Fat Suppression Strategies for Off-Resonance (IRON) Imaging of Magnetically-Labeled Stem Cells High in Iron with 0% Fat

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Introduction: Inversion Recovery with ON-resonant water suppression[1] (IRON) is an imaging method that enhances signal originating from susceptibility induced local field variations. Contrast is obtained using an on-resonant water suppression prepulse (IRON pulse). IRON has been used to improve visualization of magnetic nanoparticle-labeled stem cells. However, since the IRON method intrinsically highlights off-resonant protons, unwanted fat signal also appears signal-enhanced. Therefore, effective fat suppression approaches for IRON imaging are required.

Purpose: To theoretically and experimentally investigate different approaches for fat suppression in combination with IRON imaging.

Methods: The spatially dependent magnetic field shift induced by a paramagnetic nanoparticle, which is exposed to a static magnetic field ($\boldsymbol{B_0}$) can be modeled using the Lorentz' Sphere. The induced local field variations ($\Delta\boldsymbol{B}$) are given by the dipolar field equation, $\Delta\mathbf{B} = (\Delta\chi/3) * (a/r)^3 * (3\cos^2\theta - 1) * \mathbf{B_0}$; where $\Delta\chi$=susceptibility difference between background tissue and the superparamagnetic material, $\boldsymbol{a}$=radius of the Lorentz' sphere, $\boldsymbol{r}$=distance from the sphere, $\boldsymbol{\theta}$=angle between $\boldsymbol{r}$ and $\boldsymbol{B_0}$. It was simulated using MATLAB to study the enhancement pattern (Fig 1A). By volume integration and subsequent partial differentiation of this equation, off-resonance signal at any Larmor frequency shift was calculated and plotted using MATLAB (Fig 1B).

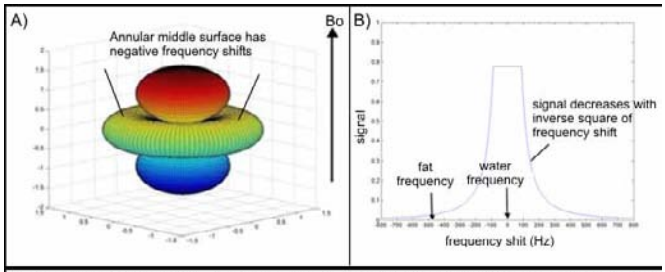

Figure 1: A) Enhancement pattern for an iron particle in the presence of the static magnetic field. B) Plot showing enhancement volume for different frequency shifts.

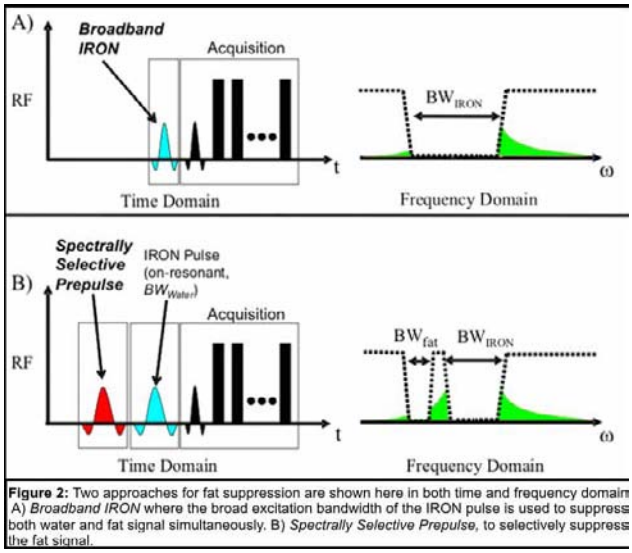

Figure 2: Two approaches for fat suppression are shown here in both time and frequency domain. A) *Broadband IRON* where the broad excitation bandwidth of the IRON pulse is used to suppress both water and fat signal simultaneously. B) *Spectrally Selective Prepulse*, to selectively suppress the fat signal.

Based on theoretical considerations, two strategies were developed to suppress fat signal for the IRON method. The **first** design, *Broadband IRON*, uses an IRON pulse with a broad excitation bandwidth (BW_{IRON}) and a center frequency set between the on-resonant protons and off-resonant fat (FA=95°, frequency offset=-240 Hz, BW_{IRON}=1020 Hz, duration=5ms), therein simultaneously suppressing both water and fat signal (Fig 2A). The **second** strategy, *Spectrally Selective Prepulse*, combines the IRON pulse (FA=95°, frequency offset=0 Hz, BW_{IRON}=145 Hz, duration=35ms) with a spectral presaturation prepulse (FA=95°, frequency offset=-480 Hz, BW=339 Hz, duration=15ms) to selectively suppress fat signal (Fig 2B).

