Computed tomographic angiography or conventional coronary angiography in therapeutic decision-making

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Aims
To evaluate non-invasive angiography using dual-source computed tomography (CT) for the determination of the most appropriate therapeutic strategy in patients with suspected coronary artery disease (CAD).

Methods and results
CT angiography (Dual Source CT, Somatom Definition, Siemens Medical Systems, Forchheim, Germany) was performed in 60 consecutive patients [51 men, median age 64 (57–70) years] scheduled for elective coronary angiography. Both techniques were used to evaluate the presence of CAD, significant stenosis, and the need for revascularization therapy. Sensitivity and specificity for the presence of significant stenosis were: per segment (n = 766) 62% (95% CI 50–72) (64/104) and 79% (95% CI 74–84) (526/662), respectively; per patient (n = 60) 100% (95% CI 91–100) (38/38) and 45% (95% CI 24–68) (10/22), respectively. In therapeutic decision-making based on CT angiography, sensitivity, specificity, positive and negative predictive values for intervention were 97% (95% CI 84–100) (36/37), 48% (95% CI 27–69) (11/23), 75% (95% CI 60–86) (36/48), and 92% (95% CI 60–100) (11/12), respectively. If a revascularization procedure was needed, the CT angiographic data indicated the appropriate modality (percutaneous coronary intervention or coronary artery bypass grafting) in 70% (26/36) of patients.

Conclusion
Although imaging qualities have improved considerably, CT angiography cannot be used for definitive therapeutic decision-making with regard to revascularization procedures in patients with suspected CAD.

Keywords
Dual-source computed tomography • Coronary angiography • Therapeutic decision

Introduction
Coronary artery disease (CAD) remains to be the leading cause of death in the western world, and its prevalence is still increasing. Despite the rapid development of computed tomography (CT) as a non-invasive technique for coronary imaging, conventional invasive coronary angiography (CAG) is the gold standard for diagnosing the presence of significant stenosis. Although the associated risk for serious complications is small,1 the inconvenience for the patient and economic deliberations have strengthened the development of CT as a non-invasive alternative.

The spatial resolution of CT is continuously improving, resulting in a current 64-slice multi-detector CT (MSCT). Recently, the dual-source multi-detector CT (DSCT) was released, further improving the temporal resolution. Studies evaluating the accuracy of DSCT in the detection of significant stenosis shows high sensitivity and specificity on a per segment, vessel, or patient level.2–6 Most studies determine the usefulness of CT in the evaluation of CAD on the ability to visualize and detect significant stenosis. However, it seems to be more important to evaluate the accuracy of the therapeutic consequences of CT as a non-invasive coronary angiography technique. Therefore, we conducted a study in which we used DSCT for the evaluation of the coronary artery tree, in order to evaluate the accuracy of DSCT-based therapeutic decision-making. We investigated whether DSCT is an accurate non-invasive technique to determine the most appropriate

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therapeutic strategy in potential candidates for a revascularization procedure, i.e. percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

Methods

Patients over 50 years of age, scheduled for elective CAG, were eligible; therefore patients with acute coronary syndrome (i.e. ST-segment elevation and non ST-segment elevation myocardial infarction) were not included. Inclusion lasted from May 2006 through May 2007. Owing to technical failure of the DSCT, inclusion was not possible during a total period of 4 months. Patients with known iodine allergy, severe renal insufficiency (creatinine levels >120 μmol/L), hyperthyroidism, arrhythmias (atrial fibrillation or frequent premature beats), unstable clinical condition, inability to follow breath-hold commands, previous PCI, or CABG were excluded. Patients were scheduled for contrast-enhanced DSCT within 1 month of CAG. The study complies with the Declaration of Helsinki and was approved by the local ethical review board. All patients signed an informed consent.

