Prospective versus retrospective ECG-gated multislice CT coronary angiography: A systematic review of radiation dose and diagnostic accuracy

Zhonghua Sun¹, Kwan-Hoong Ng²

1. Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University of Technology, GPO Box U1987 Perth, Western Australia 6845

2. Department of Biomedical Imaging, University of Malaya, Kuala Lumpur, 50603, Malaysia

Corresponding author:

Dr Zhonghua Sun, Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University of Technology, 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

**Purpose:** To perform a systematic review of the radiation dose and diagnostic accuracy of prospective versus retrospective ECG-gated multislice CT coronary angiography.

**Materials and Methods:** A search of Pubmed/Medline and Sciencedirect databases for English literature was performed to identify studies comparing prospective and retrospective ECG-gated multislice CT angiography in the diagnosis of coronary artery disease. Effective dose, dose length product, image quality and diagnostic value were compared between two groups of studies.

**Results:** 22 studies were included for analysis. The mean effective dose of prospective ECG-gated scans was 4.5 mSv (95% CI: 3.6, 5.3 mSv), which is significantly lower than that of retrospective scans, which is 13.8 mSv (95% CI: 11.5, 16.0 mSv) (p<0.001). The mean dose length product was 225 mGy.cm (95% CI: 188, 262 mGy.cm) and 822 mGy.cm (95% CI: 630, 1013 mGy.cm) for the prospective and retrospective ECG-gated scans, respectively, indicating a statistically significant difference between these two protocols (p<0.0001). The mean sensitivity and specificity of multislice CT angiography in the diagnosis of coronary artery disease was 97.7% (95% CI: 93.7%, 100%) and 92.1% (95% CI: 87.2%, 97%) for prospective ECG-gated scans; 95.2% (95% CI: 91%, 99.5%) and 94.4% (95% CI: 88.5%, 100%) for retrospective ECG-gated scans, respectively, with no significant difference for sensitivity but significant difference for specificity (p=0.047).

**Conclusion:** Multislice CT coronary angiography with prospective ECG-gating leads to a significant reduction of radiation dose when compared to that of retrospective ECG-gating, while offering comparable image quality and diagnostic value.
**Key words:** Coronary artery disease, prospective ECG-gating, radiation dose, image quality, CT angiography
Introduction

Since the introduction of 64- or more-slice CT technology, multislice CT (MSCT) angiography has been increasingly used in the diagnosis of coronary artery disease (CAD) due to its improved spatial and temporal resolution [1-4]. Studies have shown that MSCT angiography is a highly accurate method compared to invasive coronary angiography as it provides high sensitivity and specificity [1-6]. In particular, MSCT angiography has been reported to demonstrate a very high negative predictive value (more than 95%), indicating that it can be used as a reliable screening technique for patients suspected of CAD, thereby reducing the need for invasive coronary angiography [5]. The non-invasive nature of MSCT angiography and increased availability of MSCT scanners have led to rapidly increasing numbers of CT examinations performed worldwide. However, high radiation dose of MSCT angiography and its associated risk of radiation-induced malignancy have raised serious concerns in the medical field [7-10].

In response to these concerns, tremendous progress has been made to lower radiation dose for cardiac MSCT angiography, and various strategies have been proposed to address this issue. These include automatic tube current modulation, reduced X-ray tube voltage and tube current, scan range, and prospective ECG-gating [11]. Of these dose-saving strategies, prospective ECG-gated scanning represents the most recently developed approach with significant reduction of radiation dose when compared to conventional retrospective ECG-gating [12].

Radiation exposure with prospective ECG-gating has been increasingly studied and evaluated with retrospective-gating in the literature [11-14]. Despite promising results having been achieved in dose reduction, there are concerns about the image quality and diagnostic value of prospective ECG-gating, since only a portion of data is
acquired when compared to the volumetric data that is available with retrospective-gating protocol. Thus, the purpose of this study was to perform a systematic review of radiation dose and diagnostic accuracy of prospective versus retrospective ECG-gated MSCT angiography in the diagnosis of CAD, based on the currently available literature.

