Comparing Sensitivity of Magnetic Particle Imaging with 19F Magnetic Resonance Imaging for cell tracking

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Cell tracking

Cell tracking is fundamental for understanding biological processes and important for the development of novel cell-based therapies to treat disease. Current techniques face limitation because of either toxicity (tracers that produce ionizing radiation), or a lack of positive (and quantifiable) contrast.

Recently, 19-Fluorine Magetic Resonance Imaging (MRI) has been addressed [1] to overcome these issues. Even more new is the use of Magnetic Particle Imaging, a new imaging modality [2,3], for cell tracking [4].

A comparison between both modalities in terms of Signal to Noise Ratio (SNR) has not been done before but could determine the future of cell tracking research. For our research, the focus will be on Human Mesenchymal Stem Cells (hMSC).

19F MRI

Figure 1. Image of Bruker's 7T small animal MRI scanner [5].

19F MRI Physics

Signal Equation:

$$M = \frac{N\gamma^2\hbar^2 I_z(I_z+1)B_0}{3k_bT}$$

M = equilibrium nuclear magnetization
N = number of nuclear spins per unit volume
k_b = Boltzmann's constant
$\hbar$ = Planck's constant/2π
I_z = spin
T = temperature
B0 = Main magnetic field

- Detects Fluorine atoms
- Spins are 'pushed' out of equilibrium
- Spins return to equilibrium which results in a changing magnetic moment in the transverse plane. This decay is measured inductively.
- Noise is sample-dominated
- 89% as sensitive as 1H MRI

19F MRI Experimental & Preliminary results

100ul samples with different concentrations of Potassium Fluoride (KF) are placed in 50ml tube with H_20. A 1-slice 17-minute spin-echo scan is performed. SNR is approximated by ($Signal_{avg}$ – $Noise_{avg}$) / $Noise_{std}$.

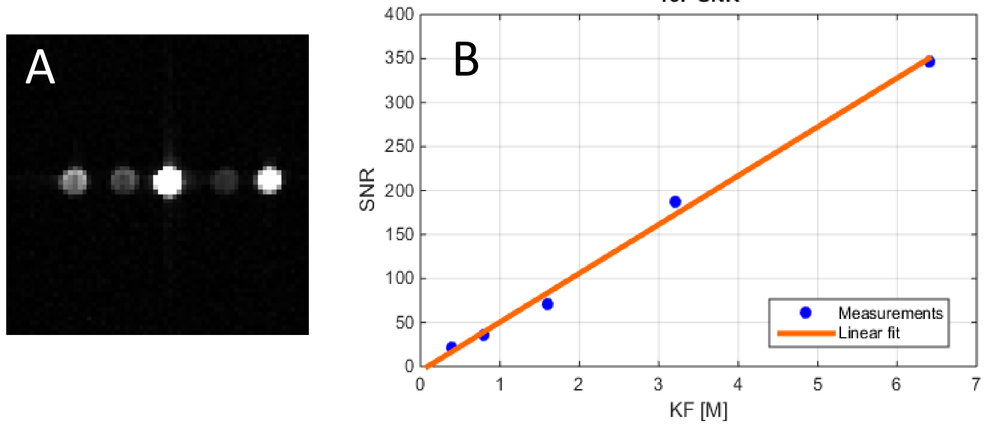

Figure 3. MRI SE image of 100ul KF samples (A) in 200ul PCR tubes inside a 50ml vial of DI H_20. Concentration from left to right: 1.6; 0.8; 6.4; 0.4; 3.2M. SNR results for different vials in (B). FOV: 45*45*2mm. Resolution: 0.7*0.7*2mm. TE: 2.5 milliseconds. Operating center frequency: 282.56MHz. Total scan time: 17 minutes. Total amount of voxels: 4096.

19F MRI Discussion

- 0.15M of F-atoms can be detected (3σ)
- Loading capacity is $7*10^{10}$ F-atoms in hMSC [7]
- Theoretical detection limit: **$1.3*10^6$ cells**
- This is for 17 minutes scan time & $4*10^3$ voxels
- Main source of noise has yet to be implemented

MPI

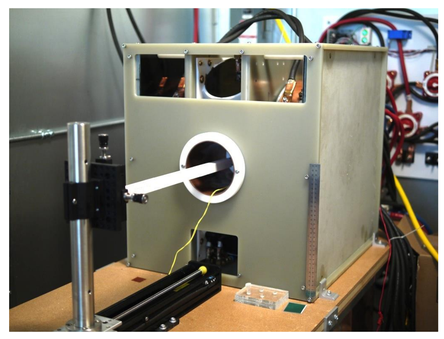

Figure 2. Image of Berkeley's 7T/m small animal MPI scanner.

