Modeling the ASL Signal Under Dynamically Changing Perfusion and Arterial Transit Time: Considerations for Event Related FMRI

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Introduction: The existing models for the ASL signal have been developed primarily for constant perfusion at the microvascular level, and constant flow velocity (transit time) at the macrovascular level. During periods of activation, perfusion becomes elevated by approximately 30%, and the mean arterial velocity increases locally such that there is approximately 100ms reduction in transit time [1,2]. While some ASL approaches are not sensitive to transit time changes [3], the faster approaches are very sensitive to them, potentially inverting the ASL signal [2,4]. Hence, as ASL becomes increasingly popular as a functional imaging tool, we must consider the system as a dynamic one in order to properly formulate models for event related experiments. We have formulated a simple numerical model for arterial spin labeling based on the analytic models proposed earlier [5,6] and consider transit time and perfusion as time-varying functions. To this end, we use the transport equation to approximate the arterial compartment and use a first order kinetics for the tissue compartment, as in [5,6]. This model can be used to study the relationship between perfusion, arterial transit time and the ASL signal during a period of activation and can be used to optimize and design acquisition parameters.

Methods: As depicted in Fig. 1, the model considers the arteries as a set of discrete compartments that feed into each other from the tagging plane to the voxel of interest and beyond. The dispersion effect of the arterial network can be approximated by smoothing the input function with a Gaussian kernel. The passage of the tag through the arterial compartment, *A(x,t)*, is characterized with the transport equation:

$$\frac{\partial A(x,t)}{\partial t} = -V_{art}(t) \cdot \frac{\partial A(x,t)}{\partial x} - R_{1art} \cdot A(x,t) \qquad (1)$$

where $V_{art}(t)$ is a time-varying arterial velocity function that reflects the observed changes in transit time. The added R_{1art} term represents the decay of the tag.. At the voxel of interest, the tag is partly taken up by a tissue compartment (defined as tissue as well as microvasculature) at a rate *f(t)* (perfusion). The tissue uptake at the voxel of interest is described by:

$$\frac{\partial T(t)}{\partial t} = f(t) \cdot A(t) - f(t) \cdot T(t) - R_{1tis} \cdot T(t) \qquad (2)$$

where *T(t)* is the tag content at the voxel of interest. The tag is assumed to spend enough time in the tissue to decay R_{1tis} completely before reaching the venous compartment, so the outflow term in equation (2) is neglected and the venous contribution to the signal is not considered [5,6].

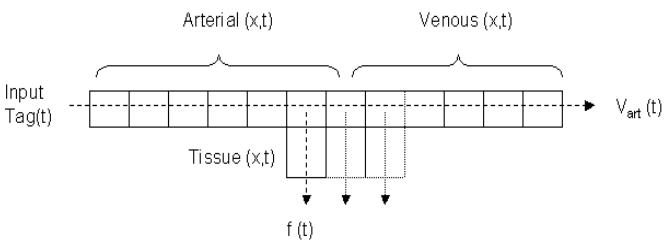

Figure 1 – Depiction of numerical ASL model

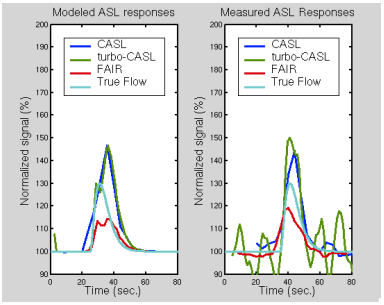

Figure 2 – Modeled and acquired data

This model was implemented using Euler's method with very small time steps (0.0001 second) to maintain accuracy. The model was verified by conducting an experiment on a perfusion phantom of our design [7], in which the arterial velocity function (*Vart(t)*) was tightly controlled by a computer driven peristaltic pump. The pump was programmed such that a canonical response function (SPM99) was repeated 10 times (once every eighty seconds). The baseline flow was 1.25 ml/min/ml and it increased up to 30% at the peak of the response function. This paradigm was repeated three times, during which ASL time series of images were collected using standard CASL and a modified turbo-CASL using a separate labeling coil, as well as FAIR. Flow crushers were used (b ~ 4 s/mm^2) in the FAIR case. Because flow crushers were not used in the CASL experiments, the arterial signal was included in the model for those cases. The trials were selectively averaged after sinc subtraction of the ASL data [8]. The resulting response functions were compared to each other and to the model's predictions.

Results and Discussion: At steady state conditions, the numerical model agrees with our previous findings about the signal dependence on TR [2] (not shown). Under activation conditions, the model also reflects the differences in signal between the three acquisition schemes (figure 2) tested and can be used to design acquisition schemes. Both CASL and Turbo-CASL can exaggerate the responses non-linearly, thus increasing the sensitivity in fMRI experiments. We are currently working on parameter fitting schemes for quantification of perfusion from this numerical model.

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References: [1] Gonzalez-At et al, MRM 43, p.739 (2000) [2] Hernandez-Garcia et al, MRM, in press [3] Alsop et al., JCBFM 16, 1236-1239(1996) [4] Wong et al, Proc. ISMRM 9 p.1162 (2001) [5] Buxton et al MRM 40 p.383, (1998) [6] Williams et al. Proc. Natl. Acad. Sci 89, p. 212-216 (1992) [7] Lee et al. Proc. ISMRM, p.1057 (2002) [8] Aguirre et al, Neuroimage 15, p.488-500(2002)