Original Article
A preliminary study on a 70 kV high-pitch dual-source CT coronary angiography using an ultra-low contrast media

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Abstract: *Objectives:* To estimate the feasibility of a 70 kV high-pitch dual-source CT (DSCT) coronary angiography using an ultra-low contrast media (CM) with iterative reconstruction (IR). *Methods:* 126 patients (BMI≤28 kg/m^2) were scanned using one of the four CM protocols: low iodine concentration (300 mgI/ml) with low flow rate (FR) (25 ml&2.5 ml/s) for protocol A and high FR (40 ml&4.0 ml/s) for protocol B; high iodine concentration (350 mgI/ml) with low FR for protocol C and high FR for protocol D. Patients were divided into different groups representing the four protocols. Results were compared among the groups. *Results:* The mean ED was 0.22±0.01 mSv. For patients with BMIs≤25 kg/m^2, the quantitative IQ scores following protocols B, C and D (respective IDR: 1.2, 0.875 and 1.4 gI/s) were significantly higher than those for patients following protocol A (IDR: 0.7 gI/s) (all P<0.05). For patients with BMIs between 25 and 28 kg/m^2, there was no significant difference in the quantitative IQ between protocols B and D (P>0.05). *Conclusions:* A 70 kV high-pitch scan in DSCT resulting in an IDR of 0.875 gI/s is feasible for patients with BMIs≤25 kg/m^2 when the CM protocol of 25 ml&2.5 ml/s (350 mgI/ml) is used; for patients with BMIs between 25 and 28 kg/m^2, the CM protocol of 40 ml&4.0 ml/s (300 mgI/ml) can be used to obtain an IDR of 1.2 gI/s.

Keywords: Coronary CT angiography (CCTA), ultra-low tube voltage, high-pitch spiral scan, ultra-low contrast media protocol, low radiation dose, Iodine delivery rate (IDR)

Introduction

Coronary artery CT angiography (CCTA) is becoming one of the most commonly used methods for screening coronary artery disease (CAD) in clinical practice [1]. Nevertheless, radiation-induced carcinogenesis and contrast-induced nephropathy, which can be caused by the CCTA examinations, remain the two main potential risks concerned by clinicians and radiologists [2].

During the past decade, CCTA data acquisition strategies and techniques for reducing the effective radiation dose (ED) have continually evolved [3, 4]. Among those ED reduction measures, lowering the tube voltage is a popular and useful technique because the radiation dose is proportional to the square of the tube voltage [5]. This is especially true for tube volt-

ages near 70 kV, which are closer to the k-absorption edge of iodine (33.2 keV) in a polychromatic X-ray beam and could increase the photoelectric effects and contrast enhancement [5, 6]. For this reason, the amount of contrast media (CM) needs to be reduced to maintain a reasonable range of attenuation enhancement and image quality (IQ) [7]. Some studies on "double-low" scanning techniques (i.e., lower radiation dose with smaller amounts of CM) have recently been conducted [2, 8-12]. However, optimized low contrast protocols with ultra-low tube voltages (70 kV) in non-obese patients have not been published.

The purpose of our study was to investigate the feasibility of ultra-low CM protocols (Iodine delivery rate [IDR]: contrast volume [CV], injection flow rate [IFR] and iodine concentration [IC]) at 70 kV using prospective high-pitch CCTA
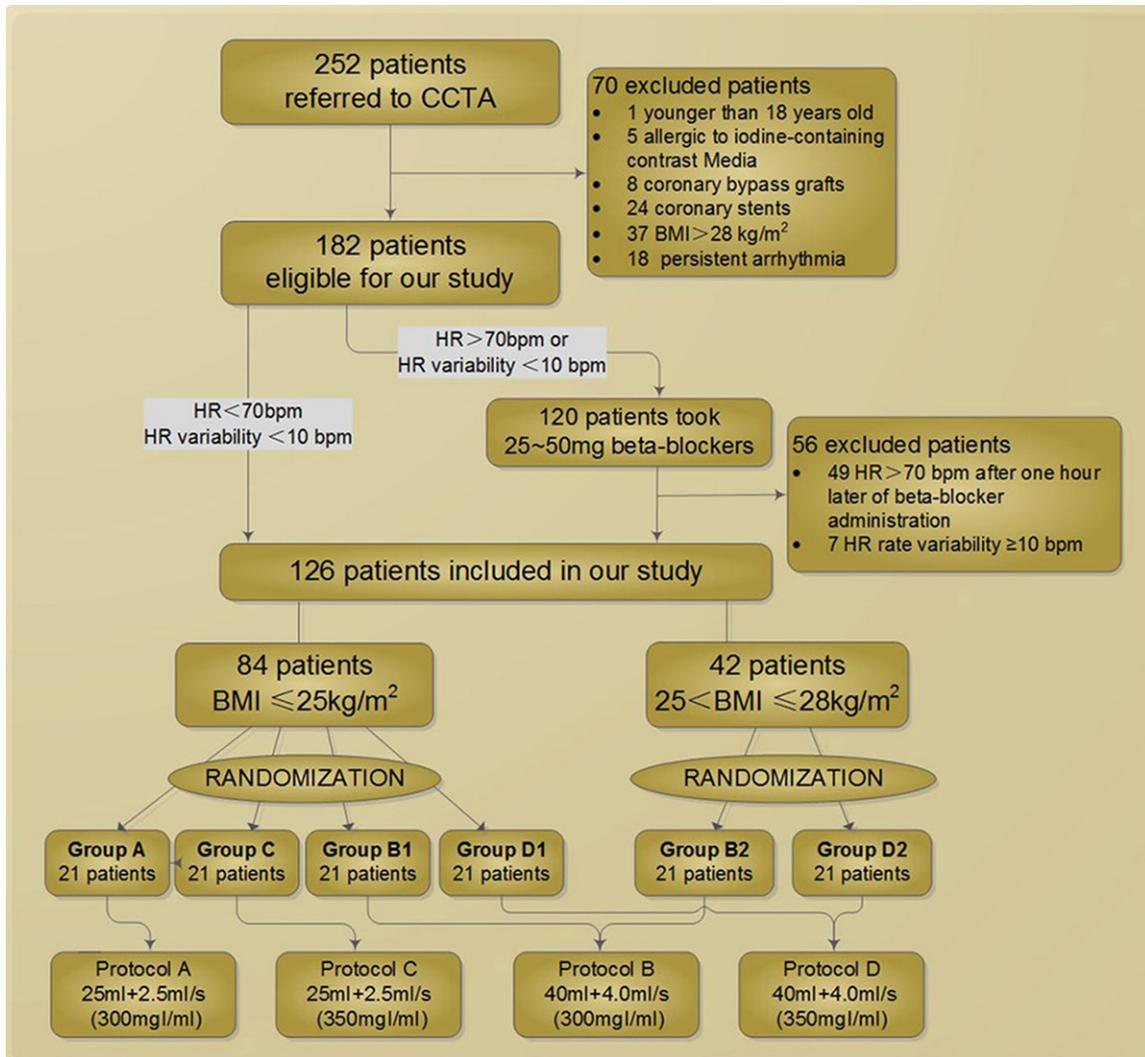
Figure 1. Flowchart of patient inclusion and study design. *CCTA*, coronary CT angiography; *BMI*, Body Mass Index; *bpm*, beats per minute.

