an individual brain image ***I*** can be modeled as

$$\mathbf{f} = \{(dx_j, dy_j, dz_j), j = 1, \cdots, n\}, \tag{1}$$

or by a $n \times 3$ vector

$$\mathbf{f} = (dx_1, dy_1, dz_1, dx_2, dy_2, dz_2, \cdots, dx_n, dy_n, dz_n) \tag{2}$$

where (dx_j, dy_j, dz_j) is a displacement vector that warps a voxel j of T to ***I***, and n is the total number of voxels in ***T***. In image registration, the deformation field is characterized either voxel-wisely or by means of linear basis functions, which generally needs a large number of parameters and requires solving a high dimensional optimization problem.

Given a set of brain image samples $\{\boldsymbol{I}_i,\ 1 \leq i \leq M\}$ and their respective deformation fields $\{\mathbf{f}_i,\ 1 \leq i \leq M\}$ (directing from $\boldsymbol{T}$), which are obtained after affine registration of these brain images to a template space, we can use PCA to get a statistical deformation model that captures the statistical variations of the training deformation fields. From all M shape deformation samples, a mean shape deformation, $\bar{\mathbf{f}} = \sum_{i=1}^{M} \mathbf{f}_i / M$, is first computed, and then a difference vector $\mathbf{f}_i - \bar{\mathbf{f}}$ for each shape deformation $\mathbf{f}_i$ is calculated to construct an overall difference matrix D:

$$D = \left((\mathbf{f}_1 - \bar{\mathbf{f}}), \ldots, (\mathbf{f}_M - \bar{\mathbf{f}})\right) \tag{3}$$

From this overall difference matrix, we can compute a covariance matrix

$$Cov(D) = \frac{1}{M} D D^T \tag{4}$$

The size of the covariance matrix of deformation fields is of $3N \times 3N$, which typically ranges from several thousands to several millions. Thus, it is not easy to directly calculate the eigenvectors and eigenvalues from this huge covariance matrix. However, the number of training samples is relatively small compared to the number of voxels. To efficiently compute the PCA model, similar to the methods described in [9, 10], we first calculate the eigenvectors and eigenvalues of the transpose matrix of equation (3)

$$Cov(D^T) = \frac{1}{M} D^T D \tag{5}$$

with $M-1$ pairs of eigenvectors $\{\mathbf{e}_i\}$ and non-zero eigenvalues $\{\lambda_i\}$ computed from $Cov(D^T)$. The first $M-1$ eigenvectors and eigenvalues of $Cov(D)$ can be calculated as $D\mathbf{e}_i$ and $\lambda_i, i = 1,2, \ldots M-1$, and the remaining $3N - M + 1$ eigenvectors all have zero eigenvalues. The eigenvalues reflect the energy distribution of the training shape deformations among each of the eigenvectors, and the eigenvectors with the largest eigenvalues generally contain the majority of the energy within the training shape deformations. Therefore, a small number of eigenvectors, serving as basis functions, can well capture the distribution of training shape deformations. By using this deformation model, any new shape deformation field $\mathbf{f}$ can be approximated as

$$\mathbf{f} \approx \bar{\mathbf{f}} + \sum_{i=1}^{t} c_i \sqrt{\lambda_i}\, D\mathbf{e}_i \tag{6}$$

where $\bar{\mathbf{f}} = \sum_{i=1}^{M} \mathbf{f}_i / M$, $t \leq M-1$, λ_i and $D\mathbf{e}_i$ are eigenvalues and eigenvectors of covariance matrix of the training shape deformation fields, and $\{c_i\}$ are the coefficients on the respective eigenvectors.

2.2 Determination of Initial Intermediate Template for a New Subject

Given a new subject image, we use the learned shape deformation statistics to generate an intermediate template very close to this new subject image from the original template. To improve the effectiveness of finding intermediate template, it is important to determine a good initial intermediate template. To achieve this goal, we first pre-calculate a number of intermediate templates and place them uniformly in the PCA space. Then, we compare the similarity of a given new subject with each pre-calculated intermediate template to find the optimal intermediate template. The sum of squared difference (SSD) of image intensity is used as the similarity metric.

Fig. 2 illustrates a number of intermediate template brain images generated by warping the template brain image using some representative deformation fields ($\mathbf{f} \approx \bar{\mathbf{f}} \pm \sqrt{\lambda_i} D\mathbf{e}_i, i = 1,2, \ldots, 5$). These intermediate template brain images demonstrate different variations of global and local brain shapes, i.e., small and large ventricles, which indicate that the statistical deformation model can potentially represent a large variation of brain image deformation.

