

# 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis

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## KEYWORDS

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**Aims** To evaluate the diagnostic accuracy of 64-slice multi-detector computed tomography coronary angiography (64-SCTA) compared with the standard reference conventional coronary angiography (CCA). **Methods and results** Based on a systematic search, 27 studies including 1740 patients were eligible for meta-analyses. Nineteen studies examined native coronary arteries ( $n = 1,251$ ), four studies examined coronary artery by-pass grafts (CABG) ( $n = 271$ ), and five studies examined coronary stents ( $n = 270$ ). Overall 18 920 segments were assessable and 810 (4%) were unassessable. The prevalence of native coronary artery stenosis in per-segment (19 studies) and per-patients (13 studies) populations were 19 and 57.5% respectively. Accuracy tests with 95% confidence intervals comparing 64-SCTA vs. CCA showed that sensitivity, specificity, positive predictive and negative predictive values for native coronary arteries were 86(85–87), 96(95.5–96.5), 83, and 96.5% by per-segment analysis; 97.5(96–99), 91(87.5–94), 93, and 96.5% by per-patient analysis; 98.5(96–99.5), 96(93.5–97.5), 92 and 99% for CABGs; 80(70–88.5), 95(92–97), 80, and 95% for stent restenosis; and 87(86.5–88), 96(95.5–96.5), 83.5, and 97% by overall per-segment analysis.

**Conclusion** The high diagnostic accuracy of 64-SCTA validates this non-invasive technique as a potential alternative to CCA in carefully selected populations suspected for coronary stenosis.

## Introduction

Non-invasive examination of coronary artery disease is an attractive and rapidly evolving possibility. Multi-detector computed tomography coronary angiography (MDCTA) is currently considered as a promising alternative to conventional coronary angiography (CCA). The technique is non-invasive, images can be obtained quickly, there are few complications and the preliminary studies show that it may be cost effective but this has to be determined.<sup>1,2</sup> Nevertheless, the available equipment suffers from several limitations compared with CCA. During the last few years, substantial technical improvement and encouraging research results have been achieved for MDCTA. The diagnostic accuracy of

MDCTA has improved after introduction of newer generations of scanners with high temporal and spatial resolution.

Many studies have addressed the accuracy of evolving generations of MDCTA in a variety of patient groups using CCA as standard reference. Several systematic reviews and meta-analyses combining results of studies using older scanner generations have been published.<sup>3–8</sup> The results of the recent studies using 64-slice MDCTA (64-SCTA) appear more promising and many studies have shown that this technique may become a potential alternative to CCA. The plausible clinical application of the currently available technique is primarily to substitute CCA as a diagnostic tool in ruling out CAD or verifying a coronary artery stenosis in selected patients suspected for CAD. In this systematic review, we have combined results of currently available published studies comparing 64-SCTA with the standard reference—CCA—to assess the diagnostic accuracy of this latest generation of MDCTA.

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## Methods

### Search strategy

We searched in the electronic databases: PubMed, EMBASE, and Cochrane for all published studies that examined patients with 64-SCTA. The following keywords were used: computed tomography, angiography, coronary artery, coronary artery disease. The search was limited until the end of April 2007. In press online published articles were also screened in the available journals. All published systematic reviews and meta-analyses were identified and their reference lists were screened.<sup>3-8</sup> Reference lists of the retrieved articles were screened as well.

### Study eligibility

Published studies were considered eligible if they included patients with proven or suspected CAD using 64-SCTA compared with CCA as standard reference. Significant coronary luminal stenosis was defined as  $\geq 50\%$  reduction in diameter using quantitative CCA or visual estimation as reference. Eligible studies should provide absolute numbers of diagnostic accuracy tests using  $2 \times 2$  tables. Studies not providing relevant data on diagnostic accuracy were excluded.

### Data extraction

Demographic, methodological and technical data, numbers of patients and segments, heart rate during scanning, numbers of true positive, false positive, true negative, and false negative values were extracted from each study. The angiographic results, reported either as per-patient or per-segment categories, were also extracted. Two authors contributed to data evaluation and extraction.

