Original Research

Estimation of Absolute Myocardial Blood Flow During First-Pass MR Perfusion Imaging Using a Dual-Bolus Injection Technique: Comparison to Single-Bolus Injection Method

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Purpose: To compare the dual-bolus to single-bolus quantitative first-pass magnetic resonance myocardial perfusion imaging for estimation of absolute myocardial blood flow (MBF).

Materials and Methods: Dogs had local hyperemia of MBF in the left anterior descending (LAD) coronary artery (intracoronary adenosine). Animals ($n = 6$) had sequential single- and dual-bolus perfusion studies with microsphere determination of absolute MBF. Perfusion imaging was performed using a saturation-recovery gradient-echo sequence. Absolute MBF was by Fermi function deconvolution and compared to transmural, endocardial, and epicardial microsphere values in the same region of interest (ROI).

Results: Signal and contrast were significantly higher for the dual-bolus perfusion images. The correlation with MBF by microspheres was $r = 0.94$ for the dual-bolus method and $r = 0.91$ for the single-bolus method. There was no significant difference between MRI and microsphere MBF values for control or hyperemic zones for transmural segments for either technique. When the ROI was reduced to define endocardial and epicardial zones, single-bolus MR first-pass imaging significantly overestimated MBF and had a significantly larger absolute error vs. microspheres when compared to dual-bolus perfusion.

Conclusion: Both single-bolus and dual-bolus perfusion methods correlate closely with MBF but the signal and contrast of the dual-bolus images are greater. With smaller nontransmural ROIs where signal is reduced, the dual-bolus method appeared to provide slightly more accurate results.

Key Words: MRI perfusion; hyperemia; adenosine; myocardial blood flow; imaging
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RELATIVE MEASURES of myocardial blood flow (MBF) can be acquired using one of a variety of noninvasive techniques. However, there are instances when absolute measures of MBF are desirable. These indications may be expanding with the developing capability to augment blood flow with external vectors. These therapies can be highly localized and their effects may be delayed for many weeks (1). Consequently, imaging endpoints need to provide quantitative measures from high spatial resolution and high signal-to-noise ratio (SNR) images. Magnetic resonance imaging (MRI) has shown some promise in this regard (2–9).

Accurate quantitative measures of MBF depend on reliable determination of the arterial input function (AIFN): that proportion of tracer available to the coronary circulation. Metallic-based contrast agents (of which gadolinium DTPA is the most commonly used) cause distortion of the MR signal if present in high concentrations in both atria and ventricles. T2* saturation effects cause the association between tracer concentration and MR signal to become nonlinear at concentrations necessary to visualize differences in tracer uptake within the myocardium (10). To preserve an accurate AIFN, previous studies using quantitative measures have focused on low doses of contrast (3,4,7). The limitation of such an approach is reduced SNR in the myocardial tissue due to the small degree of enhancement, which can be expected at doses in the 0.025–0.05 mmol/kg range.

One alternative method for the quantification of absolute MBF is by preserving an accurate AIFN and combining it with high SNR in the myocardium using a double-bolus technique (8,9). This is accomplished by using a very low-dose bolus to generate an AIFN followed by a high-dose bolus to maximize myocardial enhancement. The methodology is more complex to perform, however. The purpose of this study is to compare estimates of MBF in mL/min/g between low-dose

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Gd-DTPA single-bolus and double-bolus (low-dose AIFN high-dose enhancement), first-pass, MRI, and labeled microspheres in an animal model covering a broad range of physiologic MBF rates.

MATERIALS AND METHODS

Six beagles weighing between 9–11 kg were studied under 1%–2% isoflurane. After midline sternotomy, a portion of the left anterior descending artery (LAD) was dissected free for placement of an infusion catheter for adenosine. A left atrial catheter was placed by direct atrial puncture and a catheter was placed by surgical cutdown to the femoral artery and advanced into the descending aorta. The animals were placed in a 4-coil phased array knee coil and centered in the magnet. After cardiac localization scans the voxel containing the left ventricle (LV) was defined and the field was shimmed for optimal signal detection using stimulated echo spectroscopy (11). The magnet used was a GE Signa 1.5T system (GE Medical Systems, Milwaukee, WI).

At time zero, intracoronary adenosine infusion was started at 20 μg/min/kg. MR perfusion imaging was then performed following a 3-minute delay. Immediately thereafter the animal was withdrawn from the magnet and ≈5 million fluorescent-labeled microspheres (15 μm diameter; IMT Labs, Irvine, CA) were injected into the left atrial catheter with simultaneous reference sampling through the femoral catheter. The delay between Gd-DTPA and microsphere injection was less than 10 minutes and the intracoronary adenosine infusion was maintained throughout this time.

