Detection of myocardial perfusion abnormalities: standard dual-source coronary computed tomography angiography versus rest/stress technetium-99m single-photo emission CT

¹W CHENG, MD, ¹M ZENG, MD, ²C ARELLANO, MD, ²W MAFORI, MD, ²J GOLDIN, MD, ²M KRISHNAM, MD and ²S G RUEHM, MD, PhD

¹Department of Radiology, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China, and

²Department of Radiological Sciences, David Geffen School of Medicine, University of California Los Angeles, Peter V. Ueberroth Building, Suite 3371, 10945 Le Conte Avenue, Los Angeles, CA 90095-7206, USA

ABSTRACT. We compared coronary dual-source computed tomography angiography (corDSCTA) with technetium-99m single-photon emission computed tomography (SPECT) for the detection of myocardial perfusion abnormalities. Fifty-five consecutive patients underwent both gated myocardial perfusion SPECT and corDSCTA, the latter during a single arterial-phase injection of contrast agent. The perfusion defects visualised by corDSCTA correlated with the findings of rest/stress SPECT. Abnormal findings on stress SPECT, which were due to either ischaemia or infarct, were found in 24 patients. In comparison to SPECT at rest, corDSCTA detected perfusion defects with a sensitivity and specificity of 100% and 78%, respectively. Compared to SPECT at stress, the sensitivity and specificity values of corDSCTA were 83.3% and 90.3%, respectively. On corDSCTA, the average attenuation values of perfusion defects that corresponded to chronic infarcts (-8.5 ± 22.2 HU) were significantly lower ($p=0.002$) than those of non-infarct-related perfusion defects (43.1 ± 17.5 HU). Using rest/stress SPECT is the gold standard for the diagnosis of myocardial ischaemia, corDSCTA was able to diagnose ischaemic disease (defined as the presence of high-grade stenotic CAD ($\geq 50\%$ luminal narrowing)) with a sensitivity and specificity of 59% and 89%, respectively, in patients with no known history of myocardial infarction ($n=4$). Thus, corDSCTA may serve as a diagnostic tool for the detection of perfusion abnormalities (first) visualised by SPECT. There appears to be a limited correlation between coronary stenotic disease and SPECT findings.

Received 8 December 2008

Revised 8 June 2009

Accepted 1 July 2009

DOI: 10.1259/bjr/82257160

© 2010 The British Institute of Radiology

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality in developed countries. During the progression of atherosclerosis, the coronary artery wall undergoes pathological changes with build-up of plaque and subsequent luminal narrowing resulting in impaired blood supply to the myocardium. The focus of perfusion imaging is the detection of pathological changes in myocardial perfusion. At present, various perfusion imaging techniques are in clinical use, including nuclear medicine modalities such as single-photon emission computed tomography (SPECT), positron emission tomography (PET) and cardiac perfusion MRI.

Rest/stress myocardial perfusion SPECT imaging is a non-invasive modality that is widely used to evaluate patients with suspected CAD. Compared with conventional coronary angiography, myocardial perfusion SPECT has demonstrated sensitivities and specificities of 82–98% and 44–91%, respectively, for the detection of CAD [1, 2]. SPECT findings such as the extent, severity

and reversibility of perfusion defects have shown to be valuable for the prediction of future cardiovascular events [3]. In the absence of morphological correlation, however, SPECT is limited in allocating perfusion defects to their determining coronary lesion, which is a major precondition for accurate therapy planning [4]. As a consequence, invasive conventional coronary angiography (CCA) is often performed in cases of abnormal or equivocal SPECT findings [5]. To avoid a missed diagnosis of significant CAD, many patients whose SPECT findings are equivocal undergo further tests, the majority of which have negative results. It has been estimated that these negative evaluations cost \$10–13 billion per year in the United States alone [6].

Since the advent of multidetector computed tomography (MDCT) scanners with their greatly improved spatial and temporal resolutions, coronary CT angiography (CCTA) has been gradually evolving as a promising non-invasive method for the assessment of CAD that is less costly than invasive coronary catheter angiography. Recent studies using 64-slice MDCT to diagnose patients with CAD showed sensitivity and specificity values of 96–98% and 84–93%, respectively [7–9]. Importantly, the combined results from a number of studies have demonstrated a mean per-patient negative predictive

Address correspondence to: Weizhong Cheng, Department of Radiology, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China. E-mail: cheng.weizhong@zs-hospital.sh.cn

value of 97%. According to a recent study, the accuracy of 64-slice MDTA was comparable to that of stress nuclear perfusion imaging (SPECT) in the detection and exclusion of acute coronary syndrome in patients with chest pain [10]. Furthermore, MDCT has expanded its application beyond coronary angiography towards a more comprehensive evaluation of cardiovascular disease, including the evaluation of cardiac function, valvular disease [11], congenital abnormalities [12] and myocardial viability [13, 14]. Precise grading of stenotic CAD by CCTA is made difficult or even impossible in heavily calcified vascular segments because of blooming artefacts [15], and the diagnostic accuracy of this method is therefore limited, particularly in patients who have advanced calcified atherosclerosis, *e.g.* patients with end-stage diabetic disease. For that reason, additional diagnostic information to predict the haemodynamic relevance of stenotic CAD is desirable.

