Single Cell MRI with FIESTA: Quantitative Benefits of 3T vs 1.5T

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Introduction: The use of MRI with magnetic nanoparticles for imaging specific cells and cell populations is a rapidly growing field of research. Work in our lab has focused on developing MR tools for detecting single iron-labeled cells. Recently we showed for the first time that individual iron-labeled cells can be detected *in vivo* in mouse brain using a steady state free precession imaging sequence (FIESTA, GE Healthcare, Milwaukee, WI) and an optimized micro-imaging system on a clinical 1.5T scanner (1). This *in vivo* image data was acquired in 1.5hrs at 100x100x200μm^3 spatial resolution with an iron loading of ~50pgFe/cell. We also know that single cell contrast improves significantly with increases in spatial resolution (2). To acquire higher resolution image data at 1.5T would require scan times that are prohibitive for *in vivo* serial scanning of animal models (ie. 100µm isotropic images with the same SNR would take ~6hrs). In this study we investigate the use of higher magnetic field strength (3T) to allow for high resolution FIESTA image data acquisition in reasonable scan times, and the impact of this strategy on contrast generated by iron labeled cells.

Methods: ***Cell Labeling***: MDA-MB-231BR cells, a brain-seeking breast cancer cell line, were labeled with Dragon Green fluorescent MPIO beads (Bangs Laboratory, Fishers, IN). The mean iron content per cell was measured by MR susceptometry. ***Animal Preparation***: Mice were anesthetized and 10,000 SPIO-labeled cells were injected into the left ventricle to deliver cells to the brain. Mice were sacrificed and the heads fixed in formalin for 24 hrs before *ex vivo* scanning. ***MRI***: Scanning was performed on 1.5 and 3.0 T GE MR systems using a custom-built gradient coil insert (maximum gradient strength 600mT/m, peak slew rate 3000T/m/s) and matched solenoidal radiofrequency coils (2 cm diameter). Images of the same mouse brains were acquired at both field strengths using the FIESTA pulse sequence with the following parameter set: TR/TE 7.1/3.6ms (1.5T) or 7.2/3.5ms (3T), flip angle 30°, bandwidth +/-21 kHz, 100x100x100 μm^3 resolution. To match the SNR between field strengths, 12 scans were averaged at 3T (37min scan time) and 48 at 1.5T (146min scan time). In addition, higher resolution FIESTA images (62x62x100 μm^3 spatial resolution) were acquired at 3T with TR/TE = 7.9/3.8ms, bandwidth = +/-31 kHz, 19 NEX in 109min. ***Data Analysis:*** For each image data set the number of individual signal voids was determined manually. For every signal void, the contrast was calculated by taking the difference between the signal from the central voxel of the void (S_{cell}) and signal from background tissue containing no cells (S) and dividing by the background signal: $\Delta S/S=(S-S_{cell})/S$. The mean contrast $\Delta S/S$ was calculated for each of the three scanning conditions. SNR was measured for each data set using ROIs in the cortical gray matter and air. ***Simulations:*** We developed a simulation based on the Kaiser model of diffusion which permitted us to predict $\Delta S/S$ for the specific parameters of mc, BW, R1, R2, fip, and compared these contrast values to experimental $\Delta S/S$ values.

Results: The mean cellular MPIO content was 34 pgFe/cell. Figure 1 is a comparison of the FIESTA images obtained from each of the three scanning conditions: (A) 1.5T 100 µm isotropic, (B) 3T 100 µm isotropic, and (C) 3T 60x60x100 μm^3 resolution. Corresponding SNR values were 59, 71 and 48 for A, B & C, respectively. 71 discrete signal voids were counted in data sets A&B. The average experimental $\Delta S/S$ for signal voids identified in the matched 1.5 and 3T data (A&B) was not significantly different (0.51+/-0.21 and 0.49+\/-0.23). The ability to detect regions of signal void was improved with the higher resolution images (C). More regions of signal void were detected with the higher resolution 3T imaging protocol (89) and the mean $\Delta S/S$ was significantly greater (0.68 +/-0.17). These contrast values are slightly higher than those predicted by a theoretical model for FIESTA-based cellular MRI (theoretical values are in the range of 0.35 for 100μm^3 and 0.6 for 60x60x100μm^3), but the lack difference between 1.5T and 3T (A vs B) and the substantial increase in contrast from 100μm^3 voxels to the 60x60x100μm^3 voxels (B vs C) is predicted by this theoretical model.

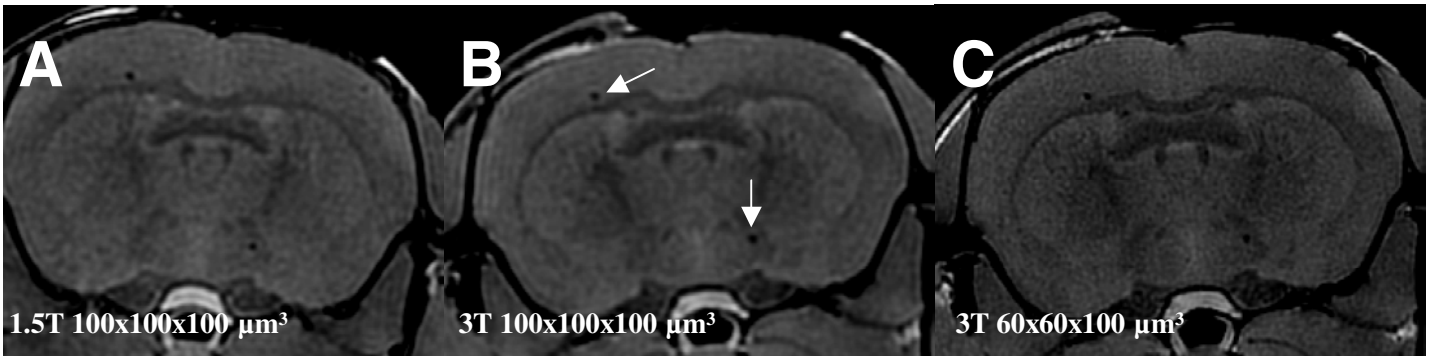

Figure 1: 3DFIESTA images of iron labeled cells in a mouse brain acquired with three different imaging conditions. Arrows = regions of signal loss

Discussion and Conclusions: This is the first study of the effect of increased field strength and decreased voxel size on FIESTA-based single cell detection by MRI. The SNR results show that despite the 4-fold decrease in scan time, the 3T 100μm^3 scans produced greater SNR than the 1.5T 100μm^3 scans. This demonstrates a greater than linear increase in signal-to-noise ratio from 1.5T to 3T. Analyzing this result further, the field strength dependence of the SNR follows a 1.4 power law and taking into account our finding of equivalent single cell contrast between 1.5T and 3T, these results imply that the same single cell detectability is achievable at 3T in a 7-fold shorter scan time. The nearly 50% increase in contrast between 100μm^3 voxels and 60x60x100μm^3 voxels is also a very significant result. The gain in SNR at 3T will allow us to pursue *in vivo* mouse brain imaging at this high spatial resolution. Finally, the lack of significant new artifact (off-resonance banding, blurring, susceptibility-based distortion or signal loss) at 3T compared to 1.5T is surprising and very encouraging to us.