Accuracy of dual-source computed tomography to identify significant coronary artery disease in patients with atrial fibrillation: comparison with coronary angiography

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Aims
It has been previously reported that the sensitivity and specificity of multislice computed tomography (CT) for detecting significant coronary artery disease (CAD) is high. However, regular sinus rhythm has been considered a prerequisite for an adequate examination, even though atrial fibrillation (AF) is common among patients evaluated for the presence of coronary heart disease. In this study, we investigated the sensitivity and specificity of dual-source CT (DSCT) to detect and rule out significant coronary stenoses in patients with AF referred for invasive coronary angiography.

Methods and results
One hundred and ten consecutive patients with AF who were admitted for a first diagnostic coronary angiogram were screened for participation. Out of these, 50 patients were excluded either due to renal insufficiency, inability to maintain an adequate breath hold or due to rapid AF non-responsive to β-blocker therapy (heart rate > 100 b.p.m.). Sixty remaining patients (mean age 71 ± 7 years) were included and subjected to CT angiography using DSCT within 24 h before invasive coronary angiography. A contrast-enhanced volume data set was acquired (330 ms gantry rotation, collimation 2 × 64 × 0.6 mm, retrospective electrocardiogram gating). Data sets were evaluated concerning the presence or absence of significant coronary stenoses and validated against invasive coronary angiography. A significant stenosis was assumed if the diameter reduction was ≥50%. Mean heart rate during CT was 70 ± 15 b.p.m. (range 32–107 b.p.m.). On a per-patient basis, the sensitivity and specificity for DSCT to detect significant coronary stenoses in vessels >1.5 mm diameter was 100% [14/14, 95% confidence interval (CI) 77–100] and 85% (39/46, 95% CI 71–94), respectively, with a negative predictive value (NPV) of 100% (39/39, 95% CI 91–100) and a positive predictive value (PPV) of 67% (14/21, 95% CI 43–85). On a per-artery basis, 240 vessels were evaluated (left main, left anterior descending, left circumflex, and right coronary artery in 60 patients, with 3 non-assessable vessels due to either severe calcification or motion artefacts which were considered positive for stenoses) with a sensitivity of 95% (21/22, 95% CI 77–100) and specificity of 94% (204/218, 95% CI 89–97); NPV was 99% (204/205, 95% CI 96–100), and PPV was 60% (21/35, 95% CI 38–80).

Conclusion
Our study demonstrates high sensitivity, specificity, and NPV of DSCT to detect significant CAD in selected patients with rate controlled AF.

Keywords
DSCT • Atrial fibrillation • Stenoses
Introduction

In patients with sinus rhythm, the diagnostic performance of coronary computed tomography (CT) angiography to rule out or identify significant coronary artery disease (CAD) has been thoroughly investigated.1–6 The introduction of dual-source CT (DSCT) in 2006 with its higher temporal resolution has lead to further progress in achieving better image quality, especially in patients with high or irregular heart rates in whom the diagnostic performance achieved with single-source CT scanners, which have lower temporal resolution, is suboptimal.7–13 Regular sinus rhythm has always been considered a prerequisite for an adequate examination.

Atrial fibrillation (AF) is the most common arrhythmia and has been an obstacle for proper assessment of the coronary arteries using coronary CT angiography. Preliminary data involving small patient cohorts comparing CT angiography to invasive coronary angiography as the gold standard in identifying significant coronary stenoses have reported promising results.14,15

In our study, we analysed the accuracy of DSCT to identify significant coronary stenoses in patients with AF referred for invasive coronary angiography.

Methods

One hundred and ten consecutive patients with AF and absence of previously known CAD admitted for a first diagnostic invasive coronary angiography were screened for study participation over a period of 15 months. Out of these, 50 patients were excluded either due to renal insufficiency defined as a serum creatinine > 1.4 mg/dL, inability to maintain an adequate breath hold or due to rapid AF non-responsive to β-blockers nor calcium-channel blockers (mean heart rate > 100 b.p.m.). Sixty remaining patients [34 males and 26 females, mean age 71 ± 7 years, mean body mass index (BMI) 29 ± 6] were included and subjected to coronary CT angiography. Figure 1 summarizes inclusion criteria. Written informed consent was obtained from each patient before the examination.

