European Heart Journal (2008) **29**, 766–776
doi:10.1093/eurheartj/ehn044

Dual-source computed tomography coronary angiography: influence of obesity, calcium load, and heart rate on diagnostic accuracy

Hatem Alkadhi[1]*, Hans Scheffel[1], Lotus Desbiolles[1], Oliver Gaemperli[2], Paul Stolzmann[1], André Plass[3], Gerhard W. Goerres[1], Thomas F. Luescher[2], Michele Genoni[3], Borut Marincek[1], Philipp A. Kaufmann[2,4], and Sebastian Leschka[1]

[1]Institute of Diagnostic Radiology, University Hospital Zurich, Raemistrasse 100, Zurich 8091, Switzerland; [2]Cardiovascular Center, University Hospital Zurich, Zurich, Switzerland; [3]Clinic for Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland; and [4]Center for Integrative Human Physiology, University of Zurich, Zurich, Switzerland

Received 5 March 2007; revised 19 December 2007; accepted 17 January 2008; online publish-ahead-of-print 21 February 2008

See page 701 for the editorial comment on this article (doi:10.1093/eurheartj/ehn052)

Aims To prospectively investigate the diagnostic accuracy of dual-source computed tomography coronary angiography (CTCA) to diagnose coronary stenoses in relation to body mass index (BMI), Agatston score (AS), and heart rate (HR) as compared with catheter coronary angiography (CCA).

Methods and results Hundred and fifty consecutive patients (47 female, mean age 62.9 ± 12.1 years) underwent dual-source CTCA without HR control. Patients were divided into subgroups depending on the median of their BMI (26.0 kg/m^2), AS (194), and HR (66 b.p.m.). CCA was considered the standard of reference. Mean BMI was 26.5 ± 4.2 kg/m^2 (range 18.3–39.1 kg/m^2), mean AS was 309 ± 408 (range 0–4387), and HR was 68.5 ± 12.6 b.p.m. (range 35–102 b.p.m.). Diagnostic image quality was found in 98.1% of all segments (2020/2059). Considering not-evaluative segments at CTCA as false-positive, overall per-patient sensitivity, specificity, positive, and negative predictive value were 96.6%, 86.8%, 82.6%, and 97.5%, respectively. High HR did not deteriorate diagnostic accuracy of CTCA. High BMI and AS were associated with a decrease in per-patient specificity to 84.1% and 77.8%, respectively, while sensitivity and negative predictive value remained high.

Conclusion Dual-source CTCA provides high diagnostic accuracy irrespective of the HR and serves as a modality to rule-out coronary artery stenoses even in patients with high BMI and AS.

Keywords Dual-source CT coronary angiography • Calcium scoring • Body mass index • Heart rate • Conventional coronary angiography • Coronary artery disease

Introduction

Several studies using computed tomography coronary angiography (CTCA) with 64-slice technology have reported a high accuracy for the diagnosis or exclusion of coronary artery disease (CAD).[1–7] In particular the high negative predictive value ranging from 98 to 100% has indicated the usefulness of CTCA to reliably exclude CAD.[2,3,6] Thus, recommendations from the European Society of Cardiology and the American Heart Association (AHA) have included the use of CTCA as a valuable alternative to conventional catheter angiography (CCA) in patients with a low- to intermediate risk for CAD.[8–10] Despite the promising results with 64-slice CT, however, a decline in diagnostic accuracy was noted by several authors that was mainly caused by a high body mass index (BMI), severe arterial wall calcifications, and elevated heart rates (HRs).[4–6]

Dual-source CTCA represents the most recently introduced CT technology and is characterized by a high temporal resolution of 83 ms through simultaneous acquisition of data with two X-ray tubes and detectors.[11] As a matter of fact, first feasibility studies

* Corresponding author. Tel: +41 1255 3662, Fax: +41 1255 4443, Email address: hatem.alkadhi@usz.ch

have shown promising results of dual-source CTCA even in patients with high HRs.[12–14]

The purpose of this study was to prospectively investigate the diagnostic accuracy of dual-source CTCA in relation to BMI, vessel wall calcifications, and average HR as compared with the reference standard CCA.

Methods

Study population

In this study, we prospectively enrolled 150 consecutive patients (47 women, 103 men; mean age 62.9 ± 12.1 years; age range 37–86 years) who were referred to CCA for clinical reasons. The patients were asked to undergo CTCA for study purposes prior to CCA. None of the 150 patients declined to take part in the study. Patients were eligible if they had stable clinical conditions, i.e. if they were in Canadian Cardiac Society class I to III, and in New York Heart Association functional class I to III. Forty-six patients (30.6%) continued taking their baseline beta-receptor antagonist medication at the time of CTCA, no additional medication for HR control was administered prior to the scan. CCA and CTCA were performed within a mean time interval of 10 ± 6 days (median 8 days; range 1–22 days). The local ethics committee approved the study protocol and written informed consent was obtained from all the patients.

Patient selection criteria

Patients were included in the present study if they suffered from chest pain and had a negative or equivocal stress test. We only included patients with an intermediate pre-test probability of CAD according to the scoring method of Morise *et al.*[15] (i.e. 9 to 15 points), because those patients represent the target population for CTCA as recommended by various international societies.[8–10] For all patients, clinical data was collected including age, gender, body weight, body height, symptoms, oestrogen status, symptoms, and common cardiovascular risk factors. Family history was considered positive if CAD was diagnosed in a first-degree relative before the age of 60 years.[15] Chest discomfort was classified according to the three categories reported by Diamond[16] (i.e. typical angina, atypical angina, and non-anginal chest pain). The BMI was calculated from body weight and body height, and obesity was defined as a BMI over 27 kg/m^2.[15] Oestrogen status was considered on the criteria previously reported.[15] Patients were excluded from the study if they had renal insufficiency (creatinine level > 130 μmol/L), previous allergic reactions to iodinated contrast material, an unstable clinical condition, known CAD, and a high (i.e. >15 points) or low pre-test probability for CAD (i.e. <9 points).

