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

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

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| Abstract: | <p>Objectives: CT coronary artery calcium scoring (CACS) is additive to traditional risk factors for predicting future cardiac events but associated with relatively high radiation doses. We assessed the feasibility of CACS radiation dose reduction using lower tube current and iterative reconstruction (IR).</p> <p>Methods: Artificial noise was added to the raw data from 27 CACS studies from symptomatic patients to simulate lower tube current scanning (75%, 50% and 25% original current). All studies were performed on the same CT scanner at 120kVp. Data was reconstructed using filtered back projection (Quantum Denoising Software [QDS+]) and IR (Adaptive Iterative Dose Reduction-3D [AIDR]-mild, standard and strong). Agatston scores were independently measured by two readers. CACS percentile risk scores were calculated.</p> <p>Results: At 75%, 50% and 25% tube currents all 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 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 percentile risk score with AIDR-mild at any tube current occurred compared with QDS+ at standard tube current ($P > 0.05$). Inter-observer agreement for AIDR-mild remained excellent even at 25% tube current (Intraclass Correlation Coefficient 0.997).</p> |

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 intra- and inter-observer variability and without altering risk classification.

Response to reviewers' comments

BJR-D-15-00780R1 "Iterative reconstruction can permit the use of lower x-ray tube current in CT coronary artery calcium scoring".

Reviewer #2:

1. A very detailed analysis of coronary artery calcification, which is a very important study at this time utilising advanced technology.
2. Details of the Agatston score are not given initially.

The use of the Agatston score for quantifying coronary artery calcification is initially discussed in the introduction, where it is referenced to the original paper. We feel it is more appropriate to provide the definition of Agatston score within the image analysis section of the methods (section 3.5), rather than in the introduction

"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."

Full title:

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

Short title:

Low dose CT CACS using iterative reconstruction and low tube current

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Conflicts of Interest or financial disclosures: None

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17/09/2015

Dear Editor,

On behalf of the authors I confirm:

1. The manuscript we submit is original, with no portion under simultaneous consideration for publication elsewhere or previously published.
2. All authors have made an important contribution to the study
4. All authors have read and approved the manuscript
5. There are no conflicts of interest or financial disclosures.

Author contributions:

Mark Rodrigues - Study concept & design, data acquisition, analysis and interpretation, drafting the manuscript and final approval.

Michelle Williams - Study concept & design, data analysis and interpretation, drafting the manuscript and final approval.

Thomas Fitzgerald - Data acquisition, drafting the manuscript and final approval.

Martin Connell - Study concept & design, data acquisition, drafting the manuscript and final approval.

Nicholas Weir - Study concept & design, drafting the manuscript and final approval.

David Newby - Study concept & design, drafting the manuscript and final approval.

Edwin van Beek - Study concept & design, data interpretation, drafting the manuscript and final approval.

Saeed Mirsadraee - Study concept & design, data interpretation, drafting the manuscript and final approval.

Yours truly,

A handwritten signature in black ink, appearing to read "Rodrigues". The signature is fluid and cursive, with a large loop at the end.

Dr Mark A Rodrigues

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

1. Abstract

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

Methods: Artificial noise was added to the raw data from 27 CACS studies from symptomatic patients to simulate lower tube current scanning (75%, 50% and 25% original current). All studies were performed on the same CT scanner at 120kVp. Data was reconstructed using filtered back projection (Quantum Denoising Software [QDS+]) and IR (Adaptive Iterative Dose Reduction-3D [AIDR]-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 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 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 percentile risk score with AIDR-mild at any tube current occurred compared with QDS+ at standard tube current ($P > 0.05$). Inter-observer

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3 agreement for AIDR-mild remained excellent even at 25% tube current (Intraclass
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5 Correlation Coefficient 0.997).
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10 **Conclusion:** Up to 75% reduction in CACS tube current is feasible using AIDR-mild.
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15 **Advances in knowledge:** AIDR-mild IR permits low tube current CACS whilst
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17 maintaining excellent intra- and inter-observer variability and without altering risk
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19 classification.
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24 **2. Introduction**

