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Original Research Article

Effect of reduced x-ray tube voltage, low iodine concentration contrast medium, and sinogram-affirmed iterative reconstruction on image quality and radiation dose at coronary CT angiography: Results of the prospective multicenter REALISE trial

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ABSTRACT

Background: Both low tube voltage and sinogram-affirmed iterative reconstruction (IR) techniques hold promise to decrease radiation dose at coronary CT angiography (CCTA). The increased iodine contrast at low tube voltage allows for minimizing iodine load.
Objective: To assess the effect of reduced x-ray tube voltage, low iodine concentration contrast medium and IR on image quality and radiation dose at CCTA.
Methods: Two hundred thirty-one consecutive patients with suspected coronary artery disease were enrolled in this prospective, multicenter trial and randomized to 1 of 2

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dual-source CCTA protocols: 120-kVp with 370 mgI/mL iopromide or iopamidol (n = 116; 44 women; 55.3 ± 9.8 years) or 100 kVp with 270 mgI/mL iodixanol (n = 115; 48 women; 54.2 ± 10.4 years). Reconstruction was performed with filtered back projection and IR. Attenuation, image noise, signal-to-noise ratio, and contrast-to-noise ratio were measured and image quality scored. Size-specific dose estimates and effective doses were calculated.

Results: There were no significant differences in mean arterial attenuation (406.6 ± 76.7 vs 409.7 ± 65.2 Hounsfield units; P = .739), image noise (18.7 ± 3.8 vs 17.9 ± 3.4 Hounsfield units; P = .138), signal-to-noise ratio (22.5 ± 5.4 vs 23.7 ± 6.1; P = .126), contrast-to-noise ratio (17.5 ± 5.5 vs 18.3 ± 6.1; P = .286), or image quality scores (4.1 ± 0.9 vs 4.0 ± 0.9; $P > .05$) between 120-kVp filtered back projection–reconstructed and 100-kVp IR-reconstructed series. Mean iodine dose was 26.5% lower (18.3 ± 0.5 vs 24.9 ± 0.9 g; $P < .0001$), mean size-specific dose estimate was 35.1% lower (17.9 ± 6.6 vs 27.5 ± 8.2 mGy; $P < .0001$), and effective dose was 34.9% lower (2.3 ± 1.0 vs 3.5 ± 1.1 mSv; $P < .0001$) with the 100 kVp compared with the 120-kVp protocol, respectively.

Conclusion: Using low x-ray tube voltage and IR allows for decreasing the iodine load and effective radiation dose at CCTA while maintaining image quality.

1. Introduction

The use of ionizing radiation and the specter of contrast-induced nephropathy (CIN) are commonly cited as limitations of CT examinations in general and of coronary CT angiography (CCTA) in particular. According to more recent insights, the risk of CIN from intravenously injected contrast media is likely small[1] and may be nonexistent.[2–4] However, because of lingering uncertainties and because the notion of CIN is still very prevalent in clinical practice, there remains motivation to restrict contrast media requirements to the smallest diagnostically appropriate amount.[5,6] Similar considerations apply to radiation dose from medical imaging, and the "As Low As Reasonably Achievable" principle is a well-supported tenet to reduce radiation exposure across the population.

Both goals are aided by lower x-ray tube voltage settings, which increase the photon absorption of iodine.[7,8] At CT angiographic applications, this simple maneuver can dramatically increase contrast signal, thus effecting similar attenuation with lower contrast media requirements, while substantially reducing radiation. However, these advantages can be partially offset by the subsequent increase in image noise. Iterative reconstruction (IR) can counterbalance increases in image noise at low tube voltage compared with filtered back projection (FBP) and can reduce radiation dose requirements by 27% to 53% while preserving or enhancing diagnostic image quality at CCTA.[9–13] Earlier works have reported the potential of combining these quality and safety measures to lower contrast media requirements in CCTA,[14] head and neck angiography,[15] and hepatic CTA.[16] However, all positive CCTA patients underwent subsequent invasive coronary angiography (ICA) in this study. This has been insufficiently explored to date. Therefore, in this prospective multicenter study we aimed at evaluating the combined effect of reduced x-ray tube voltage, low iodine concentration contrast medium, and IR on image quality and radiation dose at CCTA.

2. Methods

The study was performed at 8 centers in China. Each center's institutional review board approved the study, and written informed consent was obtained from all participating subjects. Study monitoring, data management, and statistical analysis were performed by a steering committee, which also served as the core laboratory for image interpretation. The sample size was determined by power analysis based on a type 1 error rate $\alpha = 0.05$. On the basis of historical analysis, we assumed a baseline interpretability of 95%. Using these assumptions and considering a 5% dropout rate, this study required 98 patients in each group to detect a 9% difference in image quality with 80% power.

