

# Detection of Calcified and Noncalcified Coronary Atherosclerotic Plaque by Contrast-Enhanced, Submillimeter Multidetector Spiral Computed Tomography A Segment-Based Comparison With Intravascular Ultrasound

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**Background**—We investigated the ability of multidetector spiral computed tomography (MDCT) to detect atherosclerotic plaque in nonstenotic coronary arteries.

**Methods and Results**—In 22 patients without significant coronary stenoses, contrast-enhanced MDCT (0.75-mm collimation, 420-ms rotation) and intravascular ultrasound (IVUS) of one coronary artery were performed. A total of 83 coronary segments were imaged by IVUS (left main, 19; left anterior descending, 51; left circumflex, 4; right coronary, 9). MDCT data sets were evaluated for the presence and volume of plaque in the coronary artery segments. Results were compared with IVUS in a blinded fashion. For the detection of segments with any plaque, MDCT had a sensitivity of 82% (41 of 50) and specificity of 88% (29 of 33). For calcified plaque, sensitivity was 94% (33 of 36) and specificity 94% (45 of 47). Coronary segments containing noncalcified plaque were detected with a sensitivity of 78% (35 of 45) and specificity of 87% (33 of 38), but presence of exclusively noncalcified plaque was detected with only 53% sensitivity (8 of 15). If analysis was limited to the 41 proximal segments (segments 1, 5, 6, and 11 according to American Heart Association classification), sensitivity and specificity were 92% and 88% for any plaque, 95% and 91% for calcified plaque, and 91% and 89% for noncalcified plaque. MDCT substantially underestimated plaque volume per segment as compared with IVUS ( $24 \pm 35 \text{ mm}^3$  versus  $43 \pm 60 \text{ mm}^3$ ,  $P < 0.001$ ).

**Conclusions**—The results indicate the potential of MDCT to detect coronary atherosclerotic plaque in patients without significant coronary stenoses. However, further improvements in image quality will be necessary to achieve reliable assessment, especially of noncalcified plaque throughout the coronary tree. (*Circulation*. 2004;109:14-17.)

**Key Words:** tomography ■ atherosclerosis ■ coronary disease

Direct, noninvasive imaging of coronary atherosclerotic plaque might potentially improve risk stratification for the occurrence of coronary events in selected asymptomatic individuals.<sup>1,2</sup> Initial reports of the ability of contrast-enhanced multidetector spiral computed tomography (MDCT) to visualize noncalcified coronary atherosclerotic plaque have thus received widespread attention.<sup>3-8</sup> However, the ability of MDCT to detect and quantify coronary atherosclerotic plaque in vivo has never been systematically validated. We therefore evaluated the ability of MDCT with submillimeter slice collimation to detect and quantify coronary atherosclerotic plaque in patients without significant coronary artery stenoses in comparison with intravascular ultrasound (IVUS).

## Methods

### Patients

In 22 patients (14 male, 8 female; mean age, 58 years), MDCT was performed as part of research protocols that enrolled consecutive subjects who were scheduled for invasive coronary angiography for clinical reasons. In all patients, coronary artery stenoses ( $\geq 50\%$  diameter reduction) had been ruled out by coronary angiography, and an IVUS study of the largest coronary vessel was performed. Patients with arrhythmias, contraindications to iodinated contrast agent, and unstable clinical presentation were excluded from enrollment. No patients were excluded for reduced MDCT image quality. The institutional review boards approved the research protocols, and all patients gave informed consent.

### Intravascular Ultrasound

IVUS was performed in one coronary artery per patient (40-MHz IVUS catheter, Atlantis, Boston Scientific; motorized pullback at

