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REVIEW ARTICLE

Coronary CT angiography: current status and continuing challenges

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ABSTRACT. Coronary CT angiography has been increasingly used in the diagnosis of coronary artery disease owing to rapid technological developments, which are reflected in the improved spatial and temporal resolution of the images. High diagnostic accuracy has been achieved with multislice CT scanners (64 slice and higher), and in selected patients coronary CT angiography is regarded as a reliable alternative to invasive coronary angiography. With high-quality coronary CT imaging increasingly being performed, patients can benefit from an imaging modality that provides a rapid and accurate diagnosis while avoiding an invasive procedure. Despite the tremendous contributions of coronary CT angiography to cardiac imaging, study results reported in the literature should be interpreted with caution as there are some limitations existing within the study design or related to patient risk factors. In addition, some attention must be given to the potential health risks associated with the ionising radiation received during cardiac CT examinations. Radiation dose associated with coronary CT angiography has raised serious concerns in the literature, as the risk of developing malignancy is not negligible. Various dose-saving strategies have been implemented, with some of the strategies resulting in significant dose reduction. The aim of this review is to present an overview of the role of coronary CT angiography on cardiac imaging, with focus on coronary artery disease in terms of the diagnostic and prognostic value of coronary CT angiography. Various approaches for dose reduction commonly recommended in the literature are discussed. Limitations of coronary CT angiography are identified. Finally, future directions and challenges with the use of coronary CT angiography are highlighted.

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CT has been gaining widespread acceptance in clinical practice since its invention in the 1970s. However, cardiac imaging with the use of conventional CT has been limited by the fact that cardiac motion interferes with conventional CT reconstruction algorithms and leads to loss of morphological details. Although techniques were developed in the late 1970s or early 1980s to reduce image degradation due to heart motion [1, 2], cardiac imaging has been dominated by invasive coronary angiography. However, this changed with the development of multislice CT scanners. The main applications of multislice CT in cardiac imaging are demonstrated in the detection of coronary calcium deposits, assessment of lumen stenosis or occlusion and prediction of disease outcomes.

Calcium deposition can be quantified non-invasively at a very early stage by electron beam CT (EBCT) using the Agatston method [3]. EBCT revolutionised cardiac imaging by combining high temporal resolution (50–100 ms) with prospective electrocardiographic triggering so that images free of artefacts could be acquired with this technique. The main clinical application of EBCT is in the detection and evaluation of calcification in the coronary arteries (calcium scoring), which is considered to be an indicator of coronary artery disease (CAD). EBCT has significant value in determining calcium scores, which are associated with the degree and severity of CAD, and thus assists in predicting the probability of future cardiac events [4]. The main limitation of EBCT is its inferior spatial resolution (*z*-axis resolution), which is between 1.5 and 3.0 mm. This restricts its diagnostic value in accurately evaluating the severity of CAD. After the arrival of multislice CT scanners in the late 1990s, the use of EBCT became rare. It was eventually replaced by multislice CT from 2003 onwards.

As an alternative to invasive coronary angiography, coronary CT angiography (CCTA) has been increasingly used for the investigation of suspected CAD, and rapid technological developments have led to improved spatial and temporal resolution. The early generations of 4- and 16-slice CT scanners represented a technological

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revolution in cardiac imaging [5–9], although the diagnostic accuracy in terms of sensitivity was low for grading native coronary disease. Specificity for exclusion of CAD (negative predictive value) was good, and this generation of technology also proved useful for the evaluation of coronary anomalies and bypass graft patency. Improved spatial resolution with 16-slice CT plays an important role in the reliable detection and characterisation of coronary plaques and cardiac wall changes (such as remodelling of the coronary wall due to atherosclerotic plaques). However, the image quality is compromised in patients with a high heart rate, stents or severely calcified arteries [7, 8]. In 2004, all major CT manufacturers introduced the next generation of CT scanners with 32, 40 and 64 simultaneously acquired slices, which brought about a further leap in volume coverage speed. With gantry rotation times down to 330 ms for 64-slice CT, temporal resolution for cardiac electrocardiography (ECG)-gated imaging was again markedly improved. Improvement of image quality has also been reported in the visualisation of all coronary artery branches, with high sensitivity and specificity achieved [10–12]. In patients with high heart rates, multisegment reconstruction algorithms were reported to provide diagnostic images by offering optimal temporal resolution, thus mitigating motion artefacts [13, 14].

Dual-source CT was designed to further improve temporal resolution to 83 ms, thus increasing image quality by reducing motion artefacts. Studies have shown a significant improvement with the use of CCTA in the assessment of patients with a high heart rate when dual-source CT (DSCT) is used [15–18]. The development of wide-area detector CT enables greater coverage per gantry rotation [19–21]. Expansion of multislice CT systems from a prototype 256-slice to a 320-slice system has allowed for acquisition of whole-heart coverage in one gantry rotation. Tables 1 and 2 list the number of detector rows, number of simultaneously acquired slices, maximum gantry rotation speed, effective maximum temporal resolution, method of dual-energy imaging and other special features for each of the manufacturers for their scanners of 64 slices and above.

Other new technologies have been developed by manufacturers to improve the performance of CT scanners, such as the Gemstone detector technology from GE Healthcare (Waukesha, WI) and Ingenuity CT from Philips Healthcare (Best, Netherlands) [22, 23]. The Gemstone scintillator is capable of acquiring 2.5 times as many views per rotation at the same rotating speed as the previous generation of CT products. The significantly increased amount of information enhances the spatial resolution and enables electronically switching tube energies from 80 to 140 kVp to acquire dual-energy images with a single X-ray tube during operation, thus achieving spectral imaging with a single X-ray tube [22]. The Philips Ingenuity CT uses up to 50% less dose while improving spatial resolution by up to 35% and maintaining diagnostic image quality [23].

Despite promising results having been achieved with coronary CT angiography, CCTA has the disadvantage of a high radiation dose, which leads to the concern of radiation-associated risks [24, 25]. It is generally agreed that CT is an imaging modality with high radiation exposure, as it contributes up to 70% radiation dose of all radiological examinations, although it constitutes only 15% of all radiological examinations. Radiation-induced malignancy is a problem that has been addressed by the National Research Council of the United States [26]. It is reported that radiation dose from a CT scan has been significantly underestimated by radiologists and physicians [24, 27]. Despite the increased awareness of radiation risk, many clinicians and researchers have not realised the amount of radiation exposure associated with CCTA, or the possibility of tailoring the scanning protocols to reduce radiation dose.

While the benefits of CT outweigh the harmful effects of radiation exposure in patients, concern over increasing radiation doses to the population has led to various strategies being undertaken for reduction of radiation exposure from CCTA [28, 29]. It is critical to develop methods that reduce radiation dose without compromising image quality when choosing CCTA as the main diagnostic modality in cardiac imaging. These are the challenges faced by clinicians or researchers when reducing the radiation dose, as the major goal of CT imaging is to provide clear and accurate diagnostic images. In this article, we first review the applications of CCTA on cardiac imaging, with a focus on the diagnosis of CAD, in terms of diagnostic and prognostic value. New emerging areas such as myocardial perfusion imaging of CAD with use of CCTA are also discussed. The second part of this review focuses on the radiation dose, in particular the strategies to reduce radiation dose. The final part looks at the challenges and future directions of CCTA in cardiac imaging.

