

Coronary CT angiography with prospective ECG-triggering: an effective alternative to invasive coronary angiography

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Abstract: Despite the tremendous contributions of coronary CT angiography to coronary artery disease, radiation dose associated with coronary CT angiography has raised serious concerns in the literature, as the risk of developing radiation-induced malignancy is not negligible. Various dose-saving strategies have been implemented, with some of the strategies resulting in significant dose reduction. Of these strategies, prospective ECG-triggering is one of the most effective techniques with resultant effective radiation dose similar to or even lower than that of invasive coronary angiography. Prospective ECG-triggered coronary CT angiography has been reported to have high diagnostic accuracy in the diagnosis of coronary artery disease with image quality comparable to that of retrospective ECG-gating, but with significantly reduced radiation dose. Successful performance of prospective ECG-triggering is determined by strict exclusion criteria and careful patient preparation. The aim of this article is to provide an overview of the diagnostic applications of coronary CT angiography with prospective ECG-triggering with focus on radiation dose reduction. Radiation dose measurements are discussed with aim of allowing accurate dose estimation. Diagnostic value of prospective ECG-triggered coronary CT angiography in patients with different heart rate is discussed. Finally, current status and future directions are highlighted.

Key Words: Coronary artery disease; coronary CT angiography; image quality; prospective ECG-triggering; radiation dose



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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 due to its less invasive nature and improved spatial and temporal resolution. Moderate to high diagnostic accuracy was achieved with 64- or more slice CT, owing to further technical improvements (1-5). These studies have indicated that coronary CT angiography has high accuracy for the diagnosis of CAD and could be used as an effective alternative to invasive coronary angiography in selected patients. However, coronary CT angiography has the disadvantage of high radiation dose which raises concerns

for both clinicians and manufacturers. This is reflected in the changing research directions from the early research focus on the diagnostic value of coronary CT angiography in CAD to the increasingly reported studies on dose reduction (6).

Radiation dose is becoming a major issue for coronary CT angiography, since 64- or more-slice CT shows improved and promising results in the diagnosis of CAD (7-10). It is estimated that in daily practice, effective dose of coronary CT angiography may reach up to 40 mSv in female patients if no dose-saving strategies are applied, and this is associated with radiation exposure to breast tissues (11). The radiation risks associated with coronary CT angiography have become a hot topic of debate in the

literature (12-14). The general view about radiation dose is that CT is associated with a risk of cancer development. Therefore, coronary CT angiography should be performed with dose-saving strategies whenever possible to reduce the radiation dose to patients.

Of various dose-saving strategies used in coronary CT angiography (11,15,16), prospective ECG-triggered scanning represents one of the most promising radiation saving techniques with a significant reduction of radiation dose when compared to the retrospective ECG-gating and invasive coronary angiography (17-19). Early studies demonstrated the feasibility of prospective ECG-triggering and later reports confirmed that diagnostic images could be acquired with this new technique while achieving reduction of the effective dose by up to 90% (20-23). It has been reported that the effective dose of prospective ECG-triggered coronary CT angiography is comparable to or even lower than that of invasive coronary angiography (20-27). Since prospective ECG-triggered coronary CT angiography shows promising results in the diagnosis of CAD with resultant very low effective dose, we expect that more and more studies will be conducted with this technique in cardiac imaging. It is critical to develop methods that reduce radiation dose without compromising image quality when choosing coronary CT angiography as the main diagnostic modality in cardiac imaging. The purpose of this paper is to provide an overview of coronary CT angiography with use of prospective ECG-triggering with focus on the imaging protocols, diagnostic accuracy and radiation dose when compared to traditional retrospective ECG-gating. Future directions on prospective ECG-triggered coronary CT angiography are highlighted. It is expected that this paper will provide readers with a good understanding of the current status of prospective ECG-triggering in the diagnostic applications of coronary artery disease.

Prospective ECG-triggering-general technical requirements

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 being reported in the literature due to its resultant very low radiation dose (17-27).

Prospective ECG-triggered coronary CT angiography uses the partial-scan technique to the motion of the heart,

which is defined as the step-and-shoot method, so that scan is triggered by ECG signal instead of spiral CT acquisition. This technique allows data to be acquired in a certain phase of cardiac cycle, preferably in the mid-diastolic phase, when cardiac motion is minimal.