**Materials and Methods**

*Criteria for data selection and literature searching*

A search of Pubmed/Medline and Sciencedirect databases of English literature was performed for articles comparing prospective ECG-gated MSCT angiography with retrospective ECG-gated scans in patients with suspected or confirmed CAD. Inclusion criteria required that articles must be peer-reviewed and published in the English language. The key words used in searching the references included: MSCT angiography with prospective ECG-gating/ECG-triggering, radiation dose of MSCT angiography, diagnostic value of MSCT angiography with prospective ECG-gating, and comparison of prospective with retrospective ECG-gated MSCT angiography. The literature search ranged from 2008-present as prospective ECG-gating was first reported in the literature in 2008 (last search September 2010). In addition, the reference lists of identified articles were checked to obtain additional relevant articles. Prospective and retrospective studies were included if they met some of the following criteria: (a) studies included at least 10 patients and must be performed with both prospective and retrospective ECG-gated protocols; (b) evaluation of the radiation dose by prospective ECG-gating must be addressed when compared to retrospective ECG-gating; (c) assessment of diagnostic value and image quality of both prospective and retrospective ECG-gated MSCT angiography in CAD must be addressed when
compared to conventional coronary angiography in terms of sensitivity and specificity. Since it is possible that many studies would not meet the third criterion, thus, studies were still eligible for inclusion in the analysis as long as they met the first two criteria. Exclusion criteria were: review article or a comment to the editor; case reports; conference abstracts or phantom studies.

Data extraction

Data were repeatedly extracted by two independent reviewers based on study design and procedure techniques. Each reviewer independently assessed the retrieved articles for possible inclusion according to the selection criteria. The reviewers looked for the following characteristics in each study: year of publication; number of participants; mean age; mean heart rate and body mass index (BMI) in both scanning protocols; use of beta-blockers; type of imaging unit used for MSCT coronary angiography; assessable coronary segments in each group; dose length product recorded in each study; effective dose estimated in each group; and diagnostic accuracy of MSCT angiography in CAD when compared to coronary angiography in terms of the sensitivity and specificity. Furthermore, the reviewers looked for the methods used in each study to assess image quality in terms of qualitative and quantitative image assessment. Image quality was assessed on a per-segment basis according to a three- to five-point ranking scale with excellent image quality indicating a clear delineation of the coronary segments without motion artifacts and poor image quality with severe motion artifacts. Quantitative image quality was assessed by measuring the image noise, which is derived from the standard deviation of the mean CT attenuation values in the left ventricular wall. In addition, signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated and used as
another criterion to evaluate image quality for prospective and retrospective ECG-gated protocols.

*Radiation dose values*

Radiation dose estimates for cardiac CT examinations are expressed by using the volume CT dose index in milligrays (CTDIvol) and dose length product (DLP) in milligray-centimetres, which were obtained from the patient protocol of the system. The effective dose is obtained by multiplying DLP by a conversion coefficient, $k$ (in millisieverts per milligray per centimetre), which varies depending on the body region to be examined. For cardiac CT angiography, effective dose is calculated by using a $k$ value of 0.014 or 0.017 mSv mGy$^{-1}$ cm$^{-1}$. This conversion factor is averaged between male and female models. The different tissue weighting factors are provided by the International Commission on Radiological Protection [15].

*Statistical analysis*

All of the data were entered into SPSS (version 17.0) for analysis. Mean values of effective dose, assessable segments, sensitivity and specificity estimates for each study were combined across studies using one sample test. Statistical hypotheses (2-tailed) were tested at the 5% level of significance.

*Results*

*General information*

25 studies met the selection criteria and 22 were eligible for analysis [16-40]. Three studies were excluded from the analysis as they either focused on the assessment of coronary stenting or coronary bypass instead of coronary artery disease [38-40]. There are altogether 37 comparisons from these 22 studies as seven studies involved
different scanning parameters, either due to comparison of variable tube voltage ranges [19, 26, 28, 34] or inclusion of patients with different heart rates [18, 19, 30], or application of tube current modulation [37]. The table lists patient’s characteristics and study details related to prospective and retrospective ECG-gated protocols. Of 22 studies, 12 were performed on single-source 64-slice CT, five were on dual-source CT, three were on 256-slice CT and one on 320-slice CT. The remaining study involved both single-source and dual-source 64-slice CT as it was performed in 47 study sites [36]. Figure 1 is the flow chart showing the search strategy to obtain these references.

