A Novel Approach to Measure Absolute CBV using Gd-DTPA Contrast Agent

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INTRODUCTION: Quantification of absolute Cerebral Blood Volume (aCBV), defined as ml of blood/100 ml of brain tissue, is of great importance for many neurovascular diseases (1). A means to determine aCBV would allow direct comparison between different patient groups, longitudinal studies of the same patients, as well as comparison among different imaging modalities. However, accurate measurement of aCBV using MRI is not trivial. Dynamic bolus-tracking has been used to determine the rCBV and to provide information for clinical diagnosis. One can, in principle, also calculate aCBV (2) by estimating the Arterial Input Function (AIF). However, accurate estimation of the AIF is difficult and the AIF may be voxel-dependent. Here we propose a new approach that can measure aCBV with a simple theory and few assumptions. The technique uses the T_1-relaxation effect of the Gd-DTPA contrast agent, which is limited to the intravascular space and therefore reflects the blood volume.

METHODS Theory: The method is based on the fact that the T_1 of pre-contrast blood is known, and that the contrast agent injection significantly reduces blood T_1 but has no effect on the extravascular tissue T_1. The imaging protocol consists of two identical Vascular-Space-Occupancy (VASO) experiments performed before and after contrast agent injection. The VASO sequence is a non-slice-selective inversion recovery (IR) sequence, where the inversion time (TI) is chosen to null the blood signal (Fig. 1, red) (3). The non-selective inversion makes the signal insensitive to any flow-related effects. Therefore, the pre-contrast signal is given by:

$$S_{pre} = S_{tissue} + S_{blood} = A \cdot [(C_{par} - V \cdot C_B) \cdot (1 - 2 \cdot e^{-TI/T_{1,t}}) + 0] \quad (1)$$

where *A* is a constant, and is the amount of MR signal per unit volume of water proton; C_{par} is the water density of parenchyma (ml of water per ml of parenchyma); V is the aCBV in ml of blood per ml of parenchyma; C_B is the water density of blood; $T_{1,t}$ is the tissue T_1 value. Note that the blood term is 0 because of the optimal TI to null the blood. After injection, the post-contrast signal is given by:

$$S_{post} = S_{tissue} + S_{blood} = A \cdot [(C_{par} - V \cdot C_B) \cdot (1 - 2 \cdot e^{-TI/T_{1,t}}) + V \cdot C_B \cdot (1 - 2 \cdot e^{-TI/T_{1,b,post}})] \quad (2)$$

where $T_{1,b,post}$ is the blood T_1 value after contrast agent injection. Note that the first term in Eq 2, the tissue signal (Fig. 1, black), are the same as in Eq 1 because the contrast agent is restricted in the blood, whereas the second term, the blood signal, is non-zero because the contrast agent has significantly shortened the blood T_1 and the TI used does not null the blood signal any longer (Fig. 1, blue). Therefore, the signal difference between post-contrast and pre-contrast is given by: $S_\Delta = S_{post} - S_{pre} = A \cdot V \cdot C_B \cdot (1 - 2 \cdot e^{-TI/T_{1,b,post}})$

When $T_{1,b,post}$ is small (<200ms) (4), the above equation becomes: $S_\Delta = A \cdot V \cdot C_B$. Then aCBV can be computed from: $V = \frac{S_\Delta}{A \cdot C_B}$

where A can be taken as the signal intensity in a pure CSF voxel from a long TR short TE scan and C_B is a well-known physical parameter, 0.87ml of water/ml of blood (5). Alternatively, $A \cdot C_B$ can be obtained from the sagittal sinus in the post-contrast image. We compared these two referencing methods in one subject, finding similar values ($A \cdot C_B$=2002x0.87=1742 using CSF as reference; $A \cdot C_B$=1727 using post-contrast sagittal sinus; error<1%).

Experiment: Experiments were performed on a 1.5T MR system (Siemens Medical Solutions). Six tumor patients, who were scheduled for a clinical scan, gave written consent to participate in the study. The study was focused on regions of normal brain. The post-contrast scan was performed 90s after the injection, to allow the contrast agent to reach a steady state. The scan parameters were: TR=6000s, TI=920ms, FOV=230mm, matrix=128x128, TE=6ms, 10 slices, slice thickness 5mm, scan duration 2 min 12 sec. When performing subtraction between pre and post-contrast images, it is important to identify voxels in which the sign of the magnetization has changed after injection, i.e. changing from negative to positive. In these voxels, a summation should be performed for the pre and post magnitude signals. The identification of these voxels was achieved by comparing the pre and post phase images (Fig. 2a, middle column). When a 180º phase change was detected, the algorithm will perform summation instead of subtraction.

