Extravascular BOLD effect for Different size Blood vessels over a Large range of Magnetic fields

K. Uludag[1], B. M. Müller-Bierl[2], and K. Ugurbil[1,3]

[1]Biological Cybernetics, Max Planck Institute, Tübingen, Germany, [2]Diagnostic Radiology, University Clinic Tübingen, Tübingen, Germany, [3]Center for Magn. Reson. Research, University of Minnesota, Minneapolis, MN, United States

Introduction

The blood oxygenation level dependent (BOLD) signal in the brain is caused by changes in paramagnetic deoxygenated hemoglobin and in cerebral blood volume (CBV) [1]. These physiological changes affect the signal behavior of protons both in the intra- and extravascular tissue space. Whereas the intravascular BOLD signal as a function of oxygen saturation of hemoglobin Y has been measured in blood phantoms [2], the functional dependency of the extravascular signal (ev-BOLD) on Y and CBV can currently only be evaluated by numerical simulations. Ogawa and colleagues have simulated ev-BOLD up to magnetic field strength B0 of 4T for gradient recalled echo (GRE) sequences and only to a limited extent for spin echo (SE) sequences [2]. Their results were confirmed by several other groups [3-5]. Here, we extend the results up to field strength B0 of 9.4 T for GRE and also SE sequences. We provide analytical expressions for relaxation rates R2* and R2 as a function of Y, B0 and CBV for capillary, venule and venous size cylinders (~ 3, 6, 20 μm). These results allow to model stimulus evoked BOLD signal changes for GRE and SE at different field strengths.

Methods

The blood vessel was modeled as a finite cylinder with random orientation creating spatially inhomogenous magnetic field around the cylinder. The susceptibility of the cylinder depends on Y according to $\chi = \chi_0 (1\text{-}Y)\, B_0$ with $\chi_0 = 1.6\ 10^{-6}$ (cgs) being the susceptibility of fully deoxygenated blood [4]. Using Monte-Carlo (MC) simulation, randomly placed protons diffuse $x = \sqrt{6 \cdot D \cdot \Delta t}$ within each time step $\Delta t = 200\mu s$ in the extravascular space in random direction with $D = 10^{-5}$ cm^2/s being the diffusion constant in the brain tissue. The vessel walls were regarded as impenetrable. According to the local field, each proton accumulates a magnetization phase in each time step. The resulting signal at the echo time TE for each cylinder orientation was computed by adding up all complex magnetizations of the 24 x 24 x 24 equidistributed spins. The signal from each vessel orientation was multiplied with $\sin(\theta)$ and subsequently summated with θ being the angle between vessel orientation and external magnetic field. For the calculation of R2, the phases were inverted at TE/2. The resulting signal was evaluated within the interval TE = 16-100 ms to obtain R2* and R2 values assuming an exponential relationship of the signal to R2* and R2.

Results

The relaxation rates R2* (left) and R2 (right) due to extravascular BOLD as a function of susceptibility of the blood vessel are shown for vessel radius 3μm (red), ~6μm (blue) and ~20μm (black) corresponding approximately to radii of capillary, venule and veins. The x-axis is shown in units of [χ_0·0.05·1.5T·0.02], i.e. each unit corresponds to 5% deoxy-Hb content at 1.5T field strength with 2% blood volume relative to tissue volume. With the use of these units, the plots can be easily read for other magnetic fields; for example, at 3T each unit would correspond to 2.5% deoxy-Hb content with 2% blood volume relative to tissue volume). For GRE sequences the relaxation rates of venules and veins are larger than that of capillaries for all χ (i.e. oxygenations and field strengths). In contrast, for SE sequences the venule sized cylinders have the higher relaxation rate at low χ values, and the capillaries at high χ values. These curves were fitted with a polynomial of 5th order to obtain an accurate analytical expressions for R2* and R2, i.e. R2* or $R2 = (a \cdot x + b \cdot x^2 + c \cdot x^3 + d \cdot x^4 + e \cdot x^5) \cdot \chi_0$. In the table, all coefficient were divided by a factor of 10 000.

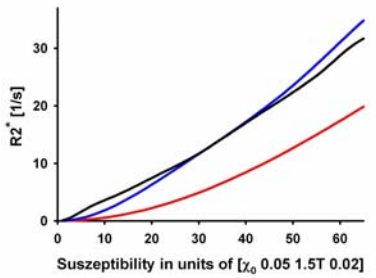

Fig. 1: Relaxation rate for ***GRE*** imaging

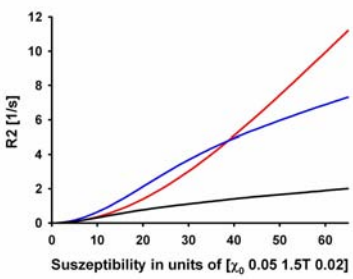

Fig. 2: Relaxation rate for ***SE*** imaging

	SE			***GRE***		
	3μm	**6μm**	**20μm**	**3μm**	**6μm**	**20μm**
a	0	.0024	.0014	.0001	-.0008	.0328
b	.164	.055	.098	.244	1.685	-.552
c	-.0837	-10.37	-2.62	.304	-32.67	15.894
d	-6.229	81.88	26.65	-10.07	310.25	167.18
e	23.119	-238.64	-96.57	32.063	-1078.8	645.47

Table: Radii and coefficients (cf. Section Results)

Discussion

The simulation results of this study are similar to those from previous studies [1, 3-5] although our results are more general (wider range for susceptibility and SE). The results illustrate that even for extravascular effects in SE, capillaries dominance requires very high magnetic fields. A 50% deoxy-Hb content in all vessels would translate into 10, 47, and 63 for 1.5, 7 and 9.4 Tesla respectively, in susceptibilty units used in the abscissa of figures shown. Capillary effects exceed small venule contribution only at 7T and more so at 9.4T. Note that, because oxygenation decreases from capillaries to venules and veins, in reality, lower χ values have to be used for the capillaries for a given χ in venules and veins. These conclusions are in agreement with recent high-resolution functional magnetic resonance imaging (fMRI) experimental results [6-7] at 9.4T showing that GRE has the highest sensitivity in superficial veins whereas SE is more sensitive to deeper layers containing mostly smaller vessels (arterioles, capillaries and venules) where as at 1.5 T, for both GRE and SE it has been found to originate from veins and venules. In ongoing studies, the dynamic behavior and compartmental contributions of the BOLD signal at different field strengths are being calculated.

References

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