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**CARDIAC**

# Low-dose coronary calcium scoring CT using a dedicated reconstruction filter for kV-independent calcium measurements

Ayman Jubran[1,2] · Domenico Mastrodicasa[1,3] · Gijs D. van Praagh[4] · Martin J. Willemink[1] · Aya Kino[1] · Jia Wang[1] · Dominik Fleischmann[1,2,3] · Koen Nieman[1,2,3]

## Abstract

In this prospective, pilot study, we tested a kV-independent coronary artery calcium scoring CT protocol, using a novel reconstruction kernel (Sa36f). From December 2018 to November 2019, we performed an additional research scan in 61 patients undergoing clinical calcium scanning. For the standard protocol (120 kVp), images were reconstructed with a standard, medium-sharp kernel (Qr36d). For the research protocol (automated kVp selection), images were reconstructed with a novel kernel (Sa36f). Research scans were sequentially performed using a higher (cohort A, $n = 31$) and a lower (cohort B, $n = 30$) dose optimizer setting within the automatic system with customizable kV selection. Agatston scores, coronary calcium volumes, and radiation exposure of the standard and research protocol were compared. A phantom study was conducted to determine inter-scan variability. There was excellent correlation for the Agatston score between the two protocols ($r = 0.99$); however, the standard protocol resulted in slightly higher Agatston scores (29.4 [0–139.0] vs 17.4 [0–158.2], $p = 0.028$). The median calcium volumes were similar (11.5 [0–109.2] vs 11.2 [0–118.0] mm$^3$; $p = 0.176$), and the number of calcified lesions was not significantly different ($p = 0.092$). One patient was reclassified to another risk category. The research protocol could be performed at a lower kV and resulted in a substantially lower radiation exposure, with a median volumetric CT dose index of 4.1 vs 5.2 mGy, respectively ($p < 0.001$). Our results showed that a consistent coronary calcium scoring can be achieved using a kV-independent protocol that lowers radiation doses compared to the standard protocol.

## Key Points

• *The Sa36f kernel enables kV-independent Agatston scoring without changing the original Agatston weighting threshold.*
• *Agatston scores and calcium volumes of the standard and research protocols showed an excellent correlation.*
• *The research protocol resulted in a significant reduction in radiation exposure with a mean reduction of 22% in DLP and 25% in CTDI$_{vol}$.*

**Keywords** Coronary artery disease · Vascular calcification · Risk factors · Tomography, x-ray computed · Radiation dosage

Ayman Jubran and Domenico Mastrodicasa contributed equally to this work.

✉ Domenico Mastrodicasa
mastro@stanford.edu

1 Department of Radiology, Stanford University School of Medicine, Stanford, CA, USA

2 Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA

3 Stanford Cardiovascular Institute, Stanford University School of Medicine, Stanford, CA, USA

4 Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, The Netherlands

## Abbreviations

| | |
|---|---|
| ACC | American College of Cardiology |
| AHA | American Heart Association |
| BMI | Body mass index |
| BPM | Beats per minute |
| CACS | Coronary artery calcium scoring |
| CNR | Contrast-to-noise ratio |
| CT | Computed tomography |
| CTDI$_{vol}$ | Volume computed tomography dose index |
| DLP | Dose-length product |
| ECG | Electrocardiogram |
| kV | Kilovoltage |
| kVp | Kilovoltage peak |
| mAs | Milliampere-second |
| mGy | Milligray |

## Introduction

Coronary artery calcium scoring (CACS) is a well-established tool for cardiovascular risk stratification [1–3]. The 2018 ACC/AHA Multisociety Guideline on the Management of Blood Cholesterol supports the use of calcium imaging for improved risk stratification and management decision-making [4]. The Agatston score is used clinically for quantifying coronary calcium, which is the function of the lesion area and maximal attenuation value per slice. The Agatston score was developed for electron-beam CT operated with a 130-kVp tube voltage [1]. For mechanical CT scanners, the standard tube voltage is 120 kVp. Contemporary CT scanners with more powerful Röntgen tubes can image the heart at substantially lower tube potentials, which reduces patient radiation exposure without sacrificing image quality [5–9]. The standard tube potential for calcium imaging has nevertheless remained at 120 kVp for sake of reproducibility of the Agatston score [10]. Recently, a new reconstruction kernel (Sa36f) has been developed with the objective of calcium imaging at lower tube potentials with similar Agatston scores [11]. A phantom study showed that with this kernel, it is possible to obtain consistent calcium scoring results while using different tube voltages [12]. We aimed to prospectively investigate this new reconstruction kernel in patients and to evaluate its potential for reduced radiation exposure. In addition, we compared the concordance of calcium scoring between standard and kV-independent protocol.

