Feasibility of cyclic myocardial perfusion variation assessment during adenosine-induced stress in rats

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Purpose

Arterial spin labeling (ASL) has become a method of choice to quantitatively map rodent myocardial blood flow. Cine-ASL has recently been proposed as an original approach to assess myocardial blood flow (MBF) (1-2). It has been validated at rest in the mouse heart by comparison with the previously used Look-Locker FAIR gradient echo (2-3). Beyond improving ASL sensitivity, this method allows dynamic mapping of MBF across the cardiac cycle. Myocardial blood volume (MBV) and MBF vary during the cardiac cycle in response to pulsatile change in coronary circulation and cyclic variation in myocardial tension. Cyclic change of regional MBV in the mouse heart has already been reported in the literature (4); however, no study has focalized on MBF variation over the cardiac cycle. In a preliminary study we have measured cyclic change of regional MBF in healthy mice at rest (5) and shown a significant MBF increase of 30% from end-systole to end-diastole. Based on this finding, we propose a new protocol, which compares cyclic MBF changes on rats between rest and during adenosine-induced stress.

Methods

Cine-ASL relies on a fast ECG-gated cine-FLASH sequence repeated over several cardiac cycles for each line of k-space. At each cardiac cycle, one single gradient-echo is substituted by a selective inversion pulse, labeling the blood at the level of the aortic root at end-systole, just before entering through the coronary system (Figure 1).

Experiments were performed on a Bruker Biospec 4.7T/30 imager. The following parameters were used: slice thickness 2 mm (Gaussian pulse), in-plane pixel size 313x625 µm², TE/TR 1.64/6 ms and flip angle 8°. The total acquisition time was approximately 9 min at a heart rate of 400 bpm. As a proof of feasibility, the protocol was tested on a healthy Wistar rat by performing a cine-ASL acquisition at rest prior to adenosine infusion via the tail vein at a rate of 140 µg kg^{-1} min^{-1}. The second cine-ASL sequence was acquired 5 min after the initial heart rate drop observed upon arrival of adenosine.

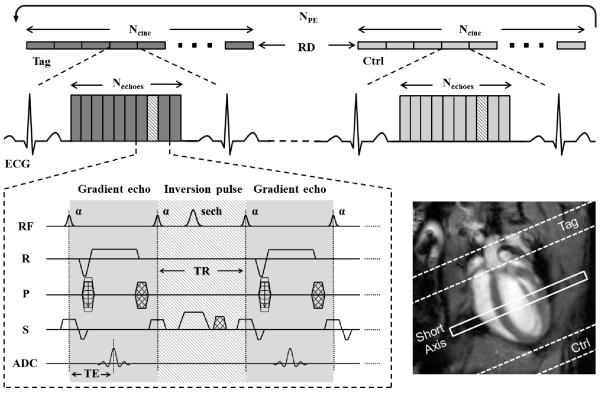

Figure 1: Schematic description of the cine-ASL pulse sequence.

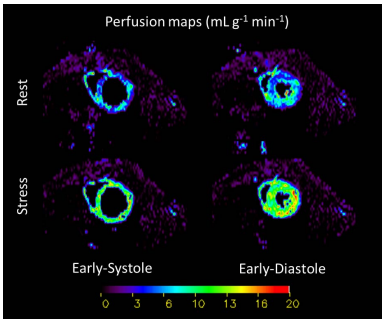

Figure 2: Perfusion maps.

Results and Discussion

Consistent spatial and temporal MBF distributions in the left myocardium within the cardiac cycle were observed. Figure 2 shows MBF maps for two specific time frames, early-systole (left) and early-diastole (right), at rest (top) and during adenosine-induced stress (bottom). Figure 3 presents MBF values obtained in the anterior wall as a function of time at rest (blue) and during stress (red). The heart rate was similar for both states (400bpm/150ms and 415bpm/145ms respectively) although the labeling pulse had to be shifted by one echo backward to match contraction timing changes during stress. Mean MBF increased from 6.8 ± 0.6 mL g^{-1} min^{-1} at rest up to 11.4 ± 0.5 mL g^{-1} min^{-1} during stress. Cyclic MBF variation was found higher at rest (28%) compared to stress (22%). Both time courses of perfusion at rest and under stress show a minimum MBF at end systole. This confirms that capillary perfusion is highest during diastole, in which the perfusion pressure gradient is highest and the resistance of the vessels to that gradient is lowest (6). One can also notice a slight delay of the MBF minimum in diastole during stress.

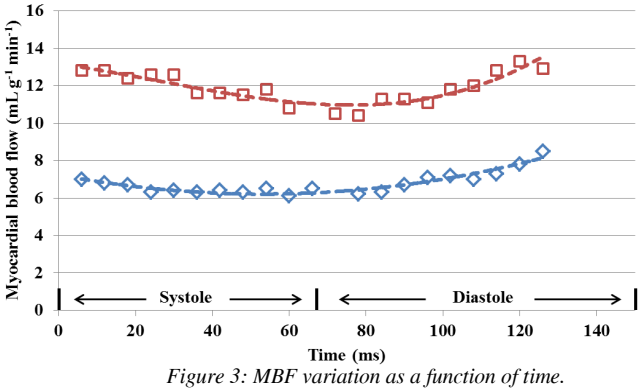

Figure 3: MBF variation as a function of time.

Conclusion

In this feasibility study, the cyclic change of regional MBF was examined by mapping MBF with a steady-pulsed ASL approach in a rat in vivo. MBF maps were obtained with high spatial and temporal resolution (6ms) demonstrating the feasibility of mapping cyclic MBF changes in vivo at rest and during adenosine-induced stress. Such measurements can be used to measure rodent coronary reserve and coronary responses to infused vasodilators in detail and may give complementary information on microvascular functional defects in non-ischemic heart disease models. Due to the relatively short acquisition time (<10min), cyclic MBF variations assessment using cine-ASL may also open new insights into the perfusion time course after onset of adenosine stress.

References

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