2.1. *Patient population*

Between June 2013 and October 2013, we approached 242 consecutive patients with suspected coronary artery disease (CAD) who were scheduled to undergo clinically indicated CCTA because of the symptom of chest pain or patients carrying ≥1 risk factors or electrocardiographic abnormalities. The serum creatinine level was obtained within 1 week before CCTA. Considered for inclusion were patients aged 30 to 80 years who were in stable baseline cardiac sinus rhythm. Exclusion criteria were serum creatinine level >120 μmol/L, prior reaction to iodinated contrast material, known or suspected pregnancy, history of prior revascularization, arrhythmia or heart rate >90 beats/minute after administration of beta-blockers, and New York Heart Association class III or IV heart failure. Eleven patients were deemed ineligible because of prior revascularization (n = 8) or a serum creatinine level >120 μmol/L (n = 3). Consequently, 231 eligible patients (139 male, 92 female; age range, 31–80 years; mean age, 54.8 ± 10.1 years) were enrolled (Fig. 1). If obtained for a clinical indication, serum creatinine levels on day 3 after the contrast-enhanced CT procedure were also recorded. In addition, patients were followed with phone interviews performed on

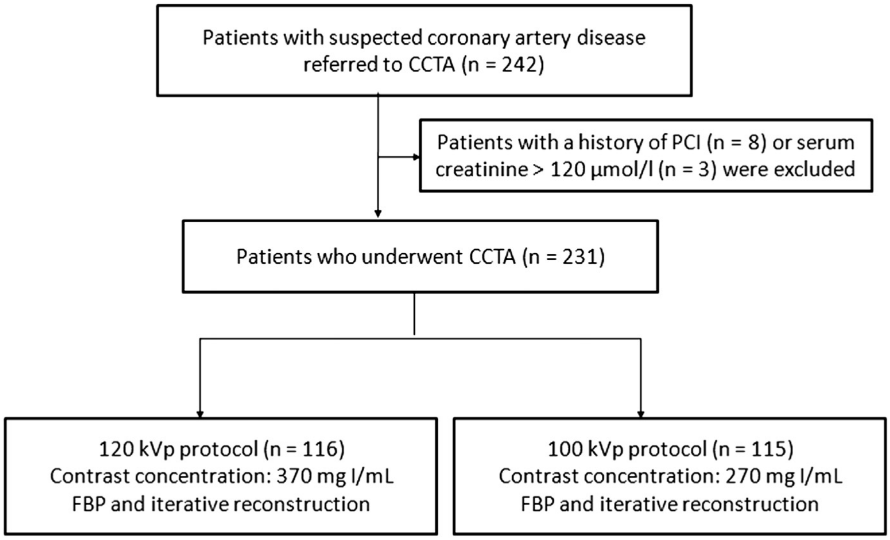

Fig. 1 – Study flowchart. Overall 242 consecutive symptomatic subjects were approached for participation and 231 patients were finally enrolled and underwent CCTA. Of these, 116 were randomly assigned to the 120-kVp with 370 mgI/mL iodine concentration agents protocol and 115 to the 100-kVp with 270 mgI/mL iodine concentration agents protocol. Reconstruction was performed with filtered back projection (FBP) and iterative reconstruction. CCTA, coronary CT angiography; PCI, percutaneous coronary intervention.

day 3 after the study to determine whether they experienced any adverse reactions from the contrast-enhanced CT procedure.

2.2. CT technique

Of the 231 patients, 116 were randomly assigned to the 120 kVp with 370 mgI/mL iopromide or iopamidol protocol and 115 to the 100 kVp with 270 mgI/mL iodixanol protocol. Randomization was performed electronically using third-party statistical software.

CT acquisition strategies were kept identical across the study arms and all participating centers. No nitroglycerines were administered as part of the study protocol. Beta-blockers (metoprolol; Betaloc; AstraZeneca, Cambridge, United Kingdom) were used in patients with a baseline heart rate >90 beats/min. This approach reflects our clinical practice, where we avoid administration of β-blockers below heart rates of 90 beats/min. Rather, we compensate for faster heart rates by adaptation of the acquisition method. All patients were examined with a second-generation dual-source CT system (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany). Scans were performed in a cranio-caudal direction in end inspiration. Noncontrast coronary calcium scoring (at 120 kV) was performed in all patients as the calcium scoring images can be used to adjust the scan length of CCTA acquisition[17] and may occasionally help clarify ambiguous findings at CCTA.[18] Per randomization, CCTA was then performed with a tube potential of either 120 or 100 kVp. Attenuation-based tube current modulation (CARE Dose4D; Siemens) was applied. All other scan parameters including the level of the reference tube current-time product were kept identical between the 120- and 100-kVp protocols. In patients with a heart rate <70 beats/min, we used a prospectively electrocardiogram-triggered sequential acquisition mode at 70% to 80% of the R-R interval (in diastole). With heart rates ≥70 beats/min, we used a prospectively electrocardiogram-triggered sequential acquisition mode at 35% to 45% of the R-R interval (in systole). For examinations at 120 kVp, vascular contrast attenuation was achieved by use of intravenous injection of 370 mgI/mL iodine concentration agents (iopromide; Ultravist 370; Bayer Healthcare, Berlin, Germany or iopamidol; Isovue 370; Bracco Diagnostics, Princeton, NJ, depending on center preference). All 100-kVp examinations were performed with a 270 mgI/mL concentration agent (iodixanol; Visipaque 270; GE Healthcare, Chalfont St. Giles, United Kingdom). All sites used a triple-phase contrast protocol: 50 to 60 mL of contrast agent, depending on scan duration, followed by 30 mL of a 30%:70% mixture of contrast medium and saline, and a 30 mL saline flush.[19] A total contrast volume of 60 to 70 mL was chosen because it reliably produces sufficient intra-arterial attenuation across various body sizes in clinical routine. Because patients with impaired renal function were not eligible for this study, strict minimization of contrast volume was not required in our study population. Flow rate was kept constant at 5 mL/s. Image acquisition was started using automated bolus tracking in the ascending aorta with a signal attenuation triggering threshold of 100 Hounsfield units (HUs) and a 6-second scan delay.

2.3. Image reconstruction

Reconstruction was performed with a section thickness of 0.75 mm and 0.5 mm increment. FBP with a vascular algorithm (B26f) and sinogram-affirmed IR (SAFIRE; Siemens) with a strength level of 3 were used, using the corresponding I26f algorithm.