in patients with body mass indexes (BMIs)≤28 kg/m². kg/m^2.

Materials and methods

This study was approved by the local institutional review board, and written informed consent forms were obtained from all patients who underwent CCTA before each examination.

Patient population

Two hundred fifty-two consecutive patients with suspected or known CAD in our hospital were referred for CCTA examination from May 2015 to July 2015. Following the inclusion and exclusion criteria (**Figure 1**), a total of 126 eligible patients (66 males; mean age, 57.4±9.3 years;

84 with BMIs≤25 kg/m²) were enrolled in this study.

CT scan and contrast injection protocols

Patients with BMI≤25 kg/m² were randomly assigned to four groups with each group using a different injection protocol (CV, IFR and IC) as A, B, C and D, respectively. Patients with BMIs between 25-28 kg/m² were randomly divided into two groups that used injection protocols B and D. The detailed protocols and group assignments were based on the different combinations of IC (high [350 mgI/ml] and low [300 mgI/ml]) and CV&IFR (high [40 ml&4.0 ml/s] and low [25 ml&2.5 ml/s]), which are illustrated in **Table 1**.

Table 1. Contrast media protocol and group assignments

Protocol	Group	Patient (N)	BMI (kg/m^2)	IDR (gl/s)	IC (mgl/ml)	CV (ml)	IFR (ml/s)
A	A	21	BMI≤25	0.7	300 (Low)	25	2.5 (low)
B	B1			1.2		40	4.0 (High)
	B2		25<BMI≤28				
C	C	21	BMI≤25	0.875	350 (High)	25	2.5 (low)
D	D1			1.4		40	4.0 (High)
	D2		25<BMI≤28				

N, Number; *BMI*, Body Mass Index; *IDR*, Iodine Delivery Rate; *IC*, Iodine Concentration; *CV*, Contrast Volume; *IFR*, Injection Flow Rate.

Table 2. Four-point grading scale for qualitative image quality score

Score	Vessel Opacification	Motion Artefacts	Noise-related Blurring	Structural Discontinuity
1	Excellent	No	No	No
2	Good	Minor	Minor	No
3	Fair	Some	Some	Minimal
4	Poor	Severe	Severe	Severe

The CM was delivered through a 20-gauge catheter inserted into an ante-cubital vein by a dual-syringe power injector (DUAL SHOT GX. Nemoto-Kyorindo, Tokyo, Japan). The baseline demographics (i.e., age, sex, risk factors, etc.) for each patient were recorded.

All patients underwent prospective high-pitch spiral CCTA on a dual-source CT (DSCT) equipment with an integrated circuit detector (Somatom Definition Flash; Siemens Healthcare) with a tube voltage of 70 kV and automatic tube current modulation (CARE Dose 4D, Siemens Healthcare, reference mAs: 370 mAs). Patients with baseline HRs>70 bpm were orally administered 25~50 mg beta-blockers (Metoprolol; Betaloc; AstraZeneca, Cambridge, United Kingdom) one hour before the scan. All patients received sublingual nitroglycerin aerosol (Jewim Pharma, Shandong, China) (0.5-1.0 mg) three minutes prior to the scan to dilate the coronary arteries. The scanning range included the entire heart, from 1 cm below the carina to the diaphragm and was initiated by a bolus-tracking technique using a region-of-interest (ROI) in the root of the ascending aorta (attenuation threshold 100HU). The scan started automatically with a delay time of 5 seconds, and all injections were followed by a 40-ml saline flush at a flow rate of 4.0 ml/s.

Date acquisition and reconstruction

The data acquisition window was automatically adapted to the HRs at ≤70 bpm, and the centre of the data acquisition window was set at 70% of the R-R interval.

All images were reconstructed using both the Filtered Back Projection algorithm (smooth convolution kernel B26f) and the Sinogram AFfirmed Iterative RE construction (SAFIRE, Siemens Healthcare) algorithm (smooth convolution kernel I26f) with a 0.75-mm slice thickness and a 0.5-mm slice increment. Strength-level 3 was used. The reconstructed image data were transferred to a dedicated workstation (Syngo MMWP, Siemens Healthcare). Multiplanar reformation, maximum intensity projection, volume rendering , and curved planar reformats were used for image interpretation.

