Noise Reduction in Multi-Slice Arterial Spin Tagging Imaging

K. S. St. Lawrence,[1]* J. A. Frank,[1] P. A. Bandettini,[2] and F. Q. Ye[2]

Attenuating the static signal in arterial spin tagging (ASSIST) was initially developed for 3D imaging of cerebral blood flow. To enable the simultaneous collection of cerebral blood flow and BOLD data, a multi-slice version of ASSIST is proposed. As with the 3D version, this sequence uses multiple inversion pulses during the tagging period to suppress the static signal. To maintain background suppression in all slices, the multi-slice sequence applies additional inversion pulses between slice acquisitions. The utility of the sequence was demonstrated by simultaneously acquiring ASSIST and BOLD data during a functional task and by collecting resting-state ASSIST data over a large number of slices. In addition, the temporal stability of the perfusion signal was found to be 60% greater at 3 T compared to 1.5 T, which was attributed to the insensitivity of ASSIST to physiologic noise. Magn Reson Med 53:735–738, 2005. Published 2005 Wiley-Liss, Inc.†

Key words: arterial spin tagging; arterial spin labeling; cerebral blood flow; blood oxygenation level dependant contrast; functional magnetic resonance imaging; physiological noise.

INTRODUCTION

Suppressing the magnetization from static tissue water (i.e., background suppression) has been shown to be an effective means of reducing noise in arterial spin tagging (AST) images (1). This approach, which is referred to as ASSIST (attenuating the static signal in arterial spin tagging), was initially developed for eliminating the extra phase noise in three-dimensional (3D) imaging caused by magnetic field fluctuations between acquisitions. Background suppression is useful for two-dimensional (2D) imaging because it reduces motion artifacts and spatially correlated noise (1,2).

There are two limitations with the original 3D version of ASSIST. First, the acquisition time for the perfusion-weighted (ΔM) images was fairly long. Typically, one ΔM imaging volume set, consisting of 8–12 slices, was collected in 30 s, which limits the ability of measuring dynamic changes in cerebral blood flow (CBF) with ASSIST (1,3). Second, BOLD-weighted images are not easily acquired in conjunction with ASSIST. Considering the interest in combining BOLD and AST data, particularly for measuring activation-induced changes in CBF and oxygen consumption (3–6), it would be advantageous to combine ASSIST and BOLD. The purpose of this work was to develop a multi-slice variation of ASSIST that overcame these limitations. A preliminary version of this work has been presented in abstract form (7).

METHODS

Multi-Slice ASSIST Sequence

The ASSIST sequence for background suppression is illustrated in Fig. 1a. It consists of a tagging pulse (P_{inv}), which alternates between slice and global inversion, a series of saturation pulses (P_{presat}), which suppress the magnetization in the imaging slab, and two global inversion pulses (P_{MIR}), which are applied during the delay (T_I) prior to imaging (1). The timings of the P_{MIR} pulses are chosen such that the image acquisition coincides with the null point of the static water's magnetization. With the multi-slice version of ASSIST, background suppression is maintained beyond the first null point by applying additional global inversion pulses (P_{180}) between slice acquisitions (see Fig. 1b). The total number of slices (N_{tot}) is divided into clusters (N_{cl}), with an inversion pulse applied between clusters. The number of inversion pulses (N_R) depends on the total number of slices and the cluster size ($N_R = N_{tot}/N_{cl} - 1$). The acquisition of each cluster of slices is timed such that the center slice is acquired at a null point. If the time between a null point and an inversion pulse is kept short relative to T_1 relaxation times, then the succeeding null point is approximately equidistant from the inversion pulse. Analogous to the P_{MIR} pulses, if the P_{180} pulses are considered ideal, then it can be shown that they have no effect on the ΔM signal, other than a possible change of sign (1).

A saturation pulse (P_{asat}) is applied inferior to the imaging slab to allow all tagged water time to reach the imaging voxels (8). Following image acquisition, the delay T_D allows the magnetization to recover before the next tagging step. BOLD-weighted images can be collected at the end of the delay, prior to the application of the next P_{inv} pulse (9).