Coronary angiography: procedure and analysis

Routine invasive CAG via the femoral or radial artery was performed. Two independent cardiologists blinded for clinical history and DSCT results evaluated the CAG. Coronary segments were analysed according to the model of the American College of Cardiology/American Heart Association. All evaluable segments were classified as normal (smooth borders), as having non-significant disease (luminal irregularities resulting in narrowing <50%), or as having significant stenosis (luminal narrowing ≥50%). In the case of multiple irregularities in a given segment, the segment was classified by the most severe irregularity. In the case of multiple abnormal segments per artery, the vessel was classified by the segment with the most severe irregularity. Patients were classified as positive for the presence of significant CAD if there was a significant stenosis in any artery. This evaluation was conducted by two cardiologists (B.dS., F.Z.), blinded for medical history and DSCT results. Moreover, based on the CAG results and clinical findings, the necessary therapeutic intervention was chosen by an experienced interventional cardiologist (R.T.), i.e. the necessity of revascularization therapy (PCI or CABG) next to conservative therapy. If revascularization therapy was needed, a decision was made whether PCI or CABG had to be done, based on the combination of clinical data (age, medical history, risk factors) and CAG, according to the guidelines of the European Society of Cardiology and the American College of Cardiology/American Heart Association,1,8

Dual-source computed tomography: procedure and analysis

A retrospectively ECG-triggered DSCT coronary angiogram (Somatom Definition, Siemens Medical Systems, Forchheim, Germany) with contrast enhancement was made with a tube current of 412 mA s/rot, tube voltage of 120 kV, and a gantry rotation time of 0.33 s for both tubes. ECG pulsing window was set at 20–70% of the RR interval and was used for all patients. The pitch was automatically adapted to the heart rate. The mean heart rate during scanning was 63 ± 12 (range 48–86) b/min. Scan direction was craniocaudal starting above the coronary ostia and ending at the diaphragm below all cardiac structures. For the contrast-enhanced scans 73 mL of non-ionic contrast agent (iomeprol 400 mg I/mL, Iomeron1 400, Bracco, Italy) was injected in an antecubital vein. Bolus triggering was used for timing with the region of interest set in the descending aorta. A 50 mL saline bolus followed the contrast bolus to maintain a compact bolus and to reduce the necessary amount of contrast. All patients were treated with sublingual nitroglycerin (0.4 mg) just prior to the scan protocol. The calculated mean effective radiation dose based on the scan protocol was 7.3 mSv.9

Reconstructions were made to select the phase with least motion artefacts to obtain motion-free images of the coronary arteries. In this phase of the RR-interval, final reconstructions were made for evaluation. Images were reconstructed using a B26f kernel, 0.6 mm slice thickness and 0.4 mm increment. Sixteen segments of the coronary artery were evaluated according to the model of the American College of Cardiology/American Heart Association.1,8 All evaluable segments were classified as normal (smooth borders), as having non-significant disease (luminal irregularities resulting in narrowing <50%), or as having significant stenosis (luminal narrowing ≥50%). In the case of multiple stenoses in a given segment, the segment was classified by the most severe stenosis. In the case of multiple abnormal segments per artery, the vessel was classified by the most stenotic segment. Patients were classified as positive for the presence of significant CAD if there was a significant stenosis in any artery. The evaluation for the presence of CAD was conducted by a dedicated investigator (R.D.), a senior experienced radiologist (M.O.) and an interventional cardiologist (R.T.), blinded for medical history and CAG results. Next, based on the DSCT results and clinical findings, an interventional cardiologist (R.T., experienced in analysing DSCT results) assessed the necessary therapeutic intervention, i.e. the necessity of revascularization therapy (PCI or CABG) next to conservative therapy. If revascularization therapy was needed, a decision was made whether PCI or CABG had to be done, based on the combination of clinical data (age, medical history, risk factors) and DSCT, according to the guidelines of the European Society of Cardiology and the American College of Cardiology/American Heart Association,1,8

