

Iron and Myelin in the Human Brain: Distribution and T₁-Contrast in Gray Matter

Carsten Stueber¹, Markus Morawski², Miriam Waehnert¹, Katja Reimann¹, Nirav Barapatre³, Stefan Geyer¹, and Robert Turner¹

¹Neurophysics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany; ²Paul-Flechsig-Institute for Brain Research, University of Leipzig, Leipzig, Germany; ³LIPSION Laboratory, Institute of Nuclear Solid State Physics, University of Leipzig, Leipzig, Germany

Introduction:

Recent progress in Ultra-High Field MRI has vastly improved the resolution of human brain images, providing an unprecedented view of mid-brain and brainstem nuclei, and allowing new insights into cortical structure. It has been shown recently that quantitative T₁ maps largely reflect the myeloarchitecture of the brain tissue, thus enabling in-vivo myeloarchitectonic cortical parcellation [1]. Furthermore it has been shown that distributions of iron and myelin overlap considerably in the cortex, as nicely seen in the myelin-rich Stria of Gennari within the visual cortex [2]. This raises the question whether spatial variations in T₁ are also correlated with iron concentration [3], given the observation that the iron-rich basal ganglia show relatively poor contrast in T₁-weighted MR sequences. Unfortunately, the co-localization of myelin and iron in the cortex makes it difficult to determine the contribution of iron as an independent source of T₁-contrast. To disambiguate these sources of contrast, we used a state-of-the-art technique, so called ion beam analysis that induces characteristic X-rays in the specimen (proton induced X-ray emission - PIXE) [4] to determine quantitatively the elemental content and elemental distribution in a given sample. Using MRI scanning of highly myelinated and iron-rich blocks of human cadaver brain tissue, before histological processing, we could also study the role of iron in T₁ tissue contrast by scanning before and after the removal of iron by deferoxamine treatment. This provides a more comprehensive picture of the specific role of this element in MRI brain contrast.

Methods:

Fixed excised blocks (motor/somatosensory cortex; visual cortex) of two human cadaver brains (post-mortem delays 36 h & 28 h) were scanned with a 7 Tesla MR scanner (MAGNETOM 7T, Siemens Healthcare Sector, Erlangen, Germany) using the MP2-RAGE-sequence with isotropic resolution of (0.25 mm)³ and (0.4 mm)³ [5]. One block of the visual cortex was soaked in a PBS-solution of 2% deferoxamine and 2% sodium dithionite for a time period of ten days to extract the iron. After this treatment the block was scanned again with exactly the same parameters. All brain blocks were sectioned at 30 µm and treated with various preparations, including stained for myelin (Myelin Basic Protein; Immunohistochemistry). Adjacent sections were left untreated to allow PIXE measurements, performed at the ion beam laboratory (LIPSION). The sections were examined with a photomicroscope (Axiolmager, Zeiss, Germany).

Results and Discussion:

Fig. 1a,b,c show the myelin, iron distribution and T₁ maps of the human somatosensory and motor cortex respectively. The similarity of all images is obvious: cortical structures as well as the boundary between gray/white matter (GM/WM) are easily visible in all three images. Nevertheless the T₁-map reflects the intracortical iron distribution rather better than the myelin density, which might indicate that iron is responsible for the underlying MR tissue contrast of the gray matter. To verify these findings we extracted the iron from one block of the visual cortex, containing the Stria of Gennari (SoG) (Fig.2). The disappearance of this myelin-rich cortical feature in the subsequent T₁ maps confirmed that iron does indeed play a significant role in brain tissue T₁ contrast.

Conclusion:

Deeper understanding of the role that brain iron plays in different types of MRI contrast will assist in strategies for in-vivo cortical parcellation, and help to provide more quantitative assessment and staging of degenerative diseases in which iron concentration appears to be a biomarker, such as Parkinson's disease. Our study of quantitative *in vivo* measurements of iron may also help to explain physiologically its mysterious substantial variations within normal gray matter and white matter.

References:

[1] Geyer et al., Front Hum Neurosci, 5 (19): 1-7 (2011), [2] Stueber et al., ISMRM 19, # 2573 (2011), [3] Ogg et al., Magn Reson Med 40, 749-753 (1998), [4] Butz et al., Nucl Instrum Meth B 161: 323-327 (2000), [5] Marques et al, Neuroimage 49 (2): 1271-1281 (2010)

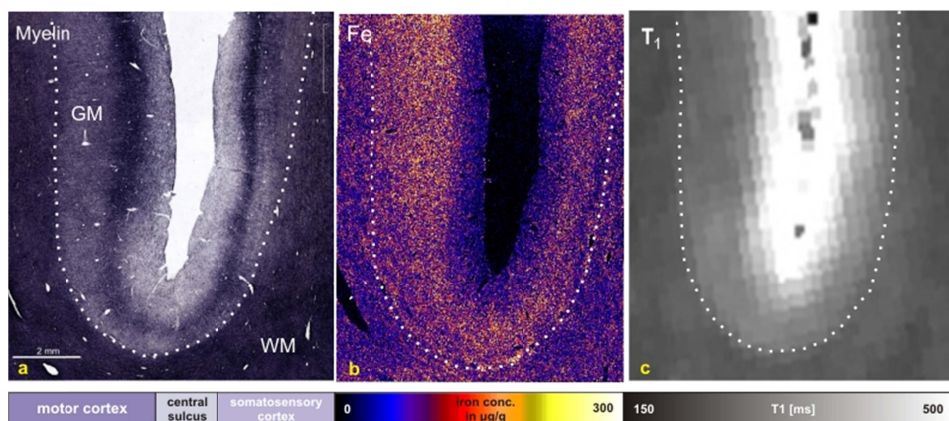


Fig. 1: Motor-/somatosensory cortex (precentral/ postcentral gyrus)

a) Myelin Basic Protein (Immunohistochemistry); b) Iron-map (ion beam analysis)
c) T₁-map (0.4 mm)³

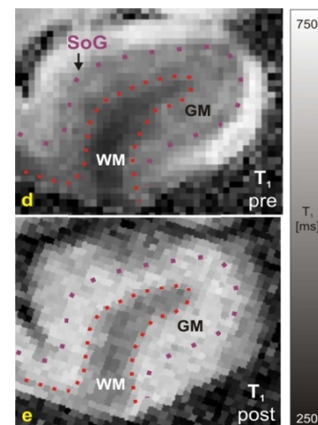


Fig. 2: Visual cortex with Stria of Gennari

d) T₁-map before iron extraction (0.25 mm)³
e) T₁-map after iron extraction (0.25 mm)³