Inferring Blood Volume, Blood Flow and Blood Oxygenation Changes from Functional ASL Data

M. W. Woolrich[1], P. Chiarelli[1], D. Gallichan[1], T. T. Liu[2]

[1]FMRIB Centre, University of Oxford, Oxford, Oxon, United Kingdom, [2]Centre for Functional MRI, UCSD, San Diego, CA, United States

Introduction

Functional MRI techniques such as Arterial Spin Labelling (ASL), Vascular Space Occupancy (VASO) and Blood Oxyenation Level Dependent (BOLD) have been developed to investigate the different haemodynamic changes of cerebral blood flow (CBF), cerebral blood volume (CBV), and blood oxygenation respectively. We propose an approach which infers these three haemodynamic changes simultaneously via a physiological model of ASL data acquired at multiple echo times. The physiological model describes the contributions of the changes in CBF, CBV and BOLD to the measured data. This can be achieved with a fairly simple model of the physiology. The method infers physiologically plausible haemodynamic changes in response to a visual task. We also demonstrate increased sensitivity in inferring CBF when compared to standard approaches of extracting it from tag-control differencing of ASL data. This approach means that a range of complementary information can be efficiently and simultaneously gathered in functional brain studies, offering enhanced detection power and improved data interpretation, particularly in studies where it is difficult to reliably reproduce conditions between sessions.

Methods

Model: To explain the observed data in undifferenced dual-echo ASL QUIPSS II data, we can not use existing models of magnetisation differences between tag and control[2]. Instead, we need to model the actual magnetisation in a voxel for both the tag and control conditions. The model we use is based in part on the ASL signal processing model introduced in [1]. The ASL signal at time t, with echo time TE_c, is modelled as $p_t = S_t \exp(-TE_c\, r_t)$, where r_t and S_t model the variation with activation of R2* and the voxel magnetisation respectively. The magnetisation, S_t, is modelled as two compartments consisting of the magnetisation due to arterial blood delivered into the voxel, and of the magnetisation in the static tissue. The delivered arterial blood compartment models the effects of (a) CBF variation with activation, (b) longitudinal relaxation of tagged, untagged and saturated blood, (c) the application of a QUIPSS II saturation pulse in the tag region, and (d) transit time delays. The static tissue compartment models (a) longitudinal relaxation effects and (b) the variation with activation of the static tissue magnetisation, M. It is this variation in M, which gives us a measure relating to blood volume under the same assumptions as VASO[3]. Note that we do not model exchange between compartments or venous outflow. We model the autocorrelation found in echo planar imaging[6] using a different autoregressive noise process (AR(1)) for each of the different echo times.

Estimation from dual echo data: The parameters we need to estimate are the R2*, CBF and M0 baselines and the % changes with activation, the transit time delay and the (autoregressive) noise parameters. The parameters are inferred using data from both echo times simultaneously using Bayesian inference. Values for T1 of arterial blood and static tissue were assumed to be 1.66s and 1.3s respectively.

Data Acquisition: We used a PICORE QUIPSS II pulse sequence on a GE Excite 3T scanner, with TI1=0.6s, TI2=1.5s, tag thickness=10cm, tag-imaging region gap=1cm, and bipolar flow crushing gradients. Flip angle was 90^o and we applied presaturation pulses to the imaging region prior to tagging. Two echos (9.1 ms and 30 ms) were acquired every TR=2s. The stimulus used was a flashing (8Hz) radial chequerboard, the first 40s were rest followed by alternating, 20s On and 40s Off, repeated 4 times. We scanned 3 subjects, each over 2 sessions. Data were motion corrected and detrended.

Results

ROI analysis: Fig1 shows typical model fits (blue) to the data (black) from an ROI analysis on an example dataset. Also shown are the separate contributions to the fit from the static tissue (green) and delivered blood (red) compartments (both include R2* weighting). These have had their means shifted for ease of display, but are unscaled. Crucially, these fits are achieved simultaneously on the data at both echo times using only free parameters which are common to both echo times. At the shorter echo time the delivered blood compartment contributes most to the signal. However, there is a clear reduction in the signal in the static tissue compartment during periods of activity due to the VASO effect of reduced static tissue magnetisation.