2.4. Effective radiation dose estimates

Volume CT dose index ($CTDI_{vol}$) and dose-length product (DLP) were obtained from the patient protocol. Effective radiation dose equivalent in mSv was estimated by multiplying the DLP with a standard chest conversion factor of 0.014.[20] To more accurately estimate size-specific radiation dose, we measured patient dimensions by anteroposterior thickness and lateral width based on CT images. Effective diameter was defined as the square root of the anteroposterior thickness multiplied by the lateral width. The sum of anteroposterior thickness and lateral width determined the conversion factor f_{size}. Size-specific dose estimate was estimated by computing the volume CT dose index with the conversion factor of f_{size}.[21]

2.5. Image analysis

CT images were transferred to a diagnostic workstation (Centricity, GE Healthcare, Waukesha, WI). All measurements and calculations were performed by 1 observer (3 years of experience in cardiac CT) who was blinded to image acquisition parameters. Circular regions of interest were placed in the aortic root at the level of the left main coronary artery ostium (size 100 mm^2) as well as in the proximal segments of the left and right coronary arteries and the left lateral ventricular wall (size 1–4 mm^2). We measured the signal intensity (CT number in HU) and noise (HU standard deviation). All regions of interests were measured 3 times, and mean measurements were used for statistical analysis. The signal-to-noise ratio (SNR) was calculated as the mean HU divided by the mean image noise measured in the aorta. The contrast-to-noise ratio (CNR) was calculated by subtracting the mean HU in the left lateral ventricular wall from the mean HU within the lumen of the proximal coronary arteries and dividing this difference by the image noise measured in the aorta.[8]

Assessment of image quality and coronary artery stenosis was performed by 2 observers independently (3 years and 5 years of experience in cardiac CT, respectively) at standardized window settings (window level 300HU, width 800HU). A third observer (18 years of experience in cardiac CT) was consulted to resolve discrepancies. All readers were blinded to the image acquisition parameters. Subjective image quality was assessed on a per-segment level using the modified 18-segment classification system of the Society of Cardiovascular Computed Tomography.[22] The overall image quality was graded on a 5-point scoring system (1, nondiagnostic; 2, limited diagnostic value; 3, adequate [presence of artifacts not limiting detection of luminal stenosis]; 4, good; 5, excellent). Mean image quality scores $\geq$3 were deemed diagnostic. The presence of coronary artery luminal diameter stenosis $\geq$50% was considered diagnostic of obstructive CAD. The presence of $\geq$50% luminal stenosis was evaluated on a per-patient basis. For stenosis detection, the readers reviewed transverse sections as well as volume-rendered displays, maximum intensity projections, and curved multiplanar reformats.

2.6. Statistical analysis

All analyses were performed using SPSS, version 16.0 (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was performed to assess the normality of data distribution. The Levene test was used to assess the equality of variance. A 2-way analysis of variance was conducted to simultaneously examine the effect of reconstruction method and tube potential on image quality. For pairwise comparison, normally distributed variables were compared with an independent Student t test for unpaired samples and the paired t test for paired samples. The chi-square test was used for categorical variables (ie, sex, scan mode, incidence of CAD, and so forth). P values $<$.05 were considered statistically significant.

3. Results

3.1. Patient demographics and CT scanning parameters

All CCTA examinations were successfully completed without complications including CIN. No adverse events were reported in the 3-day follow-up telephone interviews. A total of 116 patients (44 women and 72 men; age range, 31–78 years) were assigned to the 120-kVp protocol group, and 115 patients (48 women and 67 men; age range, 33–80 years) were assigned to the 100-kVp protocol group. Comparison between the study groups revealed no significant differences in patients' age, sex distribution, height, weight, body mass index (BMI), effective chest diameter, heart rate, pre-CT serum creatinine level, calcium score, presence of CAD, or contrast volume (all $P > .05$). In the 120-kVp group, the prospectively electrocardiogram-triggered sequential acquisition protocol was performed in systole in 50 patients and in diastole in 66 patients. In the 100-kVp group, scan acquisition was performed in systole in 47 patients and in diastole in 68 patients. Patient characteristics, CT scanning, and contrast agent administration parameters are summarized in Table 1. For 76 patients in the 120-kVp group and 89 patients in the 100-kVp group, 3-day postexamination serum creatinine levels were available. Mean levels of post-CT serum creatinine were 74.1 $\pm$ 16.7 and 75.0 $\pm$ 18.7 μmol/L in the 120- and 100-kVp groups, respectively, with no significant change from baseline in either group (both $P > .05$).

3.2. Quantitative assessment of image quality

There was a significant interaction between the effects of reconstruction method and tube potential on noise, SNR, and CNR (all $P < .001$) but not subjective image quality scores. Simple main effects analysis showed that IR-reconstructed series had significantly higher SNR and CNR than FBP-reconstructed series and that SNR and CNR were significantly higher for the 120-kVp protocol compared to the 100-kVp protocol, whereas image noise were completely opposite (all $P < .001$; Table 2). The 120-kVp series reconstructed with IR provided the lowest image noise and highest SNR and CNR ($P < .05$), whereas 100-kVp series reconstructed with FBP showed the highest image noise and lowest SNR and CNR. There was no significant difference in mean CT number between the 120- and 100-kVp protocols. Image noise (18.7 $\pm$ 3.8 vs 17.9 $\pm$ 3.4 HU), SNR (22.5 $\pm$ 5.4 vs 23.7 $\pm$ 6.1), and CNR (17.5 $\pm$ 5.5 vs 18.3 $\pm$ 6.1) were not significantly different between the 120-kVp data sets reconstructed with FBP and

Table 1 – Patient demographics, acquisition parameters, and contrast media injection protocols.