Assessment of IQ

Quantitative IQ assessment: The mean attenuation value and noise in the aortic root, proximal, middle and distal segment of the three main coronary arteries (left anterior descending artery [LAD], left circumflex [LCX] and right coronary artery [RCA]) and the adjacent connective tissue components were measured. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of each part were calculated. The circular ROI should be as large as possible but with care taken to avoid the tube wall and calcification. The calculation formula for SNR and CNR was as follows:

$$SNR = CT_{aortic}/Noise_{aortic}$$

$$CNR\ lumen = (CT_{lumen} - CT_{tissue})/Noise_{tissue}$$

Table 3. Comparison of characteristics and parameters among all the groups

Parameter	BMI≤25 kg/m²					25<BMI≤28 kg/m²		
	Group A (n=21)	Group B1 (n=21)	Group C (n=21)	Group D1 (n=21)	P value	GroupB2 (n=21)	Group D2 (n=21)	P value
B Baseline data								
Age (y)	58.50±9.10	61.85±9.64	56.50±8.83	55.75±9.90	0.170	56.48±9.08	55.33±9.11	0.686
Sex								
M (%)	14 (63.6)	10 (50.0)	8 (36.4)	10 (50.0)	0.351	12 (57.1)	13 (61.9)	0.753
F (%)	8 (36.4)	10 (50.0)	14 (63.6)	10 (50.0)	0.351	9 (42.9)	8 (38.1)	0.751
BMI (kg/m²)	22.20±1.65	23.74±1.37	22.73±1.85	23.15±2.15	0.054	27.02±0.85	26.66±0.85	0.180
Height (cm)	166.82±7.28	166.25±6.28	164.66±6.05	165.60±8.06	0.718	168.90±8.98	167.38±7.52	0.554
Weight (kg)	61.68±6.72	65.75±6.61	61.70±6.84	63.93±10.41	0.310	77.33±8.91	74.81±7.15	0.318
HR (bpm)	57.59±5.90	57.40±6.49	56.64±6.94	55.35±5.08	0.559	57.52±5.58	54.90±4.75	0.109
HR variability	3.41±1.59	3.20±1.28	4.18±2.75	3.15±1.66	0.282	4.14±3.51	3.43±1.81	0.412
Clinical Symptoms (%)	19 (86.4)	19 (86.4)	19 (86.4)	19 (86.4)	0.612	15 (71.4)	16 (72.7)	0.733
Risk Factors								
Hypertension	10 (45.5)	16 (80.0)	7 (31.8)	11 (55.0)	0.050	12 (57.1)	15 (71.4)	0.334
Hyperlipidemia	11 (50.0)	9 (45.0)	9 (40.9)	8 (40.0)	0.909	12 (57.1)	4 (19.0)	0.204
Smoking	7 (31.8)	10 (50.0)	9 (40.9)	5 (25.0)	0.379	8 (38.1)	11 (55.0)	0.352
Diabetes mellitus	11 (50.0)	10 (50.0)	3 (13.6)	1 (5.0)	0.377	5 (23.8)	1 (4.8)	0.707
Scan length	143.11±8.54	164.60±63.07	144.14±9.72	144.00±10.62	0.097	143.07±19.55	141.43±6.17	0.705
Scan Parameter								
Tube voltage (KV)	70	70	70	70	-	70	70	-
Effective tube current (mAs)	251.73±28.15	266.00±20.47	263.05±19.13	261.05±26.85	0.224	278.62±5.77	278.10±5.97	0.774
CTDI vol (mGy)	0.72±0.08	0.76±0.06	0.76±0.05	0.75±0.08	0.231	0.80±0.02	0.80±0.02	0.856
SSDE-CTDI vol (mGy)	1.04±0.01	1.05±0.07	1.08±0.08	1.05±0.08	0.469	1.03±0.05	1.05±0.04	0.100
DLP (mGy*cm)	14.72±1.38	15.50±1.23	15.47±0.99	15.35±1.69	0.195	16.03±0.44	16.17±0.55	0.391
ED (mSv)	0.21±0.02	0.22±0.02	0.22±0.01	0.22±0.02	0.238	0.22±0.01	0.23±0.01	0.432

BMI Body mass index, HR Heart rate, CAD coronary artery disease, CTDI vol CT dose index volume, SSDE-CTDI vol Size Specified Dose Estimates of CTDI vol, DLP dose-length product, ED effective dose.

Qualitative IQ assessment: Based on a modified 18-segment classification system of the coronary artery proposed by the Guidelines of the Society of Cardiovascular Computed Tomography Committee [13], the IQ for each coronary artery segment was evaluated using a Likert four-point grading scale [14], which detailed description on **Table 2**. Segments with scores of 1~3 were diagnostic. Two experienced radiologists who were blinded to each other's results independently evaluated the images. Disagreements in segments analysis between the two observers were resolved by consensus reading.

Estimation of effective dose and IDR

The CT dose index volume (CTDI vol) and the dose-length product (DLP) were recorded. The lateral width (LAT) and antero-posterior (AP) distance of the thorax for each patient were measured for the body effective diameter (= $\sqrt{LAT \times AP}$) to calculate the Size-Specific Dose Estimate of the CTDI vol (SSDE-CTDI vol) [15]. The effective radiation dose (ED, mSv) was cal-culated: ED=DLP×k [k adult =0.014 mSv/(mGy×cm)] [16].

The Iodine delivery rate (IDR; gI/s) for each protocol was calculated according to the following formula: IDR=CM iodine concentration (mgI/ml)×CM injection flow rate (ml/s) [17, 18].

