Accuracy of Multidetector Spiral Computed Tomography in Identifying and Differentiating the Composition of Coronary Atherosclerotic Plaques
A Comparative Study With Intracoronary Ultrasound
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OBJECTIVES
We evaluated the accuracy of contrast-enhanced multidetector spiral computed tomography (MDCT) for the noninvasive detection and classification of coronary plaques and compared it with intracoronary ultrasound (ICUS).

BACKGROUND
Noninvasive determination of plaque composition and plaque burden may be important to improve risk stratification and to monitor progression of coronary atherosclerosis.

METHODS
We included 46 consecutive patients with a distinctive risk profile, who were investigated by ICUS (Goldvision, 20 MHz, Jomed Inc., Rancho Cordova, California). Due to the inability to slow the heart rate below 65 beats/min (n = 7) and due to renal insufficiency (n = 2), nine of 46 consecutive patients could not be studied by MDCT (Sensation 16, Siemens, Forchheim, Germany).

RESULTS
In the remaining 37 patients, 68 vessels were investigated by ICUS, and 58 of these vessels were visualized by MDCT with image quality sufficient for analysis. In these vessels that were divided in 3-mm sections, MDCT correctly classified 62 of 80 (78%) sections containing hypoechoic plaque areas, 87 of 112 (78%) sections containing hyperechoic plaque areas, and 150 of 158 (95%) sections containing calcified plaque tissue. In 484 of 525 (92%) sections, atherosclerotic lesions were correctly excluded. The MDCT-derived density measurements within coronary lesions revealed significantly different values for hypoechoic (49 HU [Hounsfield Units] ± 22), hyperechoic (91 HU ± 22), and calcified plaques (391 HU ± 156, p < 0.02).

CONCLUSIONS
This study demonstrates that, in the case of diagnostic image quality, contrast-enhanced MDCT permits an accurate identification of coronary plaques and that computed tomography density values measured within plaques reflect echogenity and plaque composition. (J Am Coll Cardiol 2004;43:1241–7) © 2004 by the American College of Cardiology Foundation

Electron beam tomography and multidetector computed tomography (MDCT) enable an accurate noninvasive identification and quantification of calcified coronary plaques (1,2). The extent of coronary calcium is a surrogate marker for total plaque burden, and it is suggested that future coronary events may be predicted on the basis of the calcium score (3–7). In addition, it has been shown that serial calcium measurements can illustrate the effect of drug therapies (8,9). However, there is striking heterogeneity among human atherosclerotic lesions, and coronary plaques often consist of noncalcified tissue (10,11). Thus, even in coronary vessels without calcified plaques, severe atherosclerosis may be present. Furthermore, noncalcified lesions may also contribute to the development of acute coronary events (10–15). Hence, a more precise assessment of coronary atherosclerotic plaque burden and disease progression by noninvasive imaging tools that can detect and characterize calcified and noncalcified plaques can be expected to add important information.

Recently, the potential of four-slice MDCT has been demonstrated to allow detection and classification of noncalcified coronary plaques (15,16). So far, no data is available on the clinical feasibility and the diagnostic accuracy of MDCT to determine the composition of coronary plaques. Moreover, the prognostic impact of the detection and classification of noncalcified plaques needs to be evaluated and to be compared with coronary calcium scoring or traditional risk factors. We, therefore, initiated a prospective intracoronary-ultrasound-controlled study in a high-risk patient cohort to evaluate whether plaque characterization by 16-slice MDCT is suitable to predict adverse coronary events and to monitor progression of coronary atherosclerosis. As a first step, we report here on the clinical feasibility...
and the diagnostic accuracy of 16-slice CT (operating with 12 slices) to assess different types of coronary plaques.

METHODS

Patients. Forty-six patients (33 male; mean age, 63 ± 7 years) with a distinctive cardiovascular risk profile were included in the study if they fulfilled the following criteria: stable angina pectoris (Canadian Cardiovascular Society class I to III); and presence of at least two of the following risk factors: diabetes mellitus, hypercholesterolemia, hypertension, family history of premature coronary artery disease, and smoking. Exclusion criteria were atrial fibrillation, unstable angina, or unstable hemodynamic conditions. All patients gave written informed consent, and the study protocol was approved by the institutional ethical committee.