### Data synthesis

The main analyses were performed using the traditional meta-analytic methods for combining data for diagnostic accuracy tests.<sup>9,10</sup> The analyses that were performed to compare accuracy of 64-SCTA vs. CCA as reference incorporated all accuracy tests: sensitivity, specificity, predictive negative value, predictive positive value, likelihood ratios, diagnostic odds ratio, overall accuracy, and finally summarizing data in receiver operating characteristic curves. Accordingly, the absolute numbers of true positive, false positive, true negative, and false negative findings were analysed to provide sensitivity and specificity. Positive likelihood ratios  $LR+ = \text{sensitivity}/(1-\text{specificity})$  and negative likelihood ratios  $LR- = (1-\text{sensitivity})/\text{specificity}$  were calculated. The likelihood ratio for a positive result ( $LR+$ ) is a measure of how much the odds of the disease increase when a test is positive, while the likelihood ratio for a negative result ( $LR-$ ) tells how much the odds of the disease decrease when a test is negative. Thus, the combined likelihood ratios provided the diagnostic odds ratio ( $= \text{sensitivity}/(1-\text{specificity})/(1-\text{specificity})/\text{sensitivity} = \text{true positive} \times \text{true negative}/\text{false positive} \times \text{false negative}$ ). The result is a ratio of the odds of a positive test result among diseased to the odds of a positive test result among non-diseased.<sup>9,10</sup> Diagnostic odds ratio is considered as a more precise parameter for accuracy tests independent of prevalence. Moreover, prevalence in each data category (patient and segment), predictive positive and negative values were calculated as well.

The two different arms in the study by Ong *et al.*<sup>11</sup> were computed separately. The study by Malagutti<sup>12</sup> provided per-segment data on coronary artery by-pass grafts (CABG) as well as native arteries which were analysed separately. In the study by Ropers<sup>13</sup> only per-segment graft data were selected to analysis. The study by Rist<sup>14</sup> provided data on proximal, distal, and in-stent stenosis which all were combined to one result.

Due to heterogeneity, all the data were analysed by DerSimonian Laird random effects model. Sensitivity and meta-regression analyses were performed.<sup>15</sup>  $P$ -values  $< 0.05$  were considered significant.

Meta-analysis software package Meta-DiSc version 1.4 (Unit of clinical biostatistics, the Ramo y Cajal Hospital, Madrid, Spain) was used for all diagnostic accuracy analyses, generating summary receiver operative characteristic (SROC) curves and meta-regression analyses. Predictive values were calculated in MedCalc Meta-analyse package version 9.1.0.1 (Broekstrat 52, Mariakerke, Belgium).

## Results

### Search results

The search resulted in detection of 2609 hits. After exclusion of non-relevant articles by title and abstract, 87 articles were retrieved for full text evaluation, and of these 29 studies fulfilled all inclusion criteria. Two studies were excluded because of insufficient data.<sup>16-17</sup> Finally, 27 eligible studies were included in the meta-analysis (Table 1).

### Characteristics of the included studies

Characteristics of the included studies are shown in Table 1. Per-segment analysis of data was performed in all studies, thereof 19 studies examined native coronary arteries,<sup>11,12,18-35</sup> four studies examined CABGs,<sup>12,13,35,36</sup> and five studies examined implanted stent restenosis<sup>14,37-40</sup> (Table 1). The study by Malagutti<sup>12</sup> contributed both to the native coronary artery and CABG analyses. Per-patient analysis was available in 13 studies<sup>18-24,27,29,30,32-34</sup> that examined native coronary arteries. All studies defined significant luminal stenosis as cut-off  $\geq 50\%$  except two studies that defined it as  $\geq 70\%$ .<sup>23,28</sup> The included studies constituted relatively small populations ranging between 25-138 patients. The total included number of patients was 1761, of whom 21 (1.2%) were excluded for a variety of reasons. Thus 1740 were left for analyses.

