Quantifying the Intravascular SE BOLD Effect at 1.5T

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Introduction The decrease in $T_{2,blood}$ with deoxygenation is considerably greater than that of tissue so that despite a very small cerebral blood volume fraction (between 2 and 5%), almost all of the SE BOLD response [6], as well as up to 70% of the GRE BOLD signal changes at 1.5 T [1] and 35% at 3 T [3], originates in the vasculature. Various models have been put forth to describe $R_{2,blood}$ enhancement through deoxyhemoglobin compartmentalization: fast chemical exchange of water protons between the plasmatic and the erythrocytic compartments, diffusion in the intracellular, extracellular, both intra- and extracellular magnetic gradients or a combination of all of these processes. In the present study, we tested both the exchange and diffusion models of R_2 enhancement, while spanning the fMRI relevant range of blood oxygenation levels (Y) and an extensive set of refocusing intervals (τ_{180}). With the repetition time in an fMRI experiment chosen to maximize temporal resolution, the BOLD response is sensitive to the $T_{1,blood}$ variations with the Y as well: we have therefore also examined the dependence of $T_{1,blood}$ on Y and hematocrit.

Methods Both Luz and Meiboom's model of fast chemical exchange between two sites at different frequencies as well as Jensen and Chandra's model of spin-spin relaxation in the presence of diffusion in weak microscopic field inhomogeneities [4] were fitted to the T_2 estimates obtained from monoxponential decay modeling. Blood was drawn from the superficial veins of the non-dominant forearm of 4 healthy adults before, during and after alternating elbow flexion and extension (with the non-dominant arm) spanning ~4 minutes of forearm occlusion. Immediately following the phlebotomy, the filled vacutainers were placed in a plastic gear made of LEGO and secured in a wooden frame, connected to a veristaltic pump, allowing gated rotation of the vacutainers about their long axes, at ~20 rpm, thereby preventing the settling of erythrocytes. A T_2 prepared segmented EPI sequence [2] (2.3x2.3x5 mm^3, EPI factor of 3, TR of 3 s) was used for T_2 relaxometry, with τ_{180} varying from 2 to 40 ms. The order of acquisitions with different refocusing intervals was randomized and 6 effective echo times probed for each τ_{180}. The T_1 of blood was quantified using a single-slice Look-Locker sequence with a segmented EPI readout (2.3x2.3x5mm, TI of 15 ms, TE of 10 ms and TR of 4 s). The total scan time per set of four blood samples was ~80 minutes. In each case, the imaging slice was 5-mm thick and positioned axially at the centre of the vacutainer. Following the completion of the MR relaxometry measurements, the blood gas and cooximetry analysis were performed.

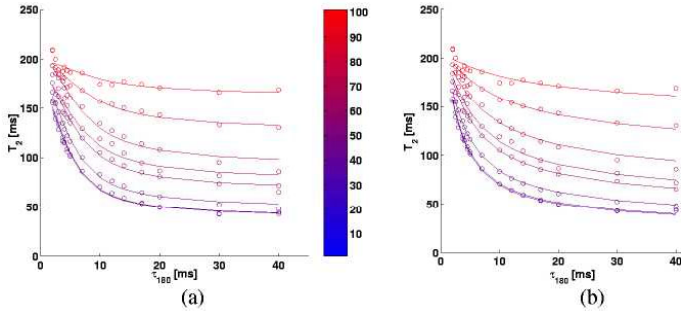

Figure 1: The T_2 blood estimates and the fits of the exchange (a) and diffusion (b) models with 17 and 10 parameters, respectively. The blood samples used had nearly equivalent hematocrit, of 51.2±0.4%.

Results For both exchange and diffusion model structures, two model orders were investigated: a constrained model, in which $T_{2,0}$ was fixed across Y and an unconstrained one, in which the $T_{2,0}$ was allowed to vary with Y. Allowing for variation of the intrinsic T_2 of blood with oxygenation level produced a better fit (at α=0.01) in the exchange but not in the diffusion modeling, as established by the F-test of the reduction in the sum of squared residuals (SSR), in going from the constrained to the unconstrained model within each model structure. Furthermore, the comparison of the SSR for the selected model order within each model structure led to the selection of the diffusion model ($SSR_{diffusion}$ ~1.85 ms^2 and $SSR_{exchange}$ ~2.49 ms^2). The estimated $T_{2,blood}$ values at different Y as well as the fits of the unconstrained exchange and constrained diffusion models to this data set are shown in Figure 1 with modeling results summarized in Table 1. In each case, the nonlinear model fitting was performed using a trust region method based on the interior-reflective Newton method. Fitting the curvature term (G_0) as a quadratic function of Y and combining the results with the above, the dependence of blood T_2 on Y and τ_{180}, at 1.5 T, for the physiologically relevant hematocrit is well modeled by the diffusion model of [4] with $T_{2,0}$ of 203±3 ms, $r_c^2/2D$ of 4.60±0.42 ms and G_0 given by: $G_0 = (4.50\pm0.51)10^{-13}[T^2](1\text{-}Y/100)^2$.

Table 1: Exchange and diffusion model parameter estimates. The exchange time (τ_{ex}) estimate was 3.0±0.2ms; the characteristic length scale for spatial variations of field inhomogeneities (r_c), 4.3±0.2μm; and the intrinsic spin-spin relaxation time from the diffusion model fitting ($T_{20,diffusion}$), 203±3ms.

Y [%]	$T_{20,exchange}$ [ms]	K_0 [10^{-14} T^2]	G_0 [10^{-14} T^2]
93	198±5	0.53±0.14	0.8±0.1
87	197±5	1.36±0.21	1.9±0.2
72	200±6	2.87±0.36	3.7±0.4
66	183±7	3.67±0.48	5.5±0.6
62	184±7	4.65±0.60	6.6±0.8
48	179±9	7.31±0.98	10.1±1.2
43	169±10	9.31±1.31	13.2±1.7
42	166±10	9.38±1.33	13.6±1.8

The dependence of the resulting T_1 estimates (from fitting to mono-exponential recovery model) on Y was obtained by linear fitting of the spin-lattice relaxation rates. The results are shown in Figure 2, corresponding to $R_1=(996\pm36)^{-1}\text{-}(0.00122\pm0.00054)10^{-3}Y$ [ms^{-1}]. Finally, two-way ANOVA reported a statistically significant effect of hematocrit on the T_1 estimates when controlling for oxygen saturation, namely $F = 123$ and $p < 10^{-9}$, the T_1 increasing with decreasing hematocrit.

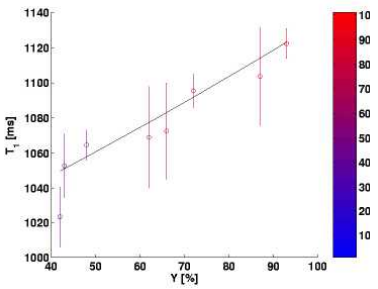

Figure 2: The spin-lattice relaxation time of blood fitted against oxygen saturation.

Conclusion The present study provides support for the application of the recently reported model of diffusion in weak microscopic field inhomogeneities in describing the spin-spin relaxation rate enhancement in human blood at 1.5 T. The parametrization of this model for the hematocrit levels pertinent to studies of functional activation is presented for ready evaluation of intravascular spin-echo BOLD changes. A linear increase of spin-lattice relaxation time with blood oxygen saturation is also observed, in agreement with recent reports [5].

References

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