Imaging of coronary atherosclerosis with multi-slice computed tomography

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Chapter 1

Advances in the Noninvasive Evaluation of Coronary Artery Disease With Multislice Computed Tomography

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Abstract

Current non-invasive detection of coronary artery disease (CAD) is based on demonstration of ischemia using stress-rest imaging: this is an indirect way of identifying CAD by demonstration of the hemodynamic consequences rather than direct visualization of the obstructive lesions in the coronary arteries. Multi-slice computed tomography (MSCT) has recently emerged as an extremely rapidly developing non-invasive imaging modality, which allows anatomical imaging of the coronary arteries, or non-invasive coronary angiography. In addition, total plaque burden, plaque morphology and (to some extent) plaque constitution can be assessed by MSCT. The technique also provides information on resting left ventricular systolic function, and possibly resting perfusion. Ideally, stress function and perfusion should also be evaluated, since this would allow detection of ischemia and would complete the picture on CAD. However, this is not routinely performed, since sequential acquisitions are associated with high radiation doses and thus pose a limitation for cardiovascular applications of MSCT. It is anticipated that, with reduction in radiation, MSCT may become an important player in the diagnostic and prognostic workup of patients with known or suspected CAD.

Introduction

Despite worldwide efforts to control cardiovascular risk factors, coronary artery disease (CAD) remains the leading cause of death in Europe and in the USA. The prevalence of CAD in American Caucasians is 5.9%; it is estimated that 700 000 Americans will present with a new coronary event and approximately 500 000 will have a recurrent event in 2006. As a result, CAD is a leading cause of death in the USA with an estimated annual cost of $142.5 billion.[1] The presence of CAD can be non-invasively assessed by demonstrating the presence of myocardial ischemia as myocardial wall motion and/or perfusion abnormalities. Accordingly, indirect information about the presence of CAD is obtained by non-invasive functional imaging techniques. The currently available modalities include nuclear imaging, echocardiography as well as magnetic resonance imaging (MRI). When the above tests are inconclusive or show the presence of ischemia, direct visualization of the coronary arteries with invasive coronary angiography, the current gold standard to diagnose CAD, is performed in order to visualize coronary stenoses, which will further guide therapeutic options. However, in up to 40% of patients with suspected CAD, invasive coronary angiography demonstrates no significant stenoses, thus serves only for diagnostic purposes and is not followed by revascularization. Ideally, invasive coronary angiography, which is associated with patient discomfort as well as a small risk of complications, would have been avoided in these patients. Accordingly, during the past years, extensive efforts have been made in search and development of alternative non-invasive anatomical imaging modalities of CAD, which focus on direct evaluation of coronary stenoses and in certain patient populations could replace invasive conventional coronary angiography. Among these, electron beam computed tomography (EBCT), multi-slice computed tomography (MSCT) and MRI have been developed and have shown promising diagnostic accuracy to detect CAD. Furthermore, the above tests (MRI and MSCT) can (potentially) provide information on multiple aspects of CAD, such as myocardial perfusion and left ventricular systolic function. Concerning left ventricular systolic function, MSCT has the advantage that this information may be derived retrospectively from the same scan performed for coronary angiography, whereas additional acquisitions are required with MRI. Having been introduced in the late 1990s, MSCT is the most recent non-invasive cardiac imaging modality. The technique allows 4D imaging of the entire heart during a single breath hold. Its relatively simple and fast image acquisition protocol has not surprisingly attracted enormous interest and the technique is considered to be at present the most robust modality for non-invasive coronary imaging. An objective of this review is to provide a summary of current status and applications of MSCT with emphasis on the diagnostic evaluation of patients with known or suspected CAD.

Non-invasive Functional Imaging of CAD

Functional imaging for the detection of CAD is based on evaluation of hemodynamic consequences of CAD (i.e. ischemia), rather than direct visualization of coronary arteries. These techniques rely on assessment of perfusion and systolic left ventricular (LV) function during stress and at rest; resting perfusion defects and/or systolic wall motion abnormalities in general indicate myocardial damage (scar formation), whereas stress-induced abnormalities indicate the presence of ischemia. Many contemporary non-invasive imaging modalities are able to demonstrate these changes indicating myocardial ischemia, including single photon emission computed tomography (SPECT), stress (contrast) echocardiography and magnetic resonance imaging (MRI). Two types of stress are used, namely exercise and pharmacological stress, the latter mostly being used in patients who are unable to exercise. A summary of the diagnostic accuracies of these functional imaging modalities to detect CAD is presented in Figure 1.

