IN VIVO ESTIMATION OF THE TRANSVERSE RELAXATION TIME DEPENDENCE OF BLOOD ON OXYGENATION AT 7 TESLA

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Purpose: Blood oxygenation level dependent (BOLD) signal changes can arise both within and around blood vessels - intravascular and extravascular BOLD, respectively. Their relative magnitude across the vascular tree depends on the local relaxation times[1]. The precise knowledge of the oxygenation dependence of the T_2^* of blood, within the physiologically relevant range will improve the quantitative understanding of the BOLD effect in gradient echo imaging at 7T. Measurements of the oxygenation dependence of T_2^* of blood at 7T have been previously performed only *in vitro*[2]. However, at high magnetic field the susceptibility gradients between the blood sample and its surroundings become more difficult to compensate *in vitro*, which can significantly confound the T_2^* estimates. Therefore *in vivo* measurement remains the best option for accurate evaluation of the oxygenation dependence of blood T_2^* at 7T. In this study, we combine T_2^* and quantitative susceptibility maps during different respiratory challenges to obtain the (de)oxygenation dependence of blood's T_2^* *in vivo* at 7 Tesla.

Methods: The study was approved by the local ethics committee and all subjects gave informed consent. Experiments were performed on a Siemens 7T MR scanner using a 24-channel head coil. Data were acquired from 6 healthy volunteers (3 male), using a 3D fully flow compensated dual echo GRE sequence[3]. During MRI data collection four different gas mixtures were administered to the subjects using a non-rebreathing gas delivery circuit: 1) 100% O_2, 2) 5% CO_2, 21% O_2 with 74% N_2, 3) 5% CO_2 with 95% O_2 (carbogen), and 4) ambient air. The administration of the gas mixtures began 3 minutes before the start of the MR acquisition and continued throughout to ensure a stable physiological state. Each scan lasted 7 min 21 s. For each volunteer a slab of 36 sagittal slices centred on the midline was acquired with TE1/TE2/TR = 5.6/19.5/40 ms, and 0.6 mm isotropic resolution. An exponential fit was applied to the magnitude images of the two echoes to yield T_2^* maps. To obtain susceptibility difference maps, the first echo phase images for each gas mixture acquisition, were subtracted from the first echo phase images during air breathing. These phase difference maps were then used to calculate quantitative susceptibility difference maps using the threshold-based k-space division method[4]. A region of interest was drawn in the superior sagittal sinus of every subject to obtain the mean venous susceptibility change. This value was corrected for global magnetic field changes during breathing of different gases by subtracting the value of an adjacent grey matter region. The susceptibility changes of the venous blood were converted to oxygenation changes, assuming a hematocrit of 0.4 for female and 0.46 for male subjects and a susceptibility difference of 3.39 ppm (SI units) between fully oxygenated and fully deoxygenated blood[5]. The venous blood oxygenation during air breathing was assumed 0.65.[6]

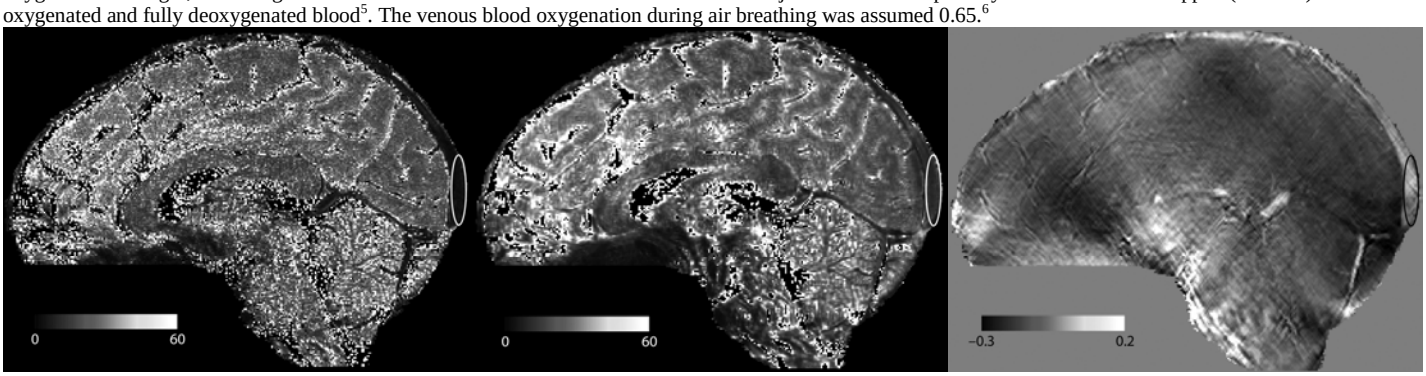

Fig. 1: A) T_2^*-map (ms) during air breathing B) T_2^*-map (ms) during carbogen breathing C) Susceptibility change map (ppm SI) air-carbogen