MR Perfusion Protocols

Double-bolus perfusion imaging with Gd-DTPA was performed with a power injector (Med-Rad Systems, Pittsburgh, PA). The double-bolus was accomplished by placing a 0.0025 mmol/kg bolus in the IV tubing, a saline flush in the first injector, four feet of high-pressure IV tubing connecting the second injector to the first filled with 0.10 mmol/kg Gd-DTPA (Berlex Labs, Wayne, NJ), and saline in the second injector. Consequently, each bolus, which was of equal volume, was pushed into the animal by a saline flush at 5 mL/sec. A 10-second delay was programmed between the two injections, and this was occasionally adjusted depending on the heart rate. Single-bolus perfusion was accomplished using a Gd dose of 0.025 mmol/kg, which was diluted to be of equal volume to the dual-bolus low- and high-concentration injections with an infusion rate of 5 mL/sec followed by a 20-cc saline flush at the same rate. There was a 2-hour recovery interval between studies. The dual-bolus was performed first on three animals and second on the other three.

First-order shimming was performed prior to each perfusion scan (11). A saturation recovery gradient echo sequence with an echo train readout was performed during the injections with the following parameters: 0.75 field of view (FOV), matrix = 128 × 96, FOV = 260 mm^2, TR = 7.6 ms, TE = 1.6 ms, saturation pulse = 70–90°, flip angle = 15°, saturation recovery time = 10 msec, echo train = 4, slice thickness = 8 mm (8,9,12,13). Three to four short axis slices with 1-cm gaps were acquired for each R-R interval over 60 cardiac cycles with a temporal resolution of each slice of 192 msec. The spacing was adjusted so that representative apical, mid-ventricular, and basal short axis slices were acquired for each animal per R-R interval.

Quantitation of MBF by MRI

The concept of deconvolution of AIFN with a shaped function to fit the tissue enhancement curve was employed as first described by Axel (5) and adapted to MRI by Jerosch-Harold et al (3). This is accomplished using a Fermi function to deconvolve the input function to fit the slope and peak of the myocardial signal in a region of interest (ROI). We have adapted this approach but have altered it to base the fit of the small bolus for the AIFN since there is a linear association between Gd-DTPA concentration and signal intensity within this low concentration range. The ratio of the Gd-DTPA small to the large bolus (0.0025 to 0.10 mmole/kg) was 40:1. Consequently, we magnified the small bolus by a factor of 40 to generate the fit for the myocardial enhancement. An IDL-based quantitative software program was created to automate these calculations but they could be adjusted to improve the fit. We used conventional single-bolus quantitation for the 0.025 mmol/kg studies where the bolus traversing the LV blood pool is used as the AIFN. There is no magnification of this function. The remainder of the deconvolution method is identical to the dual-bolus protocol. An additional analysis was performed using the high-dose injection as a single-bolus AIFN to calculate MBF from the same ROIs as the dual-bolus protocol. This was done by truncating the time intensity curve in the LV blood pool to exclude the 0.0025 mmol/kg low-concentration bolus and using the single-bolus AIFN algorithm to calculate MBF.

Images were corrected for variations in myocardial signal intensity from unequal distances from the surface coils by a 2D planar adjustment of variation in myocardial precontrast-arrival signal intensity and displayed using an IDL-based program. The ventricle was divided into eight radial segments / short axis slice. These were further subdivided into endocardial and epicardial zones. Two segments per short-axis slice were chosen for analysis based on the microsphere MBF values: a peak intervention zone and a control zone for six data points per perfusion study. We purposely did not analyze all eight segments per slice (24 data points per perfusion study) to avoid artificial inflation of statistical power (14).

SNRs were calculated for each study by measuring the mean signal intensity (SI) in the control ROI at peak Gd enhancement during first-pass perfusion and dividing this value by the standard deviation (SD) of the mean signal intensity to an ROI outside the chest cavity in air. The contrast enhancement ratio (CER) was calculated by: (peak enhancement – precontrast) SI / precontrast SI during first-pass perfusion. These measures were used to assess the physical image differences in dual vs. single-bolus first-pass perfusion experiments.

