

# Separation of Intravascular Signal in Multi-Inversion Time Arterial Spin Labelling MRI

M. A. Chappell<sup>1</sup>, B. J. MacIntosh<sup>1,2</sup>, M. J. Donahue<sup>1</sup>, M. Günther<sup>3,4</sup>, P. Jezzard<sup>1</sup>, and M. W. Woolrich<sup>1</sup>

<sup>1</sup>FMRIB Centre, University of Oxford, Oxford, United Kingdom, <sup>2</sup>Imaging Research, Sunnybrook Research Institute, Toronto, Canada, <sup>3</sup>Department of Neurology, Universitätsklinikum Mannheim, University of Heidelberg, Mannheim, Germany, <sup>4</sup>mediri GmbH, Heidelberg, Germany

**Introduction:** Arterial Spin Labelling (ASL) provides a non-invasive method to measure cerebral blood flow (CBF). After labelling of the blood using RF pulse inversion, a delay, the inversion time (TI), is inserted to permit the blood to reach the capillary exchange site. The TI may be varied to provide multi-TI ASL measurements to which a kinetic curve model may be fit. This procedure allows other parameters of interest such as the bolus arrival time (BAT) to be determined. An important artefact in ASL measurements arises from labelled blood water that is still intravascular (IV) at the time of imaging; CBF should relate to the delivery of blood water to tissue and not include blood water still within the arterial tree. One solution is to apply flow suppression (FS) gradients during acquisition [1]. We have previously proposed an alternative in multi-TI ASL, accounting for the IV signal by its inclusion in the kinetic curve model [2], but only in voxels where there is evidence in the data to support it (to avoid over-fitting). In this study we examine the reliability of this IV fitting approach and compare it to FS. We tested the hypothesis that the IV fitting approach was as effective as FS and is thus a viable alternative where FS is inappropriate, such as in current GRASE-ASL sequences [3].

**Methods:** Resting state pulsed ASL, T1-weighted structural and Time-of-flight (TOF) images were collected in four healthy subjects. In all subjects three ASL data sets were acquired: FAIR preparation with 3D-GRASE readout [3] (TR/TE 3110/23 ms, 3.44x3.44x5 mm, 64x64 matrix, 22 slices, 10 TIs, 10 averages), PICORE preparation with GE-EPI readout with and without FS ( $b=10 \text{ s/mm}^2$ , applied anterior-superior) (TR/TE 3520/18 ms, 4x4x6 mm, 64x64 matrix, 5 slices, Q2TIPS saturation after 0.7 s [4], 10 TIs, 10 averages). In one subject a further dataset was acquired with FS applied in the left-right direction. GRASE-ASL data from four patients with predominantly left ICA stenosis were also analysed (same sequence parameters as above) to investigate the reliability of IV fitting in patients.

Two models for the data were considered: **T** – tissue only, the standard ASL kinetic curve model [5] (3 parameters: CBF, BAT and bolus duration); **T+IV** – tissue plus an IV component characterised by the arterial blood volume (aBV) (6 parameters: CBF, aBV, plus BAT and bolus duration for both components). Analysis of the ASL data was performed using a probabilistic inference approach designed for multi-TI ASL [6]. Prior information was included for the BAT and bolus duration and the aBV was subject to an Automatic Relevancy Determination (ARD) prior [7], to ensure that the IV component was only applied where the data supported it.

The GRASE-ASL data was modelled using T+IV since IV contamination was expected. To confirm that the IV signal was being estimated in anatomically correct locations, the GRASE results and TOF images were aligned to the corresponding structural images and the major vessels from the TOF maximum intensity projection (MIP) highlighted via thresholding. To compare IV fitting to FS, the EPI data were analysed using a combination of the two models on the FS and non-suppressed (NS) data as in Table 1. The CBF, aBV and BAT values from these analyses were compared to examine the removal of the IV signal. An unpaired t-test (with Bonferroni multiple comparisons correction, corrected  $p<0.05$ ) was performed on the CBF differences between the FS and NS data. The IV fitting in the patient group was investigated by examining the correlation of aBV to stenotic burden within a mask including the MCA, defined from the non-stenosed side of the group mean image.

