Measurement of Cerebral Blood Volume Using LL-EPI-FAIR

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Introduction: The *in vivo* measurement of cerebral blood volume (CBV) can provide important information about brain physiology and function under both normal and pathological conditions. Together with cerebral blood flow (CBF), the quantification of CBV also allows investigation into the mechanisms underlying the BOLD response. Typically *in vivo* total CBV is obtained using contrast agents, whilst arterial CBV (aCBV) has been measured using intravascular perfluorocarbon and ^{19}F NMR. More recently, non-invasive aCBV measures have been made using EPISTAR [(2)]. However, to sample sufficiently the arterial inflow curve in this technique, several TI values are required, making experiments time consuming (~60min). Here by combining FAIR with Look-Locher EPI (LL-EPI)[(3,4,5)] we show that it is possible to form non-invasively CBV maps in under 5 minutes.

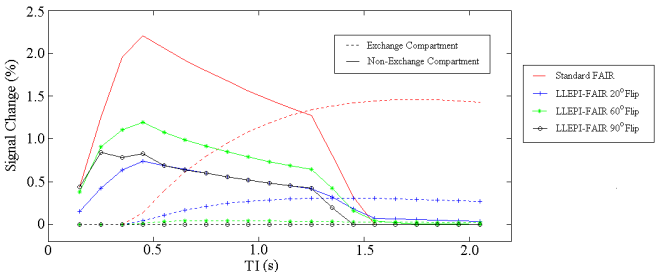


Figure 1: Simulation of the non-exchange/exchange compartment difference curves for the FAIR and LLEPI-FAIR sequences. LLEPI-FAIR curves are shown as a function of readout pulse flip angle.(Simulated assuming CBV =1.5 %, CBF =110 ml/100g/min, Δ_a =0.1s, τ_{ex} = 0.3s, Δ_C = 0.4s, and time taken for the non-selective bolus to pass through the arterial compartment = 1.3s)

Simulations: The LLEPI-FAIR sequence consists of a 180-degree inversion pulse followed by a series of readout pulses and EPI imaging modules to sample repeatedly the magnetization recovery. The inversion alternates between selective (20mm wide) and non-selective (200mm wide) and the difference signal yields information on inflowing magnetization to the imaging slice (6mm wide). A two-compartment model was used to monitor numerically the magnetisation in the non-exchange (predominantly arterial) compartment and the exchanging (tissue) compartment within the imaging slice.

Non-exchange compartment: Following an initial transit time, Δ_a tagged blood reaches the imaging plane, giving rise to a difference signal in this compartment. Blood remains in this non-exchange compartment for the 'exchange' time τ_{ex} and can be modelled as:

$$\frac{dM_{non-exchange}(t)}{dt} = 0 \quad for \quad t < \Delta_a; \quad \frac{dM_{non-exchange}(t)}{dt} = \frac{M_{non-exchange}(t) - M_{0,non-exchange}}{T_{1b}} + FM(t)_{non-exchange\_in} - FM_{non-exchange\_out}(t) \quad for \quad t \geq \Delta_a \qquad [1]$$

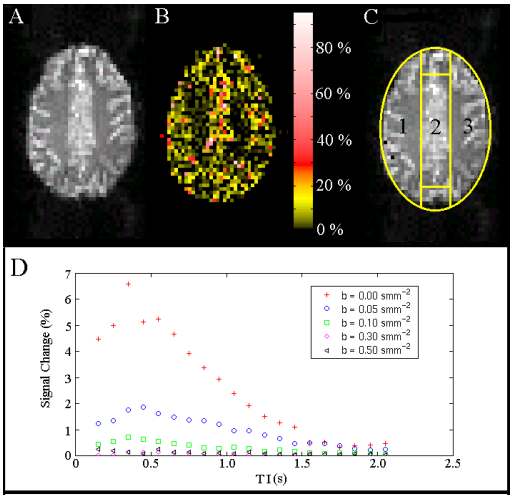
F indicates flow, and the blood volume of the non-exchange compartment can be calculated by $F\tau_{exc.}$

Exchange compartment: After a time Δ_c (~Δ_a + τ_{ex}) tagged blood then arrives at the capillary bed and tagged water exchanges between the blood and tissue. The difference signal for the exchange compartment is given by

$$\frac{dM_{tissue}}{dt} = 0 \quad for \quad t < \Delta_c; \quad \frac{dM_{tissue}}{dt} = \frac{M_{tissue}(t) - M_{0,tissue}}{T_1} + \frac{fM_{arteriole}}{\lambda} - fM_{tissue}(t) \quad for \quad t \geq \Delta_c \qquad [2]$$

where f is the perfusion rate, and λ the blood:brain partition coefficient.

