

## Myelin Sensitive Multi-Component DESPOT Imaging in Multiple Sclerosis

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### Abstract:

The relationship between multiple sclerosis (MS) and early micro-structural changes in brain tissue is at the forefront of ongoing research in the fields of neuroimaging and clinical neurology [1]. Quantitative MR imaging techniques that permit the formation of maps of underlying MR parameters such as tissue longitudinal (T1) and transverse (T2) relaxation time, have the ability to detect early disease-related changes of brain white matter (WM), and therefore are expected to play an increasingly prominent role in MS research.

### Purpose:

The main goal of this study was to utilize *multi-component Driven Equilibrium Single Pulse Observation of T1 and T2* (mcDESPOT) [2], a novel myelin-sensitive MR imaging method, and to explore its capability to depict changes in Normal Appearing White Matter (NAWM) in different types of MS. We focused on the myelin volume fraction ( $VF_M$ ) a parameter derived by mcDESPOT data processing. Clinically Isolated Syndrome (CIS) patients were included to evaluate their current definition of low risk (LR-CIS) and high risk (HR-CIS) for developing definite MS. We hypothesized that this pre-clinical state will be reflected in MR measurements.

### Method:

We acquired isotropic whole-brain mcDESPOT data that derives T1 and T2 information from sets of spoiled and fully-balanced steady-state free precession (SPGR and bSSFP, respectively) data acquired over a range of flip angles with constant TR [2]. Data from 10 patients with definite MS (relapsing-remitting [RRMS] n=3; secondary-progressive [SPMS] n=2; and, primary-progressive [PPMS] n=1) and CIS (low risk CIS, n=2, and, high risk CIS, n=1) with an averaged Extended Disability Status Scale (EDSS) score of 3.1 (max 7.5; min 0; SD 2.7) was collected using a 1.5T MR scanner (GE Signa HDx) with an 8-channel head RF coil. Imaging parameters: FOV = 22x22cm<sup>2</sup>, Matrix = 128<sup>2</sup>, slice thickness = 2mm, SPGR: TE/TR = 2.1/6.7ms,  $\alpha$  = {3,4,5,6,7,8,11,13,18}°, bSSFP: TE/TR = 1.8/3.6ms,  $\alpha$  = {11,14,20,24,28,34,41,51,67}°, 6/8 partial Fourier, total imaging time:~15min. An additional 2DFLAIR (TE/TR = 125/8800ms, TI = 2200ms, FOV = 24 x 24cm<sup>2</sup>, Matrix = 192<sup>2</sup>, slice thickness = 2mm) was acquired and co-registered to the Montreal Neurological Institute (MNI) space with the mcDESPOT data. The mcDESPOT analysis was done with FSL[3] and in-house processing software.

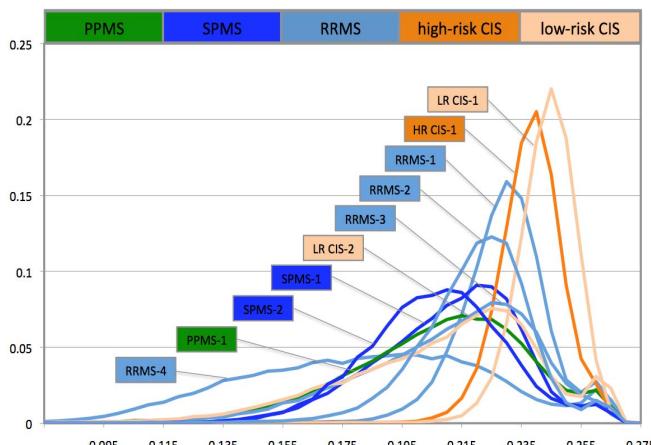


Fig.1) Myelin volume fraction histogram analysis in different types of MS

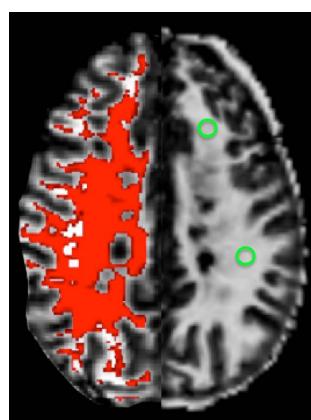


Fig.2) NAWM selection threshold vs ROI

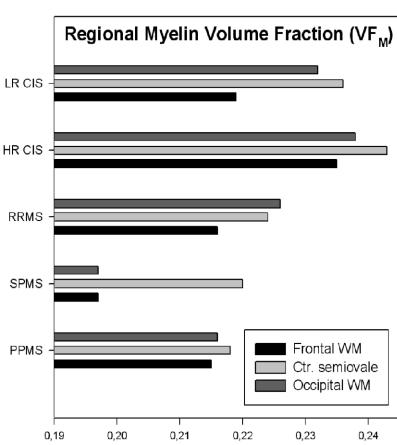


Fig.3) Regional ROI measurement results

### Result:

Global  $VF_M$  histograms (extracted from whole-brain WM) were derived from the mcDESPOT  $VF_M$  volumes, and for comparison, mean  $VF_M$  values extracted from regions of interest (ROIs) placed in supratentorial NAWM in the frontal lobe (*medial frontal gyrus* and *centrum semiovale*) and in the paramedian occipital lobe were computed. ROIs were manually placed using the FLAIR image to avoid contamination with grey matter, MS lesions and hyperintensities consistent with diffuse disease related changes. For the histogram analyses, WM was segmented using single-component DESPOT T1 maps by employing a typical WM threshold between 500ms and 750ms.  $VF_M$  histogram analysis revealed higher maximal peaks and narrower distributions of  $VF_M$  in CIS and RRMS in comparison to SPMS and PPMS [Fig.1]. However one RRMS case showed a distribution pattern deviating from the rest of the RRMS cohort, and this interestingly correlated with a 3.8-fold higher clinical disability (EDSS=5.0) compared to average EDSS of RRMS patients. By contrast, the distribution of one low risk CIS patient was similar to that of the progressive types of MS without explanatory clinical disability (EDSS=0). The ROI analysis also showed a trend toward decreasing  $VF_M$  values with progression through the disease spectrum, but with preservation of *centrum semiovale* NAWM at the transition from RRMS to SPMS. In this ROI analysis, low risk CIS presented with lower  $VF_M$  values than high risk CIS, presumably this result was affected by the LR-CIS case described above.

### Discussion and Conclusion:

mcDESPOT is a novel and rich quantitative MR imaging technique, which in this study has revealed promising correlations between measured myelin volume fraction  $VF_M$ , disease stage, and clinical disability in a spectrum of different types of MS. Based on these initial findings, our research will focus now on the tracking of early WM changes of MS and CIS by means of this technology that are invisible to standard MR imaging. We expect that this will allow us to accumulate further evidence that changes in  $VF_M$  in NAWM, measurable using mcDESPOT, will be predictive of the stage of MS development [4].

### References:

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