Dual-source computed tomography scan protocol and image reconstruction

All patients were scanned on a dual-source CT scanner (Somatom Definition, Siemens Medical Solutions, Forchheim, Germany). An initial non-enhanced scan was performed for calcium scoring. Then, all patients received a single dose of 2.5 mg isosorbiddinitrate s. l. (Isoket, Schwarz Pharma, Monheim, Germany). For CTCA, 80 mL of iodixanol (Visipaque 320, 320 mg/mL, GE Heathcare, Buckinghamshire, UK) was injected at a flow rate of 5 mL/s followed by 30 mL saline solution. Contrast agent application was controlled by bolus-tracking in the ascending aorta (signal attenuation threshold 100 HU). Scanning parameters were: detector collimation $2 \times 32 \times 0.6$ mm^3, slice collimation $2 \times 64 \times 0.6$ mm^3 by means of a z-flying focal spot, gantry rotation time 330 ms, pitch of 0.2–0.5 depending on the HR, tube current time product 350 mAs per rotation, and tube potential 120 kV. Both non-enhanced and contrast-enhanced CT scans were performed from the level of the tracheal bifurcation to the diaphragm. Electrocardiography (ECG)-pulsing for radiation dose reduction[17] was used in all patients: At mean HRs below 60 b.p.m., full tube current was applied from 60 to 70%, at 61–70 b.p.m. from 50 to 80%, and at HRs above 70 from 30 to 80% of the R–R interval. Using a similar protocol, the effective radiation dose has been reported to be between 7 and 9 mSv.[18]

Non-enhanced CT scans were reconstructed at 70% of the R–R interval using 3.0 mm non-overlapping slices (reconstruction kernel B35f). CTCA scans were reconstructed during mid-to-end diastole at 60–70% of the R–R interval. When motion artefacts were present in these datasets, additional reconstructions were performed in 5% steps within the full tube current window. CTCA images were reconstructed with a slice thickness of 0.75 mm, a reconstruction increment of 0.5 mm, and using a soft-tissue convolution kernel (B26f). In presence of vessel wall calcifications, additional images were reconstructed using a sharp-tissue convolution kernel (B46) to compensate for blooming artefacts using the previously defined reconstruction interval with least motion artefacts.

Computed tomography coronary angiography data analysis

Coronary segments were defined according to the scheme of the AHA.[19] The right coronary artery (RCA) was defined to include segments 1–4; the left main artery (LM) to consist of segment 5, the left anterior descending artery (LAD) to include segments 6–10, and the left circumflex artery (LCX) to include segments 11–15. The intermediate artery was designated as segment 16, if present, and considered to belong to the LAD. All diameter measurements were performed with an electronic calliper tool.

Calcifications were quantified with scoring software (Syngo CaScore, Siemens). All lesions on more than two contiguous pixels with attenuation values greater than 130 HU were marked by an experienced observer and the calcium load in each patient was computed by using the Agatston method.[20] The number of separate calcified lesions was noted for each coronary artery segment.

CTCA data analysis was performed by two independent observers who were both unaware of the clinical history and to the results from CCA. First, both readers independently rated the image quality of each coronary segment as being diagnostic or non-diagnostic. For segments with non-diagnostic image quality rating, the reasons for impaired visualization were selected from the following list: low signal-to-noise ratio, calcium deposits, and motion artefacts.

Then, both observers independently assessed all coronary artery segments for the presence of haemodynamically significant stenoses, defined as luminal diameter narrowing > 50%. Vessel diameters were measured on reconstructions perpendicularly oriented to the vessel's centreline. For any disagreement in data analysis, consensus agreement was appended.

Catheter coronary angiography

CCA was performed according to standard techniques and at least two views in different planes were obtained for each coronary artery. One experienced observer being aware of the patients' clinical history but blinded to the results from CTCA evaluated all angiograms with regard to the presence (diameter reduction > 50%) or absence of significant stenoses. Coronary artery segments were defined according to the scheme of the AHA,[19] similar to CTCA.

Statistical analysis

Quantitative variables were expressed by means ± standard deviations and categorical variables as frequencies and percentages. Statistical analysis was performed using commercially available software (SPSS 12.0, SPSS Inc., IL, USA, and Sigma Stat, version 3.5, Systat Software Inc., Chicago, IL, USA). The sample size of 150 patients was determined to reach a power level of 90% for detecting a difference of 5% in sensitivity. Kappa statistics were calculated for inter-observer agreements for image quality read-out and assessment of significant coronary artery stenosis with CTCA. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated from χ^2tests of contingency. CCA was considered the standard of reference. Similar to a previous publication,[21] non-evaluative segments were considered as false-positive findings, because every patient with a non-evaluative segment would undergo CCA in clinical practice. Statistics for diagnostic accuracy of CTCA were calculated on a per-segment basis. Because of the possible interdependencies between different vessel segments, the statistics were calculated on a per-vessel (i.e. at least one significant stenosis or absence of any significant stenosis in one coronary artery), and on a per-patient basis (i.e. at least one significant stenosis or absence of any significant stenosis per patient). The medians of the HR, the average BMI, and the average Agatston score (AS) were used as cut-off points to subdivide the patients into two HR-, two BMI-, and two AS-groups, respectively. Diagnostic accuracy was calculated on a patient-based and segment-based analysis for these subgroups, and any differences between individual subgroups regarding diagnostic accuracy were tested for significance by using a χ^2 test with Yates correction for comparison of cross-tables. Bias is introduced in the diagnostic performance evaluation when a single vessel contributes multiple segments with coronary artery stenosis. We took into account the clustered nature of the data (i.e. the fact that there were not 2059 independent vessel segments but instead clusters of segments in 600 individual vessels and in 150 patients). To compensate for underestimation of standard errors by clustering, we corrected the statistical calculations using the generalized estimating equations method for clustering covariates. Confidence limits were calculated for kappa values and diagnostic accuracy parameters using the data corrected for clustering. Because the same patients were assigned to three different groups and compared three times each in relation with BMI, HR, and AS, respectively, the Bonferroni method was used to account for the increased probability of experiment-wise Type I error. Thus, the α-level of 0.05 was corrected for three planned comparisons with a statistical significance level for two-sided probability values of <0.016.

Results

CTCA and CCA were successfully performed in all patients without side-effects. Clinical characteristics and demographic data of patients are summarized in *Table 1*. Mean BMI was 26.5 ± 4.2 kg/m^2 (range 18.3–39.1 kg/m^2), mean AS was 309 ± 408 (range 0–4387), and average HR during scanning was 68.5 ± 12.6 b.p.m. (range 35–102 b.p.m.). Two patients (1.3%) had HR above 100 b.p.m. A total of 2059 segments were evaluated in 150 patients (one patient had separate origins of the LAD and the LCX from the left coronary sinus).

