Assessment of Myocardial Blood Flow in Humans Using Arterial Spin Labeling: Feasibility and Noise Analysis

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INTRODUCTION

Arterial spin labeling (ASL) is a powerful tool for the quantitative measurement of tissue blood flow, and has been extensively applied to the brain. Its use in myocardial blood flow (MBF) measurement [1-4] has been limited by inadequate signal-to-noise ratio (SNR) efficiency and timing restrictions related to cardiac motion. In this work, we demonstrate MBF measurements in humans, using cardiac gated Flow-sensitive Alternating Inversion Recovery (FAIR) [5] tagging and balanced Steady-State Free Precession (SSFP) imaging at 3 Tesla, and present an analysis of thermal and physiological noise and their impact on MBF measurement error. The measured MBF was found to be inflow dependent, and increased as expected with passive leg elevation and isometric handgrip stress. We determine that myocardial ASL is critically limited by low SNR and physiological noise, which are important challenges for further investigation.

METHODS AND RESULTS

Myocardial ASL experiments were performed using the cardiac gated FAIR-SSFP sequence illustrated in Fig. 1. Inversion and imaging were both centered at mid-diastole. One pair of control and tagged images was acquired 6 s apart during a single breath-hold with an alternating order, and six breath-holds (10-12 s each) were used for signal averaging. To achieve complete cancellation of static tissue signal during subtraction, the inversion delay was kept identical for each image pair in the same breath-hold. Image acquisition was performed using a snapshot 2DFT balanced SSFP sequence with 3.2 ms TR and 50° flip angle, and the inversions were achieved using adiabatic (hyperbolic secant) pulses. Experiments were performed on a GE Signa 3.0 T EXCITE with an 8-channel cardiac array coil. Regions of septal myocardium on mid-short axis were manually segmented for each breath-hold, and MBF was estimated using Eq. 1 derived from Buxton's general kinetic model [6], where *C*, *T*, and *B* refer to the mean myocardial signal on the region of interest (ROI) in the control, tagged, and baseline (no prep) images, *RR* represents R-R interval, and *T1* corresponds to T1 of blood.

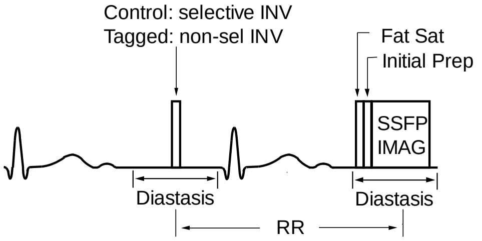

Figure 1. Cardiac gated FAIR – SSFP pulse sequence

$$MBF = \frac{C-T}{2B \cdot RR \cdot e^{-RR/T_1}} \quad (1)$$

$$\sigma_{MBF,T} = \frac{\sqrt{2/N_{avg}} \cdot \sigma_N}{2B \cdot RR \cdot e^{-RR/T_1}} \quad (2)$$

$$\sigma_{MBF,P} = \frac{\sigma_S}{\sqrt{N_{BH}}} \quad (3)$$

In-vivo Feasibility - *Resting MBF*: Fifteen scans of resting MBF measurements were performed in ten healthy volunteers with no restriction of exercise or caffeine/food intake prior to imaging. The results from all scans are summarized in Table 1. The measured MBF range was 0.74 - 2.25 ml/ml/min, which is consistent with literature values established by ^{13}N-Ammonia PET [7]. *Dependence of Inflow*: In five healthy subjects, myocardial ASL scans were performed with three different inversion slab thickness in control images to modulate the distance between the tagged volume and the imaging slice; 1) only the imaging slice (3 cm thick, same as regular MBF), 2) the entire LV myocardium up to the aortic valve plane (12 cm thick), or 3) everything (nonselective). The average ratios of MBF in case 2 and 3 with respect to case 1 were 31.9% and 18.4% respectively. *Mild Stress Imaging*: In four healthy subjects, myocardial ASL scans were performed at rest, and with two forms of mild stress. 1) Leg elevation: both the subjects' legs were passively elevated by 30-40 degrees to increase venous return. 2) Handgrip: The subjects were asked to maintain isometric handgrip at 40% of maximum voluntary contraction (MVC). The average increases in MBF were 32.2% and 28.1% for leg elevation and handgrip respectively.

