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FULL PAPER

Low contrast material dose coronary computed tomographic angiography using a dual-layer spectral detector system in patients at risk for contrast-induced nephropathy

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Objective: To evaluate the effects of virtual monochromatic imaging (VMI) using dual-layer spectral detector CT on the image quality of coronary CT angiography (CCTA) acquired by using a low contrast material (CM) dose.

Methods: We used a VMI 50keV protocol with a 50% CM dose (140 mgI kg⁻¹) to scan 30 patients with renal insufficiency and a 120 kVp with the standard CM dose (280 mgI kg⁻¹) to scan 30 controls without renal insufficiency. Quantitative parameters, including CT attenuation, image noise, and contrast-to-noise ratio (CNR), were measured. The visual image quality factors of contrast enhancement, image noise, beam-hardening artefact, vessel sharpness, and overall image quality were scored on a 4-point scale.

Results: The mean CT attenuation of the ascending aorta was significantly higher for 50 keV VMI than for 120 kVp. Image noise was significantly lower under the 50 keV VMI. CNR and the mean visual score for contrast enhancement were significantly higher for 50 keV VMI. There were no significant differences in the other visual image quality parameters between the two protocols.

Conclusion: Dual-layer spectral detector CT using 50 keV VMI enabled reducing the CM dose by 50 % without CCTA image quality degradation in patients with renal insufficiency.

Advances in knowledge: The VMI 50 keV protocol using dual-layer spectral detector CT and a CM dose reduced by 50 % (140 mgI kg⁻¹) can improve the diagnostic image quality of CCTA.

INTRODUCTION

Coronary CT angiography (CCTA) is a robust and established non-invasive imaging technique that yields high sensitivity and negative predictive values.^{1,2} However, the risk of contrast-induced nephropathy (CIN), an acute kidney injury elicited by iodinated contrast material (CM), is of concern because CIN is one of the causes of hospital-acquired acute renal failure.^{3,4} In the recent years, the incidence of CIN after intravenous administration of CM for contrast-enhanced CT remains controversial.⁵ Nevertheless, the risks and benefits of contrast injection in patients at risk of CIN must be carefully considered. Risk factors for CIN include an estimated glomerular filtration rate (eGFR) of <45 ml min⁻¹ 1.73 m⁻², severe heart disease,

dehydration, diabetes mellitus, multiple iodinated CM doses in a short time interval (<24 h) and use of nephrotoxic medications, such as non-steroidal anti inflammatory drugs and diuretics.^{6,7} These risk factors that are commonly associated with coronary artery disease should be assessed before performing CCTA using the smallest diagnostically required amount of CM in patients at risk. The Society of Cardiovascular Computed Tomography (SCCT) guidelines for the performance and acquisition of CCTA stated that the CM volume should be minimised. The guidelines also recommended lower tube voltage acquisition or virtual monochromatic imaging (VMI) using dual-energy CT for low CM dose protocols in patients at risk of CIN.⁸

Dual-energy CT can reconstruct VMI at arbitrary X-ray energies (keV) based on high- and low-energy X-ray spectral datasets. Using the greater iodine contrast in low-energy images,^{9–11} few investigators have suggested the utility of VMI (60 keV images) generated from tube-based dual-energy CT systems for the reduction of the CM dose in CCTA.^{12,13} However, this strategy has not yet been fully established, probably because the increased noise at lower keV images and inherent decrease in contrast due to reduced CM dose degrades small coronary lesion detectability and subjective image quality.

Recently, a dual-layer spectral detector CT system is commercially available.^{14–16} This system uses a detector-based dual-energy technique and simultaneously measures high- and low-energy projection data in two detector layers at the same spatial and angular location. This approach allows VMI in the projection domain without the need for temporal and angular interpolation, which may theoretically yield an accurate beam-hardening correction and cancellation of anti correlated noise in photoelectric and Compton scatter images.¹⁷ Additionally, this system allows implementation of dedicated model-based iterative reconstruction (IR) techniques, resulting in further reduction in image noise.¹⁸ Therefore, we hypothesised that lower keV VMI with a dual-layer spectral detector CT would enable a decrease in the CM dose without degrading the image quality in CCTA.

This study aimed to evaluate the effects of 50 keV VMI using a dual-layer spectral detector CT on the image quality of CCTA obtained with a 50% CM dose protocol.