All studies reported that investigators were blinded for image analyses but this point was unclear in three studies.<sup>21,27,31</sup>

### Angiography protocols in the included studies

The 64-SCTA technique scanning required patients to be in sinus rhythm without tachycardia, to be able to hold their breath for 10-15 s during scanning, be without contrast allergy, and have normal renal function. Patients not fulfilling these criteria were precluded.

Scanning protocols were almost the same in the included studies that used a 64-slice scanner. Only in the study by van Mieghem<sup>38</sup> a minority ( $n = 27$ ) of patients were scanned using 16-SCTA but the majority ( $n = 43$ ) were scanned by 64-SCTA and the study targeted proximal stents which all were assessable by both methods. Scanners gantry rotation time was 330 ms except in two studies which was 370 ms.<sup>20,25</sup> A number of studies reported a regulated rotation time to improve the temporal resolution according to heart rate.<sup>12,14,24,32,34,40</sup>

The mean volume of the injected intravenous contrast agents was 85 mL with a range of 65-100 mL. The contrast agents used were: Imeron (Iomeprol 400 mg I/mL), Omnipaque (Iohexol 300-370 mg I/mL), Ultravista 370 (Iopromide 370 mg I/mL), Visipaque (Iodixanol 320 mg I/mL), Imeron (Iomeprol 300-350 mg I/mL), Isovue (Iopamidole 370 mg I/mL), and Solustrat 300 (Iopamidole 300 mg I/mL). Either

**Table 1** Characteristics of the included 27 studies

Study	Included/excluded patients, <i>n</i>	Patient category	Unassessable segments%
<b>Studies using 64-SCTA vs. CCA to assess native coronary arteries</b>			
Ehara <sup>20</sup>	69/2	Patients with proven or suspected CAD	8
Ghostine <sup>31</sup>	66/0	Patients with LBBB without history of CAD	6
Leber <sup>30</sup>	59/4	Patients suspected for CAD	0
Leschka <sup>21</sup>	67/0	Patients suspected for CAD or prior CABG surgery	0
Meijboom-1 <sup>22</sup>	70/0	Patients before AVR	0
Meijboom-2 <sup>33</sup>	104/0	Non-ST elevation ACS	0
Mollet <sup>23</sup>	52/1	Patients scheduled for CCA	0
Muhlenbruch <sup>24</sup>	51/0	Patients suspected for CAD	5
Nikolaou <sup>25</sup>	72/4	Patients with proved or suspected CAD	10
Oncel-1 <sup>34</sup>	80/0	Patients suspected having CAD	0
Ong <sup>11</sup>	Group A: 68/0 Group B: 66/0	Symptomatic patients scheduled for CCA	6 13
Plass <sup>26</sup>	50/0	Patients with CAD and valve disease	3
Pugliese <sup>27</sup>	35/0	Patients with stable angina	3
Raff <sup>28</sup>	70/0	Patients suspected for CAD	12
Ropers-1 <sup>13</sup>	84/3	First angiography for suspected CAD	4
Schuijff <sup>19</sup>	61/1	Patients with CAD scheduled for CCA	2
Sheth <sup>29</sup>	29/0	Detection of complex lesions before revascularisation	5
Schlösser <sup>32</sup>	63/2	Patients suspected for CAD	1
<b>Studies using 64-SCTA vs. CCA to assess CABG</b>			
Malagutti <sup>12</sup>	52/0	Stable symptoms suggesting CABG obstruction	0
Meyer <sup>37</sup>	138/0	Consecutive patients after CABG suspected for graft disease	0
Pache <sup>36</sup>	31/0	Angina after CABG	0
Ropers-2 <sup>35</sup>	50/0	Patients after CABG suspected for progression of CAD	0
<b>Studies using 64-SCTA vs. CCA to assess stent restenosis</b>			
Ehara-2 <sup>40</sup>	81/0	Assessment of stent restenosis	12
Oncel-2 <sup>41</sup>	30/0	Assessment of stent restenose	0
Rist <sup>14</sup>	25/0	Assessment of stent restonsis	2
Rixe <sup>38</sup>	64/0	Assessment of stent restonsis	42
Van Mieghem <sup>39</sup>	74/4	Follow-up after LMA stenting	0

ACS, acute coronary syndrome; AVR, aorta valve replacement; CABG, coronary artery bypass-graft; CAD, coronary artery disease; CCA, conventional coronary angiography; LBBB, left bundle branch block; LMA, left main artery; 64-SCTA, 64-slice computed tomography coronary angiography.

