Reliability and Reproducibility of Arterial Spin Labeling Perfusion Measures Assessed with a Multi-Center Study

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Introduction

Arterial spin labeling (ASL) magnetic resonance imaging (MRI) is a non-invasive method for the quantitative measure of cerebral blood flow (CBF). Prior studies have shown good reproduciblity of baseline CBF measures obtained using ASL on a single MRI system over study periods ranging in duration from less than an hour to several months [1-3]. The goal of the present study was to assess the reliability and reproducibility of ASL measures of baseline CBF in a sample of healthy subjects scanned on MRI systems at three different sites.

Methods

The study was performed across three different sites (Duke, Harvard-MGH, Brigham and Women's Hospital (BWH)) that were participating in the Function Biomedical Informatics Research Network (fBIRN). Eleven healthy subjects participated in the study (5 male, ages 24 to 55). Each subject was scanned at each of the three sites, with the scans for each subject obtained over a one month period. Imaging at each site was performed with a 3T whole body imaging system (2 GE Excite systems, 1 Siemens Trio with TIM) equipped with multi-channel receive-only head coils (8-channels on GE systems, 12 channel coil with TIM Trio). Arterial spin labeling was performed using a FAIR ASL pulse sequence with both presaturation pulses and QUIPSS II post-inversion saturation pulses [4,5]. Whole-brain ASL imaging parameters were as follows: TI1/TI2 = 600ms/1600ms, 10cm tag width, 1 cm tag-slice gap, 220mm FOV, 24 slices (4 mm thick, skip 1mm), TR 4 sec, 104 reps, single-shot spiral acquisition (TE = 3ms) for the GE systems, partial Fourier EPI acquisition (TE = 11ms) for the Siemens system. In addition to the ASL scans, a scan with the inversion pulses turned off was acquired to obtain an estimate of the equilibrium magnetization of cerebral spinal fluid (CSF) and a minimum contrast image was acquired to adjust for coil inhomogeneities [6]. A per-voxel CBF estimate was obtained from the mean difference of the control and tag images in the ASL time series. This estimate was converted to physiological units of mL/(100g-min) using the CSF and minimum contrast images [7]. A high resolution anatomical scan was used to identify gray matter voxels, and the mean gray matter CBF value was computed for each subject and scan session. A repeated measures ANOVA was used to assess the effect of site and subject. We computed the intraclass correlation coefficient (ICC) as a measure of reliability, the within-subjects variation coefficient (WSC) as a measure of reproducibility, and the random noise coefficient (N) as defined in [3]. In addition, post-hoc paired t-tests were used to compare CBF values obtained between pairs of sites.

Results

Figure 1 shows representative CBF maps from one subject scanned at all three sites (the grayscale bar indicates units of mL/(100g-min)). There was not a significant effect of site ($F(2,20) = 0.36$, $p = 0.70$) on the mean gray matter CBF values, but there was a significant effect of subject ($F(10,20) = 2.7$, $p = 0.03$). ICC was equal to 0.38, WSC was -0.04, and the random noise coefficient N was 0.66. Figure 2 shows scatter plots of mean CBF values for (a) Duke vs. MGH, (b) BWH vs. MGH, and (c) BWH vs. Duke. The t-statistic and p-value associated with each paired t-test are shown in the title of each subplot, as well as the r^2 value. Consistent with the results of the repeated measures ANOVA, the post-hoc t-tests did not show a significant difference between sites (p-values ranging from 0.46 to 0.76). In addition, the scatter plots show the wide spread in mean CBF values across subjects.

Discussion

From the ANOVA analysis and the small and negative value for WSC, we conclude that measurement site was a minimal source of variance in the CBF measures. The low reliability (ICC) and relatively high random noise coefficient (N) indicates that a major source of variance is not accounted for by either site or subject alone. This source of variance most likely reflects normal physiological variations in each subject's baseline CBF levels between scan sessions, as well as an interaction term between site and subject. To assess the contribution of the interaction term, future studies will need to obtain repeated measures on each subject at each site. In summary, the current study indicates that with proper acquisition and calibration methods, quantitative CBF measures can be obtained without a significant bias introduced by site. However, further study of the additional sources of variance is needed.

Fig 1.

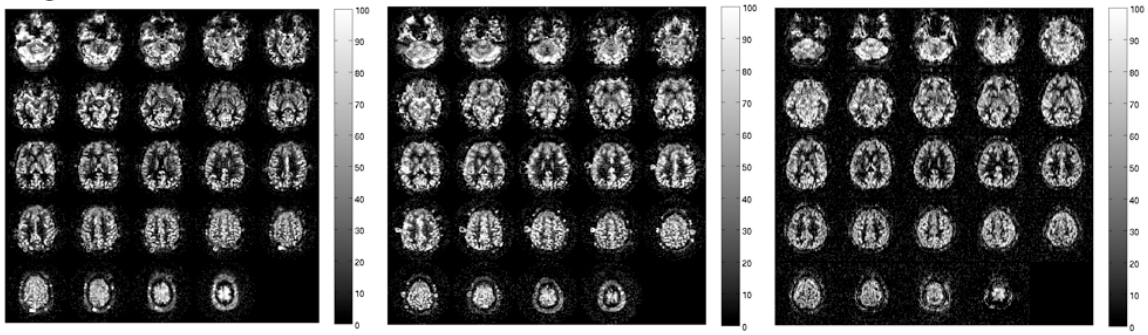
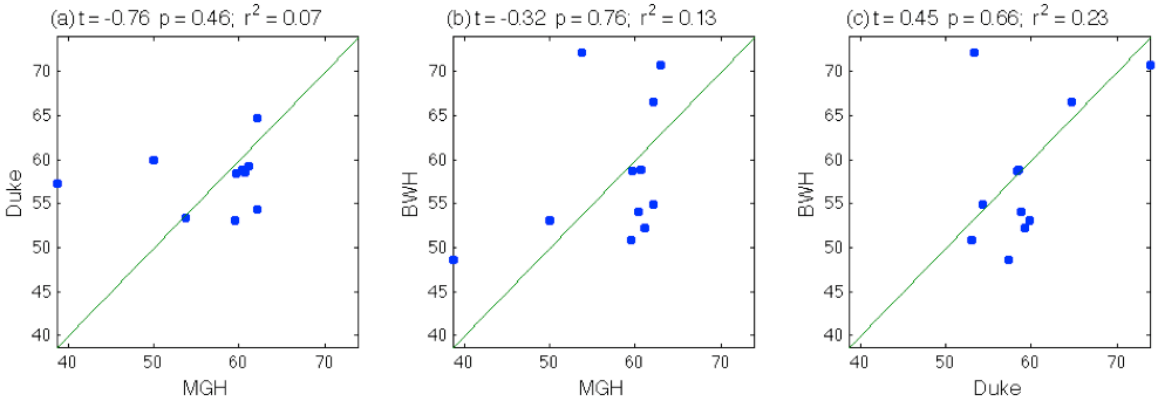


Fig 2.



References

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