Table 1
Signal Characteristics of the Single-Bolus (0.025 mmol/kg) and the Dual-Bolus (0.10 mmol/kg) Methods

Dose [Gd]	SNR			CER		
	0.025	0.10	*P*	0.025	0.10	*P*
Adenosine	16.9 ± 4.5	24.4 ± 6.7	<0.0001	0.46 ± 0.11	1.22 ± 0.41	<0.0001
Control	15.3 ± 3.4	21.7 ± 4.7	<0.0001	0.32 ± 0.06	0.89 ± 0.15	<0.0001

Pathologic Analysis

The heart was placed in 10% formalin for at least 48 hours then sliced into 4-mm short axis slices using a commercial grade slicer. These were paired to coincide with the MR perfusion images that were 8 mm in thickness. Each pair of slices was radially segmented by eight, and each of these was further subdivided into epicardial and endocardial regions for a total of 16 segments per slice. MBF was calculated from the colored microsphere content of the myocardial segments and reference samples using a conventional formula in which the number of spheres per segment was substituted for the degree of radioactivity per segment (15).

Statistical Analysis

Data are presented as mean ± SD. Unpaired *t*-tests were used to compare continuous variables by grouping variable. Paired *t*-tests were used to compare variables with paired measures. Analysis of variance was used when more than two variables were being compared simultaneously with post-hoc comparisons performed using the Fischer LSD test. Simple linear regression analysis was used to compare MR perfusion estimates to MBF by microspheres and Bland–Altman plots were constructed from these.

RESULTS

Six animals underwent perfusion imaging using single- and dual-bolus perfusion during IC adenosine infusion for quantitation of absolute MBF. There were no significant differences in MBF values by method. For the adenosine zone: single vs. dual-bolus, 2.12 ± 1.2 vs. 2.04 ± 1.26 mL/min/g, respectively (P = NS), and for control zones: 0.80 ± 0.31 vs. 0.79 ± 0.21 mL/min/g, respectively (P = NS).

The results for SNR and CER values are shown in Table 1. Despite slightly higher average hyperemia and control zone MBF, the CER was more than double for the dual-bolus protocol compared to the single-bolus protocol. SNR was also significantly higher for the dual-bolus protocol, as expected.

The correlation of both techniques with transmural microsphere-derived measures of absolute MBF are shown in Fig. 1. Both techniques reflected absolute MBF values (correlation coefficient >0.90 for both). However, the correlation coefficient was slightly better for the dual-bolus technique and the SD of the agreement was less (mean difference of [microsphere-MRI] single bolus = 0 ± 0.46 mL/min/g, dual bolus = 0 ± 0.37 mL/min/g, P = 0.12) but this did not reach statistical significance (Fig. 2). For control zone measures, the confidence intervals for the error between MRI and microsphere values were 0.72 mL/min/g for single-bolus perfusion and 0.38 mL/min/g for dual-bolus perfusion (P = NS). The results were similar in adenosine zones.

The correlation between MRI and microsphere estimates of MBF was less accurate but significant using high-dose (0.10 mmol/kg) single-bolus deconvolution (r = 0.75, $P < 0.0001$). There was significant overestimation and error introduced by this method. The mean overestimation was 1.49 mL/min/g, with nearly all MRI measures greater than microsphere values. The 95% confidence interval of the difference between these values was almost 3-fold greater (1.90 mL/min/g) using this method.

Confining the ROI to endocardial or epicardial zones (and therefore a 50% smaller ROI), some differences in the techniques were revealed. The correlation coefficients were consistently closer for the dual-bolus technique (Fig. 3). The confidence intervals of agreement with microspheres for absolute MBF values were closer for the dual-bolus approach as demonstrated in the Bland–Altman plots of Fig. 4. The difference between measures was statistically significant, with the dual-bolus approach providing closer estimates to microsphere values (Fig. 5). Figure 6 provides a visual comparison of peak enhancement images and time intensity curves for the two perfusion methods.

DISCUSSION

For most clinical questions, relative measures of MBF are sufficient and are routinely available with noninva-

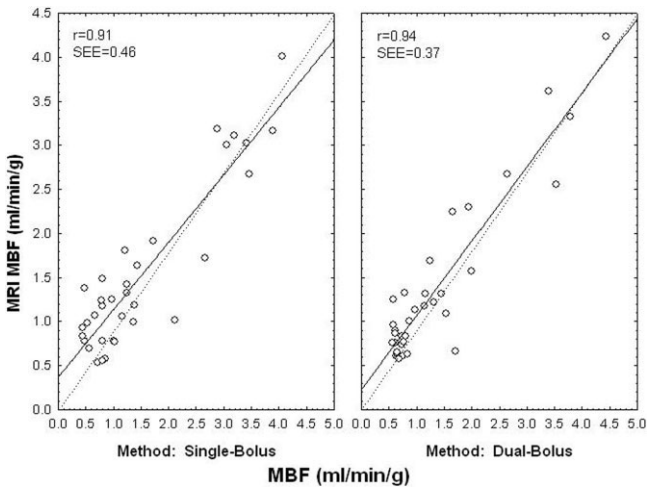

Figure 1. Transmural linear correlations between the low-contrast single-bolus method (left panel) and the high-contrast dual-bolus method (right panel).

