ZOOM and non-ZOOM Spinal Cord Diffusion Tensor Imaging protocols for multi-centre studies

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Target audience: Scientists and clinicians interested in spinal cord diffusion tensor imaging

Purpose: To develop and evaluate two spinal cord (SC) diffusion tensor imaging (DTI) protocols, implemented at multiple sites, one available on any clinical scanner, and one using more advanced options currently available in the research setting.

Introduction: The spinal cord (SC) is a common site of involvement in neurological disorders such as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), spinal cord injury and neuromyelitis optica (NMO) (1). DTI provides quantitative information about the microstructure of tissue *in vivo* and the diffusion behaviour of water molecules can be altered in pathology. By modelling the signal behaviour of diffusion using DTI in tissue, it is possible to derive several indices that may be sensitive biomarkers for characterising tissue microstructural abnormalities. These are the fractional anisotropy (FA), mean diffusivity (MD), and axial and radial diffusivities (AD and RD). However, there are many technical challenges associated with making quantitative measurements in the SC *in vivo* due to its small cross-sectional size and the potential for SC motion (both physiological and bulk motion) during scans. Additionally, various issues may arise from the use of rapid imaging techniques such as echo planar imaging (EPI), in particular geometric distortions due to susceptibility differences of air, bone and tissue, and through-plane dephasing resulting in signal drop-out (2). Various research developments have endeavoured to overcome these challenges, however such options are not necessarily widely available on standard clinical scanners. We developed two SC DTI protocols (neither requiring any pulse sequence programming); one which can be implemented on any standard clinical MRI scanner, and one utilising research options not yet commercially available, the goal being to ascertain which protocol could enter into clinical trials.

Methods: **MRI Acquisition:** Data were acquired on 3T scanners at three sites (1 – Philips Achieva (Philips Healthcare, Best, The Netherlands), 2 – Philips Achieva (Philips Healthcare, Best, The Netherlands), and 3 – TIM Trio (Siemens Healthcare, Erlangen, Germany)). Five subjects were scanned at sites 1 and 3, and four at site 2 (in total, 7M, 7F, mean age 26.8 ± 5.7 years). The first protocol used a reduced field-of-view (rFOV) sequence (zonally magnified oblique multi-slice (ZOOM) (3) for the two Philips sites and single shot 2DRF selective excitation (4) for the Siemens site). The rFOV EPI sequence (ZOOM or 2DRF) makes use of a reduced FOV (either through an inner volume imaging technique or a reduced excitation area) to achieve a shorter echo train length (ETL), thereby reducing artefacts caused by susceptibility changes between soft tissue and the adjacent vertebrae. However, this option is currently not standard on most clinical scanners, therefore we also acquired data using an outer volume suppression (OVS) technique (i.e., using saturation bands), with the best possible options available on each scanner with no research implementations. We attempted to match both protocols as far as possible between different scanner manufacturers. For both sequences 21 5mm axial slices were acquired (phase encoding anterior/posterior), with in-plane resolution 1x1mm^2, and the FOV centred at the level of the C2-3 intervertebral disc, and spanned levels C1-C7 in all volunteers. Cardiac gating via peripheral pulse oximitry was used in all protocols to reduce physiological motion. The b-value was set to 750s/mm^2 for all sequences, and 30 gradient directions and 5b0s were acquired at the Siemens site, and 32 directions and 4b0s at the two Philips sites. Other parameters specific to each protocol were:

Philips OVS: TR~7000ms, TE=72ms, matrix=100x100, saturation bands positioned anteriorly and posteriorly (A/P) to avoid aliasing; Bandwidth (BW)=893.1Hz.

Siemens OVS: Single shot EPI with twice refocusing pulse (5), TR~3000ms, TE=89ms, matrix = 96x96, partial Fourier = 6/8, saturation bands A/P; BW=1085 Hz.

Philips ZOOM: TR~7000ms, TE=50ms, matrix=64x48; BW=2097.0Hz

Siemens ZOOM: Single shot EPI 2D RF excitation with monopolar pulse, TR~2800ms, TE=89ms, matrix = 192x38, BW=1132 Hz.

Image analysis: Standard DTI parameters were obtained by a single observer using the open-source Camino toolkit (6). Mean b0 images were used for segmentation of the cord from surrounding CSF, using an active surface model (7) implemented in Jim (Xinapse systems, www.xinapse.com), with manual adjustments made where necessary. Intra- and inter-site comparisons of whole-cord parameter values were performed using Excel.

Results: Mean MD, FA, AD and RD values (± standard deviations (SD)) for each site and protocol are given in Table 1. Figure 1 shows the central 5 slices of mean b0 images for a single subject for both protocols. Images acquired using the ZOOM sequence (bottom row) appear less distorted.

