Noninvasive assessment of coronary artery stenoses by multidetector-row spiral computed tomography: comparison with conventional angiography


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Abstract. – Background. Coronary artery disease (CAD) is the most common cause of hospitalization and mortality in many industrialized countries.

We analysed the diagnostic accuracy of multi-detector row spiral computed tomography (MDCT) in determining mid- to high-grade coronary artery stenoses (> 50%).

Methods: Sixty-nine patients with suspected CAD were referred to MDCT coronary angiography. Patients with a heart rate above 60 bpm received 20-40 mg propranol before the scan. The left main (LM), the left anterior descending artery (LAD), the first diagonal branch (D1), the right coronary artery (RCA) and the proximal tract of the circumflex artery (LCX) were independently evaluated by two blinded observers and screened for >50% stenoses. The mean values of MDCT coronary narrowings assessed by two observers were compared to quantitative coronary angiography.

Results. MDCT correctly detected 95 of 123 coronary lesions (sensitivity 77.2%) and absence of stenoses was correctly identified in 388 of 426 segments (specificity 91%). The sensitivity for the LM, LAD, RCA and the proximal tract of LCX was 100%, 86.5%, 69.8% and 80% respectively. Classification of patients as having 1- vessel, 2-vessels, 3-vessels or left main disease was accurate in 75.4% (46/61) of patients.

Conclusions. MDCT technology, combined with heart rate control, allows reliable noninvasive detection of hemodynamically significant CAD.

Key words: Multidetector computed tomography, Noninvasive coronary angiography, Noninvasive imaging, Coronary artery calcium, Plaque imaging, Atherosclerosis.

Introdution

Coronary artery disease (CAD) is the most common cause of hospitalization and mortality in many industrialized countries1,2. Conventional coronary angiography (CA) is the current gold standard method to study epicardial coronary arteries and is increasingly being combined with interventional therapeutic procedures such as balloon angioplasty and stent implantation. Although CA has become a relatively safe procedure with low incidence of complications, the inconvenience for the patient as well as the economic burden have got to find an alternative, non-invasive method to visualize coronary arteries and assess intraluminal narrowings3. Therefore, noninvasive imaging modalities as Magnetic Resonance Imaging (MRI) and Electron-beam Computed Tomography (EBCT) were developed to assess calcium quantification, coronary artery morphology and flow4-6. In the last years, multidetector-row computed tomography (MDCT) scanners with simultaneous acquisition of multiple slices in less than half-second gantry rotation time have become available7,8. Multiple slice acquisition by these scanners has considerably improved cardiac application, such as noninvasive MDCT coronary angiography9,10. This study evaluates the diagnostic accuracy of MDCT angiography in determining mid- to high-grade coronary artery stenoses (>50% lumen diameter narrowing at angiography) compared with CA.
Materials and Methods

Study population
Sixty-nine patients (42 male, 27 female, mean age 60 years) who were referred for angiographic evaluation of suspected CAD were enrolled in this study. Criteria for exclusion included previous allergic reaction to iodine contrast media, renal insufficiency (serum creatinine >2 mg/dl), unstable hemodynamic situation, cardiac arrhythmias, previous bypass surgery or stent implantation, increased heart rate (>65 bpm), respiratory impairment or severe heart failure. The average interval between MDCT angiography and the catheterization procedure was 24-72 hours. Informed consent was obtained from all patients, according to institutional guidelines.

All patients received 20-40 mg propranol orally 60-90 minutes before the scan, if the heart rate was more than 60 bpm. No subject with severe obstructive pulmonary disease was present in the group we studied.

Scan Protocol and Image Reconstruction
All subjects were studied using a 4-row MDCT scanner (Somatom Volume Zoom, Siemens Medical System, Erlangen, Germany), with 0.5 sec gantry rotation time.

Subjects were positioned supine and 3 ECG electrodes were placed on the anterior chest wall in order to obtain an ECG triggering with MDCT scan. An 18-gauge i.v. cannula was placed into a superficial vein positioned in the antecubital fossa, or forearm or dorsum of the hand. Contrast administration was performed using two power injectors (EnVision CT, Medrad, Indianola, PA, USA) connected by a T tube; the first injector was filled with the contrast agent and the second injector with saline. A one-way valve was attached to the syringe with saline solution to prevent contrast agent reflux.

After the initial topogram, a preliminary unenhanced scan was performed in order to detect and quantify coronary calcium, covering a volume from the tracheal carina to the base of the heart.

