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Radiation dose and cancer risk in retrospectively and prospectively ECG-gated coronary angiography using 64-slice multidetector CT

[1]B HUANG, PhD, [2]J LI, PhD, [3]M W-M LAW, PhD, [1]J ZHANG, MD, [2]Y SHEN, PhD and [1]P L KHONG, MD

[1]*Department of Diagnostic Radiology, The University of Hong Kong, Hong Kong,* [2]*GE Healthcare China, Beijing, China, and* [3]*Department of Clinical Oncology, Queen Mary Hospital, Hong Kong*

ABSTRACT. This study aimed to estimate the radiation dose and cancer risk to adults in England, the USA and Hong Kong associated with retrospectively and prospectively electrocardiogram (ECG)-gated coronary computed tomography angiography (CTA) using currently practised protocols in Hong Kong. The doses were simulated using the ImPACT spreadsheet. For retrospectively ECG-gated CTA with pitches of 0.2, 0.22 and 0.24, the effective doses were 27.7, 23.6 and 20.7 mSv, respectively, for males and 23.6, 20.0 and 18.8 mSv, respectively, for females. For prospectively ECG-gated CTA, the effective dose was 3.7 mSv for both males and females. A table of lifetime attributable risks (LAR) of cancer incidence was set up for the English population for the purpose of estimating cancer risk induced by low-dose radiation exposure, as previously reported for US and Hong Kong populations. From the tables, the LAR of cancer incidence for a representative 50-year-old subject was calculated for retrospectively ECG-gated CTA to be 0.112% and 0.227% for English males and females, respectively, 0.103% and 0.228% for US males and females, respectively, and was comparatively higher at 0.137% and 0.370% for Hong Kong males and females, respectively; for prospectively ECG-gated CTA, the corresponding values were calculated to be 0.014% and 0.035% for English males and females, respectively, and 0.013% and 0.036% for US males and females, respectively, and again were higher at 0.017% and 0.060% for Hong Kong males and females, respectively. Our study shows that prospectively ECG-gated CTA reduces radiation dose and cancer risks by up to 87% compared with retrospectively ECG-gated CTA.

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Conventional coronary angiography is the gold standard for assessing the heart and coronary arteries, owing to its excellent spatial and temporal resolution; however, the procedure is invasive and can cause serious complications, such as thromboembolism and arterial dissection. Non-invasive imaging methods such as computed tomography angiography (CTA) can therefore be advantageous [1–4]. Applications of coronary artery CTA have, in the past, been limited by problems such as cardiac motion, respiratory motion and the small size of coronary arteries. However, technological advances with multidetector CT (MDCT) scanners have enhanced the spatial and temporal resolution achievable by CTA. Moreover, applying electrocardiogram (ECG)-gated technology, the data at diastole during each cardiac cycle can be selected and used for image reconstruction, thereby minimising motion artefacts [5]. There are two kinds of ECG-gating technologies: retrospective ECG gating and prospective ECG gating [5, 6]. For retrospective ECG gating, data are acquired during the entire cardiac cycle and only some of the data (data at the diastolic phase) are used for image reconstruction. To obtain sufficient raw data, data oversampling is used with a low pitch, which, in turn, depends on the patient's heart rate. For prospective ECG gating, initially the mean duration of a cardiac cycle is averaged over multiple heart cycles. The trigger, a predefined time-point in each subsequent cardiac cycle, is used to initiate a sequential axial scan during diastole. The acquisition time for one axial position is about 250–500 ms. All data acquired in prospectively ECG-gated scans are used for image reconstruction.

With the advent of MDCT for coronary CTA, however, radiation dose has become an important issue to be considered [7, 8]. The doses reported from coronary CTA may be even higher than for conventional angiography [9]. Using retrospectively ECG-gated CTA, doses to the organs exposed directly to X-rays are especially high: up to 114 mSv for oesophagus, 80 mSv for breast and 91 mSv for lung [10]. Recently, cancer risks from CTA, the major detriment associated with radiation exposure, have been reported in the literature [10–12]. These studies estimated lifetime cancer incidence to be up to 0.2% and 0.7% for patients undergoing coronary CTA on 16- and 64-slice CT scanners, respectively [10, 12]. Moreover, a lifetime incidence of up to 0.5% and 0.4% was reported specifically for breast and lung cancer, respectively [11]. Doses from prospectively ECG-gated CTA have been reported and were found to be much lower than those for retrospectively ECG-gated CTA [13, 14].