MR Imaging

Studies were performed on 1.5- and 3-T whole-body scanners (General Electric, Milwaukee, WI) employing standard quadrature head coils. Volunteers participated under a protocol approved by the Institutional Review Board of the National Institutes of Mental Health. Two versions of multi-slice ASSIST were used in this study: one to study functional activation and the other to collect a large imaging volume of resting-state CBF.

For functional activation, gradient echo images were acquired using a single-shot spiral gradient trajectory (10). The spiral readout gradient was 22 ms with a 64 × 64

[1]Laboratory of Diagnostic Radiology Research, Clinical Center, National Institutes of Health.

[2]Functional MRI Facility, Division of Intramural Research Programs, NIMH; National Institute of Mental Health, NIH.

*Correspondence to: Keith St. Lawrence, Lawson Health Research Institute, St. Joseph's Health Care London, 268 Grosvenor Street, London, Ontario N6A 4V2, Canada. E-mail: kstlaw@lri.sjhc.london.on.ca

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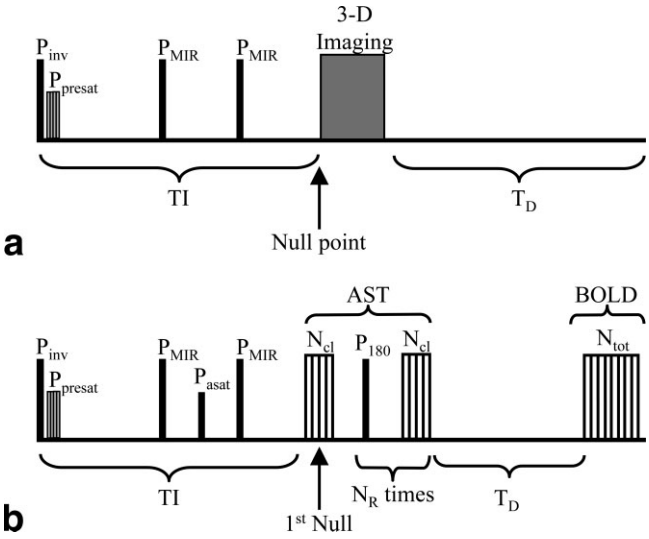

FIG. 1. **a:** Schematic diagram of the 3D ASSIST pulse sequence. The tagging component consists of an inversion pulse (P_{inv}) that alternates between slice and global inversion, followed by a delay (TI) prior to imaging. The background suppression consists of selective saturation pulses (P_{presat}) and two global inversion pulses (P_{MIR}). Following image acquisition there is a delay (T_D) to allow magnetization to recover. **b:** Schematic diagram of the multi-slice version of ASSIST. The initial procedure to suppress the background magnetization is the same as 3D ASSIST. Additional global inversion pulses (P_{180}) are applied between slice acquisitions to prevent recovery of background signal. The total number of slices (N_{tot}) is divided into clusters (N_{cl}), which are separated by inversion pulses. The number of inversion pulses (N_R) equals $N_{tot}/N_{cl} - 1$. P_{asat} saturates arterial blood proximally to the imaging slices. At the end of the delay T_D, BOLD-weighted images are collected immediately prior to the next P_{inv} pulse.

matrix and a 240-mm FOV. Six axial images were obtained with a 4-ms TE, a 5-mm slice thickness, and a 1-mm slice gap. A 16-ms sinc pulse was applied prior to each 90° slice-selective pulse to saturate the fat signal. A 600-ms rectangle pulse (P_{180}) inverted the magnetization after the acquisition of the third slice, dividing the total number of slices into two 150-ms clusters. The tagging delay (TI) was 1.65 s, T_D = 1.2 s, and TE was increased to 35 ms for the BOLD imaging. The repetition time between tagging steps was 3.75 s. To quantify CBF from the ΔM images, T_1 relaxation times were measured using a saturation-recovery Look–Locker method, consisting of a train of 12 interrogation pulses, each using a 20° flip angle, and separated by 300 ms (2).

