Quantitative BOLD: Separation of Effects from Blood Volume and Oxygen Extraction Fraction

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Introduction

Measurement of oxygen extraction fraction (OEF) is essential for understanding the baseline state of the normal human brain [1]. It is also crucial for understanding the diseases of the brain such as stroke and Alzheimer's disease [2, 3]. Knowledge of the OEF and cerebral deoxygenated blood volume (DBV) can provide important information on biophysical parameters defining blood oxygenation level dependent (BOLD) contrast in fMRI studies where the contributions from changes in DBV and OEF to BOLD signal are still under debate.

Previously proposed theoretical model [4] and experimental method [5] offer means to separate contributions from OEF and DBV into the BOLD signal. Preliminary results [6] confirmed a potential of this approach for *in vivo* applications. However, a number of issues should be resolved to make this method a robust tool for research and clinical applications. The purpose of this work is to incorporate into a BOLD signal model [4] a prior knowledge on the brain tissue composition.

Methods

Herein we assume that each voxel in the brain consists of brain tissue (white or gray matter), intravascular blood, and cerebrospinal fluid (CSF). We assume that only tissue and blood signals depend on blood oxygenation level. Accordingly, the free induction decay of MR signal from the brain tissue is described in terms of the BOLD model [4] $S_{tissue}(t) \approx exp\left(-R2_{tissue} \cdot t - DBV \cdot f_c\left(\delta\omega \cdot t\right)\right)$, where f_c is a function defining contribution of blood vessel network to the tissue MR signal decay [4], $\delta\omega = 4/3 \cdot \gamma \cdot \pi \cdot \Delta\chi_0 \cdot Hct \cdot OEF \cdot B_0$, B_0 is the external magnetic field, $\Delta\chi_0$ is the susceptibility difference between completely deoxygenated and completely oxygenated red blood cells (0.264 *ppm* [7]) and hematocrit ratio *Hct* of 0.34 is assumed for small vessels. The contribution of intravascular blood signal is described in terms of the theoretical model [8] as

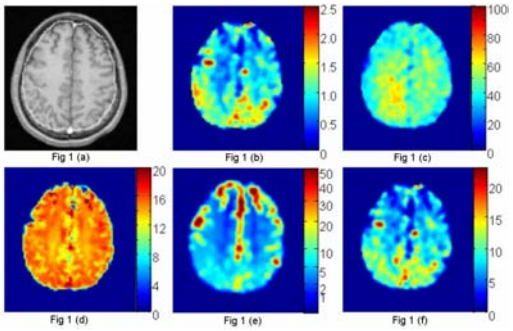
$$s_i(t) = \left[\pi/\left(3 \cdot \left|\delta\omega \cdot t\right|\right)\right]^{1/2} \exp\left(i \cdot \delta\omega \cdot t/2\right) \cdot \left[C\left(\left|3\delta\omega \cdot t/2\right|^{1/2}\right) - i \cdot sign(t) \cdot S\left(\left|3\delta\omega \cdot t/2\right|^{1/2}\right)\right],$$

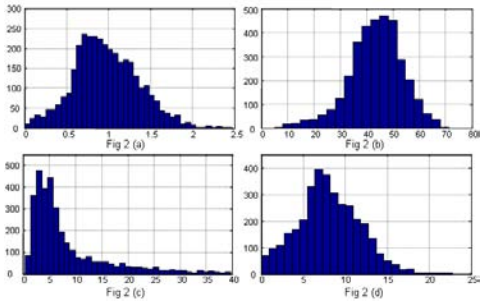
where $C(.)$ and $S(.)$ are Fresnel cosine and sine integral functions, respectively. The signal decay due to the macroscopic field inhomogeneities is quantified from the high resolution field map.

Three healthy volunteers were recruited for this study. All images were acquired on a Siemens 3.0 Tesla Allegra head scanner. MRI parameters for the double echo 3D GRE sequence to acquire high resolution field map are T_R =40 *msec*, TE = 3 and 13 *msec*, spatial resolution 1x1x2 mm^3. Gradient Echo Sampling of Spin Echo (GESSE) sequence [5] was used to acquire 21 gradient echoes with echo train spacing of 3.92 *msec*. Spin echo occurred at 4th gradient echo corresponding to 36.42 *msec*. Effective echo spacing is halved by shifting the acquisition window and read out gradient by half the echo spacing during alternated acquisitions. T_R is 1000 *msec*, image resolution is 2x2x7 mm^3, number of repetitions is eight. Model parameters (DBV, OEF, volume fractions, relaxation rates, etc) were determined by fitting theoretical model to experimental data using a multi-variable optimization procedure implemented in MatLab.

Results

The model fitting approach yields residue comparable to the background noise level of the image. Figure 1a is an example of the high resolution anatomy image. The brain area is manually segmented. Areas close to the brain surface are masked out due to the contamination from the fat signal at the brain skull. Figure 1b displays the deoxygenated blood volume fraction. The averaged value of DBV is 1.37±0.25% for gray matter and 0.67±0.11% for white matter. The OEF map shown in Fig. 1c is relatively uniform across the brain parenchyma with mean value of 43.5±11.5%. Figures 1d, 1e and 1f are maps of R_2 for brain tissue (13.9±3.0 sec^{-1}), CSF volume fraction and the deoxyhemoglobin concentration (8.1±3.7 μ*M*), respectively. High CSF volume fraction at the surface (>30%) clearly reflects brain anatomy. The averaged CSF volume fraction is 5.8±1.2 % for gray matter, and 2.0±0.5% for white matter. CSF value as low as 1.5% can be observed for deep white matter areas. Figures 2a-2d represent the histograms of DBV, OEF, CSF volume fraction and deoxyhemoglobin concentration, respectively.





Discussion

The estimated OEF value is 43.5±11.5% across the brain, compatible with the result obtained by PET [2]. The DBV map successfully resolves the contrast between gray and white matter, where a two-fold difference has been detected. The DBV estimate based on the BOLD model used in this study [4] reduces contribution of capillaries due to the effect of water diffusion not included in the model. Since the venous blood pool contributes about 30% to blood volume in brain tissue [9] (excluding large collecting veins and arteries in brain surface), the corresponding total blood volume fraction from this study is 4.7% for gray matter and 2.3% for white matter, which is compatible with the result from other studies. The CSF volume fractions for gray and white matter are also consistent with literature data [10].

We conclude that the proposed method successfully resolves contributions of OEF and DBV into the BOLD signal.

References

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