

### ***Supplementary Materials***

*Baseline predictive capabilities: those who relapsed versus those who did not (untreated group)*

During clinical follow-up (5 years), 10/15 untreated patients relapsed (all within the first 3 years). No difference was found in the baseline periventricular MTR gradient between those who relapsed compared to those who did not ( $0.462 \pm 0.084\text{pu/band}$  versus  $0.590 \pm 0.120\text{pu/band}$  respectively,  $p=0.551$ ), including after adjustment for baseline whole-brain lesion number ( $p=0.847$ ), baseline periventricular lesion number ( $p=0.607$ ) or baseline mean whole brain NAWM MTR ( $p=0.438$ ). While a significant difference was found in baseline whole-brain lesion number ( $14.6 \pm 2.8$  versus  $20 \pm 6.9$  respectively,  $p=0.043$ ), and a trend was seen in baseline periventricular lesion number ( $10.2 \pm 2.4$  versus  $13.2 \pm 4.7$  respectively,  $p=0.052$ ), no differences were found in baseline brain parenchymal fraction ( $0.713 \pm 0.008$  versus  $0.712 \pm 0.007$  respectively,  $p=0.978$ ) or baseline mean whole brain NAWM MTR ( $37.183 \pm 0.216\text{pu}$  versus  $37.036 \pm 0.275\text{pu}$  respectively,  $p=0.898$ ) between those that relapsed versus those who did not.

*Evolution over time: those who relapsed versus those who did not (untreated group)*

The rate of change in MTR gradient was significantly different between those who relapsed and those who did not ( $0.071 \pm 0.026\text{pu/band/year}$  versus  $-0.052 \pm 0.036\text{pu/band/year}$  respectively,  $p=0.001$ ), and remained significant when change in whole brain lesion number ( $p=0.006$ ), change in periventricular lesion number ( $p=0.005$ ) or change in whole brain NAWM MTR ( $p=0.003$ ) were added to the model. The rate of change in mean whole brain NAWM MTR was not significantly different between those who relapsed and those who did not ( $-0.185 \pm 0.038\text{pu/year}$  versus  $-0.181 \pm 0.053\text{pu/year}$  respectively,  $p=0.850$ ), nor were the rates of change in whole-brain lesion number ( $1 \pm 0.7/\text{year}$  versus  $0.7 \pm 0.6/\text{year}$  respectively,  $p=0.415$ ), periventricular lesion number ( $1.8 \pm 0.8/\text{year}$  versus  $1.4 \pm 0.8/\text{year}$  respectively,  $p=0.561$ ) nor brain parenchymal fraction ( $-0.002 \pm 0.001/\text{year}$  versus  $-0.005 \pm 0.001/\text{year}$  respectively,  $p=0.273$ ).