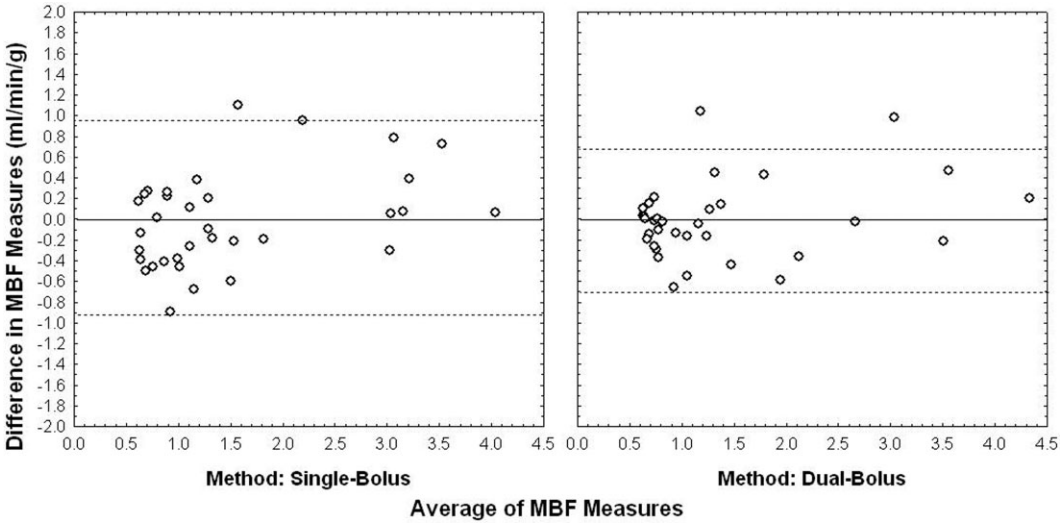

Figure 2. Bland–Altman plots of the correlations for single- and dual-bolus injection methods. The mean difference for both methods was nearly zero. The SD of these differences were single bolus = 0 ± 0.46 mL/min/g, dual bolus = 0 ± 0.37 mL/min/g, $P = 0.12$. Solid line = mean difference, dashed lines ±1.96 SD.

sive radionuclide techniques. While the augmentation of MBF is the goal of revascularization procedures, it is the improvement in symptoms and LV function that are the important clinical outcomes, rather than the quantitative change in flow. There are times when quantitation of flow is desirable, however. For example, understanding the efficacy or mechanism of therapeutic action of new agents in clinical trials whose purpose is to augment MBF. In addition, verifying the adequacy of a pharmacological stress test is not generally possible with relative perfusion images. Quantitative flow measurements could answer both of these questions.

MR cardiac imaging (CMRI) is an attractive alternative to positron emission tomography (PET) for the quantitation of MBF but has yet to be firmly established for this function. The advantages of CMRI include higher spatial and temporal resolution, inherent use of gating for image acquisition, accurate delineation of the myocardium from blood pool avoiding contamination of the AIFN, and the absence of ionizing radiation. CMRI also offers the capability of registering anatomical, functional, and viability images with the perfusion scan. Disadvantages of CMRI include the impact of arrhythmias on image acquisition, prolonged respiratory