For the resting-state perfusion-weighted images, the spiral gradient trajectory was divided into four segments, each with a readout duration of 8.2 ms. Fifteen axial images were acquired with an 80 × 80 matrix, a 240-ms FOV, TE = 4 ms, 4-mm-thick slices, and a 1-mm slice gap. The slices were divided into three clusters, each 90 ms in duration. To reduce the acquisition time, the fat saturation pulses were applied before the acquisition of the first slice and following each P_{180} pulse.

Functional Activation Study

Experiments were conducted on the 1.5-T scanner. Five subjects (one male, four females, mean age = 34 ± 6 years) participated in the study. Each subject completed the activation protocol twice: once while collecting ASSIST/BOLD data and once while collecting FAIR/BOLD data. The order of data acquisition was randomized between subjects. The FAIR data were collected using the ASSIST sequence with no background suppression pulses (i.e., P_{MIR}) applied. The activation protocol was composed of 10 alternating periods (60 s each) of rest and task. The task consisted of sequential tapping of the fingers on the right hand against the thumb at a rate of 2 Hz.

Data were processed offline using software written in interactive data language (Research Systems, Boulder, CO). All images were zero-filled to 128 × 128 and convolved with a 2D gaussian filter (kernal width = 5.6 mm). Activated voxels from the AST data were defined using z statistics with a Bonferroni-corrected P value of 0.1 (11). A third-order polynomial was used to correct the BOLD data for baseline drift and activation determined using t statistics with a Bonferroni-corrected P value of 0.025.

Temporal Standard Deviation of the Perfusion-Weighted Images

The temporal SD of the ΔM signal was measured at 1.5 and 3 T using the functional activation version of ASSIST. Eight subjects were studied at both field strengths: five males, three females, mean age = 31 ± 6 years at 1.5 T and seven males, one female, mean age = 34 ± 8 years at 3 T. Five of the subjects participated in both studies. For each voxel, the average ΔM value, normalized to the equilibrium magnetization (M_0), and SD ($\sigma(\Delta M)$) were calculated from 80 ΔM images. The $\Delta M/M_0$ and $\sigma(\Delta M)$ images were neither interpolated nor spatially filtered.

RESULTS

Figure 2 shows the activated pixels for one subject during finger tapping as detected by ASSIST/BOLD and FAIR/BOLD. Averaged over the five subjects, the activated volumes in the primary motor cortex were 1.9 ± 0.9 cm^3 for ASSIST and 0.9 ± 0.8 cm^3 for FAIR. The corresponding CBF increases were 53 ± 10 and 57 ± 3%, respectively. The average activated volume detected by ASSIST was larger than that detected by FAIR, but the difference was only significant for $P < 0.1$ due to the small group size. The BOLD data collected in conjunction with ASSIST and FAIR data were very similar. From the ASSIST/BOLD data, the BOLD signal was 1.4 ± 0.3% with an activated volume of 4.6 ± 1.2 cm^3. From the FAIR/BOLD data, the BOLD signal was 1.4 ± 0.5% with an activated volume of 3.5 ± 1.4 cm^3.

With ASSIST, the background signals were less than 6% of M_0 in all slices, whereas the background signals in the FAIR images were approximately 78% of M_0. Similar to 3D ASSIST (1), suppressing the background signal resulted in a 15 ± 3% reduction in the global ΔM signal compared to FAIR (i.e., $\Delta M/M_0$ = 0.44 ± 0.02% and 0.52 ± 0.03% for ASSIST and FAIR, respectively). Interestingly, the P_{180} pulse applied after the third slice had negligible effects on the ΔM signal.

