Modeling the Effect of Flow Dispersion in Continuous Arterial Spin Labeling

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Introduction: Arterial spin labeling (ASL) is capable of quantifying tissue perfusion non-invasively. Quantification of ASL perfusion measurements typically assumes that the flow from the labeling plane to the tissue is simple plug flow, i.e., all labeled blood requires the same transit time to the tissue. However, flow in the major arteries and branches into the brain is complicated, and may not be well approximated by simple plug flow. Flow dispersion models, including a Gaussian distribution (1,2) and a model based on fluid dynamics (3), have been used to describe the distribution of transit delay for pulsed labeling. For continuous labeling, only one model has been used to approximate flow dispersion (4). The use of dispersion models for quantification has not been widespread, in part because numerical methods are typically required to produce the signal curve. Here we propose the use of the gamma variate function without additional delay as a model distribution for perfusion quantification. The ASL signal from a gamma variate distribution can be readily expressed in terms of incomplete Gamma functions; a function that is readily available in most analysis environments, including MATLAB and IDL. The model was fit to experimental CASL data to validate the flow dispersion curve shape and estimate flow dispersion in the human brain.

Theory: A gamma variate distribution of transit times is assumed. This distribution is of the form p(δ) in Eq. [1] where η and m are parameters, Γ is the Gamma function and δ is the transit time. This mean, δ_m , and standard deviation, σ, of this distribution are shown in Eqs. [2] and [3]. A CASL kinetic model has been presented to describe the relationship between the difference signal (ΔM) and perfusion (*f*) (5,6). The standard kinetic model assuming a single transit time is shown in Eq. [4] where M_{0b} is the equilibrium magnetization of arterial blood, α is the labeling efficiency, T_{1t} and T_{1a} are the T1's of tissue and arterial blood, w is the postlabeling delay, and τ is the labeling duration. In reality, a spread in transit time may exist due to a more complicated flow velocity profile. The signal expression can be integrated over the gamma variate transit distribution to provide a result with dispersion. For infinite labeling duration, the signal is described by Eq. [5]. where Γ(m+1,x) is the incomplete gamma function readily calculated with available functions in environments such as MATLAB and IDL. For finite labeling duration the signal is given by Eq. [6].

$$p(\delta)=\frac{1}{\eta\Gamma(m+1)}\left(\frac{\delta}{\eta}\right)^m e^{-\frac{\delta}{\eta}} \quad [1] \qquad \delta_m=(m+1)\eta \quad [2] \qquad \sigma=\sqrt{(m+1)}\eta \quad [3]$$

$$\Delta M=2M_{0b}\cdot\alpha\cdot T_{1t}\cdot f\cdot e^{-\delta/T_{1a}}\cdot\left(e^{-\max(w-\delta,0)/T_{1t}}-e^{-\max(\tau+w-\delta,0)/T_{1t}}\right) \quad [4]$$

$$\langle\Delta M\rangle(w,\tau=\infty)=2M_{0b}\cdot\alpha\cdot T_{1t}\cdot f\cdot\left(e^{-\left(\frac{w}{T_{1t}}\right)}\left(1+\eta\left(\tfrac{1}{T_{1b}}-\tfrac{1}{T_{1t}}\right)\right)^{-(m+1)}\left(1-\frac{\Gamma(m+1,w\left(\frac{1}{\eta}+\left(\frac{1}{T_{1b}}-\frac{1}{T_{1t}}\right)\right)}{\Gamma(m+1)}\right)+\left(1+\frac{\eta}{T_{1b}}\right)^{-(m+1)}\frac{\Gamma(m+1,w\left(\frac{1}{\eta}+\frac{1}{T_{1b}}\right)}{\Gamma(m+1)}\right) \quad [5]$$

$$\langle\Delta M\rangle(w,\tau)=\langle\Delta M\rangle(w,\tau=\infty)-\langle\Delta M\rangle(w+\tau,\tau=\infty) \quad [6]$$

Methods: Pulsed-continuous arterial spin labeling (PCASL) (7) images were acquired on a GE 3 Tesla scanner with a 3D stack of spirals RARE sequence. Background suppression was interleaved with the labeling (8). A vessel suppression (VS) preparation pulse was applied immediately prior to image acquisition (9). The PCASL difference images were sequentially acquired with labeling duration of 2 s and nine post-labeling delays of 0.7 s, 1.0 s, 1.3 s, 1.6 s, 1.9 s, 2.2 s, 2.5 s, 2.75 s, and 3.0 s. Each acquisition was performed with six interleaves and two averages, producing a spatial resolution of 3.75 mm. The ASL data at nine post-labeling delays were pixel-by-pixel fit to the standard model and to the proposed dispersion model. Fitting was performed in MATLAB by minimizing the sum of square residuals. R square maps were calculated from both fittings.