Precontrast acquisition was performed using the following parameters: 4 x 2.5 mm collimation, with 3 mm section thickness and a reconstruction interval of 0.5 mm, 120 kV, 300 mAs. After acquisition, data sets were reconstructed at 60-70% of the R-R interval, and calcium scoring was calculated from the series with the fewest motion artefacts using the Calcium Volumetric Score (CVS) method.

The post-contrast acquisition was performed covering the distance from the tracheal carina to the diaphragmal face of the heart with the following parameters: 4 x 1 mm collimation, with a slice thickness 1.25 mm and a slice interval of 0.5 mm, 120 kV, 400 mAs. In all subjects, a standard iodine dose of 140 ml of high concentration contrast agent (Iomeron 400, Bracco, Italy) was administered with a flow rate of 4 ml/sec and delay based on a test bolus protocol.

After MDCT examination, the initial raw data set of images was reconstructed at a temporal window included between 40-70% of R-R interval with an increment of 10% and only the data set with the fewest motion and beam hardening artefacts was selected for further evaluation by an experienced radiologist.

All the reconstructed data set of images were sent to a workstation using a dedicated cardiac software package with volume rendering, maximum intensity projection (MIP), and multiplanar (MPR) capabilities and enabling the selective visualization of each coronary vessel in the 3 spatial dimensions (Vitrea 3.2, Vital Images, Minneapolis).

Two blinded reviewers independently evaluated the MDCT scans by assessment of the axial slices and with case-dependent application of post-processing tools, such as multiplanar reconstruction, maximum intensity projection, volume rendering or virtual angioscopy. Because stenoses in tiny vessels are hard to evaluate by MDCT, the assessment was restricted to coronary arteries that tend to have a lumen greater than 1,5 mm in diameter (segments 1-3, 5-9, 11 according to the American Heart Association coronary segment model)¹¹.

The investigators rated the left main coronary artery (LM, segment 5), the left anterior descending artery (LAD, segments 6, 7, 8), the first diagonal branch (D1, segment 9) the proximal tract of the left circumflex artery (LCX, segment 11) and the right coronary artery (RCA, segments 1, 2, 3) as having significant narrowing of the lumen (≥ 50% diameter reduction).
In the remaining 61 patients, 11 were on long-term β-blocker medication; 44 had a heart rate above 60 bpm and received 20-40 mg propranol orally; patients with heart rate ≤ 60 bpm (6 cases) did not receive premedication.

MDCT was performed without complications in all patients. The average scan time was 38 ± 4 seconds and the entire examination was generally completed within 20 minutes. Depending on the data quality and complexity of the coronary status, post processing and assessment required 21 ± 5 minutes.

On the basis of invasive coronary angiography, 46 patients (75.4%) had significant stenoses (1-vessel disease 15 patients; 2-vessels disease 18 patients; 3-vessels disease 10 patients; left main 3 patients), while 15 subjects (24.6%) had not significant CAD. Overall 46 of these 61 patients were correctly classified by MDCT (sensitivity 75.4%). In 2 cases, MDCT failed to demonstrate two significant stenoses of the middle LAD and of the proximal RCA respectively. In another 2 patients, 2 significant stenoses were found by MDCT but could not be confirmed by CA. Thirteen patients did not have significant CAD both on MDCT and CA.

Overall 123 stenoses >50% diameter reduction were present, and 95 of these lesions were correctly detected by MDCT (sensitivity 77.2%). In 388 of 426 segments, significant CAD could be correctly excluded by MDCT angiography, yielding a specificity of 91%. The corresponding positive and negative predictive values were 71.4% and 93.3%.

In the analysis of separate vessels, the sensitivity to detect significant stenoses in the LM and in the LAD (100% and 86.5%) was better than in the RCA (69.8%) (Table I).

Furthermore, agreement between the data obtained by means of the two technique was assessed by the method of Bland and Altman. A plot of the difference between the observers evaluation against their mean may be more informative.

The Pearson correlation coefficient and linear regression analysis were used to compare all MDCT detected coronary stenoses versus CA and by analysing separately the segments of LAD, LCX, RCA and proximal tracts of the three coronary arteries.

The interobserver variability was evaluated by the method described by Bland and Altman. A plot of the difference between the observers evaluation against their mean may be more informative.

A p value less than 0.01 was considered to be statistically significant.

Results Eight patients were excluded from the study because of their persistently high heart rate (> 65 bpm) after β-blocker administration.

In the remaining 61 patients, 11 were on long-term β-blocker medication; 44 had a heart rate above 60 bpm and received 20-40 mg propranol orally; patients with heart rate ≤ 60 bpm (6 cases) did not receive premedication.

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The following parameters indicated interobserver variability in evaluating coronary stenoses by MDCT: r = 0.90; mean difference = 0.26, standard deviation = 17.5 with standard error of estimates = 0.30.

