Received:
22 September 2015

Revised:
30 March 2016

Accepted:
6 June 2016

<http://dx.doi.org/10.1259/bjr.20150780>

Cite this article as:

Rodrigues MA, Williams MC, Fitzgerald T, Connell M, Weir NW, Newby DE, et al. Iterative reconstruction can permit the use of lower X-ray tube current in CT coronary artery calcium scoring. *Br J Radiol* 2016; **89**: 20150780.

FULL PAPER

Iterative reconstruction can permit the use of lower X-ray tube current in CT coronary artery calcium scoring

¹MARK A RODRIGUES, MB ChB, FRCR, ²MICHELLE C WILLIAMS, MB ChB, ¹THOMAS FITZGERALD, MB ChB, FRCR, ³MARTIN CONNELL, BSc, ^{3,4}NICHOLAS W WEIR, MSc, PhD, ²DAVID E NEWBY, PhD, MD, ³EDWIN J R VAN BEEK, MD, PhD and ³SAEED MIRSADEE, MD, PhD

¹Department of Radiology, Royal Infirmary of Edinburgh, Edinburgh, UK

²British Heart Foundation/University of Edinburgh Centre for Cardiovascular Science, Queen's Medical Research Institute, Edinburgh, UK

³Clinical Research Imaging Centre, University of Edinburgh, Edinburgh, UK

⁴Department of Medical Physics, Royal Infirmary of Edinburgh, Edinburgh, UK

Address correspondence to: Dr Mark Alexander Rodrigues

E-mail: mark.rodrigues@ed.ac.uk

Objective: CT coronary artery calcium scoring (CACS) is additive to traditional risk factors for predicting future cardiac events but is associated with relatively high radiation doses. We assessed the feasibility of CACS radiation dose reduction using a lower tube current and iterative reconstruction (IR).

Methods: Artificial noise was added to the raw data from 27 CACS studies from patients who were symptomatic to simulate lower tube current scanning (75, 50 and 25% original current). All studies were performed on the same CT scanner at 120 kVp. Data were reconstructed using filtered back projection [Quantum Denoising Software (QDS+)] and IR [adaptive iterative dose reduction three dimensional mild, standard and strong]. Agatston scores were independently measured by two readers. CACS percentile risk scores were calculated.

Results: At 75, 50 and 25% tube currents, all adaptive iterative dose reduction (AIDR) reconstructions decreased

image noise relative to QDS+ ($p < 0.05$). All AIDR reconstructions resulted in small reductions in Agatston score relative to QDS+ at the standard tube current ($p < 0.05$). Agatston scores increased with QDS+ at 75, 50 and 25% tube current ($p < 0.05$), whereas no significant change was observed with AIDR mild at any tested tube current. No difference in the percentile risk score with AIDR mild at any tube current occurred compared with QDS+ at standard tube current ($p > 0.05$). Interobserver agreement for AIDR mild remained excellent even at 25% tube current (intraclass correlation coefficient 0.997).

Conclusion: Up to 75% reduction in CACS tube current is feasible using AIDR mild.

Advances in knowledge: AIDR mild IR permits low tube current CACS whilst maintaining excellent intraobserver and interobserver variability and without altering risk classification.

INTRODUCTION

Coronary artery calcification is an established marker of atherosclerosis¹ and is associated with cardiovascular morbidity and mortality.^{2,3} CT can be used to quantify coronary artery calcification using various scoring systems, such as the Agatston,⁴ volume and mass scores.⁵ These have been shown to be additive to traditional risk factor scores in the prediction of future cardiac events.^{6–8}

According to current standards, calcium scoring is performed at a tube voltage of 120 kV using a filtered back-projection (FBP) reconstruction algorithm in order to standardize quantification.⁹ However, such CT coronary artery calcium scoring (CACS) is associated with a significant radiation dose, ranging from 0.8 to 10.5 mSv.¹⁰ These

radiation doses are high when compared with advances in low-dose CT coronary angiography.^{11,12} This is particularly important, as the American College of Cardiology guidelines recommend assessing coronary artery calcification for patients with low-to-intermediate cardiovascular risk, even if asymptomatic.¹³

Methods to reduce radiation dose in cardiac imaging include prospective electrocardiogram triggering, reducing the tube voltage, reducing the tube current and optimizing the scan range. These techniques can be applied to the non-contrast CT scans used for CACS, but have the potential to influence calcium quantification. Lowering the tube voltage would result in a change in Hounsfield units (HU) and therefore the Agatston score, whilst reducing

Figure 1. (a) Image noise and (b) signal-to-noise ratio: data are presented as median $\pm$ interquartile range. * $p < 0.05$ compared with Quantum Denoising Software (QDS+) at the same tube current; ** $p < 0.001$ compared with QDS+ at the same tube current. AIDR-3D, adaptive iterative dose reduction three dimensional; HU, Hounsfield units.

the tube current can lead to increased image noise and therefore false-positive results when using FBP reconstruction algorithms.¹⁴

