COMMUNICATIONS

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Turbo ASL: Arterial Spin Labeling With Higher SNR and Temporal Resolution

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A modified pulsed arterial spin labeling (ASL) technique is introduced here that has both higher temporal resolution and higher SNR per unit time than existing ASL techniques. In this technique, the time TI between the application of the tag and image acquisition is longer than the repetition time TR, allowing for the use of greatly reduced TR values without a significant decrease in the amplitude of the ASL signal. This improves both the temporal resolution and the sensitivity of ASL for functional brain mapping. Magn Reson Med 44: 511–515, 2000. © 2000 Wiley-Liss, Inc.

Key words: perfusion; cerebral blood flow; arterial spin labeling

Arterial spin labeling (ASL) techniques are becoming well established as efficient methods for measurement of cerebral blood flow (CBF) (1–3). While ASL has been used extensively for dynamic CBF measurements in the study of functional MRI (fMRI) contrast mechanisms (4–8), it has not found widespread use for fMRI itself, i.e., mapping of brain function. The reasons for this are probably several-fold, and include reduced contrast to noise ratio (CNR) and temporal resolution relative to blood oxygenation level-dependent (BOLD) techniques. However, there is now evidence that the functional ASL signal is better localized to brain parenchyma than the BOLD signal (9,10), and the use of ASL for brain mapping is therefore of current interest. In addition, the use of short echo time (TE) spirals for image acquisition in ASL greatly improves the ASL signal over the more common echo planar (EPI)-based implementations, while the advantage of spirals for BOLD imaging is less dramatic because of the requirement of longer echo times for BOLD weighting. We address here a remaining deficiency of ASL for fMRI, that of reduced temporal resolution, by introducing a modification of pulsed ASL that improves the temporal resolution of ASL by at least a factor of two relative to conventional implementations, while preserving the ASL SNR per image. We refer to this modified technique as turbo ASL.

THEORY

In pulsed ASL techniques, an RF pulse is used to tag arterial blood by magnetic inversion, and the delivery of this tagged blood to the imaging region is observed. This is usually accomplished by collecting images at regular time intervals, TR, which are alternately preceded and not preceded by an arterial inversion tag. These are referred to as tag and control images, respectively. The difference between tag and control images removes the signal contribution from static tissues and gives a signal that is proportional to the amount of blood delivered to the tissue.

In these techniques, the minimum TR is limited by two considerations. First, the bolus of inverted arterial blood must enter the imaging region before the acquisition of the tag image and after the acquisition of the previous control image. This requires that the TR be greater than the temporal width τ of the tagged bolus.

Second, the region in which the arterial blood is tagged must be refreshed with relaxed blood by inflow and/or T_1 relaxation before the application of the next tag pulse. For a tag of temporal width τ, the time required to refresh the tagging region with relaxed blood by inflow is also τ. Because the tag region is inverted in preparation for the tag images, and is not perturbed prior to the control images, this only requires that the time between tag pulses (2 TR) is greater than τ, a condition that is automatically satisfied by the first consideration above.

For an arterial tag of 10 cm length, we measured τ to be in the range of 700–800 ms (1,2). This would suggest that values of TR in this range are possible without a decrease in the ASL signal. In practice, a somewhat longer value of TR is necessary because there is a range of transit delays δt for the delivery of tagged blood to the imaging slice(s). In order for all of the tagged blood to reach the imaging slice, the tag must be applied at an inversion time TI that is at least $\delta t + \tau$ before acquisition of the tag image. In typical implementations of pulsed ASL, TR is chosen to be longer than TI, and the tag, delivery of tagged blood, and imaging all occur within one TR period of 2–4 sec (1,11,12). The presence of the transit delay δt (typically 300–1000 ms (1–3,13,14)) provides an opportunity to use values of TR that are shorter than TI. As long as TI-TR is smaller than the minimum value of δt, tagged arterial blood will not arrive in the imaging slice before the acquisition of the control image.

The conditions that should be met for turbo ASL are thus summarized by:

$$TR > \tau$$

$$TI > \delta t_{\max} + \tau$$

$$TI - TR < \delta t_{\min}.$$

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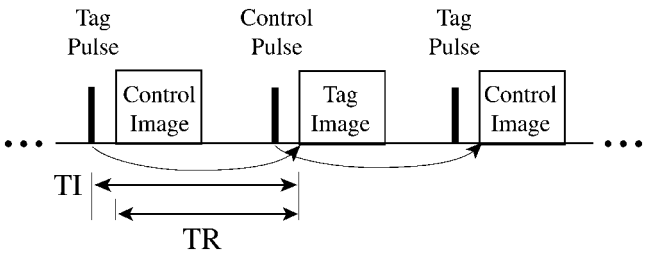

FIG. 1. Schematic diagram of turbo ASL pulse sequence.