The Pearson correlation coefficient between the coronary narrowing detected in all segments calculated by using the two technique was high: r = 0.74, p <0.01. The linear

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**X-ray Coronary Angiography**

CA was used as the gold standard method. Left and right CA was performed in multiple views by using the transfemoral Judkins approach 24-72 hours after MDCT. At each study angiographic images were obtained in at least two orthogonal views, free of vessel overlapping and foreshortening, for computed assisted quantitative coronary angiography (QCA) analysis. All angiograms were evaluated by a single blinded reader. A luminal narrowing ≥50% was considered significant.

**Statistical Analysis**

The diagnostic accuracy of MDCT to detect significant stenoses was evaluated by considering QCA as the standard reference. All vessels, regardless of the image quality, were included: none was excluded due to technical limitations. Continuous variables were expressed as means ± SD. The diagnostic accuracy was expressed as sensitivity, specificity, negative predictive value and positive predictive value. The descriptive statistics were stratified according to coronary vessels and segments. The mean values of MDCT coronary narrowing assessed by two different observers were considered for analysis. The interobserver variability was evaluated by the method described by Bland and Altman. A plot of the difference between the observers evaluation against their mean may be more informative.

The Pearson correlation coefficient and linear regression analysis were used to compare all MDCT detected coronary stenoses versus CA and by analysing separately the segments of LAD, LCX, RCA and proximal tracts of the three coronary arteries.

Furthermore, agreement between the data obtained by means of the two technique was assessed by the method of Bland and Altman. The plot of difference against mean also allows us to investigate any possible relationship between the measurement error and the true value.

A p value less than 0.01 was considered to be statistically significant.

**Results**

Eight patients were excluded from the study because of their persistently high heart rate (> 65 bpm) after β-blocker administration.
The regression equation was calculated as $y = mx + b$, by considering MDCT the dependent variable, and showed an intercept value of 18.5 and a slope value of 0.7 (Figure 1). The mean difference was $-0.28$, indicating that MDCT values underestimate the degree of coronary narrowing. The standard error of estimates was 0.27. The 95% confidence interval for the bias was $-23.32$ to $22.76$. The 95% confidence interval for upper and lower limits of agreement was $21.84$ to $23.68$ and $-24.20$ to $-22.40$, respectively. The limits of agreement observed are small enough for us to be confident (Figure 2).

By considering the estimation of proximal lesions we obtained a high correlation value: $r = 0.84$ ($p < 0.01$). The intercept value was 8.7 and slope value was 0.86. Despite this, MDCT tends to give a slight underestimation of degree of coronary stenoses. We calculated a mean difference of $-0.96$ with a standard error of estimate of 0.37. The 95% confidence interval for the bias was $-18.11$ to $16.19$. The 95% confidence interval for upper and lower limits of agreement was $14.95$ to $17.43$ and $-19.35$ to $-16.84$, respectively.

A correlation coefficient of 0.74 ($p < 0.01$) was calculated by comparing the degree of stenosis in the segments of LAD. An intercept value of 18.0 and a slope value of 0.72 were determined.

An overlapping in estimating the degree of coronary lesions by the two methods was observed in LAD segments. We calculated a mean difference of 0.06 and a standard error of estimates of 0.37. The 95% confidence interval for the bias was $21.23$ to $-21.11$. The 95% confidence interval for upper and lower limits of agreement was $19.98$ to $22.48$ and $-22.36$ to $-19.86$, respectively.

A more evident underestimation of degree of coronary stenoses by MDCT was observed in evaluating LCX segments. A mean difference of $-2.9$ and a standard error of 0.73 were measured. A correlation coefficient of 0.65 ($p < 0.05$), an intercept value of 19.5 and a slope value of 0.69 were calculated.

Despite that the limits of agreement ($-23.4$ to $17.6$) were confident (95% CI for upper and lower limits were $15.05$ to $20.15$ and $-25.95$ to $20.85$, respectively), the evaluation of degree of stenosis in RCA segments were similar by two methods. We calculated a mean difference of 0.08 with a standard error of estimates of 0.46. The correlation coefficient was 0.75 with an intercept value of 19.5 and a slope value of 0.69.

The limits of agreement were $-25.98$ to $26.14$. The 95% confidence intervals for upper and lower limits were $24.5$ to $27.71$ and $-27.55$ to $-24.41$, respectively. The limits of agreement measured are confident.

