Patch structure in white matter detected by microscopic MRI at high field strength

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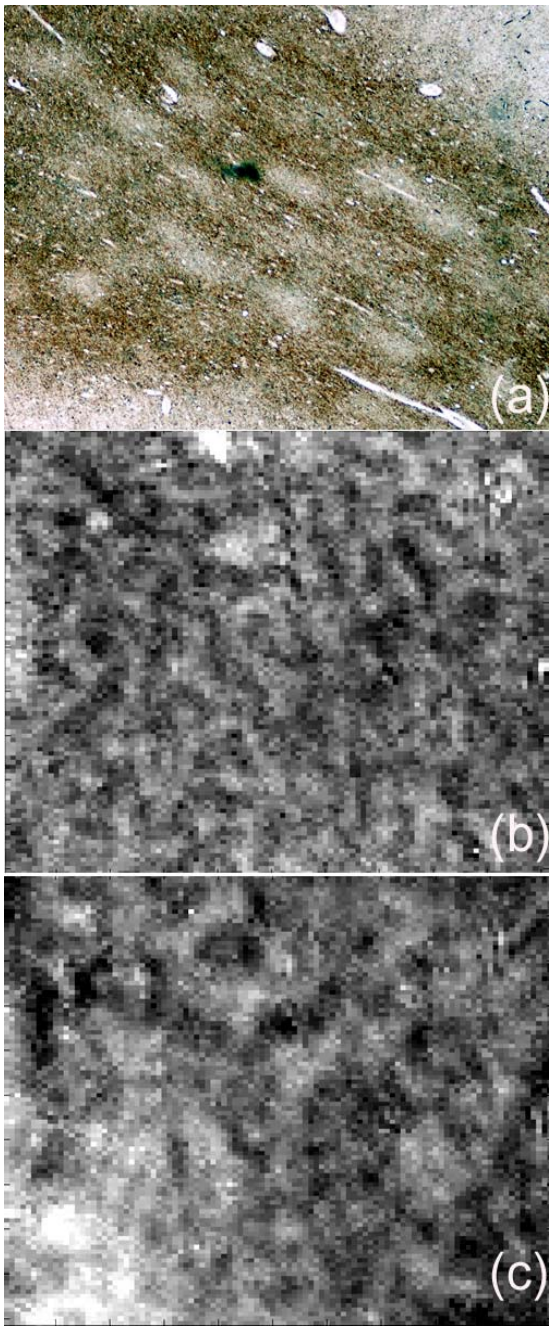
Introduction: T_2*-weighted MRI at high magnetic field strength has recently been used to reveal cortical layer structures [1] and white matter heterogeneity *in vivo* [2]. Magnetic susceptibility differences have been widely thought to give rise to most of the contrast but the precise mechanisms underlying the contrast is still poorly understood. Cell density and type, iron, and myelin contents may vary across the cortical regions and all can become the main sources for the susceptibility difference. For example, we recently demonstrated that magnetic susceptibility variations across some cortical layers are mainly associated with iron content, whereas the T2* heterogeneity among different fiber pathways is largely related to the difference in myelin content. Here, we report an interesting finding from microscopic MRI and histological studies of white matter specimens of the human brain, which may provide further clues for better understanding of the mechanisms underlying the T2*-weighted contrast.

Methods: Multiple white matter specimen of formalin-fixed brains from males (age= 66-78) who died of non-neurological related causes were extracted, washed, sealed in 15 mm NMR tubes. These samples included different white matter tissues, such as corpus callosum, cingulum fiber bundle, white matter from visual and motor cortices. The T2*-weighted microscopic MRI scans were conducted using a 11.7T experimental MRI system (Bruker Biospin) with a home build dedicated probe. Most of the MRI acquisitions were conducted over weekends to produce sufficient SNR by signal averaging. Typical scan protocol was based on a 3D multi-echo gradient-recalled echo pulse sequence. Isotropic voxel size in the range of 30-50 μm were readily achievable with overnight data sampling. some samples were even scanned at 12.5 μm isotropic resolution. Perls' iron staining was also performed in some tissue sections using DAB intensification [4]. The post-processing of the MRI data was conducted off-line using Matlab. The magnitude and phase images from the MRI scans were compared with the micrographic photos from the iron staining.

Results: Similar patch structure with almost regular signal intensity variations was observed in many white matter regions in the acquired MRI images. Typical size is in the range of 30-80μm. The variation patterns in the magnitude images are nearly opposite to these in the corresponding phase images. Line plots of the phase and magnitude data usually depict opposite contrast. Surprisingly, similar patters can also be detected in the micrographs of the iron stainning. A typical example set of images are displayed in the figs. a-c. It should be pointed out that the micrograph (a) does not match precisely the location and resolution of the MRI images shown in figs. b and c. However, the magnitude (b) and the phase image c) match precisely in location and resolution (12.5 μm).



Discussion: The results are tentatively interpreted as follows: 1. Iron deposition in white matter is clustered and varies substantially across white matte regions. 2. The similar appearance of iron staining micrograph and the T2*-weighed images suggest that the patch structure is likely to be related to iron distribution in white matter. 3. Since both myelin and iron enhance T2* relaxation but contribute oppositely to the frequency shift, the opposing contrast patterns between the magnitude and phase images indicate that the relative distribution of the local iron and myelin contents may be responsible for the observed pattern. 4. Evidence from previous studies of tissue iron extraction [5] and in vivo MRI of the line of Gennari [1,5] support the hypothesis that myelin causes a frequency shift opposing that of iron. Therefore, combined analysis of R_2* and **f**requency shifts might allow quantitative determination of the relative contribution of iron and myelin to tissue susceptibility characteristics.

References: [1]. J.H. Duyn et al. *PNAS*, **104**:11796 (2007); [2] Li,T.Q. et al. *Neuroimage*, **32**:1032 (2006). [3] Moos T. et al. *Histochem* **99**:471 (1993); [4]. Li T-Q et al. *Proc. ISMRM* 2008, 885 [5]. M. Fukunaga et al. *Proc ISMRM* 2009.