

Advances in Computed Tomography–Based Evaluation of Coronary Arteries: A Review of Coronary Artery Imaging With Multidetector Spiral Computed Tomography

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Noninvasive imaging of coronary arteries with computed tomography (CT) has become increasingly accurate with the technological advances in multidetector CT (MDCT). The authors review the utility of MDCT in quantitative and qualitative evaluations of coronary stenosis, plaques, bypass grafts, and stents. Recent studies demonstrate a high accuracy of MDCT in locating significant coronary stenosis, which may allow CT angiography to become an important screening tool for coronary artery disease in selected patient populations. Although factors such as arrhythmias, heart rate, calcifications, and patients' ability to hold their breath may limit the patient population that will ultimately benefit from this technology, MDCT coronary angiography has significant clinical potential. Studies are still needed to clarify the clinical role for CT angiography, but advances in this noninvasive technology are impressive and hold promise for clinical utility.

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Coronary artery disease (CAD) continues to be an epidemic in the United States and worldwide. The gold standard for assessing coronary artery stenosis is invasive coronary angiography (ICA). The prospect of a noninvasive coronary imaging modality is appealing, given the inherent invasiveness, risks, and cost of ICA. Recent technological advances in computed

tomography (CT) have made noninvasive imaging of the coronary arteries increasingly accurate and clinically applicable. In particular, the advancement of multidetector spiral computed tomography (MDCT) in coronary angiography has been heavily discussed. This review discusses the recent literature on CT coronary angiography, including the introduction of the 64-slice MDCT and its accuracy, limitations, and potential clinical applications.

16-Slice MDCT: The Current Generation

Accuracy of 16-Slice CT Scanners

Before the recent development of 64-slice MDCT, numerous studies investigated the use of the earlier generation of 16-slice MDCT, which is widely used in clinical settings today.¹⁻⁵ Results from those studies have provided insight into the effectiveness of MDCT. Generally, 16-slice MDCT has proved to be only moderately successful in identifying significantly stenotic lesions, with sensitivity ranging from 63% to 73% and specificity from 96% to 98%.¹⁻⁴ However, due to technological limitations, up to 43% of coronary segments were unevaluable because of poor image quality.¹ In particular, the left circumflex artery, right coronary artery, and distal coronary artery segments were often difficult to visualize or interpret. Nevertheless, per patient analyses of studies (which may be more clinically relevant) consistently demonstrated a high sensitivity (86% to 97%) for identifying at least 1 stenotic lesion in patients whose arteries were properly evaluable.¹⁻⁴ Additionally, in studies limiting analysis to segments potentially suitable for intervention and revascularization—generally defined as the left main coronary artery, the left anterior descending artery, the left circumflex artery, the

right coronary artery, and segments at least 2.0 mm in diameter—the sensitivity for identifying stenosis per segment improved to 92% to 95%, and specificity remained high at 86% to 95%.^{5,6}

Technological Limitations

Two factors that consistently limit the accuracy of CT coronary angiography in these studies are elevated heart rate and calcifications. A study by Hoffmann and colleagues⁷ found that image quality in 16-slice MDCT was best at a heart rate at or less than 75 beats/min. In most studies, beta blockers are used to attempt to lower heart rates to as low as 60 beats/min to 65 beats/min to minimize limitations due to temporal resolution. The presence of calcifications also provides a diagnostic challenge because the high density of calcified vessels and plaques tends to cause partial volume effects that obscure arterial lumens. One study, a secondary analysis limited to patients who had heart rates at or less than 65 beats/min and segments with restricted calcium levels, revealed a significant improvement in diagnostic accuracy from 36% to 91%.¹ Another limitation of CT coronary angiography includes poor visualization of small and distal segments of the coronary arteries. As a result of these limitations, many vessels and some patients were eliminated from analysis because of inadequate image quality, limiting the significance of the studies.