### Table I. Sensitivity and specificity of MDCT angiography in detecting hemodynamically significant stenoses (>50%).

<table>
<thead>
<tr>
<th>Coronary artery</th>
<th>Stenoses on</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CA</td>
<td>MDCT</td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>3</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>LAD</td>
<td>52</td>
<td>45</td>
<td>86.5</td>
</tr>
<tr>
<td>Segment 6</td>
<td>16</td>
<td>16</td>
<td>100</td>
</tr>
<tr>
<td>Segment 7</td>
<td>24</td>
<td>20</td>
<td>83.3</td>
</tr>
<tr>
<td>Segment 8</td>
<td>12</td>
<td>9</td>
<td>75</td>
</tr>
<tr>
<td>D1</td>
<td>10</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>LCX (segment 11)</td>
<td>15</td>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>RCA</td>
<td>43</td>
<td>30</td>
<td><strong>69.8</strong></td>
</tr>
<tr>
<td>Segment 1</td>
<td>18</td>
<td>15</td>
<td>83.3</td>
</tr>
<tr>
<td>Segment 2</td>
<td>18</td>
<td>11</td>
<td>61.1</td>
</tr>
<tr>
<td>Segment 3</td>
<td>7</td>
<td>4</td>
<td>57.1</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>95</td>
<td>77.2</td>
</tr>
</tbody>
</table>

CA, coronary angiography; MDCT, multidetector computed tomography; LM, left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; D1, first diagonal branch.
of coronary vessels. There is no direct visualization of wall structures. Nowadays, the major use of CA is addressed to combine diagnostic and interventional approach, when the presence of atherosclerotic disease has been suspected by noninvasive imaging. There has been an intensive search over the past years for low-risk diagnostic methods aimed at supplementing at least part of the invasive diagnostic procedures. MDCT coronary angiography seems to be the most promising technique.

Even with 4-row technology, non-invasive MDCT angiography shows a good diagnostic accuracy in the detection and quantification of lesions affecting the proximal and middle segments of the coronaries. Achenbach et al.

**Discussion**

CA has been considered the gold standard method for coronary imaging since its introduction in 1959. Balloon angioplasty and stent implantation have become the standard of care in catheter-based coronary artery revascularization for atherosclerotic disease. However diagnostic CA is an invasive procedure that yields a small but not negligible health risk and causes patient discomfort. Complications requiring emergency surgical intervention occur in approximately 0.8% of all cases. A relatively large proportion of patients with chest pain and suspected CAD may exhibit normal epicardial vessels at angiography. Furthermore, CA is restricted to the intraluminal assessment of coronary vessels. There is no direct visualization of wall structures. Nowadays, the major use of CA is addressed to combine diagnostic and interventional approach, when the presence of atherosclerotic disease has been suspected by noninvasive imaging. There has been an intensive search over the past years for low-risk diagnostic methods aimed at supplementing at least part of the invasive diagnostic procedures. MDCT coronary angiography seems to be the most promising technique.

Even with 4-row technology, non-invasive MDCT angiography shows a good diagnostic accuracy in the detection and quantification of lesions affecting the proximal and middle segments of the coronaries. Achenbach et al.
reported a sensitivity of 91% and a specificity of 84% to detect significant stenoses, when excluding vessels that could not be evaluated [14]. Nieman et al. found a sensitivity and specificity of 82% and 93% respectively to detect >50% stenoses in the assessable ≥2 mm segments. By including stenoses in nonassessable vessels, overall sensitivity decreased to 61%. Both residual motion and calcium deposits were responsible for misinterpretation.

Our data confirm these previous findings, yielding a sensitivity and a specificity of 77.2% and 91% respectively. The best visualization was achieved for the proximal tract of the epicardial arteries with more evidence for the LM and LAD (Figure 3). The RCA was more sensitive to motion artefacts and was hard to evaluate especially in middle-distal tracts (Figure 4). The assessment of the LCX was restricted to the proximal segments: this artery is small in many subjects and it easily blends with adjacent contrast-filled structures such as the great cardiac vein and the left atrium. The distal tract of the LCX and the side branches (segments 4, 10, 12-15) were not included in the evaluation. We believe this approach is reasonable for screening purposes and for assessment of coronary stenoses that would be potential target of revascularization therapy.

The image quality and the diagnostic accuracy of MDCT were significantly improved by a rigorous heart rate control and by the optimization of the reconstruction window.

Figure 3. A. Anterior view of the heart by volume rendering algorithm, showing the left main coronary artery, the left circumflex artery and the I diagonal branch. The left anterior descending artery is occluded at the end of the proximal tract (arrow). B. These findings are confirmed by conventional coronary angiography. LM = left main coronary artery; LCX = left circumflex artery; D1 = first diagonal branch; S1 = septal branch.