Coronary CT angiography: current status

Diagnostic value of coronary CT angiography in coronary artery disease

With the emergence of multislice CT and subsequent technological improvements that have increased the spatial and temporal resolution of resulting imaging, the use of invasive coronary angiography in the diagnosis of CAD has been challenged. This is reflected in the improved diagnostic value associated with different generations of multislice CT scanners [5–12, 20, 21]. Moderate diagnostic accuracy was achieved with 4- and 16-slice CT in the diagnosis of CAD, owing to limited spatial and temporal resolution, with mean sensitivity and specificity being 76% and 93% for 4-slice CCTA and 82% and 95% for 16-slice CCTA, respectively [30]. With 64-slice CT, moderate to high diagnostic accuracy was achieved owing to further technical improvements in scanning techniques, thus resulting particularly in improved temporal resolution. Several meta-analyses of studies on the use of 64-slice CT reported mean sensitivities ranging from 85 to 99% and specificities ranging from 86 to 96% [31–34]. However, the use of beta blockers to lower the heart rate to less than 65 beats per minute (bpm) is common in 64-slice CT imaging of patients with suspected CAD. The introduction of DSCT marked another technological improvement of CCTA in cardiac imaging, as the temporal resolution was further increased from 165 to 83 ms, thus reducing the need to control the heart rate during the scan [35–39].

Studies comparing DSCT with single-source CT demonstrated that DSCT maintains high diagnostic accuracy in the diagnostic examination of a wide range of patient subsets (*e.g.* patients with higher and even with irregular heart rates, including atrial fibrillation) [36, 37]. Despite slightly lower per-segment evaluability in patients with higher heart rates, DSCT did not show decrease in diagnostic accuracy for the detection of coronary stenoses [16, 38]. DSCT improves temporal resolution, which is vital in those patients who cannot have beta blockade.

Further technical developments of multislice CT scanners, such as the emergence of wide-area detector CT, enabled greater coverage per gantry rotation. Expansion of multislice CT systems from 64- to 128-, 256- and 320-slice systems has allowed for the accurate assessment of stenosis severity and atherosclerotic plaque composition, or even the acquisition of whole-heart coverage in one gantry rotation [19–21, 39]. Studies performed with 128- and 256-slice CT demonstrated the ability of CCTA for the quantification of coronary lumen stenosis and the assessment of plaque morphology and distribution in the coronary arteries [19, 40]. With 320-slice CT, 16 cm of craniocaudal coverage can be obtained in a single heartbeat, with excellent image quality and demonstration of the entire coronary arteries (64-slice CT can only achieve up to 4 cm *z*-axis coverage, depending upon the detector array width). It has been reported in a recent study that high diagnostic value, in particular a negative predictive value of 100% (including the non-diagnostic images), and diagnostic accuracy of 95% were achieved with 320-slice CT angiography for detection of >50% coronary stenosis on a patient-based analysis [39]. In patients with atrial fibrillation, 320-slice CT was reported to visualise 96% of all coronary segments with sufficient image quality to enable a diagnosis [41, 42]. Another potential advantage of wide-array detector scanning is the acquisition of images with consistent CT attenuation along the different coronary arteries [20], which maximises image quality for CCTA. Despite these advantages, 320-slice CT has the limitations of reduced gantry speed (350 ms), high radiation dose and cone beam effects, which need to be addressed in future technical developments.

Prognostic value of coronary CT angiography in coronary artery disease

High-quality multislice CT (64 slice and higher) is not only able to provide reliable information on coronary luminal changes, but also has the potential to visualise coronary artery wall morphology, characterise atherosclerotic plaques and identify non-stenotic plaques that may be undetected by conventional coronary angiography. Thus, it could be used as a non-invasive technique to provide prognostic information in patients with suspected CAD.

In recent years, several studies have reported the prognostic value of 64-slice CT in CAD. Early studies based on a single centre experience reported that findings of CCTA have been closely associated with future cardiac events, with 0 or 1% of cardiac events being reported in patients with normal cardiac CT or mild coronary artery disease, and up to 30% in patients with one- or more vessel obstructive CAD [43–45]. The extent of coronary atherosclerotic plaque as well as the presence of proximal atherosclerotic plaque were found to be associated with a significantly increased risk of a major adverse cardiac event [43]. Min et al [44] in their recent multicentre study concluded that the presence of obstructive CAD is a strong indicator of major adverse cardiac events. Furthermore, plaque compositions identified by CCTA are associated with prediction of clinical adverse cardiac events.

In a meta-analysis studying the prognostic value of 64-slice CT angiography in CAD, Abdulla et al [45] evaluated 10 relatively large studies consisting of 5675 patients during a mean follow-up period of 21 months. Their analysis showed that the rate of cumulative cardiac events over 21 months was 0.5% in patients with normal CT angiography, 3.5% in those with non-obstructive CAD and 16% in patients with obstructive CAD. The findings clearly demonstrated that 64-slice CT was able to differentiate low-risk from high-risk patients. However, future studies are required to answer the question as to whether CCTA can identify atherosclerotic plaques that are prone to rupturing and producing an acute coronary syndrome.

Coronary plaques can be characterised into the following three types based on the CT attenuation [46]: non-calcified plaques (plaques without visual calcification) are defined as lesions with a radiodensity greater than neighbouring soft tissue but with a lower density than the contrast-enhanced coronary lumen (Figure 1); calcified plaques (completely calcified plaques) indicate lesions with higher density than contrast-enhanced coronary lumen (Figure 2); and mixed plaques refer to lesions with non-calcified and calcified components (calcium component between 20 and 80%) within a single lesion or within a segment of the coronary artery (Figure 3). The detection of plaque components, the measurement of atherosclerotic plaque burden and its response

Figure 1. Coronary CT angiography of non-calcified plaque. A non-calcified plaque is found at the mid-segment of the left cunterior descending artery on a curved planar reformatted image. (Reproduced from [127].)