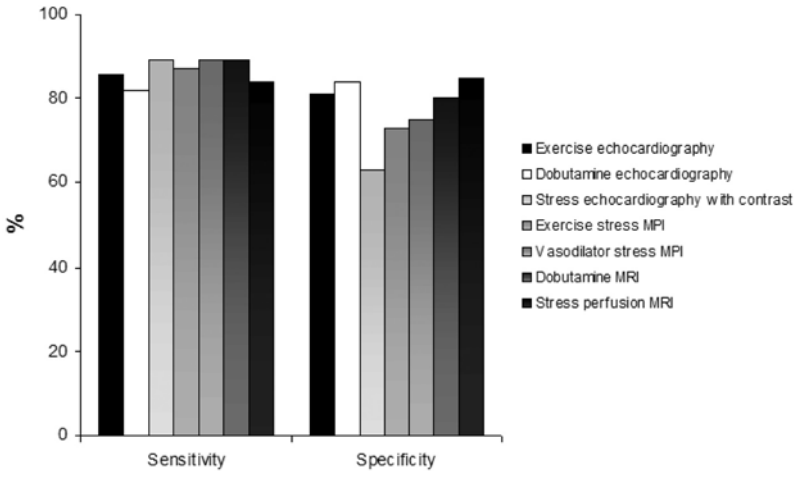

Figure 1. Diagnostic accuracies of functional non-invasive imaging modalities to detect coronary artery disease (data are based on ref. [55-60])

MPI, myocardial perfusion imaging; MRI, magnetic resonance imaging.

Non-invasive Anatomical imaging of CAD

Despite the fact that functional techniques allow reliable evaluation of the presence and extent of CAD, direct evaluation of coronary anatomy is still needed in a considerable number of patients. Thus, the ultimate goal for anatomical non-invasive imaging of CAD is to directly visualize the coronary arteries, although the small vessel size, tortuous course of the arteries and fast motion during the cardiac cycle pose significant challenges. A summary of diagnostic accuracies of non-invasive imaging modalities to detect CAD is provided in Table 1.

Table 1. Diagnostic accuracy of anatomical non-invasive imaging to detect coronary artery disease

Test	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Non-evaluable segments, %	Ref.
EBCT native coronary arteries	87	91			16	1
MRI native coronary arteries	72	87	65	90	17	5
4-slice MSCT native coronary arteries	80	94	67	97	12	5
16-slice MSCT native coronary arteries	88	96	81	98	4	5
64-slice MSCT native coronary arteries	90*	96*	75*	99*	4**	12-17
4-slice MSCT coronary artery bypass graft occlusion	93	96	89	98		21
16-slice MSCT coronary artery bypass graft occlusion	99	98	94	100		21

* Weighted mean is based on ref. [13-17]

** Weighted mean is based on ref. [12-17]

EBCT, electron beam computed tomography; MRI, magnetic resonance imaging; MSCT, multi-slice computed tomography; NPV, negative predictive value; PPV, positive predictive value.

EBCT

EBCT has been developed specifically for cardiac imaging and has been available since the early 1990s. Since its design does not require mechanical movement of an X-ray gantry, data are acquired with a very high temporal resolution (50-100 ms). As can be derived from Table 1, the technique has been proved to be accurate for detection of significant coronary stenoses with sensitivities ranging between 74 to 92% and specificities being in the range of 79 to100%.[2] However, despite the high temporal resolution, the percentage of non-evaluable segments is relatively high (7 to 25%).[2] This is

mostly due to motion artefacts, which may result from data acquisition with prospective triggering in mid-diastolic phase (80% of R-R interval) of the cardiac cycle, not taking into consideration a heart rate of an individual patient. This shortage may be partially overcome by triggering in the end-systolic phase after an increasingly shorter time interval after the previous R wave as heart rate increases. A recent study has demonstrated that with the application of the above protocol, sensitivity increases up to 91%, as compared to 69% as conventional protocol of triggering at mid-diastolic phase is used, and number of non-evaluable segments decreases from 35% to 9%, respectively.[3] Another reason of high percentage of non-enaluable segments is low spatial resolution (1.5 or 3.0 mm) and that the technique requires breath-hold of 30 to 40 s to cover the entire heart.

MRI

The first results on non-invasive coronary imaging with MRI technique were reported by Manning et al in 1993, who observed a sensitivity and specificity for breath-hold 2D MRI of 90% and 92% as compared to conventional coronary angiography.[4] Despite the substantial progress of technical acquisition protocols, such as navigator techniques, however, reported sensitivities and specificities in detecting CAD still show a wide variation, and a considerable percentage of segments suffer from degraded image quality. Currently, the performance of MSCT coronary angiography is better than of coronary MRI, as also recently indicated by Kefer et al, who performed a head-to-head comparison of 1.5 Tesla navigator gated MRI and 16-slice MSCT to invasive coronary angiography. Qualitative analysis of MRI and MSCT images showed sensitivity of 75% and 82% and specificity of 77% and 79%, respectively (p=NS). However, quantitative analysis showed improvement of diagnostic accuracy of MSCT, but not of MRI.[5] It is expected that higher field magnets of 3 Tesla may contribute to improved diagnostic accuracies in the near future.

