Myocardial CT Perfusion Imaging in a Large Animal Model

Comparison of Dynamic Versus Single-Phase Acquisitions

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OBJECTIVES This study sought to compare dynamic versus single-phase high-pitch computed tomography (CT) acquisitions for the assessment of myocardial perfusion in a porcine model with adjustable degrees of coronary stenosis.

BACKGROUND The incremental value of the 2 different approaches to CT-based myocardial perfusion imaging remains unclear.

METHODSCountry pigs received stent implantation in the left anterior descending coronary artery, in which an adjustable narrowing (50% and 75% stenoses) was created using a balloon catheter. All animals underwent CT-based rest and adenosine-stress myocardial perfusion imaging using dynamic and single-phase high-pitch acquisitions at both degrees of stenosis. Fluorescent microspheres served as a reference standard for myocardial blood flow. Segmental CT-based myocardial blood flow (MBFCT) was derived from dynamic acquisitions. Segmental single-phase enhancement (SPE) was recorded from high-pitch, single-phase examinations. MBFCT and SPE were compared between post-stenotic and reference segments, and receiver-operating characteristic curve analysis was performed.

RESULTS Among 6 animals (28 ± 2 kg), there were significant differences of MBFCT and SPE between post-stenotic and reference segments for all acquisitions at 75% stenosis. By contrast, although for 50% stenosis at rest, MBFCT was lower in post-stenotic than in reference segments (0.65 ± 0.10 ml/g/min vs. 0.75 ± 0.16 ml/g/min, p < 0.05), there was no difference for SPE (128 ± 27 Hounsfield units vs. 137 ± 35 Hounsfield units, p = 0.17), which also did not significantly change under adenosine stress. In receiver-operating characteristic curve analyses, segmental MBFCT showed significantly better performance for ischemia prediction at 75% stenosis and stress (area under the curve: 0.99 vs. 0.89, p < 0.05) as well as for 50% stenosis, regardless of adenosine administration (area under the curve: 0.74 vs. 0.57 and 0.88 vs. 0.61, respectively, both p < 0.05).

CONCLUSIONS At higher degrees of coronary stenosis, both MBFCT and SPE permit an accurate prediction of segmental myocardial hypoperfusion. However, accuracy of MBFCT is higher than that of SPE at 50% stenosis and can be increased by adenosine stress at both degrees of stenosis. (J Am Coll Cardiol Img 2013;6:1229–38) © 2013 by the American College of Cardiology Foundation

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The increase in detector width and temporal and spatial resolution over the last decade has contributed enormously to the establishment of coronary computed tomography angiography (CTA) as the noninvasive modality of choice for morphological imaging of the coronary artery system. When compared with invasive coronary angiography, coronary CTA has shown high diagnostic accuracy, particularly for patients with low-to-intermediate pre-test probability for coronary artery disease (1).

In parallel, clinical evidence favoring the hemodynamic relevance of a coronary lesion over the degree of stenosis as the most important parameter for prognosis and clinical decision making has accumulated over the last few years (2). However, there is a large body of evidence indicating that the hemodynamic relevance cannot be estimated by the degree of stenosis as measured by invasive coronary angiography or coronary CTA (3). Thus, comprehensive assessment of the hemodynamic significance remains beyond the capabilities of routine coronary CTA.

Several studies have shown that the detection of myocardial perfusion defects at rest and pharmacological stress is feasible using state-of-the-art computed tomography (CT) technology employing 2 different approaches: “single-phase CT acquisitions” at rest or adenosine-induced stress rely on a single CT acquisition after injection of an iodinated contrast agent and are characterized by relatively low radiation exposure (4). However, assessment of myocardial perfusion is limited to a qualitative or semiquantitative evaluation on the basis of mere comparisons of enhancement between apparently post-stenotic versus normal myocardial segments (single-phase enhancement [SPE]). Sequential CT acquisitions, on the other hand, enable dynamic imaging of contrast agent kinetics and permit a truly quantitative evaluation of myocardial blood flow (CT-derived MBF [MBF\textsubscript{CT}]) and other parameters at stress and at rest (5). The latter approach, however, typically is associated with higher radiation exposure. Although both approaches have been evaluated separately, a direct comparison including the evaluation of potential intrinsic limitations in an experimental setting is lacking.

