A simple model to measure arterial cerebral blood volume by arterial spin labelling

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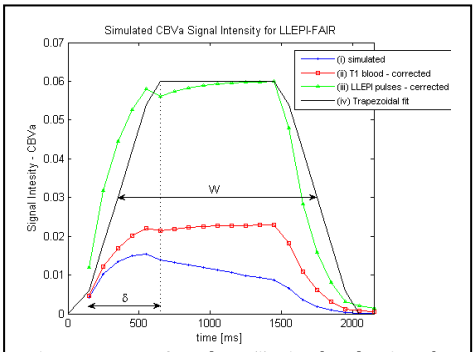

Figure 1: LL-FAIR data (i) simulated using the SCM, (ii) corrected for longitudinal recovery of blood (iii) corrected for llepi readout suppression and (iv) fitted with an ideal trapezoid function.

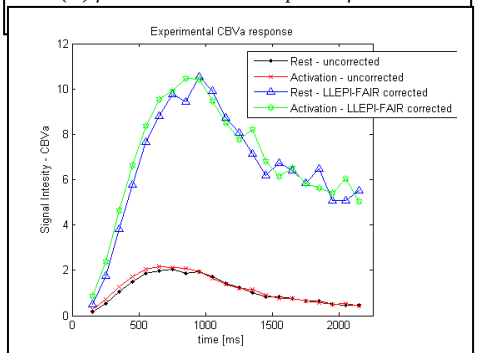

Figure 2: Experimental LL-FAIR data from an ROI with the visual cortex for activation and rest. Data is shown uncorrected and corrected as described in the theory section.

Introduction: Arterial cerebral blood volume (CBV_a) is an important parameter in assessing vascular control. Recent studies have shown that CBV_a increases on brain activation and that venous blood volume changes may, in fact, be negligible [1]. CBV_a may therefore provide a more direct, quantitative, MRI measure of brain activation than BOLD or *CBF* and may improve identification of the origin of neurovascular responses found in conventional BOLD. Pulsed arterial spin labelling (PASL) techniques measure cerebral blood flow (*CBF*), but these techniques are also sensitive to signal in the arterial blood compartment, seen as bright foci in ASL images at short post-labelling delay times (*TI*). Vascular crushing is usually used to remove this signal, but alternatively this signal can be used to measure CBV_a.

The use of standard PASL techniques (such as FAIR) to measure CBV_a is very time consuming (~ 30 mins) as several data sets must be acquired at a range of *TI*'s each with and without vascular crushing. Subtracting these data sets isolates the arterial blood volume signal which can then be modelled for CBV_a. An alternative method is to use a FAIR with a Look-Locker sampling scheme (techniques know variously as LL-FAIR, ITSFAIR and QUASAR). This scheme compares alternating non-selective and selective Look Locker inversion recovery signals acquired at a range of *TI* values in a single shot. If an optimized combination of flip angle and timing of the readout pulses is used, this sequence is only sensitive to CBV_a signals and requires no vascular crushing. CBV_a and the transit times can then be measured non-invasively from ~5 min data acquisition [3]. However a step-wise compartmental model (SCM), which iteratively estimates the signal based on repeated application of the Bloch equations, has been used to fit the data in the past.

This work aims to (i) develop a simpler method for measuring CBV_a from LL-FAIR data, (ii) validate this new model against the SCM, (iii) apply this model to measure CBV_a and changes on activation.

Theory: If the non-selective pulse has a finite width then the input function of labelled blood to the arterial compartment can be approximated as a trapezoid function of height $h = 2 * CBV_a$ **Eq.[1]**, area $A = 2 * CBV_a * (W)$ **Eq.[2],** full width at half height W, and slope length δ starting at time Δ; where δ is the time blood remains in the arterial blood compartment of the voxel, Δ is the arterial transit time (defined by the width of the selective inversion) and W is the temporal width of the non-selective inversion (Figure 1 (iv)). If LL-FAIR signals can be corrected for the effects of longitudinal recovery and suppression by the LL-EPI readout pulses, then they will approximate to this trapezoidal form and thus provide a simple method by which to measure CBV_a. Data must be (i) corrected for longitudinal recovery of the tag (multiplication by: *exp(+t/T1blood)* (Figure 1 (ii)); (ii) fitted to a trapezoid to estimate δ; (iii) corrected for the suppression of blood as it travels through the voxel, by the n LL readouts (multiplication by $\frac{(1-\cos\theta)n}{(1-(\cos\theta)^n)\sin\theta}$ where $n = \frac{\delta}{TA}$ and TA is the LLEPI readout pulse spacing) (Figure 1 (iii)).