MSCT

In the late 1990s, MSCT systems were introduced allowing the acquisition of multiple slices instead of 1 slice in a single gantry rotation. As a result, visualization of coronary arteries with this technique had become possible. The latest generations of 16- and 64-slice MSCT scanners have improved spatial and temporal resolution and reduced image acquisition time, which has resulted in significant improvement of image quality and diagnostic accuracy to detect CAD.

Non-invasive imaging of coronary arteries with MSCT
Image acquisition, reconstruction and post-processing

Over the past decade MSCT technology has evolved enormously, resulting in the development of 4-, 16- and 64- and in the near future 256-slice MSCT scanner generations. The most important improvements in the new scanner generations are faster tube rotation speed and better z-axis spatial resolution. A recently introduced development is a dual-source computed tomography (DSCT) system with two X-ray tubes and two corresponding detectors (64-slice), allowing data acquisition during one-quarter of gantry rotation resulting in temporal resolution of 83 ms or as low as 42 ms when multi-segmental reconstruction algorithm is used independent of the heart rate.[6] The first experience with 14 patients examined with DSCT without additional administration of β-blockers showed that 98% of coronary segments could be visualized unimpaired by motion artefacts.[7]

In order to avoid cardiac and breathing motion artefacts, the prerequisites of cardiac MSCT examination are regular heart rate and the ability to hold breath. A heart rate of < 65 beats per minute which can be achieved spontaneously or with the use of β-blockers is desirable for optimal image quality. The average breath hold time for 4-, 16- and 64-slice MSCT is 30 - 40 s, 20 s and 10 s, respectively. The examination of CAD begins with scanning without contrast material injection for evaluation of coronary calcium burden. Prospectively ECG-triggered or retrospectively ECG-gated spiral scanning is performed for evaluation of coronary calcium. The latter provides shorter breath hold times and has less inter-examination variability. However, an important drawback of such protocol is the higher radiation dose. For evaluation of coronary artery stenoses and plaques, the scan is performed with intravenous administration of contrast material which has to be carefully tailored either using a test bolus or automatic bolus triggering technique. Since scan times for imaging of the heart on 4-, 16- and 64-slice MSCT scanners range from 10 to 40 s, 80-140 ml of iodinated contrast with the injection rates of 4-5 ml/s is needed to maintain homogeneous vascular opacification throughout the scan. Saline chasing has proven helpful for avoiding streak artefacts arising from dense contrast material in the superior vena cava and the right atrium as well as for reduction of the volume of contrast medium needed for consistently high vascular enhancement. In contrast no data currently support improved attenuation using multi-phasic over mono-phasic contrast protocols.[8] A helical retrospectively reconstructed scan is performed for evaluation of coronary stenoses. The recent 64-slice MSCT scanners allow acquisition of nearly isotropic voxels with the z-plane resolution of 0.3-0.4 mm as compared to 0.5-0.6 mm with the previous 16-slice

MSCT and >1 mm with 4-slice MSCT. The shortest tube rotation time of 64-slice scanners is 330 ms, resulting in effective temporal resolution of 165 ms and maximal temporal resolution of 83 ms, as compared to 375 ms, 188 ms and 94 ms, respectively with the previous 16-slice MSCT scanner generation.[9] With recent introduction of DSCT scanners, a temporal resolution of 83 ms can be achieved as a single R-R interval is used for image reconstruction or as low as 42 ms when using a segmented reconstruction algorithm that combines data from two cardiac cycles.[7]

