GREY MATTER AND WHITE MATTER VOLUME MEASUREMENTS IN THE CERVICAL CORD IN-VIVO: A PILOT STUDY WITH APPLICATION TO MAGNETISATION TRANSFER

M. C. Yiannakas[1], H. Kearney[1], R. S. Samson[1], D. T. Chard[1], O. Ciccarelli[2], D. H. Miller[1], and C. A. Wheeler-Kingshott[1]
[1]Neuroinflammation, UCL Institute of Neurology, London, United Kingdom, [2]Brain Repair and Rehabilitation, UCL Institute of Neurology, London, United Kingdom

INTRODUCTION: With the advent of high magnetic field MR systems in recent years, the potential to image the spinal cord with higher spatial resolution has received growing interest. In multiple sclerosis (MS), for example, the ability to detect changes in the mean cross-sectional area of the cervical cord over time indicates the presence of cord atrophy, which correlates with neurological disability [1]. At the same time, pathological studies of the spinal cord in MS have shown that focal and diffuse abnormalities are present in both white (WM) and grey matter (GM) [2]. However, tissue specific measurements in the spinal cord with the use of clinically available MR systems is technically challenging and highly underestimated, mainly due to signal to noise (SNR) limitations coupled with the effects of motion. In this work we present an optimised high resolution *in-vivo* imaging protocol of the cervical cord using a 3T MR system. We used the optimised protocol to scan a number of healthy control subjects and then performed WM and GM volumetric measurements by means of image segmentation. Alongside the first report of WM and GM volumes estimated from cervical cord images, we present tissue-specific normal magnetisation transfer ratio (MTR) values of the cervical cord, which may be extended, in the future, to study patients with MS and other neurological diseases. It is known that MTR values correlate histologically with axonal loss and demyelination [3], which make MTR an important MR parameter to study *in-vivo* alongside volumetric measurements.

METHOD: A) Study participants: five healthy control subjects were recruited (mean age 29 years, range 27-31, 4 male, 1 female). Informed consent was obtained from all participants and the study was approved by the local institutional review board. B) MR Imaging: Using a 3T Philips Achieva MRI system with RF multi-transmit technology (Philips Healthcare, Best, Netherlands) and the manufacturer's product 16-channel neurovascular (NV) coil, the cervical cord was imaged in the axial plane (i.e. slices perpendicular to the cord) with the center of the imaging volume positioned at the level of C2-3 intervertebral disc. The following sequences were acquired: (i) for volumetric measurements, a fat-suppressed 3D slab selective fast field echo (FFE) sequence was optimised with TR = 23 ms; TE = 5ms; flip angle α = 7°; FOV= 240 x 180 mm; voxel size = 0.5 x 0.5 x 5 mm^3; NEX = 8; 10 axial contiguous slices; scanning time = 13:34 min. (ii) MTR imaging was optimised specifically to match (on a slice-by-slice basis) the resolution of the volumetric 3D FFE sequence. The details of the MTR sequence were as follows: A 3D slab selective FFE sequence with two echoes (TR=36 ms, TE1 / TE2 = 3.5 / 5.9 ms, flip angle α = 9°) was performed with and without Sinc - Gaussian shaped MT saturating pulses of nominal α = 360º, offset frequency 1 kHz, duration 16 ms. Twenty-two slices 5 mm thick were acquired in an axial orientation, with FOV = 240 x180 mm and acquisition matrix 240 x 320 (voxel size 0.75 mm x 0.75 mm, reconstructed to 0.5 mm x 0.5 mm), with SENSE acceleration factor = 2 in the foot / head direction. The total acquisition time for both the MT-on and MT-off sequences was approximately 15 minutes and the total imaging protocol was approximately 30 min. In order to minimise the effect of motion in the neck during imaging, particular attention was given to the immobilisation technique which involved the use of an adjustable MR-compatible cervical collar, similar to the ones most commonly used in cases of whiplash injuries. All subjects were imaged on 3 separate occasions with the same imaging protocol and the reproducibility of all measurements was recorded from the coefficient of variation as a percentage value (COV%). C) Imaging analysis: Using the Jim Software (Xinapse systems, www.xinapse.com) a volume of 15 mm was analysed, as previously reported [1], by extracting the same three slices (middle slice through the C2-3 intervertebral disc) from the 3D-FFE, the MT-off and MTR–map (previously calculated from the whole MTR dataset). Image segmentation and volumetric measurements were performed using the 3D-FFE dataset only, firstly by segmenting the total cord volume (TCV) of the 15 mm section using an active surface model [4] and, secondly, by extracting the total grey matter volume (TGMV) with a semi-automated method that uses the fuzzy connector tool [5] available with the Jim software (see figure 1a and 1b). The grey matter volume fraction (GMVF) was then calculated from these two volumes as the ratio between TGMV and TCV. MTR measurements were taken from the same regions on the MTR-maps (see figure 1c) by verifying the positioning of the regions (and adjusting these where necessary) on the MT-off images first. Datasets that displayed motion between the MT-off and MT-on were not included in the analysis.

