Intra and Inter-Site Reproducibility of Myelin Water Volume Fraction Values Derived using mcDESPOT

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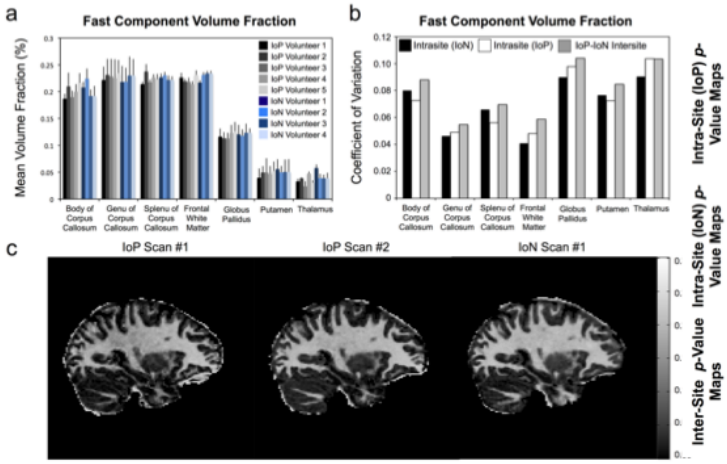
INTRODUCTION: Investigation of neuronal tissue microstructure, integrity and biochemical composition has wide neuroscience application. Multi-component relaxometry, which aims to decompose the measured MR signal into contributions from discrete micro-anatomical water components, provides specific information related to tissue micro-structure and has demonstrated utility in white matter disorders, such as multiple sclerosis[1], and psychiatric disorders, such as schizophrenia[2]. Recently introduced, mcDESPOT (multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2)[3], offers a promising alternative to conventional T_2-based multi-component relaxometry techniques. To be of broad applicability, however, the method should provide consistent estimates or have high intra-site reproducibility, of relaxation time and volume fraction parameters. Further, values should agree across imaging centres (high inter-site reproducibility) in order to permit meaningful comparisons across data from different groups, and to allow application of the technique to increasingly common multi-centre investigations. The aim of this work, therefore, was to establish the intra- and inter-site reproducibility of mcDESPOT-derived myelin water volume fraction (f_{MW}) estimates.

METHODS: 9 healthy volunteers (3 male, 6 female, 23-41 years of age) were recruited to the study. Imaging was performed across two imaging centres, the Institute of Psychiatry (IoP), and Institute of Neurology (IoN), London, UK, each equipped with GE 1.5T clinical scanners. Five of the volunteers were scanned on repeat occasions at the IoP and four volunteers were scanned on repeat occasions at the IoN (mean time between scans was 1 week). Seven volunteers were scanned at both centres (mean time between scans was, again, 1 week). A summary of acquisition parameters are provided in Table 1. Total acquisition time for each volunteer was approx. 14 minutes. Following data acquisition, volunteer images were linearly co-registered[4], non-brain signal removed[5], and f_{MW} maps calculated using mcDESPOT analysis[3]. Finally, each volunteer's data were non-linearly co-registered to MNI standard space[6]. Mean values were calculated from regions of interest were placed within 6 brain regions / tissues, including the body, genu and splenium of the corpus callosum, frontal white matter, thalamus, putamen and globus pallidus and reproducibility, defined as the absolute percent standard deviation across the repeated measures from all volunteers) was calculated for the intra-IoP, intra-IoN and inter IoP-IoN data.
Further, to verify that no site or time-point differences existed amongst the data, all maps were smoothed with a 5mm full-width-at-half-maximum 3D Gaussian kernel and voxel-wise paired t-tests were performed between the intra-IoP, intra-IoN and inter IoP-IoN data.

