Comparison of cervical cord results from a quantitative 3D multi-parameter mapping (MPM) protocol of the whole brain with a dedicated cervical cord protocol

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Synopsis

We present a comparison of cervical cord metrics obtained using both a whole brain and dedicated cord implementation of a recently introduced quantitative multi-parametric MRI protocol which provides apparent proton density, R_1, magnetisation transfer saturation (MT_{sat}) and R_2* maps sensitive to microstructural tissue changes in brain and spinal cord. Similar whole cervical cord (levels C1-C5) parameters were obtained using either protocol, and inter-subject variation was low, however in order to investigate tissue-specific cord parameters the dedicated cord protocol with higher in-plane resolution would be desirable.

Introduction

The spinal cord is commonly affected in neurological disorders such as multiple sclerosis, amyotrophic lateral sclerosis, cervical spondylotic myelopathy (CSM), and spinal cord injury(SCI)[1], however performing quantitative tissue-specific cord MRI can prove challenging due to its small cross-sectional size and potential for cord motion. Multi-parameter mapping (MPM) is a quantitative imaging technique utilising multi-echo 3D spoiled gradient echoes (SPGR) (and B_1 mapping for correction of T_1 values) to quantify several parameters including apparent proton density (APD), R_1 (=$1/T_1$), R_2* (=$1/T_2$*), and Magnetisation Transfer saturation (MT_{sat})[2-7]. We evaluated results obtained in the cervical cord (C1-C5) using 1) a whole brain MPM protocol with cord coverage to at least level C5, and 2) a dedicated cervical cord MPM protocol (potentially allowing higher in-plane resolution and coverage for a shorter acquisition time), with a view to applying the method in patients with CSM or SCI, above the injury level.

Materials and Methods

MRI Acquisition:

Seven healthy volunteers [2 females, age 32.9 ± 3.91 years (mean ± standard deviation (SD))] were scanned using a 3T Philips Achieva (Philips Healthcare, Best, The Netherlands), with a 32-channel head coil and multi-transmit technology. Both the brain and cord MPM protocols consisted of three (product) multi-echo 3D SPGR sequences (with bipolar gradients), with MT-(MTw), PD-(PDw) or T_1-weighting (T_1w) (details in Figure 1), and B_1 mapping using actual flip angle imaging (AFI)[8] (α=60°, TR1/TR2/TE=30/150/2.3ms).

Image Analysis:

Whole cord masks for each contrast acquired using both protocols were obtained semi-automatically using an active surface model[9] implemented in Jim (www.xinapse.com). These segmentations were input when co-registering different contrasts to the mean PDw volume (using spinal cord toolbox (SCT)[10]). SCT was used to label cord vertebrae and generate binary cord masks, and to perform cord segmentation, giving white (WM) and grey matter (GM) binary masks.

Processing was performed using in-house written matlab code. R_2* was estimated from the multi-echo PDw data, by linear fitting of the log of the signal. After averaging the within-contrast echoes, T_1 and APD were calculated from the PDw and T_1w images via a rational approximation of the SPGR signal[3]. The percentage MT saturation due to a single MT pulse (MTsat) was calculated from the PDw and MTw images by inserting the estimated APD and T_1 values in the approximate MT-SPGR signal equation[4,6]. T_1 maps were corrected for variations in the transmit field B_1.

Binary cord masks were applied to maps to give mean cervical cord (C1-C5) parameter values obtained using each protocol, as well as GM and WM values for the cervical cord protocol. Paired t-tests were performed to test for differences in mean whole cord parameter values between protocols.

Results

Example sagittal images with cord masks (levels C1-C5) overlaid for both protocols are shown in Figure 2.

Mean parameter values measured in the cord using both protocols are given in Figure 3, in addition to GM and WM values obtained using the cord protocol. When averaged across all the subjects for each protocol, the maximum whole cord inter-subject CoV was 26% for R_2* measured using the whole brain protocol, but was in the range of 5-12% for all other parameters measured using both protocols, consistent with literature[7].

Single slice parameter maps of the same subject obtained using both protocols at cord level C3 are shown in Figure 4.

