**MAJOR PAPER**

*In vivo Measurement of Longitudinal Relaxation Time of Human Blood by Inversion-recovery Fast Gradient-echo MR Imaging at 3T*

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Purpose: Accurate longitudinal relaxation time (\(T_1\)) of arterial blood is important in evaluating blood flow in tissue by arterial spin labeling magnetic resonance (MR) imaging. Few studies have reported the \(T_1\) of human arterial blood *in vivo*, especially using 3-tesla MR imaging. \(T_1\) values of human venous blood *in vivo* have been reported, but they differ from those measured *in vitro*. We aimed to evaluate the accurate \(T_1\) of human arterial blood *in vivo*.

Methods: We measured \(T_1\) values of blood in 10 healthy volunteers *in vivo* using an inversion-recovery fast gradient-echo sequence and 3-tesla MR imaging unit. We also measured hematocrit (Hct) values of venous blood samples. After nonselective application of the inversion pulse using a body coil, we obtained MR imaging signals of arterial blood in the abdominal aorta. Similarly, we measured the signals of venous blood in the internal jugular vein. Inversion times varied between 200 and 5000 ms for imaging of the abdominal aorta and 200 and 2500 ms for imaging of the jugular vein. We also acquired signals without the inversion pulse. We estimated \(T_1\) values from the data by nonlinear least squares fitting of a 3-parameter model.

Results: The \(T_1\) value (mean ± standard deviation) of arterial blood was 1779 ± 80 ms and of venous blood, 1694 ± 77 ms. The average Hct value was 0.47. The \(R_1\) (= 1/\(T_1\)) of arterial blood was related to the Hct value as: \(R_1 = (0.59 ± 0.16)\text{Hct} + (0.29 ± 0.07)\) (mean ± standard error) s\(^{-1}\). For the venous blood, \(R_1 = (0.70 ± 0.11)\text{Hct} + (0.27 ± 0.05)\) s\(^{-1}\).

Conclusion: We observed a \(T_1\) of human arterial blood *in vivo* of 1779 ± 80 ms at a mean hematocrit value of 0.47 as determined by 3T MR imaging; an even longer \(T_1\) value is expected with a hematocrit value less than 0.47.

**Keywords:** arterial spin labeling, MRI, perfusion, relaxation rate, \(T_1\)

**Introduction**

Accurate determination of the parameters that influence magnetic resonance (MR) signals during acquisition and interpretation of images is important. The longitudinal relaxation time (\(T_1\)) of blood is used to quantify blood flow in tissue using arterial spin labeling (ASL),\(^1,2\) and its accurate value is needed to calculate the inversion time (TI) of nulling blood signal in vascular space occupancy\(^3\) and black blood imaging.\(^4\)

The \(T_1\) of blood has been measured *in vitro*,\(^5–12\) or \(T_1\) of animal blood has been measured *in vivo*.\(^2,13\) However, those values are not necessarily equal to the \(T_1\) of human blood *in vivo*, and \(T_1\) values of human venous blood reported in recent years *in vivo*\(^14–17\) have differed from those measured *in vitro*.\(^8\) The \(T_1\) values measured *in vivo* (1783 ms,\(^15\) 1724 ms\(^17\)) are longer than that measured *in vitro* (1584 ms\(^8\)) at a field strength of 3T adjusted for a hematocrit (Hct) value of 0.42. We believe only one study has measured the \(T_1\) of human arterial blood *in vivo* at a field strength of 3T,\(^18\) and they reported \(T_1\) of 1550 ms, a value much shorter than those above of human venous blood *in vivo*.\(^8\)
We aimed to measure accurately the $T_1$ of human arterial blood in vivo using a 3T clinical MR imaging system. We also measured $T_1$ with a 1.5T system in common clinical settings. Because the $T_1$ of blood is reported to depend on hematocrit value,$^5,^7,^8,^17$ we also investigated the relationship between $T_1$ and Hct value.

**Materials and Methods**

*Data acquisition*

We recruited 10 healthy male volunteers aged 20 to 60 years (mean age, 30 years) from whom we obtained written informed consent. Our institutional review board approved the study. All subjects were scanned using a 3T Siemens Trio System (Erlangen, Germany). Further, 6 of the 10 subjects were scanned on a 1.5T Siemens Vision System.