## Methods

### Study population

For this IRB-approved and HIPAA-compliant study, we prospectively enrolled individuals scheduled for a coronary calcium CT scan between December 2018 and November 2019 at our institution, a tertiary-care academic center. Written informed consent was obtained from all individuals. Exclusion criteria were as follows: age < 40 years (to limit proportion of negative calcium scans), heart rate > 75 bpm and atrial fibrillation (to optimize intrinsic scan-rescan reproducibility), BMI > 35 kg/m$^2$ (to limit research related exposure and increase intervention benefit) and pregnancy (for safety).

### Standard and research CT acquisition protocols

Each participant underwent a clinically indicated standard coronary calcium scoring CT scan and a research calcium scan in sequence. We used a state-of-the-art 3rd-generation dual-source CT scanner (SOMATOM Force, Siemens Healthineers). The standard protocol was performed by prospectively electrocardiogram (ECG)-triggered, axial scan mode using the following parameters: tube voltage 120 kVp, automatic tube current modulation (CARE Dose4D), reference tube current–time product of 126 mAs, collimation of $2 \times 192 \times 0.6$ mm, gantry rotation time 0.25 s. The research calcium scan protocol was identical to the standard scan, except for the tube voltage, which was determined by an automatic system (CARE kV) with customizable kV selection aimed to optimize the contrast-to-noise ratio (CNR). Within the CARE kV function, the dose setting can be optimized using a slider bar that defines the level of subject contrast for a diagnostic task [13, 14]. The slider bar ranges from "0," indicating an unenhanced scan with poor structure contrast, to "11" where the contrast is expected to be high (i.e., coronary CT angiography). The principles of this setting have been previously described [13, 14]. We sequentially tested 2 slider positions: in research protocol A, the slider bar position was set on 5; in research protocol B, the slider bar was set on position 8. In brief, the rationale behind the slider bar is that in high-contrast cases, low kV will help to improve the image contrast when iodine is used intravenously. In such cases, increased noise can be tolerated without a significant change in the CNR. In cases with low subject contrast (i.e., unenhanced CT scan), there is no benefit from using low kV because the image noise is the main determinant of image quality.

### CT reconstruction parameters

All calcium scans were reconstructed with a 3.0-mm slice thickness and an increment of 1.5 mm. The standard scans were reconstructed with a conventional, medium sharp kernel (Qr36d). The research scans were reconstructed with the new Sa36f kernel. This kernel uses a tube voltage-dependent lookup table for image reconstructions, which allows generating images at any tube voltage with Hounsfield unit (HU) values equivalent to 120 kV for bone and calcium [12].

### Image analysis

Images were analyzed with a dedicated software (syngo. via VB10 Calcium Scoring) (Fig. 1). Calcifications were defined according to the Agatston convention as a plaque with an area of at least 1.03 mm$^2$ and an attenuation threshold of 130 HU. Agatston scores and calcium volumes were calculated independently by a radiologist with 7 years of experience in cardiovascular imaging and a cardiology fellow with level 2 cardiac CT training. Both observers were unaware whether the CT scan evaluated was performed with

