Multi-parameter mapping of the human cervical cord at 3.0T in less than 20 minutes

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Introduction: The spinal cord is a common site of involvement in neurological disorders such as multiple sclerosis (MS). High field post mortem MRI studies have demonstrated focal and diffuse abnormalities in cord white (WM) and grey matter (GM) (1). It has also been demonstrated that myelin content and axonal density in MS cord WM correlate with T_1, T_2, proton density (PD) and Magnetisation Transfer Ratio (MTR) at high field (2,3). However, performing quantitative cord MRI measurements *in vivo* is challenging due to its small cross-sectional size and the potential for cord motion.

A technique has been developed recently using multi-echo 3D FLASH to quantify several parameters in the brain including apparent PD, T_1, R_2^* (=$1/T_2^*$), MTR and a new parameter MT (4,5,6). We aimed to apply this imaging protocol at 3T in the cervical cord and here we present preliminary data from 12 healthy subjects.

Methods - Acquisition: 12 subjects (11 male, 1 female, aged 38.1±11.8) were scanned on a 3T Magnetom TIM Trio scanner (Siemens Medical Solutions, Erlangen, Germany) with a head, neck and spine receiver coil. For the 3D multi-parameter mapping sequences, 80 3mm thick partitions were acquired, with axial field-of-view (FOV)=200mmx200mm, 256x256 acquisition matrix, sinc interpolated in image space to 512x512, and phase encoding anterior/posterior (A/P), with GRAPPA acceleration factor 2 in the phase encoding direction. A slab selective 3D multi-echo FLASH sequence (4,5) was performed 3 times, with MT (MTw), PD (PDw) or T_1 weighting (T_1w). For the PDw images (TR=24.05ms, flip angle (α)=6º), magnitude and phase images were acquired from 8 gradient echoes at equally spaced echo times between 3.0ms and 18.55ms (425Hz/pixel BW). The MTw data were acquired with an additional 4ms off-resonance Gaussian RF pulse (nominal α=220º, offset frequency 2kHz) before each excitation pulse, and T_1w data were acquired with TR=22ms, α=20º.

The spatial distribution of the B_1 transmit field was measured using a modified 3D actual flip angle imaging (AFI) method (7) with alternative RF/gradient spoiling scheme (8), with two excitation pulses of α =60° followed by delays of 50 and 150ms and a gradient echo readout at TE=3.05ms. 40 6mm partitions were acquired, with FOV=200mmx200mm, and acquisition matrix 64x64, i.e. pixel size 3.13x3.13, sinc interpolated to 0.39x0.39, to enable correction of the T_1 maps. The total acquisition time including B_1 mapping was approximately 19 minutes.

Methods - Analysis: Processing routines developed for use with SPM8 and FSL were used for analysis (4,5,6). T_2^* was estimated from the multi-echo 'PDw' acquisition sequence, by linear fitting of the log of the signal. For the calculation of the other parameter maps, the first 6 echoes were averaged, and then T_1 and the amplitude A (apparent PD) were calculated from the PDw and T_1w images via a rational approximation of the FLASH signal (5). The parameter MT represents the additional percentage MT saturation of the longitudinal magnetization due to a single MT pulse, and is calculated by inserting the estimated A and T_1 values in the approximate signal equation for the MT-FLASH experiment (6).

Semi-automatic cord segmentation was performed on the T_1w images using a method based on an active surface model (9) implemented in the Jim software library (www.xinapse.com). Masks were generated for each subject over 5 slices centred on cervical cord level C2 and spatial mean parameter values and standard deviations (SDs) were examined. Intra-subject variation was investigated by re-calculating parameter maps for all subjects using subsets of only even or odd echoes acquired for each of the MTw, T_1w and PDw data.

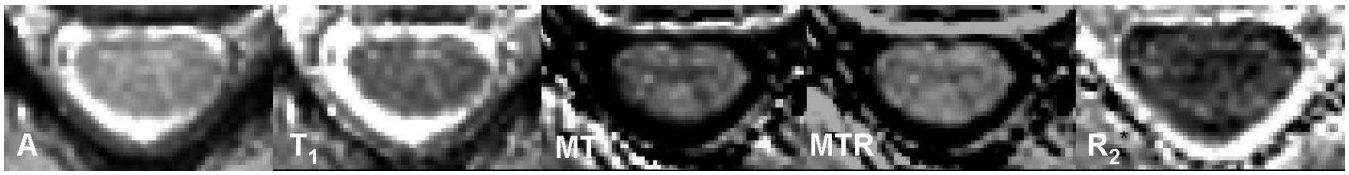

Figure 1: Example parameter maps for a single subj ect

Results: Example A, T_1, MT, MTR and R_2^* maps for a single subject at cervical cord level C2 are shown in figure 1. Grey and white matter appear to be better differentiated in the MT maps than the MTR maps, indicating enhanced sensitivity to macromolecular content differences in tissue which could be attributed to the elimination of B_1 and T_1 dependence in the MT parameter maps in comparison to the MTR (6). Table 1 gives cord parameter mean values (with SDs in brackets) measured over 5 slices centred at the level of C2.