In the LLEPI-FAIR sequence, blood in the non-exchange compartment, destined for the exchange site can be suppressed by the LLEPI readout pulses, if the readout pulses are separated by a time less than τ_{exc}. This leads to reduced sensitivity of the LLEPI sequence to the exchange component when short spacing between readout pulses and high flip angles are employed. This is illustrated in Figure 1, where the compartmental signals are compared for standard FAIR, and LLEPI-FAIR sequences at short readout spacing. In standard FAIR, two distinct maxima are observed, the first due to the non-exchange component (solid line) and the second due to the exchange component (broken line). In LLEPI-FAIR, the exchange compartment is progressively suppressed as the flip angle is increased, leaving the difference signal weighted to the non-exchange compartment. Conversely, at low flip angle (and long readout spacing) the sensitivity of LLEPI-FAIR to perfusion can be increased.



E

b (smm^{-2})	v_c (mms^{-1})	*Region 1*	*Region 2*	*Region 3*
0	*N/A*	10.2 ± 3.0 %	12.0 ± 3.0 %	8.0 ± 2.0 %
0.2	*76*	3.1 ± 1.0 %	5.0 ± 1.0 %	3.0 ± 1.0 %
0.9	*38*	1.4 ± 0.2 %	1.5 ± 0.4 %	1.5 ± 0.3 %
2.6	*22*	0.7 ± 0.4 %	1.3 ± 0.5 %	0.4 ± 0.2 %
4.4	*17*	0.3 ± 0.2 %	0.7 ± 0.4 %	0.1 ± 0.1 %

Figure 2:- A) T_1 weighted image B) CBV map C) 3 brain areas analyzed. D) The effect of diffusion weighting on the difference curve. Note blood volume is reduced as the flowing blood is crushed as diffusion weighting increases. E) Table of CBV values for different diffusion weightings and different brain regions, averaged across all 4 subjects

Methods: Data were obtained using a 3T MRI scanner, with custom-built head gradient coil and a whole head TEM RF coil. A flip angle of ~50 degrees, initial delay of 150 ms and pulse separation of 100 ms were used to allow quantification of the non-exchange blood volume. In addition, the effect of applying various diffusion weightings was investigated. Initially images were sign corrected [(6)] and motion corrected. Difference signals were obtained by calculating the difference between selective and nonselective images and normalized using the equilibrium magnetization of blood, found from the sagittal sinus. Curves were then fitted to [1] to quantify blood volume.

Results: Experiments were performed on 4 healthy volunteers. A T_1 weighted image and CBV map are shown in Figures 2A and 2B. To investigate the effect of diffusion weightings, brains were divided into 3 regions (Fig. 2C) and the mean blood volume quantified. Figure 2D demonstrates the effect of diffusion weighting on the non-exchange difference curve. Figure 2E shows the mean (n=4) percentage of blood in each region studied (Fig. 2C) as a function of diffusion weighting. As expected region 2 displays the greatest CBV as it contains the internal cerebral arteries.

Discussion: We have shown that it is possible to quantify blood volume using LLEPI-FAIR. The sequence is both more efficient and sensitive in quantifying CBV than standard FAIR. Despite the reduction in SNR per TI readout, LLEPI-FAIR samples several TI values per TR and so signal to noise per unit time is increased, allowing a CBV map to be formed in under 5 minutes. Diffusion weighting crushes signal from blood vessels where flow is greater than a critical velocity v_C (Fig 2E). The absence of any difference signal for b = 4.4 smm^{-2} and TI > 1.5 s demonstrates the insensitivity of the implemented LLEPI-FAIR sequence to perfusion (exchange compartment). Future work will replace the FAIR tagging with STAR to allow separation of venous and arterial blood volumes and the use of these methods to study changes in CBV on activation.

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References: 1) Duong *et al*, MRM 43:393-402 (2000). 2) Hoad *et al*, Proc. 13th ISMRM (2004). 3) Look, D.C. and D.R. Locher. Rev. Sci. Inst, 1970. 41(2): p. 250-251. 4) Francis, S. et al, Proc. 8th ISMRM (2000). 5) Gunther, MRM, 46: 974-984 (2001) 6) Gowland and Leach, MRM. 18: 224-231 1991.