

High Resolution *In-vivo* and *Post-Mortem* R_2^* and Phase Images of Multiple Sclerosis Lesions at 7 T

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Introduction: Gradient Echo (GRE) MRI provides an opportunity to obtain information about the chemical composition and microstructure of brain tissue. However, its underlying contrast mechanism is not well understood. For example, iron and myelin content could all play important roles in both magnitude and phase contrast [1,2]. Multiple Sclerosis (MS) is an inflammatory-degenerative condition leading to demyelination and axonal loss of the central nervous system. Abnormal iron deposition is recognized as one of the disease hallmarks from *in-vivo* imaging and experimental animal model of MS studies though no *post-mortem* evidence of iron accumulation in lesions is available. Susceptibility-weighted MRI therefore might provide an opportunity to characterize MS lesions. In this preliminary study, several brain specimens of an MS deceased patient were imaged using GRE at 7 T MR scanner and both R_2^* and phase images were investigated, and lesion appearance was compared to that observed in *in-vivo* experiments..

Methods: The study was conducted in a 7 Tesla GE (General Electric) Signa whole-body MRI scanner.

***In vivo* images acquisition** A 32-channel phase array coil (NOVA Medical) was used for signal reception. Four patients with relapsing-remitting MS (age = 28-45 y/o, Expanded Disability Status Scale score=1.0-4.5) participated in this study so far. The scanning protocol included 1) whole brain 3D MP-RAGE based T1-weighted image to localize the lesion area with a spatial resolution = $1 \times 1 \times 1 \text{ mm}^3$ and 11 minutes acquisition time; 2) 2D T_2^* -weighted Gradient Echo (GRE) images with multi-echo acquisitions. The parameters were: TE = 15.5/30.0/44.5 ms, TR = 2 s, in plane resolution = $0.31 \times 0.31 \text{ mm}^2$, slice thickness = 0.8 mm, space = 0.2 mm, flip angle = 75° , receive bandwidth = $\pm 31.25 \text{ kHz}$, 30 axial slices were acquired to cover the lesion area. A SENSE acceleration rate of 2 was used. Total scanning time was about 7 minutes. Quantitative R_2^* maps were obtained by using mono-exponential fitting. To remove phase wraps, the complex data was first smoothed by a Gaussian filter (FWHM = 30 voxels) to determine the macroscopic background phase. Continuous phase maps were then generated after subtraction of the phase background from the original data.

***Post-mortem* images acquisitions** Formalin-fixed brain specimens from a 70 y/o gentleman who had died of pneumonia linked to secondary progressive MS were scanned using multi-echo GRE sequences. The tissue slices were first scanned in 2D sequence and then cut into smaller pieces and scanned in a 6 cm diameter cylindrical container surrounded by a four-channel phase array coil using 3D sequence with a higher resolution of 0.156 mm isotropic. TE = 10.2/28.0/47.8 ms, receive bandwidth = $\pm 31.25 \text{ kHz}$. The R_2^* and phase maps were calculated using the same methods as above.

Results and Discussion: Magnitude, R_2^* and phase images of two patients and two post-mortem tissues are shown and some interesting patterns are observed. First, of all the hyper-intense MS lesions in the T_2^* -weighted images (first row), only a portion is visible in the R_2^* maps (second row) and in the phase images (third row). Second, some lesions in patient 1 appear hypointense in the R_2^* maps (B) but are much less visible in the corresponding phase image (C). A similar phenomenon is also seen in the *post-mortem* tissue (Tissue 1, H, I). On the other hand, the lesion in patient 2 appears hypointense in the phase image (F) does not appear prominently in the R_2^* image (E). This also is sometimes seen in tissue data (Tissue 2, K, L). The observations are interpreted as follows. Both iron and myelin increase R_2^* , but may have opposing phase effects. As they often colocalize in normal White Matter, phase effects there are only expected when they are changed disproportionately. For example, the strong phase contrast in F would be due to a decrease in myelin and increase in iron. Correlative MRI and iron/myelin histology will be required to support or disprove this interpretation.

References: [1] B Yao et al, *NeuroImage*, Accepted, DOI: 10.1016/j.neuroimage.2008.10.029; [2] JH Duyn et al, *Proc Natl Acad Sci USA* 104: 11796-801, 2007; [4] R Bakshi et al, *Arch Neurol* 59:62-8, 2002