This study investigated the radiation dose from retrospectively and prospectively ECG-gated coronary CTA

Address correspondence to: Pek-Lan Khong, Room 406, Block K, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. E-mail: plkhong@hkucc.hku.hk
Dr Jianying Li and Dr Yun Shen are currently employees of GE Medical System.

on 64-slice MDCT and compared the associated cancer risk imparted to adults in England, the USA and Hong Kong. Comparisons were based on the principles introduced by the Biological Effects of Ionizing Radiation (BEIR) Committee of the National Research Council in its seventh report (BEIR VII report) [15].

Methods and materials

CT dose estimation

The radiation doses associated with coronary CTA on 64-slice LightSpeed VCT and LightSpeed VCT XT (GE Healthcare, Milwaukee, WI) were evaluated. The commonly used CTA protocols for adults currently practised in our clinic were studied. The scanning protocol of retrospectively ECG-gated CTA performed using VCT was as follows: 120 kV; 0.35 s rotation time; cardiac large filter; slice acquisition 64 × 0.625 mm; 140 mA~700 mA ECG-modulated tube current (full current between 40% and ~80% of cardiac cycle, 140 mA for the rest of the cycle); and a pitch of 0.2, 0.22 or 0.24, corresponding to heart rates of 50 bpm, 60 bpm and 70 bpm, respectively. Owing to overscans in helical scan mode for the retrospectively ECG-gated CTA, we assumed a *z*-axis scan range of 16 cm to cover the cardiac region of about 12 cm. The scanning protocol of prospectively ECG-gated CTA using VCT XT was as follows: 120 kV; 450 mA; 0.35 s rotation time (half-scan, about 0.24 s ± 0.06 s padding); cardiac large filter; slice acquisition 64 × 0.625 mm; and a *z*-axis range of 12 cm. These protocols are similar to those reported in publications from some centres in Europe, America and Asia [16–18], although minor variations do exist.

To estimate the radiation dose of CTA, the spreadsheet ImPACT Version 0.99X [19] was used. This is a widely recognised tool for calculating patient organ doses and effective doses from CT examinations [20–25] including coronary angiography [21]. The scanner type, the CT dose index (CTDI) of these two scanners and the protocol parameters were input into the spreadsheet. The spreadsheet makes use of the Monte Carlo dose data published in the National Radiological Protection Board (NRPB) Report SR250 [26] and the input data to determine the organ doses from the CT scan. The effective doses were calculated by summing these organ doses weighted by organ weighting factors recommended in International Commission on Radiological Protection (ICRP) publication 103 [27].

Cancer risk estimation

Cancer risk estimation was performed by applying the principles introduced in the BEIR VII report [15] in the form of lifetime attributable risk (LAR), which is calculated using Equation 1.

$$\mathrm{LAR}(D,e) = \sum_{a} M(D,e,a)S(a)/S(e) \qquad (1)$$

where D is dose (assumed to be 100 mSv, for calculating the table), e is exposed age and a is attained age which is from $e+L$ to 100 (L is a risk-free latent period that equals 5) accounting for ''lifetime''. $S(a)$ and $S(e)$ are the probability of surviving until age a and e, respectively, which are obtained in the life table data. Hence, the ratio from $S(a)/S(e)$ is the probability of patient surviving to age a on the condition that he/she survives to age e. $M(D,e,a)$ is the excessive cancer risk in a specific year, which can be calculated using the excess relative risk (ERR) model and the excess absolute risk (EAR) model. EAR is the excess absolute cancer risk, whereas, ERR is the excess absolute cancer risk divided by the baseline rate [15]. Using the ERR model, the ERRs are assumed to be the same among different populations and $M(D,e,a)$ is given by Equation 2.

