Detection of Relevant Coronary Artery Disease Using Dual-Source Computed Tomography in a High Probability Patient Series

—— Comparison With Invasive Angiography ——

Johannes Rixe, MD; Andreas Rolf, MD; Guido Conradi, MD; Helge Moellmann, MD; Holger Nef, MD; Thomas Neumann, MD; Holger Steiger, MD; Christian W. Hamm, MD, FESC, FACC; Thorsten Dill, MD, FESC

Background
Computed tomography (CT) enables detection of coronary artery stenoses, but its use is limited by deficient evaluation at elevated heart rates. The accuracy of dual-source CT (DSCT) for the detection of coronary artery disease (CAD) was assessed in 76 patients at high probability of CAD without heart rate control and compared with quantitative coronary angiography (QCA).

Methods and Results
The 76 patients (47 males, mean age 65.5±10 years) underwent DSCT without preceding heart rate control. Data sets were evaluated by 2 observers in consensus with respect to stenoses >50% decreased diameter. QCA served as the standard of reference. Mean heart rate during scanning was 68±9 beats per min, and the average Agatston score was 337±560. Of 1,160 coronary artery segments, all but 3 were visualized artefact-free; 58 coronary stenoses were correctly detected by CT angiography. In the segment-based analysis, sensitivity was 98.3%, specificity 99.2% and accuracy 99%; patient-based analysis revealed a sensitivity of 100%, specificity of 83.3% and overall accuracy of 92.1%.

Conclusions
Even at elevated heart rates, DSCT can reliably detect coronary artery stenoses and the results correlate well with those for invasive coronary angiography. (Circ J 2009; 73: 316–322)

Key Words: Cardiac imaging; Coronary angiography; Coronary artery disease; Dual source computed tomography; Heart rate control

Because noninvasive visualization of coronary arteries and detection of relevant coronary artery stenoses using multidetector computed tomography (MDCT) have so far been challenging because of the small dimensions of the coronary arteries and their rapid motion, the improvement of temporal, as well as spatial, resolution has been the cardinal aims of scanner development over the past decade. However, coronary CT angiography (CTA) using 16-slice MDCT is still affected by numerous limitations, mostly partial volume effects caused by coronary calcification and motion artefacts because of higher coronary velocities combined with limited temporal resolution at heart rates >65 beats per min (bpm).\(^1,2\) Even visualization of coronary arteries using 64-slice MDCT with an increased temporal resolution of 165 ms is limited by severe coronary calcification and motion artefacts at heart rates >65 bpm, resulting in up to 12% of coronary segments being unsuitable for quantitative evaluation.\(^3-5\)

To overcome motion artefacts at higher heart rates, dual-source CT (DSCT) technology has recently been introduced. By using 2 X-ray tubes mounted onto a single gantry at an angle of 90°, a duplication of temporal resolution from 165 ms to 83 ms is provided with a mono-segment reconstruction mode.\(^6\) Recent studies using DSCT have shown encouraging results for visualization of the coronary arteries independent of heart rate; however, only small numbers of patients have been included and the correlation to quantitative coronary angiography (QCA) has so far barely been provided.\(^7-10\)

Thus, the purpose of the present study was to assess the feasibility of DSCT for detection of relevant coronary artery stenoses in a cohort of 76 patients with clinically suspected coronary artery disease (CAD) and compare the results with those from invasive angiography without preceding heart rate control.

Methods

Patients
During a 2-month period, 76 consecutive patients (47 males, all Caucasians; mean age, 65.5±10 years) referred for invasive coronary angiography (CAG) because of suspected CAD were included in our study. Clinical signs of CAD were typical chest pain in 50 patients (65.8%), positive stress testing in 15 (19.7%) and both indicators in 11 patients (14.5%). As it had been identically performed in previous studies, a positive stress test was not mandatory for inclusion in our study, but all patients with clinical
symptoms as the exclusive criterion for inclusion reported typical chest pain suspicious of CAD. Patient characteristics are shown in Table 1. Only patients in a stable clinical condition and without contraindications for the administration of iodinated contrast agents were investigated. Patients with coronary bypass grafts, prior stent implantation, valve prostheses and cardiac pacemakers were excluded, as were patients with atrial fibrillation, because the aim of the study was not to evaluate image quality in patients with atrial fibrillation. Written informed consent was given by all individuals included in our study, and the study was approved by the institutional review board.