A few studies have assessed the potential of cardiac CT imaging for the detection of myocardial perfusion abnormalities. Animal studies have shown that myocardial perfusion can be depicted by looking at the differences between rest and stress imaging [16]. Furthermore, dynamic CT data acquisition has been used in attempts to calculate myocardial perfusion reserve. These experimental approaches have limitations, however, including restricted ventricular coverage, high image noise, artefacts and increased radiation exposure owing to multiple CT data acquisitions. Recently, a new generation of dual-source CT (DSCT) scanners has been introduced. DSCT scanners are equipped with two X-ray tubes and two corresponding detectors mounted on the rotating gantry with an angular offset of 90°. The reconstruction of a single cross-sectional image of the heart requires the acquisition of data over a rotation of approximately 180°. Therefore, with DSCT systems, a one-quarter rotation of the gantry is sufficient for image reconstruction when both tubes and detectors are operated simultaneously. With a gantry rotation time of 330 ms, DSCT allows image acquisition with an effective scan time of 83 ms. This technology allows bisection of temporal resolution for cardiac CT scans compared with the most recent 64-slice CT scanners, obviating the need to administer beta blockers to reduce heart rate [17]. Coronary dual-source computed tomography angiography (corDSCTA) data sets are typically acquired during a single breath-hold period of 6–10 s. A bolus administration of iodinated contrast agent is given at a flow rate of 5 ml s⁻¹.

Besides visualising the coronary arteries, corDSCTA can simultaneously provide information on blood volume distribution that is based on an early arterial myocardial contrast phase. The primary aim of this study is to evaluate the performance of corDSCTA in the detection of myocardial perfusion abnormalities in comparison with rest/stress technetium-99m SPECT, which served as the gold standard. A secondary objective was to assess the potential value of corDSCTA for the detection of chronic myocardial infarcts based on the measurement of attenuation values within areas of hypoperfused myocardium (perfusion defects). A third objective was to correlate the presence of high-grade coronary disease ($\geq 50\%$ luminal narrowing) as determined by corDSCTA with perfusion defects on rest/stress SPECT.

Methods and materials

Patient population

Fifty-five consecutive patients (32 male, 23 female; median age, 60.7 $\pm$ 14.2 years) with cardiovascular risk factors and clinical suspicion of or known CAD who underwent gated myocardial perfusion SPECT were included in the study. CorDSCTA was performed within three weeks of the SPECT study. CorDSCTA was clinically indicated in all of the patients based on a combination of clinical symptoms and the results of the SPECT study. Written informed consent was obtained from all patients and the study was approved by the institutional review board.

DSCT data acquisition

All CT examinations were performed on a DSCT system (Somatom Definition; Siemens Medical Solutions, Forchheim, Germany) with a standard clinical protocol. Scanning parameters were as follows: 120 kV, effective mAs per rotation 400, 0.33 ms gantry rotation time, 32 $\times$ 0.6 mm collimation with z-flying focal spot for each detector. The pitch varied between 0.2 and 0.43, depending on the heart rate [18]. For dose reduction, an automatic tube current modulation algorithm was used. A standard volume of 85 ml of contrast material (Isovue 370; Bracco Diagnostics, Seattle, WA) was administered at 5 ml s⁻¹ followed by a 50-ml saline flush. Automatic detection of peak enhancement in the left ventricle with a detection threshold of 120 HU was used. The helical scan was started automatically following the bolus detection. A 0.4-mg tablet of nitroglycerine was sublingually administered approximately 5 min before the scan. Data sets were acquired during a single breath-hold period, and an electrocardiogram was recorded simultaneously for retrospective gating. For image evaluation, 0.75-mm slices were reconstructed starting at early systole (0% of cardiac cycle) and ending at end-diastole (95% of cardiac cycle) in steps of 5%. Electrocardiogram modulation was used with a pulsing window of 30–70%.