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27 Coronary artery calcification is an established marker of atherosclerosis¹ and is
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29 associated with cardiovascular morbidity and mortality.^{2,3} Computed tomography
30
31 (CT) can be used to quantify coronary artery calcification using various scoring
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33 systems, such as the Agatston,⁴ volume and mass scores.⁵ These have been shown
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35 to be additive to traditional risk factor scores in the prediction of future cardiac
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37 events.^{6,7,8}
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45 According to current standards, calcium scoring is performed at a tube voltage of
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47 120kV using a filtered back projection (FBP) reconstruction algorithm in order to
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49 standardise quantification.⁹ However, such CT coronary artery calcium scoring
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51 (CACS) is associated with a significant radiation dose, ranging from 0.8 to
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53 10.5mSv.¹⁰ These radiation doses are high when compared to advances in low-dose
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55 CT coronary angiography.^{11,12} This is particularly important as the American College
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57 of Cardiology guidelines recommend assessing coronary artery calcification for
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59 patients with low to intermediate cardiovascular risk, even if asymptomatic.¹³
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5 Methods to reduce radiation dose in cardiac imaging include prospective
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7 electrocardiogram triggering, reducing tube voltage, reducing tube current and
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9 optimising the scan range. These techniques can be applied to the non-contrast CT
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11 scans used for coronary artery calcium scoring, but have the potential to influence
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13 calcium quantification. Lowering tube voltage would result in a change in Hounsfield
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15 units (HU) and therefore the Agatston score, while reducing tube current can lead to
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17 increased image noise and therefore false positive results when using FBP
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19 reconstruction algorithms.¹⁴
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27 Iterative reconstruction algorithms can be applied to raw cardiac CT data and can
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29 reduce image noise to allow improved image quality and/or reduced radiation
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31 dose.^{11,12,15} Phantom studies have shown that one iterative reconstruction algorithm
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33 (Adaptive Iterative Dose Reduction-3 Dimensional [AIDR-3D; Toshiba Medical
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35 Systems, Nasu, Japan]) can permit an 80% reduction in radiation dose without
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37 significantly altering Agatston scores.¹⁶ In clinical studies other iterative
38
39 reconstruction algorithms (Iterative Reconstruction in Image Space [IRIS; Siemens
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41 Healthcare, Forchheim, Germany]) and Sinogram affirmed iterative reconstruction
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43 [SAFIRE; Siemens Healthcare, Forchheim, Germany]) showed no significant effect on
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45 Agatston score or risk stratification when used with full dose imaging.¹⁷
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54 This study assesses the effect of the AIDR-3D iterative reconstruction algorithm on
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56 coronary artery calcium score and patient risk stratification using simulated
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58 reductions in tube current in order to assess the clinical implications of applying this
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60 radiation dose reduction technique.
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3 **3. Materials and methods**
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5 *3.1. Study design*
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7 All studies were performed using a 320-multidetector row CT scanner (Aquilion ONE,
8 Toshiba Medical Systems, Nasu, Japan). First, phantom studies were performed to
9 assess whether simulated reductions in tube current would have the same effect on
10 image noise as scanning with a reduced tube current. Imaging data from 27 patients
11 was then reconstructed with five different reconstruction algorithms with various
12 levels of additional image noise to replicate the effect of reducing the tube current by
13 25%, 50% and 75%.
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27 *3.2. Phantom studies*
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29 An anthropomorphic thoracic phantom with a 20 x 30cm body diameter (QRM GmbH,
30 Moehrendorf, Germany⁹) was scanned with and without an additional 5cm muscle
31 equivalent wrap to simulate different body constitutions (large and standard
32 phantoms respectively). CT imaging of both phantoms was performed using a tube
33 voltage of 120kV and four different tube currents. For the large phantom, tube
34 currents of 320, 240, 160 and 80mA were used and for the standard phantom tube
35 currents of 200, 150, 100 and 50mA were used.
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49 *3.3. Patient studies*
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51 Participants with suspected coronary artery disease were recruited as part of the
52 SCOTHEART study (NCT01149590).¹⁸ This study was approved by the local
53 research ethics committee and informed consent was obtained from all participants.
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3 Participants underwent non-contrast CT for the assessment of coronary artery
4 calcium using a tube voltage of 120kV and tube current adjusted based on body-
5 mass index (BMI) (Appendix A). The scan range was from 20mm below the carina to
6 the base of the heart with a volume size of 80, 100, 120, 140 or 160mm. A targeted
7 acquisition at 75% of the R-R interval was obtained. Prior to imaging, patients with a
8 heart rate greater than 60 beats per minute received intravenous metoprolol as
9 previously described.¹⁸
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22 *3.4. Image reconstruction*

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24 Artificial noise was added to the raw data of the phantom images with highest tube
25 current and to the patient images to create images with simulated tube current
26 reductions of 25%, 50% and 75% (NoiseAdd, Toshiba Medical Systems, Nasu,
27 Japan). All images were reconstructed using the FC12 kernel and with five different
28 reconstruction algorithms: basic FBP (ORG), Quantum Denoising Software FBP
29 (QDS+), and iterative reconstruction (AIDR-3D) with three levels of blending (mild,
30 standard and strong). Toshiba recommend QDS+ as the standard
31 reconstruction/reference technique for calcium scoring.
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46 *3.5. Image analysis*

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48 Images were analysed by a trained observer (MAR), who was completely
49 independent from the SCOTHEART study, on a dedicated post-processing
50 workstation (Vitrea Fx, version 6.3, Vital Images, Minnetonka, USA) using calcium
51 score analysis software (VScore, Vital Images, Minnetonka, USA). Analysis was
52 performed blinded to the results of other reconstructions and in random order to
53 reduce the likelihood of recall bias. To assess inter- and intra-observer variabilities
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3 images were assessed in 24 patients, in whom all imaging data were available, by a
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5 second independent observer (TF) blinded to other results.
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10 For phantom studies the mean and standard deviation (SD) of the HU for 5 different
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12 regions of interest (ROI) (Appendix B) were calculated for each of the different
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14 simulated tube currents.
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19 The standard Agatston technique was used to quantify coronary artery calcification in
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21 patient studies. The calculation is based on the weighted density score (1 for 130–
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23 199 HU, 2 for 200–299 HU, 3 for 300–399 HU, and 4 for 400 HU and greater) given
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25 to the highest attenuation value (HU) multiplied by the area (in square millimetres) of
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27 the coronary calcification.⁴ Calcium volume scoring method was also used as
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29 described previously.¹⁹ Regions of interest were drawn in all vessels and total
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31 Agatston and volume scores were obtained by summing the weighted scores from
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33 each vessel.
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42 The absolute Agatston score was categorized as low (≤ 100 Agatston units (AU)),
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44 intermediate (101-400AU), high (401-1000AU) or very high (> 1000 AU). It was also
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46 categorized as non-extensive (≤ 400 AU) or extensive (> 400 AU) for analysis. The
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48 CACS percentile based on age, sex and ethnicity was calculated from the Agatston
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50 score using previously published distributions from a cohort of healthy asymptomatic
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52 individuals.²⁰ For patients younger than 45 years, the age 45 years was used for the
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54 calculation of the CACS percentile. These were categorized as \leq , or $> 90^{\text{th}}$ centile for
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56 analysis.
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3 For all patient reconstructions, image noise was defined as the standard deviation of
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5 HU in a 500mm² oval ROI in the ascending aorta. Signal to noise ratio (SNR) was
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7 calculated as the mean HU within the ROI divided by its standard deviation. For each
8
9 patient, the noise and SNR in the different reconstructed data sets was measured on
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11 the same image slice.
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17 *3.6. Statistical analysis*

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19 Data analysis was performed using SPSS (Version 18 for Mac, IBM) and GraphPad
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21 Prism (Version 6 for Mac). Non-normally distributed data are presented with median
22
23 and interquartile range. Statistical significance was assessed using Wilcoxon signed-
24
25 rank test. Intra- and inter-observer variabilities were assessed using Bland-Altman
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27 plots and intraclass correlation coefficient (ICC). A statistically significant difference
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29 was defined as a two-sided P value <0.05.
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37 **4. Results**