**DSCT Protocol**

DSCT was performed with a SOMATOM Definition CT scanner (Siemens Medical Solutions, Forchheim, Germany) without heart rate modulation by oral or intravenous administration of β-blockers prior to the scanning procedure, but 45 patients (59.2%) were under continuous β-blocker medication and those patients had an average heart rate of 63.6±7.9 bpm. Overall, 36 patients had a heart rate >65 bpm during scanning (47.4% of all patients), of whom 24 had a heart rate >70 bpm (31.6% of all patients included).

After placing an i.v. line in an antecubital vein, and connecting the electrocardiogram (ECG) electrodes in the standard positions, all patients received 0.8 mg of isosorbide dinitrate sublingually immediately before scanning. In agreement with previously described protocols, a test bolus approach was performed, determining the contrast agent transit time (10 ml of iopamidole contrast, containing 370 mg iodine/ml, followed by 50 ml of isotonic saline, both at 5 ml/s) by calculating the time between beginning the contrast agent injection and maximum enhancement in the ascending aorta \(^{12,13}\). For coronary artery scanning, the individual delay was calculated and 60 ml of contrast agent were injected at 5 ml/s, followed by 50 ml of saline. Data acquisition was performed from the level of the tracheal bifurcation to the diaphragm in the cranio-caudal direction using a detector collimation of 32×0.6 mm, slice acquisition 64×0.6 mm by means of a z-flying focal spot.\(^{14}\) Gantry rotation time was 330 ms; pitch 0.2–0.4, adapted manually according to heart rate. Tube current was 360 mA, and tube voltage was 120 kV for both tubes. In accordance with previously published studies for dose reduction algorithms\(^{15–17}\) ECG-gated tube current modulation and automatic radiation exposure control were both used in all patients, and the pulsing window was fixed from 65% to 70% of the RR-cycle with heart rates <70 bpm, or from 40% to 70% of the RR-cycle with heart rates >70 bpm.

**Image Reconstruction**

Retrospective ECG-gated image reconstruction was performed with a half-scan and single RR-interval reconstruction algorithm, providing for a temporal resolution of 83 ms, as described earlier\(^6\). The first image reconstruction was performed at 70% of the RR-cycle, followed by an automatically generated reconstruction using dedicated reconstruction software, which automatically generates the most quiescent phase during the RR-cycle by calculating a motion strength function between several reconstructions at low resolution over the cardiac cycle and identifying periods of low difference between neighboring phases (BestDiast/BestSyst\(^5\), Siemens Medical Solutions)\(^{18}\). If motion artefacts were present, additional reconstructions in 5% increments and decrements were rendered, as described\(^{5,19–22}\).

For image reconstruction, a slice thickness of 0.6 mm and an increment of 0.3 mm were chosen. As performed by Flohr et al, reconstructions were rendered by using a medium-sharp (B26F) convolution kernel\(^{23}\). In the presence of calcified plaques, a sharp convolution kernel (B46F) was additionally reconstructed and used for evaluation.

**Data Analysis**

For postprocessing, the DSCT data sets with highest image quality were transferred to an offline workstation (LEONARDO\(^*\), Siemens Medical Solutions) and evaluated by 2 experienced investigators in consensus blinded to each patient’s identity and clinical history. Coronary segments were defined using the American Heart Association (AHA)/American College of Cardiology (ACC) 16-segment model\(^23\). All segments were assessed for the presence of stenoses >50% lumbar reduction, as well as for the presence of occlusions. Depending on vessel morphology and image quality, various postprocessing techniques were used in the evaluation. After assessment of axial and oblique multiplanar reconstructions (MPR), oblique maximum intensity projections, curved multiplanar reconstructions (curved MPR), and 3-dimensional volume-rendering technique projections (VRT) were performed.

**QCA**

Selective conventional CAG served as the standard of reference and was performed 24–48 h after the DSCT procedure using standard techniques by a skilled observer who was unaware of the results obtained by DSCT. Quantitative evaluation was performed on an offline workstation with dedicated software (QuantCor. QCA\(^*\); PieMedical Imaging, Maastricht, The Netherlands) using the AHA/ACC 16-segment coronary model. Coronary segments with a diameter <1.5 mm were excluded from analysis, and a reduction >50% of the luminal diameter compared with the proximal reference diameter was considered a significant stenosis.

