What are the blood T1 and T2 values in neonates?

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PURPOSE: Neonatal MRI is playing an increasingly important role in studies of early brain development and diseases (1-4). Knowledge of blood T1 and T2 is of major importance in many applications of MRI in neonates. For instance, blood T1 is critical for quantification of perfusion using arterial spin labeling (ASL) (1,4). Blood T2 is important for BOLD-based techniques such as quantification of venous oxygenation and metabolic rate of oxygen (2-4). To date, there has not been a systematic study to examine blood T1/T2 relaxometry in neonates. Consequently, most of the previous studies had to assume blood T1 and T2 values based on those measured in adults (1-4). This present study intends to fill this gap. We hypothesize that T1 and T2 relaxometry of neonatal blood is different from that of adult, because of their differences in hemoglobin molecular structure, a subtype called fetal hemoglobin (HbF) in neonates (5). Using freshly collected human cord blood samples, we measured blood T1 and T2 and their dependence on common physiological factors such as hematocrit (Hct) and oxygenation at 3T. The values provided in this report may provide important reference and calibration information for sequence optimization and quantification of in vivo neonatal MRI studies.

METHODS: *Collection of cord blood samples:* 9 blood samples were collected from the umbilical cords in the delivery room at 10±1min after delivery of the neonates. The blood samples were collected as part of a larger-scale neonatal study and followed institutional and ethical guidelines. All neonates were healthy with a cord pH of 7.23±0.05. The blood was drawn from the umbilical vein and arteries in the double-clipped umbilical cord. About 3-4 ml of the cord blood was put into a heparin-coated tube and transported to the imaging center for MRI scans. All MRI studies were performed within 6 hours of the blood collection. *Blood preparation:* To ensure the results to be relevant for physiological conditions, the temperature of the blood sample during the MRI scan was maintained at 37˚C using a water bath. Blood T1 and T2 values were studied as a function of Hct and oxygenation. Oxygenation (Y) of the blood was modulated by exposing the blood to either room air (to increase Y) or N2 gas (to reduce Y). For each blood sample, 3 to 6 oxygenation levels were examined ranging from 25% to 100%. Hct of the blood was modulated by extracting top or bottom portion of the blood in the tube. Given the small volume of blood in the cord, it was not feasible to use centrifuge to accurately adjust the Hct value. At each combination of Hct and Y values, blood T1 and T2 values were determined. In one sample, we also studied the temperature dependence of blood T1, by varying the sample temperature from 20 to 40˚C at 5˚C steps. *MRI measurements:* All experiments were performed on a 3T (Philips Achieva). An inversion recovery imaging sequence was used for T1 measurements (6), with TI values of 10, 50, 100, 250, 500, 1000, 3000, and 10000 ms. T1 values was calculated by fitting the blood signals to model: $S=|S_0\cdot(1-C\cdot e^{-TI/T1})|$ (Fig.1a). Regression analyses were performed to assess the relationships between temperature and blood T1, and between T1, Y and Hct. A CPMG-T2 (inter-echo spacing τ_{CPMG}=10ms) sequence (7) was used to measure blood T2. Mono-exponential fitting of the data yields blood T2 values (Fig 1b). To establish an analytical relationship between T2, Y and Hct, the blood T2 was fitted to an exchange model described by Golay et al. (8), in which $1/T2=A+B\cdot(1-Y)+C\cdot(1-Y)^2$ and A, B and C are in turn functions of Hct (8).