38 *4.1. Phantom studies*

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40 Images with both the large and standard size phantoms showed no significant
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42 difference in mean attenuation density at any of the 5 ROIs between actual or
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44 simulated tube currents at comparative doses (P>0.05).
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51 *4.2. Objective image quality in patient studies*

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53 In the images from the 27 patients (Appendix C), AIDR-3D with mild, standard and
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55 strong levels of blending reduced noise compared with the QDS+ reconstruction
56
57 algorithm at simulated tube currents of 75%, 50% and 25% (P=0.002 for AIDR-mild
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59 at 75%; P<0.001 for all other reconstructions and simulated currents). AIDR-3D with
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3 standard and strong levels of blending also reduced image noise at 100% tube
4 current compared with QDS+ ($P<0.001$; Figure 1A). All AIDR-3D reconstructions
5 resulted in a higher SNR compared with QDS+ at 50% and 25% simulated tube
6 currents ($P<0.001$). SNR was also higher with AIDR-3D standard and strong relative
7 to QDS+ at 100% and 75% tube currents ($P<0.001$; Figure 1B).
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10 11 12 13 14 15 16 17 *4.3 Agatston score*

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19 At standard tube current (100%), AIDR-3D reconstructions at all levels of blending
20 led to a small but significant reduction in Agatston score compared to the QDS+
21 reconstruction (Reference technique) ($P<0.001$; Table 1). This reduction in Agatston
22 score relative to the reference technique was evident at all simulated tube currents
23 with all levels of AIDR-3D blending ($P<0.001$ for all).
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34 Reducing the simulated tube current led to an increase in Agatston score for QDS+
35 and ORG reconstructions and a small decrease in Agatston score for AIDR-3D at all
36 levels of blending. These differences became statistically significant at 75% tube
37 current for QDS+ and ORG reconstructions ($P<0.001$ for all), and at 50% tube
38 current for AIDR-3D standard ($P=0.174$, $P=0.003$ and $P=0.006$ [100% tube current
39 versus 75%, 50% and 25% simulated current respectively]) and strong ($P=0.112$,
40 $P=0.003$ and $P<0.001$ [100% tube current versus 75%, 50% and 25% simulated
41 current respectively]). There was no change with AIDR-3D mild at any test tube
42 current ($P=0.689$, $P=0.317$ and $P=0.253$ [100% tube current versus 75%, 50% and
43 25% simulated current respectively]; Figure 2).
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61 *4.4. Calcium volume score*

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3 At the full tube current, all levels of AIDR-3D reconstruction led to a small but
4
5 significant reduction in calcium volume scores compared to the QDS+ reconstruction
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7 algorithm ($P < 0.001$ for all; Table 2). There was no difference in volume score
8
9 between QDS+ at 100% tube current (Reference technique) and AIDR-3D mild at
10
11 50% and 25% simulated tube current ($P = 0.091$ and $P = 0.341$ respectively). Volume
12
13 scores were reduced relative to the reference technique with AIDR-3D mild at 75%
14
15 simulated tube current ($P = 0.001$), and with AIDR-3D standard and strong at 75%,
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17 50% and 25% simulated tube current ($P < 0.001$ for all except AIDR-3D standard at
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19 25% [$P = 0.033$]).
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27 Reducing the tube current led to an increase in volume score for QDS+ and ORG at
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29 75%, 50% and 25% tube current ($P < 0.001$ for all), and at 25% tube current for AIDR-
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31 3D mild ($P = 0.002$) and , whilst the volume score with AIDR-3D strong decreased at
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33 25% simulated current ($P = 0.037$).
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39 *4.5. Effect of patient BMI and degree of atherosclerosis*

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41 With the QDS+ reconstruction, increases in the Agatston score occurred with all
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43 simulated reductions in tube current in both the non-obese ($BMI \leq 30$) ($P = 0.014$,
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45 $P = 0.001$ and $P = 0.001$ [100% tube current versus 75%, 50% and 25% simulated
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47 current respectively]) and obese ($BMI > 30$) groups ($P = 0.004$, $P = 0.003$ and $P = 0.002$
48
49 [100% tube current versus 75%, 50% and 25% simulated current respectively]), as
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51 well as those with extensive atherosclerosis ($> 400AU$) ($P = 0.001$, $P = 0.002$ and
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53 $P = 0.001$ [100% tube current versus 75%, 50% and 25% simulated current
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55 respectively]). The Agatston score increased in the non-extensive atherosclerosis
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3 group (≤ 400 AU) at 50% and 25% simulated tube currents ($P=0.002$ and $P=0.001$
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5 respectively) (Tables 3 and 4).
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10 In contrast, there was no change in the Agatston scores with AIDR-3D mild at any
11
12 tested current, irrespective of BMI or degree of atherosclerosis ($P>0.05$ for all).
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15 16 17 *4.6. Intra- and inter-observer variability*

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19 Intra- and inter-observer agreements for Agatston scoring of full dose images with
20
21 QDS+ and AIDR-3D mild were excellent ($ICC=1$; Figure 3). Overall the mean intra-
22
23 observer variability was 0.3% for QDS+ and 0.3% for AIDR-3D mild, and the inter-
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25 observer variability was 1.1% and 0.3% respectively. The variability remained similar
26
27 at lower simulated currents (50% and 25% tube current), especially when using
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29 AIDR-3D mild blending (mean intra-observer variability 0.4% for QDS+ and 0.3% for
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31 AIDR-3D mild [ICC 0.998 and 0.999 respectively]; mean inter-observer 1.4% for
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33 QDS+ and 0.3% for AIDR-3D mild [ICC 0.997 and 0.998 respectively]).
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42 *4.7. Implication on risk assessment*

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44 Absolute Agatston score categories were identical to the reference technique in 25
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46 cases (92.6%) for AIDR-3D mild at 100%, 75%, 50% and 25% tube current. The two
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48 patients who were reclassified had an Agatston score with the reference technique
49
50 near a border between absolute Agatston categories (one patient had an Agatston
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52 score of 107 AU, the other 1002 AU), and therefore the small underestimation
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54 associated with AIDR-3D mild resulted in reclassification. No patients were
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56 reclassified from a zero Agatston score with the reference technique to a positive
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58 score with AIDR-3D mild reconstruction at any simulated tube current.
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5 AIDR-3D mild resulted in identical CACS percentile categories with the reference
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7 technique at all tested levels of tube current. The median calcium percentile score
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9 with the reference technique was 86 (interquartile range 74-94). The percentile
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11 scores with AIDR-3D mild at all tested levels of tube current did not differ from the
12
13 reference technique (median scores [interquartile range] at 100%, 75%, 50% and
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15 25% tube current were 86 [74-94], 87 [76-94], 87 [77-94] and 89 [83-96] respectively;
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20 P>0.05).