15 or 17 segment analysis models were used. Assessment of stenosis diameter was done by quantitative CCA (QCCA); however, three studies reported that they used visual estimation.<sup>11,23,31</sup> Assessment of coronary stenosis by 64-SCTA was performed visually using axial, multiplanar reconstruction (MPR) and maximum intensity projection (MIP) techniques in most of the studies. Six studies reported using curved MPR.<sup>14,18,21,22,29,33</sup> Only five studies on native coronary arteries reported clearly that they assessed segment stenosis in two orthogonal planes.<sup>20,25,27,29,38</sup> Only one study reported a quantitative measurement of coronary stenosis in complex lesions.<sup>27</sup>

The average estimated radiation dose during the whole electrocardiogram cycle (systole and diastole) was determined to be about 15 mSv and 20 mSv for men and women, respectively, in six studies.<sup>21,22,26,27,32,38</sup> By restricting the maximal tube current to the diastolic period, the radiation dose was reduced significantly to about 7 mSv and 14 mSv for men and women, respectively, in four other studies.<sup>13,30,34,39</sup>

### Characteristics of included patients

The mean age was 61.5 years with a range of 59–69 years. Males constituted 76.8%. Cardiovascular risk profile was

reported in 12 studies:<sup>12,18,19,21,25,26,28,30,32,35,38,39</sup> 53% had hypertension, 18% had diabetes mellitus, and 56% had hyperlipidaemia. The mean heart rate during scanning was 63/min with a range of 57–77/min. In all but four studies,<sup>18–20,25</sup> patients received additional beta-blocker either intravenous or orally to reduce heart rate below 65/min.

### Segment assessability

In per-segment analysis of native coronary arteries, a total of 18 920 segments were visualized but 806 segments were unassessable. Thus, 4% of segments (range 0–15) were excluded from analysis. All CABG segments (*n* = 810) were assessable in the four CABG studies. In one study of stents implanted in proximal vessels (left main coronary artery) it was also possible to assess all segments,<sup>38</sup> but in other two studies of smaller stents the percent of unassessable segments was high (*Table 1*).

### Results of the accuracy analyses

The results of the analyses comparing 64-SCTA vs. CCA are shown in *Table 2*. There were differences in sensitivity and specificity values in per-segment vs. per-patient analysis due to the calculated higher prevalence of CAD in per-patient data. In general, 64-SCTA demonstrated high

**Table 2** Results of the meta-analyses comparing 64-slice computed tomography coronary angiography with conventional coronary angiography: accuracy results of the group of studies

Type of analysis	Number of studies	Number of patients	Number of segments	Number of unassessable segments%	Prevalence of coronary stenosis%	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV%	NPV%	+LR (95% CI)	-LR (95% CI)	DOR (95% CI)	Overall accuracy%
Per-segment analysis of native coronary arteries	19	1251	17 695	747 (4)	19	86 (85-87)	96 (95.5-96.5)	83	96.5	22.5 (17.1-29.6)	0.11 (0.08, -0.15)	190 (121-297)	94
Per-patient analysis of native coronary arteries	13	875	—	—	57.5	97.5 (96-99)	91 (87.5-94)	93.5	96.5	7.3 (4.4, -12.2)	0.5 (0.03, -0.08)	201 (100-403)	95
Per-segment analysis of CABG	4	271	810	0 (0)	36	98.5 (96-99.5)	96 (93.5-97.5)	92	99	19.2 (10.5-35.1)	0.02 (0.00, -0.04)	962 (244-3796)	96.5
Per-segment analysis of stents	5	270	415	59 (14)	20	80 (70-88.5)	95 (92-97)	80	95	13.6 (8.5, -21.7)	0.15 (0.04-0.54)	76 (14-409)	92
Overall per-segment analysis (native, CABG and stents)	27	1740	18 920	806 (4)	19	87 (86.5-88)	96 (95.5-96.5)	83.5	97	21.1 (16.7, 26.7)	0.10 (0.07-0.14)	214 (139-330)	94