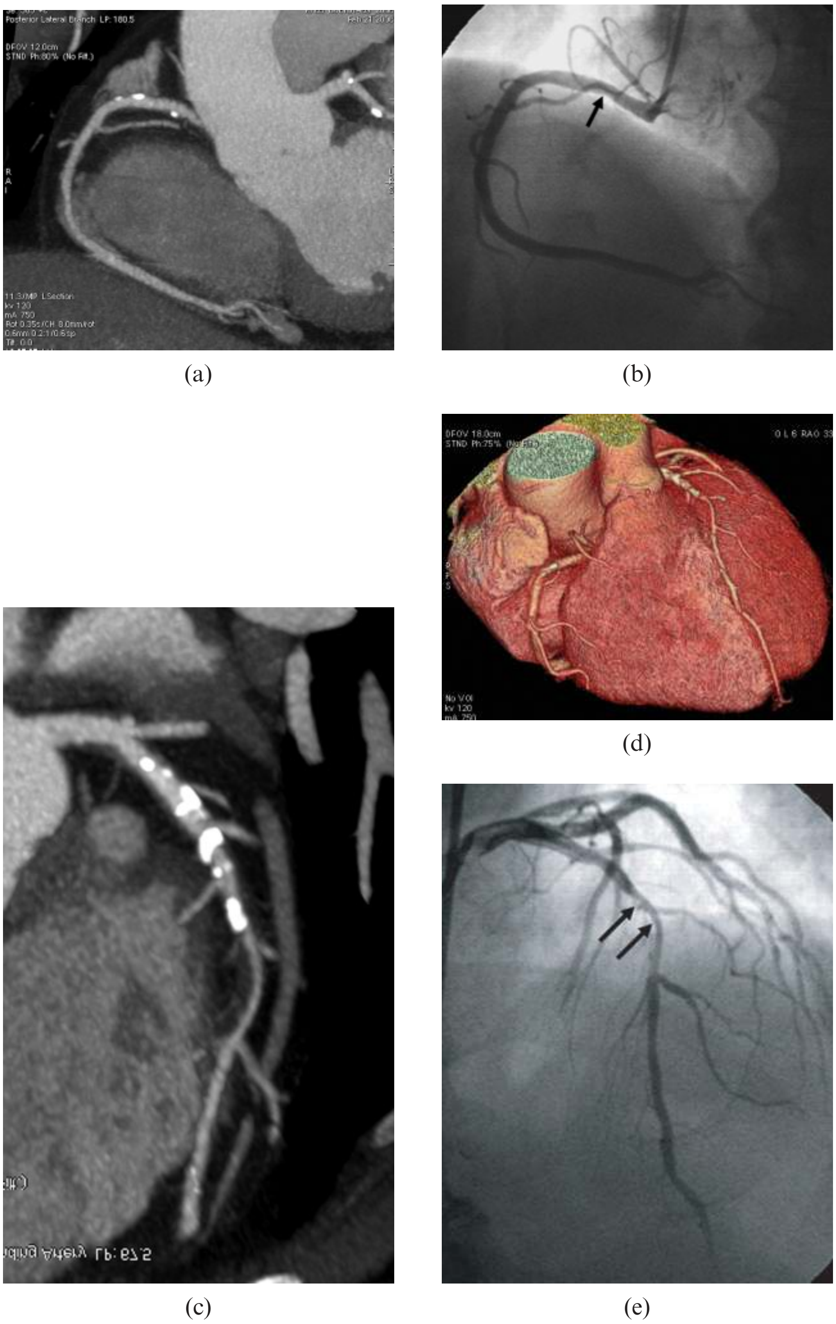


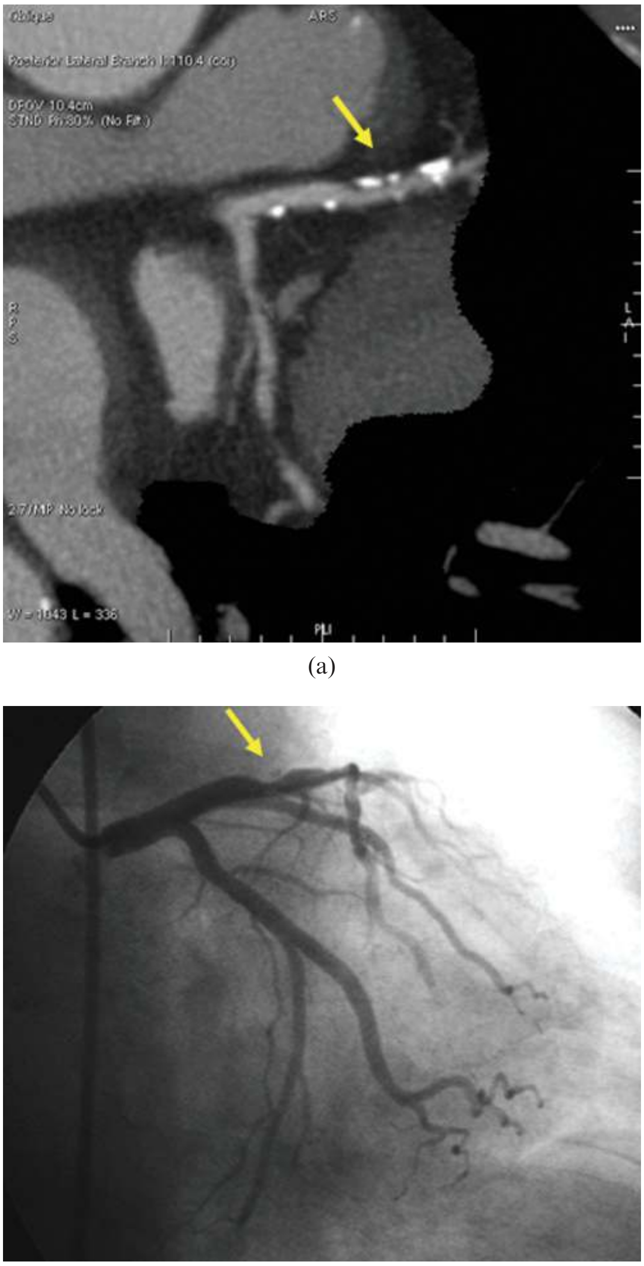
Figure 2. Coronary CT angiography of calcified plaques beyond luminography. CT maximum-intensity projection shows focally calcified plaques in the proximal segment of the right coronary artery (a). Corresponding coronary angiography shows mild coronary lumen stenosis [arrow in (b)]. Extensive calcified plaques are noticed in the proximal and middle segments of left anterior descending (LAD) on curved multiplanar reformatted (c) and volume rendering images (d). A significant stenosis of LAD is confirmed on coronary angiography [arrows in (e)].

to treatment, and the differentiation of stable plaques from those that tend to rupture play an important role in predicting the patient's risk for cardiac events.

Most of the studies include patients with intermediate to high pre-test probability of CAD, and there is a paucity of data regarding the prevalence of atherosclerotic plaques that are assessed and detected on CCTA in asymptomatic patients. Ha et al [47] found in their recent study, which enrolled 112 asymptomatic young adults who were at risk for CAD to undergo 64-slice CT angiography, that the imaging results demonstrated the presence of coronary plaques in 11% of patients. Moreover, positive modelling was noted in all the coronary segments that displayed non-calcified or mixed plaques with non-significant coronary stenosis. This suggests that CCTA is superior to coronary angiography for accurate assessment of CAD, as acute coronary syndrome has been reported to occur in young patients with normal coronary arteries confirmed by angiographic examinations [48, 49]. Positive modelling is seen in the early stages of coronary plaque formation, and it is known to be closely related to plaque instability, indicating that it is more prone to rupturing and erosion with subsequent coronary cardiac events [50, 51]. Therefore, positive vascular remodelling and plaque compositions could be used to guide patient management and risk factor modification for the asymptomatic young patients.

