Calibration and Implementation of Quantitative Blood Oxygenation Measurement at 7T

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Introduction A calibratable relationship between blood oxygenation and T_2 has been exploited for quantitative measurement of cerebral venous oxygenation [1-4]. These methods have demonstrated potential utilities in normalization of fMRI signals [5], evaluation of brain metabolism [6], and understanding brain disorders [7]. To date, all such studies have been performed at the field strength of 3T or lower. Given the field dependence of deoxyhemoglobin susceptibility effects [8], it is reasonable to expect that a higher field, e.g. 7T, may provide a unique advantage in improving the sensitivity of this technique, in addition to the SNR increase that is common to all methods at 7T [9].The goals of the present study are two-fold. First, we aim to establish a calibration plot between blood T_2 and oxygenation at 7T (using *in vitro* blood sample experiment) in the context of various hematocrit levels (Hct). Second, we implemented a recently developed T_2-Relaxation-Under-Spin-Tagging (TRUST) MRI technique [10] at 7T and determined venous blood T_2 *in vivo*. Utilizing the calibration plot, human venous oxygenation was estimated and its response to hyperoxia maneuver was demonstrated.

Methods *In vitro blood experiments* *In vitro* experiments were performed on bovine blood samples in a 7T small animal MR scanner (Varian) with a 38 mm birdcage RF coil. The temperature of the blood sample was controlled by maintaining the ambient temperature of the magnet bore at 37˚C. Experiments were performed on 7 batches of blood on separate days. Blood T_2 at three Hct levels (Hct = .34,.42,.54) were assessed. At each Hct, the T_2 dependence on oxygen saturation (Y) was examined. The blood T_2 was measured with a CPMG multi-echo T_2 sequence with τ_{CPMG} = 5 ms. Estimation of T_2 was based on standard mono-exponential fitting. The entire T_2 data (all Y and Hct values) was fitted to a 3D plot using a mathematical model to determine the relationship between T_2, Y and Hct.

In vivo human experiments *In vivo* experiments were performed using TRUST at 7T (7T Philips Achieva, 16 Ch. Nova T/R volume headcoil). The TRUST technique applies the spin labeling principle on the venous side, and subtraction of control and labeled images yields pure venous blood signal. The T_2 value of the pure venous blood is then determined using non-selective T_2-preparation pulses, which minimizes the effect of flow on T_2 estimation [10]. For implementation of TRUST at 7T, an adiabatic hyperbolic secant inversion pulse [11] was used for spin tagging (β = 400 rad/sec, μ = 8, FA = 1800˚, BW = 1020 Hz). To balance the magnetization transfer (MT) effect, an equivalent tagging pulse was played out below the imaging plane during the control acquisition. The T_2-preparation incorporates hard composite pulses, MLEV-16 phase cycled, with τ_{CPMG}=5 ms. This results in a set of label and control images with three effective TEs (eTE = 0, 20, 40 ms). Due to short blood T_2* at 7T, images were acquired with a multishot-EPI gradient echo (FOV = 220x220 mm^2, matrix = 64x64, EPI factor = 3, 8 shots, SENSE factor = 3 (AP), TE = 2 ms, 1 slice, slice thickness = 5 mm). Six subjects (2 Female /4 Male) were scanned with 7T TRUST to measure venous oxygenation in the superior sagittal sinus. The protocol for two subjects used recovery time (RT) of 9800 ms and inversion time (TI) of 1500 ms, where TR = RT + TI. All others were scanned with RT = 2500 ms, and TI between 600 and 900 ms.

Hyperoxia maneuver To demonstrate the sensitivity of the technique in detecting oxygenation changes, an additional subject (1 Female) was scanned with 7T TRUST (RT = 2500ms, TI = 700ms) during normoxia and hyperoxia (98% O_2, 2% CO_2) conditions. After the scan, 5cc of blood was drawn from the subject's arm to determine the Hct using a centrifuge. Venous oxygenation values under normoxia and hyperoxia were compared.