The first two of these apply to pulsed ASL in general, while the third applies only to turbo ASL, in which TI > TR.

The pulse sequence for turbo ASL is shown schematically in Fig. 1, and is a basic pulsed ASL sequence with an inversion time TI that is slightly longer than TR. If the conditions described above are met, then the magnitude of the ASL signal is identical to that of a conventional ASL technique with the same TI. Because the rate of image acquisition is greatly increased, the SNR per unit time is increased, as is the temporal resolution of the technique.

Note that the definition of TI used here is different from that used in the abstract that initially described this technique (15), and is more in keeping with the usual definition of TI in pulsed ASL.

METHODS

Turbo ASL was implemented on a 1.5 T GE Signa LX Echospeed system using a standard birdcage headcoil. Imaging was performed using a single shot spiral readout with the following parameters: 24 cm field of view, 8 mm slice thickness, echo time 3–10 ms, 64 × 64 matrix, PICORE (proximal inversion with a control for off resonance effects) tagging (1) with a tag thickness of 10 cm and a gap of 2 cm between the tag region and the imaging slice. For each ASL image shown, 100 images were collected (50 tag/control pairs), and the average value of control-tag displayed.

In order to evaluate the maximum value of (TI-TR) before the fastest flowing tagged blood arrives at the imaging plane and contaminates the control signal, TI was varied from 1100–1400 ms, with TR fixed at 1000 ms. In addition, a bipolar gradient was added before the spiral readout in some scans in order to dephase the signal from tagged

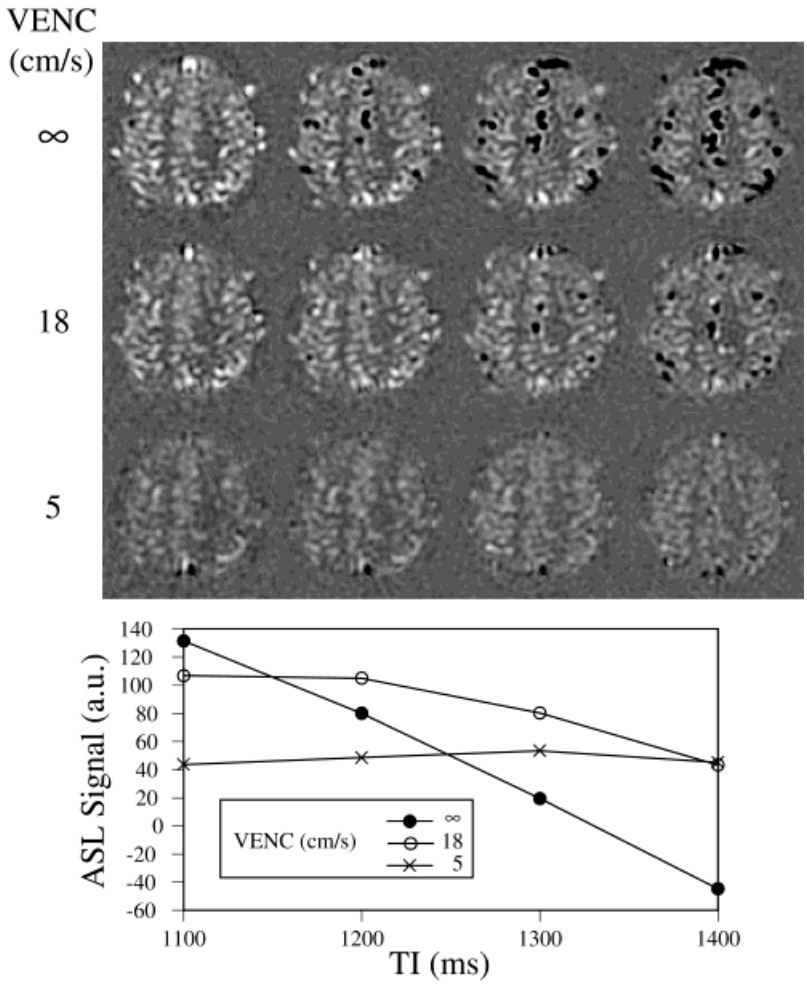

FIG. 2. ASL signal vs. TI and flow weighting for fixed TR = 1000 ms. Top: averaged ASL images. Bottom: average ASL signal in arbitrary units over a whole brain ROI. The TI axis applies to both graph and images.

