Human Blood Exhibits Gaussian Relaxation Behavior

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INTRODUCTION

Accurate knowledge of the magnetic properties of human blood is required for the precise modeling of functional and vascular flow-related MRI. It has long been assumed that the blood ^1H_2O free induction signal envelope is well modeled as an exponential governed by rate constant R_2^*. Our laboratory has made careful measurements of the transverse relaxation of fresh human blood at 1.5T at well-controlled pH and temperature. Levels of diamagnetic and paramagnetic RBC hemoglobin (Hb) were varied and accurately monitored. Careful attention to sample mixing avoided artifacts due to settling of RBC's (1). Results clearly show that the blood free induction signal envelope exhibits a significant Gaussian component in addition to the expected exponential behavior. Herein we quantify this Gaussian component, characterized by rate constant AR^*, and also exponential rate constants R_2^* and R_2, as a function of blood paramagnetic hemoglobin content. The Gaussian component should be recognized in accurate modeling of MRI phenomena that depend upon the magnetic state of blood.

METHODS

Fresh human blood samples were drawn from healthy volunteers. Lithium heparin (100 IU/7cc) was added for anti-coagulation. Sample hematocrit was varied by diluting blood samples with human plasma or by withdrawal of plasma. Blood samples were prepared at varying oxygenation levels ranging from ~30 – 100% and pH was adjusted to achieve a sample pH of 7.4 at 37°C. All MR measurements were performed on a Siemens Magnetom Vision system operating at 1.5T. Blood samples were held in horizontal NMR tubes of 5 mm o.d. and 9 in. in length aligned along the magnetic field axis. Data was acquired from a 4mm slice through the middle and orthogonal to the principal axis of single tubes following slice shimming. A slice selective spin-echo sequence with variable echo time was used with the data acquired following the refocusing pulse. During experiments blood was maintained at 37°C and red blood cell settling was eliminated via continuous rotation of the horizontally oriented sample tube. Immediately after completion of MR measurements, sample pH and the relative percentages of paramagnetic hemoglobin (deoxyHb and metHb) and diamagnetic hemoglobin (oxyHb, carbonmonoxyHb) were determined with a blood gas analyzer/cooximeter. We represent the total fraction of paramagnetic hemoglobin as (1 - Y') wherein Y' is the total fraction of diamagnetic hemoglobin.

RESULTS

A typical FID signal magnitude envelope following a spin echo, $\xi(t)$, is shown in the semilog plot of Fig. 1, which clearly shows the presence of both an exponential (R_2^*) and a Gaussian (AR^*) component. Thus, the FID signal magnitude is described by the equation:

$$\xi(t) = S_o \cdot e^{-R_2^* \cdot t - AR^* \cdot t^2}.$$

The rate constants R_2^* and AR^* vary as a function of hematocrit, spin echo time and hemoglobin paramagnetic fraction. The relaxation rate constants are well-described by

$$R_2^* = R_{2,min}^* + K_{R2^*} \cdot [(1 - Y') - 0.05]^2$$

and

$$AR^* = K_{AR^*} \cdot [(1 - Y') - 0.05]^2.$$

For Hct 0.30 and 0.40 with TE = 18 msec the AR^*, K_{AR^*} = 3872 and 4490 sec^{-2}, respectively. For R_2^*, the parameters are K_{R2^*} = 66.6 and 73.7 sec^{-1} with $R_{2,min}^*$ of 4 and 5 sec^{-1} for the respective hematocrit levels.

The transverse relaxation rate constant, R_2, was measured via spin-echo with varying echo times. The resulting modeling of the data was of the form

$$R_2(sec^{-1}) = 3.9 + 55 \cdot [(1 - Y') - 0.05]^2 \quad Hct \approx 0.30, r = 0.99$$

and

$$R_2(sec^{-1}) = 6.2 + 59 \cdot [(1 - Y') - 0.05]^2 \quad Hct \approx 0.40, r = 0.96$$

as shown in Fig. 2. Choice of independent variable [(1 - Y') – 0.05] resulted from careful modeling of the diamagnetic susceptibility of RBC and plasma (after the method of Ref. 2) and the paramagnetic part according to the Curie Law. This model predicted that matching of intracellular and extracellular susceptibility should occur at 95% diamagnetic hemoglobin. This prediction allows an excellent fit to the data, and is only slightly different than the usual assumption that the minimum in susceptibility gradient and hence relaxation rate constant occurs at 100% diamagnetic hemoglobin (3,4).

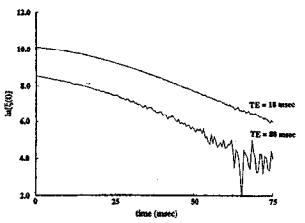

Figure 1. Semi-log plot of the FID magnitudes with spin echo time 18 msec.

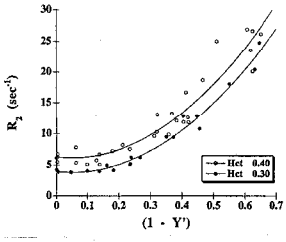

Figure 2. R_2 vs. (1 - Y') for Hct ≈ 0.40 and 0.30.

DISCUSSION

There is a substantial Gaussian signal decay component in the blood ^1H_2O FID in addition to the exponential decay which has been commonly assumed for blood. MR procedures that require accurate modeling of the evolution of blood magnetization following a sequence of rf pulses will need to consider this Gaussian component in addition to the more commonly acknowledged exponential component. The transverse relaxation rate constant R_2 is well modeled by a minima at (1-Y') = 0.05, corresponding to the predicted point of matched intracellular and extracellular susceptibility. This value of (1-Y') is also consistent with minima in the values of AR^* and R_2^*. We are currently investigating the relative contributions of transmembrane exchange and diffusion through local magnetic field gradients to the results reported herein.

REFERENCES

1. C. Gasporovic, N.A. Matwiyoff, *Magn. Reson. Med.*, **26**, 274-299 (1992).
2. M. Cerdonio, A. Congiu-Castellano, L. Calabrese, S. Morante, B. Pispisa, S. Vitale, *Proc. Natl. Acad. Sci. USA*, **75**, 4916-4919 (1978).
3. K.R. Thulborn, J.C. Waterton, P.M. Matthews, G.K. Radda, *Biochim et Biophys Acta*, **714**, 265-270 (1982).
4. G.A. Wright, B.S. Hu, A. Macovski, *J. Magn. Reson. Imag.* **1**, 275-283 (1991).