Intracoronary ultrasound (ICUS). The protocol of the present study intended that ICUS was specifically performed in all patients to compare ICUS and MDCT-derived plaque composition. Thus, the decision to use ICUS was independent from the stenting procedure. The included patients were not part of any other study. After successful stent implantation, three-dimensional ICUS was performed under fluoroscopic guidance in the target and in nontarget vessels in order to determine plaque composition and plaque burden. We used a Jomed Avanar FX ICUS-catheter (20 MHz, electronic transducer, Jomed Inc., Rancho Cordova, California) that is in accordance with the technical requirements for ICUS systems recommended by the American College of Cardiology (17). The tip of the ICUS catheter was placed in the coronary vessel distal to the stent unless a diameter <2 mm was present. The pullback was performed automatically with 0.5 mm/s (Jomed Track Back II). The complete investigation was digitally stored, and the data were assessed offline using the Jomed Goldvision software package by a cardiologist blinded to the computer tomography results. Because one ICUS pullback contains more than 1,000 frames, our analysis was performed by subsampling intervals of 1 mm (17). Plaque composition was classified according to ICUS criteria as recently reported and proposed by the American College of Cardiology (17).

Calculated plaque areas were defined as plaque tissue containing any tissue with an echogenicity as bright as or brighter than the adventitia causing acoustic shadows.

Hyperechoic plaque areas (soft plaques) were defined by plaque tissue revealing an echogenicity lower than the adventitia. No calcium detectable.

Hyperechoic plaque areas (fibrous plaques) were defined by plaque tissue producing echoes as bright as or brighter than the adventitia. No calcium detectable.

For each section, the maximum vessel diameter, defined as maximum external elastica membrane diameter, and the maximal plaque thickness, defined as plaque plus media thickness, were determined (17).

MDCT protocol. Computed tomography angiography was performed one day after the coronary intervention using a 16-slice MDCT scanner (Sensation 16, Siemens Medical Solutions, Forchheim, Germany) and a previously described protocol (18). In brief, a bolus of 80 cc contrast agent (Solutrust 300, 300 mgI/ml⁻¹, Altana, Konstanz, Germany) was injected intravenously (5 ml/s⁻¹). As soon as the signal density level in the ascending aorta reached a predefined threshold of 100 Hounsfield units (HU), the acquisition of the computed tomography data and the electrocardiogram trace was started. As in a previous study for cardiac applications, only the 12 inner detectors of the 16-detector scanner were used (18). Detector collimation was 12 × 0.75 mm; tube voltage was 120 kV at a current of 450 mAs during 55% of the cardiac cycle (diastole) and a reduction of the current by 80% during the remaining time of the R-R interval leading to an estimated mean effective radiation dose of approximately 4.3 mSv (19). Images were reconstructed with an acquisition time of 210 ms in diastole 350 to 450 ms before the R wave using retrospective electrocardiogram gating. Motion artifacts can only be avoided in the presence of a heart rate <65 beats/min (20); therefore, all patients with heart rates >65 beats/min were pretreated with 50 to 100 mg of oral metoprolol 1 h before the scan. In patients who did not reach a heart rate <65 beats/min, MDCT was not performed.

The computed tomography data set were analyzed by two independent experienced readers using the INSIGHT (Neoimagery Co., City of Industry, California) and the Vessel View (Siemens, Forchheim, Germany) software packages. In a first step, image quality was determined by the investigators on the basis of the presence of motion artefacts and based on the contrast-to-noise ratio, which has been determined by dividing the difference of mean density of coronary lumen and pericardial tissue by the image noise, which was determined as the SD of the density value measured in a region-of-interest in the aortic root (21).

