Modelling dispersion in Arterial Spin Labelling with Validation from ASL Dynamic Angiography

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Introduction: The effects of label dispersion are an established problem in the quantification of blood flow using Arterial Spin Labelling (ASL). A number of models for dispersion of the ASL labelled bolus have been proposed [1-4]. However, none has been established as suitable for routine use for the analysis of ASL data. A major obstacle to the validation of dispersion models is that the ASL signal is usually measured in the tissue, where the effects of exchange of labelled water with the extra vascular space occur. It is very difficult to separate the effects of exchange and dispersion, not least because the extent to which exchange is limited is not well quantified. A more promising solution would be to observe the ASL signal in the arteries themselves, for example [5]. Recently ASL preparations have been employed with short inversion time (TI) within dynamic angiographic sequences; these offer high temporal resolution measurements within the arterial vasculature before the labelled blood has reached the tissue. In this work we sought a model for ASL bolus dispersion that could be used in routine analysis and quantification. We assessed models according to their fit to dynamic angiographic data using an ASL preparation within a heterogeneous population of individuals with carotid artery disease.

Methods: Data were collected in 24 patients with varying degrees of carotid stenosis both pre and post carotid endarterectomy according to a protocol approved by the local ethics review board. Acquisition used a 3 T (TIM Trio, Siemens) with a 12 channel head receive coil and was centered at the level of the Circle of Willis. Flow-weighted contrast was achieved using a flow-sensitive alternating inversion recovery (FAIR) pulsed arterial spin labeling (PASL) preparation [6]. Time-resolved angiographic images were obtained using a low flip-angle Look Locker spoiled gradient echo readout [7]. In-plane resolution 1x1 mm, slab thickness 50 mm, TE=3.7ms, inflow delay=78 ms, inner TR=55ms per 3 k_y segments, label TR=1500ms, flip angle=10°, 20 inflow phases, duration was 2 minutes 42 seconds.

A selection of models of arterial bolus dispersion were fit to the data, these are summarized in Table 1. Six models were considered: 1) standard model with no dispersion [8]; 2) a Gamma Variate function (GVF) (characterised by a time-to-peak, p, and sharpness, s), which is widely used in Dynamic Susceptibility Contrast (DSC) perfusion analysis, 3) the model of Gallichan *et al.* [2] that considers the geometrical evolution of a labelled bolus in a cylindrical artery, 4) the model of Hrabe and Lewis [1], where dispersion is modelled by convolution of the initial box-car bolus shape with a Gaussian dispersion kernel, 5) the modified Hrabe-Lewis model [4], where a Gaussian dispersion kernel is also employed, but is applied to the spatial rather than temporal bolus shape, 6) the Hrabe-Lewis convolution model with a gamma shaped dispersion kernel. Model fitting was performed using a probabilistic non-linear fit that has been previously used for multi-TI perfusion ASL [9].

Models were compared using the negative free energy (FE) of the model fit in each voxel. The free energy is the natural goodness of fit measure for the probabilistic method employed; it approximates the Bayesian evidence for the model and thus includes a penalty for the number of free parameters in the model. The closer the free energy is to zero the better 'fit' is the model to the data. The mean value of the free energy was calculated within three ROIs that were manually defined at the inlets to the middle cerebral arteries (MCA-R and -L) and the vertebrobasilar artery (VBA) at the level of the Circle of Willis. The significance of an improvement in FE when using one model over another was tested using a one tailed T-test at p=0.05.

Results: Fig. 1 shows an estimated arterial blood volume (aBV) image from Model 1 with the three ROIs for that subject superimposed. Fig. 2 plots the natural logarithm of the free energy within the ROIs across all the subjects (including pre- and post-CEA). The dispersion kernel models based on the Hrabe and Lewis model produced the best fits with the modified Gaussian and gamma kernels being superior, but not readily distinguishable from each other. Table 1 gives the mean value across all subjects in the ROIs for the dispersion parameters in each model. These values indicate that dispersion was greatest in the VBA compared to MCA inlets. Fig. 3 shows an example of the model fit within a VBA voxel.