METHODS AND MATERIALS

Study population

The current study included 30 patients with and 30 without renal insufficiency (eGFR <45 ml min⁻¹ 1.73 m⁻² and >60 ml min⁻¹ 1.73 m⁻², respectively) who underwent CCTA between January and May 2017. The eGFR for the patients was calculated using the following eGFR equation¹⁹: eGFR (ml min⁻¹ 1.73 m⁻²) = 194 × age^{-0.287} × serum creatinine (Cr)^{-1.094} (×0.739 in females).

The inclusion criteria were serum Cr concentration assay performed within 2 weeks before the CT scan and an eGFR calculated using the most recent serum Cr levels before the examination. Exclusion criteria for CCTA were allergies to CM, severe renal insufficiency (eGFR <30 ml min⁻¹ 1.73 m⁻²), atrial fibrillation, history of coronary artery bypass grafting and heart failure (New York Heart Association Grades III–IV). The controls consisted of the first 30 patients without renal insufficiency (eGFR >60 ml min⁻¹ 1.73 m⁻²) who were examined during the same period and met our inclusion criteria.

A total of 30 patients with renal insufficiency were scanned using VMI and 50% reduced CM dose protocol, which is the standard of care for these patients in our institution. The 30 controls were scanned using the conventional 120 kVp protocol and standard CM dose. This retrospective study was approved by our Institutional Review Board and the patient informed consent was waived. Table 1 summarises the patient characteristics.

Table 1. Patient characteristics

	120 kVp	50 keV VMI	p-value
Sex (M/F)	18/12	17/13	0.92
Age [years]	68.7 ± 12.1	70.4 ± 14.0	0.65
Height [cm]	163.6 ± 10.4	159.6 ± 9.9	0.18
Weight [kg]	66.6 ± 12.8	61.9 ± 9.7	0.16
Body mass index [kg m ⁻²]	24.7 ± 3.0	24.4 ± 3.8	0.75
eGFR [ml ⁻¹ min ⁻¹ 1.73 m ⁻²]	62.2 ± 11.7	39.6 ± 4.4	<0.01

VMI, virtual monochromatic imaging; eGFR, estimated glomerular filtration rate.

Data are presented as the mean ± standard deviation or number.

CCTA acquisition

All patients were scanned using a dual-layer spectral detector CT scanner (iQon Spectral CT; Philips Healthcare, Best, the Netherlands). The parameters for the CCTA protocol were as follows: 64 × 0.625 mm, detector collimation; 270 ms, tube rotation time; 120 kVp, tube voltage and 0.16, helical pitch. The tube current was determined by the automatic exposure control (DoseRight; Philips Healthcare) using electrocardiogram-dependent tube current modulation. The calculated volume CT dose index (CTDI_{vol}) was 22.2–46.7 (mean, 30.3) mGy. If the baseline heart rate was >65 bpm, a beta-blocker, landiolol hydrochloride (6–10 mg, Corebeta; Ono Pharmaceutical, Osaka, Japan), was intravenously injected 4–7 min before CCTA or propranolol hydrochloride (10–20 mg, Inderal; AstraZeneca, Osaka, Japan) was orally administered 60 min before CCTA. Each patient received nitroglycerin (0.3 mg, Nitrophen; Nippon Kayaku, Tokyo, Japan) sublingually 5 min before data acquisition to dilate the coronary arteries. Using a dual-chamber power injector, iopamidol (Iopamiron; Bayer HealthCare, Osaka, Japan) was administered using 370 mg ml⁻¹ of iodine to each patient via a 20 G catheter inserted into an antecubital vein. The amount of CM was adjusted to the body weight of each patient (280 mgI kg⁻¹ for the standard 120 kVp protocol and 140 mgI kg⁻¹ for the 50 keV VMI protocol) and injected at a fixed duration of 16 s. Then, 40 ml of saline solution was injected at the same rate as that of CM. The start time of data acquisition was determined using a computer-assisted bolus-tracking programme with a trigger threshold of 100 Hounsfield units in the ascending aorta, and data acquisition started 6 s after triggering. Table 2 summarises the acquisition parameters of the two protocols.

CT image reconstruction

We reconstructed axial source images with a section thickness and interval of 0.67 mm and 0.33 mm, respectively, using a medium cardiac kernel during the mid-diastolic phase. CT images were reconstructed using a hybrid-type IR algorithm (iDose⁴; Philips Healthcare) at iDose level three for the standard 120 kVp protocol. In the VMI group, the spectral-based image data were post-processed on a dedicated workstation (Spectral Diagnostic Suite; Philips healthcare) to generate the VMI at 50 keV with a spectral level of 0.