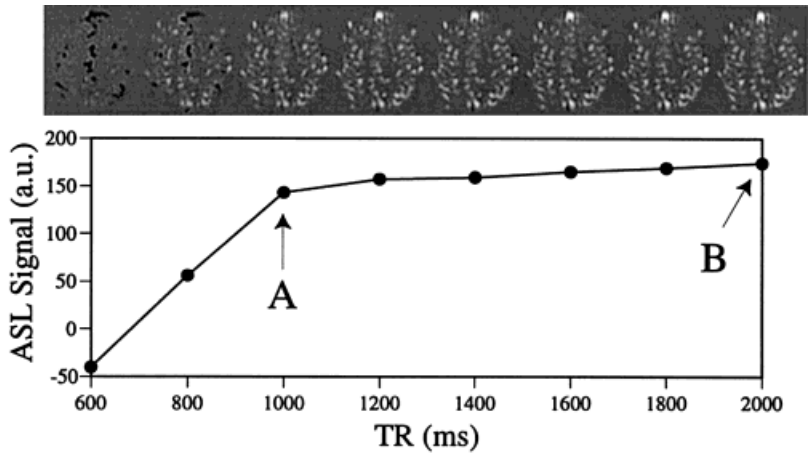

FIG. 3. ASL signal vs. TR for fixed TI = 1100 ms. Top: averaged ASL images. Bottom: average ASL signal in arbitrary units over whole brain ROI. While there is a continuous spectrum of possible TR values, the point marked A is referred to as turbo PICORE, and the point marked B is referred to as conventional PICORE. The TR axis applies to both graph and images.

spins in large arteries. These spins are the earliest to arrive in the imaging slice, and the most likely to be passing through, rather than perfusing, the imaging slice. Destroying the signal from these spins can extend the usable range of (TR-TI). In order to evaluate the lower limit of TR, a series of scans was acquired with TR ranging from 600–2000 ms with TI fixed at 1100 ms.

A functional experiment was performed in which a normal subject performed 20-sec periods of bilateral finger tapping followed by 40-sec periods of rest, repeated six times. This paradigm was repeated using conventional PICORE (TR 2000, TI 1100) and Turbo PICORE (TR 1000, TI 1100).

RESULTS

For a fixed TR of 1000 ms, turbo ASL images are shown in Fig. 2 for a range of TI values. Average values of the ASL signal over a whole-brain gray matter region of interest (ROI) are also plotted in the figure. For TI-TR longer than 100 ms without flow weighting, tagged blood in large arteries enters the imaging slice within TI-TR and gives an artifactual negative turbo ASL signal. With flow weighting that gives a VENC (velocity that gives π phase rotation) of 18 cm/sec, a value of TI-TR of up to 200 ms can be used without significant negative contribution to the turbo ASL signal from large vessels. With a VENC of 5 cm/sec, the artifactual negative signals from large vessels are nearly eliminated for TI-TR up to 400 ms, but the ASL signal itself is significantly attenuated.

For a constant TI of 1100 ms ASL images, and the average ASL signal are shown as a function of TR in Fig. 3. These demonstrate that the absolute ASL signal is relatively independent of TR over a wide range of TR values, and falls off rapidly for TR $<$ 1000 ms.

Figure 4 shows the average time courses of the absolute ASL signal over an ROI of 18 activated pixels from the motor cortex during a functional paradigm for conventional PICORE and turbo PICORE. The ROI was chosen by correlation analysis using a third independent FAIR (flow alternated inversion recovery) (12) functional ASL experiment. While the overall ASL signal is slightly lower for turbo PICORE (as in Fig. 3), the absolute signal change with activation is nearly identical. The variance of the turbo ASL time course, which is dominated by the functional signal, is reduced by only 3% from that of the conventional PICORE time course. This indicates that the sensitivity of the turbo ASL signal to functional changes in CBF is nearly the same per image as that of conventional ASL.

DISCUSSION

Turbo ASL is a modification of pulsed ASL that takes advantage of the transit delay in the delivery of tagged blood in order to increase the scan rate and thus temporal resolution of ASL. An unusual feature of turbo ASL is that this increase in temporal resolution is *not* accompanied by a large decrease in the CNR per image. The main point of this work is not specifically that one must use TI $>$ TR in order to increase the temporal resolution of ASL, but simply that TR values that are much shorter than those usually employed can be used with little reduction in the ASL