DSCT image analysis

Reconstructed images were transferred to a remote workstation running a cardiac function analysis software package (Aquarius Workstation 3.7.0.7; Terarecon Inc.). The CT data sets were analysed in a consensus reading by two experienced cardiovascular radiologists. The radiologists were unaware of the corresponding SPECT findings and any clinical patient information beyond the general suspicion of CAD. Contrast uptake in the myocardium during an early arterial phase of contrast injection was analysed subjectively and objectively. The subjective analysis was based on the visual depiction of hypoenhanced areas on reconstructed short-axis slices in a systolic phase at 35% of the cardiac cycle. A systolic phase was chosen for analysis because areas of hypoenhancement appeared to be more conspicuous during cardiac contraction. A 17-segment model was used to

determine the location of detected perfusion defects [19]. As part of the image analysis, the readers had to assign the detected perfusion defects to the appropriate coronary artery territory (right coronary artery (RCA), posterior descending artery (PDA), left anterior descending artery (LAD) or left circumflex artery (LCx)). The objective analysis included a comparison of the CT attenuation values (HU) of regions with decreased myocardial contrast uptake with those of remote normal ventricular wall. In addition, the attenuation values of both the opacified left ventricular cavity and background air, including their standard deviations (noise), were obtained. Attenuation values were determined using region of interest (ROI) measurements with an area of approximately 50 mm². Detected perfusion defects were correlated with the findings obtained on both rest and stress SPECT imaging.

To correlate stenotic disease detected by corDSCTA with the results of SPECT imaging, left main coronary artery (LMCA), LAD, LCx, RCA and PDA were assessed for the presence of stenotic disease. Stenotic disease of major side branches (first and second diagonal branch, acute and obtuse marginal branches) was assigned to the appropriate coronary vascular territory if they showed a diameter of at least 1.5 mm at the vessel origin. After visual identification of a stenosis, a computerised quantitative analysis algorithm (Vital Images, MN) was employed similarly to the technique used for quantitative coronary angiography. When minor vessel calcifications were present, the measurements were manually edited if necessary to exclude calcifications from the lumen contour. Luminal stenoses of 50% or more were defined as high grade. Vessel segments in which extensive calcifications obscured the lumen were also characterised as high grade. If one or more high-grade lesions or occlusions were present in a coronary artery, the artery was characterised as high-grade stenotic. The grading of coronary stenosis was done by two experienced radiologists in consensus.

Gated rest/stress SPECT imaging

Myocardial SPECT at rest using technetium-99m tetrofosmin (Myoview; GE Healthcare, Braunschweig, Germany) was performed using a triple-head SPECT camera system equipped with low-energy high-resolution collimators. No X-ray-based attenuation correction was used. An adenosine infusion was administered at 0.14 mg kg⁻¹ min⁻¹ for 6 min. Subsequently, technetium-99m tetrofosmin was injected at peak stress and gated SPECT images of the heart were obtained. A 20% window was used around the 140-keV energy peak of technetium-99m tetrofosmin. A total of 90 projections were obtained over a 360° circular orbit. Data were stored in a 64 × 64 matrix. Additional reconstruction yielded standard long- and short-axis projections perpendicular to the heart axis. Semi-quantitative visual assessment of short-axis slices were displayed in polar map format, and adjustment for peak myocardial activity (100%) was performed by two experienced readers in consensus. A standard 17-segment model, as proposed by the American Society of Nuclear Cardiology, was used [20]. Each segment was scored as “normal or abnormal probably

due to artefact” or “abnormal with mild, moderate or severe reduction or absence of radioisotope uptake”. The myocardial segments were then assigned to their respective coronary artery territory according to the segment model as described above.

Statistical analysis

Categorical data SPSS 11.5 (Chicago, IL) were used for statistical analysis. Rest/stress myocardial perfusion gated SPECT was used as the reference standard. Values for sensitivity, specificity and diagnostic accuracy for the detection of perfusion defects were obtained on both a per-patient and a per-segment basis [21]. κ values were used to assess agreement in the detection of perfusion between imaging modalities (<0.4 = poor agreement; 0.4–0.60 = fair agreement; 0.61–0.80 = good agreement; and >0.8 = almost perfect agreement) [22]. Continuous variables are presented as means $\pm$ SDs. Comparison of myocardial attenuation among groups was performed with a one-way analysis of variance (ANOVA) test. A *p*-value <0.05 was considered statistically significant.

Results

CorDSCTA provided images of diagnostic quality in all 55 patients included in the study. The clinical symptoms of patients were as follows: 33 had chest pain, four felt occasional chest pressure during exercise and two complained of shortness of breath. Ten asymptomatic patients were evaluated for ischaemic heart disease on the basis of a combination of risk factors, such as family history, elevated lipid profile and hypertension. A summary of patient characteristics including average heart rate during data acquisition and radiation dose (volume CT dose index) during coronary CT is presented in Table 1.

