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CLINICAL RESEARCH

Imaging

FASTTRACK Feasibility of low-dose coronary CT angiography: first experience with prospective ECG-gating

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Aims	To determine the feasibility of prospective electrocardiogram (ECG)-gating to achieve low-dose computed tomography coronary angiography (CTCA).
Methods and results	Forty-one consecutive patients with suspected ($n = 35$) or known coronary artery disease ($n = 6$) underwent 64-slice CTCA using prospective ECG-gating. Individual radiation dose exposure was estimated from the dose-length product. Two independent readers semi-quantitatively assessed the overall image quality on a five-point scale and measured vessel attenuation in each coronary segment. One patient was excluded for atrial fibrillation. Mean effective radiation dose was 2.1 ± 0.6 mSv (range, 1.1–3.0 mSv). Image quality was inversely related to heart rate (HR) (57.3 ± 6.2 , range 39–66 b.p.m.; $r = 0.58$, $P < 0.001$), vessel attenuation (346 ± 104 , range 110–780 HU; $r = 0.56$, $P < 0.001$), and body mass index (26.1 ± 4.0 , range 19.1–36.3 kg/m ² ; $r = 0.45$, $P < 0.001$), but not to HR variability (1.5 ± 1.0 , range 0.2–5.1 b.p.m.; $r = 0.28$, $P = 0.069$). Non-diagnostic CTCA image quality was found in 5.0% of coronary segments. However, below a HR of 63 b.p.m. ($n = 28$), as determined by receiver operator characteristic curve, only 1.1% of coronary segments were non-diagnostic compared with 14.8% with HR of >63 b.p.m. ($P < 0.001$).
Conclusion	This first experience documents the feasibility of prospective ECG-gating for CTCA with diagnostic image quality at a low radiation dose (1.1–3.0 mSv), favouring HR <63 b.p.m.
Keywords	Low dose • Computed tomography coronary angiography • Feasibility • Prospective ECG-gating

Introduction

Since the introduction of 64-slice computed tomography (CT) and dual source CT technology, CT coronary angiography (CTCA) plays an increasing role in the clinical assessment of coronary artery disease (CAD).^{1–5} CTCA has been suggested to be most useful in patients with a low to intermediate pre-test probability for CAD.^{6–8} As the number of CTCA-capable scanners is constantly increasing, its role in clinical routine is likely to gain widespread acceptance.^{9,10}

However, radiation exposure of CTCA and its association to the risk of cancer induction has remained an issue of discussion.¹¹ This is even more eminent in the emerging field of hybrid cardiac imaging^{12–14} where the patient is additionally exposed to even higher radiation dose from nuclear perfusion scanning.¹⁵

New CTCA acquisition protocols have been proposed with prospective electrocardiogram (ECG) triggering.¹⁶ With this, radiation is only administered at predefined time points of the cardiac cycle, rather than the entire cardiac cycle as in the so far used

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helical mode. The former is likely to be associated with a substantial reduction of radiation dose. However, the feasibility of the new technique has not been investigated in a clinical setting.

Therefore, it was the purpose of this study to determine prospectively the feasibility of low-dose CTCA with prospective ECG triggering, by determining the applied effective radiation dose.

Methods

Patients

After introducing prospective gating at our clinical service, the first consecutive 41 patients (12 women, 29 men; mean age 54.9 ± 13.0 years; age range 30–85 years) scheduled for CTCA were prospectively enrolled in the present feasibility study if none of the following exclusion criteria were present: hypersensitivity to iodinated contrast agent, renal insufficiency (creatinine levels $>150 \mu\text{mol/L}$ or $>1.7 \text{ mg/dL}$), non-sinus rhythm, or haemodynamic instability. Patients were referred because of suspected CAD ($n = 35$, 85%) based on at least one of the following symptoms such as dyspnoea ($n = 3$), typical angina pectoris ($n = 8$), atypical chest pain ($n = 18$), pathological exercise test or ECG ($n = 16$), because of high cardiovascular risk factors ($n = 1$), or patients with known CAD ($n = 6$, 15%) were referred for stent ($n = 1$) or bypass control ($n = 1$), or for a hybrid SPECT/CT scan ($n = 4$) to identify culprit lesions.¹³

The study protocol was approved by the institutional review board and written informed consent was obtained from all patients.