2.3 Optimization of Intermediate Template

Using the statistical deformation model, the estimation of shape deformation field $\mathbf{f}$ from the template space $\boldsymbol{T}$ to a new brain image $\boldsymbol{I}$ can be modeled as an optimization problem to find appropriate parameters $\{c_i\}$ for the shape deformation field $\mathbf{f}$ (as described in equation (6))

$$\arg max_{c_i}\, s(\mathbf{f}(\boldsymbol{T}), \boldsymbol{I}) \tag{7}$$

where $s(\cdot)$ measures the sum of squared difference (SSD) of image intensity between the warped template $\mathbf{f}(\boldsymbol{T})$ and a subject $\boldsymbol{I}$ to be registered. The warped template $\mathbf{f}(\boldsymbol{T})$ is generated from $\boldsymbol{T}$ by applying a shape deformation $\mathbf{f}$.

To further make the intermediate template as close as possible to the given new subject, we use Powell's optimization algorithm to optimize the coefficients $\{c_i\}$ of the shape deformation model. Based on the initialization method mentioned in the above subsection, we can obtain initial coefficients for $\{c_i\}$. By adjusting the coefficient $\{c_i\}$, the similarity between the updated intermediate template and the given subject will be changed. The search range for each coefficient $\{c_i\}$ is between -3 and +3, thus ensuring the generation of valid intermediate template.

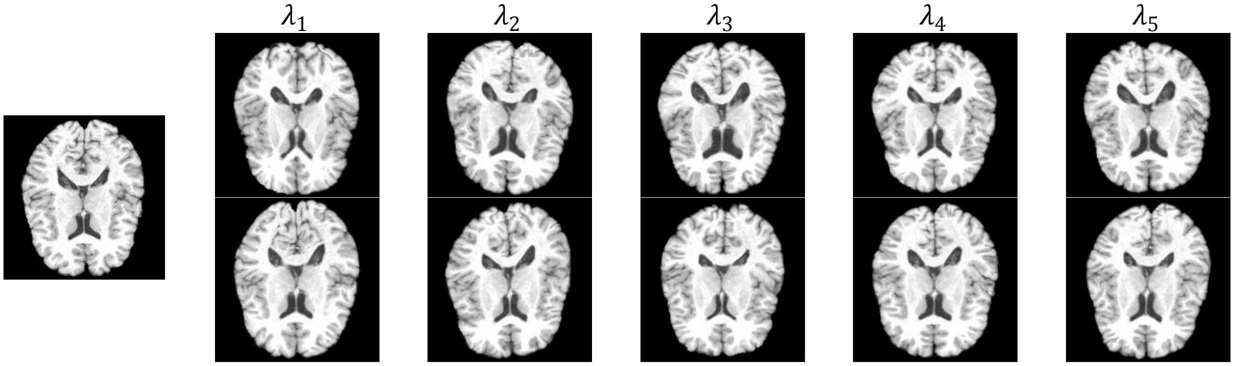


Fig.2. The template image is shown in the first column, and some intermediate template images generated by the deformation fields corresponding to the first 5 largest eigenvalues are shown from columns 2 to 6.

2.4 Refinement of Registration

The goal of generating intermediate template is to use the learned shape statistics to rapidly warp the template as close as possible to a given new subject. Since the shape statistics learned from a limited number of samples cannot capture the complete variations of brain shape deformations, the best estimated intermediate template is not well matched with the given subject, although the shape difference could be very small. To better align them, a conventional registration algorithm, namely HAMMER registration algorithm, is applied. Since the shape difference between the intermediate template and the image to be registered is relatively small, the registration can be achieved very fast.

To illustrate how RABBIT works, Fig. 3 shows all the intermediate results during the image registration of a brain scan to the template image. The template image is shown in Fig. 3(a), to which the brain scan in Fig. 3(c) is to be registered. Fig. 3(b) shows the initially estimated intermediate template for the brain scan in Fig. 3(c), based on only the similarity with the pre-generated intermediate templates. It can be observed that, compared to the original template, the initially estimated intermediate template is more similar to the given brain scan. Furthermore, with the constructed deformation model, the initially estimated intermediate template can be refined, with the final intermediate template shown in Fig. 3(d). The remaining difference between the final intermediate template and the brain scan is estimated by HAMMER, with the final registration result shown in Fig. 3(e), which is visually very similar to the brain scan in Fig. 3(c). For comparison, the registration result obtained by HAMMER is also shown in Fig. 3(f). These experimental results visually demonstrate the procedure of RABBIT, as well as its comparable performance with HAMMER.

