Implicit Reference-Based Group Registration of Diffusion Tensor Imaging

X. Geng[1], H. Gu[1], T. J. Ross[1], G. E. Christensen[2], and Y. Yang[1]

[1]Neuroimaging Research Branch, National Institute on Drug Abuse, NIH, Baltimore, MD, United States, [2]Electrical and Computer Engineering, The University of Iowa, Iowa City, IA, United States

Introduction

Group analysis of fractional anisotropy (FA) derived from diffusion tensor imaging (DTI) is a popular technique to study white matter alterations within and between populations [1]. Common registration approaches in DTI analysis include selecting an image as template, registering all images to it pair-wise, and making statistical analyses in the template image space. The template selection may induce bias [2] which would affect the sensitivity to detect FA changes at a group level. Recently, unbiased group registration methods have been suggested [2-5]. Here we propose a novel group-wise registration method to jointly estimate transformations from each FA image to an implicit reference. This implicit reference-based group (IRG) registration method does not require a template selection, and the implicit reference has been proven to be the mean of the population in a general metric space [6]. Our results show that the deformed FA images have smaller variance and the shape is closer to the group mean compared to reference-based registration techniques.

Methods

Data Acquisition and preprocessing. Healthy subjects (n=30) were scanned on a Siemens 3T Allegra scanner. An EPI-based spin echo pulse sequence was used to acquire diffusion-weighted MRI images. For each subject, 35 axial images were prescribed to cover the whole brain with a 128×128 inplane matrix at a resolution of 1.719×1.719×4 mm^3. Beside the non-diffusion weighted reference image, 12 directions were used to apply the diffusion-sensitive gradients with a *b*-factor of 1000 s/mm^2. For EPI, TR/TE = 5000/87ms, BW= 1700Hz/Pixel, and NEX=4. Three-dimensional T1-weighted anatomical images were also acquired. Each structural image was automatically normalized to Talairach space using the AFNI software package (National Institute for Mental Health, http://afni.nimh.nih.gov/afni). The 12 diffusion weighted images (DWIs) were aligned to their corresponding structure images for correction of motion and image artifacts using mutual information based affine registration [7], provided by the FSL package (http://www.fmrib.ox.ac.uk/fsl/). Normalization matrices were applied to DWIs, and FA and mean diffusivity (MD) images were then calculated from the diffusion tensor.

Group registration and data analysis. The proposed IRG minimizes the summation of the intensity difference between each pair of deformed images, and the total cost function is defined as $C=C_{SIM}+C_{REG}$. The similarity cost function is defined as $C_{SIM} = \sum_i \sum_j \int_\Omega \| I_i(h_{iR}(x)) - I_j(h_{jR}(x)) \|^2 \, dx$, where I_i represents the *ith* image in the group, and h_{iR} is the transformation from I_i to the implicit reference. The regularization cost C_{REG} is a small deformation linear-elastic regularization constraint [8] to penalize transformations with large and unsmooth distortion. The 30 images were simultaneously registered to the implicit reference space using the IRG method. To compare with reference-based techniques, the FSL package (http://www.fmrib.ox.ac.uk/fsl/) was used to provide two alternative templates. The first one was obtained by aligning every FA image to each other (a total of 30x29=870 pair-wise registrations) and selecting the "most representative" one, which had the minimum energy to register to other images. The second template was the FA standard space image provided by FSL. This standard image is a high-resolution average of 58 well-aligned high quality FA images, which is in the MNI152 standard space. It was converted to Talaraich space before registration. Two pair-wise registration techniques were applied to register images to each template respectively. The first one B-spline based free-form deformation (BFF) is provided by IRTK (Image Registration Toolkit, www.doc.ic.ac.uk/~dr), embedded in the FSL package. The second is Fourier based small deformation elastic (SDE) registration [8]. The IRG method uses the SDE model under an implicit reference-based registration framework. To assess the effectiveness of these registration techniques, region of interest (ROI) based intensity variance of the deformed FA images was computed and compared between IRG and reference-based registration. The ROI was computed by taking the intersection of the FA masks from different registration methods, and each FA mask was obtained by thresholding the average deformed FA images at FA of 0.3.

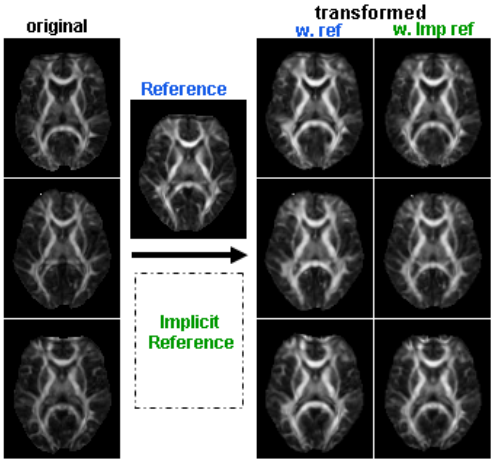
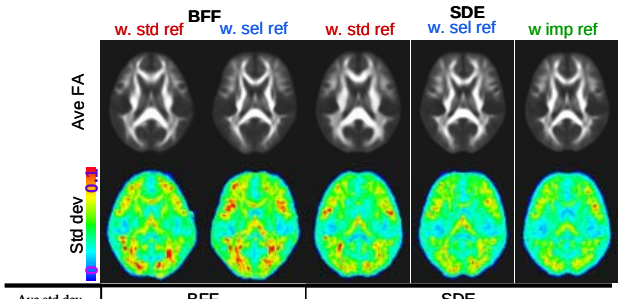


Fig.1 FA images before and after reference-based or IRG registration.

Results and Discussion

Fig.1 shows FA images from 3 randomly selected subjects and their deformed images after reference-based or IRG registration. The deformed images using reference-based registration have similar shapes as the reference, whereas the ones using IRG have similar shapes to each other, which are closer to the general mean of the group. Mean and standard deviation of the deformed FA maps using the two different references and the implicit reference are shown in Fig.2. The IRG registration reduces the variance compared to the reference-based techniques using both BFF and SDE models. This is due to the fact that IRG registration deforms images to the implicit template which is the group mean. IRG requires less registration energy compared to that deforming images to a selected or standard reference, and therefore produces less registration error. Although there is only a small amount of decrease in the variance compared to the selected reference-based registration using SDE, the computation cost of IRG is $\mathbf{O}(n)$ which is much less than the reference-selection method with $\mathbf{O}(n^2)$.



Ave std dev	BFF		SDE		
FA ROI	.05755	.06145	. 05110	.04989	.04858
Whole brain	.04860	.04659	.04313	.04311	.03887

Fig.2 Mean and standard deviation (S.D.) of deformed FA images after reference-based (using the standard or selected reference) or IRG registration. The average S.D. is computed on the FA ROI or the whole brain.

Conclusion

The proposed implicit reference-based group-wise registration produces smaller inter-subject variance compared to reference-based registration, which is important for accurate group analysis of DTI data.

References

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