STATISTICALLY-CONSTRAINED DEFORMABLE REGISTRATION OF MR BRAIN IMAGES

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ABSTRACT

Statistical models of deformations (SMD) capture the variability of deformations of a group of sample images, and they are often used to constrain deformable registration, thereby improving their robustness and accuracy. Although low- dimensional statistical models, such as active shape and appearance models, have been successfully used in statistically-constrained deformable models, constraining of high- dimensional warping algorithms is a more challenging task, since conventional PCA-based statistics are limited to capture the full range of anatomical variability. This paper first proposes an SMD that is built upon the wavelet-PCA model and then uses it to constrain the deformable registration, wherein the template image is adaptively warped based on SMD during the registration procedure. Compared to the original template image, the adaptively deformed template image is more similar to the subject image, *e.g.*, the deformation is relatively small and local, and it is less likely to be stuck in undesired local minima. In experiments, we show that the proposed statistically-constrained deformable registration is more robust and accurate than the conventional registration.

Index Terms— Biomedical image processing, magnetic resonance imaging, image registration, statistics

1. INTRODUCTION

Conventional deformable registration methods [1, 2, 3, 4, 5] aim to find a deformation field between two images by maximizing the image-similarity measure and simultaneously constraining/regularizing the deformation field according to various deformable models. When training samples are available, statistical models that capture the variability of these deformations can be utilized to constrain the registration procedure in order to obtain more robust registration results [6]. Nevertheless, a good statistical model must effectively limit the searching space of deformations and, at the same time, accurately capture complex nature of deformation fields.

The popular principal component analysis (PCA)-based algorithms [7, 8, 9] can be used to capture the variability of deformations using the principal modes of shape variation. However, they fail when applied to deformation fields, due to under-training in practical settings, *e.g.*, high dimensionality and small training samples. Different statistical algorithms have been proposed to deal with these problems, among which the wavelet-PCA model [10, 11], applying PCA model in each wavelet band of deformation fields, has been approved to be more accurate and effective for estimating pdfs of deformations. To alleviate possible discontinuity or some negative Jacobians that could be generated by the wavelet-PCA model, we proposed the SMD [12], which uses additional constraints to regularize deformation fields, including wavelet-PCA models of both deformations and their Jacobian determinants coupled with a Markov random field (MRF).

This paper proposes a statistically-constrained deformable registration, using the Bayesian framework formulation. The basic idea is to adaptively deform the template image according to the statistics of deformations (*i.e.*, SMD) and register the input subject image and the deformed template image by using a conventional algorithm. Since the intermediate deformed template image is more similar to the input subject image than the original template image, the registration between them is much easier, due to relatively small and local deformations between these two images.

Experimental results show that the statistically-constrained deformable registration provides more robust and accurate registration results than only using the HAMMER registration algorithm [4]. Notice that this statistical registration framework can be applied to other conventional image registration algorithms.

2. METHOD

2.1. Statistical Model of Deformations (SMD)

Denoting $\mathbf{f}(\mathbf{x}), \mathbf{x} \in \Omega_t$, as the deformation field defined over the template image domain Ω_t, the goal of SMD is to estimate the pdf of $\mathbf{f}$, *i.e.*, $p(\mathbf{f})$, from a relatively small number of training samples. In order to capture finer and more localized variations of $\mathbf{f}$, SMD follows and extends the wavelet-based PCA model [11]. The wavelet-PCA model decomposes $\mathbf{f}$ using the wavelet packet transform (WPT) and subsequently captures within-scale statistics via PCA in each wavelet band. The fundamental assumption in wavelet-PCA is that the wavelet-based rotation renders the covariance matrix of deformation $\mathbf{f}$ close to block-diagonal, thereby enabling a more accurate estimation of the statistical distribution in each block (wavelet band) from a limited set of examples, compared to the usual sample covariance estimation, due to both of lower dimensionality and relatively strong correlations among variables.