The principle of prospective ECG-triggering is that data acquisition only takes place in the selected cardiac phase by selectively only turning on the x-ray tube when triggered by the ECG signal, and turning it off or dramatically lowering it during the rest of the R-R cycle (*Figure 1*). This contrasts significantly to the retrospective ECG-gated coronary CT angiography, which acquires the volume data during spiral scanning at a very low pitch (0.2-0.5) so as to produce volume coverage without gaps in each phase of the cardiac cycle with multiple overlapping regions (*Figure 2*). Prospective triggering is also referred to as sequential data acquisition with an effective pitch of 1.0. The main advantage of this scanning protocol is the very low radiation dose as the x-ray exposure time is short. Most importantly, this prospective ECG-triggered method is still accurate in diagnosing coronary artery disease. However, it suffers from several limitations.

First, it is limited to heart rate less than 70 or 65 beats per minute (bpm). Estimation of the next R-R interval may be incorrect when heart rate changes are present such as arrhythmia (28). Second, ECG-triggered sequential scan is usually restricted to scanning with non-overlapping adjacent slices, or slice increments with only small overlap. The scan time to cover the heart volume is thus directly proportional to the slice increment. Consequently, prospective ECG-triggering puts high demand on the z-axis coverage, therefore, it is normally performed with 64-slice or more slice scanners. Presence of misalignment due to acquisition of images in 4-5 heart beats to cover the entire heart with 64-slice CT is an example of this limitation (*Figure 3*). This can be overcome with the latest 320-slice CT scanner, which enables coverage of the cardiac volume in a single heartbeat. Last, cardiac images are acquired during only a small portion of the R-R interval as ECG-triggered acquisition targets only a specific phase of the cardiac cycle; thus, functional information about cardiac valve or ventricular wall motion is not available (17,27).

Prospective ECG-triggering can also be performed with high-pitch spiral scan which is a new type of spiral acquisition developed specifically for dual-source CT (DSCT) scanner, Siemens Definition Flash. This scanning protocol enables acquisition of 128 slices simultaneously (flying focal spot) (29-31). The pitch can be increased

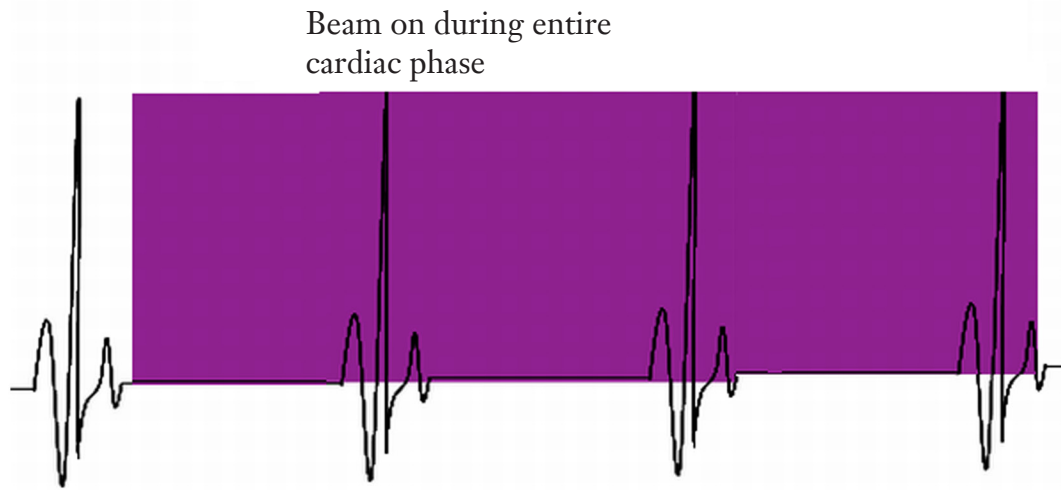


Figure 1 Conventional retrospective ECG-gated coronary CT angiography. X-ray beam is turned on during the entire cardiac cycle without adjusting the tube current, allowing for acquisition of volume data

