MULTI-CONTRAST DIFFUSION TENSOR IMAGE REGISTRATION WITH STRUCTURAL MRI

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ABSTRACT

We present a diffeomorphic diffusion tensor image (DTI) registration technique with multi-contrast images extracted from DTI and conventional structural MRI data. DTI provides microstructure information in white matter. However due to the acquisition protocols used in many clinical studies, DTI has lower SNR and spatial resolution compared to structural MRI. Complementary information can be used to improve the registration of white and gray matter. The proposed registration framework is constructed by a vector-valued large deformation diffeomorphic demons approach. Fractional anisotropy (FA) and eigenvalues are included as DTI components. T1-weighted image serves as the structural MRI component. The performance of the proposed method is compared with DTI only multi-contrast and full tensor based registration methods. Incorporation of structural data reduces FA variance in white matter adjacent to cortical regions. Compared to tensor based registration, the multi-contrast methods generate smaller shape variance but less directional consistency. We also demonstrate that the proposed method reduces fiber tract variations across individuals and creates a denser fiber tract probability map compared to DTI based registrations.

Index Terms— Diffusion tensor imaging, T1-weighted (T1w) MRI, multi-contrast registration, diffeomorphic demons

1. INTRODUCTION

Diffusion tensor magnetic resonance imaging (DTI) [1] is widely used for studies of white matter properties in normal brain development and neuropathological disorders. Accurate registration of tensor images is important in DTI analysis. It has been shown that incorporating the full tensor information [2, 3], multi-channel [4], multi-contrast [5] images, or features extracted from tensors[6] improves the registration performance compared to using a single DTI index, e.g., fractional anisotropy (FA). DTI provides significant white matter microstructure information compared to conventional T1-weighted (T1w) or T2-weighted (T2w) structural MRI modalities. Diffusion weighted images (DWIs) used for DTI reconstruction, however, are obtained by applying diffusion gradients which cause signal attenuation and lower SNR compared to structural images. Eddy current and head motion are also factors that affect DTI quality. Structural MRI has higher SNR, greater spatial resolution in many areas, such as tissue boundaries and gray matter structure. The two modalities provide complementary information and registering them simultaneously potentially improves the alignment of both white and gray matter. Another motivation of the current work is the emerging brain anatomical connectivity studies [7], which require diffusion and structural MRI to jointly generate cortio-cortical fiber connectivity matrices. The group level analysis needs to register both cortical and white matter regions accurately to an atlas space. Most current techniques register DTI and structural data separately.

In this work, we present a multi-contrast image registration method combining DTI and T1w MRI data. Invariant diffusion properties including FA and three eigenvalues are employed as DTI components, and the T1w image is added as the structural component. A vector-valued multi-resolution large deformation diffeomorphic demons registration framework was implemented to estimate transformation fields that register DTI and structural data simultaneously. Experiments were performed with human infant datasets. To evaluate the proposed method and compare it with registration techniques using only DTI, the variance of registered FA maps and the dyadic coherence [2] of principal eigenvectors were computed. The probability maps of cortico-spinal tracts (CST) were also constructed with various registration methods. The proposed method reduces FA variance and fiber variations, and produces denser tract probability maps compared to DTI only multi-contrast and full tensor based registrations. A related image registration work [8] incorporates DTI with conventional structural MRI with a mutual information criterion, and demonstrated that including DTI in the structural MRI registration improved the localization of tissue volume changes in studies of neurodegenerative condition.

2. MATERIALS AND METHODS

2.1. Similarity Cost of the Multi-Contrast Registration

For DTI components, we use FA to characterize the shape of tensors and three eigenvalues (λ_1, λ_2 and λ_3, where $\lambda_1 >$

$\lambda_2 > \lambda_3$) to represent the tensor size and diffusivity along major and minor principle directions. Unlike DTI components that are quantitative measures, the conventional structural images are T1 or T2 weighted and the intensities may not be consistent across different scans. Intensity histogram matching is applied to the structural data by linearly stretching or squeezing the intensities so that all input structural images have consistent intensity values for similar tissue types.

