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FULL PAPER

Accuracy of coronary artery calcium scoring with tube current reduction by 75%, using an adaptive iterative reconstruction algorithm

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Objective: To assess the accuracy of an iterative reconstruction (IR) technique for coronary artery calcium scoring with reduced radiation dose.

Methods: 163 consecutive patients underwent twofold scanning by 320-row detector CT at 120 kVp. A low-dose scan at 25% tube current but with standard scan length (14 cm) was followed by a standard dose scan with routine tube current but reduced scan length (10 cm). Reduced dose images were constructed using filtered back-projection (FBP) and IR (adaptive iterative dose reduction in three dimensions). The standard dose scan reconstructed with FBP served as the gold standard for comparisons. Image noise and Agatston coronary calcium scores were determined and compared between the groups.

Results: Compared with FBP at standard dose, noise at reduced dose increased markedly with FBP but remained

low with IR. Mean Agatston score with FBP at reduced dose showed a significant increase as compared with FBP at standard dose. No significant difference was observed when applying IR at reduced dose. At reduced dose, 38 (23.3%) patients were reassigned to a different cardiovascular risk category with FBP but only 8 (4.9%) with IR. Out of 47 patients with a zero Agatston score, 15 patients (31.9%) were false-positive with FBP at reduced dose, but no false positives were found with IR.

Conclusion: IR allows accurate coronary artery calcium scoring with a radiation dose reduced by 75%.

Advances in knowledge: The application of adaptive iterative dose reduction in three dimensions allows the maintenance of accurate Agatston scores and risk stratification at significantly reduced tube current, thus reducing the patient's exposure to ionizing radiation.

INTRODUCTION

The amount of coronary artery calcium (CAC) is considered to reflect the coronary artery plaque burden of an individual patient, and is associated with the probability of future adverse cardiac events.^{1,2} While cardiac CT is the standard method for detecting and quantifying CAC in clinical routine, it exposes patients to ionizing radiation with an effective radiation dose reported to range typically between 1 and 2 mSv, although values as high as 10 mSv have been reported when a standard filtered back-projection (FBP) reconstruction algorithm is used.³

Recently, several new iterative reconstruction (IR) algorithms have been introduced by the various CT manufacturers.⁴ All these algorithms have been designed with the main purpose of improving image quality by reducing image noise. As a result, IR is expected to allow image acquisition at lower radiation dose levels without loss of image quality or

diagnostic information. Since its introduction, the potential of IR has been investigated for a wide range of CT applications, including various cardiac applications.^{5,6} In general, these investigations have indeed shown that improvements in either image quality or radiation dose levels can be achieved when IR is used. However, concerns have arisen as to whether the use of IR may affect the accuracy of CAC scoring and thus result in incorrect cardiovascular risk assessment (*i.e.* assessment of an individual's 10-year risk of atherosclerotic cardiovascular disease events). Indeed, differing results have so far been reported.^{7–9} Therefore, for each individual, IR algorithm rigorous testing of the algorithm's effects on CAC scores seems crucial before its use can safely be recommended in clinical practice.

A recently published phantom study using a dedicated IR algorithm, Adaptive Iterative Dose Reduction in 3 Dimensions (AIDR3D, Toshiba Medical Systems, Otawara, Japan) showed that novel IR algorithms do not necessarily alter

CAC quantification.¹⁰ In addition, that experimental study suggested that novel IR algorithms may allow substantial reduction of the radiation exposure by up to 80%. In a recent study by Rodrigues et al, scanning at lower tube voltages was simulated by adding artificial noise to CAC scans from 27 patients, indicating that tube current reduction by up to 75% is feasible when AIDR3D is used.¹¹ However, there is still little information available from larger prospective intraindividual validation studies in subjects undergoing CAC scoring in routine clinical practice using AIDR3D.