Results & Discussions: R square difference maps (Fig. 1f) show that the dispersion model produces a better or equivalent fit across all brain voxels compared to the standard model. Typical fitting quality is shown in Fig. 2. The curve from the dispersion model is smoother, unlike the standard model with the physiologically unlikely peak shape. The dispersion model gives similar fit quality for the red voxel (Fig. 2f, m=287 and η=0.0039) and clearly better fit for the green voxel (Fig. 2h, m=2.79 and η=0.42) compared with the standard model. Indeed, the dispersion model will converge to the standard model when m goes to infinity and η goes to zero. This indicates that the transit delay of the red voxel is close to plug flow but not the green pixel. The signals in the spatial locations with large flow dispersion will be better described by the dispersion model, but not by the standard model. Therefore, The R square difference map reflects the degree of flow dispersion. It can be seen that deep gray matter regions have less dispersion and posterior regions have more, consistent with results reported with the PASL (10). The mean and standard deviation of transit time calculated from Eqs. [2] and [3] in the dispersion model are shown in Fig. 1b and Fig. 1g. The standard deviation of transit time is a quantitative measure of dispersion, which shows a similar distribution to the R square difference map. The histogram of fractional dispersion, defined as a ratio of the standard deviation to the mean of transit time, demonstrates that the overall fractional dispersion of gray matter voxels is approximately 0.2.

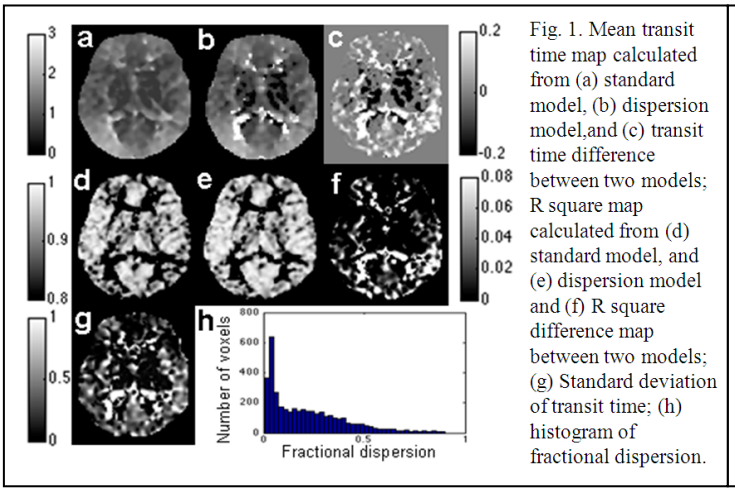

Fig. 1. Mean transit time map calculated from (a) standard model, (b) dispersion model,and (c) transit time difference between two models; R square map calculated from (d) standard model, and (e) dispersion model and (f) R square difference map between two models; (g) Standard deviation of transit time; (h) histogram of fractional dispersion.

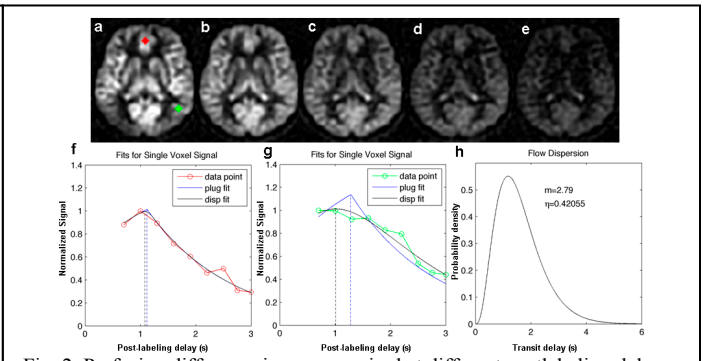

Fig. 2. Perfusion difference images acquired at different postlabeling delays: (a) 0.7 s, (b) 1.3 s, (c) 1.9 s, (d) 2.5 s, (e) 3.0 s; (f) fits to the signals from single voxel shown as red pixel in (a); (g) fits to the signals from single voxel shown as green voxel in (a); (h) the dispersion produced from the fit in (g) using dispersion model.

References: 1. Wu et al, IEEE Trans Med Imaging 2007;26(1):84-92. 2. Hrabe et al, J Magn Reson 2004;167(1):49-55. 3. Kazan et al, IEEE Trans Biomed Eng 2009;56(6):1635-1643.4. Gonzalez-At et al, Magn Reson Med 2000;43:739-746. 5. Buxton et al, Magn Reson Med 1998;40:383-396. 6. Alsop et al, Journal of Cerebral Blood Flow and Metabolism 1996;16:1236-1249. 7. Dai et al, Magn Reson Med 2008;60(6):1488-1497. 8. Dai et al, 18th ISMRM 2010:1748. 9. Dai et al, 17th ISMRM 2009:1512. 10. Gallichan et al, Magn Reson Med 2008;60(1):53-63.