The aim of this in vivo animal study was to compare dynamic with single-phase CT acquisition techniques for myocardial perfusion imaging in a large animal model with different degrees of coronary artery stenosis.

**METHODS**

The study was approved by the governmental animal protection committee and the institutional review board for the care of animal subjects. All animal studies were performed in accordance with the “Position of the American Heart Association on Research Animal Use.”

**Animal experiments.** All experiments were performed at the Walter-Brendel-Centre of Experimental Medicine, Ludwig-Maximilians-University (Munich, Germany).

Experiments included 6 young country pigs of either sex weighing between 25 and 30 kg; all animals were fed 75 mg of clopidogrel (Ratiopharm, Ulm, Germany) daily for 2 days before the experiment. General anesthesia was induced by intramuscular administration of acepromazine (Vetranquil, Biokema, Crissier, Switzerland), atropine (B. Braun, Melsungen, Germany), and ketamine (B. Braun), followed by a bolus of intravenous midazolam (0.1 mg/kg) (Dormicum, Roche Pharma, Basel, Switzerland). After endotracheal intubation, anesthesia was maintained by continuous intravenous administration of fentanyl (6 μg/kg/h) (B. Braun) and propofol (2%, 10 to 15 ml/h) (MCT, Fresenius, Bad Homburg, Germany) using perfusion pumps connected to an intravenous drip of normal saline and hydroxyethyl starch plasma expander (50%/50%). Automatic mechanical ventilation was performed with a tidal volume of 150 ml and a breathing frequency of 40 breaths/min. To ensure adequate oxygenation, a pulse oximeter was attached to the tail tip. A 4-lead electrocardiogram was recorded continuously throughout the experiment and synchronized with the CT scanner. After intravenous administration of 500 mg of aspirin (Aspirin i.v., Bayer Healthcare, Berlin, Germany) and 1,000 IE of heparin (Heparin-Calcium, Ratiopharm), 2 catheters (8-F sheath) were introduced through the carotid...
arteries into the left ventricle (for delivery of fluorescent microspheres [FM]) and into the left anterior descending coronary artery. A double-lumen central venous catheter (8-F sheath) was placed into the superior vena cava through the right internal jugular vein for contrast agent. Adenosine was administered through a peripheral vein.

Variable degrees of coronary stenosis (50% and 75% area stenoses) were created using a model previously validated by Boekstegers et al. (6) with a percutaneously implanted stent/balloon assembly: in a dedicated animal catheter suite, a 3-mm stent (Biotronik, Pro-Kinetik Energy, Buelach, Switzerland) was placed in the mid segment of the left anterior descending coronary artery. By controlled balloon inflation, different degrees of luminal obstruction were simulated (50% and 75% area stenoses).

**CT imaging protocol.** All animals were positioned on the CT table in a supine, head-first position. All acquisitions were performed on a dual-source CT scanner (Definition FLASH, Siemens Healthcare, Erlangen, Germany). The following scan techniques were applied (Fig. 1):