At CTCA, diagnostic image quality was found in 98.1% of all segments (2020/2059), while image quality of 39 segments (1.9%; RCA, $n = 15$; LM, $n = 0$; LAD, $n = 11$; LCX, n=13) was considered non-diagnostic. Inter-observer agreement for image quality ratings between readers was good (kappa = 0.72; 95% confidence interval, 0.62–0.83). Non-diagnostic image quality was most often present in distal segments (segment 3, $n = 6$; segment 8, $n = 5$; segment 13, $n = 4$), side-branches (segment 4, $n = 7$; segment 10, $n = 5$; segment 12, $n = 3$; segment 14, $n = 4$; segment 15; $n = 2$), and only in three more proximal segments (segment 2, $n = 3$). Reasons for image quality impairment for non-diagnostic segments were extensive wall calcification with beam hardening artefacts impairing arterial lumen visualization in 38.5% (15/39), motion artefacts in 33.3% (13/39), and low signal-to-noise ratio in 28.2% (11/39). Non-diagnostic segments were found in 11 patients (7.3%) with a mean BMI of 27.1 ± 4.1 kg/m^2 (range 20–33), mean AS of 690 ± 1018 (range 0–2594), and mean HR of 67.2 ± 13.1 b.p.m. (range 54–96 b.p.m.).

Prevalence of coronary artery stenosis

CCA identified 225 significant stenoses in 59 patients (39.3%). Single-vessel disease was found in 12.7% (19/150) and multi-vessel disease in 26.7% (40/150). Significant coronary artery stenosis was absent in 60.7% of patients (91/150). Coronary artery stenosis was most commonly present in the LAD (43/150; 28.7%), and less often in the LCX (35/150; 23.3%), the RCA (25/150; 16.7%), and LM (12/150; 8.0%).

Dual-source computed tomography coronary angiography and catheter coronary angiography for the evaluation of coronary stenosis

The kappa value for coronary artery stenosis detection with CTCA was 0.80 (95% confidence interval, 0.71–0.90) indicating an excellent inter-observer agreement between readers. CTCA correctly recognized 215 of the 225 significant stenoses detected with CCA (95.6%). In 29 segments lesions were incorrectly graded as being stenosed on CTCA. Including all 39 non-evaluable segments into analysis and considering them as false-positives, a total of 68 false-positive ratings were present. In 10 segments CTCA underestimated the severity of stenosis. On a vessel-based analysis, CTCA correctly identified 115 of the 119 vessels having at least one significant stenosis at CCA (96.6%). Ten vessels were incorrectly classified as being stenotic and four vessels were incorrectly classified as having no stenosis with CTCA. Non-diagnostic segments resulted in false-positive ratings in 2.2% of the vessels (13/599; RCA, $n = 5$; LM, $n = 0$; LAD, $n = 4$; LCX, $n = 4$), as no stenosis was present in the other evaluable segments of the vessel. On a per-patient analysis, CTCA correctly identified at least one significant coronary artery stenosis in 96.6% of patients (57/59) having significant stenoses at CCA, while diagnosis was missed in two patients (3.4%). In three patients without CAD at CCA, CTCA suspected significant stenosis (3.3%; 3/91). In nine of the 11 patients with non-diagnostic segments (81.8%), no significant CAD was present at CCA. Thus, unnecessary CCA would have been performed in clinical practice and these patients were considered as false-positives in the per-patient analysis. Diagnostic accuracy of CTCA on a per-segment, per-vessel, and on a per-patient analysis is summarized in *Table 2*.

Table 1 Patient characteristics

	Total	BMI groups		Calcium score groups		Heart rate groups	
		≤26.0 kg/m²	>26.0 kg/m²	≤194	>194	≤66 b.p.m.	>66 b.p.m.
No. of patients	150 (100%)	75 (50%)	75 (50%)	75 (50%)	75 (50%)	75 (50%)	75 (50%)
Age (years)	62.9 ± 12.1	62.3 ± 13.1	63.1 ± 10.5	60.3 ± 12.9	65.0 ± 10.2	61.9 ± 11.7	63.5 ± 12.0
Male/female	103/47	50/25	53/22	50/25	53/22	52/23	51/24
BMI (kg/m²)	26.5 ± 4.2	23.2 ± 1.9	29.7 ± 3.2	26.2 ± 4.3	26.7 ± 4.2	26.7 ± 4.3	26.2 ± 4.2
Average heart rate (b.p.m.)	68.5 ± 12.6	69.6 ± 12.6	67.7 ± 13.3	66.3 ± 12.8	70.9 ± 12.7	58.4 ± 5.9	78.9 ± 9.4
Calcium score	309 ± 408	523 ± 849	597 ± 741	42 ± 53	1078 ± 861	552 ± 799	568 ± 807
Cardiovascular risk factors							
Arterial hypertension	76 (50.7%)	30 (40.0%)	46 (61.3%)	34 (45.3%)	42 (56.0%)	37 (49.3%)	39 (52.0%)
Diabetes mellitus type II	29 (19.3%)	13 (17.3%)	16 (21.3%)	11 (14.7%)	18 (24.0%)	15 (20.0%)	14 (18.7%)
Smoking	62 (41.3%)	27 (36.0%)	35 (46.7%)	25 (33.3%)	37 (49.3%)	29 (38.7%)	33 (44.0%)
Positive family history	21 (14.0%)	13 (17.3%)	8 (10.7%)	11 (14.7%)	10 (13.3%)	13 (17.3%)	8 (10.7%)
Hyperlipidemia	57 (38.0%)	20 (26.7%)	37 (49.3%)	26 (34.7%)	31 (41.3%)	25 (33.3%)	32 (42.7%)
Obesity[a]	62 (41.3%)	–	62 (82.7%)	30 (40.0%)	32 (42.7%)	35 (46.7%)	27 (36.0%)
Symptoms							
Typical angina	32 (21.3%)	14 (18.7%)	18 (24.0%)	12 (16.0%)	20 (26.7%)	15 (20.0%)	17 (22.7%)
Atypical angina	91 (60.7%)	48 (64.0%)	43 (57.3%)	49 (65.3%)	42 (56.0%)	44 (58.7%)	47 (62.7%)
Non-anginal chest pain	27 (18.0%)	13 (17.3%)	14 (18.7%)	14 (18.7%)	13 (17.3%)	16 (21.3%)	11 (14.7%)

[a]Obesity was defined as BMI ≥ 27 kg/m².
BMI, body mass index; b.p.m., beats per minute.