Parameters	120 kVp (n = 116)	100 kVp (n = 115)	P values
Baseline characteristics			
Male-to-female ratio	72:44	67:48	.592
Age (y), mean ± SD	55.3 ± 9.8	54.2 ± 10.4	.390
Height (cm), mean ± SD	167.7 ± 7.4	166.0 ± 7.8	.099
Weight (kg), mean ± SD	70.3 ± 9.3	68.8 ± 9.7	.220
Body mass index (kg/m^2), mean ± SD	25.0 ± 2.7	24.9 ± 2.5	.767
Effective chest diameter (mm), mean ± SD	283.3 ± 22.0	281.7 ± 20.9	.575
Heart rate (beats/min), mean ± SD	68 ± 9	68 ± 11	.876
Baseline serum creatinine (μmol/L), mean ± SD	74.6 ± 18.7	76.4 ± 16.6	.433
Calcium score, mean ± SD	122.5 ± 315.6	145.4 ± 343.6	.598
Hypertension, n (%)	66 (56.9)	58 (50.4)	.357
Hyperlipidemia, n (%)	32 (27.6)	45 (39.1)	.070
Smoking, n (%)	35 (30.2)	30 (26.1)	.559
Diabetes mellitus, n (%)	17 (14.7)	14 (12.2)	.700
Angina pectoris, n (%)	7 (6.0)	10 (8.7)	.463
Family history of CAD, n (%)	41 (35.3)	35 (30.4)	.484
No. of patients with CAD, n (%)	27 (23.3)	19 (16.5)	.249
Scanning parameter			
Scan mode (systolic/diastolic)	50/66	47/68	.790
Contrast injection protocol			
Iodine concentration (mgI/mL)	370	270	NA
Contrast medium volume (mL), mean ± SD	67.4 ± 2.5	67.9 ± 2.0	.121

CAD, coronary artery disease; NA, not applicable; SD, standard deviation.

the 100-kVp series reconstructed with IR (all $P > .05$; Fig. 2). The mean CT number in studies of 5 obese patients (BMI, 30.1–31.1 kg/m^2) in the IR-reconstructed 100-kVp series was 379.4 ± 88.3 HU. Mean image noise in this group was 20.0 ± 2.6 HU, which was considered in the range of acceptable image quality. Mean SNR and CNR were 19.3 ± 5.1 and 15.1 ± 6.2, respectively.

To evaluate the robustness of image quality vis-a-vis body size, we divided the cohort into lower and higher BMI groups. Because the mean BMI in this study was 24.9 kg/m^2, we used this value as the cutoff threshold. As IR was superior to FBP reconstruction, we aimed to explore whether the 100-kVp images reconstructed with IR had image quality comparable to the standard protocol using 120-kVp acquisition and FBP reconstruction. This analysis revealed that there was no significant difference in mean CT number, image noise, SNR, and CNR between the 2 protocols in either group with lower (<24.9 kg/m^2; n = 119) and higher BMI (>24.9 kg/m^2; n = 112; Table 3).

3.3. Qualitative assessment of image quality

Assessment of ≥50% luminal stenosis on a per-patient level was completely consistent between the readers as the coronary artery calcium score was relatively low in this study. None of the examinations were deemed nondiagnostic. A total of 1740 and 1725 coronary artery segments were present in 120-kVp and 100-kVp series, respectively (mean: 15 segments per patient). Overall, image quality scores on per-segment level as determined by 3 readers were worse for the 100-kVp series reconstructed with FBP ($P < .05$) and similar for 120-kVp series reconstructed with FBP and the 120- and 100-kVp data sets reconstructed with IR ($P > .05$; Table 4). Of 1740 segments in 120-kVp series reconstructed with FBP and IR, 25 segments (1.4%) in 5 patients (4.3%) and 23 segments (1.3%) in 5 patients (4.3%) were deemed nondiagnostic (image quality score <2). Of 1725 segments in 100-kVp series reconstructed with FBP and IR, 49 segments (2.8%) in 8 patients (7.0%) and 26 segments (1.5%) in 5 patients (4.3%) were deemed nondiagnostic. Nondiagnostic image quality was most frequently observed in the 100-kVp series reconstructed with FBP than 120-kVp data sets and 100-kVp data sets reconstructed with IR ($P < .05$).

3.4. Findings at CCTA and ICA

Luminal stenosis ≥50% was detected by CCTA in 27, 26, 21, and 19 patients and in 47, 46, 39, and 32 vessels in the 120-kVp

Table 2 – Objective image quality parameters in the overall study cohort.

Parameter	120 kVp (n = 116)			100 kVp (n = 115)		
	FBP, mean ± SD	IR, mean ± SD	P value	FBP, mean ± SD	IR, mean ± SD	P value
CT number (HU)	406.6 ± 76.7	406.6 ± 76.5	.860	410.1 ± 66.2	409.7 ± 65.2	.616
Image noise	18.7 ± 3.8	13.7 ± 2.7	.000	20.3 ± 3.1	17.9 ± 3.4	<.001
Signal-to-noise ratio	22.5 ± 5.4	30.5 ± 7.4	.000	20.6 ± 4.2	23.7 ± 6.1	<.001
Contrast-to-noise ratio	17.5 ± 5.5	23.7 ± 7.5	.000	15.9 ± 4.4	18.3 ± 6.1	<.001

FBP, filtered back projection; HU, Hounsfield unit; IR, iterative reconstruction; SD, standard deviation.