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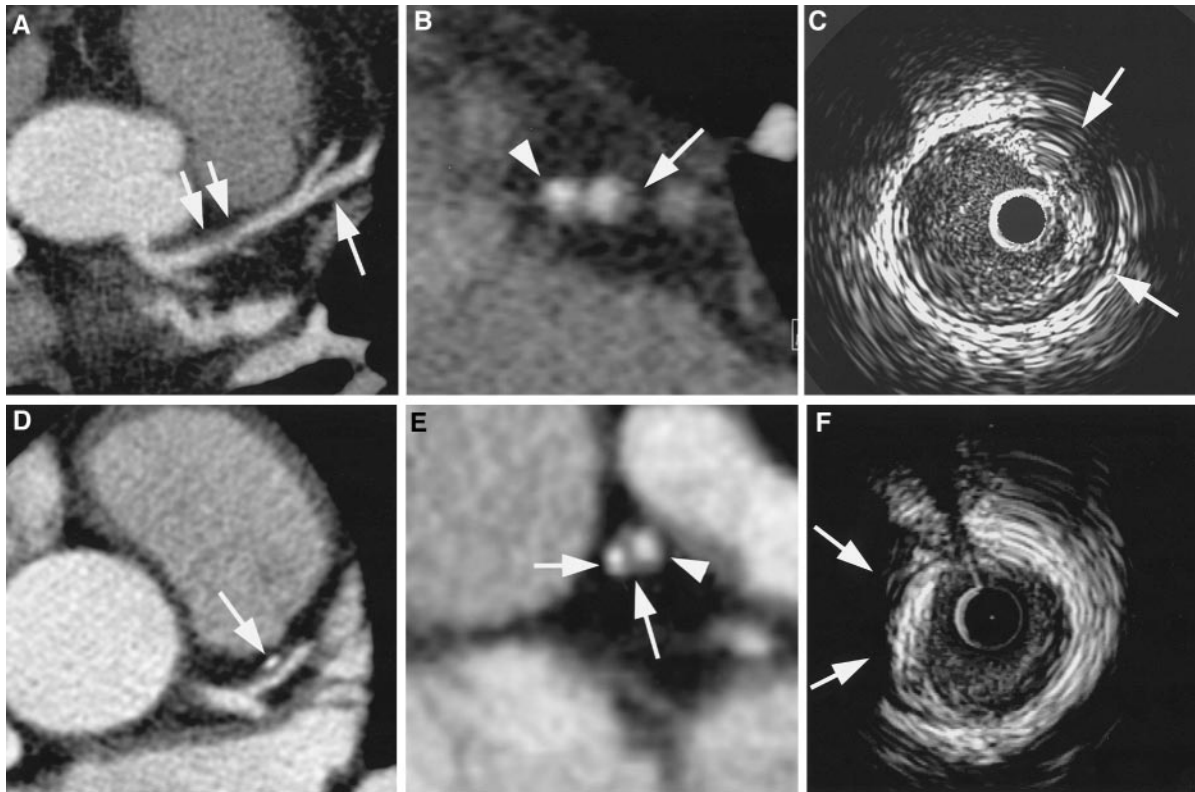
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**Figure 1.** A through C, Patient with noncalcified plaque in segments 6 and 7 of left anterior descending coronary artery (LAD). A, Axial MDCT image showing noncalcified plaque in segments 6 (proximal LAD; small arrows) and 7 (LAD distal to diagonal branch; large arrow). B, Multiplanar reconstructed MDCT image showing cross section of LAD segment 7 with plaque (arrow). Arrowhead indicates diagonal branch. C, IVUS image showing noncalcified plaque in segment 7 (arrows). D through F, Patient with calcified and noncalcified plaque components in proximal LAD (segment 6). D, Axial MDCT image showing partly calcified plaque in proximal LAD (arrow). E, Multiplanar reconstructed MDCT image showing cross section of proximal LAD with plaque (large arrow), including calcification (small arrow). Arrowhead indicates contrast-enhanced lumen. F, IVUS image showing partly calcified plaque in proximal LAD (arrows).

0.5 mm/s). The right coronary artery (segments 1, 2, and 3 according to the American Heart Association classification<sup>9</sup>) was imaged in 3 patients; the left main and left anterior descending coronary artery (segments 5, 6, 7, and 8) in 17 patients; and the left main, proximal left circumflex, and obtuse marginal branch (segments 5, 11, and 12) in 2 patients. Two independent investigators blinded to MDCT results analyzed IVUS data off-line. Coronary segments were identified by side branches, and the presence of calcified and noncalcified plaque was determined for every segment. Plaque area (external elastic membrane cross-sectional area minus luminal area) was measured by manual tracing in 1-mm increments to determine the plaque volume for each coronary segment. In distal segments (3, 8, and 12), analysis was limited to the proximal 20 mm.

### Multidetector Spiral Computed Tomography

Patients with a heart rate  $>60$  bpm received 50 mg atenolol 1 hour before the MDCT scan (Sensation 16, Siemens Medical Solutions). The mean heart rate during MDCT was  $59 \pm 6$  bpm (range, 53 to 69). MDCT data were acquired using  $12 \times 0.75$ -mm collimation, 420-ms gantry rotation, 2.8-mm table feed per rotation, 400 mAs with ECG modulation,<sup>10</sup> and tube voltage of 120 kV, with an estimated average radiation dose of 4.3 mSv.<sup>10</sup> Contrast agent (80 mL) (350 mg iodine/mL) was injected intravenously (4 mL/s). Transaxial images (slice thickness 1.0 mm, increment 0.5 mm) were reconstructed using an ECG-gated half-scan reconstruction algorithm (temporal resolution 210 ms) and kernel B35f. The position of the reconstruction window within the cardiac cycle was individually optimized to minimize motion artifacts.<sup>10</sup>