Table 2 Diagnostic accuracy of dual-source computed tomography coronary angiography as compared with catheter coronary angiography in all 93 patients

	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	LR+	LR−
Segments (*n* = 2059)	215	1766	68	10	95.6% (215/225) [92.0–97.9]	96.3% (1766/1834) [95.3–97.1]	76.0% (215/283) [70.6–80.8]	99.4% (1766/1776) [99.0–99.7]	25.8 [20.4–32.6]	21.7 [11.8–39.7]
Vessels (*n* = 599)	115	457	23	4	96.6% (115/119) [90.5–99.9]	95.2% (457/480) [91.8–98.0]	83.3% (115/138) [75.0–90.2]	99.1% (457/461) [96.7–100]	20.2 [13.5–30.1]	28.3 [10.8–74.2]
RCA (*n* = 150)	25	117	7	1	96.2% (25/26) [79.3–100]	94.4% (117/124) [86.6–98.8]	78.1% (25/32) [58.9–91.8]	99.2% (117/118) [94.3–100]	17.0 [8.3–35.1]	24.5 [3.6–167.7]
LM (*n* = 149)	12	136	1	0	100% (12/12) [72.4–100]	99.3% (136/137) [94.9–100]	92.3% (12/13) [62.9–99.9]	100% (136/136) [96.2–100]	137.0 [19.4–965.6]	–
LAD (*n* = 150)	43	98	7	2	95.6% (43/45) [83.9–99.9]	93.3% (98/105) [85.8–98.3]	86.0% (43/50) [72.3–95.2]	98.0% (98/100) [92.0–100]	14.3 [7.0–29.4]	21.0 [5.4–81.5]
LCX (*n* = 150)	35	106	8	1	97.2% (35/36) [84.5–100]	93.0% (106/114) [85.6–97.9]	81.4% (35/43) [65.6–92.6]	99.1% (106/107) [93.9–100]	13.9 [7.1–27.1]	33.5 [4.8–231.4]
Patients (*n* = 150)	57	79	12	2	96.6% (57/59) [87.2–99.9]	86.8% (79/91) [77.2–93.9]	82.6% (57/69) [70.7–91.6]	97.5% (79/81) [90.5–99.9]	7.3 [4.3–12.4]	25.6 [6.5–100.2]

Note: raw data is in parentheses and 95% confidence intervals in brackets.
TP, true-positive; TN, true-negative; FP, false-positive; FN, false-negative; LR+, positive likelihood ratio; LR−, negative likelihood ratio; RCA, right coronary artery; LM, left main artery; LAD, left anterior descending artery; LCX; left circumflex artery. PPV, positive predictive value; NPV, negative predictive value.

Influence of obesity on diagnostic accuracy

The median of the BMI over all 150 patients was 26.0 kg/m^2; thus 75 patients (50.0%) had a BMI $\leq$ 26.0 kg/m^2 (mean 23.2 $\pm$ 1.9 kg/m^2) and 75 patients (50.0%) a BMI $>$ 26.0 kg/m^2 (mean 29.7 $\pm$ 3.2 kg/m^2). Non-evaluable segments were present in 1.4% of segments (14/1019) in patients with a BMI $\leq$ 26.0 kg/m^2, and in 2.4% of segments (25/1040) in patients with a BMI $>$ 26.0 kg/m^2. Diagnostic accuracy in the segment-based and patient-based analysis was comparable in both BMI groups (*Tables 3* and *4*) (*Figure 1*). The observed differences in diagnostic accuracy among both groups neither reached a level of significance for sensitivity [$\chi^2 < 0.01$, $P = 0.97$ (per segment); $\chi^2 = 0.03$, $P = 0.86$ (per patient)], specificity [$\chi^2 < 0.01$, $P = 0.96$ (per segment); ($\chi^2 = 0.10$, $P = 0.76$) (per patient)], positive predictive value [$\chi^2 = 0.08$, $P = 0.77$) (per segment); $\chi^2 = 0.01$, $P = 0.92$ (per patient)] nor negative predictive value [$\chi^2 < 0.01$, $P = 0.98$ (per segment); $\chi^2 < 0.01$, $P = 0.96$ (per patient)].

Influence of calcium load on diagnostic accuracy

The median of the AS over all 150 patients was 194; thus 75 patients (50.0%) had an AS $\leq$ 194 (mean 42 $\pm$ 53) and 75 patients (50.0%) an AS $>$ 194 (mean 1078 $\pm$ 861). Non-evaluable segments were present in 2.1% of segments (21/1023) in patients with an AS $\leq$ 194, and in 1.7% of segments (18/1036) in patients with an AS $>$ 194. The rate of stenosed coronary artery segments was higher in patients with an AS $>$ 194 (16.9%; 175/1036) than in patients with lower AS (3.9%; 40/1023). On a per-segment analysis, positive predictive value was lower in patients with an AS $<$ 194 (60.6%) than in the higher AS group (80.7%), while other diagnostic accuracy parameters were comparable (*Table 3*) (*Figure 2*). On a per-patient analysis, specificity was lower at high AS (77.8%) in comparison with the low AS group (92.7%; *Table 4*). Differences in diagnostic accuracy among both groups did not reached the level of significance for sensitivity [$\chi^2 = 0.02$, $P = 0.89$ (per-segment); $\chi^2 < 0.01$, $P = 0.95$ (per-patient)], specificity [$\chi^2 = 0.10$, $P = 0.75$ (per-segment); $\chi^2 = 0.16$, $P = 0.69$ (per-patient)], positive [$\chi^2 = 1.35$, $P = 0.25$ (per-segment); $\chi^2 = 0.02$, $P = 0.88$ (per-patient)] or negative predictive value [$\chi^2 < 0.01$, $P = 0.99$ (per-segment); $\chi^2 < 0.01$, $P = 0.96$ (per-patient)].