64-Slice MDCT: The Next Generation

The recent introduction of 64-slice MDCT represented a major improvement in CT technology, with the new “z-axis flying focus technology.”⁸ Whereas the previous generation of scanners had 16 detectors along the axis of the gantry, 64-slice MDCT uses 32 central detectors that oscillate

between 2 positions along the z-axis, allowing for a total of 64 slices per rotation. This technology results in a marked improvement in spatial resolution (to an isotropic voxel resolution of as high as $0.4 \times 0.4 \times 0.4$ mm³) and in temporal resolution (165 milliseconds). As a result, image quality is improved, and the partial volume phenomenon, especially that due to calcification, is diminished. Motion abnormalities caused by individual heartbeats are also decreased by improved temporal resolution. In addition, scan time can be reduced to about 12 seconds or less (compared with about 20 seconds with 16-slice MDCT), which not only reduces exposure to radiation and dye but also shortens the duration for which patients must hold their breath to limit respiratory motion abnormalities. The introduction of 64-slice MDCT was clearly a significant technological improvement over the previous generation of 16-slice MDCT.

Qualitative Accuracy of 64-Slice MDCT Versus ICA

Several studies have demonstrated the accuracy of 64-slice MDCT (Table 1). A study by Leschka and colleagues⁹ of 67 patients was the first that used the 64-slice scanner to compare MDCT with the gold standard of ICA. Despite the lack of beta-blocker use (other than the patients' personal medications), visualization of vessels at least 1.5 mm in diameter was impressive, with a sensitivity of 94% and a specificity of 97% for identifying stenotic lesions. Every patient with at least 1 significantly stenotic lesion was properly identified, showing the high accuracy of 64-slice MDCT. Fine and colleagues¹⁰ reported similar findings, with a sensitivity and specificity of 95% and 96%, respectively, for detecting stenosis of at least 50% in vessels at least 1.5 mm in diameter.

Table 1
Diagnostic Accuracy of 64-Slice Multidetector Computed Tomography (vs Invasive Coronary Angiography) for Detecting Significant Stenotic Lesions

Study	Per Evaluable Segment Analysis						Per Patient Analysis				
	Segments Evaluable	Number of Segments	Sensitivity	Specificity	PPV	NPV	Number of Patients	Sensitivity	Specificity	PPV	NPV
Leschka S et al ^{9*}	100%	1005	94%	97%	87%	99%	67	100%	100%	—	—
Fine JJ et al ^{10*}	100%	245	95%	96%	97%	92%	—	—	—	—	—
Mollet NR et al ¹¹	100%	725	99%	95%	76%	100%	51	100%	92%	97%	100%
Raff GL et al ¹²	88%	938	86%	95%	66%	98%	70	95%	90%	93%	93%
Pugliese F et al ¹³	—	494	99%	96%	78%	99%	35	100%	90%	96%	100%

Significant stenosis defined as $\geq 50\%$ luminal obstruction. Per evaluable segment analysis and per patient analysis as provided by the study authors.

PPV, positive predictive value; NPV, negative predictive value.

*Vessels < 1.5 mm excluded from analysis.

Mollet and coworkers¹¹ used 64-slice MDCT to evaluate every coronary segment, regardless of size, in 52 patients with atypical chest pain, unstable angina, or non-ST-elevation myocardial infarction. The true magnitude of the technological advance was demonstrated as a sensitivity of 99% and a specificity of 95% for identifying significant stenosis ($\geq 50\%$) per segment. Per patient (1 patient excluded because of an inconclusive CT scan), no patient with significant stenosis was missed, and only 1 patient's disease was overestimated by MDCT. The authors suggested that based on these results, CT coronary angiography could be considered an alternative to diagnostic ICA. Other studies confirmed the high qualitative accuracy of MDCT to detect significant stenosis, with sensitivity ranging from 86% to 99% and specificity from 95% to 96% for identifying significantly stenotic lesions per segment.^{12,13}

