Noninvasive Detection of Coronary Lesions Using 16-Detector Multislice Spiral Computed Tomography Technology
Initial Clinical Results
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OBJECTIVES
The aim of our study was to evaluate the feasibility of detecting coronary artery lesions using a new computed tomography (CT) scanner with 16 detectors and faster gantry rotation.

BACKGROUND
Computed tomography angiography of the coronaries permits assessment of the coronaries; however, image quality is still impaired by motion artifacts and calcifications.

METHODS
Sixty patients scheduled for conventional coronary angiography (CCA) were additionally studied by multislice spiral computed tomography (MSCT). Calcium scores and a contrast-enhanced visualization of the coronaries were performed and analyzed regarding evaluability, presence of coronary artery lesions, and correct clinical diagnosis.

RESULTS
Calcium scoring was successful in all patients; 58 of 60 patients had a diagnostic contrast-enhanced scan. Mean calcium score was 506 ± 743 Agatston score equivalent (ASE); 13 of 58 (22%) patients had an ASE >1,000, 46 of 58 (78%) patients <1,000. In 763 coronary segments, CCA detected a total of 75 lesions ≥50%. The MSCT correctly assessed 54 of these. Twenty-one lesions were missed or incorrectly underestimated. Sensitivity was 72%, specificity 97%. When restricting analysis to patients with an ASE <1,000, 40 significant lesions ≥50% were seen on CCA, and MSCT correctly detected 39 lesions (sensitivity 98%, specificity 98%). Regardless of any threshold, the correct clinical diagnosis could be obtained in 58 of 60 (97%) of all patients.

CONCLUSIONS
In individuals with low-to-moderate amounts of coronary artery calcium, 16-detector CT coronary angiography has high sensitivity and specificity for the diagnosis of significant coronary artery stenosis. (J Am Coll Cardiol 2004;44:1230–7) © 2004 by the American College of Cardiology Foundation

In 1999, mechanical multislice spiral computed tomography (MSCT) systems with simultaneous acquisition of four slices and half-second scanner rotation became available. Multi-row acquisition with these scanners allows for considerably improved visualization of the coronary arteries in comparison to single-slice spiral scanners (1–10). Initial experiences have shown that coronary lesions can be detected with promising sensitivity and specificity (11–18).

However, a number of factors are known to impair image quality and image interpretation. The two factors mostly held responsible are severe calcifications and higher heart rates (HRs) (3,4,7,16,19,20).

Since 2002, new MSCT scanners with faster gantry rotation speed and more than four detector rows were introduced. First publications suggest an improved image quality and possibly improved clinical robustness in comparison with four-slice scanners (21,22).

The aim of our study was to evaluate its feasibility, image quality, and clinical accuracy in detecting coronary artery lesions.

METHODS

Study population. A total of 60 patients were included in this study. To recruit patients, every patient that was referred to our institution for conventional invasive coronary angiography (CCA) was screened for possible contraindications to participate in this study (irregular HR, patients with prior stent implantation, known allergy to iodinated contrast media, and elevated serum creatinine levels >1.5 mg/dl). If no contraindication was present, the patient was asked to participate in the study, regardless of the primary indication for conventional angiography. If the patient gave informed consent, he/she was included in the study. Not all patients principally suitable for the study gave their consent and, therefore, were not included in the study. The local ethics committee had approved the study protocol. All patients underwent computed tomography (CT) angiography one day before CCA. An oral premedication with β-blocker was attempted in all patients. Contraindications for β-blocker medication was atrioventricular block

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Manuscript received June 25, 2003; revised manuscript received April 13, 2004, accepted May 25, 2004.
was acquired using the following protocol: 12 × 0.75 mm collimation, table feed 3.8 mm/rotation, tube current 500 mAs at 120 kV.

**Image reconstruction.** For image reconstruction, the standard built-in reconstruction algorithm was used. The reconstruction window was set to start at 60% RR-interval for all native images as well as the contrast-enhanced scan. If coronary segments were present with motion artifacts that allowed for limited diagnostic only, a test-series reconstructing single slices at a given z-position was performed. The range was 35% to 75% relative to the RR-interval in 2% steps. Thus, the reconstruction interval with the fewest motion artifacts was determined. The time point with least motion artifacts was then chosen to reconstruct the entire stack of images of the CTA scan.

