Multisite DTI of the spinal cord with integrated template and white matter atlas processing pipeline

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Target audience. Scientists and clinicians interested in spinal cord diffusion tensor imaging and template-based group analysis.

Purpose. Spinal cord MRI has tremendous potential for improving diagnosis/prognosis in neurodegenerative diseases and trauma as well as for investigating pathophysiological processes that could be then targeted by the development of new drugs. In particular, multi-parametric MRI, which combines several semi-quantitative techniques (e.g., diffusion-weighted imaging, magnetization transfer) provides a variety of biomarkers sensitive to white matter integrity and neuronal function [1]. However, spinal cord MRI in research and clinical settings is underutilized, a direct consequence of the difficulties related to the acquisition and processing techniques. In fact, only very few multi-disciplinary centers around the world can benefit from state-of-the-art multi-parametric quantitative MRI techniques in the spinal cord. *Objectives*. To propose and validate a standard acquisition protocol and processing pipeline for DTI of the spinal cord and demonstrate its applicability within a small-scale multi-site study.

Methods. *Acquisition*. Data were acquired at 3T at three sites: London (Achieva, Philips Healthcare), Vanderbilt (Achieva, Philips Healthcare) and Montreal (TIM Trio, Siemens Healthcare). Five subjects were recruited in London and Montreal, four at Vanderbilt (in total 7M, 7F, mean age 26.8 ± 5.7years). The acquisition protocol was based on a reduced-FOV acquisition, matched across vendors at far as possible, while benefiting from the best protocol at each site. The reduced-FOV protocol consisted of the ZOOM sequence [2] (London and Vanderbilt sites) and the 2DRF selective excitation technique [3] (Montreal site). Common parameters were: single shot EPI, single refocusing pulse, cardiac gating, in-plane resolution = 1x1mm^2, slice thickness = 5mm, number of slices = 21, coverage: C1-C7, b-value = 750 s/mm^2, number of gradient directions = 30. Specific parameters were: Montreal: TR~2800ms, TE=89ms, matrix=192x38, bandwidth=1132 Hz/pixel; London/Vanderbilt: TR~7000ms, TE=50ms, matrix=64x48; BW=2097Hz. *Processing*. All data were preprocessed in the native space by a single person (R.S.) using the Camino toolkit. All data were then registered to the spinal cord template MNI-Poly-AMU [4]. Using ANTS, a series of affine and diffeomorphic transformations were estimated between the b=0 image, the anatomic data and the template. The combined transformations were then applied to the DTI indices. *Quantification*. A newly-developed atlas of white matter tracts that takes into account partial volume effects and that is merged to the template was used to quantify DTI indices (FA: fractional anisotropy, MD: mean diffusivity) within the dorsal fasciculus gracilis and lateral corticospinal tracts (CST). Values were then compared intra- and inter-site and a 3-way ANOVA was performed to test the effect of site, subject and laterality (right/left).

Results. The bottom left figure shows the result of the within site-averaged b=0 and FA at a single slice centered at the C3 vertebral body. Data from all sites were adequately registered to the template (shown on the top right panel). The bottom right panel shows the white matter tracts selected for quantifications from the white matter atlas (red: left CST, green: right CST, blue: left gracilis, yellow: right gracilis). Results of ANOVA on the CST using FA show no effect for site (p=0.09), subject (p=0.06) and laterality (p=0.35). Results of ANOVA on the CST using MD show an effect of site (p=0.005), no effect for subject (p=0.14) and no effect for laterality (p=0.90). Similar results were obtained on the fasciculus gracilis. Average FA and MD are plotted on the bottom right figure (L=London, V=Vanderbilt, M=Montreal).

Discussion. This study shows the feasibility of acquiring spinal cord DTI data at different vendor sites, processing them with a unique pipeline, registering them to an external template and quantifying metrics with atlas-based regions. Different subjects were scanned across sites, to reproduce the setting of multicenter trials where the reproducibility of a healthy population is key as well as the sensitivity to change (for which longitudinal data would be needed). The analysis method is applicable to other quantitative MRI techniques, such as magnetization transfer and functional MRI.

References. **[1]** J Cohen-Adad et al., *NeuroImage*, 2011. 55(3): p. 1024-33. **[2]** CA Wheeler-Kingshott et al., *NeuroImage*, 2002. 16(1): p. 93-102. **[3]** J Finsterbusch et al, *J Magn Reson Imaging*, 2009. 29(4): p. 987-93. **[4]** VS Fonov et al. *Proc. ISMRM* 2013: p. 1119.

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