Assessment of image-based registration of diffusion-weighted images acquired at high *b*-value

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Introduction There is growing interest in the use of high *b*-value diffusion MRI to model complex white matter fibre structures in the brain. One disadvantage of such techniques is the reduction in signal-to-noise ratio (SNR) of the diffusion-weighted (DW) images due to the large signal attenuation at high *b*-value. This is thought to cause problems when DW images, for example those acquired using echo-planar imaging, need to be corrected for eddy-current induced distortions and bulk-patient motion using image-based registration techniques. Here, we tested whether one popular multimodal registration algorithm, FLIRT (www.fmrib.ox.ac.uk) (1), can register DW images with low SNR within error tolerance. The possibility of using registration techniques at such low SNR would facilitate quantitative pixel-by-pixel analysis in diffusion imaging techniques using very high *b*-values.

Methods Sets of 5-mm thick T_2-weighted images of a synthetic human brain were generated using the Montreal Simulated Brain Database (http://www.bic.mni.mcgill.ca/brainweb). These noise-free synthetic T_2-weighted images were segmented into grey matter, white matter and CSF based on the signal intensity in each pixel, and a single apparent diffusion tensor representative of normal brain was assigned to each of these tissues types. Noise-free DW images were then created from this synthetic data by applying $S = S_0 \exp\{-\mathbf{BD}\}$ to each voxel in the T_2-weighted images. The *b*-matrix was defined as $\mathbf{B} \equiv \{b_{ij} = 1/3b\}$ with $b \in \{1000, 7000\}$ s/mm^2. Gaussian random noise was then added in quadrature to both T_2-weighted and DW images to produce a range of SNR values comparable to those seen at different *b*-values in human brain studies using the same voxel size. To mimic the magnification (M), translation (T) and shear (S) caused by eddy currents on image geometry, the synthetic DW images at each *b*-value were distorted using two sets of parameters representing stretching, $\{M, T, S\} = \{1.06, 5.6$ mm, 0.06 mm column$^{-1}\}$, and shrinking $\{M, T, S\} = \{0.97, -5.8$ mm, -0.06 mm column$^{-1}\}$ in the phase-encoding direction determined from phantom experiments. FLIRT transformation matrices, $\mathbf{T}$, were created with combinations of the distortion parameters in each set and applied to the DW images to distort them. Since all the synthetic images were originally perfectly registered, it should only be necessary to apply the inverse of the distortion transformation ($\mathbf{T}^{-1}$) to co-register the DW images to the T_2-weighted image in each case.

All the distorted DW images at each *b*-value were registered to the corresponding undistorted T_2-weighted images using FLIRT and the resultant transformations $\mathbf{R}$ saved. The root mean square (RMS) deviation was used to compare $\mathbf{R}$ to $\mathbf{T}^{-1}$ (2). An RMS error > 1 mm will be taken as the tolerance for satisfactory registration (3). This test was performed using two different similarity measures as cost functions in FLIRT, correlation ratio (CR), which is the default cost function, and mutual information (MI). A second test of the accuracy of registration was performed using principal component analysis (PCA) of each set of synthetic images. PCA identifies statistical patterns in the data. Mis-registration effects contribute to the high order principal components (PC), increasing their share of the total variance. Therefore, the higher the % of the variance in the first PC (%var1), the better the image registration. PCA was also performed on a dataset with *b* set to 0 (i.e. all T2-weighted images), and infinite SNR with and without distortions, before registration to provide a baseline value of % variance against which to compare the registration results at different *b*-values.

Results The RMS deviation showed that FLIRT error was below the tolerance of 1 mm for *b*-values less than 6000 s mm^{-2} (SNR > 1.5) for CR and 5000 s mm^{-2} (SNR > 1.9) for MI, indicating that the performance of MI is slightly poorer than CR at low SNR. At higher *b*-values and lower SNR, the error increased rapidly for both cost functions. No difference was found between using stretching or shrinking parameters.

Results from PCA corroborated these findings. Figure 1 shows how the total variance is shared between the first six PC for DW images generated with different *b*-values, distorted using stretching parameters and registered with FLIRT using CR. The legend indicates (SNR) and %var1. PCA showed a distribution of the total variance in the PC very close to the undistorted ideal case for *b*-values up to 5000 s/mm^2, demonstrating an excellent performance of FLIRT at SNR > 1.9. The %var1 decreases slightly from this *b*-value but still shows a considerable improvement in the registration at 6000 s/mm^2. However, at higher *b*-values the effect of FLIRT in the images is actually to decrease %var1 dramatically as compared to the result from the unregistered images, indicating that FLIRT registration is actually worsening the alignment of the images rather than improving it when the SNR of the images is below 1.5. This effect is shown in the FA maps. Figure 2 shows misregistration artifacts and ill defined white matter fibres in FA maps calculated from unregistered DW images acquired at *b*-value of 1000 (a), 4000 (b) and 7000 (c) s/mm^2. FLIRT reduced these artifacts, in images acquired with 1000 (d) and 4000 (e) s/mm^2 but not with 7000 s/mm^2 (f). When using FLIRT in such low SNR DW images, the registration is so deficient that the resulting FA map has poorer quality than when unregistered images were used.

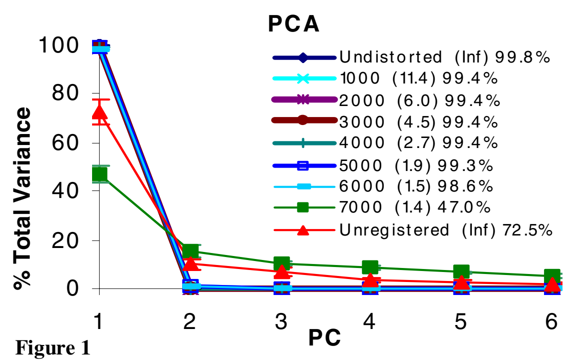

Figure 1

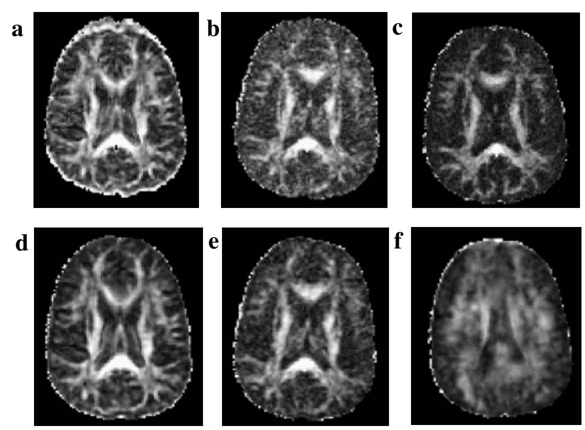

Figure 2

Conclusions FLIRT, and possibly other image based registration methods using multimodal similarity measures such as CR and MI, can be used to correct distortions from DW images with SNR > 1.5. This facilitates the use of diffusion imaging modalities at high *b*-values where an accurate correspondence between same pixels in different images is required.

References (1) Jenkinson M,.Smith S. Med Image Anal 2001;5:143-156. (2) Jenkinson M. FMRIB Technical Report TR99MJ1. (3) Haselgrove JC, Moore JR. Magn Reson Med 1996;36:960-964.