Quantification of Cerebral Blood Volume during Brain Activation with Grey Matter Nulled fMRI

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Introduction

MR signal change measured by grey matter nulled (GMN) fMRI [1] is affected by partial volume effect of cerebrospinal fluid (CSF), causing errors in estimation of absolute cerebral blood volume (CBV). In this study, we present a method to quantify CBV both at baseline and during activation by assessing CSF fraction in a voxel using GMN fMRI data acquired with multiple TRs. These data were fitted into a tissue model comprising of multiple parenchymal compartments to determine absolute CBV in the brain.

Method and Material

The MR signal from a typical voxel consisting of blood, tissue and CSF can be expressed by:

$$S = X_b S_b + X_t S_t + X_c S_c = (1-X_c)CBV \cdot C_b \cdot M_b(TR,TI)\cdot e^{-TE/T^*_{2,b}} + (1-X_c)(C_{par} - CBV \cdot C_b)\cdot M_t(TR,TI)\cdot e^{-TE/T^*_{2,t}} + X_c C_{CSF}\cdot M_{CSF}(TR,TI)\cdot e^{-TE/T^*_{2,CSF}} \quad [1]$$

where S_b, S_t and S_c are signals from the blood, pure tissue and CSF respectively, X_b, X_t and X_c are the corresponding component fractions that satisfy $X_b + X_t + X_c = 1$, C_b, C_{par} and C_{CSF} are the water proton densities in blood, parenchyma and CSF respectively, M_b, M_t and M_{CSF} are the longitudinal magnetisation of blood, pure tissue and CSF, respectively, and CBV is the fraction of blood volume relative to the parenchymal volume in unit of *ml blood/100 ml parenchyma*. Assuming that the tissue consists of pure grey matter (GM), the MR signal after nulling the GM signal can be simplified to

$$S = (1-X_c)CBV \cdot C_b \cdot M_b(TR,TI)\cdot e^{-TE/T^*_{2,b}} + X_c C_{CSF}\cdot M_{CSF}(TR,TI)\cdot e^{-TE/T^*_{2,CSF}} \quad [2]$$

Considering that there is no signal change from CSF during brain activation because of absence of perfusion in CSF, the relative signal change can be expressed by

$$P = \frac{\Delta S}{S} = \frac{(1-X_c)\cdot C_b \cdot M_b(TR,TI)\cdot\left(CBV_{act}\cdot e^{-TE/T^{*,act}_{2,b}} - CBV_{rest}\cdot e^{-TE/T^{*,rest}_{2,b}}\right)}{(1-X_c)CBV_{rest}\cdot C_b \cdot M_b(TR,TI)\cdot e^{-TE/T^{*,rest}_{2,b}} + X_c \cdot C_{CSF}\cdot M_{CSF}(TR,TI)\cdot e^{-TE/T^{*,rest}_{2,CSF}}} \quad [3]$$

where $M_b(TR, TI)$ and $M_{CSF}(TR, TI)$ are expressed by

$$M_b = M_0\left(1-2\cdot e^{-TI/T_{1,b}} + e^{-TR/T_{1,b}}\right) \quad [4]$$

and

$$M_{CSF} = M_0\left(1-2\cdot e^{-TI/T_{1,CSF}} + e^{-TR/T_{1,CSF}}\right) \quad [5]$$

In Eq.[3], $C_b = 0.87$ [2], $C_{CSF} = 1$ [2], $T_{1,b} = 1627$ ms at 3T [3] and $T_{1,CSF} = 3817$ ms at 3T [4]. $T_{2,b}$* at baseline and activation at 3T can be determined by [Ref. 5]

$$1/T^*_{2,b} = 18.82 + 188.28\times(1-Y_b)^2 \quad [6]$$

where Y_b is 0.61 and 0.796 at baseline and during activation, respectively [5]. The respective $T_{2,b}$* values for baseline and activation states are 21.1 and 37.5 ms. In Eq.[3], only three parameters, CSF fraction (X_c) and CBV at baseline and activation, are unknown. We use the least square fitting approach to determine these parameters. Specifically, we minimise

$$E(X_c, CBV_{rest}, CBV_{act}) = \sum_{TR}\left[Z_{TR} - P_{TR}(X_c, CBV_{rest}, CBV_{act})\right]^2 \quad [7]$$

by fitting the suitable parameters from the measured data Z acquired at variable TR. Note that Eq.[3] depends on TR only because TI also relies on TR. In the process of numerical fitting, we cover X_c from 0 to 0.3, baseline CBV from 5 to 6.5 ml/100 ml and activation CBV from 5 to 8 ml/100 ml with increment of 0.1 in each step of fitting.