Dual-source computed tomography examination

All patients were in AF at the time of the scan. Patients with a mean heart rate > 100 beats/min received 100 mg of atenolol orally 45–60 min before DSCT. If the mean heart rate remained > 100 beats/min at the time of scanning, up to four doses of metoprolol 5 mg or a single dose of diltiazem 5 mg were given intravenously. All patients received isosorbide dinitrate 0.8 mg sublingually before DSCT.

Coronary CT angiography was performed in all patients using DSCT (Definition, Siemens Medical Solutions, Forchheim, Germany) within 24 h before invasive coronary angiography. A contrast-enhanced volume data set was acquired with retrospective electrocardiogram (ECG) gating without using tube current modulation to allow reconstructions during all phases of the cardiac cycle. Data acquisition parameters for CT angiography were 0.6 mm collimation, 330 ms rotation time, 120 kV tube voltage in 37 patients (BMI > 30), and 100 kV in 23 patients (BMI < 30). Tube current was 400 mAs for patients scanned with a tube voltage of 120 kV and 360 mAs for patients scanned with 100 kV. Scan direction was cranio-caudal, and scan volume ranged from the mid-pulmonary artery to below the diaphragmatic face of the heart. After placing an antecubital 18-G intravenous access, contrast agent transit time (iopromide, 370 mg of iodine/mL; Ultravist 370, Schering, Berlin, Germany) was assessed by injecting a test bolus of 10 mL followed by a saline flush of 50 mL, both at a flow rate of 6 mL/s using a dual-head power injector (CT Stellant, Medrad Inc., Indianola, PA, USA). Contrast transit time was defined as the time between the start of contrast injection and maximum enhancement in the ascending aorta at the level of the coronary ostia. For angiographic CT data acquisition, a delay of 2 s longer than the contrast transit time was used to ensure adequate contrast enhancement of the coronary arteries. The volume of contrast agent injected for the scan depended on the estimated scan duration. Contrast was injected at a flow rate of 6 mL/s for the same duration as data acquisition, but for at least 10 s. Overall quantity varied from 60 to 110 mL. Contrast injection was followed by a 50-mL saline chaser bolus (6 mL/s).

Image reconstruction

Using a half-scan reconstruction algorithm (temporal resolution was 83 ms), overlapping axial cross-sectional images with 0.75 mm slice

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**Figure 1** Flow diagram showing patients eligible for scanning.
thickness and 0.4 mm increment were reconstructed using a medium sharp convolution kernel (B26f). In the presence of significant calcification, images were reconstructed with 0.6 mm slice thickness and 0.3 mm increment using a sharp convolution kernel (B46f). For each patient a diastolic phase using relative percentage approach (70–80% of R-peak to R-peak interval), a diastolic absolute delay (100 ms before R-peak) as well as a systolic phase using absolute delay reconstruction (300 ms after R-peak) were rendered. Further diastolic or systolic absolute delay reconstructions in increments of 25 ms were rendered for each patient if necessary to achieve optimum image quality free of artefacts if the three default reconstructions were not sufficient. In addition, the trigger signal was manually edited, deleted, or added to compensate for very long or very short cardiac cycles. Electrocardiogram editing aimed at skipping data sampling just before beats with the shortest coupling interval, whereas maintaining sampling in cardiac cycles with a relatively long diastole.

Image analysis
Rendered reconstructions were displayed on dedicated workstations (Leonardo; Siemens Medical Solutions, Forchheim, Germany). Two readers, each with >3 years of experience in coronary CT angiography, jointly analysed the DSCT data sets. Review of the original transaxial images, multiplanar reconstructions, and curved multiplanar reconstructions were used to evaluate the data sets. All evaluable coronary artery segments >1.5 mm were visually evaluated for the presence of significant stenoses, defined as a diameter reduction of >50%.