Ideally, if the wavelet-PCA model captures the statistics of deformation $\mathbf{f}$ accurately, we can just use it as the statistical model; however, the assumption that the covariance matrix of $\mathbf{f}$ is block-diagonal in the wavelet packet basis does not hold exactly. Although it is well-known that for broad classes of signals, correlations across scales diminish rapidly, they are nonetheless non-negligible for adjacent scales. In order to alleviate this problem, we observe that additional constraints imposed on the deformation fields can be used to define subspaces in which the deformation must belong to. Therefore, SMD requires that a valid deformation field belongs to the intersection of the following three subspaces:

The first subspace: The Wavelet-PCA model applied to the sample deformation fields.

The second subspace: The wavelet-PCA model of the Jacobian determinants of the sample deformation fields. The reason to use Jacobian is that they reflect local volume changes of anatomical structures, which are important from the perspective of spatial distribution of the amount of brain tissue. It also makes sure that the deformation fields have valid Jacobian determinants and are topologically correct.

The third subspace: A nested MRF regularization applied to eliminating the potential discontinuities of deformations.

Given an input deformation field, we can iteratively project it onto each of the three subspaces, and generate the SMD-regularized deformation field according to these priors. This procedure is referred to as the *SMD regularization algorithm*, and it consists of the following five steps,

Step 1. Project the deformation field onto the wavelet-PCA model of valid deformation fields;

Step 2. Project the Jacobian of the deformation field onto the wavelet-PCA model of valid Jacobian determinants;

Step 3. Find new deformation field with Jacobians matching the one generated in Step 2;

Step 4. Apply the nested MRF regularization to imposing spatial smoothness on the deformation at all scales;

Step 5. Go to step 1 and iterate until convergence, *i.e.*, until the MRF-regularized deformation field belongs to the subspaces of valid Jacobians and deformations.

SMD has been approved to be more accurate in capturing the statistics of deformation fields than the conventional PCA-based method and been used for simulating realistic images for evaluation of atlas-based registration and segmentation algorithms [12].

2.2. Statistically-Constrained Deformable Registration

After estimating the statistical model of deformation fields, we can use it to constrain a deformable registration. Let T and S be the template and the subject images, the deformed template image can be denoted as $T(\mathbf{f}(\mathbf{x}))$, where $\mathbf{f}$ is the deformation of the template image. Let $\mathbf{h}$ be the deformation between the deformed template $T(\mathbf{f}())$ and the subject image S, the statistically-constrained deformable registration estimates both $\mathbf{h}$ and $\mathbf{f}$ (see Fig.1), according to the Bayesian framework, *i.e.*, $\mathbf{h}$ and $\mathbf{f}$ can be obtained by maximizing their joint posterior distribution, $p(\mathbf{h},\mathbf{f}|S,T)$,

$$p(\mathbf{h},\mathbf{f}|S,T) = \frac{p(\mathbf{f})p(S,T|\mathbf{f})p(\mathbf{h}|\mathbf{f},S,T)}{p(S,T)} \tag{1}$$

where $p(\mathbf{f})$ is the prior distribution of deformation fields, and $p(S,T|\mathbf{f})$ is the likelihood of the images for a given deformation $\mathbf{f}$, thus to maximize $p(\mathbf{f})p(S,T|\mathbf{f})$ we need to find an $\mathbf{f}$ according to its prior districution, which also aligns the template and the subject images well. $p(\mathbf{h}|\mathbf{f},S,T)$ is the conditional likelihood of $\mathbf{h}$. To maximize this likelihood, we need to find a deformation $\mathbf{h}$, which registers the deformed template and the subject images accurately. These two tasks are accomplished by the respective two steps described below. Fig.1 illustrates the relationship between the template and the subject images, as well as $\mathbf{h}$ and $\mathbf{f}$. For simplicity, the template image is the one generated using the mean deformation.

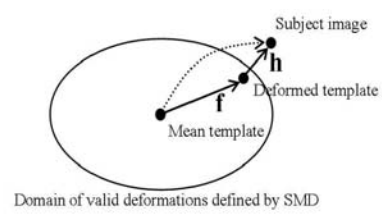

Fig. 1. Instead of directly registering the template image with the subject image (illustrated by the dotted line), in this work, the template image is first warped toward the subject image in the space of SMD (by deformation $\mathbf{f}$), and a conventional registration is then performed for the deformed template and the subject images (using deformation $\mathbf{h}$).