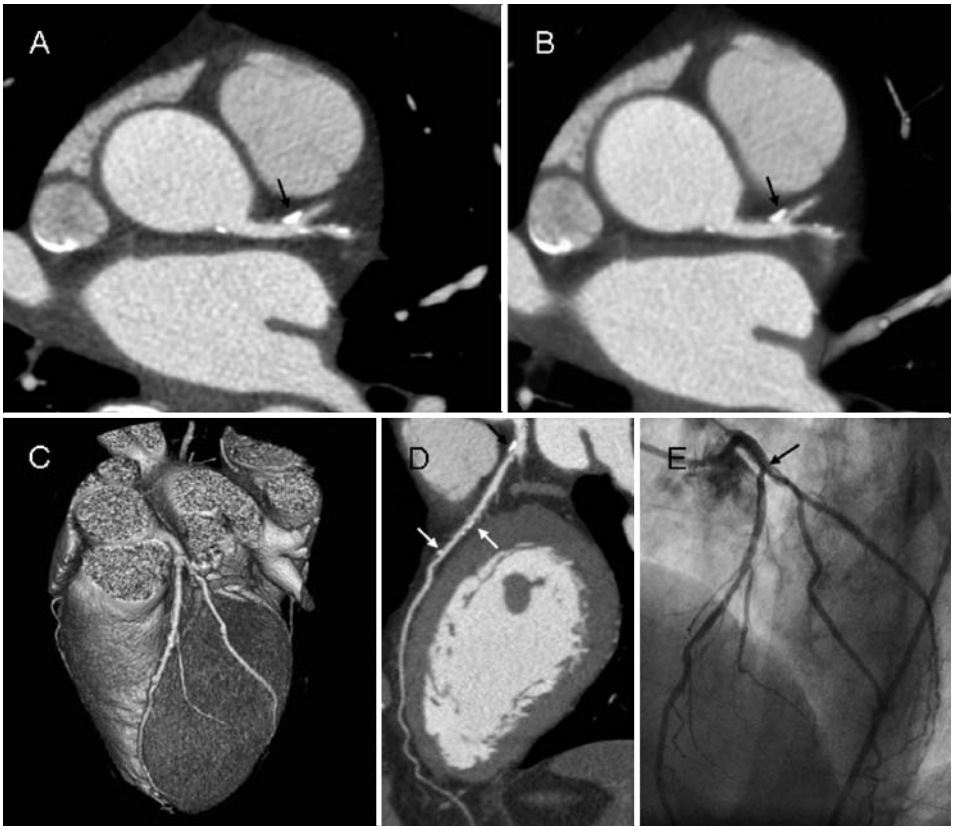

Figure 2. Evaluation of coronary plaques with different post-processing techniques. (A) Axial slice of 0.5 mm thickness is depicted. (B) MIP of 8 mm thickness allows better volumetric evaluation of coronary vessel. (C) 3D volume rendering of the heart. A cMPR is allows the whole course of the coronary artery to be depicted in 2D plane (D). Multiple mixed plaques of LAD are seen in all available reconstructions (white and black arrows). A borderline significant stenosis is seen in the proximal LAD (black arrows), which was confirmed with conventional coronary angiography (E).

LAD, left anterior descending coronary artery; MIP, maximum intensity projection; cMPR, curved multiplanar reconstruction.

Several image post-processing techniques are available to allow clinically useful information to be extracted from several hundreds of individual axial images generated during single MSCT examination.[9,10] The evaluation often begins with the scrolling through axial images, which are considered to be the source images for image post-processing. Multiplanar reconstructions are generated from the volume data set reconstructed from axial images in several arbitrary imaging planes with all available data being represented in the images. Depending on the vascular tissue densities encountered by each ray in the 3D volume, maximum intensity projection reconstructions of various thicknesses may be performed. Volume rendering reconstructions are used to obtain an anatomical overview of the heart and the coronary arteries. Examples of images performed with the available post-processing techniques are provided in Figure 2.

Examination of native coronary arteries

Although diagnostic accuracy to detect significant coronary artery stenoses with the first 4-slice MSCT generation was promising, still 20% of coronary segments had to be excluded from analysis due to non-diagnostic quality.[11] Substantial improvement was achieved by the introduction of 16-slice scanners with submillimeter collimation as well as faster tube rotation times. The sensitivities ranged between 70 to 98%, whereas the specificities varied between 93 to 98%, with on average only 4% (ranging between 0% to 17%) of coronary segments being excluded as non-evaluable.[11] With the introduction of 64-slice MSCT systems, further substantial improvement in image quality has been observed. Examples of coronary angiography with 64-slice MSCT are shown in Figure 2. Currently available data using 64-slice MSCT in comparison to invasive coronary angiography demonstrate sensitivities of 93 to 99% and specificities of 95 to 97% to detect significant coronary stenoses on segment based analysis (Table 2) and 96 to 100% and 90 to 92% on patient based analysis.[12-15] When quantitative analysis is employed, the sensitivity decreases, being 81 and 86%.[16,17] While in some studies all available coronary segments could be included in the analysis,[12,13,15] others have reported exclusion of still 3 to 12% of segments.[14,16,17] In general, the specificity and negative predictive value of MSCT is extremely high and the likelihood of significant CAD if no abnormalities are demonstrated on MSCT is extremely low. Accordingly, the technique may be particularly suitable to exclude CAD and as a result substantially decrease the number of diagnostic catheterizations.

Table 2. Diagnostic accuracy of 64-slice MSCT

Author	Sensitivity, % (no. of segments)	Specificity, % (no. of segments)	PPV, % (no. of segments)	NPV, % (no. of segments)	Evaluable, % (no. of segments)
Leschka et al [13]	94 (165/176)	97 (805/829)	87 (165/189)	99 (805/816)	100 (1005/1005)
Mollet et al [12]	99*	95*	76*	100*	100 (725/725)
Ropers et al [14]	93 (39/42)	97 (1010/1041)	56 (39/70)	100 (1010/1013)	96 (1083/1128)
Pugliese et al [15]	99 (66/67)	96 (408/427)	78 (66/85)	99 (408/409)	100 (494/494)
Raff et al** [16]	86 (79/92)	95 (802/843)	66 (79/120)	98 (802/815)	88 (935/1065)
Leber et al** [17]	81 (59/75)	97 (700/723)	72 (59/82)	98 (700/716)	97 (798/825)

* not specified.

** diagnostic accuracies are based on quantitative evaluation of coronary stenoses with MSCT coronary angiography.

MSCT, multi-slice computed tomography; NPV, negative predictive value; PPV, positive predictive value.