Thermal Noise Analysis - Based on Eq. 1 and the i.i.d. additive white Gaussian model of thermal noise in the image domain, the MBF measurement error is expected to follow a Gaussian distribution with zero mean and standard deviation shown in Eq. 2 where N_{avg} is the total number of voxels averaged (over a ROI and multiple breath-holds), and σ_N is the standard deviation of the Gaussian thermal noise affecting each voxel in each source image (tagged and control). Using this distribution, the probability of MBF measurement error being < 0.1 ml/ml/min was calculated for each scan. The range of the probability was 70.0 - 98.5 % (yellow column).

Physiological Noise Analysis - Standard deviation of the six measurements σ_S was measured as an estimate of physiological noise. Based on a Gaussian model for physiological noise, the MBF measurement error also follows a Gaussian distribution with zero mean and standard deviation shown in Eq. 3 where N_{BH} is the number of breath-holds. The probability of MBF measurement error being < 0.1 ml/ml/min using this distribution was 18.2-94.0 % (blue column), showing a substantially wider range compared to that of thermal noise only.

DISCUSSION

We have demonstrated the feasibility of MBF assessment in humans using ASL at 3 Tesla. MBF measurements in healthy volunteers at rest were consistent with MBF ranges established by the quantitative PET literature. These MBF measurements were inflow-dependent, and increased with passive leg elevation and handgrip stress as expected. This study has also determined that myocardial ASL is limited by SNR. The fact that intrinsic myocardial SNR when using 8-channel cardiac coils is roughly 3-3.5 times lower than gray matter SNR when using 8-channel head coils (measured on our 3 T scanner) explains the need for signal averaging over a ROI and multiple breath-holds to achieve a higher number of averages compared to brain ASL. Our result also demonstrates that physiological noise ($\sigma_{MBF,P}$) is about 3.4 times higher than thermal noise ($\sigma_{MBF,T}$). There is substantial opportunity for improved tagging and imaging methods that may increase SNR efficiency while reducing physiological noise up to thermal noise level (theoretical lower limit of physiological noise).

MBF (ml/ ml/ min)	ROI size (cm^3)	Confidence (%)	
		Thermal noise only	Physiological noise
0.74	21.0	96.1	94.0
0.83	8.1	70.5	73.6
1.11	12.6	90.6	35.3
1.16	15.3	71.2	42.0
1.16	20.8	97.0	62.6
1.17	14.1	84.3	50.6
1.21	14.7	70.0	23.7
1.27	39.2	98.5	38.1
1.33	14.5	88.4	46.8
1.37	22.4	75.8	28.0
1.60	24.5	94.0	18.2
1.62	17.8	92.8	32.4
1.77	18.7	82.9	42.2
1.85	17.5	80.5	18.2
2.25	17.0	89.6	20.2

Table 1. Measured MBF at rest, septal ROI size, and confidence (probability that measurement error is < 0.1 ml/ml/min) based on thermal noise only (yellow) and physiological noise (blue).

REFERENCES

[1] Poncelet BP *et al,* MRM 41:510, 1999. [2] Wacker CM *et al,* JMRI 18:555, 2003. [3] An J *et al*, 13th ISMRM p253, 2005. [4] Zhang H *et al*, MRM 53:1135, 2005. [5] Kim SG, MRM 34:293, 1995. [6] Buxton RB *et al*, MRM 40:383, 1998. [7] Chareonthaitawee P *et al*, Cardiovascular Research 50:151, 2001.