The algorithm is implemented using the following two iterative steps (see the structure in Fig.2):

Step 1. Use the *SMD regularization algorithm* to regularize the combined deformation $\mathbf{h}(\mathbf{f})$ and generate a new deformation $\mathbf{f}$ and a new deformed template image $T(\mathbf{f})$;

Step 2. Apply a conventional registration algorithm to register the deformed image $T(\mathbf{f})$ with the subject image S and generate a new deformation $\mathbf{h}$.

Fig.3 gives an example of the statistically-constrained deformable registration. It can be seen that compared to the original template image in Fig.3(a), the intermediate deformed template image in Fig.3(c) is more similar to the subject image in Fig.3(b), which renders the registration between Fig.3(b) and Fig.3 (c) relatively easy than that between Fig.3(a) and Fig.3(b), *e.g.*, the deformation between them is relatively small and local. In experiments, we have used the HAMMER registration algorithm in our framework to register images $T(\mathbf{f})$ and S, referred to as SMD+HAMMER. Other registration algorithms could also be used instead.

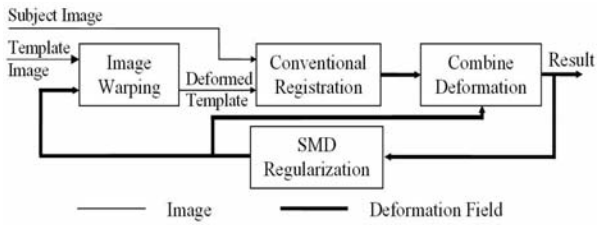

Fig. 2. The structure of the statistically-constrained deformable registration.

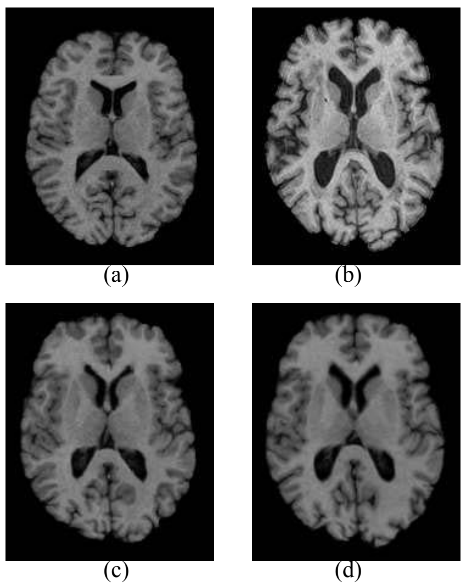

Fig. 3. An example of the registration results. (a) the template image; (b) the subject image; (c) the intermediate deformed template image; (d) final registration result: the warped template image;

Notice that the deformation in this paper consists of two parts, one is a deformation of the template image defined according to SMD, and the other is a nonlinear deformation by registering the warped template with the subject image using a conventional registration; whereas in our previous work [13, 14], only the former, *i.e.*, the deformation regularized by SMD, is regarded as the registration result.

3. RESULTS

3.1. Comparison of Accuracy of Registration Using Simulated Deformations and Images

Simulated deformations and images are used to compare the registration accuracy of HAMMER and SMD+HAMMER. First, we used two groups of T1-weighted MR brain images (79 for each group) as the training samples for two SMDs, respectively. Then, one SMD was used for simulating new deformations and images, and another was used for constraining the registration. We have simulated 9 such images and registered them onto the template image space, and then calculated the deformation errors between the registration results and the simulated ground truth. The histogram of these voxel-wise deformation errors of all the 9 images are shown in Fig.4. It can be seen that SMD+HAMMER yields more accurate registration than HAMMER, with respective population means as 0.59mm and 0.86mm.

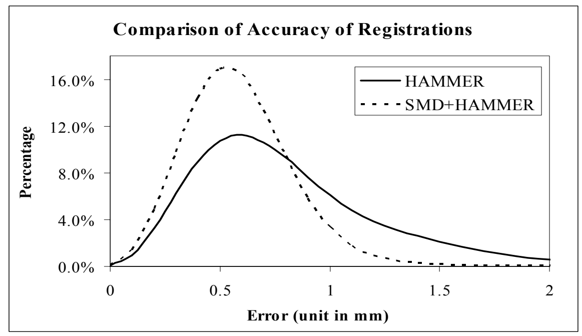

Fig. 4. Comparison of accuracy of registrations.

