# Pathological Differences in Neuromyelitis Optica Reflected Differently by Two Myelin Water Imaging Techniques

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## INTRODUCTION:

Neuromyelitis optica (NMO) is an inflammatory central nervous system disorder that typically affects the spinal cord and optic nerves. The associated demyelination led NMO to be previously classified as a variant of multiple sclerosis (MS). However, the discovery of an antibody against the aquaporin-4 water channel revealed that NMO has pathological characteristics distinct from those in MS, and a different mechanism of demyelination[1]. It remains controversial whether normal appearing white matter (NAWM), which is known to be abnormal in MS, is affected in NMO. Given NMO's predominant optic nerve and spinal cord involvement, two brain regions likely to be implicated in NMO are the optic radiations (OR) and corticospinal tract (CST). This work examined NMO and healthy controls using two MRI methods believed to be sensitive to myelin: multi-echo $T_2$ relaxation[2] using a 32-echo gradient spin echo (GRASE) sequence[3], and multi-component driven equilibrium single pulse observation of $T_1$ and $T_2$ (mcDESPOT)[4]. **We hypothesized that compared to healthy controls, myelin measurements would be reduced in NMO OR and CST, but normal in regions believed to be unaffected in NMO such as the corpus callosum (CC) or the average of all cerebrum NAWM.**

## METHODS:

Ten NMO patients (EDSS 2.0-6.0) and 35 healthy controls were scanned on a Philips 3T Achieva MRI scanner. MRI included a 32-echo GRASE sequence (TE/TR=10/1000ms, 1x1x5mm, 20 slices, EPI factor=3) and mcDESPOT imaging (1.7x1.7x1.7mm, whole brain). Both acquisition techniques yield estimates of the proportion of signal originating from the water trapped between the myelin bilayers, the myelin water fraction (MWF) for GRASE or fraction myelin water ($f_M$) for mcDESPOT. The 3-pool mcDESPOT analysis technique[5] also yields several other parameters including: $T_1$ and $T_2$ of the intra/extracellular (IE) water peak ($IET_1$, $IET_2$), $T_1$ and $T_2$ of the myelin water peak, the myelin water residence time, and cerebrospinal fluid (CSF) fraction. Each parameter was calculated voxelwise across the whole cerebrum, and average values were calculated for regions of interest (ROI) from the OR, CST and CC. MRI metrics were compared using Student's t-tests.

## RESULTS:

As hypothesized, NMO NAWM did not have a significantly reduced MWF (p=0.2) or $f_M$ (p=0.8) compared to controls. Furthermore, NMO CC also showed similar MWF (p=0.7) and $f_M$ (p=0.4) to controls. While both regions expected to be affected in NMO had reduced MWF (OR: -16%, p=0.0006; CST: -6%, p=0.05), there was **no** reduction in $f_M$ (OR: 0%, p=0.9; CST: 0%, p=0.9) compared to controls. However, other mcDESPOT parameters did show differences for NMO compared to controls for the OR ($IET_1$: 5%, p=0.002; $IET_2$: -4%, p=0.02; residence time: -10%, p=0.05) and the CST ($IET_1$: 3%, p=0.03). Applying Holm-Bonferroni correction for multiple comparisons, only the decrease in MWF and increase in $IET_1$ in NMO OR remained statistically significant.

## DISCUSSION:

While the decrease in MWF in NMO OR and CST was expected, it was surprising not to detect a decrease in $f_M$ in these regions. Previous work has shown that MWF and $f_M$ are not equivalent, as each technique may be influenced differently by factors such as changes in water content, magnetization transfer effects, or residence times[6]. However, in a study using the same 3-pool mcDESPOT analysis method[5] as used here, MWF and $f_M$ were shown to correlate in a cohort of MS patients and healthy controls (R=0.9 across a variety of tissue types, R=0.7 in white matter alone)[7]. In the same study, $f_M$ was found to be significantly *more* sensitive than MWF to differences between MS and controls in all regions including the OR and CST.

The finding that MS OR and CST had significantly reduced MWF *and* $f_M$, but NMO OR and CST only had decreased MWF, suggests different underlying pathology in the two diseases. Given the observed shifts in $IET_1$ and residence times, possible candidates include changes in water content or exchange. The CST is known to have different $T_2$ distributions from other structures[8] which could be due to its broad distribution of axon diameters, myelin content or exchange; these factors may affect how pathological changes are reflected by each technique. Future work will include examining the $T_2$ distributions, characterising changes in total water content, and correlating results to optical coherence tomography measurements of axonal health in the optic pathways.

## CONCLUSIONS:

The myelin water measured using the GRASE approach found differences between NMO and controls in the OR and CST as hypothesized, while mcDESPOT did not. As both approaches were able to detect reductions in these regions in MS, this finding implies that the damage in NMO differs from that in MS NAWM.

**REFERENCES:** [1]Morrow J Neuroopthamol 2012;32:154. [2]MacKay MRM 1994;31:673. [3]Praskloski NeuroImage 2012;63:533. [4]Deoni MRM 2013;70:147. [5]Deoni MRM 2014 Jan 24 epub. [6]Zhang MRM 2014 Feb 11 epub. [7]Kolind AAN 2014; S44-004. [8]Russell-Schulz MRI 2013; 31:329.