Quantitative Accuracy of 64-Slice MDCT Versus ICA

The ability of MDCT to identify stenotic lesions qualitatively, how-

ever, does not compare with the diagnostic ability that an interventionalist has to quantify lesions with diagnostic ICA. Furthermore, the reference range of 50% stenosis is somewhat arbitrary, and its clinical significance is questionable. Two studies reviewed here have used 64-slice MDCT to evaluate the accuracy of MDCT in assessing coronary lesions quantitatively rather than qualitatively. Leber and colleagues¹⁴ studied 59 patients with stable angina and found an overall correlation coefficient (r) of 0.54 for degree of stenosis measured by MDCT versus ICA. However, when categorizing stenotic lesions as less than 50%, at least 50%, and at least 75%, MDCT showed moderate accuracy, with respective sensitivities of 79%, 73%, and 80%, and a specificity of 97%. Raff and coworkers¹² reported more promising results in a study of 70 patients referred for elective ICA. They found an r of 0.76 for MDCT versus ICA, with a mean difference in percentage stenosis of $1.3\% \pm 14.2\%$, although 17% of lesions could not be quantitatively analyzed. Additionally, 92% of quantitative MDCT

readings were within 1 stenosis score ($\pm 25\%$) of the ICA reading. These results suggest that MDCT has a moderate capacity not only for identifying lesions but also for grading them. However, studies of this generation of MDCT have not provided enough proof to suggest that this technique might be a diagnostic alternative to ICA.

Plaque Visualization

Although MDCT is becoming increasingly effective at identifying stenosis, there are other facets of coronary artery anatomopathology to consider. Higher grades of coronary artery stenosis are associated with increased risk of acute coronary events,¹⁵ but the majority of events are associated with stenotic grades of less than 50%.¹⁶ The composition as well as the size of individual coronary plaques are of clinical significance, and both have been studied as risk factors for acute coronary events. Intravascular ultrasound (IVUS) is now the invasive method of choice for evaluating coronary plaques because ICA can visualize only stenotic lesions and may miss

Table 2
Diagnostic Accuracy of Multidetector Computed Tomography (vs Intravascular Ultrasound)
for Detecting Nonstenotic Coronary Plaques

Study	Number of Coronary Segments Evaluated	Sensitivity	Specificity	PPV	NPV	Correlation of Measured Plaque Volumes
Studies using 16-slice MDCT						
Achenbach S et al ¹⁷	83	82%	88%	91%	76%	$r = 0.8$
Leber AW et al ¹⁸	525	78%, 78%, 95%*	92%	—	—	—
Studies using 64-slice MDCT						
Leber AW et al ¹⁴	99	84%	91%	—	—	$r = 0.73^{\dagger}$
Leber AW et al ²⁰	365	90%	94%	—	—	$r^2 = 0.69$

Per evaluable segment analysis reported. MDCT, multidetector computed tomography; PPV, positive predictive value; NPV, negative predictive value; r , correlation coefficient.

*Sensitivity of detection of hypoechoic, hyperechoic, and calcified plaque areas, respectively.

[†]Correlation of plaque area.

plaques because of positive remodeling (a compensatory widening of vessels in response to plaque formation). MDCT has been studied to determine its worth in identifying and evaluating coronary plaques (Table 2).

Accuracy of Plaque Localization Using 16-Slice MDCT

In a study using the current generation of 16-slice CT scanners, Achenbach and colleagues¹⁷ found that MDCT had an overall sensitivity and specificity of 82% and 88%, respectively, for detecting nonstenotic coronary plaques, compared with IVUS. However, multiple studies have shown a difference in the ability of 16-slice CT scanners to detect calcified versus noncalcified plaques. Plaques with limited or no calcification were detected with a sensitivity of 53% to 78%, whereas calcified plaques were better visualized, with a sensitivity of 91% to 95%.^{17,18} In another study, Achenbach and coworkers¹⁹ also found that 16-slice MDCT had a moderate ability to identify and quantify positive remodeling (remodeling index for MDCT vs IVUS, $r^2 = 0.82$). However, as in

other studies, image quality from 16-slice MDCT suffered from limited resolution.

