Simultaneous Measurements of CBV and CBF Changes using VASO-FAIR

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Introduction

Most methods relating BOLD changes to quantitative physiological parameters, such as metabolic rate of oxygen (CMRO2) or oxygen extraction fraction (OEF) require knowledge of the quantitative relationship between cerebral blood flow (CBF) and blood volume (CBV). Conventionally, the empirical Grubb equation is used ($CBV = \beta CBF^{\alpha}$ with α=0.38, β=0.8) [1], based on experimental data from monkey experiments. Recently, the exponential factor α has been challenged, and van Zijl et al. [2] found that Grubb's data in the physiological range can also be fitted well using a simple cylindrical model for blood vessels (α=0.5), resulting in β=0.5 and a correlation coefficient (r^2) better than the original values. Thus, both values can be used within experimental errors. In this work, we propose a new sequence to simultaneously measure CBF and CBV changes and apply it to a graded visual activation experiment to evaluate the Grubb equation. This sequence is based on the flow-alternating inversion-recovery (FAIR) sequence [3], and its timing has been optimized to acquire all images at the zero-crossing of the blood signal, allowing therefore to get vascular space occupancy (VASO) [4] related signal in the control acquisitions.

Methods

All experiments were performed on a Philips Intera 3.0T system (Best, the Netherlands), using body coil transmission and six-channel head coil reception. The activation paradigm used a flashing black-white checkerboard, and six different conditions, flashing at 4Hz or 8Hz, with 33% 66% and 100% contrast (15° visual angle). The paradigm lasted 4'40'', with three 40' activation periods interleaved with four 40' resting state. Informed written consent was obtained in each of the n=6 volunteers, and the study was approved by local ethical committee. The VASO-FAIR sequence used: EPI, TR = 4s, TI = 1s (based, on T_{1b}=1680ms at Hct=0.38 [5]), TE = 5.6ms, FA=90°, FOV=24cm, slice thickness = 5mm, Matrix=80 (reconstructed=128), SENSE factor 2, halfscan (60%), adiabatic (hyper-secant) inversion pulse. A single axially angulated slice was positioned parallel to the calcarine fissure. All data from the 6 experiments were processed using in-house IDL-based software. The processing consisted of motion-correction using AIR [6], 8mm FWHM Gaussian smoothing, activation detection based on T-test between resting state and all activated state of the CBF maps (T>3.5, cluster>3, p<.0001). The time courses from ROIs including all actived voxels were gathered, and baseline CBF, average ΔCBF and ΔCBV changes were calculated according to Calamante [7] and the VASO equations [4] with blood and water densities assumed equal:

$$CBF = \left(\frac{2\alpha_0}{\lambda} \frac{M_0}{\Delta M} \left(\frac{e^{-TI \cdot R_{1app}} - e^{-TI \cdot R_{1b}}}{R_{1b} - R_{1app}} \right) \right)^{-1}, \quad \frac{\Delta CBF}{CBF} = \frac{\Delta S_{FAIR}}{S_{FAIR}} \quad \text{and} \quad \frac{\Delta CBV}{CBV} = -\frac{\Delta S_{VASO}}{S_{VASO}} \left(\frac{1-\xi^{rest}}{\xi^{rest}} \right)$$

with α_0=1, λ=0.9ml/g, $R_{1app}=1/T_{1app}=0.91s^{-1}$ (corresponding to T_{1app}=1.1s) $R_{1b}=1/T_{1b}=0.59s^{-1}$ (corresponding to T_{1b}=1.68s) and ξ^{rest} = resting state vascular space occupancy (4), which equals the microvascular blood volume fraction (ml blood/ml parenchyma). In order to evaluate Grubb's equation, the baseline CBV was calculated according to $CBV = \beta CBF^{\alpha}$, and was therefore not fixed. A non-linear fit for both α and β was then performed under the condition that the mean baseline CBV was equal to 4.37 ml/100g tissue (equivalent to ξ^{res} = 4.59%) [2]. Such a condition was necessary to avoid the fit to diverge.

Results and Discussion

Fig. 1 shows positive activated pixels overlaid on a representative VASO image for better delineation of the anatomy, as well as a native FAIR image. Please note that some large vessels are still visible, due to the rather short inversion time used in our experiment necessary to achieve blood nulling. In all volunteers the activated area encompassed mainly the primary visual cortex. The mean baseline CBF in the activated pixels was 66 ± 14 ml/min/100g. Fig. 2 shows CBV vs. CBF, for each individual condition in all volunteers. One condition in one volunteer was discarded due to lack of attention from the volunteer. The best fit gave the values α = 0.47 and β = 0.60 (r^2 = 0.89). Furthermore, by refitting the data using β=0.5, one get α = 0.51 (r^2 = 0.89) with a calculated mean baseline CBV = 4.21ml/100g ≡ 4.42%. These results would suggest that the relationship between CBV and CBF follows the basic fluid dynamics principles when one consider cylindrical tubes of constant length. It would therefore be in line with most neurophysiological studies [8] excluding any capillary recruitment upon brain activation.

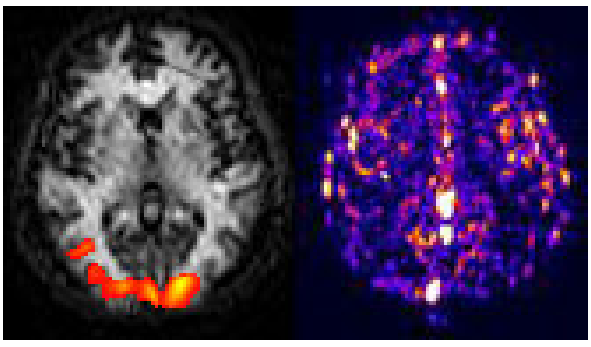

Figure 1: Left: Activated area overlaid on a native VASO image for anatomical reference (T > 3.5, p < 0.001). Right: The corresponding FAIR image. Due to the short inversion time (1sec), some large vessels are visible. They are however not included in the activated area (e.g. sagittal sinus)

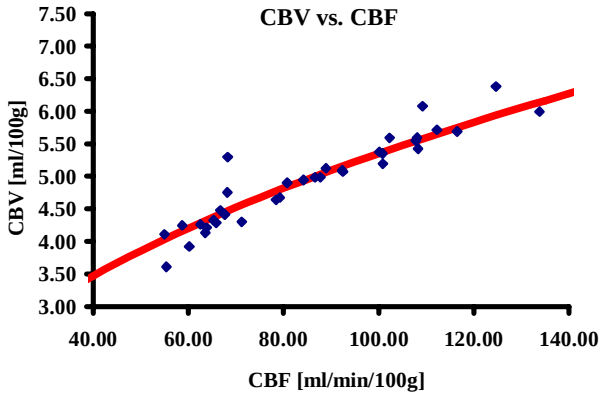

Figure 2: Plot of the absolute blood volume changes in function of the absolute cerebral blood flow changes upon activation for each condition (N=6) in each volunteer (n=6). The theoretical curve is $CBV = 0.60 \cdot CBF^{0.47}$

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