**Statistical Analysis**

Quantitative variables are described as mean±standard deviation, and categorical variables are presented as counts and percentages. Diagnostic accuracy for detection of relevant coronary lesions by DSCT was expressed as sensitiv-
ty, specificity, positive predictive value (PPV) and negative predictive value (NPV), calculated from the chi-square test of contingency.

Calculations were performed for coronary segments, coronary arteries and in patient-based analysis. If at least 1 coronary segment was unevaluable on DSCT, it was regarded as having a relevant stenosis because of the clinical consequence of invasive angiography if the presence of a stenosis could not be ruled out.

Results

DSCT was performed successfully and without complications in all 76 patients enrolled; the mean scan and breathhold time for CTA scan was 9.68±1.73 s. Mean heart rate during scanning was 68±9 bpm (range 49–85 bpm) and the average Agatston score was 337±560 (range 0–2,650).

Assessment of Image Quality

A total of 1,080 coronary segments and 304 coronary arteries were included in our study, of which 1,072 coronary segments (99.3%) and 296 coronary arteries (97.4%) could be assessed without artefacts; 80 coronary segments with a diameter <1.5 mm were excluded from analysis, but no coronary segment impaired by artefacts because of motion or blurring was excluded. Three patients (3.9% of all patients enrolled, 0.28% of all coronary segments) had CT angiograms severely affected by motion artefacts, of which all were because of premature beats of supraventricular (n=2) or ventricular origin (n=1). No coronary segment was considered unevaluable because of motion artefacts because of elevated heart rates. In 5 patients (6.6% of all patients) with an average Agatston score of 988±1,010, 5 coronary segments (0.5% of all segments included) severe coronary calcifications were present, significantly impairing image quality by obliterating the coronary lumen. These 5 segments were regarded as having significant stenosis.

Under exclusion of the automated reconstruction tool described in the Methods, the overall number of different time instants necessary for each data set to obtain diagnostic image quality was 1±0.3.

In our patient series, optimal image quality could be achieved using exclusively diastolic reconstructions at 65% or 70% of the RR-cycle in 55 patients (72% of all patients). These data sets were acquired at a mean heart rate of 65±4 bpm, which was significantly lower than the mean heart rate of patients whose raw data were ideally reconstructed at systolic time instants of the cardiac cycle (the corresponding mean heart rate was 76±5.3 bpm, P<0.05). The optimal time instants for systolic reconstructions were 35% and 40%, respectively, with a total of 21 data sets (28% of all patients). In a subanalysis of patients with heart rate >65 bpm (n=36), a systolic reconstruction of raw data proved satisfactory only for patients with heart rate >70 bpm, as all data sets with best image quality at 35% or 40% were obtained in patients with a heart rate >70 bpm.

Comparison of DSCT and QCA

QCA demonstrated CAD in 40 patients (prevalence in total patients, 53%). Among these 40 patients, 59 coronary stenoses >50% diameter reduction were detected by QCA (2 in left main, 29 in left anterior descending, 15 in left circumflex and 13 in right coronary artery; Fig 1).

Of the 1,072 coronary segments classified as evaluable on DSCT, 58 showed significant stenoses. One stenotic lesion of coronary segment 3 was found to be >50% reduced on QCA but was missed by DSCT. Nine coronary segments were classified as false-positive by DSCT: 8 were unevaluable and thus estimated as having significant stenosis, but did not show stenosis on QCA. One further segment was evaluated as false-positive because the degree of lumen reduction was overestimated; the remaining 1,012 coronary segments were assessed as true negative on DSCT (Fig 2).

Thus, on a per-segment analysis, DSCT revealed a sensitivity of 98.3%, specificity of 99.1%, and the NPV and PPV were 99.9% and 86.6%, respectively. Vessel-based and patient-based analyses revealed a sensitivity of 98.3% (patient-based 100%) and specificity of 97.1% (patient-based 83.3%). The NPV and PPV values were 99.6% and 89.4% in the vessel-based and 100% and 86.9% in the per-patient analyses, respectively (Table 2).

Overall diagnostic accuracy was 99.1% in the coronary-segment-based analysis; vessel- and patient-based analyses

![Fig 1. Maximum intensity projection of the right coronary artery (A) demonstrates a significant stenosis in the proximal portion. Reconstructed slice thickness is 5 mm, and heart rate is 65 beats per min. The time instant of image reconstruction was 71% of the RR-cycle. The patient was referred for conventional angiography and the stenosis was confirmed (B).](image-url)
revealed an overall accuracy of 97% and 92.1%, respectively.