Coronary CT angiography on revascularised patients: coronary bypass follow-up

Promising results were reported for the evaluation of bypass patency with the early generation of multislice



(a)

(b)

Figure 3. Coronary CT angiography of mixed plaques. Mixed plaques are observed in the proximal segment of the left anterior descending (LAD) artery with >50% stenosis (a, arrow). Coronary angiography confirms the significant stenosis of the LAD (b, arrow).

CT scanners; however, a high percentage of bypass grafts could not be evaluated [52]. With improved spatial and temporal resolution achieved in 16- and 64-slice CT, a more accurate assessment of the patency or atherosclerotic changes of coronary artery bypass grafts (CABG) could be expected. According to a systematic review of the usefulness of mutislice CT for the detection of CABG patency and stenosis [53], the sensitivity and specificity for complete occlusion were 93 and 96% with 4-slice CT, and 99 and 98% with 16-slice CT, respectively. However, the sensitivity for >50% stenosis was only 75% for the 4-slice CT and 88% for the 16-slice CT. Similar results were reported by Anders et al [54] regarding the diagnostic value of 16-slice CT for evaluation of CABG patency and bypass stenosis, with high sensitivity (100%) and specificity (98%) being achieved with 16-slice CT for the detection of bypass occlusion, but moderate sensitivity (82%) and specificity (88%) for the detection of bypass stenosis.

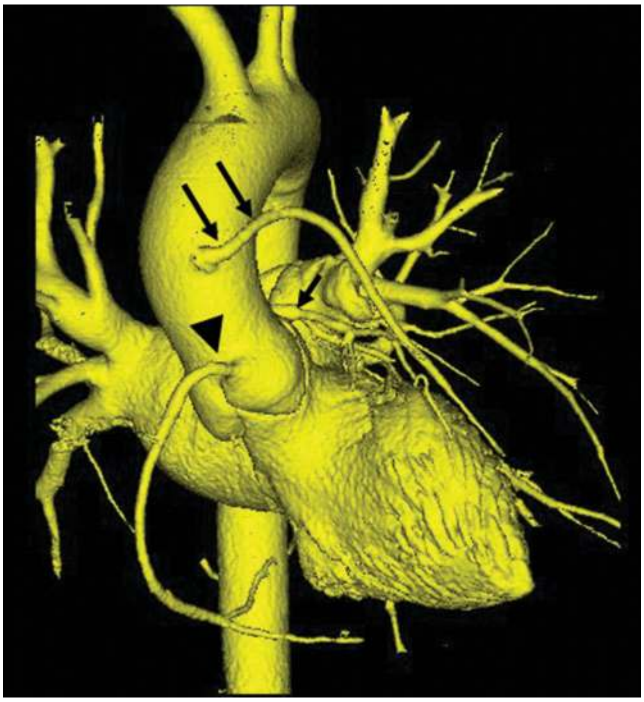


Figure 4. Coronary CT angiography follow-up of a coronary bypass graft. Three-dimensional surfaced shaded display shows a patent saphenous vein graft (long arrows) in a patient treated with a coronary artery bypass graft because of significant stenosis in the left coronary artery. The short arrow indicates the left coronary artery while the arrowhead indicates the right coronary artery.

High sensitivity and specificity (>90%) have been achieved with 64-slice CT for CABG assessment and detection of significant stenosis in CABG [55, 56]. Artefacts are less problematic with the improved spatial resolution of 64-slice CT, and complete visualisation of the entire course of the arterial grafts is possible with 64-slice CT, which shows superiority over 4-slice and 16-slice CT (Figure 4). Meyer et al [55] reported that 64-slice CT angiography allowed the non-invasive assessment of venous and arterial bypass graft patency and stenoses with high diagnostic accuracy even in patients with arrhythmia during the scanning. They also noticed that the diagnostic accuracy of CCTA for the detection of graft occlusion or stenosis did not differ between venous and arterial bypass grafts [55].

The assessment of native coronary arteries in patients after CABG is challenging owing to poor run-off, more extensive calcification and diffusely narrowed arteries with small dimensions. Non-invasive CCTA might be used as a first-line diagnostic tool for graft patency owing to its excellent negative predictive value, while invasive coronary angiography should only be performed after coronary CT angiography, when grafts are occluded or stenotic, and when interventional procedures such as percutaneous coronary intervention are needed as part of the therapy.

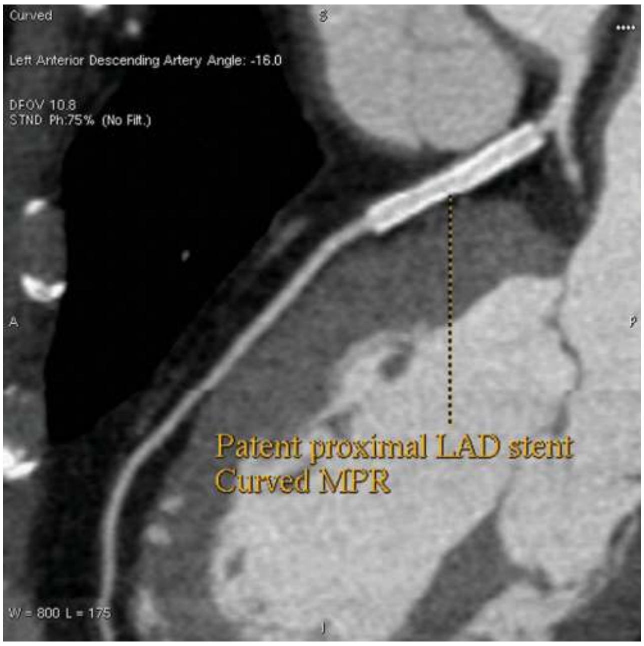


Figure 5. Coronary CT angiography of a patent stent. A patent coronary stent is noticed in the proximal left anterior descending (LAD) artery on a curved multiplana reformatted (MPR) image with clear demonstration of the intrastent lumen without in-stent restenosis.

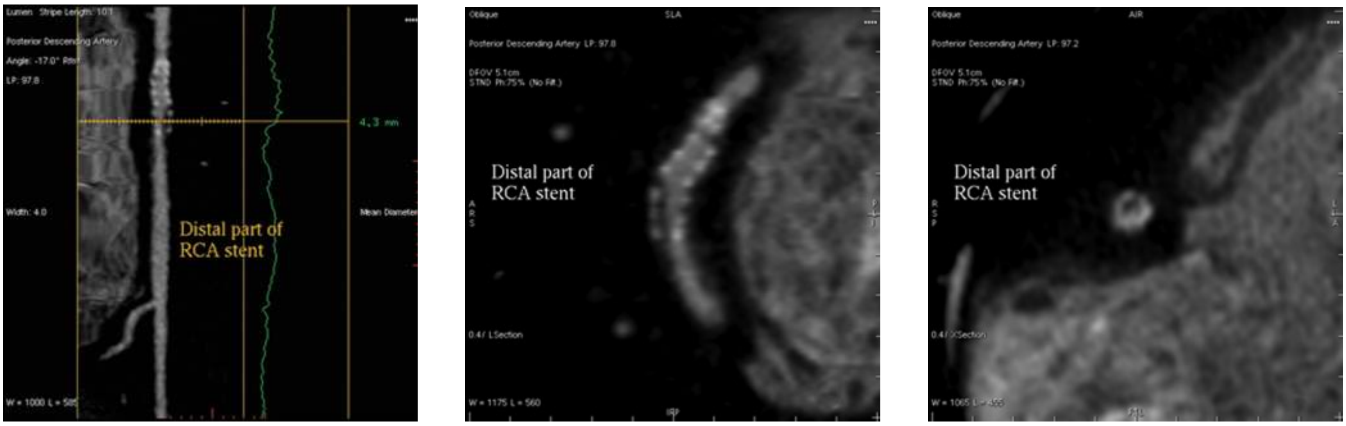
Coronary CT angiography on revascularised patients' coronary stenting

