Sensitivity to bolus dispersion in continuous and pulsed multi-TI ASL techniques

Roman Fleysher[1], Mark Wagshul[1], Michael Lipton[1], and Craig Branch[1]
[1]*Gruss Magnetic Resonance Research Center, Department of Radiology, Albert Einstein College of Medicine, Bronx, NY, United States*

Introduction. In both clinical and research settings, arterial spin labeling (ASL) is used to provide information on regional CBF non-invasively using MRI. In elderly patients and those with cardiovascular disease, variable transit delays and label dispersion lead to bias in CBF measurements. The magnitude of the bias, therefore, is a function of the status of the disease which undermines comparisons across subjects and determination of absolute thresholds for normal and abnormal regional CBF. Several models have been proposed to describe delay and dispersion in pulsed and continuous ASL experiments[1-5] as well as deconvolution-based model free Quasar ASL to avoid such modeling all together[6]. These techniques rely on acquisition at multiple inversion (TI) times. Radiologists, MRI researchers and scanner manufactures are, consequently, interested in determining which of the ASL techniques is capable of handling the issue most effectively. To address this question Gaussian dissipation and single compartment Kety models are typically employed[1,3,6]. However, both were found to be inadequate for description of ASL experiments because (*i*) bolus disperses continuously as it travels down the vascular tree and must be modeled as such all the way to the capillary level and (*ii*) exchange through the capillary wall is not instantaneous[7].

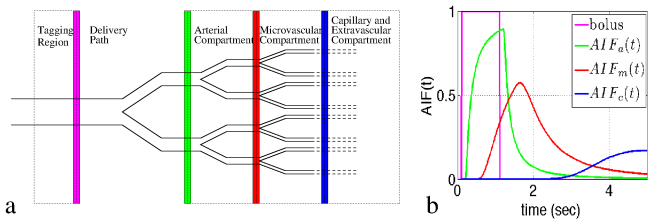

Fig.1 Schematic representation of vessels leading from the tagging region into the capillary/extravascular compartment of the voxel **(a)** as well as the corresponding arterial input functions in the absence of T1 decay **(b)**. Initial dispersion takes place while bolus travels along the delivery path. It arrives into the arterial compartment of the voxel with speed above flow crushing velocity cutoff, disperses and slows down before reaching microvasculature where the speed is below cutoff, disperses and slows down further arriving to capillary where exchange with extravascular space is possible.

The purpose of this work is to evaluate accuracy of ITS-FAIR[5], QUASAR[6] and CASL[2] multi-TI methods using a recent model of continuous bolus dispersion[4] and restricted water permeability of capillary walls[7] which was found to match the experimental data well[4,8,9].

Methods. The vascular tree, starting from the level of small arteries down to capillaries, can be described by a space-filling fractal[4]. Number of vessel bifurcations in the delivery, arterial and microvascular compartments was set to 2, 5 and 18 respectively[4] (see Fig.**1a**). Identical vessel geometry and initial 1sec-long bolus were used in all simulations. Partial label saturation due to repeated excitations of the Look-Locker train in ITS-FAIR and Quasar was simulated by a decaying exponential[5], $\exp(-\delta R t)$, where $\delta R=-\ln(\cos(\phi))/\Delta TI$, ϕ is its flip angle and ΔTI=200ms is its time step. Signal in CASL was simulated at the same set of multiple single TI's, where label does not suffer such saturation. Flow crushing gradients are simulated by excluding signal contribution from the arterial compartment where blood speed is high. In our vascular tree model this corresponds to 3cm/sec crushing velocity cutoff.

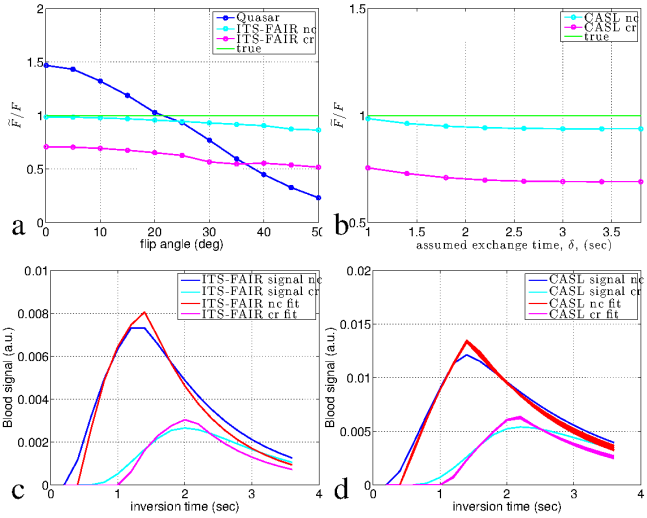

Fig.2 Ratio of estimated to true CBF as function of flip angle in ITS-FAIR and Quasar ASL **(a)** and as function of assumed exchange time in CASL **(b)**. Corresponding simulated signals and fits **(c,d)**. Quasar fits data perfectly by the virtue of the method[6], thus not shown.

Results. Degree of bolus dispersion as it travels down the vascular tree is demonstrated in Fig.**1b**. Ratio of the estimated to true flow is shown in Fig.**2a,b**. Simulated signals and fits are shown in Fig.**2c,d**. Quasar fits data perfectly by the virtue of the method[6], thus not shown.

Discussion. The fits of the CASL[2] and ITS-FAIR[5] models to the data are not perfect, but certainly not bad enough to explain the discrepancy in the flow estimation. ITS-FAIR and CASL perform well in the absence of flow crushing gradients because simulations do not include pass-through vessels. In practice, flow crushing is used to suppress pass-through vessels carrying blood to other voxels.

Conclusion. Simulations reveal that Quasar at ϕ=20°, ΔTI=200msec, handles bolus dispersion most effectively while CASL and ITS-FAIR demonstrate similar 30-50% CBF underestimation, which is known to be caused by unaccounted bolus dispersion[10]. Such underestimation worsens in cardiovascular diseases which may cause even greater bolus dispersions than simulated in this study.

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