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Coronary CT angiography: technical developments, clinical applications and radiation dose issue

Zhonghua Sun[1], Mansour Almoudi[1]

1. Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, Perth, Western Australia, 6845, Australia

Corresponding author:

Associate Professor Zhonghua Sun, Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, GPO Box, U1987, Perth, Western Australia 6845, Australia

Tel: +61-8-9266 7509

Fax: +61-8-9266 2377

Email: z.sun@curtin.edu.au

Abstract

High diagnostic accuracy has been achieved with coronary CT angiography using 64- and more slice CT scanners, and in selected patients, coronary CT angiography is considered a reliable alternative to invasive coronary angiography. Coronary CT angiography is able to detect variable densities in the coronary atherosclerotic plaques and demonstrate the corresponding intraluminal changes due to presence of plaques, thus providing prognostic value of disease extent. Despite the tremendous contributions of coronary CT angiography to cardiac imaging, coronary CT angiography suffered from high radiation dose, which has raised serious concerns in the literature. The aim of this review is to provide an overview of the clinical applications of coronary CT angiography in coronary artery disease with focus on diagnostic and predictive value of coronary CT angiography; technical developments of cardiac CT imaging and different approaches for radiation dose reduction.

Keywords: Coronary artery disease, coronary CT angiography, diagnostic value, predictive value, radiation dose.

Introduction

Over the last decade a great deal of interest has been focused on imaging and diagnosis of coronary artery disease (CAD) using coronary CT angiography (CCTA) due to its less invasive nature and improved spatial and temporal resolution. Moderate to high diagnostic accuracy has been achieved with 64- or more slice CT, owing to further technical improvements [1-5]. These studies have indicated that CCTA has high accuracy for the diagnosis of CAD and could be used as an effective alternative to invasive coronary angiography in selected patients [6].

In addition to the diagnostic value, CCTA demonstrates the potential to visualize coronary artery wall morphology, characterize atherosclerotic plaques and identify non-stenotic plaques. Studies have shown that CCTA demonstrates high prognostic value in CAD, as it is able to differentiate low-risk from high-risk patients [7, 8], with very low rate of adverse cardiac events occurring in patients with normal CCTA, and significantly high rate of these events in patients with obstructive CAD.

CCTA with 3D visualization has been explored as a new imaging modality for the assessment of cardiac valves, including both original and artificial ones [9-11]. Transesophageal echocardiography and transthoracic echocardiography are the primary imaging modalities for valve assessment as these techniques provide both anatomical and functional information. However, they fail to detect the anatomical substrate that causes prosthetic heart valve dysfunction [10]. CCTA, with its capability to produce 3D/4D visualizations, is emerging as a new diagnostic modality for the evaluation of heart valve morphology and function.

Despite these promising reports, CCTA has the disadvantage of high radiation dose, which leads to the concern of radiation-induced malignancy [12, 13]. 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 comprises only 15% of all radiological examinations. Radiation-associated risk is a problem that has been addressed by the National Research Council of the United States [14], and there is an increased awareness of radiation risk associated with CCTA among physicians and manufacturers, which is reflected in the changing research directions from the early research focus on the diagnostic value of CCTA in CAD to the increasingly reported studies on dose reduction in the literature [15]. The purpose of this paper is to provide an overview of CCTA with a focus on the diagnostic accuracy and prognostic value in CAD. Radiation dose issues associated with CCTA and corresponding dose-reduction strategies are discussed, and future directions of CCTA are highlighted.

Technological developments in coronary CT angiography

The history of cardiac CT is closely related to technological improvements that occurred with each successive generation of CT scanner. Imaging of the heart has become clinically practicable with the introduction of multislice CT angiography (MSCT) and development of electrocardiogram-synchronized gating and the z-axis extended coverage from the MSCT scanners [16, 17]. The technological developments in these MSCT scanners determine the diagnostic performance of CCTA in terms of spatial and temporal resolution, which in turn decides the diagnostic value of CCTA in CAD. This is discussed in detail in the following sections.

4- and 16-slice coronary CT angiography

The early generations of 4- and 16-slice CT scanners represented a technological revolution in cardiac imaging [18-20], although the diagnostic accuracy in terms of sensitivity was low for determining the degree of CAD. Specificity for exclusion of CAD (in particular, the 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 characterization of coronary plaques and cardiac wall changes (such as remodelling of the coronary wall due to atherosclerotic plaques). Improved spatial (0.75 vs 1-1.25 mm) and temporal resolution (105-210 vs 165-330 ms) can be obtained with 16-slice CT when compared to early type of 4-slice CT scanners [21, 22]. However, the image quality is compromised in patients with high heart rate, or with stents or severely calcified arteries [23, 24]. In order to overcome the limitations of 16-slice CT, multisegment reconstruction was used to improve the temporal resolution to 93 ms compared to the 185 ms acquired with the standard halfscan reconstruction [25]. Diagnostic accuracy of multisegment reconstruction has been improved due to a reduction of motion artefacts, but at the expense of high radiation exposure resulting from a lower pitch [25, 26].

