High Resolution, Quantitative Imaging of Multiple Sclerosis at 3Tesla MRI

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Introduction: Multiple sclerosis (MS) is an autoimmune disease affecting the nervous system and causing various neurological complications mainly due to demyelination and axonal lo ss. Although there are different types of MS lesions, most appear as areas of demyelination in the brain's white matter (WM). MRI has played an important role and emerged as a powerful non-invasive technique to assist in the diagnosis and monitoring of multiple sclerosis. The use of MRI in MS has been increasing in the field of research in recent years. Standard MRI techniques for MS now include central nervous system atrophy, T1 and T2 weighted imaging and gadolinium enhancement. These measures provide a better understanding to the underlying mechanisms of MS disease and have uncovered remarkable information about MS in recent years. However, the contribution of MRI conventional measures to MS is only at the macroscopic level. They lack the specificity required to understand the MS disease process and have thus failed to provide a complete picture of the underlying pathology which leads to a so called clinico-radiological paradox. In other words, the clinical status of MS patient does not correlate well with MRI findings. Advanced quantitative MRI measures are capable of revealing a range of changes that occur in the normal appearing brain tissue (NABT) which cannot be detected on standard MR images. These advanced quantitative MRI measures include magnetization transfer (MT), T1 and T2 relaxometry, magnetic susceptibility mapping, diffusion imaging and magnetic resonance spectroscopy (MRS). The increased signal to noise ratio (SNR) and spatial resolution available at ultra high field MRI also improves specificity as well as sensitivity to MS lesions and diffuse changes in the central nervous system (CNS). A reduction in scanning time is of importance for most MS patients especially those who are debilitated and thus cannot stay still in the scanner for long time. The main aim of this work is to study the diffuse occult disease outside the macroscopic lesions in the NABT (including the deep grey matter structures) in MS patients using advanced quantitative imaging techniques at 3 Tesla MRI mentioned above.

Methods:

Subjects: So far, nine patients with relapsing remitting multiple sclerosis (RRMS) and two patients with secondary progress multiple sclerosis (SPMS) were recruited from King Hussien Medical Center. No single healthy volunteer has been scanned yet. All subjects were consented according to local ethics approval. The Extended Disability Status Scale (EDSS) score was calculated for each patient.

MR Imaging: Scanning was performed on a 3T Siemens Trio MR system, equipped with 8-channel head coil. The imaging protocol included the following imaging sequences: High resolution 3D-T1 weighted MPRAGE with spatial resolution = 0.9 mm^3 isotropic resolution; reconstruction matrix = 224×256×144; TE = 3.4 ms; TR = 1900 ms; inversion time = 900 ms; flip angle = 9°; number of slices = 144; scan time = 5:53 min. High resolution 3D-T2* weighted gradient echo sequence with spatial resolution = 1 mm^3 isotropic resolution, reconstruction matrix = 192×192×104; TE = 20 ms; TR = 33 ms; flip angle = 15°; number of slices = 104; scan time = 5:30 min. Both magnitude and phase images were reconstructed for further analysis. 2D-T2 weighted Fluid Attenuated Inversion Recovery (FLAIR) with spatial resolution = 0.5×0.5×4 mm^3; reconstruction matrix = 464×512×28; TE = 93 ms; TR = 9000 ms; flip angle = 130°; number of slices = 28; scan time = 4:50 min. 2D-dual echo (proton density-T2 weighted) spin echo with spatial resolution = 0.9×0.9×5 mm^3; reconstruction matrix = 256×256×19; TE_1 = 38 ms; TE_2 = 84 ms; TR = 3880 ms; flip angle = 150°; number of slices = 19; scan time= 2:10 min. 3D Magnetization Transfer (MT) prepared-gradient echo sequence with spatial resolution = 1×1×2 mm^3; reconstruction matrix = 256×256×26; TE = 5 ms; TR = 60 ms; flip angle = 10°; number of slices = 26; scan time = 3.23 min. The MT RF pulse was applied at 1.05 kHz off resonance to water. The same sequence was repeated with similar parameters but with the MT RF pulse 'off'. T1 maps were created from 3D-T1 weighted MPRAGE (short MPRAGE) images acquired at 8 different inversion times (130, 400, 250, 600, 900, 1200, 1600, 2200 ms) with spatial resolution = 1×1×3.6 mm^3; reconstruction matrix = 192×192×16; TE = 2.28 ms; TR = 8000 ms; flip angle = 9°; number of slices = 16; scan time per inversion time = 2.26 min.

Post Processing and Analysis:

High resolution 3D-T1 weighted MPRAGE images were used in FreeSurfer (http://surfer.nmr.mgh. harvard.edu) for cortical thickness and volumetry. The reference scan of the MT-GRE sequence acquired with the MT RF pulse OFF was co-registered to the short MPRAGE repeat-acquired with inversion time that nulled the grey matter-using rigid body registration with 6 degrees of freedom in FSL (FMRIB, Oxford UK) and the co-registration matrix was applied to the MT-GRE sequence acquired with the MT RF pulse ON so that the two volumes of MT-GRE sequences are co-registered to the short MPRAGE sequence. MTR maps were then calculated on voxel by voxel basis using [MTR=(So-S_{mt})/So]. T1 maps were calculated from the repeated 3D-T1 weighted MPRAGE images using Neuroi software. The 3D-short MPRAGE repeat acquired with inversion time that nulled the grey matter was used in SPM8 to segment the white matter and produce a binary mask of the normal appearing white matter tissue (NAWM). NAWM mask was then applied to the calculated MTR and T1 maps to extract the corresponding maps of the normal appearing white matter which were used in MATLAB (www.mathworks.com) for further analysis. For the magnetic susceptibility maps, phase images were unwrapped, filtered and converted into susceptibility maps on which different region-of-interest (ROIs) were drawn to cover the caudate nucleus, Putamen, Globus Pallidus, Thalamus, Pulvinar, red Nucleus and Substantia Nigra. Furthermore, the posterior horn of internal capsule was also drawn and their magnetic susceptibility values were used as a reference for normalization. Lesion load was then calculated using the 'lesion segmentation tool' (LST) in SPM8 using both the T1 weighted MPRAGE and T2 weighted FLAIR image.

Results: We have not performed any statistical analysis to compare with health controls yet. Only processing steps have been carried out on MS patients. In next coming weeks, more subjects will be scanned along with age and sex matched controls and results will be analyzed and presented by the time of oral presentation.

Conclusion: No conclusion has been driven yet. Results will be discussed and a conclusion could be derived by the time of oral presentation.

References: (1) Mougin et al, NeuroImage. 2010. 49: p 272-81 (2) Blakeley,J.O. et al, Neurology 2007. 68 : A288 (3) S. Ropele et al, MRM. 2005. 53 : p 134-140 (4)R. Samson et al. MR I. 2006. 24 : p 255-263, Wharton et al Magnetic Resonance in Med icine 2010,63, p 1292–1304.