Determination of CBF and CBV using Short and Long TR Vascular Space Occupancy (VASO)-MRI

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Introduction. Quantification of cerebral blood volume (CBV; ml/ml) and blood flow (CBF; ml/100g/min) requires knowledge of an arterial input function (AIF) or post-labeling delay time, which can often be only approximated. Recently, it was shown that vascular space occupancy (VASO) MRI (1), an approach to obtain CBV-weighted images by nulling intravascular blood water, is proportional to CBV at long TR, and to both CBF and CBV at short TR (2). This is due to an arterial spin labeling effect through the use of a nonselective inversion pulse for blood nulling (2). As all blood is labeled by this pulse, the CBF effect has an instantaneous AIF. Here, we investigate the possibility of extracting CBF and CBV from short and long TR VASO experiments using a brief breath hold paradigm.

Methods. *Experiment.* Gradient-echo VASO-fMRI was performed on healthy volunteers (n=5) at 3T for TR/TI=2/0.711s and TR/TI=5/1.054s. A paradigm with 60s normal breathing, 4s exhale, and 14s breath hold was repeated three times. Signal changes (ΔS/S) in voxels meeting activation criteria (cc<-0.15, cluster size≥3) were calculated. Experiments were repeated one month later to assess reproducibility. Other parameters: FOV=240mm, matrix=80x80, slice thickness=3mm, TE=15ms. *Fitting*. The model of Donahue et al. (2) was fit to ΔS/S at TR=2s and TR=5s using constrained nonlinear optimization. Assuming only gray matter (GM) signal changes between rest and activation, ΔS/S, in terms of MR signal S and volume fractions X, may be written,

$$\frac{\Delta S_{Total}}{S_{Total}^{rest}} = \frac{\left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{act}\right) - \left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{rest}\right)}{\left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{rest}\right)} \quad [1]$$

for $S_{CSF} \sim C_{CSF} \cdot M_{CSF}(TR,TI) \cdot e^{-TE/T_{2,CSF}^{*}}$ [2] and $S_{GM} \sim (C_{GM} - CBV_{GM} \cdot C_b) \cdot M_{GM}(TR,TI,CBF) \cdot e^{-TE/T_{2\cdot GM}^{*}}$ [3]

where C is water density, $M_{CSF}(TR,TI)$ is steady-state CSF water magnetization and $M_{GM}(TR,TI,CBF)$ is the CBF-dependent steady-state GM magnetization. Resting CBF and CBV (CBFres, CBVres), breath hold CBF and CBV (CBFact, CBVact) and X_{CSF} all influence ΔS/S in VASO experiments (2). A measured average X_{CSF} = 0.1 was used (2) and fitting possibilities were explored using different combinations of CBF and CBV as unknowns. Fitting was considered for ΔS/S determined in three ways. First, averaged over all subjects. Second, averaged over all voxels within a subject. Third, on a voxel-by-voxel basis for each subject.

Results. Larger ΔS/S was found at TR=2s versus TR=5s in all subjects, in-line with the expected CBF contribution at short TR (Fig. 1). In addition, mean ΔS/S (n=5) showed excellent reproducibility one month removed: First scan, ΔS/S=-0.026±0.003 (TR=2s); ΔS/S=-0.014±0.001 (TR=5s). Second scan, ΔS/S=-0.026±0.005 (TR=2s); ΔS/S=-0.014±0.001 (TR=5s). In all subjects, 3/4 hemodynamic parameters could be uniquely determined if the Grubb relationship (3), here with α=0.5 (4), was applied between CBF and CBV (Fig. 2). Table 1 lists the fit results obtained for different CBFres=45-65 ml/100g/min (5) or CBVres=0.045-0.055 (6), calculated from individual subject ΔS/S. Table values are consistent with fit results found from subject-averaged ΔS/S: CBFres=55 ml/100g/min (held constant) CBFact=76.5, CBVres=0.038, CBVact=0.045. When fitting was performed on a voxel-by-voxel basis, 60.8%±5.3% voxels yielded fit convergences: CBFres=55 ml/100g/min (held constant), CBFact=82.1±4.9, CBVres=0.058±0.01, CBVact=0.065±0.01.

Discussion. CBF and CBV can be uniquely determined from a combined experiment with short and long TR VASO data. While experimental reproducibility is excellent, several factors influence fit results. First, fitting requires either CBFres or CBVres to be assumed (or measured) and the Grubb relationship to be applicable. In regions where both parameters may vary independently or where vascular compliance is affected, this Grubb assumption may not hold. Second, at short TR where CBF, inflow, and lower SNR contribute (2), ΔS/S varies more noticeably between breath hold periods (Fig. 1). This variation should be considered when interpreting fit results: When CBFres is held constant, there is a broad range of CBV within error (Fig. 2); when CBVres is held constant, there is a broad range of CBF within error. Third, if X_{CSF} is overestimated, CBV will be underestimated (and vice versa). From this study and others, mean X_{CSF}~0.1 at the current resolution, but will vary with location. Fourth, unique CBF and CBV values can be obtained when fitting to averaged ΔS/S or single-subject ΔS/S. However, small fluctuations in ΔS/S (<0.5%) will significantly influence CBF and CBV, so care must be taken in ensuring proper task performance. Finally, only 60.8% of individual voxels gave fit convergences. We tentatively attribute this to large variations in partial volume contributions with CSF between voxels, which can be alleviated in the future by determining X_{CSF} on a voxel-by-voxel basis. Thus, we showed that it is possible to quantify CBF and CBV with instantaneous AIF using multi-TR VASO-fMRI, however care should be taken in interpreting CBF and CBV values.