Therefore, the aim of the present study was to perform a prospective clinical investigation of the accuracy of AIDR3D for CAC scoring, with reduced tube current using FBP images obtained with standard tube current as reference and including as representative a population as justifiable.

METHODS AND MATERIALS

Patients

Outpatients referred for CAC scoring in the context of comprehensive clinical cardiovascular risk assessment were screened for participation in the study. The ethical standards for research on human subjects have been adhered to. In particular, no patient was exposed to additional radiation. The local Ethics Committee approved the study, and informed consent was obtained from all patients.

Data acquisition

Patients with a heart rate above 65 beats min⁻¹ received oral beta-blocking medication (25–100 mg atenolol; Tenormin, AstraZeneca, London, UK) 1 h before imaging. CAC imaging was performed using a second-generation volume CT scanner (Aquilion ONE™ Vision Edition, Toshiba Medical Systems, Otawara, Japan). Each patient underwent non-contrast enhanced CT for CAC scoring twice. The first scan was performed with a tube current reduced by 75% followed by a second scan at standard tube current. To minimize the total radiation exposure to the patient, the first scan was used for planning of the second scan, as follows: First, a projection radiograph in the anteroposterior and lateral directions was obtained. These projections were used to plan the craniocaudal scan length of the first CAC scan, from the level of the tracheal bifurcation to the level of the left lateral pleural recess. By using the axial images of the first scan, the craniocaudal extension of the coronary artery system was identified. The craniocaudal scan length of the second CAC scan was then planned by adding at least 0.5 cm to the cranial and 0.5 cm to the caudal border of the coronary artery tree, in order to account for possible changes in inspiration depth between the two scans. Accordingly, the scan with higher tube current was acquired with a shorter scan length. As a result, radiation exposure was considerably lower than it would have been if a standard CAC examination had been performed, allowing the total radiation dose administered to the patient within this protocol to be minimized.

Imaging was performed with the patient in the supine position during a breath-hold after mild inspiration. The scanned slice thickness was 0.5 mm with a scanned field of view of 320 ×

320 mm. Both scans were acquired within one rotation at 275 ms exposure time using prospective electrocardiogram triggering set at 75% of the R–R interval. A constant tube voltage of 120 kV was used and tube current was determined by the system's automatic exposure control feature (SureExposure, Toshiba Medical Systems, Otawara, Japan). Target maximum image noise was 23 Hounsfield units (HU) for both scans. Patients were excluded if their excessive obesity meant that the automatic exposure control would have exceeded the maximum tube current, so that the target image quality (*i.e.* image noise target of 23 HU) could not have been guaranteed. The first scan was performed applying IR with the tube current lowered by 75% (nominal value on the apparatus, 80%) compared with scanning using FBP. Scan length, CT dose index and the dose–length product were obtained for each scan. The effective dose was calculated from the dose–length product using the conversion factor 0.014 mSv mGy⁻¹ cm⁻¹ for each scan.

Data reconstruction

All data sets were automatically reconstructed with a slice thickness of 3 mm at 3 mm increment in a field of view of 200 × 200 mm with a matrix of 512 × 512 pixels. In 19 patients, an obvious displacement of (small) calcium deposits between the two acquisitions was found. This was due to partial volume effects resulting from different axial slice positions in the cranio-caudal direction for both scans. These data sets were reconstructed again and axial slice positions were adjusted manually for a perfect match of the two acquisitions. The IR reconstruction was performed with the manufacturer-recommended settings for AIDR3D using the preset “standard” (of the three available options “mild”, “standard” and “strong”). For both IR and FBP, the manufacturer-recommended smooth filter convolution kernel without beam-hardening correction (FC12), which is routinely used for soft tissue reconstructions, was applied.

Image noise

Image noise was measured as the standard deviation of attenuation values in a region of interest placed in the ascending aorta. For each patient, the noise measurements in the different reconstructed data sets were done on the same location.