Recently, coronary CT angiography has been increasingly used for assessment of coronary stent patency or restenosis [57, 58]. However, imaging of coronary stents by multislice CT is more difficult than imaging of a native coronary artery. This is because of the presence of metal within the stents which can cause artefacts, interfering with the interpretation of lumen patency. While the accuracy of stent lumen analysis was low or modest with 4- and 16-slice CT scanners, 64-slice CT (single-source and dual-source) scanners allow for more accurate stent visualisation and characterisation owing to increased spatial and temporal resolution [59–61] (Figures 5 and 6). Recent meta-analyses of the diagnostic value of CCTA in coronary stenting showed that the diagnostic value of 64-slice CT angiography is significantly higher than that of 16-slice CT angiography (91 *vs* 81%) as a result of the increased spatial and temporal resolution [62, 63]. Stent diameter and beam hardening artefacts are two common factors that affect the visualisation of coronary stents or in-stent restenosis. Thus, the inclusion of coronary stents of >3.0 mm and the use of dedicated edge-enhancing convolution kernels improve the diagnostic accuracy of CCTA in the follow-up of coronary stenting [63].

Coronary CT angiography: myocardial perfusion imaging

Although multislice CT presents excellent ability to completely assess the entire coronary tree with good diagnostic accuracy in the identification of significant coronary stenosis, anatomically significant coronary stenosis is not always indicative of functional stenosis. This is particularly true for the assessment of intermediate-type coronary lesions [64, 65]. According to the guidelines of the European Society of Cardiology and the American College of Cardiology/American Heart Association, the decision to perform interventional procedures such as coronary angioplasty or bypass surgery should integrate anatomical information with a test that provides objective proof of ischaemia [66, 67].

Myocardial perfusion imaging modalities, comprising stress echocardiography, nuclear myocardial perfusion tests (single-photon emission CT and positron emission tomography) and MR myocardial perfusion imaging, rely on the visualisation of myocardial perfusion or related regional cardiac wall motion abnormalities. CCTA and invasive coronary angiography only allow for direct visualisation of the anatomical details about the degree of coronary lumen stenosis, and thus they are categorised as anatomical imaging modalities. Although CCTA has been reported to provide potentially important additional information on myocardial perfusion and chronic myocardial infarction, a limited correlation was noticed between stenotic coronary disease and single-photon emission CT (SPECT) findings [68]. However, with the emergence of dual-energy CT (DECT), which



(a) (b) (c)

Figure 6. Coronary CT angiography of in-stent restenosis. An in-stent restenosis is present at the distal part of the right coronary atery (RCA) stent which is demonstrated as the low-attenuating area on longitudinally straightened (a), curved multiplana reformatted (b) and cross-sectional images (c).

offers fascinating new applications such as the mapping of the iodine distribution, acquisition of both anatomical and functional information is possible [22, 69].

Early reports support the feasibility of using DECT for comprehensive imaging of CAD: with a single-contrast enhanced scan, DECT coronary angiography allows for the assessment of coronary anatomy, detection of coronary stenosis and evaluation of myocardial perfusion imaging [69, 70]. Ruzsics et al [71] compared DECT with SPECT to evaluate the diagnostic performance of DECT for imaging coronary artery morphology and assessing myocardial blood supply. In a group of 36 patients with suspected or known CAD, >90% diagnostic accuracy was achieved with DECT for detecting any type of myocardial perfusion defect observed on SPECT. Nagao et al [72] used the iodine map that is available with DECT to detect alterations in coronary flow during adenosine stress and rest. This is the first non-invasive method to provide a functional assessment of coronary artery flow using cardiac CT.

Dual-energy cardiac CT imaging can also be achieved with a single X-ray tube. GE Healthcare's Discovery CT750 HD spectral imaging is based on fast kilovolt switching-dynamic switching between two different energy levels of X-rays from view to view during a single rotation [22]. This allows for demonstration of different material densities as scatter plots, histograms and region of interest, thus enabling myocardial perfusion analysis of cardiac function. Despite these promising results, however, large patient cohorts are needed to confirm the potential application of a single protocol for anatomical and myocardial perfusion assessment of CAD.

Coronary CT angiography: radiation dose issue

Coronary CT angiography is routinely performed with retrospectively ECG-gated cardiac CT examination, which indicates that helical CT scanning is performed while an ECG trace of heart movement is recorded simultaneously. Thus, volumetric data are acquired with this approach and the acquired data are selected for image reconstruction with respect to the pre-defined cardiac phase based on ECG signal, thus ensuring the fewest motion artefacts present in the final reconstructed data. Very low pitch values (0.2–0.4) are typically required for coronary data acquisition to ensure continuous z-axis coverage between image stacks reconstructed from consecutive cardiac cycles. The main disadvantage of this approach is higher radiation exposure, as the table is advanced by less than one detector width during each gantry rotation; thus, the same anatomical area is exposed to X-ray radiation during consecutive rotations of the gantry.

The general view about radiation dose is that coronary CT angiography is associated with a risk of cancer development. The National Academies' seventh report on the biological effects of ionising radiation (BEIR VII Phase 2) provides a framework for estimating cancer risk associated with radiation exposure from coronary CT angiography [26]. BEIR VII develops risk estimates for cancer from exposure to low-level ionising radiation using the most current data and epidemiological models available on the health effects of radiation. According to the report, it is estimated that 1 in 2000 people will develop cancer owing to an exposure of 10 mSv. Brenner and Hall [24] estimated that approximately 1.5–2% of all cancers in the USA may be caused by radiation exposure from CT examinations [24].

The calculation of the effective dose of CCTA takes into account the biological effect of the radiation on the heart because each organ is given a tissue weighting depending on its individual susceptibility to the effects of ionising radiation. The tissue weightings are derived from the International Commission on Radiological Protection (ICRP), which focuses on all aspects of protection from ionising radiation. In 2007, the ICRP released the ICRP 103 publication, updating the 16-year-old ICRP 60 data setusing the latest available scientific information on the biology and physics of radiation exposure. In particular, the tissue weighting for breast tissue has increased from 0.05 to 0.12 [73]. The conversion factor used to calculate effective dose from cardiac CT angiography has been upgraded from 0.014 to 0.028; thus, doses from cardiac CT angiography could be significantly underestimated owing to failure to use a cardiac-specific conversion factor in the recent ICRP documentation [74, 75]. Appropriate conversion factors are needed to accurately estimate effective dose.