Iterative reconstruction (IR) algorithms can be applied to raw cardiac CT data and can reduce image noise to allow improved

image quality and/or reduced radiation dose.^{11,12,15} Phantom studies have shown that one IR algorithm [adaptive iterative dose reduction three dimensional (AIDR-3D) (Toshiba Medical Systems, Nasu, Japan)] can permit an 80% reduction in radiation dose without significantly altering Agatston scores.¹⁶ In clinical studies, other IR algorithms [Iterative Reconstruction in

Table 1. Agatston scores (in Agatston units) for different simulated tube currents and reconstruction algorithms

Tube current (%)	QDS+	bFBP	AIDR-3D mild	AIDR-3D standard	AIDR-3D strong
100	397 (107–983)	401 (109–987) ^a	360 (96–934) ^a	349 (87–919) ^a	317 (77–860) ^a
75	416 (108–988) ^b	419 (110–991) ^{a,b}	357 (88–930) ^a	340 (85–909) ^a	295 (76–843) ^a
50	432 (112–993) ^b	443 (113–1001) ^{a,b}	330 (88–921) ^a	306 (79–890) ^{a,c}	291 (75–834) ^{a,c}
25	475 (193–1053) ^b	478 (203–1064) ^{a,b}	303 (88–896) ^a	293 (77–887) ^{a,c}	293 (74–821) ^{a,b}

AIDR-3D, adaptive iterative dose reduction three dimensional; bFBP, basic filtered back-projection; QDS+, Quantum Denoising Software. Data are presented as median (interquartile range).

^a $p < 0.001$ compared with QDS+ at 100% tube current (reference technique).

^b $p < 0.001$ compared with 100% tube current with the respective reconstruction algorithm.

^c $p < 0.05$ compared with 100% tube current with the respective reconstruction algorithm.

Image Space (Siemens Healthcare, Forchheim, Germany)] and sinogram-affirmed iterative reconstruction (Siemens Healthcare, Forchheim, Germany) showed no significant effect on the Agatston score or risk stratification when used with full-dose imaging.¹⁷

This study assessed the effect of the AIDR-3D IR algorithm on coronary artery calcium score and patient risk stratification using simulated reductions in tube current in order to assess the clinical implications of applying this radiation dose reduction technique.

METHODS AND MATERIALS

Study design

All studies were performed using a 320-row multidetector CT scanner (Aquilion™ ONE, Toshiba Medical Systems, Nasu, Japan). First, phantom studies were performed to assess whether simulated reductions in tube current would have the same effect on image noise as scanning with a reduced tube current. Imaging data from 27 patients were then reconstructed with 5 different reconstruction algorithms with various levels of additional image noise to replicate the effect of reducing the tube current by 25, 50 and 75%.

Figure 2. Images of the right coronary artery reconstructed with Quantum Denoising Software (QDS+) (a-d) and adaptive iterative dose reduction three dimensional (AIDR-3D) mild (e-h) at various tube voltages. The calcium scoring software highlights the tissues fulfilling the Agatston scoring inclusion criteria. Images a-d are reconstructed with QDS+ (100, 75, 50 and 25% tube currents, respectively). A “real” calcified plaque is indicated by the open arrows. As the current is reduced, there is an increase in noise, leading to multiple spurious calcified plaques (closed arrows in images c-d). Images e-h are the corresponding images reconstructed with AIDR-3D mild. The markedly reduced number and size of spurious plaques at 25% tube current can be noticed (h).

Phantom studies

An anthropomorphic thoracic phantom with a 20 × 30-cm body diameter (QRM GmbH, Moehrendorf, Germany) was scanned with and without an additional 5-cm muscle equivalent wrap to simulate different body constitutions (large and standard phantoms, respectively). CT imaging of both phantoms was performed using a tube voltage of 120 kV and four different tube currents. For the large phantom, tube currents of 320, 240, 160 and 80 mA were used and for the standard phantom, tube currents of 200, 150, 100 and 50 mA were used.

Patient studies

Participants with suspected coronary artery disease were recruited as part of the Scottish computed tomography of the heart (SCOT-HEART) study (NCT01149590).¹⁸ This study was approved by the local research ethics committee, and informed consent was obtained from all participants.

Participants underwent non-contrast CT for the assessment of coronary artery calcium using a tube voltage of 120 kV, and the tube current was adjusted based on the body mass index (BMI) (Appendix A). The scan range was from 20 mm below the carina to the base of the heart with a volume size of 80, 100, 120, 140 or 160 mm. A targeted acquisition at 75% of the R–R interval was obtained. Prior to imaging, patients with a heart rate >60 bpm received i.v. metoprolol as previously described.¹⁸

Image reconstruction

Artificial noise was added to the raw data of the phantom images with highest tube current and to the patient images to create images with simulated tube current reductions of 25, 50 and 75% (NoiseAdd; Toshiba Medical Systems, Nasu, Japan). All images were reconstructed using the FC12 kernel and with five different reconstruction algorithms: basic FBP (bFBP), Quantum Denoising Software (QDS+) FBP and IR (AIDR-3D) with three levels of blending (mild, standard and strong). Toshiba recommend QDS+ as the standard reconstruction/reference technique for calcium scoring.