Coronary artery calcium scoring

All images were analysed in a soft-tissue window (default setting: width 350 HU, centre 50 HU) on a standalone workstation using dedicated image-processing software with integrated application for CAC scoring (Vitrea v. 6.3, Vital Images, Toshiba Medical Systems, Otawara, Japan) by a skilled radiologist with 15 years' experience in cardiac imaging. Calcified lesions were manually identified by selecting automatically visualized (colour-coded highlighted) regions that were located within the coronary arteries. The amount of CAC was quantified in a standardized fashion and expressed as the traditional Agatston score for all data sets using the reference 130 HU CT number threshold. To avoid reader recall, data sets were analysed in different reading sessions with an interval of at least 1 week and with the order of data sets randomized. Agatston scores were classified into six commonly used risk categories (0, 1–10, 11–100, 101–400, 401–1000, and >1000). In addition, the respective age- and

sex-adjusted Agatston score percentile was determined for each data set and assigned to one of six percentile-based risk categories (0, 1–25, 26–49, 50–75, 76–95, and >95%, respectively).

To determine the variability of repeated measurements, CAC scoring was repeated (i) by the same reader several months after the initial measurement, to calculate intraobserver variability, and (ii) by a second reader (a radiologist with 6 years' experience in cardiac imaging) to calculate interobserver variability.

Statistical analyses

FBP reconstruction at standard dose served as the gold standard for comparisons with FBP and IR reconstructions at reduced dose. Continuous data are presented as mean $\pm$ standard deviation. The two-sided paired *t*-test with Bonferroni correction was used for pairwise comparison of mean values. κ statistics were used to assess the agreement on cardiovascular risk stratification according to cut-off values for the Agatston score. The variability of repeated assessment pairs was quantified by expressing the difference between the two measurements as a percentage of their mean and then calculating the average percentage difference. Where the score was 0 at both measurements, the variability was defined as 0. In addition, the agreement of repeated assessments was analysed by calculating Pearson's correlation coefficient (*r*) as well as Bland–Altman 95% limits of agreement and associated 95% confidence intervals. One-way analysis of variance (random effects model) was used and a two-sample *F*-test was applied for a pairwise comparison of variances.

Two-sided *p*-values below 5% were regarded as significant. All analyses were performed using PASW statistics v. 18.0.0 (IBM Corporation; Armonk, NY).

RESULTS

A total of 220 patients were screened; 16 patients with heart rates above 65 beats min^{-1} (despite previous beta-blocker medication), 4 patients with visible motion artefacts despite a low heart rate, and 37 patients who were highly obese (meaning that the automatic exposure control would have exceeded the maximum tube current, so that the target image quality could not be guaranteed) were excluded. Thus, 163 patients were included in the study; all provided full data sets.

Baseline characteristics of the study patients are summarized in Table 1. In total, 163 patients [99 (61%) female, average age 65 ± 12 years] were studied. Average body mass index was $24.8 \pm 3.1 \text{ kg m}^{-2}$ with a range of 19.7–33.6 kg m^{-2} . Data acquisition was successful for all patients, and diagnostic image quality was achieved in all scans. Scan and dose parameters are provided in Table 2. Mean tube current at standard dose was $345.0 \pm 140.5 \text{ mA}$ vs $91.1 \pm 40.4 \text{ mA}$ at reduced dose ($p < 0.05$). Accordingly, effective dose was 0.44 mSv when the reduced dose protocol was followed, as compared with 1.77 mSv when the standard dose protocol with identical scan length was used, representing a reduction in radiation dose by 75% ($p < 0.05$).