Beta-blockers were used in both prospective and retrospective ECG-gating groups in 17 studies to lower the heart rate less than 75 beats per minute (bpm). In four studies, patients were carefully selected with inclusion of those with stable and heart rate less than 65 bpm in the study groups [19, 24, 25, 26], thus, no beta-blocking agents were administered prior to CT scans. In the remaining study, this information was not available since the study was conducted at 47 international study sites and there is no record of use of the beta-blockers [36].

The number of patients included in the prospective and retrospective ECG-gating studies was 1535 and 2293, respectively. In 16 out of 22 studies, the number of patients included in the studies was matched in both groups, while in four studies a significantly small number of patients were included in the prospective ECG-gating group when compared to that included in the corresponding retrospective gating group [27, 28, 30, 36]. In the remaining two studies, the number of patients included in the prospective gating group is more than 3 times of that included in the retrospective groups [32, 37]. Patients’ age, heart rate and BMI were matched in both
groups in all of the studies except in one study, where significantly younger patients were selected in the prospective ECG-gating group [27].

**Comparison of radiation dose between prospective and retrospective gated scans**

DLP was available in 12 studies, while in another study only CTDIvol was provided. In the remaining nine studies, DLP was not provided. There exists a wide variation between the DLP values for retrospective ECG-gating scans, as it ranged from 395 mGy.cm to 1242 mGy.cm among these studies, with DLP more than 1000 mGy.cm reported in four studies. In contrast, the DLP value for prospective ECG-gating scans ranged from 129 mGy.cm to 337 mGy.cm with DLP more than 300 mGy.cm reported in only two studies. The mean DLP was 225 mGy.cm (95% CI: 188, 262 mGy.cm) and 822 mGy.cm (95% CI: 630, 1013 mGy.cm) for the prospective and retrospective ECG-gating scans, respectively, indicating a statistically significant difference between these two protocols (p<0.0001).

Effective dose was estimated by multiplying the DLP with a conversion factor of 0.017 in 17 out of 22 studies, while in the remaining five studies, the conversion factor was chosen to be 0.014 [22, 30, 32, 36, 37]. Tube current modulation was applied in retrospective ECG-gating scanning in six studies [22, 30, 31, 33, 34, 37]. The mean effective dose was 4.5 mSv (95% CI: 3.6, 5.3 mSv) and 13.8 mSv (95% CI: 11.5, 16.0 mSv) for the prospective and retrospective ECG-gating scans, respectively, indicating a significant difference of radiation dose between the two groups (p<0.001) (Fig 2). The highest effective dose of prospective ECG-gating scans was 12.6 mSv due to acquisition of images in 2 R-R interval, which was reported in one study with the use of 320-slice CT due to the inclusion of patients with high heart rate [18]. In the remaining studies, the effective dose was lower than 10 mSv in prospective gating.
studies with dose less than 5 mSv in 67% of the studies. In contrast, the effective dose was higher than 10 mSv in 69% of the retrospective gating studies with dose more than 20 mSv reported in four studies.

A kVp value of both 100 and 120 was applied and compared in four studies with use of prospective ECG-gating, and a reduction of effective dose by up to 55% was found in the studies scanned with 100 kVp when compared to those with 120 kVp, indicating a further dose reduction of radiation dose with use of lower kVp values in patients with BMI less than 30 kg/m^2.

Padding was applied in four studies performed with prospective ECG-gating [22, 28, 29, 32]. The purpose of adding padding 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 60 bpm or when there exists apparent heart rate variability. Application of padding helps to generate diagnostic images in patients with high heart rate variations, however, this leads to an increase of effective dose by up to 42% when compared to that without padding groups.

Assessable segments and image quality assessment

Evaluation of assessable coronary segments was available in 19 studies with no significant difference found between prospective and retrospective ECG-gating groups (p=0.843). The mean value of assessable segments was 97.3% (95% CI: 95.4%, 99.2%) and 96.8% (95% CI: 94.0%, 99.7%) for prospective and retrospective
ECG-gating scans, respectively. Qualitative assessment of image quality was performed in 14 studies with a five-, four- and three-point ranking scale used in three, eight and three studies, respectively, while in the remaining studies, information about qualitative assessment was unavailable. Quantitative assessment of image quality was reported in five studies with use of SNR and CNR as the criteria, in addition to the subjective scoring for assessment of image quality. Although image noise (standard deviation) was increased in prospective gating scans when compared to that measured in retrospective gating scans, there is no significant difference in SNR and CNR between the prospective and retrospective gating groups.