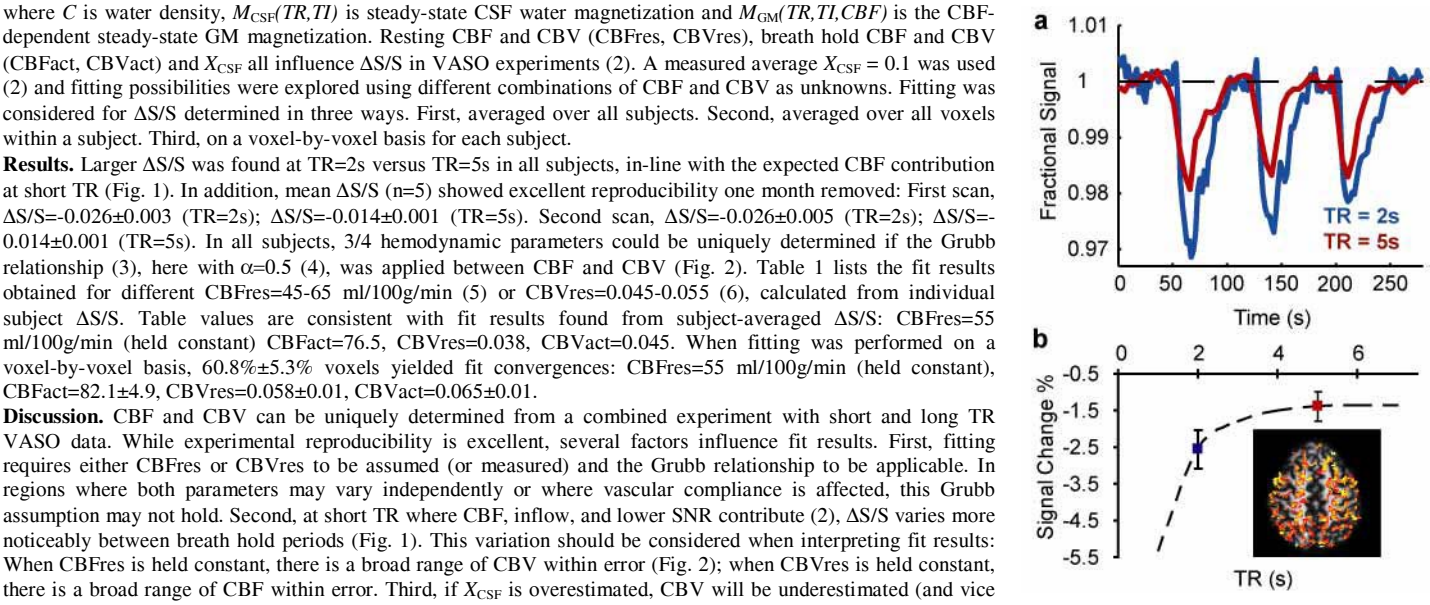

Fig. 1. TR=2s and TR=5s time courses averaged over all subjects (a) with fitting to ΔS/S and example of TR=5s activation map (b).

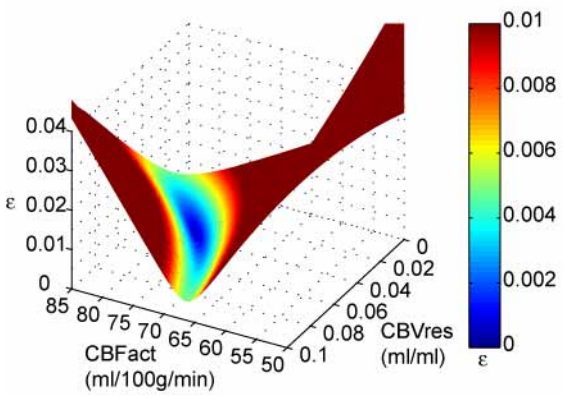

Fig. 2. Surface plot of CBFact vs. CBVres assuming CBFres=55 ml/100g/min and X_{CSF} =0.1, color-mapped according to magnitude of residuals ε. A unique minima at CBVres=0.038 and CBFact=77 ml/100g/min (Grubb-calculated CBVact=0.045 ml/ml) is apparent.

CBFres*	CBFact	CBVres	CBVact
45	67±3	0.033±0.004	0.040±0.005
55	77±3	0.040±0.006	0.047±0.006
65	86±3	0.047±0.006	0.053±0.007

CBFres	CBFact	CBVres*	CBVact
74±17	95±19	0.045	0.052±0.001
84±14	105±16	0.050	0.056±0.001
90±16	111±17	0.055	0.061±0.001

Table 1. Fit results assuming constant CBFres (above; ml/100g/min) or constant CBVres (below; ml/ml). Error is SEM over five subjects. * denotes held constant.

References. 1. Lu et al. MRM. 2003Aug;50(2):263-74. **2.** Donahue et al. MRM. 2006 Oct 30; [Epub]. **3.** Grubb et al. *Stroke* 1974;5:630-639. **4.** van Zijl et al. Nat Med. 1998Feb;4(2):159-67. **5.** Donahue et al. NMR Biomed.2006 Aug 31; [Epub]. **6.** Lu et al. JMRI. 2005Jul;22(1):13-22. Funding: NCRR RR15241, NIBIB EB004130, Philips Medical systems