Image analysis

Images were analyzed by a trained observer (MAR), who was completely independent from the SCOTHEART study, on a dedicated post-processing workstation (Vitrea Fx, v. 6.3, Vital Images, Minnetonka, MN) using calcium score analysis software (VScore,

Vital Images, Minnetonka, MN). Analysis was performed blinded to the results of other reconstructions and in random order to reduce the likelihood of recall bias. To assess interobserver and intraobserver variabilities, images were assessed in 24 patients, in whom all imaging data were available, by a second independent observer (TF) blinded to other results.

For phantom studies, the mean and standard deviation (SD) of the HU for five different regions of interest (ROIs) (Appendix B) were calculated for each of the different simulated tube currents.

The standard Agatston technique was used to quantify coronary artery calcification in patient studies. The calculation is based on the weighted density score (1 for 130–199 HU, 2 for 200–299 HU, 3 for 300–399 HU and 4 for 400 HU and greater) given to the highest attenuation value (HU) multiplied by the area (in square millimetres) of the coronary calcification.⁴ Calcium volume scoring method was also used as described previously.¹⁹ ROIs were drawn in all vessels and total Agatston and volume scores were obtained by summing the weighted scores from each vessel.

The absolute Agatston score was categorized as low (≤ 100 AU), intermediate (101–400 AU), high (401–1000 AU) or very high (> 1000 AU). It was also categorized as non-extensive (≤ 400 AU) or extensive (> 400 AU) for analysis. The CACS percentile based on age, sex and ethnicity was calculated from the Agatston score using previously published distributions from a cohort of healthy asymptomatic individuals.²⁰ For patients younger than 45 years, the age 45 years was used for the calculation of the CACS percentile. These were categorized as ≤ 90 th percentile or > 90 th percentile for analysis.

For all patient reconstructions, image noise was defined as the SD of HU in a 500-mm² oval ROI in the ascending aorta. Signal-to-noise ratio (SNR) was calculated as the mean HU within the ROI divided by its SD. For each patient, the noise and SNR in the different reconstructed data sets were measured on the same image slice.

Statistical analysis

Data analysis was performed using SPSS® v. 18 for Mac (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) and GraphPad Prism® v. 6 for Mac (GraphPad Software, Inc., La

Table 2. Calcium volume scores (in cubic millimetres) for different simulated tube currents and reconstruction algorithms

Tube current (%)	QDS+	bFBP	AIDR-3D mild	AIDR-3D standard	AIDR-3D strong
100	348 (120–762)	353 (125–766) ^a	320 (121–760) ^a	310 (112–759) ^a	295 (104–756) ^a
75	355 (122–767) ^b	359 (135–771) ^{a,b}	317 (118–760) ^c	309 (112–756) ^a	296 (105–756) ^a
50	384 (166–783) ^b	394 (172–796) ^{a,b}	318 (120–761)	307 (111–757) ^a	282 (103–753) ^a
25	430 (267–885) ^b	510 (270–935) ^{a,b}	323 (140–768) ^d	299 (110–761) ^c	265 (102–755) ^{a,d}

AIDR-3D, adaptive iterative dose reduction three dimensional; bFBP, basic filtered back-projection; QDS+, Quantum Denoising Software. Data are presented as median (interquartile range).

^a $p < 0.001$ compared with QDS+ at 100% tube current (reference technique).

^b $p < 0.001$ compared with 100% tube current with the respective reconstruction algorithm.

^c $p < 0.05$ compared with QDS+ at 100% tube current (reference technique).

^d $p < 0.05$ compared with 100% tube current with the respective reconstruction algorithm.

Jolla, CA). Non-normally distributed data are presented with median and interquartile range. Statistical significance was assessed using Wilcoxon signed-rank test. Intraobserver and interobserver variabilities were assessed using Bland–Altman plots and intraclass correlation coefficient (ICC). A statistically significant difference was defined as a two-sided p -value <0.05 .

RESULTS

Phantom studies

Images with both the large- and standard-size phantoms showed no significant difference in the mean attenuation density at any of the five ROIs between actual or simulated tube currents at comparative doses ($p > 0.05$).

Objective image quality in patient studies

In the images from the 27 patients (Appendix C), AIDR-3D with mild, standard and strong levels of blending reduced noise compared with the QDS+ reconstruction algorithm at simulated tube currents of 75, 50 and 25% ($p = 0.002$ for adaptive iterative dose reduction mild at 75%; $p < 0.001$ for all other reconstructions and simulated currents). AIDR-3D with standard and strong levels of blending also reduced image noise at 100% tube current compared with QDS+ ($p < 0.001$) (Figure 1a). All AIDR-3D reconstructions resulted in a higher SNR compared with QDS+ at 50 and 25% simulated tube currents ($p < 0.001$). SNR was also higher with AIDR-3D standard and strong relative to QDS+ at 100 and 75% tube currents ($p < 0.001$) (Figure 1b).