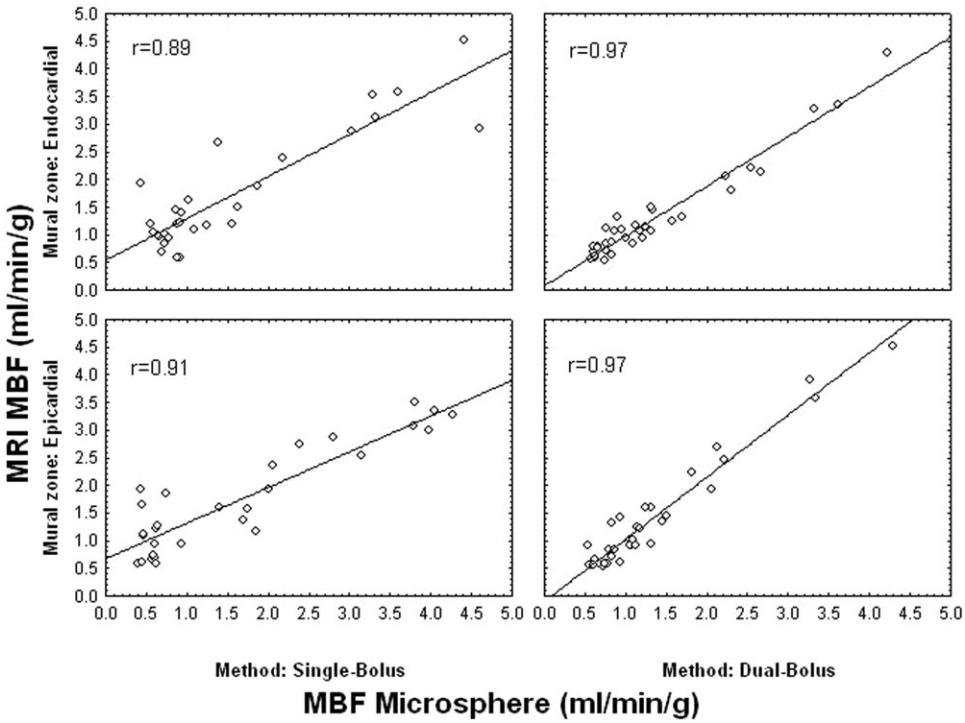

Figure 3. Linear correlations between the low-contrast single-bolus method (left panels) and the high-contrast dual-bolus method (right panels) for endocardial and epicardial zones which reflect a 50% reduction in the region of interest compared to transmural zones.

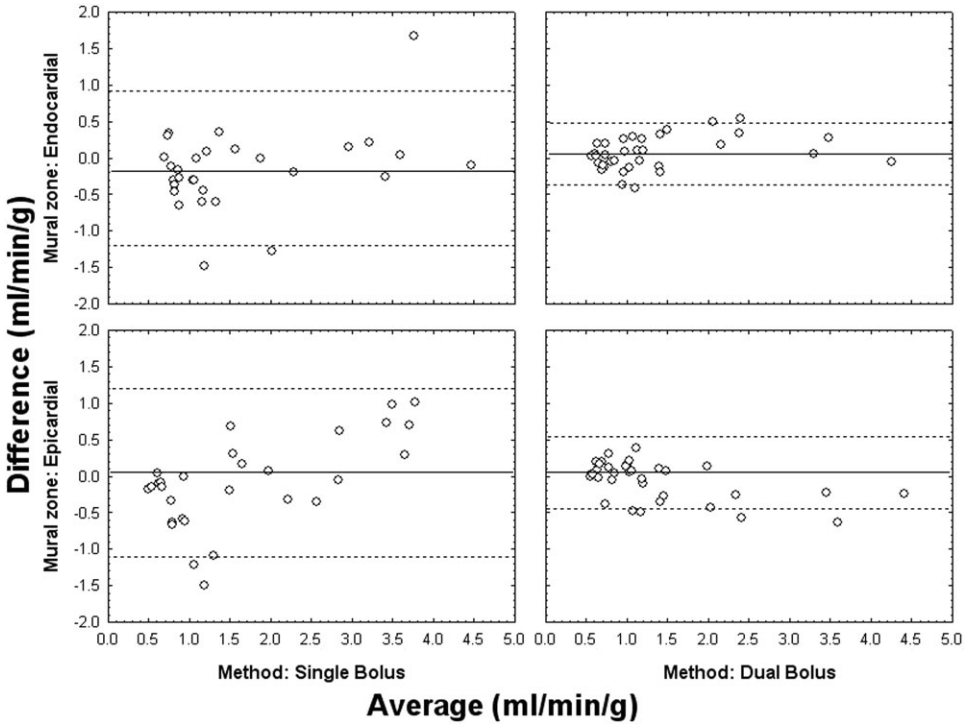

Figure 4. Bland–Altman plots of the correlations for single- and dual-bolus injection methods by endocardial and epicardial ROI. The mean difference for single-bolus endocardial and epicardial measures was −0.16 ± 0.55 and 0.09 ± 0.62 mL/min/g, respectively. The mean difference for dual-bolus endocardial and epicardial measures was 0.06 ± 0.22 and 0.06 ± 0.26 mL/min/g, respectively. Solid line = mean difference, dashed lines ±1.96 SD.

suspension and respiratory artifacts, susceptibility artifacts, and contrast agents that have both intravascular and extravascular compartments. On balance, there remains keen interest in developing the quantitative aspect of perfusion imaging with MRI.