Accuracy of Plaque Localization and Characterization Using 64-Slice MDCT
 Leber and colleagues^{14,20} conducted early studies comparing IVUS with 64-slice MDCT in identifying and evaluating coronary plaques. MDCT (compared with IVUS) had a good ability to properly identify coronary plaques (sensitivity 84% to 90%), but tended to underestimate both plaque area (correlation value = 0.69 to 0.73) and vessel obstruction. However, the composition of plaque influenced interpretation: calcium-rich plaques tended to cause overestimation of lesions through partial volume effects due to the high attenuation of calcium by CT, whereas mixed and noncalcified lesions were underestimated. MDCT was moderately successful at categorizing plaques as either calcified, mixed, or noncalcified (overall, 86% of lesion categorization was in consensus with IVUS).²⁰ Furthermore, MDCT (compared with IVUS) had moderate success in identifying patterns of lipid

pools (70%) and patterns of spotty calcification (90%), 2 findings that researchers suggest are characteristic of “vulnerable plaque.”^{21,22}

The moderate success of these studies seems promising, because evaluation of coronary plaques may allow clinicians to better risk-stratify patients with CAD and may influence treatment plans. Serial angiography with IVUS is proposed to be more useful than a single angiography at evaluating plaques, and the noninvasive MDCT would have benefits over ICA, such as lower cost and less procedural risk. However, these studies of MDCT have been very small, so any promise of success is guarded at best. Another limitation in studies of the use of MDCT for evaluating coronary plaques is the high level of interobserver variability and lack of reproducibility, making interpretation highly reader-dependent.¹⁴

Visualization of Bypass Grafts

Another potential use of MDCT is in evaluation of coronary bypass grafts. ICA is the gold standard for assessing the patency of bypass grafts, but

Table 3
Diagnostic Accuracy of 16-Slice Multidetector Computed Tomography (vs Invasive Coronary Angiography) for Detecting Significant Stenosis in Bypass Grafts

Study	Number of Grafts	Grafts Evaluable	Anastomoses Evaluable	Sensitivity	Specificity	PPV	NPV
Martuscelli E et al ²³	285	88%*	—	97%	100%	—	—
Schlosser T et al ^{24†}	131	96%	74%	96%	95%	81%	99%

Significant stenosis defined as $\geq 50\%$ luminal obstruction. PPV, positive predictive value; NPV, negative predictive value.

*Percentage of patients with evaluable grafts.

†Per study protocol, only 12 of 16 detector rings used.

again, there are cost and risk considerations that would make noninvasive evaluation desirable. There are no early studies that have used the new generation of 64-slice MDCT to evaluate bypass grafts, but studies using the commercially available 16-slice MDCT have shown promising results (Table 3). In 2 studies, MDCT was able to visualize 100% of patent bypass grafts and assess for significant stenosis at a sensitivity of 96% to 97% and specificity of 95% to 100%.^{23,24} Visualization of distal anastomoses was more challenging, with one study reporting that only 74% of distal anastomoses were evaluable.²⁴ However, in those vessels, the sensitivity for identifying stenotic lesions was 90%. Evaluation of coronary bypass grafts by 16-slice

MDCT is highly accurate, and performance with 64-slice MDCT is expected to be even better, providing a noninvasive alternative for assessing bypass grafts.

Visualization of Coronary Stents

The evaluation of coronary stents by MDCT is challenging because of the high attenuation of metal components by CT, yet it remains an important clinical aspect of the evaluation of coronary arteries. To date, the majority of studies involving evaluation of stents by MDCT have been done with the current generation of 16-slice MDCT scanners (Table 4). Compared with ICA, 16-slice MDCT has shown good sensitivity (78% to 100%) and specificity (92% to 100%)

for detecting in-stent restenosis in evaluable stents in 3 studies.²⁵⁻²⁷ However, in the 2 studies that evaluated all stents, only 69% to 77% were evaluable by MDCT.^{25,26} Consistently, small stents and stents with thicker struts were more difficult to visualize, given the higher relative partial volume effects of metals. Visualization tended to be easier in larger vessels. Stents in the left main coronary artery or in arteries greater than 3.5 mm in diameter were evaluable in 93% and 88.6% of cases, respectively.^{26,27} Peri-stent stenosis is also vulnerable to partial volume effects from metal stents, but 16-slice MDCT has shown a sensitivity and specificity of 75% and 96%, respectively, for detecting significant stenosis in peri-stent segments.²⁵