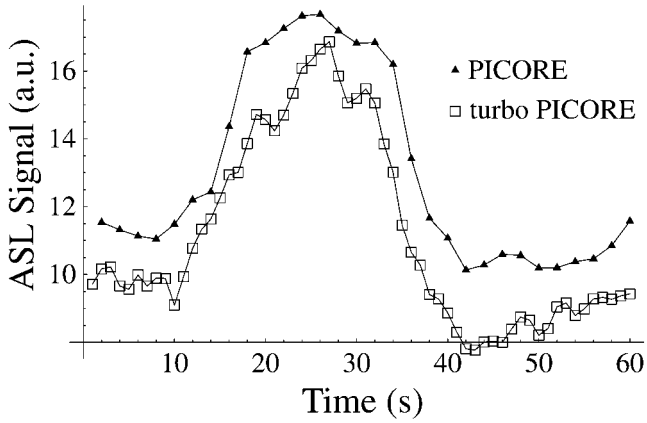

FIG. 4. ASL signal over time for conventional PICORE (triangles) and turbo PICORE (boxes). The absolute scale is the same (in arbitrary units), and the temporal resolution is 2 sec for PICORE and 1 sec for turbo PICORE. While the overall signal is decreased in turbo PICORE, the signal change due to activation, and therefore the sensitivity to activation is nearly identical.

signal. In Fig. 3, for example, the data that were acquired with TR > 1100 ms are acquired in the usual way with TR > TI. The transition in the data to TR < TI is smooth, and the signal falls off only when TR is short enough that the conditions outlined above in the THEORY section are not met.

Silva and Kim (16) introduced a modified continuous ASL technique for improving the temporal resolution of ASL by separating the tag and control conditions into two separate experiments, each sampled at high temporal resolution and then subtracted. This works well in the rat preparation for which it was intended; however, there are three obstacles to the routine use of this technique in humans. First, because the tagged blood is imaged as it enters a slice, tagged blood that is flowing through the slice to more distal tissues is counted as perfusion of the imaging slice. Second, this saturates tagged blood as it flows through the most proximal slice, eliminating the possibility of multislice applications. Third, this technique requires very high signal stability (and reproducibility of functional activation) across experiments in order to obtain good subtractions between tag and control images. None of these problems are present in turbo ASL.

A feature that cannot be used in a straightforward way with turbo ASL is QUIPSS II (quantitative imaging of perfusion using a single subtraction) (1). This modification uses an additional saturation pulse applied to the tagging region to control the temporal duration of the tag, and is essential for the quantitation of CBF, in particular lending insensitivity to the effects of transit delays from the tagging region to the imaging slice. The application of this additional pulse would perform the intended function, but because it perturbs the tagging region during every TR period a much longer TR would then be required in order that the tagging region be replenished with relaxed blood. Because QUIPSS II cannot be implemented, we consider turbo ASL to be a qualitative CBF imaging technique that is very well suited for brain mapping, but like FAIR, EPISTAR (echo planar imaging and signal targeting using alternating radiofrequency) (11), and PICORE without the QUIPSS II modification, not appropriate for quantitative analysis of CBF, unless multiple TI points are collected, and the data fit to a model.

A multislice implementation of turbo ASL is straightforward, and involves rapid acquisition of multiple slice locations during each image acquisition period. If TI is to be greater than TR for maximum time efficiency, then one must ensure that for all slices the tagged blood does not reach the slice before acquisition of the preceding control image. The image acquisition should be sequential from proximal to distal, and such that the propagation of slice acquisitions stays ahead of the leading edge of the wave of tagged blood. As indicated by Fig. 2, the range of possible values for TI is widened by the use of small flow weighting gradients to dephase the fastest flowing tagged spins. These issues are currently under experimental investigation in our laboratory.

Turbo ASL can also be used for combined CBF/BOLD studies. While the ASL signal is most efficiently acquired using a short TE imaging technique, such as a spiral, the BOLD signal can be efficiently acquired using the second echo of a dual echo spiral sequence. The BOLD images are alternately positively and negatively flow-weighted and the average of consecutive pairs of images is nearly flow-independent (13).

For the FAIR technique, the tag is applied by nonselective inversion, and the tag size is thus limited not by the characteristics of the RF pulse, but by the length of the RF coil that produces the pulse. For head coil excitation, the tag is usually short enough that the refreshment of the tag region is dominated by inflow from outside the RF coil, while for body coil excitation T_1 relaxation is the only mechanism for bringing relaxed blood into the tagging region, and the optimal TR may be longer.

We have introduced here a new method for fMRI using ASL that has at least twice the temporal resolution of conventional ASL techniques and only a minimal reduction in CNR per image. It can thus be used to obtain the same functional sensitivity in about half the scan time, or improve the CNR by nearly $\sqrt{2}$ or the same length scan.

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