Results and Discussion The *in vitro* blood data results are shown in Figure 1. As expected, the 7T blood T_2 values are shorter than those measured at lower magnetic fields with the same τ_{CPMG} (5 ms). For venous blood (Y=0.6) the T_2 values of blood with Hct = 0.42 are 132 [12], 76 [13], and 20 ms [this study] for 1.5, 3, and 7T respectively. For arterial blood (Y = 1) the T_2 values of blood with Hct = 0.42 are 193 [12], 164 [13], and 70 ms [this study] for 1.5, 3, and 7T respectively. A representative 7T TRUST data set is shown in Figure 2.The *in vivo* 7T data resulted in an average blood T_2 value of 24.7 ± 4.1 ms in the sagittal sinus. Using the model of the *in vitro* blood data and assuming a Hct of .42, the *in vivo* blood T_2 data can be converted to an average measured venous oxygen saturation of 64.8 ± 4.6 %. The T_2 and calculated Y values for each subject lie within the expected physiologic range for venous blood. To test the sensitivity of TRUST at 7T, normoxia and hyperoxia conditions from one subject with Hct = 0.40 were compared. In normoxia, we measured T_2 = 26.0 ms, which corresponds to Y = 65%. Hyperoxia resulted in T_2 = 31.1 ms, which corresponds to Y = 70%. This increase in T_2 and Y is a promising indication that TRUST at 7T is responsive to changes in blood oxygenation.

To the best of our knowledge, the present report is the first study to quantitatively estimate blood oxygenation at 7T. Our results provide a calibration plot for accurate conversion of blood T_2 to oxygenation levels. Such data can be used to calibrate a number of venous oxygenation techniques including TRUST, QUIXOTIC [14], VSEAN [15], and others. Our *in vivo* results also demonstrate the feasibility of TRUST at 7T and provide a basis for further technical development of these methods at high field.

References [1] Wright et al. JMRI 1:275 (1991). [2] Golay et al. MRM 46:282 (2001). [3] Oja et al. JCBFM 19:1289 (1999). [4] Qin et al. MRM 65:471 (2011). [5] Lu et al. MRM 2:364 (2008). [6] Xu et al. MRM 62:141 (2009). [7] Ge et al. ISMRM (2010). [8] Thulborn et al. BBA 2:265 (1982). [9] Vaughan et al. MRM 46:24 (2001). [10] Lu, et al. MRM 2:357 (2008). [11] Golay, et al. MRM 1:15 (2005). [12] Stefanovic, et al. MRM 52:716 (2004). [13] Lu, et al. MRM, in press (2011). [14] Bolar et al. MRM, in press (2011). [15] Guo et al. ISMRM (2010).

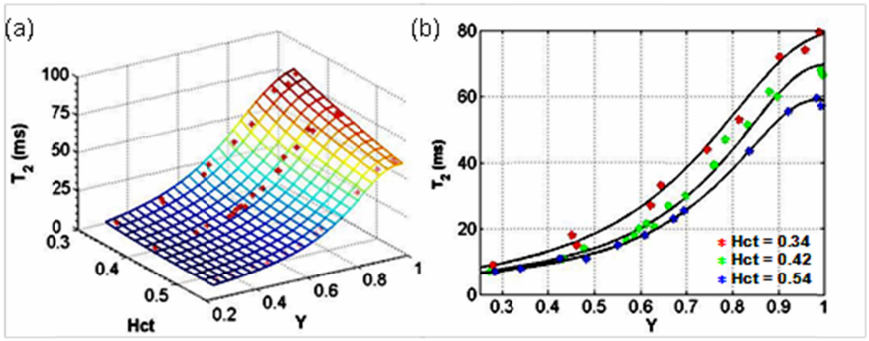

Figure1: *In-vitro* blood T_2 dependence on Y. (a) All blood data and fitted model. (b) 2D cross-sections of the model for each Hct.

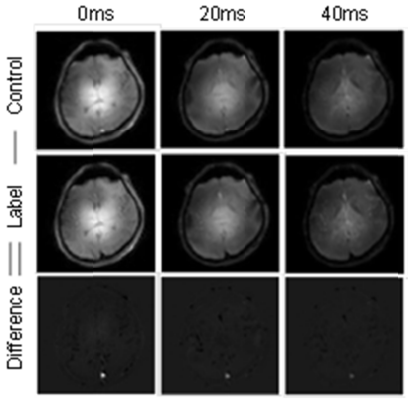

Figure 2: 7T TRUST data, with Control and Label images, and the resulting Difference image for eTE = 0, 20, 40 ms.