21 22 23 24 25 **5. Discussion**

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

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44 One of the main difficulties limiting radiation dose reduction in CT CACS is the fixed
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46 tube voltage (120kVp) required for Agatston scoring. Attempts to reduce dose by
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48 decreasing tube current with FBP reconstruction have resulted in false-positive
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50 lesions.¹⁴ However recent studies^{22,23} showed that FBP did not affect the Agatston
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52 score when the dose was reduced by up to 80%. These ex-vivo studies used a single
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54 standard sized phantom (30 x 20cm) and it is not clear whether the results would be
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59 reproducible in an in-vivo setting with larger patients.

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3 The present study showed that AIDR-3D reduced image noise and yielded superior
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5 SNR at low tube currents (up to 75% reduction) compared to FBP, which is in
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7 keeping with results from several other studies.^{11,17,24,25,26} The benefit of AIDR-3D
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9 was most apparent at lower tube currents.
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15 As the CACS in this study are obtained by volume imaging without mA modulation,
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17 and the scan length and kV are constant, dose length product has straight
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19 relationship to mA. Therefore, the potential reduction in dose is by a factor of 4 when
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21 the mA is quartered.
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27 In line with a recent ex-vivo study, the lowest level of iterative reconstruction (AIDR-
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29 3D mild) was the most promising for Agatston scoring and calcium volume.²³
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32 However even AIDR-3D mild significantly reduced Agatston scores relative to FBP at
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34 normal dose settings. This underestimation with iterative reconstruction is in
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36 accordance with several other studies^{16,22,27} and is partly attributed to a reduction in
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38 the blooming effect of calcified plaques seen with FBP methods, leading to down
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40 staging of the plaque size with iterative reconstruction algorithms.^{12,17} This is
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42 supported by the observation that calcium volume was significantly lower with all
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44 AIDR-3D reconstructions compared to FBP at normal dose settings.
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51 In contrast with FBP, there was no change in Agatston score with AIDR-3D mild
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53 when tube current was reduced by up to 75%, regardless of patient BMI or degree of
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55 atherosclerosis, with intra- and inter-observer agreement remaining excellent. This is
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57 in agreement with phantom studies,^{16,22} suggesting dose reduction is feasible with
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59 AIDR-3D mild.
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5 A recent in vivo study assessing a type of hybrid iterative reconstruction (iDose,
6 Philips Medical Systems, the Netherlands) demonstrated tube current reduction of
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8 80% was possible without affecting the Agatston score or calcium volume. However
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10 the effects of tube current reduction on clinical scoring were not assessed.²⁸ A further
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12 study has recently shown excellent correlation of clinical risk groups between FBP
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14 and hybrid iterative reconstruction at full dose scanning.²⁹ In the present study, there
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16 remained excellent agreement of absolute and percentile risk scores with the
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18 reference technique (FBP at normal dose settings) when using AIDR-3D mild at a
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20 tube current as low as 25%. The patients who were reclassified with AIDR-3D mild
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22 were the result of small absolute changes in Agatston scores in patients who were
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24 either on the borderline between categories or relatively young, so that a small
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26 absolute change resulted in reclassification.
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37 Some limitations should be considered. This was a small feasibility study using
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39 simulated reductions in tube current. Artificially adding noise allowed the effect of
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41 different reconstruction algorithms on multiple different tube currents to be assessed
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43 without exposing the patients to further ionizing radiation. However this results in
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45 estimated rather than true reductions in current. Larger studies assessing actual
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47 tube current reductions are therefore needed to validate our findings, and establish
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49 the degree of dose reduction possible. Second, the software to calculate mass
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51 scores, another validated measure used to quantify coronary artery calcification, was
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53 not available at the time of the study. Future work should assess the effects on this
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55 score, as well as vessel- and lesion-specific calcium scoring, in addition to the
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57 Agatston and volumes scores. We only assessed software from a single vendor.
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3 However the iterative reconstruction algorithms employed by different manufacturers
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5 differ, and in experimental models, Willemink et al demonstrated significant
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7 differences in Agatston score between different vendors' iterative reconstruction
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9 software.^{22,30} Accordingly, multivendor studies should be performed. The degree of
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11 dose reduction with other scanners and scanning protocols may differ, if for example
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13 there is tube current modulation, and the feasibility of dose reduction in these cases
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15 must be studied separately. Finally, our patient cohort consisted of symptomatic
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17 patients, with a median Agatston score of nearly 400. This may limit the validity of our
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19 results to other patient groups, such as asymptomatic screening populations,
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21 especially as there were higher percentage changes in those without extensive
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23 atherosclerosis (<400AU), and such absolute changes are likely to have the biggest
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25 effect on percentile classifications.²⁷
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34 **Conclusion**

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37 Reduction of CT CACS tube current by up to 75% is feasible with the use of AIDR-3D
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39 mild. As suggested by Blobel et al¹⁶ a correction factor may be considered as AIDR-
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41 3D mild results in a small but significant underestimation of Agatston scores.
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3 **Figure legends**

