


In vitro evaluation of a new iterative reconstruction algorithm for dose reduction in coronary artery calcium scoring

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Abstract

Background: Coronary artery calcium (CAC) scoring is a widespread tool for cardiac risk assessment in asymptomatic patients and accompanying possible adverse effects, i.e. radiation exposure, should be as low as reasonably achievable.

Purpose: To evaluate a new iterative reconstruction (IR) algorithm for dose reduction of in vitro coronary artery calcium scoring at different tube currents.

Material and Methods: An anthropomorphic calcium scoring phantom was scanned in different configurations simulating slim, average-sized, and large patients. A standard calcium scoring protocol was performed on a third-generation dual-source CT at 120 kVp tube voltage. Reference tube current was 80 mAs as standard and stepwise reduced to 60, 40, 20, and 10 mAs. Images were reconstructed with weighted filtered back projection (wFBP) and a new version of an established IR kernel at different strength levels. Calcifications were quantified calculating Agatston and volume scores. Subjective image quality was visualized with scans of an ex vivo human heart.

Results: In general, Agatston and volume scores remained relatively stable between 80 and 40 mAs and increased at lower tube currents, particularly in the medium and large phantom. IR reduced this effect, as both Agatston and volume scores decreased with increasing levels of IR compared to wFBP ($P < 0.001$). Depending on selected parameters, radiation dose could be lowered by up to 86% in the large size phantom when selecting a reference tube current of 10 mAs with resulting Agatston levels close to the reference settings.

Conclusion: New iterative reconstruction kernels may allow for reduction in tube current for established Agatston scoring protocols and consequently for substantial reduction in radiation exposure.

Keywords

Cardiac, heart, radiation safety, calcium score, iterative reconstruction

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Introduction

The risk of coronary heart disease-related events correlates significantly with the grade of coronary artery calcifications (CAC), as measured by non-contrast cardiac computed tomography (CT) (1,2). Despite several attempts to establish mass or volume scores for CAC scoring, the first scoring method for quantification of CAC introduced by Agatston et al. in 1990 still represents the most frequently used and worldwide established method for CAC quantification (3).

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Although nowadays the radiation dose for CAC scans may be considered relatively low while simultaneously maintaining highest image quality, emphasis on dose reduction and further development strides to that effect continue to gain scientific and public attention (4). Particularly in view of increasing screening examinations of healthy individuals, radiation exposure will become considerable on a population level (5).

Radiation exposure is mainly influenced by tube potential and tube current. Nowadays there are different options for image reconstruction which have been proven to influence not only image quality, but also radiation dose (6). Typically, CAC scans are reconstructed with filtered back projection (FBP), which represented the standard reconstruction algorithm in CT for a long period of time. Within the last decade, iterative reconstruction (IR) techniques have been gradually established in clinical routine. This promising development is largely attributed to increased distribution and widespread availability of powerful computer technology. The current concern is to take advantage of these IR techniques to provide better image quality while simultaneously evaluating their potential for further reduction of radiation dose (7–9). Use of IR algorithms for coronary CT angiography is now standard, whereas CAC scorings continue to be computed with FBP as it remains up to debate to what extent coronary calcium scores might be influenced by use of IR algorithms. Over time, proportional radiation exposure of CAC scoring has increased with regards to total exposure dose in cardiac CT including coronary CT angiography.

Therefore, the aim of this study was to assess and quantify the possible dose reduction while maintaining both image quality and Agatston scores using a third-generation dual-source CT in combination with a new IR algorithm.

Material and Methods

The study design consisted of a phantom study using small, medium, and large phantoms for CAC scoring at different acquisition parameters. Subsequently, an ex vivo evaluation of a human heart was performed to demonstrate not only quantitative, but also visual image quality when applying different radiation doses and IR levels, respectively.