64-slice coronary CT angiography

In 2004, all major CT manufacturers introduced the next generation of MSCT scanners with 32, 40, and 64 simultaneously acquired slices, which brought about a further leap in volume coverage speed in cardiac CT imaging. With gantry rotation times being down to 330 ms for 64-slice, the spatial (0.5-0.6 mm) and temporal resolution (up to 165 ms) for cardiac ECG-gated imaging is again markedly improved, thus, enabling longitudinal cardiac coverage (3.2-4 cm for 64-slice CT vs 1.2 cm for 16-slice CT).

The increased temporal resolution of 64-slice CT has the potential to improve the clinical strength of ECG-gated cardiac examinations at higher heart rates, thereby reducing the number of patients requiring heart rate control. In contrast to previous studies, high diagnostic accuracy has been achieved despite the presence of severely calcified coronary plaques [27, 28]. In addition, using 64-slice CT the scanning time is reduced to less than 15 seconds, allowing a decreased breath-hold time, better utilization of contrast medium with fewer enhancements of adjacent structures and a lower dose of applied contrast medium [24]. Improvement of image quality has also been reported in the visualization of all coronary artery branches with high sensitivity and specificity achieved [29, 30] (Fig 1). Although multisegment or multiphase reconstruction approach increases temporal resolution, the effectiveness of these algorithms depends on the relationship between heart rate, gantry rotation time, and pitch [31]. Although image quality has been shown to improve with use of multsegment reconstruction, diagnostic accuracy was not affected [32].

The improvements in cardiac CT imaging led to the development of even faster CT scanners. Dual-source CT (DSCT) was designed to improve temporal resolution to 75 ms, thus increasing image quality by reducing motion artefacts and eliminating the need to control the heart rate during the scan [33, 34]. Studies have shown that cardiac CT image quality of coronary artery is independent of heart rate with DSCT [35, 36] (Fig 2), so this indicates a significant improvement of CCTA in the assessment of patients with high heart rate. Table 1 summarizes the diagnostic value of CCTA based on 64-slice CT, according to a number of systematic reviews and meta-analyses.

64-slice beyond coronary CT angiography

The development of wide area detector CT enables greater coverage per gantry rotation [37-39]. Expansion of MSCT systems from a prototype 256-slice to a 320-slice system has allowed for acquisition of whole heart coverage in one gantry rotation with a slice thickness of 0.5 mm. This eliminates “stair-step” artefacts that are observed during 64-slice CCTA scans. Full cardiac coverage with one gantry rotation allows for evaluation of coronary arteries in patients with arrhythmias, such as with atrial fibrillation. The imaging principle of 320-slice CT is different from previous generations of MSCT scanners as there are is no need to piece together image sub-volumes acquired over several heartbeats (normally 4-5 heartbeats for 64-slice CCTA) to reconstruct the entire cardiac volume. With 320-slice CT, a 16 cm of craniocaudal coverage can be obtained in a single heartbeat, with excellent image quality and demonstration of the entire coronary arteries. Initial experience using 256- and 320-slice CT in cardiac imaging is promising [39-41], although further work with inclusion of large cohort of patients is required to investigate the effect on image quality and diagnostic value when scanning protocols are adjusted to lower radiation and contrast doses.

Despite extended z-axis coverage with use of 256- and 320-slice CT, temporal resolution of these scanners is still inferior to that of the second-generation of DSCT scanners, which enable acquisition of 128 slices simultaneously [42, 43]. This DSCT mode allows CCTA to be performed by combining high pitch value of up to 3.4 with large detector coverage, thus, the acquisition time of CCTA is reduced to a quarter of a second, allowing depiction of the entire heart within a single heartbeat.

Clinical applications of coronary CT angiography

Coronary CT angiography has been increasingly used in the diagnosis of coronary artery disease and prediction of major adverse cardiac events owing to its less invasiveness and improved diagnostic performance. The diagnostic accuracy of CCTA has been significantly enhanced with the developments of MSCT scanners, from 4-slice CT to the latest models of 256- and 320-slice CT. Similarly, the predictive outcomes of CCTA with use of 64- or more slice CT scanners show promising results.

