Continuous Arterial Spin Labeling at 9.4T: How Long to Label?

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Introduction Arterial spin labeling (ASL) techniques utilize the T_1 effects resulting from blood flow, and T_1 values are field strength-dependent. In ASL quantification, a "steady-state" condition has often been assumed. However, when T_1 values are remarkably increased at high fields, such as 9.4T, the steady-state condition may not be satisfied when the tagging duration is not sufficiently long, which could introduce substantial quantification errors. To our knowledge, this issue has not been fully addressed in the literature. In the present study, we performed theoretical and experimental analyses to address this question.

Theory Assuming negligible magnetization transfer (MT) effects, the Block equation describing tissue water magnetizaton with blood perfusion is given by (1,2): $\frac{dM(t)}{dt} = \frac{M^0 - M(t)}{T_1} + (1-2\alpha)\frac{f}{\lambda}M^0 - \frac{f}{\lambda}M(t)$. Here, f is tissue perfusion rate in ml/g/sec; λ is the brain:blood partition coefficent; α is arterial blood tagging efficiency defined as $(M_a^0 - M_a)/(2*M_a^0)$ with M_a^0 being the longitudinal magnetization per milliliter of arterial blood. The superscript "0" indicates longitudinal magnetization under fully relaxed conditions. These equations can be used to derive time-dependent magnetization changes between tagging and control conditions, given by: $\frac{\Delta M(t)}{M^0} = \frac{2\alpha f}{\lambda(1/T_1 + f/\lambda)} \cdot (1 - e^{(-t/(1/T_1 + f/\lambda))})$. This equation suggests that ASL signal is a functon of perfusoin rate and T_1 value of brain tissue. Under the assumption of "steady-state conditon", this equation reduces to $\Delta M(t)/M^0 = 2\alpha f/(\lambda(1/T_1 + f/\lambda))$, which has been widely used for ASL qunatificaitons. The assumption of "steady-state condition" is valid when the tagging duration is sufficiently long. However, for pratical reasons and instrumental constraints, the tagging duration is limited. Given the fact that T_1 value increases as field strength increases, two questions arise: 1) how long should the tagging duration be for reaching a steady-state at 9.4T; and 2) how much error could be potentially introdcued when such assumption is not satisfied.

Methods A three-coil continuous ASL technique was implemented on a Bruker 9.4T scanner. A tagging coil was designed to have a curvature that minimizes the distance between the coil and the common carotid artery, and was driven by a separate RF amplifier. Tagging efficiency was measured using the method described in Ref. 2. The volume transmit coil, the tagging coil and the surface MR signal reception coil were actively decoupled (InsightMRI, Worcester, MA). Control and tagging images were acquired in an interleaved version using a single-shot gradient echo EPI sequence. Scan parameters were: FOV = 3 × 3 cm^2, matrix size = 64×64, TE = 16 ms, 7 slices with a thickness of 1.5 mm. The tagging pulse was a continuous square wave with a tagging duration of 1.2, 3.2, 4.8, 6.4 or 9.6s, in a pseudo-random order. The tagging plane was typically 2.1 cm away from the isocenter of the magnet. No post-labeling delay was employed. Instead, bi-polar diffusion weighting gradients (b=167 s/mm^2) were applied to minimize ASL signal originating from arteries of relatively large sizes (3). Animal preparation procedure was similar to a previous report (4) and was approved by the Animal Care and Use Committee of the National Institute on Drug Abuse, NIH. Briefly, four rats were intubated and artificially ventilated under isoflurane anesthesia (1.3-1.5%). Femoral artery and vein were catheterized for blood pressure monitoring and drug delivery. Core body temperature and blood gases were maintained within normal ranges.

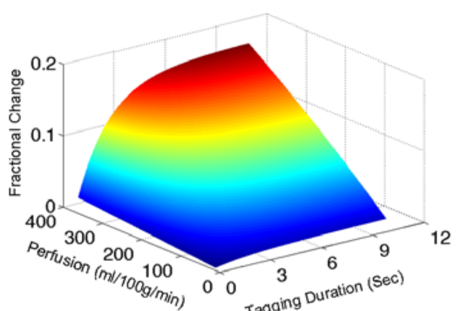

Fig. 1.

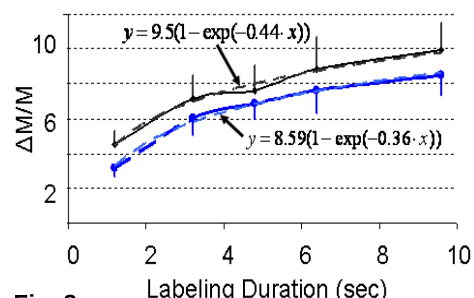

Fig. 2.

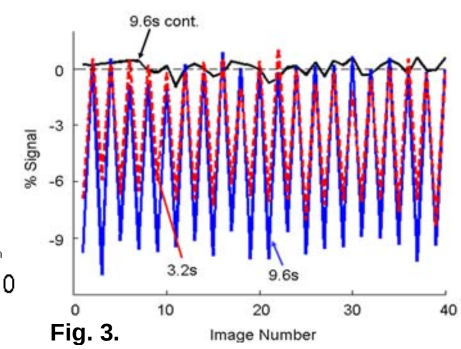

Fig. 3.

Figure1. Simulated ASL signal as a function of tagging duration and perfusion rate. Figure 2. Measured perfusion signals in the striatum (black) and cortex centered at S1FL,(blue), each averaged from 28~32 voxels (n=4 rats). Figure 3. Normalized tagging-control signal time courses with the tagging duration of 3.2s (red) and 9.6s (blue) from one voxel. To examine potential MT effects on the ASL signal, the rat was sacrificed while maintained at the same location and was scanned using the same sequence as a control. The resulting ASL signal is shown in black (9.6s cont.).

Results Figure 1 shows simulated ASL signal with the tagging duration varying from 0.3s to 10.3s and the perfusion rate varying from 20 to 400 ml/100g/min. λ was set to 0.9 (1), T_1 was set to 2.1s and tagging efficiency was set to 0.75 based on our measurements. Tagging efficiency reduction due to blood transit delay from the tagging plane to the imaging plane was ignored for the simulation. It appears that ASL signal reaches a plateau at a tagging duration ≥6s. Figure 2 shows measured ASL signal in the cortex centered at the primary somatosensory cortex of the forelimb region (S1FL blue) and striatum (black). With a tagging duration of 3.2s, the ASL signal was about 30% smaller than that at 9.6s. There was no significant difference in ASL signals at the tagging durations of 6.4s and 9.6s ($P<0.05$, 2-tailed paired t-test).

Long tagging duration is known to induce significant MT effects in single-coil ASL (5-7). Given the fact that ASL signal was enhanced at longer tagging period, a concern was whether this was caused by potential MT effects, even though a separate small coil was used for tagging. As a control procedure, a rat was sacrificed with overdose pentobarbital while maintained the same location inside the magnet. The same ASL experiment was repeated. The resulting ASL signal is shown in Fig. 3 (9.6s cont.). There were no systematic signal modulations between the tagging and control pairs. For comparison, time courses before the sacrifice are also shown. These data demonstrate that the enhanced ASL signals at longer tagging durations were not the result of potential MT effects.

Discussion A steady-state condition has often been assumed for ASL quantification. Our data suggest that, at 9.4T, short tagging duration (≤4.8s) does not satisfy the "steady-state" assumption, systematically underestimating resting-state perfusion values by ~30%. A correction procedure may be required for accurate perfusion quantifications when a short tagging duration is applied (8).

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