Six healthy volunteers (two males, four females, age from 24 to 47 years) were recruited, each providing a signed informed consent before taking part in the fMRI study. GMN fMRI scans were acquired with a 3T MR system (Philips Medical Systems, Best, The Netherlands). The GMN fMRI data were collected at variable TRs ranging from 2000 to 5000 ms. A GM $T_1 = 1122$ ms at 3T [6] was adopted for the determination of appropriate TIs. TIs for TR = 2000, 3000, 4000 and 5000 ms are 603, 703, 746 and 765 ms, respectively. GMN fMRI scans were collected as follows: single shot GE-EPI, TR = 2000, 3000, 4000 and 5000 ms, FA = 90°, FOV = 224 mm, matrix = 112x112, SENSE factor = 2.5, slice thickness = 5 mm, TE = 10 ms, and TI = 603, 703, 746 and 765 ms. A single oblique axial slice covering the primary visual cortex was manually selected. Visual stimulation consisted of two cycles with B/W checkerboard (45 sec OFF and 45 sec ON) flashing at 8 Hz. GMN fMRI scans at each TR lasted for 225 s. Activation maps were obtained using FEAT (FMRI Expert Analysis Tool), part of FSL package (http://www.fmrib.ox.ac.uk/fsl). Routines under IDL 6.0 (Research Systems Inc., Boulder, CO) were used to determine fMRI signal change amplitudes for each TR and further to quantify CSF fraction in each voxel and CBV at baseline and activation using least squares fitting approach.

Results

Table 1 shows the results for CSF fraction and CBV obtained from six volunteers. The fraction of CSF in the activated brain region by GMN fMRI was 0.16 ± 0.03 (mean ± SD, n = 6) at spatial resolution of 2x2x5 mm^3. The average CBV in the visual cortex was 5.5 ± 0.04 ml/100 ml (mean ± SD, n = 6) at baseline and it increased to 7.8 ± 0.08 ml/100 ml during activation, giving an increase of 42 ± 2 % to visual stimulation.

Discussion and Conclusion

The grey matter CBV of 5.5 ± 0.04 ml/100 ml that we determined is consistent with previously reported 5.5 ± 0.2 ml/100 ml [7], but the CBV increase of 42 ± 2 % is higher than that obtained by a different MRI technique (32.4 ± 11.9%) [5]. We observed that the present value for CBV increase satisfies Grubb's empirical equation ($CBV_{act}/CBV_{rest} = (CBF_{act}/CBF_{rest})^{\alpha}$) [8] with $\alpha = 0.5$ considering the increase in CBF by 100%, which is within a typical range of CBF increase (60 - 150%) induced by visual stimulation [9]. Our study demonstrates that least squares fitting to multiple tissue compartment model using inputs from multiple TR measurements is feasible, providing physiologically acceptable results. In the multi-compartment tissue model, we consider no change in the blood magnetisation during brain activation based on a study in GMN fMRI showing that perfusion causes negligible change in blood magnetisation [1]. The method presented here offers a useful tool to quantifying the absolute CBV as well as the hemodynamic response in the brain. The method can be applied not only to fMRI studies but also potentially to clinical cases where CBV is desired.

Reference

[1] Shen Y, et al; Proc. ISMRM 2007; 27.
[2] Lu H, et al; NeuroImage 2002; 17:943-955.
[3] Lu H, et al; Magn Reson Med 2004; 52:679-682.
[4] Donahue MJ, et al; Proc. ISMRM 2006; 459.
[5] Gu H, et al; NeuroImage 2006; 30:377-387.
[6] Lu H, et al; J Magn Reson Imaging 2005; 22:13-22.
[7] Lu H, et al; Magn Reson Med 2005; 54:1403-1411.
[8] Grubb RL, et al; Stroke 1974; 5:630-639.
[9] Uludag K, et al; NeuroImage 2004; 23:148-155.

Table 1. Quantification of CSF fraction and CBV in healthy subjects.

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Mean±SD
Fraction of CSF	0.12	0.18	0.16	0.18	0.13	0.2	0.16±0.03
CBV_{rest} (ml/100 ml)	5.6	5.5	5.5	5.5	5.5	5.5	5.5±0.04
CBV_{act} (ml/100 ml)	7.8	7.9	7.9	7.9	7.7	7.8	7.8±0.08
$\Delta CBV/ CBV_{rest}$ (%)	39.3	43.6	43.6	43.6	40.0	41.8	42±2