Noise or Artifact: Detrimental Effects of BOLD Signal in Arterial Spin Labeling fMRI at High Field Strength

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INTRODUCTION: High magnetic fields (e.g. 3.0 Tesla) are expected to provide significant improvement for arterial spin labeling (ASL) perfusion imaging due to increased signal-to-noise ratio (SNR, proportional to the static field strength) and increased T_1 (1), leading to slower decay of the blood label. While these advantages have been well demonstrated in baseline ASL studies, functional experiments often show less than the expected improvement in sensitivity. One possible reason is that BOLD effects, which are much more pronounced at high field, may have an adverse effect on the measured ASL signal, even at short TE. In this study, we investigated the contamination of ASL signal by BOLD effects using experiment and simulation. It was found that, due to the interleaved acquisition of labeled and control images, the difference signal contains considerable BOLD-related artifacts, which CAN NOT be alleviated by averaging over multiple trials or over multiple subjects. Various aspects concerning this artifact are discussed. A correction method using linear interpolation is proposed to minimize the artifact and to improve the ASL fMRI sensitivity.

METHODS Experiment: Studies (n=4) were performed on a 3.0T MR scanner (Philips Medical Systems) using body coil transmission and SENSE head coil reception. FMRI of visual stimulation (checkerboard, visual angle=25º, frequency=8Hz, 10s ON, 50s OFF, 4 trials) was performed with: TR=2s, FA=90º, matrix=80x80, SENSE factor 2, single slice (5mm). The ASL experiment used Transfer-Insensitive-Labeling-Technique (TILT) (2) which is similar to EPISTAR in that only the proximal side is labeled. The labeling slab thickness was 120mm and TI was 1500ms. Shortest TE of 14.4ms was used. A BOLD fMRI (TE=35.0ms) was also performed. Activation detection criteria: cross-correlation, cc>0.22, cluster>3, p<0.005.

Simulation: Water in a voxel was simulated as consisting of two components: static spins (S_{static}) that are not replaced by labeled blood during the inversion time (TI); fresh spins (S_{flow}) that enter the voxel from labeling slab. The total signal $S=S_{static}+S_{flow}$, where S_{static} is not affected by the label/control pulses and S_{flow} on the other hand is. The fractions of these two pools are determined by the perfusion values. At baseline,

f_{flow}= 60ml of blood/100 ml of tissue/min x 1.5 seconds of delay = 1.5ml of blood/100ml of tissue = 1.5% and $f_{static}=1-f_{flow}$

Therefore, the MR signals can be written as: $S_{static} = (1-f_{flow}) \cdot M_{static} \cdot (1+BOLD_{static})$ and $S_{flow} = f_{flow} \cdot M_{flow} \cdot (1+BOLD_{flow})$

where M_{static} and M_{flow} are factors related to longitudinal relaxation. In TILT, a presaturation pulse was applied before the labeling pulses to suppress the static signal in the imaging slice. Therefore, $M_{static}=1-\exp(-TI/T_{1,gray})\approx 0.7$, where $T_{1,gray}$=1200ms. $M_{flow}=1-2*\exp(-TI/T_{1,blood}) \approx 0.2$ for labeling scan, and $M_{flow}=1.0$ for the control scan. The term "*BOLD*" is the fractional BOLD signal change. In the simulation for a functional experiment, *f* and "*BOLD*" vary as a function of time while the other parameters remain constant. The assumed BOLD curve was based on the experimental data obtained in the BOLD fMRI but scaled down according to the actual amplitude of the BOLD effect in the ASL experiment (TE=14.4ms, $BOLD_1$ peak=1.6%). The CBF curve was taken as the positive part of the BOLD curve and scaled to the measured changes (CBF peak=50%). Three different processing strategies were applied in the calculation of CBF signals (Fig. 1).

