

Cervical Cord Abnormalities in Primary Progressive Multiple Sclerosis: Atrophy and Myelin Water Changes

C. Laule¹, I. M. Vavasour², J. D. Vavasour¹, J. Oger³, D. W. Paty³, A. L. MacKay^{1,2}, D. K. Li²

¹Physics, University of British Columbia, Vancouver, BC, Canada, ²Radiology, University of British Columbia, Vancouver, BC, Canada, ³Medicine, University of British Columbia, Vancouver, BC, Canada

Introduction: Involvement of the spinal cord in primary progressive multiple sclerosis (PPMS) is common and likely an important element in disability (1). However, as conventional imaging gives little information about what pathological processes are responsible for injury and destruction, innovative techniques have been developed with the hope of providing more sensitive and specific data. Volumetric measurements of cervical cord are believed to give information about neuronal atrophy and shrinkage (2) and myelin water imaging as measured by T₂ relaxation is thought to be a quantitative measure of myelin content in-vivo (3). **The goal of this study was to investigate changes in cervical cord area and myelin water fraction in PPMS patients over 2 years as compared to age and gender matched controls, with the hope of better defining sources of disability in PPMS.**

Methods: Twenty-four patients with clinically definite PPMS [16 male, 8 female; mean age 51yrs (range 32-66yrs), median EDSS=6.0 (range 3.0-6.5), mean disease duration=8yrs (range 2-20yrs)] enrolled in a therapeutic trial (PROMISE trial) underwent serial MR examinations at baseline, year 1 (n=20), and year 2 (n=18). Twenty-four age and gender matched healthy controls were also scanned twice, one year apart. Scans were acquired at the C2/C3 level including sixty 1mm thick 3D spoiled gradient echo (TR=13.5ms, TE=4.2ms, flip angle=20°) and a single 5mm thick 32 echo T₂ relaxation slice with (TR=3000ms, TE=10-320ms) with a preparatory inversion recovery pulse to null signal from CSF. Area measurements were performed across 15mm centred at C2/C3 using a series of radial median cuts to determine a 120-sided polygonal representation of the structural boundary. T₂ relaxation decay curves were decomposed into an unspecified number of exponentials by using a non-negative least squares algorithm and myelin water fraction (MWF) was the ratio of the signal with T₂ below 50ms divided by the total signal in the T₂ distribution.

Results: Area - Mean cord area at baseline was found to be significantly lower in MS patients than controls (mean (and standard error, SE): 63.1(2.1) mm² and 73.3(1.4) mm² respectively, p<0.0001) as seen in Figure 1A. At year 1, 9/20 patients had a significant decrease in mean cord area, and at year 2, 10/18 patients had a significant decrease in mean cord area (Figure 1B), both relative to baseline (p<0.05).

Myelin Water - Mean MWF was also found to be significantly lower in MS patients than controls at baseline (mean and SE: 0.198(0.017) compared to 0.257(0.014), p=0.0004), as shown in Figure 2A. Patients also showed decreases in myelin water over time (Figure 2B).

Correlations - Mean MWF and cervical cord area were correlated at baseline (R=0.60, p=0.002). A correlation was found between disease duration and baseline EDSS (R=0.55, p=0.006), as well as between disease duration and cervical cord area (R=0.43, p=0.04; R=0.58, p=0.02; R=0.58, p=0.01 at baseline, year 1 and year 2 respectively). No correlation was found between EDSS and cervical cord area or MWF. No correlation was found between change in area and change in MWF at either year 1 or year 2.

Conclusion: The findings of a reduction in both the area of, and amount of myelin associated water in, the C2/C3 cervical cord region give evidence for more specific substrates of clinical disability and progression in primary progressive multiple sclerosis. Lack of correlation with EDSS may be because only a limited transverse plane was measured. Volumetric measurements provide information about neuronal swelling and atrophy, while myelin water imaging specifically studies myelin pathology. Decreases in cervical cord area can be caused by a combination of axonal loss and demyelination. The partial correlation between the cervical cord area and the myelin water fraction and the poor correlation between their respective changes suggests that changes in myelin are only partially contributing to spinal cord atrophy.