These two approaches were implemented on a Philips 3T Achieva scanner and compared *in vitro* in a gelatin phantom. Three 15ml samples were embedded in the gelatin containing **1.** agarose doped with $CuSO_4$; **2.** doped agarose with iron-labeled C17.2 murine neural stem cells (~2 million); and **3.** mineral oil. Stem cells were magnetically labeled by magnetoelectroporation[2]. Coronal images were obtained using the IRON method combined with a fast spin-echo image acquisition (TE/TR=10ms/3000ms, FA=90°, FOV/matrix=220mm/512, slice thickness=3mm, echo spacing=10ms, echo train length=24). For image analysis, regions-of-interest were manually selected within the agarose, oil and stem cells. Subsequently, signal-to-noise ratio (SNR) for the enhanced cell signal and contrast-to-noise ratio (CNR) between the cells/fat, cells/agarose and agarose/fat were determined for both approaches.

Results: The MATLAB simulation of the dipolar field equation shows the anticipated shifts in the Larmor frequencies and the characteristic dipolar pattern when a superparamagnetic particle is exposed to a static magnetic field B_0 (Fig 1A). Positive frequency shifts are associated with the upper and lower lobes, and negative shifts are associated with the annular middle surface (Fig 1A-arrows). Volume integration shows that the volume enclosed by the positive lobes is identical to that enclosed by the annular surface. Hence, there is equal amount of signal coming from protons with both positive and negative frequency shifts. Further, the partial differentiation suggests that the amount of signal originating from all protons with a particular frequency shift decreases with the inverse square of that frequency shift (Fig 1B).

Using the IRON method *in vitro* without fat suppression, significant enhancement of the iron-labeled cells was observed but the fat signal also appeared hyper-enhanced, as expected (Fig 3A). However, by using the *Broadband IRON* pulse that suppresses on-resonant protons and fat simultaneously, moderate suppression of water and fat signal was observed, and the enhancement from the negative frequencies was concurrently suppressed, as anticipated (Fig 3B-arrows). In contrast, excellent fat and water suppression was obtained using the *Spectrally Selective Prepulse* in combination with IRON imaging (Fig 3C).

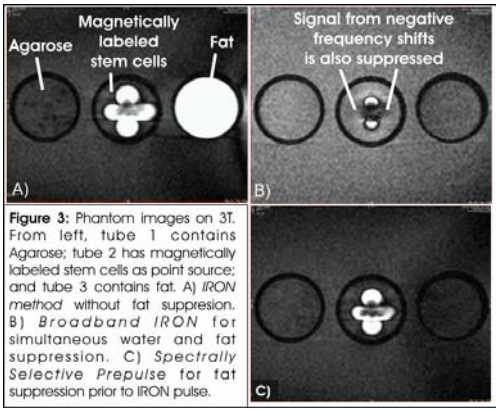

Figure 3: Phantom images on 3T. From left, tube 1 contains Agarose; tube 2 has magnetically labeled stem cells as point source; and tube 3 contains fat. A) *IRON method* without fat suppresion. B) *Broadband IRON* for simultaneous water and fat suppression. C) *Spectrally Selective Prepulse* for fat suppression prior to IRON pulse.

Conclusions: Effective fat suppression with IRON imaging was demonstrated *in vitro*; while hyper-enhanced visualization of iron-labeled stem cells was obtained using both fat suppression techniques. Excellent signal enhancement and fat suppression were observed using the IRON method with the *Spectrally Selective Prepulse*. The use of this technique resulted in superior cell SNR and CNR as compared to the *Broadband IRON* approach. Although suppression was generally reduced with the *Broadband IRON* approach, the short preparation time associated with this design may lend itself to be useful in rapid imaging strategies.

	Imaging Method	IRON pulse without fat suppression	Fat suppression using *Broadband IRON*	Fat suppression using *Spectrally Selective Prepulse*
1	SNR_{cells}	95.01	38.38	78.37
2	SNR_{fat}	180.47	19.89	13.52
3	$SNR_{agarose}$	21.02	30.16	23.05
4	$CNR_{(cells/agarose)}$	73.99	8.22	55.32
5	$CNR_{(cells/fat)}$	85.46	18.49	64.85
6	$CNR_{(agarose/fat)}$	159.45	10.27	9.53

Table 1: SNR and CNR Comparisons

References:

[1] Stuber M, *et al*, Proc. ISMRM 13 (2005).

[2] Walczak P, *et al*, MRM 54, 769-774 (2005).