Using SWIFT T1 mapping to quantify iron oxide nanoparticles uptake and biodistribution in organs in-vivo

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Purpose Recent advances in nanotechnology have allowed for the effective use of iron oxide nanoparticles (IONP) for cancer imaging and therapies. Noninvasive and quantitative imaging techniques for the assessment and tracking of IONP uptake, bio-distribution and clearance processes in tumors and tissues, including the reticuloendothelial system organs of liver and spleen, will be necessary to accurately assess IONP-based therapies in clinical studies. At the same time, IONPs have proven to be useful in a variety of MRI applications as contrast agents. However, most methods exploit the T_2-shortening properties of IONPs to create negative contrast and provide quantitative information only at relatively low concentrations of IONPs compare to the concentration used in IONP-based therapies. In this study, the positive contrast due to T_1-shortening from IONPs created by SWIFT sequence [1], which can preserve signal with ultra-short T_2*, was applied to quantify the in-vivo bio-distribution of IONPs at high concentration in major organs of mouse.

Methods and materials In-vivo studies were done on both five nude mice. The superparamagnetic iron oxide nanoparticles (SPIONs) (EMG-308, Ferrotec, USA) coated with mesoporous silica and polyethylene glycol at concentrations of 0, 0.06, 0.09, 0.16, 0.18 mg Fe/(g of body wt) were delivered by intravenous (IV) injection. (1 mg Fe/ml=17.8 mM of Fe). SWIFT images and R_1 (=1/T_1) maps were acquired 24 hours after IV injection on a 9.4 T animal MRI scanner (Agilent Technologies, USA) using a home-made three-loop surface coil, with BW=384 kHz, TR=1.2 ms. The SWIFT T_1 map was acquired by the SWIFT Look-Locker method [2], with total acquisition time = 7 minutes. GRE images were also acquired, at BW=150 kHz, TR=4.2 ms, TE=2.1 ms. Iron content of different organs (liver, spleen and kidney) were measured by ICP-Mass Spectrometry (MS) separately.

Results and discussions From Fig. 1a, it can be seen in the post-injection case most IONPs deposited in liver, spleen, or kidney and appeared as a void in GRE images. SWIFT images show T_1-weighted contrast over the whole body with much higher signal to noise ratio than GRE images. Apparent differences were observed between the quantitative SWIFT R_1 (=1/T_1) maps before and post-injection, especially in organs with high iron deposition (liver, spleen, kidney). Larger difference between the two R_1 maps indicates higher iron deposition. It is also interesting to see sizeable amounts iron deposited in bone marrow of femur. In Fig. 1b and 1c, the average R_1 (=1/ T_1) in liver or kidney post-injection both show linear dependence on the iron concentration in corresponding organ measured by ICP-MS. Here, we assume the iron concentration measured is distributed homogeneously over the whole organ. The maximum average iron concentration in liver is up to 2 mg Fe/ml (=35 mM). The measured relaxivity r_1 is different for liver and kidney, probably due to different water accessibility from different micro-structures of organs.

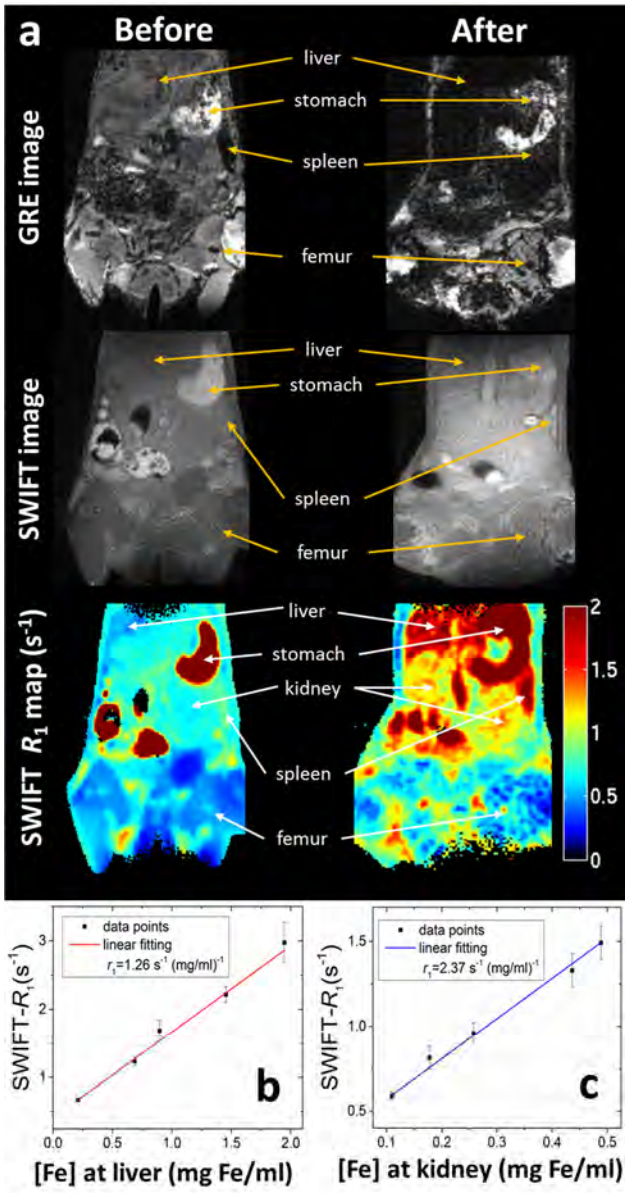

Fig. 1 a) GRE images, SWIFT images and SWIFT R_1 (=1/T_1) maps of mouse body (head up) before or after IV injection of SPIONs. b) and c) are plots of average R_1 of liver and kidney post-injection versus iron concentration measured by ICP-MS of the corresponding organ. High iron deposition was found in liver, spleen, kidney and bone marrow. From the linear dependence, the biodistribution of iron oxide nanopartilces in different organs can be quantified by SWIFT R_1 maps in-vivo.

Conclusions In this study, it has been demonstrated that SWIFT T_1 mapping technique has the ability to quantify invivo biodistribution of SPIONs in major organs of mouse at concentration up to 2 mg Fe/ml (=35 mM Fe). It appears to be a promising tool for assessing SPION uptake, biodistribution and clearance processes in major organs in applications involving nanoparticle-based therapies like thermal therapy or drug delivery systems.

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