**Fig. 1** Upper row: axial view of the research scan reconstructed with the novel Sa36d kernel at 3 mm. Lower row: axial view of the same patient scanned with the standard protocol and reconstructed with the Qr36d kernel at 3 mm. Qr36d = conventional, medium sharp kernel; Sa36f = novel kernel
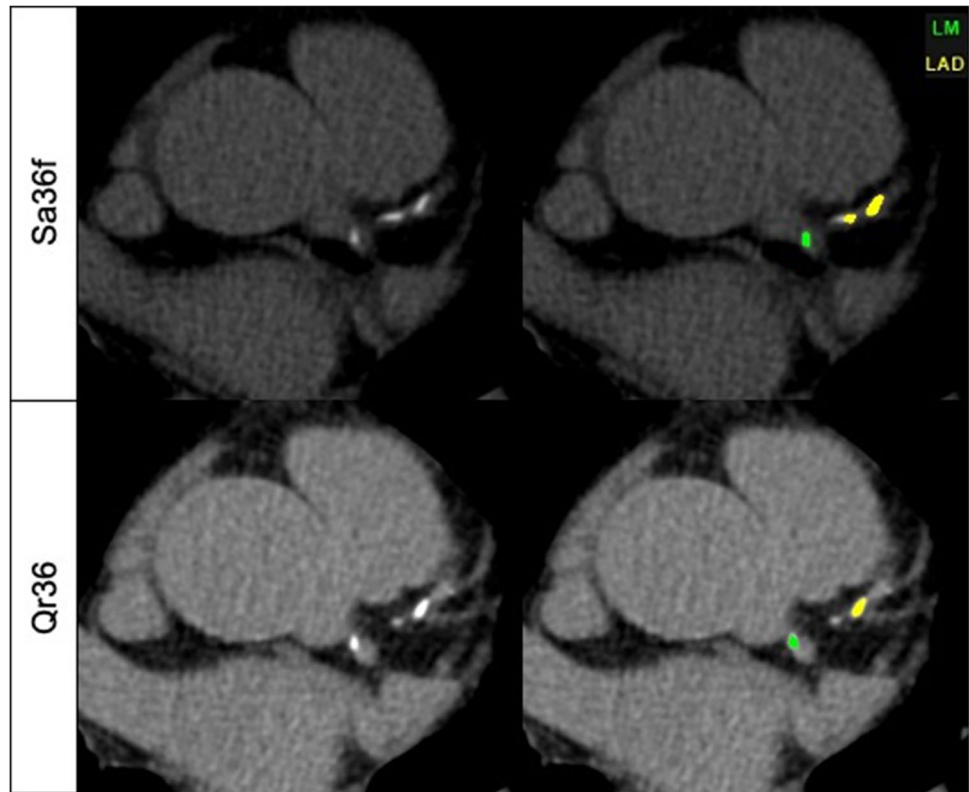
the standard or the research CT protocol. Agatston score risk categories were defined as follows: 0, 1–10, 11–100, 101–400, and > 400. The tube voltage, tube current, volumetric CT dose index (CTDIvol), effective tube current–time product, and dose-length-product (DLP) were recorded for both standard and research scans.

## Inter-scan variability

We conducted a phantom study to systematically determine the effect of acquisitions with different tube voltages and the Sa36f kernel. A commercially available anthropomorphic phantom (QRM Thorax Phantom) with a 10-cm cardiac calcification insert (QRM CCI) containing nine hydroxyapatite inserts and an extension ring (QRM extension, large) was used. The routine clinical protocol (120 kVp) was applied as described above. Additionally, tube voltage was decreased to 100 kVp and 80 kVp to assess inter-scan variability. Acquisition and reconstruction parameters are listed in Supplementary Table 1.

## Statistical analysis

SPSS version 26.0 (IBM) was used for statistical analysis. Continuous variables were expressed as medians with interquartile ranges (IQR). Normal distribution was assessed using the Kolmogorov–Smirnov test. Wilcoxon testing was used to compare Agatston scores and calcium volumes as well as kV, mAs, DLP, and CTDIvol. Pearson's correlation coefficients were calculated to compare the Agatston between the standard and the research CT protocol. Bland–Altman analysis was performed to assess the agreement between the two protocols. $p$ value $\leq 0.05$ was considered statistically significant.