*Diagnostic value of prospective versus retrospective ECG-gating in CAD*

Diagnostic value of prospective versus retrospective ECG-gating for detection of CAD was reported in four studies (with seven comparisons) when invasive coronary angiography was used as the gold standard [20, 29, 31, 35]. The mean sensitivity and specificity were 97.7% (95% CI: 93.7%, 100%) and 92.1% (95% CI: 87.2%, 97%) for prospective gating scans; 95.2% (95% CI: 91%, 99.5%) and 94.4% (95% CI: 88.5%, 100%) for retrospective gating scans, respectively. There is no significant difference in the mean sensitivity between these two groups (p=0.310), however, a marginally significant difference was reached for the mean specificity between the two groups (p=0.047).

**Discussion**

Our analysis presents three findings which we consider important for clinical application of MSCT angiography in CAD: first, prospective ECG-gating leads to a significant reduction of DLP and effective dose by more than 60% (up to 90% in some studies) when compared to retrospective ECG-gating. Second, diagnostic image
quality of prospective ECG-gating is comparable to that of retrospective ECG-gating, in terms of both subjective and objective assessment of coronary segments. This indicates that prospective ECG-gating is a feasible technique for evaluation of CAD. Third, high diagnostic value (>90%) is achieved with prospective ECG-gating in patients with a regular and low heart rate and this is comparable to that of retrospective ECG-gating; therefore, prospective ECG-gating can be reliably used in the diagnosis of CAD, although more studies are needed to confirm its diagnostic value.

Prospective ECG-gating utilises the same technique as that used in electron-beam CT which is defined as the step-and-shoot method. The scan is performed in a non-helical way with acquisition of a series of axial images instead of volumetric data, thus, X-ray tube is turned on only at the selected cardiac phase and turned off during the rest cardiac cycle. Therefore, a significant reduction of radiation dose can be expected from prospective ECG-gating. This is confirmed in our analysis as prospective ECG-gating results in a significant reduction of both DLP and effective dose when compared to the corresponding retrospective ECG-gating.

Radiation dose can be further reduced by lowering the kVp value in the prospective ECG-gating protocol. Our analysis shows that in four studies comparing 100 kVp and 120 kVp protocols, a reduction of radiation dose from 42% to 55% with diagnostic image quality was achieved, even if in the presence of heart rate more than 70 bpm. Effective dose lower than 5 mSv was reported in 67% of the studies performed with prospective ECG-gating, and this is comparable to invasive coronary angiography which delivers an effective dose of 7 mSv [41]. For comparison, the average yearly background radiation dose is around 3 mSv [42]. Depending on the technique used
and the dose-saving algorithms implemented, MSCT angiography may have a comparable or even lower effective dose than invasive coronary angiography.

This analysis shows that in characterising a cardiac CT study, DLP is a more objective physics metric than effective dose. The variability of DLP between different study sites observed in this review is striking. Median DLP at the highest dose sites was more than 3 times that at the lowest dose sites, and doses ran the range in between these extremes. Thus, cardiac CT angiography may be associated with significantly higher or lower effective dose than standard 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 [43].

Diagnostic value of MSCT angiography in CAD has been significantly improved with use of 64-CT. Several meta-analyses of 64-slice CT studies with use of conventional retrospective ECG-gating indicated that MSCT, especially with 64-or more-slice CT, has high diagnostic accuracy for detection of CAD and could be used as an effective alternative to invasive coronary angiography in selected patients [5, 44-46]. Although prospective ECG-gating shows promising results in dose reduction, its diagnostic value in CAD has not been confirmed due to lack of sufficient evidence. In this systematic review, only four studies were identified which provided information about diagnostic value of prospective ECG-gating in CAD, with mean high diagnostic sensitivity and specificity (>90%) reported in these studies. This is consistent with recent reports which showed a high diagnostic performance achieved with 64 or dual-
source CT prospective ECG-gating with low radiation dose [47, 48]. Despite limited studies available in the literature; this analysis shows that prospective ECG-gating could be used as a reliable alternative modality for the diagnosis of CAD. Prospective ECG-gating demonstrated higher diagnostic value in the evaluation of assessable segments than that acquired with corresponding retrospective ECG-gating and early reports of 64-slice CT studies (97.2% vs 96%) [5]. Further studies should be conducted with a focus on the diagnostic value of prospective ECG-gating in CAD with inclusion of patients with high heart rate.