The grading criteria for image quality were as follows: high image quality: no motion artefacts and contrast-to-noise ratio >8; moderate image quality: motion artefacts present, but vessel still evaluable and/or contrast-to-noise ratio between 4 and 8; poor image quality: motion artefacts present that make vessel delineation impossible and/or contrast-to-noise ratio <4. Only vessels with high and moderate image quality were considered for further analysis. Sections containing a stent were not considered for analysis.

Coronary plaques were defined as structures >1 mm²
within and/or adjacent to the coronary artery lumen, which could be clearly distinguished from the vessel lumen and the surrounding pericardial tissue. For plaque analysis and tissue differentiation, the optimal image display setting was chosen on an individual basis, in general at a window between 600 and 900 HU and at a level between 40 and 250 HU. Structures with densities above the adjacent vessel lumen were defined as calcified, and structures with densities below the vessel contrast as noncalcified plaques (15,16).

**Comparison ICUS versus MDCT.** It is difficult to differentiate and separate single coronary plaques in coronary vessels, because the nature of the atherosclerotic process infrequently presents as a strictly focal lesion but instead involves a large segment or the entire coronary vessel, ranging from initial atherosclerotic changes to advanced calcified or noncalcified plaques. We, therefore, divided the coronary tree into 3-mm sections (Fig. 1), and each interval was morphologically classified according to ICUS (hypoechoic, hyperechoic, calcified) and computed tomography criteria (calcified, noncalcified). After blinded and independent assessment of the computed tomography and ICUS data sets, each 3-mm section was compared site by site. To ensure that always the same corresponding coronary sections were compared with ICUS and MDCT, we selected a fiduciary point, such as a side branch for the distal starting reference, as has been proposed for serial ICUS investigations previously (17). The complete distance from the fiduciary point to the coronary ostium was measured using the longitudinal reconstructed ICUS data set and multiplanar reconstructions of the computed tomography data set to ensure that distance measurements were the same with both methods. Starting from the distal reference point, the coronary vessel was analyzed in 3-mm intervals, and the morphology of each section was directly compared with both methods. A similar approach has been shown to be very accurate in previous studies (22,23).

**MDCT density measurements.** For each 3-mm coronary section, three axial slices with a thickness of 1 mm were analyzed. Each slice was then divided into a raster with boxes of 1 mm². In each box that contained plaque tissue,
five density measurements were randomly performed. The mean density for the entire plaque area within a 3-mm segment was calculated by averaging the density measurements obtained from the raster boxes within the plaque. In order to avoid oversampling of certain tissue types in mixed plaques, density measurements for calcified plaques were only performed in hyperdense parts (raster boxes) of the plaques and measurements for noncalcified plaques only in hypodense tissue. Only density values determined in plaque areas that corresponded to plaques detected by ICUS were considered for retrospective calculation of density values of different plaque types.

**Statistical analyses.** All statistical calculations were performed using Microsoft Windows Excel (version 9.0) (Microsoft Co., Redmond, Washington) and SPSS (version 10.0) (SPSS Inc., Chicago, Illinois) installed on a desktop computer. For proportions (sensitivity, specificity), the 95% confidence interval was determined. To compare the mean density values of different plaque types, the nonparametric Kruskal-Wallis test was employed. To identify potential within-patient effects, a repeated measures analysis of variance was performed controlled for interaction of the factors patient group (group 1: patients in whom one vessel was investigated by ICUS; group 2: two vessels investigated; group 3: three vessels investigated) and plaque type (hypodense, hyperechoic, calcified). All calculations were considered to be significant in the presence of a p value <0.05.

**RESULTS**

Intracoronary ultrasound was performed only in one vessel (target vessel) in 18 of 46 patients. In 25 of 46 patients, in addition to the target artery, a second coronary vessel, and in three of 46 patients, three major coronary arteries were assessed by ICUS.

Of 46 included patients (mean age: 63 ± 8 years) who initially underwent coronary catheterization and ICUS, nine patients were not investigated by contrast-enhanced MDCT because their heart rate could not be reduced below 65 beats/min (n = 7) or they revealed serum creatinine levels that exceeded the maximal limit of 1.5 mg/dL. Of the 37 patients who were investigated by MDCT, 21 were investigated in the ICUS group (group 1), 15 in the group 2, and one in group 3.