CABG, coronary by-pass graft; CI, confidence interval; DOR, diagnostic odds ratio; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

accuracy particularly by its high negative predictive values. The accuracy was highest in assessing CABG (96.5%) and lowest in stented segments (92%).

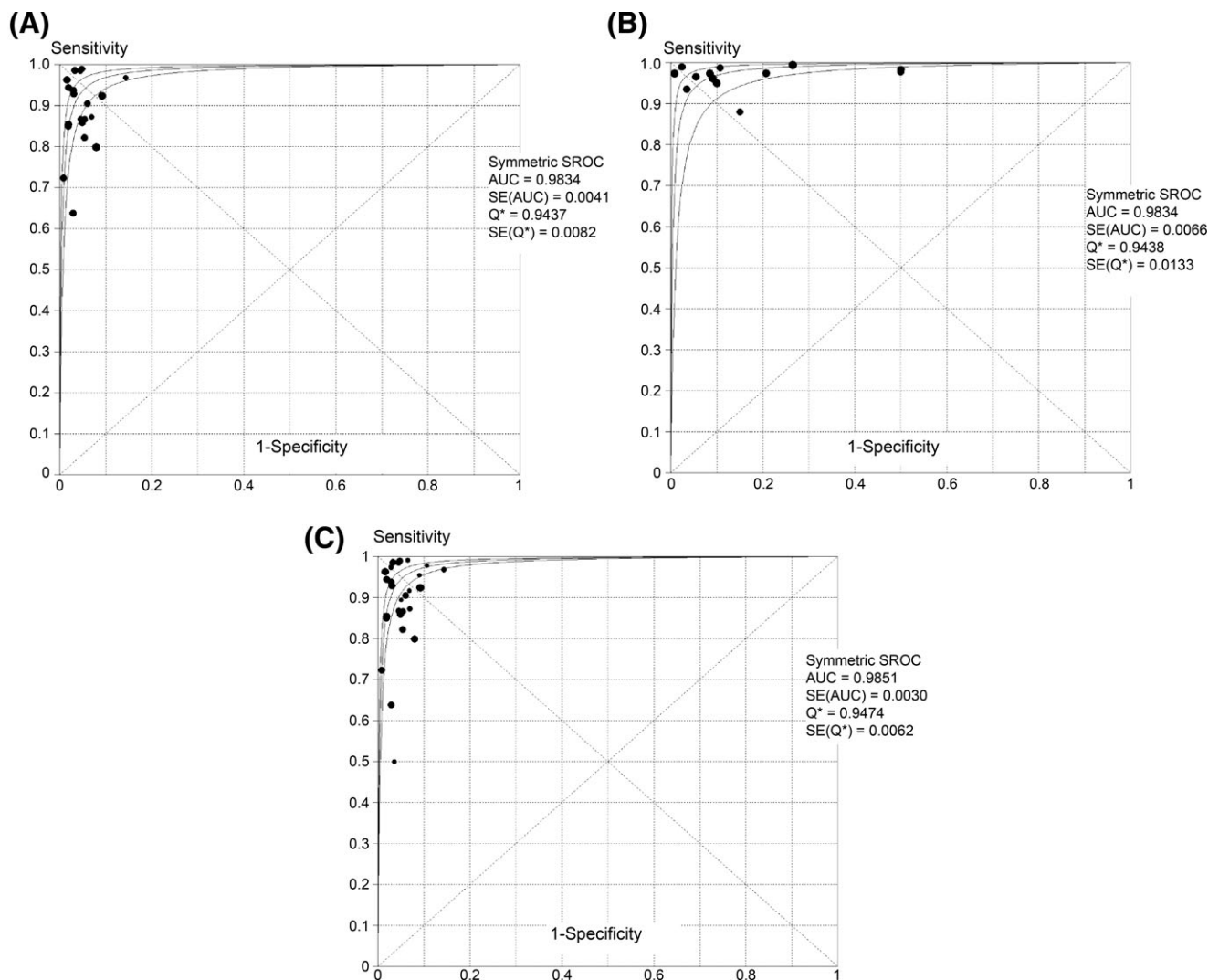
We ran also the analyses by including only the studies that used quantitative coronary angiographic method for assessment of stenosis diameter and by excluding three studies that used visual estimation.<sup>11,23,31</sup> The results of 16 studies on per-segment analysis of native coronary arteries showed an increased sensitivity of 88(86–90)% and unchanged specificity of 96(95.5–96.5)%, the studies were heterogeneous  $P < 0.001$ . The results of 11 studies on per-patient analyses of native coronary arteries showed unchanged sensitivity of 97.5(96–99)% with  $P = 0.079$  for heterogeneity and an increased specificity of 92(88.5–95.5)% with  $P = 0.004$  for heterogeneity.