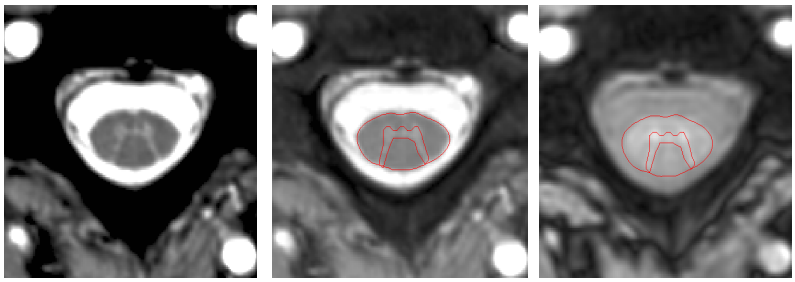

Figure 1. a) Axial 3D-FFE image (resolution 0.5 x 0.5 x 5 mm) through the C2-3 intervertebral disc b) segmentation boundaries from where TCV and TGMV are measured c) segmentation boundaries displayed on the MT-off image from where the MTR values were then obtained from the MTR-map.

Measure	case1	case2	case3	case4	case5
TCV mm³ (COV%)	1472 (0.4)	1344 (2.2)	1240.7 (1.4)	1245 (0.6)	1300 (0.8)
TGMV mm³ (COV %)	207 (3.4)	201 (2.1)	195.4 (11.1)	181.7 (6.7)	202.9 (1.9)
GMVF (COV %)	0.16 (3.3)	0.18 (4.9)	0.19 (6.3)	0.17 (8.4)	0.18 (2.3)
WM-MTR (COV %)	51.7 (0.5)	53.5 (2.7)	52.1 (2.2)	52.3 (0.8)	51.1 (0.9)
GM-MTR (COV %)	51.1 (0.8)	53.2 (3.1)	50.7 (1.5)	50.7 (2.6)	49.9 (0.7)

Table 1. Volumetric and MTR measurements shown separately for each participant.

RESULTS: Mean TCV for the 5 control subjects was 1320.3 (± 94.8) mm³, mean TGMV was 197.7 (± 13.2) mm³ and GMVF was 0.18 (± 0.01). Mean total volume WM-MTR was 52.1 (± 0.9) and total volume GM-MTR was 51.1 (± 1.3). Table 1 shows the results for each of the 5 control subjects separately along with the COVs from the reproducibility study (3 repeated measurements).

CONCLUSION: A method has been presented here which enables tissue specific volumetric measurements in the cervical cord of healthy control subjects with the use of a clinically available MR system. Careful optimisation of the MR parameters for use within the imaging protocol coupled with special attention to the immobilisation technique has been shown here to allow GM and WM volumetric measurements, with a good inter and intra-subject reproducibility. The clinical relevance of this finding will be assessed in future studies of the cervical cord. As well as the volumetric measurements, we have reported tissue-specific MTR values, as determined with the specific MT pulse and sequence used in this study. Future investigations will be directed at improving the acquisition protocol presented here, by refining the image segmentation methods used and also by introducing image registration methods to correct for differences in cord position in multi-parametric acquisitions.

REFERENCES: 1) Losseff N. A et al, (1996), Brain, 119: 701-708. **2)** Gilmore C. P et al, (2009), Multiple Sclerosis, 15: 180-188. **3)** Bot J. C. J et al, (2004), Radiology, 233: 531-540. **4)** Horsfield M, A et al, (2010), Neuroimage, 50: 446-455. **5)** Udupa JK, Samarasekera S. (1996), Graphical Models and Image Processing, 58: 246-261.