Statistical analysis

Statistical analysis was performed using SPSS 12.0 for Windows (Chicago, IL, USA) and Stata 10.0 (Stata Corporation, College Station, TX, USA). All data were expressed as mean ± SD. For skewed data, median and interquartile range were given. Accuracy of stenosis detection was described as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Sensitivity, specificity, PPV, and NPV were calculated for segment, vessel, and segment level, we used robust standard errors to account for within-person correlation.9 Sensitivity and specificity were computed with the CAG result as the dependent variable; PPV and NPV were computed with the DSCT result as the dependent variable. As we sought to investigate the relationship between stenoses seen by DSCT and CAG and the clinical implications, we included 60 patients. This number of patients is comparable with the previous studies comparing CAG and CT angiography.

Results

Clinical characteristics of the patient population

Sixty patients were enrolled during the period from May 2006 through May 2007. An additional 22 patients were screened but excluded; 14 because of arrhythmias (atrial fibrillation, frequent
extrasystoles) found during examination before DSCT, one because of known contrast allergy, six because of severe renal insufficiency, and one because of hyperthyroidism. Six patients declined to undergo DSCT. All DSCT and CAG were performed without complications. The characteristics of each patient are shown in Table 1. Table S1. Table 1 shows a summary of the patient characteristics. Thirty-eight patients (64%) had significant CAD. Although the Framingham Risk Score showed similar 10-year risk of cardiovascular disease, patients with significant CAD were older [65 (59–70) vs. 58 (53–66), P < 0.05], more often hypertensive [35 (92%) vs. 10 (46%), P < 0.05] and had diabetes mellitus [13 (34%) vs. 2 (13%), P < 0.05], compared with patients without significant CAD.

### Table 1: Patient characteristics (n = 60)

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Age (years)</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>64 (57–70)</td>
<td>51 (85%)</td>
</tr>
<tr>
<td>Hypcholesterolaemia</td>
<td>46 (77%)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>28 (47%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15 (25%)</td>
<td></td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>34 (57%)</td>
<td></td>
</tr>
<tr>
<td>Obese (body mass index &gt; 30 kg/m²)</td>
<td>11 (18%)</td>
<td></td>
</tr>
<tr>
<td>10-year risk of CVD (%)</td>
<td>10 (6–13)</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical findings
- Typical complaints, ischaemia proven: 25 (42%)
- Atypical complaints, ischaemia proven: 8 (13%)
- Typical complaints, no ischaemia proven: 21 (35%)
- Atypical complaints, no ischaemia proven: 6 (10%)

### CAG findings
- No CAD: 2 (3%)
- Non-significant CAD: 20 (33%)
- Single-vessel disease: 16 (27%)
- Multi-vessel disease: 22 (37%)

The 10-year risk of developing CVD is calculated according to the Framingham Risk Score. CAD, coronary artery disease. CAG, conventional coronary angiography. CVD, cardiovascular disease.

### Table 2: Diagnostic accuracy of DSCT compared with CAG for detection of significant lesions in patients

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n = 60)</td>
<td>38/38</td>
<td>100% (91–100)</td>
<td>10/22</td>
<td>45% (24–68)</td>
</tr>
<tr>
<td>Arteries (n = 240)</td>
<td>62/71</td>
<td>87% (77–94)</td>
<td>115/169</td>
<td>68% (59–76)</td>
</tr>
<tr>
<td>Segments (n = 766)</td>
<td>64/104</td>
<td>62% (50–71)</td>
<td>526/662</td>
<td>79% (74–84)</td>
</tr>
<tr>
<td>Proximal segments (n = 239)</td>
<td>31/38</td>
<td>82% (63–92)</td>
<td>145/201</td>
<td>72% (64–79)</td>
</tr>
<tr>
<td>Remaining segments (n = 527)</td>
<td>33/66</td>
<td>50% (38–62)</td>
<td>381/461</td>
<td>83% (77–87)</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, PPV, and NPV are presented as percentage (95% CI). CAD, coronary artery disease. CAG, conventional coronary angiography. DSCT, dual-source computed tomography. NPV, negative predictive value; PPV, positive predictive value.