Computed tomography data acquisition and post-processing

All patients received a single dose of 2.5 mg isosorbiddinitrate sublingual (Isoket, Schwarz Pharma, Monheim, Germany) 2 min prior to scan. In addition, intravenous metoprolol (5–20 mg) (Beloc, AstraZeneca, London, UK) was administered prior to CTCA examination if necessary to achieve a target heart rate (HR), $<65 \text{ b.p.m.}$ For CTCA, 80 mL of iodixanol (Visipaque 320, 320 mg/mL, GE Healthcare, Buckinghamshire, UK) at a flow rate of 5 mL/s followed by 50 mL saline solution was injected into an antecubital vein via an 18-gauge catheter. Bolus tracking was performed with a region of interest (ROI) placed into the ascending aorta, and image acquisition was started 4 s after the signal density reached a predefined threshold of 120 Hounsfield units.

All CTCA examinations were performed with a LightSpeed VCT XT scanner (GE Healthcare) and prospective gating,¹⁶ using a commercially available protocol (SnapShot Pulse, GE Healthcare) and the following scanning parameters: slice acquisition $64 \times 0.625 \text{ mm}$, smallest X-ray window (only 75% of the RR-cycle), z-coverage value of 40 mm with an increment of 35 mm, gantry rotation time 350 ms, body mass index (BMI) adapted tube voltage (100 kV: BMI $<25 \text{ kg/m}^2$, 120 kV: BMI $\geq 25 \text{ kg/m}^2$) and effective tube-current (450 mA: BMI $<22.5 \text{ kg/m}^2$, 500 mA: BMI 22.5–25 kg/m^2 , 550 mA: BMI 25–27.5 kg/m^2 , 600 mA: BMI 27.5–30 kg/m^2 , 650 mA: BMI $>30 \text{ kg/m}^2$). Scanning was performed from below the tracheal bifurcation to the diaphragm, choosing three to four scan blocks (field of view, 11–14.5 cm). By choosing the smallest possible window at only one distinct end-diastolic phase of the RR-cycle (i.e. 75%), we ascertained the lowest achievable effective dose delivery. It may be worth mentioning that although prospective gating with mechanical non-dynamic CT has been the initial acquisition mode for pioneering studies on cardiac CT imaging more than two decades ago to evaluate the patency of coronary artery bypass grafts,¹⁷ the temporal resolution of conventional CT scanners has for long time not been sufficient to visualize native

coronary arteries. This problem has been solved by the introduction of scanners with gantry rotation times $<350 \text{ ms}$, such as in the present study.

The effective radiation dose of CTCA was calculated as the product of the dose-length product (DLP) times a conversion coefficient for the chest ($k = 0.017 \text{ mSv/mGy cm}$).¹⁸ HR variability was assessed as the standard deviation of the HR throughout the scan as reported previously.¹⁹

Computed tomography coronary angiography images were reconstructed with a slice thickness of 0.6 mm, using a medium-soft tissue convolution kernel (standard). In case of vessel wall calcifications, additional images were reconstructed using a sharp-tissue convolution kernel (detail) and preferably analysed using a bone window setting (window width: 1500 HU; window level: 500 HU) to compensate for blooming artefacts. All images were transferred to an external workstation (AW 4.4, GE Healthcare).

Computed tomography image analysis

For analysis of CTCA data, coronary arteries were segmented as suggested by the American Heart Association:²⁰ the right coronary artery was defined to include segments 1–4, the left main artery and the left anterior descending artery to include segments 5–10, and the left circumflex artery to include segments 11–15. The intermediate artery was designated as segment 16, if present. All segments with a diameter of at least 1.5 mm at their origin were included.