Comparison of the mean image noise is provided in Figure 1. As compared with FBP standard dose reconstructions, mean image

Table 1. Patients' clinical characteristics

Characteristic	N = 163
Age (years)	64.6 ± 11.8 (34–79)
Sex (male/female)	
Male	64 (39%)
Female	99 (61%)
Weight (kg)	69.8 ± 10.7 (53–102)
Height (m)	1.68 ± 9.4 (152–191)
Body mass index (kg m^{-2})	24.8 ± 3.1 (19.7–33.6)
Heart rate (bpm)	60.8 ± 8.7 (43–67)
Hypertension	104 (64%)
Diabetes mellitus	34 (21%)
Hypercholesterolemia	93 (57%)
Family history of coronary artery disease	52 (32%)
Smoking	83 (51%)
Asymptomatic	24 (15%)
Chest pain	124 (76%)
Dyspnea	59 (36%)
Other symptoms (syncope)	11 (7%)
Abnormal exercise electrocardiogram	46 (28%)
Abnormal stress imaging	18 (11%)

Mean $\pm$ standard deviation (range) or absolute number (%).

noise increased significantly for FBP reconstructions at reduced dose, but remained similar for IR reconstructions at reduced dose.

On the FBP standard dose images, mean Agatston score was 185 ± 346 as compared with 215 ± 380 for FBP reconstructions at reduced dose and 185 ± 351 for IR reconstructions at reduced dose. As expected on the basis of the study design, linear regression analysis revealed excellent correlations between Agatston scores from both FBP at reduced dose ($y = 1.09x + 13.5$, $r = 0.995$, $p < 0.0001$) and IR at reduced dose ($y = 1.01x - 1.6$, $r = 0.997$, $p < 0.0001$) with Agatston scores derived from FBP standard dose. However, as compared with the gold standard, a systemic bias was observed for Agatston scores derived with FBP at low dose with a mean difference of 30.4 ± 50.4 ($p < 0.0001$). In contrast, mean Agatston score derived from low-dose scans reconstructed with IR showed no systemic deviation (mean difference 0.52 ± 25.2 , $p > 0.05$ (not significant)). Details, including the mean differences per risk score category, are shown in Table 3.

On FBP standard dose, coronary calcium (Agatston score > 0) was identified in 116 patients, whereas a negative score was obtained in the remaining 47 patients. On the reduced dose images, no false negatives were seen with either FBP or IR reconstruction. However, reconstruction with FBP at reduced dose resulted in an additional 15 patients with (incorrect) positive Agatston scores. No false positives

Table 2. Scan and dose parameters

	Reduced dose (full scan length)	Standard dose (reduced scan length)	Standard exposure (standard dose, full scan length) ^a
Tube current (mA)	91.1 ± 40.4 ^b	345.0 ± 140.5	341.7 ± 147.5
Scan length (cm)	14.0 ^b (fixed)	10.05 ± 0.62	14.0 (fixed)
CTDI _f (mGy)	2.24 ± 1.02 ^b	7.00 ± 2.99	9.02 ± 3.98
Dose-length product (mGy-cm)	31.4 ± 14.3 ^b	70.9 ± 31.4	126.5 ± 55.7
Effective dose (mSv)	0.44 ± 0.2 ^b	0.99 ± 0.44	1.77 ± 0.78

CTDI, CT dose.

Mean ± standard deviation and range are given unless indicated otherwise.

^aSimulated for comparison only; not administered.

^bStatistically significant difference ($p < 0.05$) as compared with the standard dose, with reduced scan length.

^cNote the CTDI value depends on the scan length and the dependence of radiation dose and scan length is subject to a power law greater than linear.

were seen when applying IR at reduced dose. More details regarding the individual risk classification based on Agatston score categories are provided in Table 4. In total, 38 (23%) patients were assigned to a different risk category because of a changed Agatston score as compared with FBP standard dose [agreement 77%, $k = 0.70$, 95% CI (0.62–0.78)]. When IR was used, excellent agreement was observed, with only 8 (5%) patients being reclassified [agreement 95%, $k = 0.94$, 95% CI (0.89–0.98)]. Additionally, the impact on age- and sex-adjusted percentile risk classification was assessed

(Table 5). Applying reduced tube current with FBP reconstruction would have resulted in reclassification of 26 (16%) patients to a different risk percentile. In 15 (9%) patients, the difference was more than 1 category. All these patients were in the 0% risk category but shifted to a substantially higher risk owing to the occurrence of false positive calcium detection in the reduced-dose FBP reconstruction. Reconstruction of the reduced-dose scans with IR resulted in a reclassification of 7 (4%) patients. In none of these patients was the difference more than 1 risk category. More details are provided in Table 5.

