Three-compartment modeling of the arterial-spin-labeling data at different post-labeling delays with and without flow-attenuating gradient

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[Introduction] Several models have been published to quantify cerebral blood flow (CBF) data using arterial spin labeling (cASL) techniques. A one-compartment model without distinguishing vascular contribution is widely used. Recently, a two-compartment model that separate tissue and vessel component has been proposed. Arterial and capillary components were however not distinguished in this model. We observed that three major regions of the brain (cortical gray matter (GM), white matter (WM) and caudate-putamen (CP)) showed three distinct patterns of ΔS/S versus post labeling delays and these patterns were modulated by flow attenuating gradients, suggesting perfusion parameters including arterial and capillary contributions may be uniquely different among these regions. We thus hypothesize that different arterial and capillary contribution in different brain region is likely a major factor. In this study, we propose to a three-compartment model to include different vascular contributions to the cASL signals. We modulated the vascular contribution by performing cASL measurement at different post-labeling delays and by applying flow-attenuating gradient to preferentially eliminate the arterial component.

[Material and Methods] Rhesus monkeys (n =5, 6.2-7.5 kg) were anesthetized under 0.9-1.1% isoflurane. MRI was performed on a 3T Siemens Trio. CBF was measured using a separate neck coil for cASL (1) with and without a diffusion gradient (b = 30 s/mm^2, n=3). The MRI parameters were: single shot GE EPI, TR/TE = 4900/55 ms, FOV = 96×96 mm, matrix = 64×64, thickness 1.5 mm, labeling duration 2.0 s, labeling gradient of 0.3 G/cm, 16 slice, and eight post-labeling delay (ω), ranging from 100ms to 1500 ms for the first imaging slice. ω for subsequent slices took into account the slice acquisition time. T_1 maps were acquired to segment GM and WM. ΔS/S was analyzed for GM, WM and CP. Our three-compartment is based on Alsop's formalism (2). Three different transit times to the artery (δa), capillary (δc), and water exchange (δex) were incorporated to account for three compartments (**Fig 1**). For the single-compartment model, $\Delta S/S = A\,f\,Ct \times Ktis$ (1); for the two-compartment, $\Delta S/S = A\,f\,(Ct \times Ktis + Cc \times Kc)$; and for the three-compartment model, $\Delta S/S = A\,f\,(Ct \times Ktis + Cc \times Kc + Ca \times Ka)$; where f=CBF, $A=2\alpha/\lambda$, Ct, Cc and Ca are contribution of tissue/capillary/arterial component. Ct+Cc+Ca=1. $Ktis = T_1ns \exp(-\delta ex/T_1a) \times [\exp(\min(\delta ex - \omega), 0)/T_1ns) - \exp(-\omega/T_1ns)(1 - T_1s/T_1ns)]$, $Kc = T_1a\,[\exp((\min(\delta c - \omega, 0) - \delta c)/T_1a) - \exp((\min(\delta ex - \omega) - \delta ex)/T_1a)]$, $Ka = T_1a\,[\exp((\min(\delta a - \omega, 0) - \delta a)/T_1a) - \exp((\min(\delta c - \omega) - \delta c)/T_1a)]$. δex and venous contribution was ignored here.

[Results & Discussion] **Fig 2** shows the simulations of ΔS/S versus the post-labeling delays (ω) data with and without diffusion gradient assuming Cc=0.1. At long ω, there were no differences between with and without diffusion gradient at each Ca contribution as expected because arterial component is minimized at long ω. At short ω, differences between with and without diffusion gradient became larger with increasing arterial contribution (Ca). **Fig 3** shows the effect of diffusion gradient on Cc contribution assuming Ca=0.01. With increasing capillary contribution (Cc), a difference at ω ~1.0-1.5 s became evident. This is likely due to T1 difference between blood and tissues (i.e., labeled waters in the vessels decay with blood (T_1a) and once exchange with tissue will decay with tissue T_1 was also found to play a role).

Experimental cASL data were acquired at different ω with and without flow-attenuating gradients to modulate the arterial contribution. These results are plotted for 3 tissue types: WM, GM and CP (Fig 4). At long ω, there were no differences in ΔS/S between with and without diffusion gradient. At short ω, ΔS/S attenuation by diffusion gradient was the strongest in CP and smallest in WM. This is because the CP has high density of perforating arteries, less in GM and smallest in WM. The three-compartment models with and without considering arterial component adequately fitted our data without and with diffusion gradient. The resultant parameters from fitting were: Ca = 0, 0.05 and 0.4 in WM, cGM and CP, respectively, and Cc = 0.1-0.2 over all three tissue types. A possible explanation of this observation is that CP has a large density of perforating arteries, whereas capillary density (Cc fraction) is expected to be similar across the three tissue types.

[Conclusion] The density of perforating artery is remarkably different in different brain regions. Three-compartment model accounting for different vascular contributions fitted the ΔS/S versus post-labeling delay data over a wide range of post-labeling delays with and without arterial component. These results suggest that accounting for arterial and capillary contributions is likely to be important to better understand the CBF signal sources.

[References] 1) Zhang X et al. Neuroimage in press, 2006. 2) Alsop DC and Detre JA, JCBFM 16, 1236-1249, 1996.

Fig 1. Schematic Diagram of transit time

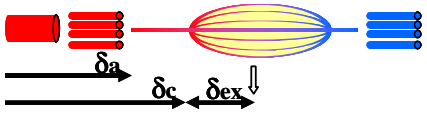
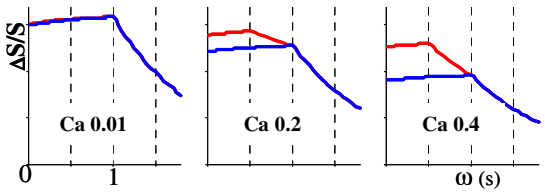
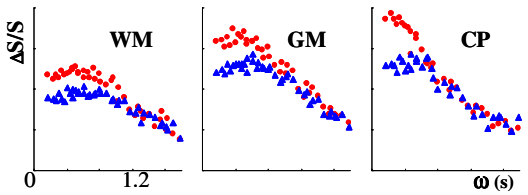
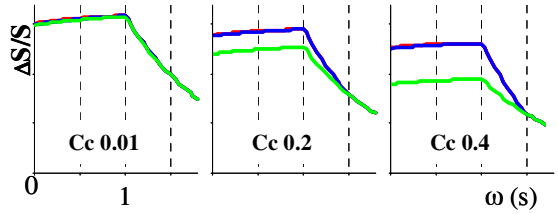


Fig 2. Simulation of ΔS/S dependence on Ca without (red) and with (blue) diffusion gradient





⇐ **Fig 3**. Simulation of ΔS/S dependence on Cc without (red) and with (blue) diffusion gradient tissue component (green)



⇐ **Fig 4**. ΔS/S vs delay ω without (red) and with (blue) diffusion gradient.