Invasive angiography
Invasive coronary angiography served as the standard of reference to validate DSCT and was performed within 24 h after Coronary CT angiography. Standard projections were obtained after intracoronary injection of 0.2 mg isosorbide dinitrate and evaluated offline by an independent observer. The diameter stenosis was determined visually by taking into account the luminal narrowing from two orthogonal projections. A significant stenosis was assumed if the diameter reduction was ≥50%.

Effective radiation dose
The effective dose of DSCT angiography was derived from the product of the dose length product (DLP) and a conversion factor of 0.014 for chest CT in adults.16

Statistical methods
Statistical analysis was done using SPSS for Windows release 15.0 (SPSS Inc., Chicago, IL, USA). All data are expressed as mean ± SD for continuous variables and as percentage ratio for categorical data. For continuous variables, t-test was used to detect statistical significance. P-values of <0.05 were considered significant.

Before starting the study, sample size estimate using the method described by Buderer et al.17 was calculated. Assuming a sensitivity of DSCT of 90% to detect patients with at least one significant stenosis in our patient cohort, a confidence interval (CI) of 10% and a 60% prevalence of significant disease, a sample size of 58 patients was estimated to calculate the need for adequate sensitivity.

Diagnostic accuracy for the detection of significant lesions by DSCT in comparison to invasive coronary angiography was expressed as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% CIs. The primary form of evaluation in our study was the per-patient analysis. This analysis was performed for any significant stenosis where patients with a detectable stenosis, as well as patients with at least one unevaluable vessel, were classified as ‘positive’ (because the presence of a stenosis could not be ruled out and invasive angiography would be the clinical consequence). Patients in whom all vessels were evaluable and no significant stenosis was present were classified as ‘negative’. Calculations were also done on a per-artery basis. In this analysis, vessels classified as unevaluable were considered positive for stenoses.

To eliminate bias introduced by the fact that observations in several coronary arteries of the same patient are not independent, we reported the CIs for sensitivity, specificity, NPV, and PPV using the method described by Drake et al.18 for covariance calculation combined with Wilson19 score interval calculation that handles the issue of centre shift for CIs.

Results
Coronary CT angiography was successfully performed in all 60 patients (34 males and 26 females, mean age 71 ± 7 years, mean BMI 29 ± 6). Indications for invasive coronary angiography were unexplained left ventricular dysfunction (n = 9), high pretest probability of CAD (n = 24), intermediate probability of CAD with a positive or an inconclusive stress test (n = 21) or preoperative assessment prior to non-coronary cardiac surgery (n = 6). The pretest probability for CAD for both patient groups was calculated on the basis of age, gender, and symptoms.20

Seventy-seven per cent of the patients (46/60) were on long-term β-blockers whereas only 32% (19/60) were on long-term medication with cardiac glycosides. All patients were in AF at the time of the scan (39 patients with permanent AF and 21 with persistent AF). Mean heart rate was 70 ± 15 b.p.m. (range 32–107 b.p.m.). Additional medication was given in 32 patients (53%, 3 patients

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<th>Table 1 Patient characteristics</th>
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<td>Long-term β-blocker therapy, n (%)</td>
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<td>Effective radiation dose, mean ± SD (range)</td>
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received only 100 mg atenolol orally, 8 patients diltiazem 5 mg as a single dose slowly intravenously, and 21 patients 5–20 mg metoprolol intravenously). In 30 patients (50%) additional reconstructions with or without ECG editing in addition to the previously described default reconstructions were needed to achieve diagnostic image quality. Diastolic reconstructions were found to be diagnostic in 40% of the patients (24/60), systolic reconstructions in 37% (22/60), and in 23% of patients (14/60) reconstructions in both diastole and systole were needed to adequately assess the entire coronary tree. In only two patients, the diastolic phase reconstruction using relative percentage approach (70–80% of R-peak to R-peak interval) was sufficient for assessment, otherwise in the remaining 58 patients (97%) absolute delay reconstructions with or without ECG editing were necessary. Among diastolic reconstructions, reconstructions using −100 ms absolute delay from the peak of the R-wave yielded the best image quality in most patients, whereas among systolic reconstructions using 300 ms absolute delay following peak R-wave most frequently yielded best systolic image quality. Patient characteristics are shown in Table 1.

