Volumetric Measurement of Perfusion and Arterial Transit Delay Using Hadamard Encoded Continuous Arterial Spin Labeling

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Introduction: Arterial spin labeling (ASL) is capable of quantifying tissue perfusion non-invasively. However, a major confounding factor for quantitative ASL perfusion measurement is the time that the labeled blood takes to travel through the arteries from the labeling location to the tissue of interest (1-4). This arterial transit delay, ATD, may cause perfusion to be underestimated or overestimated depending on its length relative to the labeling timing. Though a number of investigators have proposed methods to minimize ATD errors by the choice of labeling parameters (1-3), these approaches are imperfect and require reasonable estimates of the ATD in order to optimize labeling. Directly measuring the ATD could help improve perfusion measurement and might provide an additional measure with diagnostic significance, especially for vascular disease. Current ATD measurement techniques typically require ASL measurements with multiple different labeling timings, but these can be very time consuming and tend to have low signal-to-noise ratio (SNR) (5-8). Hadamard encoding of continuous ASL has been proposed as an approach to increasing the SNR and time efficiency of multiple labeling timing acquisitions (9-10). The potential of this method was demonstrated in a small animal study using a single-slice CASL technique, but has not been rigorously evaluated with volumetric acquisition or in humans. Here we investigate the feasibility and potential SNR (per unit time) improvement of the Hadamard encoded CASL technique for ATD and perfusion measurements of humans in volumetric acquisition.

Theory: The measurement of ATD typically requires acquiring ASL images at multiple (N) different labeling delays or durations. If the multiple ASL images are acquired in a sequential manner, i.e. one image after another, one needs to acquire N×2 images (N label images and N control images). With Hadamard encoded acquisitions, a long ASL preparation period is divided into N smaller time blocks (either evenly or unevenly). A total of N+1 Hadamard encoded acquisitions are acquired, each with a mixture of label and control signals from all the small time blocks. Images representing each block of labeling are reconstructed by the appropriate linear combination (or Hadamard transformation) of the (N+1) images. Theoretically, SNR for each delay of a Hadamard acquisition should be square root of N times better than sequential acquisition, because the signal for each delay is averaged across N+1 acquisitions, instead of 2 for the sequential acquisition, and the entire acquisition is 2N/(1+N) times shorter than sequential acquisition.

Methods: Pulse sequence: Two keys to realizing the potential of Hadamard encoding are a long labeling period, to allow sufficient blocks of labeling, and background suppression to minimize the contribution to noise from motion and other instabilities. We employed interleaved labeling and background suppression (11) to create a long labeling period (from 700ms to 4900 ms) while preserving excellent background suppression. Background suppression was optimized as previously described (12). Vessel suppression preparation (13) was employed to minimize pulsatility and bright signal artifacts from vessels. Pulsed-continuous arterial spin labeling (PCASL) (14) was used for all labeling and a 3D stack of spirals RARE acquisition was employed. The 4200 ms labeling period was divided into seven 600ms blocks for ATD estimation.
In-vivo studies. Six volunteers were imaged on a GE 3 Tesla scanner using an 8-channel head coil receive array. Because we have previously proposed that low-resolution measurements are sufficient for ATD estimation (19), both high-resolution (8 spiral interleaves, 3.1mm in plane resolution) and low-resolution (1 spiral interleave, 12.1mm in-plane resolution) acquisitions were performed with both Hadamard and sequential encoding. In addition, a high-resolution acquisition with a single block of long labeling performed for the entire 4200ms was acquired. This long labeling sequence can be combined with the low-resolution transit map to quantify perfusion (15) (Perfusion Imaging with a LOw resolution Transit Scan (PILOTS)). Repeated scans were used to assess noise and test-retest reliability.
Analysis: ROIs were drawn on a single slice to calculate signal and noise. ATD and perfusion maps were calculated from multi-delay data by fitting data to a kinetic model (ref). Perfusion from the long labeling acquisition was corrected using the ATD map calculated from the low-resolution Hadamard encoding. Reproducibility of ATD and perfusion maps were quantified by the standard deviation from the distribution of fractional change between repeated scans. Simulations were performed to determine the consistency between our experimental results and the theoretical predictions of the relative SNR of different ATD and perfusion measurement methods.

Results & Discussion: Images from Hadamard encoded acquisition showed identical signal, lower noise and consequently superior SNR compared to sequential acquisitions (Fig. 1). The noise ratio between sequential and Hadamard encoded acquisition across all delays were 1.97 ± 0.07, which is consistent with the theoretical value of 2. The ATD measurement from the low-resolution Hadamard acquisition was more reproducible than from the high-resolution Hadamard acquisition (Table 1). This is expected due to the increased SNR from the low-resolution acquisitions. The perfusion measurement using the PILOTS scheme was more reproducible than using the high-resolution Hadamard encoded method (Table 1 & Fig. 2). Simulations confirmed that noise should be reduced using the PILOTS method. In conclusion, we have demonstrated the feasibility of the Hadamard encoded method in humans and improved SNR for ATD and perfusion measurements.

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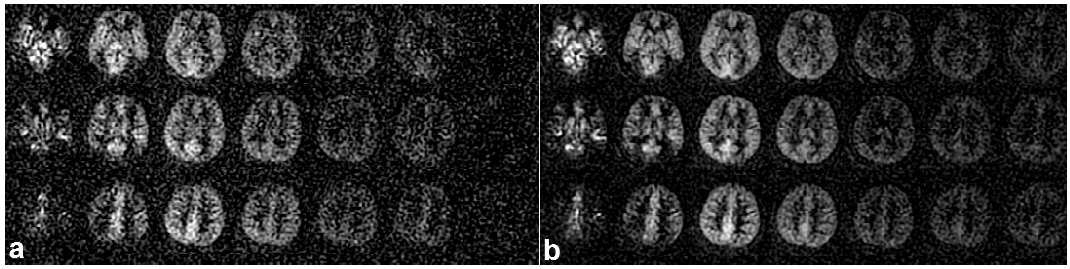

Fig. 1. Perfusion difference images derived from multi-delay (a) sequential (14 min) and (b) Hadamard (8 min) acquisitions showing higher SNR in less time with Hadamard.

Table 1. Standard deviations of fractional changes in ATD and perfusion

	ATD Low Res Hadamard	ATD Hi Res Hadamard	Perfusion using PILOTS	Perfusion using Hadamard
Average SD	0.07 ± 0.03	0.14 ± 0.03	0.16 ± 0.06	0.28 ± 0.06

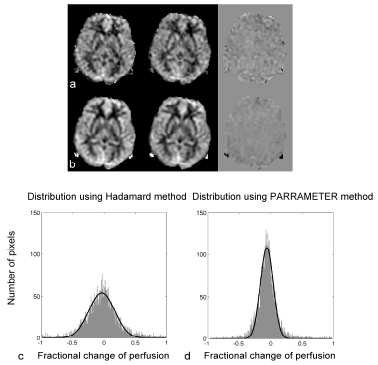

Fig. 2. The perfusion map from two repeated scans and the difference perfusion map using a) Hadamard and b) PILOTS method; the distributions for fractional change between the two repeated scans using c) Hadamard and d) PILOTS method.