Table 4
Diagnostic Accuracy of 16-Slice Multidetector Computed Tomography (vs Invasive Coronary Angiography) for Detecting Significant In-Stent Restenosis

Study	Number of Stents	Stents Evaluable	Sensitivity	Specificity	PPV	NPV
Schuijff JD et al ²⁵	65	77%	78%	100%	—	—
Kitagawa T et al ²⁶	61*	69%	100%	100%	100%	100%
Gilard M et al ^{27†}	29	93%	100%	92%	100%	92%

Significant in-stent restenosis defined as $\geq 50\%$ luminal obstruction; analysis performed per evaluable stent. PPV, positive predictive value; NPV, negative predictive value.

*Only 21 stents in 16 patients compared with invasive coronary angiography.

†Only the left main coronary artery evaluated.

These studies show that 16-slice MDCT has a moderate ability to detect in-stent restenosis, but that many stents and segments are not evaluable with this technology. Early in vitro studies suggest that the 64-slice scanners will allow superior visualization of stent lumen and in-stent stenosis.²⁸ Further in vivo studies will evaluate the ability of 64-slice MDCT to overcome the limitations of 16-slice scanners in stent assessment.

Limitations of MDCT

We have focused mainly on the strengths and benefits of MDCT, but it is equally important to understand its limitations, so as to understand which patients may benefit the most from this technology (Table 5). Some limitations are caused by the contraindications and inherent problems of CT scanners in general. Patients who are allergic to iodinated contrast or who have renal failure are not candidates for CT angiography. Also, there is a relatively high radiation burden for patients undergoing

CT angiography. The estimated dose using 64-slice MDCT has been reported to be as high as 15.2 mSv for men and 21.4 mSv for women.¹¹ With conventional ICA, doses are 2.1 mSv for men and 2.5 mSv for women.²⁹ The radiation burden becomes of particular concern in applications of MDCT that require serial scans.

Limitations specific to CT angiography include issues related to heart rate and rhythm and the patients' ability to hold their breath. As mentioned above, image resolution with MDCT is best with heart rates at or less than 75 beats/min.⁷ Beta-blockers are one method for slowing heart rates, but patients with contraindications or allergies to beta-blockers are less ideal candidates for MDCT. The newer 64-slice MDCT scanners, however, have shown some success in imaging the coronary arteries at higher heart rates. One ideal requirement for patients being considered for MDCT is a normal heart rhythm. Images are collected using electrocardiogram-gating, and in the presence

of an abnormal heart rhythm such as atrial fibrillation, proper imaging is currently much more challenging. Finally, 64-slice MDCT has shortened the scan time to less than 12 seconds, but to prevent respiratory motion abnormalities, patients must be able to hold their breath for the duration of the scan. These factors should be considered in selecting potential candidates for CT coronary angiography.

Potential Applications of MDCT

Technological advancements in MDCT have led to an increased diagnostic accuracy of CT angiography. CT angiography will never be a replacement for ICA—which has not only diagnostic but also therapeutic functions. However, the evidence suggests that it may become a powerful tool for risk stratification of CAD in patients who present with chest pain. Specifically, there may be a role for CT angiography as a screening test to diagnose or evaluate CAD in patients being considered for ICA. At the present time, many

Table 5
Overview of the Advantages and Disadvantages of Multidetector Computed Tomography (MDCT) Versus Invasive Coronary Angiography (ICA)

Advantages of MDCT	Disadvantages of MDCT
Noninvasive	Limited by computed tomography contraindications/limitations
Less expensive than ICA	Allergy to iodinated dye
High accuracy of qualitative detection of stenosis	Renal failure/insufficiency
High negative predictive value in detection of stenosis—may be useful as screening test	Morbid obesity
Ability to detect and describe nonstenotic coronary plaques	Cannot be performed in presence of arrhythmia
Ability to evaluate bypass grafts	Requires breath-holding time of about 12 seconds
Ability to evaluate coronary stents	High radiation exposure
Potential to evaluate surrounding intra-thoracic disease such as pulmonary embolism and aortic dissection	Less accurate in the presence of high coronary calcifications or high heart rates
	Only moderate quantitative accuracy
	No therapeutic benefit

patients are undergoing ICA that reveals no significantly stenotic lesions. Studies have consistently shown that 64-slice MDCT has a very high negative predictive value (92% to 100%) for assessing significant segment stenosis, and thus it may

gies of chest pain such as pulmonary embolism or aortic dissection in an emergency setting. Although there is no evidence on evaluation of bypass grafts and limited evidence on the evaluation of stents with 64-slice MDCT, research