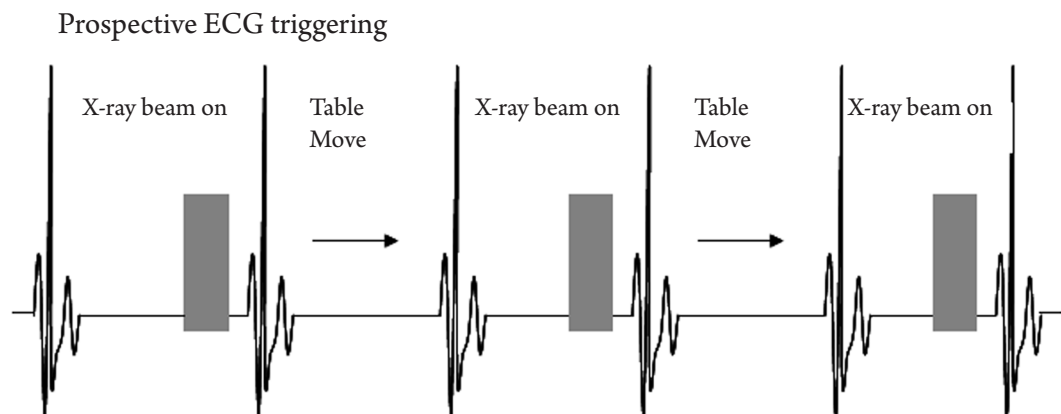


Figure 2 Prospective ECG-triggering with X-ray beam on during a portion of cardiac cycle, while in the remaining cardiac phase, the X-ray beam is turned off

substantially while still allowing image reconstruction due to dual-source geometry. Overlapping radiation dose is avoided, thus substantially reducing the effective radiation dose to the patient. According to Achenbach and Alkadhi's reports, a very high pitch value (up to 3.4) was used to cover the volume of the heart in a very short (approximately 0.260 s), enabling acquisition of complete data in a single cardiac cycle with excellent image quality at a consistent dose lower than 1.0 mSv (29,31). Thus, high-pitch spiral cardiac CT angiography seems to be very attractive in the future due to its very low dose.

Radiation dose measurements in prospective ECG-triggering

Radiation dose estimates for coronary CT angiography are best expressed as volume CT dose index (CTDIvol), dose-length product (DLP), and effective dose. These parameters are accurately defined and allow comparisons of the radiation doses of various cardiac CT imaging protocols. Clinicians referring for performing coronary CT angiography should fully understand the radiation doses associated with various CT scanning protocols.



Figure 3 Prospective ECG-triggered coronary CT angiography curved planar reformatted image shows presence of misalignment, affecting visualization of the right coronary artery

This may aid in making decisions as to whether a cardiac CT examination is medically justified and which protocol addresses the clinical question properly with the least radiation exposure to patients (32).

Dose-length product

The DLP is an indicator of the integrated radiation dose of an entire CT examination. DLP increases with an increase in total scan length or variables that affect the CTDI_{vol} (tube voltage or tube current or pitch). A recent systematic review of coronary CT angiography with use of prospective ECG-triggering versus retrospective gating shows that in characterising a cardiac CT study, DLP is a more objective physics metric than effective dose (33). The variability of

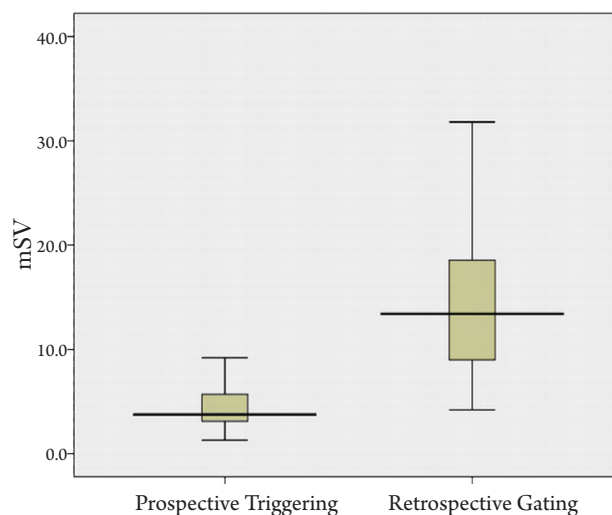


Figure 4 Box plot shows the mean effective dose reported in the studies with use of retrospective ECG-gating and prospective ECG-triggering. It is obvious that the radiation dose of prospective ECG-triggered coronary CT angiography is significantly lower than that of retrospective gating protocol according to a systematic review (32). Horizontal line in each box shows median and top and bottom lines of boxes show interquartile range.