As the use of cardiac CT grows, particularly in young adult patients, concern over the population dose from CT is being widely expressed in the scientific literature [24, 25, 28]. It has become clear that the responsible use of CT is absolutely necessary in terms of justifying and adjusting scanning techniques. In response to these concerns, the radiology community (radiologists, medical physicists and manufacturers) has worked to implement as low as reasonably achievable principles in CT imaging [76, 77]. The guiding principle for dose measurement in cardiac CT is that the right dose for a cardiac CT examination takes into account the specific patient attenuation and the specific diagnostic purpose.

Dose reduction strategies: optimisation of scanning protocols

All dose reduction strategies are implemented with the assumption that the CT radiation dose levels and image quality fall within manufacturer specifications and general image quality criteria. CT dose in cardiac CT imaging is a more complicated issue compared with non-cardiac CT applications. The first reason is that dose, noise and pitch demonstrate different relationships in cardiac CT compared with non-cardiac CT imaging [78]. The second reason is that the dose in cardiac CT is dependent on the patient's heart rate. In addition, as only a portion of the projection data from one gantry rotation are used for image reconstruction, relatively high milliampere values are normally required to provide an acceptable image noise for diagnostic cardiac CT imaging. Thus, cardiac CT examinations have until now been associated with a higher radiation dose than other non-cardiac CT procedures.

A number of dose-saving strategies have been recommended, and numerous investigations have shown that radiation dose can be significantly reduced to a level equivalent to (or even lower than) that from invasive coronary angiography, without compromising image quality [28, 29]. ECG-controlled tube current modulation is one of the most effective approaches for dose reduction in coronary CT angiography. Effective doses of CCTA up to 20 mSv have been reported in the literature [29]. Moreover, the average dose per site was reported to demonstrate significant variability, ranging from 5 to 30 mSv [25]. Early studies using ECG-controlled tube current modulation reported radiation dose reduction by 30–50% for 4- and 16-slice CT [79, 80]. Later reports with 64-slice and DSCT reported that effective doses for CCTA could be reduced to lower than 10 mSv with the use of ECG-controlled tube current modulation [81, 82]. Weustink et al [82] studied three groups of patients with different heart rates using DSCT, and their results suggested that radiation dose could be significantly reduced with ECG-controlled tube current modulation, particularly in patients with low or high heart rate, with the effective dose being 6.8 and 4.2 mSv, respectively.

Appropriate use of lower peak kilovoltage values (80 or 100 kVp) for CCTA examinations can further reduce radiation dose without compromising image quality. Early studies have shown that decreasing the X-ray tube voltage from 120 to 100 or 80 kVp resulted in up to a 70% reduction in radiation exposure for a constant tube current using 16- and 64-slice CT, with increased image noise and unchanged contrast-to-noise ratio [81, 83]. Recent studies utilising DSCT compared a 100 kVp protocol with the routine 120 kVp for coronary CT angiography and demonstrated a dose reduction of 25–54%, with an estimated effective dose as low as 4.4 mSv [84, 85]. It should be emphasised that changing the tube voltage needs to be correlated with the patient's body mass index (BMI). Lowering the tube voltage from 120 to 100 kVp is appropriate when the patient's BMI is $<25\,\mathrm{kg\,m^{-2}}$. Reduction of the tube voltage to 80 kVp should only be considered in children and slim young adults with a BMI $<20\,\mathrm{kg\,m^{-2}}$.

Additional dose reductions can be achieved using prospective ECG triggering or the step-and-shoot method. Prospective ECG triggering with non-helical scan was used a long time ago with electron beam CT for calcium scoring; however, it was recommended recently for multislice CT cardiac imaging, and this imaging protocol is increasingly reported in the literature owing to its resultant very low radiation dose [86–90]. The principle of prospective ECG triggering is that data acquisition only takes place in the selected cardiac phase by selectively turning on the X-ray tube only when triggered by the ECG signal, and turning it off or dramatically lowering it during the rest of the R–R cycle (*i.e.* the time elapsing between two consecutive R waves in an electrocardiogram).

Studies using prospective ECG triggering with single-source 64-slice or DSCT have reported a reduction in the effective dose of up to 90% when compared with retrospective ECG-gating technique, with diagnostic image quality being achieved in >90% of the cases [86–90]. A direct comparison of prospective ECG triggering with retrospective ECG gating in some studies has shown a very high diagnostic value (>90% sensitivity and specificity) of prospective ECG triggering for the evaluation of coronary arteries with assessable coronary segments of >95% [91–93]. It has been reported that the effective dose of prospective ECG triggering CCTA in CAD is comparable with, or even lower than, that of invasive coronary angiography [89, 90]. The main limitation of prospective ECG triggering is that the technique is strictly restricted to patients with a low and regular heart rate, as the CT scan is triggered by the ECG signals that require the heart rate to be regular and <65 bpm. Thus, pharmacological measures for heart rate control are commonly required for prospective gating. After all, some patients will have low enough heart rates and ivabradine can help in those intolerant of beta blockade.

The development of DSCT is a solution to overcome this problem. Patients with a high heart rate, who would normally be excluded from the retrospective ECG gating with use of single-source CT, can be imaged with DSCT, achieving diagnostic images. Although DSCT can scan accurately at higher heart rates than single-source CT, it is achieved at the expense of higher doses of retrospective ECG gating. Another limitation of prospective ECG triggering is the presence of misalignment due to acquisition of images in 4–5 heartbeats to cover the entire heart with 64-slice CT. This can be overcome with the latest 320-slice CT, which allows coverage of the cardiac volume in a single heartbeat.

It is well known that radiation dose is inversely proportional to the pitch value. A high pitch (1.0–2.0) is recommended for non-cardiac CT angiography, with the aim of reducing radiation dose while achieving diagnostic image quality. However, for CCTA, a very low pitch (0.2–0.4) is routinely used to produce volume coverage without gaps in each phase of the cardiac cycle with multiple overlapping regions, thus resulting in high radiation exposure. Increasing pitch to a higher value was made possible with the development of the second generation of DSCT scanners, Siemens's Definition Flash (Siemens Healthcare, Erlangen, Germany), which enabled acquisition of 128 slices simultaneously (flying focal spot) [89, 90, 94, 40] (Table 2). The Flash mode is predicted on low heart rate just as prospective schema is. This DSCT mode allows coronary CT angiography to be performed at a high pitch value of >3.4 with significant reduction of radiation dose. By combining high pitch and large detector coverage, the acquisition time of coronary CT angiography is reduced from the previous 5–10 s to a quarter of a second, allowing depiction of the entire heart within a single heartbeat. >90% of all coronary segments were assessable with DSCT coronary angiography at a high pitch of 3.4, resulting in a radiation dose <1 mSv [89, 90]. The new scan mode, with a temporal resolution of 75 ms, is regarded as an extremely attractive alternative to invasive coronary angiography owing to the very low dose and high image quality, as well as cardiac function evaluation.