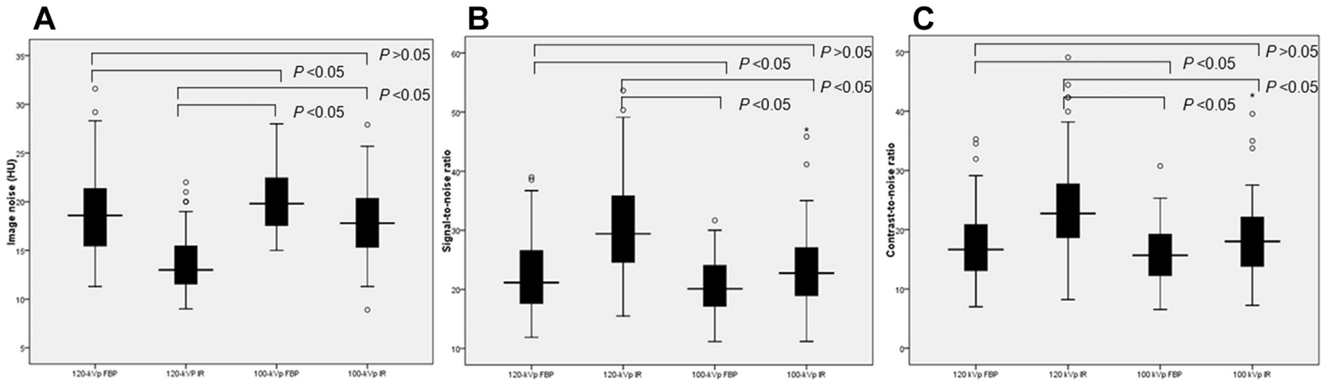

Fig. 2 – Comparison of objective image quality in the overall study cohort. Box plots demonstrate significant differences in image noise (A), signal-to-noise ratio (SNR; B), and contrast-to-noise ratio (CNR; C) (all $P < .05$) between the 120-kVp data sets reconstructed with filtered back projection (FBP) and the 100-kVp data sets reconstructed with FBP but no significant differences between the 120-kVp data sets reconstructed with FBP and the 100-kVp data sets reconstructed with iterative reconstruction (IR; $P > .05$). The 120-kVp series reconstructed with IR provided the lowest image noise and highest SNR and CNR ($P < .05$), whereas 100-kVp series reconstructed with FBP showed the highest image noise and lowest SNR and CNR. *indicates extreme values.

protocol with FBP, 120-kVp protocol with IR, 100-kVp protocol with FBP, and 100-kVp protocol with IR, respectively. Eighty-six coronary vessels in 48 patients showed ≥50% luminal stenosis in at least 1 reconstruction. These patients were referred for ICA, which confirmed ≥50% luminal stenosis in 45 patients and 79 coronary vessels (26 and 19 patients and 46 and 33 vessels in the 120-kVp and 100-kVp protocol, respectively; Figs. 3, 4). There was 1 false-positive patient in the 120-kVp protocol group, and there were 2 false-positives in the 100-kVp protocol group reconstructed with FBP. Of the 45 patients demonstrating ≥50% luminal stenosis at ICA, 9 had 3-vessel disease (including 2 with left main disease), 16 had 2-vessel disease (including 2 with left main disease), and 20 had single-vessel disease.

3.5. *Radiation dose and iodine load*

Table 5 lists radiation dose descriptors analyzed for 2 patient size categories. The decreases in size-specific dose estimates and DLPs were more pronounced in heavier patients than in leaner patients. Overall, mean DLP was 34.9% lower for the 100-kVp protocol compared to the 120-kVp protocol (163.7 ± 72.5 vs 251.7 ± 80.7 mGy·cm; $P < .001$), corresponding to a 34.9% reduction in estimated radiation dose for the 100-kVp protocol ($P < .001$; Fig. 5). Mean iodine dose was 26.5% lower for the 100-kVp compared to the 120-kVp protocol (18.3 ± 0.5 vs 24.9 ± 0.9 g; $P < .0001$; Fig. 5).

4. Discussion

This prospective, randomized, multicenter study demonstrates that radiation and contrast media requirements can be substantially reduced by the combined use of 100-kVp x-ray tube voltage and IR techniques. The combination of 100 kVp, lower contrast iodine concentration, and IR yielded comparable SNR, CNR, and image quality with a 26.5% reduction in iodine load and a 34.9% reduction in effective radiation dose compared with a standard protocol using 120 kVp, higher contrast concentration, and conventional FBP reconstruction. The implication of our study results is that the investigated "double-low" technique is a promising strategy for reducing both radiation dose and iodine load while maintaining image quality and should thus be routinely used in CCTA examinations.

Lowering contrast media requirements is desirable to further defuse the notion of CIN risk from intravenously injected contrast media, particularly in patients perceived to

Table 3 – Objective image quality parameters: comparison between 120-kVp with filtered back projection and 100 kVp with iterative reconstruction protocols in patients with BMI ≤24.9 and >24.9 kg/m².