Given two vector valued images $\mathbf{I_i} = [I_{i1}, I_{i2}, ..., I_{iC}]$ $(i = 1, 2)$ where C is the number of components, and the diffeomorphic transformation Φ_{12}: $\Omega \in R^3 \rightarrow R$, the similarity metric using vector L2-norm is defined as:

$$\begin{aligned} C_S &= \int_\Omega D(\mathbf{I_1} \circ \Phi_{12}(x), \mathbf{I_2}(x))dx \\ &= \sum_{c=1}^{C} \frac{1}{n_c} \int_\Omega ||I_{1c}(\Phi_{12}(x)) - I_{2c}(x)||^2 dx \quad (1) \end{aligned}$$

where n_c is the weighting parameter for each component image I_c. The weighting parameter for FA is set to 1. The n_cs for λ_is are equal to each other and set to the maximum of the L2-norm of $(\lambda_1(x), \lambda_2(x), \lambda_3(x))$, so that the Frobenius norm of the diffusion tensors in the input data has a range of $[0, 1]$. The n_c for structural MRI is set to $\max(I_c(x))/\sqrt{2}$. Therefore, the DTI shape denoted by FA and size referred by λ_is have similar weight, and the structural channel contributes equally in the cost term compared to the DTI components.

2.2. Vector-Valued Diffeomorphic Registration

To map multi-contrast images with large shape differences, an extended diffeomorphic demons framework [9] is used to estimate diffeomorphic transformations. The vector-valued image registration is formulated as estimating the transformation Φ that minimizes the cost function:

$$\begin{aligned} C &= C_S(\mathbf{I_1} \circ \Phi_{12}^t, \mathbf{I_2}) + D(\Phi_{12}^t, \Psi_{12}^t)^2 + C_R(\Psi_{12}^t, v_{12}^t) \\ &= \sigma \sum_{c=1}^{C} \frac{1}{n_c} \int_\Omega ||I_{1c}(\Phi_{12}(x)) - I_{2c}(x)||^2 dx \\ &+ \rho \int_\Omega ||\Phi_{12}^t(x) - \Psi_{12}^t(x)||^2 dx \\ &+ \lambda_\Psi \int_\Omega || \bigtriangledown (\Psi_{12}^t(x))||^2 dx \\ &+ \lambda_v \int_\Omega || \bigtriangledown (v_{12}^t(x))||^2 dx \quad (2) \end{aligned}$$

where v_{12}^t is the velocity field at time t which parametrizes a diffeomorphism via $\Phi^t = \int_{\tau=0}^{t} v^\tau d\tau$; Ψ is another introduced transformation variable to separate the minimization of the similarity and regularization costs [9]; the distance term between Φ and Ψ, $D(\Phi_{12}^t, \Psi_{12}^t)$ is to constrain Ψ close to Φ; the regularization term is to ensure smooth velocity and transformation fields, defined as an isotropic differentiable operator $\bigtriangledown(\cdot)$; σ, ρ, λ_Ψ and λ_v are weighting parameters for each cost term. We set σ to $\frac{1}{\sum_{c=1}^{C} \frac{1}{n_c} ||I_{1c}(\Phi_{12}^t(x)) - I_{2c}(x)||^2}$, vary ρ to keep the largest update field less than 1 at each iteration, and set λ_Ψ and λ_v to be 0.5 and 0.2 after examining the smoothness of the velocity and transformation fields by varying them with the following pairs (0.2, 0), (0.2, 0.2), (0.5, 0.2), (0.5, 0.5), (1, 0.2), (1, 0.5), (1, 1). After linear approximation of the similarity term in Eq.(2) using Taylor expansion, the first two terms in Eq.(2) can be written as:

$$C_S(v^t) \approx || \begin{bmatrix} \mathbf{I_1} \circ \Phi_{12}^t - \mathbf{I_2} \\ 0 \end{bmatrix} + \begin{bmatrix} \sqrt{\sigma} \bigtriangledown \mathbf{I_1} \circ \Phi_{12}^t \\ \sqrt{\rho} I \end{bmatrix} v_{12}^t ||^2$$

The update of v^t can be calculated by

$$v_{12}^t = \frac{-\sum_{c=1}^{C} (\bigtriangledown I_{1c}(\Psi_{12}^t)(I_{1c}(\Psi_{12}^t) - I_{2c})}{|| \sum_{c=1}^{C} \bigtriangledown I_{1c}(\Psi_{12}^t)||^2 + \frac{\rho}{\sigma}}. \quad (3)$$

Details can be found in [9]. Modifications were made to suit vector image registration [10].