Figure 1. Noise for FBP reconstruction at standard dose vs FBP and IR reconstructions at reduced dose. For the FBP reconstruction at standard dose, the median noise was 14.0 HU (quartiles 12.9 and 15 HU). When the dose was reduced, FBP reconstruction gave a much higher median noise (27.3 HU; quartiles 24.7 and 29.3 HU). However, the use of IR, even at reduced dose, gave a median noise only slightly greater than FBP at standard dose (16.2 HU; quartiles 14.6 and 17.5 HU). *compared with FBP standard dose. FBP, filtered back-projection; HU, Hounsfield unit; IR, iterative reconstruction.

Table 3. Comparison of mean Agatston scores across the various risk categories

CAC risk classification	<i>n</i>	FBP standard dose	FBP reduced dose	IR reduced dose	Difference FBP reduced dose—FBP standard dose	Difference IR reduced dose—FBP standard dose
All patients	163	184.8 ± 346.4	215.2 ± 380.1 ^a	185.3 ± 351.3	30.4 ± 50.4 ^a	0.5 ± 25.2
0	47	0 ± 0	1.3 ± 3.0 ^a	0 ± 0	1.3 ± 3.0 ^a	0 ± 0
1–10	7	3.6 ± 2.9	11.4 ± 4.5 ^a	3.9 ± 3.2	7.9 ± 5.6 ^a	0.3 ± 1.7
11–100	50	54.5 ± 25.1	70.3 ± 34.2 ^a	52.2 ± 26.0	15.8 ± 17.2 ^a	–2.4 ± 9.1
101–400	36	225.4 ± 88.2	266.6 ± 103.8 ^a	222.3 ± 97.2	41.3 ± 30.2 ^a	–3.1 ± 24.2
401–1000	19	605.9 ± 181.9	717.8 ± 225.7 ^a	621.4 ± 196.3	112.0 ± 86.6 ^a	15.5 ± 61.7
>1000	4	1935.0 ± 241.7	2045.5 ± 299.6	1939.3 ± 278.1	110.5 ± 76.9	4.3 ± 37.9

CAC, coronary artery calcium; FBP, filtered back-projection; IR, iterative reconstruction.

^aStatistically significant difference as compared with FBP standard dose.

All in all, of the 47 patients without calcium on the standard examination, 15 (32%) would have been incorrectly classified as having coronary artery disease on the basis of the FBP reduced dose images. Overall, 38 (23%) patients would have been assigned to a different category because of an elevated Agatston score as compared with standard-dose FBP. In addition to absolute scores, adjusted percentiles for that person's age and sex are also frequently used.^{12,13} For 5 of the 47 patients

without any calcium the false positive detection of CAC would have meant a shift in age- and sex-adjusted CAC risk from 0% to the uppermost quartile. A clinical example is provided in Figure 2.

Intra- and interobserver agreement was excellent for all series of measurements, as demonstrated by close correlations with small differences and an overall low variability with limits

Table 4. Agreement in overall CAC risk classification

A		FBP reduced dose						
		FBP standard dose	0	32	14	1	–	–
–	47		0	1–10	11–100	101–400	401–1000	>1000
Total	1–10		–	2	5	–	–	–
7	11–100		–	–	40	10	–	–
50	101–400		–	–	–	30	6	–
36	400–1000		–	–	–	–	17	2
19	>1000		–	–	–	–	–	4
4	Total	32	16	46	40	23	6	163
B		IR reduced dose						
		0	1–10	11–100	101–400	401–1000	>1000	Total
FBP standard dose	0	47	–	–	–	–	–	47
	1–10	–	7	–	–	–	–	7
	11–100	–	–	48	2	–	–	50
	101–400	–	–	3	33	–	–	36
	400–1000	–	–	–	2	16	1	19
	>1000	–	–	–	–	–	4	4
	Total	47	7	51	37	16	5	163

CAC, coronary artery calcium; FBP, filtered back-projection; IR, iterative reconstruction.

