Impact of Model Choice on Quantitative Perfusion Measurements using Continuous Arterial Spin Label Imaging

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Introduction: Quantitative perfusion in units of ml blood/100 g/min may be derived from arterial spin label (ASL) images using models with different underlying assumptions. These may be divided into "tissue-based" and "blood-based" models based on whether the model is formulated from the standpoint of the imaged voxel or labeled blood, respectively. In tissue-based models [1-2], perfusion is proportional to the ratio of the difference (control - label) images and control images ($\Delta M/M_{control}$), while in blood-based models [3-4], perfusion is proportional only to the difference signal (ΔM). This study compares perfusion levels calculated with four previously reported models using a continuous ASL method under typical clinical imaging conditions to assess whether significant perfusion differences may occur solely due to post-processing model choice.

Methods: Multislice CASL [5] was performed in 16 volunteers (age 34±7, range 22-52 yrs) with a Philips 1.5 T Intera magnet. TR/TE/label time/post-label delay = 4300/32/2500/1000-1675 ms, SE-EPI, 6 mm thick, 3.75 mm in-plane resolution, with collection of 34 pairs of control and label images for a total imaging time of 5 min. Conversion of the raw data to perfusion levels was performed using four models: a two-compartment tissue-based model [1], a four-compartment tissue-based model [2], and full [3] and simplified [4] blood-based models. Segmentation into cortex, deep gray, and white matter was achieved using SPM2. The following parameters were derived from previous reports: α=0.71, λ_{blood} = 0.76, λ_{brain}=0.90, arterial arrival time=0.8 s, $T1_{gray}$ without and with RF=0.92 and 0.75 s; $T1_{white}$ without and with RF=0.79 and 0.64 s, respectively; $T1_{csf}$=4.2 s, $T1_{blood}$=1.2 s, $T2_{blood}$ =0.24 s, ρ_{blood} = 1.05 g/cc. CSF signal intensity was used to determine $M_{0,blood}$ for blood-based perfusion measurements [4]. $p<0.05$ using repeated-measures ANOVA was considered significant.

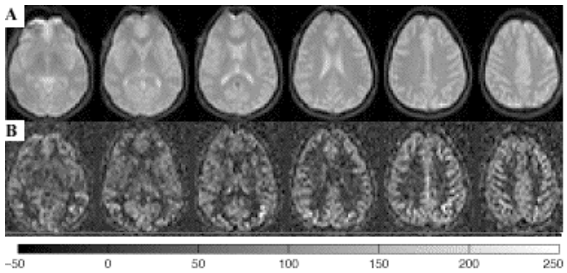

Fig 1: Selected (a) anatomic images (b) perfusion images calculated using model 3. Scale is in ml blood/100g/min

Perfusion (ml/100g/min)	Cortex	Deep Gray	White	
Model 1 Two-compartment	111±28	80±21	62±23	A
Model 2 Four-compartment	81±20	58±15	33±12	B
Model 3 Full blood-based	84±20	54±14	39±14	B
Model 4 Simple blood-based	67±16	47±11	23±8	C

Table 1: Models joined by the same letter at right are not significantly different at $p<0.05$.

Results: Fig 1 shows selected (a) anatomic and (b) perfusion maps created with the full blood-based model (#3). Table 1 demonstrates no difference between the four-compartment tissue-based model (#2) and full blood-based model (#3); however, they were significantly different from the two-compartment model (#1) and simplified blood-based model (#4). Given this, perfusion measurements of the four-compartment tissue-based model and the full blood-based model (#2&3) were averaged together to use as a baseline for further comparisons. These models were chosen for the baseline since they were found to be equivalent and because the four-compartment model is the only ASL model to be compared with 15-O water PET [6]. Bland-Altman plots, which plot the difference between two data sets as a function of their mean, are used to evaluate for systemic differences between data sets. Plots of difference vs. the mean for Models 1 and 4 demonstrate highly significant linear fits with near zero intercept, corresponding to direct proportionality (Fig 2). Converting these slopes to percent change demonstrates that the two-compartment model overestimates the baseline perfusion measurements by an average of 40%, 47%, and 78% in cortex, deep gray, and white matter, respectively; the simplified blood-based model underestimates the baseline measurement by 21%, 21%, and 38% in these same regions. Within-subject standard deviations of the individual voxel perfusion measurements were different for all 4 models, with the simple blood-based model being the lowest (Least mean squares, all regions: Model 1: 55±2, Model 2: 35±2, Model 3: 40±2, and Model 4: 28±2 ml/100 g/min, all significantly different, $p<0.05$).

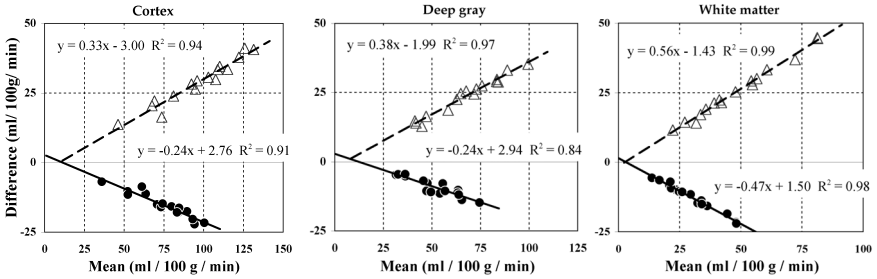

Figure 2: Bland-Altman plots of perfusion difference vs. mean. △ two-compartment tissue-based (#1); ● simple blood-based (#4); Baseline is mean of Models #2&3. Each point is a measurement in a separate individual.

Discussion: Since different ASL post-processing models yield different calculated perfusion values when given the same raw data, attention to the model used to derive quantitative perfusion levels is necessary. Equivalence between the four-compartment tissue-based model and full blood-based model was demonstrated under clinical imaging conditions in young volunteers. The smaller scatter of voxel perfusion levels within the same individual may favor the use of the four-compartment model over the full blood-based model.

Of the two methods, perfusion images created using tissue-based models must be careful masked, since the ratio ($\Delta M/M_{control}$) used in its calculation is highly variable if the control signal intensity is low. Blood-based methods avoid this problem, but may be inaccurate in the setting of inhomogeneous receive coils, surface coils, or in regions with signal loss due to susceptibility, given the model's assumption of uniform sensitivity to the labeled blood. In general, blood-based methods would be expected to yield lower perfusion values, as they assume that the labeled protons never experience the lower T1 relaxation times of either white or gray matter (compared with blood). For both methods, the possibility that mean white matter arrival times are significantly different from gray matter arrival times may bias estimates of white matter perfusion. Unfortunately, direct measurement of arrival times is not currently feasible in the clinical setting.

References: 1. Wang et al., MRM 48:242-254 (2002); 2. McLaughlin et al., MRM 37:501-510 (1997); 3. Buxton et al., MRM 40:383-392 (1998); 4. Chalela et al., Stroke 31:680-687 (2000); 5. Alsop et al., Radiology 208:410-416 (1998); 6. Ye et al., MRM 44:450-456 (2000).