DLP between different study sites observed in that review was striking, as the DLP reported in the studies ranged from 129 to 337 mGy cm. Median DLP at the highest dose sites was more than 3 times that at the lowest dose sites. Thus, coronary CT angiography may be associated with significantly higher or lower dose than invasive coronary angiography, depending on how CT angiography is performed at a study site. The DLP represents most closely the radiation dose received by an individual patient and may be used to set reference values for a given type of CT examination to help ensure patient doses at CT are as low as reasonably achievable. It is recommended that DLP should be recorded for each study and serve as the cornerstone of quality assurance efforts (34).

Effective dose

Effective dose is a single parameter used to reflect the relative risk from exposure to ionizing radiation. The calculation of the effective dose in the current literature is based on a method proposed by the European Working Group for Guidelines on Quality Criteria in CT (35),

deriving radiation dose estimates from the product of the DLP and an organ weighting factor for the chest as the investigated anatomic region ($k=0.014$ or $0.017 \text{ mSv}\cdot\text{mGy}^{-1}\cdot\text{cm}^{-1}$) averaged between male and female models from Monte Carlo simulations (36).

According to a number of systematic review and meta-analysis reports, the mean effective radiation dose for prospective ECG-triggered coronary CT angiography in patients with a low and regular heart rate ranges from 2.7 to 4.5 mSv (33,37,38), which is significantly lower than that for retrospective ECG-gated coronary CT angiography (*Figure 4*). Further reduction of radiation dose can be achieved in prospective ECG-triggered coronary CT angiography with use of lower kVp values and high-pitch mode. A reduction of effective dose by up to 55% has been reported in prospective ECG-triggering with application of 80 and 100 kVp without compromising image quality (33,38). Therefore, a combination of prospective ECG-triggering with a low kVp protocol should be recommended in patients with body mass index (BMI) less than 25 kg/m^2 , since changing tube voltage needs to be correlated with the patient's BMI.

The prospective ECG-triggered high-pitch mode further and significantly lowers the radiation dose to less than 1 mSv while maintaining the image quality and high diagnostic performance, as reported in some studies (29-31). This technique can only be achieved with the second generation of DSCT as it requires high temporal resolution to allow single cardiac cycle reconstruction without motion artefacts. For the high-pitch mode, only patients with a low and stable heart rate ($<65 \text{ bpm}$) and $\text{BMI} <30 \text{ kg/m}^2$ are eligible to accommodate the long image acquisition window and allow accurate triggering of the image acquisition process. Both high and irregular heart rates preclude the use of high-pitch coronary CT angiography because inconstant heart rates would compromise image quality by causing data acquisition in an unfavourable segment of the cardiac cycle. In addition, the broader detector width of 128-slice scanner reduces the misalignment artefacts that are observed in 64-slice CT scanners.

Diagnostic value of prospective ECG-triggering at low heart rate

A significant dose reduction has been reported in several studies performed with prospective ECG-triggered coronary CT angiography (39-41), however, diagnostic value of prospective ECG triggering in the assessment of coronary arteries or CAD has not been systematically studied. Achieving high diagnostic accuracy with

Sun. Coronary CT angiography with prospective ECG-triggering

prospective ECG-triggering is essential to ensure that this scanning technique can be reliably used as an alternative to high-dose retrospective ECG-gating or invasive coronary angiography in the diagnosis of CAD.

Assessable coronary segments and image quality evaluation

Most of the studies performed with prospective ECG-triggered coronary CT angiography that are available in the literature focus on the assessment of coronary artery segments and image quality evaluation, in addition to the reduction of radiation dose. The mean assessable segments for prospective ECG-triggered coronary CT angiography were more than 97% (*Figure 5*), which are comparable to those for retrospective ECG-gated scans, according to recent analyses. On average, less than 3% of the coronary segments were reported to be non-diagnostic image quality in prospective ECG-triggered scans (37,38).

