Simultaneous quantification of oxygen extraction fraction, vessel radius and cerebral blood volume by respiratory-calibrated MRI

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Purpose

Recently there has been some success using combined hyperoxic and hypercapnic gas challenges to determine SvO_2, and from there estimate the oxygen extraction fraction[1,2] (OEF). In parallel to the development of these techniques, hyperoxic and hypercapnic gas challenges have been used for MRI measurement of vessel size[3,4]. In each of these techniques certain physiological assumptions are required to estimate the OEF or vessel size. In this work we present a novel method that combines vessel size imaging with a simultaneous estimate of OEF and CBV. The new technique removes the assumption of a fixed vessel size from the OEF estimate and simultaneously removes the need to assume a baseline oxy-haemoglobin saturation in the vessel size estimate.

Theory

It has been demonstrated[1,2] that the resting OEF can be estimated by fitting to hyperoxic and hypercapnic measurements of the BOLD calibration parameter M. To calculate M it is common practice to use a fixed value of the exponent β in the calibration equations, thus assuming a uniform contribution from diffusion effects to the BOLD signal. By including a measurement of the vessel scale in the signal analysis the effects of the vessel geometry can be included, reducing the number of assumptions in the model, and expanding the scope of the technique. One method of quantifying the BOLD sensitive vessel scale is to acquire gradient-echo (GE) and spin-echo (SE) data during a gas challenge[3]. This method can readily be incorporated into a standard calibration experiment, with only the addition of a spin-echo to the dual GE-EPI sequence. However, as β is a compound parameter it is difficult to directly relate it to the measured vessel scale. Therefore a new formulation of the calibration problem is needed to integrate the vessel size information. Rather than create a new analytical model, we propose the use of a look-up table technique to interrogate the results of a Monte-Carlo signal model directly. The fundamental parameter driving the signal contrast in our simulations is the blood susceptibility χ. Reframing the problem in terms of χ, rather than M, means new calibration equations are needed. These equations can be derived under the same physiological assumptions used in the original calibration methods; producing the following equations for hyperoxic and hypercapnic challenges respectively:

$$\Delta\chi = -2.3\text{x}10^{-4}\cdot\Delta P_{ET}O_2 \quad \text{and} \quad \chi_0/\chi = CBF/CBF_0,$$

where χ is in ppm, $P_{ET}O_2$ is the end-tidal partial pressure of oxygen (mmHg), and CBF is the cerebral blood flow. The derived calibration equations demonstrate that while a hyperoxic challenge causes an additive change in blood susceptibility, a hypercapnic challenge results in a multiplicative change. Thus, the two challenges create independent probes of the BOLD signal. By including a spin-echo readout in the protocol a further probe is introduced that allows for the simultaneous calculation of OEF and the mean vessel size.

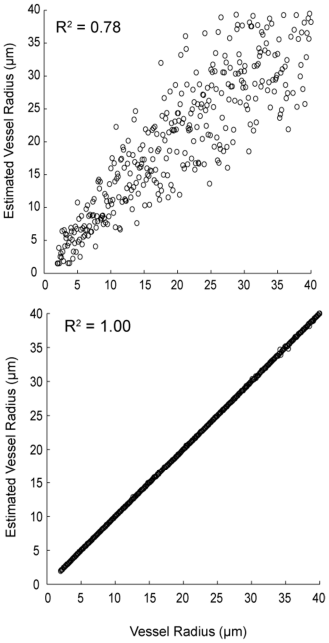

Figure 1. Sensitivity of vessel size estimates to resting OEF. Top: hyperoxia. Bottom: calibrated hyperoxia and hypercapnia.

Methods

Monte-Carlo modelling of the BOLD signal from a vascular network was performed as described in Ref 5. The modelling method is unchanged for a hyperoxic stimulus. However, in keeping with the derived calibration equations, the susceptibility change is modelled as χ_0/χ for hypercapnic simulations, rather than $\Delta\chi$. Additionally, a hyperemia induced increase in venous blood volume has been included in the modelling. Extravascular diffusion was assumed to be 0.76μm^2/ms, a post-capillary resting blood volume fraction of 3% was assumed and GE and SE echo times were chosen to be 30 and 80ms. Six healthy volunteers were scanned at 3T with a Siemens Verio. Imaging data were acquired with a pseudo-continuous arterial spin labelling sequence (1200ms tagging duration and 960ms post-labelling delay). Three echo-planar readouts were employed: two GE readouts at 10 and 30ms, and one SE readout at 80ms. After the first readout, bi-polar spoiler gradients (first gradient moment 200s/m) were used to suppress intravascular signal[5]. Images were acquired with a GRAPPA factor of 3, 3x3x6mm^3, 12 slices, TR: 3.5s. The paradigm consisted of two 2-minute periods of hyperoxia and hypercapnia interleaved with 2-minute periods of air (total 18mins). The gases were delivered to the subject via a nasal cannula at 8L/min to achieve FiO_2~0.5 and $FiCO_2$~0.05. The change in CBF was estimated from the first gradient-echo readout by fitting a general linear model to the expected time courses using FEAT, as per Ref 1. Parametric maps were calculated in MATLAB by fitting to the BOLD time courses using a Delayed Rejection and Adaptive Metropolis Markov chain Monte Carlo algorithm[6].

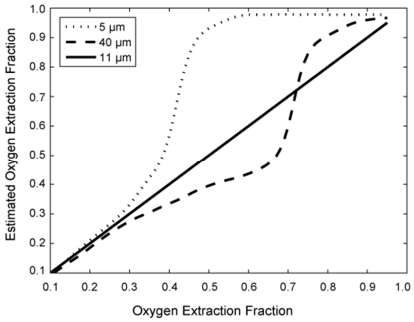

Figure 2. Sensitivity of gradient-echo only estimates of OEF to true vessel size. (Assumed vessel size 11 μm)

Results

Figure 1 compares the sensitivity in vessel size estimates of an existing method (hyperoxic stimulus) with the proposed method for a range of randomly sampled parameter values: OEF (0.1 to 0.95), $\Delta\chi$ (-0.02 to -0.1ppm) and χ_0/χ (1.15 to 1.45). It is clear that the proposed method of vessel size estimation is significantly more accurate (R^2=1.0 vs 0.78). Figure 2 shows the sensitivity of gradient-echo only estimate of OEF to the true vessel size. In each curve the vessel size is assumed to be 11 μm while the true vessel size is altered. The proposed method is insensitive to variations in vessel size (because it is simultaneously estimated), while the gradient-echo only method appears to be highly inaccurate above an OEF of approximately 0.4 when the vessel size is unknown. The results from the pilot data (OEF = 0.36±0.05, CBV = 3.5±1%, vessel radius = 13.5±1.7 μm) are in agreement with expected values for healthy subjects. Maps of CBV show the expected white/grey matter contrast, while maps of vessel radius are more uniform.

Conclusions

Our modelling results show that the resting OEF, CBV and vessel size can be calculated by calibrating GE and SE acquisitions against estimated changes in blood susceptibility. The simultaneous estimation of all three parameters appears to remove a large degree of uncertainty in the estimation of both vessel size and OEF. The new technique is applicable to a wider range of physiological states, and thus has the potential to become a valuable tool in the assessment of diseases such as dementia, stroke and cancer.

References

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