Phantom study

The phantom study was performed with a commercially available 30-cm-wide anthropomorphic calcium scoring phantom (QRM, Moehrendorf, Germany) with a total of six cylindrical inserts (three inserts of 5 mm and three inserts of 3 mm) containing

hydroxyapatite at different concentrations (800, 400, 200 mg/cm³). Details and composition of the phantom have been described before (10). Each acquisition was conducted three times, i.e. without additional attenuation ring, as well as with small (35 cm wide) and large (40 cm wide) attenuation rings for simulation of a slim, average-sized, and large patients. More detailed information concerning design and composition of the phantom has been described before (11).

All scans were performed with a third-generation dual-source CT (SOMATOM Force, Siemens Healthineers, Forchheim, Germany) at 120 kVp tube potential using a standard high-pitch calcium scoring protocol. Reference tube current was set to 80 mAs for standard and then stepwise reduced to 60, 40, 20, and 10 mAs, respectively. Images were reconstructed with a slice thickness of 3.0 mm, an increment of 1.5 mm, and a standard weighted filtered back projection (wFBP) kernel. Additional reconstructions were performed with a new version of an established iterative reconstruction kernel (ADMIRE, Siemens Healthineers) at different strength levels, ranging from 1 (lowest) to 5 (highest). Further details and operation mode of the ADMIRE kernel have been discussed before (12). For each series, calcifications were quantified by calculation of Agatston scores as described by Agatston et al. and by calculation of volume scores (3).

A dedicated non-commercial custom software solution (Siemens Healthineers) was developed to allow the semi-automatic Agatston scoring of the inserts. The nature of the anthropomorphic calcium scoring phantom allowed the evaluation in an automatic fashion as the location of the inserts can be determined by predefined ROI locations. The software was validated by comparison with a commercial software package (Syngo.via VA30A, Siemens Healthineers) on a selected number of images with manual lesion labeling by an experienced reader. The overall agreement for the automatic method if applied to the reference phantom is within 5% relative uncertainty. The semi-automatic extraction of the Agatston score in the phantom was chosen to allow for exclusion of human bias in lesion detection in a non-blinded phantom experiment.

Ex vivo study

For the ex vivo part of the study, a heart from a deceased male patient was examined. Informed consent to donate his body to medical education and research had been obtained from the patient ante-mortem. In addition, a statement of non-objection was issued by the local ethics committee. The explanted heart was fixed in alcohol and positioned in a water barrel (Fig. 1): first, to achieve attenuation similar to surrounding tissue in vivo; and, second, to allow all

intraluminal air to escape from the heart chambers and especially the coronary arteries. All acquisitions were performed as in the phantom study, i.e. with a fixed tube potential of 120 kVp and reference tube currents of 80, 60, 40, 20, and 10 mAs.

Statistical analysis

Comparison between FBP and the different strength levels of the new ADMIRE reconstruction algorithm was performed with the Wilcoxon signed-rank test for



Fig. 1. Ex vivo examination of a human heart in a water barrel.

between-group comparisons with the Bonferroni correction applied for multiple testing. Statistical analyses were performed with IBM SPSS Statistics 21 (IBM Corp., Armonk, NY, USA). Statistical significance was assumed at $P < 0.05$.

Results

Total Agatston scores for the three different phantom sizes calculated from FBP and ADMIRE at different tube currents are shown in Fig. 2. In general, Agatston scores were found to be slightly decreasing with increasing ADMIRE levels ($P < 0.001$). When lowering tube current, Agatston scores proved to remain relatively stable between 80 and 40 mAs and increased at lower tube currents, particularly in the medium and large phantoms.

Total volume scores for the three different phantom models are displayed in Fig. 3. Comparable to Agatston scores, volume scores were found to be in the range of 600 mm^3 between 80 and 40 mAs reference tube current. Likewise, they decreased with increasing levels of iterative reconstruction and remained relatively stable down to a tube current of 40 mAs. As for Agatston scores, the increase of volume scores at

