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

Contrast

Clemens Diwoxy, Daniel Gungl, Andreas Reinsich, Nicole Anette Hofmann, Dirk Strunk, and Rudolf Stollberger

1Institute of Medical Engineering, Graz University of Technology, Graz, Austria, 2Stem Cell Research Unit, Dept. of Hematology, Univ. Clinic of Internal Medicine, Medical University of Graz, Graz, Austria

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 sensitivity [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.g. a single labeled cell) is produced. Due to the 3D radial half-echo acquisition, off-resonant magnetization is shifted to a sphere with radius \( r = \Delta B_0/\text{bandwidth/pixel} \) \([2]\) (\(\Delta B_0\) given in Hz, radius in pixel-units). An additional B0 offset (\(\Delta B_{\text{add}}\)) 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 \(\Delta B_{\text{add}}\) 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: \( S_{\text{mod}} = S \exp(m2\pi\Delta B_{\text{add}}\alpha) \) whereas \( \alpha = 0 \) at k-space center and \( \alpha = NT\text{DT} \) 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, \(\alpha = 60\), TE=0.1ms, matrix=256, FOV: 50mm, 256² spokes, 200Hz/pixel; In-vivo: TR= 5.8ms, \(\alpha = 20\), TE=0.1ms, matrix=320, FOV: 51mm, 320² spokes, 256Hz/pixel. Cell-labeling: 3g/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 \(\Delta B_{\text{add}}\) 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 5x5x5 voxels with a discretization of 10µm, 200µm voxel size and a magnetic perturber (cell) with \(m=50pgFe\), radius=7µm.

Results:
Simulations (Fig.1) show the generation of the spherical contrast with increasing \(\Delta B_{\text{add}}\). At \(\Delta B_{\text{add}} = 300\text{Hz} \) cells showed a remarkable contrast in-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 \(\Delta B_{\text{add}}\): 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 \(\Delta B_{\text{add}}\) is feasible.

References:

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

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