Possible evidence for multiple vascular pathways in cerebral ASL perfusion measurements

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INTRODUCTION: Arterial Spin Labelling (ASL) offers a non-invasive method to measure Cerebral Blood Flow (CBF). The ASL signal, the difference image with and without the presence of magnetically tagged blood, is small compared to the noise present, hence it is typically necessary to measure data at various time points and fit to some physiological model. Kinetic Curve models (e.g. [1, 2]) describe the transit of a bolus of blood after magnetic inversion has been applied. The use of a kinetic model allows the effects of various physiological variables to be taken into account, for example the variable delay time, Δt , for the bolus to reach different areas of the imaged region. It is generally assumed that the ASL data can be explained by the arrival of a single bolus. However, it is possible that, at least in some subjects, the blood supply to some regions of the brain arrives by more than one route. Thus, multiple boluses each with a different Δt (since each path is likely to be of differing length) might explain the observed ASL signal.
We have recently developed a method for inferring the parameters of a kinetic curve model using a Bayesian approach [3]. This permits the physiological parameters to be determined from measured data, whilst allowing uncertainty in the various model parameters to be incorporated. Here, this method has been modified using Automatic Relevance Determination (ARD), which has been used previously to automatically determine the number of crossing fibres in diffusion tractography [4]. Here it allows us to test the relative ability of models incorporating either a single or two boluses to explain observed ASL data.

METHODS: The data each at voxel is modelled by a kinetic curve model plus additive white Gaussian noise. The Variational Bayes method seeks to infer the parameters of both the model and the noise from the data via Bayes' theorem [5]. By using a Bayesian approach prior information about the variability of the parameter values can be incorporated, e.g. uncertainty in T_1 . To test whether there is evidence for a second bolus a modified kinetic curve model was used: The two bolus model is the sum of two (single bolus) kinetic curves using the model of [1], where each curve has its own perfusion and delay time parameters, the other parameters (e.g. T_1) being common to both boluses.
To test for the appearance of a second bolus in ASL data the Variational Bayes algorithm was modified to include ARD. This is applied to the perfusion contribution of the second bolus, the prior for which is initially set to be uninformative with zero mean, but is itself updated during the Variational Bayes inference procedure. If the data supports the second bolus then the prior retains a large variance, hence the perfusion corresponding to the second bolus can take a non-zero value. If, however, there is no support for the extra complexity introduced by the second bolus then the variance collapses and it is suppressed.

RESULTS AND DISCUSSION: The results presented here are from data acquired using a pulsed ASL sequence of Q2TIPS with PICORE [6]. Data was collected for 10 TI points (0.3, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2.1, 2.5, 3.0 seconds), each of which was repeated for 30 pairs. The data was smoothed using 2D Gaussian filter with a standard deviation of 1 voxel. Figure 1 shows the maps of perfusion for the first and second bolus for two subjects. It can be seen that in certain areas of the brain the ASL perfusion data can be explained by the presence of two separate boluses arriving after different delays post-inversion. Figure 2 shows kinetic curves from voxels where there is significant perfusion associated with the second bolus. These show to what extent a second bolus is supported by data at the later TI points. Figure 3 shows the distributions of delay time in the two boluses for both the subjects considered here.

