Multi-modal post mortem MRI at 7T to detect and quantify multiple sclerosis cortical grey matter pathology

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Introduction: Multiple sclerosis (MS) is a demyelinating and degenerative disease of the central nervous system (CNS) white matter (WM) and grey matter (GM). However, using standard MRI techniques focal pathological changes can only be detected easily in the WM. High resolution MR imaging using high field MRI systems promises better detection and quantification of MS GM pathology, thus enabling a more comprehensive depiction of MS pathology in vivo. Cortical GM pathology in MS can be divided into demyelinated GM lesions (GML) and non-lesional GM (NLGM) with no apparent demyelination [1]. To further explore the pathophysiology of MS in vivo it is important to be able to separate (i) GML from NLGM and (ii) both GML and NLGM from the white matter (WM) and cerebro-spinal fluid (CSF) compartments. Recent studies investigating GML in vivo have used either (i) double inversion recovery (DIR) and phase sensitive inversion recovery (PSIR) at 3T [2-4] or (ii) T2*-weighted (T2*-w) MRI as 7T [5].

Aim: In this study we aim to optimize multimodal 3D MRI acquired at 7T for (i) cortical GML detection and (ii) quantitative assessment of GML and NLGM. Isotropic voxel size is chosen to enhance lesion detection, delineation and volume assessment of the lesions, and for registration between the modalities.

Method: A formalin fixed hemisphere of post mortem brain from a 47-year-old female with MS was used. Time between death and tissue fixation was 39 hours. For scanning the brain hemisphere was taken out of its 10% formalin bath placed in a purpose-designed holder, and immersed in perfluoropolyether (to avoid susceptibility artefacts at the tissue-air interface).

MRI was performed on an Achieva 7T MRI scanner (Philips Medical Systems) equipped with a whole body gradient coil, a head only quadrature transmit RF coil and a NOVA 32 channel receiver coil. Sequences acquired were as follows: (i) T2*w volume acquired at 300μm isotropic resolution using a 3D-TFE (TE/TR=15/46ms, FA=15° (6h)) onto which all the other sequences were registered; (ii) T2-weighted (T2,w) MRI at 350μm isotropic resolution acquired with a 3D-TSE (TE/TR=90/3500 (12h11min)), (iii) PSIR acquired at 350μm isotropic with a 3D-TFE (TE/TR=9/3500ms, TI of 210ms (3h)), (iv) magnetization transfer ratio (MTR) maps at 350μm isotropic resolution acquired with a 3D-MT-TFE sequence (saturation via n= 20 off-resonance pulses with amplitude B1sat of 3.79μT, T= 50ms, bandwidth of 250Hz, applied at 1 kHz off resonance chosen to be sensitive to CEST effects observed in the spectra at 3.5 ppm) with TE/TR=10/21ms, FA=8° (5h45min), (v) double inversion recovery (DIR) at 350μm isotropic resolution acquired using 3D-TSE (TE/TR=144/10000ms, TI1/TI2=1850/260ms (5h)). Quantitative T1, T2 and T2* maps were also acquired (at coarser resolution).

All images were registered to the T2* volume using fs software (http://www.fmrib.ox.ac.uk/fsl/) and volumes of interest (VOI) were manually drawn on each slice of the different volumes. Two independent researchers reviewed the different modalities and classified the lesions as: 1: purely cortical, 2: mixed, 3: subpial [1]. VOIs of five mixed and five purely cortical lesions, as well as adjacent NLGM were analysed on each modality independently, and results are summarized in figure 2.

Results: A similar amount of lesions were classified as mixed (N=137) as purely cortical (N=111), with no sub-pial lesion being detectable with confidence. Imaging parameters were successfully optimized for fixed post mortem MS brain (figure 1) and Contrast to Noise Ratio (CNR) was highest in the T2*w images followed by T2* for the different lesion types.

Conclusion: This study has shown that T2*w MRI is the best technique to detect cortical GML in fixed post mortem MS brain, confirming earlier work[6] obtained using a small bore 9.4T system, and showing best contrast in structure (myelin loss) occurring in GML. Post mortem brain MRI at 7T will allow comparison of the MR characteristics of pathological changes in GM due to MS, and will allow the MR properties of these lesions to be fully investigated. Our inability to detect sub-pial lesions may be due to (i) the limited sample size (N=1 brain hemisphere) (ii) the lack of non-MS-brain for comparison or (iii) the need for pathological confirmation of the MRI findings. We will therefore increase our sample size, include control brain in our study, and explore pathological correlates of the MRI techniques used.