1. A test bolus to determine contrast transition time using axial slices at the level of the mid ascending aorta obtained every 2 s (100 kV, 45 mAs); for the test bolus, 15 ml of iopromide (Ultravist 370, Bayer Healthcare) were injected at a flow rate of 3.5 ml/s, followed by 15 ml of normal saline at the same flow rate;
2. A prospectively triggered CT angiography of the heart, verifying the position of the catheter (delay: time to peak in test bolus scan + 4 s; acquisition triggered to a time point of 200 ms within the R-R-interval, 100 kV, 300 mAs, 2 × 128 slices, 0.28-s rotation time), and injecting 35 ml of iopromide at a flow rate of 3.5 ml/s, followed by 15 ml of saline at the same flow rate;
3. A single-phase high spiral-pitch acquisition triggered to end-systole (100 kV, 300 mAs) with a delay set to 6 s following peak opacification in the ascending aorta; for this phase, 20 ml of iopromide were injected at 3.5 ml/s, followed by 15 ml of normal saline at the same flow rate;
4. A dynamic CT perfusion scan (100 kV, 300 mAs) with sequential acquisitions triggered to 200 ms of the R-R interval and initiated 4 s before opacification of the ascending aorta. As published previously (7), data were acquired at 2 alternating table positions.
in electrocardiogram-triggered mode using end-systolic timing, with the table moving forward and backward between both positions to cover a scan range of 73 mm with a temporal sampling of 2.5 to 3.0 s (8) for 17 consecutive phases. For the dynamic perfusion acquisition, 20 ml of iopromide were injected.

Step 3 (single-phase, high-pitch acquisition) and step 4 (dynamic acquisition) were repeated 3 times to allow for acquisitions at rest and during adenosine-induced stress at both degrees of coronary stenosis (50% and 75% area stenoses). Adenosine stress was induced by continuous intravenous injection of 140 μg/kg/min adenosine (Adenoscan, Sanofi, Munich, Germany) for at least 2 min before image acquisition.

Between each pair of acquisitions (single-phase and dynamic), an intermission of approximately 30 min was set, allowing for the renal elimination of applied contrast material. The duration of the induced coronary stenosis (balloon time) was 20 min on average. The time between single-phase and dynamic acquisitions was approximately 10 min. At the end of the experiment, all animals were euthanized, and their hearts were excised and fixed in formaldehyde for 6 to 8 days. Overall, the average duration of the experimental protocol was 6.2 ± 0.6 h.

**Fluorescent microspheres.** FM (Molecular Probes, Eugene, Oregon) were applied for each degree of stenosis at rest and at stress, immediately after the respective CT acquisition. Microspheres labeled with different fluorescent colors were randomly selected for application. Before application, FM was dispersed and stirred to ensure proper mixing (~5 × 10⁶ FM in physiological saline solution) and injected at a constant rate for 60 s into the left ventricle immediately after each of 4 corresponding pairs of CT perfusion acquisitions and single-phase high-pitch acquisitions (50% rest and stress, 75% rest and stress). Reference blood samples from the abdominal aorta were simultaneously withdrawn into anticoagulation syringes (3.1% sodium citrate, 5 ml) at a constant rate (4.1 ml/min for 3 min) using an automated withdrawal pump (model 640A, Harvard Apparatus, South Natick, Massachusetts).

**CT data post-processing and analysis.** All datasets were transferred to an off-line work station for further analysis (MMWP, Siemens Healthcare, Forchheim, Germany). The dynamic perfusion datasets (rest and stress) were reconstructed employing a medium-soft reconstruction algorithm (B30f) at 3-mm slice width (2-mm increment) and further processed using a commercially available software tool (syngo VPCT Body, as integrated in syngo CT Workplace, Syngo CT 2012B, VA44A Siemens Healthcare, Forchheim, Germany). As previously described, a parametric deconvolution technique, based on a 2-compartment model of intra- and extravascular space, was applied to fit the time attenuation curves (7,9). The algorithm calculated MBFₜₚ by applying the maximum slope approach onto the model curve that was fit for every voxel.

Single-phase high-pitch acquisitions were reconstructed using a smooth reconstruction algorithm (B23f) at 3-mm slice thickness and 2-mm reconstruction increment (“axial single-phase series”). Corresponding MBFₜₚ and single-phase series were simultaneously loaded into a multiplanar reformation tool, and short-axis reformations of both series were generated in an identical orientation (Fig. 2).