Statistical analysis

Statistical analysis was performed using statistical software (SPSS 18.0; SPSS Inc., Chicago, IL). All of the continuous variables were expressed as mean ± SD, the categorical variables were reported as frequencies or percentages. Independent Student's t-test and Chi-square test were used for results comparison among all groups. Inter-observer agreement in qualitative IQ grading was assessed using the Kappa statistics (the kappa value of >0.81, 0.61-0.80, 0.41-0.60 and <0.20 were considered excellent, good, moderate and poor, respectively). The significance level set at $P<0.05$.
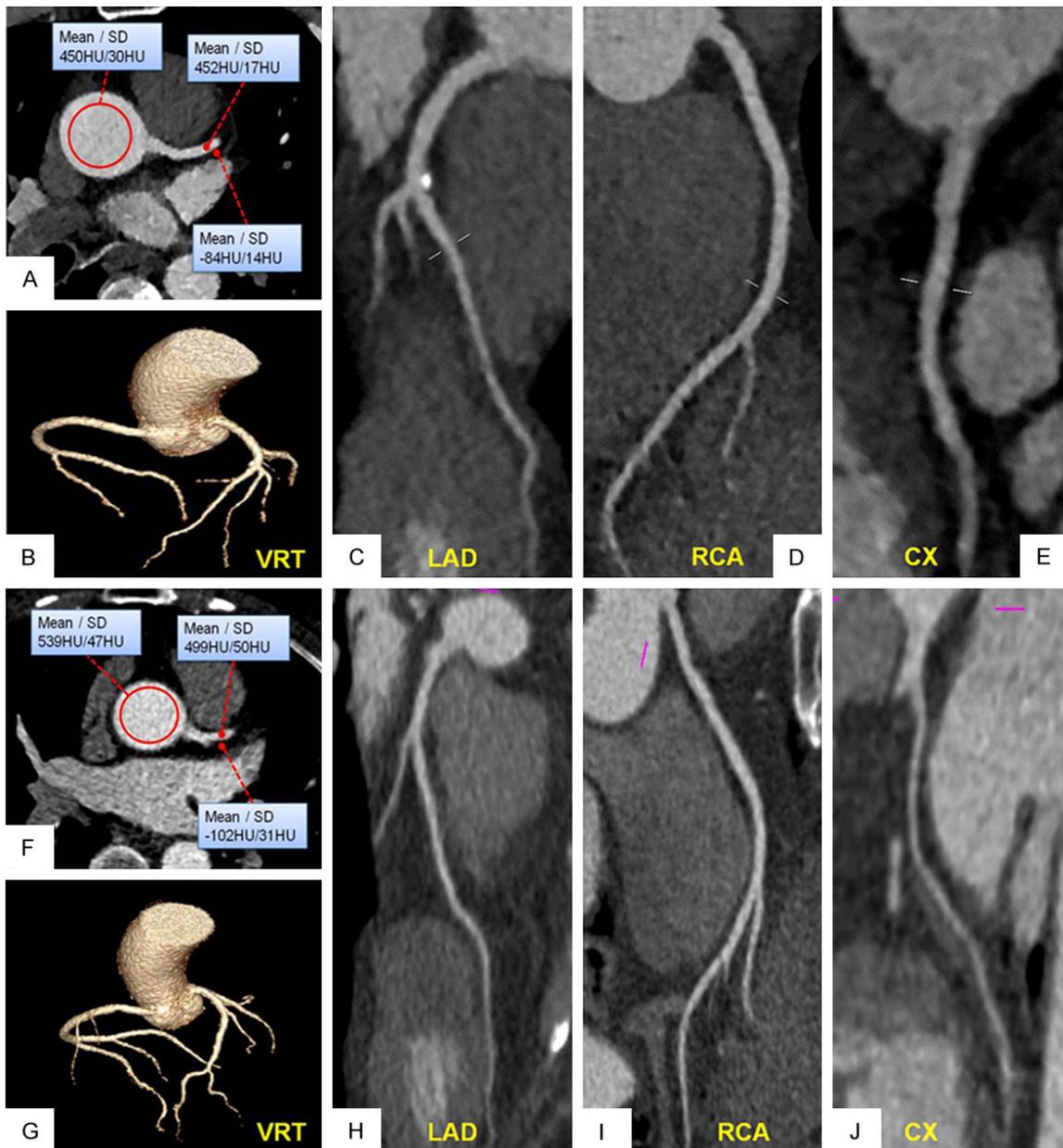
Figure 2. Comparison of case 1 from Protocol A with the SAFIRE algorithm and case 2 from Protocol D (Group D1) with the FBP algorithm.

Results

Patient demographics

All of the enrolled patients successfully underwent CCTA with no complications. The statistical analysis showed that there were no significant differences among the patients regarding baseline characteristics (age, gender distribution, height, weight, BMI, etc.) (all $P>0.05$). **Table 3** summarizes the detailed patient characteristics parameters.

IQ assessment

In each group, with the same level of CT mean attenuation, SNR and all the CNR values from the SAFIRE reconstruction were significantly higher than those from Filtered back projection (FBP) ($P<0.05$).