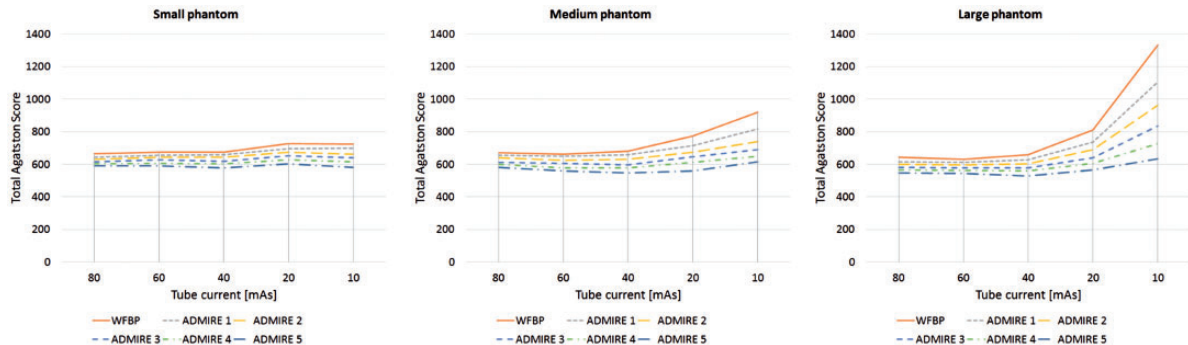


Fig. 2. Total Agatston scores for the three different phantom sizes calculated from FBP and ADMIRE.

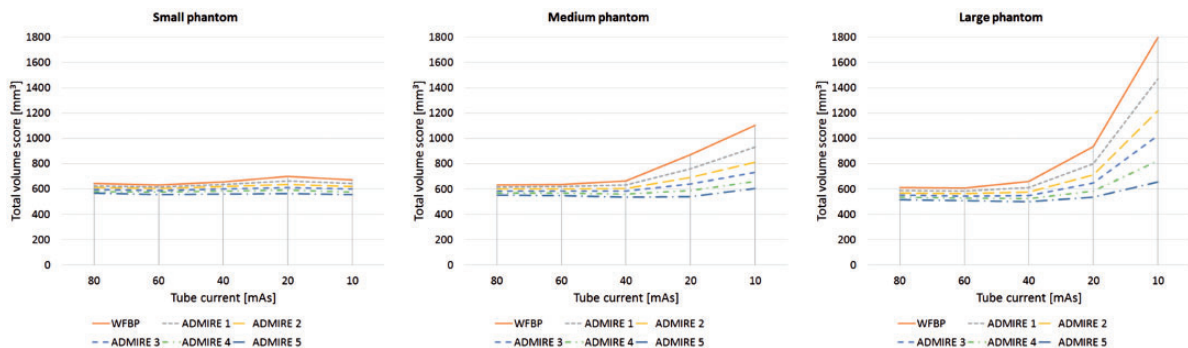


Fig. 3. Total volume scores for the three different phantom sizes calculated from FBP and ADMIRE.

Table 1. Total and individual Agatston scores of hydroxyapatite inserts.

Tube current (mAs) Reconstruction	Small phantom			Medium phantom			Large phantom			
	80 FBP	10 ADMIRE 1	Δ	80 FBP	10 ADMIRE 3	Δ	80 FBP	10 ADMIRE 5	Δ	
Hydroxyapatite inserts	200 mg/cm ³ – 3 mm	10.3	8.4	-1.9	10.7	15.1	4.4	4.7	5.4	0.8
	200 mg/cm ³ – 5 mm	56.0	85.9	29.9	59.7	70.9	11.1	53.4	75.2	21.8
	400 mg/cm ³ – 3 mm	35.7	31.9	-3.8	29.1	33.6	4.5	35.4	24.1	-11.3
	400 mg/cm ³ – 5 mm	190.3	190.0	-0.3	187.7	185.5	-2.2	174.5	165.6	-8.9
	800 mg/cm ³ – 3 mm	84.4	94.1	9.8	90.6	79.5	-11.1	82.9	80.3	-2.6
	800 mg/cm ³ – 5 mm	288.8	289.8	1.1	292.7	299.5	6.7	291.7	278.9	-12.8
	Total	665.5	700.1	34.6	670.5	684.1	13.6	642.6	629.5	-13.1

Table 2. Radiation doses depending on tube current for the different phantom sizes.