Two readers who were blinded to all other information independently performed image analysis on corresponding short-axis series on a segmental basis as standardized by the American College of Cardiology/American Heart Association 16-segment model (excluding the apex); discrepancies were solved by consensus (10). MBFₜₚ was determined in each of the 16 myocardial segments by manually placing a region of interest (ROI) of ~0.5 cm² in a representative myocardial region, excluding a 1-mm subendocardial zone directly adjacent to the contrast-filled left ventricle, and a 1-mm subepicardial zone, to avoid any influence of measurements by beam hardening artifacts or partial volume effects. ROIs were then copied to the according short-axis single-phase series, measuring myocardial enhancement (SPE).

**Post-processing of heart specimens.** The excised and fixed hearts were further dissected into samples of equal size according to the American Heart Association classification. The anterior, lateral, and inferior walls of the left ventricle were dissected into 16 wedge-shaped transmural tissue pieces and processed, in order to determine MBFₘₑₗₚ by spectrofluorometry according to the method described by Glenny et al. (11). Samples were lysed, and microsphere fluorescence was measured using a Tecan Safire microplate reader (Tecan, Männedorf, Switzerland) (12).

**Statistical analysis.** Continuous data are provided as mean ± SD and as absolute and relative frequencies for binary data. MBFₜₚ and SPE measurements were compared between the different degrees of luminal narrowing using linear regression with random effects to account for the clustering of segments within the animals. The association between MBFₜₚ and SPE and MBFₘₑₗₚ was determined using the Pearson product-moment
correlation coefficient. As there were only minor differences of association between pigs, the correlation coefficient was not adjusted for the clustered structure of the data. To determine different degrees of discriminatory power between the 2 approaches, receiver-operating characteristic (ROC) curve analysis with subsequent calculation of the area under the curve (AUC) were performed. AUC values are reported with 95% confidence intervals. For the comparison of correlated AUCs, the method published by DeLong et al. (13) was used, applying a nonparametric approach to the analysis of areas under correlated ROC curves.

All analyses were performed using SAS (version 9.2, SAS Institute, Cary, North Carolina), R (version 2.13.1, R Foundation for Statistical Computing, Vienna, Austria), and MedCalc (version 12.5.0.0, MedCalc Software, Ostend, Belgium); a 2-sided p value <0.05 was considered to indicate statistical significance.

RESULTS

All study procedures were performed without complications, and all 6 animals completed the study protocol. Among a total of 384 myocardial segments, 16 (4.2%) were considered non-evaluable due to wire artifacts, and were excluded from subsequent analysis. During adenosine-induced stress, a significant increase of the heart rate was observed (95 ± 12 beats/min vs. 80 ± 10 beats/min, p = 0.04) (Table 1). Each dynamic acquisition was associated with an average dose of 11.3 ± 2 mSv, whereas the average dose for single-phase acquisitions was 0.88 ± 0.15 mSv.

With a threshold of 1.8 ml/g/min, 4 animals showed perfusion defects in 4 myocardial segments (segments 7, 8, 13, and 14), and 2 animals showed perfusion defects in 5 myocardial segments

Table 1. Average Animal Weight, HR at Baseline and Stress, and Detailed Scan Protocol Parameters for Dynamic as Well as Single-Phase Acquisitions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Weight, kg</td>
<td>27.5 ± 1.9</td>
</tr>
<tr>
<td>HR at baseline, beats/min</td>
<td>80 ± 10</td>
</tr>
<tr>
<td>HR at stress, beats/min</td>
<td>95 ± 12</td>
</tr>
<tr>
<td><strong>Dynamic acquisition</strong></td>
<td></td>
</tr>
<tr>
<td>Tube voltage, kVp</td>
<td>100 ± 0</td>
</tr>
<tr>
<td>Tube current time product, mAs</td>
<td>300 ± 0</td>
</tr>
<tr>
<td>Contrast volume, ml</td>
<td>20 ± 0</td>
</tr>
<tr>
<td>Flow rate, ml</td>
<td>3.5 ± 0.0</td>
</tr>
<tr>
<td><strong>Single-phase acquisition</strong></td>
<td></td>
</tr>
<tr>
<td>Tube voltage, kVp</td>
<td>100 ± 0</td>
</tr>
<tr>
<td>Tube current time product, mAs</td>
<td>300 ± 0</td>
</tr>
<tr>
<td>Contrast volume, ml</td>
<td>20 ± 0</td>
</tr>
<tr>
<td>Flow rate, ml/s</td>
<td>3.5 ± 0.0</td>
</tr>
</tbody>
</table>

