Bayesian inference of Kinetic Curve models for ASL perfusion measurements

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INTRODUCTION: By manipulating the magnetic properties of blood Arterial Spin Labeling (ASL) techniques allow Cerebral Blood Flow (CBF) to be estimated without intravascular tracers. Blood is 'tagged' by magnetic inversion before entering the imaging region and an image collected after a delay: the inversion time (TI). Subtraction of this image from a control, taken once the residual magnetization has cleared, allows flow of blood to be estimated, assuming that the static magnetization in the two images is identical.

In practice local effects mean that the difference image cannot directly be used as an accurate measure of CBF. For example, tagging is performed in a region distant from the imaging region, hence there is some delay before the tagged blood arrives, Δt , which varies across the brain. The time evolution of the magnetization in the ASL process, called the kinetic curve, can be described in terms of a simple kinetic model [2]. Thus, one solution to the above problem is to collect images at multiple inversion times and fit the resulting data to the kinetic curve, allowing the estimation of both Δt and CBF. Previously this has been achieved using some form of curve fitting procedure, e.g. [2]. However, this approach cannot incorporate the uncertainty of other parameters in the model, such as the T_1 of blood, which might bias the estimates. Here we propose an alternative Bayesian inference method, which not only allows Δt and CBF to be inferred from the data, but also permits the variance on these estimates and an estimate of the noise in the data to be calculated, as well as allowing our prior knowledge about the parameters to be incorporated.

METHODS: The data at each voxel, *y*, is modeled as:

$$y = g\left(TI, \Delta t, CBF, T_1\right) + \varepsilon\left(TI\right),$$

where *g* is the (non-linear) kinetic curve model describing the difference signal at TI in terms of the physiological parameters and ε is additive white noise. A separate noise model is used for each TI, allowing the individual variance of the data at each TI point to be incorporated. Since a Q2TIPS sequence is used (see below) the tagged bolus width is assumed to be fixed, in this case at 0.7 seconds. Parameters in the model are estimated from the data by using an inference scheme based on Bayes' theorem:

$$P\left(\Delta t, CBF, T_1 \mid y\right) \propto P\left(y \mid \Delta t, CBF, T_1\right) \cdot P\left(\Delta t, CBF, T_1\right),$$

i.e. the probability of the model parameters taking a value given the data presented, is proportional to the probability of generating the data given those parameter values (the likelihood) and the parameters' prior probabilities. The most probable parameter values are those that maximize this posterior probability. The likelihood is calculated from the difference between the data and the model predictions, and the prior probability distributions are chosen as Table 1 reflecting pre-existing knowledge about the parameters.

Since it is not possible analytically to determine the posterior probability, the Variational Bayes' [3] approach was taken, whereby the posterior is factorized into terms separately representing physiological and noise parameters. Additionally, since the kinetic curve model is non-linear, a linear approximation is made about the mean of the posterior distribution. Estimation of the measures of these distributions then follows an iterative approach, alternating between updating physiological and noise distributions.

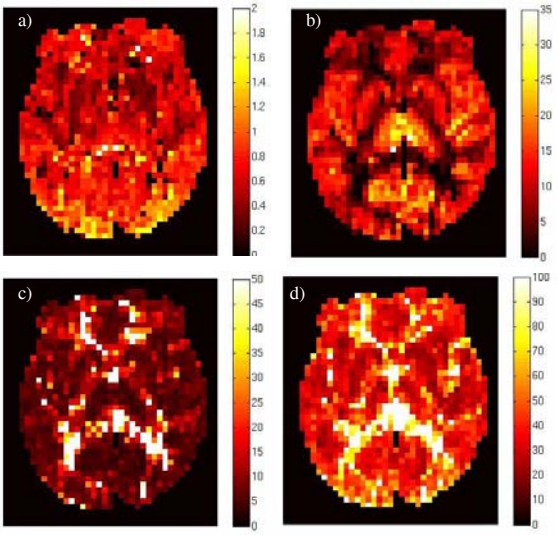

Figure 1: Maps of a) Δt (seconds), b) CBF estimates (arbitrary units), c) variance on Δt estimates (%) and d) variance on CBF estimates (%).

Table 1: Prior distribution measures for parameters.

Parameter	Mean	Standard deviation
Δt	0.7 s	2 s
CBF	0	1000*
T_1	1664 ms	40 ms [1]

*uninformative prior: no pre-existing information about CBF assumed

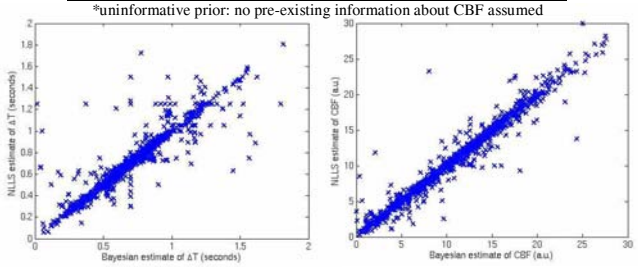

Figure 2: Comparison of Δt (left) and (right) estimates from Non-linear Least Squares (NLLS) regression and Bayesian inference.

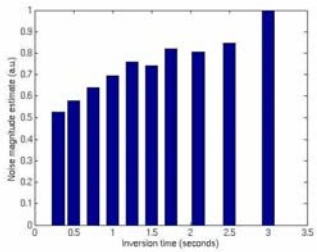

Figure 3: Estimated noise magnitude at each inversion time.

RESULTS AND DISCUSSION: The results presented here are from data acquired using a pulsed ASL sequence of Q2TIPS with PICORE [4]. 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. Figure 1 shows the estimated maps of Δt and CBF for one subject along with the associated variance estimates of the two parameters. Across the slice Δt varies between 0.3 and 2 seconds, with the larger delay times in the occipital cortex. As would be expected, CBF values are greater in the gray than white matter. Additionally, predicted CBF values are almost zero in the CSF with a large variance, implying, as expected, that in this region there is little evidence for the kinetic curve model.

Estimates of Δt and CBF produced by non-linear least squares regression produces results that appear similar to those of the Bayesian inference method, although a more detailed comparison, as shown in Figure 2, indicates significant differences for a number of voxels. For both parameters there is greater than 10% difference in the estimate in approximately 20% of the voxels. This may be at least partially explained by the more accurate modeling of the noise process within each TI point in the Bayesian approach. This is illustrated in Figure 3, where the estimate of noise magnitude at each TI point is shown. As might be expected, the noise increases approximately linearly with TI, which arises from the pre-saturation applied at inversion to suppress the tissue signal. Post-inversion the tissue signal recovers and likewise the noise on this signal, which itself will be evident once the tag image is subtracted from the control.

The Variational Bayes method produced results for multiple-TI ASL data consistent with the existing methods. However, it has it has the advantage of incorporating uncertainty in the model parameters along with variation of the within-TI noise.

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