## Results

A total of $n = 61$ individuals underwent both standard and research calcium scoring CT scan and were included in the final analysis. The first 31 (51.6%) participants were scanned with research protocol A (slider bar on 5), and the last 30 (48.4%) participants with research protocol B (slider bar on 8). The median age of participants was 62 (55–69) years, and the median BMI was 23.8 (22.5–28.3) kg/m$^2$. There was no significant difference in age and BMI between both cohorts ($p > 0.05$). Further baseline characteristics are presented in Table 1.

### Agatston scores and calcium volumes

Agatston scores of the standard scans were higher (29.4 [0–139]) than of the research scans (17.4 [0–158], $p = 0.028$), while the total calcium volumes were similar

| Demographics | Total |
|---|---|
| $N$ | 61 |
| Male | 37 (61%) |
| Age, years | 62 (55–69) |
| Body-mass index, kg/m$^2$ | 23.8 (22.5–28.3) |
| Dyslipidemia | 27 (44%) |
| Hypertension | 26 (43%) |
| Diabetes mellitus | 2 (3%) |
| Current smoker | 4 (7%) |
| Current statin use | 12 (20%) |

Values are reported as median (interquartile range) or $n$ (%)

(11.5 [0–109] versus 11.2 [0–118], $p = 0.176$), respectively (Table 2). Despite the difference in absolute Agatston scores, the median relative difference between both scans was small: 0 (0–8) (Table 2) [10]. The intraclass correlation coefficients between the standard and research protocols were excellent for the Agatston scores and calcium volumes: 0.994 (95% CI 0.990–0.996) and 0.996 (95% CI 0.994–0.998), respectively (Table 2). The number of detected calcified lesions was also similar between the standard (2 [0–6]) and the research protocol (2 [0–7], $p = 0.092$) (Table 2). Bland–Altman plots (Fig. 2) revealed a slight difference in Agatston score and calcium volume between the standard and research scans: for the Agatston score, the mean difference was 10.7; limits of

agreement $-88.8$ to $+67.2$, and for the calcium volume the mean difference was 5.6, limits of agreement $-52.5$ to $+41.3$ (Fig. 1). One patient was reclassified to another risk category with the research protocol. In this case, the Agatston score was 0 based on the standard protocol, and 3.0 based on the research protocol (Table 3; Fig. 3; Supplementary Table 2).

## Radiation exposure

For the standard protocol, tube potential was 120 kVp for all individuals. For the research protocol, tube potential was 70 kVp ($n = 6$, 10%), 80 kVp ($n = 18$, 30%), 90 kVp ($n = 15$, 25%), 100 kVp ($n = 16$, 26%), or 110 kVp ($n = 6$, 10%) (Table 2). Median current was lower in the standard protocol (136 [101–176] mAs) compared to the research protocol (270 [221–334] mAs, $p < 0.001$). The scans resulted in a median CTDI$_{vol}$ of 5.2 (3.8–7.0) mGy for the standard protocol, which decreased to 4.1 (3.1–6.3) mGy ($p < 0.001$) for the research protocol (Table 2). Similarly, DLP was 74.8 (55.2–93.7) mGy·cm for the standard protocol, which decreased to 59.3 (40.7–86.6) mGy·cm ($p < 0.001$) for the research protocol.

## Effect of dose setting variation

Spearman's correlations of calcium scores between the standard protocol and research protocol A (slider position at 8) were excellent (Agatston score: 0.997; volume:

Table 2 Comparison between standard and research CT scanning protocol and results

| Protocol comparison | Standard protocol | Research protocol | $p$ value | ICC or kappa | 95% CI |
|---|---|---|---|---|---|
| Tube voltage (kVp) | 120 (120–120) | 90 (80–100) | **< 0.001** | | |
| 70 kVp | | 6 (10%) | | | |
| 80 kVp | | 18 (30%) | | | |
| 90 kVp | | 15 (25%) | | | |
| 100 kVp | | 16 (26%) | | | |
| 110 kVp | | 6 (10%) | | | |
| 120 kVp | 61 (100%) | 0 (0%) | | | |
| Tube current (mAs) | 136.0 (101.0–179.0) | 270.0 (221.0–333.5) | **< 0.001** | | |
| CTDI$_{vol}$ (mGy) | 5.2 (3.8–7.0) | 4.3 (3.1–6.3) | **< 0.001** | | |
| Dose-length product (mGy·cm) | 74.8 (55.2–93.7) | 59.3 (40.7–86.6) | **< 0.001** | | |
| Lesions | 2 (0–6) | 2 (0–7) | 0.092 | 0.604* | |
| Agatston score | 29.4 (0–139.0) | 17.4 (0–158.2) | **0.028** | 0.994** | (0.99–0.996) |
| Calcium volume (mm$^3$) | 11.5 (0–109.2) | 11.2 (0–118.0) | 0.176 | 0.996** | (0.994–0.998) |
| Agatston relative difference | | 0 (0–7.8) | | | |