It is well known that the high-density calcification produces blooming artefacts, which lead to overestimation of the degree of coronary stenosis, thus affecting the assessment of coronary segments and resulting in low positive predictive value. Although it has been reported that the rate of nondiagnostic segments in patients with a higher calcium score was significantly higher than the rate of nondiagnostic segments in patients with a lower calcium score (42), the diagnostic accuracy was not affected in patients with higher calcium loads (38).

Qualitative assessment of image quality was normally performed by a likert-scale point score system (3 to 5-point ranking scale) in most of the studies, while quantitative assessment of image quality with use of signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) was only reported in a few studies (33). Although image noise (standard deviation) was slightly increased in prospective ECG-triggered coronary CT angiography when compared to that measured in retrospective gated scans, there is no significant difference in SNR and CNR between the two groups (33).

Diagnostic accuracy

Information about diagnostic value of prospective ECG-triggered coronary CT angiography in CAD is limited, as the majority of currently available studies focus on reduction of radiation dose with acceptable diagnostic images. Two meta-analyses of studies on the use of prospective ECG-triggered 64-or more slice coronary CT angiography reported that the mean patient-based sensitivities and

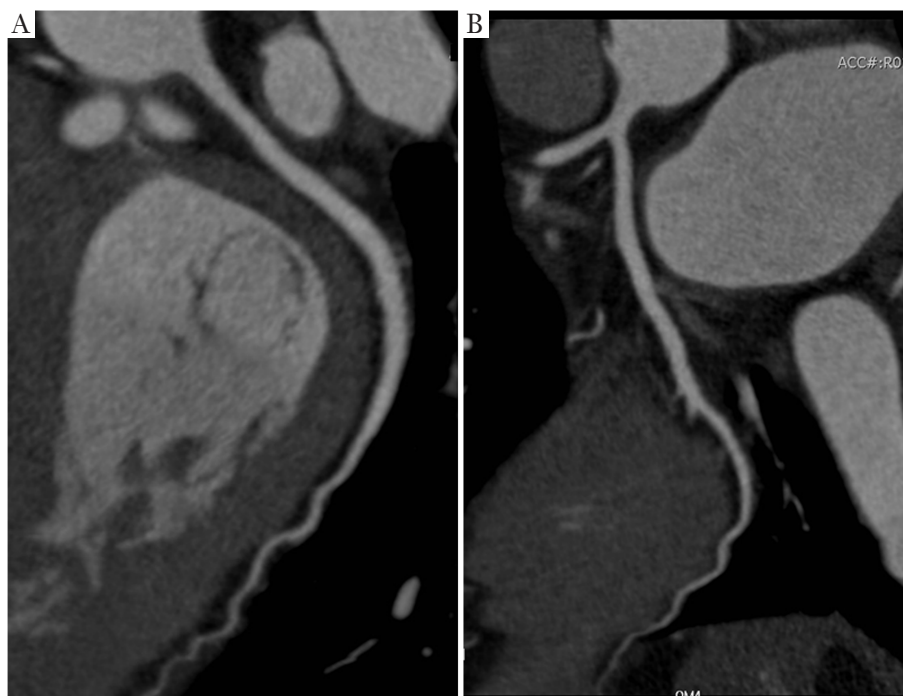


Figure 5 Prospective ECG-triggered coronary CT angiography curved planar reformatted images of the right coronary artery (A) and left coronary artery branches (B) with excellent vessel visualization and no artefacts

specificities ranged from 99% to 100%, and 89% to 91%, respectively (37,38). The vessel- and segment-based estimates showed lower sensitivities and higher specificities, which ranged from 95% to 97% and 93% to 95%; 91% to 92% and 96% to 97%, respectively. Early evidence indicates that coronary CT angiography with prospective ECG-triggering has high sensitivity and good specificity for the diagnosis of significant CAD. The very high negative predictive value of prospective ECG-triggered coronary CT angiography with low radiation dose suggests that this imaging technique can be used as a reliable test for ruling out CAD.

Based on the individual studies and meta-analyses, it can be concluded that for the group of patients with a low and regular heart rate (less than 70 bpm) examined to date with coronary CT angiography, use of a prospectively triggered scan has not been shown to change patient-based, vessel-based and segment-based sensitivity or specificity when compared to the existing data for retrospectively gated exams (1-5).