3. EXPERIMENTAL RESULTS

The performance of RABBIT is evaluated with respect to registration accuracy, speed, and sensitivity in detecting brain atrophy by using both simulated and real MRI brain images.

3.1 Statistical Deformation Model

To build a statistical deformation model, we selected a normal brain from our database as a template, and 50 T1-weighted MR brain images as training data (with spatial resolution of 1.5×0.9375×0.9375 mm^3). We register all training data to the standard template space using affine registration followed by HAMMER algorithm. It is worth noting that other deformable image registration algorithms with reasonable performance can be also used to estimate brain deformations.

The cumulative energy represented by the largest eigenvectors is shown in Fig. 4, indicating that the first 5 eigenvectors with the largest eigenvalues (or principal components) cover almost 90% of the energy, while the first 10 can cover over

95% of the energy. Therefore, a deformation model with the first 10 principal components might be good enough to represent the brain deformations, as confirmed by the experiments below.

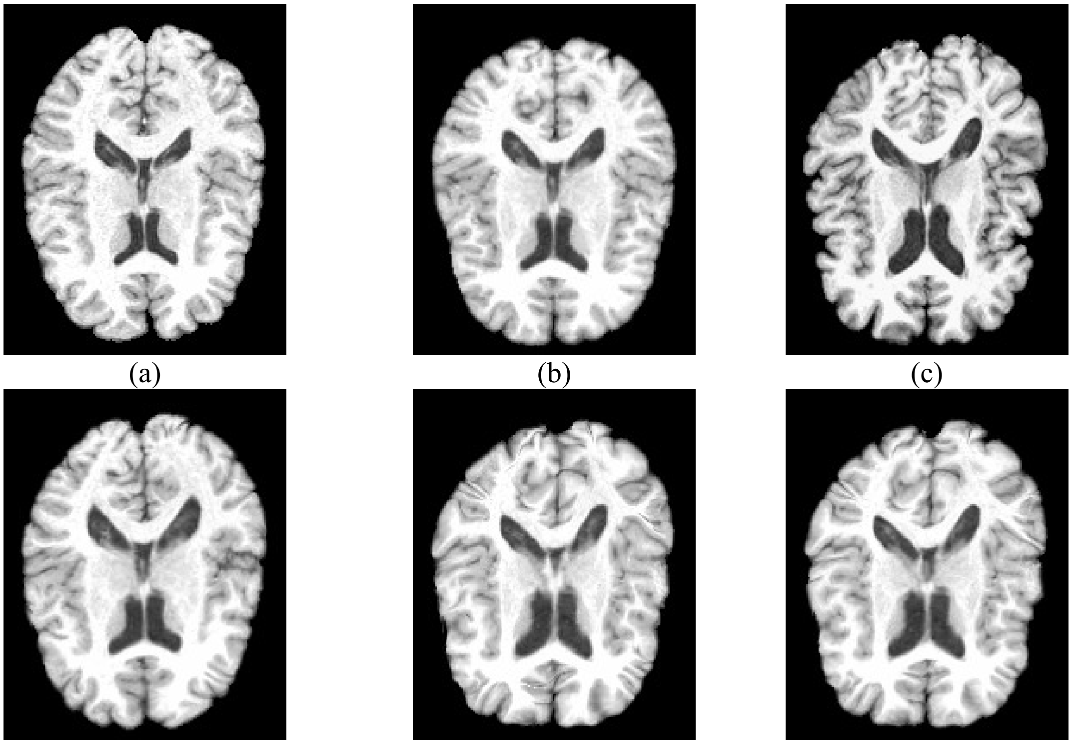

(a) (b) (c)
(d) (e) (f)

Fig.3. The step-by-step demonstration of RABBIT in aligning a template (a) with a new brain scans (c). The initially estimated intermediate template (using the pre-generated intermediate templates) is shown in (b), while the final estimated intermediate template is given in (d). The final warped template is shown in (e). For comparison, the template warping result by HAMMER is also displayed in (f), which indicates that our final warping result is comparable to the one obtained by HAMMER. The advantage of RABBIT is the significant deduction of the computational time.