Parameter	BMI ≤24.9 kg/m²			BMI >24.9 kg/m²		
	120 kVp (n = 58), mean ± SD	100 kVp (n = 61), mean ± SD	P values	120 kVp (n = 58), mean ± SD	100 kVp (n = 54), mean ± SD	P value
CT number (HU)	426.4 ± 77.1	426.7 ± 60.5	.983	386.7 ± 71.5	390.4 ± 65.5	.772
Image noise	17.9 ± 3.6	17.2 ± 3.3	.256	19.4 ± 4.0	18.8 ± 3.3	.388
Signal-to-noise ratio	24.5 ± 5.5	25.7 ± 6.3	.272	20.5 ± 4.6	21.4 ± 5.0	.339
Contrast-to-noise ratio	19.0 ± 6.1	20.2 ± 6.1	.263	15.9 ± 4.4	16.1 ± 5.3	.889

BMI, body mass index; HU, Hounsfield unit.

Table 4 – Subjective image quality score separated by each reader and obtained from 3 readers in the overall study cohort.

Reader	120-kVp with FBP, mean ± SD	120-kVp with IR, mean ± SD	100-kVp with FBP, mean ± SD	100-kVp with IR, mean ± SD
Reader 1	4.0 ± 0.9	4.1 ± 0.9	3.9 ± 0.9	4.0 ± 0.9
Reader 2	4.1 ± 0.9	4.1 ± 0.9	3.9 ± 0.9	4.0 ± 0.9
Overall	4.1 ± 0.9	4.1 ± 0.9	3.9 ± 0.9	4.0 ± 0.9

FBP, filtered back projection, IR, iterative reconstruction; SD, standard deviation.

be at risk for CIN owing to pre-existing renal conditions. In this study, we chose a lower iodine concentration contrast agent to reduce contrast media requirements at a vascular CT application, which may be beneficial with regard to the more universal availability and lower cost compared with high-concentration agents.

Constant CNR with use of a lower iodine concentration contrast agent is enabled by lower x-ray tube voltage, which more closely approaches the *k* edge of iodine and thus increases intravascular attenuation. The increased image noise associated with lower tube voltage may present a challenge, especially in obese patients. However, IR has previously been shown to decrease image noise at CCTA overall and also in obese patients.[10,23] Thus, increased iodine attenuation and IR can compensate for increased image noise at low tube voltage setting across a variety of body types. Our findings confirm that IR is superior to FBP for low-dose CCTA. In our study, a statistically significant interaction between tube voltage and reconstruction method was observed; the beneficial effect of IR on SNR and CNR was stronger at 120 kVp compared to 100 kVp.

The observations on radiation dose in our investigation are in line with and go beyond the data from previous studies. The international PROTECTION II trial[8] demonstrated that reducing x-ray tube voltage from 120 to 100 kVp resulted in a 31% radiation dose reduction. A smaller single-center study found a 25% to 54% dose reduction for 100-kVp CCTA compared to 120-kVp CCTA.[24] These results are comparable with our finding of a 34.9% dose reduction. A previous study comparing prospectively electrocardiogram-triggered CCTA with reduced tube voltage (80 or 100 kVp, depending on BMI) to standard tube voltage (100 or 120 kVp, depending on BMI) found a 50% dose reduction for the reduced tube voltage protocol.[7] This is consistent with another study that found 56.4% and 51.9% radiation dose reduction in BMI <25 kg/m^2 and BMI ≥ 25 kg/m^2, respectively.[14] This study further demonstrated that the diagnostic accuracy of CCTA is not compromised at reduced tube voltage. It has been demonstrated that decreasing tube voltage from 100 to 80 kVp can further decrease radiation dose by nearly 50%.[25] We chose 100 kVp for the low tube potential group in our study as the 100-kVp setting can be applied to a wide range of patients and thus represents a more conservative and realistic approach for radiation dose saving in clinical routine.

Our study adds to existing data by investigating the combination of low-concentration contrast material, decreased tube potential, and IR at CCTA. Although 120 kVp with IR provided the best image quality, the combination of 100 kVp, 270 mgI/mL, and IR allowed for lower radiation dose and iodine load at CCTA without compromising image quality or jeopardizing diagnostic value compared with 120-kVp