Examination of coronary artery bypass grafts

In patients after bypass surgery, graft occlusion remains a clinically relevant problem as occlusion may occur in up to 15% of venous grafts within a year.[19] In contrast, patency rates are much higher for arterial grafts with occlusion of 5% to 15% of grafts after 10 years.[20] Accordingly, examination of patients with recurrent chest pain complaints after coronary artery bypass graft surgery is another possible application of MSCT. As recently shown in a meta-analysis of the available literature, graft occlusion can reliably be assessed with MSCT.[21] An increasingly better diagnostic accuracy has been shown with the new scanner generations both, to detect coronary bypass graft occlusion and to assess bypass graft stenoses. A pooled analysis of 12 studies where 441 patients with 1246 grafts examined with 4-slice MSCT were included showed overall sensitivity to detect bypass occlusion of 93% and specificity of 96%. Two studies with 144 patients and 416 grafts examined with 16-slice MSCT showed even better sensitivity and specificity of 99% and 98%, respectively.[21] However, observed ability of the technique to detect bypass graft stenosis was lower and the sensitivity was demonstrated to be 70 to 85% with 4- and 16-slice MSCT, respectively.[20] Also, limited data are available on the diagnostic accuracy to detect CAD in the native coronary arteries after coronary artery bypass surgery. This is an important issue, since CAD in the native coronary arteries is more advanced and extensive coronary calcifications are present. Another limitation of coronary bypass graft imaging is the use of metal clips, which potentially cause metal artefacts and hamper evaluation of bypass graft lumen. Currently, no data are yet available on the diagnostic accuracy to detect coronary

artery bypass graft patency with 64-slice MSCT.

Another potential application of MSCT coronary angiography is the evaluation of anatomical information of native vessels and the arterial conduits prior to minimally invasive coronary artery bypass surgery, such as the precise localization of the course of left anterior descending coronary artery, internal mammary arteries and left subclavian artery.[22]

Examination of coronary stents

Despite substantial improvements in interventional revascularization of coronary arteries, the rate of in-stent restenosis remains in the range of >20% in routine clinical practice.[23] Patients presenting with complaints suggestive of in-stent restenosis may accordingly be another subgroup which could benefit from non-invasive imaging of the coronary arteries with MSCT. Coronary stent patency has been extensively evaluated with previous MSCT scanner generations. Four-slice MSCT failed to allow stent lumen assessment regardless of stent type and diameter and the patency of stent was assessed mainly by evaluating the presence of contrast filling in the segment distal to stent.[24] With the introduction of 16-slice MSCT with superior temporal and spatial resolution, the visualization of stent lumen became possible, with 65 to 77% of stents being regarded as evaluable.[25,26] However, stents with larger diameter (>3 mm) were more often regarded as evaluable and rendered higher diagnostic accuracy to detect in-stent restenosis, smaller stents with thicker struts being the main reason for excluding stents from analysis.[25,26] In a study with 40-slice MSCT, a superior diagnostic accuracy to detect in-stent restenosis was observed, as compared to 16-slice MSCT.[27] Only 4.5% of stents were excluded as not evaluable. All except one stent with non-significant in-stent restenosis on MSCT were confirmed with invasive angiography. The sensitivity and specificity to detect restenosis of ≥50% were 63.6% and 87.6%, respectively, with a particularly high negative predictive value of 90.7%. Similar results were observed in a phantom study evaluating the feasibility of stent assessment with 64-slice MSCT, where it has demonstrated that artificial lumen reduction was significantly less with 64-slice than with 16-slice CT, and average visible

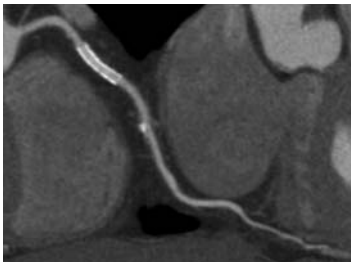

Figure 3. Curved MPR of coronary stent, placed in the right coronary artery. No in-stent restenosis is observed. MPR, multiplanar reconstruction.

stent lumen was 53.4% and 47.5%, respectively.[28] However, a relevant part of the stent lumen is still regarded as not assessable with 64-slice MSCT and the evaluation of subtle neo-intima hyperplasia therefore remains unlikely at least in the near future. In Figure 3, a patent coronary stent imaged with 64-slice MSCT is depicted.