Radiation dose of prospective ECG-triggering at high heart rate

It is an essential step to control patients' heart rate to 70 bpm or lower in coronary CT angiography using prospective

ECG-triggering in order to guarantee image quality and low effective dose, as shown in previous studies (17-27). In patients with high or irregular heart rate, higher radiation dose has been reported in studies due to the use of padding (43-45).

The purpose of adding padding (additional surrounding X-ray beam on time) is to provide additional phase information to compensate for variations in heart rate by adding time before and after the centre phase of the acquisition. Padding is described in the range of 0-200 ms and is added to both sides of the centre of the acquisition with padding 0 corresponding to a window of 100 ms scanning time and padding 100 corresponding to a window of 200 ms scanning time. Padding is generally used when the heart rates are more than 65bpm or when there is apparent heart rate variability (heart rate variation is more than 10 bpm) (33). LaBounty *et al.* in their recently published large multicentre study showed that the use of minimal padding was associated with substantial reduction in radiation dose with preserved image interpretability (46). Use of no or reduced padding should be considered in dose-saving strategies. Freeman *et al.* in their prospective study consisting of 2025 patients undergoing prospective ECG-triggered 64-slice coronary CT angiography reported that the mean effective dose was 2.75 mSv in patients without use of

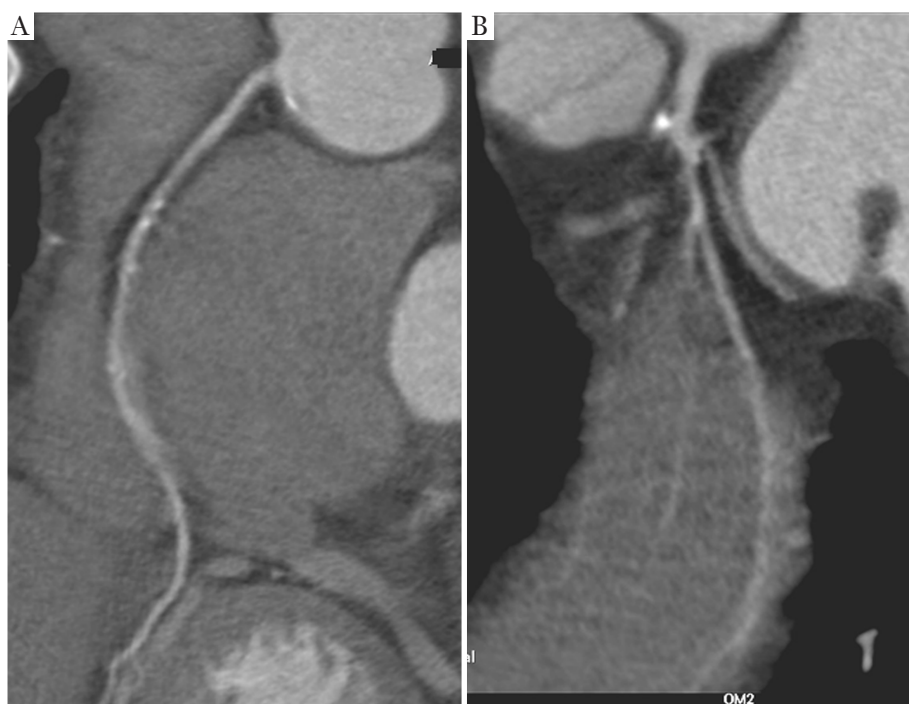


Figure 6 Prospective ECG-triggered coronary CT angiography curved planar reformatted images of the right (A) and left coronary arteries (B) with blurred borders due to moderate artefacts

padding, while the mean effective dose was increased to 5.88 mSv in patients studied with padding (44). Similarly, Hoe and Toh in their study performed with 320-slice CT coronary angiography showed that radiation dose has been significantly increased in patients with heart rate >65 bpm or irregular heart rate when compared to the low heart rate group (45). The mean effective was 5.7 mSv in patients scanned by one-heart beat protocol, but the dose was increased to 13.0 and 17.5 mSv in patients scanned by two- and three-heart beat protocols, respectively. Modification of the prospective ECG-triggered protocols is necessary to enable further dose reduction in these patients with high or irregular heart rate.