4 Figure 1. A. Image noise and B. Signal to noise ratio. Data are presented as median
5 \pm interquartile range. *P<0.05 compared to QDS+ at the same tube current, **P<0.001
6 compared to QDS+ at the same tube current.
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10 Figure 2. Images of the right coronary artery reconstructed with QDS+ (A-D) and AIDR-
11 3D mild (E-H) at various tube voltages.
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14 The calcium scoring software highlights tissues fulfilling the Agatston scoring inclusion
15 criteria in pink. Images A to D are reconstructed with QDS+ (100% tube current, 75%,
16 50% and 25% respectively). A “real” calcified plaque is indicated by the open white
17 arrow. As the current is reduced there is an increase in noise, leading to multiple
18 spurious calcified plaques (closed white arrows images C & D) . E to H are the
19 corresponding images reconstructed with AIDR-3D Mild. Notice the markedly reduced
20 number and size of spurious plaques at 25% tube current (Image H).
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28 Figure 3: Bland-Altman plots showing intra- (A) and inter- (B) observer variability for
29 Agatston calcium score using QDS+ and AIDR-3D mild reconstructions at different
30 tube currents. (Dotted lines represent bias and limits of agreement).
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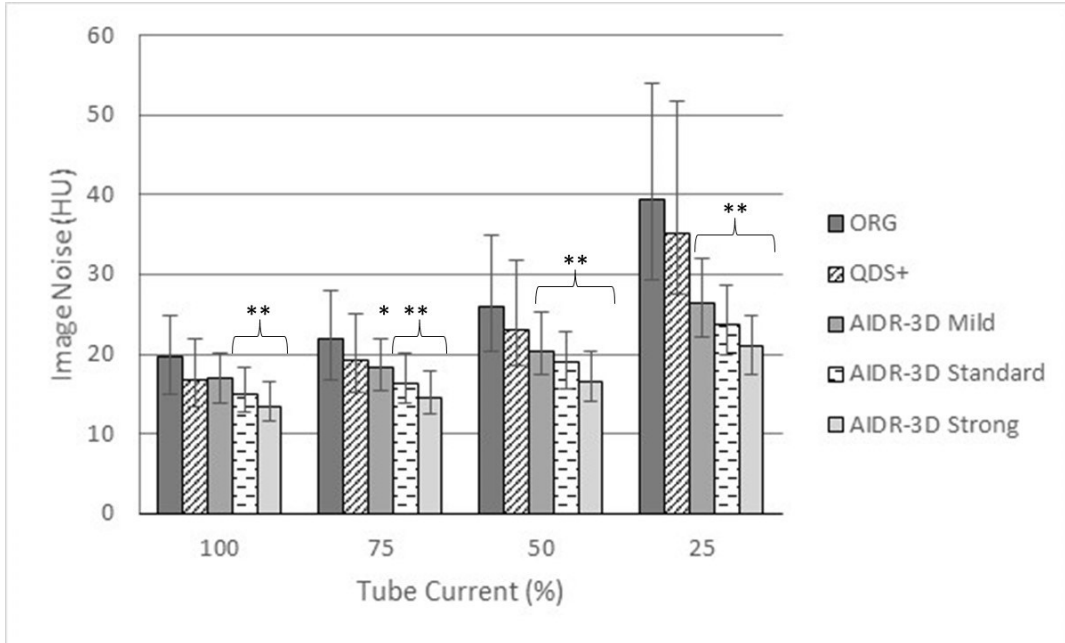
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Figure 1. A. Image noise and B. Signal to noise ratio. Data are presented as median \pm interquartile range. *P<0.05 compared to QDS+ at the same tube current, **P<0.001 compared to QDS+ at the same tube current.

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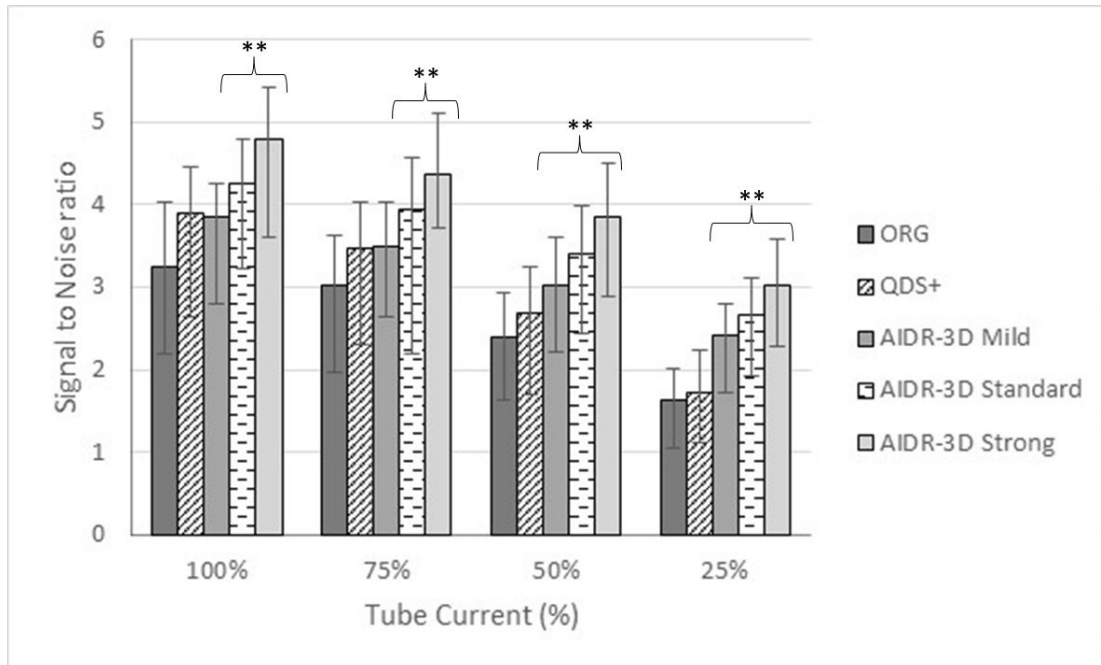


Figure 2. Images of the right coronary artery reconstructed with QDS+ (A-D) and AIDR-3D mild (E-H) at various tube voltages.

