Measurement of Parenchymal Extravascular R2* using Multi-echo VASO MRI at 7T

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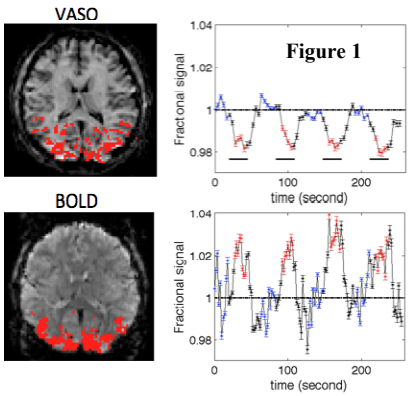
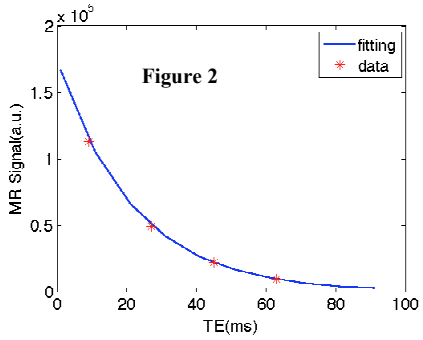
Introduction: Parenchymal extravascular R_2^* is an important parameter for quantitative blood-oxygenation-level-dependent (BOLD) measurements. While total R_2^* values have been reported in many studies (1), it is not trivial to separate out the extravascular compartment, for which the BOLD theory is better established than for total tissue (2). Vascular-space-occupancy (VASO) MRI (3) can be employed to null blood signal while keeping substantial extravascular tissue signal, based on the different T_1 relaxation times of blood and tissue. Lu et al. previously determined parenchymal extravascular R_2^* values at 1.5T and 3T using multi-echo VASO fMRI (4) (Table 1). Donahue et al. used bipolar crusher gradients to suppress fast flowing blood signal and measure the extravascular R_2^* change (ΔR_2^*) during visual stimulation at 7T (5) (Table 1). However, the absolute parenchymal extravascular R_2^* in human brain has not yet been reported at 7T. In this study, we use multi-echo VASO MRI to measure this in human brain at 7T. This R_2^* together with measured extravascular and total ΔR_2^* during visual stimulation, will be used to assess the intravascular and extravascular contributions to the BOLD effect at 7T.

Methods: Studies were performed on a 7T Philips Achieva system (Philips Healthcare, Best, The Netherlands) using a quadrature transmit head coil and a 32-channel phased array receive coil (Nova Medical). Four healthy volunteers were recruited for this study. Three fMRI scans (2 VASO (TR/TI=4s/1293ms) and one BOLD (TR=2s) scans) were performed on each participant with visual stimulation of yellow/blue flashing checkerboard (40s/24s off/on; 4 repetitions). The VASO scan was repeated once to get signal-to-noise ratio (SNR) comparable to the BOLD scan. Single-shot gradient echo (GE) echo-planar-imaging (EPI) readout was used, and images were acquired at four TEs (TE/echo spacing (ES)=9/18ms) to allow R_2^* fitting. Common imaging parameters: flip angle=68.3˚, matrix=80x80, voxel=2.5x2.5x2.5mm^3, single slice, SENSE factor=4, halfscan=0.6, fat suppression (SPIR). Second order shimming on the brain was applied. A magnetization-reset module (90˚ RF pulse followed by spoiler gradients) (6) was deployed immediately after the end of readout in both VASO and BOLD scans in order to suppress blood inflow effects. *Data analysis:* All fMRI images were co-registered and detrended with SPM8. The VASO images from all four echoes were used to extrapolate to the effective TE of 0ms, in order to avoid BOLD contaminations. Activated voxels were detected with VASO (TE=0ms) and BOLD (TE=27ms, second echo) data. Requirements for voxel activation were t-score>1.5 (BOLD), t-score>1 (VASO), p<0.05, SNR>20, and cluster size>4. Only voxels activated in both modalities were used for further calculations, in order to exclude voxels containing big vessels and to localize the signal predominantly in parenchyma. Voxel based R_2^* fitting was conducted using a two-parameter model.