Diagnostic accuracy of coronary CT angiography

Early studies with use of 4- and 16-slice CT showed moderate diagnostic accuracy in the diagnosis of CAD due to technical limitations [44]. Image quality of coronary artery visualization was impaired and suboptimal in a number of cases with 4-slice CT as the unassessable coronary segments could be as high as more than 33% [18, 44]. With 16-slice CT, thinner detector rows increased the spatial resolution and further shortened the total scan time. Therefore, image quality in 16-slice CT angiography has become more consistent with the reported sensitivities and specificities ranging from 83% to 98% and 96% to 98%, respectively [19, 21, 22, 45]. Further increased diagnostic accuracy was achieved with 64-slice CT due to improved spatial and temporal resolution, thus leading to shorter examination times. Several meta-analyses of 64-slice CT studies in the diagnosis of CAD reported that the sensitivities were more than 90% and specificities more than 96% in most of the studies [1-5].

Heart rate control with use of beta-blockers is necessary in 64-slice CCTA as image quality is affected by motion artefacts in patients with heart rates more than 65 bpm (beats per minute). This limitation has been overcome with the introduction of DSCT as the temporal resolution was increased from 165 ms to 75 ms, thus image quality and diagnostic value of CCTA was less dependent on heart rates. Salavati et al in their meta-analysis reported that only 8% of the total number of patients undergoing DSCT coronary angiography received beta-blocker [46], and this is significantly lower than the 41%-76% of patients that received beta-blocker undergoing 64-slice CCTA [1, 4]. Apart from beta-blockers, ivabradine can also be used as an alternative to reduce heart rate. Oral ivabradine has been reported to be a safe and effective heart rate lowering agent when compared to the beta-blockers, according to a recent study [47]. Despite a wide range of different heart rates being included in the CCTA, DSCT coronary angiography shows improved diagnostic performance [48, 49].

Results using 320-slice CCTA are compared favourably to the studies using 64-slice and DSCT coronary angiography [39-41, 50-52]. van Velzen et al in their recent study reported sensitivity and specificity of 100% and 85% for 320-slice CCTA in 106 patients with acute chest pain admitted to the Emergency Department [50]. Pellicia et al in their prospective study consisting of 118 unselected consecutive patients with suspected CAD demonstrated the excellent results with 320-slice CT, with more than 90% of sensitivity, specificity, positive predictive value and negative predictive value achieved at the per-patient, per-vessel and per-segment analysis [51]. These results indicate that 320-slice CT has the potential to broaden the use of CCTA to more patients, such as patients with atrial fibrillation.

In summary, the sensitivity of CCTA has been significantly improved with 64- or more slice CT scanners when compared to the early generations of 4- and 16-slice scanners, however, the specificity and negative predictive value remains consistently high (>90%), regardless of the type of CT scanners. This indicates the main role of CCTA is to rule out significant CAD, thus reducing the need for invasive coronary angiography. The prime indication of CCTA is to diagnose patients with a low and intermediate probability of CAD as a simple non-invasive testing, while patients with a high probability of CAD will benefit from invasive coronary angiography.

Diagnostic value of coronary CT angiography: effect of coronary artery calcium score

The diagnostic performance of CCTA may be limited due to presence of severe calcification in the coronary lumen, yielding false positive results. Several studies performed with 64-slice CT have demonstrated vessel calcification was a serious limitation to the specificity in patients with coronary calcium score above 400 [52-54]. However, the current literature shows that there is controversial evidence as to whether coronary calcium score should be used as a reference for recommending CCTA [55, 56]. den Dekker MA et al in their recent systematic review and meta-analysis concluded that with 64-slice and new CT scanners, CCTA has high sensitivity and specificity for diagnosis of significant CAD in the presence of severe calcification, thus, a coronary calcium score cut-off for performing CCTA is no longer indicated [56].

Prognostic value of coronary CT angiography

The anatomy-based approach is a well-established method for risk stratification of patients as demonstrated by invasive coronary angiography, which clearly delineates the severity and extent of significant coronary stenosis. High risk coronary anatomy (three-vessel CAD, stenosis of left main coronary artery) is directly related to poorer outcome [57-59], while normal coronary artery is associated with an excellent prognosis [60]. Coronary calcium score has demonstrated incremental prognostic value over traditional risk factors, with a seven-fold increase in the incidence of cardiac events for Agatston scores >100 when compared with patients with zero calcium score [61, 62]. Despite many reports showing the prognostic value of coronary calcifications detected on non-enhanced CT scans, it is not until very recently that the prognostic value of CCTA has been made clear.