Influence of heart rate on diagnostic accuracy

The median of the HR over all 150 patients was 66 b.p.m.; thus 75 patients (50.0%) had a HR $\leq$ 66 b.p.m. (mean 58.4 $\pm$ 5.9 b.p.m.) and 75 patients (50.0%) a HR $>$ 66 b.p.m. (mean 78.9 $\pm$ 9.4 b.p.m.). Non-diagnostic segments were present in 1.6% of all segments (17/1041) in patients with HR $\leq$ 66 b.p.m., and in 2.2% of all segments (22/1018) in patients with HR $>$ 66 b.p.m. Diagnostic accuracy was comparable in both HR subgroups on a per-segment and per-patient analysis (*Tables 3* and *4*) (*Figure 3*). Both on a per-segment and per-patient analysis, the differences in diagnostic accuracy parameters among the different HR groups were neither significant for sensitivity [$\chi^2 < 0.01$, $P = 0.96$ (per segment); $\chi^2 = 0.03$, $P = 0.86$ (per patient)], specificity [$\chi^2 < 0.01$, $P = 0.99$ (per segment); $\chi^2 = 0.02$, $P = 0.90$ (per patient)], positive [$\chi^2 = 0.11$, $P = 0.74$ (per segment); $\chi^2 = 0.02$, $P = 0.90$ (per patient)] nor negative predictive value [$\chi^2 < 0.01$, $P = 0.98$ (per segment); $\chi^2 = 0.02$, $P = 0.88$ (per patient)].

Discussion

High diagnostic accuracy for the assessment of coronary artery stenosis has been repetitively reported with 64-slice CTCA. Although reported sensitivities vary between 73[1] and 99%[3,6] and specificities vary from 90[5] to 97%,[1,2] negative predictive values were invariably high ranging between 98 and 100%.[2,3,6] This led to the widely accepted conclusion that a normal CTCA reliably rules-out significant CAD and further invasive workup with CCA can be omitted. This concept presumes that the entire coronary artery tree can be imaged with a diagnostic image quality and no segment must be excluded from analysis. However, even with 64-slice CT up to 12% non-evaluative coronary segments were found[5] that were caused by a high calcium load, high BMI, and high HRs.[2,5,6] The present study demonstrates that dual-source CTCA provides a high diagnostic accuracy for the diagnosis of significant coronary stenoses with a per-segment sensitivity of 95.6% and specificity of 96.3%. While these values somewhat resemble the reported sensitivities of 73–99% and specificities of 90–97% with 64-slice CT,[1–5] we performed no HR control prior to CT and did not exclude non-diagnostic segments from analysis but rather considered these as false-positive ratings on an intent-to-diagnose basis.

Heart rate

With 64-slice CTCA, the temporal resolution was not high enough to compensate for motion artefacts with higher HRs.[1–3,5,6,22] Consequently, beta-receptor antagonists were administered in most studies in patients with HRs above 65–70 b.p.m.[1,3–6] Dual-source CTCA provides HR independent temporal resolution of 83 ms by using a mono-reconstruction algorithm.[11] Similar to this study, Scheffel *et al.*[12] observed no differences regarding diagnostic accuracy in patients with HR above and below 70 b.p.m. Thus, our results suggest omitting pre-medication for HR control with beta-receptor antagonists when using dual-source CTCA. Parallel to the consistently high diagnostic accuracy at high HRs, the rate of non-evaluable segments appears to be decreased with dual-source CTCA (i.e. 1.9% in this and 1.4% in the study of Scheffel *et al.*[12]) as compared with most 64-slice CTCA studies.[1,4,5]

Body mass index

Correct evaluation of CTCA might be difficult in obese patients due to higher image noise. Raff *et al.*[5] reported with 64-section CT a deterioration of diagnostic accuracy in obese patients. The present findings employing dual-source CT are consistent with and extend those of the previous 64-section CTCA study. We found a comparable decrease in specificity and positive predictive value in both the segment- and patient-based analysis with higher BMI. In addition, the rate on non-evaluable segments was 1.4% in patients with low BMI but higher in overweight and obese patients (i.e. 2.4%). This deterioration of diagnostic accuracy might be explained by scattering and absorption of radiation in obese

Table 3 Effect of body mass index, calcium score, and heart rate on diagnostic accuracy of dual-source computed tomography coronary angiography as compared with catheter coronary angiography in a segment-based analysis

	Sensitivity	Specificity	PPV	NPV	LR+	LR−
BMI groups						
≤26.0 kg/m^2	94.5% (86/91) [87.6–98.2]	96.6% (896/928) [95.2–97.6]	72.9% (86/118) [63.9–80.7]	99.5% (896/901) [98.7–99.8]	27.4 [19.4–38.7]	17.6 [7.5–41.2]
>26.0 kg/m^2	96.3% (129/134) [91.5–98.8]	96.0% (870/906) [94.5–97.2]	78.2% (129/165) [71.1–84.2]	99.4% (870/875) [98.7–99.8]	24.2 [17.6–33.4]	25.7 [10.9–60.8]
Calcium score groups						
≤194	90.9% (40/44) [78.3–97.5]	97.3% (953/979) [96.1–98.3]	60.6% (40/66) [47.8–72.4]	99.6% (953/957) [98.9–99.9]	34.2 [23.2–50.6]	10.7 [4.2–27.3]
>194	96.7% (175/181) [92.9–98.8]	95.1% (813/855) [93.4–96.4]	80.7% (175/217) [74.8–95.7]	99.3% (813/819) [98.4–99.7]	19.7 [14.6–26.5]	28.7 [13.1–63.0]
Heart rate groups						
≤66 b.p.m.	95.1% (97/102) [88.9–95.4]	96.2% (903/939) [94.7–97.3]	72.9% (97/133) [64.6–80.3]	99.5% (903/908) [98.7–99.8]	24.8 [18.0–34.3]	19.6 [8.3–46.1]
>66 b.p.m.	95.9% (118/123) [90.8–98.7]	96.4% (863/895) [95.0–97.5]	78.7% (118/150) [71.2–84.9]	99.4% (863/868) [98.7–99.8]	26.8 [19.1–37.8]	23.8 [10.1–56.0]

Note: raw data is in parentheses and 95% confidence intervals in brackets.
BMI, body mass index; b.p.m., beats per minute; TP, true-positive; TN, true-negative; FP, false-positive; FN, false-negative; LR+, positive likelihood ratio; LR−, negative likelihood ratio. PPV, positive predictive value; NPV, negative predictive value.

