Quantification of cerebral blood volume changes in response to a visual stimulus in humans

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INTRODUCTION

An infusion of a paramagnetic contrast agent (CA) has previously been used [1-3] to measure the fractional change in total cerebral blood plasma volume (CBV_{tot}) during a stimulus. A key limitation of this technique is an inability to measure these changes quantitatively. Quantitative maps of resting CBV_{tot} have long been produced [4] by bolus tracking methods. We propose to combine this technique with the fractional CBV_{tot} (ΔCBV_{tot}) method. The ΔCBV_{tot} method measures the change in BOLD signal intensity in response to a change in intravascular contrast agent concentration ([CA]). Previously the change in [CA] has been achieved by using a steady infusion of CA yielding an approximately linear increase in [CA] with time, but in this experiment we use a bolus injection of CA and rely on the excretion of the agent through the kidneys to provide an exponentially reducing [CA]. We have applied this technique at 3.0 T and 7.0 T.

THEORY

The change in the transverse relaxation rate (R_2^*) in the presence of a CA can be modelled [3] by Eq. [1] and [2]. The superscripts *act* and *rest* refer to the on and off periods of the stimulus paradigm. Blood plasma volume, *V*, is either arterial (*a*) or venous (*v*) and χ_{agent} is the susceptibility contribution of the CA. The R_2^* change on activation is indicated by Δ and the change due to the presence of a CA by δ. Assuming that vessels in a voxel are uniformly and randomly oriented, the relaxivity constants κ_v and κ_a are equal. If we combine these equations we find that their ratio is equivalent to ΔCBV_{tot} (Eq. [3]). Therefore the ratio of the gradients of plots of ΔR_2^{*act} and R_2^{*rest} versus CA concentration will yield a measure of ΔCBV_{tot}. Maps of CBV_{tot} were created by tracking the first pass of a bolus of CA. An arterial input function (AIF) was determined from a large arterial vessel. This time-course, along with those from the slices of interest, were converted to a concentration time-course using Eq.[4], where *k* is a proportionality constant. By integrating through time, from the start of the bolus injection to the beginning of the second pass, it is possible to calculate CBV_{tot} using Eq.[5], where ρ is the density of brain tissue (1.04g/ml).

$$\delta(\Delta R_2^{*act})_{agent} = (\kappa_v \Delta V_v + \kappa_a \Delta V_a)\chi_{agent} \quad (1)$$

$$\delta(R_2^{*rest})_{agent} = (\kappa_v V_v + \kappa_a V_a)\chi_{agent} \quad (2)$$

$$\Delta CBV_{tot} = \frac{\delta(\Delta R_2^{*act})_{agent}}{\delta(R_2^{*rest})_{agent}} = \frac{\Delta V_{tot}}{V_{tot}} \quad (3)$$

$$C_m(t) = \frac{k}{TE}\ln\left(\frac{S(t)}{S_0}\right) \quad (4)$$

$$CBV_{tot} = \frac{1}{\rho}\frac{\int C_m(t).dt}{\int AIF(t).dt} \quad (5)$$

METHOD

Imaging was performed on Phillips Achieva 3.0 T (1 subject) and 7.0 T (1 subject) systems. At 3.0 T multi-echo GE-EPI images (4 echoes) were acquired using an 8-channel SENSE coil with the following parameters; 64×64 matrix, 3×3mm in-plane resolution, 2.5mm slice, SENSE 2, TR=2.4s, TE/ΔTE=12.4/22.0 and 10 slices. Imaging at 7.0 T had the following differences; 16-channel SENSE coil, 3mm slice, TE/ΔTE=13.6/24.6, 4 slices, TR=1.2s,. The increased temporal resolution allowed the first pass bolus to be better characterised. Initially a functional localiser was performed to select the optimal slices through the visual cortex for the study. The slices were divided into two stacks, with one stack containing a single slice through the internal carotid arteries (ICA) and the other stack slices through the visual cortex as identified from the localizer. Each stimulus cycle consisted of 20s of red LED goggles flashing at 8Hz followed by 40s of darkness. The experimental paradigm comprised 4 cycles of the stimulus, a single dose bolus of ProHance was then given followed by another single dose 1 minute later. After a further minute 8 stimulus cycles were presented during the CA washout. This yielded measurements of the BOLD haemodynamic response at several different levels of CA concentration. Images were realigned, and statistical maps of BOLD activation produced, using the FEAT [5] tool within FSL. Further analysis to generate maps of CBV_{tot} and time-courses of ΔCBV_{tot} using Eq. [1]-[4] was performed in MATLAB. As a proof of concept only the first echo at each field strength was used in this analysis.

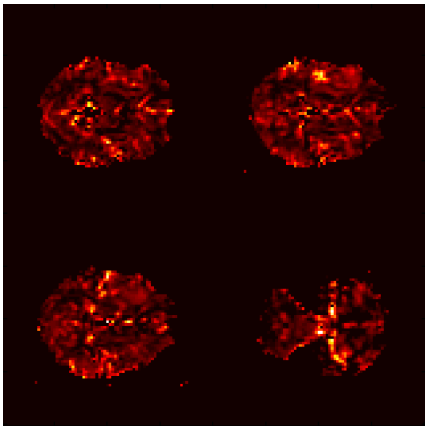

Fig. 1 – CBV_{tot} map acquired at 7.0 T. Colour scale 0 (black) → 97.9 ml/100g (white).

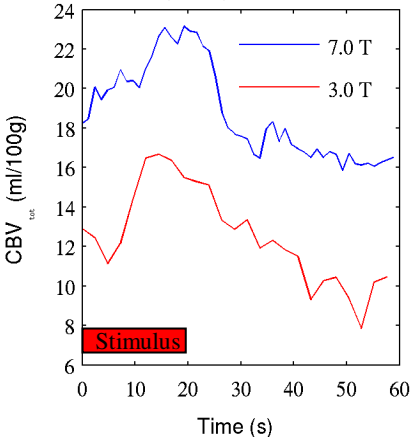

Fig. 2 – Quantitative measurements of ΔCBV_{tot} in response to a 20s visual stimulus at 3.0 T and 7.0 T.

RESULTS AND DISCUSSION

Figure 1 shows a map of resting CBV_{tot} acquired at 7.0 T. The map consists of three slices in the visual cortex, and a lower slice at the level of the ICA. This fourth slice allowed a pure arterial blood voxel to be obtained improving the determination of the AIF and hence the accuracy of the map. Figure 2 shows the result of combining CBV_{tot} and ΔCBV_{tot} data averaged over the activated region to produce a quantitative time-course of blood plasma volume change during a visual stimulus. The resting CBV_{tot} in the activated region was measured to be 11.7±1.9ml/100g tissue at 3.0 T and 17.4±1.1 ml/100g tissue at 7.0 T. These values are slightly higher than the grey matter CBV_{tot} values quoted by Rempp et al. [4]. However the region of interest in this study is likely to contain draining veins leading to these elevated values.

CONCLUSIONS

In this work we have shown that it is possible to produce high quality maps of resting total cerebral blood plasma volume at 7.0 T. We have also shown that it is possible to quantitatively measure changes in total cerebral blood plasma volume in response to a visual stimulus in humans using this bolus tracking method. This technique can be applied at ultra-high field, despite short T_2^* values at 7.0 T. This technique will allow the measurement of Grubb's constant when combined with ASL techniques measuring CBF. The relative contribution of arterial and venous blood volume to total blood volume change will also be considered by measuring arterial blood volume quantitatively [6].

REFERENCES

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