The SROC graphs (Figure 1A–C) showed a symmetric area under the curve of 0.98 for per-patient, per-segment, and overall analyses.

## Heterogeneity and sensitivity analyses

The per-segment analyses showed significant heterogeneity for all accuracy analyses, all  $P < 0.001$ . The heterogeneity was significant ( $P < 0.001$ ) even after excluding the small studies with populations below 50 patients. Therefore, meta-regression analyses (27 studies) were performed by including four important covariates, which we presumed to be the most likely source of heterogeneity. These were: age, prevalence of CAD, heart rate during scanning, and percent of unassessable segments. The results showed that age, prevalence of CAD, and heart rate had no significant influence on heterogeneity  $P = 0.69$ ,  $P = 0.64$ ,  $P = 0.83$ , respectively. Percent of unassessable segments had significant influence,  $P = 0.03$ , and after including all the other covariates in the model this influence was still border-line significant,  $P = 0.053$ .

The per-patient analyses showed significant heterogeneity only for the specificity  $P < 0.001$  and positive likelihood ratio  $P < 0.001$ .



**Figure 1** (A–C) Plot of per-segment (19 studies), per-patient (13 studies), and overall (27 studies) symmetric receiver operating characteristics comparing 64-slice computed tomography coronary angiography vs. conventional coronary angiography. The diagnostic accuracy is shown by plotting 1-specificity against sensitivity, area under curve (AUC), and Q\* statistic with their standard errors (SE). The upper and lower lines indicate 95% confidence intervals. SROC, summary receiver operating characteristic.



A comparison between results of the current meta-analysis with the previous meta-analyses is shown in *Table 3*.

## Discussion

The results of the current meta-analysis demonstrate that 64-SCTA has high diagnostic accuracy and assessability of coronary artery segments (*Tables 2 and 3*). The estimated high negative predictive value by per-patient analysis validates 64-SCTA technique as an alternative to CCA in carefully selected patients suspected for CAD. The accuracy of the technique is robust in assessing bypass grafts but limited in assessing in-stent restenosis. The accuracy of 64-SCTA has also been compared with the other non-invasive methods and shown that 64-SCTA has higher accuracy compared with magnetic resonance imaging angiography and stress nuclear imaging in detecting CAD.<sup>3,41–43</sup> Thus, 64-SCTA can be considered as a major option to be used in examining patients suspected for CAD. However, it should be emphasized that these three methods provide different and complementary structural and functional information on CAD.

Although 64-SCTA seems to be an attractive alternative non-invasive method, several limitations remain in clinical practice. In this review, it can be noticed that some preclusion criteria restricted the number of eligible patients prior to scanning, leaving eventually selected groups who were potential candidates for 64-SCTA. Perhaps due to the rigid preclusion criteria, the number of excluded patients during the studies was low, only 1.2%. The number of assessable segments by 64-SCTA was high (96%), but still a considerable number (4%) was not well assessed and might need re-evaluation with CCA (*Table 2*).

