T_2^*-weighted MRI at 7T accurately predicts eventual diagnosis of MS in cases with diagnostic uncertainty

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Introduction: Hyperintensities on conventional MRI are not specific for demyelination, often causing diagnostic delay and sometimes misdiagnosis of patients with suspected MS[1]. In-vivo T2*-weighted MRI at high field has been shown to consistently depict central blood vessels within a higher proprtion of lesions in patients with established MS (>40%) compared with patients with microangiopathic white-matter (WM) brain lesions (<40%) [2]. In this work, we prospectively assess the predictive value of T2*-weighted imaging at 7T for an eventual diagnosis of MS in patients who were undiagnosed following standard neurological evaluations and were referred for additional paraclinical testing and clinical follow up.

Methods: 25 patients were recruited - 18 females, 7 males, mean age 49.7 years (range 30.6 – 74.6) who remained undiagnosed despite assessment by a consultant Neurologist and interpretation of conventional hospital MRI scanning by a consultant Neuroradiologist. T_2^*-weighted images were acquired using a Philips Acheiva 7T system equipped with whole-body gradients and a 16-channel head-only SENSE receive coil (NovaMedical). Images were acquired using a turbo-gradient-echo acquisition with 0.5-mm isotropic voxels, 20-ms TE, 150-ms TR, 14° flip angle, EPI factor 3, acquisition time 8.8 min, as previously described [2]. Lesions were outlined on the 7T images for each patient, by a Neurology research fellow blind to patient history; lesion volume, lesion location and the presence or absence of a vessel are recorded. Patients continue under follow-up by their treating Neurologist for a current average of 1.5 years (range 0.9 to 2.2).

Results: 20 of the 25 patients scanned have since received a clinical diagnosis from their Neurologist. 13 patients received a diagnosis for MS; the remaining 7 patients were diagnosed with microangiopathic WM lesions. A total of 441 lesions was identified on the T_2^*-weighted images (mean 17.6 per patient, range 5 – 47; mean lesion volume 129 ml, range 1.1 – 5500). The proportion of lesions containing a visible vein was consistently and significantly higher for the patients diagnosed with MS compared with the non-MS group ($p<0.0001$, Figure 1): all of the "MS" patients had central veins visible in >40% of lesions (mean 91%. range 70% – 100%); all of the "non-MS" patients had central veins visible in <40% of lesions (mean 21%, range 9% to 33%). The difference between groups was most pronounced for small lesions (Figure 2). 15 patients underwent lumbar puncture as part of their clinical testing; of these, 8 had positive CSF oligoclonal bands and none of these 8 had detectable central veins in <40% of lesions. Based on a binomial distribution, if 10 lesions were selected at random from a patient's T2*-weighted image, 99.6% of patients diagnosed with demyelinating disease and 0.1% of patients diagnosed with microangiopathic WM lesions would have detectable central veins in 6 or more lesions.

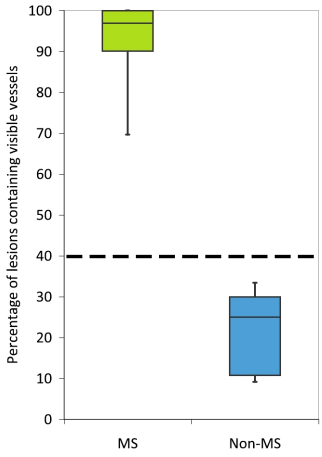

Figure 1 – Box and whisker plot showing quartiles in percentage of lesions containing detectable veins for MS patients (left) and non-MS patients (right). Dashed line shows threshold suggested for diagnosis in [2].

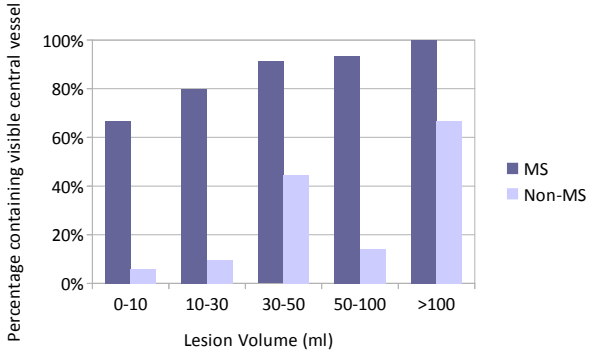

Figure 2 – Percentage of lesions containing visible vessels as a function of lesion volume, for MS and non-MS patients

Discussion: In this cohort, the presence of visible central vessels in >40% of WM lesions on T2*-weighted MRI at 7T was a reliable way to predict eventual clinical diagnosis of MS, with 100% positive and negative predictive value. The identification of all lesions and veins in patients with high lesion counts would be very time-consuming; however, binomial distribution theory suggests that analysis of only 10 lesions per patient, selected at random, would yield accuracy comparable with that obtained by analysing all lesions. With the advent of effective treatments of MS, the need for a test which allows early diagnosis is increased. This technique may speed up diagnosis of MS in patients who would otherwise be difficult to diagnose using conventional methods, as well as eliminate the need for lumbar puncture. This test could be accessible for general physicians and primary care doctors, leaving more time for Neurologists to concentrate on prognosis and treatment. Because of the limited availability of 7T systems, translation of this technique to lower field would be of benefit for clinical use.

Conclusion: In the current cohort, T2*-weighted imaging at 7T had 100% positive and negative predictive value for MS in patients with initial diagnostic doubt. Translation of this technique to clinically available 3T systems may be of benefit for future diagnosis.

References: [1] Fazekas F, et al. Neurology 1999; 53: 448. [2] Tallantyre EC, et al. Neurology 2011; 76: 534.

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