Vasculature Visualisation using Blood Pool USPIO Contrast Agent Ferumoxytol in Humans

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Introduction: Characterization and visualisation of the cerebral vasculature provide valuable information in many diseases, such as stroke and tumor. Ultrasmall Superparamagnetic Iron Oxide (USPIO) contrast agents have a strong T2* effect, which opens many new possibilities in clinical MR imaging, including steady-state high-resolution quantitative Cerebral Blood Volume (CBV) mapping [1], and more sensitive functional activation measurements with CBV based fMRI (fBVI) [2]. Due to its strong T2* effect, USPIO is also ideally suited for enhancing the imaging details of small vascular structures that are otherwise indiscernible. Ferumoxytol (Feraheme, AMAG Pharmaceuticals Inc., Cambridge, MA) is an USPIO compound recently approved for human use as a treatment for iron-deficiency anemia. Here, we demonstrate the potential of the high resolution contrast enhancement of vascular systems using a 3D multi-echo GRE sequence and a custom developed 3D multi-shot multi-echo EPI sequence that allows quantitative T2* mapping with whole brain coverage in 7-8 minutes.

Materials and methods: The study was approved by the local Institutional Review Board. MR imaging was performed at a 3T scanner with an 8-channel head coil (MR750, GE Healthcare Systems, Waukesha, WI). Six subjects were scanned with the following protocol: A 3D T1-weighted inversion recovery spoiled gradient echo (IR-SPGR) sequence covering the entire brain was acquired. A 3D multi-echo gradient echo sequence sequence (TR=75ms, 16 echoes, TE=3.3 to 63.8ms, ΔTE=4ms, FOV=22*22, slice thickness (ST)=1mm, 256*256, 12 slices, acq. time=4min) was performed before and after injection of ferumoxytol (approx 7 mg/kg at a rate of 1mL/s). Two of the subjects were followed by at about 4 and 22 hrs after the scan, respectively, and a 3D multi-shot multi-echo EPI sequence that allows R2* mapping with coverage of the entire brain in about 7-8 minutes (3 echoes TE = 16.8ms, 40.3ms and 63.8ms, echo train length = 6, FOV= 224x 192, Voxel size = 1mm x 1mm, slice thickness = 1mm, number of slices = 170). Raw k-space data was saved and reconstructed to obtain both magnitude and phase images. To enhance the imaging feature, composite magnitude images were calculated from all the echoes using their TE as weighting factor using the following formula: $S = \sqrt{\sum(S_i \cdot TE_i)^2}$, where S_i and TE_i are the signal intensity and TE of the i-th echo respectively. Further enhancement was performed using the standard susceptibility weighted imaging (SWI) technique by modulating the magnitude image using the phase imaging using the formula $S = S_0 \cdot (\frac{\varphi}{\pi} + 1)^4$, where φ equals filtered phase when the filtered phase is less then zero or zero otherwise [3]. To avoid phase aliasing, phase image from the eighth echo (TE = 31.5ms, approximately optimal for non-contrast enhancement at 3T) was used for pre-contrast SWI processing, whereas the phase image of the second echo (TE=7.4ms) was used for post-contrast SWI enhancement due to significantly higher susceptibility value of USPIO. Minimum intensity projection was performed over 5 consecutive slices.