RESULTS and DISCUSSION: Only voxels that were activated in both BOLD and ASL fMRI were included in averaging. Fig. 2a shows the experimental results of unsubtracted MR signals (mean±SEM). The signal is characterized by high-frequency fluctuations due to interleaved labeled and control scans that are modulated by BOLD effects. Fig. 2b shows the time-courses of CBF-weighted (i.e. subtracted) signals using the three different strategies in Fig. 1. It can be seen that E2 and E3 are essentially the downsampling of E1. The E1 curve (blue) has significant fluctuation which CAN NOT be solely attributed to random noise (relatively small error bars). In fact, a nearly identical pattern is seen in the noise-free simulation results (Fig. 2c). The comparison between experiment and simulation suggests that the measured CBF dynamics contain significant BOLD-related artifacts. Such artifacts are consistent for different trials and different subjects, and therefore can not be removed by averaging. In E2 and E3, the artifacts result in a systematic deviation from the true CBF curve (red in Fig. 2c). It is more pronounced at higher field strength due to larger BOLD effects. The artifacts exist for all ASL techniques but are more severe when static tissue signal is large, as in the cases of QUIPSS, EPISTAR and TILT. To correct for such an artifact, the BOLD effects in the labeled and control images need to be matched. This can be achieved by interpolating the labeled images (odd points in Fig. 2a) and control images (even points in Fig. 2a) separately, and then performing a subtraction. This approach essentially uses two neighboring time-points to estimate the missing points that should have the matched BOLD effects. Fig. 2d shows the results after the correction. It was found that more activated voxels were detected (18±5%, n=4, p<0.01) and the CBF time-courses were significantly improved (Fig. 2e). The proposed correction method is essential for accurate measurement of CBF time-courses and for high sensitivity of ASL fMRI at high field.

REFERENCES: 1) Lu MRM 52: 679 2004; 2) Golay JMRI 9: 454 1999;

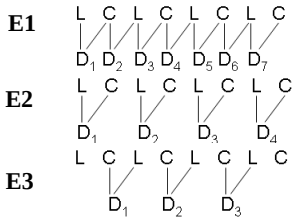

Fig. 1: Different subtraction strategies for perfusion estimation. L-labeling scan; C-control scan; D-difference image. E1 has higher temporal resolution, although consecutive difference images are not completely independent.

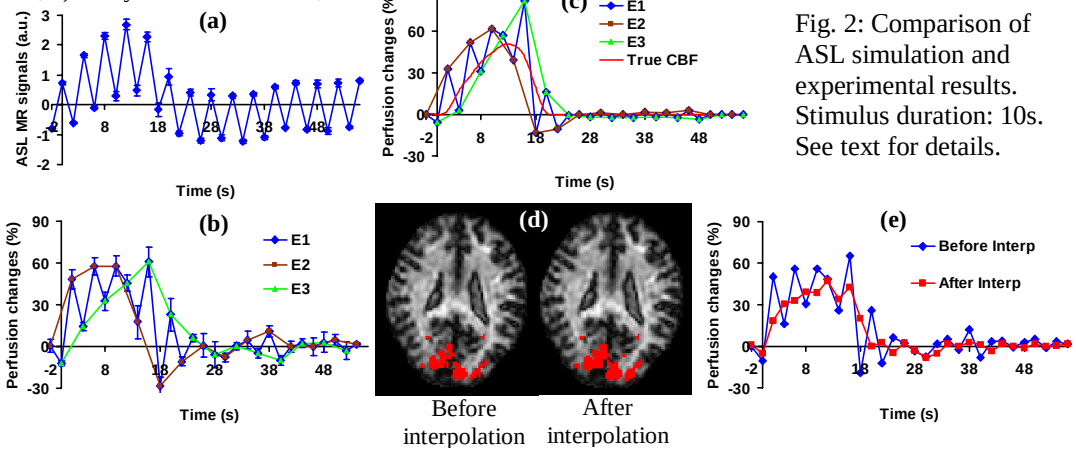

Fig. 2: Comparison of ASL simulation and experimental results. Stimulus duration: 10s. See text for details.