

Quantification of Myocardial Blood Flow and Flow Reserve in Rats Using Arterial Spin Labeling MRI, Comparison with a Fluorescent Microsphere Technique

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Introduction

Non-invasive quantification of MBF reserve may play an important role in grading the severity of the cardiac damage in disease such as diabetes, hypertension and coronary artery disease. In earlier studies, myocardial blood flow reserve was assessed using arterial spin labeling MRI in rats anesthetized with pentobarbital which is known to depress cardiac function. The purpose of this study was to non invasively quantify myocardial blood flow reserve in isoflurane-anesthetized rats using a Look-Locker flow-alternating inversion recovery gradient-echo arterial spin labeling technique (LLFAIRGE-ASL), and to compare the results with the fluorescent microsphere (FM) technique.

Materials and Methods

Male Wistar rats (weight=200-240g, n=21) were anesthetized with 2.0% isoflurane. Hemodynamic parameters were recorded. In 7 rats, MBF was assessed on a Bruker Biospec 4.7T MR system using an ECG- and respiration-gated LLFAIRGE-ASL technique (pixel size=234×468μm², TE=1.52ms). This technique acquires one phase-encoded gradients echo per heart cycle (Kober 2004) after a slice selective or global adiabatic spin inversion. The measurement was performed at rest and during continuous adenosine infusion through a catheter placed in the tail vein (140μg/kg/min). A mixture of 200,000 FM was injected into a second group of rats at rest and during adenosine infusion (n=7 each), under similar physiologic conditions. Hearts and skeletal muscle samples were processed for fluorescence spectroscopy. Two-tailed unpaired, paired Student's t-test and ANOVA were used to compare groups.

Results

Figure 1 shows two typical perfusion maps at rest (left) and under stress (right). MBF measured with LLFAIRGE-ASL was 5.2±1.0mL/g/min at rest and 13.3±3.0 mL/g/min during adenosine infusion. Results obtained with fluorescent microspheres yielded 5.9±2.3 mL/g/min (non significant vs LLFAIRGE-ASL, p=0.9) at rest and 13.1±2.1mL/g/min (non significant vs LLFAIRGE-ASL, p=0.4) during adenosine infusion. Myocardial blood flow reserve measured using LLFAIRGE-ASL and FM were not significantly different (2.5±0.6 vs 2.4±0.9 respectively; p=0.8). Hemodynamic parameters during the experiments were not different between the groups. For comparison, skeletal muscle blood flow measured with FM and LLFAIRGE-ASL at rest was 0.1±0.1 mL/g/min and 0.3±0.4 mL/g/min, respectively, and not statistically different from zero.

Conclusion

Myocardial blood flow reserve determined under isoflurane anesthesia was 2.5±0.6 which was not different from the value obtained with FM. This value is in agreement with although in the higher range of flow reserve values reported in the literature in rodents in response to adenosine. Reported MBF reserve values vary between 1.2 to 2.5 in rats and mice using different measurement techniques (Croteau 2004, Raher 2007, Waller 2000, Vandsburger 2007). A recent study by Vandsburger *et al.* used ASL in mice with an A2A adenosine receptor agonist (ATL313) in intra peritoneal injection during anesthesia with isoflurane and found a coronary reserve around 2. Waller *et al.* (Waller 2000) found a MBF reserve of 1.2 in rats using pentobarbital anesthesia and arterial spin labeling MRI. Most likely, the difference in hemodynamics during stress is a function of the anesthetic used. A comparison of results between these different settings therefore appears difficult. The finding of a significant MBF reserve using isoflurane is important, since this anesthetic is commonly used in imaging experiments due to its good maintenance of cardiac function and physiology in general.

LLFAIRGE-ASL has provided MBF maps with high spatial resolution in rats under isoflurane anesthesia. Arterial spin labeling MRI in general, and LLFAIRGE in particular is a non invasive measurement to assess myocardial blood flow reserve and therefore provides an interesting tool for cardiovascular research.

References

C Waller et al, *Radiology*. 2000; **215**: 189-197, MJ Raher et al, *Circulation*. 2007; **116**: 1250-1257, E Croteau et al, *J Nucl Med*. 2004; **45**: 1924-1930, MH Vandsburger et al, *Eur Heart J*. 2007; **28**: 2792-2798, MH Vandsburger et al, *Magn Reson Med*. 2010; **63**: 648-657, F Kober et al. *Magn Reson Med*. 2004; **51**: 62-67

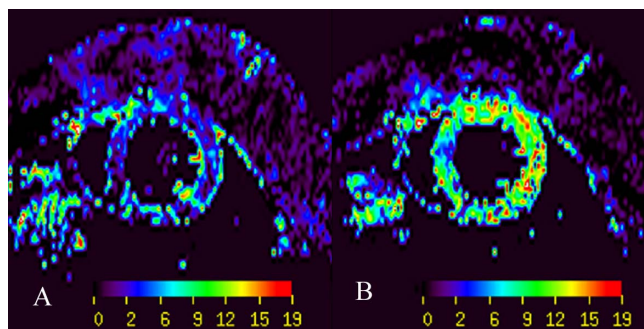


Figure 1