Investigation of Vascular-Space-Occupancy (VASO) MRI for Quantitative Measurement of Cerebral Blood Volume (CBV)

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INTRODUCTION Vascular-Space-Occupancy (VASO) MRI has been used to estimate absolute Cerebral-Blood-Volume (CBV) in units of ml blood/100ml brain (1). This method uses the T1-shortening effect of Gd-DTPA under steady state, and employs a pre/post-contrast image subtraction approach to estimate CBV (1). In comparison with Dynamic-Contrast-Susceptibility (DSC) techniques, VASO MRI has several potential advantages: 1) does not require the knowledge of arterial input function (AIF); 2) the absence of echo-planar-imaging (EPI) related image distortion; 3) flexible slice orientation which allows the acquisition of coronal/sagittal sections. Compared with other T1-based steady state methods (2,3), the VASO method does not need to find a whole blood voxel for signal reference, utilizes fully the T1-relaxivity of the Gd-DTPA (pre-contrast signal 0 and post-contrast signal 1), and has minimal inflow effect. On the other hand, several confounding factors need to be investigated for VASO MRI to fully optimize the method for accurate measurement of CBV, some of which are issues shared by other T1-based steady state methods. Here we investigate the echo-time (TE) dependence, acquisition timing dependence, acquisition technique dependence (gradient-echo vs. spin-echo), and water-exchange effects in the VASO method. Experimental data are compared with numerical simulations. Recommendations for parameter selections are provided.

METHODS: Nine young (age 24±2 years), healthy subjects were studied on a 3T system (Philips Achieva) after consent was obtained. An FDA-approved contrast agent Gd-DTPA (Magnevist®) was used with a standard dosage (0.1 mmol/kg) via a power injector (MEDRAD). The VASO MRI protocol was similar to a previous study (1) except that 8 echoes were acquired after each RF excitation and the post-contrast VASO was repeated 10 times (Fig. 1). Spin-echo, SE (T2-weighted), and gradient-echo, GE (T2*-weighted), acquisition schemes were used in separate sub-groups (n=5 for SE, n=4 for GE). The imaging parameters were: FOV=230×230mm^2, matrix size =128×128, single-slice, slice thickness=5mm, EPI factor=7, TE=10ms(SE), TE=6ms(GE), and TR=6s. Each VASO scan took 2 min 16s and 2 min 10s for SE and GE scans, respectively. The post-contrast images were co-registered to the pre-contrast image using FSL (Oxford University, UK) and the CBV maps were calculated with the algorithm described in the literature (1). Multi-echo data were extrapolated to that at TE of 0, thereby eliminating T2/T2* effect. Gray matter voxels were identified based on the histogram of pre-contrast VASO image and spatial average was performed. Numerical simulations were performed using a two-compartment relaxation model (4) that accounts for capillary water exchange.

RESULTS and DISCUSSION: Fig. 2 illustrates the CBV maps from different echoes and acquisition times. Fig. 3 plots the normalized CBV of gray matter as a function of echo time and post-injection time. The CBV values have been normalized against the extrapolated CBV at 7-12 min after injection (reason given below). It can be seen that SE (Fig. 3a) and GE (Fig. 3b) data manifest similar patterns. The estimated CBV decays as echo time increases. At the first echo (10ms for SE, 6ms for GE), the under-estimation was 15.5±1.4% for SE and 16.3±3.5% for GE. The T2* effect was more pronounced and the calculated white-matter CBV can become negative at long echo times (data not shown), when the T2* effect dominates over the T1 effect. The time-courses of gray matter T2 and T2* are shown in Fig. 4. As expected, T2* shows a considerable drop after contrast injection, then slowly recovers back toward the pre-contrast value. Surprisingly, the T2 curve only shows a very small dip. Since the gray matter contains blood and extra-vascular tissue, we believe that the pure tissue T2 change will be even smaller, suggesting that the Gd-DTPA does not significantly affect the tissue T2 (at refocusing interval of 10ms) even in the presence of diffusion. As predicted from the VASO theory, the estimated CBV value is relatively insensitive to the acquisition timing (Fig. 3), even though the concentration of the contrast agent changes considerably within that period (Fig. 5). The CBV starts to reduce noticeably only after 15 min. Another important feature is that immediately following the injection, the CBV is actually over-estimated and then rapidly (within 5 min) drops to the plateau level. We conducted simulations and explain this feature in terms of water exchange in capillary. Water exchange occurs in capillary across the blood-brain-barrier (BBB). Therefore even though the Gd-DTPA stays inside blood vessels, some tissue water can also be affected by the T1-relaxivity of Gd, resulting in an over-estimation of the blood space. This is well known for slow-exchange models (3) such as the one used in VASO. Our simulation using physiologic permeability-surface (PS) values (5) yielded excellent agreement with the experimental data (Fig. 6). Based on these data, we believe that VASO measurements immediately following the injection have contributions from both CBV and water exchange, resulting in a CBV over-estimation of as large as 22.6±12.1% according to our experiments. As the concentration of Gd decreases, the water exchange effect reduces significantly but the CBV contribution is minimally affected as long as the Gd concentration is still above the threshold. When the Gd concentration further reduces to a level violating the VASO assumptions (>15min post-injection), systematic under-estimation is observed. Therefore, we believe the extrapolated (TE=0) value using the 7-12 min post-contrast VASO scans is most close to the true CBV value. In summary, this work demonstrates that water exchange can cause over-estimation and T2/T2* effects can cause under-estimation in VASO CBV measurement. A post-contrast scan between 5-15 min with a multiple-echo acquisition scheme is recommended for accurate estimation of absolute CBV.

