

# Investigation of magnetic susceptibility contrast across cortical grey matter and white matter

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## Introduction

Magnetic susceptibility contrast in high field MRI has been used to reveal contrast variations within gray matter (GM) of the human brain [1]. Intriguingly, this contrast, to a certain extent, reflects the layer structure of cortical gray matter and is quite variable across brain regions.  $R_2^*$  and particularly phase contrast are quite strong in the primary visual cortex (VC) of the occipital lobe and allow identification of the line of Gennari, a prominent layer with high myelin content. In a previous study, we have demonstrated that laminar susceptibility variations in VC strongly correlate with local iron content, which generally co-localized with myelin as determined from histochemical stains [2]. It was further reported that iron was the dominant source of these susceptibility variations. Here, we expand this investigation of susceptibility contrast to the temporal and parietal lobes and included white matter (WM) as well.

## Materials and Methods

The formalin-fixed, coronally sectioned brain slabs, including part of the parietal and temporal lobules, were derived from a patient with no history of neurological disease (Female, 27 y.o.). Postmortem fixation time was about 8 months. The brain tissue was soaked in saline for at least 24 hours to restore tissue hydration and bring relaxation values closer to in-vivo levels. High resolution 3D multi-echo gradient echo (GRE) acquisition was performed on a 7.0 T whole-body MRI scanner (GE Healthcare) with a volume transmit coil and a 24 channel receive-only detector array specifically designed in-house for imaging of tissue slabs. The scanning parameters were as follows: TR: 500 ms, TE: 13.5/31.5/49.4 ms, flip angle: 45 degrees, field of view: 160x160x19.2 mm, matrix size: 800x800x96 (200  $\mu$ m isotropic voxel size), bandwidth: 15.6 kHz, total scan time: 7 hours 40 minutes. Data processing, including image reconstruction, calculation of magnitude and phase images and  $R_2^*$  maps was performed with IDL 7.1 (ITT Visual Information Solutions) software. Images were reconstructed using a phase-sensitive noise-weighted channel combination. For removing low frequency variation of background phase changes (macroscopic field inhomogeneity), a fifth-order 2-dimensional polynomial was fitted to the phase data and removed. After that phase was converted to frequency. After the MRI scan, Perls' non-heme ferric ( $Fe^{3+}$ ) iron staining with DAB enhancement and Luxol Fast Blue myelin staining without nuclear counter stain were performed on 10  $\mu$ m-thick serial sections from the same tissue slab. The stained images were digitally scanned and co-registered to the  $R_2^*$  and frequency images.

## Results and Discussion

The high resolution GRE images showed laminar structure in sensory-motor cortex (Fig.1), precuneus and cingulate cortex in the parietal lobe (Fig.2; rows labeled 1,2,3 are zoomed views corresponding to the areas in the yellow squares in the top row).  $R_2^*$  in GM ranged from 14 to 45  $s^{-1}$ . Additionally, bi-level contrast was distinguishable in nearly all of cortex. Infragranular layer showing higher  $R_2^*$  than supragranular layer. Increased  $R_2^*$  was frequently observed at their boundary, and in a thin layer of subcortical white matter. Similar laminar contrast was also seen in the iron and in the myelin stain images. In frequency images, layers with positive frequency shift were highly correlated with the level of iron content (Fig.1). On the other hand, the optic radiation (Fig.3 arrows), which constitutes a major fiber bundle in temporal-occipital WM, shows high  $R_2^*$  in the absence of iron while myelin is high. The results suggest that iron contributes significantly to susceptibility contrast across cortical GM and subcortical WM; however, not iron but myelin is the dominant source of susceptibility in WM bundles. Further investigation is needed to quantify the major source of susceptibility contrast in WM.

Fig. 1

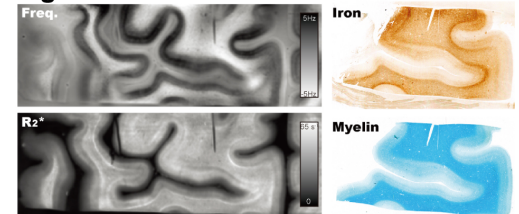


Fig. 2

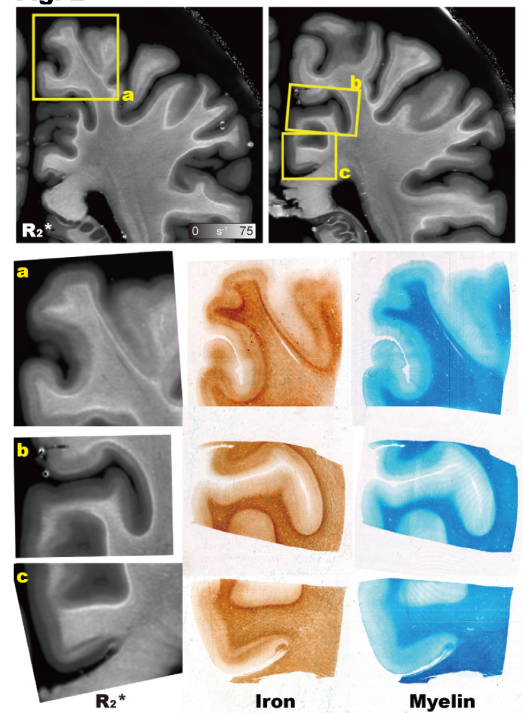
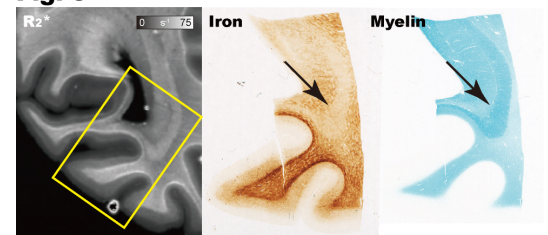


Fig. 3



References : [1] Duyn et al., PNAS 104:11796 (2007), [2] Fukunaga et al., PNAS 107:3834 (2010).