Correlation between muscle magnetization transfer ratio and muscle strength in chronic inflammatory demyelinating polyneuropathy

C. D. Sinclair1,2, M. A. Miranda1,2, P. Cosley3, M. Reilly1, J. S. Thornton1,2, and T. A. Yousry1,2

1Institute of Neurology, University College London, London, United Kingdom, 2Lysholm Department of Neuroradiology, National Hospital for Neurology and Neurosurgery, London, United Kingdom

Objectives Though relatively unexplored in this context, quantitative MRI may provide valuable outcome markers for trials of new therapies in neuromuscular disorders. While muscle magnetization transfer ratio (MTR) has previously been shown to decline relative to controls in other muscle diseases [1], our purpose here was to investigate for the first time the specific relationship between muscle MTR and clinically assessed muscle strength in a group of patients with chronic inflammatory demyelinating polyneuropathy (CIDP), an acquired peripheral neuropathy [2].

Methods Nine adult patients suffering from CIDP and 10 healthy control subjects were scanned at 1.5T (GE Healthcare, Milwaukee, WI). An interleaved 2D gradient echo sequence was used to measure MTR in 5mm axial slices of both lower legs (TR/TE = 1500/7 ms; magnetization transfer saturation pulse offset 2kHz) using an abdominal phased array receive coil. A radiologist placed elliptical regions of interest (ROIs) manually on the resulting MTR maps (Fig.1) over the 4 principle muscle compartments in the lower leg (the posterior superficial compartment (PSC), posterior deep compartment (PDC), anterior compartment (AC) and lateral compartment (LC)) for both the right and left lower legs of all subjects. Clinical disease severity in the CIDP patients was quantified by manual muscle strength testing of ankle dorsiflexion by a neurologist using the standard 5 point MRC Score ordinal scale of manual muscle strength [3]. An MRC score of 0 corresponds to the most severe impairment and 5 corresponds to healthy status.

Results The ROI mean MTR in the AC was highly correlated with MRC strength score for ankle dorsiflexion in both the right and left legs of the CIDP patients, MTR declining with reduced muscle function (Spearman's $\rho=0.91, p=0.001$ right leg, $\rho=0.83, p=0.006$ left leg)(Fig. 2). The ROI mean MTR measured in the other muscle compartments (PSC, PDC, LC) did not significantly correlate with MRC score for ankle dorsiflexion, consistent with this particular clinical strength test being primarily a measure of AC muscle function in the lower leg. However, for both right and left limbs, the group median MTRs for each of the 4 muscle groups were reduced in the CIDP group compared to healthy controls (2-tailed Mann-Whitney U test, $p<0.05$ for all muscle groups except left LC ($p=0.053$)), further supporting the hypothesis that reduced MTR is a good correlate of myopathy in CIDP. MTR combined across all muscle compartments and both legs was also significantly less in CIDP than in controls (CIDP MTR = 39.3 (35.1, 45.8) %.; Control MTR = 50.5 (47.2, 50.8) %, both median(IQR); $p=0.03$, 2-tailed Mann-Whitney test).

Conclusions We have shown for the first time that MTR in the lower leg muscles of CIDP patients is consistently reduced compared to that in healthy controls, strongly suggesting that MTR provides a sensitive index of muscle pathology. Furthermore, in measurements specific to the anterior musculature of the leg, MTR was highly correlated with muscle strength and function as tested by a standard clinical method. The reduced muscle MTR with muscle function in CIDP presumably reflects a progressive shift in the balance between free and bound tissue water with disease severity, the precise underlying mechanism for which awaits explanation. MTR shows promise as a non invasive biomarker of disease status in CIDP, such indices being essential for future therapeutic trials in CIDP and other neuromuscular diseases.