Values are mean ± SD. HR = heart rate.
Comparison of Average MBFCT, SPE, and MBFMIC Values in Post-Stenotic Versus Reference Segments

Table 2. Comparison of Average MBFCT, SPE, and MBFMIC Values in Post-Stenotic Versus Reference Segments

<table>
<thead>
<tr>
<th></th>
<th>MBFCT Post-Stenotic (ml/g/min)</th>
<th>MBFCT Reference (ml/g/min)</th>
<th>p Value</th>
<th>SPE Post-Stenotic (HU)</th>
<th>SPE Reference (HU)</th>
<th>p Value</th>
<th>MBFMIC Post-Stenotic (ml/g/min)</th>
<th>MBFMIC Reference (ml/g/min)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% stenosis, rest</td>
<td>0.65 ± 0.10</td>
<td>0.75 ± 0.16</td>
<td>0.0012</td>
<td>128 ± 27</td>
<td>137 ± 35</td>
<td>0.1707</td>
<td>1.7 ± 0.5</td>
<td>2.3 ± 0.4</td>
<td>0.04</td>
</tr>
<tr>
<td>50% stenosis, stress</td>
<td>0.42 ± 0.18</td>
<td>0.86 ± 0.23</td>
<td>&lt;0.0001</td>
<td>127 ± 11</td>
<td>144 ± 38</td>
<td>0.0242</td>
<td>1.8 ± 0.6</td>
<td>2.9 ± 0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>75% stenosis, rest</td>
<td>0.45 ± 0.14</td>
<td>0.9 ± 0.24</td>
<td>&lt;0.0001</td>
<td>96 ± 28</td>
<td>148 ± 25</td>
<td>&lt;0.0001</td>
<td>1.4 ± 0.4</td>
<td>2.5 ± 0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>75% stenosis, stress</td>
<td>0.47 ± 0.18</td>
<td>1.12 ± 0.28</td>
<td>&lt;0.0001</td>
<td>97 ± 39</td>
<td>155 ± 23</td>
<td>&lt;0.0001</td>
<td>1.4 ± 0.5</td>
<td>3.2 ± 0.7</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are mean ± SD. MBF values are shown for different degrees of stenosis (50% and 75%) and rest and stress, along with tests for significance of differences.

HU – hounsfield unit; MBFCT – computed tomography-derived myocardial blood flow; MBFMIC – microsphere-derived myocardial blood flow; SPE – single-phase enhancement.

Table 2 (continued)

(All p values are corrected for multiple testing.)

The table shows that MBFCT and SPE values in post-stenotic segments at rest were 128 ± 28 HU and 96 ± 27 HU for 50% and 75% stenosis, respectively, and were apparently not influenced by adenosine-induced myocardial stress (at 50% stenosis: 127 ± 20 HU, p = 0.94; at 75% stenosis: 97 ± 38 HU, p = 0.88). Differences of SPE values between post-stenotic and reference segments were significant for 75% stenosis regardless of adenosine administration (rest: p < 0.01; adenosine stress: p < 0.01) (Table 2), whereas at 50% stenosis, differences were significant under adenosine stress, but not at rest (p < 0.01 and p = 0.17, respectively).

Comparison of dynamic versus single-phase technique. MBFCT and SPE showed a moderate positive correlation on a per-segment level across both degrees of stenosis and rest or stress conditions (r = 0.57, p < 0.01). However, the degree of correlation was different between the different perfusion states. Specifically, the agreement was highest for 75% stenosis at stress and at rest (r = 0.64 and r = 0.64, respectively, both p < 0.01) (Figs. 4A and 4B) and lowest at 50% stenosis at stress (r = 0.44, p < 0.01) (Fig. 4C). Correlation between SPE and MBFCT was not significant for 50% stenosis at rest (r = 0.13, p = 0.21) (Fig. 4D).

