DTI Geometric Distortion Correction by Non-Linear Registration and Field Map Correction: Quantitative Analysis of DTI Tractography and Fractional Anisotropy

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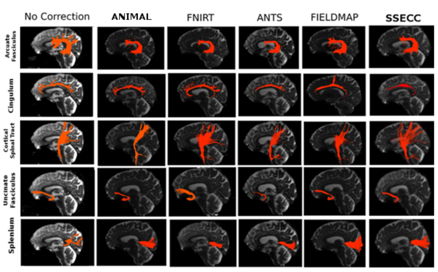
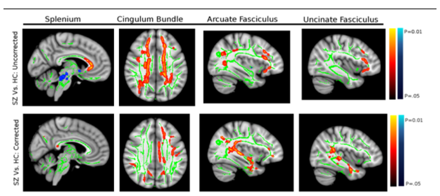
Target Audience: Researchers who utilize tractography and/or fractional anisotropy measures for diffusion-weighted imaging (DWI) data collected with echo planar imaging (EPI).

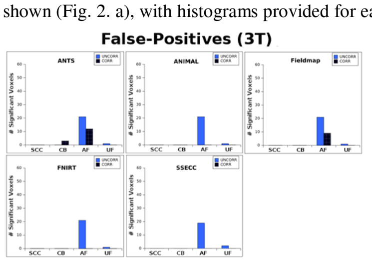
Purpose: Diffusion tensor imaging (DTI) is utilized to study white matter (WM) *in vivo* by estimating local tissue properties using scalar metrics derived from the diffusion tensor such as fractional anisotropy (FA) or tractography. DTI is typically collected with echo planar imaging (EPI) sequences, prone to geometric distortion in the phase-encode direction. Geometric distortion in EPI images can be minimized by non-linear registration to an anatomical reference image, or by using b_0 field maps [1]. In this work we perform an investigation of both field mapping and non-linear registration distortion correction techniques, to evaluate their effect on standard downstream diffusion tensor imaging metrics and tractography. We also present *SSECC (Simultaneous Susceptibility and Eddy Current Correction),* which corrects for the unique eddy-current and geometric distortions affecting each diffusion image, in an integrated fashion, using non-linear registration tuned to map diffusion weighted images directly to T2-weighted images The pipelines have been developed for easy inclusion of different non-linear registration algorithms, to investigate multiple non-linear registration algorithms, and their effect on diffusion weighted data.

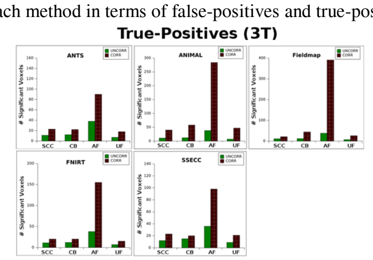




Methods: Imaging data were collected for 10 healthy controls (age 42 ± 11, 5M, 5F) and 10 participants with schizophrenia (age 45 ± 16, 5M, 5F), at 3T (GE Discovery MR750, General Electric Medical Systems, Milwaukee, WI) at the Centre for Addiction and Mental Health. DWI: (b=1000 s/mm^2, 60 diffusion encoding directions, 5 b=0, matrix 128x128, FOV 25.6 cm, Phase Encode (IS)), T2: 2D oblique (0.85x0.85x3mm, matrix (256x256), TE=11ms, slice thickness=3mm, fat saturation). Artifact correction was achieved as follows: a) The b=0 image underwent affine registration to each DW-image, creating a set of 'template' images with b=0 image contrast but similar eddy-current artifacts to the original DW-images. These template images, owning to their T2-contrast (without diffusion sensitization), underwent non-linear registration via: ANTs, ANIMAL or FNIRT to the T2-anatomical. This method has the advantages that 1) We calculate a unique non-linear transformation for each DW-image, 2) A unified Jacobian determinant map can be used to correct local brightness modulations resulting from signal compressions and rarefactions [2]. *SSECC* utilizes ANTs non-linear registration with mutual information, to simultaneously correct eddy-current and susceptibility induced image distortions, by direct registration of each DW image to the T2-anatomical without relying on a b=0 intermediate. This also allows brightness modulation via a Jacobian determinant. Furthermore this method does not assume independence between the two artifacts, thereby accounting for any non-linear or high order effects, resulting from their combination. Both methods include correction for rigid motion and B-matrix correction for rotation. An 'uncorrected' dataset with affine registration correction only (i.e. eddy-current correction), was used for comparison to fully corrected data. Deterministic tractography was performed in Slicer (4.1.1) using an unscented Kalman filter with free water correction, with seed regions selected to elicit the Splenium of the Corpus Callosum (SCC), Cingulum Bundle (CB), Arcuate Fasciculus (AF), Uncinate Fasciculus (UF) and Coritcal Spinal Tract (CST) [3, 4]. Previous literature has indicated WM tracts in which FA is reduced patients with schizophrenia compared to healthy controls in particular the SCC, CB, AF and UF[5, 6]. Lacking a ground truth, these 4 tracts were used to indicate regions of interest in which increases in FA between schizophrenia participants compared to controls could be considered false-positives. The number of such false-positives was quantified by thresholding the multiple comparison corrected t-statistic skeleton maps, to include only those values above the statistical threshold ($p < 0.05$), and masking the skeleton with regions of interest corresponding to those tracts identified above from the Mori John Hopkin's University WM atlas [7], and summing the number of remaining voxels.