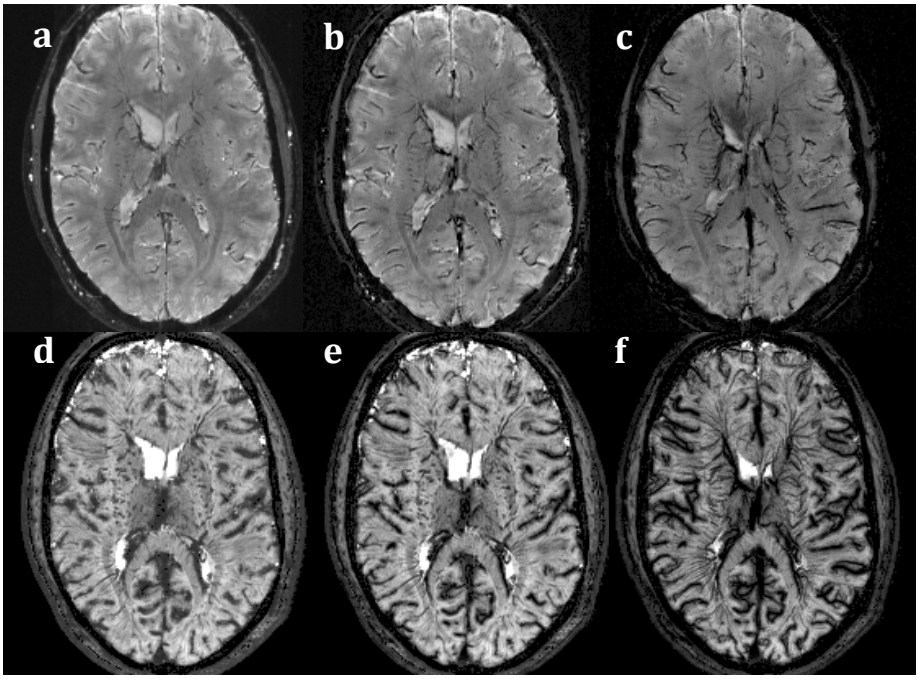

Fig 1 (a-c) pre contrast images, (d-f) post contrast images: (a, d) TE weighted combination of magnitude images ; (b, e) phase modulated SWI images ; (c, f) minimum intensity image projection of SWI images over 5 slices.

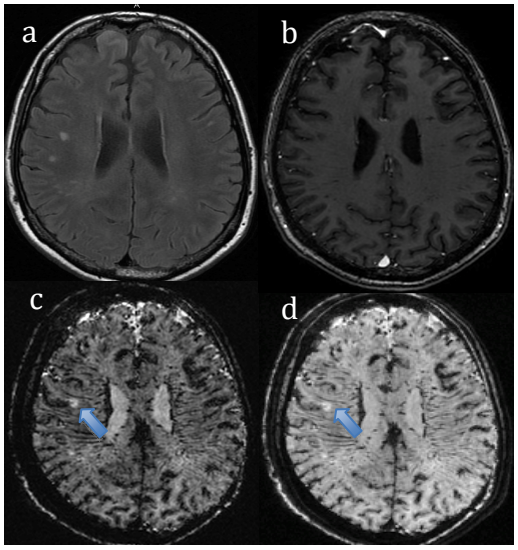

Fig 2 (a) T2 FLAIR image, (b) T1 weighted image, (c)3D Multi-shot multi-echo EPI, last echo, (d) composite image created from the three gradient echoes with TE as a weighting factor. An arrow points to a subcortical white matter lésion (UBO) which shows up as bright, indicating very low CBV.

Results: Figure 1 shows the composite magnitude, SWI, minimum intensity projected SWI before and after contrast injection. The post-contrast composite images show substantially improved delineation of microvasculature than the pre-contrast composite and SWI images. Phase modulation of post-contrast composite image using a SWI technique further improves the vasculature delineation. A Minimum Intensity Projection (minIP) allows appreciation of small vessels perfusing in the white matter (Fig 1f) at the level that is not possible without contrast. Known past presentation of a tiny non-specific subcortical white matter lesion ("unidentified bright object [UBO]") was followed up using the 3D multi-shot multi-echo EPI sequence. The UBO is depicted as a detailed hyperintense region, suggesting that it has very low blood volume (Fig 2, arrow).

Conclusion: In this study, we explore the use of USPIO for enhanced vasculature visualisation. Small vascular structures that are otherwise invisible are clearly depicted, which is more profound than in previous USPIO animal studies [4]. We further demonstrate that UBOs present as bright areas in the USPIO enhanced imaging, suggesting very low blood volume in the lesions. In conclusion, USPIO allows significantly improved visualisation of small vessels, and is potentially useful for vasculature visualisation and characterization in many diseases.

References: [1] Troprès I. 2001. Magn Reson Med. 45:397-408. [2] Mandeville J. 2010. Proc ISMRM. p1110. [3] Haacke EM. 2004. MRM. 52:612-618. [4] Hamans B. 2006. Proc ISMRM. p964.

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