The estimation of Φ_{12} can be summarized as follows: (1) initialize Φ_{iR} and Ψ_{iR} to be identity fields; (2) let $\Phi_{12}^n = \Psi_{12} \circ (I + v_{iR}^n)$ and estimate the velocity field v_{12}^{n+1} according to Eq.(3); (3) regularize v by taking the Gaussian kernel of it: $v_{12}^{n+1} = \lambda_v K * v_{12}^{n+1}$; (4) let $\Psi_{12}^{n+1} = \lambda_\Psi K * \Psi^n \circ (\exp v_{12}^{n+1})$, and $\Phi_{12}^{n+1} = \Psi_{12}^{n+1}$; (5) repeat steps 1–4 until convergence: $C_{Sim} < \epsilon$, or $n > N_{max}$, where N_{max} is the iteration number and set to 20 at each resolution level.

2.3. Data Acquisition and Preprocessing

We demonstrate the performance of the proposed method using MRI scans of ten one-year old infants recruited for an ongoing early brain development study. Images were acquired on a 3T Siemens MRI scanner. A single shot EPI spin-echo sequence was used to acquire DWIs with the following parameters: TR/TE=5,200/73 msec, slice thickness=2mm, and in-plane resolution=2x2mm^2. Seven images were acquired, one with b=0 and six with b=1,000 sec/mm^2 along six diffusion gradients. DWIs were acquired five times and averaged to improve the SNR. MPRAGE sequence was applied for T1w: TR=1,820msec, TI=400msec, TE=4.38msec, flip angle=7^o, and spatial resolution=$1 \times 1 \times 1$mm^3.

DTI was estimated following automated and visual quality control as well as motion and eddy current correction [11]. FA and λ_is were then calculated and up-sampled to the same resolution as the T1w image. T1w images were rigidly aligned to the corresponding b0 images with normalized Mutual Information metric. B0 images were rigidly aligned to the average of the original images, and then affine aligned to the average of the rigid aligned b0s. The affine matrices were then applied to the DTI scalar maps and T1w images. After intensity histogram matching of the structural data, the multi-contrast images were ready for nonlinear registration. Fig. 1 (a) gives an example of a multi-contrast input. The affine aligned images were averaged to serve as a reference image.

We performed a hierarchical multi-resolution registration scheme of $[1/8, 1/4, 1/2, 1]$ in this study.

3. RESULTS

We applied three registration methods to register each dataset to the reference: multi-contrast DTI registration using FA and λ_is, the proposed method using DTI and T1w MRI, and a tensor based DTI registration [2] in the DTI-ToolKit (http://www.nitrc.org/projects/dtitk). Default parameters were used for all methods. Once the transformation fields were estimated, the original DTI data were deformed by the composition of the affine and diffeomorphic transformation. Tensors were reoriented by the local Jacobian of the transformation using the preservation of principle direction [12], and were interpolated with Log-Euclidean metric. Fig. 1 (b) shows the Log Jacobian of the transformations obtained by registrations using DTI contrasts, T1w contrast, and combined DTI and T1w contrasts. The transformation with combined contrasts reflects similar pattern to the one with DTI contrasts in major white matter regions, and shows a similar pattern to the one with T1w image in cortical and fine white matter regions. Fig. 1 (c) shows the averages of registered FA and T1w images with the proposed method.

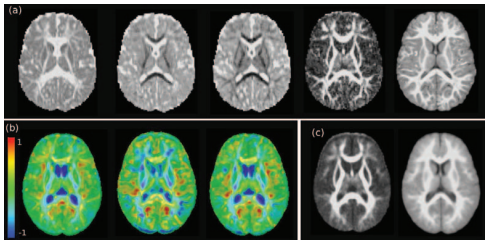


Fig. 1. (a)An example of a set of multi-contrast images including λ_1, λ_2, λ_3, FA, and T1w from left to right. (b) Log Jacobian of the transformation fields estimated using DTI contrasts only, T1w only, and DTI and T1w contrasts. (c)Average FA and T1w images after the proposed registration.

Normalized standard deviation (NSTD) of the FA maps was computed to indicate the shape variance of the registered DTI data. The dyadic coherence (DC) of principle eigenvectors was used to measure the directional consistency, and the computation can be found in [2]. DC=0 indicates that the principal eigenvectors are randomly scattered, whereas DC=1 means the principal eigenvectors are perfectly aligned.