$$M(D,e,a) = \mathrm{ERR}(D,e,a)\lambda_I^c(a) \qquad (2)$$

where $\lambda_I^c(a)$ represents sex- and age-specific baseline cancer incidences (cases in 100 000 people), which can be obtained from the cancer statistics. For the EAR model, EARs are assumed to be constant among different populations and equal to $M(D,e,a)$. In the BEIR VII report, ERR(D,e,a) and EAR(D,e,a) modelling are based on the cohorts exposed to excess radiation, including A-bomb survivors. Two LARs were acquired using the ERR and EAR models, and a weighted LAR was then calculated by weighting these two on a logarithmic scale. In the BEIR VII report, to calculate the table for the US population, weights of 0.3 for the EAR model and 0.7 for the ERR model are given to most cancer sites, based on an analysis of risk transport between the Japanese and US population [15]. The final LAR table data were acquired by dividing the weighted LAR(D,e) by a dose and dose-rate effectiveness factor (DDREF) of 1.5, to account for the lower risk of the low-dose radiation. In this way, the LAR of each organ for 100 000 US subjects exposed to 100 mSv radiation at a specific age was derived and tabulated in the BEIR VII report. Each organ's LAR for a specific radiation dose can be calculated according to data in the table and applying linear extrapolation.

In our study, to calculate the LAR for the English population, an LAR table similar to the one derived for the US population in the BEIR VII report [15] was calculated using the Cancer Registration Statistics England 2005 [28] and United Kingdom Interim Life Tables 2005–07 [29]. The weights of EAR and ERR for the English population were chosen to be the same as those used in the BEIR VII report for the US population, as no weights were suggested for other populations in the BEIR VII report. A DDREF of 1.5 was also used to account for the lower risk of the low-dose radiation.

The tables of LAR for the USA and Hong Kong population have been established and presented in our previous publication [30]. We performed the analyses of cancer risks for England, USA and Hong Kong adult populations ranging between 20 and 80 years of age. To study the detriment of the associated cancer risk, the proportion of the total lifetime cancer incidence contributed by the LAR was also calculated. The total lifetime cancer incidence was calculated by summing the

baseline lifetime cancer incidence acquired from the cancer statistics [28, 31, 32] and the LAR.

Results

Radiation dose

Organ doses and effective doses from CTA performed on LightSpeed VCT and LightSpeed VCT XT are presented in Table 1. For females, the effective doses of retrospectively ECG-gated coronary angiography with a heart rate of 50 bpm, 60 bpm and 70 bpm (corresponding to pitches of 0.2, 0.22 and 0.24, respectively) were 23.6 mSv, 20.0 mSv and 18.8 mSv, respectively; for males, the corresponding values were 27.7 mSv, 23.6 mSv and 20.7 mSv, respectively. The effective doses for males were higher than those for females. The organ doses and effective doses decreased when the pitch increased. A high radiation burden was observed in the lung, breast and oesophagus, all of which were directly exposed to radiation. Doses imparted to these directly exposed organs ranged from 45 mSv to 73 mSv. The organs not exposed directly, including gonad, colon and bladder, contributed less than 6% of the overall effective dose. The effective dose from prospectively ECG-gated CTA was 3.7 mSv for both males and females, less than one-quarter of the dose from retrospectively ECG-gated coronary CTA. We also made a comparison table of doses from other types of CT scans that have been reported in the literature (Table 2).

Cancer risk

The LAR data calculated for the English population are presented in Table 3. The table shows lifetime cancer cases per 100 000 persons (males or females, independently) exposed to 100 mSv radiation. As shown in the table, the excess risks for females are higher than for males, except for colon and liver.

LARs of cancer incidence induced by the radiation dose for English (Figure 1a,b), USA (Figure 1c,d) and Hong Kong (Figure 1e and f) populations from 20 to 80 years of age are illustrated in Figure 1. We used 50-year-old subjects as representative examples. For retrospectively ECG-gated CTA, for the English population, the LAR in 50-year-old males undergoing a single examination was 0.112% (*i.e.* 1 case in 893 males), 0.096% (1 in 1042) and 0.084% (1 in 1190) for pitches of 0.2, 0.22 and 0.24, respectively; in 50-year-old females the corresponding values were 0.227% (1 in 441), 0.192% (1 in 521) and 0.170% (1 in 588), respectively. For the US population, the LAR in 50-year-old males was 0.103% (1 in 971 males), 0.087% (1 in 1149) and 0.077% (1 in 1299) for pitches of 0.2, 0.22 and 0.24, respectively; in 50-year-old females the corresponding values were 0.228% (1 in 439), 0.193% (1 in 518) and 0.171% (1 in 585), respectively. For the Hong Kong population, the LAR in 50-year-old males was 0.137 % (1 in 730), 0.116% (1 in 862) and 0.102% (1 in 980) for pitches of 0.2, 0.22 and 0.24, respectively; in 50-year-old females the corresponding values were 0.370% (1 in 270), 0.313% (1 in 319) and 0.287% (1 in 437), respectively. The risks for the USA population are similar to those for the English population (less than 10% difference, depending on age), whereas the risks for the Hong Kong population were about 1.2–1.9 times the risks for the English population.