Values are reported as $N$ (%), median (interquartile range) or $n$ (%). All $p$ values are based on Wilcoxon signed ranks test. Significant $p$ values are indicated in bold

$CTDI_{vol}$ volume computed tomography dose index; $DLP$ dose-length product; $kVp$ peak kilovoltage; $mAs$ milliampere-second; $mGy$ milligray; $Qr36d$ conventional, medium sharp kernel; $Sa36f$ novel kernel

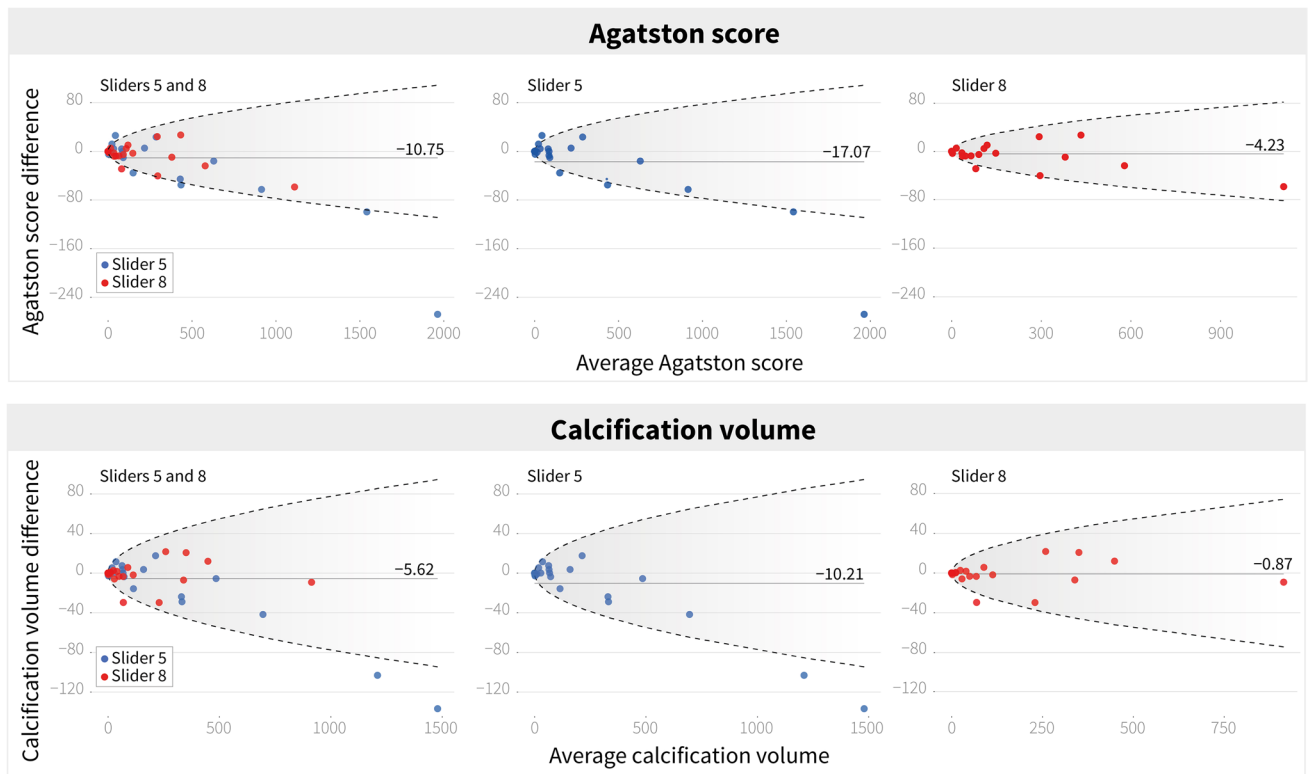*Cohen's kappa

**Intra-class correlation coefficient

**Fig. 2** Bland–Altman plots of the Agatston (upper row) and calcium volumes (lower row) between the standard and research scans