Agatston score

At standard tube current (100%), AIDR-3D reconstructions at all levels of blending led to a small but significant reduction in Agatston score compared with the QDS+ reconstruction (reference technique) ($p < 0.001$) (Table 1). This reduction in Agatston score relative to the reference technique was evident at all simulated tube currents with all levels of AIDR-3D blending ($p < 0.001$ for all).

Reducing the simulated tube current led to an increase in Agatston score for QDS+ and bFBP reconstructions and a small decrease in Agatston score for AIDR-3D at all levels of blending. These differences became statistically significant at 75% tube current for QDS+ and bFBP reconstructions ($p < 0.001$ for all) and at 50% tube current for AIDR-3D standard [$p = 0.174$, $p = 0.003$ and $p = 0.006$ (100% tube current vs 75, 50 and 25% simulated current, respectively)] and AIDR-3D strong [$p = 0.112$, $p = 0.003$ and $p < 0.001$ (100% tube current vs 75, 50 and 25% simulated current, respectively)]. There was no change with AIDR-3D mild at any test tube current [$p = 0.689$, $p = 0.317$ and $p = 0.253$ (100% tube current vs 75, 50 and 25% simulated current, respectively)] (Figure 2).

Calcium volume score

At the full tube current, all levels of AIDR-3D reconstruction led to a small but significant reduction in calcium volume scores compared with the QDS+ reconstruction algorithm ($p < 0.001$ for all) (Table 2). There was no difference in the volume score between QDS+ at 100% tube current (reference technique) and AIDR-3D mild at 50 and 25% simulated tube current ($p = 0.091$ and $p = 0.341$, respectively). Volume scores were reduced relative to the reference technique with AIDR-3D

Table 3. Agatston scores [in Agatston units (AU)] and calcium volume (Vol) scores (in cubic millimetres) for different simulated tube currents and reconstruction algorithms according to body mass index (BMI)

BMI	≤ 30 ($n = 15$)						> 30 ($n = 12$)					
	QDS+			AIDR-3D mild			QDS+			AIDR-3D mild		
Tube current (%)	AU	Vol	AU	AU	Vol	Vol	AU	Vol	AU	AU	Vol	Vol
100	458 (228–1044)	413 (254–900)	456 (207–1031)	411 (249–889)	412 (248–890)	335 (11.5–706.5)	307.5 (19.75–656)	300.5 (10–698.75) ^a	300.5 (9.25–689.25)	289 (13–638.5)	287.5 (13.5–652.75)	288 (15–666.25)
75	460 (225–1056) ^a	414 (255–934) ^a	459 (207–1031)	412 (248–890)	409 (243–905)	350.5 (15.5–727.75) ^a	316.5 (26.75–668.75) ^a	300.5 (10–698.75) ^a	300.5 (9.25–689.25)	288.5 (9–702.5)	288.5 (15–666.25)	293.5 (28.5–684.5) ^a
50	457 (240–1104) ^a	419 (255–967) ^a	461 (203–1028)	409 (243–905)	410 (253–926) ^a	366 (33–770.75) ^a	341.5 (54.25–733) ^a	288.5 (9–702.5)	288.5 (9–702.5)	288.5 (15–666.25)	293.5 (28.5–684.5) ^a	293.5 (28.5–684.5) ^a
25	475 (315–1187) ^a	430 (267–1063) ^a	456 (209–1037)	410 (253–926) ^a	410 (253–926) ^a	431 (118–875) ^a	469.5 (233–840) ^a	276.5 (13.25–674)	276.5 (13.25–674)	276.5 (13.25–674)	276.5 (13.25–674)	276.5 (13.25–674)

AIDR-3D, adaptive iterative dose reduction three dimensional; QDS+, Quantum Denoising Software. Data are presented as median (interquartile range).

^a $p < 0.05$ compared with 100% tube current with the respective reconstruction algorithm.

mild at 75% simulated tube current ($p = 0.001$) and with AIDR-3D standard and AIDR-3D strong at 75, 50 and 25% simulated tube current [$p < 0.001$ for all, except AIDR-3D standard at 25% ($p = 0.033$)].

Reducing the tube current led to an increase in the volume score for QDS+ and bFBP at 75, 50 and 25% tube current ($p < 0.001$ for all) and at 25% tube current for AIDR-3D mild ($p = 0.002$), whilst the volume score with AIDR-3D strong decreased at 25% simulated current ($p = 0.037$).

Effect of patient body mass index and degree of atherosclerosis

With the QDS+ reconstruction, increases in the Agatston score occurred with all simulated reductions in tube current in both the non-obese group ($BMI \leq 30$) [$p = 0.014$, $p = 0.001$ and $p = 0.001$ (100% tube current vs 75, 50 and 25% simulated current, respectively)] and obese group ($BMI > 30$) [$p = 0.004$, $p = 0.003$ and $p = 0.002$ (100% tube current vs 75, 50 and 25% simulated current, respectively)], as well as those with extensive atherosclerosis (>400 AU) [$p = 0.001$, $p = 0.002$ and $p = 0.001$ (100% tube current vs 75, 50 and 25% simulated current, respectively)]. The Agatston score increased in the non-extensive atherosclerosis group (≤ 400 AU) at 50 and 25% simulated tube currents ($p = 0.002$ and $p = 0.001$, respectively) (Tables 3 and 4).

