Cross-field analysis of the accuracy of hypercapnia calibrated BOLD

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Introduction: The calibrated BOLD method enables the BOLD response to be quantified in terms of oxygen metabolism[1]. The Davis model (Eq. [1]) describes the fractional BOLD signal change (δS) as a function of normalised changes in blood flow (f=F/F$_0$) and oxygen metabolism (r=R/R$_0$). Changes in blood volume are accounted for by modelling the coupling of flow and volume with the constant α. The relationship between changes in blood oxygenation and the BOLD signal are modelled by the exponent β. Values for α and β were initially optimised for 1.5T[1], and were later revised for 3T[2]. However, with the arrival of 7T systems it is unclear what these values should be and how the accuracy of measurements of oxygen metabolism are affected. In this study we extended an existing detailed model of the BOLD signal[3] to simulate the BOLD response to stimulus and hypercapnia at 1.5T, 3T and 7T. This model was employed to examine the accuracy of the calibrated BOLD method across these field strengths using commonly suggested values of α and β.

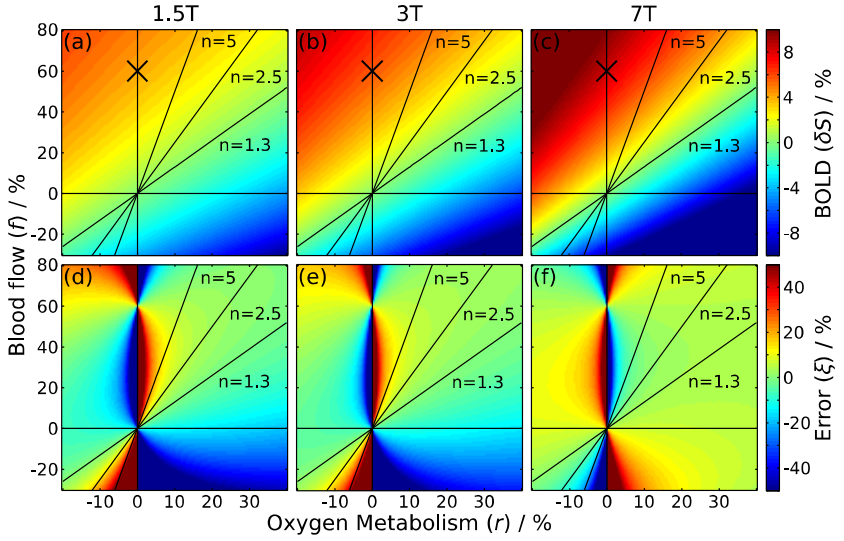
$$\delta S = M\left(1 - f^{\alpha-\beta} r^{\beta}\right) \quad \text{Eq. [1]}$$

$$\xi = \frac{r_{meas} - r_{truth}}{r_{truth} - 1} \quad \text{Eq. [2]}$$

$$n = \frac{f-1}{r-1} \quad \text{Eq. [3]}$$

Simulations: The detailed BOLD signal model[3] includes both intra- and extravascular signal contributions from three vascular compartments; arteries, capillaries and veins. It was extended in the following ways. Changes in extravascular R_2^* in the capillary compartment were described by updated Monte Carlo results[4] that take account of the transition of capillary sized vessels from quadratic to linear relaxivity at ultra-high field. Intravascular R_2^* and resting extravascular R_2^* were modelled using cross-field blood relaxivity measurements[5] and grey matter relaxometry[6], respectively. Typical BOLD weighted echo times were used at each field strength: 50ms, 35ms and 25ms for 1.5T, 3T and 7T, respectively. The standard physiology of the original model was otherwise retained. The BOLD response to hypercapnia was simulated as f=1.6 and r=1. This simulated BOLD response was used to calculate M using Eq. [1] and values for α and β suggested in the literature. A constant value of α=0.2 was used across field strengths[7]. Values[1,2,4] of β=1.5, 1.3, and 1.0 were used for 1.5T, 3T and 7T, respectively. For simulations of the stimulus evoked BOLD response, f was varied in the range 0.7 to 1.8 and r between 0.8 and 1.4. When combined with the simulated M value and Eq. [1], the measurement of oxygen metabolism (r_{meas}) was simulated. The percentage error, ξ, in the fractional change in oxygen metabolism (r_{meas}-1) with respect to the true value (r_{truth}-1) was calculated using Eq. [2].

Fig. 1 - Simulation results: (top row) BOLD response as a function of blood flow and oxygen metabolism. (bottom row) Error in calibrated BOLD oxygen metabolism measurement. (left to right) Increasing magnetic field strength.



Results: Fig. 1a-c displays the amplitude of the BOLD response using a colour scale across the flow-metabolism plane, where X marks the BOLD response to hypercapnia. The amplitude of the BOLD response can be seen to increase with field strength, as expected[6]. The coupling between blood flow and metabolism is often described by the coupling constant n (Eq. [3]). Fig. 1 plots lines for n=1.3, (where a zero BOLD response is observed), n=2.5, (the coupling generally observed in the calibrated BOLD literature), and n=5, (observed in early PET work). The following values for M were simulated: 9%, 14% and 26% for 1.5T, 3T and 7T, respectively. The colour scale on Fig. 1d-f displays the error in the oxygen metabolism measurement. Low error (light green = 0) is observed across all field strengths for typical stimulus derived BOLD responses, i.e 5>n>1.3 and f>0.

Discussion: The simulations presented in this work are the first to consider the implications for the calibrated BOLD method of moving to ultra-high field. Simulated M values provide a guide to the expected increase in M. The values for α and β suggested in the literature for the field strengths under investigation provide accurate measurements of oxygen metabolism for standard stimuli. This would not be the case for caffeine where n=-0.8 has been observed[3]. Further improvements in accuracy are likely to be achieved by abandoning the physical meaning of α and β and optimising their value to minimise the error across the flow-metabolism plane[3].

References: 1. Davis T, *et al.*, PNAS, 95:1834 (1998), 2. Mark C, *et al.*, Neuroimage, 54:1102 (2011), 3. Griffeth V, *et al.*, Neuroimage, 58:198 (2011), 4. Uludag K, *et al.*, Neuroimage, 48:150 (2009), 5. Blockley *et al.*, MRM, 60:1313 (2008), 6. van der Zwaag W, *et al.*, Neuroimage, 47:1425 (2009), 7. Chen J and Pike G, NMR Biomed, 22:1054 (2009).