High Resolution Cerebral Blood Volume Mapping in Humans at 7T with Hyperoxic Contrast

D. T. Pilkinton[1], S. Gaddam[1], M. A. Elliott[1], and R. Reddy[1]
[1]Center for Magnetic Resonance and Optical Imaging, University of Pennsylvania, Philadelphia, PA, United States

Introduction

Increasing the inspired fraction of oxygen (FiO_2>0.21) has been shown to produce positive contrast enhancement in T_2^*-weighted images based on the blood oxygenation-dependent (BOLD) effect [1]. Recently, it has been shown that cerebral blood volume (CBV) can be accurately calculated by measuring signal changes in echo-planar images (EPI) at 3T during short epochs (<6min) of mild hyperoxia (0.5 FiO_2) [2]. Typically, images acquired in this fashion have low spatial resolution (approximately 4x4x6mm) because of the need for: (a) high contrast-to-noise ratio (CNR), since tissue signal changes are typically small, and (b) high temporal resolution to average the signal fluctuations inherent to heavily T_2^*-weighted EPI. Ultra-high field strengths (>7T) can enhance the CNR of this experiment due to the nonlinear increase in BOLD contrast with field strength, potentially allowing for significantly increased spatial resolution. However, performing a high-resolution CBV experiment using the EPI technique described above at 7T is difficult for a number of reasons. Geometric distortions and signal dropout in EPI due to B_0 inhomogeneity near air-tissue interfaces are substantial problems at 7T. Even more significantly, quantifying CBV with this method requires that the BOLD contrast be primarily intravascular. Since venous blood at 7T has a T_2^*<10ms, a short echo time (TE<9 ms) and readout length are required that are less than standard EPI sequences can produce even at high bandwidth and with partial-Fourier (PF) encoding. Furthermore, acquiring thin slices using a 2D approach is difficult to do due to slice profile imperfections. To address these problems, we hypothesized that high resolution (1x1x2mm) CBV maps can be produced robustly at 7T using a steady-state acquisition segmented 3D EPI with PF encoding in the phase direction.

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 a loose-fitting mask during five alternating epochs lasting approximately six minutes each. Images were acquired on Siemens Magnetom 7T using a vendor-supplied CP head coil. A product-standard segmented EPI sequence was used with a 3D slab-selective pulse with 16 slice encodes, 256 phase encodes with 11 segments and 6/8 PF factor, and TE/TR: 8.4/35ms, allowing a complete k-space acquisition every 15.5secs. Twenty-five volumes were acquired during each epoch. The field-of-view was 256x256x32mm, producing a nominal resolution of 1x1x2mm.

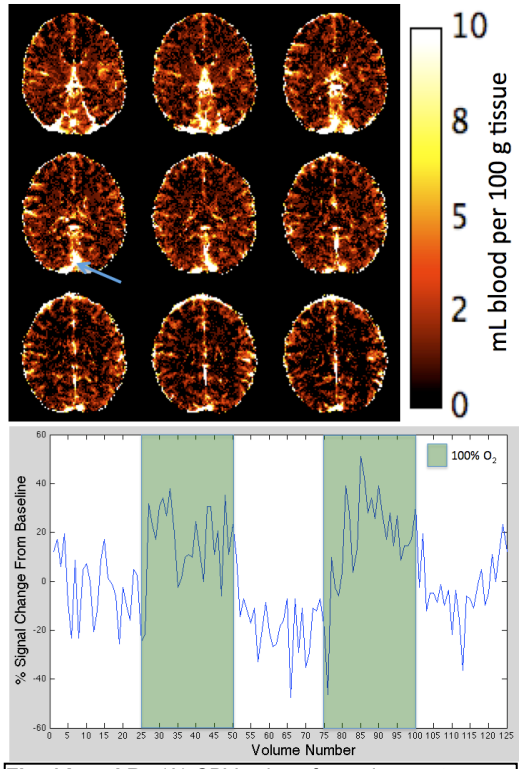

Fig. 1A and B. (A) CBV values from nine center partitions. (B) Signal time course versus volume number for sagittal sinus voxel (blue arrow)

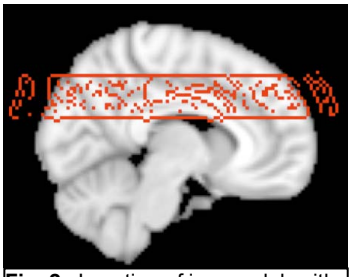

Fig. 2. Location of image slab with respect to standard space

Prior to the final analysis, the images were brain-extracted, motion-corrected, high-pass filtered to remove long-term signal drift, spatially-smoothed with a 2x2x2mm kernel, and linearly affine registered to the standard MNI brain atlas using FSL Tools [3]. Signal intensities changes between air and oxygen breathing were converted to CBV values according to **Equation 1** [2], which normalizes the tissue signal changes to those occurring in a pure vein voxel. $S_{tissue,0}$ and $S_{vein,0}$ represent the mean signal during air breathing while $S_{tissue,j}$ and $S_{vein,j}$ represent signal during the plateau period (first five volumes of each epoch were discarded) of oxygen breathing. The constants correct for tissue density (ρ=1.04g/mL) and for the fact that hematocrit (Hct) is greater in the large vessels (h=(1-Hct)/(1-r*Hct)). Hct was set equal to 0.48 based on a normal healthy male average, and r was set equal to 0.85 based on PET data [2].

$$CBV = \frac{h}{n\rho}\sum_{j=0}^{n}\frac{ln(\frac{S_{tissue}(j)}{S_{tissue,0}})}{ln(\frac{S_{vein}(j)}{S_{vein,0}})}$$

Equation 1

Results

Fig.1 shows the final values produced for CBV from the nine center slices from Equation 1 (in mL blood per 100g tissue). Slices at the ends of the slab suffered from aliasing artifacts and are not shown. **Fig. 1B** shows the voxel signal from tip of the blue arrow in **Fig. 1A**. The voxel was averaged along with several others in the sagittal sinus vein region to produce the pure vein voxel ratio. **Fig. 2** shows the result of the registration of the image slab to standard space; the red border shows the sagittal location of slab with respect to the atlas.

Discussion

The qualitative contrast enhancement (i.e. contrast primarily weighted towards veins and capillaries) and the quantitative values of CBV in this study are very close to those obtained by Bulte, et al [2]. The particularly high contrast associated with large veins indicate that the shorter TE is an appropriate modification for 7T. Furthermore, this acquisition approach would not work well at 3T, since longer T_2^* venous blood at 3T would result in less BOLD contrast, and the longer TE necessary to regain contrast would also increase TR, substantially reducing temporal resolution. The geometric distortions and signal dropout seen here are less than those typically seen in standard EPI at 7T, even when a good shim has been obtained. The high spatial resolution of this approach also benefits from reduced total voxel volume, which yields significantly less sensitivity to macroscopic field fluctuations caused by respiration and motion that are particularly problematic at 7T. In summary, we have presented an effective method of obtaining high resolution CBV mapping at 7T in agreement with published values.

References

[1] Losert, et al. *Magn. Reson. Med.* (2002); [2] Bulte, et al. *J. Magn. Reson. Imag.* (2007); [3] Smith SM, et al. *Neuroimage* (2004).