Both types of analyses—per-segment and per-patient—that were performed provided high negative predictive values, though the estimated prevalence of CAD based on per-segment compared with per-patient analysis was as expected much lower (19 vs. 57.5%). However, segmentation separates the coronary tree and individuals as a whole leading clinically to an unrealistic distribution of the disease. An independent analysis based on diseased segments can therefore be misleading and provides no useful information in practice. Accordingly, the results provided by the per-patient analysis in populations with high prevalence of CAD can be considered clinically relevant and the

overall results of accuracy in the current study seem therefore to be acceptable.

The rapid technical evolution in the recent few years indicates that solutions for the restricting technical factors could be possible in the near future. Increasing number of detectors, shortening gantry rotation time, and using dual source technique are possible solutions. Important remaining issues are artefacts due to cardiac, pulmonary and body motion, beam hardening due to metallic objects (surgical clip, marker, wire, and stents), extensive calcifications, and overlying cardiac veins.<sup>44,45</sup> Image quality might be worsened by arrhythmias and inability to hold breath.<sup>45,46</sup> These are not uncommon problems in patients with heart and lung diseases. Faster acquisition time and increasing resolution by the newer generations of scanners might minimize artefact problems.

The high radiation dose is probably the most undesirable disadvantage concerning the safety of 64-SCTA. The estimated mean effective radiation dose per patient in the included studies was about 15 and 20 mSv and with modulated protocols 7 and 14 mSv for males and females, respectively. This dose is markedly higher compared with the dose associated with an uncomplicated CCA which is about 5–7 mSv,<sup>47,48</sup> but is almost similar to the patient dose administered when using nuclear cardiac stress scanning (with technetium is about 6–8 mSv and up to 27 mSv with thalium).<sup>49–50</sup>

Modulated radiation protocols with dose-saving algorithms are therefore important in daily practice to reduce the risk of radiation and at the same time maintain relevant image quality.<sup>51</sup> Patient's age is an important issue when 64-SCTA is chosen as first method, because younger patients have higher lifetime risk of developing cancer as a result of exposure to X-ray. Younger females are in further increased risk of breast radiation and cancer.<sup>52</sup> Thus, these patient categories may have higher lifetime cancer mortality than older people in case of repeated examinations with higher cumulative radiation.<sup>52,53</sup> A recently published study estimating the radiation risk in phantom male and female models underscored the increased lifetime attributable risk of cancer in younger patients and particularly females.<sup>54</sup> However, as noticed in this paper the mean age of patients scheduled for 64-SCTA was 61.5 years, in whom the lifetime cancer risk might be considered relatively lower.<sup>54</sup> The risk of contrast agents on renal function and

**Table 3** Diagnostic accuracy of computed tomography coronary angiography compared with conventional coronary angiography based on per-segment analyses of native coronary arteries in the successive meta-analyses using different generations of scanners

Author of meta-analysis and number of studies	Patients number	Assessable segments%	Type of scanner	Sensitivity%	Specificity%
Schuijf 2006, <sup>3</sup> 26 studies	1300	87	4–16–64 slice	85	95 <sup>a</sup>
Stein 2006, <sup>4</sup> 33 studies	1861	87	4 slice	83	93 <sup>a</sup>
			16 slice	88	97
Sun 2006, <sup>5</sup> 47 studies	3142	NA	4–16–64 slice	83 (79–89)	93 (91–96)
Hamon 2006, <sup>6</sup> 27 studies	2024	93	4–16–64 slice	81(72–89)	93 (90–97)
			Only 64 slice (9 studies)	87(80–94)	96 (95–97)
Abdulla 2007, 19 studies	1251	96	Only 64-slice	86 (85–87)	96 (95.5–96.5)

<sup>a</sup>Confidence intervals were not reported in these studies.  
NA, not available.