Reference tube current (mAs)	Small phantom		Medium phantom		Large phantom	
	Effective tube current (mAs)	CTDI (mGy)	Effective tube current (mAs)	CTDI (mGy)	Effective tube current (mAs)	CTDI (mGy)
80	26	0.88	54	1.78	122	4.01
60	20	0.66	40	1.34	92	3.05
40	12	0.41	26	0.88	62	2.06
20	10	0.33	12	0.43	32	1.05
10	10	0.32	10	0.33	16	0.56

a tube current of 20 and 10 mAs decreased with higher levels of iterative reconstruction. In particular, with ADMIRE level 5 only a mild increase could be observed in the medium and large phantom models.

Based on the results for total Agatston scores, the individual hydroxyapatite inserts were further evaluated (Table 1). Comparison was performed between Agatston scores at 80 mAs with FBP as reference setting and 10 mAs with different levels of iterative reconstruction, depending on the level with total results closest to the reference setting. Correspondingly, levels of iterative reconstruction closest to the reference were level 1 in the small phantom, level 3 in the medium phantom, and level 5 in the large phantom. In general, differences in Agatston scores between the reference setting and IR at a tube current of 10 mAs were largest in the 5-mm insert with a concentration of 200 mg/cm³, ranging between 29.9 in the small and 11.1 in the medium phantom.

Radiation doses depending on tube current for the different phantom sizes are displayed in Table 2. In the small phantom, CTDI at the standard reference tube current of 80 mAs was 0.88 mGy and could be lowered to 0.32 mGy at a reference tube current of 10 mAs. Of note, the effective tube current was already 10 mAs at a

reference tube current of 20 mAs and could not be further reduced as 10 mAs is the lowest possible tube current for operation of the scanner. In the medium phantom, CTDI could be reduced from 1.78 mGy at a reference tube current of 80 mAs to 0.33 mGy at a reference tube current of 10 mAs. The highest reduction in radiation dose could be achieved in the large phantom. Here, CTDI was lowered from 4.01 mGy at 80 mAs reference tube current to 0.56 mGy at 10 mAs reference tube current.

An example of image quality at different tube currents and the influence of varying strength levels of IR is provided in Figs. 4 and 5, respectively. Both show a slice through the calcified origin of the left coronary artery from the aorta and the left ventricle surrounded by epicardial fat in the human heart. In Fig. 4, all images were reconstructed with FBP and reference tube current was gradually reduced from 80 mAs (Fig. 4a) to 10 mAs (Fig. 4e), resulting in an apparent increase in image noise. The effect of the iterative reconstruction algorithm is displayed in Fig. 5. The left (Fig. 5a) is a slice reconstructed with FBP at 10 mAs tube current. Then, from left to right the same slice reconstructed with increasing levels of iterative reconstruction is shown, ranging from level 1 (Fig. 5b) to level 5