**Table 3** Risk category reclassification

| | Agatston score | Risk Category Research Group | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 23 | 1 | 0 | 0 | 0 | 24 |
| | 1-10 | 0 | 4 | 0 | 0 | 0 | 4 |
| **Risk Category Standard Group** | 11-100 | 0 | 0 | 15 | 0 | 0 | 15 |
| | 101-400 | 0 | 0 | 0 | 9 | 0 | 9 |
| | > 400 | 0 | 0 | 0 | 0 | 9 | 9 |
| | Total | 23 | 5 | 15 | 9 | 9 | 61 |

Reclassifications ($N$, %): 1, 1.6%

Cohen's kappa: 0.978

0.992) (Fig. 4). Similarly, Spearman's correlations between the standard protocol and research protocol B (slider position at 5) were also excellent (Agatston scores: 0.990; calcium volume: 0.991). The Bland–Altman plot revealed mean difference of $17.1 \pm 53.2$ between the standard and research scans for the research protocol A, and a mean difference of $4.2 \pm 16.3$ for the research protocol B. For calcium volumes, the mean difference was $10.2 \pm 31.7$ mm$^3$ and $0.9 \pm 10.2$ mm$^3$ for research protocol A and B, respectively (Table 4). CTDI$_{vol}$ and DLP were lower for research protocol B (CTDI$_{vol}$ 3.7 [2.7–4.8] mGy; DLP 52.7(39.2–69.3) mGy·cm) compared to research protocol A (CTDI$_{vol}$ 6.0 [4.1–7.2] mGy, $p = 0.002$; DLP 75.9 [53.5–93.4] mGy·cm, $p = 0.008$) (Table 4) (Supplementary Fig. 1).

## Inter-scan variability

The reference Agatston score of the phantom at 120 kVp with the Qr36d kernel was 659 (Supplementary Fig. 2). Decreasing the kVp with the conventional Qr36d kernel resulted in a slight increase of Agatston scores, ranging from 675 at 100 kVp to 734 at 80 kVp, respectively. While these scores with the Sa36f kernel increased to 703 at 120 kVp, and decreased to 587 at 100 kVp and 618 at 80 kVp, respectively.

