INTRODUCTION

Although functional magnetic resonance imaging based on blood oxygenation level dependent (BOLD) contrast has become a widely used tool in neuroscience, the physiological changes that underpin the BOLD effect are still not completely understood. In particular the relationship between the changes in blood oxygenation (ΔY) and cerebral blood volume (CBV), occurring in active brain tissue, and the variation in signal intensity of T₂*-weighted images is not fully characterised. In probing this relationship, it has generally been assumed that the brain vasculature can be represented as an arrangement of randomly oriented infinite cylinders (IC) of varying size (1, 2) – a model which it has recently been shown produces similar susceptibility-related signal changes to those generated by a more realistic model of the vasculature (RV) (3). Here we describe simulations based on a finite difference method (3), which have been used to characterise the dependency of relaxation rate, R₂*, on blood volume and oxygenation, for signal from both extra- and intra-vascular compartments. Both models (IC and RV) were considered.

METHODS

The simulations spanned two different ranges of intra-extra-vascular susceptibility difference, χ, reflecting: (i) BOLD contrast at 3 T (oxygenation fraction of the blood varied from 0.5 to 0.8); (ii) exogeneous contrast agents (1 to 4 mM MION- at 3T)(4), which could also be considered representative of BOLD effects at high field (> 9T). Blood volume fraction, V, and vessel sizes were also varied, potentially allowing the overall behaviour of the relaxation processes to be parameterised.

Intra and extravascular compartments were studied separately. (a) The extravascular signal was assumed to be characterised by a mono exponential decay, exp(-R₂*TE).

The relaxation rate obtained was parameterised as αVχR₂*, where V is measured as a percentage and χ is measured in ppm . (b) The intravascular decay was characterised by a term resulting from the distribution of cylinder orientations (1) multiplied by an exponential decay due to dephasing resulting from field inhomogeneities generated by neighbouring vessels (this term is not calculable with the IC model).

RESULTS AND DISCUSSION

Figure 1 shows the parameters that best fit the calculated R₂* values for the extra-vascular signal as a function of the vessel diameter showing a significant difference for simulations carried out with χ-values typical of BOLD and exogeneous contrast at 3T. The haemodynamic response can be represented as a path on the χ-V surface over which AR₂* varies. Figure 2a shows a typical path (black line) calculated using the balloon model (5) with relaxation rate coded in color (blue contour lines for lower fields and red contour lines for higher fields). Figure 2b shows the shape of the corresponding BOLD signal variation with time for the two different regimes. As would be expected from experiment, the initial dip is more visible at the higher field, reflecting: (i) BOLD contrast at 3 T (oxygenation fraction of the blood varied from 0.5 to 0.8); (ii) exogeneous contrast agents (1 to 4 mM MION- at 3T)(4).

Once analysis (a) and (b) had been carried out, it was possible to write the signal intensity following a GE sequence at 3T as a function V and χ, 

\[ Signal(t, V, \Delta \chi) = M_{0GM} \frac{100 - V}{100} e^{-R_2^{GM}} \exp(-2.73V^{1.1}T_1) + M_{0V} \frac{V}{100} e^{-R_2^{Blood}(\chi)} \exp(-3.5V^{1.2}T_1) e^{(40V^{-0.1} \chi^{1.2}T_1)} \]

where the first term represents a physiologically (appropriate weighting of the various vessel length scales) sensible average extravascular contribution to the signal, whilst the second term represents the intravascular contribution. The latter term has various contributions: (i)I(t) refers to the isotropically oriented vessels; (ii) the second term refers to the the unaccounted effect of relaxation due to diffusion around red blood cells (this was not simulated because such dependence can be measured in vitro with much more reliability); (iii) the third term refers to static dephasing that should be the same as for gray matter at the static regime (Fig. 1 at large length scales) because the intravascular frequency shift distribution of the RV model was found to be well described by a convolution of extravascular frequency distribution of the RV model and that expected from isotropically oriented cylinders; (iv) the last term is an averaged effect through different length scales due to diffusion in the complex distribution of field shift, this relaxation value is positive because the diffusivity along the vessels, actually delays the process of dephasing described earlier as I(t);