### Dual-source computed tomography compared with coronary angiography for detection of significant stenosis

DSCT images were used to evaluate the presence, extent, and severity of CAD. All the 60 patients could be analysed for the presence of CAD. DSCT correctly detected significant stenosis in all the 38 cases for an overall sensitivity of 100% (95% CI 91–100) (Table 2). In 10 of 22 patients, the absence of significant stenosis was correctly detected by DSCT, for an overall specificity of 45% (95% CI 24–68). Accurate detection of the absence or presence of significant CAD was made in 48 of 60 patients, resulting in an accuracy of 80%.

Overall, 766 of 827 segments could be interpreted by DSCT; 61 segments were not evaluable because of movement artefacts (7; 0.8%), poor filling (5; 0.6%), too small luminal calibre (32; 3.9%), severe calcification (2; 0.2%), or not visible (15; 1.8%). On a per-segment base, DSCT had a sensitivity of 62% (95% CI 50–71) (64 of 104) in detecting significant stenosis on CAG, and a specificity of 79% (95% CI 74–84) (526 of 662) (Table 2). Of all the segments, 590 were evaluated correctly, giving an accuracy of 77%.

Two hundred and thirty-nine proximal segments were evaluable by DSCT. Five segments were not evaluable because of proximal occlusion and one segment 11 because of motion artefacts. In the proximal segments, sensitivity and specificity were 82% (95% CI 63–92) and 72% (95% CI 64–79), respectively. In the remaining segments (n = 527), the sensitivity and specificity were 50% (95% CI 38–62) and 83% (95% CI 77–87), respectively.

### Therapeutic strategy based on DSCT compared with CAG

Based on DSCT results, a therapeutic strategy was defined, i.e. the necessity of revascularization therapy next to conservative therapy. The gold standard was therapeutic strategy eventually chosen based on CAG. DSCT correctly predicted the necessary strategy in 47 of 60 patients (78%) (Table 3). Sensitivity for predicting the need of revascularization therapy was 97% (95% CI 84–100) (36 of 37 patients), whereas specificity, PPV, and NPV were 48% (95% CI 27–69), 75% (95% CI 60–86), and 92% (95% CI 60–100), respectively (Table 4). In the population with significant CAD, DSCT correctly predicted the necessary strategy in 35 of 38 patients (92%). In two patients revascularization therapy...
was proposed according to DSCT and in one patient no revascularization therapy was needed based on DSCT results. In the population without significant CAD, DSCT correctly predicted that there was no need for revascularization therapy in 10 of 22 patients (45%).

According to CAG, 37 patients needed revascularization therapy (Table 3). In 26 of these patients (70%) the appropriate revascularization therapy (PCI or CABG) was chosen based on DSCT results. Moreover, in 10 patients an incorrect decision towards CABG was made based on DSCT results.

### Discussion

Our study shows that the decision to perform revascularization therapy cannot be based reliably on the results of a DSCT; DSCT predicted in 78% of the patients the appropriate therapeutic strategy. If we consider the decision of giving conservative therapy, PCI, or CABG, the right therapeutic strategy was chosen based on DSCT in 62% of the patients.

In case a patient is suspected of having CAD, the following process of therapeutic decision-making can be divided into three steps. The first step is to determine whether the patient has CAD. It is known that MSCT as well as DSCT allows safe and reliable rule out of CAD. Similar results for NPV were found in our study. So far, little is known about the long-term NPV of CT coronary angiography; Pundziute et al. studied the prognostic value of MSCT in 100 patients who were referred for further cardiac evaluation owing to suspicion of significant CAD. No events occurred in 20 patients with no signs of CAD on CT coronary angiography, whereas patients with non-obstructive CAD had an 8% event rate and with obstructive CAD a 63% event rate (mean follow-up of 16 months).