In contrast, there was no change in the Agatston scores with AIDR-3D mild at any tested current, irrespective of the BMI or degree of atherosclerosis ($p > 0.05$ for all).

Intraobserver and interobserver variability

Intraobserver and interobserver agreements for the Agatston scoring of full-dose images with QDS+ and AIDR-3D mild were excellent ($ICC = 1$) (Figure 3). Overall, the mean intraobserver variability was 0.3% for QDS+ and 0.3% for AIDR-3D mild, and the interobserver variability was 1.1 and 0.3%, respectively. The variability remained similar at lower simulated currents (50 and 25% tube current), especially when using AIDR-3D mild blending [the mean intraobserver variability was 0.4% for QDS+ and 0.3% for AIDR-3D mild (ICC 0.998 and 0.999, respectively)]; the mean interobserver variability was 1.4% for QDS+ and 0.3% for AIDR-3D mild (ICC 0.997 and 0.998, respectively)].

Implication on risk assessment

Absolute Agatston score categories were identical to the reference technique in 25 (92.6%) cases for AIDR-3D mild at 100, 75, 50 and 25% tube currents. The two patients who were reclassified had an Agatston score with the reference technique near a border between absolute Agatston categories (one patient had an Agatston score of 107 AU and the other had an Agatston score of 1002 AU), and therefore the small underestimation associated with AIDR-3D mild resulted in reclassification. No patients were reclassified from an Agatston score of 0 with the reference technique to a positive score with AIDR-3D mild reconstruction at any simulated tube current.

AIDR-3D mild resulted in identical CACS percentile categories with the reference technique at all tested levels of tube

Table 4. Agatston scores [in Agatston units (AU)] and calcium volume (Vol) scores (in cubic millimetres) for different simulated tube currents and reconstruction algorithms according to the degree of atherosclerosis (extensive atherosclerosis = Agatston score >400 AU, non-extensive atherosclerosis = Agatston score ≤ 400 AU)

Degree of atherosclerosis	Non-extensive atherosclerosis ($n = 14$)						Extensive atherosclerosis ($n = 13$)					
	QDS+			AIDR-3D mild			QDS+			AIDR-3D mild		
	AU	Vol		AU	Vol		AU	Vol		AU	Vol	
100	136 (24.5–306.5)	147 (25.25–270.75)		127.5 (23.75–300.25)	144 (23–261.75)		983 (691–1074.5)	762 (611.5–925)		934 (670.5–1036.5)	760 (606–910)	
75	133.5 (28.5–309.75)	146.5 (28.25–282.5) ^a		120 (24–300.75)	140 (22.5–263)		988 (706.5–1091) ^a	767 (634.5–950.5) ^a		930 (675.5–1031.5)	760 (617.5–919.5)	
50	143 (35–308.5) ^a	170 (64.75–302.25) ^a		122 (19–299.75)	141.5 (23–264.25)		993 (744.5–1125) ^a	783 (657–981) ^a		921 (681–1035)	761 (628.5–931)	
25	215 (117.25–361) ^a	302.5 (174.25–407) ^a		118 (15.75–286)	153.5 (33.5–272) ^a		1053 (848–1221) ^a	885 (742–1094) ^a		896 (674–1038.5)	768 (647.5–932.5) ^a	

AIDR-3D, adaptive iterative dose reduction three dimensional; QDS+, Quantum Denoising Software.

Data are presented as median (interquartile range).

^a $p < 0.05$ compared with 100% tube current with the respective reconstruction algorithm.

Figure 3. Bland-Altman plots showing the intraobserver variability (a) and interobserver variability (b) for Agatston calcium score using Quantum Denoising Software (QDS+) and adaptive iterative dose reduction three dimensional (AIDR-3D) mild reconstructions at different tube currents. Dotted lines are representing the bias and limits of agreement.

current. The median calcium percentile score with the reference technique was 86 (interquartile range 74–94). The percentile scores with AIDR-3D mild at all tested levels of tube current did not differ from the reference technique [median scores (interquartile range) at 100, 75, 50 and 25% tube currents were 86 (74–94), 87 (76–94), 87 (77–94) and 89 (83–96), respectively; $p > 0.05$].

DISCUSSION

Keeping radiation exposure as low as reasonably achievable whilst maintaining diagnostic quality is an important challenge in CT imaging. This is particularly pertinent to CT CACS, as guidelines that recommend its use as a screening tool in patients who are asymptomatic with intermediate and low-to-intermediate risk of cardiovascular disease are likely to result in a substantial increase in medical ionizing radiation exposure.^{13,21}

One of the main difficulties limiting radiation dose reduction in CT CACS is the fixed tube voltage (120 kVp) required for Agatston scoring. Attempts to reduce dose by decreasing tube current with FBP reconstruction have resulted in false-positive lesions.¹⁴ However, recent studies^{22,23} showed that FBP did not

affect the Agatston score when the dose was reduced by up to 80%. These *ex vivo* studies used a single standard-sized phantom (30 × 20 cm) and it is not clear whether the results would be reproducible in an *in vivo* setting with patients who are larger.