At the present time, many patients are undergoing invasive coronary angiography that reveals no significantly stenotic lesions.

allow clinicians to rule out significant CAD in some patients, preventing unnecessary invasive catheterization. At this time, the burden of proof for performing noninvasive, quantitatively diagnostic angiography rather than ICA has not been satisfied, but perhaps future generations of CT scanners will be able to do so.

The patient population for which this test would be most useful is still uncertain. Patients with the contraindications discussed above (cardiac arrhythmia, allergy to contrast, renal failure, and inability to hold their breath) would not benefit from MDCT. Older patients with high levels of coronary artery calcification may also have less accurate scans. Finally, a study of high-risk patients with positive stress tests who were evaluated by 16-slice MDCT showed a meager negative predictive value of only 75%,⁴ suggesting that high-risk patients may benefit less from MDCT. However, this study was performed with the previous generation of MDCT technology, and it is possible that 64-slice MDCT would yield improved results. Based on the current evidence, however, a low-risk population with minimal comorbidities would likely benefit the most from CT angiography. Additionally, a low-risk patient presenting with chest pain would also be able to be evaluated for noncoronary etiolo-

gies with the previous generation of 16-slice scanners suggests that these patient populations would also benefit from CT angiography.²³⁻²⁷

The success of CT angiography studies has dictated organizational actions. The American College of Cardiology Foundation and the American Heart Association have recently published a clinical competence statement on cardiac imaging, including MDCT,²⁹ as well as a statement on the training requirements for CT imaging.³⁰ The Society for Cardiac Computed Tomography was formed to foster the development and use of the technology. However, at this time, there is no clear indication for routine use of MDCT angiography, although early recommendations have been proposed.³¹ In addition, there is no clinical evidence demonstrating the utility of CT angiography for risk stratification, and 64-slice MDCT is not widely used at the present time. Further studies using CT angiography are needed to define the clinical role of this technology and to clarify its utility in conjunction with, and in comparison with, other tools available for evaluating CAD, such as a stress test and myoperfusion imaging. Still, considering the impressive progress of MDCT, in the future it is likely to prove a powerful diagnostic tool and may change the way that chest pain and CAD are evaluated.

Conclusion

The development of 64-slice MDCT has led to a major improvement in the diagnostic accuracy of noninvasive coronary angiography. MDCT has a high accuracy for qualitatively identifying significant coronary stenosis, but quantitative accuracy and ability to visualize coronary plaques are only moderate with the current technology. Although factors such as arrhythmias, heart rate, calcifications, and patients' ability to hold their breath may limit the patient population that will ultimately benefit from this technology, MDCT coronary angiography has significant clinical potential. More studies are needed to clarify the clinical utility of MDCT, but its potential as a diagnostic tool for evaluating the coronary arteries is very promising. ■

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Main Points

- The early generation of 16-slice multidetector computed tomography (MDCT) scanners proved moderately successful in identifying significant stenotic lesions; up to 43% of coronary segments were unevaluable.
- Per patient analyses demonstrated a high sensitivity for identifying at least 1 stenotic lesion in patients whose arteries were properly evaluable.
- The more recent 64-slice MDCT provides a marked improvement in spatial and temporal resolution.
- Studies show 64-slice MDCT has a sensitivity of 86% to 99% and specificity of 95% to 97% for identifying stenotic lesions.
- Intravascular ultrasound is the invasive method of choice for evaluating coronary plaques, but 64-slice MDCT has a good ability to identify plaques and is moderately successful at categorizing plaques as calcified, mixed, or noncalcified.