**MSCT image interpretation.** Two reviewers, blinded to the results of CCA and all clinical information, evaluated the MSCT scans in a joint reading manner. Each case was investigated by the use of axial slices and 4-mm thin slab maximum intensity projections (MIPs) in axial and double oblique orientation adapted to the specific anatomy of the vessel using the scanners standard workstation (Wizard, Siemens). Three-dimensional volume-rendering techniques and curved MIP projections were used for display only. Curved MIP projections were created on a separate workstation (Vitrea 2, Vital Images, Plymouth, Minnesota).

Vessel wall calcifications were assessed visually, and they were quantitatively determined on an offline workstation (Leonardo, Siemens), based on the standard built-in algorithm using an Agatston score equivalent (ASE) adapted for MSCT and also based on the determination of the total calcium mass in mg calcium hydroxiapatite (CaHA).

Image quality was classified as “excellent” (no motion artifacts present), “good” (minor motion artifacts present), “moderate” (substantial motion artifacts present, but luminal assessment regarding significant stenosis still possible), “heavily calcified” (vessel lumen obscured by calcification), or “blurred” (only contrast visualization inside the vessel possible, no luminal assessment regarding significant stenosis possible). The readers assessed significant lesions ≥50% by visual estimation. Results were documented separately for all coronary segments using a modified American Heart Association classification (right coronary artery: 1 = proximal, 2 = middle, 3 = distal, and 4 = combined posterior descending and posterolateral branches; 5 = left main stem; left anterior descending: 6 = proximal, 7 = middle, 8 = distal, 9 = first diagonal, 10 = second diagonal; left circumflex: 11 = proximal, 12 = distal, 13 = first marginal branch) (23). Each bypass graft was counted as an additional segment. Additionally, the results per patient were compared with the findings of CCA. The diagnosis made by MSCT was considered to be correct if MSCT ruled out any significant lesion >50% or MSCT detected correctly at least one significant >50% lesion that was detected using CCA.

**Quantitative coronary angiography.** In all patients, CCA were obtained using 4Fr catheters the day after the MSCT.
exam. The CCA procedure itself was done under normal routine conditions, and the examiner actually performing the CCA was not explicitly informed that the patient was part of a study. To avoid any examination bias, all patients themselves were also asked not to inform the examiner that he/she actually was part of a study. Any clinical consequence and treatment decisions drawn from CCA, such as percutaneous transluminal coronary angioplasty procedure, stent placement, or coronary artery bypass grafting procedure were solely based on the results of CCA.

A second examiner aware of the study conditions but blinded to the CT results was asked to analyze the CCA again for study purposes and to perform a quantitative coronary angiography. His reading results, however, had no influence on the clinical treatment of the patient. All angiograms were evaluated by quantitative coronary analysis with automated vessel contour detection and manual correction. The catheter was used for calibration (Quantitative Coronary Analysis, Philips Medical Systems, Eindhoven, the Netherlands). The projection with the most severe degree of stenosis was used for evaluation. Nitrates were used at examiners discretion. Lesions with a diameter stenosis >50% were considered to be significant lesions.

**Statistics.** The diagnostic accuracy of MSCT to detect significant lesions was evaluated regarding QCA as the standard of reference. If a coronary vessel segment contained more than one lesion, the most severe lesion within the segment determined the diagnostic accuracy of the assessment. Two statistical analyses were performed, one on a per-patient basis and one based on individual segments. Evaluation criteria for the per-patient analysis was the ability of MSCT to correctly detect at least one significant lesion ≥50% diameter stenosis or to correctly rule out the presence of any lesion ≥50% diameter stenosis per patient.

In the per segment evaluation, the ability of MSCT to correctly identify lesions ≥50% diameter stenosis in any given segment was analyzed.

Standard descriptive statistics were used. Categorical data were presented with absolute frequencies and percentages. Computations were performed using SAS-PC for Windows (version 8.0, SAS Institute Inc., Cary, North Carolina).

**RESULTS**

**Image quality.** The MSCT was performed without complications in all patients; 56 of 60 (93%) patients received a beta-blocker regimen before the scan (two patients had an HR <48 beats/min, one patient had a blood pressure of 105/70, and one patient refused the β-blocker regimen). The mean HR was 63.5 ± 10.3 beats/min. Two patients were excluded from the statistical analysis regarding sensitivity and specificity but were kept in the study with respect to the assessment of the correct diagnosis; exclusion reasons were development of ventricular tachycardia in one case (related to the injection of contrast, but no allergic reaction; it recessed after the exam without any medical treatment) and one insufficient breath hold maneuver in another case leading to non-interpretable image quality.

