Separation of SPIO and air bubbles for molecular imaging

T. Liu[1,2], R. Wong[1,2], P. Spincemaille[2], and Y. Wang[1,2]

[1]Biomedical Engineering, Cornell University, Ithaca, NY, United States, [2]Radiology, Weill Cornell Medical College, New York, NY, United States

Introduction: Dark T2* contrast of SPIO has been widely used in cell tracking in molecular MRI [1, 2], but this negative contrast may be indistinguishable from ones generated by air bubbles that are commonly observed in gel phantoms due to their porous nature. In this study, we propose to distinguish air bubbles from SPIO labeled cells by quantifying the magnetization at two different field strengths, 1.5T and 3T, using the fact that SPIO magnetization is typically saturated, relative to water, at fields greater than 1T, while the magnetization of air increases linearly with field strength.

Materials and Methods: Due to the limited resolution, cellular MRI is in actuality imaging magnetization inside each individual voxel, whose volume is usually at least 100 times greater than a single cell. However, cells labeled using nano or micro SPIO particles may have the same magnetization as a larger air bubble with paramagnetic susceptibility, giving rise to an identical outside field observed by MRI. The magnetization of an SPIO (Feridex) is nearly saturated at 0.8T [3], while that of an air bubble scales with the external field. As a result, the magnetization of an air bubble will be double at 3T compared to 1.5T while the magnetization of SPIO should only have moderate change. Therefore, the ratio of magnetization between two field strengths is a criterion to differentiate air bubbles from cells.
To prove this concept, a water phantom containing 5 tubes (Fig. 1) was constructed. Four of the tubes were filled with different concentrations of an FDA-approved SPIO Feridex, and one tube was left empty with only air. Another water phantom without any tubes but otherwise identical was also scanned as a reference. Experiments were conducted at 1.5T (GE Signa EXCITE 14.0) using a modified fast gradient echo sequence to acquire multiple TEs in an interleaved manner. A 110×110×76 voxel field of view covered the entire phantom with an isotropic resolution of 1mm. Bandwidth, TR and flip angle were ±31.25kHz, 20ms and 30˚. Four TEs were used at 1.9, 2.4, 4.4 and 14.4ms. Phantoms were rotated around the AP direction and scanned from three orientations at 0˚, -120˚, +120˚. Afterwards, the scans were repeated at 3T (GE Signa EXCITE 14.0) using identical parameters. Susceptibility maps were calculated by inverting the dipole fields measured from multiple orientations [4], which performs a weighted least square fitting of the field map using a conjugate gradient algorithm. On the resulting images, the magnetization of each tube was calculated as the sum of the susceptibility in a circular ROI of 20 pixel diameter (20 mm) in the central slice multiplied with the field strength. The ratio of magnetizations between 3T and 1.5T was subsequently calculated. An empirical value of 1.6 was chosen as the threshold ratio to differentiate air and Feridex.

Results: Air and 4~5% Feridex were indistinguishable at TE=1.9ms at both 1.5 and 3T as negligible signal was observed in magnitude images (Fig. 1). In contrast, susceptibility maps revealed positive contrast corresponding to the susceptibilities of air and Feridex (Fig. 2). The ratio of magnetization is 1.93 for air, and 1.12, 1.06, 1.26, 1.21 for 2, 3, 4 and 5% concentrations of Feridex, respectively. The 1.6 threshold successfully distinguished air and Feridex.

Discussion and conclusion: We have shown that susceptibility mapping at 2 field strengths can be utilized to indicate the presence of air or SPIO due to the differing magnetic saturation properties of each. The magnetization quantification was accomplished by inverting the dipole field from multiple orientation measurements; this technique does not require any knowledge of the magnetic source's geometry or volume, thus avoiding the confusion of air and cells caused by limited resolution, and could potentially be used to better identify a single cell in *in vitro* single cell imaging.

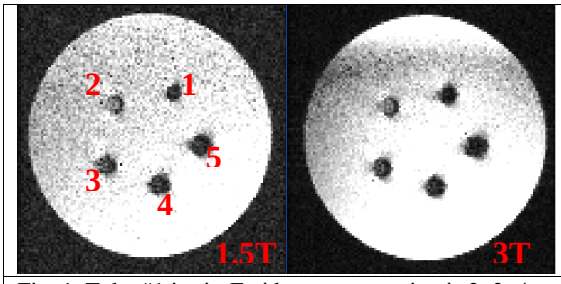

Fig. 1. Tube #1 is air. Feridex concentration is 2, 3, 4 and 5% for tube #2, 3, 4, and5.

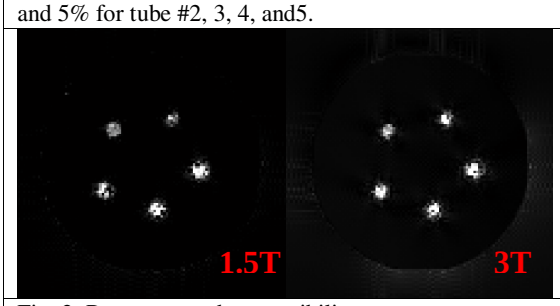

Fig. 2. Reconstructed susceptibility map

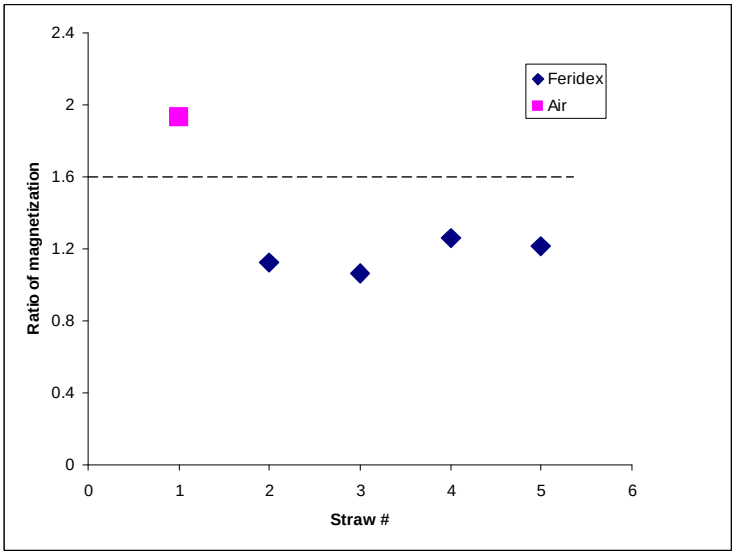

Fig. 3 Ratio of magnetization

Ref: [1] Shapiro et al., MRM: 55: 242-249. [2] Foster-Gareau et al., MRM: 49: 968-971. [3] Jung et al., MRI: 13(5): 661-674. [4] Liu et al, ISMRM 2008, p.643