This study demonstrated a close overall agreement between quantitative MR estimates of MBF and those obtained by labeled microspheres. The approach chosen for quantitation focuses on a deconvolution of the AIFN to fit an impulse response of the myocardial tissue and closely parallels the methodology proposed by prior investigators (3,5,16). The confidence intervals of the difference between microsphere values and MRI-derived values in control zones were very close to those reported for those of single acquisition O–15 PET in pigs at rest for the single-bolus method in subendocardial and epicardial zones (17) and somewhat better with the dual-bolus method (PET: 0.90–0.98 mL/min/g, dual-bolus MRI: 0.43–0.51). Both the single-bolus low-contrast concentration method and the dual-bolus method provided close approximations with absolute MBF, with the latter tending to have less variance from identity. The physical characteristics of the images favored the dual-bolus technique. Indeed, the contrast enhancement ratio using the dual-bolus protocol was more than 2-fold higher than in animals receiving the 0.025 mmol/kg dose.

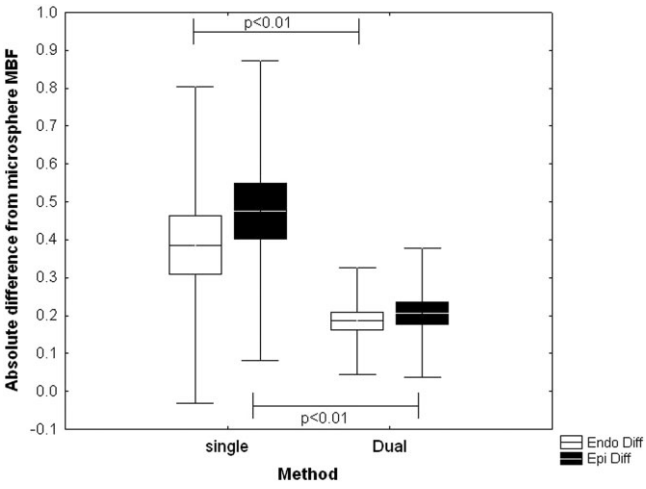

Figure 5. Absolute difference between microsphere and MRI first-pass MBF values by method and myocardial zone. The error vs. microsphere values was significantly less for dual-bolus perfusion imaging for both endocardial and epicardial analyses.

Schwitter et al (18) have recently demonstrated an excellent correlation with PET flow using semiquantitative first-pass high-dose (0.1 mmole/Kg) Gd-DTPA MRI perfusion. The present study essentially combines these two approaches, providing an accurate AIFN with the higher contrast necessary for optimal signal generation. Alternative approaches for full quantification of MBF by MRI have been reported. Gatehouse et al (19) have shown a linear association of an AIFN acquired using a very short T1 saturation recovery sequence with known Gd-DTPA concentrations in a phantom. This method maintains linearity of the signal related to changes in T1 but may lose linearity between signal intensity and gadolinium concentration since larger pixels magnify the effects of T2*. However, further studies have shown this loss to be less than 10% of the true AIFN using a short TE time (20).

Eliminating the low concentration bolus and using a single high-dose bolus provided a marked overestimation in absolute MBF and considerably more variability. This is likely due to the truncation of the AIFN due to

