Supplementary data

Supplementary Table 1. Comparison of baseline clinical and radiological demographics in those with and without follow up at two and five years.

	People with optic neuritis		**Significance**
	People with clinical follow-up	**People without clinical follow-up**	
N	N = 58	N = 13	
Mean age, years ± SD (range)	33.5 ± 6.4 (27-48)	33.6 ± 8.1 (21-46)	$p = 0.966$
female : male	40 : 18	9 : 4	$p = 1.000$
Median baseline EDSS (range)	1 (0-3)	1 (0-2)	$p = 0.585$
Number with abnormal T2 scan (excluding symptomatic lesion)	46	9	$p = 0.471$
Number with periventricular lesions	40	6	$p = 0.197$
Number with Gd-enhancing lesions	19	3	$p = 0.741$
Mean brain parenchymal fraction ± SD	0.85 ± 0.04	0.85 ± 0.03	$p = 0.388$
Mean inner MTR gradient ± SE	0.05 ± 0.02	0.09 ± 0.04	$p = 0.378$

Comparative results: capability of mean MTR in ring 1 and ring 5 for predicting conversion to CDMS and EDSS at 5 years

Conversion to CDMS – ring 1.

In one-way ANOVA, the mean MTR of ring 1 in the ON group who developed CDMS within two years was significantly smaller than in healthy controls, but was not significantly different when compared to the ON group who did not develop CDMS within two years (converters vs healthy controls p=0.000; converters vs non-converters p=0.077; non-converters vs healthy controls p=0.007). The results for conversion at five years were broadly similar (converters vs healthy controls p=0.000; converters vs non-converters p=0.301; non-converters vs healthy controls p=0.014).

Conversion to CDMS – ring 5.

In one-way ANOVA, the mean MTR of ring 5 in the ON group who developed CDMS within two years was not significantly smaller than in healthy controls or the ON group who did not develop CDMS within two years (converters vs healthy controls p=0.062; converters vs non-

converters p=0.893; non-converters vs healthy controls p=0.012). The results at five years were broadly similar (converters vs healthy controls p=0.031; converters vs non-converters p=0.764; non-converters vs healthy controls p=0.017).

Disability

We found no correlation between the mean MTR values in rings 1 and 5 with EDSS score at five years (p=0.165 and p=0.540 respectively).

Effect of conversion to CDMS before MTR scan.

As a confirmatory analysis we excluded those 8 ON subjects who converted to MS in the interval between the baseline clinical MRI and the MTR acquisition. Despite the reduced power, the pattern in group differences in periventricular MTR gradients was maintained: ON vs healthy controls (0.050 pu/mm ± 0.022 vs. -0.033 pu/mm ± 0.028, p=0.022); ON converting to CDMS within two years vs HC (0.114 pu/mm ±0.051 vs. -0.033 pu/mm ± 0.028, p=0.016); ON converting to CDMS within two years vs non-converters (0.114 pu/mm ±0.051 vs. 0.016 pu/mm ± 0.028, p=0.102).

MTR gradient threshold calculations

The range of periventricular MTR gradients found in those who developed CDMS within 2 years (-0.20 to 0.40 pu/mm) compared to those who did not (-0.41 to 0.62 pu/mm) - and in those who developed McDonald MS within two years (-0.41 to 0.40 pu/mm) compared to those who did not (-0.35 to 0.62 pu/mm) - overlapped substantially, and there was no clear cut off beyond which

conversion from a CIS to MS was inevitable. The same pattern was seen when examining conversion versus no conversion at 5 years (CDMS: -0.41 to 0.40 pu/mm; -0.35 to 0.62 pu/mm) (McDonald MS: -0.41 to 0.40 pu/mm; -0.35 to 0.62 pu/mm).

When we use the mean MTR gradient of the group who did not develop CDMS within 2 years as a cut-off (n=40), 13/18 (72%) of those converting to CDMS within 2 years had a greater MTR gradient; if a mean + 1 SD threshold is used, 7/18 (39%, expected by chance 16%); and greater than the mean + 2 SD 1/18 (6%, expected by chance 2%). In comparison, the proportion of controls exceeding these thresholds were: mean 14/37 (38%); mean + 1 SD 3/37 (8%); mean + 2 SD 1/37 (3%). When we repeated this using the mean MTR gradient of controls as the threshold (n=37), 15/18 (83%) of those converting to CDMS within 2 years had a greater MTR gradient compared to 26/40 (65%) of those not converting within 2 years; if a mean + 1 SD threshold was used, respectively 9/18 (50%) and 9/40 (23%) exceeded the threshold, and greater than the mean + 2 SD 4/18 (22%) and 1/40 (3%).