(A) FBP standard dose compared with FBP reduced dose [agreement 77%, $k = 0.70$, 95% CI (0.62–0.78)]. (B) FBP standard dose compared with IR reduced dose [agreement 95%, $k = 0.94$, 95% CI (0.89–0.98)]. Numbers in rows and columns give the CAC risk classification. The diagonal elements (shaded) represent complete agreement; off-diagonal numbers represent differences.

Table 5. Agreement in age- and sex-adjusted percentile CAC risk classification

A		FBP reduced dose						
		0%	1–25%	26–49%	50–75%	76–95%	>95%	Total
FBP standard dose	0%	32	–	–	10	5	–	47
	1–25%	–	4	1	–	–	–	5
	26–49%	–	–	20	2	–	–	22
	50–75%	–	–	–	33	5	–	38
	76–95%	–	–	–	–	37	3	40
	>95%	–	–	–	–	–	11	11
	Total	32	4	21	45	47	14	163
B		IR reduced dose						
		0%	1–25%	26–49%	50–75%	76–95%	>95%	Total
FBP standard dose	0%	47	–	–	–	–	–	47
	1–25%	–	5	–	–	–	–	5
	26–49%	–	2	20	–	–	–	22
	50–75%	–	–	1	35	2	–	38
	76–95%	–	–	–	1	39	–	40
	>95%	–	–	–	–	1	10	11
	Total	47	7	21	36	42	10	163

CAC, coronary artery calcium; FBP, filtered back-projection; IR, iterative reconstruction.

(A) FBP standard dose compared with FBP reduced dose [agreement 84%, $k = 0.80$, 95% CI (0.72–0.87)]. (B) FBP standard dose and IR reduced dose [agreement 96%, $k = 0.95$, 95% CI (0.91–0.99)]. Numbers in rows and columns indicate the percentiles. The diagonal elements (shaded) represent complete agreement; off-diagonal numbers represent differences.

of agreement in a relatively narrow range. However, for all measuring series (FBP standard dose, FBP reduced dose and IR reduced dose, respectively) statistical analysis revealed a significantly higher interobserver than intraobserver variability ($p < 0.0001$ for all comparisons) with larger limits of agreement. Moreover, for FBP reduced dose significantly higher intra- and interobserver variabilities with substantially

larger limits of agreement were observed when compared with FBP standard dose and when compared with IR reduced dose, respectively ($p < 0.0001$ for all comparisons). Interestingly, IR reduced dose showed a slightly, but significantly lower intraobserver variability ($p < 0.001$) with somewhat smaller limits of agreement than FBP standard dose, whereas no discrepancies between both methods were found for interobserver variability

Figure 2. Clinical example of a 76-year-old female presenting for cardiovascular risk assessment. The image in panel (a) was obtained using the reference protocol with standard radiation dose (CTDI = 8.5 mGy) and reconstructed with FBP (noise $N = 12.1$). Total Agatston score was 0. Images in panels (b, c) were acquired using reduced radiation dose (CTDI = 2.6 mGy). In panel (b), FBP reconstruction was applied. Increased noise ($N = 32.5$ HU) can be observed as also reflected by a potential false-positive lesion (arrow). Total Agatston score was calculated to be 3. In panel (c), reconstruction with IR resulted in reduced noise ($N = 15.2$ HU) and an Agatston score of 0, comparable to the reference standard. CTDI, CT dose index; FBP, filtered back-projection; HU, Hounsfield unit; IR, iterative reconstruction.