Two readers semi-quantitatively assessed independently the overall image quality on a 5-point scale as reported previously¹⁹ (1, excellent image quality; 2, blurring of the vessel wall; 3, mild artefacts; 4, severe artefacts; 5 non-evaluative). Step artefacts at junctions of different image blocks may not necessarily lead to misinterpretations. However, as a hidden lesion within the artefact cannot be definitely excluded, we have categorized any step artefact as non-evaluative. For any disagreement in data analysis between the two observers, consensus agreement was achieved.

Furthermore, two observers independently placed an ROI in each available coronary segment to estimate vessel attenuation (Figure 1). The ROIs were positioned by carefully avoiding calcifications, plaques, stenoses, and vessel walls. The mean attenuation of both observations was calculated for further evaluation.

Statistical analysis

Quantitative variables were expressed as mean \pm SD and categorical variables as frequencies, or percentages.

Kappa statistics were performed for inter-observer agreement of image quality assessment. Pearson correlation coefficient and Bland–Altman (BA) analysis were used to determine the inter-observer agreement for vessel attenuation. The relationship between BMI, HR, HR variability, and image quality was analysed with Spearman rank-order correlation coefficients. Mann–Whitney *U*-test was performed to determine the image quality differences between coronary segments with physiologically high vs. low motion velocities, as well as between large and small coronary segments. Furthermore, Mann–Whitney *U*-test was used to determine the differences in HR, HR variability, BMI, and vessel attenuation between segments with diagnostic and non-diagnostic image quality. χ^2 test was performed to determine whether the amount of non-diagnostic coronary segments was more frequent when HRs were $\geq 63 \text{ b.p.m.}$, a cut-off determined by receiver operator characteristic (ROC) analysis. A *P*-value of <0.05 was considered statistically significant. SPSS software (SPSS 12.0.1, Chicago, IL, USA) was used for statistical testing.

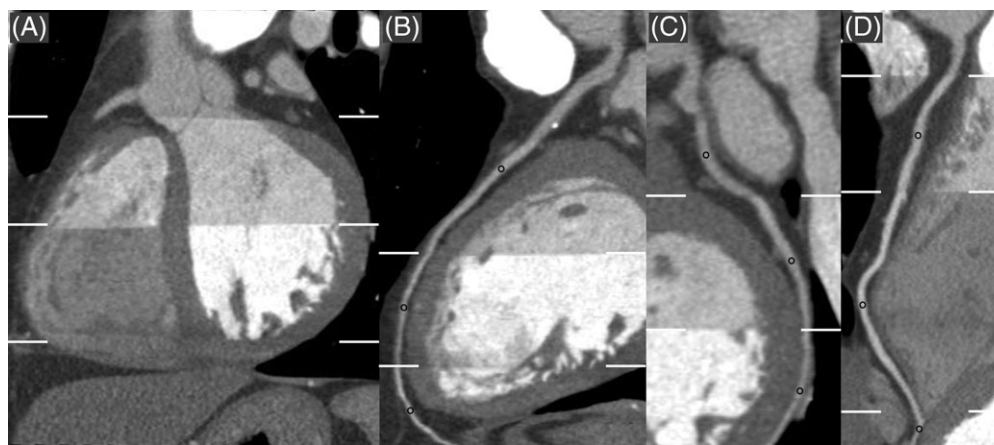


Figure 1 During computed tomography coronary angiography scanning with prospective ECG-gating (SnapShot Pulse technology), data are acquired with a z-coverage of 40 mm (indicated by white lines). To allow time for table movement, dataset is acquired at every second heart beat, which gives the contrast medium bolus time to travel, as demonstrated in (A)–(D) [differing contrast medium concentrations can be appreciated, especially in the ventricle; (A) oblique multiplanar reconstruction of the left ventricle, (B) curved multiplanar reconstruction of the left anterior descending artery, (C) curved multiplanar reconstruction of the circumflex artery, (D) curved multiplanar reconstruction of the right coronary artery]. To determine whether different concentration of contrast media has an impact on image quality in computed tomography coronary angiography, vessel attenuation was measured in every coronary segment (indicated by black circles)

