Non-Monoexponential Signal Decay Due to Single SPIO Loaded Cells

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PURPOSE Superparamagnetic iron oxide (SPIO) nanoparticles have been used to image cell migration with MRI by exploiting the capability of certain cell types to ingest small particles through phagocytosis [1]. Even the detection of single SPIO labeled cells has been reported [2-5], but the MR signal decay characteristics in presence of single labeled cells have not been addressed so far. Our study is aimed at a deeper understanding of how single SPIO labeled cells affects the MR signal decay. As based on numerical simulations and experimental findings, we show that the gradient echo signal decay in presence of a single labeled cell per MR imaging voxel is non-monoexponential.

METHODS Cells loaded with SPIO produce strong dipolar fields around the cell such that diffusion has a minimal effect on the MR signal decay [6]. The field perturbation δB_z in presence of a magnetic dipole was computed to $\delta B_z(r,\varphi) = (\delta\chi \cdot B_0 \cdot (3\cdot\cos^2\varphi - 1)\cdot a^3) / (3\cdot r^3)$ for r > a ($\delta\chi$ magnetic susceptibility, a radius, r distance from the dipole center, φ angle relative to the vector B_0). The frequency distribution was studied in a static 3D numerical model. The related free induction signal decay (FID) was assessed by Fouriertransforming the computed frequency distribution. The magnetic susceptibility $\delta\chi$ was 1300×10^{-6}, the magnetic field strength was B_0 = 1.5 Tesla and the volume fraction (volume of magnetic dipole / 3D volume) was 0.01%.

SK-Mel28 human melanoma cells were labeled by means of incubation with SH U 555A, resulting in an average iron content of 20 pg Fe / cell. 50×10^3 SPIO labeled cells were homogeneously suspended in 50 ml of agar gel. Assuming a homogeneous distribution of cells throughout the sample, the preparation resulted in a concentration of a single cell / μl_{gel}. The control consisted of agar gel without SPIO labeled cells. MR measurements were carried out to study the multi-echo gradient echo signal decay in presence of a single SPIO labeled cell per MR imaging voxel. For that purpose, the size of the MR imaging voxel was 1 µl. Experiments were performed at a whole-body MR unit operating at 1.5 Tesla. Overally 40 echoes were acquired with an echo spacing ΔTE = 5 ms between TE_1 = 5 ms and TE_{40} = 200 ms.

RESULTS As shown in **Fig. 1** the 3D frequency distribution around a magnetic dipole was computed. For a single magnetic dipole the computed frequency components were distributed unsymmetrical with respect to $\delta\nu$ = 0 Hz. Moreover, the maximum of frequency distribution was shifted towards positive frequencies. The related signal decay, as assessed by Fouriertransforming the frequency distribution, was non-monoexponential. As expected, the signal decay was faster in the sample containing SPIO labeled cells (see **Fig. 2**). Moreover, we observed monoexponential signal decay for the agar gel control sample, while non-monoexponential signal decay was observed for samples doped with SPIO labeled cells.

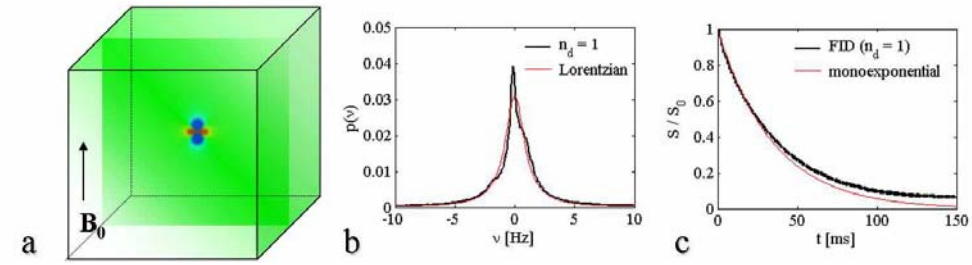

Figure 1 (a) Representative cross section through the 3D magnetic field distribution around a single magnetic dipole, which was calculated with respect to the vector $\mathbf{B_0}$ of the homogeneous magnetic field. **(b)** 3D frequency distribution. **(c)** The free induction signal decay (FID) as assessed by Fouriertransforming the computed frequency distribution.

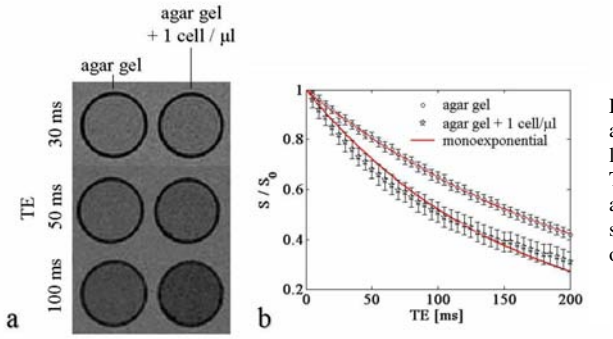

Figure 2 (a) MR images of samples containing no (i.e., agar gel) and a single (i.e., agar gel + 1 cell / µl) SPIO labeled cell per µl agar gel. Images were acquired at 1.5 Tesla using a gradient echo sequence with TE 30, 50, and 100 ms (from top to bottom). **(b)** Measured relative signal decays. Non-monoexponential signal decay was observed in case of a single labeled cell.

DISCUSSION We treated SPIO loaded cells as magnetic dipoles in a homogeneous magnetic field. Using a static numerical model we showed that the frequency distribution is likely to be non-lorentzian in presence of single magnetic dipoles, what led to non-monoexponential signal decay. Experimental findings confirmed non-monoexponential signal decay induced by a single labeled cell per MR imaging voxel. In conclusion, non-monoexponential signal decay can result directly from magnetic field inhomogeneities caused by SPIO loaded cells. Under in vivo conditions similar signal characteristics can be expected as the underlying physical principles are comparable.

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