Table 4 Effect of body mass index, calcium score, and heart rate on diagnostic accuracy of dual-source computed tomography coronary angiography as compared with catheter coronary angiography in a patient-based analysis

	Sensitivity	Specificity	PPV	NPV	LR+	LR−
BMI groups						
≤26.0 kg/m^2	96.4% (27/28) [81.0–100]	89.4% (42/47) [76.2–97.2]	84.4% (27/32) [66.5–95.4]	97.7% (42/43) [87.0–100]	9.1 [4.0–20.8]	25.0 [3.6–171.9]
>26.0 kg/m^2	96.8% (30/31) [82.6–100]	84.1% (37/44) [69.3–94.1]	81.1% (30/37) [64.1–92.7]	97.4% (37/38) [85.5–100]	6.1 [3.1–12.0]	26.1 [3.8–180.0]
Calcium score groups						
≤194	100% (20/20) [82.5–100]	92.7% (51/55) [81.7–98.7]	83.3% (20/24) [62.6–95.3]	100% (51/51) [93.0–100]	13.8 [5.4–35.3]	–
>194	94.9% (37/39) [82.0–99.9]	77.8% (28/36) [60.2–90.6]	82.2% (37/45) [67.3–92.6]	93.3% (28/30) [77.2–99.8]	4.3 [2.3–7.9]	15.3 [3.9–54.3]
Heart rate groups						
≤66 b.p.m.	96.8% (30/31) [81.1–100]	86.4% (38/44) [72.1–95.4]	83.3% (30/36) [66.6–94.2]	97.4% (38/39) [85.8–100]	7.1 [3.4–15.0]	26.8 [3.9–184.8]
>66 b.p.m.	96.4% (27/28) [85.6–100]	87.2% (41/47) [73.5–95.8]	81.8% (27/33) [63.8–93.6]	97.6% (41/42) [86.7–100]	7.6 [3.6–16.0]	24.4 [3.6–167.9]

Note: raw data is in parentheses and 95% confidence intervals in brackets.
BMI, body mass index; b.p.m., beats per minute; TP, true-positive; TN, true-negative; FP, false-positive; FN, false-negative; LR+, positive likelihood ratio; LR−, negative likelihood ratio. PPV, positive predictive value; NPV, negative predictive value.

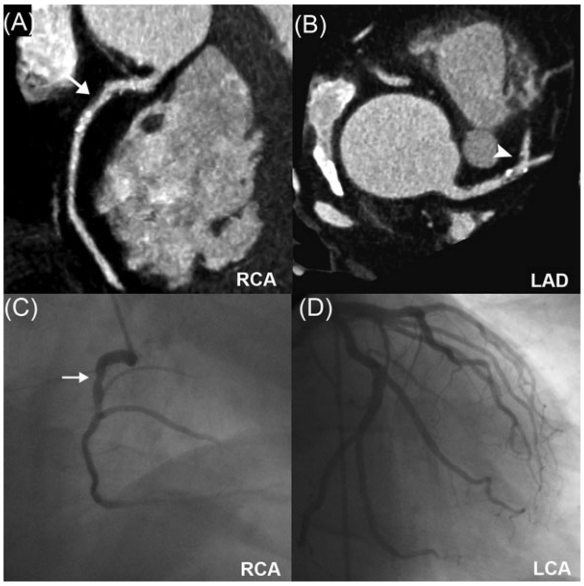

Figure 1 Dual-source computed tomography coronary angiography and catheter coronary angiography (CCA) in a 64-year-old man with typical chest pain. Body mass index was 35.1 kg/m^2, Agatston score was 386, and heart rate was 56 b.p.m. Curved multiplanar reformations of the right coronary artery (RCA, *A*) and left anterior descending artery (LAD, *B*) show moderate, non-significant luminal narrowing in the proximal segment of the RCA (arrow) and mid-segment of the LAD (arrowhead). Corresponding CCA of the RCA and left coronary arteries (LCA) confirms the computed tomography (CT) diagnosis of non-significant stenoses. Note the increased image noise of CT images in the obese patient.

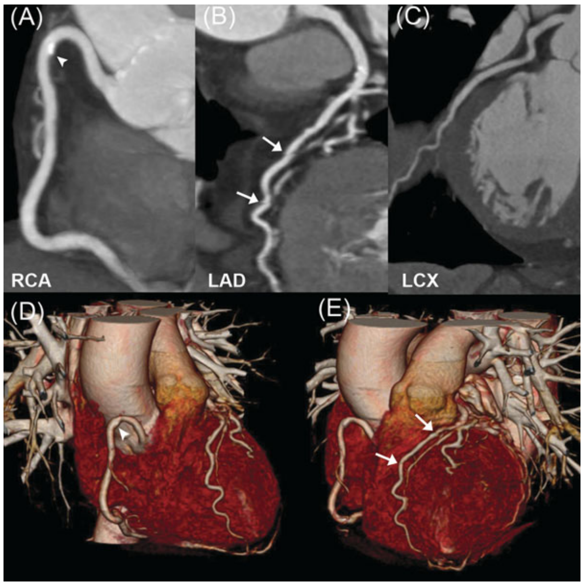

Figure 2 Dual-source computed tomography coronary angiography in a 67-year-old woman with tachycardia and atypical chest pain. Body mass index was 18.6 kg/m^2, Agatston score was 8, and heart rate was 99 b.p.m. Curved planar reformations of the right coronary artery (RCA, *A*), left anterior descending artery (LAD, *B*), and left circumflex artery (LCX, *C*) demonstrate normal coronary arteries without significant stenosis. A small calcified wall deposit is shown in the proximal RCA resulting in minor luminal narrowing (arrowhead). Some slight motion artefacts are present in mid to distal LAD (arrows), but image quality was rated diagnostic in those segments. Volume rendered images (*D* and *E*) delineate the three-dimensional course of the coronary arteries and show minor motion artefacts in the LAD (arrows). Catheter coronary angiography (CCA) confirmed absence of significant stenoses.

patients resulting in poorer image quality of CT images due to increase in image noise and decrease in signal-to-noise ratio.[23] Since absorption mainly occurs in the softer part of the radiation beam hereby causing beam hardening, images in patients with a higher BMI are produced by harder radiation beam than images in patients with a lower BMI. In addition, low vessel opacification may occur in overweight and obese patients due to differences in distribution of blood volume in peripheral venous and central pulmonary circulation in various body constitutions when injecting a constant contrast medium amount.[23]