In ROC analyses, MBFCT provided significantly higher power than SPE for the detection of ischemia at 50% stenosis on a segmental level both at rest (AUC: 0.74 [0.64 to 0.83] vs. 0.57 [0.46 to 0.68], p = 0.045) and during adenosine-stress (AUC: 0.88 [0.80 to 0.94] vs. 0.61 [0.50 to 0.71], p < 0.01) (Fig. 5A). Similarly, the discriminatory power to identify ischemic segments at 75% stenosis under stress was significantly higher for MBFCT than SPE (AUC: 0.99 [0.94 to 1.00] vs. 0.89 [0.81 to 0.95], respectively, p = 0.005) (Fig. 5B). By contrast, differences between techniques were not significant for 75% stenosis at rest (AUC: 0.84 [0.74 to 0.91] vs. 0.80 [0.70 to 0.90], p = 0.08).
0.87 [0.79 to 0.93] for MBF_{CT} and SPE, respectively, p = 0.42).

For SPE, no significant differences in accuracy of ischemia detection were found between rest and stress conditions for either degree of stenosis (at 50%: AUCs 0.57 vs. 0.60, p = 0.76; at 75%: AUCs 0.87 vs. 0.89, p = 0.59). For MBF_{CT}, however, the respective differences were significant for both degrees of stenosis (at 50%: AUCs 0.74 vs. 0.88, p = 0.02; at 75%: AUCs 0.84 vs. 0.99, p < 0.01).

**DISCUSSION**

In this experimental validation study, we compare CT-based myocardial perfusion imaging on the basis of dynamic acquisitions with single-phase acquisitions in a large animal model for myocardial ischemia, simulating different degrees of coronary stenosis. Our results indicate that dynamic acquisition techniques allow the identification of more subtle perfusion changes at moderate stenosis (50%), whereas both techniques permit the identification of high-grade stenosis (75%), with moderately higher test performance of MBF_{CT} (AUC under adenosine stress: 0.99 vs. 0.89, p < 0.05).

Our results show that generally, both strategies are able to detect hypoperfusion in post-stenotic myocardial segments. Specifically, myocardial attenuation measured during single-phase acquisition correlates well with MBF derived from dynamic acquisitions for high degrees of stenosis for rest or stress. With this study, we confirm prior pre-clinical and clinical studies indicating that both the single-phase and the dynamic approach can detect hypoperfused myocardium (4,5,14–18).

Previous studies, including a number of in vivo animal validation studies, have shown that single-phase acquisitions are able to detect myocardial perfusion defects similar to single-photon emission computed tomography (15). Applying an experimental stenosis of the left anterior descending coronary artery in a canine model, hence reducing the MBF by 50%, George et al. (19) demonstrated that density measurements on single-phase acquisitions correlate well with microsphere-derived estimates of MBF. Using a large animal model (dogs and pigs), it has also been shown that single-phase CT acquisitions may characterize acute and healed myocardial infarction (20). Our results confirm that single-phase CT in general allows the detection...
of ischemic myocardium in a large animal model. However, our findings extend previously published results in that, for moderate degrees of coronary artery stenosis, the discriminatory power of dynamic acquisitions appears to be superior. One explanation may be the relatively low signal-to-noise ratio of the myocardium (with relatively high SD), which is even more pronounced when applying high-pitch acquisition techniques.

We confirm previous observations made in in vivo animal experiments demonstrating that dynamic acquisitions allow the detection and quantification of ischemic myocardium (5,21). In a prior large animal validation study, we demonstrated that MBF_{CT} derived from dynamic acquisition can differentiate various degrees of coronary artery stenosis (7). Rossi et al. (22) showed that MBF_{CT} measurements correlated well with fractional flow reserve measurements performed at intermediate (15% to 39%) or severe (40% to 95%) flow reduction in a porcine model.

