On the effect of contrast agent internalization in a two compartment diffusion model

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Introduction

Contrast agents (CA) are commonly used in MRI to generate a detectable contrast between areas of interest and the surrounding tissue. However, the CA may accumulate in a specific area. In this situation it is possible that the exchange of water molecules between the area with CA and the surrounding tissue is not fast enough to preserve the conditions of the fast exchange limit and diffusion can become a limiting factor on the relaxation rate. An example are CAs internalized in cells.

This effect has been investigated for T1 relaxation using an exchange model [1]. In this work diffusion between different compartments was not considered explicitly, but modeled implicitly by size dependent residence times of the spins in the according compartment.

The effect of diffusion in similar problems has been treated by different authors [2,3,4,5]. The focus of this work is the behavior of the CAs relaxivity if the CA is not homogeneously dispersed but accumulated in small parts of the volume. This is done in terms of a diffusion model.

Materials and Methods

The problem is modeled by two concentric spheres with monoexponential relaxation in both compartments (cf. Fig 1). A constant relaxivity of the CA is assumed corresponding to linear relationship between relaxation rates and the current concentration. Due to its spherical symmetry the model is described by the one dimensional Bloch Torrey Equation $\partial/\partial t\, m(r,t) = r^{-2}\, \partial/\partial r\, [r^2\, \partial/\partial r\, m(r,t)] - m(r,t)/T$ with reflective boundary conditions at $r=0$ and $r=R$. This equation is solved numerically using an implicit finite difference scheme [6,7]. The relaxation rates are calculated in the mean relaxation time approximation [5].

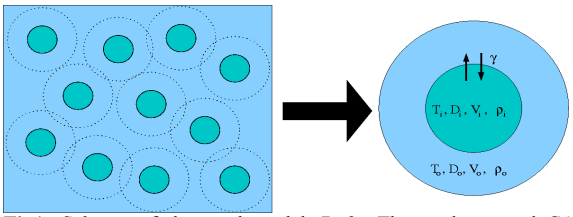

Fig1: Scheme of the used model. **Left:** The agglomerated CA influences a specific surrounding area (dashed volume). This structure is periodically continued giving the macroscopic volume. **Right**: T, D, V and ρ are the relaxation time, diffusion coefficient, volume and the proton density of the respective compartment. The compartments are separated by a permeable membrane γ.

Results

Different situations have been simulated numerically. In Fig. 2a) the relaxation rate of a constant amount of CA for different inner compartment sizes is shown. It can be seen that with decreasing volume fraction the relaxation rate decreases, too. Furthermore, independent from the relaxation rate of the dispersed CA a limiting value on the averaged relaxation rate is found for small volume fractions. In Fig 2b) and c) the relaxation rate is given for different sizes of the inner compartment but constant volume fraction η. In b) the total amount of CA is kept constant while in c) concentration of the CA does not change. It can be seen that independent of the volume fraction for smaller inner compartments the relaxation rate tends towards the averaged relaxation rate obtained for the fast exchange limit. However, the rate of convergence depends on the relaxation rate of the internalized CA (not shown). The spatial distribution of the transverse magnetization of a FLASH sequence is shown in Fig 2d). A strong spatial dependence can be found for short repetition times and large flip angles. For small flip angles as well as long repetition times the spatial difference in the transverse magnetization is less pronounced (not shown).

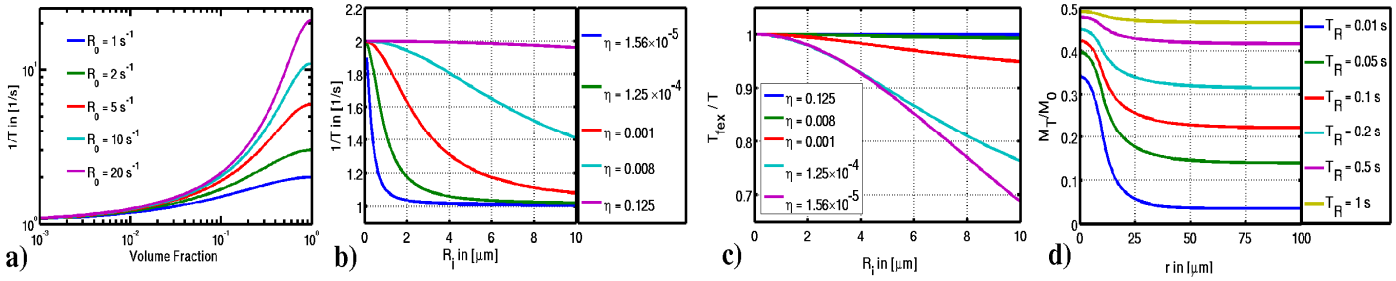

Fig2: Simulation results. **a) A**pparent relaxation rate in dependence on the volume fraction (const. V_o). The curves correspond to different relaxation rates of the completely dispersed CA (outer radius = 100 µm). **b)** Apparent relaxation rate in dependence of the radius of the inner compartment. The total amount of the CA is kept constant. The curves correspond to different volume fractions η (relaxation rate of CA for η=1: 1 s^{-1}**). c)** Normalized relaxation rate in dependence of the inner compartments radius. The concentration of the CA in the inner compartment is kept constant. The quantity $1/T_{fex}$ is the relaxation rate in the fast exchange limit (relaxation rate of CA: 100 s^{-1}). **d)** Radial distribution of the steady state transverse magnetization in a FLASH sequence. The curves correspond to different repetition times. (Flip angle: 30°, inner radius 10 µm, relaxation rate of CA = 100 s^{-1}). **all subfigures)** T_o = 1 s, $D_{i,o}$ = 2.3 10^{-9} m^2/s, γ=1**,** $\rho_{i,o}$=1

Discussion & Conclusion

The influence of the diffusion on the efficiency of CAs in compartmentalized systems was studied. Applying a simple two compartment system with diffusion it was shown that the agglomeration generally decreases the apparent relaxivity of the CA. Additionally the simulation shows that for given T_o, $D_{i,o}$, $V_{i,o}$, $\rho_{i,o}$ *and* γ a limiting apparent relaxation rate exists. These results are in agreement with Strijkers et al. [1]. However, this model also allows to investigate the spatial distribution of the magnetization which can be useful for studying the signal evolution and contrast of steady state sequences or dephasing in microscopic field inhomogeneities.

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