Two subsets of odd and even echoes were used in the processing routines to recalculate parameter maps of A, T_1, MT and MTR, i.e. using only half the data in each case, but with the same effective echo time. This could be assumed to approximate an upper limit of intra-subject reproducibility in parameter values. Paired t-tests were then performed on the two sets of parameter values for each subject, and demonstrated that the sample means were not significantly different (the p-values obtained ranged from 0.12 to 0.77).

Table 1: Mean parameter values for 12 subjects

Parameter	Mean Histogram Peak Location (± SD)
A (a. u.)	4367 (± 667)
T_1(ms)	1535 (± 185)
MT (pu)	1.20 (± 0.11)
MTR (pu)	36.43 (± 1.64)
R_2^* (s^{-1})	20.46 (± 1.56)

Cervical cord T_1, R_2^* and MTR mean values are consistent with previously reported 3T values (10), and parameters are similar to those obtained using the same technique in the brain at 3T (5,6). Intra-subject variation, as estimated by repeating the processing with subsets of odd or even echo data, was found to be between 0.01 and 15 % for all parameters in all subjects, although this was much less than 10% in 9 of 12 subjects in all parameters. These estimates of the maximal intra-subject variation are low, especially considering that they were obtained using only half the data in each case.

Discussion: The method described here provides measurements of several quantitative and semi-quantitative MRI parameters at 3.0T in the cervical cord in a clinically feasible time (<20min in total). Cervical cord measurements in 12 healthy volunteers yielded parameter values consistent with literature values measured at 3T in the brain using this technique (5,6), and cord (via alternative methods) (10), demonstrating the accuracy of the technique, and the low intra-subject variation in mean parameter values demonstrates the reproducibility of measurements made using this method. Inter-subject coefficients of variation (CoV) are low, and comparable to literature values. The CoVs for MTR and MT are just 4.5% and 8.8% respectively, which are lower than those observed in a reproducibility study of another MT measure applied in the spinal cord at 3T (approximately 10%) (11). The R_2^* CoV is also very low (7.6%), but CoVs in T_1 and A are larger (12.1% and 15.3% respectively). A recent study that measured T_1 and T_2 in WM and GM regions in the cervical cord at 3.0T found the T_1 reproducibility to be slightly lower (between 5 and 10%), but these are for separate GM and WM regions on a single slice at the C3 level so are not directly comparable to the results presented here (12).

B_1 inhomogeneity proved to be a major source of variation in signal intensity in the acquired images, and was accounted for by B_1 correction in the maps of A and T_1. However receive inhomogeneity is not accounted for in the A maps and may have contributed to the inter-subject variation observed. Therefore inclusion of receive sensitivity mapping in the protocol may be desirable. Also, although inhomogeneities in the transmit/receive RF field are intrinsically compensated in the parameter MT, since we used slab-selective excitation to avoid signal wrap-around, in contrast to the non-selective excitation of the same technique applied in the brain (5,6), we could not assume that transmit B_1 errors are optimally cancelled in all areas.

The technique described is rapid and provides several quantitative MRI measures, which could be applied to examine changes in studies of neurological disease affecting the spinal cord, either on a region-of-interest or volumetric basis. In addition to standard relaxation parameters, the parameter MT is of particular interest since, unlike the MTR (13), it is minimally affected by T_1 relaxation and is less sensitive to B_1 inhomogeneities.

References: [1] Gilmore CP *et al* Mult Scler 15: 180-188 (2009), [2] Mottershead JP *et al* J Neurol 250: 1293-1301 (2003), [3] Bot JCJ *et al* Radiology, 233: 531-540 (2004), [4] Weiskopf N & Helms G Proc ISMRM 16: 2241 (2008), [5] Helms G *et al* MRM 59:667-72 (2008), [6] Helms G *et al* MRM 60: 1396-1407 (2008), [7] Yarnykh V *et al* MRM 57 (1): 192-200 (2000), [8] Lutti A *et al* MRM 64: 229-38 (2010), [9] Horsfield MA et al NeuroImage 50 (2010) 446-455, [10] Stanisz GJ et al MRM 54:507-12 (2005), [11] Smith SA *et al* NMR in Biomed 23:207-17 (2010), [12] Smith SA *et al* MRM 60: 213-9 (2008), [13] Helms G *et al* MRM 64: 177-85 (2010)

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