Table 1: Comparison of fitted CBV_a values (%) obtained at rest and on activation using the SCM and peak signal amplitude (Method 1)

Subject	Rest		Activation	
	SCM	Method I	SCM	Method I
1	7.9	7.7	8.2	7.8
2	9.1	9.6	9.5	9.9
3	14.4	10.2	15.7	10.7
4	5.3	5.0	5.6	5.2

Validation: Monte Carlo modelling was used to validate this simpler approach compared to the SCM. Data sets were simulated using the SCM (Δ = 100-300 ms, δ = 500-700 ms, CBV_a = 2-3 %, W = 1500 ms) and Gaussian noise added (mean = 0 stdev = 0.01). CBV_a was estimated from the data using 4 different methods: (I) peak amplitude of the simulated signal (Eq.[1]); (II) area under curve of simulated signal (Eq.[2]) (III); height (*h*) of fitted trapezoid (IV); area of fitted trapezoid. This was repeated 1000 times for each simulated data set and the errors in the measurement of CBV_a for the different values of Δ, δ and CBV_a were assessed.

Experimental Methods and Data analysis: The LL-FAIR sequence was implemented on a Philips 3T Achieva scanner using a body transmit and SENSE receive head gradient coil. Sequence timings used were those previously optimised for CBV_a at 3T [3] (TI = 150 ms, TA = 100 ms, $\alpha = 50^0$ (final readout 90^0), 21 readout pulses, selective width = 30 mm, non-selective width = 200 mm). The jittered TR was 2.4 s. Image resolution was 3 x 3 x 5 mm^3 and GE-EPI TE = 16 ms. Four healthy volunteers participated in a visual experiment using 4.8s red LED goggles flashing at 8Hz followed by 26.4 s rest repeated for 14 cycles. Data was realigned [3] and the LL-FAIR difference signals (S-NS) (normalised to the equilibrium blood magnetization $M_{b,0}$, [3]) were extracted. This normalised data was then fitted using methods (I-IV) and the SCM and estimates of CBV_a were compared.

Results: Results of Monte Carlo simulations showed that the measured peak signal (method (I)) provided the most reliable estimate of CBV_a (for noise <0.01). As Δ increased the accuracy of CBV_a was reduced due to the increased noise in the data as a result of the longer period available for T1 recovery of blood. As δ increased the accuracy of CBV_a was reduced, particularly for those methods II and IV that are based on area since the onset/offset slopes, which are of length δ, are not well matched to a trapezoid function (Figure 1). Figure 2 shows experimental LLEPI data taken from an ROI. Table 1 shows the fitted values of CBV_a for each subject.

Discussion: It has been shown that CBV_a can be simply estimated from the peak LL-FAIR signal using simple correction factors. This opens up the possibility of conveniently applying this technique to fMRI studies, where CBV_a may provide a more direct measure of neuronal activation than the BOLD effect. The model described here assumes that the input function is trapezoidal, but in practice variation of vessel sizes within an ROI and dispersion of the label will lead to deviations from a trapezoid (fig 2). Future work will use voxel-by-voxel analysis of the data to form CBVa maps. The use of LL-FAIR will also provide an opportunity to study the exact form of the arterial input function of the label to the voxel.

References: [1] Kim, et al, J Cerebrl Blood Flow & Metabolism (2007) 27, 1235–1247, 2007[2] Kim, T. and Kim, S-G., MRM, 55,1047-1057, 2006. [3] Brookes et al., MRM 58,41-54, 2007. Acknowledgements: This work was supported by the MRC.