For prospectively ECG-gated CTA, the LARs were 0.014% and 0.035% for 50-year-old English males and females, respectively. For 50-year-old USA males and females, the LARs were 0.013% and 0.036%, respectively. For 50-year-old Hong Kong males and females, the LARs were 0.017% and 0.060%, respectively. Similar to retrospectively ECG-gated CTA, the LARs for the Hong Kong population were around 1.2–2.0 times those of the English population. Comparing retrospective and prospective ECG-gating techniques, the LARs of cancer incidence from retrospectively ECG-gated CTA were between 4 and 8 times higher than those from prospectively ECG-gated CTA (Figure 1) across all ages in England, the USA and Hong Kong.

Table 1. Radiation doses from a single coronary CT angiography examination

Organ	Dose from coronary CT angiography (mSv)							
		VCT, 50 bpm		VCT, 60 bpm		VCT, 70 bpm		VCT XT
	W_T	Male	Female	Male	Female	Male	Female	Male/female
Gonad	0.08	0.0	0.1	0.0	0.1	0.0	0.1	0.0
Colon	0.12	0.2	0.1	0.2	0.1	0.1	10.0	0.0
Stomach	0.12	11.1	9.7	9.5	8.3	8.5	7.3	1.2
Lung	0.12	72.9	61.8	61.8	52.3	54.4	46.2	9.7
Breast	0.12	73.9	62.8	62.8	53.3	55.3	47.1	12
Bone marrow	0.12	15.2	13.2	13.3	11.4	11.8	10.0	2.0
Thyroid	0.04	2.2	1.9	1.9	1.6	1.7	1.5	0.2
Liver	0.04	19.2	16.2	16.2	13.3	13.6	11.8	1.8
Bladder	0.04	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Oesophagus	0.04	71.9	61.8	61.8	52.3	53.5	45.3	5.7
Bone surface	0.01	27.3	23.3	23.8	20.0	20.9	17.2	3.5
Skin	0.01	10.1	9.0	9.0	7.7	7.9	6.7	1.3
Brain	0.01	0.1	0.1	0.1	0.1	0.1	0.1	0.0
Remainder tissues	0.13	2.8	2.4	2.3	2.0	2.1	1.8	0.3
Effective dose (mSv)	–	27.7	23.6	23.6	20.0	20.7	18.8	3.7

W_T, tissue-weighting factors recommended in the International Committee on Radiological Protection (ICRP) publication 103 [27].

Table 2. Radiation doses and cancer risks reported from various CT studies and for the background radiation

Study type and reference	Effective dose[b] (mSv)	Lifetime excess cancer incidence (%) (mainly for 20-year-old patients)
Retrospectively ECG-gated coronary CTA[a]	18.8–27.7	0.23 (males), 0.70 (females)
Prospectively ECG-gated coronary CTA[a]	3.7	0.03 (males), 0.11 (females)
Head CT [38]	8.7 (to thyroid only)	0.039 (to thyroid gland only)
Chest CT [39,40]	5.4	0.025
Paediatric abdominal CT [41]	11	0.18
Whole body CT [20]	12.1	0.135 (mortality)
Background radiation per year [42]	3	–

[a]Data obtained from the present study.
[b]Effective dose given for an average of genders.

The LARs for both protocols were comparatively higher in younger cubiects and decreased with increasing age for both genders in England, the USA and Hong Kong (Figure 1). For example, for retrospectively ECG-gated CTA with pitch 0.2, the LAR of Hong Kong males decreased from 0.229% at 20 years of age to 0.042% at 80 years of age. LARs for women were higher than for men across all ages; this was mainly because females' breasts receive high doses and carry a higher relative risk of developing cancer.