This is the first systematic in vivo validation study to our knowledge that reports differences between single-phase and dynamic myocardial perfusion acquisitions at lower degrees of coronary stenosis, which may have implications for future research efforts. There may be similarities with acute stroke imaging in which dynamic acquisition is increasingly used as a first-line diagnostic tool to distinguish infarct core from penumbra, showing that quantitative measures of cerebral perfusion provide diagnostic accuracies approaching magnetic resonance imaging–based diffusion-weighted imaging (23). Thus, it can be anticipated that only quantitative CT-derived parameters might be of sufficient accuracy to allow for the evaluation of myocardial perfusion in clinical routine.

The most significant advantage of single-phase perfusion imaging is lower radiation exposure. Although it had been shown that on former CT scanner generations, a comprehensive workup, including single-phase acquisitions at rest and at stress, could be performed with radiation doses similar to myocardial single-photon emission computed tomography of ~12 mSv (15), the introduction of high-pitch imaging has reduced doses below 3 mSv (4).

Figure 4. Scatter Diagrams With Regression Lines Analyzing Correlations Between MBF and SPE Values
MBF values and SPE values are for different degrees of coronary stenosis at rest or adenosine-stress. Correlation is highest for 75% stenosis at adenosine stress (A), as well as at rest (B), and considerably lower for 50% stenosis at stress (C). For 50% stenosis at rest, correlation was not statistically significant (D). HU = Hounsfield units; other abbreviations as in Figure 1.
Our results are in line with findings by Feuchtner et al. (4) (average exposure at single-phase acquisitions at rest: 1.59 ± 1.3 mSv) and show that the dynamic scan was associated with an approximately 7-fold higher radiation exposure (average exposure 11.3 ± 2 mSv). However, there is early evidence that future optimization and the adoption of iterative reconstruction techniques may substantially reduce radiation exposure at similar image quality (24).

We observed that the quantitative measurements of perfusion by MBFCT were significantly lower than the corresponding MBFMIC values. Although there are different theoretical explanations for potential systematic underestimation—such as inaccuracies in the underlying mathematical algorithms—the contrast injection protocol, as well as the adenosine dose used, in our study are likely major factors. In fact, in one prior study, higher values for reference blood flow were obtained by applying considerably higher adenosine doses (500 μg/kg/min) (22). Furthermore, we deliberately chose a contrast volume of only 20 ml for each injection to facilitate full renal clearance of contrast material between acquisitions. Thus, further validation and optimization of the underlying algorithms will be necessary to provide values for MBFCT that are in line with values obtained by reference methods.

Study limitations. First, this is an animal study, and thus, the results may not be generalizable to a clinical setting. However, a large porcine model was selected because it optimally approximates human cardiac anatomy and physiology while allowing for a standardized comparison of various acquisition techniques. Thus, our results may help in understanding the value of the different techniques but will need to be confirmed in clinical studies. Second, timing of the single-phase acquisitions is critical to detect the ideal phase of contrast accumulation in the myocardium. We employed a standard delay for coronary CT angiography and adding 2 s to assure the enhancement of the myocardium, which is similar to studies made in humans. Third, all analyses, including the employed gold standard of FM, were restricted to the assessment of myocardial perfusion on a segmental basis. Although this approach has been validated previously, it may introduce some bias because the entire myocardial segment may not have been affected by ischemia. However, we used a representative ROI measurement for each myocardial segment.

CONCLUSIONS

This in vivo animal validation study indicates that both approaches to CT-based myocardial perfusion imaging, dynamic and single-phase acquisitions, allow for an assessment of myocardial perfusion states at higher degrees of coronary stenosis. However, our
results also suggest that \( \text{MBF}_{\text{CT}} \) derived from dynamic myocardial perfusion imaging may be more sensitive for the detection of subtle differences of myocardial perfusion as compared with CT-density/enhancement measurements derived from single-phase acquisitions. Further clinical validation studies will be necessary to prove the clinical value of either approach in the management of patients with known or suspected coronary artery disease.

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REFERENCES


Key Words: cardiac CT • infarct • ischemia • myocardial perfusion.