Counterbalancing mismatched magnetization differences in functional arterial spin labeling

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INTRODUCTION:

While the advent of Arterial Spin Labeling (ASL) offers new possibilities for brain activation studies, functional ASL is difficult for several reasons: SNR is low, resulting in relatively poorer detection and characterizing of transients, as compared to those obtained by BOLD-fMRI. In addition, severe fluctuations have been observed particularly at the beginning and end of stimulation epochs, where the large dynamic changes in cerebral blood flow (CBF) challenge the assumption of steady state condition, which are needed for pair-wise subtraction. During both onset and decline of the perfusion signal due to functional stimulation, a pair-wise subtraction can result in either large positive or negative differences in the subtracted magnetization ΔM, depending on the relative position of the labeling or control pulses with respect to the stimulation epoch. Such effects are particularly evident in multi-time point ASL sequences [1,2]. Stimulation paradigms that use an even number of volumes per baseline and activation block will result in the same type of scan (control or label) for each corresponding volume of each cycle. Here, we propose a simple method for counterbalancing the large fluctuations in multi-time-point ASL data at the transition between baseline and stimulation blocks using an odd number of volumes between stimulation periods.

METHODS: ***Experiments*.** All sequences were implemented on a clinical 3.0T imager (Philips Medical Systems) with parallel imaging capabilities (SENSE). Four healthy subjects (2 males, 2 females; age 32±2.8) were presented with visual stimuli and scanned twice in the same session using the QUASAR pulse sequences [2].

MR parameters. The following parameters were used for the ASL sequences: slices=1, thickness=5 mm, gap=1 mm, θ=27°, TR/TE=3000/21 ms, ΔTI=170 ms, time points=16, SENSE factor=3, labeling slab=150 mm, inversion gap=30-50 mm, crusher encoding velocity Venc=[∞, 3 cm/s]. Labeling and control acquisitions were acquired alternatively; starting with a labeling scan. A single slice per subject was acquired along the calcarine sulcus to image the primary visual area. The functional paradigm was a gray-white checkerboard pattern (50% contrast, 8Hz frequency) that alternated with a baseline condition (iso-luminance gray (50%) background). Both ASL runs had 6 blocks of visual stimuli (10 volumes/block) regularly alternating with 7 blocks of baseline condition. The first 'counterbalanced' run had 21 volumes per baseline block. The odd-numbered stimulus paradigm ensured that there was a control scan for every labeled scan at each corresponding time-point in each of the six stimulation cycles. The second 'conventional' (non-counterbalanced) run had only 20 volumes per baseline block, thus resulting in a regular label-control occurrence.

Data Analysis. Functional images were realigned if necessary. Linear interpolation of the control and labeled data was done before pair-wise subtraction in order to eliminate the detrimental BOLD effects on activation [3]. RS-tests (p<0.001, uncorrected) were performed on a phase-by-phase basis to determine the commonly significant phases for use in region-of-interest (ROI) detection. CBF was estimated using the 3-parameter model [4]:

$$\Delta M_T(t) = \frac{-2M_{a,0} \cdot f}{\delta R} e^{-R_{1,a} \cdot t}\left(1 - e^{-\delta R(t-\tau_a)}\right)$$

RESULTS & DISCUSSION: The time-courses for each of the two ASL scans were averaged using only commonly activated voxels across time and subjects. Figure 1 shows an example of a typical ROI for a subject. From Figure 2, the 'counterbalanced' CBF time-course appears smoother, especially around the beginning and end of the stimulation period. The conventional ('non-counterbalanced') CBF time-course on the other hand, fluctuates quite severely around the edges of the stimulation period. This effect is due to very bad fitting results at the rising and falling edges of the stimulation periods, as the magnetization signal of the individual control and labeled volumes prior to subtraction have mismatched rising and falling edges, since it is not possible to have both control and labeled volumes acquired simultaneously. Figure 3 illustrates this point: the magnetization change (dM) for the conventional scan in the 2nd volume after the stimulation period is starkly larger than that of the counterbalanced scan and the averages of the resting steady state condition. This volume corresponds to volume 12 in Figure 2, where a huge CBF fluctuation can be seen. In single time-point ASL methods, such timing issues can be in part resolved by Lu et al's method of interpolating the controls and labels separately [3]. However, this method cannot take care of spurious BOLD effects in multi time-points ASL dataset, in which individual time points after a control or labeling pulse will be acquired during a transient BOLD signal. Our method of counterbalancing the acquisition of controls and labels throughout the stimulation paradigm helps to achieve a smoother time-course upon averaging, as each pair of labeled and control time-course will be acquired alternately at identical transient times. Please note from Figure 2 that the large variations at the rising and falling edges of the stimulation period cannot be explained uniquely by random noise, as the standard error bars do not overlap. One of the potential drawbacks of our method is that it may induce some artificial reduction of the up-rise and down-slope of the functional ASL signal.

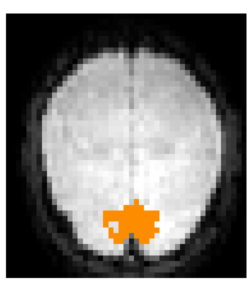

Figure 1: A representative ASL dataset from one subject showing overlaid activation in the primary visual cortex.

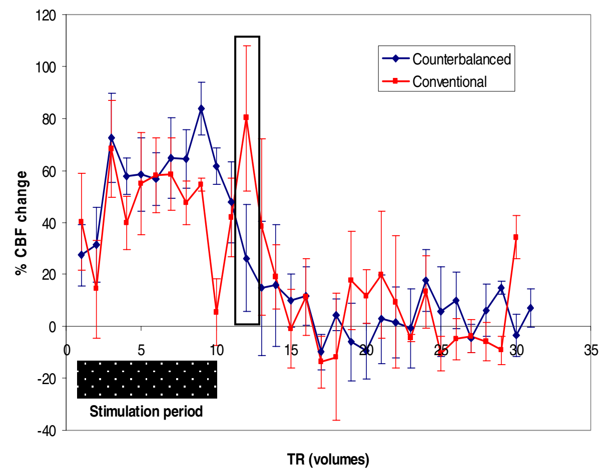

Figure 2: Averaged CBF % changes for the counterbalanced scans (blue) and the conventional scans (red).

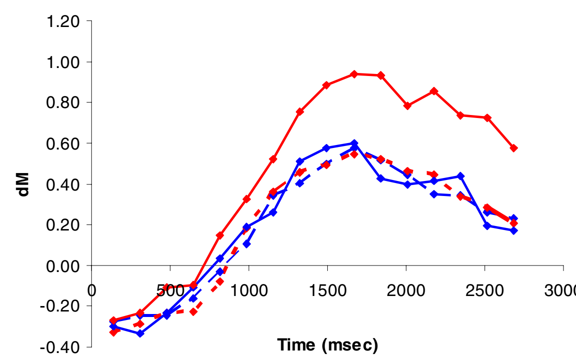

Figure 3: Averaged magnetization changes (dM) in the 2nd volume of the baseline blocks (volume 12 in Figure 2 – black box) for the counterbalanced scans (solid blue) compared to the conventional scans (solid red). The steady-state baseline dMs are plotted in broken lines with similar colour coding for comparison.

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