In-vivo Measurement of arterial cerebral blood volume using LL-EPI-FAIR and LL-EPI-STAR

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Introduction: The *in vivo* measurement of arterial cerebral blood volume (aCBV) can provide important information about brain physiology. Also, the accurate quantification of aCBV should allow new insights into the biophysical mechanisms underlying the BOLD response. It has been shown that aCBV can be obtained non-invasively using arterial spin labeling (ASL) techniques[(1)]. However, in order to separate the arterial blood volume signal from the perfusion signal, two experiments are required, both with and without diffusion weighting, making the acquisition time consuming. Recently, we have shown that Look-Locher-Echo Planar Imaging (LL-EPI) [(2,3)] can be combined with Flow sensitive Alternating Inversion Recovery (FAIR) in order to quantify accurately and non-invasively aCBV[(4)]. Since the LL-EPI readout pulses perturb spins as they flow through the imaging slice, blood magnetization is progressively suppressed in the capillary compartment (perfusion signal), whilst inflowing arterial blood magnetization is maintained. This suppression makes the LL-EPI-ASL techniques sensitive solely to blood in the arterial compartment and hence to aCBV. Here, we extend our previous observations by comparison of LL-EPI-FAIR with LL-EPI-STAR (Signal Targeting by Alternating Radiofrequency flow encoding with LL-EPI sampling). We show that the two sequences yield similar results in the measurement of resting state aCBV, and that LL_EPI_STAR provides additional flow directional information.

Methods: The LLEPI pulse sequence consists of a single 180-degree hyperbolic secant inversion pulse followed by a series of readout pulses and EPI imaging modules. This allows the repeated sampling of longitudinal magnetization as it recovers. The LL-EPI-FAIR routine was implemented as shown in Figure 1A, with a 6 mm imaging slice, a 20 mm selective inversion slab and a 200 mm non-selective inversion slab, all centred at the origin. The LL-EPI-STAR routine was implemented as shown in figure 1B, with a 6 mm imaging slice centred at the origin, a 90 mm 'tag' inversion slab centred 55 mm inferior from the origin, and a 90 mm 'control' inversion slab centred 55 mm superior to the origin. In both FAIR and STAR, a 90 mm bolus of labeled arterial blood flows into the imaging slice thus making their sequence geometry equivalent. In LL-EPI-STAR, the sequence was preceded by a saturation pulse in order to suppress inaccuracy in inversion slab profile.

LL-EPI sequence parameters were optimized to suppress blood magnetization in the capillaries (perfusion signal) and retain arterial blood magnetization (aCBV). The delay between the inversion pulse and the first LL-EPI readout pulse (t_i) was set to 150 ms, delays between subsequent readout pulses (Δ) were set to 100 ms and a flip angle (FA) of 50° was used. The delay (TR) between LL-EPI sets was 3 s. Previous work shows that these parameters allow measurement of signal from arterial blood whilst suppressing perfusion signals [(4)].

Sequences were implemented on a 3T MRI scanner with head gradient coil and whole head TEM RF coil. A total of 20 readout pulses were applied following each inversion pulse in order to sample the arterial inflow curve (Figures 2C and 2D). MBEST EPI images with an in plane resolution of 4 mm x 4 mm and a slice thickness of 6 mm were acquired using a matrix size of 64 x 64. An echo time of 35 ms was used. Incremental spoiler gradients followed each readout pulse[(5)]. A total of six healthy volunteers took part in the study. For each subject 90 LL-EPI sets (45 selective/tag and 45 non-selective/control) were acquired for both LL-EPI-FAIR and LL-EPI-STAR. LL-EPI-FAIR images were sign corrected by assessment of phase change[(7)]. In both LL-EPI-FAIR and LL-EPI-STAR, difference images were generated and the difference signal fitted for aCBV using a previously described model[(4)]. Since in LL-EPI-STAR, the inversion slabs do not cover the imaging slice, sign correction of the data is not required.

