Changes in T1 and T2 in Formalin Fixed Tissue Compared to Fresh Tissue at 7 Tesla

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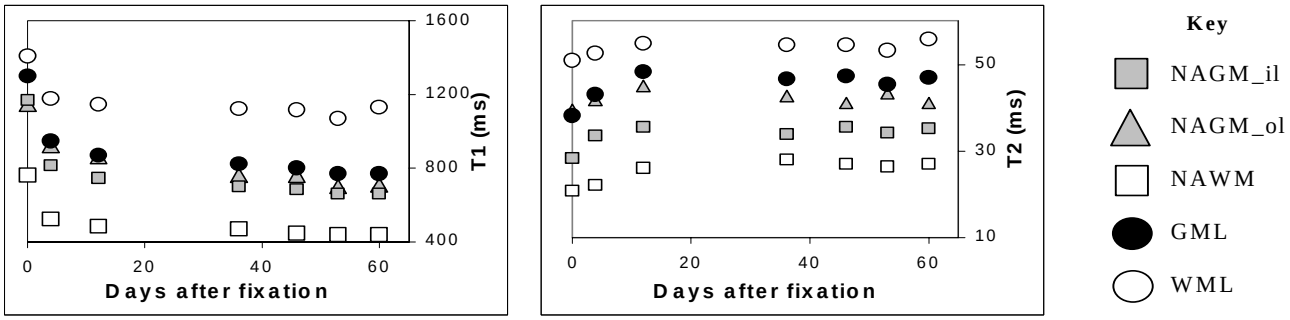
Introduction: High resolution MR imaging of post mortem (PM) multiple sclerosis (MS) brain offers the potential to study in detail the pathological correlates of quantitative MR changes. Access to fresh PM MS brain is limited. Hence, the use of brain tissue after fixation is desirable. However, few data are available on changes of MR indices due to fixation(1). The aim of this study was to evaluate the changes of fundamental MR parameters (T1, T2) in PM MS brain tissue due to (i) fixation and (ii) time of fixation. The feasibility of high resolution studies of white matter and grey matter MS lesions in fresh and formalin fixed tissue at 7 Tesla is addressed.

Sample and Methods: A fresh coronal PM brain slice of a patient with MS was obtained through the UK MS Tissue Bank. One tissue block (size, 2x2x1cm) was used for this study. The sample was kept at 2-8^{0}C before the first scan was performed 91 hrs post-mortem. After scanning under fresh conditions, the specimen was fixed in 10% formaldehyde solution. For scanning at each timepoint the specimen was placed in a syringe and immersed in perfluoropolyether. All measurements were performed on a 7T Bruker Biospec spectrometer using a 2cm diameter saddle coil. Images were acquired with a field of view of 3cm, an image matrix of 192x256 pixels and a slice thickness of 0.5cm; multiple contiguous slices were obtained through the whole of the sample. Four sets of inversion recovery images were acquired with imaging parameters: TE = 16ms, TR = 5000ms and inversion times (TI) = 100ms, 1000ms, 2000ms and 4000ms. A non-linear least squares fit to the exponential recovery of longitudinal magnetisation was performed on a pixel to pixel basis to produce a T1 parameter map. Two sets of spin-echo images were acquired with imaging parameters: TE = 20ms and 60ms, TR = 2000ms. A log-linear fit to the data was performed on a pixel-by-pixel basis to produce a T2 parameter map. For one slice at each timepoint, co-registered to the initial scan, regions of interest were defined in the inner and outer layers of the normal appearing grey matter (NAGM_il, probably reflecting cortical layers 4-6, containing abundant myelin, and NAGM_ol, probably reflecting cortical layers 1-3, containing little myelin), the normal appearing white matter (NAWM) and grey and white matter lesions (GML and WML). Figure 1 shows T1 and T2 maps at 60 days fixation with these areas denoted.



Results:

The graphs show the evolution of T1 and T2 from day 0, when the tissue was fresh and un-fixed, to 60 days post fixation. T1 was longest in the unfixed tissue; in normal appearing tissue areas T1 was approximately 40% shorter at 60 days compared to fresh tissue ($p< 0.01$; paired t-test). T2 was shortest in the unfixed tissue; in normal appearing tissue areas T2 was longer by 10% in GM_il, 25% in GM_ol and 30% in NAWM at 60 days compared to fresh tissue ($p< 0.01$; paired t-test). Thus tissue contrast was similar in both T1 and T2 maps at 60 days compared to fresh tissue.

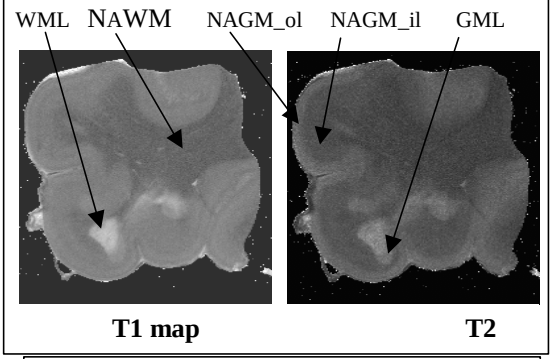


Figure 1: T1 and T2 maps after 60 days

Discussion: Formaldehyde fixation leads to changes in the microstructure of tissue with subsequent changes of T1 and T2. The decline of T1 in our sample following fixation is in line with earlier reports at lower field strengths(2). However, the increase in T2 following fixation at 7 Tesla is in contrast to the decrease of T2 seen at lower field(1).. Moreover, the contrast between NAWM and NAGM for both T1 and T2 did not change substantially in our sample as opposed to studies at lower field. T1 and T2 change with field strength because the amplitude of the spectral density function at the relevant resonant frequency is different. It is not unreasonable that the behaviour of T2 after fixation should be different at high field compared to low field. Good contrast was seen between the WML and NAWM for both T1 and T2, whereas between the GML and the NAGM_il into which the lesion protruded only T2 showed good contrast. Our observations suggest that high resolution imaging of PM MS formalin fixed brain tissue can be a useful tool in the detailed study of MS GM and WM lesions.

References: [1] Blamire AM *et al*, Acta Radiologica 40: 593, 1999. **[2]** Tovi M & Ericsson A, Acta Radiologica 33: 400, 1992.

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