Numerical Simulation of Magnetic Field Distortions Caused by Cells Loaded with SPIO Nanoparticles

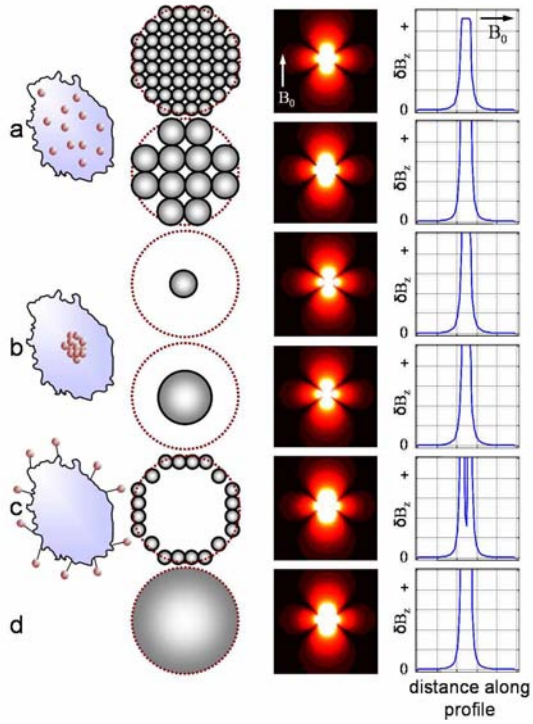
J. Pintaske[1], B. Mueller-Bierl[1], F. Schick[1]

[1]Section on Experimental Radiology, University Hospital Tuebingen, Tuebingen, BW, Germany

PURPOSE The use of MRI for cellular imaging is rapidly increasing and to combine the versatile diagnostic information of MRI applications with superparamagnetic iron oxide (SPIO) nanoparticles for cellular targeting is currently the focus of research worldwide [1, 2]. Several effective approaches to label different cell types with SPIO contrast media have been reported [1-7]. Exploiting the capability of certain cell types to ingest small particles through phagocytosis, the particles are either homogeneously distributed within the cell or specifically targeted to intracellular structures forming magnetic subcompartments. Moreover, SPIO complexes targeting to specific cell membrane components (receptor-mediated labeling) have been under investigating in order to image pathologic processes associated with disease.

Cells loaded with SPIO cause significant signal dephasing due to the magnetic field inhomogeneities induced in water molecules near the cell. In terms of a reliable in vivo quantification of labeled cells it is of critical importance to identify and to understand the various factors affecting the MR signal decay in isolation. The SPIO induced magnetic field distortions are one of the most important in that context. In this study we treat SPIO particles as magnetic dipoles in a homogeneous magnetic field and compute the field distribution using a numerical approach. This work is aimed to investigate the magnetic field distortions caused by SPIO loaded cells in dependence on the distribution of SPIO nanoparticles on the cellular level as resulting from the above mentioned labeling approaches.

METHODS We treated SPIO particles as magnetic dipoles in a homogeneous magnetic field and modelled the different distribution of SPIO on the cellular level by varying the spatial distribution of magnetic dipoles within a sphere and on the surface of a sphere, with the spherical volume representing the cell. The geometrical considerations to model these effects are summarized in **Table 1** and displayed in **Fig 1**. 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 total magnetic moment of a SPIO labeled cell is the sum over the magnetic moments p_m of each magnetic dipole assigned to the cell. For n particles the total magnetic moment is given according to $P_m = n \cdot p_m \propto n \cdot a^3 \cdot \chi \cdot B_0$. According to the distribution of magnetic dipoles (SPIO nanoparticles) with respect to the spherical volume (labeled cell) this total magnetic moment P_m is assigned to the cell in a differently geometrical manner (see **Fig. 1**). By smearing out this magnetic moment over the entire spherical volume it is suitable to introduce an effective radius $\tilde{a}$ and an effective magnetic susceptibility $\tilde{\chi} = n \cdot \chi \cdot (a/\tilde{a})^3$ for that homogeneously magnetized sphere by assuming the total magnetic moment to be $P_m \propto \tilde{a}^3 \cdot \tilde{\chi} \cdot B_0$. **Table 1** lists the simulation parameters radius and magnetic susceptibility in units of $\tilde{a}$ and $\tilde{\chi}$, respectively, for all investigated dipole distributions.



RESULTS For all geometrical arrangements of magnetic dipoles under investigation the magnetic field distributions, computed with respect to the vector of the homogeneous magnetic field B_0, are shown in **Fig. 1.** Moreover, the magnetic field distribution along the distance of the profile parallel to B_0 is plotted. As expected, the magnetic field distribution within and close to the sphere depends strongly on the inner-sphere distribution of magnetic dipoles, with the distance between the magnetic dipoles and their magnetization being of critical importance. In distance to the spherical distribution of magnetic dipoles the computed magnetic fields could not be distinguished from the field created by a spherical particle with the same total magnetic moment (see **Fig. 1d**).

CONCLUSIONS The investigation of the magnetic field distribution caused by iron loaded cells is of critical importance in order to interpret and to understand the MR signal decay observed under in vivo conditions, and to develop reliable models that allow for the in vivo quantification of labeled cells using MRI. The magnetic field around labeled cells originates from the magnetic dipoles (SPIO nanoparticles) ingested in the cell or targeted to the cell surface. We have shown numerically, that the magnetic field is sensitive to its shape and intracellular distribution of magnetic dipoles only in close proximity to the cell. From a physical point of view, outside this region, the magnetic field cannot be distinguished from the magnetic field created by a spherical particle with the same total magnetic moment. Because the total volume of SPIO loaded cells is small as compared to the typical size of an MRI voxel, the majority of tissue molecules that contribute to the signal decay will experience only the magnetic dipole field around the SPIO loaded cell.

Figure 1 (right side) Numerical modelling of the magnetic field distribution with respect to the vector of the homogeneous magnetic field B_0 for various cell label characteristics as described in Table 1. The magnitude of the computed planar field distribution is colour-encoded. The outer right column plots the field distribution along the profile parallel to the vector B_0 through the center of the dipole distribution.

Table 1 Description of the geometrical arrangement and magnetic properties of magnetic dipoles used for numerical modelling of SPIO cell label characteristics. The simulation parameters radius and magnetic susceptibility are listed in units of a homogeneously magnetized sphere radius $\tilde{a}$ and susceptibility $\tilde{\chi}$, respectively.

Cell Label Characteristics	Numerical Modelling	Magnetic Dipoles Number n	Magnetic Dipoles Radius a	Magnetic Dipoles Susceptibility χ
a) Homogeneous intracellular SPIO distribution (phagozytotic uptake)	Distribution of magnetic dipoles throughout the entire volume of a sphere	52	1/8 $\tilde{a}$	9.85 $\tilde{\chi}$
		12	1/4 $\tilde{a}$	5.33 $\tilde{\chi}$
b) SPIO attached to intracellular target structures (magnetic subcompartments)	Highly magnetized magnetic dipole assigned to the sphere's center	1	1/4 $\tilde{a}$	64 $\tilde{\chi}$
		1	1/2 $\tilde{a}$	8 $\tilde{\chi}$
c) Target components at cell surface (receptor-mediated targeting)	Distribution of magnetic dipoles on the surface of a sphere	20	1/8 $\tilde{a}$	25.6 $\tilde{\chi}$
d)	Homogeneously magnetized sphere	1	$\tilde{a}$	$\tilde{\chi}$

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