Calcium load

Arterial wall calcifications are characteristic of CAD and are often found in early stage arteriosclerosis.[24] At CT, large and dense calcified plaques cause blooming artefacts and result in a virtual increase of plaque volume and thus may obscure the coronary lumen. Consequently, high calcium load represents the main contributor to stenosis overestimation and false-positive ratings with CT.[2,5,6,25,26] Morgan-Hughes *et al.*[26] reported a calcium score threshold of >400 and Heuschmid *et al.*[25] a threshold of >1000 above, which the diagnostic accuracy of CTCA for stenosis evaluation significantly decreases. On the other hand, Cademartiri *et al.*[27] did not find a significant impairment of accuracy in the presence of high calcium load. Ong *et al.*[4] investigated the diagnostic accuracy of 64-slice CTCA with a median score of 142 as cut-off and found a decrease in sensitivity, specificity, and negative predictive value in the high calcium group in the per-segment analysis. In addition, the rate of non-evaluative segments increased from 2.7 to 13.1% with higher calcium scores. Raff *et al.*[5] reported in a 64-slice CTCA study, a significant deterioration in specificity and negative predictive value in patients with a calcium score >400. In our study, we found a similar deterioration in specificity on a per-patient analysis but a milder decrease in negative predictive value. As spatial resolution of dual-source CT is the same as that of single-source 64-slice CT, the higher diagnostic performance in our patients with higher HRs indicates superimposition of blooming by additional motion artefacts, as previously suggested.[12]

Limitations

There are several study limitations. First, dual-source CT offers technical abilities that have not been explored in this investigation, such as the use of multisegment reconstruction algorithms resulting

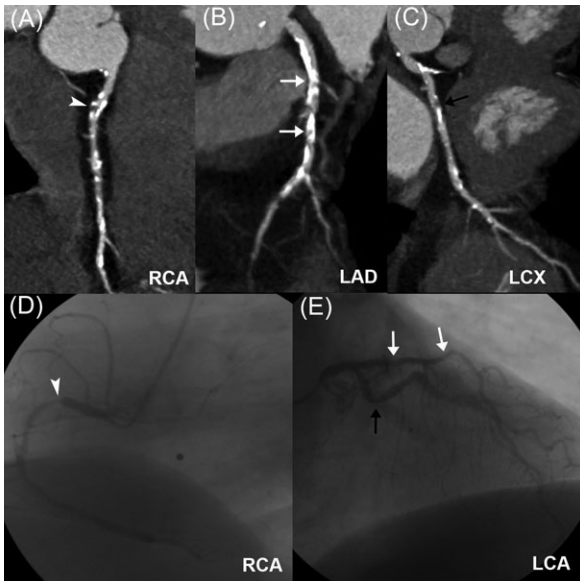

Figure 3 Dual-source computed tomography coronary angiography and catheter coronary angiography (CCA) in a 69-year-old man with typical chest pain. Body mass index was 28.0 kg/m^2, Agatston score was 1.317, and heart rate was 52 b.p.m. Curved planar reformation of the right coronary artery (RCA, *A*) shows a high-grade stenosis in the proximal segment (arrowhead) and multiple non-significant stenoses in the mid and distal RCA. In the proximal and mid-segment of the left anterior descending artery (LAD, *B*), dense calcified deposits were present and significant coronary stenoses were suspected at computed tomography (CT) (white arrows). Curved planar reformation of the left circumflex artery (LCX, *C*) shows moderate, non-significant luminal narrowing in the proximal segment (black arrow). Corresponding CCA of the RCA (*D*) and left coronary arteries (LCA) confirms diagnosis of significant stenosis in the proximal segment of the RCA (arrowhead) and non-significant coronary stenosis in the proximal segment of the LCX (black arrow). The suspected coronary stenoses in the proximal and mid-segment of the LAD were estimated as being non-significant resulting in false-positive classifications by CT.

in a temporal resolution of 42 ms at dedicated HRs[11] or scanning with two different energies for better plaque differentiation and lumen visualization.[28] In addition, we did not use dedicated dual-source CT obesity protocols in which the scanner operates both X-ray tubes with a total power of 160 kW. Secondly, stenosis assessment with CT coronary angiography was restricted to visual, semi-quantitative estimation, and no quantification of the degree of stenosis was performed. Thirdly, the prevalence of coronary artery stenosis was heterogeneous throughout the subgroups, which may have affected in particular the positive and negative predictive value. Finally, our study selection criteria may have introduced a bias because only patients with an intermediate pre-test probability of CAD who were referred for CCA to our hospital were included in the study. On the other hand, patients with intermediate risk of CAD represent the target population for CTCA as recommended by various international societies.[8–10]

In conclusion, dual-source CTCA provides a high diagnostic accuracy for the diagnosis or exclusion of significant coronary stenosis as compared with the reference standard CCA. While the high diagnostic accuracy is maintained even at high HRs, obesity and high calcium load still increase the rate of false-positive judgments and thus lead to a decline in specificity and positive predictive value. Nevertheless, sensitivity and negative predictive values are invariably high even in obese patients and in patients with high AS, further substantiating the modality to be a valuable tool for non-invasive exclusion of CAD and obviating the need for invasive workup.

Conflict of interest: none declared.

Funding

This work was supported by the National Center of Competence in Research, Computer Aided and Image Guided Medical Interventions of the Swiss National Science Foundation.

References

1. Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, Wintersperger B, Reiser M, Becker CR, Steinbeck G, Boekstegers P. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005;**46**:147–154.
2. Leschka S, Alkadhi H, Plass A, Desbiolles L, Grunenfelder J, Marincek B, Wildermuth S. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. *Eur Heart J* 2005;**26**: 1482–1487.
3. Mollet NR, Cademartiri F, van Mieghem CA, Runza G, McFadden EP, Baks T, Serruys PW, Krestin GP, de Feyter PJ. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. *Circulation* 2005;**112**:2318–2323.
4. Ong TK, Chin SP, Liew CK, Chan WL, Seyfarth MT, Liew HB, Rapaee A, Fong YY, Ang CK, Sim KH. Accuracy of 64-row multidetector computed tomography in detecting coronary artery disease in 134 symptomatic patients: influence of calcification. *Am Heart J* 2006;**151**:1323 e1–6.
5. Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *J Am Coll Cardiol* 2005;**46**:552–557.
6. Pugliese F, Mollet NR, Runza G, van Mieghem C, Meijboom WB, Malagutti P, Baks T, Krestin GP, deFeyter PJ, Cademartiri F. Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. *Eur Radiol* 2006;**16**: 575–582.
7. Ropers D, Rixe J, Anders K, Kuttner A, Baum U, Bautz W, Daniel WG, Achenbach S. Usefulness of multidetector row spiral computed tomography with 64- x 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. *Am J Cardiol* 2006;**97**:343–348.
8. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, Guerci AD, Lima JA, Rader DJ, Rubin GD, Shaw LJ, Wiegers SE. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American

Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 2006;**114**:1761–1791.