DSCT coronary angiography shows promise in examining patients with different heart rate. Few data are available to show the diagnostic value of DSCT coronary angiography with use of prospective ECG-triggering. Sun *et al.* investigated the diagnostic performance of DSCT prospective ECG-triggered coronary angiography in patients with low to high heart rate, and their results showed no significant difference among low, medium and high heart rate groups in terms of diagnostic image quality, and mean effective dose (43). Despite encouraging results, patients with irregular heart rate or heart rate

more than 90 bpm were excluded from their study due to potential failure or unpredictable image quality (Figure 6). Xu *et al.* explored feasibility of DSCT prospective ECG-triggered coronary CT angiography in patients with heart rate higher than 70 bpm, and their results indicated that prospective ECG-triggering is feasible in patients with a heart rate between 70 and 110 bpm with excellent depiction of coronary segments and 57% dose reduction compared to retrospective gating (47). The second generation of DSCT system with capability of achieving 75 ms temporal resolution could be a promising solution for patients with irregular or high heart rate with use of prospective ECG-triggering technique.

Current status and future directions

Current available data indicate that achieving low-dose coronary CT angiography using prospective ECG-triggering is feasible in an everyday population but requires the use of strict exclusion criteria and careful patient preparation (44,48). Heart rate control is crucial for performing a successful coronary CT angiography with prospective ECG-triggering with use of either 64- or 128- or 320-slice scanners (20-24,44,49-52).

A regular heart rate control of less than 70 bpm is achieved through oral or intravenous administration of β -blockers, and this is conducted in almost all of currently available reports. This may result in the exclusion of patients who do not respond or have known contraindications to β -blockers. DSCT coronary angiography offers potential opportunities for inclusion of patients with different heart rate, although more studies are needed to confirm the diagnostic value and image quality.

The tissue weightings of estimating the effective dose of prospective ECG-triggered coronary CT angiography are derived from the International Commission on Radiological Protection (ICRP) which focuses on all aspects of protection from ionizing radiation. In 2007, ICRP released the 103 publication updating the 16-year old ICRP 60 dataset, following the latest available scientific information of the biology and physics of radiation exposure, particularly the tissue weighting for breast tissue has increased from 0.05 to 0.12 (53). The conversion factor used to calculate effective dose from coronary CT angiography has been upgraded from 0.014 to 0.028, thus, doses from coronary CT angiography could be significantly underestimated due to failure of using a cardiac specific conversion factor in the recent ICRP documentation(54,55). Gosling *et al.* compared the effective dose using the latest ICRP 103 tissue-weighting factors with that calculated with previously published chest conversion factors (54). Their results showed that the use of chest conversion factors (0.014-0.017) significantly underestimated the effective dose when compared to the dose calculated using the conversion factor of 0.028. A conversion factor of 0.028 would give a better estimation of the effective dose from prospectively ECG-triggered coronary CT angiography. Appropriate conversion factors are needed to accurately estimate effective dose. A conversion factor of 0.014 or 0.017 is commonly used in many cardiac CT studies to estimate the effective dose associated with coronary CT angiography, thus, this could lead to variations in the reported effective dose. As a result, the DLP or CTDIvol is recommended to compare the radiation exposure of coronary CT angiography (33).

Most of the current studies on prospective ECG-triggering are performed by the same expert groups at a single academic centre, thus, further studies at multiple centres are needed before widespread implementation of this technique can be recommended.

Summary and conclusions

There is sufficient evidence to confirm that coronary CT

angiography with prospective ECG-triggering results in high diagnostic image quality and is associated with a low radiation dose. Prospective ECG-triggered coronary CT angiography is regarded as a reliable alternative to retrospective ECG-gated coronary CT angiography in the assessment of coronary arteries in patients with a regular and low heart rate. It is important to note that the current effective doses from prospective ECG-triggered coronary CT angiography are at the same level or even lower than those acquired from invasive coronary angiography. Therefore, according to the currently available data in the literature, the achievements in radiation dose reduction in coronary CT angiography have been tremendous. Further studies based on large cohorts with inclusion of patients with different heart rate, and with focus on the diagnostic value are needed to confirm its clinical accuracy.

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