

# Gradient Distortion Correction for 3D Diffusion Tensor Microscopy

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**INTRODUCTION:** Diffusion tensor imaging (DTI) is a promising tool for characterizing the tissue structure, and useful in studying the structure-function relationships of ordered tissues. The DTI dataset consists of images acquired in the presence of diffusion-sensitizing gradients in different directions. However, these large gradients can cause significant image distortions by, for example, eddy current induced magnetic fields [1, 2]. The distortion varies in the different gradient directions and one needs to develop a correction technique in order to create accurate tensor maps. Previous work carried out to correct this distortion assumed the distortion to be present only in the phase encode direction [1]. Moreover, the technique was developed and tested for multi-slice images, and estimated the distortion for relatively lower diffusion weighting and then used that information to extrapolate for higher diffusion weighting [1]. However, this has often been found to be inadequate in the presence of noise for higher diffusion weighting [2]. Another technique [2] that models the magnetic field to perform a calibration operation invariably needs additional acquisitions. Post processing techniques based on image registration using mutual information have been developed, but are primarily used for a multi-slice acquisition where the deformation is assumed to be present only in the phase encoding direction and is a simple slice dependent affine deformation [3]. Since our work primarily deals with true 3D DT images, we have made no such assumptions about the distortion model. Here we perform a systematic comparison of factors that influence mutual information based image registration [4] and present a generalized 3D correction technique without a-priori assumption of the distortion source.

**METHODS:** Mutual information (MI) has been shown to be a suitable measure for cross-modality medical images [4], but has often been found to result in mis-registration if the mutual information function is ill defined having local maximum, mainly due to interpolation effects [5]. We propose the use of Fourier based translation and shear; and evaluate the performance of interpolation schemes such as bilinear, bicubic, and Fourier scheme.

Another factor that affects the reliability of MI based registration techniques is the selection of the cost function. The reliability of the registration using MI can be improved by using spatial information in the form of the angle between the image gradients [6]. We compare the performance of various cost functions suggested in [6] to evaluate the efficacy of including spatial information along with the mutual information. We perform registration on a-priori determined deformation on test diffusion weighted images (N=24) using four cost functions, namely, Mutual Information (MI), Normalized Mutual Information (NMI), MI modified by spatial information (MIGR) and NMI modified by spatial information (NMIGR). We use Fourier based translation and shear as suggested earlier to deform the images and use normalized cross-correlation as a metric indicating the registration for these datasets.

Subsequently, we extended the above MI based registration technique for true 3D image registration for fixed mouse brain high-resolution DTI datasets N=5, 256 x 128 x 128, 100-micron isotropic resolution obtained from a separate study. The Levenberg-Marquardt optimization technique is used to register each diffusion-weighted to the non-diffusion weighted volume. To study the performance of the 3D registration, we created a standard deviation (STD) map by computing the STD for each voxel in all the gradient directions along with the non-diffusion weighted direction. Fractional anisotropy (FA) maps before and after registration were computed to assess the effectiveness of the correction. In addition, the root mean square (RMS) deviation of the DT principal eigenvector with the six neighboring voxels was averaged over the white matter (FA>0.3).

**RESULTS AND DISCUSSION:** Figure 1 shows the dependence of the MI function on translation in the readout direction, which is representative of other registration parameters as well. Bilinear and bicubic interpolation techniques result in false maxima in the MI function, which may complicate the search for true MI maximum. The Fourier based translation and shear keeps the mutual information function smooth with no local maxima leading to reliable convergence. Table A reveals that the different cost functions performed statistically comparable to each other. The reason being the fact that the Fourier based method compensates for most of the problems associated with linear, cubic interpolators. The different cost functions using spatial information were used to correct for the interpolation effects, hence the performance of these various cost function do not yield much difference. Figure 2 shows the STD maps for the (a) unregistered and the (b) registered set. As expected the unregistered STD maps shows higher STD at diagonal edges, which has been clearly corrected by registration, which shows less variation in the series of images. Figure 3b and 4b show a visible improvement in the FA maps for the registered dataset as compared to unregistered set in 3a and 4a, where we see qualitative improvement in the visualization mainly by virtue of less background and more visible detail in the structure. Table B consists of the RMS deviation angles for the unregistered and registered datasets revealing a statistically significant reduction in the RMS values for the registered datasets, which is expected as the regions in close proximity tend to have the principal eigen vectors in the same direction. Hence the lower RMS deviation angle between the neighbors indicates better alignment of the various diffusion-weighted images.

**Table A: these are mean (N=24) ± std of measured normalized cross-correlation of registered images with respect to the target test image as a function of the cost-function.**

Cost Func.	MI	NMI	MIGR	NMIGR
Mean NCC	0.58±0.0061	0.58±0.0066	0.58±0.0064	0.58±0.0069
One way repeated measure ANOVA		F value: 1.1458	P Value: 0.3368	

**Table B: these are RMS deviation angles for 5 datasets**

Dataset	1	2	3	4	5
UnReg	0.4117	0.6007	0.6405	0.4869	0.5423
Reg	0.3212	0.5064	0.5505	0.4095	0.4552
Paired Student t-test		T-value 30.62		P value: << 0.001	

**CONCLUSIONS:** Fourier interpolation can make mutual information function more reliable by circumventing the problem of false maxima that leads to improvement in the detection of the global optimum. Significant improvements in the quality of DTI data (e.g. FA map and “fiber” orientation) have been achieved by correcting the distortion in true 3D DT images by application of the technique developed above.

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