DESPOT: application and optimisation for *postmortem* multiple sclerosis brain

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INTRODUCTION: DESPOT1 and DESPOT2 (driven equilibrium single pulse observation of T_1 and T_2, respectively) allow a rapid and signal-to-noise ratio (SNR) efficient (SNR per unit scan time) means for voxelwise mapping of both longitudinal (T_1) and transverse (T_2) relaxation times over large image volumes (eg whole brain) and with high spatial resolution (eg 1mm^3 isotropic voxels) (1,2). Multiple sclerosis (MS) is a common inflammatory demyelinating condition of the central nervous system in which both potential tissue specificity of quantitative MRI as well as short duration of image acquisition is highly desirable. *Post mortem* brain tissue allows acquisition of ultra high spatial resolution images and subsequent correlation with matched histology of the same specimen thereby facilitating the development of MRI biomarkers (3). Due to tissue changes *post mortem* and tissue fixation there are significant challenges, however, including dramatically reduced T_1 and T_2 values (4) and SNR, which require optimization of acquisition parameters (TE, TR, flip angle, etc.). For this reason we optimized in this study DESPOT1 and DESPOT2 using a whole *post mortem* MS brain.

METHODS: Sample preparation: The whole brain of a man who died at the age of 92 years with a clinical diagnosis of secondary progressive MS was used. MS disease duration was 60 years, and the patient had been wheelchair bound for 20 years prior to death. Brain weight (unfixed) was 1310g, time between death an tissue fixation was 23 hours, and the brain was then fixed in 10% formalin solution for 47 months. For MRI the specimen was taken out of its formalin bath and inserted into a tightly sealed plastic container within which the specimen was immersed in perfluoropolyether. Data acquisition & processing: All imaging was performed on a GE Signa Excite 1.5T clinical scanner with an 8-channel head receive-only RF array coil. Scanning was performed at room temperature. T_1 was calculated from a series of 3D spoiled gradient-recalled-echo (SPGR) images acquired over 13 flip angles (α, from 26º to 2º in steps of 2º) with constant repetition time (TR) of 6.4ms and echo time (TE) 2.9ms. Number of excitations (NEX) was 1. T_2 was calculated from a series of 3D fully balanced steady-state free precession (SSFP) images over 13 α's (from 50º to 1º in steps of 3.3º) with TR=5.2ms and TE=2.5ms (NEX=2). Sixty-six axial slices were acquired for both T_1 and T_2 maps. Voxel size was 0.7 x 0.7 x 1.5mm. Regions of interest were placed in the normal appearing white matter (NAWM), diffusely abnormal ("dirty) white matter (DAWM), white matter lesions (WML), cortical grey matter with – on visual inspection – high (GM-H) and low (GM-L) signal intensity, respectively, the medial thalami and caudate nuclei.

RESULTS: Example axial slices of DESPOT1 and DESPOT2 map volumes are shown in Figures 1 and 2. Mean values obtained are summarized in the table. For comparison, *in vivo* estimates from the same brain regions from the literature are shown, which demonstrate the dramatic reduction in T_1 and T_2 values. Note the difference between GM-H and GM-L indicating a large dynamic range within the cortical grey matter.

FIGURE 1 A: T_1 map **1 B:** Close-up of cortex **FIGURE 2 A:** T_2 map **2 B:** Close-up of cortex

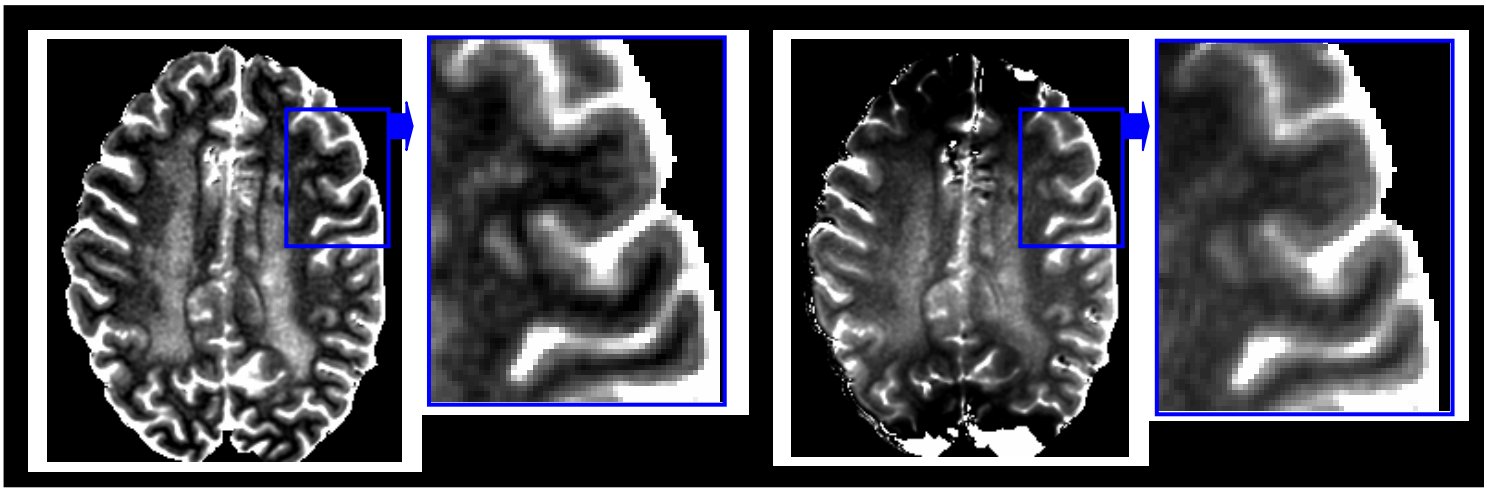

TABLE T_1 and T_2 values [ms] in multiple sclerosis *post mortem* brain, and comparison with *in vivo* values from the literature. NAWM= normal appearing white matter; DAWM= diffusely abnormal white matter; WML= white matter lesions; GM-H= grey matter with high signal intensity on visual inspection; GM-L= grey matter with low signal intensity on visual inspection.

*values obtained from references 1&2.

Brain tissue	T_1 *post mortem*	T_1 *in vivo**	T_2 *post mortem*	T_2 *in vivo**
NAWM	145	608	20	54
DAWM	272	--	34	--
WML	430	--	50	--
CGM-H	264	1065	45	98
CGM-L	210		36	
Thalamus	195	~900	29	~100
Caudate N	215	1064	30	89

CONCLUSION: MRI of fixed *post mortem* specimens offers the unique opportunity for investigating imaging biomarkers of disease through comparison with histology. For quantitative MRI techniques, this also presents a direct means for validating derived anatomically-related parameters. In this study we have demonstrated the ability to acquire quantitative T_1 and T_2 data with high spatial resolution in fixed MS brain using DESPOT implemented on a clinical MR system operating at 1.5T. Our results suggest that DESPOT may be a powerful tool to explore MS. The dynamic range in the cortical grey matter, particularly of T_1 values (figure 1), is intriguing; pathological examination will help to clarify the histological substrate of this finding. Potential limitations of DESPOT2 include the assumption of monoexponential T_2 relaxation. Future work will therefore include quantification of multicomponent relaxation from multi-angle SSFP data using mcDESPOT (5).

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