REFERENCES: 1) Lu H et al. Magn Reson Med 54: 1403 (2005); 2) Moseley ME and Chew WM Magn Reson Med 23:21 (1992); 3) Shin W et. Al. Magn Reson Med 56:138 (2006); 4) Hazlewood CF et.al. Biophys. J. 14:583 (1974); 5) Zhou J et al. J Cereb Blood Flow Metab 21:440 (2001)

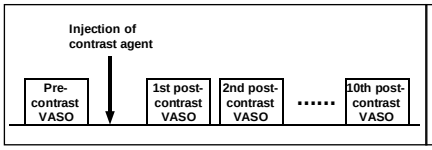

Fig. 1 VASO-MRI experiment protocol

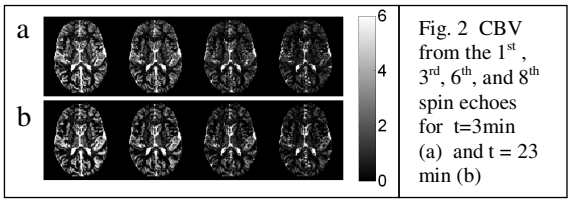

Fig. 2 CBV from the 1st, 3rd, 6th, and 8th spin echoes for t=3min (a) and t = 23 min (b)

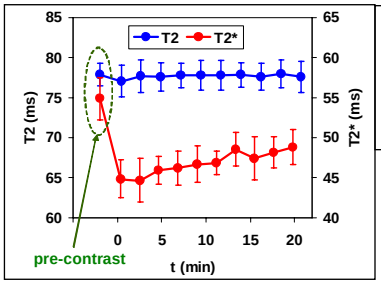

Fig. 4 Time-courses of gray matter T2 and (left axis) T2* (right axis)

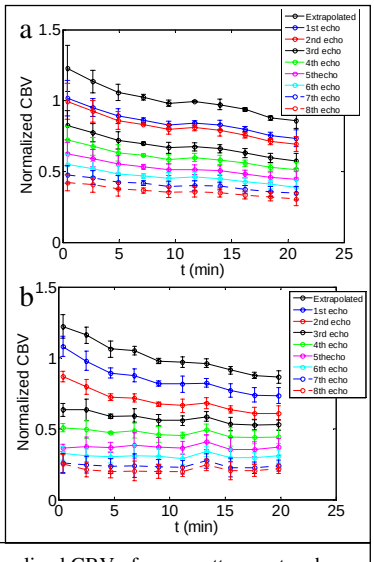

Fig. 3 Normalized CBV of gray matter w.r.t. echo times and post-injection times for SE (a) and GE

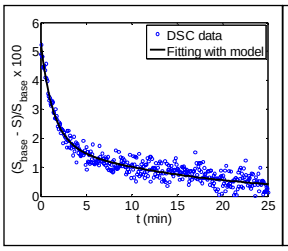

Fig. 5 DSC data, S, normalized by baseline, S_{base}, during 25 min post-injection times reflecting the concentration change of contrast agent

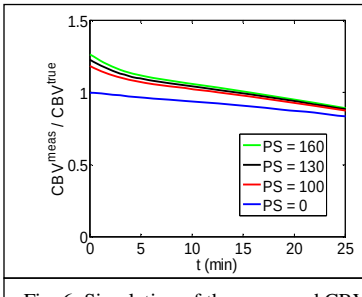

Fig. 6 Simulation of the measured CBV. PS is in ml water/100 ml brain /min