MPI Physics

Signal Equation:

$$M = M_s\left[coth\left(\frac{\mu_0 mH}{k_bT}\right) - \left(\frac{k_bT}{\mu_0 mH}\right)\right]$$

M = magnetization
M_s = saturation magnetization of SPIO
μ_0 = vacuum permeability
m = magnetic moment
k_b = Boltzmann's constant
T = temperature
H = Magnetic field

- Detects Super Paramagnetic Iron Oxides (SPIO's)
- Employs a moving magnetic 'field free point (FFP)'
- Within this FFP, an external oscillating magnetic field flips the magnetic moment of SPIO's. Changes in magnetic moment are detected inductively.
- Noise is coil-dominated

MPI Experimental & Preliminary results

0.5ul 'point source' samples with different amount of SPIO's are placed in 50g of chicken breast. A 3D, 10 minute scan is performed. SNR in the maximum projection image is approximated by ($Signal_{avg}$ – $Noise_{avg}$) / $Noise_{std}$.

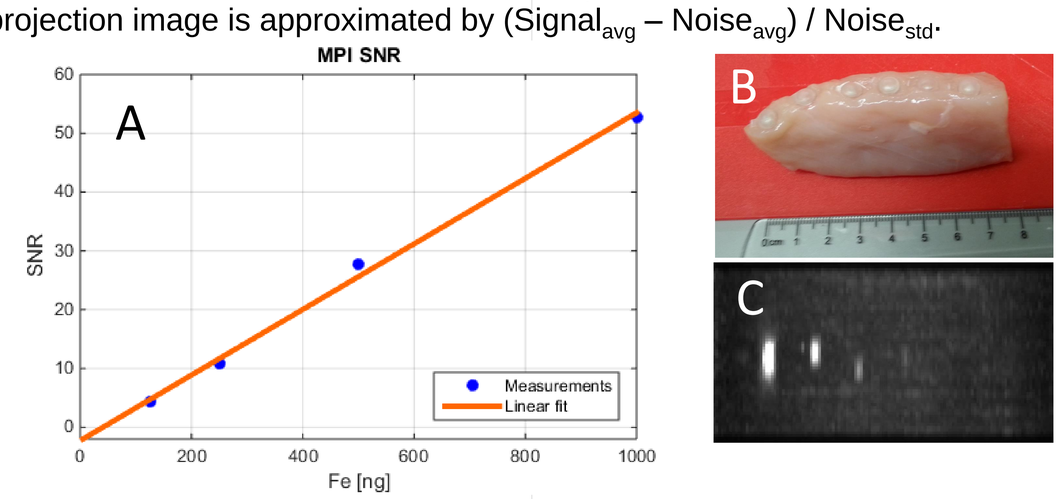

Figure 4: 0.5ul samples of 'MPI tailored' SPIO's [6] are placed in chicken (B). The resulting MPI projection image (C) holds amounts of iron from left to right: 1000; 500; 250; 125ng. SNR results for different samples in (A). Lower amounts (67 & 33ng) are not detected. FOV: 30*30*80mm. Estimated resolution: $3.8mm^3$. Total scan time: 10 minutes. Estimated amount of voxels: $2*10^4$.

MPI Discussion

- 100ng of Fe can be detected (3σ)
- Loading capacity of Resovist is 123pg per hMSC[8]
- Current theoretical detection limit: **800 cells**
- This is for 10 minutes scan time & $2*10^4$ voxels
- Optimization of scanner and SPIO's could decrease detection limit 100-fold

Conclusion & Outlook

Preliminary results match data in literature and theoretical detection limits have been calculated. MPI seems to have a lower detection limit of hMSC's, even though MRI hardware has a 30-year advantage. Advances in MPI hardware and particle design could increase detection limit significantly.

MPI has the potential to be more sensitive than 19F MRI

Now, actual cell-based experiments have to be performed where we will focus on:

- Similar (clinical relevant) scan time: 10 mins
- Similar amount of voxels
- A relevant source of noise for MRI
- Optimal cell loading

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