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Research article

Reduced radiation dose with model based iterative reconstruction coronary artery calcium scoring

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A R T I C L E I N F O

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A B S T R A C T

Assessing coronary artery calcium (CAC) is a valuable tool for individualizing cardiac risk assessment. In CAC scanning, this technical report assesses the use of a true model-based iterative reconstruction algorithm using forward projected model-based iterative reconstruction ("FIRST") and assess whether FIRST allows for reduced radiation dose CAC scanning on 320-detector row computed tomography (320-CT). Here, 100 consecutive patients prospectively underwent reduced and standard dose scans. For the patients (59 ± 9 years, 61% male) stratified by Agatston categories 0, 1–10, 11–100, 101–400, > 400, agreement between reduced dose with FIRST versus standard dose with FBP was excellent at 81% (95% CI: 73–88%) with kappa 0.74 (95% CI: 0.64–0.85). Median radiation exposure was 75% lower for reduced (0.35 mSv) versus standard dose (1.37 mSv) scans. In conclusion, agreement was excellent for reduced dose with FIRST and standard dose with FBP in 320-detector row CT CAC imaging in well-established categories of cardiovascular risk. These methods make it possible to reduce radiation exposure by 75%.

1. Introduction

Assessing coronary artery calcium (CAC) by non-contrast cardiac computed tomography (CT) is valuable in assessing an individual's risk of coronary heart disease events [1–3]. Furthermore, the recent introduction of iterative reconstruction (IR) reduces image noise and enables lower radiation for CT angiography, but is more established against conventional filtered back projection (FBP) in CT angiography rather than CAC scoring [4–9]. Previous iterative reconstruction methods are rooted in filtered back projection and retain some of its limitations. In contrast, forward projected model-based iterative reconstruction (FIRST) is a true, fully implemented model-based iterative reconstruction algorithm, meaning a forward projection step is performed for every iteration [10,11]. FIRST has rarely been applied in CAC scanning. Thus, this study assesses whether CAC scanning with FIRST can achieve significant radiation dose reduction with similar risk prognostication.

2. Methods

The study was approved by the Institutional Review Board (IRB) and Radiation Safety Committee of the National Institutes of Health and National Heart, Lung, and Blood Institute (URL: https://clinicaltrials.gov/ct2/show/NCT01621594. Unique identifier: NCT01621594).

100 consecutive patients were prospectively scanned at a standard radiation dose and at a reduced radiation dose in a randomized order. Each scan underwent reconstruction at standard dose with filtered back projection ("Standard w FBP") and at reduced radiation dose with forward projected model-based iterative reconstruction ("Reduced w FIRST", Canon Medical Systems, Otawara, Japan). Standard w FBP was the reference standard. Patient characteristics were prospectively obtained.

All patients had non-contrast cardiac CT using an axial 320 x 0.5 mm detector row CT (AquilionONE ViSION, Canon Medical

Abbreviations: CAC, coronary artery calcium; CHD, coronary heart disease; IR, iterative reconstruction; CT, computed tomography; FBP, Filtered Back Projection; FIRST, Forward Projected Model-Based Iterative Reconstruction; IRB, institutional review board; SCCT, Society of Cardiovascular Computed Tomography; mSv, millisievert; EBCT, electron beam computed tomography; MDCT, multidetector computed tomography

