Shedding Light on the Dark Spot with IRON - A Method that Generates Positive Contrast in the Presence of Superparamagnetic Nanoparticles

M. Stuber[1], W. D. Gilson[2], M. Schaer[3], J. W. Bulte[4], D. L. Kraitchman[2]

[1]Radiology, Medicine, and Electrical Engineering, Johns Hopkins University, Baltimore, MD, United States, [2]Radiology, Johns Hopkins University, Baltimore, MD, United States, [3]Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland, [4]Radiology and Institute for Cell Engineering, Johns Hopkins University, Baltimore, MD, United States

Introduction

The use of superparamagnetic materials has shown promise for contrast generation in atherosclerosis imaging, stem cell research, and catheter tracking. However, the associated negative contrast created by susceptibility artifacts can be difficult to discriminate from other potential sources of signal voids (absence of tissue, motion artifacts, calcifications, etc.). For these reasons, we have developed **I**nversion-**R**ecovery **ON**-Resonant water suppression (***IRON***), an imaging methodology that enables the signal-enhanced visualization of non-diamagnetic materials. The technique is introduced and first in-vitro results obtained in iron-loaded stem cells are discussed.

Methods

The local external field-shift of a non-diamagnetic spherical particle exposed to the static magnetic field (B_0), can be described as

$$\Delta B(r,\Theta)_{External} \sim \frac{\Delta K}{3}\frac{a^3}{r^3}\left(3\cos^2\Theta - 1\right)B_0 \qquad \text{[Equation 1]},$$

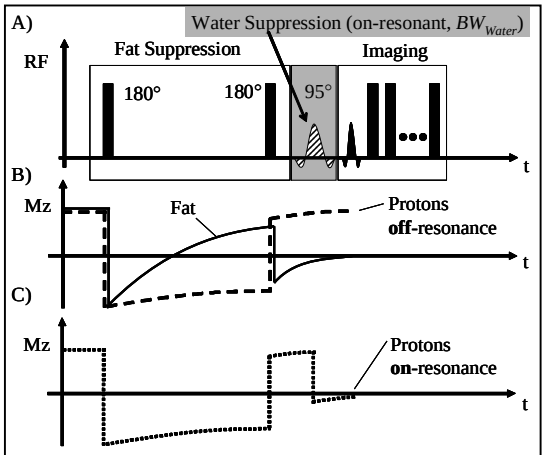

Figure 1 IRON pulse sequence (A) for signal-enhanced visualization of non-diamagnetic objects and the corresponding Mz of fat (B), off-resonant (B) and on-resonant (C) protons. High signal is obtained from off-resonant protons while both fat and on-resonant water appear signal-suppressed.

in which ΔK is the difference in susceptibility, and $\boldsymbol{r}$ and a refer to the distance from the particle and to its radius, respectively. The angle between $\boldsymbol{r}$ and $\boldsymbol{B_0}$ is Θ. External to the particle, the frequency shift is $\Delta\omega_{External}=\gamma\Delta B_{External}$. *Concept IRON:* Using a spectrally selective saturation pre-pulse with the center frequency ω_0 and the bandwidth BW_{Water}, the signal originating from on-resonant protons can be suppressed (Figure 1). However, this saturation pulse does not affect off-resonant protons in close proximity to the non-diamagnetic particles (Figure 1B). Therefore, signal enhancement adjacent to these particles can be generated while the on-resonant background appears signal-attenuated (Figure 1C). With $r\sim(BW_{Water})^{1/3}$, the size of the signal-enhanced area can be controlled by adjusting BW_{Water}. Fat saturation is obtained by adding a preceding dual-inversion pre-pulse. (Figure 1 A, B). *Implementation:* IRON was implemented on a 1.5T Philips Intera system and fast spin-echo imaging of a 5mm thick slice perpendicular to $\mathbf{B}_0$ (FOV/matrix=180mm/256, TE/TR=4.6ms/2RR, Inter echo spacing=4.6ms, ETL=24, 2 NSA) was performed *with* (BW_{Water}=100Hz, 50ms duration, excitation angle=95°) and *without* on-resonant water suppression in an agarose phantom (T1=850ms) in which a strand (anterior-posterior orientation) of $1.5\text{x}10^7$/mL iron-loaded (PLL Feridex) mesenchymal stem cells was injected (Figure 2). In a second experiment (2mm slice thickness) with slice orientation perpendicular to the strand of cells, imaging was performed with BW_{Water}=100Hz, 170Hz, and 340Hz (Figure 2C-E) and the areas of signal enhancement were measured. On all images, contrast-to-noise (CNR) between signal-enhanced and signal-suppressed areas was quantified. On the image of Figure 2C, Θ_0 between $\mathbf{B}_0$ and the axis $\boldsymbol{r}$ with minimal signal enhancement was manually determined.

Results

While a signal void is obvious at the injection site of the cells on the conventional fast spin-echo image in Figure 2A (CNR~14), the use of IRON leads to a substantial signal enhancement in the same region (Figure 2B). In this figure, the surrounding agarose appears signal-attenuated and a CNR of ~47 was measured. In Figure 2C-E, consistent with Equation 1, the characteristic dipolar field surrounding the cells can be appreciated as signal enhancement. With BW_{Water} of 100Hz, 170Hz and 340Hz, CNR amounted to 40, 24 and 7 while the signal-enhanced area was 24mm^2, 16mm^2, and 6mm^2, respectively. The measured Θ_0 where signal-enhancement is zero was 54° while 54.73° is predicted by Equation 1 ($\gamma\Delta B(\Theta_0)=0$).

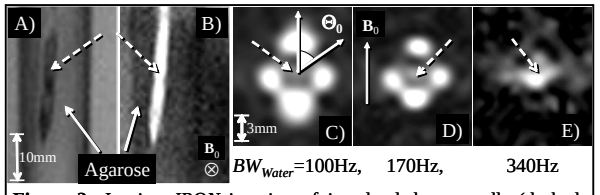

Figure 2 In-vitro *IRON* imaging of iron-loaded stem cells (dashed arrows) was performed *without* (A) and *with* (B) on-resonant water suppression. Imaging perpendicular to the vein (C-E) with incremental BW_{Water} leads to a change in size of the dipolar signal-enhanced area surrounding the cells. Θ_0 refers to the polar angle between maximum and minimum signal intensity.

Discussion and Conclusions

IRON is an MRI methodology that enables the selective signal-enhanced visualization of superparamagnetic nanoparticles with very high positive contrast. A good quantitative and qualitative agreement between theory and practice was found, and the size of the signal-enhanced area can be controlled by adjusting BW_{Water}. The first successful in-vitro results were obtained in iron loaded stem cells. Additional potential applications include the visualization of iron uptake of macrophages and passive catheter tracking. The method remains to be compared with alternative approaches [1, 2].

References

1.) Seppenwoolde *et al*, Magn Reson Med 50:784-790 (2003). **2.)** Coristine *et al*, Proc Intl. Soc. Mag. Reson. Med. 11(2004).