The present study showed that AIDR-3D reduced image noise and yielded superior SNR at low tube currents (up to 75% reduction) compared with FBP, which is in keeping with results from several other studies.^{11,17,24–26} The benefit of AIDR-3D was most apparent at lower tube currents.

As the CACS in this study is obtained by volume imaging without milliamperage (mA) modulation, and the scan length and tube potential are constant, the dose-length product has a straight relationship with mA. Therefore, the potential reduction in dose is by a factor of 4 when the mA is quartered.

In line with a recent *ex vivo* study, the lowest level of IR (AIDR-3D mild) was most promising for Agatston scoring and calcium volume.²³ However, even AIDR-3D mild significantly reduced Agatston scores relative to FBP at normal dose settings. This

underestimation with IR is in accordance with several other studies^{16,22,27} and is partly attributed to a reduction in the blooming effect of calcified plaques seen with FBP methods, leading to downstaging of the plaque size with IR algorithms.^{12,17} This is supported by the observation that calcium volume was significantly lower with all AIDR-3D reconstructions than with FBP at normal dose settings.

In contrast with FBP, there was no change in the Agatston score with AIDR-3D mild when the tube current was reduced by up to 75%, regardless of the patient BMI or degree of atherosclerosis, with intraobserver and interobserver agreement remaining excellent. This is in agreement with phantom studies,^{16,22} suggesting dose reduction is feasible with AIDR-3D mild.

A recent *in vivo* study assessing a type of hybrid IR (iDose; Philips Medical Systems, Best, Netherlands) demonstrated that tube current reduction of 80% was possible without affecting the Agatston score or calcium volume. However, the effects of tube current reduction on clinical scoring were not assessed.²⁸ A further study has recently shown the excellent correlation of clinical risk groups between FBP and hybrid IR at full-dose scanning.²⁹ In the present study, there remained excellent agreement of absolute and percentile risk scores with the reference technique (FBP at normal dose settings) when using AIDR-3D mild at a tube current as low as 25%. The patients who were reclassified with AIDR-3D mild were the result of small absolute changes in Agatston scores in patients who were either on the borderline between categories or relatively young, so that a small absolute change resulted in reclassification.

Some limitations should be considered. This was a small feasibility study using simulated reductions in tube current.

Artificially adding noise allowed the effect of different reconstruction algorithms on multiple different tube currents to be assessed without exposing the patients to further ionizing radiation. However, this results in estimated rather than true reductions in current. Larger studies assessing actual tube current reductions are therefore needed to validate our findings and establish the degree of dose reduction possible. Second, the software to calculate mass scores, another validated measure used to quantify coronary artery calcification, was not available at the time of the study. Future work should assess the effects on this score, as well as vessel- and lesion-specific calcium scoring, in addition to the Agatston and volume scores. We only assessed software from a single vendor. However, the IR algorithms employed by different manufacturers differ, and in experimental models, Willemink et al^{22,30} demonstrated significant differences in the Agatston score between different vendors' IR software. Accordingly, multivendor studies should be performed. The degree of dose reduction with other scanners and scanning protocols may differ, if for example there is tube current modulation, and the feasibility of dose reduction in these cases must be studied separately. Finally, our patient cohort consisted of patients who were symptomatic, with a median Agatston score of nearly 400. This may limit the validity of our results to other patient groups, such as asymptomatic screening populations, especially as there were higher percentage changes in those without extensive atherosclerosis (<400 AU), and such absolute changes are likely to have the biggest effect on percentile classifications.²⁷

CONCLUSION

Reduction of CT CACS tube current by up to 75% is feasible with the use of AIDR-3D mild. As suggested by Blobel et al,¹⁶ a correction factor may be considered as AIDR-3D mild results in a small but significant underestimation of Agatston scores.