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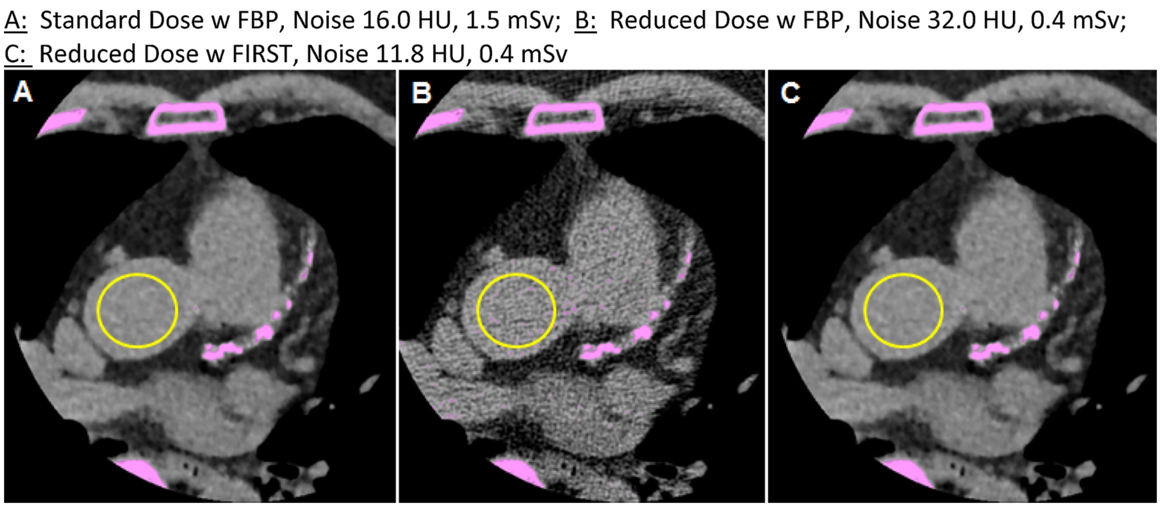

Fig. 1. Example of CTs with a region of interest (ROI) in the ascending aorta measuring the image noise as the standard deviation (SD) of the ROI in Hounsfield Units (HU):
A: Standard Dose w FBP, Noise 16.0 HU, 1.5 mSv; B: Reduced Dose w FBP, Noise 32.0 HU, 0.4 mSv;
C: Reduced Dose w FIRST, Noise 11.8 HU, 0.4 mSv.

Table 1
Baseline Characteristics.

Age, years ± **SD**	59 ± 9 years
Male, n (%)	61 (61%)
Body Mass Index, kg/m^2 ± SD	28 ± 5.8
Ethnicity	
White, n (%)	65 (65%)
Black, n (%)	19 (19%)
Asian, n (%)	7 (7%)
Hispanic, n (%)	9 (9%)
CAD Risk Factors	
Hypertension, n (%)	52 (52%)
Diabetes Mellitus, n (%)	17 (17%)
Hyperlipidemia, n (%)	39 (39%)
Family History of CAD, n (%)	27 (27%)
Current Smoker, n (%)	9 (9%)
Former Smoker, n (%)	18 (18%)

Abbreviations: SD = Standard Deviation; CAD = Coronary Artery Disease; ACE-I = Angiotensin converter enzyme-inhibitor; ARB = Angiotension Receptor Blocker.

Systems, Otawara, Japan) at gantry rotation time of 275 ms, 0.5 mm slice thickness and tube voltage of 120 kV with reconstructions at contiguous 3 mm slice thickness using prospective electrocardiogram-triggered gating [12]. To briefly discuss the iterative reconstruction algorithm, whereas the prior adaptive iterative dose reduction 3D (AIDR) was a hybrid model-based IR with FBP algorithm, FIRST is a fully model based IR algorithm. As described by Maeda, et al and Wu, et al., FIRST jointly optimizes image quality in both the sonogram and images spaces. By including both a forward and statistical model in the projection data, FIRST enables high spatial resolution with reduced image noise [13,14]. Radiation dose was modulated through automated exposure control (Sure Exposure 3D, Canon Medical Systems, Otawara, Japan). Effective radiation dose was estimated by multiplying the dose length product by a k-factor of 0.014 mSv/mGy cm by standard methodology [15].

CAC quantification was performed per Society of Cardiovascular Computed Tomography (SCCT) standard methodology and the Agatston approach [12,15–21]. Reduced versus standard dose scans were interpreted in random order in separate sessions by an experienced cardiologist.

2.1. Statistical analysis

Data are presented as mean ± SD or frequency (percentage) for patient characteristics and median with 5th and 95th percentile for coronary artery calcium (CAC) scores. The inter-scan variability was assessed between the low dose FIRST and standard dose FBP Agatston CAC scores through the Bland-Altman plot and the repeatability coefficient (RC). The RC was calculated using the method of Sevrukov et al. to obtain an approximate 95% confidence band for the difference between the two scans as a function of the average of the two scans [22]. The percent agreement and simple Kappa statistic were also assessed for the standard Agatston categories defined as 0, 1–10, 11–100, 101–400, and > 400.

