Advantages of Gradient Echo Plural Contrast Imaging for Identifying MS Abnormalities in Postmortem Brain Tissue

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Introduction: Recently introduced MRI technique, Gradient Echo Plural Contrast Imaging (GEPCI), allows acquisition of co-registered T1-weighted images, quantitative T2* maps and GEPCI-FLAIR images from a single MRI scan [1-2]. Application of GEPCI technique for *in vivo* evaluation of brain MS lesions demonstrated substantial improvement in image quality and saving of acquisition time as compared to current clinical MR sequences [3]. This technique has the potential to provide quantitative information about the disease progression. However, *ex vivo* studies and comparison with pathology is required to validate this method. Herein we apply GEPCI technique for investigations on MS postmortem brains and compare results with data obtained by standard MRI protocols.

Methods: Two postmortem brain slices (1 MS formalin-fixed for 4 years and 1 control fixed for 2 months) were placed in a cylindrical container filled with formalin (10%). Images were acquired using 1.5T Siemens Magnetom Sonata and a manufacture RF knee coil. Standard 2D T1-weighted (T1w), proton density-weighted (PDw) and T2-weighted (T2w) images were acquired with protocols proposed previously [4-5]: TR=400ms and TE=15ms for T1w-SE; TR=2760ms, TE1=45ms and TE2=91ms for PDw/T2w-TSE. The 3D multi-gradient-echo GEPCI sequence was used with TR=50ms, TE1=3.4ms, Echo Spacing=3.4ms, 13 echoes as for in-vivo [2]. From GEPCI dataset, T1w images and quantitative T2* maps were generated by post-processing methods [1-3]. All images were obtained with the same voxel size ($0.5\times0.5\times2mm^3$).

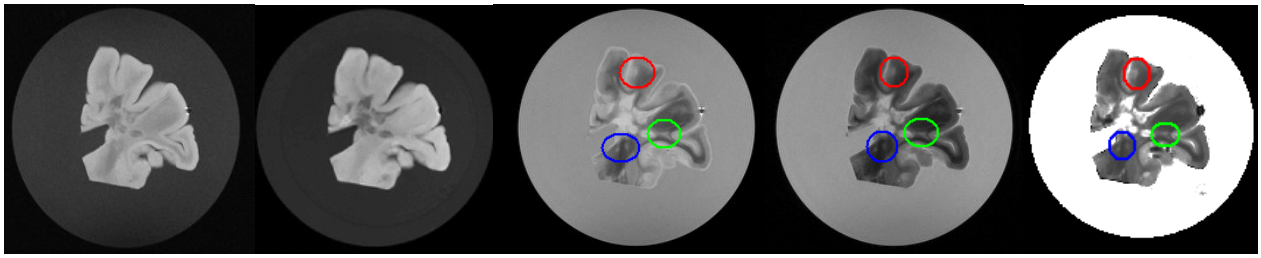

Figure 1: **T1w-SE** **T1w-GEPCI** **PDw-TSE** **T2w-TSE** **T2* map GEPCI**

Results and Discussion: Examples of the obtained results are shown in Fig. 1. One can first observe the massive distribution of black holes depicted by both T1w-SE and T1w- GEPCI images. These black holes are seen as hyperintense lesions on PDw-TSE image, T2w-TSE image and GEPCI T2* map. These three last images also show the extension of the severe lesions (green circle) in WM. Note that other MS lesions (blue circle) exist in WM and one cortical lesion (red circle) can be observed in one gyrus. Note also the axonal sparing of several U-fibers connecting different cortical gyri. Focusing now on the quantitative information provided by GEPCI T2* maps shown in Fig. 2, one can first observe that control tissue (Fig. 2a) shows a completely homogeneous mapping throughout the WM. Cortical GM layer is also very homogeneous with slightly higher T2* values than WM. Note that the partial volume effect is at the origin of the yellowish layer surrounding the formalin/cortical GM interface. T2* map of MS tissue is shown in Fig. 2b (the same slice as in Fig. 1). First we note substantial difference between T2* values of abnormal MS tissue as compared to the normal control tissue. Importantly, we can see that all the lesions, already depicted in Fig. 1, show in fact distinctive patterns and different range of relaxation T2* times which might correspond to different pathology substrates and/or different degree of damage severity. In particular the cortical lesion, which is believed to have a different pathological mechanism than WM lesions, shows much lower T2* values than black holes in WM. This quantitative mapping also clearly demonstrates the axonal sparing by showing normal T2* values for the spared U-fiber (black circle).

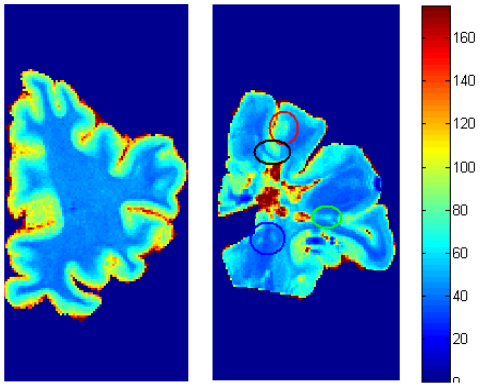

Figure (2a) **Figure (2b)** **ms**

Conclusion: We show that GEPCI technique is effective for investigations of MS abnormalities in postmortem tissues. Due to its quantitative nature, GEPCI approach has a potential to provide new information about the abnormalities in MS tissue while being as reliable as conventional MRI techniques for detection of MS lesions. Hence, this technique has the potential to provide new information about the disease development which could be transferred and applied to in-vivo studies.

References: **1.** Yablonskiy DA, *Gradient Echo Plural Contrast Imaging (GEPCI)*, ISMRM (2000); **2.** Bashir A and Yablonskiy DA, *Gradient Echo Plural Contrast Imaging (GEPCI)*, ISMRM (2006); **3.** Sati P, Cross AH, Bashir A, Yablonskiy DA. *Evaluation of Multiple Sclerosis lesions using Gradient Echo Plural Contrast Imaging*, Abstract at Proceedings of World Congress on MS, Multiple Sclerosis (2008), 14: S5-S27; **4.** Schmierer K *et al*., *Quantitative Magnetic Resonance of Post mortem Multiple Sclerosis Brain before and after Fixation*, Magn Reson Med. (2008), 59(2):268-277. **5.** van Walderveen MAA *et al*., *Histopathologic correlate of hypointense lesions on T1-weighted spin-echo MRI in Multiple Sclerosis*, Neurology (1988), 50:1282-1288.