Acknowledgements: Thank you to the MS patients and controls, MRI technologists, Teva and the MS Society of Canada.

- (1) Lycklama GJ *et al.* Spinal cord magnetic resonance imaging in suspected multiple sclerosis. *European Radiology*. 10(2):368-76, 2000.
- (2) Kidd D *et al.* MRI Dynamics Of Brain And Spinal Cord In Progressive Multiple Sclerosis. *J Neurol Neurosurg Psychiatry* Jan;60(1):15-9,1996
- (3) Whittall KP *et al.* In vivo measurement of T₂ distributions and water contents in normal human brain. *MRM* 37(1):34-43,1997

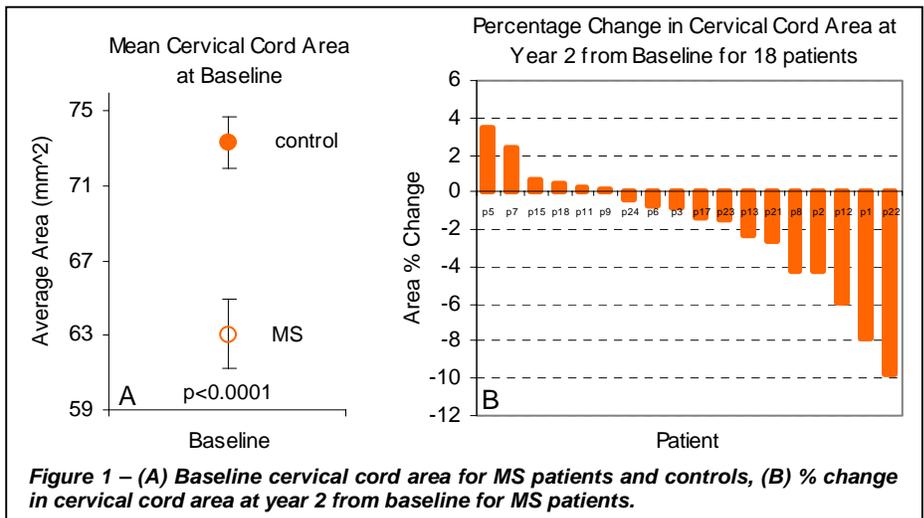


Figure 1 – (A) Baseline cervical cord area for MS patients and controls, (B) % change in cervical cord area at year 2 from baseline for MS patients.

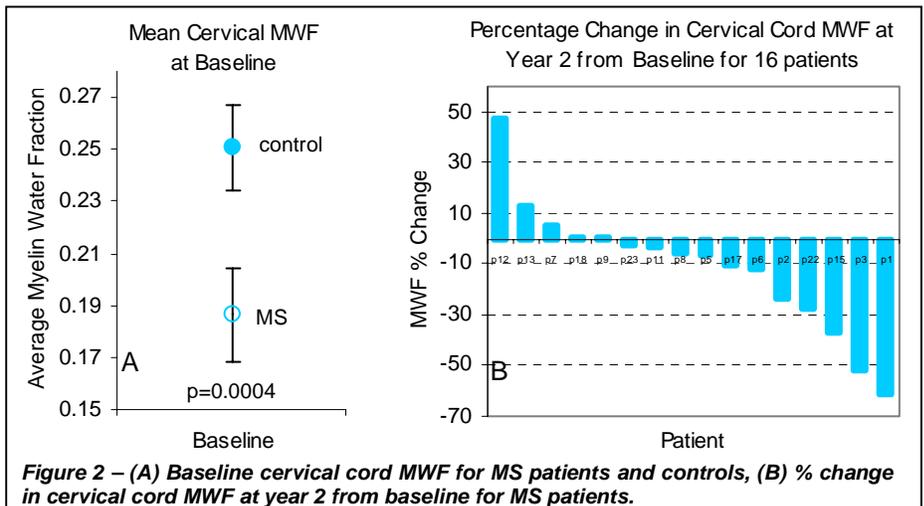


Figure 2 – (A) Baseline cervical cord MWF for MS patients and controls, (B) % change in cervical cord MWF at year 2 from baseline for MS patients.