9. Fox K, Garcia MA, Ardissino D, Buszman P, Camici PG, Crea F, Daly C, De Backer G, Hjemdahl P, Lopez-Sendon J, Marco J, Morais J, Pepper J, Sechtem U, Simoons M, Thygesen K, Priori SG, Blanc JJ, Budaj A, Camm J, Dean V, Deckers J, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo J, Zamorano JL. Guidelines on the management of stable angina pectoris: executive summary: the Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology. *Eur Heart J* 2006;**27**:1341–1381.
10. Hendel RC, Patel MR, Kramer CM, Poon M, Carr JC, Gerstad NA, Gillam LD, Hodgson JM, Kim RJ, Lesser JR, Martin ET, Messer JV, Redberg RF, Rubin GD, Rumsfeld JS, Taylor AJ, Weigold WG, Woodard PK, Brindis RG, Douglas PS, Peterson ED, Wolk MJ, Allen JM. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *J Am Coll Cardiol* 2006;**48**:1475–1497.
11. Flohr TG, McCollough CH, Bruder H, Petersilka M, Gruber K, Suss C, Grasruck M, Stierstorfer K, Krauss B, Raupach R, Primak AN, Kuttner A, Achenbach S, Becker C, Kopp A, Ohnesorge BM. First performance evaluation of a dual-source CT (DSCT) system. *Eur Radiol* 2006;**16**:256–268.
12. Scheffel H, Alkadhi H, Plass A, Vachenauer R, Desbiolles L, Gaemperli O, Schepis T, Frauenfelder T, Schertler T, Husmann L, Grunenfelder J, Genoni M, Kaufmann PA, Marincek B, Leschka S. Accuracy of dual-source CT coronary angiography: first experience in a high pre-test probability population without heart rate control. *Eur Radiol* 2006;**16**:2739–2747.
13. Achenbach S, Ropers D, Kuettner A, Flohr T, Ohnesorge B, Bruder H, Theessen H, Karakaya M, Daniel WG, Bautz W, Kalender WA, Anders K. Contrast-enhanced coronary artery visualization by dual-source computed tomography–initial experience. *Eur J Radiol* 2006;**57**:331–335.
14. Johnson TR, Nikolaou K, Wintersperger BJ, Leber AW, von Ziegler F, Rist C, Buhmann S, Knez A, Reiser MF, Becker CR. Dual-source CT cardiac imaging: initial experience. *Eur Radiol* 2006;**16**: 1409–1415.
15. Morise AP, Haddad WJ, Beckner D. Development and validation of a clinical score to estimate the probability of coronary artery disease in men and women presenting with suspected coronary disease. *Am J Med* 1997;**102**:350–356.
16. Diamond GA. A clinically relevant classification of chest discomfort. *J Am Coll Cardiol* 1983;**1**:574–575.
17. Leschka S, Scheffel H, Desbiolles L, Plass A, Gaemperli O, Valenta I, Husmann L, Flohr TG, Genoni M, Marincek B, Kaufmann PA, Alkadhi H. Image quality and reconstruction intervals of dual-source CT coronary angiography: recommendations for ECG pulsing windowing. *Invest Radiol* 2007;**42**:543–549.
18. Stolzmann S, Scheffel H, Schertler T, Frauenfelder T, Leschka S, Husmann L, Flohr T, Marincek B, Kaufmann PA, Alkadhi H. Radiation dose estimates in dual-source computed tomography coronary angiography. *Eur Radiol* 2007; DOI 10.1007/s00330-007-0786-8.
19. Austen WG, Edwards JE, Frye RL, Gensini GG, Gott VL, Griffith LS, McGoon DC, Murphy ML, Roe BB. A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. *Circulation* 1975;**51**:5–40.
20. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;**15**:827–832.
21. Garcia MJ, Lessick J, Hoffmann MH. Accuracy of 16-row multidetector computed tomography for the assessment of coronary artery stenosis. *JAMA* 2006;**296**:403–411.
22. Leschka S, Wildermuth S, Boehm T, Desbiolles L, Husmann L, Plass A, Koepfli P, Schepis T, Marincek B, Kaufmann PA, Alkadhi H. Noninvasive coronary angiography with 64-section CT: effect of average heart rate and heart rate variability on image quality. *Radiology* 2006;**241**:378–385.
23. Husmann L, Leschka S, Boehm T, Desbiolles L, Schepis T, Koepfli P, Gaemperli O, Marincek B, Kaufmann P, Alkadhi H. [Influence of body mass index on coronary artery opacification in 64-slice CT angiography]. *RoFo* 2006;**178**:1007–1013.
24. Watson KE. Pathophysiology of coronary calcification. *J Cardiovasc Risk* 2000;**7**:93–97.
25. Heuschmid M, Kuettner A, Schroeder S, Trabold T, Feyer A, Seemann MD, Kuzo R, Claussen CD, Kopp AF. ECG-gated 16-MDCT of the coronary arteries: assessment of image quality and accuracy in detecting stenoses. *AJR Am J Roentgenol* 2005; **184**:1413–1419.
26. Morgan-Hughes GJ, Roobottom CA, Owens PE, Marshall AJ. Highly accurate coronary angiography with submillimetre, 16 slice computed tomography. *Heart* 2005;**91**:308–313.
27. Cademartiri F, Mollet NR, Lemos PA, Saia F, Runza G, Midiri M, Krestin GP, de Feyter PJ. Impact of coronary calcium score on diagnostic accuracy for the detection of significant coronary stenosis with multislice computed tomography angiography. *Am J Cardiol* 2005;**95**:1225–1227.
28. Boll DT, Hoffmann MH, Huber N, Bossert AS, Aschoff AJ, Fleiter TR. Spectral coronary multidetector computed tomography angiography: dual benefit by facilitating plaque characterization and enhancing lumen depiction. *J Comput Assist Tomogr* 2006;**30**: 804–811.