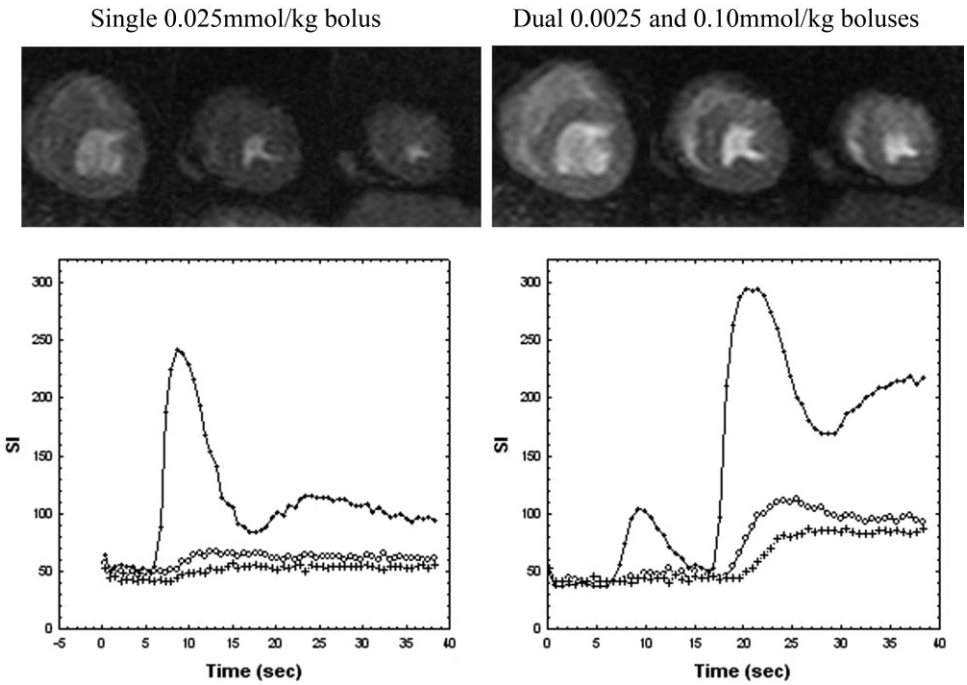

Figure 6. Basal, mid-ventricular and apical images from two animals receiving either a single-bolus low-contrast injection (left) or a high-contrast dual-bolus injection (right) during adenosine infusion down the LAD using identical window and leveling. The adenosine blush can be seen in the anterior wall clearly on the images. The time intensity curves for each type of injection at mid-ventricular level are shown below. The solid line is the LV arterial input function (AIFN), open circles reflect the change in signal in the adenosine zone, and the crosses reflect time signal change in the control zone. The curves have less variability for the dual-bolus method and the image quality is subjectively better.

T2* effects, making it smaller in magnitude than would be expected if there was a linear relation between signal intensity and concentration in the blood pool (10,21). The truncation may be multifactorial between subjects, which may contribute to the wider variability in the results with this technique. It appears that methods that can minimize T2* impact on the AIFN, such as lower Gd-DTPA concentrations or very short TE times, are necessary for absolute quantification.

Steady-state free-precession (SSFP) imaging may provide images with high SNR but at Gd-DTPA doses that allow measurement of the AIFN. Favorable results with semiquantitative techniques have been reported (22,23) but the impact of the SSFP sequence on the homogeneity of the AIFN remains to be determined. Finally, imaging at 3T will improve SNR for perfusion images but T2* effects will be amplified and may necessitate a reduction in Gd-DTPA concentration. The final interplay of these factors on quantitative assessment of MBF is also unknown.

With any study in which ROI analysis correlates with pathology there are unavoidable misalignments in registration that contribute to a background of data noise. Great care was taken to align images with pathology samples but misregistration was certainly present. The concept of deconvolution of the AIFN to fit the tissue response of the contrast agent to estimate mean transit time assumes a tracer which is intravascular. Clearly, Gd-DTPA is not wholly an intravascular agent. There was a marked difference in the profiles of the time–activity curves in control and hyperemic segments. Although an intravascular agent might have shown better agreement with MBF, the Fermi function performed reasonably well in control and adenosine zones. The perfusion acquisition parameters used dictated that short axis slices were acquired serially within a 1 R-R interval. This limits the number of slices obtainable (3–4 8 mm slices in this study) and dictates that they reflect different phases of the cardiac cycle (whereas the microsphere analysis represents the entire R-R interval averaged over many heartbeats). It is difficult to estimate the impact of this variability. The dual-bolus approach had superior imaging characteristics compared with the conventional, low-contrast single-bolus approach. We did not compare these methods in low MBF states where the advantages of higher signal may have greater weight.

In conclusion, quantitation of MBF by first-pass MR perfusion can be accomplished using either a low-contrast single-bolus method or a high-contrast dual-bolus method. The dual-bolus method provided more accurate estimates when smaller endocardial and epicardial regions were analyzed, likely as a result of the higher myocardial signal present in the myocardium compared to the low-dose single-bolus method. Consequently, the additional effort of performing a dual-bolus acquisition may be warranted for this specific purpose. Further clinical application of quantitative perfusion imaging appears warranted.