Per-patient analysis

In the per-patient analysis, arteries classified as unevaluable by DSCT were regarded as positive for presence of stenoses. Invasive angiography identified 14 patients with at least one significant stenosis. The accuracy of DSCT for accurately detecting—or ruling out—patients with at least one significant stenosis was 88% (53/60), sensitivity was 100% (14/14, 95% CI 77–100), and specificity was 85% (39/46, 95% CI 71–94). Negative predictive value was 100% (39/39, 95% CI 91–100) and PPV was 67% (14/21, 95% CI 43–85). In three patients, one artery was considered unevaluable in DSCT [1 left main coronary artery (LM) due to heavy calcification and 2 right coronary arteries (RCAs) due to motion artefacts]. Out of those three patients only one patient was identified to have a significant stenosis in invasive angiography.

Per-artery analysis

A second analysis was performed on a per-artery basis. Coronary segments <1.5 mm in diameter were excluded from the analysis (26 out of 790 coronary segments). Out of 240 vessels in 60 patients [LM, left anterior descending artery (LAD), left circumflex coronary artery (LCX), RCA], 3 vessels (1%) were considered unevaluable due to either heavy calcification (1 artery, LM) or motion artefacts (2 arteries, RCA) and were considered positive for the presence of stenoses. Invasive angiography classified 22 arteries as having significant stenosis and 218 arteries as free of significant disease. The sensitivity of DSCT for detection of significant

![Figure 2](image-url)

**Figure 2** Patient with high grade stenosis in left anterior descending artery. Left anterior descending artery stenosis was well identified in dual-source computed tomography. Mean heart rate 68 b.p.m. (A) Curved multiplanar reconstruction of the left main and left anterior descending coronary artery. High grade left anterior descending artery stenosis marked by the arrow. (B) Invasive angiogram of the left anterior descending coronary artery showing high grade stenosis. (C) Curved multiplanar reconstruction of the left main and left circumflex coronary artery showing diffuse disease yet no significant stenosis. (D) Invasive coronary angiogram of the left circumflex coronary artery. (E) Curved multiplanar reconstruction of the right coronary artery showing plaques with no relevant stenoses. (F) Invasive coronary angiogram of the right coronary artery. No significant stenoses present.
stenosis compared with invasive angiography as the gold standard was 95% (21/22, 95% CI 77–100) and specificity was 94% (204/218, 95% CI 89–97). Negative predictive was 99% (204/205, 95% CI 96–100) and PPV was 60% (21/35, 95% CI 38–80) (Figures 2 and 3). DSCT failed to identify a significant stenosis in the LCX in 1 patient (vessel heavily calcified) and overestimated the degree of stenoses in 11 lesions (8 patients). The three arteries classified as unevaluable in DSCT and hence considered as positive for stenoses, were classified as free of significant disease in invasive angiography.

**Effective radiation dose**

The mean DLP for all 60 patients was $1186 \pm 375$ mGy*cm (range: 630–2038 mGy*cm). Using a conversion factor of 0.014 for chest CT in adults, this corresponds to a mean effective dose of $16 \pm 5$ mSv. For 37 patients scanned with a tube voltage of 120 kV (mean BMI 32) the mean DLP was $1439 \pm 239$ mGy*cm which corresponds to a mean effective radiation dose of $20 \pm 3$ mSv. For 23 patients scanned using a tube voltage of 100 kV (mean BMI 27), DLP was significantly lower with a mean DLP of $789 \pm 109$ mGy*cm corresponding to a mean effective radiation dose of $11 \pm 1$ mSv ($P$-value of $<0.001$).