Examination of coronary atherosclerosis: coronary artery calcium scoring

The evaluation of coronary calcium burden is possible using EBCT and MSCT, both providing similar measures.[29] The most widely applicable technique of evaluating coronary calcium burden is the determination of Agatston score.[30] However, it has been shown that volume and mass indexes are superior to traditional calcium score for comparing the results of EBCT and MSCT.[31] Although coronary calcium scoring provides an indication of the extent of atherosclerosis, it does not resemble the total coronary plaque burden, as it identifies only calcified atherosclerotic lesions. Nonetheless, it has been shown that the likelihood of having obstructive CAD increases in parallel with the coronary artery calcium score.[32] Still, coronary artery calcium is not site-specific meaning that calcified segments are not necessarily significantly obstructed and vice versa.[33]

Coronary artery calcium score assessed by EBCT has been studied extensively for risk stratification in asymptomatic patients, and a calcium score <100 has been associated with excellent outcome, with an increase in event rate paralleling the increase in calcium score. Also, the technique has been demonstrated to be an independent predictor of cardiovascular events, thereby potentially refining Framingham risk stratification.[34]

Examination of coronary atherosclerosis: plaque imaging

It has been shown, that the risk of acute coronary syndromes caused by plaque disruption and thrombosis depends on plaque composition rather than stenosis severity.[35,36] In this context, an important advantage of non-invasive coronary angiography with MSCT as compared to conventional coronary angiography is the ability to image the vessel wall. Figure 2 demonstrates evaluation of coronary plaques with 64-slice MSCT. Coronary plaque imaging with MSCT relies on a difference in densities (expressed in Hounsfield Units, HU) in different types of coronary lesions. It has been shown by Schroeder and colleagues that significantly different mean densities of 419±194 HU, 91±21 HU and 14±26 HU can be detected respectively in calcified, intermediate and soft plaques (with intravascular ultrasound serving as standard of reference).[37] Recently Kunimasa et al have demonstrated

that low density coronary plaques detected with 16-slice MSCT were significantly more often observed in patients presenting with acute coronary syndromes as compared to those having stable CAD.[38] Similarly, MSCT allows assessment of coronary artery remodeling. Achenbach et al have demonstrated that the mean remodeling index measured by MSCT was significantly higher in nonstenotic than in stenotic lesions (1.3±0.2 versus 1.0±0.2, $p<0.001$). Moreover, remodeling indices measured by MSCT correlated closely to intravascular ultrasound ($r=0.82$).[39] However, available data on plaque imaging with MSCT are still limited and prospective studies are required whether MSCT can indeed play a role in identification of patients at elevated risk for coronary events based on the plaque distribution and type. Moreover, further distinction of low-density plaques in fibrous and lipid content appears not feasible as their signal intensities on MSCT are highly overlapping.

Additional diagnostic information with MSCT; LV function and perfusion

Image acquisition, reconstruction and post-processing

Assessment of LV function with MSCT is only possible at rest, since repeated scanning during stress and resting conditions is not justifiable due to the high radiation dose. The same set of axial slices acquired during helical scanning of the coronary arteries is used for LV function imaging. For the assessment of LV systolic function, the entire heart is reconstructed in the short-axis plane in 10 or 20 cardiac phases (using a step of 10% and 5% of the R-R interval on the electrocardiogram, respectively) with the various reconstructed slice thickness and reconstruction increment.[40,41] The set of axial images is then transferred to the remote workstation with dedicated software for analysis of global and regional LV systolic function. For LV perfusion analysis, the density of the hypoperfused and normally perfused myocardial areas is assessed and expressed in HU. The hypoperfused areas may be quantitatively assessed with the use of available software. An example of evaluation of global LV systolic function and myocardial perfusion with 64-slice MSCT is provided in Figure 4.

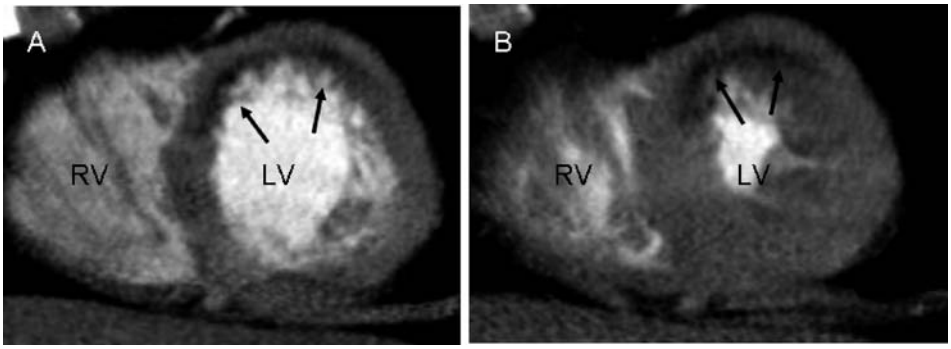

Figure 4. Evaluation of LV function in a patient with a history of anterior myocardial infarction. (A) End-diastolic phase. (B) Myocardial thickening in end-systolic phase. Perfusion defects are seen in anterior segments (arrows), confirming the presence of previous myocardial infarction.
ED, end-diastole; ES, end-systole; LV, left ventricle; RV, right ventricle.

Systolic left ventricular function

In ischemic heart disease cardiac function provides both diagnostic and prognostic information.[42,43] Decreased LV function has been related to worse prognosis after myocardial infarction.