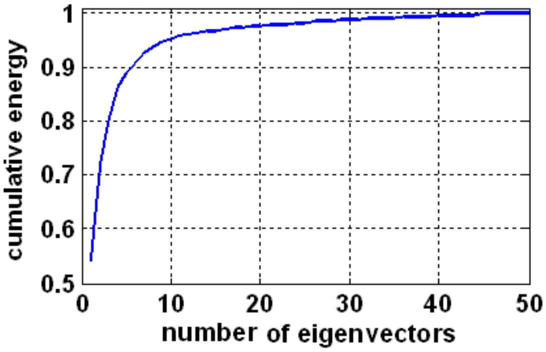
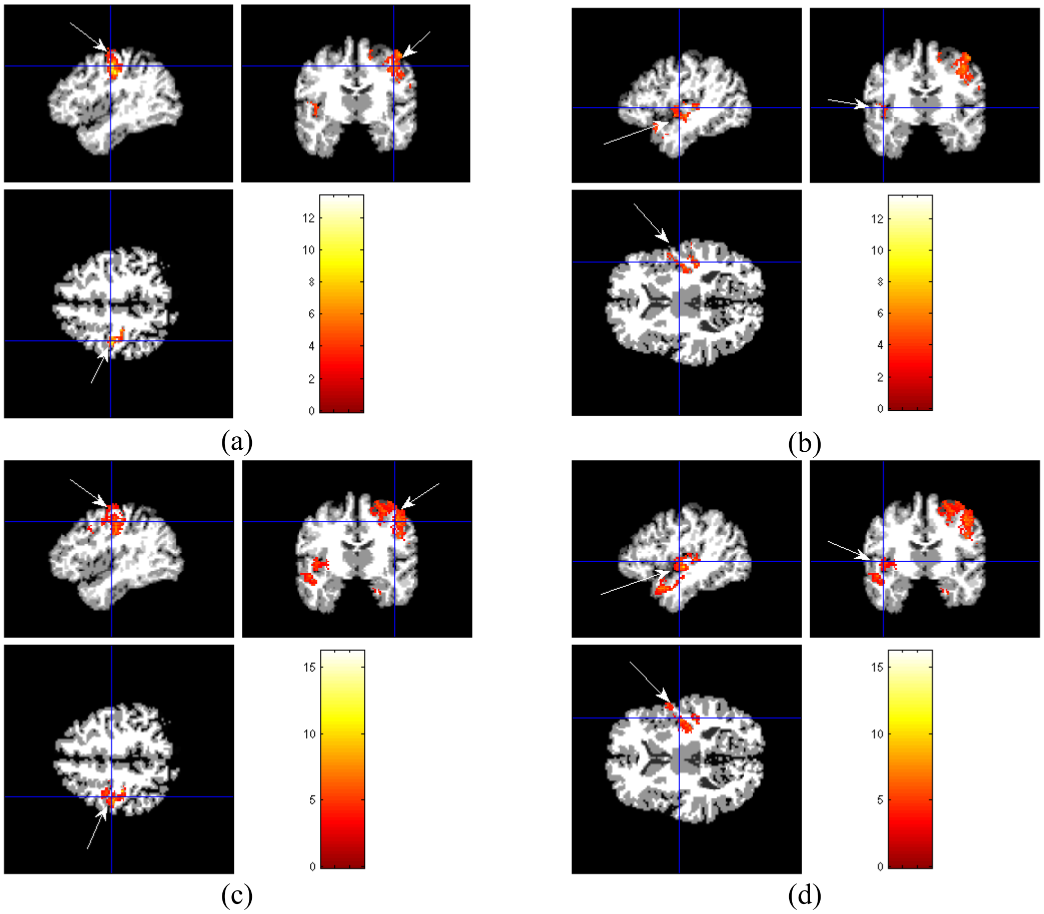


Fig.4. The change of cumulative energy with respect to the number of used eigenvectors.

3.2 Simulated Data

In this experiment, we use 12 normal T1-weighted MR brain images to simulate the atrophy at both precentral gyrus and superior temporal gyrus at each image [11]. All of these 24 images, including 12 original images and 12 images with simulated atrophy, are spatially normalized onto a template space by RABBIT and HAMMER, respectively. Then, we exam the ability of each registration algorithm in detecting simulated atrophy from the tissue density maps computed using the estimated deformation fields. In particular, tissue density maps, called RAVENS maps [12], are first calculated from shape deformation fields to directly reflect the regional volumetric changes. We perform a paired t-test on GM tissue density maps of the normal and the atrophy groups. Notice that in the paired t-test, smaller p values or larger t values indicate the better separation between two groups. We use an equal p value (p=0.005) to compare the t-score obtained by RABBIT with that by HAMMER. As a result, differences are detected at both simulated locations of the precentral gyrus and the superior temporal gyrus by the proposed method and HAMMER. Fig. 5 shows those detected differences with overlay on the top of the template image.

