Saturation by Off-resonance Irradiation: An Alternative Contrast with Superparamagnetic Particles

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Introduction:

Currently, superparamagnetic contrast agents, such as monocrystalline iron oxide nanoparticles (MION), are typically used as contrast agents based on their effect on T2 or T2*. Because these particles cause local field inhomogeneities, it is also possible, by the application of off-resonance irradiation, to exploit the effect of field inhomogeneity as an alternative contrast mechanism for these agents. In this work, we examine the effect of off-resonance irradiation on the image intensity in the presence of MION, demonstrate that an off-resonance effect, distinct from the MT effect, exists, investigate its dependence on off-resonance frequency and MION concentration and explore its potential as an alternative contrast mechanism.

Theory:

In the presence of an external magnetic field, superparamagnetic particles become aligned along the external field. This in turn causes an alteration in the magnetic field surrounding each particle. Consequently, application of appropriate off-resonant irradiation will saturate protons in some volume surrounding the particle and diffusion will lead to an apparent partial saturation, causing a signal reduction similar to that in magnetization transfer. From the spatial distribution of a dipole field, it is furthermore anticipated that larger off-resonance ($\Delta\omega$) occurs in small shells near the particle, leading to smaller effect, and smaller $\Delta\omega$ occurs in larger volumes, corresponding to greater effects. In this work, the effect of off-resonance irradiation in the presence of MION is experimentally investigated.

Methods:

MION particles, (2.5mM Fe in citrate buffer) with average diameter 5nm, were prepared in house (courtesy of Dr. Hui Mao Emory University School of Medicine). Dilutions were made using de-ionized water. Imaging was performed on a 3T Siemens TRIO scanner. Off-resonant irradiation was accomplished by adding a 6-ms Gaussian pulse prior to each TR in both a spin-echo sequence and a FLASH sequence.

Results:

The off-resonance irradiation results in a decrease in signal that is dependent on concentration and offset frequency (see Figure 1). In the figure, the line for pure water represents signal loss due to direct saturation, and is therefore viewed as baseline for assessment. Our data suggests a useful offset range of 500Hz < $|\Delta\omega|$ < 1500Hz, less than which direct saturation is high and beyond which the off-resonant effect diminishes. In Figure 2, a FLASH image obtained without off-resonance irradiation (left) and an image corresponding to the ratio, $1-M_{sat}/M_o$, (right), where M_{sat} was obtained with 1500 Hz offset irradiation, are shown. The latter is analogous to the magnetization transfer ratio in MT imaging. In the ratio image, it can be seen that pure water shows little signal and MION particles can be identified at concentrations as low as 20µM. Figure 3 shows a phantom made from 2% agar and embedded with cylinders of agar containing various concentrations of particles. The locations of embedded particles can be identified on the right image within the agar (which also shows MT effect) indicating this effect is distinct from magnetization transfer.

Discussion:

This off-resonance effect is presumably dependent on several factors. One is the fraction of volume being directly saturated by the off-resonance irradiation, which depends on $\Delta\omega$ and particle concentration. The exact dependence on the frequency can be examined with numerical simulation which is being conducted. The dependence on the concentration should be linear for small concentration and nonlinear when the particles become closely packed. Another factor is how the off-resonance irradiation is applied. Here, a pulse was applied every TR and any steady state would depend on time of applied RF, diffusion of water molecules, and magnetic characteristics of particles.

In conclusion, this work demonstrates a new vehicle to exploit the contrast of superparamagnetic particles. In conjunction with obtaining a T2 image, an off-resonant image may be obtained to provide further characterization of the agent. This can be especially useful in molecular imaging where it may be difficult to obtain high in-vivo concentrations of contrast agent.

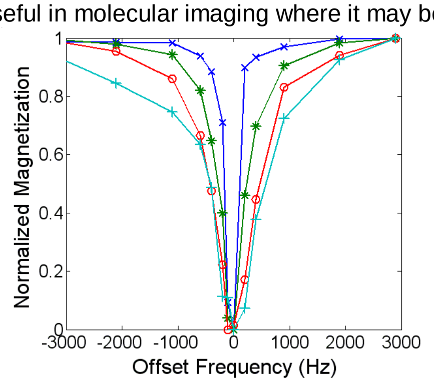

Fig. 1 Normalized magnetization vs. offset frequency. x- H_2O, *- 0.03mM, o-0.15mM, +-0.45 mM

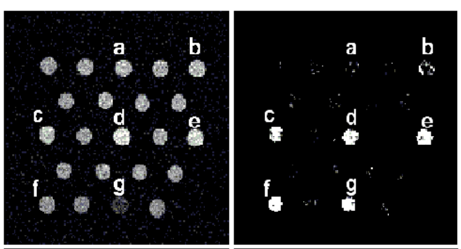

Fig. 2 FLASH imaging of MION solutions. (mM). a) 0.0025 b) 0.01 c) 0.02 d) 0.03 e) 0.06 f) 0.15 g) 0.45. All other vials are water. The left image is taken without off-resonance, and the image on right is the ratio $1-M_{sat}/M_o$ where M_{sat} is the image taken with saturation pulses (image not shown). TR 35 ms, TE 4.8ms, flip angle 20º, offset 1500 Hz .

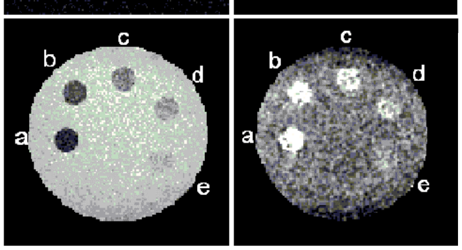

Fig. 3 Agar phantom (2%) with embedded particles; in mM: a) 0.5 b) 0.25 c) 0.125 d) 0.63 e) 0.31. The left image is taken without off-resonance pulses, and the image on right is the ratio $1-M_{sat}/M_o$ where M_{sat} is the image taken with saturation pulses (image not shown). TR 35 ms, TE 4.8ms, flip angle 20º, offset -700 Hz.

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