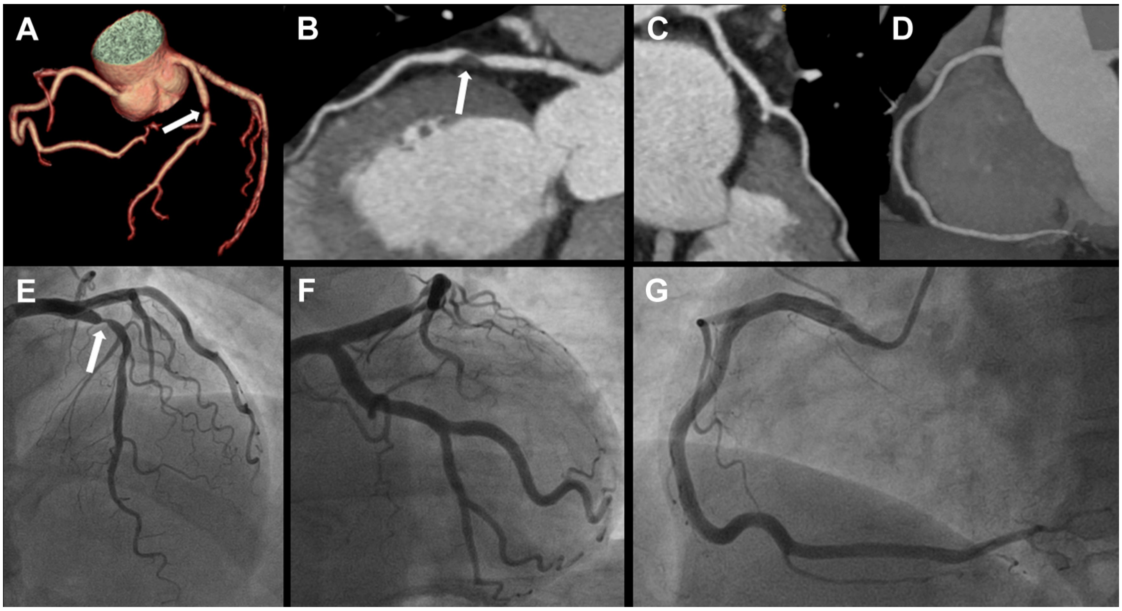

Fig. 3 – Representative images from a patient in the 120-kVp group. CCTA with 120-kVp, 370 mgI/mL iopamidol and filtered back projection was performed in a 48-year-old man (BMI, 28.0 kg/m^2; heart rate, 67 beats/min) with suspected coronary artery disease. High-grade stenosis (*arrow*) and noncalcified plaque (*arrow*) of the left anterior descending coronary artery are shown in volume rendering (A) and curved multiplanar reformat (B) displays. The lesion (*arrow*) was confirmed by coronary catheter angiography (E). The left circumflex and right coronary artery (C and D, F and G) are free of obstructive disease. Size-specific dose estimate was 27.2 mGy. Effective radiation dose was 3.5 mSv. Iodine dose was 25.5 g.

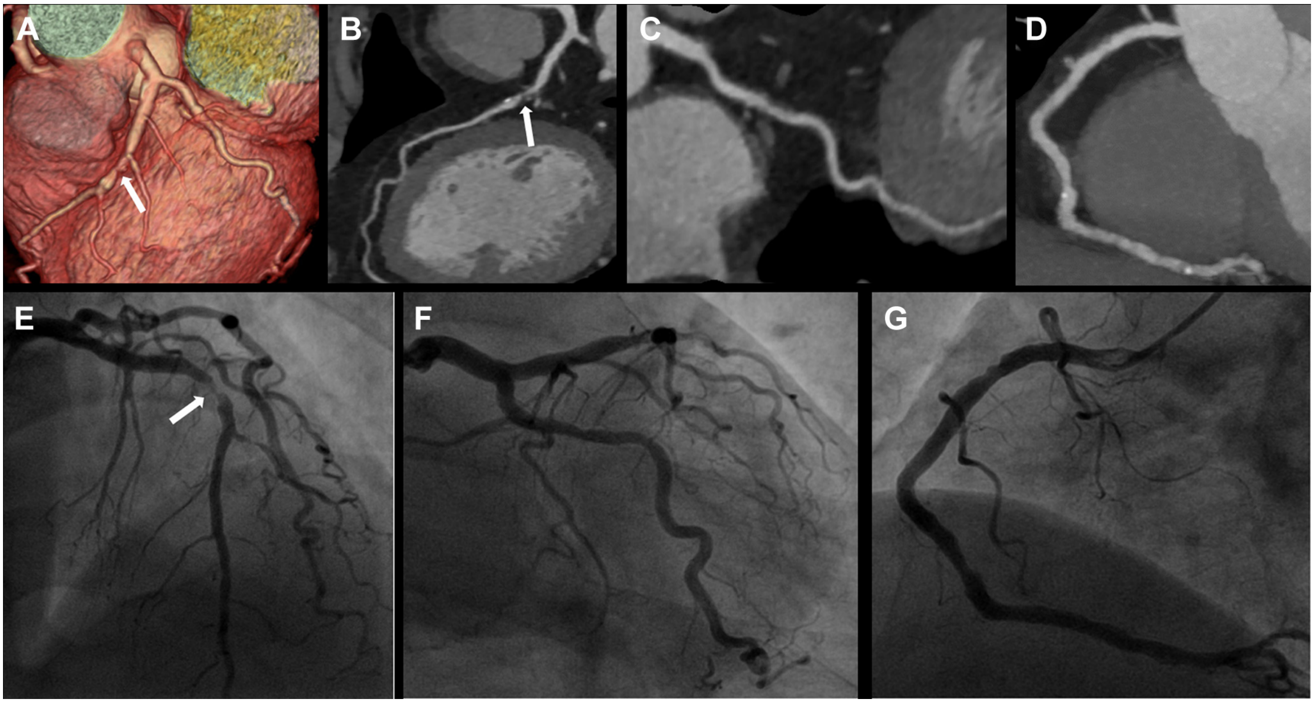

Fig. 4 – Representative images from a patient in the 100-kVp group. CCTA with 100 kVp, 270 mgI/mL iodixanol and iterative reconstruction was performed in a 53-year-old woman (BMI, 28.7 kg/m^2; heart rate, 64 beats/min) with suspected coronary artery disease. High-grade stenosis (arrow) and noncalcified plaque of the left anterior descending coronary artery are shown on volume rendering (A) and curved multiplanar reformat (B) displays. The lesion (*arrow*) was confirmed by coronary catheter angiography (E). The left circumflex and right coronary artery (C and D, F and G) are free of obstructive disease. Size-specific dose estimate was 19.5 mGy. Effective radiation dose was 2.4 mSv. Iodine dose was 18.6 g.

acquisitions reconstructed with FBP. There was no significant difference in SNR and CNR for the whole study cohort between protocols and in the subgroup of patients with a BMI >24.9 kg/m^2. This points toward the possibility that heavier patients may also benefit from our proposed 100-kVp protocol with reduced radiation dose and iodine load.