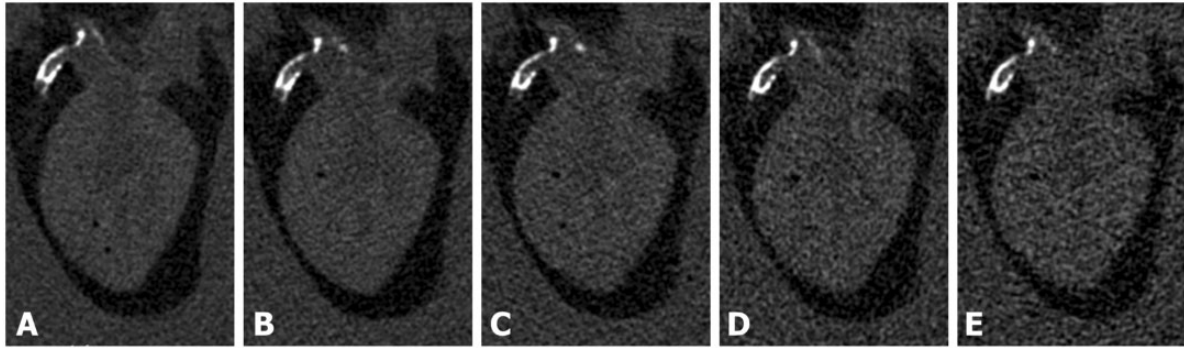


Fig. 4. Image quality at 80 mAs (a), 60 mAs (b), 40 mAs (c), 20 mAs (d), and 10 mAs (e) reference tube current. All images reconstructed with FBP. Image shows a slice through the calcified origin of the left coronary artery in the explanted human heart.

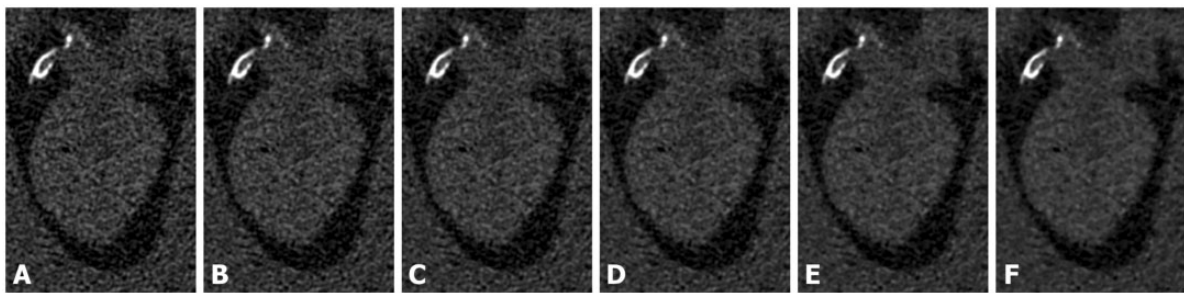


Fig. 5. Influence of IR on image quality. Same slice as in Figure 4 at 10 mAs tube current. Reconstruction with FBP (a) and with increasing levels of IR, ranging from level 1–5 (b–f, respectively).

(Fig. 5f), resulting in a stepwise decrease of image noise. Of note, Figs. 4 and 5 were generated for demonstration purposes only. Agatston and volume scores were calculated only from the phantom study as the phantom setup was considered to provide more reliable results in repetitive scans.

Discussion

CAC scoring has been shown to be a valuable tool for cardiac risk assessment in asymptomatic patients (2,13–16). As for all examinations in healthy individuals with potential follow-ups, on the one hand possible adverse effects to the patient are to be avoided as far as possible, i.e. radiation exposure should be as low as reasonable achievable (ALARA-principle). On the other hand, high accuracy and reproducibility are desired. Previous studies have shown that the variability for Agatston scores in repeated measurements with identical acquisition parameters and scanners settles in the range of 8–20.1% (17,18). Moreover, even just slightly shifting the starting point of the reconstruction of the 3.0-mm slices used for assessment of a single examination can have a substantial effect on resulting Agatston and volume scores (19). Therefore, when

comparing different acquisition parameters, variations may not necessarily reflect a substantial difference solely based on differences in the acquisition settings.

Due to the categorization/stratification of patients into different risk groups, variability in Agatston scores is not necessarily associated with a change in clinical management. Yet, in cases where the score is close to the border of another risk group, even small changes could influence medical therapy and possibly prognosis. A recent study by the MESA (Multi-Ethnic Study of Atherosclerosis) group revealed that approximately one-half of patients eligible for statin therapy according to current ACC/AHA guidelines can be reclassified to not eligible due to the absence of coronary calcifications, i.e. an Agatston score of 0 (20). These findings could not only lead to considerable savings in the public health sector but also stress the importance of correctly identifying even the presence of small calcifications.