**Table 1.** Sensitivity of MDCT in the Detection of Different Coronary Plaques in Evaluable Vessels (58 of 68) and Specificity to Exclude Coronary Lesions

<table>
<thead>
<tr>
<th>Plaque Type</th>
<th>Soft Sensitivity</th>
<th>Fibrous Sensitivity</th>
<th>Calcified Sensitivity</th>
<th>Total Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCA</td>
<td>(12/16) 75%</td>
<td>(27/34) 79%</td>
<td>(49/49) 100%</td>
<td>94/102 92%</td>
</tr>
<tr>
<td>LAD</td>
<td>(44/54) 81%</td>
<td>(47/62) 76%</td>
<td>(76/83) 92%</td>
<td>294/315 93%</td>
</tr>
<tr>
<td>RCX</td>
<td>(6/10) 60%</td>
<td>(13/16) 82%</td>
<td>(25/26) 96%</td>
<td>96/108 89%</td>
</tr>
<tr>
<td>Total</td>
<td>(62/80) 78%</td>
<td>(87/112) 78%</td>
<td>(150/158) 95%</td>
<td>484/525 92%</td>
</tr>
</tbody>
</table>

Values are (n), %, (95% confidence interval).

LAD = left anterior descending coronary artery; MDCT = multidetector computer tomography; RCA = right coronary artery; RCX = right circumflex artery.

**Table 2.** Quantitative Characteristics of MDCT Detected Versus Nondetected Coronary Plaques

<table>
<thead>
<tr>
<th></th>
<th>Detected</th>
<th>Not Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque thickness</td>
<td>1.5 ± 0.3 mm</td>
<td>0.9 ± 0.3 mm</td>
</tr>
<tr>
<td>Vessel size (EEM CSA)</td>
<td>4.5 ± 1.2 mm</td>
<td>3.6 ± 1.1 mm</td>
</tr>
<tr>
<td>% Plaque cross-sectional area</td>
<td>42 ± 16%</td>
<td>22 ± 5%</td>
</tr>
</tbody>
</table>

p <0.05 for all categories.

EEM CSA = external elastic membrane cross-sectional area; MDCT = multidetector computer tomography.

**Figure 2.** Computed tomography (CT) density values for hypoechoic, hyperechoic, and calcified plaques. Each box describes the distribution of density values within one SD. The whiskers above and below each box are describing the range between the lowest and highest observed density value. The differences of the mean CT density values between hypoechoic, hyperechoic, and calcified plaques were significant with a p value <0.02.
levels >1.5 mg/dl (n = 2). In the remaining 37 patients (mean heart rate 59 ± 3 beats/min), 68 coronary vessels (right coronary artery [RCA], n = 10; left anterior descending artery [LAD], n = 35; right circumflex artery [RCX], n = 23) were investigated by ICUS. The mean length of the investigated vessels was 52 ± 8 mm. Of 68 vessels in 37 patients, 45 of 68, 13 of 68, and 10 of 68 vessels were assessable with high-, moderate-, and poor-image quality, respectively. Poor image quality was due to motion artifacts in five vessels (RCA, n = 2; RCX, n = 2; LAD, n = 1) and in five cases due to image noise and poor contrast (RCX, n = 4; LAD, n = 1). For plaque analysis, only vessels providing good or moderate computed tomography image quality were considered.

The accuracy determined for MDCT in the detection of different plaque types is given in Table 1. Coronary plaques that were not detected on MDCT had a smaller maximum plaque thickness (0.9 mm ± 0.3 vs. 1.5 ± 0.3, p < 0.001) and were located in coronary sections with a smaller external elastic membrane diameter (3.6 mm ± 1.1 vs. 4.5 ± 1.2, p < 0.02) (Table 2). A total of 41 sections were incorrectly classified as containing plaques; 36 of these sections were misclassified as containing noncalcified plaque. Twenty of these sections were located adjacent to a severely calcified section or a stent, and nine were located in vessels providing only moderate image quality. The mean computed tomography density values for hypoechoic, hyperechoic, and calcified plaques were 49 HU ± 22 (range, 14 to 82 HU), 91 HU ± 22 (range, 34 to 125 HU), and 391 HU ± 156 (range, 162 to 820 HU), respectively (p < 0.02; Fig. 2).