Regarding patients with elevated heart rates, sub analyses for patients with >65 bpm or >70 bpm revealed a sensitivity, specificity, PPV and NPV that were not substantially different to the statistical parameters of the patient series in general. At least, sensitivity and NPV values remained remarkably constant, whereas sensitivity ranged from 98.3% in the segment- and coronary-based calculations to 100% in all patient-based analyses, and the NPV ranged from 99.6%
Table 2 Comparison of DSCT and QCA

<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>Evaluable</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segment-based</td>
<td>1,072 (99.3%)</td>
<td>98.3%</td>
<td>99.1%</td>
<td>86.6%</td>
<td>99.9%</td>
</tr>
<tr>
<td>95%CI</td>
<td>89.7–99.9</td>
<td>98.3–99.6</td>
<td>75.5–93.3</td>
<td>99.4–100</td>
<td></td>
</tr>
<tr>
<td>Coronary-based</td>
<td>296 (97.4%)</td>
<td>98.3%</td>
<td>97.1%</td>
<td>89.4%</td>
<td>99.6%</td>
</tr>
<tr>
<td>95%CI</td>
<td>89.9–99.9</td>
<td>93.9–98.5</td>
<td>78.8–95.3</td>
<td>97.3–100</td>
<td></td>
</tr>
<tr>
<td>Patient-based</td>
<td>68 (89.5%)</td>
<td>100%</td>
<td>83.3%</td>
<td>86.9%</td>
<td>100%</td>
</tr>
<tr>
<td>95%CI</td>
<td>89.1–100.0</td>
<td>66.5–93.0</td>
<td>73.0–94.6</td>
<td>85.9–100</td>
<td></td>
</tr>
<tr>
<td>Patients with HR &gt;65 bpm</td>
<td>34 (94.4%)</td>
<td>100%</td>
<td>88.2%</td>
<td>90.5%</td>
<td>100%</td>
</tr>
<tr>
<td>95%CI</td>
<td>79.0–100.0</td>
<td>62.3–97.9</td>
<td>68.2–98.3</td>
<td>74.7–100</td>
<td></td>
</tr>
<tr>
<td>Patients with HR &gt;70 bpm</td>
<td>22 (91.7%)</td>
<td>100%</td>
<td>83.3%</td>
<td>85.7%</td>
<td>100%</td>
</tr>
<tr>
<td>95%CI</td>
<td>65.5–100.0</td>
<td>56.2–97.5</td>
<td>50.1–97.1</td>
<td>69.9–100</td>
<td></td>
</tr>
</tbody>
</table>

In segment-based, vessel-based and even patient-based analyses; individuals with at least 1 coronary segment considered unevaluable on DSCT were regarded as having irrelevant coronary stenosis.

DSCT, dual-source computed tomography; QCA, quantitative coronary angiography; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval. Other abbreviation see in Table 1.

Discussion

Our study demonstrates that the improvement in temporal resolution for coronary artery imaging by CT enables accurate detection of relevant coronary artery stenoses, even at elevated heart rates, and thus broadens the spectrum of patients that can be assessed non-invasively.

CAG using 16- and 64-slice MDCT has become an increasingly reliable tool for visualizing the coronary arteries and has proved particularly reliable for ruling out of CAD in selected patient cohorts. The high NPV for ruling out CAD has prompted the current European Society of Cardiology (ESC) guidelines on management of stable angina to recommend MDCT for patients with a low pre-test probability of CAD and inconclusive stress testing. Additionally, recently published studies underline the feasibility of coronary CTA to even detect coronary plaque and therefore clinically silent CAD. A certain prognostic impact on the detection of coronary calcification and non-obstructive CAD is therefore assumed.

However, in clinical practice 2 major limitations are apparent: Firstly, coronary calcifications lead to overestimation of coronary stenoses because of blurring artefacts and total obstruction of the coronary lumen, and may significantly impair diagnostic accuracy and thus lead to unnecessary invasive angiography. Secondly, the occurrence of motion artefacts at elevated heart rates is a common problem, which most frequently affects the right coronary artery because of its extensive motion during the cardiac cycle. A low heart rate during scanning has therefore been an essential requirement to obtain a data set suitable for quantitative analysis. Hence, the mean heart rate during scanning in studies using 64-slice MDCT is considerably below 65 bpm.

