Adiabatic Pulse Preparation for Imaging Iron Oxide Nanoparticles

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Introduction

Superparamagnetic iron-oxide (SPIO) nanoparticles have found broad applications in clinical and research settings. While their initial detection with MRI was based on T2 and T2* shortening, a number of techniques producing positive contrast, including using unbalanced gradients [1] and spectrally selective RF pulses [2], have emerged. These methods produce hyperintensities as a result of the bulk susceptibility effects of the SPIO nanoparticles. We introduce a method sensitive to the local magnetic field inhomogeneity produced by the individual nanoparticles [3] to selectively prepare and image the effect of SPIO particles. Specifically, we use adiabatic pulses which are amplitude and frequency modulated RF pulses that rotate the magnetization with the effective B_1 field provided the adiabatic condition is met [4]. Near the SPIO particles, the adiabatic condition is violated due to large frequency offsets and the adiabatic pulse does not work as expected. We hypothesized that adiabatic pulses can therefore be used to detect the microscopic changes in the magnetic field surrounding the nanoparticles to produce a positive contrast and tested this hypothesis numerically and experimentally.

Methods

Monte Carlo simulations were preformed in MATLAB with 250 spins randomly assigned starting positions within simulated environments of varying particle concentrations. For each 1 microsecond time-step the local magnetic field was calculated and the Bloch equation was used to simulate the effect under the influence both the adiabatic pulse and the local magnetic field, taking into account three-dimensional diffusion within the local variations of the magnetic field. Phantoms were made with Feridex (Advanced Magnetics, Inc., Cambridge, MA, USA) in water and 2% agar gel. Imaging was preformed on a 3T Siemens Magnetom Trio using a spin-echo sequence. Images were acquired after preparation with either an adiabatic full passage pulse (10 msec with a 1000-Hz maximum frequency offset) or an adiabatic zero passage (two adiabatic full passage pulses applied back-to-back). The adiabaticity and maximum B_1 power were determined experimentally in the absence of SPIOs. SPIO sensitive images were generated by taking the difference of images acquired with and without adiabatic preparation and then normalizing to the non-prepared image. For comparison, off resonance saturation was preformed using a FLASH sequence with 6 msec, 1000 Hz offset Gaussian preparation pulses [5].

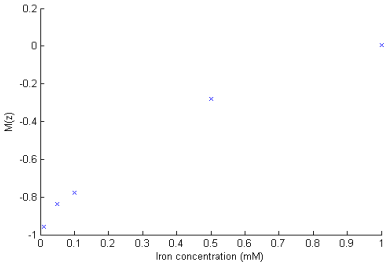

Figure 1: *Simulation shows that the failure of the adiabatic condition in the region surrounding the nanoparticles reduces the longitudinal magnetization at the end of the preparation pulse.*

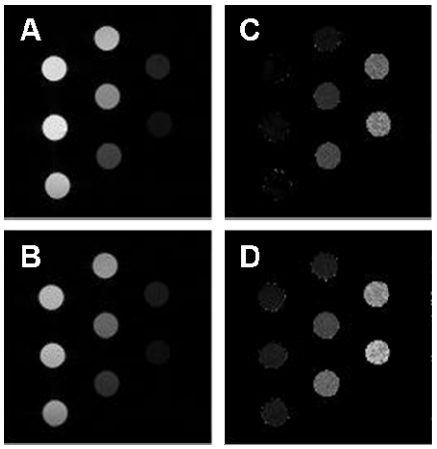

Figure 2: *Spin-echo images show decreased signal with increasing iron concentration in (A) water and (B) agar gel. Normalized difference images demonstrate positive contrast with increasing concentration in (C) water and (D) agar gel. Iron concentrations: (left, top-down) 0.0, 0.025, 0.05 (middle, top-down) 0.1, 0.25, 0.5 (right, top-down) 0.75, 1.0 mM.*

Results

The simulation data show a decrease in the magnitude of the longitudinal magnetization at the end of the applied adiabatic full passage as a function of the SPIO concentration (Fig. 1). For spins diffusing in regions near the nanoparticles the adiabatic condition is destroyed resulting in incomplete inversion. In Fig. 2 experimentally acquired non-prepared images show signal loss with increasing particle concentration in (A) water and (B) agar gel. The normalized difference images with and without adiabatic full passage preparation show positive contrast at higher particle concentration in (C) water and (D) agar gel. The linear correlation of this contrast with increasing iron concentration is evident both in the adiabatic full passage (Fig. 3a) and zero-passage (Fig. 3b) prepared conditions. Compared to using the off resonance saturation technique [5], the adiabatic preparation generated contrast does not saturate within the range of particle concentrations studied and appears less sensitive to magnetization transfer (Fig 3c).

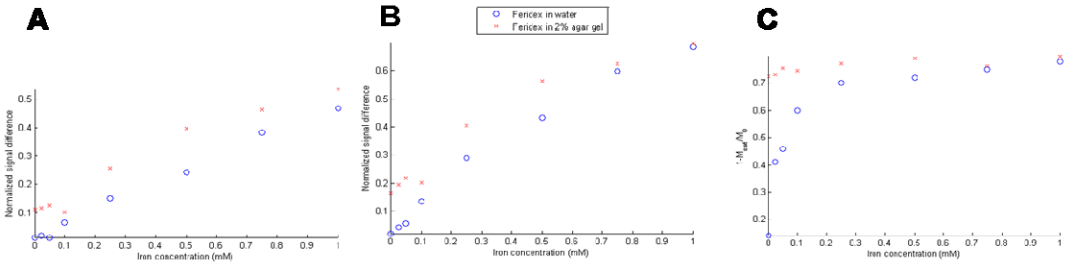

Figure 3: *Increasing normalized difference intensity with increasing iron concentration with (A) single adiabatic full passage and (B) double, zero passage adiabatic full passage preparation, and (C) off resonance saturation method provided for comparison.*

Discussion

Taken with the simulation data, our experimental data suggest that the failure of the adiabatic condition in the region surrounding the nanoparticle is the origin of this microscopic imaging contrast. The flexibility of the adiabatic pulse offers several potential options for modifying contrast from the proposed technique. The ability to modulate the pulse duration, RF power and frequency sweep may produce varying contrasts based on diffusion and other off-resonance processes. Adiabatic pulses may be especially useful for detecting and quantifying nanoparticles *in vivo*, where the complex environment demands a more specific imaging contrast. In addition, the linear relationship of the contrast with increasing iron concentration allows for quantification of a broad range of particle concentrations and the small increase in the contrast due to the presence of agar indicates that the present approach is not very sensitive to magnetization transfer.

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References: [1] Seppenwoolde JH et al. Magn Reson Med 2003; 50(4):784-790. [2] Stuber M et al. Magn Reson Med 2007;58(5):1072-1077. [3] Schenck JF. Med Phys 1996; 23(6):815-850. [4] Garwood M, DelaBarre L. J Magn Reson 2001;153(2):155-177. [5] Zurkiya O, Hu X. Magn Reson Med 2006; 56(4):726-732.