3.2. Comparison of Robustness of Registration for Group Analysis

In order to test the robustness of registration, from a group of normal MR brain images (10 images), we simulated atrophy on the superior temporal gyrus and the precentral gyrus [15], and then registered all these images onto the template image. Using the tissue density maps, *i.e.*, the RAVENS maps [15] of gray matter (GM), white matter (WM), and ventricular CSF (VN) calculated from the resultant deformation fields, we performed a paired t-test for group analysis using the Statistical Parametric Mapping (SPM) software package. A smaller p-value or a larger t-value of this t-test indicates better separation. Table 1 shows the statistical measures for the two clusters detected in the locations of the precentral gyrus and the superior temporal gyrus, respectively. It can be seen that smaller p-values (both of $p_{FWE-corr}$ and $p_{FDR-corr}$) and larger t-values are obtained by SMD+HAMMER. Thus, according to these experiments, SMD + HAMMER generated more robust and stable deformation fields and is more powerful in detecting group differences.

Table 1. Paired t-test for the two image groups.

Cluster	HAMMER	SMD+HAMMER
Cluster 1: *precentral gyrus*	$p_{FWE-corr} = 0.017$ $p_{FDR-corr} = 0.02$ $T = 17.44$	$p_{FWE-corr} = 0.003$ $p_{FDR-corr} = 0.003$ $T = 21.58$
Cluster 2: *sup-temp gyrus*	$p_{FWE-corr} = 0.19$ $p_{FDR-corr} = 0.02$ $T = 12.79$	$p_{FWE-corr} = 0.043$ $p_{FDR-corr} = 0.006$ $T = 15.50$

3.3. Comparison of Robustness of Registration By Registering Serial Images

Robustness of registration can also be observed by warping serial images of the same subject. For the serial images captured from normal subjects, the longitudinal changes are relatively small, thus a robust registration should be able to accurately measure these subtle longitudinal changes or provide temporally consistent/smooth results, even without using any temporal smoothness constraints. Voxel-wise temporal smoothness (TS) of the serial deformation fields, *i.e.*, the average of the absolute values of temporal gradients of deformations along longitudinally corresponding points, can be used to reflect such kind of longitudinal consistency. A smaller TS value means the longitudinal deformation is temporally smooth, and vise versa. To illustrate the TS values of SMD+HAMMER relative to those of HAMMER, we calculated the histograms of the differences of TS maps between SMD+HAMMER and HAMMER, for the six series of images tested (see Fig.5). From the figure, we can see that most of the TS values of SMD+HAMMER are smaller than those of HAMMER, indicating that SMD+HAMMER generates more longitudinally-consistent registration.

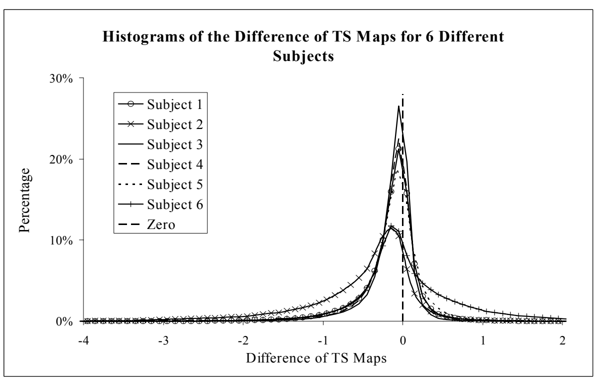

Fig. 5. Histograms of the difference of TS values between SMD+HAMMER and HAMMER.

4. CONCLUSION

This paper proposed a statistical model of deformation (SMD) and uses it to constrain deformable registration. The template image can be adaptively warped according to SMD during the registration procedure, and the conventional registration is performed by aligning the input subject image with the intermediate deformed template image. More robust and accuracy registration is achieved compared to the conventional registration. The proposed framework can be easily applied to other conventional deformable registration methods.

The software package of SMD (so is HAMMER) is publicly available and can be used to construct statistical models of deformations, to simulate new deformations and images, and to constrain a conventional registration algorithm.

5. REFERENCES

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