To overcome the occurrence of motion artefacts at higher heart rates, 2 technical approaches have been developed; multi-segment reconstruction algorithms combine data sets from 2 or even more cardiac cycles for reconstruction, achieving improved temporal resolution, but they disregard the inter-heartbeat variability of coronary artery position and require low table pitches. By providing a temporal resolution of 83 ms in a monosegment reconstruction mode, DSCT enables motion artefact-free visualization of coronary arteries, independent of heart rate, and therefore a significant decrease of motion artefacts in clinical practice.

In this prospective study we assessed the feasibility of new DSCT technology to detect coronary artery stenoses in a cohort of 76 consecutive patients without precedent heart rate lowering medication. An overall diagnostic accuracy of 99.1% and excellent NPV of 99.9% in segment-based analysis was achieved without excluding any coronary segments from statistical analysis because of artefacts. Only 0.7% of all coronary segments were unevaluable on DSCT, and thus regarded as having significant stenosis, but none of these was assessed unevaluable because of motion artefacts caused by elevated heart rate.

There are only a few published studies evaluating the feasibility of DSCT for the identification of relevant coronary artery stenoses in patients, which differs significantly from our study of patients with a relatively high pre-test probability for CAD. Considering the study by Busch et al, DSCT presents itself superior to 64-slice MDCT for the detection of CAD: in a small cohort of 10 patients each, DSCT was superior to 64-slice MDCT for the detection of CAD; DSCT demonstrated a sensitivity and specificity of 100% for both, whereas thea 64-slice scanner achieved a sensitivity of 100%, but a reduced specificity of 90%; the mean heart rate of patients examined with the DSCT scanner was 80 bpm, but the mean heart rate of patients scanned by MDCT was not given.

Similar to the results of our study, Leber et al, Scheffel et al, and Ropers et al demonstrated, that an excellent overall diagnostic accuracy and an NPV of 99% in per segment analysis can be achieved using DSCT for the detection of CAD in their studies with 90, 30, and 100 enrolled patients, respectively. The patients enrolled in the studies of Scheffel et al and Leber et al had mean heart rates of 73 and 70.3 bpm, respectively, and a pre-test likelihood of CAD ranging from “low” to “intermediate” in the study by Leber et al to “high” in the study by Scheffel et al. In the study by Ropers et al, the mean heart rate was 64±13 bpm, which is in fact at the level of earlier studies with 64-slice MDCT. In addition, the prevalence of CAD in the latter study is
lower than in all studies of DSCT previously published (only 41%). The potential of DSCT technology is better tested in a cohort of patients with a higher prevalence of CAD (eg, 53% in our study), while acknowledging that patients with a high pre-test likelihood for CAD do not represent the patient cohort recommended for coronary MDCT by current European guidelines.23

The recently published study by Husmann et al also included patients with a high probability for CAD, but in fact there were only 25 patients in the high-risk subgroup, and furthermore, the authors describe an improved PPV for the diagnosis of relevant CAD in that subgroup.22 Taking into account that patients with a high probability for CAD tend to have higher amounts of calcification, this conclusion appears to be relatively implausible.

**Study Limitations**

A major limitation is that the mean heart rate during scanning was 68±9 bpm, which is not considerably higher than that reported in studies using 64-slice MDCT.10,13,35 However, in comparison with those studies, our data suggest a considerably increased diagnostic accuracy, which might be at least partially related to optimized image quality at elevated heart rates. Another limitation is that we did not enrol patients with coronary stents or atrial fibrillation, both clinically relevant conditions that should be the subject of further studies.

In conclusion, this study demonstrates that noninvasive CAG using CT has become a reliable alternative to invasive diagnostic procedures. The present patient cohort tested with a high prevalence of 53% for CAD was very well suited to testing the accuracy of the new DSCT technique, while acknowledging that it is not the patient group that is aimed for investigation with noninvasive CTA.25 This study revealed a high accuracy for the detection of relevant coronary artery stenosis, even in a patient series of high pre-test probability for CAD, and confirmed the high NPV in patients with higher heart rates, and thus using DSCT may avoid the unnecessary invasive procedures related to inconclusive findings on CTA by previous scanner generations.

**Disclosure**

None.

**References**