We compared Group A (CM protocol A: low IC [300 mgI/ml] with low CV&IFR [25 ml&2.5 ml/s]) under the SAFIRE algorithm and Group D1 (CM protocol D: high IC [350 mgI/ml] with
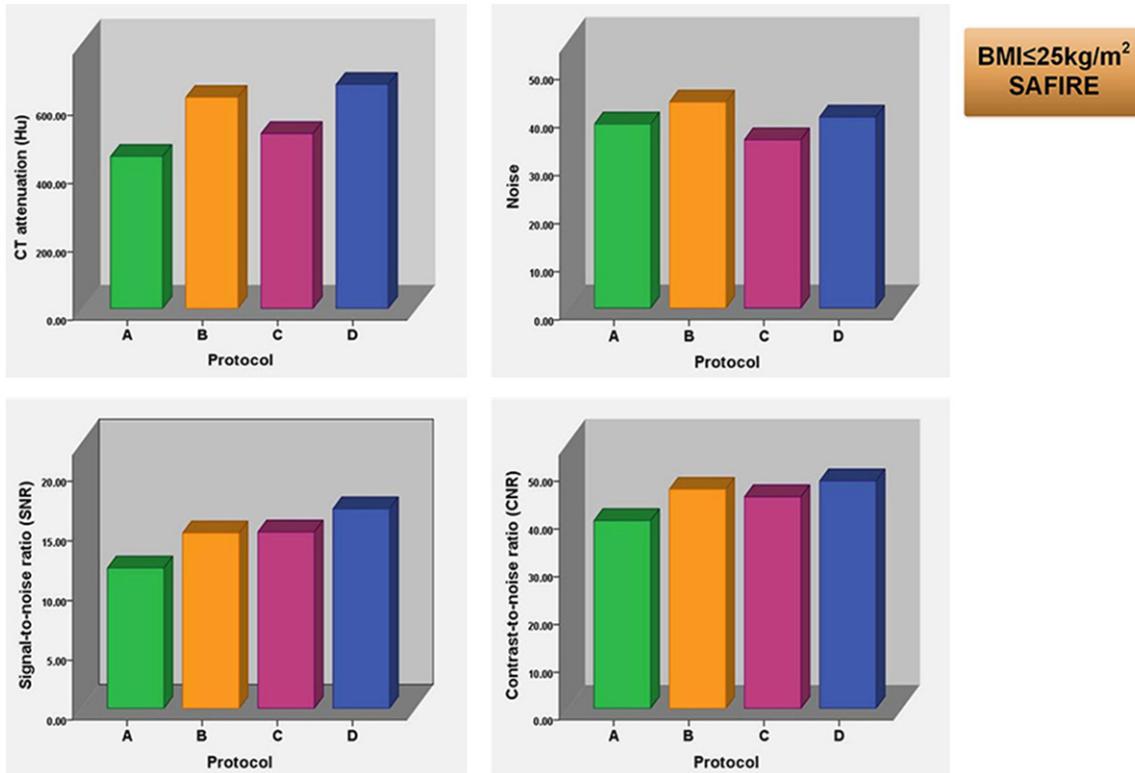
Figure 3. Comparison of quantitative IQ among the four protocols (A-D) of patients with normal BMI (BMI≤25 kg/m^2) under the SAFIRE algorithm. The CT attenuation of the aortic root in Protocols B and D was higher than that in Protocols A and C (all *P*<0.05). The noise in the aortic root in Protocols C and D was slightly lower than that in Protocols A and B (both *P*<0.05). The Signal-to-noise ratio (SNR) and Contrast-to-noise ratio (CNR) in the proximal segment of the left anterior descending (LAD) artery from Protocol A were slightly lower than those in Protocols B and D (all *P*<0.05); however, no significant differences were found among Protocols B-D (all *P*>0.05). *BMI*, Body Mass Index; *SAFIRE*, Sinogram affirmed iterative reconstruction, *FBP*, Filtered back projection, two iterative reconstruction products of Siemens Healthcare.

high CV&IFR [40 ml&4.0 ml/s]) under the FBP algorithm, and found that the former IQ was much better than the latter (*P*<0.05) (**Figure 2**).

For patients with BMI≤25 kg/m^2, the quantitative IQ in both Protocols B (low IC [300 mgI/ml] with a high CV&IFR [40 ml&4.0 ml/s]) and C (high IC [350 mgI/ml] with low CV&IFR [25 ml&2.5 ml/s]) were significantly higher than that in Protocol A (both *P*<0.05), especially for the mid- and distal segments (*P*<0.001). However, no significant difference was found in the quantitative IQ scores among Protocols B, C, and D (all *P*>0.05), except that the mean CT attenuation was higher in Protocols B and D than in Protocol C in all vessel locations of interest (**Figure 3**).

For patients with BMIs between 25-28 kg/m^2, there were no significant differences in quantitative IQ between Protocols B and D (*P*>0.05) (**Figures 4**, **5**).

Overall, 126 patients with 1872 coronary artery segments were available for qualitative IQ evaluation. **Table 4** shows the results of the IQ scores (1-4) and the coronary artery diagnostic segments. No significant difference was found regarding the percentage of diagnostic segments among all of the groups (χ^2=2.23, *P*>0.05). Among all of these patients, 11 patients (8.7%) from the SAFIRE reconstruction and 14 patients (11.1%) from the FBP groups had non-diagnostic segments. The segments with non-diagnostic IQ scores were located on the RCA (n=15) and LCX (n=9), which resulted from the coronary motion artefacts. The inter-observer agreement values for the MPR images, MIP images, CPR images and VR images were good (kappa=0.71, 0.78, 0.69, and 0.80, respectively).