Voxelwise analysis: Fig2 shows the spatial maps of changes in R2*, CBF and M for an example visual dataset. This shows z-statistic maps corresponding to the different fractional changes thresholded at z=3 (top), and the inferred mean percentage changes (bottom). R2*, CBF and M all show activation within the primary visual cortex (V1) for the visual dataset. The amount of activity inferred is greatest in R2*. However, the R2* map alone has a focus of activation in an area which may contain the large draining vein of the sagittal sinus[3,4].

CBF sensitivity: Fig3 shows results which are consistent with the proposed method being more sensitive than pairwise differenced GLM analysis (of ASL data from the shortest echo time) for inferring CBF. This is because using Bayesian inference on the full physiological model allows us to utilise all of the available undifferenced data at both echo times.

CBV and Grubb exponents: Under the same assumptions as VASO[3], if we assume that the baseline CBV is 5%, then the % changes in M that we obtain from our ROI analysis (from -0.5% to -2.3%) give percent changes in CBV from 12% to 44%. Since we are estimating CBF and M simultaneously, we can also calculate Grubb exponents[5] for assumed baseline CBV values, and vice versa. Fig4(top) shows the baseline CBV map for an assumed Grubb exponent of 0.4 for an example dataset. Given both the Grubb exponent and the baseline CBV are unknown, it is useful to plot the solution space consistent with our estimations of % changes in M and CBF. This is shown in fig4(bottom) (shading indicates group mean +/- group standard deviation) from the ROI analyses from all datasets and supports plausible values of baseline CBV=0.05 and Grubb exponent=0.4 (red lines).

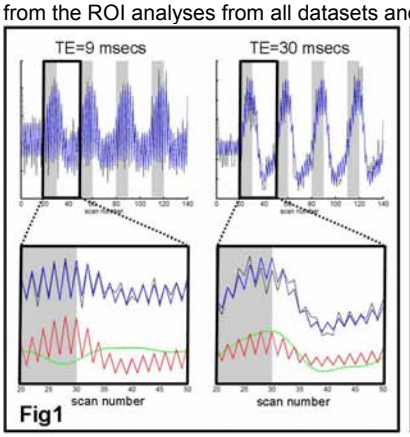

Fig1

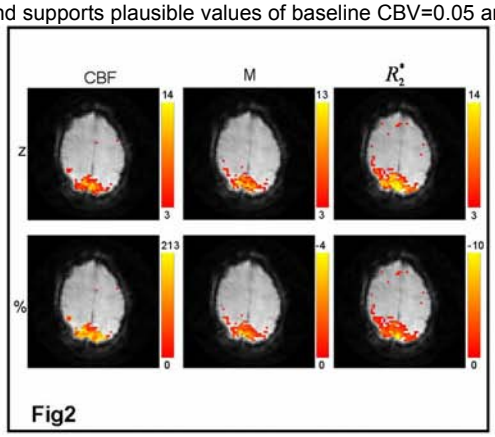

Fig2

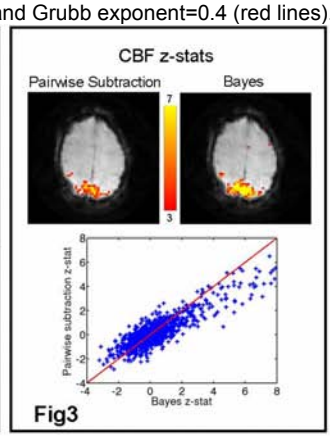

Fig3

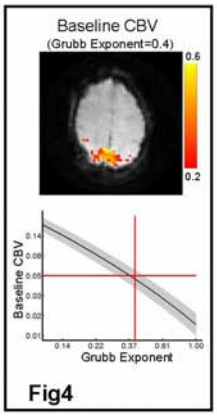

Fig4

[1] Liu, NI 2005 [2] Wong, MRM 1998 [3] Lu, MRM 2003 [4] Yang, MRM 2004 [5] Grubb, Stroke 1974 [6] Woolrich, NI 2001