Centre	Manufacturer	Field of View	Image Matrix	SPGR Parameters		SSFP Parameters	
IoP	GE	22 cm^2 x 15 cm	128^2 x 86	***TE / TR / BW***	***Flip Angles***	***TE / TR / BW***	***Flip Angles***
				2.5ms/5.3ms/38kHz	[3, 4, 5, 6, 7, 8, 11, 13, 18]	1.8ms/3.6ms/100kHz	[10, 14, 19, 24, 28, 34, 41, 51, 67]
IoN	GE	22 cm^2 x 15 cm	128^2 x 86	***TE / TR / BW***	***Flip Angles***	***TE / TR / BW***	***Flip Angles***
				2.8ms/6ms/38kHz	[3, 4, 5, 6, 7, 8, 11, 13, 18]	2ms/4ms/100kHz	[10, 14, 19, 24, 28, 34, 41, 51, 67]

Table 1: mcDESPOT Acquisition parameters at the IoP and IoN imaging centres.

RESULTS: Mean f_{MW} values calculated for each volunteer across each of the 6 brain tissues are shown in Fig. 1a and reveal strong agreement across the healthy population. Intra- and inter-site reproducibility values are shown in Fig. 1b for each brain region investigated, with coefficient of variation values ranging from 0.045 in the genu of the corpus callosum and frontal white matter, to 0.107 in the grey matter globus pallidus and thalamus. Averaged over all regions, the intra-site coefficient of variation was 0.07 for both the IoP and IoN, with the inter-site coefficient of variation found as 0.08. Results of the voxel-wise paired *t*-tests are shown in Fig. 2. Even without false discovery rate (FDR) correction, no voxels were found to be statistically different between the two time-points or across centres.



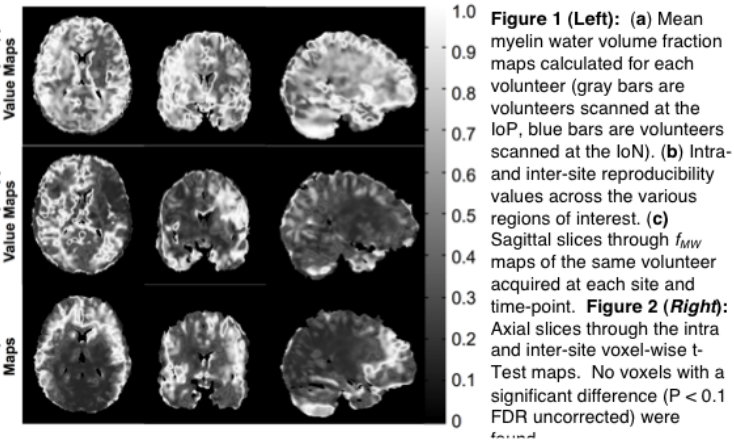


Figure 1 (Left): (**a**) Mean myelin water volume fraction maps calculated for each volunteer (gray bars are volunteers scanned at the IoP, blue bars are volunteers scanned at the IoN). (**b**) Intra- and inter-site reproducibility values across the various regions of interest. (**c**) Sagittal slices through f_{MW} maps of the same volunteer acquired at each site and time-point. **Figure 2 (*Right*):** Axial slices through the intra and inter-site voxel-wise t-Test maps. No voxels with a significant difference ($P < 0.1$ FDR uncorrected) were found.

DISCUSSION / CONCLUSIONS: Results of this study demonstrated the high reproducibility of the mcDESPOT multi-component relaxometry technique, both longitudinally and across different imaging centres. A perceived advantage of quantitative imaging, compared with conventional qualitative T_1 or T_2-weighted imaging, is the insensitivity of derived estimates to acquisition parameters or hardware, allowing data to be acquired at multiple different sites and pooled for analysis. Here we have demonstrated the ability to pool mcDESPOT data acquired at two different imaging sites without observing significant site biases.

REFERENCES: [1] Laule C et al. Mult. Scler. 2006; 12: 747-753 [2] Flynn SW et al. Molecular Psych. 2003; 8: 811-820. [3] Deoni SCL. et al. Magn. Reson. Med. 2003; 46:515-526, [4] Jenkinson M, Smith SM. MIA. 2001; 5: 143-156. [5], Zhang Y, et al. IEEE Trans Med. Imag. 2001; 20: 45-57. [6] Collins DL. et al. J Comput. Assist. Tomogr. 1994; 18: 192-205.