Table 2. Scanning and contrast material parameters

	120 kVp	50 keV VMI
Iodine dose (mgI/kg)	280	140
Injection duration (sec)	16	
Timing method	Bolus track	
Scan mode	Retrospective electrocardiogram gating	
Peak tube voltage (kVp)	120	
Tube current	Automatic exposure control (dose right index = 36)	
Rotation time (sec)	0.27	
Helical pitch	0.16	
Reconstruction	iDose ⁴ level 3	VMI 50 keV
Slice thickness (mm)	0.67	

VMI, virtual monochromatic imaging.

Quantitative image quality analysis

A cardiovascular radiologist, with 8 years of experience in CCTA, performed the following measurements on axial source images: (1) The mean CT attenuation of the ascending aorta, proximal and distal segments of the right coronary artery (RCA), left main coronary artery (LMA) and distal segments of the left anterior descending and left circumflex artery (LAD, LCX). For these measurements, a circular region of interest (ROI) was placed in the not-so-small and not-so-large area of the vessels to prevent pixel variability and to avoid the edges of the vessel, respectively. The sizes of ROI in the ascending aorta and proximal and distal segments of the coronary artery were approximately 300 mm², 6 mm² and 4 mm², respectively. (2) Contrast enhancements of the ascending aorta, proximal and distal segments of the RCA, LMA and distal segments of the LAD and LCX were calculated as the difference between the mean attenuation in the lumen of the contrast-enhanced vessel and the adjacent perivascular fatty tissue. (3) Image noise was determined as the standard deviation of the attenuation value in a single circular ROI placed in the ascending aorta. (4) The contrast-to-noise ratios (CNRs) of the ascending aorta, proximal and distal segments of the RCA, LMA and distal segments of the LAD and LCX were calculated as CNR = contrast enhancement/image noise. These parameters were compared between the two reconstruction methods.

Qualitative image quality analysis

All images were reviewed and interpreted using PACS (EV Insite; PSP Corp., Tokyo, Japan). Available images were axial source images and multiplanar- and curved multiplanar reconstructions. The image series acquired using the two reconstruction methods were intermixed. Two cardiovascular radiologists, with 8 and 12 years of experience in CCTA, were blinded to the protocol settings, and they independently graded the images for coronary arterial contrast, image noise, beam-hardening artefacts, vessel sharpness and overall image quality. These radiologists used a 4-point subjective scale to grade the image noise and beam-hardening artefacts (1, present and unacceptable; 2, present and interfering the depiction of coronary arteries; 3, present but not interfering their depiction and 4, minimal or

absent). Vessel sharpness was graded as 1 (blurry), 2 (poorer than average), 3 (better than average) and 4 (sharpest). Coronary arterial contrast and overall image quality were also graded as 1 (unacceptable), 2 (acceptable), 3 (good) and 4 (excellent). In cases of inter observer disagreement, final decisions were achieved by consensus. Adjustment of the window level and width was allowed during qualitative assessments.

Further, we performed coronary segmental evaluation by assessing the image quality of each segment according to the SCCT guidelines²⁰ on a 4-point scale (1, unacceptable; 2, acceptable; 3, good and 4, excellent) to assess the effects of reduced CM dose protocol on the assessability of each coronary segment. We recorded the number of assessable segments (score, ≥ 3) for each patient and used these data to compare the two protocols.

Statistical analysis

All numeric values are reported as the mean $\pm$ standard deviation. All qualitative and quantitative image parameters obtained using the 120 kVp and 50 keV VMI protocols were compared. Differences in the mean values between the two protocols with normally and non-normally distributed data were determined using the two-tailed independent *t*-test and the Mann-Whitney *U*-test, respectively. The degree of agreement between the two observers for their visual evaluation was measured using the κ statistic with a value of 0, no; >0 but <0.20 , poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial and 0.81–0.99, almost perfect agreement. A *p*-value < 0.05 was considered statistically significant. Statistical analyses were performed using the Excel statistics software package for Microsoft Windows (BellCurve for Excel; SSRI, Tokyo, Japan).