Early studies investigating the short to mid-term outcomes of patients undergoing 64-slice CT angiography reported that CCTA is able to provide independent prognostic information for predicting cardiac events and mortality in patients with known or suspected CAD [63, 64]. Findings of CCTA based on a single center experience have been closely associated with the future cardiac events, with 0% or 1% 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 [65, 66]. Recently, two meta-analyses of studies on the prognostic value of CCTA showed that cumulative major adverse cardiac events with a mean follow-up of 20 to 21 months ranged from 0.17% to 0.5% in patients with normal CCTA findings, 1.4% to 3.5% in those with non-obstructive CAD and 8.8% to 16% in patients with obstructive CAD by 16- and 64-slice CT angiography [7, 67]. Compared to a normal CCTA, non-obstructive CAD was associated with a significant increased risk of major adverse cardiac events, while obstructive CAD was associated with a greatly increased further significant risk. The presence and extent of nonobstructive plaques have been reported to enhance prediction of incidental mortality beyond traditional clinical risk assessment [68, 69]. The prediction of excellent prognosis together with the high negative predictive value makes CCTA the appropriate imaging modality to exclude CAD and prognosticate populations with different pre-test likelihoods for CAD.

Prospective multi-centre trials evaluating patients presenting to the emergency department with acute chest pain symptoms further confirmed the prognostic value of CCTA [70-72]. Incorporating CCTA into a triage strategy improved the efficiency of clinical decision making and allowed the safe, expedited discharge from the emergency department of many patients who would otherwise be admitted [73, 74]. These findings demonstrated that the presence and severity of atherosclerotic plaque on CCTA acted as independent predictors of acute coronary syndrome. Table 2 is a summary of clinical indications of CCTA in CAD.

Integration of coronary CT angiography with myocardial perfusion imaging

Although CCTA with use of 64- and more slice scanners 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 [75, 76]. 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 ischemia [77, 78].

Contrast-enhanced dual-energy (DECT) with DSCT has been reported to depict myocardial ischemia using the myocardial blood pool images [79, 80]. Blankstein et al reported that adenosine stress CT detected stress-induced myocardial perfusion defects with a diagnostic accuracy comparable to that of SPECT [80]. Nagao et al recently demonstrated functional assessment of coronary artery flow using cardiac CT, with change in coronary artery flow under adenosine stress closely related to the physiological significance of coronary stenosis [81]. These early reports along with a recently published study by Wang et al indicate that dynamic stress myocardial CT perfusion imaging offers diagnostic accuracy comparable to that of SPECT for detecting myocardial perfusion defects [82]. A more comprehensive and accurate assessment of coronary stenosis and myocardial perfusion with a single modality consisting of CT perfusion and CCTA could be achieved without increasing radiation dose.

Radiation dose associated with coronary CT angiography

Radiation dose is becoming a major issue for CCTA, since CT is associated with a risk of cancer development. The general view about radiation dose is that coronary CT angiography is associated with a risk of cancer development. The National Academies' Biological Effects of Ionising Radiation 7th Report (BEIR VII Phase 2) provides a framework for estimating cancer risk associated with radiation exposure from coronary CT angiography [14]. 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 due to an exposure of 10 mSv. Brenner and Hall estimated that approximately 1.5% to 2% of all cancers in the United States may be caused by radiation exposure from CT examinations [12]. Therefore, CCTA should be performed with dose-saving strategies whenever possible to reduce the radiation exposure to patients.

Previous studies have reported that CCTA with use of retrospectively ECG-gated technique results in very high effective dose, which ranged from 13.4 mSv to 31.4 mSv [83]. A number of techniques have been introduced to reduce the radiation dose in coronary CT imaging in order to accomplish the 'as low as reasonably achievable' (ALARA) rule. These dose-reduction techniques include ECG-controlled tube current modulation, lower x-ray tube voltage, high pitch, prospective ECG-triggered scanning and reconstruction algorithms [6, 84].

Dose-reduction strategies

Radiation dose in CT can be reduced significantly by applying the approach of tube current modulation. Either ECG-controlled or anatomical-dependent tube current modulation results in effective dose reduction significantly between 22% and 52% compared to retrospective ECG-gating without any modifications [85, 86]. In ECG-controlled modulation, the tube current is reduced to the level between 46% and 80% from its maximum at diastole (60–80% of R-R interval) [86]. A recent phantom study comparing different dose-saving techniques demonstrate a significant reduction of about 65% in effective dose with ECG-controlled tube current modulation when compared with the corresponding retrospectively ECG-gated protocol [87].