Comparing with the baseline lifetime cancer incidence, the proportion of LAR that contributed to total lifetime cancer risk (sum of LAR and baseline lifetime cancer incidence) was, for retrospectively ECG-gated CTA, 0.1%–0.4% and 0.5%–1.6% for males and females, respectively, in England, 0.1%–0.4% and 0.3%–1.5% for males and females, respectively, in the USA and 0.3%–0.7% and 1.3%–2.9% for males and females, respectively, in Hong Kong. For prospectively ECG-gated CTA, the proportion of LAR that contributed to total lifetime cancer risk was 0.03%–0.05% and 0.10%–0.26% for males and females, respectively, in England, 0.02%–0.05% and 0.07%–0.25% for males and females, respectively, in the USA, and 0.05%–0.09% and 0.3%–0.5% for males and females, respectively, in Hong Kong. Again, this was comparatively higher in younger ages and decreased with increasing age.

Table 3. Table of lifetime attributable risks (LAR) of cancer incidence for the English population

Cancer site	Exposed age (years)						
	20	30	40	50	60	70	80
Male							
Stomach	51	36	35	33	28	19	8
Colon	172	122	119	110	92	61	26
Liver	29	20	20	18	15	10	4
Lung	162	111	111	106	94	70	37
Prostate	42	30	30	28	23	13	6
Bladder	92	67	66	65	58	42	21
Other solid	340	215	190	158	115	67	27
Thyroid	17	7	6	6	5	4	2
Female							
Stomach	57	40	39	36	32	24	13
Colon	101	71	69	64	54	38	18
Liver	27	19	19	17	14	10	5
Lung	347	238	236	226	200	151	79
Breast	407	240	135	67	30	12	4
Uterus	2	1	1	1	1	1	0
Ovary	54	38	34	29	22	13	6
Bladder	97	69	68	66	60	46	25
Other solid	403	260	213	176	129	80	36
Thyroid	71	29	24	20	16	12	7

The numbers shown are cancer cases in the lifetime of 100 000 persons exposed to a radiation dose of 100 mSv.

Discussion

Our dose results for both retrospectively and prospectively ECG-gated coronary CTAs are similar to the published dose reports in the literature using 64-MDCT [10, 13, 14, 17]. To make comparisons with previous published studies in which effective doses were calculated based on tissue weighting factors in ICRP publication 60, the effective dose in the present study was recalculated according to ICRP publication 60. For retrospectively ECG-gated coronary CTA (pitch 0.2), the recalculated dose was found to be 21 mSv for males and 18 mSv for females, in good accordance with the average effective dose estimated to be 20.0 $\pm$ 3.5 mSv by Hirai et al [13]. For prospectively ECG-gated CTA, the reported effective doses ranged from 3.0 mSv to 4.2 mSv [13, 14, 17], which are also similar to the recalculated effective dose in our study (2.6 mSv). Einstein et al [10] reported the LAR associated with retrospectively ECG-gated coronary CTA on 64-slice MDCT to be 0.70% and 0.15% for 20-year-old US women and men, respectively, similar to our estimated LAR results (Figure 1).

Our results showed that both the doses and risks change markedly with heart rate using the retrospective ECG-gating technique (Table 1 and Figure 1). This has been reported and explained in our previous publication [33]. Briefly, there are two reasons for this observation. First, for lower heart rates a lower pitch is used, as this is necessary to avoid discontinuities in images of the heart from consecutive cardiac cycles [34]; however, this would then increase the radiation dose when other CT parameters remain the same [35]. Second, the tube current during CT scan is different for different heart rates with the use of ECG modulation, and this would affect the dose. The effective doses from prospectively ECG-gated CTA were less than 20% of those from retrospectively ECG-gated CTA (Table 1) and the estimated LARs less than 25% (Figure 1), even for the highest pitch. This was observed in both males and females in England, the USA and Hong Kong across all ages. The lower dose is a result of the shortened time period of radiation exposure, because the other parameters of the two protocols in our study were similar. For example, in our study, the total exposure time of retrospectively ECG-gated CTA is up to 7 s (pitch 0.2),