**Discussion**

Atrial fibrillation is a major challenge for coronary CT angiography. Until recently, given the relatively low temporal resolution offered by single-source CT scanners, AF was considered a contraindication for performing an adequate CT coronary angiogram. Attempts to improve temporal resolution in single-source CT scanners by using multi-cycle reconstruction algorithms are not of benefit in AF patients owing to the variable R–R intervals. With the introduction of DSCT, which provides a temporal resolution of 83 ms with single-cycle reconstruction, it seems more feasible to achieve adequate image quality in patients with AF. Recent data with small patient cohorts comparing diagnostic accuracy of DSCT in identification of significant CAD to invasive angiography reported promising results.14,15

We performed coronary CT angiography in 60 patients (mean HR 70 ± 15 b.p.m., mean age 71 ± 7 years) referred for invasive coronary angiography. On a per-patient basis, sensitivity and specificity for identifying significant CAD in DSCT was 100% (14/14, 95% CI 77–100) and 85% (39/46, 95% CI 71–94), respectively. On a per-artery basis, sensitivity was 95% (21/22, 95% CI 77–100) and specificity was 94% (204/218, 95% CI 89–97).
Figure 4 Patient with normal coronaries. Curved multiplanar reconstructions using different cardiac phases as well as electrocardiogram editing. Mean heart rate 80 b.p.m. Invasive angiography correlation showing normal coronaries. (A, B, C) Curved multiplanar reconstructions of the left main coronary artery, left anterior descending artery, left circumflex coronary artery, and right coronary artery using different reconstructions. (A) Reconstruction at 70% R-peak to R-peak interval. (B) Absolute delay reconstruction −100 ms before R-peak with no electrocardiogram editing. (C) Absolute delay reconstruction −100 ms before R-peak with electrocardiogram editing. Beats with short coupling intervals were skipped to try to maintain regular intervals. Obvious improvement of the image quality and of the motion artefacts after electrocardiogram editing. (D, E, F) Invasive angiogram of left main coronary artery, left anterior descending artery, left circumflex coronary artery, and right coronary artery showing normal coronaries.
97). In a recent study, Rist et al.\textsuperscript{15} reported a sensitivity of 90%/89% and specificity of 82%/98% on a per-patient/per-segment basis, respectively, to identify significant CAD in 21 patients who underwent DSCT angiography and invasive coronary angiography. The lower sensitivity in their cohort may be explained by the fact that in their study only two reconstructions were used for the assessment of the data sets. These two default reconstructions included a diastolic phase 70\% from the R-peak to R-peak interval and a systolic phase using absolute delay reconstruction 300 ms from the peak R-wave. Further reconstructions were not done, nor was ECG editing used. In a study by Oncel et al.\textsuperscript{14} reporting their initial experience with 15 patients with AF, in whom DSCT data sets were compared with invasive angiography, per-patient sensitivity and specificity was 89 and 83\%, respectively. On a per-artery basis, a sensitivity of DSCT to identify significant CAD was 87\% and specificity was 96\%. In the Oncel study, reconstructions were obtained in all cardiac phases in increments of 50 ms, yet no ECG editing was reported. This may have contributed to the lower sensitivity as compared with our results. We observed that ECG editing was required to optimize image quality in 50\% of the patients (Figure 4). Cademartiri et al.\textsuperscript{21} previously reported an improved image quality using ECG editing in patients with mild irregularities. Furthermore the mean heart rates in the Oncel and Rist studies were higher than mean heart rate in our study (83 ± 9 and 77 ± 25 b.p.m., respectively, vs. 70 ± 15 b.p.m.).

In the previously mentioned studies, the percentage of unevaluable CT data sets ranged between 6 and 8\%. Rist et al. and Oncel et al. reported 6\% of the data sets as un evaluable, whereas Wolak et al.\textsuperscript{22} reported a percentage of 8\%. In our study, three patients (5\%) had one un evaluable artery and were considered positive for coronary stenoses in the per-patient and per-artery analysis. In those patients, invasive angiography did not identify significant stenoses in the arteries considered un evaluable in CT.