Radiation dose estimation and protocols' IDR

The average DLP, CTDI vol, SSDE-CTDI vol and ED analyses revealed no statistically significant
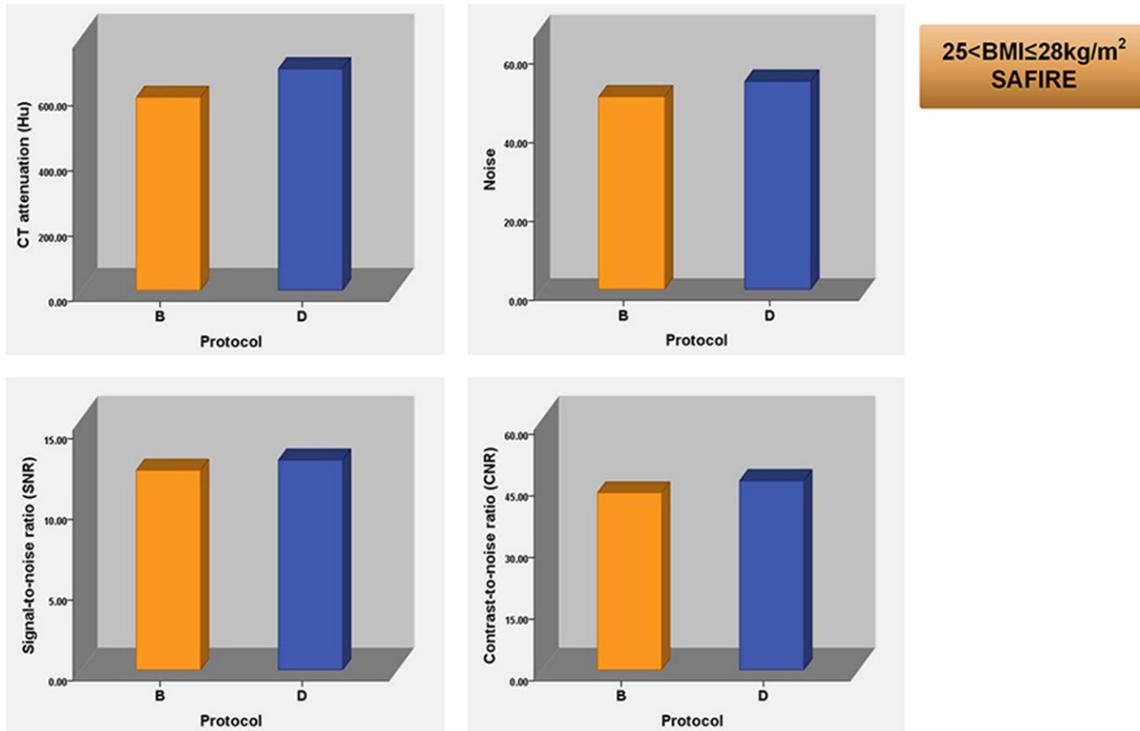
Figure 4. Comparison of quantitative IQ between the two protocols (B and D) of patients with BMIs between 25 and 28 kg/m^2 under the SAFIRE algorithm. No significant differences were found between Protocols B and D in CT attenuation of the aortic root, noise in the aortic root, Signal-to-noise ratio (SNR) or Contrast-to-noise ratio (CNR) in the proximal segment of the left anterior descending (LAD) artery (all *P*>0.05). *BMI*, Body Mass Index; *SAFIRE*, Sinogram affirmed iterative reconstruction, an iterative reconstruction product of Siemens Healthcare.

differences among the four protocols (*P*>0.05). The dosimetric parameters are shown in **Table 3** where the mean DLP, CTDI vol, SSDE-CTDI vol, and ED for the study population were 15.54±1.04, 0.76±0.05, 1.05±0.05, and 0.22±0.01 mSv, respectively.

The IDRs for Protocols A, B, C and D were 0.7, 1.2, 0.875 and 1.4 gI/s, respectively.

Discussion

In this pilot study, we showed that high-pitch CCTA on DSCT at an ultra-low tube voltage (70 kV) can lead to substantial reductions in CM-IC, CV and IFR in overweight patients (BMIs between 25-28 kg/m^2) without compromising the IQ. For normal BMI patients (BMI≤25 kg/m^2), the CM usage can be even lower.

With the booming development of CT technology and its excellent sensitivity and negative predictive value, CCTA is already the technology of choice for screening and diagnosing CAD in clinical practice [1]. However, the accompany-

ing ED and difficult-to-avoid usage of CM, are still the two main concerns for clinicians and radiologists in its application [2].

The America Heart Disease Committee considers a CT examination with an effective dose of 10 mSv as associated with an increase in the possibility of fatal cancer to approximately 1 in 2000 [19]. Many approaches have been considered to reduce the ED. It is well understood that reducing the tube voltage to 70 kV is the most effective method because the ED is proportional to the square of the tube voltage. Additionally, this voltage is much closer to the k-absorption edge of iodine (33.2 keV) in a polychromatic X-ray beam than the previously used 80 and 100 kV voltages, which will result in increased photoelectric effects and increased contrast enhancement [5, 6]. Thus, it seems reasonable to decrease the ED and CM load at the same time. In this study, we have successfully achieved a mean ED for all the patients as low as 0.22±0.01 mSv, which is nearly comparable to the dose of two chest X-rays.
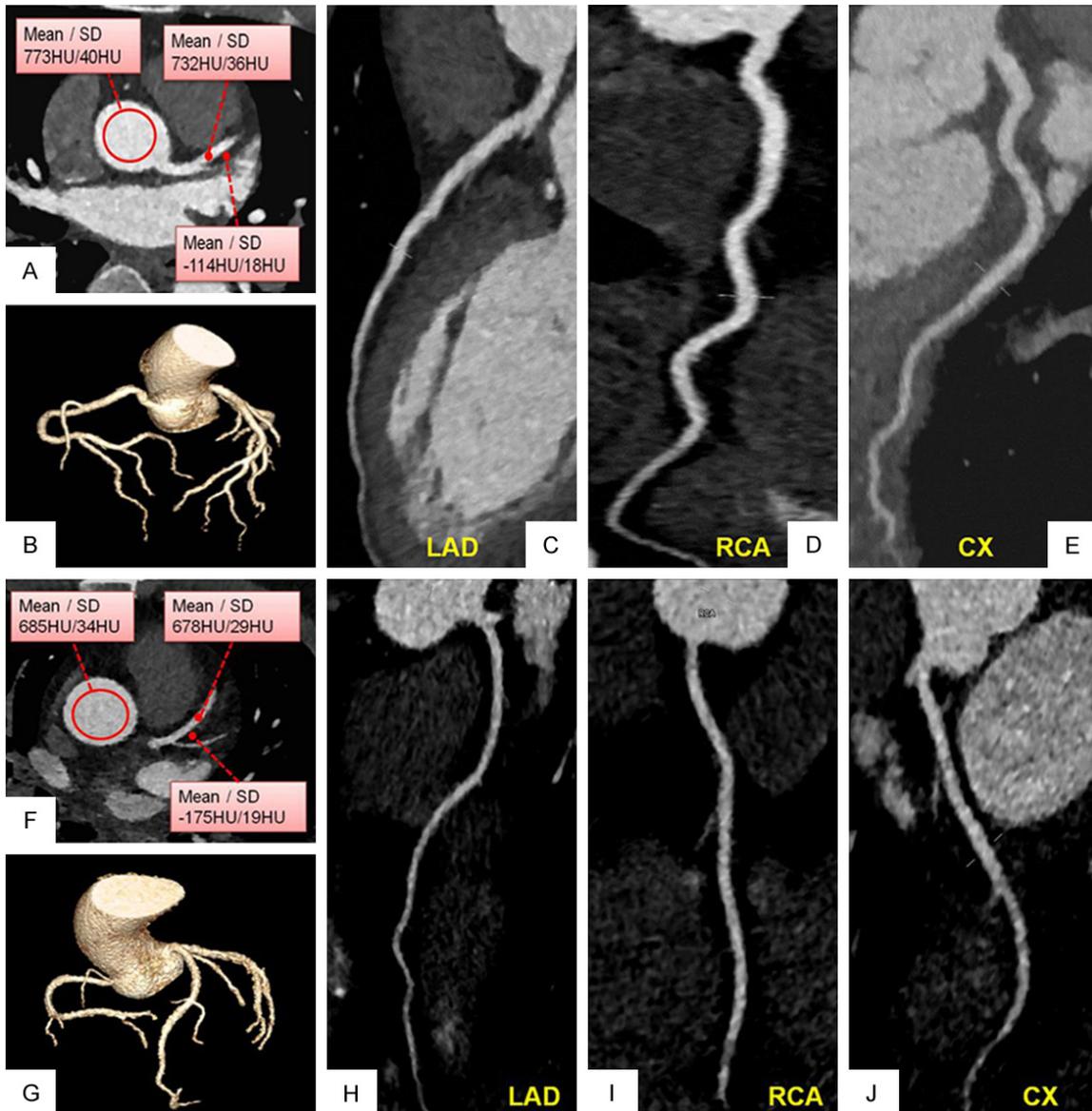
Figure 5. Comparison of case 3 from Protocol B (Group B2) with the SAFIRE algorithm and case 4 from Protocol D (Group D2) with the SAFIRE algorithm.

