Whole-Brain Mapping of Venous Vessel Size in Humans Using the Hypercapnia-Induced BOLD Effect

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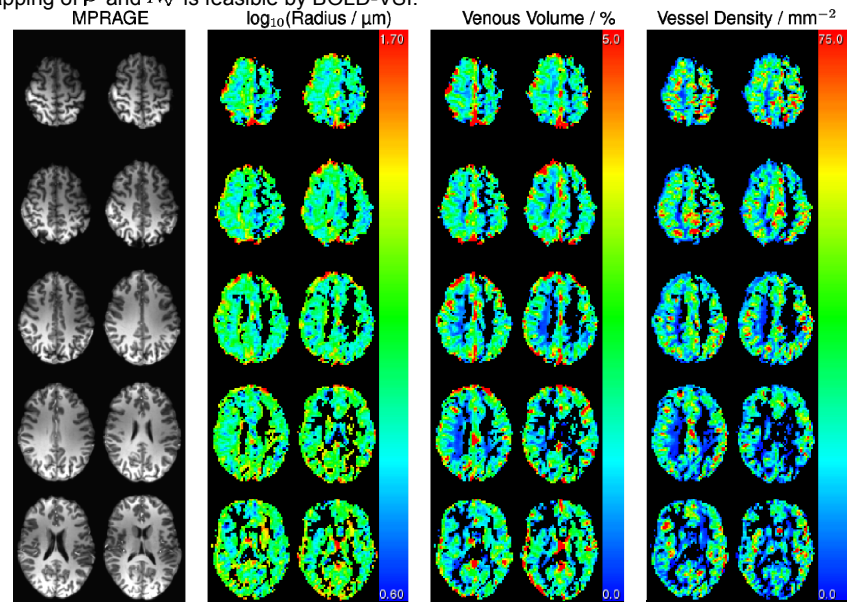
Introduction The approach of *vessel-size imaging* (VSI) [1-3] for characterizing cerebral tumor vascularization has recently drawn much attention [4-9]. VSI employs the ratio of the change between the transverse gradient-echo (GE) and spin-echo (SE) relaxation rates, ΔR_2^* and ΔR_2, in response to an intravascular contrast agent. This non-invasive method allows quantitative mapping of the microvasculature, i.e. of the mean vessel radius, r_v, on a spatial scale of several micrometers. Despite the great potentials of VSI, the method has not found widespread use in clinical practice due to the lack of experience with healthy subjects, as the injection of the contrast agent is often ethically difficult to justify for methodological purposes. We propose, therefore, to employ the easily-accessible hypercapnia-induced *blood oxygenation level dependent* (BOLD) effect for VSI of the venous vasculature [1, 10]. It is demonstrated in this work that whole-brain BOLD-VSI is possible in humans by using the administration of carbogen (5% CO_2, 95% O_2). Furthermore, it is shown that maps of venous vessel size can be utilized to calculate the venous blood volume fraction, β, and vessel density, N_v.

Materials and Methods Measurements were performed on a Siemens 7 Tesla Magnetom using ODIN [11]. A single-shot, multi-slice, combined GE-SE sequence was used to obtain maps of ΔR_2^* and ΔR_2 simultaneously and with high temporal resolution. Two GE-EPI readouts with short nominal TEs of 7.3 and 17.6 ms, respectively, were employed. The SE was sampled by a single EPI at TE = 55.9 ms. Other sequence parameters were: 3 × 3-mm in-plane resolution; 10 axial slices (3-mm thickness); repetition time, TR = 2 s; 159-kHz receiver bandwidth; 75% partial Fourier acquisition with GRAPPA reconstruction (reduction factor 2). Healthy subjects were breathing air and carbogen for 3 minutes in an alternating fashion for 27 minutes in total. Maps of r_v were obtained from the ratio $q = \Delta R_2^*/\Delta R_2$ [10]. Furthermore, β was estimated by using the decomposition $\Delta R_2^* = \beta \cdot F(r_v)$, which is valid for $\beta \ll 1$. The function $F(r_v)$ represents the blood-volume-normalized, vessel-size-dependent GE-BOLD effect and was obtained from the MC-simulated $\Delta R_2^*(r_v)$. By measuring r_v and ΔR_2^*, β and $Nv = \beta/(2r_v^2)$ can be calculated.

Results The figure shows maps of the calculated parameters and the table list values averaged over different regions. The values for r_v correspond well with previous results [10] and β is in the expected range, i.e. approximately half of the total blood volume.

Discussion and Conclusions The present work lays the foundations for BOLD-VSI in humans by providing reproducible maps of venous vessel size at 7 T based on carbogen-induced hypercapnia. Compared to VSI based on an exogenous contrast agent, BOLD-VSI offers a simple and safe technique to map the microstructure of the (venous) vasculature. It has broader applicability than just for the brain, for instance for mammographic screening. The next obvious steps are to test the feasibility of BOLD-VSI on tumor patients at lower, clinically available field strengths, possibly with a higher resolution. Furthermore, the present work demonstrates experimentally that quantitative mapping of β and N_v is feasible by BOLD-VSI.



	GM			WM		
Subject	r_v / µm	β / %	N_v / mm^{-2}	r_v / µm	β / %	N_v / mm^{-2}
1	13.0	2.38	29.5	13.2	1.32	17.5
2	12.2	2.47	35.2	11.5	1.32	24.9
3	11.5	2.00	34.4	11.2	0.94	19.3
4	14.8	2.50	25.0	14.7	1.33	14.8
All	12.9 ± 1.4	2.34 ± 0.23	31.0 ± 4.8	12.6 ± 1.6	1.22 ± 0.19	19.1 ± 4.3

Venous Vessel Size (r_v), Blood Volume (β) and Vessel Density (N_v) separately for gray matter (GM) and white matter (WM). The last row lists mean and standard deviation over subjects.

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