Both the Oncel study and the Rist study agree that systolic phase reconstructions, namely 300 ms after peak R-wave yielded the best diagnostic images.\textsuperscript{14,15} In the study performed by Wolak et al.\textsuperscript{22} systolic reconstructions alone were sufficient in 18\%, diastolic reconstructions alone in 27\% and in 55\% of the cases both phases were needed to assess the coronary tree. Our results show that in 33\% of the patients, systolic reconstructions alone were sufficient for assessment of the entire coronary tree, diastolic reconstructions alone in 42\% and reconstructions in both phases were needed in 25\% of the cases. The superiority of systolic phase reconstructions in the Oncel\textsuperscript{14} and Rist\textsuperscript{15} study may be explained by the slightly higher mean heart rate in their study as well as lack of ECG editing in their adopted reconstructions.

Tube current modulation was not adopted in our study to allow reconstructions through the entire cardiac cycle, as different phases were required for assessment of the coronary arteries.

Effective radiation dose in our patient cohort was 16 ± 5 mSv (for all patients) which is lower than mean effective radiation dose reported by Wolak et al.\textsuperscript{22} (26 ± 7 mSv) and higher than the mean doses reported by Rist et al.\textsuperscript{15} (13.2 mSv) and Oncel et al.\textsuperscript{14} (13.8 mSv). Effective radiation dose ranged from 9 to 28 mSv. This can be explained by the wide range of heart rates (32–107 b.p.m.) resulting in different pitch values and subsequently different radiation doses. Using lower tube voltage in 23 patients with a BMI below 30 (mean BMI 27) resulted in a significantly lower mean effective radiation dose (11 mSv) compared with 37 patients (mean BMI 32, 20 mSv) scanned using a tube voltage of 120 kV (P-value of <0.001). We therefore recommend reduction of the tube voltage in patients with average BMI. In spite of reducing tube voltage in patients with lower BMI, mean effective radiation dose in our study was higher than would currently be considered standard. This is due to the fact that tube current modulation protocols were not adopted in our data acquisition protocol, in order to allow for reconstructions at any desired time instant in the cardiac cycle. This will, of course, substantially limit the use of CT angiography in patient with AF, particularly if they are of younger age.

To our best knowledge, this is the largest study to date which compares DSCT to invasive coronary angiography for the detection of coronary artery stenoses (Table 2). In our study, DSCT displayed a high sensitivity, specificity, and NPV to identify significant CAD as compared with invasive coronary angiography in patients with rate controlled AF. However, the results of our study represent a single centre experience and can therefore be generalized only with limitations. Moreover, mean effective radiation dose in our cohort is relatively high (16 mSv). This is due to absent tube current modulation to allow for flexible reconstructions at every point of the cardiac cycle. Herzog et al.\textsuperscript{23} recently reported significantly lower effective radiation doses in patients examined using low dose CT angiography protocols, compared with invasive angiography. Unfortunately those protocols cannot be applied in AF patients due variable R–R intervals. In patients with controlled AF (HR < 100 b.p.m.), with carefully performed reconstructions using absolute delay algorithms and meticulous ECG editing, DSCT angiography may be an alternative to invasive coronary angiography in ruling out CAD.

### Funding
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| Table 2 Detection of coronary artery stenosis for all patients |
|----------------|----------------|---------------|----------------|---------------|
| Analysis       | Sensitivity (%) | Specificity (%) | NPV (%)        | PPV (%)       |
| Per-patient    | 100 (14/14) 95\% CI (77–100) | 85 (39/46) 95\% CI (71–94) | 100 (39/39) 95\% CI (91–100) | 67 (14/21) 95\% CI (43–85) |
| Per-artery     | 95 (21/22) 95\% CI (77–100) | 94 (204/218) 95\% CI (89–97) | 99 (204/205) 95\% CI (96–100) | 60 (21/35) 95\% CI (38–80) |
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References