RESULTS and DISCUSSION: Fig. 2a shows an example of the VASO images and the resulting aCBV map. It can be seen that the pre and post-contrast images show clear difference, which is most visible in large vessels regions (arrow) corresponding to high aCBV. The phase images are crucial for accurate measurement of aCBV, especially in regions with significant CSF partial volume. Fig. 2b shows a 10-slice aCBV map in one patient, who had a tumor in the lower right hemisphere. Table 1 lists the averaged aCBV values in the normal brain regions of the patients. The values are in excellent agreement with values in the literature (1). Compared to conventional dynamic bolus-tracking method, the approach proposed here does not require the knowledge of AIF and is not dependent on the relationship between contrast agent concentration and R_2* change, which is often different for small vessels and large vessels. Furthermore, it does not employ dynamic imaging, thereby avoiding EPI-related distortion or signal loss in some brain regions. We believe that this method can provide accurate and precise estimation of absolute CBV, and is valuable for clinical applications as well as animal studies using long half-life contrast agents.

REFERENCES: 1) Tomita, in "Cerebral hyperemia and ischemia: from the standpoint of cerebral blood volume", (1988); 2) Ostergaard MRM 36: 726 (1996); 3) Lu MRM 50: 263 (2003); 4) Wendland, MRM 32: 319 (1994); 5) Herscovitch JCBFM 5: 65 (1985)

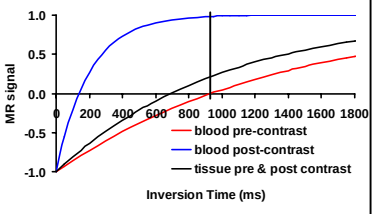

Fig. 1: Simulation of the signals (as a function of TI) before and after contrast agent injection for blood and tissue. The blood curve changes dramatically before and after the injection, whereas the tissue curve does not change, because the contrast agent is located only in the intravascular space.

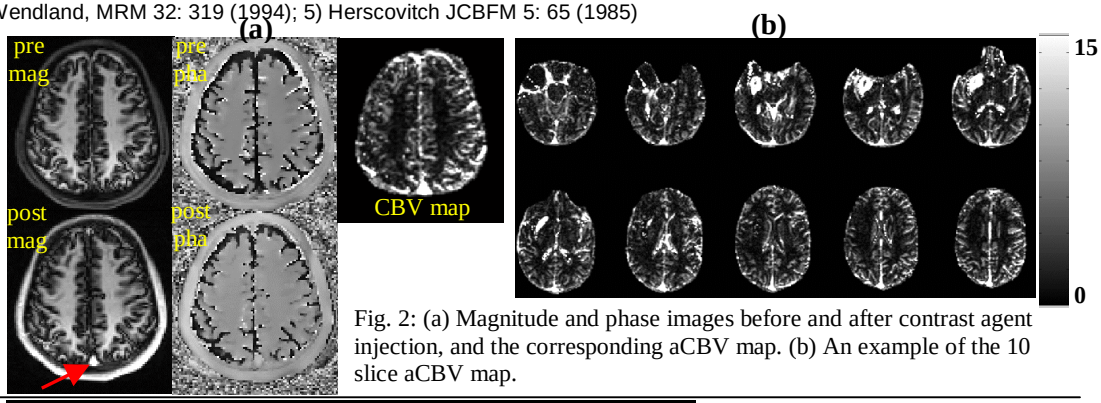

Fig. 2: (a) Magnitude and phase images before and after contrast agent injection, and the corresponding aCBV map. (b) An example of the 10 slice aCBV map.

	gray matter	white matter	thalamus	basal ganglia
aCBV (ml/100ml of brain)	5.4±0.6	1.7±0.1	3.5±0.4	4.8±0.5

Table 1: Absolute CBV values in typical brain regions (mean±SEM, n=6).