Quantitative Assessment of Myocardial Flow Reserve in a Porcine Model of LAD Stenosis

B. P. Poncelet#, M. K. Atalay#, H. L. Kantor*, T. G. Reese#, T. J. Brady# and R. M. Weisskoff#
*Massachusetts General Hospital #NMR Center-Radiology, Charlestown, MA and *Cardiac Unit, Boston, MA*

Introduction

Current imaging measurements of cardiac perfusion require the injection of an exogenous contrast agent. Recently, noninvasive measurement of myocardial perfusion has been demonstrated in isolated hearts at 4.7T using arterial spin labeling [1-2]. We have developed a double-gated FAIR method, enabling the steady-state measurement of myocardial perfusion at 1.5T and in vivo, both in humans and in animal models [3]. The purpose of this study was: 1) to assess the accuracy of our method using radiolabeled microsphere flow measurements, and 2) to test the sensitivity of our method at 3T for the detection of regional differences in myocardial perfusion reserve in a porcine model of LAD stenosis.

Methods

Porcine model - Nine Yorkshire pigs (50-70 kg) were studied, using a closed-chest model previously published [4]. Following sedation, a catheter with a Delran stenosis (81% lumen reduction) attached at its tip, was placed under fluoroscopy into the proximal segment of the left anterior descending (LAD) coronary artery. Another catheter was placed into the left atrium for injection of radiolabeled microsphere and a femoral artery was canulated for reference blood withdrawal.

MR acquisition - FAIR imaging was performed with an IR EPI pulse sequence (3T GE-ANMR system), alternating between selective and non-selective inversions (IR slab=12 mm/∞) and gating the inversion and excitation pulses at the same cardiac phase in consecutive heart beats (i.e. double-gated, TI=3RR≈1.6s). For each series, 54 pairs of short-axis IR images (slice=5mm, TE=22ms, pixel=3x3mm, FOV=20x40cm) were acquired at mid-level of the heart and double-gated at end-systole (TR≈6s, Tacq≈12mins). The animal respirator was gated to the image acquisition.

Pairs of FAIR and microsphere flow measurements were collected at rest and during graded intravenous infusion of adenosine (IV ADO 140, 280 and 420 μg/kg/min). Changes in heart rate and blood pressure between doses were minimized by infusion of phenylephrine.

At the conclusion of each experiment, 3 injections were perfomed into the LAD catheter: 1) a small dose of microspheres was injected for delineation of the perfusion territory distal to the stenosis, 2) a multislice series of T2*-weighted EPI images were acquired during injection of Gd-DTPA for MR registration and, 3) a bolus of methylene blue was injected for visual inspection at autopsy.

MR myocardial blood flow (MBF) and flow reserve (MFR) were calculated as previously described [3]:

$$MBF = \Delta S\ \lambda / (\alpha\ Mo\ TI_{avg}\ \exp^{(-TIavg/T1insel)})$$

and $$MFR = MBF_{ADO} / MBF_{rest}.$$

Results and Discussion

The average T1 of the myocardium, determined from the non-selective IR data, was 1443 ± 82ms (n=8) and blood T1 was approx. 1820ms. The average myocardial signal change at rest between selective and non-selective data, ΔS/Mo, was 2.0 ± 08%, corresponding to a calculated myocardial flow of 1.15 ± 0.34 ml/g/min. The noise of our calculated flow in 1.5 cc wall segment was 0.22 ml/g/min.

FAIR allowed in all 9 pigs the successful detection of pharmacologically induced regional differences in myocardial flow reserve (see **Fig.1** and **Fig.2**). Myocardial flow increased significantly more in the control territory than in the LAD territory ($MFR_{control}$ = 3.8 ± 1.1 vs MFR_{LAD} = 1.5 ± 0.8, p<.001).

Comparison with radiolabeled microsphere flow measurements showed a good correlation across all LV wall segments ($flow_{MR}$ = 0.62 + 0.61 x $flow_{\mu sphere}$; n=9, r=0.89), though with a positive offset and a slope < 1. Such systematic differences between methods will require further investigation to elucidate the source of discrepancies from the arterial spin labeling model.

Conclusion

Our data indicate that FAIR measurement of MBF can detect pharmacologically induced focal ischemia without contrast agent. Given the precision of our data, we can estimate the increased flow that would be required in a pharmacologic stress protocol to reliably distinguish between normal and abnormal tissue. Stress induced increases in flow under stress must exceed 3 ml/g/min to reliably detect severe ischemia (absence of reserve), and must exceed 4 ml/g/min to detect moderate ischemia (less than a doubling of flow).

References

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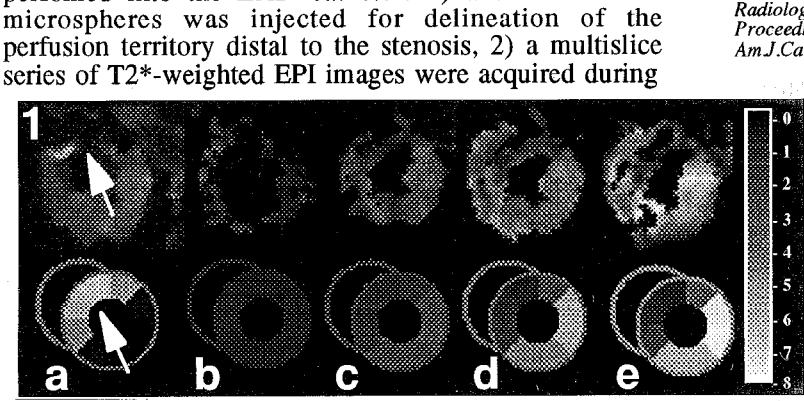

Figure 1. Calculated flow maps (in ml/g/min) by MR (top) and microsphere (bottom) in swine at rest (b) and during graded IV ADO infusion (140, 280 and 420 μg/kg/min) (c-e). Reference T2*-weighted image acquired during Gd-DTPA injection into the LAD (a, top) shows the extent of the LAD territory distal to the stenosis (see arrow). Reference LAD microsphere map (a, bottom) reveals the same antero-septal LAD territory (see arrow). Note the lack of flow increase in the LAD territory and the progressive flow increase in the other LV walls (control).

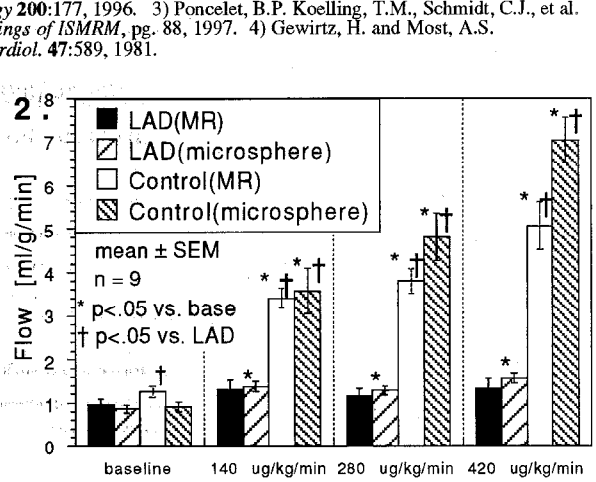

Fig 2. Comparison of MR and microsphere flow measurementss at rest and during graded IV ADO infusion in LAD and control LV walls.