3. Results

A majority (n = 63, 63%) of patients had CAC (Agatston score > 0) detected on standard w FBP scanning. The CAC for the cohort encompassed a wide range of standard FBP Agatston scores (0–1590), but with 95% of the scores ≤ 739. Baseline characteristics of the patient population (n = 100) were representative of a wide range of cardiovascular risk (Fig. 1) (Table 1).

Reduced w FIRST Agatston scores were classified within the same Agatston group as Standard w FBP 81% (81/100) of the time with a 95% CI of 73–88% (Fig. 2). This corresponded to a kappa = 0.74 and 95% CI of 0.64-0.85. For the 44 patients with zero CAC on standard w FBP scans, 36/44 (82%) had a zero calcium score on both standard radiation dose and reduced radiation dose scans. By Bland-Altman, the absolute differences for low dose FIRST and standard w FBP were nominal at small values and increased across increasing CAC scores with a reproducibility coefficient = 4.8 (Fig. 3).

Scan parameters and radiation dose are listed in Table 2. The median (5th-95th percentiles) radiation exposure was 75% (95% CI: 51%–76%) lower for reduced versus standard dose scans corresponding to overall medians of 0.35 mSv (5th, 95th: 0.15, 1.03) for reduced dose scans and 1.37 mSv (5th, 95th: 0.49, 3.15; $p < 0.0001$ for standard dose scans).

4. Discussion

This study uniquely evaluated reduced radiation dose CAC scoring

		Standard w FBP				
		0	1-10	11-100	101-400	>400
Reduced Dose w FIRST	0	36	1	0	0	0
	1-10	8	6	0	0	0
	11-100	0	4	10	0	0
	101-400	0	0	3	18	1
	>400	0	0	0	2	11

Overall Agreement = 81%
K=0.74 (95% CI: 0.64 – 0.85)

Fig. 2. Overall Agreement of Standard Dose w Filtered Back Projection (FBP) vs. Reduced Dose w Forward projected model-based iterative reconstruction ("FIRST") by standard Agatston categories. In this specific comparison, Reduced w FIRST Agatston scores were classified within the same Agatston group as Standard w FBP 81% (81/100) (95% CI: 73–88%) and kappa 0.74 (95% CI: 0.64-0.85).

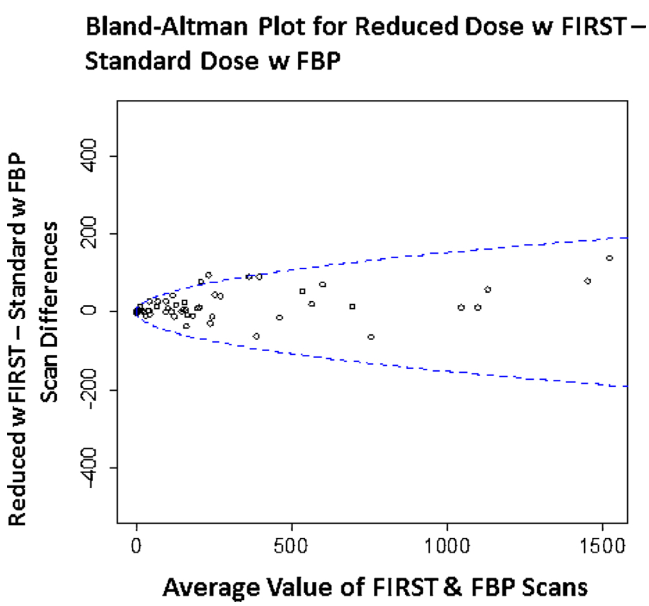

Fig. 3. Difference Between Reduced Dose w FIRST – Standard Dose w FBP Agatston Score: Bland-Altman Plot of Difference between Reduced w FIRST and Standard w FBP scans with upper and lower 95% confidence bounds shown. The difference between FIRST w IR and Standard w FBP was small at low values (< 400) and increased as the mean scores increased. The 95% repeatability bounds for the Reduced w FIRST – Standard w FBP scan differences are ± 4.8 $\sqrt{average\ value}$.

via true model-based iterative reconstruction on a 320-detector row CT scanner. Iterative Reconstruction in CAC has evolved from anthropomorphic phantom studies to application in patients at standard radiation dose to assess image noise improvement and most recently reduced radiation dose [12,23–30] (Fig. 4).

