Dynamic Measurement of Functional Changes in Venous Cerebral Blood Volume at 3 T

J. J. Chen[1], and G. B. Pike[1]
[1]Montreal Neurological Institute, Montreal, Quebec, Canada

Introduction

While the cerebral blood volume (CBV) component of the BOLD signal depends primarily upon venous CBV (CBV_v), non-invasive MR techniques for continuous monitoring of CBV_v changes have been scarce. The venous refocusing for volume estimation (VERVE) technique exploits blood's unique spin-spin relaxation properties as a function of the CPMG refocusing interval (τ_{180}) and oxygen saturation in order to isolate venous CBV change, and was demonstrated in human subjects at 1.5 T [1]. Since the underlying principles of VERVE are field-dependent, we sought to establish the feasibility and validity of VERVE at high field, as well as to optimize its implementation. We demonstrate here the use of VERVE to obtain CBV_v measurements at 3T, present simultaneous CBF and CBV_v data, and compare our findings to predictions based on Grubb's power-law [2].

Methods

First, human whole blood relaxometry measurements (presented in another abstract) were performed to validate and optimize the VERVE sequence at 3T. For this purpose, whole-brain cortical grey matter (GM) relaxometry was also performed (at 3T) on 5 healthy adult subjects. Optimization of VERVE parameters was performed based on simulations and the relaxometry data. Following this, CBF and CBV_v were measured in 4 healthy adult subjects on a Siemens Trio 3T system using a QUIPSS II-based PASL [3] and the VERVE method [1], respectively. The common parameters were: FOV=256mm, matrix=64x64, slice-thickness=5mm, TR = 3500ms. The PASL parameters were: TI=1300ms, TE=23ms, labeling thickness=100mm, labeling gap=5mm. In the VERVE implementation, T1 preparation for CSF suppression was applied at TI=1100ms. Also, static field (B0) and RF-field (B1) inhomogeneities were minimized using composite $90°_x$-$180°_y$-$90°_x$ pulses and MLEV phase cycling in the refocusing train, with RF chopping between excitations. An EPI readout was employed to minimize signal decay, with BW=752Hz/voxel. The optimized VERVE refocusing parameters are presented below. Visual activation was induced using a radial yellow/blue checkerboard at full contrast with 8 Hz contrast reversal, with a uniform grey field as baseline, in 5 repetitions of 35s/140s/105s off/on/off blocks. A 3D T1-weighted scan served as anatomical reference. The visual activation region-of-interest (ROI) was delineated for each subject by thresholding the CBF and CBV_v *t*-maps at $p<0.05$ (corrected for multiple comparisons). The overlap between CBF- and CBV_v-based visual cortex ROIs was used to calculate average steady-state ΔCBF(%) and ΔCBV_v(%). Finally, α was estimated from $rCBV_v=rCBF^{\alpha}$, through non-linear least-square fitting ($rCBV_v=1+\Delta CBV_v$, $rCBF=1+\Delta CBF$).

Results

Whole-brain cortical GM relaxometry at 3T showed a 5.1% T2 decrease (5.3±3.6ms) for τ_{180} increasing from 4 ms to 24 ms. This minimal T2 dependence on τ_{180} at 3T is attributable to the small content of partially deoxygenated blood in GM. On the other hand, human whole blood relaxometry demonstrated that the dependence of T2 on τ_{180} and Y in partially-oxygenated blood was enhanced at 3T, thus establishing VERVE as a technique for isolation of venous blood at high field. The optimal VERVE refocusing train parameters were obtained by maximizing the contrast between activation and baseline venous blood while maintaining the signal-to-noise ratio and minimizing the intravascular spin-echo BOLD effect [1]. The resulting implementation employs 64 fast-refocusing nonselective RF pulses spaced by τ_{180}=3.02ms and 8 slow-refocusing pulses spaced by τ_{180}=30ms, and TE =196 ms. The term ΔVERVE is defined as the normalized difference between ΔS during activation and baseline, where ΔS is the signal difference between the fast and slow refocusing regimes [1]. Sample CBF and CBV_v *t*-maps following visual stimulation are shown in Fig. 1. Based on simulations using a multi-compartmental voxel model [1], we derived a linear approximation between ΔVERVE and ΔCBV_v at 3T (r^2=0.95), accounting for the IV SE BOLD effect. The group-average ΔCBF and ΔCBV_v time courses are shown in Fig. 2. In the steady-state, the average ΔCBF was 120.9%±30.6%, and the average ΔCBV_v was 18.4%±7.9%. Using these values, α was estimated to be 0.21±0.09 from the fits to Grubb's relationship.

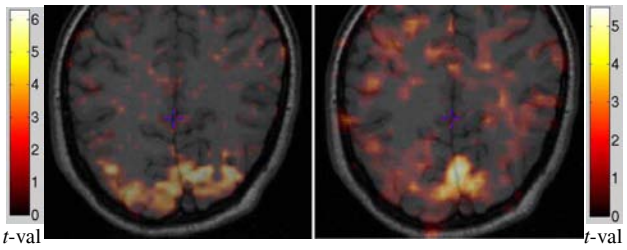

Figure 1. CBF (left) and VERVE vCBV (right) *t*-stat maps from one subject overlaid with the T1-weighted anatomical scan reveals visual cortex activation.

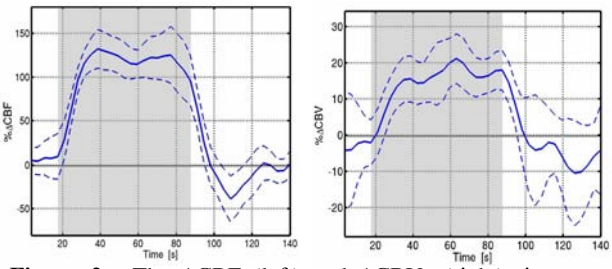

Figure 2. The ΔCBF (left) and ΔCBV_v (right) time courses (mean: solid, standard error: dashed) are averages across all subjects and voxels with $p<0.05$ (shaded region = stimulus-on period). A Hanning filter with FWHM=12s was applied.

Conclusion

The VERVE sequence has been shown to benefit from enhanced blood T2 dependence on Y and τ_{180} at 3T, and has provided robust activation maps. The 3T VERVE ΔCBV_v measurements are in excellent agreement with 1.5T measurements [1] and with animal data from Lee *et al.* [4]. The power-law coefficient (α) estimated from these initial results (α=0.21) is lower than the widely-adopted 0.38, originally measured by Grubb *et al.* in anesthetized monkeys using $H_2{}^{15}O$ PET [2]. Our observations echo those by Lee *et al.* [4] from rats using perfluorocarbons, and might be explained by exclusive venous ΔCBV contribution, which was estimated to make up 62% of the total CBV change [5]. These results can have important consequences for the accurate modeling of the BOLD signal, which is modulated primarily by venous blood oxygenation changes. To further improve the VERVE technique at 3T, EPI can be replaced with HASTE to minimize T2* weighting incurred during readout.

[1] Stefanovic *et al.* Magn Reson Med 2005;53:339-41; [2] Grubb *et al.* Stroke, 1974 :5 :630-9; [3] Warnking *et al.* Magn Reson Med 2004;52 :1190-9; [4] Lee *et al.* Magn Reson Med 2001;45:791-800; [5] Mandeville *et al.* Magn Reson Med 1998:39:615-24.