Table 1: Dispersion models with mean estimated value (across all subjects) for dispersion parameters, higher value corresponds to a more dispersed bolus.

#	Model		Parameter	Mean estimated value MCA-R	MCA-L	VBA
1	Standard	[8]	-			
2	GVF		1/s	0.96	0.90	1.60
			p	1.00	0.92	1.34
3	Gallichan et al.	[2]		2.81	3.37	2.73
4	Hrabe & Lewis	[1]	σ	0.21	0.20	0.29
5	Modified H & L	[4]	k	0.56	0.52	1.00
6	Gamma kernel		1/s	0.16	0.13	2.63
			p	0.11	0.12	0.38

Discussion: From this dataset the use of a dispersion kernel appears to be most appropriate with either the modified Gaussian or gamma kernel, these two models being virtually indistinguishable. It has been established that the Hrabe and Lewis model may result in non-causal solutions with the Gaussian kernel [2]. This was addressed by the modification of [4], although symmetrical dispersion of label along the vessel is still permitted. The gamma dispersion kernel both guarantees causal solutions and assumes that the dispersion occurs asymmetrically, consistent with flow in the vessel.

None of the models investigated here reflects the greater physiological accuracy that might be achieved by a more thorough modelling of the fluid dynamics within the arterial vasculature, as in [3]. However, the mathematical form of these models is sufficiently simple to compute and could therefore be routinely incorporated into ASL perfusion analysis. A limitation for the use of dispersion models in ASL tissue signal analysis is the specification of the values for parameters in the model, since it is unlikely that they can be estimated accurately from tissue data. The values in Table 1 are indicative of those expected *in vivo* and represent a first estimate for use in tissue modelling. However, additional dispersion effects are to be expected further along the vascular network, for instance in grey matter tissue.

The cohort considered here is older and contains atypical vasculature arising from stenosis and thus might be expected to exhibit greater effects of dispersion than a younger healthier group. The results indicate that it is feasible to employ models of dispersion within such a population and by implication that this should also be possible within other groups. Future work could address whether dispersion differences can be quantified between population cohorts, for example.

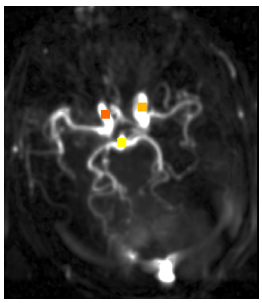

Figure 1: Estimated aBV in one subject using model 1 showing arterial ROIs.

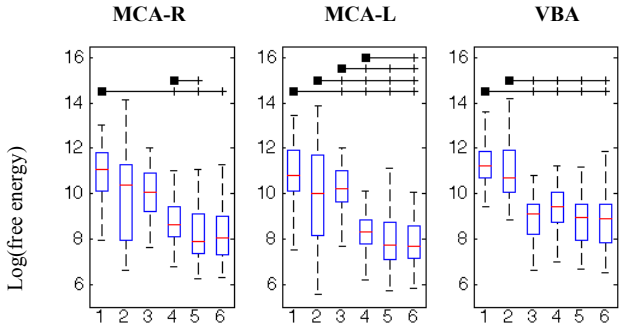

Figure 2: Mean of the natural logarithm of the free energy across all subjects in the three arterial ROIs. Significant improvements shown by horizontal bars (one tailed t-test, p<0.05).

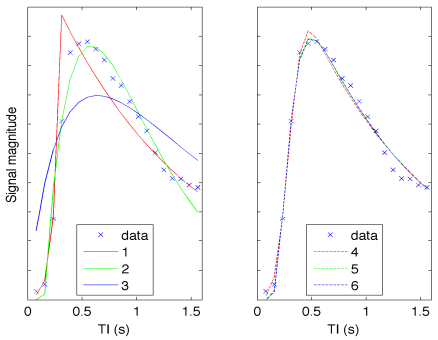

Figure 3: Example model fits from a VBA voxel in one subject (same data on both axes).

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