In addition to the tube voltage, we employed the prospective Electrocardiogram-triggered high-pitch spiral scan modality on the second-generation DSCT, which uses an increased rotation rate to significantly reduce the scan time [20]. In this study, the average scan time for all of the patients was 0.46±0.05 s. As a result, we could finish the scan without asking the patients to hold their breaths. In this way, some patients who cannot hold their breath well during the examination can also be examined, which is beneficiary for elder patients or patients with cardiopulmonary insufficiency.

Furthermore, it has been reported that contrast-induced nephropathy was ranked as the third leading cause of hospital-acquired acute kidney injuries [6, 21]. Thus, lowering the iodine load for patients is of great practical importance, especially because chronic renal insufficiency and kidney disease are very common among patients with CAD. However, the traditional CM protocols in clinical practice around the world are still at relatively high levels; normally the CM volumes are 60-100 ml and the CM-IFR are 5-6 ml/s [14, 22]. Although several previous studies investigated the promising

Table 4. Image quality scores and assessable percentage

Group	Segments (n)	1 points n (%)		2 points n (%)		3 points n (%)		4 points n (%)		Assessable n (%)		Mean score	
		FBP	SAFIRE	FBP	SAFIRE	FBP	SAFIRE	FBP	SAFIRE	FBP	SAFIRE	FBP	SAFIRE
A	317	78 (24.6%)	119 (37.5%)	132 (41.6%)	135 (42.6%)	101 (31.9%)	59 (18.6%)	6 (1.9%)	4 (1.3%)	311 (98.1%)	313 (98.7%)	2.11±0.79	1.83±0.77
B1	308	83 (26.9%)	101 (32.8%)	142 (46.1%)	158 (51.3%)	77 (25.0%)	44 (14.3%)	6 (2.0%)	5 (1.6%)	302 (98.0%)	303 (98.4%)	2.01±0.77	1.85±0.72
B2	311	92 (29.6%)	123 (39.5%)	147 (47.3%)	152 (48.9%)	66 (21.2%)	33 (10.6%)	6 (1.9%)	3 (1.0%)	305 (98.1%)	308 (99.0%)	1.95±0.76	1.73±0.68
C	320	85 (26.6%)	123 (38.4%)	151 (47.2%)	149 (46.6%)	81 (25.3%)	46 (14.4%)	3 (0.9%)	2 (0.6%)	317 (99.1%)	318 (99.4%)	2.01±0.75	1.77±0.71
D1	316	73 (23.1%)	99 (31.3%)	141 (44.6%)	147 (46.5%)	96 (30.4%)	66 (20.9%)	6 (1.9%)	4 (1.3%)	310 (98.1%)	312 (98.7%)	2.11±0.77	1.92±0.75
D2	312	71 (22.8%)	105 (33.7%)	143 (45.8%)	122 (39.1%)	93 (29.8%)	81 (25.9%)	5 (1.6%)	4 (1.3%)	307 (98.4%)	308 (98.7%)	2.10±0.76	1.94±0.80

FBP Filtered back projection, SAFIRE Sinogram affirmed iterative reconstruction, an iterative reconstruction product of Siemens Healthcare, The value is showed as the number of segments (%).