RESULTS

Quantitative image quality analysis

Table 3 shows the results of our quantitative image quality assessment. The mean CT attenuation values of the ascending aorta, LMA and proximal RCA were significantly higher with the 50 keV VMI protocol than that with 120 kVp protocol. However, no significant differences were observed in the mean CT attenuation values of the distal LAD, distal LCX and distal RCA. Image noise was significantly lower with the 50 keV VMI protocol than that with 120 kVp protocol ($p < 0.01$). CNR was significantly higher with the 50 keV VMI protocol than that with 120 kVp protocol in all evaluated sites ($p < 0.01$).

Qualitative image quality analysis

Table 4 shows the results of our qualitative image quality assessment. The mean score for coronary arterial contrast was significantly higher with the 50 keV VMI protocol than that with 120 kVp protocol ($p < 0.01$). However, no significant differences were observed in the other image quality parameters (image noise, beam-hardening artefact, vessel sharpness and overall image quality) between the two protocols.

A total of 431 and 436 coronary artery segments for the 120 kVp and 50 keV VMI protocols, respectively, were subjected to visual scoring in our segmental evaluation. The images obtained in 403 of 431 segments (93.5%) using the 120 kVp protocol were

Table 3. Quantitative assessment of image quality

	120-kVp	50-keV VMI	<i>p</i> -value
Ascending aorta			
Mean CT attenuation (HU)	402.9 ± 62.7	478.8 ± 74.3	<0.01
Image noise (HU)	25.4 ± 5.0	21.8 ± 4.3	<0.01
Contrast-to-noise ratio	20.5 ± 5.0	29.3 ± 8.5	<0.01
LMA			
Mean CT attenuation (HU)	388.9 ± 63.9	436.7 ± 69.6	0.02
Contrast-to-noise ratio	19.8 ± 4.8	27.2 ± 7.7	<0.01
Proximal RCA			
Mean CT attenuation (HU)	387.4 ± 61.5	431.8 ± 80.1	0.04
Contrast-to-noise ratio	19.6 ± 4.4	26.9 ± 6.6	<0.01
Distal LAD			
Mean CT attenuation (HU)	350.2 ± 70.4	363.6 ± 76.6	0.53
Contrast-to-noise ratio	18.3 ± 4.6	23.9 ± 6.7	<0.01
Distal LCX			
Mean CT attenuation (HU)	357.7 ± 71.8	403.1 ± 92.2	0.07
Contrast-to-noise ratio	18.4 ± 4.8	26.0 ± 9.9	<0.01
Distal RCA			
Mean CT attenuation (HU)	373.8 ± 75.7	412.3 ± 73.4	0.08
Contrast-to-noise ratio	19.1 ± 4.1	25.8 ± 6.1	<0.01

HU, Hounsfield unit; LAD, left anterior descending artery; LCX, left circumflex artery; LMA, left main coronary artery; RCA, right coronary artery; VMI, virtual monochromatic imaging.

Data are presented as the mean ± standard deviation or number.

of assessable quality than those obtained in 405 of 436 segments (92.9%) using 50 keV VMI protocol (Figure 1), but the difference between the two protocols was not significant ($p = 0.84$). Inter observer agreement for visual grading was moderate to substantial for the two protocols (κ value = 0.58–0.69).

Figure 2 shows the representative cases.

Radiation dose

The mean CTDI_{vol} and estimated effective radiation dose were 36.5 ± 8.2 mGy and 8.9 ± 2.0 mSv with the 120 kVp protocol and

33.3 ± 8.1 mGy and 7.7 ± 2.1 mSv with 50 keV VMI protocol, respectively. No significant differences were observed in the mean CTDI_{vol} and estimated effective radiation dose between the two protocols.

DISCUSSION

Our results demonstrated that the 50 keV VMI protocol using a dual-layer spectral detector CT and a CM dose that decreased by 50% (140 mgI kg^{-1}) yielded sufficient coronary arterial contrast enhancement relative to that of the standard 120 kVp protocol using the standard CM dose (280 mgI kg^{-1}), which provided significantly improved CNR and visual image quality equivalent to that of the standard 120 kVp protocol on CCTA. This observation is practically important because CCTA using a lower CM dose may reduce risks of CIN without compromising the quality of diagnostic information, especially in patients with renal insufficiency.

