Measurement Stability in Arterial Spin Labeling Investigated Using Multiple Sites

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Introduction

Cerebral Blood Flow (CBF) measurements are a primary tool in the study of neurophysiological processes. Using Arterial Spin Labeling (ASL) methods, inflowing blood from the arteries is tagged and imaged, quantifying the principal mechanism of metabolic delivery within the brain. The measurements are generally used alone as either an absolute measure of perfusion[1] or as a change in flow associated with a corresponding change in function[2], due to metabolic demands of local neuronal activity. Recently, studies have shown ASL to be effective as a calibration measurement for fMRI imaging due to its coupling to the BOLD response[3]. In all cases, ASL measurements are highly susceptible to noise and require a significant number of temporal acquisitions with relatively low temporal resolution, resulting in long scan times. This study uses multiple scanners to investigate the effect of varying the number of repetitions used in CBF measurement of Gray Matter tissue (GM) and establishes recommendations for the minimum scan time necessary for a stable calculation.

Methods

Data was combined across two traveling subjects studies composed of 6 separate 3T scanners, with two different manufacturers. The first traveling subjects study included 18 volunteers at 4 sites, site 1 had a repeat visit. The second traveling subjects study included 21 volunteers and were imaged on the same day, albeit at different scanners. Sequence parameters were made as similar as possible and were based on established community guidelines for multi-site studies (http://www.nbirn.net). Despite these efforts, manufacturer constraints meant sites 3, 4, 5A and 5B used spiral acquisitions while sites 1 and 2 used Cartesian acquisitions (64 x 64 MAT; F. Enc. R/L; N_{AVG} 1; TE Min; TR 4s; FA 90°; FOV 220 mm x 220 mm; T_{SCAN} 7:04 minutes). Calibration and minimum contrast scans were acquired for intensity and RF coil inhomogeneity corrections respectively. Standard motion correction, registration to high resolution anatomical scans, tissue segmentation and a surround subtraction were performed using an in-house Matlab script with numerous calls to both FSL and AFNI packages. Keeping the entire analysis pipeline constant, a mean and standard deviation of GM masked CBF values were calculated for each subject with the number of repetitions increasing in pairs from 16 to 104. The extracted mean and standard deviation values were used to evaluate stability within subjects, across subjects and across sites.

Results

A typical superior axial slice of a single subject (Site 3) perfusion map is accompanied by a Gaussian fit to CBF statistics in figure 1. Anatomy is evident by 16 TRs and midway through the series at 42 TRs the mean perfusion measurement is stabilizing (GM mask outline in white), followed by gains in SNR evident at the full 104 TRs. Single subject measurements at site 2 are shown in figure 2. Significant instabilities in mean CBF are seen early on (2a,c), but subject-wise differentiation sets in quickly, followed by diminishing returns in SNR gains shadowed in the GM CBF spatial standard deviation asymptotic approach (2b,d). Finally, figure 3 demonstrates mean and variance statistics across subjects at all 6 sites. The convergence to stable mean GM CBF values varies by site but can be generalized to have

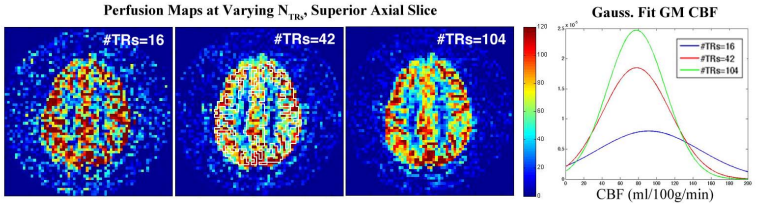

Figure 1. Perfusion map example, single subject with accompanying statistics, Site 3.

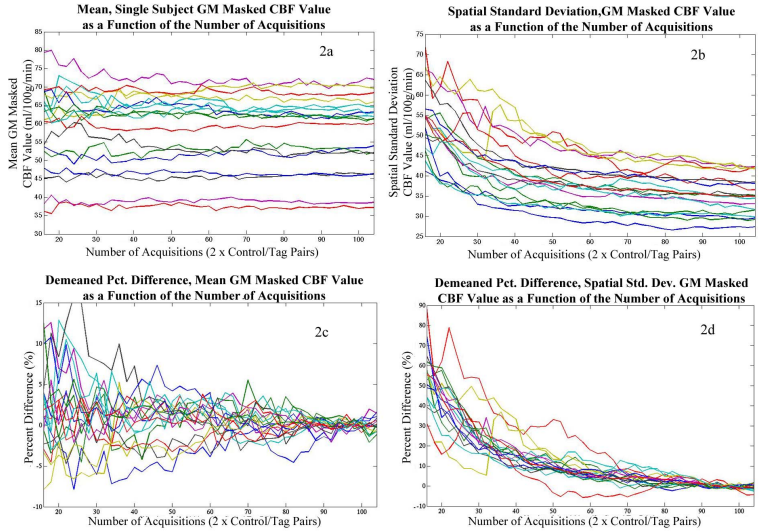

Figure 2. GM masked mean and spatial std. dev. of CBF values (2a, 2b) at Site 2. Demeaned, as a percent difference (2c, 2d) from the final steady state value.

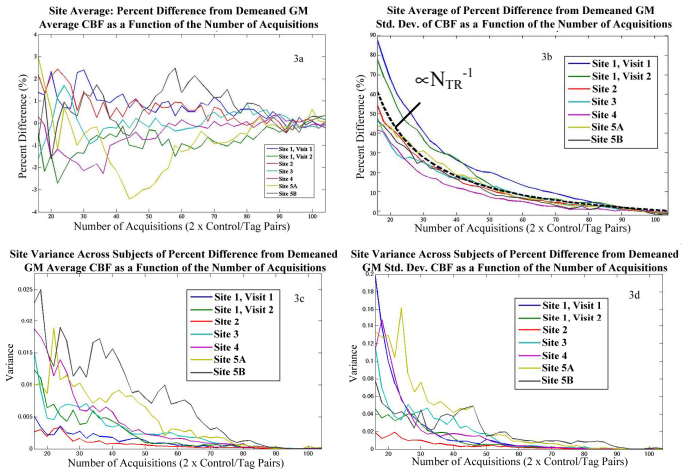

Figure 3. GM Masked mean and spatial std. dev. of CBF values averaged (3a, 3b) across subjects for each site. Variance across subjects at each site (3c, 3d).

come within 1% of steady state mean CBF (3c) and minimal variance (3d) by 92 TRs (46 tag and control pairs). The rate of convergence in spatial standard deviation was also site dependent and primarily noise driven as evidenced by the $1/(N_{TR}/2)$ trend (Adjusted R-squared=.99) of GM CBF standard deviation (3b).

Discussion

These results suggest that investigators can safely design experiments with a number of acquisitions greater than 92 and is the current FBIRN recommendation. It is recommended that individual sites perform similar analysis to determine what is ideal, as a number of factors can affect the quality of data. In addition, diminishing returns occur quickly and the level of specificity required and time demands for a particular study may not suit the above recommendation. Based on these results, given careful observation and analysis, it may be possible to differentiate between subjects or groups with significantly less temporal acquisitions. These results do not necessarily generalize to regional CBF and functional CBF measurements, although the future aim of this research is to address these issues in kind.

References

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