# Myelin Water Imaging in Multiple Sclerosis: Quantitative Correlations with Histopathology

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**Introduction:** Various *in-vivo* magnetic resonance (MR) techniques have been used to study the pathological evolution of multiple sclerosis (MS). However, few studies have quantitatively investigated the correlation between MR derived measurements and histopathology. One MR parameter believed to be a quantitative marker for myelin is the myelin water signal as measured by a multi-echo $T_2$ relaxation experiment (1). Previous work has shown little change in the myelin water signal immediately after death and upon tissue fixation (Figure 1) when compared to *in-vivo* values. As well, a good qualitative correspondence between myelin water imaging and luxol fast blue (LFB) staining for myelin has been observed (2). ***The goal of this study was to determine if an in-vivo measure of myelin water content, based on the short $T_2$ signal, quantitatively correlated with histopathologic markers.***

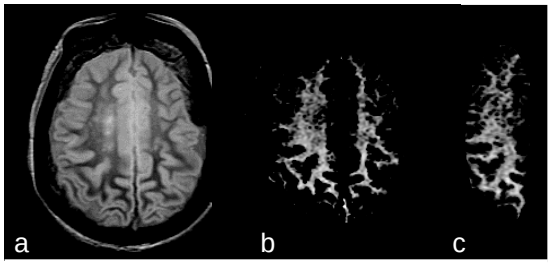


*Figure 1. In-situ (a) MRI and (b) myelin water map of an MS patient, (c) formalin fixed brain myelin water map.*

**Methods:** Eighteen brain slices, fixed in 10% formalin, from 12 patients with clinically definite MS were examined (8 female, 4 male; mean age = 66 yrs (range 41-80 years); mean disease duration = 26 years (range 2-49 yrs)). MR studies were performed in a head coil on a 1.5T scanner using a single slice 32 echo $T_2$ relaxation measurement (TR=3000ms, TE=10ms, matrix=256x256, thickness=3mm, 8 averages). Various regions of interest (ROI's) in white matter, grey matter and lesions were outlined and the $T_2$ relaxation decay curves were decomposed into an unspecified number of exponentials by using a non-negative least squares algorithm (2). The myelin water fraction (MWF) was defined as the fraction of the $T_2$ signal below 30ms divided by the total signal in the $T_2$ distribution. The tissue slices were then embedded in paraffin, sectioned into 10μm thick slices and stained with LFB for myelin and Bielschowsky for axons. ROI's from the $T_2$ relaxation experiment were mapped onto the histopathology images registered to the TE=10ms MR image and mean optical density (OD) was determined using Image Pro Plus. Correlations were investigated between LFB OD and MWF, Bielschowsky OD and MWF, and LFB OD and Bielschowsky OD for each tissue sample using a Spearman rank correlation coefficient.

**Results:** Myelin water maps showed good qualitative correlation with both LFB and Bielschowsky staining, as shown in Figure 2. On average, MWF correlated strongly with LFB OD [mean (and range) $R^2$ = 0.67 (0.48-0.92), p<0.0001] and Figure 3 shows an example of a strong correlation between MWF and OD of LFB for various regions of interest in one sample. Likewise, a correlation was found between MWF and Bielschowsky OD [mean (and range) $R^2$ = 0.59 (0.32-0.85), p<0.0001]. A strong correlation was also found between LFB and Bielschowsky OD [mean (and range) $R^2$ =0.70 (0.50-0.92), p<0.0001].

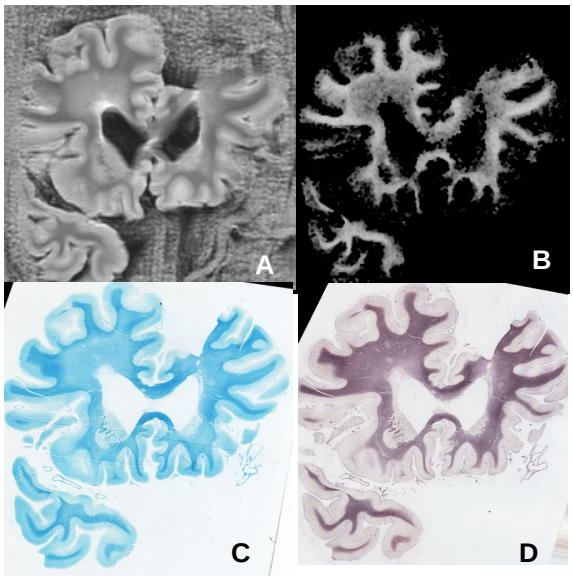


*Figure 2: Good qualitative correlation between (A) TE=10ms, (B) myelin water image, (C) LFB and (D) Bielschowsky.*

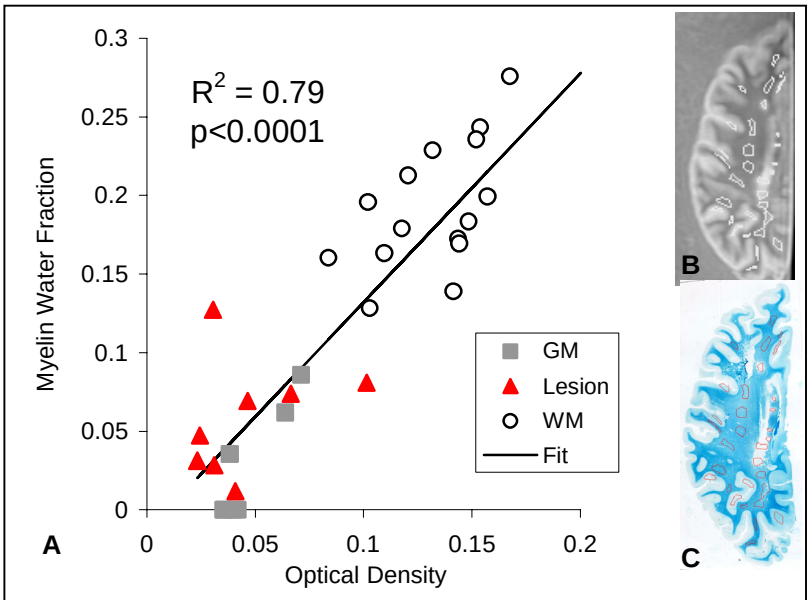


*Figure 3: (A) Example of the strong correlation between myelin water fraction (B) and optical density of LFB (C) for various regions of interest in one sample.*

**Conclusion:** This study validates MWF as a myelin marker. The close relationship between myelin and axons is reflected in the strong correlation between the LFB and Bielschowsky stains which also explain the good correlation between MWF and the Bielschowsky OD. This study supports the use of myelin water imaging to study myelin pathology and the role of demyelination and remyelination in MS.

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1. Whittall KP *et al*. In vivo measurement of $T_2$ distributions and water contents in normal human brain. MRM 1997;37(1):34-43.
2. Moore GR *et al*. A pathology-MRI study of the short-$T_2$ component in formalin-fixed multiple sclerosis brain. Neurology 2000;55(10):1506-1510.