FA NSTD and DC maps masked by a common white matter region are shown in Fig.2 after different registrations. The mask was generated by taking the average of all deformed FA maps after three nonlinear registration methods and thresholding the average FA map with FA > 0.15 (unmatured white matter and lower FA values in infants compared to adults). Compared to the method with DTI contrast, the proposed

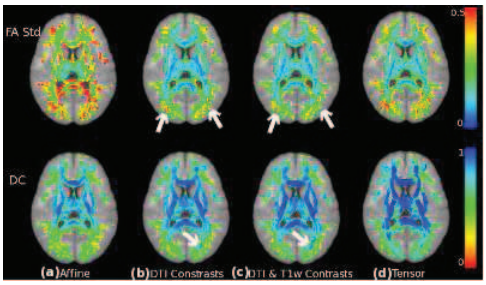
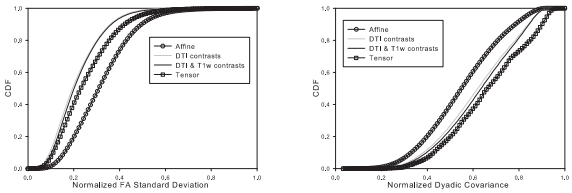


Fig. 2. Normalized standard deviation of FA maps and Dyadic coherence maps after (a)affine alignment, (b) DTI multi-contrasts, (c) DTI and T1w multi-contrasts, and (d) tensor based DTITK registration methods.



(a) (b)

Fig. 3. Empirical CDF of (a) FA normalized standard deviation and (b) DC maps after different registration methods.

method shows smaller FA variance in occipital and frontal superficial white matter regions, and higher directional consistency in occipital white matter regions. Both contrast based methods produce lower FA variance, but lower directional consistency compared to tensor based registration. Fig.3 plots the CDFs of FA NSTD and DC over the whole brain region. We found that overall FA variance and DC have similar value distributions between DTI contrasts and DTI plus T1w contrasts methods. Contrast based methods again show reduced FA variance but lower DC compared to tensor based method.

Another validation was applied to compare probability maps of fiber tracts with different registrations. We constructed the bilateral cortico-spinal tracts (CSTs) in individual space and transformed them to the reference space. Whole brain white matter fiber tracts were generated using "Trackvis" (http://trackvis.org/). The CST tract was defined as fibers connecting cerebral peduncle and precentral gyrus (PreG). The PreG and brain stem, generated by Freesurfer, were acted as"AND" ROIs to generate the CST tract. Manual editing was performed when tracts passing cerebellum. Fig. 4 shows four representative fiber tracts in individual spaces. The tracks were projected to an image grid, where the voxel was set to 1 if more than two fibers pass it, and 0 otherwise. The projected fiber images were transformed and averaged to generate the probability maps with affine, DTI contrast,

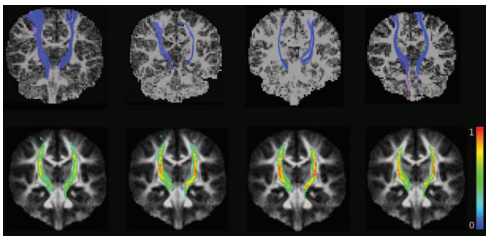


Fig. 4. The probability maps of bilateral cortico-spinal tracts (CSTs). Top row shows four CSTs in individual space. Bottom row shows the probability maps with affine, DTI contrasts, DTI and T1w contrasts, and tensor based registrations (left to right). The probability maps were thresholded by 0.3.

DTI and T1w contrast, and tensor based registrations (see bottom row in Fig. 4). The average values of the probability maps were 0.434(Left)/0.381(Right), 0.559(L)/0.511(R), 0.596(L)/0.532(R) and 0.543(L)/0.506(R), respectively. Combining T1w MRI reduces fiber variations and produces denser tract probability maps. The average probability with the proposed method was about $10\%/6\%$ (L/R CST) higher compared to registrations using DTI contrasts or tensors.

4. DISCUSSION

Our results show that DTI registration combining structural MRI helps to reduce shape variances and the deformed tensor images have higher directional consistency in superficial white matter regions compared to methods with only DTI contrasts. Multi-contrast registrations produce smaller FA variation but less directional consistency compared to tensor based registration. However, the multi-contrast registration with T1w MRI reduces variation of individual fiber tracts and generates denser tract probability maps compared to the tensor based method, indicating that, higher directional consistency itself does not ensure variation reduction of fibers across individuals. Our results indicate that in studies where DTI does not have great quality and high resolution, the conventional structural MRI may help to reduce fiber variations in regions adjacent to gray matter cortex. The emerging multi-modal neuroimaging studies also boost the need of simultaneous processing of diffusion and structural images.

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