Paired t-tests showed no significant differences between whole cord parameters acquired using either protocol, except for APD (p=0.047).

Discussion

Cervical cord parameter values measured at 3T in healthy volunteers using a whole brain and dedicated cord protocol were consistent with literature values[7,11,12], demonstrating the accuracy of both protocols, developed using only product sequences. With the exception of APD, mean whole cord parameters obtained from either protocol are within 10% of each other.

Paired t-tests showed no significant differences between parameters obtained from either protocol, except APD, which we attribute to the lack of calibration applied here (in the brain APD values are calibrated to the mean WM APD, however this was not possible since brain data were only acquired in one of the

protocols).

Conclusions

It is possible to obtain several quantitative cervical cord parameters in a clinically feasible time (~17/12mins for brain/cord protocols) using both a protocol set up for whole brain MPM, and a dedicated cervical cord protocol. Inter-subject variation is low using either protocol, and both protocols give similar whole cord parameter values. Using the dedicated cord approach, it is feasible to perform accurate GM segmentation, giving tissue-specific measurements in addition to whole cord values. Improvements in image analysis and segmentation methods would be necessary to fully exploit cord data acquired using the brain protocol[12].

Acknowledgements

References

[1] Wheeler-Kingshott, CAM et al Neuroimage 84:1082-93 (2014);

[2] Weiskopf N, Helms G Proceedings ISMRM 16: 2241 (2008);

[3] Helms G et al Magnetic Resonance in Medicine 59:667-72 (2008);

[4] Helms G et al Magnetic Resonance in Medicine 60: 1396-1407 (2008);

[5] Helms G et al Magnetic Resonance in Medicine 64: 177-85 (2010);

[6] Weiskopf N et al Frontiers of Neuroscience7: 95 (2013);

[7] Samson RS et al. NMR in Biomedicine 26(12):1823-30 (2013);

[8] Yarnykh V et al Magnetic Resonance in Medicine 57(1):192-200 (2007) ;

[9] Horsfield MA et al. NeuroImage 50: 446-455 (2010);

[10] De Leener B et al NeuroImage 15:145(Pt A):24-43 (2017);

[11] Smith SA et al Magnetic Resonance in Medicine 60(1): 213–219 (2008);

[12] Battiston M et al Magnetic Resonance in Medicine; in press, published online 24th July 2017;

[12] Prados F et al NeuroImage 152 :312-329 (2017).

Figures

Acquisition parameter	Sagittal whole brain protocol			Axial cervical cord protocol		
	MTw	PDw	T1w	MTw	PDw	T1w
TR (ms)	30	18	18	30	18	18
TE1 (ms)	2.4	2.4	2.4	2.4	2.4	2.4
ΔTE (ms)	2.4	2.4	2.4	2.4	2.4	2.4
Number of echoes	6	6	6	6	6	6
Flip angle α (°)	9	4	23	9	4	23
Field-of-view (mm³)	256x240x170	256x240x170	256x240x170	212x212x90	212x212x90	212x212x90
Resolution (mm)	1x1x1	1x1x1	1x1x1	0.6x0.6x3	0.6x0.6x3	0.6x0.6x3
Bandwidth (Hz/pixel)	481.4	481.4	481.4	480.3	480.3	480.3
MT pulse flip angle (°)	220			220		
MT pulse duration (ms)	8			8		
MT pulse offset frequency (kHz)	1.0			1.0		
Parallel imaging acceleration factor	2 (A/P), 1.25 (R/L)	2 (A/P), 1.25 (R/L)	2 (A/P), 1.25 (R/L)	2 (A/P), 1.25 (R/L)	2 (A/P), 1.25 (R/L)	2 (A/P), 1.25 (R/L)
Partial Fourier	5/8	5/8	5/8	5/8	5/8	5/8
Signal Averages	1	1	1	3	3	3
Acquisition time (mins)	3:39	3:39	6:05	2:45	2:45	4:36