The second step in therapeutic decision-making is to determine, whether the detected CAD is significant. This also implies the ensuing therapeutic strategy; the choice between conservative management or revascularization. In four recent studies, the accuracy of DSCT to determine the severity of CAD has been studied in a total of 274 patients. These studies have shown a sensitivity, specificity, PPV, and NPV on segment level of 88–96%, 74–96%, and 92–99%, respectively, and a sensitivity, specificity, PPV, and NPV on patient level of 95–100%, 73–90%, 61–89%, and 97–100%, respectively, for the detection of significant stenosis. In contradiction, we found a sensitivity and specificity on segment level of 62% and 79%, respectively, and on patient level of 100% and 45%, respectively. The PPV and NPV are 32% and 93%, respectively, on segment level, and 76% and 100% on patient level. These findings are in-line with the multicentre study of Garcia et al. in which a higher number of false-positive detection of significant CAD was reported. Kaiser et al. studied the accuracy of CT angiography in a population similar to ours, and found comparable results. The observed difference can at least in part be explained by the high prevalence of CAD in our study population when compared with the other studies. However, the most important findings, namely the PPV and NPV on a patient level are comparable. Nevertheless, our study shows that DSCT is not really accurate in detecting significant stenosis, as only 77% of the segments were correctly evaluated and only 80% of the patients. The remaining patients were incorrectly classified as having significant CAD, thus underlying the tendency of DSCT to overestimate lesion severity. A very important observation is that no patient was incorrectly classified to have non-significant CAD. This underlines the usefulness of DSCT in ruling out significant CAD.

To take the third step in therapeutic decision-making, whether the patient with significant CAD needs PCI or CABG, it is important to consider the clinical characteristics of the patient such as...

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**Table 3** Therapeutic strategy based on DSCT compared with CAG

<table>
<thead>
<tr>
<th>DSCT</th>
<th>Conservative</th>
<th>Intervention</th>
</tr>
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<tbody>
<tr>
<td>CAG</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>PCI</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

The upper part of the table shows the relation of therapeutic strategy based on DSCT and CAG. The lower part of the table shows the distribution of both the interventional strategies (i.e. PCI and CABG) decided on DSCT and CAG. CAG, conventional coronary angiography; DSCT, dual-source computed tomography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery.

**Table 4** Therapeutic decision for revascularization therapy based on DSCT compared with CAG

<table>
<thead>
<tr>
<th>DSCT</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>36/37</td>
<td>97% (84–100)</td>
<td>11/23</td>
<td>48% (27–69)</td>
</tr>
<tr>
<td>Significant CAD</td>
<td>34/35</td>
<td>97% (83–100)</td>
<td>1/3</td>
<td>33% (2–87)</td>
</tr>
<tr>
<td>No significant CAD</td>
<td>2/2</td>
<td>100% (2–100)</td>
<td>10/20</td>
<td>50% (28–72)</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, PPV, and NPV are presented as percentage (95% CI). CAD, coronary artery disease; CAG, conventional coronary angiography; DSCT, dual-source computed tomography; NPV, negative predictive value; PPV, positive predictive value.
age, co-morbidity, and ensuing individual risk. Furthermore, the entire coronary artery tree must be evaluable. Weustink et al. found comparable sensitivity and specificity for the detection of significant CAD of proximal and remaining segments, 95% and 93–96%, and 94% and 89–97%, respectively. Our results show a sensitivity and specificity of 82% and 72%, respectively, in proximal segments, compared with a sensitivity and specificity of 50% and 83%, respectively, for the remaining segments. Our results show that the distal branches are less good evaluable, as critical evaluation of all distal branches is necessary prior to a decision to perform PCI or CABG. This can partly explain why in only 26 of 37 (70%) patients, eventually scheduled for a revascularization procedure, the appropriate modality was proposed based on DSCT. In 10 patients, based on DSCT results an inappropriate advice for CABG was given; in nine patients because of overestimation of CAD severity and in one patient because DSCT did not detect collateral filling of the right coronary artery. Nevertheless, as previously mentioned coronary anatomy is not the sole determinant of which intervention is best suitable for the patient. His or her clinical condition certainly should always be taken into account.