Results

One of the 41 consecutively enrolled patients presented with atrial fibrillations and was therefore not scanned according to the predefined exclusion criteria. CTCA was successfully performed in the remaining 40 patients (12 women, 28 men; mean age 54.6 ± 13.0 years; age range 30–85 years) of whom 13 were smokers (33%), three had diabetes (8%), 15 had a positive family history for CAD (38%), 19 had dyslipidaemia (48%), and 18 were hypertensive (45%). CTCA revealed unknown CAD in five patients (13%) who consequently underwent myocardial perfusion imaging to determine haemodynamic significance of the lesions. In six patients (15%) with known CAD, CTCA revealed an open stent (one patient), an occluded bypass (one patient), and several lesions in four patients in whom the culprit lesions were identified with hybrid nuclear CT imaging. In 29 patients, CAD was ruled out with CTCA (72.5%).

The mean BMI of the study population was 26.1 ± 4.0 kg/m² (range 19.1–36.3 kg/m²), the mean HR 57.3 ± 6.2 b.p.m. (range, 39–66 b.p.m.), and the HR variability 1.5 ± 1.0 b.p.m. (range, 0.2–5.1 b.p.m.). Ten of 40 patients (25%) were on beta-blocker medication as part of their baseline medication. Additional intravenous beta-blockers were administered for HR control prior to CTCA in 30 patients (75%) (10.5 ± 5.9 mg, range, 5–20 mg). The field of view was 11 cm in 14 patients (35%) and 14.5 cm in 26 patients (65%). The mean scan time was 6.6 ± 1.2 s (range, 4.6–9.1 s) with a mean radiation time of 0.7 s in 14 patients (35%) and 0.9 s in 26 patients (65%). No major HR variabilities occurred; therefore, prospective scanning was continuously performed at every second heart beat in all patients.

The mean DLP from the CTCA was 124.9 ± 37.3 mGy cm (range, 65.0–179.0 mGy cm) resulting in an estimated mean applied radiation dose of 2.1 ± 0.6 mSv (range, 1.1–3.0 mSv).

In 40 patients, a total of 160 vessels and 519 coronary artery segments with a diameter of ≥ 1.5 mm were evaluated (of theoretically 640 possible segments in 40 patients with 16 coronary segments, 73 segments were missing because of anatomical variants and 48 had a diameter < 1.5 mm at their origin). Inter-observer agreement for image quality rating was good ($\kappa = 0.69$).

Four-hundred and ninety-three coronary segments (95.0%) were of diagnostic image quality (score 1–3) (Figure 2), i.e. 269 segments (54.6%) were rated to have excellent image quality (score 1), 166 (33.7%) had blurring of the vessel wall (score 2), and 58 (11.8%) had minor artefacts (score 3).

Non-diagnostic coronary segments (scores 4 and 5) were found in 26/519 coronary segments (5.0%) of 9/40 patients (23%) [score 4 in six patients (15%) and 13 segments (2.5%), score 5 in four patients (10%) and 13 segments (2.5%)]. Non-diagnostic image quality was caused by severe coronary motion ($n = 12$) (46%), stair step artefacts caused by incorrect fusion (Figure 3) of two adjacent datasets ($n = 12$) (46%), or by streak artefacts caused by intracardial electrodes ($n = 2$) (8%). With ROC curves, a cut-off HR of 63 b.p.m. was determined (Figure 4) and subsequently, non-diagnostic coronary segments were significantly less frequent [four of 370 coronary segments (1.1%) in two of 28 patients (7.1%)] when HRs were < 63 b.p.m., compared with HRs ≥ 63 b.p.m. [22/149 coronary segments (14.8%) in seven of 12 patients (58%); $P < 0.001$].

Mean coronary vessel attenuation was 346 ± 104 HU (range, 110–780 HU). Correlation between attenuation measurements of both readers was $r = 0.93$, Bland–Altman limits of agreement were -75.7 to 78.7 HU with a mean difference of 1.5 HU.