Perfusion defects

SPECT imaging at stress showed perfusion defects in 24 of 55 patients (43%). The perfusion defects were

Table 1. Summary of patient characteristics (*n*=55) and radiation dose (volume CT dose index)

Variables	
Age (years)	60.7 $\pm$ 14.2
Women/men	23/32
Hypercholesterolemia (>6.2 mmol l ⁻¹)	23 (42%)
Diabetes mellitus	15 (27%)
Hypertension	34 (62%)
Current smoker	9 (16%)
Family history of CAD	12 (22%)
Mean heart rate (bpm) ¹	74.3 $\pm$ 13 (53–115)
Body mass index (kg m ⁻²)	26.3 $\pm$ 3.2
Mean DLP (mGy*cm)	926 $\pm$ 441
Effective dose (mSv)	15.7 $\pm$ 7.4

Values are mean $\pm$ SD (range) or number (per cent); DLP, dose-length product. ¹Heart rate was measured during data acquisition.

located in the following vascular territories: RCA ($n=4$), ($n=17$) and LCx ($n=3$). The rest portion of SPECT showed perfusion defects in 14 patients: RCA ($n=2$), LAD ($n=10$) and LCx ($n=2$).

corDSCTA detected hypoenhanced areas of myocardium (perfusion defects) in 23 patients in the following vascular territories: RCA ($n=4$), LAD ($n=16$) (Figure 1), LCx ($n=3$). Comparing corDSCTA with stress SPECT, a perfusion defect was assigned to the same coronary artery vascular territory by both imaging modalities in 20 cases (Figure 2).

All of the perfusion defects detected by rest SPECT ($n=14$) were detected by corDSCTA.

In four cases, perfusion defects detected by stress SPECT were not detected by corDSCTA, whereas, in three cases, perfusion defects detected by corDSCTA were visualised by neither stress nor rest SPECT imaging.

There was a good agreement ($\kappa=0.61-0.8$) between corDSCTA and rest SPECT ($\kappa=0.64$) as well as between corDSCTA and stress SPECT ($\kappa=0.74$) for the detection of perfusion defects. A summary of findings comparing the results of corDSCTA and SPECT is displayed in Table 2. With stress SPECT serving as gold standard, corDSCTA diagnosed perfusion defects with an overall sensitivity and specificity of 83.3% (20 of 24 patients) and 90.3% (28 of 31 patients), respectively; compared with rest SPECT, sensitivity and specificity values were 100% and 78%, respectively (Table 3).

Quantitative analysis of perfusion defects

Eleven of the 14 patients with fixed defects had a known history of myocardial infarction. The average attenuation

Figure 1. Images of a 78-year-old woman with atypical chest pain. (a) Vertical long-axis view of corDSCTA shows an area of subendocardial hypoenhancement in the distal anterior wall and apex, as indicated by the arrowhead. (b) Rest SPECT shows no abnormal findings. (c) A perfusion defect is identified in the anterior wall and apex, as indicated by the arrowhead, consistent with stress-induced ischaemia in LAD territory. (d) Thin maximum intensity processing (MIP) reconstruction of corDSCTA demonstrates occlusion of the mid-portion of LAD with a prominent first diagonal branch, as indicated by the arrowhead. Presence of coronary calcifications challenges accurate grading of stenosis.

Figure 2. Images of a 67-year-old man with recurrent chest pain and a history of myocardial infarction. (a) Short axis view of corDSCTA shows a near transmural area of low density in the anterolateral wall of the left ventricle. On the basis of low attenuation values and myocardial thinning, corDSCTA suggests chronic infarct. (b,c) SPECT shows a fixed defect in the corresponding myocardial region consistent with myocardial infarct.

values determined on corDSCTA of perfusion defects designated as fixed on SPECT (-8.5 ± 22.2 HU) were significantly lower ($p=0.002$) than those of SPECT-designated reversible defects (43.1 ± 17.5 HU). Furthermore, the average attenuation difference between perfusion defect versus normal myocardium was significantly

greater ($p=0.004$) for fixed defects (101.0 ± 36.1 HU) than for reversible defects (58.5 ± 24.6 HU). A summary of the measurements is presented in Table 4. Average opacification values for the left ventricular cavity were not statistically different in patients with reversible defects, fixed defects and no defects.

Table 2. Summary findings for rest and stress SPECT versus corDSCTA for detection of perfusion defects

	Rest SPECT		Stress SPECT		Total
	Normal	Perfusion defects	Normal	Perfusion defects	
corDSCTA					
Normal	32	0	28	4	32
Perfusion defects	9	14	3	20	23
Total	41	14	31	24	55
Overall agreement	$\kappa=0.644$		$\kappa=0.740$		

Table 3. Overall diagnostic accuracy of corDSCTA in comparison with rest and stress SPECT for the detection of myocardial perfusion abnormalities in 55 patients

	Compared with rest SPECT	Compared with stress SPECT
Sensitivity (%)	100 (14/14)	83.3 (20/24)
Specificity (%)	78.0 (32/41)	90.3 (28/31)
Negative predictive value (%)	100 (32/32)	87.5 (28/32)
Positive predictive value (%)	60.9 (14/23)	87.0 (20/23)
Accuracy (%)	83.6 (46/55)	87.3 (48/55)

Correlation of stenotic disease with perfusion defects

Of the 44 patients with no history of myocardial infarct ($n=44$), 13 patients had high-grade stenotic CAD ($\geq 50\%$) upon corDSCTA. A total of 23 vascular territories (RCA, LAD, LCx) were affected. Patients with a known history of myocardial infarction were excluded from this part of the analysis because they had undergone interval revascularisation treatment by percutaneous transluminal coronary angioplasty ($n=7$) or coronary bypass surgery ($n=4$). No high-grade stenosis of the LMCA was detected by corDSCTA.

