Off-Resonant Reconstruction of Balanced 3D-Radial Acquisitions with Half-Echo Sampling for Unique Cell Tracking Contrast

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Introduction:

Over the past years magnetic resonance imaging showed a great potential to track stem cells in human-like animal models. Cells have to be labeled ex-vivo with super paramagnetic iron oxide nanoparticles (SPIOs) prior to their transplantation. Subsequently imaging with gradient-echo or balanced steady state free precession (bSSFP) sequences allows in-vivo cell detection with high sensitivitiy [1]. Nevertheless homogeneity of the background signal and motion close to the region of interest are limiting the success of these methods. Within this work, we could show a new contrast for SPIO labelled cells. By off-resonant reconstruction a characteristic ring around the cells, easy to distinguish from the background, is produced. We present this contrast within in-vitro single-cell phantoms as well as in-vivo cell-islets with cell densities down to 1 cell/mm³. A complete simulation of the intra-voxel signal including the point spread function for off-resonant 3D half-echo acquisition (3DPSF) is used to confirm this contrast.

Theory:

Our approach is based on a motion-insensitive 3D radial balanced SSFP acquisition with half-echo sampling and a simple post-processing step. Adding a frequency shift to each half-echo before reconstruction, a unique ring-shaped contrast around voxels containing a strong magnetic perturber (e.q. a single labeled cell) is produced. Due to the 3D radial half-echo acquisition, off-resonant magnetization is shifted to a sphere with radius r = ΔB0/bandwidth/pixel [2] (ΔB0 given in Hz, radius in pixel-units). An additional B0 offset ($\Delta B0_{add}$) applied to the rawdata prior reconstruction shifts magnitude and phase information to neighbouring pixels causing signal cancellation or enhancement. Depending on the magnetic moment of the perturber and the chosen $\Delta B0_{add}$ at the reconstruction, different spherical structures are the result.

Methods:

Measurements and Reconstruction:

Fully-balanced 3D-radial half-echo [3] datasets were acquired on a 3T clinical system using a volume coil for mice. Prior to reconstruction, each rawdata line (S) is modulated: $S_{mod} = S^*\exp(j2\pi\Delta B0_{add} *t)$ whereas t=0 at k-space center and t=N*DT for the last k-space point (with N the resolution and DT the sampling dwell-time). On the modulated rawdata a NUFFT with Kaiser-Bessel window and density compensation is performed. Acquisition:

In-vitro: TR=7.5ms, α=60, TE=0.1ms, matrix=256, FOV: 50mm, 256² spokes, 200Hz/pixel; In-vivo: TR= 5.8ms, α=20, TE=0.1ms, matrix=320, FOV: 51mm, 320² spokes, 256Hz/pixel. Cell-labeling: 3µg/ml protamine sulfate and 200µg/ml Fe SPIO Resovist (Schering, Germany) solution within 24 hours. Suszeptometric measurements [4] showed an average iron load/cell of 48pg. For in vivo cell detection, a 300µl matrigel plaque containing 1.6 million unlabeled ECFCs, 0.4 million unlabeled MSCs mixed with 0, 400, 2000 and 10000 labeled ECFCs was injected subcutaneously in nude mice (left/right to the lungs, left/right to the pelvis). Imaging was performed on day7 post implant. In-vitro: cells were resuspended in 1% agarose gel to reach cellular densities of: 1,2,5,10,25 cells/µl and filled into 5mm NMR glastubes.

Simulations (Fig.1): A full intra-voxel bSSFP simulation with a centered spherical magnetic perturber [1, 5] was performed. Resultant intra-voxel signals are modulated with $\Delta B0_{add}$ and a convolution with the half-echo off-resonant 3DPSF is performed. 3DPSF was calculated prior including the sampling parameters gradient-ramp-up and readout-bandwidth. The simulation volume covered 5x5x5voxels with a discretization of 10µm, 200µm voxel size and a magnetic perturber (cell) with m_c=50pgFe, radius=7µm.

Results:

Simulations (Fig.1) show the generation of the spherical contrast with increasing $\Delta B0_{add}$. At $\Delta B0_{add}$ = 300Hz cells showed a remarkable contrast in-vitro and in-vivo (Fig.2 b,e,g). In-vitro, the borders of the vials holding the agarose-embedded cells are duplicated. In-vivo, just borders between fat/water changed slightly, but did not interfere with the detectability of the cells. Figure 2 c,f shows the contrast evolution over $\Delta B0_{add}$: 0-100-200-300Hz whereas the same signal behaviour was observed for in-vitro and in-vivo scans.

Discussion:

Despite the unique contrast for single labelled cells, at higher cellular concentrations this feature is lost. We observed in-vitro that 10 cells/µl at an isotropic resolution of 200µm seems to be the limit, indicating that at least 1-2 bordering voxels should be free of magnetic perturbers.

Further investigations are needed to investigate if a quantification of the iron-load or amount of cells within one voxel, given a set of reconstructed images of different $\Delta B0_{add,}$ is feasible.

References:

[1] Lebel at al. MRM 55: 583-591 (2006)
[2] Brodsky et al., MRM 59: 1151-1164 (2008)
[3] Diwoky, Stollberger, p327, ISMRM 2011
[4] Bowen et al., MRM 48: 52-61 (2002)
[5] Freeman, Hill, *JMR* 4:366-383 (1971)

Fig.1: Top: Flowchart of the simulation. Bottom: Results of the full bSSFP model with a 50pgFe magnetic perturber with 3DPSF+$\Delta B0_{add}$ =0,100,200,300Hz.

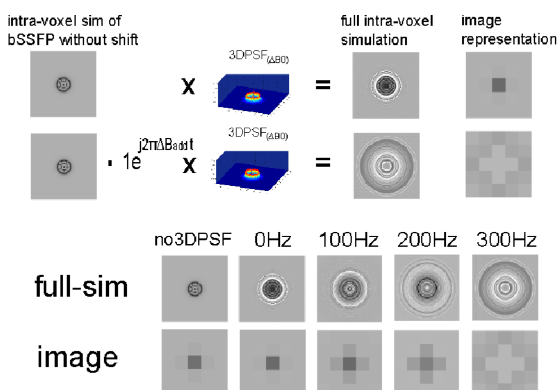

Fig.2: Single-cell phantom $\Delta B0_{add}$ = 0Hz (a), and $\Delta B0_{add}$ =300Hz (b). In-vivo image showing a cell-islet (~7cells/µl) with $\Delta B0_{add}$ =0Hz (d) and $\Delta B0_{add}$ =300Hz (e). Panel (c) and (f) presents the signal for 0-100-200-300Hz $\Delta B0_{add}$. (g) in-vivo coronal slice showing all cell-islets with 0,400,2000,10000 labeled cells at $\Delta B0_{add}$ =300Hz.