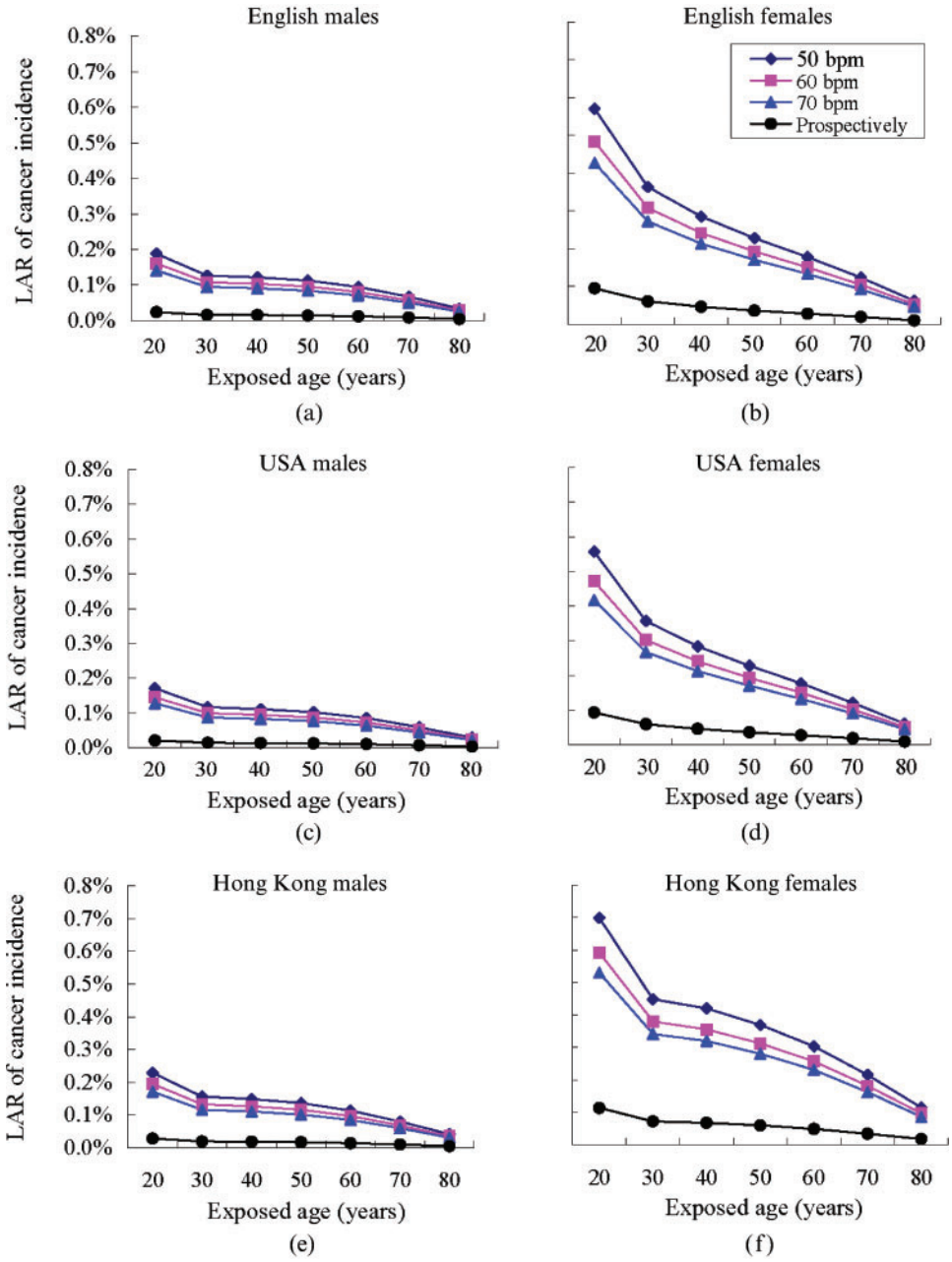

Figure 1. Estimated lifetime attributable risks of cancer incidence associated with radiation dose from a single electrocardiogram (ECG)-gated CT angiography examination at different ages. Retrospectively ECG-gated CT angiography was studied on LightSpeed VCT with three different heart rates (50, 60 and 70 bpm) corresponding to different pitches (0.2, 0.22 and 0.24); prospectively ECG-gated CT angiography was studied on LightSpeed VCT XT. The risks to (a) English males, (b) English females, (c) USA males, (d) USA females, (e) Hong Kong males and (f) Hong Kong females are shown independently.

whereas for the prospectively ECG-gated scan it is only about 1 s (three times a 0.35 s rotation time).