The calcium scoring software highlights tissues fulfilling the Agatston scoring inclusion criteria in pink. Images A to D are reconstructed with QDS+ (100% tube current, 75%, 50% and 25% respectively). A “real” calcified plaque is indicated by the open white arrow. As the current is reduced there is an increase in noise, leading to multiple spurious calcified plaques (closed white arrows images C & D). E to H are the corresponding images reconstructed with AIDR-3D Mild. Notice the markedly reduced number and size of spurious plaques at 25% tube current (Image H).

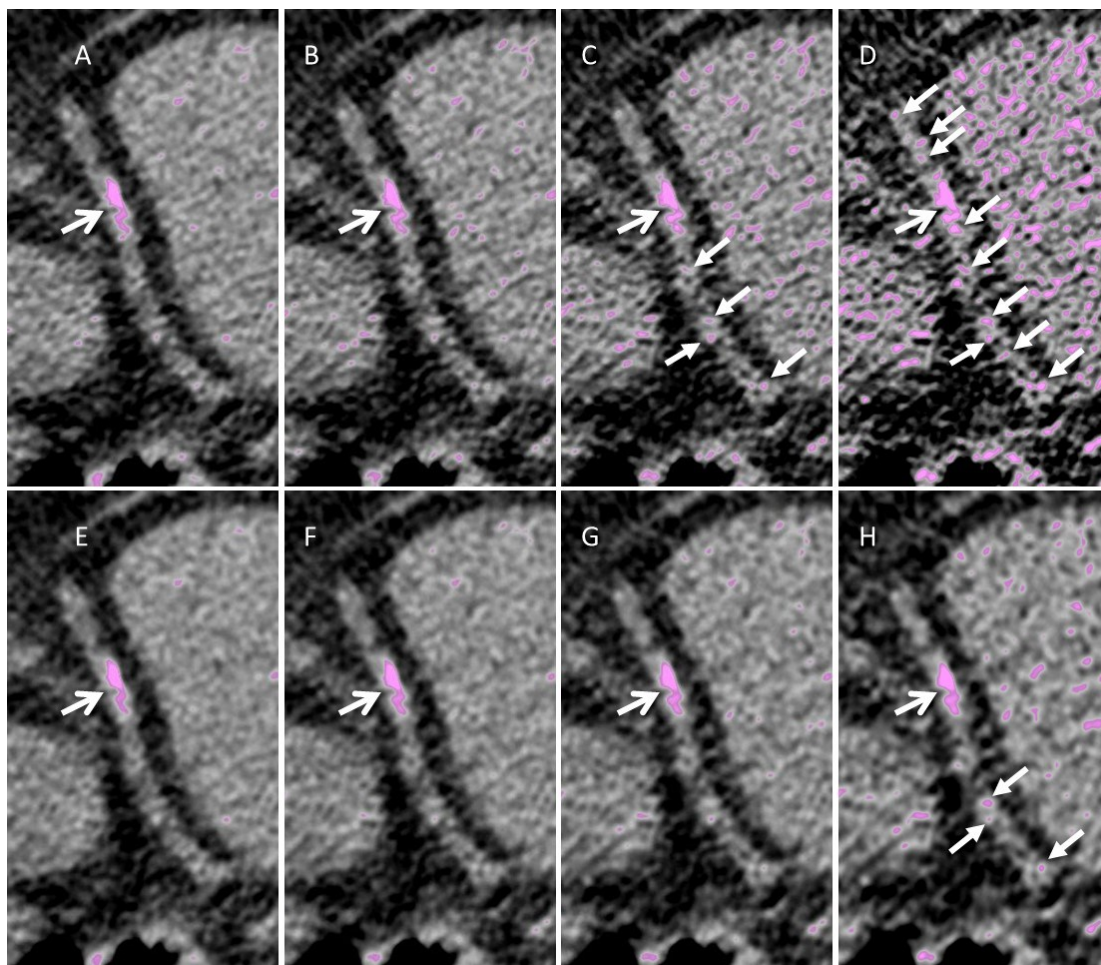
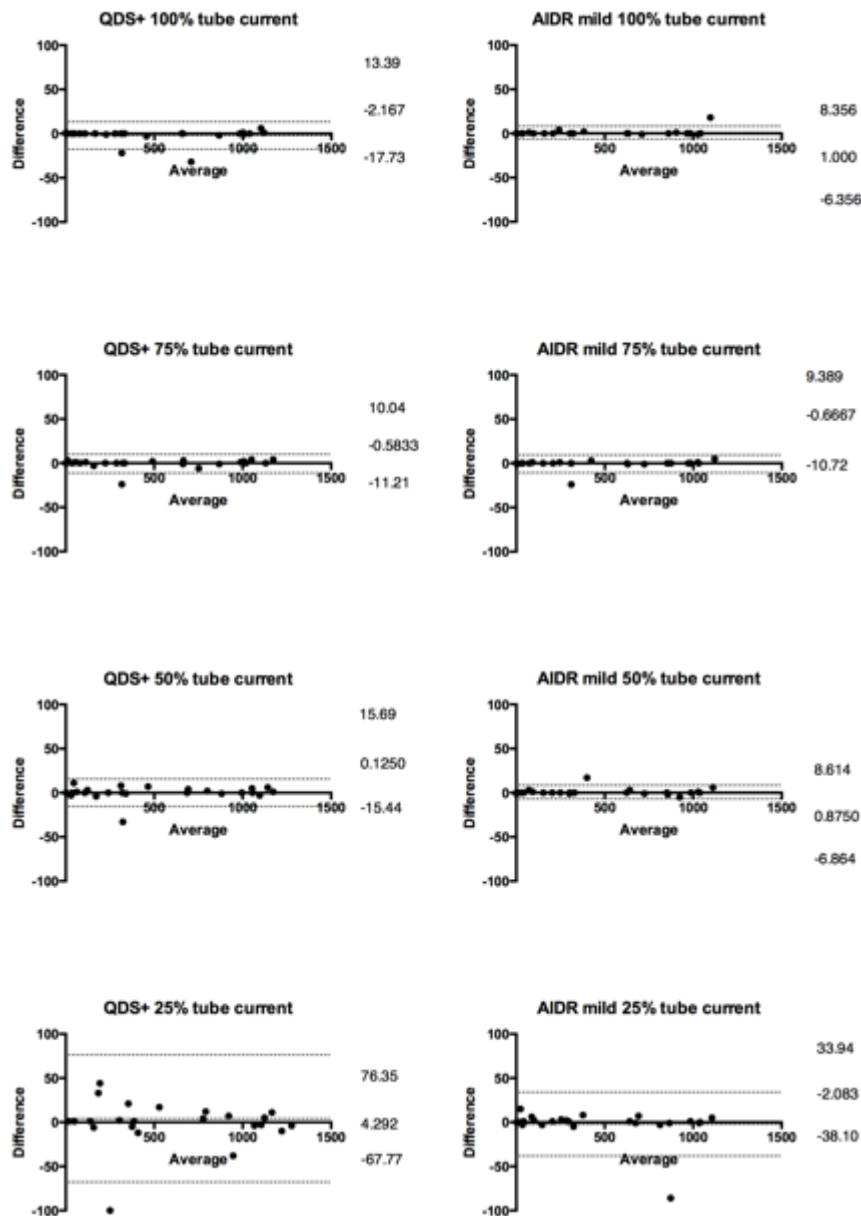