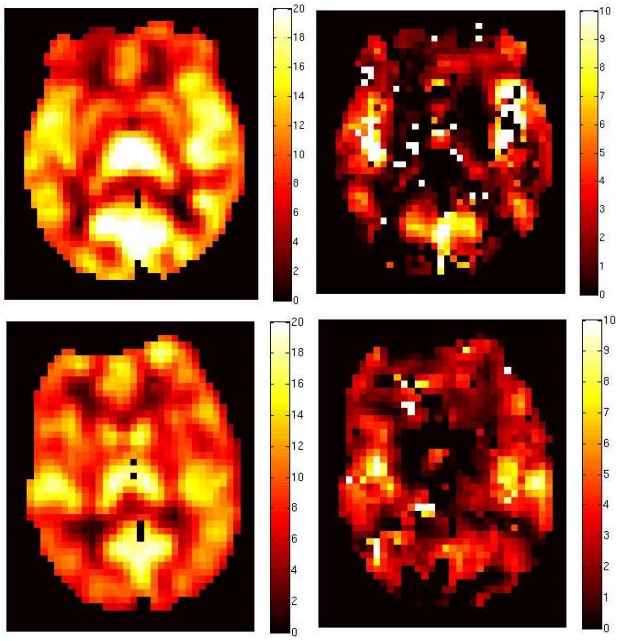

Figure 1: Maps of perfusion contribution from the two boluses (left and right) in two subjects (1: upper, 2: lower).

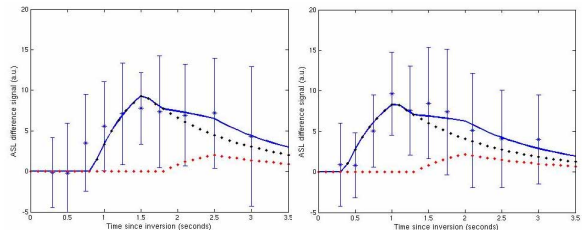

Figure 2: Time series plots from the two subjects of Figure 1 (1: right and 2: left), showing the orignal data (mean ± 1 s.d.), model fit (blue) and the two boluses (black and red).

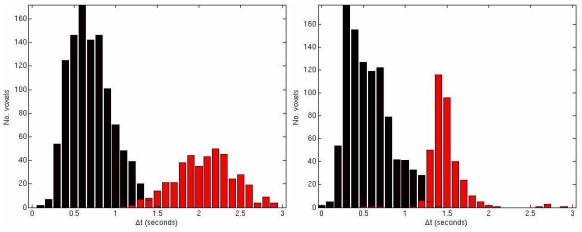

Figure 3: Distribution for delay times for first (black) and second (red) bolus, for the two subjects of Figure 1(1: right and 2: left).

A total of 8 subjects have been analysed and significant variation in the maps for the perfusion contributed by the second bolus was observed. This may be expected, as it is likely that there will be significant inter-subject variation [7].
The deviation of the measured data from the kinetic curve may also be partly due to dispersion of the bolus as it travels through the circulation. It is possible to include dispersion within the Variational Bayes framework, for example using a modified kinetic curve model [2]. Preliminary results suggest that both dispersion and two boluses partially explain the observed data. Further investigation will be required to investigate the effects of both dispersion and multiple boluses on ASL measurements.
Ultimately these results support the possibility that in some subjects the ASL perfusion data can be explained by two boluses of blood arriving via differing vascular routes. For example, this may in part be due to separate tagging of blood in the carotids and the vertebrals. However, these preliminary results are far from conclusive. A significant difficulty is that evidence for a second bolus is present in the later TI points, which typically contain greater noise. It is hoped that the appearance of multiple boluses can be investigated by acquiring more data at longer inversion times, and by selectively tagging blood in individual vessels entering the brain, e.g. using selective ASL [7].

REFERENCES:

1. Buxton, R.B., et al., Magnetic Resonance in Medicine, 1998. **40**(3): p. 383-96.
2. Hrabe, J. and D.P. Lewis, Journal of Magnetic Resonance, 2004. **167**(1): p. 49.
3. Chappell, M.A., et al., Proc. ISMRM, Berlin, 2006, submitted.
4. Behrens, T.E.J., et al., Neuroimage, 2006: in press.
5. Attias, H., Proc. Advances in Neural Information Processing Systems, 2000. p. 49-52.
6. Luh, W.M., et al., Magnetic Resonance in Medicine, 1999. **41**(6): p. 1246-54.
7. Van Laar, P.J., et al., NeuroImage, 2006. **29**(1): p. 136.