	air	100% O_2		5% CO_2 in air		Carbogen	
subject	T_2^*	oxygenation change	T_2^*	oxygenation change	T_2^*	oxygenation change	T_2^*
1	8.7	4.0	11.9	11.5	13.5	14.9	17.6
2	10	6.0	10.9	9.7	14.8	12.6	15.9
3	7.7	5.8	9.2	12.1	12	20.6	19
4	6.8	4.7	7.2	9.4	9.1	17.9	15.1
5	9.8	5.3	11.8	14.9	14.3	20.9	21.1
6	9.4	2.8	11.6	8.7	15.3	17.2	26.8
mean ± STD	8.7 ± 1.3	4.8 ± 1.2	10.4 ± 1.9	11.1 ± 2.3	13.2 ± 2.3	17.4 ± 3.2	19.3 ± 4.3

Tab. 1: Venous blood oxygenation increases (in %) and T_2^* (ms) for all experiments across subjects

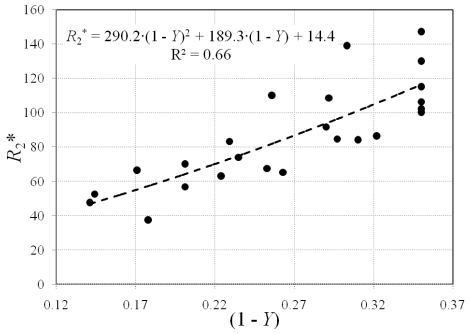

Fig. 2: Scatter plot R_2^* vs. blood deoxygenation level *in vivo*

Results: Fig. 1 A) and B) show the T_2^* maps (in ms) during air and carbogen breathing, respectively, whereas C) displays the corresponding susceptibility difference map. The ellipses indicate the regions used to estimate the venous T_2^* in A) and B) and the venous susceptibility change in C). In Fig. 1 C) positive values correspond to regions which are more paramagnetic during air breathing, while areas with negative values are more paramagnetic during carbogen breathing. Table 1 lists the increases of venous blood oxygenation (in %) in the posterior portion of the sagittal sinus and the corresponding T_2^* values (in ms) for all the gas experiments across subjects. Fig. 2 presents a scatter plot of the *in vivo* $R_2^* = 1/T_2^*$ values vs. blood deoxygenation level (1-Y) for all subjects and breathing conditions. The data were fitted using a quadratic function of (1-Y) as suggested by theory[7]. Furthermore, the fitting coefficients and the R^2 value obtained are also included in Fig. 2.

Discussion: The measured venous oxygenation increase due to breathing 5% CO_2 in air is consistent with values obtained in previous reports for this challenge[6]. The scatter in the data may be attributed to differences in hematocrit and baseline venous oxygenation across subjects. Another source of inter-subject variability of the measured T_2^* is the difference in the shim quality in the chosen ROIs. The coefficients in Fig. 2 can be used to obtain the venous oxygenation from the measured T_2^* value. The procedure presented here can also be easily translated to lower magnetic fields to validate previous in vitro results[7].

Conclusion: The approach proposed can reliably determine the oxygenation dependence of the effective transverse relaxation time of blood (T_2^*), in vivo at 7T, within the physiologically relevant range. The observed dependency of T_2^* on (de)oxygenation can be applied to estimate more accurately the intravascular contribution to the BOLD effect in gradient echo imaging at 7T across the vascular tree.

References: 1. Uludag K, et al. Neuroimage: 2009; 48: 150-165; **2.** Blockley NP, et al. MRM: 2008; 60: 1313-1320; **3.** Deistung A, et al. JMRI: 2009; 29: 1478-1484; **4.** Wharton S, et al. MRM: 2010; 63: 1292-1304; **5.** Spees WM, et al. MRM: 2001; 45: 533-542; **6.** Jain V, et al. JCBFM: 2011; 31: 1504-1512; **7.** Silvennoinen MJ, et al. MRM: 2003; 49: 47-60