USPIO Enhanced Susceptibility Weighted Magnetic Resonance Imaging of the Mouse Brain Vascular Architecture

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Introduction

The cerebral vascular structure plays an important role in brain oxygenation and nutrition. Visualizing brain vascular structure is usually performed with techniques such as magnetic resonance angiography using endogenous contrast or by using exogenous contrast agents such as Gd-DTPA or iron oxide particles in T1 and T2*-weighted imaging. Recently susceptibility-weighted imaging (SWI) has been introduced in humans [1, 2] and rats [3] as a novel approach. With SWI, small veins in the brain are enhanced using advanced post-processing, making use of susceptibility differences between certain structures such as the susceptibility difference between blood (deoxyhaemoglobin) in vessels and its surrounding tissue. In this paper we propose to use additional exogenous contrast for a substantial enhancement of local susceptibility effects allowing for even smaller structures like mouse brain capillaries to be visualized. By injecting superparamagnetic iron oxide nanoparticles (USPIO) as a blood pool agent, additional local magnetic field in-homogeneities will be introduced, resulting in both a reduction of T2* and greater susceptibility differences between vessels and their surroundings than only caused by deoxyhaemoglobin. To test this hypothesis susceptibility-weighted imaging was performed on the mouse brain before and after USPIO injection. Mice provide an excellent model system to study brain vasculature by MR, for instance to evaluate the effect of anti-angiogenic therapy in brain tumour [4].

Material and Methods

MRI Experiments were performed on a 7 T / 12 cm horizontal-bore magnet (MR Research Systems, UK). The magnet is equipped with a gradient insert of gradient strength 150 mT / m and rise time 150 ms. Healthy C57Bl6 mouse (25 g) were used in this study. They were anesthetized using 1.5–2% Isoflurane in a N2O/O2 mixture of 70:30 and positioned in a MR cradle. A 16 mm diameter 1H brain surface coil was positioned over the mouse skull and used as a transmit/receive coil. Gradient echo images were acquired in three perpendicular directions for anatomical localization of the mouse brain. 3-D T2*-weighted gradient echo measurements with flow compensation in all three directions were performed before and directly after administration of USPIO (12,5 mg / kg) (Sinerem, Guerbet, France). Imaging parameters were as follows: TR = 30 ms, TE = 15 ms, FOV = 12,8 x 12,8 x 12,8 cm3, matrix= 128 x 96 x 128, flip angle= 20º, scan time 6 min 9 sec. Reconstruction and post processing was performed using IDL (RSI, USA). Unwrapped images of the data were created by homodyne filtering in three dimensions using a 3-D Hamming window with a width of 64 x 48 x 64. Phase masks were created by setting all positive phases to 1 and by scaling negative phases linearly between 0 and 1. These were then multiplied four times with the corresponding magnitude image to create susceptibility-weighted images. To allow for better visualization of the data 5 slices (500 μm) were combined to form a minimum intensity projection (mIP).

Results

In a pre-contrast T2*-weighted mIP, shown in figure 1a, little brain vasculature can be discriminated, however in the pre-contrast susceptibility-weighted mIP, shown in figure 1b, some small vessels in the deep nuclei become visible (yellow arrows). The post USPIO injection T2*-weighted mIP, shown in figure 2a, displays a significant decrease of intensity outlining the major vascular architecture in detail. The post-contrast susceptibility-weighted mIP , shown in figure 2b, shows substantially more detail in the deep nuclei as compared to the pre-contrast susceptibility-weighted mIP. Moreover, as compared to the post-contrast T2*-weighted mIP substantially more detail of smaller vessels can also be observed (red arrows).

Discussion

This study demonstrates that by using USPIO the vascular information content provided by SWI is substantially enhanced. Due to the small size of the mouse brain, intrinsic susceptibility differences are generally too small to provide enough phase differences to allow large effects on susceptibility-weighted images, however with USPIO enhanced SWI this is dramatically improved allowing extensive visualization of mouse brain vasculature at 7 T.

References

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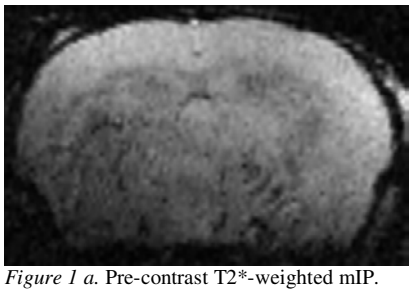
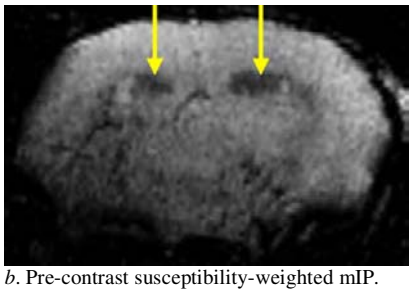


Figure 1 a. Pre-contrast T2*-weighted mIP.



b. Pre-contrast susceptibility-weighted mIP. SWI allows for some small vessels in the deep nuclei to be visualized (yellow arrows).

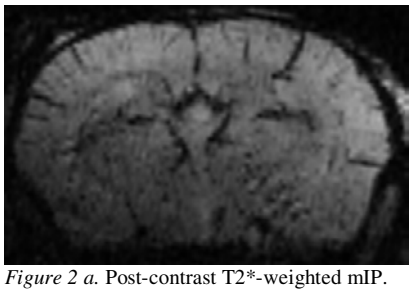
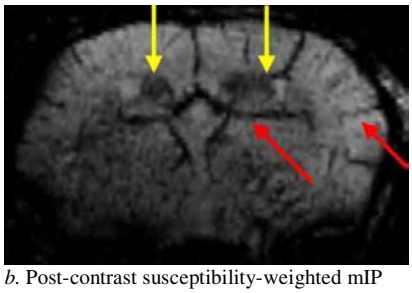


Figure 2 a. Post-contrast T2*-weighted mIP. Major brain vessels can be distinguished in this projection.



b. Post-contrast susceptibility-weighted mIP showing additional enhancement in the deep nuclei compared to pre-contrast susceptibility-weighted mIP (yellow arrows) as well as additional detail in vascular structure compared to the post-contrast T2*-weighted mIP (red arrows).