Monitoring multiple sclerosis lesions over a period of five years using MR frequency shift imaging

Vanessa Wiggermann[1,2], Enedino Hernández Torres[1,3], Irene M. Vavasour[1,3], Alex L. MacKay[2,3], David K.B. Li[1,3], Anthony Traboulsee[3,4], and Alexander Rauscher[1,3]

[1]Radiology, University of British Columbia, Vancouver, BC, Canada, [2]Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada, [3]UBC MRI Research Centre, Vancouver, BC, Canada, [4]Neurology, University of British Columbia, Vancouver, BC, Canada

Target Audience: Clinicians, MR physicists, Radiologist, Neurologists

Purpose: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system, characterized by the appearance of focal lesions and diffuse abnormalities in the brain and spinal cord, episodic inflammation and axonal damage. MR frequency images contain quantitative information related to the magnetic susceptibility of the tissue and the tissue's microstructure[1]. As shown in a previous study[2], MR frequency increases sharply when new lesions appear and remains elevated for at least 6 months. Here, we performed long-term follow up (LTF) scans in 8 out of the 20 MS patients of the original short-term study cohort. We hypothesize a reduction in the MR frequency signal, in agreement with theoretical predictions[3], due to axonal destruction and axonal loss alongside demyelination.

Methods: 8 subjects with relapsing-remitting MS (at LTF: age: 34-57yr, mean: 44.5yr, Expanded Disability Status Scale (EDSS): 1-4.5, median EDSS: 2.5, disease duration: 7-30yr, mean: 15.4yr) were scanned over six months at one-month intervals and received one long-term follow up scan after 3.2 – 5.6 years on a 3T system (Philips Achieva) using an 8-channel head coil. Data from 3 healthy controls was collected at scans 0, 6 and LTF. FLAIR (Fluid Attenuated Inversion Recovery) and Gd-enhanced T1-weighted images were acquired for lesion detection. Single echo frequency shift images were acquired using a 3D single gradient echo sequence (FOV=240x166x64mm^3, reconstructed voxel size=0.43x0.43x1mm^3, TR/TE=40/20ms). Images were registered using FSL's FLIRT. Regions of Interest were manually defined on MR frequency shift images for focal enhancing lesions, normal-appearing white matter (NAWM) and normal WM (NWM) in corresponding regions in controls. Statistical analysis was performed using a linear mixed effect model in R, co-varying for differences in age, EDSS and disease duration and LTF time.

Results: The left panel of Fig. 1 shows a lesion 6 months after enhancement (top) and at LTF (bottom). The comparison of both images demonstrates qualitatively the nearly vanishing contrast in MS lesions on frequency shift images. The graph on the right hand side shows the average frequency shifts and standard error for all 21 lesions that enhanced within the first 6 months. The numbers above the curve indicate the available data (number of lesions) at each time point, respectively. After the initial increase in MR frequency (as described in [2], here p=0.001), the frequency in the same MS lesions decreases over time while no such changes are observed in control regions (NAWM in subjects, p = 0.3; and NWM in controls, p = 0.8). The observed decrease at LTF was significant when compared to month 2-6, which showed elevated frequency (p=0.004).

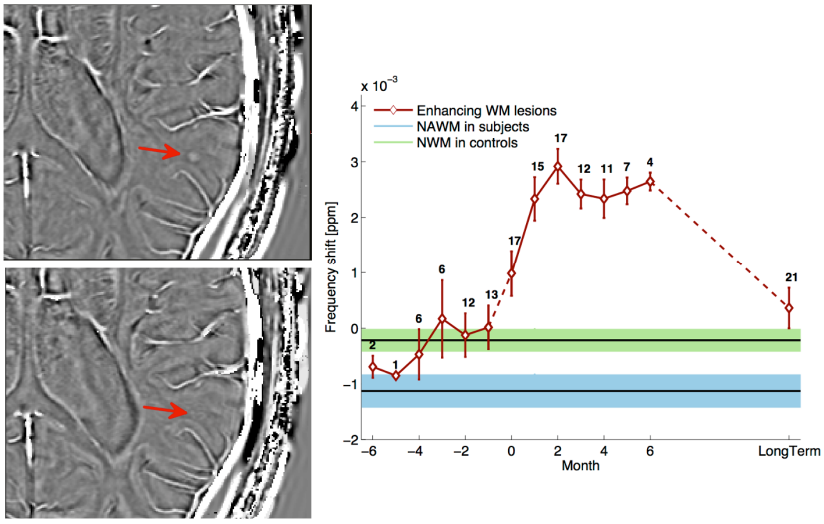

Fig 1: Demonstration of contrast changes in enhancing lesions over time. Left panel: Visually inspection of frequency images: Lesion is clearly visible at month 6 (top) and vanishes after 5.5 years (bottom). Right panel: Steep increase in frequency at lesion appearance (month 0) and prominent decrease after 3-5 years.

Discussion: Most long-term studies of lesions and MS patients involve quantitative MRI measures. However, these measures are mostly limited to the description of lesion load, size and shape of MS lesions. Magnetization Transfer Imaging (MT) and Diffusion Tensor Imaging (DTI) have been used to measure quantitative changes in MS lesions and NAWM[4,5]. MTR is reduced in NAWM before lesion appearance[4] and diffusion changes are detectable between MS lesion types[5]. Frequency shift imaging has the advantage to provide high-spatial resolution and an excellent signal-to-noise ratio, which is often not available from other quantitative MR acquisitions. Our results demonstrate the sensitivity of frequency shifts to measure microstructural changes in MS lesions, which occur due to the destruction of the myelin sheath and axonal damage. Remyelination could also explain the observed decrease of frequency in lesions. Our findings in control regions illustrate that no changes in MR frequency are observed in unaffected regions.

Conclusion: MR frequency shifts may provide us with an exciting high-resolution tool to measure short and long term quantitative changes in MS lesion indicating demyelination and axonal loss. Our data is in good agreement with theoretical predictions to contrast changes in MS lesions on frequency images.

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