REFERENCES

1. Simons M, Bonow RO, Chronos NA, et al. Clinical trials in coronary angiogenesis: issues, problems, consensus. An expert panel summary. Circulation 2000;102:E73–86.
2. Wilke N, Jerosch-Herold M, Wang Y, et al. Myocardial perfusion reserve: assessment with multisection, quantitative, first-pass MR imaging. Radiology 1997;204:373–384.
3. Jerosch-Herold M, Wilke N, Stillman AE. Magnetic resonance quantification of the myocardial perfusion reserve with a Fermi function model for constrained deconvolution. Med Phys 1998;25: 73–84.
4. Kraitchman DL, Wilke N, Hexeberg E, et al. Myocardial perfusion and function in dogs with moderate coronary stenosis. Magn Reson Med 1996;35:771–780.

5. Axel L. Tissue mean transit time from dynamic computed tomography by a simple deconvolution technique. Invest Radiol 1983;18: 94–99.
6. Kroll K, Wilke N, Jerosch-Herold M, et al. Modeling regional myocardial flows from residue functions of an intravascular indicator. Am J Physiol 1996;271:H1643–H1655.
7. Panse P, Klassen C, Panse N, et al. Magnetic resonance quantitative myocardial perfusion reserve demonstrates improved myocardial blood flow after angiogenic implant therapy. Int J Cardiovasc Imaging 2007;23:217–224.
8. Christian TF, Rettmann DW, Aletras AH, et al. Absolute myocardial perfusion in canines measured using dual-bolus first-pass MR imaging. Radiology 2004;232:677–684.
9. Hsu LY, Rhoads KL, Holly JE, Kellman P, Aletras AH, Arai AE. Quantitative myocardial perfusion analysis with a dual-bolus contrast-enhanced first-pass MRI technique in humans. J Magn Reson Imaging 2006;23:315–322.
10. Wendland MF, Saeed M, Yu KK, et al. Inversion recovery EPI of bolus transit in rat myocardium using intravascular and extravascular gadolinium-based MR contrast media: dose effects on peak signal enhancement. Magn Reson Med 1994;32:319–329.
11. Haase A, Frahm J, Matthaei D, et al. MR imaging using stimulated echoes (STEAM). Radiology 1986;160:787–790.
12. Ding S, Wolff SD, Epstein FH. Improved coverage in dynamic contrast-enhanced cardiac MRI using interleaved gradient-echo EPI. Magn Reson Med 1998;39:514–519.
13. Epstein FH, London JF, Peters DC, et al. Multislice first-pass cardiac perfusion MRI: validation in a model of myocardial infarction. Magn Reson Med 2002;47:482–491.
14. Christian TF. Anatomy of an emerging diagnostic test: computed tomographic coronary angiography. Circulation 2005;112:2222–2225.
15. Domenech RJ, Hoffman JI, Noble MI, Saunders KB, Henson JR, Subijanto S. Total and regional coronary blood flow measured by radioactive microspheres in conscious and anesthetized dogs. Circ Res 1969;25:581–596.
16. Clough AV, al Tinawi A, Linehan JH, Dawson CA. Regional transit time estimation from image residue curves. Ann Biomed Eng 1994; 22:128–143.
17. Rimoldi O, Schafers KP, Boellard R, et al. Quantification of subendocardial and subepicardial blood flow using ^{15}O-labeled water and PET: experimental validation. J Nucl Med 2006;47:163–172.
18. Schwitter J, Nanz D, Kneifel S, et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation 2001;103:2230–2236.
19. Gatehouse PD, Elkington AG, Ablitt NA, Yang GZ, Pennell DJ, Firmin DN. Accurate assessment of the arterial input function during high-dose myocardial perfusion cardiovascular magnetic resonance. J Magn Reson Imaging 2004;20:39–45.
20. Kellman P, Aletras AH, Hsu LY, McVeigh ER, Arai AE. T2* measurement during first-pass contrast-enhanced cardiac perfusion imaging. Magn Reson Med 2006;56:1132–1134.
21. Utz W, Niendorf T, Wassmuth R, Messroghli D, Dietz R, Schulz-Menger J. Contrast-dose relation in first-pass myocardial MR perfusion imaging. J Magn Reson Imaging 2007;25:1131–1135.
22. Klocke FJ, Simonetti OP, Judd RM, et al. Limits of detection of regional differences in vasodilated flow in viable myocardium by first-pass magnetic resonance perfusion imaging. Circulation 2001;104:2412–2416.
23. Wang Y, Moin K, Akinboboye O, Reichek N. Myocardial first pass perfusion: steady-state free precession versus spoiled gradient echo and segmented echo planar imaging. Magn Reson Med 2005; 54:1123–1129.