Off-Resonance Spin Echos for Probing the Cellular Microenvironment

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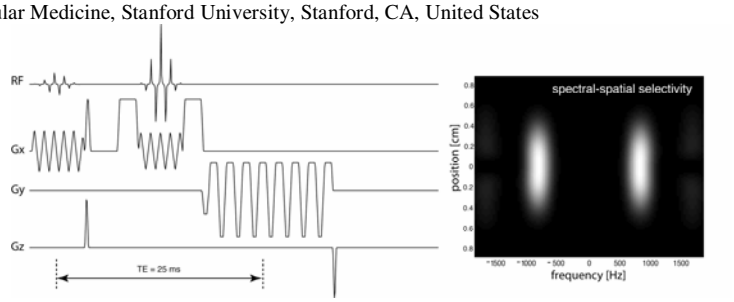
INTRODUCTION Several methods have recently been proposed [1-6] for obtaining positive contrast when imaging regions of concentrated superparamagnetic iron oxide (SPIO). In all of these methods, the spins imaged are those that usually contribute to the negative contrast, with the mechanism being dephasing in the presence of the strong field inhomogeneity surrounding the particles (static dephasing [7]). These spins are re-focused by means of a gradient or RF refocusing, and the other spins are suppressed by means of crusher gradients or by simply not being excited. In this abstract, the principle that the positive contrast signal can carry information about the local microenvironment surrounding the particles is demonstrated.



METHODS A new pulse sequence consisting of spectral-spatial excitation/refocusing pulses and an optional oscillating readout gradient was developed for these experiments (see Fig. 1). The use of spectral-spatial pulses offers a significant advantage over our original method in that regions that can cause contamination of the positive-contrast signal, such as air-tissue boundaries, can be excluded from the excited volume. The oscillating gradient provides a spectroscopic imaging mode so that the frequencies surrounding the cells can be resolved and spatial shifts corrected.

The method was tested by imaging phantoms implanted with mouse embryonic stem cells (mESC), as well as a rat with 3x10^6 cells injected into the wall of the left ventricle. The cells were labeled with ferumoxides at 100 ug/mL iron concentration. All experiments were performed on a GE Signa 1.5T system with 40 mT/m, 150 mT/m/ms gradients. The frequency to be excited was changed by manually changing the scanner center frequency.

The ability to rapidly measure the interaction between the positive-contrast signal and a second contrast agent was tested. A plastic tube with a conical tip containing 5 x 10^7 mESCs labeled with ferumoxides was suspended in 250 mL of tap water, within a cylindrical container. The pulse sequence was tuned to -400Hz from resonance so that only signal from a thin layer surrounding the cells was excited/refocused. During data acquisition, 0.5 mL of Gd-DTPA (Magnevist, Berlex Labs) was injected and stirred.

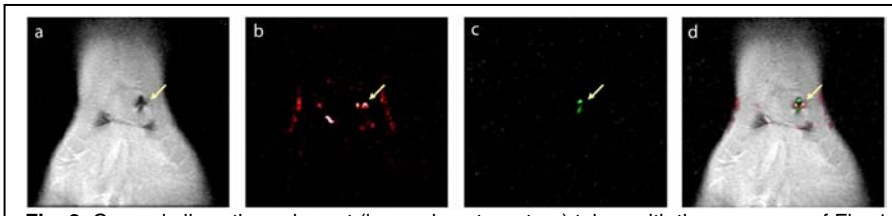


Fig. 2: Coronal slices through a rat (imaged post-mortem) taken with the sequence of Fig. 1 with center frequency (a) on resonance (b) at -420 Hz and (c) at +420 Hz. (d) Fused images show the frequency distribution around the cells. Acquisition parameters: 7.6cm receive coil, TR=600ms, TE=25ms, 128x256 matrix, FOV=10cm, bw=15.6kHz.

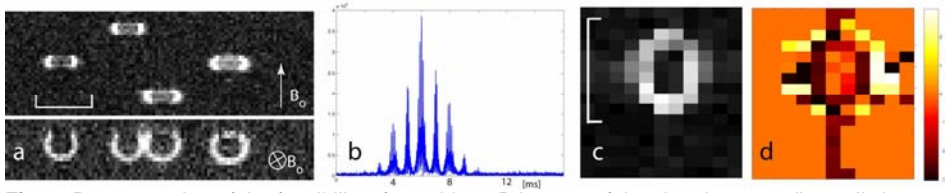


Fig. 3: Demonstration of the feasibility of acquiring 3D images of the signal surrounding cells in an agar phantom. (a) A coronal (upper) and an axial projection through the 3D data set are shown, with each bright region being the signal surrounding 2x10^6 cells. (b) With the oscillating readout gradient, several spatial k-space traversals can be completed during the spin echo (the average of 128 excitations is shown). By applying phase encoding in the other directions, each of these echoes can be used to create an image (c), with the multiple echoes combined to create a frequency map (d) (units of radians/2ms k-space traversal). The scales in (a) and (c) show 1 cm.

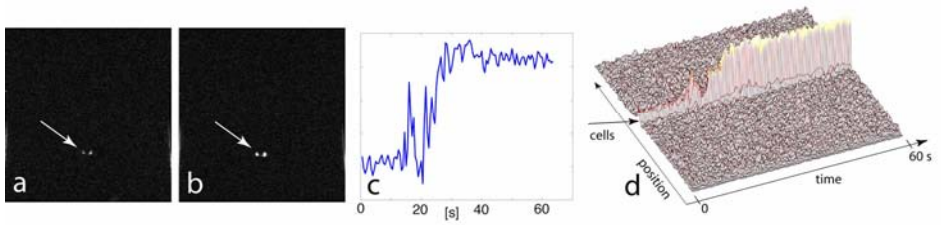


Fig. 4: Dynamic Gd-DTPA enhancement study. Images before (a) and after (b) injection of Gd-DTPA show the enhancement. (c) The amplitude of echoes (no phase encoding) acquired during the injection/mixing show the dynamics of the second agent as it mixes with the water immediately adjacent to the cells. (d) With a spatial-encoding gradient applied during each echo, a localized signal is resolved vs. time. Note that the signal remains localized to the cells. TR=500ms, TE=25ms, FOV=16cm.

CONCLUSIONS Positive contrast methods for imaging SPIO agents result in a signal, as opposed to a lack of signal as with conventional methods. It was demonstrated that this signal can carry information such as the local phase distribution surrounding the cells, which could be used for iron quantification. Also, a proof-of-principle experiment showed that information about a complementary contrast agent such as Gd-DTPA can be measured in the positive contrast signal. The spatial localization provided by the off-resonance excitation enabled a complete measurement every TR (500 ms) giving dynamic information. This dynamic information could be useful for probing local angiogenesis or measuring the interaction of targeted probes with the cells.

[1] Coristine et al. Proceedings of the ISMRM, 163 (2004) [2] Cunningham et al. Magnetic Resonance in Medicine 53:999-1005 (2005) [3] Grant et al. Proceedings of the ISMRM, 2209 (2005) [4] Stuber et al. Proceedings of the ISMRM, 2608 (2005) [5] Carmichael et al. Proceedings of the ISMRM, 2613 (2005) [6] Foltz et al. Proceedings of the ISMRM, 2627 (2005) [7] Bowen et al. Magnetic Resonance in Medicine 48:52-61 (2002)