Figure 3: Bland-Altman plots showing intra- (A) and inter- (B) observer variability for Agatston calcium score using QDS+ and AIDR-3D mild reconstructions at different tube currents. (Dotted lines represent bias and limits of agreement).

A.

Intra-observer variability



B.

Inter-observer variability

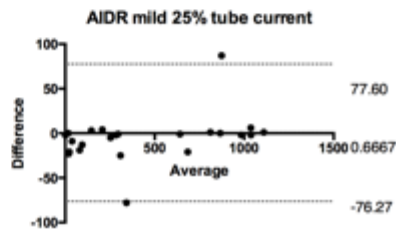
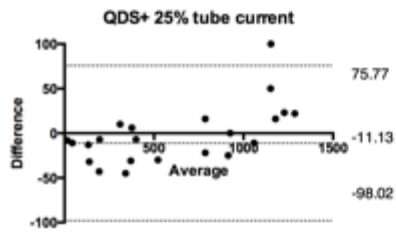
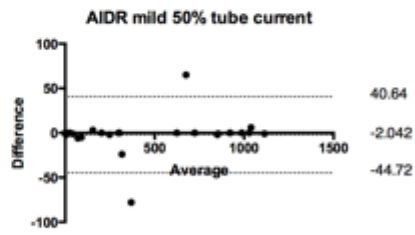
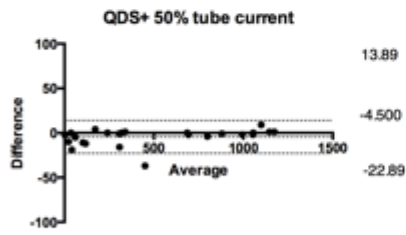
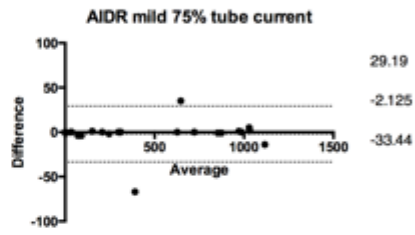
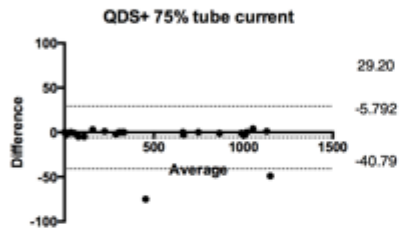
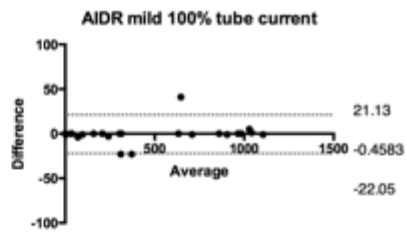
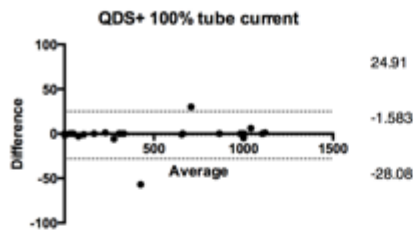


Table 1. Agatston scores (Agatston units) for different simulated tube currents and reconstruction algorithms.

| Tube current | QDS+ | ORG | AIDR-3D Mild | AIDR-3D Standard | AIDR-3D Strong |
|---------------------|------------------|--------------------|---------------------|-------------------------|-----------------------|
| 100% | 397 [107-983] | 401 [109-987]* | 360 [96-934]* | 349 [87-919]* | 317 [77-860]* |
| 75% | 416 [108-988]## | 419 [110-991]* ## | 357 [88-930]* | 340 [85-909]* | 295 [76-843]* |
| 50% | 432 [112-993]## | 443 [113-1001]* ## | 330 [88-921]* | 306 [79-890]* # | 291 [75-834]* # |
| 25% | 475 [193-1053]## | 478 [203-1064]* ## | 303 [88-896]* | 293 [77-887]* # | 293 [74-821]* ## |

*Data are presented as median [interquartile range]. *P<0.001 compared to QDS+ at 100% tube current (Reference technique). # P<0.05 and ## P<0.001 compared to 100% tube current with the respective reconstruction algorithm.*

Table 2. Calcium volume scores (mm³) for different simulated tube currents and reconstruction algorithms.

| Tube current | QDS+ | ORG | AIDR-3D Mild | AIDR-3D Standard | AIDR-3D Strong |
|---------------------|---------------|-----------------|---------------------|-------------------------|-----------------------|
| 100% | 348 [120-762] | 353 [125-766]** | 320 [121-760]** | 310 [112-759]** | 295 [104-756]** |

| | | | | | |
|-----|-----------------|--------------------|----------------|-----------------|----------------------|
| 75% | 355 [122-767]## | 359 [135-771]** ## | 317 [118-760]* | 309 [112-756]** | 296 [105-756]** |
| 50% | 384 [166-783]## | 394 [172-796]** ## | 318 [120-761] | 307 [111-757]** | 282 [103-753]** |
| 25% | 430 [267-885]## | 510 [270-935]** ## | 323 [140-768]# | 299 [110-761]* | 265 [102-755]** # |

