

Characterization of Blood Pool Half Life of USPIO Contrast Agent Ferumoxytol in Humans

Deqiang Qiu¹, Thomas Christen¹, Wendy W Ni¹, Greg Zaharchuk¹, and Michael E Moseley¹
¹Radiology, Stanford University, Stanford, CA, United States

Introduction: 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], more sensitive functional activation measurements with CBV based fMRI [2], and imaging of inflammation processes in various diseases. Ferumoxytol (Feraheme, AMAG Pharmaceuticals Inc., Cambridge, MA) is an USPIO compound recently approved for human use as a treatment for iron-deficiency anemia. Whole brain R2* values before and after contrast injection as well as at follow-up sessions were obtained and the vascular half-life time was calculated.

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). Two 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 (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 to obtain R2* map before (**R2* pre**) and after (**R2* post**) injection of ferumoxytol (approx 7 mg/kg at a rate of 1mL/s). They were followed up at about 4 and 22 hrs after the scan, respectively, and R2* map (**R2* flw**) was also obtained using 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). The half-life was calculated using a mono-exponential decay model. The 3D T1 weighted image and R2* maps were registered using SPM8, and the 3D T1 weighted image were segmented to create brain masks for calculation of mean R2* values before and after contrast injection, and at follow up scans.

Results:

Fig 1 shows the R2* map before and after contrast injection and at follow-up scan. The R2* map after contrast injection showed enhanced signal contrast between gray and white matter, which is due to the difference in CBV between gray and white matter. Table 1 shows the mean R2* values before, after contrast injection, and at follow up scans. The mean increase of R2* value was about 30.7 s⁻¹ at the current dosage (about 7 mg Fe/kg). The intravascular half-life of ferumoxytol was estimated to be between 12.1 and 22.6 hrs.

Conclusion: This abstract is a part of a series of studies that aim to explore the use of USPIO's for high-resolution steady state CBV mapping and CBV-based blood volume fMRI (fBVI) for enhanced sensitivity in humans. Here we characterize the R2* value before and contrast injection as well as at follow up scans. The blood half-life of contrast agent was estimated to be from 12.1 to 22.6 hrs, which is longer than in non-human primates (4.6 hrs) [3]. This prolonged blood half-life enables many imaging methodologies that promise to improve cerebrovascular and functional MRI brain studies.

References: [1] Tropès I. 2001. Magn Reson Med. 45:397-408. [2] Leite FP. 2002. NeuroImage. 16:283-293. [3] Mandeville. 2010. Proc ISMRM. p1110.

Acknowledgements :National Institute of Health (2R01NS047607, 1R01NS066506, 5P41RR09784), Lucas Foundation and Oak Foundation

Table 1 : Mean R2* values of the brain before, after contrast injection and at follow up scans.

Subject	R2* pre s ⁻¹	R2* post s ⁻¹	R2* flw s ⁻¹	Follow-up interval	Half life
60 y.o. M	22.1	53.2	37.9	22.0 hrs	22.6 hrs
38 y.o. F	19.4	49.7	43.0	4.3 hrs	12.1 hrs

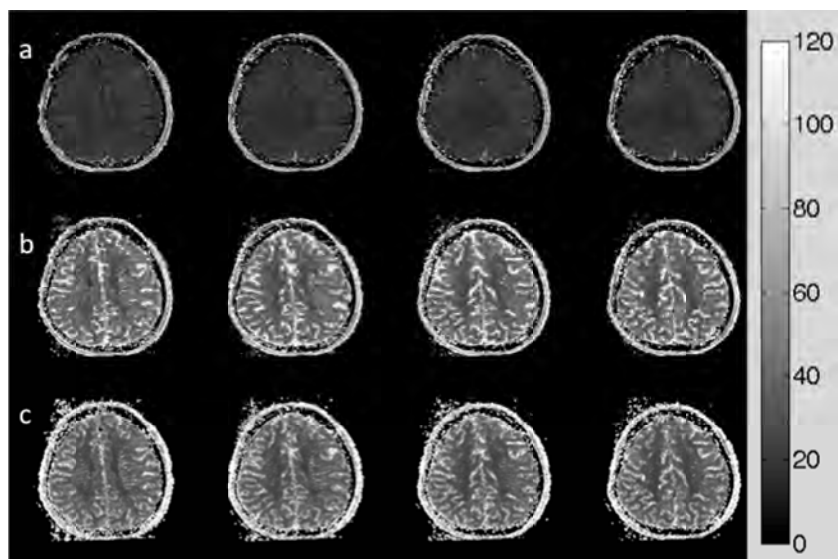


Fig 1 R2* map (a) before and (b) after contrast injection, and follow-up at 4 hours after the acquisition of (b).