Determinates of image quality

There was a significant impact of HR, BMI, and vessel opacification on image quality, while the HR variability had no impact (Spearman

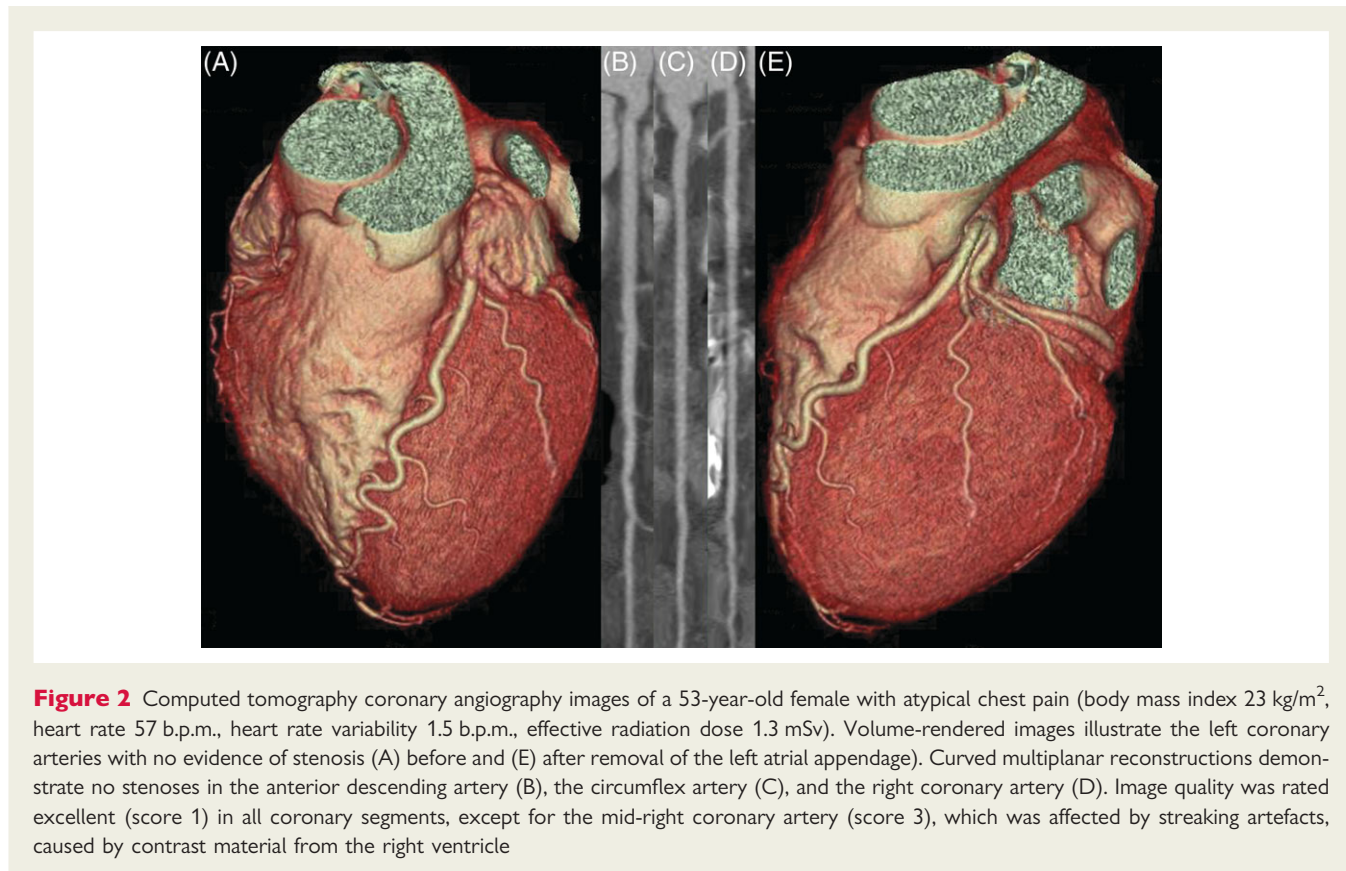


Figure 2 Computed tomography coronary angiography images of a 53-year-old female with atypical chest pain (body mass index 23 kg/m², heart rate 57 b.p.m., heart rate variability 1.5 b.p.m., effective radiation dose 1.3 mSv). Volume-rendered images illustrate the left coronary arteries with no evidence of stenosis (A) before and (E) after removal of the left atrial appendage). Curved multiplanar reconstructions demonstrate no stenoses in the anterior descending artery (B), the circumflex artery (C), and the right coronary artery (D). Image quality was rated excellent (score 1) in all coronary segments, except for the mid-right coronary artery (score 3), which was affected by streaking artefacts, caused by contrast material from the right ventricle