The more recent availability of automated, user-independent, anthropometry-based tube potential selection from the patient-specific attenuation of the planning range (“scout,” “topogram”) acquisition has been shown to reduce radiation dose compared to the use of standard BMI cutoffs, without differences in image quality.[26,27] The expected increasing integration of automated x-ray tube voltage selection, automated anatomic tube current modulation, and contrast media injection strategies will likely facilitate protocol choices that optimize the interrelationship between x-ray tube settings and contrast media injection algorithms to the individual patient and the respective diagnostic task.

Several limitations of our study merit consideration. First, patients’ BMI in this study was lower than that of the general European and North American populations as we investigated an Asian population that tends to have leaner body types than

Table 5 – Comparison of radiation dose between 120-kVp and 100-kVp protocols in patients with BMI ≤24.9 and >24.9 kg/m^2.

Parameters	120-kVp (n = 116), mean ± SD	100-kVp (n = 115), mean ± SD	Relative difference (%)	*P* values
SSDE (mGy)	27.5 ± 8.2	17.9 ± 6.6	35.1	$P < .0001$
BMI ≤24.9	26.4 ± 9.2	17.7 ± 7.3	32.9	$P < .0001$
BMI >24.9	28.6 ± 7.1	18.1 ± 5.8	36.9	$P < .0001$
DLP (mGy·cm)	251.7 ± 80.7	163.7 ± 72.5	34.9	$P < .0001$
BMI ≤24.9	230.5 ± 82.2	156.0 ± 74.4	32.3	$P < .0001$
BMI >24.9	272.8 ± 74.0	172.5 ± 70.0	36.8	$P < .0001$
ED (mSv)	3.5 ± 1.1	2.3 ± 1.0	34.9	$P < .0001$
BMI ≤24.9 kg/m^2	3.2 ± 1.2	2.2 ± 1.0	32.5	$P < .0001$
BMI >24.9 kg/m^2	3.8 ± 1.0	2.4 ± 1.0	36.9	$P < .0001$

DLP, dose-length product; ED, effective dose; SSDE, size-specific dose estimates.

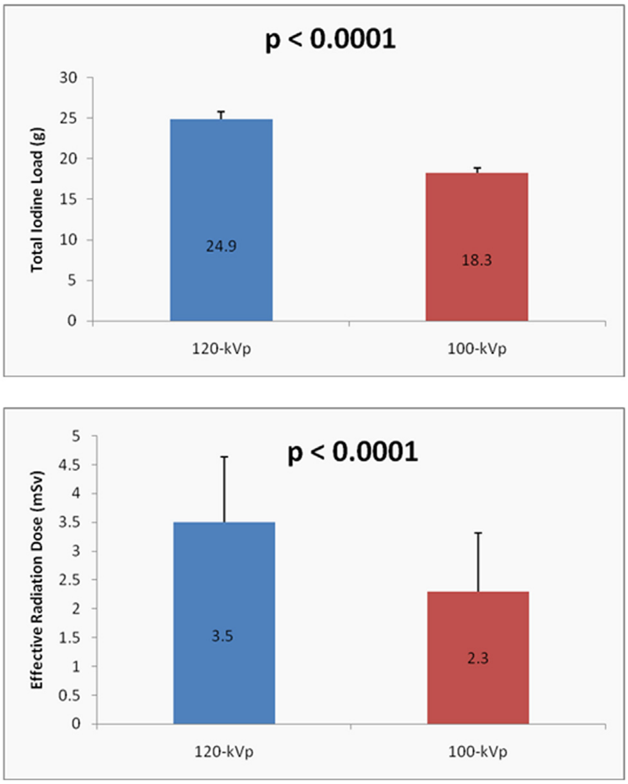

Fig. 5 – Comparison of total iodine load and effective radiation dose. Mean values and standard deviations of total iodine load (in g; A) and effective radiation dose (in mSv; B) are shown for the 120-kVp (*blue bars*) and the 100-kVp (*red bars*) CCTA protocols. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

the average patient in Western societies. However, IR was effective at achieving acceptable image noise levels and diagnostic image quality with low iodine contrast concentration and low tube voltage setting even in the 5 obese patients (BMI >30 kg/m^2) in this study. Although we recruited patients who had been clinically referred for CCTA, the average age in our cohort was younger than in most comparable investigations. It may therefore not be reflective of the population of patients undergoing clinically indicated CCTA according to current guidelines. Second, it is not possible to effectively blind observers to specifics of the protocol-embedded and reconstruction technique. Third, the assessment of diagnostic accuracy for detecting coronary artery stenosis compared to coronary catheter angiography was limited to those individuals where CCTA suggested obstructive CAD; however, this approach represents actual clinical practice, where the high negative predictive value of CCTA is increasingly used to avoid unnecessary invasive testing. Fourth, in our study, we aimed to investigate luminal imaging and coronary artery stenosis rather than identify or quantify coronary plaques. Therefore, we only analyzed noise, SNR, and CNR. The effect of low-contrast resolution in applications beyond coronary luminology may be limited. Fifth, we did not use nitroglycerin and only administered beta blockers in patients with heart rates >90 beats/min. This reflects clinical routine at many Asian centers with high patient volumes but represents a limitation of our study as it is against SCCT recommendations.[28] Lastly, we only reconstructed image data with SAFIRE, and other IR algorithms should be tested with the CCTA protocols in our study for effectiveness.

5. Conclusion

In conclusion, our data demonstrate that the combined use of a lower iodine concentration contrast medium, 100 kVp, and IR at CCTA results in image quality comparable to a standard protocol using higher iodine concentration, 120 kVp, and conventional FBP reconstruction while effective radiation dose and iodine load are substantially reduced.

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