Distinguishing Neuromyelitis Optica from Multiple Sclerosis with Myelin Water Imaging

Margarita Gorodezky[1], Lucy A.E. Matthews[2], Anthony Traboulsee[3], Jacqueline Palace[2], and Shannon Kolind[3]

[1]Goethe Universitaet Frankfurt, Frankfurt am Main, Germany, [2]Oxford University and Oxford Radcliffe Hospitals NHS Trust, Oxford, United Kingdom, [3]University of British Columbia, Vancouver, BC, Canada

Background: Neuromyelitis optica (NMO) is a demyelinating disease of the central nervous system that resembles multiple sclerosis (MS) but has distinct pathological features and is likely a separate disorder[1]. A method of clinical differentiation has significant importance since prognosis and optimal treatment for these two diseases diverge; however differentiation can be difficult due to clinical similarities.
Multi-component relaxation imaging allows interrogation of the myelin water fraction (MWF), a measure related to myelin content[2]. Multi-component driven equilibrium single pulse observation of T1 and T2 (mcDESPOT)[3] is a high-resolution whole-brain multi-component relaxation imaging technique that affords us the opportunity to study diffuse myelin changes throughout the brain in a clinical setting.
In this work, we applied mcDESPOT imaging to cases of both NMO and MS in comparison with healthy controls as a novel marker of demyelination with the aims of furthering understanding of pathology and aiding in differentiating between these diseases clinically.

Methods: Fifteen people with relapsing remitting MS (mean age = 43 years (range 22-62); median Expanded Disability Status Scale (EDSS) = 3.5 (range 0.5-5), mean disease duration = 93 months (range 24-240)), 15 people with NMO (mean age = 48 years (range 20-76); median EDSS = 4 (range 2-6), mean disease duration = 71 months (range 12-186)) and 17 healthy individuals (mean age = 49 years (range 19-76)) were included in the study. Whole-brain mcDESPOT MRI data were acquired on a Siemens Verio 3T scanner with a 1.7mm isotropic resolution in less than 14 minutes. mcDESPOT processing was performed to derive voxel-wise MWF maps for each participant[3]. To compare individual patient MWF maps to the healthy population, a normative 3D 'atlas' representing the MWF mean and standard deviation was created from a population of age-matched healthy controls[4]. The healthy MWF maps were non-linearly aligned to the MNI standard space template[5] using a multi-scale approach, and averaged. To restrict our analysis to consistent anatomical voxels (those with a high correspondence between individuals, i.e., white and deep grey matter), voxels with a MWF CoV across subjects of greater than 75% were excluded. Patient MWF maps were non-linearly aligned to the atlas (via registration to the MNI template) following lesion masking. Finally, for each voxel, a Z-score was calculated comparing the individual patient MWF values to the control group distribution. Voxels with a Z-score of less than -4 were considered significantly reduced.

Results: MS patients had a greater volume ($p<0.05$) of normal appearing tissue with significantly reduced MWF values (see Figure 1). The volume of significantly reduced MWF values correlated significantly with EDSS for MS ($R=0.6$, $p<0.02$) but not for NMO ($R=-0.3$, $p=0.2$) (see Figure 2).

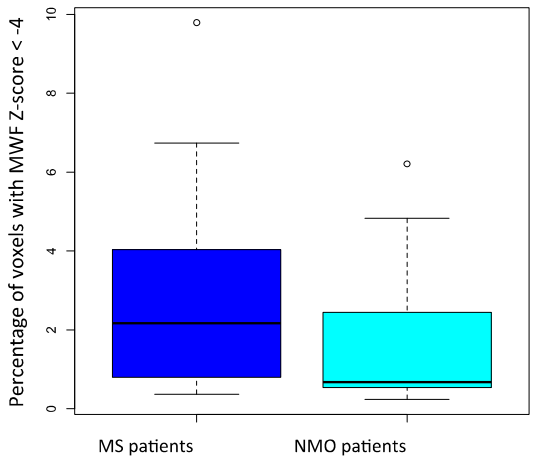

Figure 1: MS patients had a significantly greater volume of reduced MWF than NMO patients ($p<0.05$).

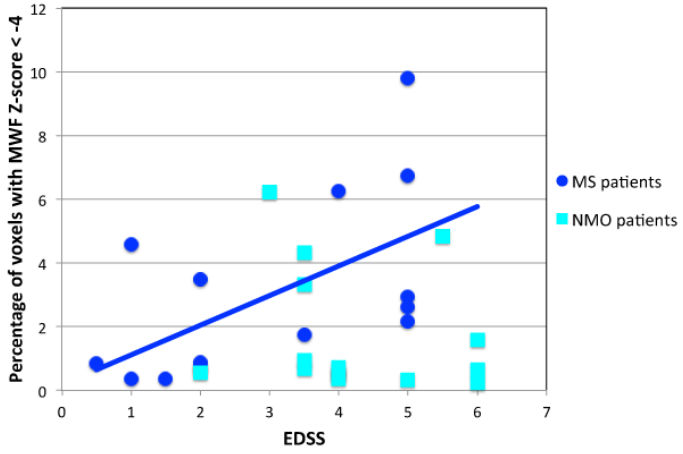

Figure 2: MS patients demonstrate a significant relationship between reduced MWF and EDSS that NMO patients do not (MS: $R=0.6$, $p<0.02$; NMO: $R=-0.3$, $p=0.2$).

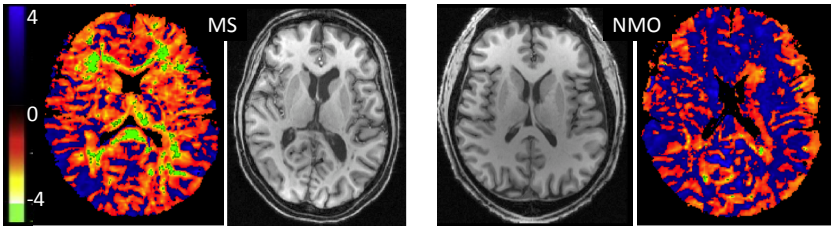

Figure 3: MWF Z-score (scale far left) and conventional image for (left) an MS patient (age 47 y, EDSS 4, disease duration 36 m) and (right) an NMO patient (age 40 y, EDSS 5, duration 36 m), demonstrating the greater change to normal appearing tissue in MS.

Figure 3 illustrates a demonstrative case of one MS and one NMO patient with similar EDSS and disease duration, but drastically different MWF Z-score maps.

Conclusions: mcDESPOT demonstrates significantly greater change in normal appearing MS brain tissue than NMO brain tissue, with a strong relationship between this change and clinical disability for MS that is lacking in NMO. This supports differences in pathological mechanisms of disability in these two diseases, and may provide a significant aid in clinical differentiation, particularly for patients at higher EDSS values.

References: [1] Morrow et al. J Neurooptham ol 2012;32:154. [2] MacKay et al. MRM 1994;31:673. [3] Deoni et al. MRM 2008;60:1372. [4] Kolind et al. Neuroimage 2012;60:263. [5] Collins et al. J Comput Assist Tomogr 1994;18:192.