Table 1 summarizes the statistical measures obtained at the locations of the precentral gyrus and the superior temporal gyrus. It can be observed that both p_{PWE_corr} and p_{FDR_corr} are smaller and t-values are larger for the proposed method. This indicates that the PCA-based deformation model, combined with HAMMER, is powerful in brain atrophy detection.



(a) (b)

(c) (d)

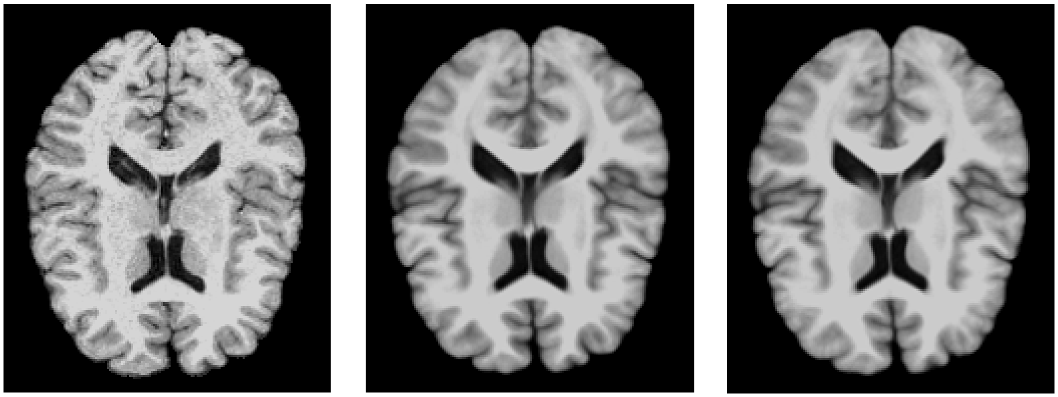
Fig.5. Atrophy detection results in GM, using the simulated atrophy data. The arrows indicate the detected atrophy locations. (a) and (b) show the atrophies detected in the precentral gyrus and the superior temporal gyrus by HAMMER. (c) and (d) show the atrophies detected in the precentral gyrus and the superior temporal gyrus by RABBIT.

Table 1. Paired t-test results on detection of simulated brain atrophy.

	RABBIT			HAMMER		
	p_{PWE_corr}	p_{FDR_corr}	t-value	p_{PWE_corr}	p_{FDR_corr}	t-value
Cluster 1 (GM, precentral gyrus)	0.001	0.002	16.20	0.004	0.002	13.40
Cluster 2 (GM, superior temporal gyrus)	0.005	0.002	13.00	0.076	0.005	9.95

3.3 Real Data

Eighteen real MR brain images are used to generate average brains, to visually evaluate the performance of RABBIT. These 18 brain images are spatially normalized onto a template by RABBIT and HAMMER, respectively. Fig. 6 shows the average brains built by RABBIT and HAMMER, respectively. By visual inspection, the average brain by RABBIT is very similar to that generated by HAMMER. After calculating the SSD of average brain and template, the SSD values of RABBIT and HAMMER are 14.53 and 17.18, respectively. This indicates that the proposed method has the same registration accuracy with HAMMER.



Template RABBIT HAMMER

Fig.6. Average brain images constructed from 18 brain images using RABBIT and HAMMER, respectively.

3.4 Speed

For each brain image, HAMMER takes over 4800 seconds on average. RABBIT takes about 250 seconds for the deformation model to estimate a reasonable intermediate template, and about 600 seconds for the HAMMER-based refinement. The total cost for RABBIT is less than 900 seconds, which is over five times fast than HAMMER.

4. CONCLUSION

We have presented a PCA-based technique to capture the statistics of shape deformations between the template and individual samples, and use the learned shape statistics to fast determine a close intermediate atlas and perform fast registration with a new subject. Compared to HAMMER, the proposed registration method can perform the same image registration over 5 times fast. Also, it can improve the statistical power in detecting group difference and can build average brain as good as HAMMR. In the future, we will test using more number of eigenvectors for statistical predication. Also, we will use more training samples to construct our statistical model of shape deformation, for improving the statistical representation. The proposed fast registration method will be also applied to the large clinical studies, to test its capability in detecting brain atrophy produced by brain diseases such as Alzheimer's disease (AD) or schizophrenia.

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