The study by, Choi et al. using adaptive iterative dose reduction is the largest comparative study at n = 200 patients and showed similar radiation dose reduction of 75% with minimal interscan variability on a 320-detector row platform [31]. Rodriguez et al. and Tatsugami et al.

Table 2
Scan Parameters and Radiation Dose.

N = 100	Standard Dose	Reduced Dose
Current ± SD, mA	392.3 ± 212.6	120.5 ± 85.2
Z-Coverage ± SD, mm	117 ± 7	117 ± 7
Scans at 120 mm Z-coverage, n (%)	78 (78%)	78 (78%)
DLP, mGy * cm Median (5th, 95th)	98.0 (35.2, 225.2)	24.3 (10.7, 73.9)
Effective Dose, mSv Median (5th, 95th)	1.4 (0.46, 3.2)	0.35 (0.15, 1.0)
Heart Rate ± SD, beats per minute	58 ± 8	58 ± 8

Abbreviations: mA = milliamps; mm = millimeters; DLP = Dose Length Product; mSv = millisievert; SD = Standard Deviation.

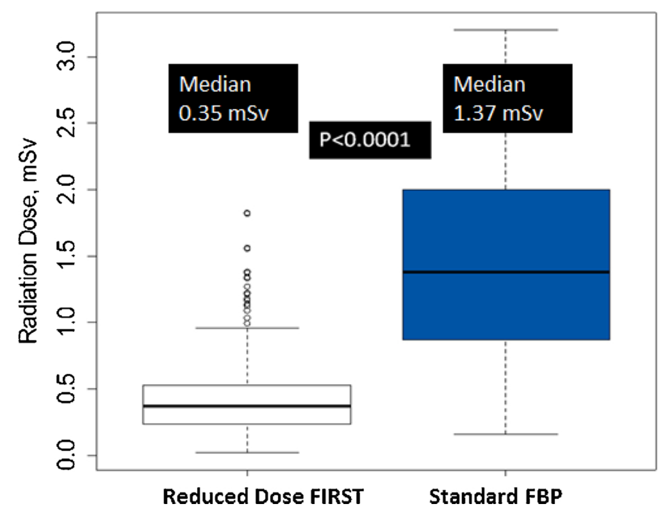

Fig. 4. Radiation Exposure for Reduced vs. Standard Dose Scans: As shown in the following box and whisker plots, median radiation exposure for Reduced Dose was median 0.35 mSv (5th, 95th: 0.15, 1.17) and for Standard Dose was median 1.37 mSv (5th, 95th: 0.46, 3.18). For patients with educed dose scans, the outliers represent patients with high BMI (36–45 kg/m^2) where the automatic exposure control calculated a higher mA for scans. For standard dose scans, the scanner reached maximal x-ray tube output so there are no outliers beyond the 1.5 * interquartile range. The median radiation reduction was 75% for Reduced w FIRST vs. Standard w FBP Dose Scans (p < 0.0001).

have also confirmed these findings in n = 27 patients and n = 54 patients, respectively [30,32].

There have been varied approaches to reduced radiation dose calcium scanning on different scanning platforms. Tesche et al. retrospectively investigated the accuracy and radiation dose reduction using tin pre-filtration with iterative beam-hardening correction (IBHC) (Siemens Healthcare, Forchheim, Germany) in 62 patients who underwent a clinically indicated CACS acquisition and found that there was excellent correlation and agreement in Agatson scores between the standard method and IBHC method while also achieving a 75% reduction in radiation dose [33]. den Harder compared a hybrid IR and model based IR approach (Philips Healthcare, Best, The Netherlands) and found that radiation dose for coronary calcium scoring could be safely reduced in a small (n = 28) cohort to a slightly higher dose than our study, 0.4 mSV without compromise in image quality [34]. Hecht et al. and Matsuura et al. tested the use of a hybrid IR algorithm based on Poisson denoising algorithm (iDose, Phillips, Best, Netherlands) in 102 consecutive patients and 77 patients respectively [35,36]. Willemink et al. evaluated IR in 30 patients at four dose levels and found CAC reclassifications rates remained within 15% at 20% of the routine radiation dose [37]. A summary of these findings is included in Table 3.

To place these findings within a clinical context, the current analysis

Table 3
Summary of Selected Patient Studies Evaluating Low Dose Radiation with Iterative Reconstruction.