Table 1: Mean MD, FA, AD and RD values (± SD) for each site and protocol

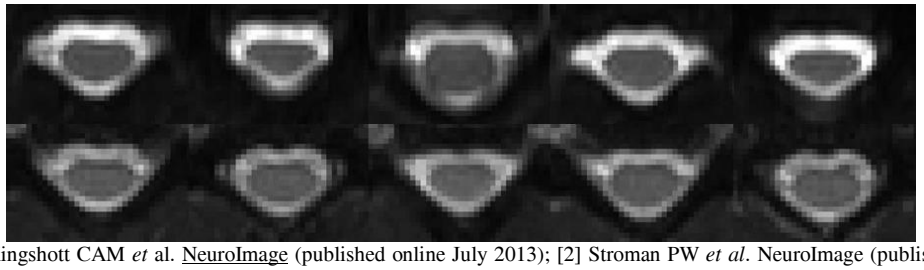
DTI parameter	1 – OVS	2 – OVS	3 – OVS	1 – ZOOM	2 – ZOOM	3 - ZOOM
MD	1.39 (±0.15)	1.32 (±0.32)	1.45 (±0.30)	1.21 (±0.07)	1.17 (±0.15)	0.88 (±0.15)
FA	0.59 (±0.04)	0.59 (±0.08)	0.54 (±0.09)	0.61 (±0.04)	0.61 (±0.04)	0.58 (±0.05)
AD	2.20 (±0.16)	2.22 (±0.33)	2.27 (±0.27)	2.13 (±0.12)	2.06 (±0.13)	1.49 (±0.31)
RD	0.84 (±0.14)	0.86 (±0.31)	1.05 (±0.32)	0.75 (±0.09)	0.72 (±0.16)	0.58 (±0.09)

Discussion and Conclusions: SC MD, FA, RD and AD values obtained using both sequences at all sites were consistent with previous measurements made at 3T (8,9). Intra-site SDs were larger for all parameters measured using the OVS sequence than the ZOOM sequence. Site 3 showed a large difference in DTI indices between the OVS and ZOOM sequences. Inter-site coefficients of variation (CVs (%)) for MD, FA, AD and RD were 6.30, 5.22, 12.5 & 1.37 respectively for the OVS sequence and 16.4, 2.51, 13.4 & 18.6 for the ZOOM sequence. However, it should be acknowledged that the two implementations of the rFOV protocol are very different, for instance, the Siemens protocol has a longer TE which has an impact on signal-to-noise ratio (SNR), and in turn can affect the accuracy of the fitted DTI parameters. Ongoing work is investigating other acquisition issues such as shimming and cardiac gating. Encouragingly, for the two Philips sites alone these CVs were reduced to 1.37, 0.56, 0.94 & 2.23 for OVS and 1.05, 0.60, 0.67 & 1.81 for ZOOM. For the two Philips sites the inter-site CVs are lower for the ZOOM sequence than the OVS sequence, with values of less than 2%, which is reassuring considering that the volunteers were different at different sites.

Since Philips scanners do not allow the possibility of interleaving b0 images within the diffusion-weighted images without the use of pulse programming), it was not possible to reliably motion correct our data, which may improve reproducibility of measured DTI indices. A larger multi-centre study including scan-rescan tests, and scanning of the same subjects at different sites are also required to further evaluate the protocols developed.

The lower intra- and inter-site reproducibility (for the same manufacturer and acquisition details) of ZOOM compared to the OVS sequence supports the idea that making research options such as ZOOM more widely available would improve accuracy of measurements obtained in multi-centre clinical trials. Future multi-centre studies should also aim to SNR-match all sequences from different manufacturers/sites in order to avoid any bias in measured DTI parameters.

Figure 1: Example single subject mean b0 images acquired using the OVS (top) and ZOOM sequence (bottom) (acquired at site 2)



References: [1] Wheeler-Kingshott CAM *et* al. NeuroImage (published online July 2013); [2] Stroman PW *et al*. NeuroImage (published online May 2013); [3] Wheeler-Kingshott CAM *et al* NI 2002; 16:93–102; [4] Finsterbusch *et al.* JMRI 2009; 29(4):987-93; [5] Reese TG *et al*. Magn Reson Med 2003; 49:177–182; [6] Cook PA *et al* Proc 14th Annual Meeting ISMRM 2006, Seattle, USA, 2759; [7] Horsfield MA *et al*. NI 2010; 50: 446-455; [8] Uda T *et al.* J Cran Junc Spine 2011; 2(2): 77-81; [9] Brandner A *et al*. Acta Radiol (published online Aug 2013)

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