Improved Arterial Spin Labeling After Myocardial Infarction In Mice Using Respiratory and Cardiac Gated Look-Locker Imaging with Fuzzy C-Means Clustering for T1 Estimation

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Introduction

Quantitative arterial spin labeling (ASL) of myocardial perfusion has previously been demonstrated in mice[1,2]. However, due to erratic respiratory patterns and increased variability of the ECG, this technique has not been successfully applied to mouse models of acute myocardial infarction (MI) and post-MI infarct healing. Prior methods for minimizing respiratory artifacts include manually removing artifact-ridden frames[1], using velocity-compensated gradients, and signal averaging[2]. We developed a cardio-respiratory gated Look-Locker spiral ASL sequence which uses a fuzzy C-means (FCM) clustering algorithm to reconstruct ASL images and assign image inversion times (TIs). This method markedly reduced motion artifacts and enabled the quantitation of myocardial perfusion in mice after experimental MI.

Methods

A Look-Locker spiral ASL sequence was implemented on a 7T Clinscan MR system (Bruker, Germany) using combined respiratory gating and ECG triggering, where ECG triggers were detected only during the quiescent phase of expiration. Upon detection of a respiratory-gated ECG trigger, a 5ms hyperbolic secant RF inversion pulse was applied. At 30 subsequent respiratory-gated ECG triggers, a low-flip-angle RF excitation pulse was applied and a time-stamped gradient-echo spiral interleaf was acquired. After a delay of at least 5 sec between inversion pulses, the pulse sequence was repeated until multiple averages of all spiral interleaves were acquired. For each complete scan, data sets were acquired using both non-selective and slice-selective inversion pulses. For image reconstruction, a FCM clustering algorithm[3] was used to sort the data, which were cardio-respiratory gated, and, consequently, acquired at inconsistent inversion times. Specifically, the time-stamped TIs for all spiral interleaves were used to identify TI clusters and to determine the membership of each interleaf within each cluster. Images were reconstructed using primary cluster membership, and missing interleaves were filled with closest matches based on cluster membership values. After image reconstruction, the myocardium was manually segmented in one image and pixel-wise T1 maps were calculated for the data sets acquired using both the non-selective and slice-selective inversion pulses. T1 estimation used Bloch equation simulations to account for the effects of the RF excitation pulses. After estimation of the T1 values, myocardial perfusion (P) was calculated according to Kober et al[1]. The method was successfully validated by scanning stationary phantoms without and with cardio-respiratory gating from live mice. The method was then applied to mice at baseline (n=7) and 1 day following experimental reperfused MI (n=6). During MRI, mice were anesthetized using 1.25% isofluorane and body temperature was maintained at 36.3±0.6°C. Cardiac and respiratory gating were performed using a dedicated system for small animal MRI (SAII, Inc, Stony Brook, NY). Specific ASL parameters included slice thickness = 2.5mm for the slice-selective inversion, flip angle = 15°, TE = 0.67ms, TR = 5sec, averages = 3, number of spiral interleaves = 87, slice thickness = 1mm, FOV = 3.0 x 3.0 cm^2, and matrix = 128x128. Following collection of ASL data after MI, delayed contrast enhancement (DCE) images were acquired to determine the infarct region.

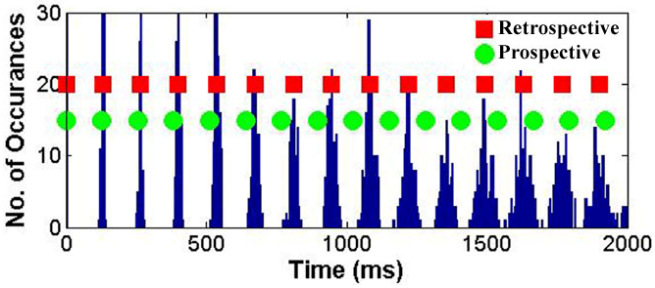

Figure 1. Histogram of TI distribution for a cardio-respiratory gated ASL scan of a mouse. Green circles indicate image TI values assigned by prospective estimation. Red squares represent the TI values for each reconstructed ASL image calculated using an FCM clustering algorithm.

Results

Figure 1 shows an example histogram of the post-inversion TIs of the cardio-respiratory gated spiral interleaves from a mouse. Prospective assignment of image TIs based on average heart rate is indicated by green circles, whereas retrospective assignment of image TIs computed by the FCM clustering algorithm is indicated by red squares. The red squares more accurately reflect the TIs of the data clusters, and lead to more accurate estimates of T1. Cardio-respiratory gated ASL images showed marked reduction of motion artifact compared to images that were not respiratory gated. For the cardio-respiratory gated sequence, example post-infarct T1 maps for non-selective and slice-selective inversion pulses, and the corresponding perfusion map are shown in Fig. 2. The ASL perfusion defect (Fig. 2C, blue) closely matches the infarct region as delineated in the delayed hyperenhancement image (Fig. 2D). For the mice studied at baseline, myocardial perfusion by cardio-respiratory gated ASL was 3.5 ± 0.3 (ml/g·min) (mean±SEM). After MI, perfusion in the noninfarcted zone (P_{remote}) was 4.5 ± 0.4 (ml/g·min) ($p<0.05$ vs. baseline) and in the reperfused infarcted zone ($P_{infarct}$) was 1.9 ± 0.3 (ml/g·min) ($p<0.05$ vs. baseline and P_{remote}). Perfusion was also assessed in 3 mice post-MI without respiratory gating, where P_{remote} was 11.1 ± 0.9 (ml/g·min) and $P_{infarct}$ was 4.0 ± 1.0 (ml/g·min), demonstrating the large errors that can occur if respiratory motion is not accounted for.

Conclusions

Use of cardio-respiratory gating during image acquisition and implementation of an FCM clustering algorithm for ASL image reconstruction reduced respiratory artifact and enabled measurement of myocardial perfusion following MI in the mouse heart. This method, when applied to genetically-engineered mice, will enable studies of the roles of individual genes in myocardial perfusion after MI and during infarct healing.

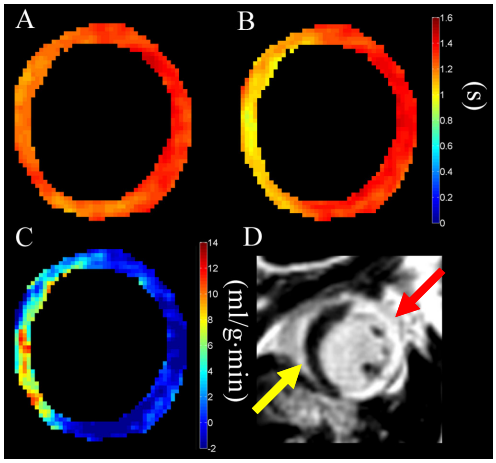

Figure 2. T_1 maps for non-selective (A) and slice-selective (B) inversions. Myocardial perfusion (C) was significantly lower in the infarct zone one day after MI. DCE image (D) shows high intensity infarcted myocardium (red arrow) and a low intensity remote zone (yellow arrow).

[1]Kober et al., *MRM*, 2005; 43; 601-606
[2]Streif et al., *MRM*, 2005; 53; 584-592
[3]Fukunaga., *Intr. Stat. Pattern Recognition*, 1990; 508-562

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