rank correlation coefficients for image quality and HR: $r = 0.58$, $P < 0.001$; BMI: $r = 0.45$, $P < 0.001$; vessel opacification: $r = 0.56$, $P < 0.001$; HR variability: $r = 0.28$, $P = 0.069$). Similarly, in coronary segments with non-diagnostic image quality, HR was significantly higher ($P < 0.001$). However, BMI, vessel attenuation, and HR variability did not significantly differ in diagnostic and non-diagnostic coronary segments ($P = 0.89$, 0.11, and 0.65, respectively) and ROC curves determined no cut-off values (area under the curve: 0.49, 0.39, and 0.52, respectively).

Furthermore, image quality was significantly lower in small coronary segments (i.e. segments 3, 4, 8, 9, 10, 12, 13, 14, 15, and 16) compared with larger coronary segments (i.e. segments 1, 2, 5, 6, 7, and 11) ($P < 0.05$). And, image quality was significantly lower in coronary segments with physiologically higher velocity (i.e. segments 1, 2, 3, 4, 9, 12, 13, and 14) compared with coronary segments with less coronary motion (i.e. segments 5, 6, 7, 8, 10, and 11)²¹ ($P < 0.001$).

Discussion

The present study is the first to demonstrate the feasibility of low-dose CTCA using prospective ECG-gating. Diagnostic image quality was achieved in 93% of patients (or 99% of coronary segments) with a very low effective radiation dose exposure (1.1–3.0 mSv), when HRs are <63 b.p.m.

With the introduction of CTCA into clinical routine, radiation exposure has remained an issue of concern.¹¹ Previous CTCA studies have reported the estimated radiation doses of up to

21.4 mSv without the use of the ECG-pulsing technique⁵ and down to 9.4 mSv with the use of ECG-pulsing technique.²² A recent dual source CTCA study using two different ECG-pulsing protocols reported the estimated mean effective doses of as low as 7.8 mSv with optimized acquisition protocol parameters.²³ With the estimated mean effective dose of 2.1 mSv, documented in the present study, another substantial dose reduction appears to be feasible and may be considered in the debate about radiation exposure vs. image quality and diagnostic yield. This is particularly important in view of the emerging field of hybrid imaging by integrating CTCA with nuclear techniques,²⁴ as such the combination would result in a considerable radiation exposure.¹⁵ Therefore, any attempt to lower exposure seems welcome, and this should hopefully stimulate introduction of modern protocols to lower radiation doses also for myocardial perfusion imaging in SPECT (currently 8–10 mSv for ^{99m}Tc tracers) to reach values currently achieved by PET scanning (2–3 mSv with ⁸²Rb or ¹³NH₃).¹⁸

In the present study, intravenous beta-blocker medication was administered in 75% of the patients, resulting in a mean HR of 57 b.p.m. which is substantially lower than in some of the previous reports.^{19,25} This is at least in part attributable to the slightly higher beta-blocker dose in the present study compared with some^{1,2,19,26} but not all³ previous studies. Nevertheless, we could still observe a significant impact of HR on image quality in our study. Furthermore, we found a cut-off HR of 63 b.p.m., below which low-dose CTCA is feasible in 93% of the patients with diagnostic image quality in all coronary segments. In contrast to previous reports,¹⁹ however, no relevant impact of the HR



Figure 3 Demonstration of a stair step artefact in the distal segment of the left anterior descending artery (arrows) caused by imperfect fusion of two image blocks (arrow heads). As a coronary lesion within the artefact may be missed all stair step artefacts were graded as non-evaluative (image quality score 5)

variability on image quality could be determined, most likely because the range of HR variability was too small following high rates of beta-blocker administration.