"double-low" technique, most of them limited the CM volume to 40-60 ml with a tube voltage of 80 kV or even higher [2, 8-12]. Recently, Zhang LJ et al. [23] performed CCTA with a 30-ml CM volume at 70 kV in patients with BMIs<25 kg/m^2. However, none of above studies attempted ultra-low CM protocols-ultra-low IC, low CV&IFR combined with ultra-low tube voltage (70 kV) in relatively bigger patients (BMIs between 25-28 kg/m^2) to investigate the optimal scan protocol and CM injection protocol of CCTA with diagnostic IQ. Compared with previous studies, we reduced the CM volume to 25 ml, which was almost reduced by 60% in contrast with 60 ml, or by 75% in contrast with the traditional clinical practice level (100 ml). Furthermore, we lowered the IC to 300 mgI/ml and 350 mgI/ml, consequently reducing the iodine burden by more than 60% compared with 370 mgI/ml (60 ml), which is the most commonly used concentration in present clinical application. Last but not least, the CM-IFR was thereupon slowed to 2.5 ml/s, which allowed small needles to be used, especially on patients suffering from immune, systemic or chronic diseases and having really weak vessel conditions. In addition, slowing down the CM-IFR is one of the most important methods in relieving patient discomfort and feverish feelings.

Even though we reduced the iodine load to a low level, the mean CT attenuation in the root of the ascending aorta and coronary artery segments were still as high as 400-500HU, which was sufficient for obtaining diagnostic quality images. Previous studies confirmed that the optimal CT attenuation for coronary artery stenosis detection on CCTA is approximately 350HU [24]. In general, a high intra-lumenal CT value of more than 250HU is recommended for satisfactory images [12]. We have found that all groups have shown great diagnostic qualities in qualitative IQ assessment. Even the IQ of protocol A, which showed a significant difference when compared with other groups in the CNR and SNR, can still meet the clinical diagnostic requirements for subjective and objective assessments. The percentage of diagnostic segments of all segments was 98.65%, and the mean value was more than 98% in each group.

As a result of using the 70 kV voltage, the image noise may increase and result in IQ impairment. When analysed with the SAFIRE algorithm, which has been demonstrated to decrease the image noise effectively [25], the CNR and SNR can be mostly maintained.

Thus, the SAFIRE algorithm can greatly compensate for the ultra-low iodine load because the quantitative IQ results in protocol A (low IC, CV and IFR) with the SAFIRE algorithm were significantly higher than those obtained in protocol D (high IC, CV and IFR) [26].

As shown in these results, for normal BMI (BMI≤25 kg/m^2) patients, protocols B (low IC with high CV&IFR), C (high IC with low CV&IFR) and D were all feasible, and protocol C (25 ml&2.5 ml/s with 350 mgI/ml IC) was the most advantageous due to its lowest CM iodine load. Similarly, for overweight (BMIs between 25-28 kg/m^2) patients, both protocols B and D were feasible, whereas protocol B (40 ml&4.0 ml/s with 300 mgI/ml IC) was more practical for its lower iodine load.

Recently, multiple studies [17, 18, 27, 28] have shown that IDR is the most important factor for achieving diagnostic intra-vascular CT attenuation of the coronary artery. Because the CM protocols and CM-IC usages differ significantly among global medical centres, IDR can be used to popularize the reduction of CM dose and the design of individualized protocols. In our study, the results confirmed the decisive impacts of IDR in different ultra-low CM protocols. For patients with normal BMIs (BMI≤25 kg/m^2), although the qualitative IQ assessment results showed no significant difference among all patients, the quantitative IQ results in Protocol A (IDR: 0.7 gI/s) were much lower than those in all other protocols. However, Protocol C (IDR: 0.875 gI/s) showed no significant difference when compared with Protocols B (IDR: 1.2 gI/s) and D (IDR: 1.4 gI/s) for IQ. A potential feasible lower bound of IDR for normal BMI patients has been proposed between 0.7-0.875 gI/s. For overweight patients (BMIs between 25-28 kg/m^2), the two protocols (B and D) both fulfilled diagnostic requirements, which demonstrated that an IDR of 1.2 gI/s is adequate. Further studies can be conducted to explore a more precise IDR lower bound.

All the patients' non-diagnostic segments were found located on RCA and LCX due to the coronary motion artefacts. This can be explained by the increased susceptibility of RCA and LCX to

motion artefacts compared with the LAD because the former segments have a larger excursion and faster movements [29]. Another potential reason for this observation might be the relatively strict inclusion criteria of our study.

Several limitations of our study are worth consideration. First, because we focused on the IQ, the diagnostic accuracy was not evaluated by the gold standard of invasive coronary angiography. Second, the sample size of each group in this study was relatively small. Further studies with larger populations are necessary to confirm our findings, and further multi-centre studies will need to be arranged to invite more participants in the innovation of CM protocols in CCTA. Third, we did not evaluate the lumen and the plaque specifically, which will be investigated in follow-up studies. Fourth, we only designed four protocols to investigate the feasibility of ultra-low CM usage; a larger number of different protocols need to be tested to explore a more accurate lower bound of IDR under certain tube voltage and scan conditions. In addition, because of the limited technology, the inclusion criteria of this study were relatively confined. As the third Generation of DSCT comes into clinical application with improved techniques and fewer patient restrictions [6, 30], larger studies with more general patient cohorts are expected in the near future.

This study demonstrates that the ultra-low CM protocols in prospective 70 kV high-pitch CCTA were feasible for all non-obese patients, and the SAFIRE algorithm played a critical role in maintaining the IQ. For normal BMI patients (BMI≤25 kg/m^2), the CM protocol with a high IC (350 mgI/ml) and a low CV&IFR (25 ml&2.5 ml/s) (IDR: 0.875 gI/s) was feasible; for patients with BMIs between 25-28 kg/m^2, the CM protocol with a low IC (300 mgI/ml) and a high CV&IFR (40 ml&4.0 ml/s) (IDR: 1.2 gI/s) was practical.

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Disclosure of conflict of interest

None.

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