Of all remaining 763 coronary artery segments scanned (58 patients each with 13 segments + 9 bypasses), 189 were found to be of excellent image quality, 198 of good image quality, and 218 segments were considered of moderate image quality. Forty-six coronary segments were severely affected by calcifications to such an extent that the assessment of the lumen was not possible, and 112 segments were of “blurred” image quality, so that no luminal assessment was possible. A total of 79.3% segments showed an image quality that permitted luminal assessment; in all other segments luminal assessment was not possible. Mean HR was 63.5 ± 10.3 beats/min for the whole study group, 61.2 ± 7.1 beats/min for patients with severe calcifications/ASE >1,000, and 64.2 ± 11.2 beats/min in patients with mild-to-moderate calcifications. When looking at the distribution of segments affected by motion artifacts, 80 to 112 (71%) belonged to distal segments (segment 4 [n = 25], 8 [n = 5], 12 [n = 14]) or side branches (segment 9 [n = 9], 10 [n = 8], or 13 [n = 14]). Only 16 of 112 (14%) belonged to proximal segments (segment 1 [n = 3], 2 [n = 4], 5 [n = 2], 6 [n = 0], 7 [n = 1], 11 [n = 6]).

**Native scan and calcium scoring.** The assessment of calcifications was successfully performed in all patients. Only those patients with diagnostic contrast-enhanced scans were included in the further analyses (58 of 60 patients). The mean calcium score expressed as total calcium mass in mg Ca-HA was 83.7 mg ± 129.5 CaHA (506 ± 743 ASE) for all 58 patients. In a second step, the patients were divided into two groups: ASE <1,000 and ≥1,000 score points to account for the most severe calcifications.

A total of 12 of 58 (21%) patients had scores ≥1,000 C. In that group the total Ca-mass was 296.1 ± 122.4 mg CaHA (1,718 ± 579 ASE), whereas, in those 46 patients with an ASE <1,000, the total Ca-mass was 25.8 ± 39.9 mg CaHA (147 ± 231 ASE).

**Lesion detection per coronary segment.** In a total of 763 coronary segments, CCA detected a total of 75 lesionings/ASE. MSCT correctly assessed 54 (72%) of these. Twenty-one lesions were missed or incorrectly underestimated (three lesion missed due to motion artifacts, nine had important calcifications, and nine lesions were underestimated despite sufficient image quality). Twenty-one lesions were overestimated and counted as false positive. Sensitivity was 72%, specificity 97%, the positive predictive value 72%, and the negative predictive value was 97%. The distribution of missed lesions per vessel was as follows: right coronary artery (RCA); 2 of 19 (11%), left main: 0 of 2 (0%), left anterior descending coronary artery (LAD): 7 of 27 (26%), left circumflex coronary artery (LCX): 12 of 26 (46%), identifying the LCX as most difficult vessel to assess.

When limiting the analysis to patients with a threshold of 1,000 ASE [n = 46, 12 patients had an ASE >1,000] as criteria for severe calcifications, CCA detected a total of 40 lesions >50%. The MSCT correctly assessed 39 (95%) of
these. One lesion was missed in a marginal branch, and 10 lesions were overestimated and counted as false positive.

Threshold-corrected sensitivity was 98%, specificity 98%, the positive predictive value 80%, and the negative predictive value was 99.8%. The distribution of missed lesions per vessel for this group was as follows: RCA: 0 of 10 (0%), left main: 0 of 2 (0%), LAD: 0 of 14 (0%), LCX: 1 of 14 (7%), identifying the LCX also most difficult vessel to assess. However, statistically there is an over-representation of missed lesions in the LCX in the patient collective with an ASE >1,000.

Bypass grafts indicate the presence of significant lesions in the vessel proximal to the insertion site and thus constitute a non-neglectable examination bias. A third analysis was performed without the four bypass patients, who had a total of eight venous grafts and one arterial graft and a mean calcium score of 1,235 ASE. All grafts were identified as patent by MSCT and CCA; no significant lesion was detected. In these four patients, a total of 10 significant lesions were detected other than those proximal to the graft insertion site; 7 of these were correctly identified (70%).