To measure the $T_1$ of blood, we used inversion-recovery (IR)-prepared fast low-angle shot (IR-turbo FLASH) gradient-echo sequence$^{19}$ (Fig. 1) with a k-space filling of centric ordering in the phase-encoding direction without cardiac gating. We examined 20-mm-thick transaxial sections of the upper abdomen (for the abdominal aorta) and neck (for the internal jugular vein), where the blood flow was nearly perpendicular to the imaging slice (Fig. 2).

To measure the $T_1$ of flowing blood, we acquired blood signals after applying a nonselective IR pulse using a body coil that extended well over the upstream region of the blood flow so that the IR pulse would affect all blood flowing into the imaging slice. Specifically, to obtain the blood signal in the abdominal aorta, we applied the pulse to a region between the neck and upper abdomen. To obtain the blood signal of the internal jugular vein, we applied the pulse to the entire head and neck regions.

The times from the IR pulse to signal acquisition, i.e., inversion times (TI) were 200, 300, 450, 500, 550, 600, 2000, 3000, 4000, and 5000 ms for the abdominal aorta and 200, 300, 450, 500, 550, 600, 1500, and 2500 ms for the internal jugular vein. The reason why we set the maximum TI for the abdominal aorta of 5000 ms is as follows. Blood that did not receive the IR pulse would not flow into the imaging slice for the abdominal aorta within 5000 ms since the average circulation time of blood from the right ventricle to the left ventricle in resting healthy men is 6.6 s.$^{20}$ We determined a maximum TI of 2500 ms for the internal jugular vein by considering the shorter circulation time in the brain. We set the interval between IR pulses to more than 20 s for the longitudinal magnetization to recover completely. So, acquisition time for the set of images to estimate $T_1$ value was approximately 4 min.

The receiver gain of the system was fixed. The subjects were instructed to hold their breath from initiation of the IR pulse to the end of image acquisition. On the 3T system, images were also acquired without the IR pulse, and they were regarded as images obtained with infinite TI.

The acquisition parameters on the 3T system were: repetition time (TR)/echo time (TE), 3.0/1.24 ms; field of view (FOV), 400 × 300 mm; scan matrix, 256 × 192; and flip angle, 10°. Parameters on the 1.5T system were: TR/TE, 11/4.2 ms; FOV, 320 × 320 mm; scan matrix, 256 × 128; and flip angle, 5°.

Hematocrit values were measured from venous blood samples collected from the subjects within one week before and after MR imaging, and mean and variance were calculated for each subject.

*Data analysis*

Image data were transferred to a personal com-

![Fig. 1. Pulse sequence diagram of inversion-recovery (IR)-prepared fast low-angle shot (IR-turbo FLASH) sequence. Following a nonselective (NS) 180° inversion pulse, the longitudinal magnetization is sampled by FLASH sequence: a series of slice-selective (SS) excitation pulses (10° flip angle on 3T system, 5° on 1.5T system) and gradient-echo acquisitions (ACQ) with rectilinear k-space filling of centric phase ordering. $N_p$, number of phase-encoding steps; TI, inversion time; TR, repetition time.](image-url)
computer, and subsequent analyses were performed using Mathematica 8.0 (Wolfram Research Inc, Champaign, IL, USA). We placed a region of interest (ROI) in the blood vessel lumen on each image (Fig. 2) and obtained mean signal intensity (SI). The ROI was identical for the set of images with various TIs to estimate $T_1$. The ROI on the neck images was placed in the larger of the right or left internal jugular vein.

Because the SI was based on an absolute value, it was positive even when acquired at short TI. The recovery of longitudinal magnetization after an inversion pulse is naturally expressed as a monotonically increasing function of TI. To obtain such data, the SIs obtained with TIs less than (or equal to) 600 ms were multiplied by $(-1)$.

A 3-parameter model that shows the recovery of longitudinal magnetization, i.e., $SI = p_1 + p_2 \exp (-TI/T_1)$, where $p_1$, $p_2$, and $T_1$ are the parameters to be estimated, was fitted to the MR imaging data using a nonlinear least squares method. After calculating the longitudinal relaxation rates ($R_1 = 1/T_1$) from the estimated $T_1$ values, we analyzed the relationship between $R_1$ and Hct value by weighted linear regression, where the weight is the inverse of the variance of Hct values measured twice for each subject. The difference in $T_1$ values between arterial and venous blood was estimated by Wilcoxon signed-rank test at a significance level of 0.05.