All 83 coronary segments covered by IVUS were included in the analysis. Two investigators, blinded to IVUS results, independently

evaluated the MDCT data sets using axial and multiplanar reformatted images. Contrast enhancement in each coronary segment was measured by placing a 4-mm<sup>2</sup> region of interest in the vessel lumen. Data sets were visually evaluated for the presence of atherosclerotic plaque. Any discernible structure that could be assigned to the coronary artery wall, had a computed tomography density below the contrast-enhanced coronary lumen but above the surrounding connective tissue, and could be identified in at least 2 independent planes was defined as noncalcified coronary atherosclerotic plaque. To maximize sensitivity for calcium detection, any structure with a density of 130 Hounsfield units (HU) or more that could be visualized separately from the contrast-enhanced coronary lumen (either because it was "embedded" within noncalcified plaque or because its density was above the contrast-enhanced lumen), could be assigned to the coronary artery wall, and could be identified in at least 2 independent planes was defined as calcified atherosclerotic plaque (see Figure 1). For every coronary artery segment, identified via side branches, the investigators decided whether calcified plaque, noncalcified plaque, both, or neither was present in MDCT. In case of disagreement, agreement was reached in a joint reading. To measure plaque volume in each coronary segment, contiguous 1-mm-thick cross-sectional images of the coronary arteries were rendered and displayed with a fixed setting (700-HU window, 200-HU level). Plaque areas were manually traced and volume calculated by multiplying area and slice increment. In distal segments (3, 8, and 12), analysis of plaque volume was limited to the proximal 20 mm.

### Statistical Analysis

Sensitivity and specificity of MDCT for detection of segments with any plaque, calcified plaque, or noncalcified plaque were deter-

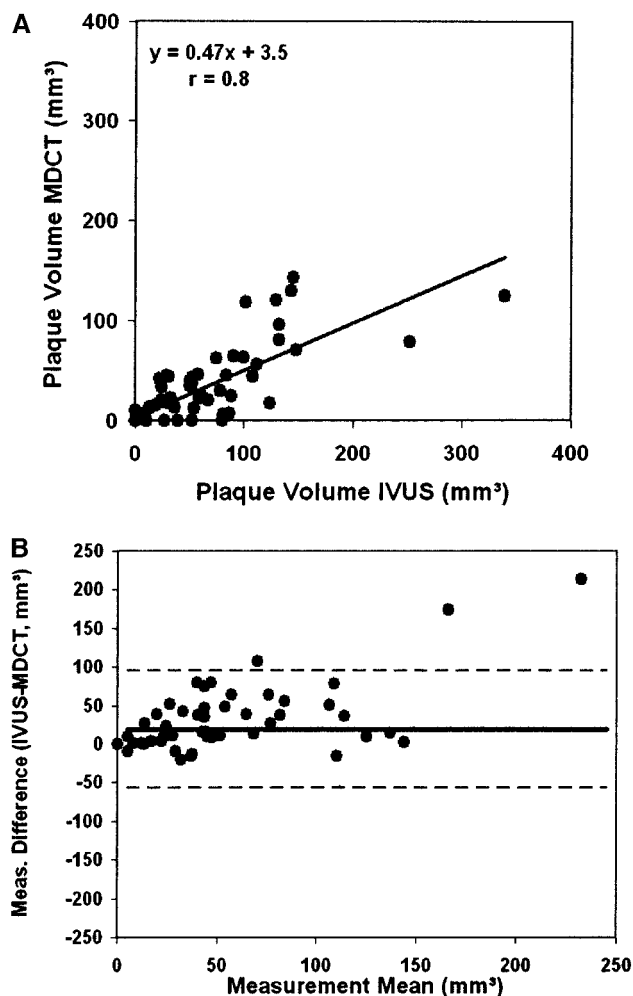
mined. Cohen's  $\kappa$  was calculated to determine interobserver agreement. Plaque volumes in MDCT and IVUS were compared with Pearson's correlation, Bland-Altman analysis, and Wilcoxon test. Maximum IVUS plaque areas within coronary segments with true-positive and false-negative MDCT results were compared by using Mann-Whitney  $U$  test.