*Data are presented as median [interquartile range]. *P<0.05 and **P<0.001 compared to QDS+ at 100% tube current (Reference technique). # P<0.05 and ##P<0.001 compared to 100% tube current with the respective reconstruction algorithm.*

Table 3. Agatston scores (Agatston units) and calcium volume scores (mm³) for different simulated tube currents and reconstruction algorithms according to BMI. (AU - Agatston unit, Vol – calcium volume).

| BMI | ≤30 (n=15) | | | | >30 (n=12) | | | |
|--------------|--------------------|--------------------|-------------------|-------------------|-------------------------|--------------------------|----------------------|------------------------|
| Tube current | QDS+ | | AIDR-3D Mild | | QDS+ | | AIDR-3D Mild | |
| | AU | Vol | AU | Vol | AU | Vol | AU | Vol |
| 100% | 458 [228-1044] | 413 [254-900] | 456 [207-1031] | 411 [249-889] | 335 [11.5-706.5] | 307.5 [19.75-656] | 300 [9.25-689.25] | 289 [13-638.5] |
| 75% | 460 [225-1056]* | 414 [255-934]* | 459 [207-1031] | 412 [248-890] | 350.5 [15.5-727.75]* | 316.5 [26.75-668.75]* | 300.5 [10-698.75] | 287.5 [13.5-652.75] |
| 50% | 457 [240-1104]* | 419 [255-967]* | 461 [203-1028] | 409 [243-905] | 366 [33-770.75]* | 341.5 [54.25-733]* | 288.5 [9-702.5] | 288 [15-666.25] |
| 25% | 475 [315-1187]* | 430 [267-1063]* | 456 [209-1037] | 410 [253-926]* | 431 [118-875]* | 469.5 [233-840]* | 276.5 [13.25-674] | 293.5 [28.5-684.5]* |

Data are presented as median [interquartile range]. *P<0.05 compared to 100% tube current with the respective reconstruction algorithm.

Table 4. Agatston scores (Agatston units) and calcium volume scores (mm³) for different simulated tube currents and reconstruction algorithms according to the degree of atherosclerosis. (Extensive atherosclerosis = Agatston score greater than

400 Agatston units, non-extensive atherosclerosis = Agatston score \leq 400). (AU - Agatston unit, Vol – calcium volume).

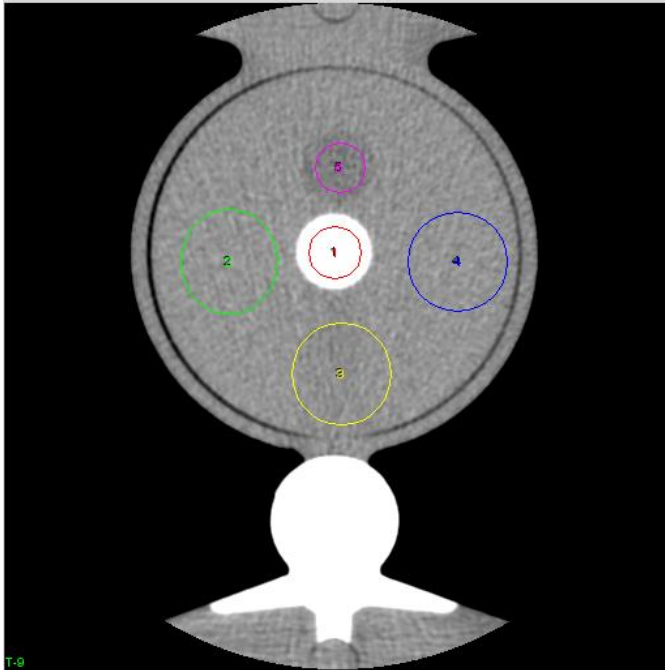
| | Non-extensive atherosclerosis (n=14) | | | | Extensive atherosclerosis (n=13) | | | |
|--------------|--------------------------------------|-----------------------------|-----------------------------|--------------------------|----------------------------------|---------------------------|---------------------------|---------------------------|
| Tube current | 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]* | 120 [24- 300.75] | 140 [22.5- 263] | 988 [706.5- 1091]* | 767 [634.5- 950.5]* | 930 [675.5- 1031.5] | 760 [617.5- 919.5] |
| 50% | 143 [35- 308.5]* | 170 [64.75- 302.25]* | 122 [19- 299.75] | 141.5 [23- 264.25] | 993 [744.5- 1125]* | 783 [657- 981]* | 921 [681- 1035] | 761 [628.5- 931] |
| 25% | 215 [117.25- 361]* | 302.5 [174.25- 407]* | 118 [15.75- 286] | 153.5 [33.5- 272]* | 1053 [848- 1221]* | 885 [742- 1094]* | 896 [674- 1038.5] | 768 [647.5- 932.5]* |

Data are presented as median [interquartile range]. *P<0.05 compared to 100% tube current with the respective reconstruction algorithm.

Appendix A. Tube current was optimized for the individual patient based on body mass index according to the following protocol.

| Body mass index (kg/m²) | 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 5 regions of interest assessed (1 = hydroxyapatite insert, 2-4 = tissue equivalent and 5 = water equivalent).



Appendix C. Patient demographic and CT acquisition characteristics.

| Characteristic | n |
|--------------------------------------|----------------------|
| Number of patients | 27 |
| Gender (Number of Males) | 19 (70.1%) |
| Age | 61.3 ± 7.8 (44 - 72) |
| Body mass index (kg/m ²) | 30.2 ± 5.4 (23 – 42) |
| Tube voltage (kVp) | 120 |
| Tube current (mAs) | 295.2 ± 51.5 |
| Dose length product (mGy.cm) | 124.2 ± 27.9 |

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