For translation of our results into clinical routine, some factors have to be considered. First, lower tube current resulted in higher Agatston and volume scores, especially at tube currents of 20 or 10 mAs. Second, this increase was higher, the larger the diameter of the phantom was presumably caused by higher image

background noise resulting in overestimation of the calcifications. Third, IR was shown to reduce scores, especially at higher strength levels, most likely caused by “sharpening” the calcifications and thus reducing the number of pixels with densities over the scoring threshold. Therefore, to avoid false low or high scores, a balance has to be found between tube current, strength of IR, and object diameter. In our study setup, iterative reconstruction strength level 1 in the small phantom, level 3 in the medium phantom, and level 5 in the large phantom in combination with a reference tube current of 10 mAs resulted in scores comparable to the standard calcium scoring setting of 80 mAs reference tube current with FBP. Notably, by choosing these settings, i.e. reducing reference tube current from 80 mAs to 10 mAs, radiation dose could be reduced by as much as 86% in our phantom study in the large phantom.

Several previous studies have evaluated different methods of various vendors for dose reduction in coronary calcium scoring. One possibility for dose reduction is lowering the tube potential (21). Although reduction of tube potential in CT leads to decreased patient dose, it is considered to be a doubtful method in context with the evaluation of CAC, mainly due to altered CT density levels at lower tube potentials. Deprez et al. assessed the influence of reduced tube potential protocols on Agatston score results and concluded that due to the multi-threshold measurement, modified Agatston scores acquired at tube potentials lower than 120 kVp cannot be reliably converted to standard Agatston scores by using a single, adjusted calcium attenuation threshold (10).

Another possibility for reduction of radiation dose is lowering tube current, resulting in increased image noise, false positive identification of CAC, and consecutively higher Agatston scores when using standard FBP for image reconstruction. Several previous publications, all using multi-row single source CT, have discussed the benefits and pitfalls of different IR algorithms for noise and dose reduction in CAC evaluation. In particular, the publications on hybrid IR algorithms and model-based IR (iDose4 and IMR, Phillips Healthcare, Best, The Netherlands), as well as adaptive iterative dose reduction algorithms (AIDR 3D, Toshiba Corp. Medical Systems, Tokyo, Japan) attract attention (6,10,22–24). IR algorithms allow for a significant reduction in image noise and could allow for substantial reduction in radiation dose while maintaining diagnostic accuracy as has been previously shown for other vendors than the one in the present study (22,25,26). Yet, in the current literature, use of IR in CAC scoring remains up to debate. Matsuura et al. argued that tube current can be lowered and hybrid IR applied without influencing CAC scores (23). Caruso et al. concluded that IR renders comparable results to filtered back

projection in CAC scoring when a correction factor is applied (27). In contrast, Li et al. arrived at the conclusion that CAC scores significantly decreased with use of IR and tended to be underestimated at least for female anatomy in their phantom study (28).

In the future, strength of IR in patient studies could be selected depending on patient diameter, i.e. lateral chest width measured on the topogram, as has been suggested for selection of effective tube current in recent guidelines (29). An alternative would be selecting an optimized protocol for all patients irrespective of size. Based on the results of our phantom study, a reference tube current of 40 mAs with IR level 1 could result in Agatston scores and volume scores in the range of the standard setting with reference tube current of 80 mAs and wFBP reconstruction (Figs. 2 and 3). However, these settings need to be further evaluated in a clinical study to assess reliability of reproducibility of the low dose protocol.

Our study has some limitations. First, as this is an *in vitro* study, possible influence of *in vivo* motion has to be taken into account. However, usually coronary calcium scoring is performed with ECG-gating in diastole during breath-hold and therefore motion is limited as far as possible. Second, possible effects of reduced tube current and use of IR on reclassifications between risk groups are to be considered and should be further evaluated in patient studies. Third, due to the different IR algorithms from different vendors the results from our study may not necessarily be transferrable to other CT systems.

In conclusion, as coronary calcium scoring is a main, widespread tool for cardiac risk assessment in asymptomatic patients, accompanying possible adverse effects, i.e. radiation exposure, should be held as low as reasonably achievable. Tube current reduction and use of new IR algorithms and possibly individualized strength levels of IR instead of wFBP hold the potential for substantial dose reduction in CAC scoring.

Declaration of conflicting interests

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