As BMI is another known factor to influence the image quality in CT examinations in general^{3,27–29} and specifically in CTCA by decreasing coronary artery attenuation and increasing image noise,^{30,31} we have adapted tube potential and current to BMI. As a result, we found only a weak correlation between BMI and image quality and no detectable cut-off value by ROC to predict non-diagnostic image quality from BMI.

Also, vessel attenuation in CTCA has been discussed to affect the accuracy of quantitative CTCA.^{32–34} Although we anticipated that this effect might be pronounced by the use of prospective gating, as datasets are acquired only at every second heart beat, allowing the contrast medium bolus time to dissipate this proved not true. In fact, no meaningful attenuation cut-off value could be observed.

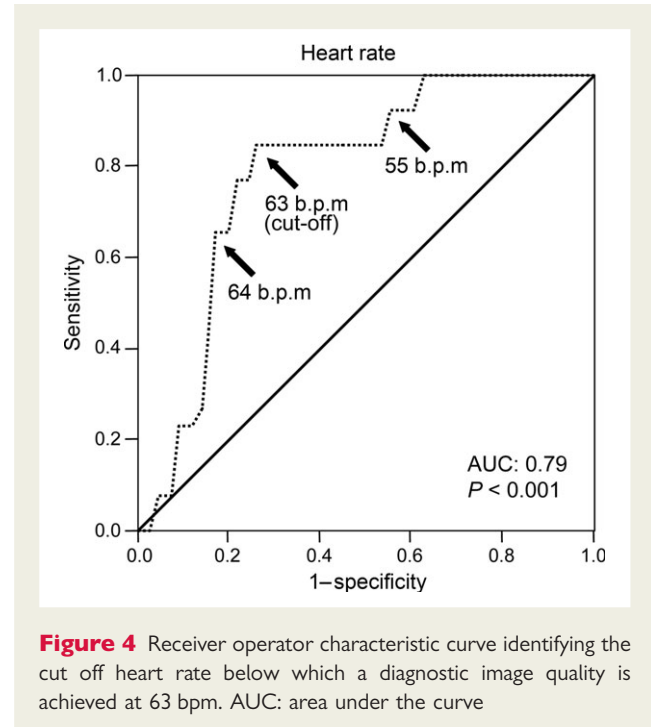


Figure 4 Receiver operator characteristic curve identifying the cut off heart rate below which a diagnostic image quality is achieved at 63 bpm. AUC: area under the curve

We acknowledge the following limitations to our study. We included a relatively small group of patients and did not assess the diagnostic accuracy of CTCA by comparing our findings with the reference standard invasive coronary angiography. Therefore, future studies on diagnostic accuracy of low-dose CTCA with larger patient populations are required.

Furthermore, the image quality scoring may have been biased by subjectivity; however, high kappa-values indicated good inter-observer agreement and may argue against such a bias.

In addition, as the acquisition is limited to one phase, the use of prospective ECG-triggering does not allow functional assessment of the left ventricle. This, however, is generally assessed primarily with other modalities such as echocardiography or a gated nuclear examination if hybrid imaging is performed.³⁵

Finally, although it appears that prospective ECG gating represents an important step forward for the CTCA technique, it is still in its infancies especially with current 64-slice technology and rotation times ~ 350 ms. However, this low-dose acquisition protocol has a great potential in combination with further refinements of CT scanners including higher rotation speed and higher number of detectors (scanners with 256 and 320 slices have been announced) with full heart coverage.

This first experience documents the feasibility of prospective ECG-gating for CTCA with diagnostic image quality at a low effective radiation dose (1.1–3.0 mSv), favouring HRs < 63 b.p.m.

Conflict of interest: Authors who are not employee or consultants for GE Healthcare, Milwaukee, had control of inclusion of any data and information that might present a conflict of interest for the author (O.A.) who is an employee of that company.

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