More recently, different iterative image reconstruction methods for reducing radiation dose without compromising image quality have been developed by all major CT manufacturers: adaptive statistical iterative reconstruction and model-based iterative reconstruction by GE Healthcare, iterative reconstruction in image space by Siemens Healthcare, adaptive iterative dose reduction by Toshiba Medical Systems (Ottawara, Japan) and iDose

Table 1. 64-slice CT scanner characteristics for four main manufacturers

	Single-source 64-slice CT				**Dual-source 64-slice CT**				
Manufacturer	**Number of detector rows**	**Number of acquired slices**	**Maximum gantry rotation speed**	**Effective maximum temporal resolution**	**Number of detector rows**	**Number of acquired slices**	**Maximum gantry rotation speed**	**Effective maximum temporal resolution**	**Other special features**
GE Healthcare	64×0.625	64	350 ms	175 ms					
Philips Healthcare	64×0.625	64	400 ms	200 ms					
Siemens Healthcare	64×0.6	64	300 ms	150 ms	$2\times32\times0.6$[a]	64	330 ms	165 ms	Dual energy function
Toshiba Medical Systems	64×0.5	64	350 ms	175 ms					

[a] *z*-flying focal spot technique is used to acquire 64 slices. In addition, dual-energy CT is available with two tubes emitting X-ray spectra of different energy levels.

by Philips Healthcare [95]. Clinical evaluation has shown >60% dose reduction compared with standard filtered back projection while maintaining diagnostic images [96]. Coronary CT angiography incorporating iterative reconstruction resulted in a significant reduction in the effective dose.

Justification of use of coronary CT angiography

There is no doubt that, with increasing technological improvements, coronary CT angiography will continue to play an important role in the detection and diagnosis of CAD. Justification is a shared responsibility between requesting physicians and radiologists. For cardiac imaging exposures, the primary tasks of the medical imaging specialists are to collaborate with referring cardiologists to direct patients to the most appropriate imaging modality for the required diagnostic task and to ensure that all technical aspects of the examination are optimised so that the acquired image quality is diagnostic while keeping the doses as low as possible [97]. This is particularly important for young individuals, especially women, for whom alternative diagnostic modalities that do not involve the use of ionising radiation should be considered, such as stress electrocardiography, echocardiography or MRI. The benefit-to-risk ratio for imaging patients suspected of CAD must be driven by the benefit and appropriateness of the CCTA examination requested by the physicians. The American College of Radiology's appropriateness criteria provide evidence-based guidelines to help physicians in recommending an appropriate imaging test [98]. Similarly, the European Commission's guidelines and UK's Royal College of Radiologists' referral guidelines for imaging also provide a detailed overview of clinical indications for imaging examinations including CT [99]. Physicians need to follow guidelines like national diagnostic reference levels for reducing radiation dosages.

Coronary CT angiography: limitations

The diagnostic value of CCTA is widely known to be hampered by the heavy calcification in the coronary artery tree. According to several meta-analyses [30–34], high-density calcification produces blooming artefacts, which lead to overestimation of the degree of coronary stenosis, thus resulting in low positive predictive value. Patients with high Agatston calcium scores are generally excluded from studies using CCTA. Specifically, calcium scores >400 were found to significantly reduce the diagnostic specificity. This was confirmed by the recently published ACCURACY prospective multicentre study, which included patients with high calcium scores [100]. Patient-based specificity of 83% was reported in detecting ≥70% coronary stenosis. In contrast, another study, which excluded patients with a calcium score of >600, reported a specificity of 90% [101]. These conflicting findings represent the limitations of the current studies due to the different study designs used in each single centre and the degree of strictness applied in controlling bias in the study. It has been shown that significant statistical heterogeneity exists among published studies, with smaller studies reporting higher diagnostic accuracy of CCTA in CAD [102]. Therefore, reports of the diagnostic value of CCTA in CAD in the literature need to be interpreted with caution.

A normal CCTA has been demonstrated to allow the clinicians to rule out the presence of haemodynamically relevant coronary artery stenoses with a high degree of reliability owing to its very high negative predictive value (>95%) [103]; thus, no further work-up is required to demonstrate the absence of coronary disease [104]. Furthermore, in those patients with coronary disease, the likelihood that an individual coronary plaque will result in acute coronary syndrome is related to many factors, independent of the degree of vascular narrowing [105]. Therefore, CCTA could be used as a valuable technique for triage of low to intermediate pre-test probability patients, which remains its main strength when compared with invasive angiography.

There is a lack of uniform criteria for the assessment of the coronary arteries and associated branches or segments. A 14- to 17-segment classification according to the American Heart Association is used in the majority of studies, which indicates a variation of the data analysis, thus affecting the results to a greater extent. Similarly, a significant variation was reported on a vessel-based evaluation [106, 107]. Another limitation of CCTA is the criterion of determining significant coronary stenosis, which is set at >50% lumen stenosis, as this is normally performed in most of the studies. Diagnostic performance of CCTA, as reported in a recent study, is optimal for predicting the haemodynamically significant stenosis when the degree of stenosis is >60% [108]. Future

Table 2. 128-, 256- and 320-slice CT scanner characteristics for four main manufacturers

Manufacturer/scanner	128-slice CT				256-slice CT				320-slice CT			
	Number of detector rows	Number of acquired slices	Maximum gantry rotation speed	Effective maximum temporal resolution	Number of detector rows	Number of acquired slices	Maximum gantry rotation speed	Effective maximum temporal resolution	Number of detector rows	Number of acquired slices	Maximum gantry rotation speed	Effective maximum temporal
GE Healthcare (Waukesha, WI)	$2 \times 64 \times 0.625^a$	128	350 ms	44 ms								
Philips Healthcare (Best, Netherlands)	128×0.625	128	270 ms	135 ms	$2 \times 128 \times 0.625^b$	256	270 ms	135 ms				
Siemens Healthcare (Erlangen, Germany) Definition AS	64×0.6^c	128	300 ms	150 ms/75 ms								
Siemens Definition Flash	$2 \times 64 \times 0.6^d$	2×128	280 ms	75 ms/37.5 ms								
	$2 \times 64 \times 0.6^e$	2×128	280 ms	75 ms								
	$2 \times 64 \times 0.6^f$	2×128	280 ms	75 ms								
Toshiba Medical Systems (Tochigi, Japan)	128×0.5	128	500 ms	250 ms	256×0.5	256	500 ms	250 ms	320×0.5	320	350 ms	175 ms

[a] Conjugate cone-beam back projection uses sets of counteropposed projections to provide 128 distinct projection measurements per rotation for an axial and a helical acquisition mode to significantly improve *z*-resolution. Axial reconstruction provides up to 128 reconstructed slices for 1 rotation.

[b] Dynamic *z*-focal spot technique is used to double the sampling in the slice direction, resulting in 256 simultaneous slices.

[c] *z*-sharp technology doubles the X-ray projections reaching each detector segment, resulting in a full 128-slice acquisition. Temporal resolution can be down to 75 ms for Syngo HeartView CT.