Results: Better anatomical correspondence is observed between all distortion corrected data with the T2 anatomical reference, than is observed between the uncorrected data and the T2 anatomical references. The uncorrected images demonstrate that geometric distortion resulted in an overall stretching of the image in the inferior-superior direction, causing misalignment for both the cortical surfaces and WM projections. This is mitigated by distortion correction, however, each algorithm has provided a slightly different fit, such that ANIMAL appears to be superior to the other algorithms. Tractography results for the AF and CB appear to be more robust compared to uncorrected data (Fig 1.). For each tract of interest mean FA was shown to increase after distortion correction compared to eddy-current correction only. Each algorithm performed similarly with respect to the relative increase of FA, however ANTs consistently resulted in the smallest increase in FA for the regions of interested investigated. TBSS statistic maps are presented for ANIMAL non-linear registration as it showed the fewest incidences of 'false-positives'. Contrasts between corrected and uncorrected data for the two cohorts shown multiple regions of statistically significant differences. Contrasts between schizophrenia participants and healthy controls without and with correction are shown (Fig. 2. a), with histograms provided for each method in terms of false-positives and true-positives indicated by statistically significant voxels with higher FA in schizophrenia subjects compared to controls, in the four tracts investigated: CB, AF, UF, SCC (Fig. 2. b and c).





Conclusion: Despite having received little attention in the literature, geometric distortion may have a profound impact on both tractography and diffusion metrics, specifically FA, which appears to be substantially affected throughout the imaging volume.

1.Wu, M., et al., *Comparison of EPI distortion correction methods in diffusion tensor MRI using a novel framework.* Med Image Comput Comput Assist Interv, 2008. **11**(Pt 2): p. 321-9. 2.Jezzard, P., A.S. Barnett, and C. Pierpaoli, *Characterization of and correction for eddy current artifacts in echo planar diffusion imaging.* Magn Reson Med, 1998. **39**(5): p. 801-12. 3.Fedorov, A., et al., *3D Slicer as an image computing platform for the Quantitative Imaging Network.* Magn Reson Imaging, 2012. **30**(9): p. 1323-41. 4.Lienhard, S., et al., *A full bi-tensor neural tractography algorithm using the unscented Kalman filter.* EURASIP J Adv Signal Process, 2011. **2011**. 5.Oh, J.S., et al., *Thalamo-frontal white matter alterations in chronic schizophrenia: a quantitative diffusion tractography study.* Hum Brain Mapp, 2009. **30**(11): p. 3812-25. 6.Ohtani, T., et al., *Abnormalities in white matter connections between orbitofrontal cortex and anterior cingulate cortex and their associations with negative symptoms in schizophrenia: a DTI study.* Schizophr Res, 2014. **157**(1-3): p. 190-7. 7.Mori, S. and P. van Zijl, *Human white matter atlas.* Am J Psychiatry, 2007. **164**(7): p. 1005.