**Results**

The average Hct value was 0.47 (range, 0.41 to 0.52). At 3T, the $T_1$ of arterial blood (mean ± standard deviation across individual subjects) was 1779 ± 80 ms (corresponding $R_1$ value, 0.563 ± 0.025 $s^{-1}$), and the $T_1$ of venous blood was 1694 ± 77 ms.
(R₁, 0.592 ± 0.027 s⁻¹). Table lists the individual T₁ values; Fig. 3 shows their distributions. The difference in T₁ values between arterial and venous blood was statistically significant (P = 0.01). Figure 4 shows the relation between R₁ and Hct value. For arterial blood, R₁ was related to Hct value as R₁ = (0.59 ± 0.16)Hct + (0.29 ± 0.07) (mean ± standard error) s⁻¹; for venous blood, as R₁ = (0.70 ± 0.11) Hct + (0.27 ± 0.05) s⁻¹. At 1.5T, the T₁ of arterial blood (mean ± SD across individuals) was 1499 ± 74 ms (R₁ is 0.668 ± 0.034 s⁻¹). The mean hematocrit value was 0.467 for the 6 subjects scanned at 1.5T. The R₁ of arterial blood was related to Hct value as R₁ = (0.74 ± 0.16)Hct + (0.32 ± 0.07) (mean ± standard error) s⁻¹.

**Discussion**

The T₁ of arterial blood at 3T in our study was about 180 ms longer than the value measured in vitro⁸ and 230 ms longer than the value measured in human cardiac ventricles.¹⁸ The latter discrepancy might result from an error in estimating the T₁ of blood in the cardiac study. The efficiency of the inversion might not be estimated properly in that study because the maximum TI (800 ms) used¹⁸ is too small to track the entire recovery process of longitudinal magnetization after inversion pulse. The T₁ of human venous blood measured in the present study at 3T is consistent with values recently reported in in vivo human studies,¹⁵-¹⁷ and these values are about 200 ms longer than the previously measured in vitro value.⁸ Because deoxyhemoglobin, which is paramagnetic and can reduce T₁, is more abundant in venous than arterial blood, T₁ is longer in arterial than venous blood. A difference of 79 ms has been reported for arteriovenous T₁ in vitro at 3T.⁸ Our observation of an 85-ms difference in this study agrees well with the in vitro difference,⁸ though the absolute values in our study are much longer than the in vitro values for both arterial and venous blood. Therefore, the T₁ of arterial blood obtained in this study at 3T may be as reliable as that for venous blood.

Paramagnetic contamination may affect in vitro T₁ value,¹⁶ and different blood methemoglobin (MetHb) levels may cause the difference between T₁ values measured in vivo and in vitro. Though Lu and colleagues⁸ noted in their in vitro study that they used only fresh blood (MetHb < 1.5%) to avoid possible MetHb accumulation, the level of MetHb reported in vivo (0.64% per Young et al.²¹) may be much lower than the level in vitro. MetHb is paramagnetic, and the relaxivity is about 2 s⁻¹ mM⁻¹ at 3T.²² If the amount of MetHb increases by 1% of hemoglobin in the blood sample (the increase will be 0.15 g/dL = 0.023 mM), the relaxation rate of the blood will increase by 0.046 s⁻¹. This result corresponds to a difference of 135 ms in the T₁ of arterial blood at 3T and is comparable to the observed difference of 180 ms.

The reported range of T₁ values of human blood in vivo at 1.5T is 1205 to 1540 ms.¹⁴,²³-²⁵ The estimated T₁ of 1499 ms in our study falls within this range and may be used in measuring blood flow in
In quantifying the blood flow in tissue by ASL, the pulsed ASL signal is proportional to the difference (unlabeled minus labeled) in longitudinal magnetization \( \Delta M: \Delta M = 2M_{0b}T_1\alpha \exp \left(-T_1/T_1^{\text{blood}}\right)q_0(T_1) \), where \( M_{0b} \) denotes the equilibrium magnetization of arterial blood; \( \alpha \), the period during which the labeled blood continues to be delivered to the imaging voxel within \( T_1 \); \( \alpha \), the efficiency of the labeling; \( f \), the tissue blood flow; and \( T_1^{\text{blood}} \) the \( T_1 \) of the arterial blood that flows into the tissue, and \( q_0(T_1) \) has a value close to one. Therefore, the tissue blood flow calculated from the ASL signal is proportional to \( \exp \left(T_1/T_1^{\text{blood}}\right) \).