Rest/stress SPECT detected perfusion defects suggestive of haemodynamically relevant vessel narrowing in 13 patients in a total of 17 vascular territories. Ten of the 17 coronary arteries with perfusion defects on SPECT showed stenoses ($\geq 50\%$) in matching vascular territories on corDSCTA, whereas 13 of the 23 coronary arteries found to have stenoses $\geq 50\%$ on corDSCTA did not result in any perfusion defects on SPECT. The data converted into sensitivity and specificity values for corDSCTA for the detection of perfusion abnormalities seen on rest and stress SPECT in patients with no known history of prior myocardial infarction of 59% and 89%, respectively.

Discussion

Both multislice CT (MSCT) angiography and SPECT are valuable techniques for the non-invasive evaluation of patients with known or suspected CAD. However, the modalities differ in the information they provide. Multislice CTA of the coronary arteries is generally focused on providing information relating to the lumens of the coronary arteries and to pathological changes in the vessel walls caused by atherosclerotic plaque. Recent

studies have shown that 64-slice coronary MSCT is highly accurate for the detection of high-grade coronary artery stenoses, even in patient cohorts where the prevalence of CAD is low [23]. However, accurate quantification of stenosis severity by MSCT remains difficult in the presence of heavily calcified coronary arteries, which often results in an overestimation of stenosis severity [24]. Additional information to determine the functional relevance of coronary stenoses and the cardiac risk stratification would therefore be desirable.

Myocardial SPECT aims to assess the haemodynamic relevance of coronary atherosclerosis but does not provide detailed anatomical information. In multiple large-scale studies, the extent and severity of myocardial perfusion defects as demonstrated by SPECT have served as a strong predictor of cardiac death, with an increasing death rate proportionate to the displayed perfusion abnormalities [25].

Because of the inherent differences between SPECT and coronary MSCT, both techniques are highly complementary. In considering the complementary nature of the two modalities, the focus of this study was to evaluate how far myocardial perfusion information can be derived from standard corDSCTA and to determine the degree of correlation with the perfusion information provided by SPECT.

To our knowledge, this study is unique as it utilised the recently introduced DSCT technology for the assessment of myocardial perfusion in clinical patients. DSCT imaging provides a number of advantages, particularly for cardiac imaging. The combination of high temporal and spatial resolution provided by DSCR means that routine administration of beta blockers is not necessary to obtain images of the coronary arteries of diagnostic quality [26]. It has been reported that the administration of beta blockers can alter myocardial blood flow and lead to hyperaemia, particularly in the presence of myocardial ischaemia [27], and therefore may confound myocardial perfusion measurements. Clearly, fast data acquisition (typically less than 10 s to capture the whole heart) and lack of beta blocker administration may be highly beneficial to the assessment of myocardial perfusion and may even offer the opportunity to assess myocardial perfusion at stress, *e.g.* following the administration of dipyridamole or adenosine.

A recent report has suggested that the impact of beta blocker therapy on the detection of perfusion defects by adenosine SPECT may actually be limited [28]. As part of that study, patients were not specifically instructed to abstain from beta blockers before their CT examination.

Table 4. Regions of decreased CT attenuation (HU) of different SPECT findings

Attenuation on corDSCTA (HU)	SPECT finding		
	RPD ($n=10$)	FPD ($n=14$)	Normal ($n=31$)
Perfusion defects attenuation	43.1 $\pm$ 17.5	-8.5 $\pm$ 22.2	n.a.
Remote (normal) attenuation	104.7 $\pm$ 22.1	96.6 $\pm$ 15.3	111.5 $\pm$ 20.7
Difference in attenuation between perfusion defect and remote tissue	58.5 $\pm$ 24.6	101.0 $\pm$ 36.1	n.a.
Left ventricular cavity	365.3 $\pm$ 90.4	303.2 $\pm$ 65.7	318.7 $\pm$ 110.2

FPD, fixed perfusion defect; RPD, reversible perfusion defect.