Although, most reports stress the usefulness of CT coronary angiography in significant CAD detection, in our opinion it is far more important to evaluate the accuracy of the therapeutic decision-making based on CT coronary angiography. Our study shows that DSCT cannot be used accurately in therapeutic decision-making with regard to revascularization therapy.

Recently, the COURAGE trial showed no additional benefit of PCI to optimal medical therapy in reducing the risk of death and non-fatal myocardial infarction in patients with stable CAD; PCI does not protect destabilization of plaques not stented.15 As DSCT often shows more extensive CAD than is diagnosed with CAG, multiple non-significant plaques that may potentially destabilize in the future are identified using DSCT. Given the rapid technical developments, DSCT may become useful in detecting the vulnerable plaques by using specific plaque characteristics, like calcium-spotted core.16

Some limitations of DSCT and CAG should be discussed. First, although temporal resolution has increased with the introduction of DSCT compared with MSCT (83 ms vs. 165 ms) and the high spatial resolution (0.4 mm), CAG is still superior with a spatial and temporal resolution of 0.2 mm and 5 ms, respectively. DSCT enables motion-free imaging of patients with a heart rate over 80 b.p.m., but several cardiac arrhythmias are still an insurmountable challenge. In our study, only 0.8% of the segments were not evaluable because of motion artefacts. Our patients did not receive beta-blockers to reduce heart rate. However, arrhythmia was an exclusion criterion.

Secondly, CAG allows ad hoc performance of coronary interventions such as balloon dilatation or coronary stent placement. However, only one-third of all CAG in Europe are performed in conjunction with a revascularization procedure, while the rest are performed only for diagnostic purposes.17 So, CT angiography could prevent the application of some invasive diagnostic procedures.

Thirdly, although DSCT has a high spatial resolution, the accuracy of stenosis detection is limited in distal branches of the coronary artery tree. In our study, DSCT could visualize 93% of the segments visualized by CAG. However, from CAG studies it is known that the clinical significant stenosis are most often seen in more proximal segments with a luminal diameter of 2–5 mm.18 Moreover, only vessels with a luminal diameter larger than 2 mm are the targets of PCI, and there is also a minimum vessel diameter to allow CABG.

Fourth, DSCT has higher radiation burden than CAG. The calculated mean effective radiation dose based on our DSCT scan protocol was 7.3 mSv.9 For comparison, CAG is associated with an effective dose of about 5.6 mSv.19 As the availability and subsequently the use of CT increases, clinicians must be more aware of this consequence. However, the risk of artery access complications related to CAG must also be taken into account.

Study limitations
As all patients were referred for CAG, there was a high incidence of CAD in our population. The high burden of atherosclerosis in this selected population is also reflected by the number of excluded patients (n = 22, 27%), mainly for arrhythmias and poor renal function. As this study did not include patients with suspected acute coronary syndromes, further research is needed to establish the degree of accuracy in that population.20 Furthermore, the degree of stenosis was based on eye-balling and not quantitatively analysis. Therefore, we could not correlate percentage stenosis, but our purpose was to approach the normal clinical setting in which therapeutic decision-making is performed.

Clinical implications
Although a normal CT angiogram has a very high NPV and is useful for excluding CAD, when this technique is used in a population with high probability of CAD, DSCT is of limited use for therapeutic decision-making with regard to revascularization procedures. If significant stenosis is suggested, a CAG still has to be performed to precisely evaluate the coronary artery tree, and to make sure that appropriate therapeutic strategy is chosen.

Supplementary material
Supplementary material is available at European Heart Journal online.

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Conflict of Interest: none declared.

References