Relaxivity of blood pool contrast agent depends on the host tissue as suggested by semianalytical simulations

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Introduction

Concentration of MRI contrast agents (CA) cannot be measured directly and is commonly determined indirectly using their relaxation effect. This requires knowledge of the relaxivity of the used CA. Quantitative perfusion studies involve measurement of CA concentration during a bolus passage. Relaxation is commonly converted into concentrations assuming identical relaxivities for tissue and blood (1,2). We show that the relaxivity of blood pool CA depends significantly on both host tissue and pulse sequence. The result agrees with experimental data by Johnson et al. (3). In particular, the relaxation effect of Gd-based CA in brain tissues is several-fold larger than in bulk blood. The enhanced relaxation effect in tissue is due to dephasing of water protons in extravascular (EV) field gradients created by vessels filled with paramagnetic CA because of a difference in magnetic susceptibility. We developed a comprehensive model to describe this effect and created a program for fast, realistic simulation of transverse relaxation in perfused tissues. Beyond perfusion measurements, this method can be applied to quantitation of functional MRI and to vessel size imaging.

Methods

Simulations are performed as follows: First, the EV relaxation caused by one vessel is calculated using the newly developed model, which consists of Monte Carlo simulations embedded in the framework of analytical theory (4,5). This calculation is performed for each vessel in the voxel. This simulation is effectively two dimensional. The signal is calculated by including these calculations in a simulation program modeling tissue using analytical theory (6). The simulation uses available experimental gradient echo (GE) data for the relaxation effect of CA in blood, (7,8), described by the empirical formula: $R_2 = r_b \cdot c + q_b \cdot c^2$, with parameters summarized in Table 1. The authors are not aware of any corresponding experimental data for spin echo (SE). The simulation used experimental data for GE which provided an upper limit for SE.

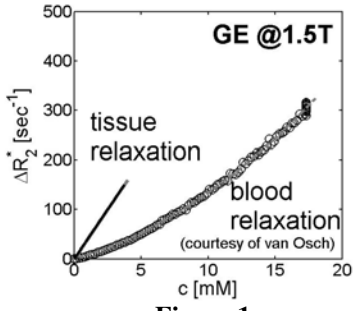

Figure 1

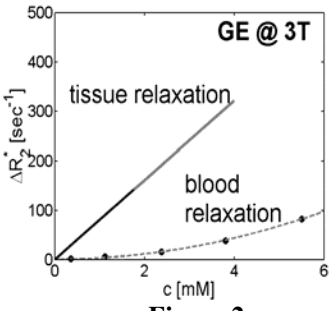

Figure 2

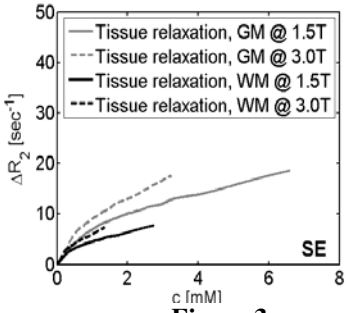

Figure 3

r [(mM·ms)$^{-1}$]	
r_b (exp, 1.5T, ref. 7)	0.0076
r_t (sim, 1.5T)	0.044
r_b (exp, 3T, ref. 8)	0.00049
r_t (sim, 3T)	0.087
q [(mM^2·ms)$^{-1}$]	
q_b (exp, 1.5T, ref. 7)	0.00057
q_b (exp, 3T, ref. 8)	0.0026

Table 1

Results

We performed simulations for both gray matter (GM) ($\zeta = 0.06$, gray lines) and white matter (WM) ($\zeta = 0.025$, black lines), where ζ is the blood volume. The change in relaxation rate, ΔR_2, of CA for GE is shown in Figure 1 and 2 as a function of the tissue concentration of CA, c. The latter is related to the blood concentration, c_b, via $c_t = c_b/\zeta$. The predicted relaxation in tissue is almost linear as a function of CA concentration. The calculated relaxivities are seen in Table 1 and they suggest a scaling proportional to the main magnetic field in agreement with analytical results in the static dephasing regime, (4,5). The values of the relaxivity are in agreement with the relaxivity found in animal studies (3,9) as demonstrated in (10). The tissue relaxation for GM and WM coincide for GE because of the similar vessel geometry in the two types of tissue. Experimental data for the relaxivity of bulk blood are shown for comparison. The increased relaxation in tissue is attributed to the dephasing of water protons in the EV space because of indirect relaxation caused by magnetic field gradients. This fact is supported by a calculating of the relaxivity of tissue, only taking the EV signal into account, which changed the result less than 3% for both field strengths. This demonstrates that the EV signal dominates the relaxation, which also was stated in (6). The effect of CA on the transverse relaxation of SE is shown in Figure 3. This dependence is nonlinear which reflects the proportionality of ΔR_2, to the power 2/3 of the magnetic susceptibility of blood in the static dephasing regime, (4).

Discussion

It was demonstrated previously (6) that the perfusion measurements using dynamic susceptibility contrast inherently overestimate the cerebral blood flow and volume. In view of the present result, this is attributed to the significant difference in the relaxivity of the CA in brain tissues compared to blood. The relaxivity is shown to be geometry dependent, because the magnetic field gradients caused by susceptibility differences are shape dependent, (11). The standard data analysis method of perfusion data neglects this difference, (1,2) and due to the linearity of the deconvolution in the standard data processing the ratio r_t/r_b becomes the overestimation factor in the blood flow and volume. This correction factor, r_t/r_b, is important for all methods that involves the relaxation effect of different tissues.

References: (1) Østergaard, L et al., *MRM* 36:715-725, 1996. (2) Østergaard, L et al., *MRM* 36:726-736, 1996. (3) Johnson, KM et al. *MRM* 44:090, 2000. (4) Kiselev, Posse, *Phys. Rev. Lett.* 81:5696–5699, 1998. (5) Yablonskiy DA and Haacke EM., *MRM* 32:749-763. 1994. (6) Kiselev, VG, *MRM*. 46:1113-1122, 2001. (7) van Osch MJ et al, *MRM* 49:1067-1076, 2003. (8) Akbudak E et al. Syllabus of the ISMRM workshop in Venice 2004. (9) Bjørnerud, A et al. *MRM* 47:461, 2002 (10) Jensen, BF et al, submitted in *MRM*. (11) Kiselev, Novikov. *Phys. Rev. Lett*. 89: 278101, 2002.