Whereas 17 patients were on beta blocker therapy (50 mg Metoprolol p.o.) within 3 months of the CT study, only 3 patients took beta blockers within the 3–5-hour period prior to the corDSCTA study. These three patients showed fixed perfusion defects on SPECT. How far beta blockers may impact the visual or semi-quantitative assessment of perfusion defects in cardiac CT warrants further investigation. Various nuclear medicine studies have addressed the effect of nitroglycerine on the detection of myocardial perfusion abnormalities. It appears that nitroglycerine may improve the detection of perfusion defects by nuclear medicine stress studies [29]. It remains unclear to what extent nitroglycerine affects the detection of perfusion abnormalities on cardiac CT studies at rest. Because nitroglycerine is typically administered for coronary vasodilation in routine coronary CTA, we decided not to withdraw nitroglycerine as part of our CT study protocol.

In our study, corDSCTA detected all of the perfusion defects visualised on rest SPECT, resulting in both sensitivity and negative predictive values of 100%. The sensitivity and negative predictive values of corDSCTA for the detection of perfusion defects at stress SPECT were lower, at 83.3% and 87.5%, respectively. This is not surprising as the corDSCTA data were acquired at rest without pharmacological stimulation. Three of the perfusion defects detected by corDSCTA had no correlating defect at either stress or rest SPECT, resulting in specificities of 78% (SPECT at rest) and 90.3% (SPECT at stress). A possible explanation for this discrepancy may be the higher spatial resolution of corDSCTA, which may offer advantages, particularly for the depiction of small subendocardial defects.

There is a potential for false-positive CT findings caused by beam hardening owing to the influx of highly concentrated contrast agent in the superior vena cava, right atrium or right ventricle. This can cause streak artefacts that result in areas of dark myocardium, which may mimic perfusion abnormalities. In addition, artefacts have been described at the endocardial surface because of the density of contrast in the left ventricle, and these too may generate false-positive findings. However, beam-hardening artefacts do not follow the distribution of the coronary arteries and have a typically triangular shape, as they originate from a focus of high density that does not respect morphological borders, hence they can generally be differentiated from myocardial perfusion defects. Overall, there was a good agreement between corDSCTA and SPECT at both rest ($\kappa=0.64$) and stress ($\kappa=0.74$). A number of recent studies have addressed the topic of CT myocardial perfusion in both animals [16] and humans [30, 31]. Animal studies have demonstrated that MDCT can be utilised to evaluate myocardial perfusion differences at rest and stress [16].

The present study aimed to analyse the myocardial perfusion defects displayed by volumetric data acquired from the whole heart. The data were collected in a helical mode during an early arterial phase of rapid intravenous contrast administration, as consistent with standard protocol for coronary CTA used in clinical practice. This approach differs fundamentally from dynamic scanning at a fixed pre-defined slice location of the heart over a period of time in order to assess the wash-in and wash-out of contrast agent, a technique that has been

investigated by both electron beam CT [32] and MDCT [33] and is similar to the technique used by cardiac perfusion MRI [34]. When used for cardiac CT, however, this technique results in the patient being repeatedly exposed to radiation. Furthermore, it does not allow the comprehensive display of the coronary arteries unless used in addition to a standard CT protocol, which would require additional contrast administration and result in even more radiation exposure.

Hacker et al [35] evaluated cardiac CT perfusion imaging with a clinical protocol primarily aimed at the detection of coronary artery pathology compared with cardiac perfusion MRI as the standard [35]. For the detection of ischaemic perfusion abnormalities, they obtained a specificity of 92%. However, they detected only three of six ischaemic perfusion defects (sensitivity: 50%), all located in the cardiac apex. Interestingly, they utilised 16-slice CT technology with scan times for the heart of around 20 s, which is at least double the acquisition time for the DSCT used in the present study. In addition, cardiac imaging with 16-slice CT mandates the use of beta blockers in patients with heart rates higher than 60 beats per min. These technical factors may serve as an explanation for the lower sensitivity compared with our results.

The correlation between high-grade stenotic ($\geq 50\%$) CAD and perfusion abnormalities on SPECT showed only limited agreement on corDSCTA. In 45 patients with no history of myocardial infarction, corDSCTA showed high-grade stenotic coronary CAD ($\geq 50\%$) in 13 patients and 23 coronary arteries (RCA, LAD and LCx). 10 of the 17 coronary arteries in which perfusion defects were detected on SPECT showed stenoses ($\geq 50\%$) in matching vascular territories on corDSCTA, whereas 13 of 23 coronary arteries with stenoses $\geq 50\%$ detected on corDSCTA did not correspond to arteries with perfusion defects on SPECT, resulting in a sensitivity and specificity for corDSCTA of 59% and 89%, respectively. These results are in agreement with previous studies that suggest that MDCT is not able to predict the functional relevance of coronary artery stenosis. They may also point to the heterogeneous aetiology of myocardial perfusion abnormalities, including small vascular disease, which is not displayed by current angiographic techniques.