Adjusting the tube voltage, kVp according to patient's BMI (body mass index) is an effective approach to reduce radiation dose during CCTA. Early studies have shown that decreasing the X-ray tube voltage from 120kVp to 100 kVp or 80 kVp resulted in up to 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 [88, 89]. Later reports utilising DSCT compared a 100 kVp protocol to the routine 120 kVp for CCTA, and demonstrated a dose reduction of 25-54%, with an estimated effective dose as low as 4.4 mSv [90, 91]. It should be noted that lowering tube voltage from 120kVp to 100 kVp is recommended when the patient's BMI is less than 25 kg/m^2. Reduction of the tube voltage to 80 kVp should only be considered in children and slim young adults with BMI below 20 kg/ m^2.

Additional dose reductions can be achieved using prospective ECG-triggering or 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 has been increasingly used in recent years for CCTA due to its resultant very low radiation dose. Studies performed with prospectively ECG-triggered CCTA have reported reduction of the effective dose by up to 90% when compared to retrospectively ECG-gated technique, with diagnostic image quality being achieved in more than 90% of the cases [92-94]. A direct comparison of prospective ECG-triggering with retrospective ECG-gating has shown high diagnostic value (more than 90% of sensitivity and specificity) of prospectively ECG-triggered CCTA for evaluation of coronary arteries with assessable coronary segments of more than 95% [95-97]. The effective dose of prospectively ECG-triggered CCTA is comparable to, or even lower than that of invasive coronary angiography [95, 96]. Thus, low radiation dose can be achieved in low and regular heart rate with prospectively ECG-triggered CCTA, regardless of the CT scanner generation. It has been reported that BMI is identified as the main factor that significantly affects the radiation dose in prospectively ECG-triggered CCTA [98].

Further dose reduction can be achieved by a combination of prospective ECG triggering with high pitch spiral acquisition, which results in a consistent low dose [99, 100]. This is only achievable with the second generation of DSCT scanners, Siemens definition Flash, with acquisition of 128 slices per gantry rotation, and high temporal resolution of 75 ms. This DSCT mode allows CCTA to be performed at a pitch value of up to 3.4 with significant reduction of radiation dose. By combining high pitch and large detector coverage, the acquisition time of CCTA is reduced from the previous 5-10 sec to a quarter of a second, allowing depiction of the entire heart within a single heartbeat. More than 90% of all coronary segments were assessable with DSCT coronary angiography at a high pitch of 3.4, resulting in a radiation dose less than 1 mSv [99, 100].

More recently, iterative image reconstruction has emerged as an exciting new tool in cardiac CT imaging offering opportunities for dose reduction and improvements in image quality [101, 102]. Clinical evaluation has shown up to 60% dose reduction compared to standard filtered back projection while maintaining diagnostic images [103]. CCTA incorporating iterative reconstruction resulted in a significant reduction in the effective dose.

Summary and conclusion

Coronary CT angiography represents the most rapidly developed imaging modality in cardiac imaging, with satisfactory results having been achieved. The technological advances in multislice CT scanners have gradually overcome the technical and diagnostic challenges, thus, these advances have led to a dramatic impact on its accuracy in diagnosing CAD and predicting major adverse cardiac events.

Radiation dose associated with coronary CT angiography has increased substantially over the last decade with the development of multislice CT scanners and widespread use of cardiac CT. This has raised a serious concern, which needs to be drawn to the attention of both clinicians and manufacturers. Various dose-saving strategies have been undertaken in the past few years to lower radiation exposure to patients undergoing coronary CT angiography with tremendous progress having been achieved. Effective dose reduction has been accomplished by employing techniques with a radiation dose of less than 10 mSv to as low as 1 mSv in some studies. However, much effort is still required to ensure that coronary CT angiography is safely performed in imaging patients with suspected coronary artery disease.

Appropriate utilization of coronary CT angiography must be defined as to whether it leads to the greatest benefit and whether the radiation risk may be greater than the benefit expected from the cardiac CT examinations.

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Figure legends

Figure 1. A mixed coronary plaque (long arrow in A) is present within a lesion at the proximal segment of left anterior descending artery as shown on a curved planar reformatted image in a 55-year-old man undergoing 64-slice coronary CT angiography. A calcified plaque is also noticed at the mid-segment of the same left coronary artery (short arrow in A). Three-dimensional (3D) volume rendering demonstrates significant stenosis in the left anterior descending due to the calcified plaque (arrows in B).

Figure 2. Coronal maximum-intensity projection images acquired with a dual-source 64-slice coronary CT angiography shows normal right (A) and left coronary artery branches (B) in a 47-year-old man with atypical chest pain. 3D volume rendering images (C and D) demonstrate right and left coronary arteries with excellent visualization of the main coronary and side branches.