In 2016, the first dual-layer spectral detector CT instrument was commercially available (iQon Spectral CT; Philips Healthcare). The instrument uses a single X-ray source and acquires dual-energy information by measuring low-energy regions of the emitted spectrum through the upper layer of the detector; high-energy photons penetrate this layer and are measured by the deeper layer of the detector.²¹ This new technology facilitates simultaneous acquisition of low- and high-energy data at the same spatial position, and the dual-energy information is retrospectively available for every scan; hence, no *a priori* decision on the suitability or need of dual-energy acquisition prior to the examination is required. Based on our literature review, this is the first investigation to demonstrate the utility of VMI using dual-layer spectral detector CT for CM dose reduction in CCTA by comparing its image quality with that of the standard 120 kVp and using the standard CM dose as reference. In the present study, the low noise level was obtained at 50 keV, which is in contrast to the results of previous studies using different dual-energy systems.²² This may have been achieved by exploiting the anti correlated noise suppression and implementing a dedicated model-based IR in the projection domain, where the exactly matched high- and low-energy datasets can be post-processed without the need for angular and temporal interpolation.^{18,23–26}

We evaluated the image quality of low-keV VMI using 120 kVp reference standard images. However, comparisons with low-kVp images (e.g. 100 kVp) could also be an interesting research target. Low-kVp scans allow not only a reduction in the CM dose but also a considerable reduction in the radiation dose.²⁷ In contrast, dual-layer spectral detector CT enables the use of spectral-based imaging techniques, such as virtual non-contrast imaging, iodine maps and effective anatomical number maps, and optimisation of iodine contrast based on the demand for each examination and organ of interest or reduction of artefacts by reconstructing the VMI at arbitrary mono-energetic levels.^{28,29} Moreover, when using a dual-layer spectral detector CT, the dual-energy information for all acquisitions is retrospectively available using the usual protocols. The acquisition of spectral data is dependent on the detector rather than the X-ray tube. Hence, before the scan,

Table 4. Qualitative assessment of image quality

	120-kVp	50-keV VMI	<i>p</i> -value
Coronary arterial contrast	3.5 ± 0.6	3.8 ± 0.4	0.04
Image noise	3.5 ± 0.6	3.5 ± 0.5	0.89
Beam-hardening artifacts	3.6 ± 0.6	3.4 ± 0.5	0.11
Vessel sharpness	3.5 ± 0.5	3.4 ± 0.6	0.93
Overall image quality	3.5 ± 0.5	3.5 ± 0.5	0.96

VMI, virtual monochromatic imaging.

Data are presented as the mean ± standard deviation or number.

Figure 1. Results of qualitative coronary segmental image quality assessment (a) The images obtained in 403 of 431 segments (93.5%) using the 120 kVp protocol were of assessable quality as those obtained in 405 of 436 segments (92.9%) using the 50 keV VMI protocol (b) The difference between the two protocols was not significant.

Figure 2. A 74-year-old male with chest pain (body weight, 58.1 kg; body mass index, 23.3 kg m^{-2}). Axial source images, curved multiplanar reconstruction of the right coronary artery (RCA) and volume-rendered images were obtained using the 120 kVp protocol with the standard contrast material (CM) dose (280 mgI kg^{-1}) (a-c). A 68-year-old male with chest pain (body weight, 62.6 kg; body mass index, 24.2 kg m^{-2}). Axial source images, curved multiplanar reconstruction of the RCA and volume-rendered images were obtained using the 50 keV VMI protocol with a 50% CM dose (140 mgI kg^{-1}) (d-f). Both patients had similar quantitative and qualitative image quality.

there is no need to decide whether or not to use a special protocol for spectral analysis.

The present study had some limitations. First, we did not evaluate the diagnostic performance of our individual protocols for detecting coronary stenoses. Further, we did not correlate our imaging findings with the results of coronary catheterisation because the incidence of coronary stenosis was too low in our patients and we did not have any standard reference for most of their lesions. Rather, we focused on comparing the quality of CCTA images obtained using low-keV VMI and a 50% CM dose with scans performed using 120 kVp and the standard CM dose. Second, the study population was small; thus, our techniques need to be rigorously evaluated in large-scale prospective studies.

Third, the body size of our Japanese patients (mean body mass index, approximately 24 kg m^{-2}) was smaller than those of North Americans and Europeans. In patients with a large body size, low-keV VMI CCTA may yield images of poorer quality because of radiation scattering and absorption. Finally, all patients and CCTA examinations in the present study were from a single institution. Multicentre prospective clinical trials are required to validate these results.

CONCLUSION

The 50 keV VMI protocol using dual-layer spectral detector CT decreased the CM dose by 50% without compromising the image quality in CCTA.

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