In the remaining 56 patients, 56 lesions were detected by CCA, of which 39 were correctly detected by MSCT, 17 lesions were missed, and 17 lesions were incorrectly identified as significant lesion resulting in a sensitivity of 70%, specificity 98%, positive predictive value of 70%, and a negative predictive value of 98%.

Correct clinical diagnosis in individual patients. Independently of any single vessel segment evaluation, 58 of 60 (97%) of all patient studies were correctly diagnosed using MSCT. The diagnosis was considered to be correct if any significant lesion >50% was ruled out or at least one significant lesion >50% lesion was detected and confirmed by CCA.

Both patients excluded from segmental analysis due to non-diagnostic image quality had no significant coronary artery disease, which could not be demonstrated by MSCT.

DISCUSSION

The most important findings of this study are that 16-detector MSCT technology provides a further improved image quality and diagnostic accuracy in the detection of coronary artery lesions in comparison with four-slice systems. Current limitations seem to remain severe calcifications and smaller vessels.

Lesion detection. Nieman et al. (21) as well as Ropers et al. (22) could demonstrate similar results in a comparable patient population using the same 16-slice CT technology. Also, their analysis adhered to specific thresholds. While Nieman et al. (21) focused their analysis on major branches with a vessel size ≥2 mm, Ropers et al. (22) focused their analysis on patients with an HR <60 beats/min. In our study we focused on patients with non-excessive calcifications using an ASE <1,000 as threshold. In this study, all coronary segments, regardless of their size, were included, and no HR limit was used. In that patient population, the study yields a sensitivity of 98%, specificity of 98%, a positive predictive value of 80%, and a negative predictive value of 100%. Lesion detection could be performed with better accuracy when compared with recently published studies using four-slice scanners (14).

However, the most relevant clinical information in clinical practice is to either correctly rule out or correctly identify patients with significant coronary artery disease. In the present study, this information could be obtained in all but two patients (97%). A major reason for this result seems to be the further improved image quality of the new MSCT scanner generation with a smaller susceptibility of heart-rate related motion artifacts (Figs. 1 and 2).

HR and motion artifacts. We could recently demonstrate that HR has a major impact on image quality, when using four-slice scanning systems (20). Our findings revealed a highly significant inverse relationship between HR and segmental visibility. Vessel visibility was best for HRs <65 beats/min. These data are supported by recent results published by Giesler et al. (3), Becker et al. (1), and others (14,15). The reason for this HR limitation can be explained by the limited temporal resolution of four-slice CT systems.

With a gantry rotation time of 420 ms, the new system provides a maximal temporal resolution of 210 ms when using a single-phase (single-heart-beat) algorithm to reconstruct an image. For higher HRs (>70 beats/min), a biphasic reconstruction algorithm uses two heartbeats to reconstruct an image, achieving a minimized temporal resolution up to 105 ms (24).

In our study population, with 56 of 60 (93%) patients having received oral beta-blockade before the scan, HR was 63.5 ± 10.3 beats/min. The improved image quality compared to four-slice scanners and the fact that relatively few proximal segments were affected by motion artifacts can be explained by two factors. Faster gantry rotation allows for an improved temporal resolution (250 vs. 210 ms) and second, a strict β-blockage assures favorable HRs. Both factors combined seem to sufficiently decrease motion artifacts of especially proximal segments (14%) to a level where accurate diagnosis is little impaired by them. Ropers et al. (22) could demonstrate that β-blockage using about 50 mg atenolol decreases HR 8 beats/min in their study. Also, their average HR was comparable with ours (62 ± 10 beats/min vs. 64 ± 10 beats/min).

Lesion detection in presence of calcifications. The second major cause for non-diagnostic images of the coronaries acquired by four-slice systems are severe calcifications. Early reports describe the effect that already minor calcifications impair the diagnostic image quality because the lumen obstruction cannot sufficiently be visualized (2,14,25). Our data suggest that this limitation might be reduced when using 16-detector technology. In our study population a statistical coincidence of over-representation of missed lesions in the LCX in the group of patients with an ASE.
>1,000 may overestimate the beneficial effect of low calcium scores (Table 2).