Table 6. Intra- and interobserver agreement of repeated CAC measurements

	Correlation coefficient (<i>r</i>)	Paired difference mean (95% CI)	Limits of agreement lower to upper 95% limit (95% CI)	Variability
Intraobserver agreement				
FPB standard dose	0.999 ^a	0.04 (−0.35, 0.44) ^b	−4.9 (−5.6, −4.3) −5.0 (4.4, 5.7)	0.22%
FBP reduced dose	0.999 ^a	0.03 (−0.72, 0.78) ^b	−9.5 (−10.8, −8.3) −9.6 (8.3, 10.9)	0.95%
IR reduced dose	0.999 ^a	−0.20 (−0.49, 0.09) ^b	−3.9 (−4.4, −3.4) −3.5 (3.0, 4.0)	0.25%
Interobserver agreement				
FPB standard dose	0.999 ^a	1.13 (−0.27, 1.87) ^b	−6.9 (−7.9, −6.0) −7.5 (6.6, 8.5)	0.41%
FBP reduced dose	0.999 ^a	1.14 (−0.33, 2.60) ^b	−17.5 (−20.0, −15.0) −19.7 (17.2, 22.2)	1.96%
IR reduced dose	0.999 ^a	−0.10 (−0.66, 0.45) ^b	−7.2 (−8.1, −6.2) −7.0 (6.0, 7.9)	0.54%

CI, confidence interval.

^a*p* < 0.0001 (correlation highly significant).

^b*p* > 0.05 (difference not significant).

(*p* = 0.74). Results for intra- and interobserver variability are provided in detail in Table 6.

DISCUSSION

In the present study, an intraindividual comparison of CAC scores obtained at standard and reduced (25%) tube current was performed. FBP reconstruction at standard dose served as the gold standard. FBP reconstruction of the CAC images at reduced tube current resulted in significantly higher noise and, as a result, a significant deviation in Agatston scores. In contrast, reconstruction of the reduced dose scans with IR resulted in significant noise reduction and superior image quality. Importantly, using IR, the average Agatston score remained similar to the FBP gold standard. While reconstruction of the reduced dose images with FBP resulted in reclassification of 23% of patients to a different risk category, this percentage was minimal (5%) when applying IR. Accordingly, these observations indicate that using AIDR3D standard for image reconstruction, accurate CAC scoring can be performed with the radiation dose reduced by 75%.

In clinical practice, noise thresholds of <20 HU and <23 HU are recommended for small-/medium- and large-sized patients.¹⁴ Reduction of the tube current by 75% resulted in a significant increase in median noise from 14 to 27 HU when FBP was used for image reconstruction. The impact of this almost twofold increase in noise is reflected by the significantly higher average Agatston score on FBP reduced dose images as compared with the gold standard. In other words, the increased noise can result in “false-positive” lesions, while the apparent size of true lesions may be artificially increased. False-positive lesions may have considerable impact on risk stratification, as set out in the “Results” section. In practice, risk assessment would have been incorrectly revised upward in these patients on the basis of the international guidelines on cardiovascular disease prevention.^{12,13} Application of IR by means of AIDR3D standard to the reduced dose images resulted in a much better noise profile. Median noise was significantly reduced from 27 to 16 HU, close to the noise level on standard CAC images. As a result, image quality was more comparable to the gold-standard images and, importantly, no false positive scores occurred. In addition, no

significant deviation of the average Agatston score was observed, with only a very small difference of 0.5 on average. Reclassification of risk category was limited, with only ≤5% of patients being reclassified to another either absolute or age- and sex-adjusted percentile risk. These values are well within accepted ranges; in fact, larger percentages of reclassified patients have been reported when comparing different scanners or even different reconstruction intervals.^{8,15} Finally, none of the patients in the current study were shifted by more than one category when IR at reduced dose was used. Clinicians should be aware, however, that in contrast to FBP reconstruction, which invariably results in higher calcium scores, downgrading because of lower calcium scores can occur with IR.

