Depiction of Cortical Lesions in Multiple Sclerosis at 7T: Comparison with Immunohistochemistry

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Introduction: Pathology studies have demonstrated that cortical lesions are widely present in Multiple Sclerosis (MS), and it is thought that they may better correlate to cognitive impairment and seizure activity than white matter lesion load [1,3]. The objective of this postmortem specimen study was to gather ground truth data for optimized clinical patient MR imaging 1) by evaluating how lesion detection is influenced by spatial resolution, SNR and contrast achieved with different sequences including sequences that can be implemented into patient care or research animal imaging, and 2) to validate lesions with immunohistology.

Methods: Formalin fixed sections of a 42y male SPMS brain (12y past onset) were immersed in buffer solution and imaged at 7T (Philips Achieva) using a T/R knee coil. T1 measurements with IR-TSE found T1 of 370, 310, 410 and 2090ms for GM, WM, WM lesions, and buffer solution respectively. B1 and B0 maps showed limited problems with inhomogeneity. Images were acquired with 3D- white matter attenuated IR-TFE (*WHAT*: shot interval TS=40000ms, TI=90ms, shortest TR/TE, $\alpha=8^{o}$ for the TFE readout), and PD/T2* susceptibility weighted imaging (*SWI*: TR/TE/α=25/12/5^{o}). Spatial resolution ranged from 150x150x300 to 250x250x1000µm. Number of signal averages, NSA, were adjusted to give similar final SNR with resulting scan times ranging from 6min to 3hr. Lesions were classified as mixed (MX) or intracortical (IC), counted and compared with pathology. Following MRI, tissue was transferred through 10-30% sucrose. Brain blocks were then cut at 50 mm thickness on a sliding microtome. Sections were incubated for 5 days in primary antibody against myelin basic protein (DAKO) and processed with secondary antibody and the avidin/biotin staining kit (Vector) with diaminobenzidene as the chromogen. Photomicrographs were taken with a DP71 digital camera attached to a BX41 Olympus microscope.

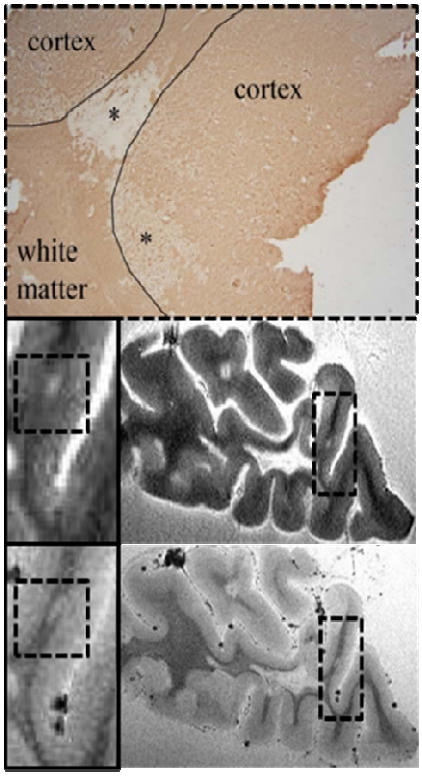

Fig 1: Pure intracortical lesion and adjacent white matter lesion

Results: Grey matter SNR normalized for resolution, matrix size and NSA was 8-fold higher in *SWI* compared to *WHAT*. Both *SWI* and *WHAT* had excellent GM/WM contrast (*SWI/WHAT*: GM signal 44% /74% higher than WM), but lesion depiction was significantly improved with *WHAT* (*SWI/WHAT*: lesion 14%/78% higher than GM). *SWI* phase images were unimpressive. **Figure 1** shows a comparison of *WHAT, SWI*, and pathology. **Table 1** shows comparison of lesion counts with different sequences and different resolutions. Compared to *WHAT*, pure intracortical lesions were poorly depicted with *SWI* especially at lower resolution; conversely mixed lesions were often better depicted with *SWI* compared to *WHAT*. In fact, 4 of 9 IC lesion seen in the 3hr *SWI* data (* in Table) appeared to be mixed. Overall, optimized contrast is most crucial for cortical lesion detection even at the expense of SNR and spatial resolution. High in-plane resolution may be more critical than slice resolution (for slice thickness <1mm).

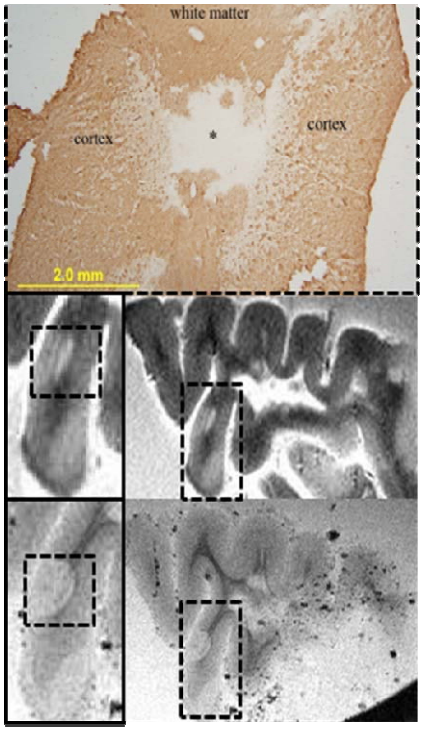

Fig 2: Mixed GM./WM lesion

Discussion: Our specimen study indicates that 7T WHAT is highly promising for cortical lesion MRI at 7T. The findings will lead to further optimization studies to implement robust imaging of cortical lesions at high and ultrahigh field in the hope to further advance the non-invasive assessment of MS disease state, progression and therapeutic effects.

References : [1] Geurts JG, Lancet Neurol 2008;7;841-851; [2] Geurts JG, J Neurol 2008 255,183-191; [3] Nelson F, Multi Scler 2008,14,1214

Lesion Type	WHAT		SWI	
	8min	1:47hr	12min	3hr
IC	7	14	3	9*
MX	9	12	9	10

(8min) 250x250x1000µm, SNR(GM)=8
(1:47hr) 250x250x500µm, SNR(GM)=15
(12min) 250x250x500µm, SNR(GM)=38
(3hr) 150x150x300µm, SNR(GM)=25