Quantitative assessment of hematocrit, hemoglobin concentration and oxygenation effects on the longitudinal relaxation time of blood

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Target audience: Physicians and researchers who are interested in water proton T_1 in blood.

Purpose: To develop a theory to quantitatively describe interrelations between water proton T_1 in blood and the basic physiological parameters: hematocrit, oxygenation and hemoglobin concentration, which can be used to predict blood T_1 at multiple fields.

Method: Bovine blood (an analogue of human blood with typical mammalian erythrocytes) was prepared and pumped into a flowing loop with constant temperature at 37°C[1]. The oxygenation was controlled carefully by mixing N_2 and air. Inversion-recovery experiments were done at 3T, 7T, 9.4T, 11.7T and 16.4T for determining T_1 (flow is stopped during pulse) of whole blood samples with different hematocrit or lysed blood with different Hb concentrations. MATLAB was used for data processing and fitting.

Results and discussion: In terms of magnetic properties, water in blood can be considered predominantly as a two-compartment system[2]. The first part is in plasma which contains albumin and has a constant T_1 at a certain magnetic field. The second part is inside red blood cells (RBC) which contain ~5mM hemoglobin (Hb, 4-unit structure) and have a water T_1 depending on the Hb concentration (ctHb) and oxygenation fraction (Y). Because the water exchange rate between these two compartments (~100 s^{-1}) is very fast compared to R_1 (= $1/T_1$), the blood longitudinal relaxation rate is weighted sum of R_1 of plasma and RBC, i.e. $R_1 = f_{water} \times R_{1plasma} + (1 - f_{water}) \times R_{1RBC}$ where Hct is hematocrit and $f_{water} = \frac{Hct}{1.2-0.2\times Hct}$ is the water fraction in RBC calculated according to the water mass percentage inside and outside RBC. To study R_{1RBC}, lysed blood experiments (good mimic of inner part of RBC) were performed as shown in Fig.1 and Fig. 2a. Fig. 1 shows that under fully oxygenated conditions, R_{1RBC} linearly depends on the molality of hemoglobin b_{Hb} (b_{Hb}=6.5 × 10^{-3}mol/kg in normal RBC). This field dependent relaxation results from diamagnetic effects primarily related to the interaction between water and hemoglobin. Combined with the paramagnetic effect from deoxy-hemoglobin, we can derive an R_1 equation for inner part of red blood cells: $R_{1,RBC} = R_{1plasma} + r_{1protein} \times b_{Hb} + r_{1para} \times ctHb \times (1 - Y)$ where $r_{1protein}$ is the relaxivity due to water hemoglobin interaction, r_{1para} is relaxivity of deoxy-Hb and Y is the oxygenation fraction of Hb. This equation is validated from lysed blood experiments at 11.7T with different oxygenations fractions and Hb concentrations (Fig 2a). Therefore, combining the two equations above, the blood longitudinal relaxation rate can be expressed as $R_1 = f_{water} \times R_{1plasma} + (1 - f_{water}) \times [R_{1plasma} + r_{1protein} \times b_{Hb} + r_{1para} \times ctHb \times (1 - Y)]$. This equation describes different mechanisms contributing to T_1 relaxation, and employs only three parameters to predict blood T_1 for certain Hct, Y and ctHb at one magnetic field. To test the theory, we applied it to a series of whole blood T_1 experiments with different Hct and Y under 3T, 7T, 9.4T, 11.7T and 16.4T (Fig. 2 b-f). The good fitting performance (R^2≈1), well consistent between experimental plasma $R_{1plasma}$ and $R_{1plasma}$ fitted from whole blood data (Table 1), and good agreement between $r_{1protein}$ fitted from whole blood and lysed blood data validate our theory.

B_0 (T)	3.0	7.0	9.4	11.7	16.4
Experimental $R_{1plasma}$ (s^{-1})	0.38	0.33	0.32	0.30	0.30
Lysed $r_{1protein}$ ((mol/kg×s)$^{-1}$)		63.4	48.6	41.6	37.8
Whole $R_{1plasma}$ (s^{-1})	0.38	0.31	0.30	0.31	0.29
Whole $r_{1protein}$ ((mol/kg×s)$^{-1}$)	75.5	62.7	52.5	39.0	38.4
Whole r_{1para} ((g/dL×s)$^{-1}$)	7.48×10^{-3}	6.82×10^{-3}	9.58×10^{-3}	9.88×10^{-3}	5.36×10^{-3}

Table 1. Experimental R_1 for plasma and fitted parameters for lysed and whole blood data.

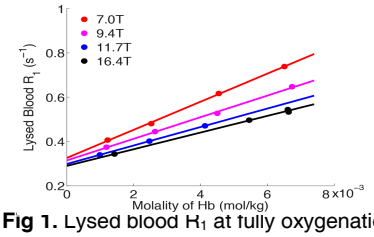

Fig 1. Lysed blood R_1 at fully oxygenation

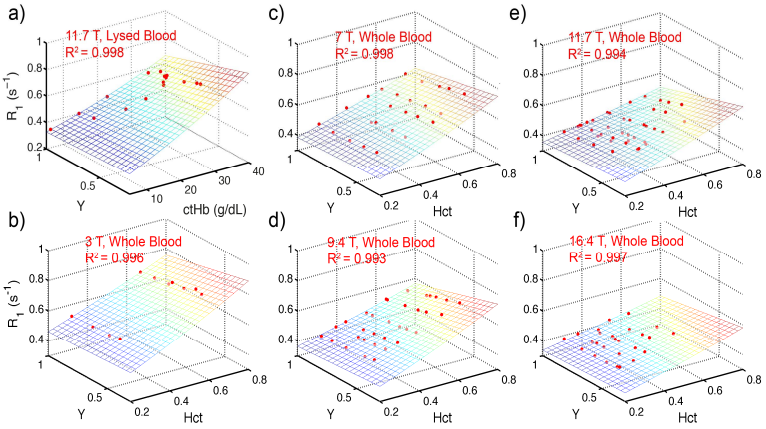

Fig 2. Fitting of lysed blood data (a, red dots) and whole blood data (b-f, red dots) at different ctHb, hematocrit and oxygenation ratio.

Conclusion: We have derived expressions for the effects of hemoglobin concentration, hematocrit and oxygenation on the water proton T_1 in blood, and confirmed the equations experimentally in lysed and whole blood at multiple magnetic fields. In addition, the theory presented here and the fitted parameters in Table 1 provide a good calibration set for blood T_1 prediction at arbitrary Hb concentration, hematocrit and oxygenation at multiple fields, which is useful for perfusion-based quantification experiments such as ASL and VASO.

Reference:

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