REFERENCES

- Wexler L, Brundage B, Crouse J, Detrano R, Fuster V, Maddahi J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Writing Group. *Circulation* 1996; **94**: 1175–92. doi: <http://dx.doi.org/10.1161/01.CIR.94.5.1175>
- Hou ZH, Lu B, Gao Y, Jiang SL, Wang Y, Li W, et al. Prognostic value of coronary CT angiography and calcium score for major adverse cardiac events in outpatients. *JACC Cardiovasc Imaging* 2012; **5**: 990–9. doi: <http://dx.doi.org/10.1016/j.jcmg.2012.06.006>
- Rosen BD, Fernandes V, McClelland RL, Carr JJ, Detrano R, Bluemke DA, et al. Relationship between baseline coronary calcium score and demonstration of coronary artery stenoses during follow-up MESA (multi-ethnic study of atherosclerosis). *JACC Cardiovasc Imaging* 2009; **2**: 1175–83. doi: <http://dx.doi.org/10.1016/j.jcmg.2009.06.014>
- Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990; **15**: 827–32. doi: [http://dx.doi.org/10.1016/0735-1097\(90\)90282-T](http://dx.doi.org/10.1016/0735-1097(90)90282-T)
- Rumber JA, Kaufman L. A rosetta stone for coronary calcium risk stratification: agatston, volume, and mass scores in 11,490 individuals. *AJR Am J Roentgenol* 2003; **181**: 743–8.
- Detrano R, Guerci AD, Carr JJ, Bild DE, Burke F, Folsom AR, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008; **358**: 1336–45. doi: <http://dx.doi.org/10.1056/NEJMoa072100>
- Raggi P, Callister TQ, Cooil B, He ZX, Lippolis NJ, Russo DJ, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron-beam computed tomography. *Circulation* 2000; **101**: 850–5. doi: <http://dx.doi.org/10.1161/01.CIR.101.8.850>
- Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* 2004; **291**: 210–15. doi: <http://dx.doi.org/10.1001/jama.291.2.210>
- McCollough CH, Ulzheimer S, Halliburton SS, Shanneik K, White RD, Kalender WA. Coronary artery calcium: a multi-institutional, multimanufacturer international standard for quantification at cardiac CT. *Radiology* 2007; **243**: 527–38. doi: <http://dx.doi.org/10.1148/radiol.2432050808>

10. Marwan M, Mettin C, Pflederer T, Seltmann M, Schuhback A, Muschiol G, et al. Very low-dose coronary artery calcium scanning with high-pitch spiral acquisition mode: comparison between 120-kV and 100-kV tube voltage protocols. *J Cardiovasc Comput Tomogr* 2013; **7**: 32–8. doi: <http://dx.doi.org/10.1016/j.jcct.2012.11.004>
11. Moscariello A, Takx RA, Schoepf UJ, Renker M, Zwerner PL, O'Brien TX, et al. Coronary CT angiography: image quality, diagnostic accuracy, and potential for radiation dose reduction using a novel iterative image reconstruction technique—comparison with traditional filtered back projection. *Eur Radiol* 2011; **21**: 2130–3138. doi: <http://dx.doi.org/10.1007/s00330-011-2164-9>
12. Renker M, Nance JW Jr, Schoepf UJ, O'Brien TX, Zwerner PL, Meyer M, et al. Evaluation of heavily calcified vessels with coronary CT angiography: comparison of iterative and filtered back projection image reconstruction. *Radiology* 2011; **260**: 390–9. doi: <http://dx.doi.org/10.1148/radiol.11103574>
13. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2010; **56**: e50–103. doi: <http://dx.doi.org/10.1016/j.jacc.2010.09.001>
14. Shemesh J, Evron R, Koren-Morag N, Apter S, Rozenman J, Shaham D, et al. Coronary artery calcium measurement with multi-detector row CT and low radiation dose: comparison between 55 and 165 mAs. *Radiology* 2005; **236**: 810–14. doi: <http://dx.doi.org/10.1148/radiol.2363040039>
15. Williams MC, Weir NW, Mirsadraee S, Millar F, Baird A, Minns F, et al. Iterative reconstruction and individualized automatic tube current selection reduce radiation dose while maintaining image quality in 320-multidetector computed tomography coronary angiography. *Clin Radiol* 2013; **68**: e570–7. doi: <http://dx.doi.org/10.1016/j.crad.2013.05.098>
16. Blobel J, Mews J, Schuijff JD, Overlaet W. Determining the radiation dose reduction potential for coronary calcium scanning with computed tomography: an anthropomorphic phantom study comparing filtered backprojection and the adaptive iterative dose reduction algorithm for image reconstruction. *Invest Radiol* 2013; **48**: 857–62. doi: <http://dx.doi.org/10.1097/RLI.0b013e31829e3932>
17. Schindler A, Vliegthart R, Schoepf UJ, Blanke P, Ebersberger U, Cho YJ, et al. Iterative image reconstruction techniques for CT coronary artery calcium quantification: comparison with traditional filtered back projection *in vitro* and *in vivo*. *Radiology* 2014; **270**: 387–93. doi: <http://dx.doi.org/10.1148/radiol.13130233>
18. Newby DE, Williams MC, Flapan AD, Forbes JF, Hargreaves AD, Leslie SJ, et al. Role of multidetector computed tomography in the diagnosis and management of patients attending the rapid access chest pain clinic, the Scottish computed tomography of the heart (SCOT-HEART) trial: study protocol for randomized controlled trial. *Trials* 2012; **13**: 184. doi: <http://dx.doi.org/10.1186/1745-6215-13-184>
19. Callister TQ, Cooil B, Raya SP, Lippolis NJ, Russo DJ, Raggi P. Coronary artery disease: improved reproducibility of calcium scoring with an electron-beam CT volumetric method. *Radiology* 1998; **208**: 807–14. doi: <http://dx.doi.org/10.1148/radiology.208.3.9722864>
20. McClelland RL, Chung H, Detrano R, Post W, Kronmal RA. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2006; **113**: 30–7. doi: <http://dx.doi.org/10.1161/CIRCULATIONAHA.105.580696>
21. Kim KP, Einstein AJ, Berrington de González A. Coronary artery calcification screening: estimated radiation dose and cancer risk. *Arch Intern Med* 2009; **169**: 1188–94. doi: <http://dx.doi.org/10.1001/archinternmed.2009.162>
22. Willemink MJ, Takx RA, de Jong PA, Budde RP, Bleys RL, Das M, et al. The impact of CT radiation dose reduction and iterative reconstruction algorithms from four different vendors on coronary calcium scoring. *Eur Radiol* 2014; **24**: 2201–12. doi: <http://dx.doi.org/10.1007/s00330-014-3217-7>
23. den Harder AM, Willemink MJ, Bleys RL, de Jong PA, Budde RP, Schilham AM, et al. Dose reduction for coronary calcium scoring with hybrid and model-based iterative reconstruction: an *ex vivo* study. *Int J Cardiovasc Imaging* 2014; **30**: 1125–33. doi: <http://dx.doi.org/10.1007/s10554-014-0434-8>
24. Willemink MJ, de Jong PA, Leiner T, de Heer LM, Nievelstein RA, Budde RP, et al. Iterative reconstruction techniques for computed tomography part 1: technical principles. *Eur Radiol* 2013; **23**: 1623–31. doi: <http://dx.doi.org/10.1007/s00330-012-2765-y>
25. Willemink MJ, Leiner T, de Jong PA, de Heer LM, Nievelstein RA, Schilham AM, et al. Iterative reconstruction techniques for computed tomography part 2: initial results in dose reduction and image quality. *Eur Radiol* 2013; **23**: 1632–42. doi: <http://dx.doi.org/10.1007/s00330-012-2764-z>
26. Willemink MJ, Takx RA, de Jong PA, Budde RP, Bleys RL, Das M, et al. Computed tomography radiation dose reduction: effect of different iterative reconstruction algorithms on image quality. *J Comput Assist Tomogr* 2014; **38**: 815–23. doi: <http://dx.doi.org/10.1097/RCT.0000000000000128>
27. Gebhard C, Fiechter M, Fuchs TA, Ghadri JR, Herzog BA, Kuhn F, et al. Coronary artery calcium scoring: influence of adaptive statistical iterative reconstruction using 64-MDCT. *Int J Cardiol* 2013; **167**: 2932–7. doi: <http://dx.doi.org/10.1016/j.ijcard.2012.08.003>
28. Matsuura N, Urashima M, Fukumoto W, Sunamori H, Tatsugami F, et al. Radiation dose reduction at coronary artery calcium scoring by using a low tube current technique and hybrid iterative reconstruction. *J Comput Assist Tomogr* 2015; **39**: 119–24. doi: <http://dx.doi.org/10.1097/RCT.0000000000000168>
29. Obmann VC, Klink T, Heverhagen JT, Stork A, Lagmani A, Adam G, et al. Impact of hybrid iterative reconstruction on agatston coronary artery calcium scores in comparison to filtered back projection in native cardiac CT. *Rofo* 2015; **187**: 372–9. doi: <http://dx.doi.org/10.1055/s-0034-1398850>
30. Willemink MJ, Vliegthart R, Takx RA, Leiner T, Budde RP, Bleys RL, et al. Coronary artery calcification scoring with state-of-the-art CT scanners from different vendors has substantial effect on risk classification. *Radiology* 2014; **273**: 695–702. doi: <http://dx.doi.org/10.1148/radiol.14140066>

