

# Myelin as a primary source of phase contrast demonstrated in vivo in the mouse brain

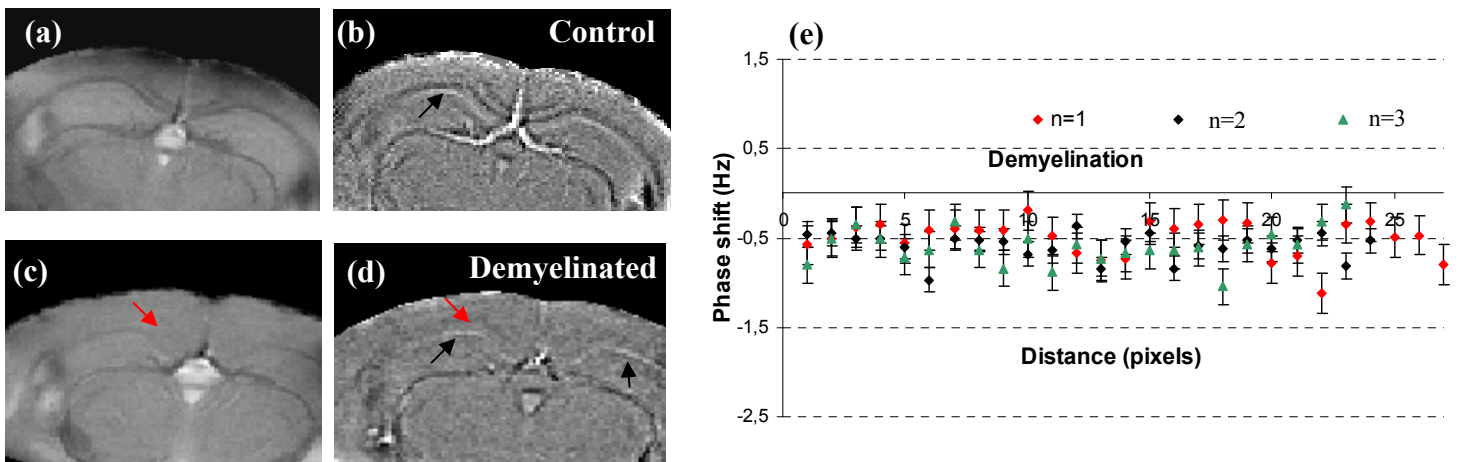
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## INTRODUCTION

While most of MRI studies are focused on the magnitude data, the phase contrast has only recently proved its ability to improve the contrast to noise in high-resolution images at high-field strength [1]. The origin of phase contrast between white matter (WM) and gray matter (GM) has been widely discussed; several sources were suggested including paramagnetic blood deoxyhemoglobin, tissue iron concentrations, water-macromolecules exchange or tissue myelin content [1,2]. In the present study we examine the contribution of tissue myelin content to the phase contrast by exploiting the frequency shift variation in a chronic model of cuprizone induced demyelination [3].

## MATERIALS AND METHODS

C57BL/6 mice were scanned after 12 weeks of cuprizone treatment. Experiments were performed on a Bruker 9.4 T Biospec System with 600 mT/m gradient set. 2D gradient echo flow compensated images were acquired with the following parameters:  $TR = 400$  ms,  $TE = 14$  ms, flip angle = 20 degrees,  $FOV = 20 \times 20$  mm<sup>2</sup>, slice thickness 500  $\mu$ m, matrix =  $256 \times 256$ , leading to a  $0.078 \times 0.078 \times 0.500$  mm<sup>3</sup> spatial resolution and an acquisition time of 13 minutes 39 s. Images were processed offline off-line with custom-made software developed in Matlab to calculate both magnitude and phase maps. Because we are interested in preserving the small-scale phase variations caused by local tissue structure, a spatial high-pass filtering was applied on the phase images to remove the unwanted macroscopic background phase variations (e.g. air tissue interfaces) [4]. Magnitude and the resulting high-passed phase images are displayed in Figure 1 for one control and one cuprizone treated mice. Frequency shift variations were computed over 25 projections perpendicular to the surface of gray matter, running along the corpus callosum to the center of hippocampus.



**Figure 1:** (a) GE magnitude and (b) high-pass filtered phase images of a control mouse brain. Note the higher contrast of the phase data in WM structures (corpus callosum) and vessels. (c) GE magnitude and (d) phase images of a demyelinated mouse brain. As expected, the phase contrast between WM and GM is diminished due to the lower tissue myelin content. (e) Frequency difference between WM and GM structure measured over 25 perpendicular projections along the corpus callosum for each demyelinated mouse (n=3).

## RESULTS/DISCUSSION

As expected, the phase image yields a higher contrast-to-noise ratio between GM/WM compared to the magnitude data. As a general remark, we noticed that the frequency shifts along the corpus callosum of demyelinated mice were much smaller (and still negative) compared to controls. In several regions their measured values did not exceed -0.2 Hz, values which can be related to regions with important myelin loss. Correlation with histochemical myelin staining will be performed for confirming this assumption. The measured frequency difference between WM and GM in demyelinated mice reaches  $-0.56 \pm 0.19$  Hz and  $-1.21 \pm 0.18$  Hz in controls. The frequency shifts ( $1.25 \pm 0.25$  Hz (demyelination case) and  $1.32 \pm 0.24$  Hz (control)) of the hippocampus pyramidal cell layer (black arrow) were measured as well. Since no significant variation was observed between both cases, their positive value can serve as reference in quantifying the frequency shifts between GM/WM in regions of severe myelin loss. The frequency plots from the demyelinated mice are illustrated in Fig 1e showing the stability of the data. The variations occurred in some of the selected projections could be explained by a higher myelin content (Fig 1d, red arrow).

## CONCLUSION

In this study we demonstrate that the tissue myelin content induce a significant effect on the WM/GM frequency difference. The frequency ratio dropped considerably reaching values close to -0.2 Hz in regions of severe myelin loss. However, further confirmation is still needed. Future measurements will be performed to correlate the presented results with histochemical myelin staining.

## REFERENCES

[1] Duyn JH *et al*, PNAS, 2007; 104:11796-1180. [2] K Zhong *et al*. NeuroImage 40: 1561–1566, 2008. [3] Harsan LA *et al*, J Neurosci. 2008; 28:14189-201; [4] Haacke EM *et al*, MRM, 2000; 12:525-533.