Figure 4. A. MDCT of a 68 year-old male patient showing a significant stenosis (70%) of the right coronary artery in the proximal tract (arrow), followed by a complete occlusion of the vessel in the middle tract (arrowhead). B. These findings are confirmed by conventional coronary angiography.
The temporal resolution of four-slice MDCT is adequate only at low heart rate (< 65 bpm)\textsuperscript{9,21}. To achieve optimal image quality, β-blocker or other negative chronotropic drugs should be administered before the CT investigation if no contraindications exist\textsuperscript{9,21,22}. For cardiac CT applications, the synchronization of data acquisition with the cardiac cycle can be performed in a prospective ECG-triggered or retrospective ECG-gated way. The procedure of prospectively triggering scan acquisition to sequential diastolic phases is routine in cardiac EBCT\textsuperscript{21}. EBCT only acquires a single phase of the cardiac cycle, representing a compromise for assessment of all coronary arteries. From cineangiographic studies, however, it is known that each of the coronary arteries has a distinct motion pattern in the course of the cardiac cycle. Because of their position in the coronary groove, the RCA and the LCX have more rapid diastolic motion than the LAD, caused mainly by atrial contraction during end-diastole. The different motion pattern of coronary arteries calls for an individual reconstruction for each vessel in regard to position in the cardiac cycle. This can only be obtained with ECG-gated MDCT, which acquires a three-dimensional data set of the entire heart including data from all phases of the cardiac cycle. The retrospective selection in the cardiac cycle of the phase with least motion and the adaptation of the reconstruction window to each coronary artery provide optimal image quality\textsuperscript{9,21,23,24}.

The presence of extensive calcium deposits in the coronary artery walls made a substantial number of scans only partially interpretable. Heavy calcification that appears to obliterate the coronary lumen can be associated with a wide range of luminal narrowing\textsuperscript{18}. These artefacts hamper assessment and cause misinterpretations\textsuperscript{13,20,24}. Nevertheless, severe calcification is related to coronary artery disease, and its detection will contribute to clinical decision-making\textsuperscript{25}.

The good specificity of MDCT suggests that this technique may be suitable for exclusion of stenoses in patients with a low likelihood of extensive CAD, such as young patients with atypical chest pain\textsuperscript{26,28}. Furthermore, cardiologists show a growing interest in using this technology for screening of coronary atherosclerosis\textsuperscript{21,22}. The rationale for investigating the presence of preclinical CAD relies on the consideration that more than half of all first coronary events are sudden cardiac death or acute myocardial infarctions in previously asymptomatic individuals\textsuperscript{25}. So, detection of coronary artery stenoses and calcifications by MDCT may be included in more sophisticated models for cardiovascular risk assessment\textsuperscript{29}. Clinical studies are expected to establish whether the potential benefits of MDCT are large enough to justify its employment as screening method in asymptomatic subjects with cardiovascular risk factors.

More recent 16-slice MDCT scanners have a minimum gantry rotation time of 0.375 sec and offer simultaneous acquisition of 32 slices in 0.75 sec. Higher spatial resolution, through reduction of partial volume effects, improves diagnostic accuracy of 16-slice MDCT and allows visualization of small-in-calibre vessels, whereas advantages of shorter scan time are a more comfortable breath-hold (approximately 18 sec) and a lower volume of contrast agents\textsuperscript{30,33}. Dedicated algorithms using only the data from a half gantry rotation per slice, provide a temporal resolution of < 210 msec, permitting to scan patients with heart rate > 65 bpm\textsuperscript{20}. However, to obtain excellent image quality, a lower heart rate is preferable\textsuperscript{21,23}. Ropers et al. have recently demonstrated that 16-slice MDCT depicts coronary artery stenoses with high accuracy, and a low rate of not assessable arteries (sensitivity 92%, specificity 93%)\textsuperscript{19}. Nieman et al. have reported a sensitivity of 95% and a specificity of 86% for detection of stenoses ≥50% in 59 patients\textsuperscript{20}.

A limitation of MDCT is the use of ionizing radiation that is slightly higher as compared to single slice spiral CT. All manufacturers provide several means to reduce X-ray exposure, by significantly improving the quality of detectors and by modulating throughout the acquisition the mAs (milliAmpère/second)\textsuperscript{34}.

In our study, as in others, the coronary arteries were described by segments. This approach cannot be done as precisely for MDCT as for CA and its use with MDCT has not been evaluated. Another limitation is the difference in the method of evaluation of coronary stenoses, which was based on quantitative analysis in CA and on visual estimation in MDCT.

The equipment of MDCT are progressing rapidly and in the near future this technique will challenge the supremacy of CA in the evaluation of patients with suspected or proven CAD.
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