Results & Discussion: Fig. 1 shows representative activation maps superimposed on VASO and BOLD images and the average time courses of relative signal changes from one subject. In VASO, a negative signal change is normally expected upon neuronal activation because the concomitant vasodilatation results in a reduced tissue signal. Fig. 2 shows a typical R_2^* fitting. The fitted results are summarized in Table 2. The extravascular R_2^* values were slightly smaller than the corresponding total R_2^* values (P<0.3), which is in agreement with the fact that venous blood has a larger R_2^* (1) than extravascular tissue. As expected, both extravascular and total R_2^* values are higher at 7T than those at lower fields (Table 1). The R_2^* changes (ΔR_2^*) during visual stimulation and extravascular ΔR_2^* fraction (extravascular ΔR_2^*/total ΔR_2^*) were in line with those reported in (5). Both our data and the Donahue study (5) show that the extravascular ΔR_2^* fraction is approximately 90% at 7T, indicating a much larger contribution from the extravascular compartment to the BOLD effect compared to 1.5T and 3T (4). This is in line with the prediction that intravascular BOLD contributions are decreased at higher field due to the faster R_2^* decay of venous blood (thus diminishing intravascular signal) (7,8).



Conclusion: We demonstrated that by using multi-echo VASO MRI, we can measure the parenchymal extravascular R_2^* value in human visual cortex at 7T to be 43.78±2.82 s^{-1} at baseline and 42.71±3.32 s^{-1} during visual stimulation. The values can be used in quantitative modeling of the BOLD effect.

Reference: (1) K. Uludağ *et al.* NeuroImage 2009;48:150. (2) Yablonskiy *et al.*, MRM 1994;32:749. (3) Lu *et al.* MRM 2003;50:263. (4) Lu *et al.* MRM 2005;53:808. (5) Donahue *et al.* NMR in Medicine 2011;24:24. (6) Lu *et al.* ISMRM Proceedings 406, Toronto, Canada, 2008. (7) Silvennoinen *et al.* MRM 2003;49:47. (8) Zhao *et al.* MRM 2007;58:592

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Table 1: Literature values.

	Extravas. $R_{2,rest}^*$ (s^{-1})	Extravas. $R_{2,act}^*$ (s^{-1})	Extravas. ΔR_2^* (s^{-1})	Total $R_{2,act}^*$ (s^{-1})	Total $R_{2,rest}^*$ (s^{-1})	Total ΔR_2^* (s^{-1})	Extravas. ΔR_2^* fraction (%)
1.5 T [4]	16.1 ± 0.64	15.89 ± 0.63	-0.25 ± 0.02	16.78 ± 0.65	16.21 ± 0.67	-0.57 ± 0.10	47 ± 7
3.0 T [4]	21.15 ± 0.66	20.77 ± 0.69	-0.38 ± 0.05	22.06 ± 0.84	21.48 ± 0.82	-0.58 ± 0.09	67 ± 6
7.0 T [5]			-1.25 ± 0.11			-1.37 ± 0.34	91 ± 4

Table 2: Summary of results.

	Extravas. $R_{2,rest}^*$ (s^{-1})	Extravas. $R_{2,act}^*$ (s^{-1})	Extravas. ΔR_2^* (s^{-1})	Total $R_{2,rest}^*$ (s^{-1})	Total $R_{2,act}^*$ (s^{-1})	Total ΔR_2^* (s^{-1})	Extravas. ΔR_2^* fraction (%)
Subject 1	42.59	41.34	-1.25	44.51	43.07	-1.44	86.8
Subject 2	45.93	44.67	-1.26	46.25	45.02	-1.23	102
Subject 3	40.35	39.61	-0.74	40.46	39.66	-0.80	92.5
Subject 4	46.25	45.24	-1.01	46.16	44.84	-1.32	76.5
Mean	**43.78**	**42.71**	**-1.06**	**44.34**	**43.15**	**-1.20**	**89.6**
STD	**2.82**	**3.32**	**0.24**	**2.70**	**2.48**	**0.28**	**10.8**