Several studies have shown excellent correlation and agreement between LV volumes and ejection fraction (EF) obtained by MSCT and 2D echocardiography.[41,44-47] Schuijf et al compared global LV systolic function with 4-slice MSCT and 2D echocardiography. Bland-Altman analysis in comparison of LVEF showed a mean difference of -0.48±3.8%, which was not significant from 0.[44] Similarly, another study with 16-slice MSCT showed an excellent correlation (r=0.96) between the two modalities in the evaluation of global LV systolic function.[46] The comparison of global LV systolic function with MRI showed similar results.[41,48] Salm et al demonstrated fair correlation (r=0.86) between 16-slice MSCT and MRI in the assessment of LVEF.[41] Another study by Mahnken and coworkers demonstrated that MSCT multisegmental image reconstruction improved the quantitative assessment of global LV systolic function, as compared to MRI, resulting in better agreement between the two modalities.[48] Besides global LV systolic function, the presence of regional wall motion abnormalities can be assessed from the cine-loop images. In a study with 4-slice MSCT, a good correlation was demonstrated between myocardial wall motion as compared to 2D echocardiography, overall agreement was 88% with a weighted kappa value of 0.84.[45] Sixteen-slice MSCT has shown even better correlation of qualitative assessment of wall motion abnormalities as compared to 2D echocardiography. In a study by Schuijf et al, the

agreement between the two modalities for assessment of regional contractile function was excellent (91%, kappa statistic 0.81).[47] In the comparison of regional systolic LV function detected with MSCT multisegmental reconstruction algorithm and MRI overall agreement was 92.5%.[48] Another study comparing regional wall motion assessed with 16-slice MSCT and MRI showed a good agreement of wall motion scores with kappa value of 0.8.[49]

Although an MSCT scan is not justifiable to solely assess systolic LV function, the functional parameters obtained during the same scan performed for coronary angiography may importantly add to the diagnostic (and potentially prognostic) work-up of patients with suspected or known CAD.

Myocardial perfusion

As described above, only myocardial perfusion at rest may be justifiable, as repeated scanning during stress and resting conditions is associated with a high X-ray dose. Perfusion abnormalities at rest may be observed in the early phase of the contrast bolus. Several reports have evaluated the diagnostic performance of MSCT in the diagnosis of the myocardial infarction. Nikolaou et al observed a sensitivity and specificity of 4-slice MSCT to detect myocardial infarction with invasive ventriculography serving as standard of reference to be 85% and 91%, respectively.[50] Moreover, the authors have demonstrated the ability of MSCT to differentiate old and recent myocardial infarction on the basis of the tissue density expressed in HU, old infarctions having lower CT densities as compared to recently infarcted areas (44±17 HU versus 63±19 HU; p=0.0465).[50] Due to high spatial resolution of MSCT, the differentiation of subendocardial and transmural infarctions is possible, which may have additional prognostic information. Wada et al have demonstrated poor recovery of regional and global systolic left ventricular function in patients having transmural infarction at 6 months after the onset of acute myocardial infarction, whereas the subendocardial infarction group exhibited good recovery of LV function.[51] Sporadic studies have also examined the ability of MSCT to evaluate myocardial viability, based on assessment of myocardial perfusion. Mahnken et al evaluated myocardial perfusion with 16-slice MSCT in the early phase of the contrast bolus and 15 min after contrast injection. An excellent agreement was demonstrated between the infarct size on late enhancement of MRI and late enhancement of MSCT.[52] Theoretically, also evaluation of perfusion during stress may be possible, as was recently explored by Kurata et al in 12 patients, showing an 83% agreement between MSCT and SPECT to detect stress induced (by means of adenosine triphosphate) hypoperfusion areas.[53] However, further evaluation is necessary to define the clinical role of myocardial perfusion assessment with MSCT.

Limitations of MSCT

Despite the enormous development of MSCT technique during the last decade, several important limitations still remain. The newer scanner generations with improving spatial resolution are associated with high radiation. The effective dose of 64-slice MSCT scanner is substantially higher (14 mSv) than that of conventional coronary angiography (6 mSv).[54] MSCT techniques have been developed to reduce radiation exposure, such as the reduction of X-ray tube current at early systolic and diastolic phases of the R-R interval, or the use of prospective triggering for coronary calcium scoring. At present, the technique is therefore not suitable for repeated imaging to monitor disease progression/regression or to allow sequential imaging of LV function during stress and resting conditions. Although the amount of injected iodinated contrast is decreasing with the shorter scan time of the newer scanner generations, the use of contrast limits examination of patients with impaired renal function. A stable and low heart rhythm is an important prerequisite of cardiac MSCT. Although reconstruction algorithms are available to improve image quality in patients with heart rates above 65 beats per minute, artificial lowering of the heart rate is still preferable to obtain best results. Technical advancements, such the introduction of DSCT, may potentially assist in overcoming the need of lowering of heart rate. Also, atrial fibrillation and frequent extrasystoles often require deferring the procedure due to unacceptable motion artefacts. To date, mostly qualitative analysis of coronary stenoses is available and quantitative evaluation needs to be developed and validated. The presence of coronary artery calcifications is another serious limitation for MSCT coronary angiography, hampering precise evaluation of the degree of coronary stenoses. Although the technique allows accurate evaluation of coronary stenoses, its capacity of functional imaging is limited, as compared to radionuclide imaging, MRI and echocardiography which allow evaluation of a wider range of LV functional parameters.