**Results:** Figure 1 shows the aBV image (thresholded at 0.1%) from an individual subject at the level of the Circle of Willis, with the major vessels from the TOF MIP overlaid. There was good agreement between regions of high aBV and vessel locations in all subjects. Figure 2 shows a comparison of images from the EPI data in one subject: modelling both tissue and IV components from the non-suppressed data (top row) produced a similar CBF image to that of the FS data (tissue only model, middle row). However, there were areas of higher CBF, with corresponding shorter BAT, in the FS data not present in the NS data. This was confirmed by examining the differences in CBF and BAT in regions of high aBV. Inclusion of the IV component in the analysis of the FS data removed these discrepancies, indicating that it was possible to identify some remaining IV signal in the FS data. The results of the statistical comparisons of CBF estimates, figure 3, showed a marked reduction in the CBF differences when the FS data were analysed using the T+IV model, supporting the supposition that there remained IV signal in the FS data. The same effect was seen when the FS direction was altered (Figure 3b, dashed line). Figure 4 shows the mean aBV image in the patient group along with the correlation ( $r^2=0.67$ ) between mean aBV and stenotic burden within a mask incorporating the MCA, consistent with flow changes within the macro vasculature.

**Discussion:** Both FS and IV fitting were able to remove contamination of CBF by IV signal arising from macro vascular vessels. IV fitting appeared to be more effective at removal of the IV signal than FS, even ‘residual’ IV signal in the FS data. The FS implementation was in one direction only, which may not be the most effective strategy, since some component of the IV blood is likely to have been perpendicular to the FS direction. More effective FS strategies using multiple directions can be employed, though typically at the expense of longer acquisition or echo times. Whilst the patient data are preliminary, the aBV results were consistent with reductions in the macro vascular flow arising from their stenotic burden, implying that the method is applicable in pathological as well as healthy subjects.

**Conclusions:** It is possible in multi-TI ASL to isolate the macro vascular IV signal by employing a probabilistic inference approach and including an extra component within the kinetic curve model. This is a viable alternative to flow suppression where this is not desirable or feasible, such as in GRASE-ASL.

Table 1: Analysis applied to EPI data

Data	Model	
	Tissue only	Tissue + IV
No suppr.	-	NS (T+IV)
Flow suppr.	FS (T)	FS (T+IV)

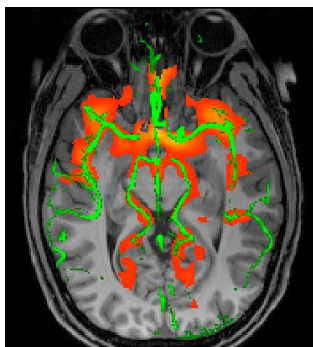


Figure 1: aBV (>0.1%) in an individual, with vessels from TOF MIP.

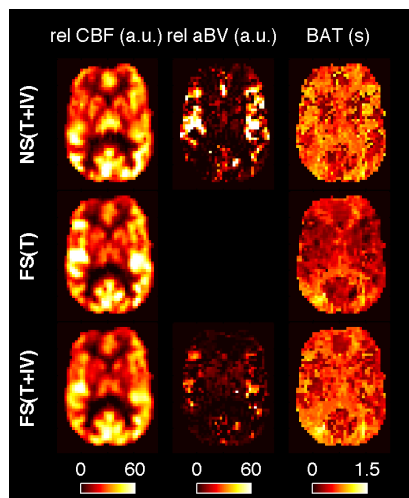


Figure 2: Images from EPI data, results for all three analyses in table 1.

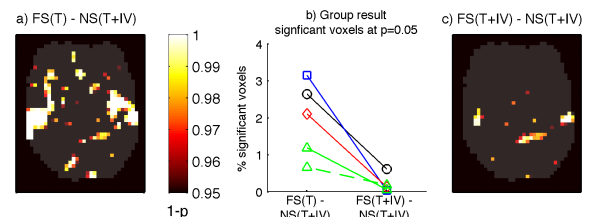


Figure 3: Statistical differences in CBF between FS and NS data, reduction seen when IV model included for analysis of FS data.

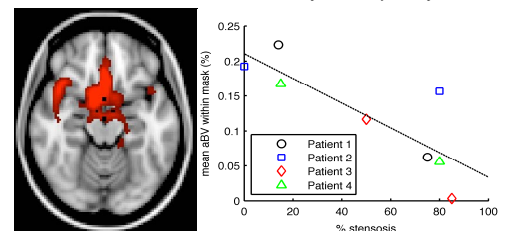


Figure 4: Results from patient group, group mean aBV (left), aBV within group MCA mask against stenotic burden (right).

## References:

- Ye, F.Q., et al., Magn Reson Med, 1997. 37:226.
- Chappell et al., in Proc. ISMRM Hawaii, 2008.
- Günther, M., et al., Magn Reson Med, 2005. 54: p. 491-498.
- Wong E.C. et al., Magn Reson Med, 1998. 39:702-708.
- Buxton, R.B., et al., Magn Reson Med, 1998. 40:383-396.
- Chappell, M.A., et al., IEEE Trans Sig Proc, 2009. 57:223-236.
- Mackay, D., Network: Computation in Neural Systems, 1995. 6:469-505.