In this study, we showed that corDSCTA has the potential to identify chronic myocardial infarcts on the basis of significantly lower attenuation values ($p=0.002$) in infarcted myocardium (-8.5 ± 22.2 HU) compared with non-infarct-related perfusion defects (43.1 ± 17.5 HU). The lower attenuation values reflect scar tissue with fatty replacement, as has been demonstrated in previous studies [36, 37].

This study has several limitations. The potential influence of heart rate, body weight and height on image quality was not evaluated as part of this study. A comparative analysis of radiation exposure between corDSCTA and SPECT was not performed. Furthermore, patients already on beta blockers were not excluded from the study. Therefore, it remains unclear how far beta blocker administration may have influenced the results in selected patients. Our CT data were not acquired in “dual energy” mode, which offers fascinating new applications such as the mapping of the iodine distribution, and therefore of the perfused blood pool volume within the

myocardium [38]. However, dual-energy technology has only recently become available and was not accessible to us at the time of this study. Furthermore, this technology requires the operation of both X-ray tubes at different energy levels. This reserves this technique for patients with low heart rates or alternatively requires the administration of beta blockers.

In summary, this study indicates that clinically indicated corDSCTA can provide potentially important additional information on myocardial perfusion and chronic myocardial infarction similar to that provided by SPECT. It may therefore improve risk stratification in patients with suspected CAD beyond the angiographic display of stenotic disease.

References

- Beller GA, Zaret BL. Contributions of nuclear cardiology to diagnosis and prognosis of patients with coronary artery disease. *Circulation* 2000;101:1465–78.
- Frans J, Wackers FJ. SPECT detection of coronary disease. In: Dilsizian V, Narula J, eds. *Atlas of Nuclear Cardiology*. Philadelphia, PA: Current Medicine, Inc, 2003:63–77.
- Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. *Circulation* 1998;97:535–43.
- Taillefer R, DePuey EG, Udelson JE, Beller GA, Latour Y, Reeves F. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. *J Am Coll Cardiol* 1997;29:69–77.
- Brown KA, Rowen M. Prognostic value of a normal exercise myocardial perfusion imaging study in patients with angiographically significant coronary artery disease. *Am J Cardiol* 1993;71:865–7.
- McCaig LF, Burt CW. National hospital ambulatory medical care survey 2003. Emergency department summary: advance data from vital and health statistics, No.358. Hyattsville, MD: National Center for Health Statistics, 2005.
- Ropers D, Baum U, Pohle K, Anders K, Ulzheimer S, Ohnesorge B, et al. Detection of coronary artery stenoses with thin-slice multi-detector row spiral computed tomography and multiplanar reconstruction. *Circulation* 2003;107:664–6.
- Hoffmann MH, Shi H, Schmid FT, Gelman H, Brambs HJ, Aschoff AJ. Noninvasive coronary imaging with MDCT in comparison to invasive conventional coronary angiography: a fast-developing technology. *AJR Am J Roentgenol* 2004;43:2265–70.
- Raff GL, Goldstein JA. Coronary angiography by computed tomography: coronary imaging evolves. *J Am Coll Cardiol* 2007;49:1830–3.
- Gallagher MJ, Ross MA, Raff GL, Goldstein JA, O'Neill WW, O'Neil B. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low-risk chest pain patients. *Ann Emerg Med* 2007;49:125–36.
- Manghat NE, Rachapalli V, Van Lingen R, Veitch AM, Roobottom CA, Morgan-Hughes GJ. Imaging the heart valves using ECG-gated 64-detector row cardiac CT. *Br J Radiol* 2008;81:275–90.
- Datta J, White CS, Gilkeson RC, Meyer CA, Kansal S, Jani ML, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. *Radiology* 2005;235:812–8.
- Henneman MM, Schuijf JD, Jukema JW, Lamb HJ, de Roos A, Dibbets P, et al. Comprehensive cardiac assessment with MSCT: evaluation of LV function and perfusion in addition to coronary anatomy in patients with previous myocardial infarct. *Heart* 2006;92:1779–83.
- Lardo AC, Cordeiro MA, Silva C, Amado LC, George RT, Saliaris AP, et al. Contrast enhanced multidetector computed tomography viability imaging following myocardial infarction: characterization of myocyte death, microvascular obstruction and chronic scar. *Circulation* 2006;113:394–404.
- Schlosser T, Mohrs OK, Magedanz A, Nowak B, Voigtlander T, Barkhausen J, et al. Noninvasive coronary angiography using 64-detector-row computed tomography in patients with a low to moderate pretest probability of significant coronary artery disease. *Acta Radiol* 2007;48:300–7.
- George RT, Silva C, Cordeiro MA, DiPaula A, Thompson DR, McCarthy WF, et al. Multidetector computed tomography myocardial perfusion imaging during adenosine stress. *J Am Coll Cardiol* 2006;48:153–60.
- Achenbach S, Ropers D, Kuettner A, Flohr T, Ohnesorge B, Bruder H, et al. Contrast-enhanced coronary artery visualization by dual-source computed tomography — initial experience. *Eur J Radiol* 2006;57:331–5.
- Vanhoeacker PK, Heijenbrok-Kal MH, Van Heste R, Decramer I, Van Hoe LR, Wijns W, et al. Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis. *Radiology* 2007;244:419–28.
- Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002;105:539–42.
- Klocke FJ, Baird MG, Lorell BH, Bateman TM, Messer JV, Berman DS, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging — executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging). *Circulation* 2003;108:1404–18.
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–10.
- Fleiss JL. Statistical methods for rates and proportions. 2nd Ed. New York: Wiley, 1981: 218.
- Leber AW, Johnson T, Becker A, von Ziegler F, Tittus J, Nikolaou K, et al. Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. *Eur Heart J* 2007;28:2354–60.
- Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005;46:147–54.
- Vanzetto G, Glover DK, Ruiz M, Calnon DA, Pasqualini R, Watson DD, et al. 99mTc-N-NOET myocardial uptake reflects myocardial blood flow and not viability in dogs with reperfused acute myocardial infarction. *Circulation* 2000;101:2424–30.
- Ropers U, Ropers D, Pflederer T, Anders K, Kuettner A, Stilianakis NI, et al. Influence of heart rate on the diagnostic accuracy of dual-source computed tomography coronary angiography. *J Am Coll Cardiol* 2007;50:2393–8.