Compared with that of retrospectively ECG-gated CTA, image quality of prospectively ECG-gated CTA has been reported to be at least similar [17] or even significantly higher [18]. Hence, prospectively ECG-gated CTA is a promising method for evaluating coronary arteries, owing to its non-invasive nature, good image quality and lower radiation dose. The prospective ECG-gating technique does have some limitations, however. First, it cannot be applied in patients with cardiac arrhythmias [6], because the time-point of triggering the CT scan in the cardiac cycle can be estimated only from the preceding cardiac cycle. Second, image quality is more severely degraded at higher heart rates (>70 bpm) in patients imaged with prospective gating as compared with retrospective gating [36]. Third, prospective gating does not allow for cardiac functional analysis, which requires reconstruction of images at all time-points during the cardiac cycle [36]. Finally, prospective ECG gating is performed with an axial rather than a helical scan and therefore does not allow for the acquisition of true volumetric raw data; such data can be potentially useful in the correction of motion artefacts [37].

LARs were calculated based on the dose from the CT protocols used in our clinic, hence there might be some variation in risks, depending on the protocols used

across centres and in different countries. Nevertheless, our results, allowing comparisons of the computed risks among the three populations in the UK, USA and Hong Kong, are also of interest. As the life tables and cancer statistics data for the English and US populations are similar [28, 29], the LARs for these two populations showed little difference (Figure 1). For the same radiation dose exposure, cancer risks to the Hong Kong population were found to be higher than for the US population (or English population), as found in our previous study [30, 33]. This is due to the longer life expectancy in the Hong Kong population and the fact that this population has higher baseline cancer incidence in most of the organs that are more sensitive to radiation dose [30]. As the US and English populations have a higher baseline lifetime cancer incidence than the Hong Kong population plus a lower LAR, the proportion contributed by the LAR to total cancer incidence was lower in the USA and the English populations than in the Hong Kong population. Hence, our results suggest that radiation risk from coronary CTA may have a greater impact on the Hong Kong population than on the USA and English populations.

There are limitations in our estimation of doses and cancer risks in this study. According to Groves et al [25], the doses simulated using ImPACT are about 15% lower than the doses measured by them using thermoluminescent detectors directly. This underestimation by the ImPACT spreadsheet may be attributed to differences between the Rando humanoid phantom (used for measurement in the work of Groves et al [25]) and the MIRD phantoms (used in ImPACT). As ImPACT results are used to determine organ doses for a standard size person, variations in patient size and tissue composition can lead to discrepancies in the organ dose estimation. Despite these variations, the doses simulated using ImPACT are robust enough and have been reported widely in the literature [20–25]. The limitations in calculating the LAR of cancer incidence have been discussed in our previous study [30]. Briefly, these limitations are twofold: first, their are uncertainties in the method for estimating the cancer risk according to the principles of the BEIR VII report [15]; second, there are no experimental data to verify the linear extrapolation assumption for doses in the range of CTA (*i.e.* less than 100 mSv). In addition, one should bear in mind that the BEIR VII risk estimates are applicable to the general population with the typical life expectancy for age and sex, as our LAR tables were set up based on these data. These estimates are less applicable in individual subjects with decreased life expectancy, for example from exposure to risk factors and chronic illnesses (such as patients with post-acute myocardial infarction).

Conclusion

According to our study, radiation doses of up to 27.7 mSv and a lifetime risk of cancer incidence of up to 0.37% (for 50-year-old subjects) are associated with retrospectively ECG-gated coronary CTA. By contrast, prospectively ECG-gated coronary CTA dramatically reduces the doses and cancer risks by up to 86% (dose) and 88% (cancer risk), respectively. Prospectively ECG-gated CTA, when feasible, is the preferred choice in evaluating the coronary arteries, in terms of minimising radiation exposure. However, retrospectively ECG-gated coronary CTA is still the technique used for patients when the prospectively ECG-gated technique is not suitable or is unavailable. In this case, CT protocols should be tailored to decrease the potential detriments of radiation exposure.

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