APPENDIX A

TUBE CURRENT WAS OPTIMIZED FOR THE INDIVIDUAL PATIENT BASED ON BODY MASS INDEX (BMI) ACCORDING TO THE FOLLOWING PROTOCOL

BMI (kg m^{-2})	Tube current (mA)
17–18	180
19–20	200
21–22	220
23–24	240
25–26	260
27–28	280
29–30	290
31–32	300
33–35	310
36–38	320
39–40	400
>40	450

APPENDIX B

TRANSVERSE CT IMAGE OF THE ANTHROPOMORPHIC PHANTOM SHOWING THE FIVE REGIONS OF INTEREST ASSESSED (1 = HYDROXYAPATITE INSERT, 2–4 = TISSUE EQUIVALENT AND 5 = WATER EQUIVALENT)

APPENDIX C

PATIENT DEMOGRAPHIC AND CT ACQUISITION CHARACTERISTICS

Characteristic	<i>n</i>
Number of patients	27
Gender (number of males)	19 (70.1%)
Age (years)	61.3 $\pm$ 7.8 (44–72)
BMI (kg m^{-2})	30.2 $\pm$ 5.4 (23–42)
Tube voltage (kVp)	120
Tube current (mAs)	295.2 $\pm$ 51.5
Dose-length product (mGy cm)	124.2 $\pm$ 27.9

BMI, body mass index.

Data are mean $\pm$ standard deviation or number (percent), with range in parentheses.