One of the main limitations of prospective ECG-gating is inclusion of patients with a low and regular heart rate, since the CT scan is triggered by the ECG signals which require the heart rate to be regular and less than 65 bpm. Mean heart rate less than 65 bpm was found in 18 studies, while in the remaining two studies performed with dual-source and 256-slice CT, patients with heart rate more than 70 bpm was included in the prospective ECG-gating group. This indicates the superiority of dual-source CT in imaging patients with high heart rate. It has been reported that high diagnostic value could be achieved with dual-source CT angiography in the diagnosis of CAD, with image quality independent of heart rate [49]. The improved temporal resolution of dual-source CT results in a robust image quality within a wide range of heart rates; thus provides the opportunity to image patients with higher heart rates without requiring pre-examination beta-blockage.

Another limitation of prospective ECG-gating is the lack of cardiac functional evaluation of left ventricle or cardiac valves. The limitation of no functional information has also been overcome with use of the new generation of CT techniques since myocardial perfusion imaging can be obtained with 256 or 320-slice prospective gating. Early studies showed the accuracy of 256- and 320-slice CT perfusion
imaging for the simultaneous evaluation of coronary atherosclerosis and its physiological significance with a mean dose of 13.5 ± 3.5 mSv [50, 51]. Apparently the radiation dose is higher than that acquired with prospective ECG-gating technique, thus, further technical improvement to reduce radiation dose is necessary.

Some limitations exist in this study. First, the publication bias exists and may affect the results as non-English publications were excluded. However, it is reported that language-restriction meta-analyses overestimated the treatment effect by only 2% on average compared with language-inclusive meta-analyses [52]. Although it is apparent that more studies are being performed on 64- or more slice CT scanners (especially with dual-source CT), it was difficult to include all of the potential studies in the analysis, especially those studies currently being undertaken or under review. Second, lack of uniform criteria of assessment is another limitation inherent in most of the studies. Different ranking scales were used in these studies that were analysed, and objective assessment of image quality was available in a small number of studies. Subjective assessment of image quality without using any ranking scale was used in nearly 20% of the studies, and this could introduce biased opinion to the study results. Third, MSCT angiography was performed in patients referred for invasive coronary angiography, creating a selection bias of patients with a relatively high prevalence of significant CAD patient selection. Fourth, we did not include studies with evaluation of coronary stents or coronary artery bypass grafting, which should be investigated in the future studies. Finally, effective dose based on a conversion factor of 0.014 or 0.017 is only an estimate. The calculation of the effective dose in these studies is based on a method proposed by the European Working Group for Guidelines on Quality Criteria in CT [53], 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 0.107 mSv·mGy^{-1}·cm^{-1} averaged between male and female models from Monte Carlo simulations [54]. Because the mathematical modelling done to compute organ doses is based on a standard adult (70kg), effective dose estimation can underestimate the risk for children and thin patients and overestimate the risk for obese patients. Therefore, one should remember that the uncertainty associated with the effective dose estimations could vary as much as 40% in some cases. One has to adopt a correction factor when making comparisons with different studies. Although the use of effective dose estimates for assessing the exposure of patients has severe limitations, the effective dose is still widely used as a dose parameter to reflect the radiation risk, compare doses from different diagnostic and therapeutic procedures and compare the use of similar technologies and procedures in different hospitals and countries as well as of different technologies for the same medical examinations.

In conclusion, this analysis shows that MSCT angiography with prospective ECG-gating leads to a significant reduction of radiation dose when compared to that with use of retrospective ECG-gating, while achieving comparable image quality and diagnostic value in the diagnosis of CAD in patients with a regular and low heart rate. A wide variation of DLP was present in both retrospective and prospective ECG-gating groups, leading to a significant difference of radiation dose associated with these studies. This emphasises the importance of using diagnostic reference levels of DLP as another approach for radiation dose limitation. Prospective ECG-gating can be used as a reliable alternative to invasive coronary angiography in selected patients, although further studies are needed to verify its diagnostic accuracy.
References


**Figure legends**

Figure 1. Flow chart shows the search strategy used to identify eligible references.

Figure 2. Mean effective dose reported in the studies by comparing prospective with retrospective ECG-gating is shown in the box plot.