**DISCUSSION**

An accurate assessment of coronary plaque composition and plaque burden remains challenging even by using invasive methods (17,24). The modality of choice so far is ICUS...
(17). A number of investigations indicate that plaque composition, plaque burden, and progression of coronary atherosclerosis may be important factors influencing the risk of adverse coronary events (10–15, 24–26). Thus, noninvasive imaging tools that allow reliable determination of plaque burden and plaque composition may be important for risk stratification and monitoring of coronary atherosclerosis. In the present study, we evaluated the clinical feasibility and the diagnostic accuracy of recently developed 16-slice MDCT (operating with 12 detectors) with improved spatial and temporal resolution to detect and characterize coronary plaques. A potential strength of the present study is the fact that ICUS was used to assess plaque burden for large segments (52 mm) of up to three coronary arteries in a set of consecutive patients. Therefore, we were able to define the potential and the current limitations of MDCT concerning coronary plaque detection.

The results of our study suggest that, in a clinical setting, MDCT is feasible to assess coronary plaques with considerable high accuracy (Fig. 3). We observed a strong correlation between computed tomography density measurements within the plaques and the lesion echogenicity on ICUS.

Feasibility of MDCT. Sufficient heart rate reduction by a beta-blocker was not achieved in seven of 46 patients, and in another two patients administration of contrast agent had to be avoided due to significantly elevated serum creatinine levels. Multidetector computer tomography imaging was, therefore, suitable for 80% of consecutive patients with a distinctive risk profile who were scheduled for MDCT one day after coronary stenting. In these patients, diagnostic computed tomography image quality was not obtained in 15% of the coronary vessels, predominantly due to motion artifacts. This finding is concordant with a previous contrast-enhanced MDCT study using a 16-slice scanner (27).

Accuracy of plaque detection. In the case that adequate image quality was achieved, MDCT was able to identify calcified coronary lesions with high accuracy in all coronary sections. The visualization of noncalcified lesions, however, was limited by plaque and vessel size. Smaller plaques predominantly located in smaller coronary sections were not reliably identified by MDCT.

Plaque composition. We could demonstrate that lesion echogenicity of ICUS correlates well with computed tomography density measurements in coronary plaques. Mean computed tomography values for hypoechoic, hyperechoic, and calcified lesions were statistically different. The overlap we observed in the density measurements of different plaque types appears to be inherent to atherosclerotic plaque development, as they, in general, contain different plaque components ranging from necrotic, lipid-rich, to collagenous fibrous tissue. Our measurements are in a similar range to those described in a prior coronary four-slice computed tomography study (16) and indicate that the computed tomography attenuation reflects the major plaque composition. This appears of special interest, as plaques with high-lipid content (i.e., plaques with a large lipid core) that reveal low echogenicity on ICUS might be identified on the basis of their low computed tomography attenuation. However, the prognostic impact of density based characterization of noncalcified plaques needs to be evaluated.

Study limitations. Although this is a multivessel ICUS study, we did not assess all three major coronary vessels by ICUS in the majority of patients. In agreement with a recent study (27), we were able to visualize all three major coronary arteries (RCA, LAD, RCX) by MDCT in 31 of 37 patients with diagnostic image quality. The accuracy data, however, certainly reflect only vessels that were analyzed by ICUS and MDCT. As a consequence, the results for plaque detection in the RCA and RCX are based on smaller sample sizes than for the LAD, and the overall result might be affected if more RCA and RCX were included. Furthermore, our study population consisted of preselected symptomatic patients with a high prevalence of coronary plaques, and accuracy for plaque detection might be lower in a set of asymptomatic patients with a lower prevalence for atherosclerotic plaques. However, it is difficult to justify invasive investigations like ICUS in asymptomatic patients.

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