The spatial resolution of the four-slice systems of 24 line pairs/cm in xy-direction and 9 line pairs in z-direction, which corresponds to a voxel size of $0.6 \times 0.6 \times 1.0$ mm (compared with 50 line pairs in CCA), provides assessment of structures >0.9 to 1 mm (1,17). With the new system, a maximal spatial resolution of $0.5 \times 0.5 \times 0.6$ mm is possible (24). This also seems to be sufficient to assess the coronary lumen of the relevant coronary segments. Because
calcifications obscure the lumen also due to beam hardening artifacts, this maximum spatial resolution may not be applicable in the presence of major calcifications. As a clinical consequence, the same amount of calcium may not obscure the lumen in larger coronary segments, while in smaller segments the same amount of calcium may totally obscure the lumen and, hence, may impair a correct assessment of luminal obstruction (Fig. 3).

Correct clinical diagnosis in the individual patient. We were able to demonstrate that 58 of 60 (97%) patient studies were correctly diagnosed using MSCT. In comparable studies, the investigative focus lies mostly on determination of sensitivity and specificity of lesion detection in each single coronary segment or coronary artery regardless of the individual patient (21,22). In our study we sought to demonstrate that even with some unevaluable coronary segments present, the majority of our collective could be diagnosed correctly with respect to the presence or absence of significant coronary artery lesions. Because MSCT is not considered a replacement for coronary angiography but might become a useful tool to rule out significant lesions in patients with a low pretest probability, this is an important factor when considering an MSCT exam for an individual patient.

Study limitations and dose considerations. We sought to assess feasibility, scanning technique, and accuracy of diagnosis using a new 16-detector CT system with a gantry

Table 2. Lesion Detection Stenosis ≥50%

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<thead>
<tr>
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<th>All Segments</th>
<th>Patients With Ca Score &lt;1,000</th>
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<tbody>
<tr>
<td>Patients (n)</td>
<td>60</td>
<td>46</td>
</tr>
<tr>
<td>Segments (n)</td>
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<td>598</td>
</tr>
<tr>
<td>Lesions by CCA (n)</td>
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<td>40</td>
</tr>
<tr>
<td>Correct positive lesions by MSCT (n)</td>
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<td>39</td>
</tr>
<tr>
<td>False positive (n)</td>
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<td>10</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.72</td>
<td>0.98</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.97</td>
<td>0.98</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>0.72</td>
<td>0.80</td>
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<tr>
<td>Negative predictive value</td>
<td>0.97</td>
<td>1.0</td>
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CCA = conventional coronary angiography; MSCT = multislice spiral computed tomography.
rotation speed of 420 ms. Our collective of 60 patients so far in a single-center setting is a small group to assess every aspect of MSCT angiography of the coronaries with satisfying statistical power. Especially in our collective, the coincidental statistical effect mentioned above call for verification in larger collectives in a multicenter setting. Especially our arbitrarily chosen threshold of 1,000 ASE cannot be taken as a definite threshold for the decision when to perform an enhanced scan; however, it gives a first idea that only severe calcifications prohibit accurate diagnosis.

Dose measurements of the protocol used in this study revealed an effective dose of 5.4 mSv (male) using an electrocardiogram-dependent tube current modulation at 60 beats/min and 10.1 mSv (male) without tube current modulation (26). Each R-peak detected by the algorithm triggers a constant full dose interval of 400 ms. At low HRs, fewer R-peaks are detected during a given scan and, thus, fewer intervals with full dose are triggered, causing the total dose to be lower than at higher heart for the same scan (27,28). As a consequence, a controlled HR not only provides better image quality but also minimizes the radiation exposure to the patient.

Radiation exposure of CCA is examiner-dependent, and published data vary considerably, but it is generally agreed that CCA has a lower radiation exposure than MDCA (29).

Conclusions. The MSCT image quality could be furthermore improved with 16 slices. Severe calcifications, however, still limit interpretability of contrast-enhanced investigations. Thus far, primary native scans appear to be mandatory to evaluate the usefulness of contrast-enhanced visualization of the coronaries. Also, controlled HRs are warranted for the MSCT exam because this condition not only provides for better image quality but also minimizes the radiation exposure for the patient.

Acknowledgments
The authors would like to thank our radiographers, Ayser Birinci, Nicole Sachse, and Henriette Hehners, for their excellent work and their continuous dedicated commitment to our CT team.

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