Consequently, assumption of a smaller \( T_1^{\text{blood}} \) may lead to overestimation of blood flow. If the \( T_1^{\text{blood}} \) of the reported values of 1550 ms (measured in the cardiac ventricle)\(^{18}\) or 1600 ms (\textit{in vitro} measurement of Lu et al.\(^8\) at Hct value = 0.47) is adopted instead of 1780 ms (this study), the calculated blood flow will be 1.18 or 1.13 times larger in a case of \( T_1 = 2000 \) ms, for example.

The slopes of the \( R_1 \)-Hct relationships, \( \frac{dR_1}{d(\text{Hct})} \), observed in this study at 3T, \( (0.59 \pm 0.16) \text{ s}^{-1} \) for arterial blood and \( (0.70 \pm 0.11) \text{ s}^{-1} \) for venous blood, agree with those of the \textit{in vitro} study,\(^8\) \( (0.52 \pm 0.15) \text{ s}^{-1} \) for the arterial blood and \( (0.83 \pm 0.07) \text{ s}^{-1} \) for the venous blood, within the estimated precision. However, the \( R_1 \)-Hct relationships in this study vary widely (Fig. 4). Inaccurate Hct values can cause the \( R_1 \)-Hct to vary. We measured Hct values on days when MR imaging was not performed. Intraindividual variation in Hct values with time may have led to dispersion of the measured \( R_1 \)-Hct relationship.

Differences in serum protein levels might also cause these variances. Human blood contains albumin and globulins. The relaxation rate of the solution of serum proteins in water (at one T and room temperature)\(^{26}\) increases with albumin concentration as \( 0.035 \text{ s}^{-1} (\text{g/dL})^{-1} \) and increases more rapidly with globulin concentration as \( 0.045-0.052 \text{ s}^{-1} (\text{g/dL})^{-1} \). Therefore, a normal range of serum total protein (6.7 to 8.3 g/dL) will cause \( R_1 \) variation of at least 0.056 (=0.035 \times [8.3 - 6.7]) \text{ s}^{-1}. Although the \( R_1 \) value will be slightly smaller at 3T and body temperature, interindividual variability in serum protein concentration can affect blood \( T_1 \) values. The \( R_1 \) variation of 0.05 \text{ s}^{-1} is compatible with the variation observed in Fig. 4.

In this study, the first gradient-echo signal acquired after the inversion pulse was placed in the center of the k-space, and the subsequent signals were used to fill the rest of the k-space. Although the signal in the center of the k-space will determine image contrast, the signals near the center of the k-space would also affect contrast. Because the speed of arterial flow changes at around 0 to one mm/ms during a cardiac cycle, the amount of blood that flows into the imaging slice after TR of 3 ms would differ every time the gradient-echo signal is acquired without cardiac gating. The difference might have affected estimated \( T_1 \) values because it would cause variation in image contrast under the condition of 20-mm slice thickness. However, this variation would occur randomly, and the effect may

\[
\text{Table. Estimated } T_1 \text{ values in 10 healthy subjects}
\]

<table>
<thead>
<tr>
<th>Subject</th>
<th>Hematocrit value</th>
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<tr>
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<td>0.481</td>
</tr>
<tr>
<td>10</td>
<td>0.522</td>
</tr>
</tbody>
</table>

| Mean ± SD\(^{\dagger}\) | 1779 ± 80 | 1694 ± 77 | 1499 ± 74 |

\(^{\dagger}\) The standard errors are shown as the precision of the estimations for each subject.
\(^{\dagger}\) Standard deviation across subjects.
have been alleviated in the fitting procedure using a dataset of 11 images with various TIs. Table shows the estimated precisions of $T_1$ values as standard errors.

Conclusion

We measured the proton $T_1$ of blood flowing in the human body and found that the $T_1$ of arterial blood at 3T at a hematocrit value of 0.47 is 1779 ± 80 ms, which is approximately 180 ms greater than the reported in vitro value and 230 ms greater than the previously reported in vivo value. It should be noted that the value will be even greater for people with hematocrit values less than 0.47 and that assumption of a smaller $T_1$ value in ASL leads to overestimation of tissue blood flow. The arterial blood $T_1$ at 1.5T was estimated to be 1499 ± 74 ms at a mean hematocrit value of 0.47.

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References