[d] Dual-source cardio acquistion modes: *z*-flying focal spot technique is used to acquire 128 slices. Syngo HeartView Flash (Siemens Healthcare) provides 75 ms temporal resolution independent of the heart rate (≤37.5 ms using two-segment reconstruction, except Flash Spiral).

[e] Dual source Flash Spiral modes for increased scan speed ≥400 mm s^{-1}, resulting in temporal resolution of 75 ms.

[f] Dual-source, dual-energy acquisition modes with the parallel utilisation of two sources with different kilovolt settings and selective photon shield, resulting in improved differentiation.

studies adopting the suitable cut-off value of stenosis degree are required to ensure the validity of diagnostic performance of CCTA in CAD.

Attention should be paid to quantify the degree of coronary stenosis between concentric and eccentric stenoses since multislice CT is different from invasive angiography, as the latter is a gold standard of ''luminography'' that provides little information about vessel wall morphology or the course of the vessel at the occluded segment [109]. Coronary CT angiography allows differentiation between luminal enhancement and adjacent structures such as calcifications and indwelling stents with the support of a number of post-processing techniques, especially the curved planar reformation. However, the dense calcification present in the coronary artery tree may degrade the accuracy of the assessment of stenosis owing to beam-hardening artefacts.

Coronary CT angiography: challenges

Technological challenges in coronary CT angiography

The main challenge in CCTA is that there is a strong demand for high temporal resolution, which translates into the time required to acquire cardiac images in a very short period. A temporal resolution of 75 ms is achieved with recent models of DSCT scanners, which demonstrates a significant improvement in cardiac imaging; however, heart rate control is still necessary to produce the best images, and the lowest dose methods also require low heart rates. Despite the excellent spatial resolution available with 64-, 256- and 320-slice CT (isotropic voxel $0.5\times0.5\times0.5\,\mathrm{mm}^3$ or $0.6\times0.6\times0.6\,\mathrm{mm}^3$), the temporal resolution of these models (165–175 ms) is still significantly inferior to that of invasive coronary angiography, which is 20 ms. Thus, aggressive approaches such as heart rate control with the use of beta blockers are necessary in studies performed with these CT models.

The demand for new CT technology has been accelerating over the past few years, and the GE Healthcare HD system equipped with the Gemstone scintillator presents an example of CT technological improvements. The HD system significantly enhances the dual-energy CT imaging (spectral imaging) and enables temporal registration of the dual-energy samples at 0.5 ms, which is 165 times faster than a DSCT scanner [22].

Coronary CT angiography has been reported in some studies as a useful imaging modality in the triage of patients presenting with chest pain, which looks at the coronary arteries, the pulmonary arteries and the thoracic and abdominal aorta [110–112]. Tailored protocols, often referred to as triple-rule-out (TRO) protocols, have been designed to evaluate all thoracic vascular structures in a single examination. The challenge of a TRO protocol is to evaluate the three most common vascular causes of chest pain (obstructive CAD, acute aortic syndrome and pulmonary embolism) in a single examination [113]. A recently published prospective study concluded that in a low- to moderate- risk acute coronary syndrome population, TRO coronary CT angiography identified non-coronary pathologies, limiting additional diagnostic tests to a small population and facilitating a safe, rapid discharge of the majority of patients with suspected acute coronary syndrome [114]. However, the design of a TRO protocol, which includes an ECG-gated cardiac CT, is technically challenging as the contrast injection and scanning protocols for TRO CT studies vary significantly from one clinical centre to another [115–117]. The main concerns about TRO protocols refer to the radiation dose and the amount of contrast medium used. A radiation exposure of 15–20 mSv has been reported in TRO protocols performed on 64-slice CT scanners [118–120], which is above that of dedicated cardiac CT examinations. A reduction in radiation dose and contrast medium volume has been reported in a recent study using 320-slice CT compared with previously published TRO protocols [113]. Dose-saving strategies are recommended to be applied in TRO protocols.

Morphological challenges in coronary CT angiography

A comprehensive evaluation of atherosclerotic plaques requires the detection of both lumen and outer vessel wall borders throughout the coronary tree. Semi-automatic multislice CT approaches have been reported to quantify plaque volume, burden and the degree of remodelling [121, 122]. However, automatic detection of outer artery wall borders remains a major challenge, as it is usually affected by subtle differences in image gradients, particularly in the peripheral coronary segments [123]. Thus, the development of advanced quantitative algorithms in combination with advances in CT scanner technology may lead to improved quantification of plaque characteristics and guide percutaneous coronary interventions.

Despite these promising results, coronary CT angiography is unable to determine which plaques are ''vulnerable'' or unstable from those that are stable [124]. Therefore, differentiation of lipid-rich content from fibrous content with multislice CT remains challenging owing to considerable overlap in the attenuation values of lipid and fibrous tissue [125]. Atherosclerotic plaque dimension and geometry play an important role in the natural progression of the disease and may have an important clinical predictive value. It is widely accepted that plaque composition rather than the degree of luminal narrowing may be predictive of the patient's risk for cardiac events.

Radiation challenges in coronary CT angiography

With increasing application of CCTA in the diagnosis of CAD, the research focus has shifted from the previous emphasis on diagnostic accuracy to the current focus on reduction of radiation dose with acceptable diagnostic images. This is reflected in the increasing publications reported in the literature. Using many of the technologies and strategies discussed above, it is possible to lower the dose to $<5\,\mathrm{mSv}$, where doses of $<1\,\mathrm{mSv}$ have been reported in the literature [89, 90]. Doses that are consistently $<1\,\mathrm{mSv}$ for CCTA can be achieved with prospective ECG triggering in patients with a BMI of $<30\,\mathrm{kg\,m^{-2}}$ and a heart rate of $<70\,\mathrm{bpm}$. Thus, dose-saving strategies should be applied in cardiac CT imaging whenever possible. This can be achieved through the collaborative efforts of cardiologists, radiologists and medical physicists. The reduction of radiation dose in CCTA remains a continuing challenge, and it is expected that more research will be conducted in cardiac imaging with the use of multislice CT.

Summary and conclusion

There is sufficient evidence to confirm that coronary CT angiography represents the most rapidly developed imaging modality in cardiac imaging, with satisfactory results having been achieved. While coronary CT angiography demonstrates high diagnostic accuracy, the reported results must be interpreted with caution as there are a number of limitations in these reports, including varying study designs and recruitment of patients from different risk groups. Multislice CT scanning protocols in cardiac imaging should be standardised across institutions with the aim of reducing dose variation across patients and facilities.

The radiation dose associated with CT imaging has increased substantially over the last decade with the development of multislice CT scanners. This has raised a serious concern which needs to be drawn to the attention of both clinicians and manufacturers. Tremendous progress has been made to reduce the radiation dose; however, much effort is still required to ensure that coronary CT angiography is safely performed in imaging patients with suspected coronary artery disease. Utilisation of coronary CT angiography must be defined in terms of whether it leads to the greatest benefit and whether the radiation risk may be greater than the benefit expected from the CT examinations.

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