Expert opinion

An alternative, less expensive non-invasive diagnostic test to be used in order to avoid a substantial number of invasive coronary angiographies could have a major impact on clinical practice and cost effectiveness. While diagnostic accuracies and assessability to detect CAD with the first MSCT generations were not sufficient for the application of the technique in clinical practice, the results of the latest 64-slice scanners are excellent. Consistently high negative predictive values have been reported with MSCT, making the technique particularly suitable to exclude CAD in patients with previously unknown CAD at intermediate risk. Nonetheless, most studies have focused on examining patients with high pretest likelihood of CAD thus far and the technique still needs additional validation in patients with lower prevalence of the disease.

Five-year view

Although a possibility to evaluate CAD non-invasively with MSCT is an important development in clinical practice, the evaluation of hemodynamic consequences of CAD (hypoperfusion in ischemic areas and/or induction of systolic LV dysfunction) is essential in the diagnosis of CAD and subsequent choice of therapeutic strategy. Therefore, combined SPECT or PET-CT systems are under development, which will allow fusion of anatomical and functional information on CAD in a given patient. This combination will serve not only for detection of coronary lesions, but also for assessment of hemodynamic consequences of these lesions. Future investigations should be directed to evaluate the integration of these parameters.

Finally, current state-of-the-art MSCT allows non-invasive evaluation of the vessel wall. Evaluation of plaque burden and plaque composition will become increasingly important and will further aid in improved management of patients with CAD.

Key issues

- Multi-slice computed tomography (MSCT), electron beam computed tomography (EBCT) and magnetic resonance imaging (MRI) are the currently available non-invasive imaging modalities to detect coronary artery stenoses.
- The sensitivity and specificity to detect significant stenoses in native coronary arteries with 64-slice MSCT is as high as 93 to 99% and 95 to 97%, respectively, making MSCT the most promising non-invasive imaging modality for anatomical evaluation of coronary artery disease (CAD).
- Evaluation of coronary artery bypass graft occlusion with MSCT is highly accurate; however, the assessment of native coronary arteries of patients after coronary artery bypass graft surgery is problematic due to advanced and diffuse calcifying CAD.
- Precise evaluation of neo-intima hyperplasia in stents remains unlikely with MSCT in the near future due to insufficient spatial resolution of the current scanner generations.
- Evaluation of coronary plaque burden and constitution with MSCT is possible and appears promising.
- MSCT allows evaluation of left ventricular perfusion and systolic function at rest, however, due to high radiation dose associated with repeated scanning, it does not allow detection of CAD by demonstrating myocardial ischemia during stress conditions.
- The major limitations of MSCT are high radiation dose and insufficient temporal resolution, requiring at present a low and stable heart rate during MSCT examination.

Outline of the thesis

The aim of this thesis was to evaluate the role of MSCT in non-invasive imaging of coronary atherosclerosis in patients with suspected CAD. In **Part I**, the ability of MSCT to demonstrate obstructive atherosclerotic lesions in the coronary arteries was explored. The diagnostic accuracy of 64-slice MSCT in detecting obstructive coronary stenoses as compared with conventional coronary angiography was evaluated in **Chapter 2**. In **Chapter 3**, the diagnostic accuracy of 64-slice MSCT coronary angiography in detecting obstructive lesions in male and female patients was investigated. The impact of calcium accumulation in the coronary arteries on the diagnostic accuracy of the previous 16-slice MSCT and the more recent 64-slice MSCT in detecting obstructive lesions was explored in **Chapter 4**. The accuracy of 64-slice MSCT to detect in-stent restenosis was described in **Chapter 5**. In **Chapter 6**, direct comparison between findings on bicycle exercise testing and MSCT coronary angiography is provided.

Part II focuses on characterization of coronary atherosclerotic plaque extent and composition on MSCT. The prognostic value of coronary plaque characteristics on MSCT was explored in **Chapter 7**. Head-to-head comparison of coronary plaque composition between non-invasive MSCT and invasive virtual histology intravascular ultrasound was performed in **Chapter 8**. Coronary plaque characteristics were investigated both on non-invasive MSCT and on invasive virtual histology intravascular ultrasound in patients presenting with acute coronary syndromes and stable CAD in **Chapter 9**. The patterns of coronary atherosclerosis on MSCT in patients with type 2 diabetes were investigated in **Chapters 10** and **11**. Finally, coronary atherosclerosis was explored in men and women with suspected CAD both on MSCT and on gray-scale and virtual histology intravascular ultrasound (**Chapter 12**).

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