Quantification of SPIO iron: Comparison of three methods

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Introduction

A superparamagentic iron oxide (SPIO) labeled region affects B_0 well outside the labeled region itself, while signal from within or near the labeled region may not be detectable. Various methods exploit these distant fields to detect iron (1-5). We compared Cunningham's off resonant excitation, standard gradient echo images, and a new phase difference approach for measuring iron quantity (not concentration) without the need for calibration.

Methods

In Cunningham's bright T2* spin echo method (1), off resonant pulses played without gradients excite and refocus only spins with Larmor frequency in the bandwidth of the RF pulses, $f - \delta f$ to $f + \delta f$. If these frequencies are known, the extent of the pattern in the image determines the amount of iron producing the effect. For positive offsets, rearranging expressions for dipole fields and Larmor frequencies gives

$$M_{Fe} = (f - \delta f)\, z^3 / (2\gamma) \qquad [1]$$

Iron magnetization, M_{fe}, is given in emu, z (half the length along B_0) in cm, and γ is 4258 Hz/gauss. Our SPIO have ~110 emu/g.

In gradient echo sequences, the amount of iron can be estimated absolutely from phase or magnitude images. Using the phase difference between images with different TE and standard expressions for dipole fields,

$$M_{Fe} = z^3 / (4\gamma\,(TE2\text{-}TE1)) \qquad [2]$$

where z is the distance in cm along B_0 from the center of the dipole to the point where the dipole produces a 180° phase shift. Similar expressions for iron content use distance to the point where the phase shift is 540° or to the 180° point perpendicular to B_0.

The phase of the magnetization within a voxel is not uniform. A pixel with ~360° across it appears black through intravoxel dephasing. This provides another absolute iron estimate. With z the radius of the black spot along B_0 and Δz the pixel size in consistent units,

$$M_{Fe} = z^4 / (6\gamma\, \Delta z\, TE) \qquad [3]$$

Experiments were performed on a 1.5T SIGNA imaging system (GE Healthcare Technologies, Milwaukee, WI) in a custom 6-turn, 50 mm ID solenoid receive coil. A 4.4 mm silicone ball containing 29 μg SPIO was placed in a rat brain suspended in agarose gel in a 50 ml centrifuge tube. Imaging parameters were for the 3D gradient echo (negative T2* contrast and phase difference): TR 50 ms, TE = 7.5 or 23.5ms, 10° flip angle, 6 cm FOV with 128 x 128 matrix, 1 mm slice thickness with 32 partitions. The off-resonance excitation (positive T2* contrast) spin echo (SE) approach had parameters of: TR/TE 700/20ms, 6 cm FOV, 256x128 matrix, thick slice projection. The iron mass was then estimated using Eqns.[1-3] and compared with the mass spectrometric measurement, with the observers blinded to the actual iron mass contained in the SPIO.

Results and Discussion

In Figs. 1-3, coronal images are presented at the same scale with frequency readout direction L/R and the direction of the B_o field (and phase encode) top to bottom. Estimated iron masses are tabled by method. The three different approaches gave estimates of iron from 25-45 μg.

TE ms	7.5	23.5
Fe μg	38	45

Grad echo black spot

Δϕ	180° z	540° z	180° x
Fe μg	32	27	20

Gradient echo phase difference

f Hz	+800
Fe μg	25

Off resonant excitation SE

As expected, positive contrast off-resonant images (Fig.1) and negative contrast GRE images (Fig.2) show an asymmetrical pattern with distortion in the readout (frequency) direction. In contrast, the phase difference image (Fig.3a) showed the expected $3\cos^2\theta - 1$ pattern with much less distortion than the simple phase image from the GRE acquisition (Fig.3b). The *ex-vivo* brain itself does not appear to interfere with the dipole pattern produced by the SPIO. Image based absolute iron measurement appeared to be best along the undistorted phase encode (z) rather than the frequency distorted read direction (x). The phase difference images gave an accurate estimate of iron mass (27-32μg) and reproduced the expected field perturbation pattern from the SPIO, lending confidence to the identification of SPIO.

Conclusion

Determining the concentration of iron by T2* requires interpretation of signal intensities in the labeled region. We have demonstrated that positions of signals outside the labeled region can give absolute estimates of the amount of iron present, without error prone interpretation of intensities.

Acknowledgment Professor Charles H. Cunningham kindly provided code for his pulse sequence.

References 1. CH Cunningham MRM 53:999-1005 (2005). 2. CJ Bakker MRM 55:92-7 (2006). 3. V Mani MRM 55:126-35 (2006). 4. AJ Coristine proc ISMRM 2004:163. 5. M Stuber proc ISMRM 2005:2608.

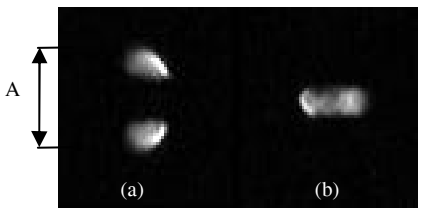

Fig.1: Positive contrast SE images with resonant offsets (a) 800Hz and (b) –800Hz. The spatial extent of the frequency range, A = 0.75 cm. Images with other frequency offsets gave somewhat larger estimates of iron mass.

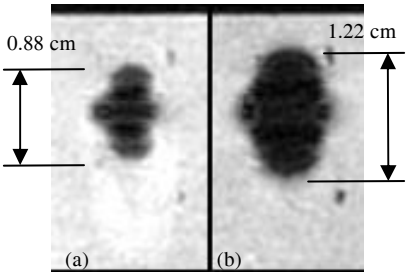

Fig. 2: Magnitude 3D gradient echo images at (a) TE = 7.5ms, (b) TE= 23.5 ms. The measured spatial extent is shown in the z (phase encode) direction.

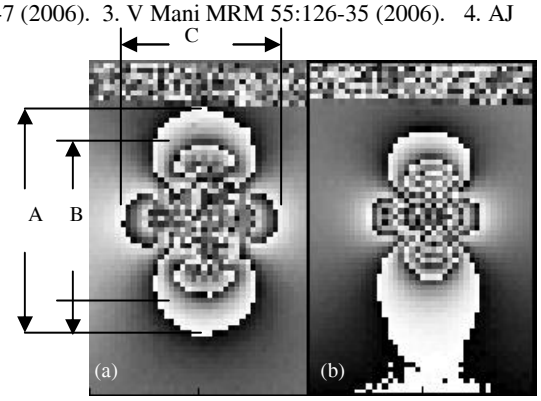

Fig. 3: 3D gradient echo images showing (a) phase difference between TE=7.5 and 23.5 ms. (b) phase image for TE 7.5 ms. Measured spatial extents were: A=1.97 cm, B=1.29 cm, C=1.33 cm