27. Koepfli P, Wyss CA, Namdar M, Klainguti M, von Schulthess GK, Lüscher TF, et al. Beta-adrenergic blockade and myocardial perfusion in coronary artery disease: differential effects in stenotic versus remote myocardial segments. *J Nucl Med* 2004;45:1626–31.
28. Lakkireddy D, Aronow WS, Bateman T, McGhee I, Nair C, Khan IA. Does beta blocker therapy affect the diagnostic accuracy of adenosine single-photon-emission computed tomographic myocardial perfusion imaging? *Am J Ther* 2008;15:19–23.
29. Batista JF, Pereztol O, Valdés JA, Sánchez E, Stusser R, Rochela LM, et al. Improved detection of myocardial perfusion reversibility by rest-nitroglycerin Tc-99m-MIBI: comparison with TI-201 reinjection. *J Nucl Cardiol* 1999;6:480–6.
30. George RT, Jerosch-Herold M, Silva C, Kitagawa K, Bluemke DA, Lima JA, et al. Quantification of myocardial perfusion using dynamic 64-detector computed tomography. *Invest Radiol* 2007;42:815–22.
31. Nikolaou K, Sanz J, Poon M, Wintersperger BJ, Ohnesorge B, Rius T, et al. Assessment of myocardial perfusion and viability from routine contrast-enhanced 16-detector-row computed tomography of the heart: preliminary results. *Eur Radiol* 2005;15:864–71.
32. Knollmann FD, Muschick P, Krause W, Hausmann H, Hetzer R, Felix R, et al. Detection of myocardial ischaemia by electron beam CT. Experimental studies. *Acta Radiol* 2001;42:386–92.
33. Nagao M, Matsuoka H, Kawakami H, Higashino H, Mochizuki T, Murase K, et al. Quantification of myocardial perfusion by contrast-enhanced 64-MDCT: characterization of ischaemic myocardium. *AJR Am J Roentgenol* 2008;191:19–25.
34. Gebker R, Jahnke C, Paetsch I, Kelle S, Schnackenburg B, Fleck E, et al. Diagnostic performance of myocardial perfusion MR at 3 T in patients with coronary artery disease. *Radiology* 2008;247:57–63.
35. Hacker M, Jakobs T, Hack N, Nikolaou K, Becker C, von Ziegler F, et al. Sixty-four slice spiral CT angiography does not predict the functional relevance of coronary artery stenoses in patients with stable angina. *Eur J Nucl Med Mol Imaging* 2007;34:4–10.
36. Nieman K, Cury RC, Ferencik M, Nomura CH, Abbara S, Hoffmann U, et al. Differentiation of recent and chronic myocardial infarction by cardiac computed tomography. *Am J Cardiol* 2006;98:303–8.
37. Becker CR, Nikolaou K, Muders M, Babaryka G, Crispin A, Schoepf UJ, et al. Ex vivo coronary atherosclerotic plaque characterization with multi-detector-row CT. *Eur Radiol* 2003;13:2094–8.
38. Schwarz F, Ruzsics B, Schoepf UJ, Bastarrika G, Chiaramida SA, Abro JA, et al. Dual-energy CT of the heart — principles and protocols. *Eur J Radiol* 2008;68:423–33.