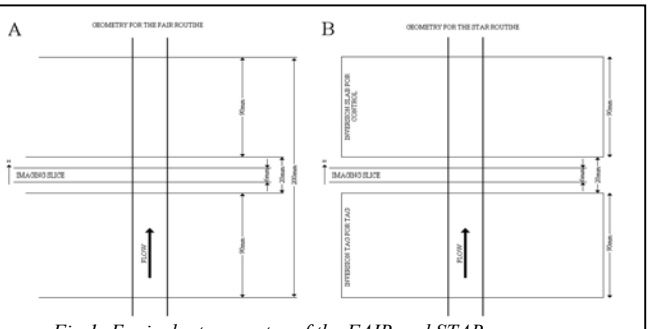

Fig 1: Equivalent geometry of the FAIR and STAR sequences

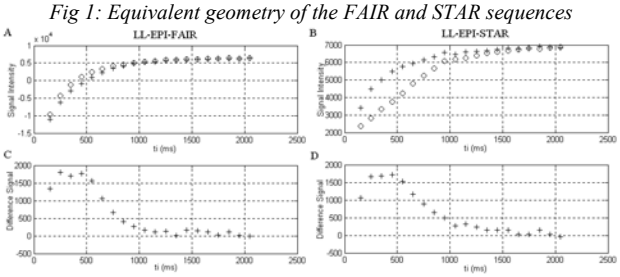

Fig 2: Raw and difference signals for LL-EPI-FAIR and LL-EPI-STAR

Subject	FAIR Region 1	STAR Region 1	FAIR Region 2	STAR Region 2
SL	3.2 ± 0.8 %	3.8 ± 0.6 %	0.9 ± 0.2 %	0.7 ± 0.1 %
AJ	5.6 ± 0.2 %	5.1 ± 0.1 %	1.2 ± 0.3 %	1.3 ± 0.2 %
PW	1.4 ± 0.3 %	1.5 ± 0.3 %	1.1 ± 0.2 %	1.2 ± 0.2 %
LJ	4.0 ± 0.9 %	3.2 ± 0.8 %	1.0 ± 0.2 %	1.2 ± 0.2 %
JM	3.5 ± 0.9 %	4.5 ± 0.6 %	0.9 ± 0.2 %	1.1 ± 0.2 %
IC	3.0 ± 0.6 %	3.2 ± 0.4 %	1.2 ± 0.2 %	1.2 ± 0.2 %

Table 1: Comparison of aCBV values measured in the two ROI's.

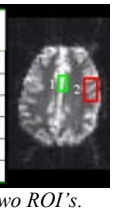

Fig 3: The relative positioning of the ROI's.

Results: Figure 2A shows the averaged LL-EPI-FAIR signal taken from a region of interest in grey matter, crosses show the data acquired following a non-selective inversion pulse whilst circles show data acquired following a selective inversion pulse. Figure 2B shows the LL-EPI-STAR signal from the same region, crosses show data acquired following a control inversion and circles show that acquired following a tag inversion. Notice that whilst LL-EPI-FAIR follows an approximate inversion recovery, the STAR follows a saturation recovery (due to the pre-saturation pulse applied prior to inversion in LL-EPI-STAR). Despite the obvious difference in raw signals, the two sequences yield approximately equivalent difference signals (figures 2C and 2D). In order to compare quantitatively the LL-EPI-FAIR and LL-EPI-STAR techniques across the ($n = 6$) subject group, two regions of interest were defined as shown in Figure 3. Region 1 was positioned over a region containing mainly the large cerebral arteries, and Region 2 contained mostly grey matter. Table 1 shows the aCBV values calculated across these regions.

Discussion: The results presented show that both LL-EPI-FAIR and LL-EPI-STAR can be used to produce reliable measurements of aCBV in the resting state brain. Good quantitative agreement was observed between values of aCBV calculated using LL-EPI-FAIR and LL-EPI-STAR. As expected, the aCBV values the regions containing the large internal arteries (Region 1) are on average higher than those calculated in grey matter regions (Region 2). The values recorded for grey matter in Table 1 are in agreement with results published elsewhere[(7, 8)]. It should also be noted that LL-EPI-STAR yields flow direction sensitivity. Here LL-EPI sequences have provided a method of accurately quantifying resting state aCBV in less 5 minutes, a significantly shorter acquisition time than using more traditional methods This, along with the inherent suppression of the perfusion signal using the sequence parameters chosen, represents the major advantage of LL-EPI techniques.

Conclusion: Both LL-EPI-FAIR and LL-EPI-STAR techniques yield equivalent aCBV results confirming the validity of either technique. However LL-EPI_STAR provides additional directional flow sensitivity and since no sign correction is required, is easier to analyse making this the technique of choice.

Acknowledgements: This Work is supported by a Programme Grant from the Medical Research Council (MRC).

References: 1) Hoad *et al*, Proc. 12th ISMRM (2004). 2) Look, D.C. and D.R. Locher. Rev. Sci. Inst, 1970. 41(2): p. 250-251. 3) Gowland and Mansfield, MRM 30 351-354 (1993). 4) Brookes *et al*, Proc. 13th ISMRM (2005). 5) Wang *et al.* MRM. 50 599-607. 6) Gowland and Leach, MRM. 18: 224-231 1991. 7) Petersen *et al*, Proc. 13th ISMRM (2005). 8) Duong *et al*, MRM 43:393-402 (2000).