The average whole-brain values for $\Delta M/M_0$ and $\sigma(\Delta M)/\Delta M$ were 0.43 ± 0.04 and 0.93 ± 0.16% at 1.5 T and

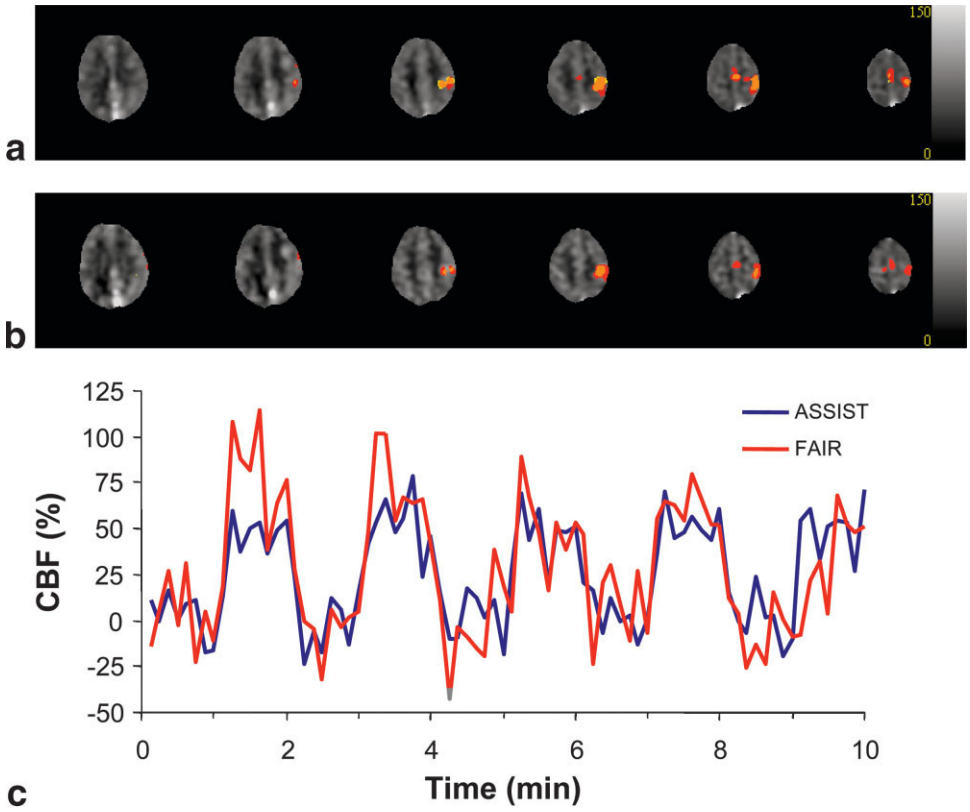

FIG. 2. Activated pixels from the (**a**) ASSIST/BOLD and the (**b**) FAIR/BOLD data sets obtained from one subject. Activation maps have been overlaid onto their respective resting-state CBF images (scale on the right side is in units of milliliters per 100 g per minute). The three colors indicate activated pixels common to both data sets (orange), pixels activated only in BOLD data (red), and pixels activated only in CBF data (yellow). Average gray matter CBF was 61 and 67 mL/100 g/min for ASSIST and FAIR, respectively. **c:** Time course of relative CBF in the primary sensorimotor cortex as determined from the ASSIST and FAIR data sets.

0.47 ± 0.07 and $0.53 \pm 0.09\%$ at 3.0 T. Although there was no change in the ΔM signals, there was a significant reduction in $\sigma(\Delta M)/\Delta M$ at 3 T ($P < 0.001$).

DISCUSSION

The purpose of this work was to improve the temporal resolution ASSIST and enable the simultaneous collection of perfusion and BOLD data. The 3D imaging sequence used in the original ASSIST was replaced with 2D multi-slice imaging. The recovery of the background signal, which limits the number of slices that can be collected, was avoided by applying inversion pulses between slice acquisitions. With this approach, the background magnetization was less than 6% of M_0. Using single-shot SPIRAL imaging, ΔM images were acquired every 7.5 s. In contrast, 3D ASSIST acquired ΔM images over a similar slab thickness every 30 s (3). One potential limitation with using multi-slice imaging instead of 3D imaging is transit time differences between slices. To minimize any potential effects, SPIRAL trajectories were used to keep the total imaging time to less than 300 ms.