Figure 1: Acquisition details of the sagittal whole brain and dedicated axial cervical cord MPM protocols. The sequences were set up so as to give approximately equivalent signal-to-noise ratio (SNR) in each protocol, with voxel volumes approximately equal (1x1x1mm³ for brain and 0.6x0.6x3mm³ for cord), and 3 signal averages acquired for the cord protocol to compensate for the lower number of phase encoding steps for a reduced field-of-view (FOV). Other acquisition parameters (TE, ΔTE, TR, flip angle, MT pulse details, etc) were the same for both protocols.
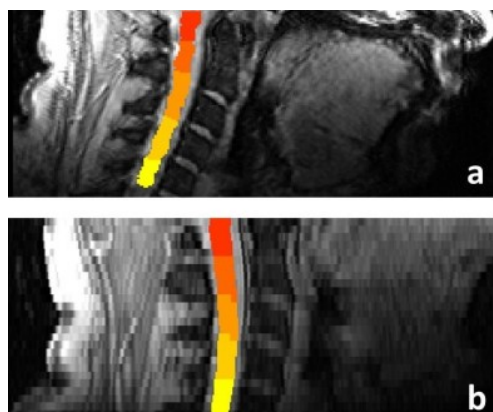
Figure 2: Sagittal images with cervical cord masks (levels C1-C5) overlaid on mean PDw images acquired using (a) the sagittal whole brain protocol, and (b) the axial cervical cord protocol. Vertebral levels range from C1 (red) to C5 (yellow).

MPM parameter	Sagittal brain protocol whole cord value	Axial cervical cord protocol		
		Whole cord	GM	WM
APD [A. U.]	$7.75 (\pm 0.89) \times 10^6$	$6.87 (\pm 1.42) \times 10^6$	$7.25 (\pm 1.23) \times 10^6$	$6.59 (\pm 1.05) \times 10^6$ ***
T_1 (s)	1.16 (±0.062)	1.08 (±0.08)	1.19 (±0.11)	1.06 (±0.08) ***
MT_{sat} (pu)	2.81 (±0.31)	3.08 (±0.36)	2.90 (±0.32)	3.19 (±0.34) **
R_2^* (s⁻¹)	23.4 (±6.13)	23.0 (±2.01)	20.9 (±1.12)	24.0 (±1.24) ***

Figure 3: Mean whole cervical cord (levels C1-C5) parameter values obtained using the sagittal brain MPM protocol and whole cord, grey (GM) and white matter (WM) parameters measured using the dedicated axial cervical cord protocol: PD* (arbitrary units (A.U.)), T_1 (s), MT_{sat} (percent units (pu)) and R_2^* (s⁻¹). Cervical cord WM and GM values were found to be significantly different from each other (**$p<0.01$, ***$p<0.001$).
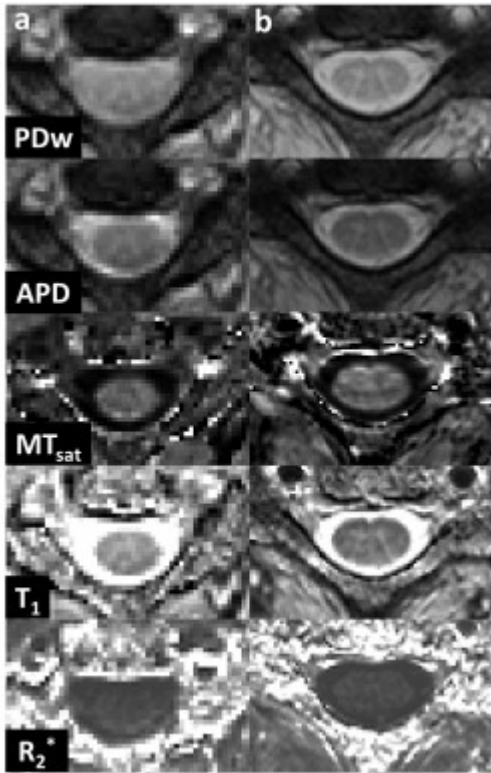

Figure 4: Axial single slice mean PDw image (at cervical level C3) and corresponding parameter maps acquired using (a) the whole brain protocol, and (b) the cervical cord protocol.