risk of allergy remain important for both procedures. Nevertheless, it should be noticed that the estimated overall risk associated with 64-SCTA is still considered lower than CCA.<sup>48,55</sup>

In summary, the current 64-SCTA technique can therefore not be recommended for examination of patients with high probability of CAD and coronary intervention and neither for screening of asymptomatic patients. Ideally, cardiologists should use a pretest probability of CAD in order to avoid further interventions associated with increased radiation risk. Appropriate selection of patients can be performed by a pretest probability of CAD,<sup>56</sup> assessment of lifetime cancer risk, probability of artefacts induced by motion and arrhythmias, as well as patients' ability to cooperate.<sup>57,58</sup>

Compared with CCA, 64-SCTA is a non-invasive approach that would more likely be preferred by most of the patients, has the advantage of shorter patient preparation time, provides insight in surrounding tissues and plaque morphology, can construct images both on the coronary tree, cardiac and the other intra-thoracic structures and finally personnel will not be exposed to radiation. While the disadvantages are increased radiation risk for patient, lower resolution, longer analysis time, need for a work-station, patients need to hold breath and finally inadequate image quality in case of arrhythmias and artefacts.

An important issue when comparing the diagnostic accuracy of 64-SCTA with CCA is not only assessment of a significant stenosis by quantitative CCA as reference, but also how the stenosis is reliably assessed by 64-SCTA. The core analysis is usually done by evaluating the axial source images and MPR. These images provide parallel and orthogonal views of the vessels, which are instrumental in detecting and assessing stenosis severity. These can be supplied by MIP technique images, but the disadvantage of this technique is that the presence of calcifications can obscure lower density structures of interest like non-calcified plaques.<sup>59</sup> A visual comparison of the stenotic area with the distal and proximal luminal areas as reference provides a qualitative assessment of the stenosis.<sup>59-61</sup> In case of excellent image quality, a planimetric measurement of the cross-sectional area can provide a quantitative assessment.<sup>60,61</sup> Based on the results of the included studies in this meta-analysis, the method of data evaluation and assessment of coronary artery stenosis varied across the studies and was qualitative. This underscores the need for optimal image quality as well as consensus on using a standard qualitative and quantitative assessment of luminal stenosis by 64-SCTA.

The results of the current and previous meta-analyses showed significant heterogeneity between the included studies. However, the current meta-analysis of studies using only 64-SCTA showed a reduced heterogeneity in per-patient data. Analyses by excluding small size studies or studies using visual estimation of coronary stenosis had no influence on heterogeneity. Exploring for source of heterogeneity by meta-regression analyses showed that age, prevalence of CAD, and heart rate had no influence. The only reasonable source of heterogeneity was a significant difference in the numbers of assessed segments among studies, which might have influenced the absolute numbers of true and false stenoses reported in each study. This variation in segment analysis can be attributed to level of

experience with 64-SCTA used in different centres where the studies were performed. Improvement of technical quality and clinical experience might minimize this difference.

There is no consensus about using quality scores in assessment of diagnostic accuracy studies and even the suggested scores have shown no major role in systematic reviews of diagnostic accuracy tests.<sup>62</sup> However, identifying inclusion and exclusion criteria and study populations were well described, the reference method used was the same, the index test was well described, the majority of studies used blinded methods in image analysis, and finally the number of unassessable segments and excluded patients were well reported in the studies included in this meta-analysis.

## Clinical implication

The results of this study show that 64-SCTA can be used to rule out or detect the presence of CAD in carefully selected populations suspected for CAD. The method is attractive due to many advantages, however, clinicians should be cautious about the high radiation dose and risk of re-evaluation with CCA in case of failure of adequate assessment by 64-SCTA.

## Limitations of the study

It is likely that the results of this study are biased by the fact that the included populations were of small sizes, selected patients and investigators had a better experience compared with the real-life centres which usually examine larger and more broad-spectrum populations and may have less experience with the technique. The included studies were also likely to be associated with some observational bias due to inter-observer variations.

**Conflict of interests:** none declared.

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