SPIO Positive contrast in-vivo by the use of Diagonal-SPRITE

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Introduction

Superparamagnetic iron oxide particles (SPIOs) have been extensively used in *in-vivo* molecular imaging by MRI for detecting cells (1) and gene expression (2). However, being iron based, imaging of such particles causes attenuation of the signal intensity due to severe shortening of T2*, which may be difficult to discern from signal attenuation arising from bulk susceptibility. In order to detect the short T2* SPIOs, a novel UTE(3) technique, Diagonal-SPRITE (4), was used. This technique was used to determine the T2* of phantoms containing either a SPIO-containing solution or saline, followed by *in-vivo* work.

Method

Phantom experiment: Two 1ml syringes containing either saline or SPIOs (CD4 microbeads, Miltenyi Biotec, Bisley, UK) were prepared for MRI.

In-vivo experiment: CBA mice (Harlan UK) were anaesthetized and given an intramuscular dose of SPIOs (15µl, CD4 microbeads) in a hindleg and saline (15µl) into the contralateral leg. The mouse was then placed inside the rf coil and anaesthesia maintained with a 1.5% isoflurane oxygen mix, and body temperature maintained throughout at 37°C by warm air.

Scanning: MRI was performed on a 9.4T horizontal bore Varian scanner (Palo Alto, CA) using a 25mm ID birdcage rf coil (Magnetic Laboratories, Oxford UK). For the phantom experiment, parameters for Diagonal-SPRITE were: TR = 0.5ms+Tp (phase encoding time); Tp of 0.25, 0.32, 0.6, 0.9, 1.2, 1.5, 2.1, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6 ms, matrix 120x120x21, FOV 30x30x30mm, 5 averages, slice thickness = 6mm, flip angle=5°. For the *in vivo* mouse experiment, the slice thickness was decreased to 1.5mm and Tp values were 0.32, 0.9, 1.5, 2.1, 2.5 ms. (Total scan time for the *in vivo* mouse experiment was 2 hours, the long scan time arising from inefficiency of single point imaging).

Results and Discussion

Fig.1 shows the change in signal intensity of the SPIOs (fit curve in red triangles) and saline (fit curve in blue dots) phantom versus Tp time. A value of approximately 2ms was measured for the T2* of the SPIOs from the exponential curve fit and a longer value of 6ms for the T2* of saline by Diagonal-SPRITE. Despite differences in TR between different scans, a relationship still exists between signal intensity and T2*. In fact it can be shown that by using the signal equation in reference (5) adapted for SPRITE with no steady-state T1 magnetization, when a small flip angle is used the T1 effect is minimized and the signal becomes predominantly dependent on T2*. The signal coming from the leg muscle containing SPIOs was fitted for the five Tp values used *in-vivo* and a T2* of approximately 2ms was achieved. Unsurprisingly, the T2* of SPIOs *in-vivo* presented the same value as in free solution in the phantom. Fig.2B shows the attenuation of signal intensity in the hindleg given an injection of SPIOs with a Tp of 2.1ms. Fig.2A shows Tp=0.32ms signal intensities from long, short and ultra-short T2* tissue components are comparable and there is very little contrast in the image. By subtracting image Fig2B from Fig2A, signal attenuation arising from the presence of SPIOs gives rise to positive contrast (arrows, Fig.2C). Note, fat has high signal intensity for Tp=2.1ms (Fig.2B) but its signal is attenuated when Tp=0.32ms (Fig.2A) due to performing MRI at 9.4T where there is a shift in phase of 180 degrees between fat and water every 0.35 ms.

Conclusion

Diagonal-SPRITE may be used to detect the presence of iron concurrent with susceptibility, therefore allowing iron-containing tissues to be distinguished from those with high susceptibility, eg, the lungs, and opens the door to positive contrast detection of iron based contrast agents.

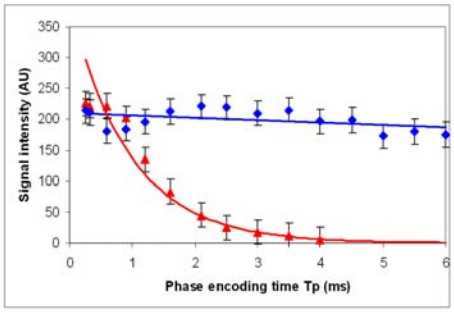

Fig.1: Fit of signal versus Tp for the saline (blue dots) and SPIOs (red triangles) phantoms. The T2* of SPIOs can be evaluated to be approximately 2ms and the T2* of saline to be much longer than

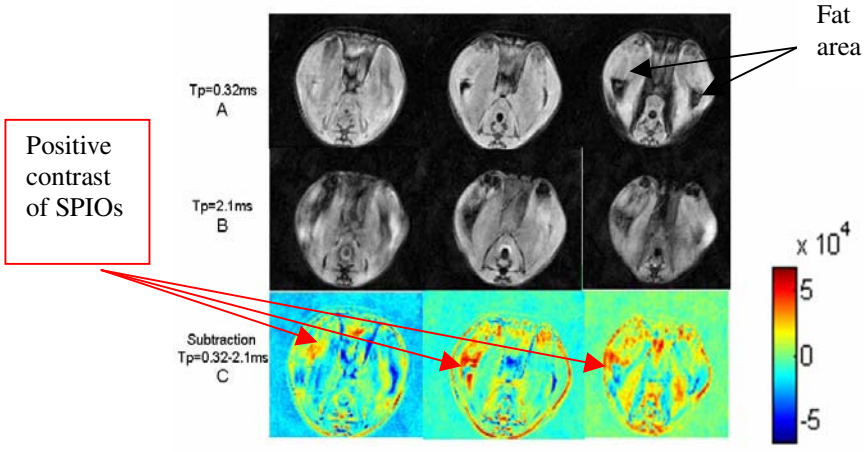

Fig.2: *In vivo* diagonal-SPRITE consecutive transverse images of the hindlegs of a mouse at (A) Tp=0.32ms and (B) Tp=2.1ms following injection of SPIOs and saline into the muscles of the left and right legs, respectively. A subtraction image (C) was obtained to highlight the comparatively shorter T2* of SPIOs in the left leg.

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