Author	Year	n	IR Algorithm	Vendor	Standard vs Low Radiation Effective Dose	Agatston Category Risk Reclassification
Hecht, et al[35]	2014	102	HIR	Philips Healthcare	0.76 mSv vs 0.37 mSv (mean)	8%
Matsuura, et al[36]	2015	77	HIR	Philips Healthcare	1.20 mSv vs 0.24 mSv (mean)	n/a
Willemink, et al[37]	2015	30	HIR	Philips Healthcare	0.7 mSv vs 0.2 mSv (< 80 kg pts only) (median)	15%
Choi, et al[31]	2015	200	AIDR3D	Canon Medical	1.38 mSv vs 0.37 mSv (median)	11%
Tatsugami F, et al[30]	2015	54	AIDR3D	Canon Medical	2.2 mSv vs 0.7 mSv (mean)	n/a
den Harder, et al[34]	2016	28	HIR	Philips Healthcare	0.9 mSv vs 0.4 mSv (mean)	18%
Sulaiman[39]	2017	100	ASIR	GE Healthcare	2.3 mSv vs 1.8 mSv (mean)	3%
Choi, et al (current paper)	2018	100	FiRST	Canon Medical	1.37 mSv vs 0.35 mSv (median)	19%

n = number of patients; IR = iterative reconstruction; HIR = hybrid iterative reconstruction; AIDR = adaptive iterative dose reduction; ASIR = adaptive statistical iterative reconstruction; FiRST = forward projected model-based iterative reconstruction.

included an evaluation of the CAC reclassification by Agatston prognostication categories. The results showed risk reclassification in 19% of cases. This is consistent with prior reported literature showing that Agatston risk reclassification ranges from anywhere from 3 to 18% (Table 3). It is also consistent with prior analysis of the Multi-Ethnic Study of Athersclerosis by Detrano, et al. that interscan variability of the same patient on the same scanning platform is 20% [38].From the subjective perspective of the authors, while there is increased image noise with the FiRST images, there was no significantly added time or difficulty required to interpret the scans.

Recently published 2018 American College of Cardiology/American Heart Association (ACC/AHA) multisociety guidelines for cholesterol management place an added emphasis on CAC for clinical decision making for patients at low-intermediate risk [39]. The results of the present study suggest a nominal increase in risk categorization for a small proportion of patients previously classified with a zero score. However, based on recently published analysis by Mitchell, et al, this change does reach a threshold (CAC > 100) where there is evidence of significant benefit to additional pharmacologic treatment with statin therapy [40]. Thus, reduced radiation dose CAC imaging will have a minimal, but non-negligible clinical impact on risk reclassification. However, shared decision making should continue to be a key aspect for clinicians and patients in approaching a nominally elevated CAC score as espoused in the aforementioned 2018 American College of Cardiology/American Heart Association guidelines

Several limitations for this study are acknowledged. This study was single-center and single platform. This specific proprietary algorithm may only be applied to the 320-detector CT system from Canon Medical Systems which limits its applicability to older scanners on other vendors. The use of both a standard dose and reduced dose scan increased radiation exposure to patients, though overall radiation dose delivered was within an accepted limit as specified by both the IRB and NIH Radiation Safety Committee and written informed consent was obtained in all subjects. The 75% radiation dose reduction we used may have been conservative and a greater radiation dose reduction may be achievable without a significant change in risk prognostication.

In conclusion, when compared to standard w FBP, FIRST achieves a median radiation dose of 0.35 mSv, which represents a 75% radiation dose reduction with similar image quality. These methods make it possible to perform individualized cardiac risk stratification with CAC at negligible radiation doses when utilized on a 320-detector row CT platform.

Guarantor

The scientific guarantor of this publication is Dr. Marcus Chen.

Conflict of interest

Dr. Marcus Chen has an Institutional Research Agreement with Canon Medical
Systems Corporation.

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Role of the funding source

This funding source had no role in the study design, execution, analyses, interpretation of the data, or decision to submit results.

Statistics and biometry

Dr. Eric Leifer has significant statistical expertise.

Informed consent

Written informed consent was obtained from all patients in the study.

Ethical approval

National Heart, Lung and Blood Institute Institutional Review Board approval was obtained.

Methodology

Prospective diagnostic study, performed at one institution

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