Recently, reduction of the radiation dose associated with CAC scanning has received increasing attention. Basically, two main approaches have been described, reducing either the tube voltage or the tube current, in combination with novel reconstruction algorithms. Use of lower tube voltages requires careful recalibration and is, therefore, considered harder to implement in daily clinical practice.^{16–18} Much effort has, therefore, been focussed on tube current reduction in combination with IR. Varying results have been reported.^{7,9,19–22} While some studies reported no loss in CAC score accuracy, less favourable observations have also been described, even including the disappearance of detectable calcium.⁹ Such findings highlight the importance of testing the allowable dose reduction for each IR algorithm individually.

Our current observations are in line with earlier studies using the same IR algorithm AIDR3D, and they build further on these observations. In a phantom study using rigorous image quality and CAC score accuracy control, Blobel et al determined a dose reduction potential of around 80% without loss in score accuracy when using AIDR3D in comparison with the dose currently used for image processing with FBP.¹⁰ The feasibility of considerable dose reduction using AIDR3D was further investigated by Rodrigues et al, who performed a small patient study in combination with phantom experiments.¹¹ Instead of repeated scanning at lower dose, artificial noise was added to the raw data from 27 CAC scoring studies obtained with standard radiation

exposure, confirming no change in absolute Agatston scores or percentile risk scores when simulating tube current reduction by 75%. In a more recent study from the USA, Choi et al performed 74% reduced-dose acquisition reconstructed with AIRD3D and standard-dose acquisition using FBP reconstruction and for each of these reported excellent rescan agreement after single repetition of each scan in a large cohort of patients.²³ Our current study, providing a more extensive analysis of both the absolute Agatston scores and the implications for risk assessment in a large series of (non-obese) patients in Europe, provides a definite confirmation that accuracy is maintained at the reduced dose of 25%.

We found almost perfect agreement for repeated measurements, with variability values ranging between 0.2 and 1% for intraobserver and between 0.4 and 2% for interobserver comparison. These values are in fact lower than frequently found in the literature (e.g. respectively 1 and 3%,²⁴ presumably because of the relatively large proportion of calcium-free data sets and the exclusion of data sets with elevated noise levels or recognizable movement artefacts). Interestingly, the variability for “FPB reduced dose” was greater for “FPB standard dose” or for “IR reduced dose”, which suggests that greater image noise may influence the (reproducibility of) visualization of calcification.

Importantly, in our current study, patients were enrolled in the context of comprehensive clinical cardiovascular risk assessment, thus representing the target population for CAC scoring. In addition, a novel approach was used to allow repeated scanning for intraindividual comparisons without any dose penalty.

An important limitation of our study is that the effects on volume or mass scores were not assessed. Although these quantification methods may be more accurate, the Agatston score, however, is the most commonly used method. For similar practical reasons, only one level of IR (AIRD3D “standard”) was investigated. The effect of other IR settings was not investigated, since AIRD3D “standard” is the recommended setting for quantitative cardiac applications. The mean image noise values were lower than the 23 HU target value. To avoid false-positives, it is important that the actual scan parameters take the increased absorption in the liver region (caudal part of the CAC scan) into account. If this is not the case, actual noise might exceed the target values, with the risk of degraded image quality and accuracy. Note that we do not regard the exclusion of excessively obese patients as a significant limitation of the study. This was a technical feature that allowed us to conduct the study in a manner that was safe for the patients and guaranteed adequate image quality for comparisons. There seems to be no reason why the methodological conclusion of the study (i.e. the potential of IR for reducing radiation dose) should not be generalizable to patients of any weight.

In conclusion, the application of IR by means of AIRD3D “standard” allows one to maintain accurate Agatston scores and cardiovascular risk stratification when the tube current is reduced by 75%, thus substantially decreasing the patient’s exposure to ionizing radiation.

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