

# Measurement of Cerebral Blood Flow and Cerebral Blood Volume in Humans Using Washout of Hyperoxic Contrast

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## Introduction

Hyperoxic contrast-enhanced MRI, performed by increasing the inspired fraction of oxygen ( $FiO_2 > 0.21$ ), have been shown in numerous studies to produce positive contrast enhancement in  $T_2^*$ -weighted images based on the blood oxygenation-dependent (BOLD) effect [1],[2],[3]. It has been long thought that hyperoxia substantially alters the hemodynamics of the brain, confounding attempts to measure hemodynamic quantities with hyperoxic contrast. However, it has been recently shown [2] that cerebral blood flow (CBF) experiences only a small (<4%) reduction upon breathing low to moderate oxygen concentrations ( $FiO_2 \leq 0.5$ ) -- flow changes that are too low to be produce signal changes that can be detected by typical BOLD  $T_2^*$ -weighted EPI. Since hyperoxic contrast exhibits fast washout times [2], accurate measurements of dynamic parameters are feasible. Our group has recently shown substantial negative contrast enhancement in  $T_2^*$ -weighted images near arteries in the brain that we believe is due to excess dissolved paramagnetic molecular oxygen in the plasma (data is submitted in another abstract). This negative contrast enhancement provides the means to infer the relative excess oxygen content in the arteries feeding the brain and thereby measure an arterial input function. Bulte et al. [3] have recently presented a method of measuring cerebral blood volume (CBV) using hyperoxic contrast enhancement measured during steady-state. In this study, we hypothesize that accurate measurements of CBV and CBF can be made dynamically during the washout of hyperoxic contrast using indicator-dilution theory in a manner akin to traditional dynamic susceptibility contrast (DSC) measurements.

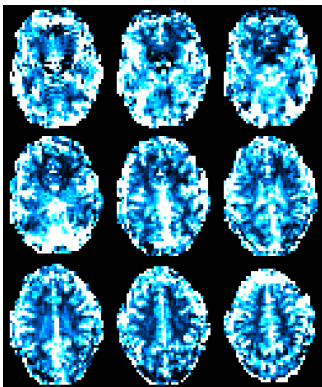
## Materials and Methods

A single male subject was imaged under a protocol approved by our Institutional Review Board. The subject first breathed medical air followed by 100% oxygen at 15L/min from nasal cannula (generally accepted to be less than  $FiO_2 < 0.6$ , due to the entrainment of room air) during three alternating epochs lasting approximately five minutes each. Images were acquired on Siemens Trio 3T using a vendor-supplied 8-channel receiver head coil. A product-standard EPI sequence was used with TE/TR: 34/4500ms, FOV: 256x256, 64 phase encodes, 24 slices at 6mm thickness (nominal resolution of 4x4x6mm). Sixty full volume acquisitions were acquired during each epoch. Prior to the final analysis, the images were brain-extracted, motion-corrected, high-pass filtered to remove signal drift, spatially-smoothed with a 4x4x4mm kernel using FSL Tools [4].

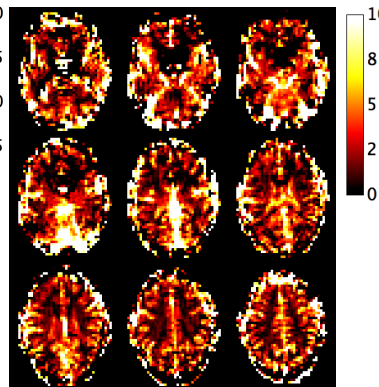
Our analysis assumed a linear relationship between concentration of paramagnetic contrast (whether this contrast is molecular oxygen (arteries) or deoxyhemoglobin (veins and capillaries)) and the change in  $R_2^*$  such that  $C(t) = k \ln(S(t)/S(0))/TE$ , where  $S(0)$  is the signal intensity after complete contrast washout and  $k$  is a correction constant. CBV and CBF measurements were made during the first minute (12 time points) of the washout of hyperoxic contrast. To convert arterial input function, which involves a negative contrast (molecular oxygen) to the positive contrast (deoxyhemoglobin) downstream, the time signal curve from the artery was demeaned, inverted, and scaled to the magnitude measured in a pure vein voxel. CBV was calculated according to **Equation 1** where  $\rho$  is the tissue density and  $h$  corrects for the fact that hematocrit is greater in large vessels. Relative CBF (relCBF) was calculated in the manner presented by Ostergaard, et al. [5], which involves solving for flow,  $F_i$ , in **Equation 2** by deconvolving the tissue concentration time curve with the arterial input function,  $R(t)$ , using truncated singular value decomposition. Approximate quantitative values of CBF were calculated by scaling final CBF values to the known constant value 22 mL/min per 100g tissue found in a white matter [5]. All calculations were performed using MATLAB (Mathworks, Inc.).

$$CBV = \frac{h}{\rho} \frac{\int_0^t C_{tissue}(t) dt}{\int_0^t C_{artery}(t) dt}$$

**Equation 1**



**Fig. 1.** relCBF with approximate CBF values in mL/min per 100g tissue



**Fig. 2.** CBV values in mL per 100g tissue

## Results

Fig. 1 and Fig. 2 show the values produced for CBF and CBV from the same nine slices using the approach described above. CBF values are displayed in mL/min per 100g tissue, and CBV values are mL per 100g.

## Discussion

Hyperoxia produces BOLD contrast in tissues, which is primarily associated with veins and end capillaries. Therefore, relCBF and CBV maps presented here are primarily sensitive to regions with a high density of veins and capillaries. Moreover, these measurements are somewhat confounded in and around regions with high arterial blood volume due to the negative contrast enhancement there (issue is explored in another submitted abstract). The values of CBF in gray and white matter reported here are similar to those widely reported in literature (60 and 20 mL/min per 100g, respectively). The values of CBV computed in this study are very close to those using similar method (Bulte, et al. 2007 JMRI). White matter regions are typically noisier than gray matter regions using in this approach since white matter has significantly less venous CBV and therefore less contrast than gray matter. Although this technique has drawbacks, it may present a viable alternative to dynamic susceptibility contrast imaging where the injection of an intravenous contrast agent is unsuitable. In summary, we have demonstrated that accurate whole-brain measurements of cerebral blood flow and volume can be performed using the washout of hyperoxic contrast.

## References

- [1] Losert, et al. *Magn. Reson. Med.* (2002); [2] Bulte, et al. *J. Cereb. Blood Flow Metab.* 2007; [3] Bulte, et al. *J. Magn. Reson. Imag.* (2007); [4] Smith SM, et al. *Neuroimage* (2004); [5] Ostergaard, et al. *Magn. Reson. Med.* (1996).