### Results

IVUS showed the presence of coronary atherosclerotic plaque in 50 of 83 coronary artery segments (calcified and noncalcified plaque in 31 segments, exclusively calcific plaque in 4, and exclusively noncalcified plaque in 15). In MDCT, mean contrast enhancement within the coronary lumen was  $343 \pm 55$  HU in proximal segments (1, 5, 6, and 11),  $324 \pm 52$  HU in mid segments (2, 7, and 12), and  $278 \pm 77$  HU in distal segments (3 and 8). MDCT correctly detected 41 of 50 segments with any atherosclerotic plaque (sensitivity 82%), and the presence of any plaque was correctly ruled out in 29 of 33 segments (specificity 86%, positive predictive value 91%, negative predictive value 76%, and intermodality  $\kappa$  0.68). For segments with calcified plaque, sensitivity was 94% (33 of 35), and specificity was 94% (45 of 47). Segments containing noncalcified plaque, alone or in combination with calcified plaque, were detected with a sensitivity of 78% (35 of 45) and specificity of 87% (33 of 38). Of 15 segments with exclusively noncalcified plaque, 8 (53%) were correctly detected by MDCT. If analysis was limited to the 41 proximal segments (American Heart Association segments 1, 5, 6, and 11), sensitivity and specificity were 92% (23 of 25) and 88% (14 of 16) for the detection of any plaque, 95% (18 of 19) and 91% (20 of 22) for calcified plaque, and 91% (20 of 22) and 89% (17 of 19), respectively, for segments with calcified and noncalcified plaque. Correlation of plaque volumes measured in MDCT and IVUS was relatively close ( $r=0.8$ ,  $P<0.001$ ), but MDCT systematically and significantly underestimated plaque volume per segment ( $24 \pm 35$  mm<sup>3</sup> versus  $43 \pm 60$  mm<sup>3</sup>,  $P<0.001$ ; see Figure 2). Mean plaque volume and maximum plaque area measured by IVUS within the 9 segments with a false-negative MDCT result were  $47 \pm 11$  mm<sup>3</sup> and  $8 \pm 3$  mm<sup>2</sup>, as compared with  $76 \pm 10$  mm<sup>3</sup> and  $11 \pm 4$  mm<sup>2</sup> for the 41 segments with a true-positive MDCT result ( $P=0.2$  and  $P=0.08$ ). Interobserver agreement about the presence of any plaque was achieved in 73 of 83 segments (88%) by MDCT (Cohen's  $\kappa$  0.65) and in 80 of 83 segments (96%) by IVUS (Cohen's  $\kappa$  0.91).

### Discussion

Several previous studies have documented the ability of MDCT to visualize coronary atherosclerotic plaque in vivo.<sup>3-8</sup> Possible applications in risk stratification of asymptomatic individuals have been discussed<sup>2</sup> but require close scrutiny of the actual ability of MDCT to detect nonstenotic coronary plaque. In comparison with IVUS, we found a sensitivity of 82% to detect coronary artery segments containing atherosclerotic plaque in patients without significant coronary artery stenoses. However, segments containing exclusively noncalcified plaque were identified with a sensitivity of only 53%, and MDCT substantially underestimated plaque burden. Expectedly, accuracy for plaque detection was



**Figure 2.** A, Plaque volumes measured by MDCT and IVUS in 83 coronary segments show a significant correlation ( $r=0.8$ ,  $P<0.001$ ), but MDCT systematically underestimates plaque volumes. B, Bland-Altman analysis. Solid line indicates systematic error (mean difference, 19 mm<sup>3</sup>); hatched lines, limits of agreement (95% confidence interval,  $-55$  to 93 mm<sup>3</sup>).

lower for smaller plaques and in distal versus proximal vessel segments.

### Limitations

Even though we limited our analysis to patients without significant coronary artery stenoses to reduce bias introduced by an artificially high prevalence of coronary plaque, patients were somewhat preselected because they were scheduled for invasive coronary angiography, and thus, a higher prevalence of risk factors and, consequently, coronary plaque than would be found in the general population must be assumed. The achieved contrast enhancement within the coronary lumen may not have been optimal for plaque detection and quantification.<sup>11</sup> MDCT analysis was based on visual assessment, and the accuracy for calcium detection may have been artificially low because the threshold of 130 HU we used may not have been optimal and no nonenhanced scan was performed. Smaller calcified plaques with a density equal to the contrast-enhanced lumen may thus have been missed in

MDCT. However, calcified plaques were missed only in 2 segments.

In summary, the present study provides the first assessment of the accuracy of MDCT in detecting and quantifying noncalcified coronary atherosclerotic plaque in vivo. It indicates the potential of MDCT to visualize such plaques but also demonstrates that in spite of the increased spatial and temporal resolution of the latest scanner generation, reliable detection and quantification of noncalcified plaque throughout the coronary tree are currently limited.

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