With multi-slice ASSIST, BOLD-weighted images are collected at the end of the delay period preceding the next P_{inv} pulse. Since the background suppression technique begins with saturating the magnetization in the imaging slices, collecting BOLD-weighted images had no effect on the ΔM signal. As a feasibility study, the combined ASSIST/BOLD technique was used to measure the simultaneous CBF increase and BOLD signal during motor activation. There was good agreement between the CBF increases measured with ASSIST and FAIR. However, there was a trend toward a larger activated volume detected by ASSIST, which could be attributed to a reduction in the sensitivity to physiologic noise. Preliminary data collected at 3 T showed similar results (data not shown).

If the signal-to-noise ratio is considered proportional to field strength, performing experiments at higher field strengths should improve the inherently poor sensitivity of AST techniques (12,13). In recent reports, the anticipated improvement was not evident when comparing the temporal stability of MR signals at different field strengths (13–15). This lack of improvement for field strengths $\geqq$ 3.0 T was attributed to an increase in physiologic noise, which is considered proportional to the signal (15). Since the ASSIST technique suppresses the static magnetization, it also reduces physiologic noise. This is evident by comparing the temporal SD of the ΔM signals at the two field strengths. The $\sigma(\Delta M)/\Delta M$ value at 3.0 T was 1.75 times smaller than the value measured at 1.5 T, which suggests that ASSIST can be used to reduce physiologic noise in perfusion imaging at higher field strengths.

The improved temporal stability at 3.0 T enables higher resolution ΔM images to be collected. Figure 3 shows one example consisting of 15 oblique slices covering the visual, motor, and frontal cortices. The background signals in all images were reduced to less than 4% of M_0 by applying two P_{180} pulses. Susceptibility artifacts, which are common in the frontal areas, were avoided by using a segmented-spiral trajectory. The ASSIST technique is well suited for segmented acquisitions since it is insensitive to shot-to-shot signal variations. However, the tradeoff is a reduction in the temporal resolution.

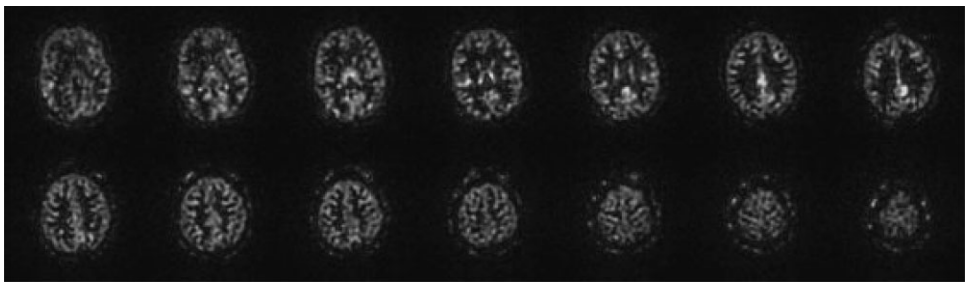

FIG. 3. Perfusion-weighted images obtained with the segmented-SPIRAL version of ASSIST. The images were collected with a matrix size of 80 × 80, interpolated to 160 × 160, and convolved with a gaussian filter (kernal width = 3.6 mm). The image resolution prior to interpolation was 3 × 3 × 4 mm and the scan duration was 12 min.

In this study, a multi-slice version of ASSIST was presented that improved the temporal resolution of the technique and enabled simultaneous collection of CBF and BOLD data. The static background signal was suppressed in all slices by applying inversion pulses between slice acquisitions. Due to the insensitivity of ASSIST to physiologic noise, the temporal stability of the ΔM signal increased with increasing field strength.

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