RESULTS and DISCUSSION: The mean Hct level of our blood samples was 0.42±0.08, which covers the typical range of neonatal Hct values. *Blood T1:* It was found that similar to adult blood (6), 1/T1 (in s^{-1}) of neonatal blood was strongly dependent ($p<0.001$) on Hct (Fig. 2a for Y=0.97±0.03). However, neonatal blood T1 was longer than that of adult blood (Fig. 2a). Relevant for ASL quantification, typical arterial T1 in neonate was 1825±184ms (Hct=0.42±0.08). Neonatal blood T1 was also found to be dependent on Y ($p=0.005$). Specifically, venous blood had a shorter T1 compared to arterial blood. There was also an interaction effect between Hct and Y ($p=0.04$). That is, the dependence of T1 on Y was more prominent in high hematocrit blood (Fig. 2b) compared to plasma, as expected. *Blood T2:* Fig. 3a illustrates the relationship between neonatal blood T2, Y and Hct. The symbols indicate the experimental data points and the mesh shows the model-fitted surface, which can be written as $1/T2=[-1.1+1.5\cdot Hct-21.4\cdot Hct^2]+[-5.1\cdot Hct+29.4\cdot Hct^2]\cdot(1-Y)+[242.9\cdot Hct\cdot(1-Hct)]\cdot(1-Y)^2$. T2 is longer in arterial blood and in low hematocrit blood. Furthermore, as can be seen in a 2D profile in Fig. 3b, neonatal blood has a longer T2 than adult blood. At a typical Hct of 0.42, the arterial T2 of neonatal blood is 191ms, whereas the arterial T2 of adult blood is 147ms (7). Relevant for T2-based methods to estimate blood oxygenation (2-4), if one were to use adult T2-Y relationship to calibrate neonatal T2 data, an overestimation in blood oxygenation is expected. *Temperature dependence of T1:* Fig. 4 showed that blood T1 is significantly correlated with temperature ($p<0.001$). Measurement of T1 at room temperature (20˚C) resulted in an underestimation by 24% comparing to that measured at body temperature (37˚C). Therefore, it is important to maintain the blood temperature at 37˚C in *in vitro* experiments in order for the data to be applicable for *in vivo* studies.

CONCLUSION: The present work represents the first *in vitro* quantification blood T1 and T2 relaxometry for neonates. Using healthy cord blood samples, we established a comprehensive relationship between hematocrit, oxygenation and neonatal blood T1/T2. We found that neonatal blood has a longer T1 and T2 comparing to adult blood. The T1 values reported in this work can be utilized in ASL-CBF quantification as well as in other MRI techniques requiring knowledge of blood T1. To give a quantitative example, if adult arterial T1 (1664ms, (6)) were to be used in ASL quantification for neonates, it would lead to an overestimation of CBF by 16%. The T2-Y relationship can be used to estimate blood oxygenation *in vivo*, which can lead to the quantification of an important functional index, cerebral metabolic rate of oxygen. Several in vivo studies have demonstrated the successful implementation of this principle (2-4), and the present work should allow the refinement of those results. In summary, the neonatal blood T1 and T2 characteristics reported in this work may serve as a useful reference for future *in vivo* studies aiming to assess hemodynamic function in neonates.

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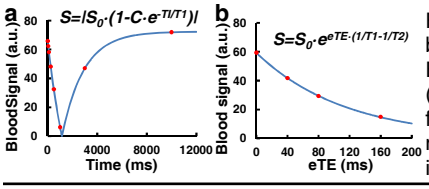

Fig. 1: Determination of blood T1 and T2. (a) Example of T1 fitting. (b) Example of T2 fitting. Red dots indicate measured value. Line indicates fitting curve.

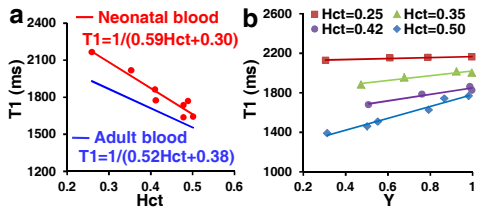

Fig. 2: Results of cord blood T1 measures. (a) Arterial T1 decreases with Hct level. Blood T1 is higher in neonates than in adults. (b) Neonatal T1 decreases with Y. Symbols indicate measured T1 values. Lines are linear fitting curves.

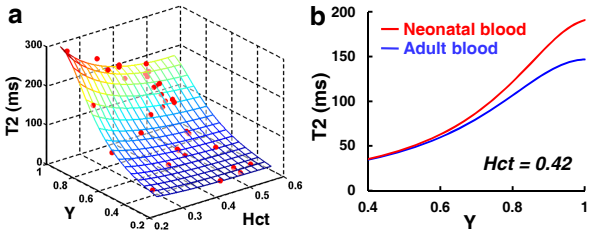

Fig. 3: Results of cord blood T2 measures. (a) 3D calibration plot showing the dependence of blood T2 on oxygenation, Y, and hematocrit (Hct). 3T, τ_{CPMG}=10ms. (b) Neonatal blood T2 is different from adult blood T2 (7).

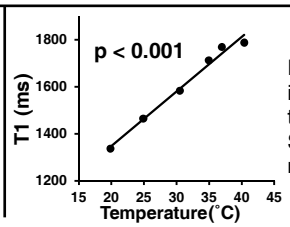

Fig. 4: Blood T1 increases with temperature. Symbols are measured T1.