**Fig. 3** Coronary artery calcium scoring CT scan (axial view) of the only patient who was reclassified. The Agatston score was 3.0 based on the research protocol (upper row), and 0 based on the standard protocol (lower row). Qr36d = conventional, medium sharp kernel; Sa36f = novel kernel
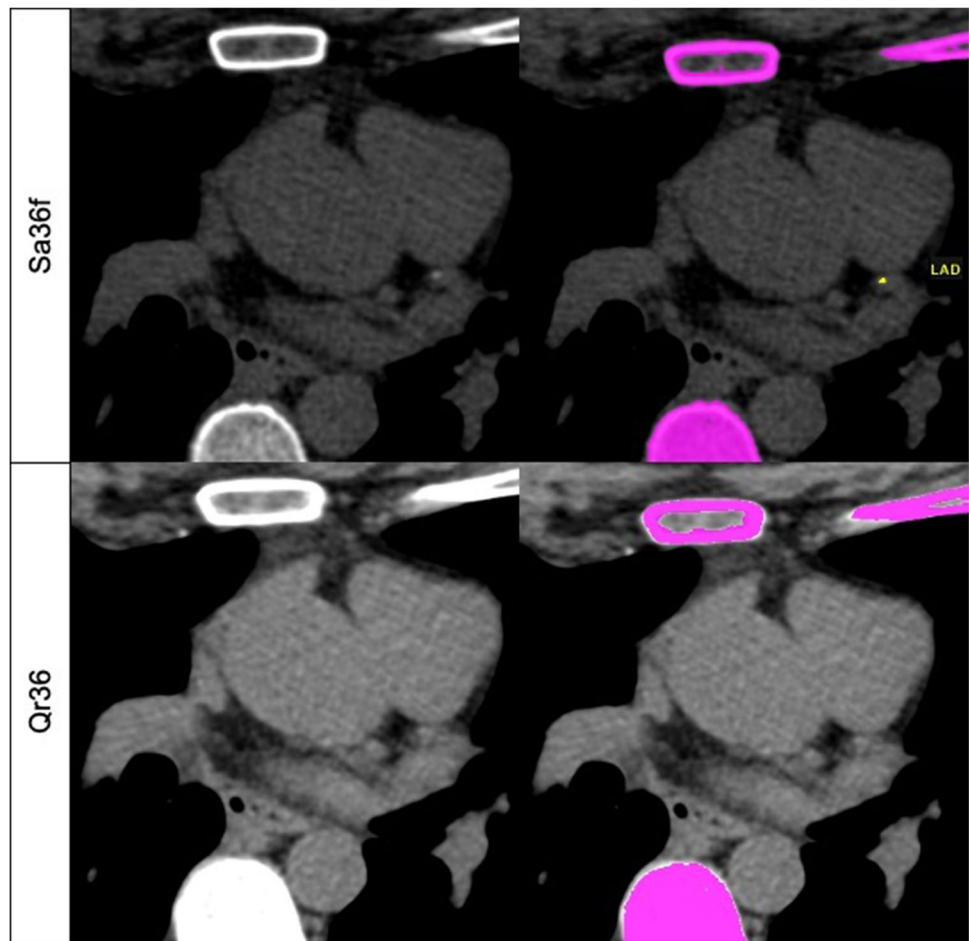


## Discussion

Our pilot study demonstrated that a low-dose calcium CT protocol with patient-optimized kV setting and similar Agatston scores can be achieved using a dedicated novel image reconstruction kernel (Sa36f). The reduced tube voltage resulted in significantly lower radiation exposure while maintaining an excellent reproducibility of the calcium measurements. The Sa36f kernel uses a voltage-dependent lookup table based on raw data for image reconstruction of non-contrast CT acquisitions. It can produce images with Hounsfield units equivalent to 120 kV for bone and calcium. The standard HU threshold for calcium classification is 130 HU. Previous studies that investigated low-kV calcium scans required an increased HU threshold or used conversion factors to recalibrate the Agatston scores [15, 16]. The Sa36f kernel reproduces 120 kV-equivalent images and similar Agatston scores for a range of tube voltage settings without the need for changing the calcium threshold or converting results. Although in our study there was a small but significant difference in the absolute Agatston scores between the research and standard calcium scan, the relative difference was small and resulted in no more than a single risk group

re-classification (2%). Moreover, the small difference of 0 (0–7.6%) easily falls within the published limits of inter-scan variability (11–27%) [17–20]. It is well known that the Agatston score has limited reproducibility [10, 21, 22]. Willemink et al. demonstrated that different CT scanners may produce significantly different Agatston scores and result in risk category reclassification [23]. Detrano et al. showed a mean Agatston score relative difference of 20.1 between two scans performed with the same scanner and protocol [10]. Apfaltrer et al. showed Agatston score relative difference of 16.4 between a high-pitch scan mode with tin filtration and standard 120-kVp high-pitch acquisition; however, Agatston score categories and percentile-based risk categories showed excellent agreement [24]. The Bland–Altman plots in this study (Fig. 2) indicated that the mean difference in Agatston score between the standard protocol and the research protocol was 11, which is well in range with the published scan-rescan reproducibility for calcium imaging [17–20]. The small mean difference appears to be caused by a small number of patients with relatively high calcium scores, more suggestive using the slider 5 protocol than the slider 8 protocol. Although the effect on clinical reclassification should be minimal, confirmation in larger cohorts
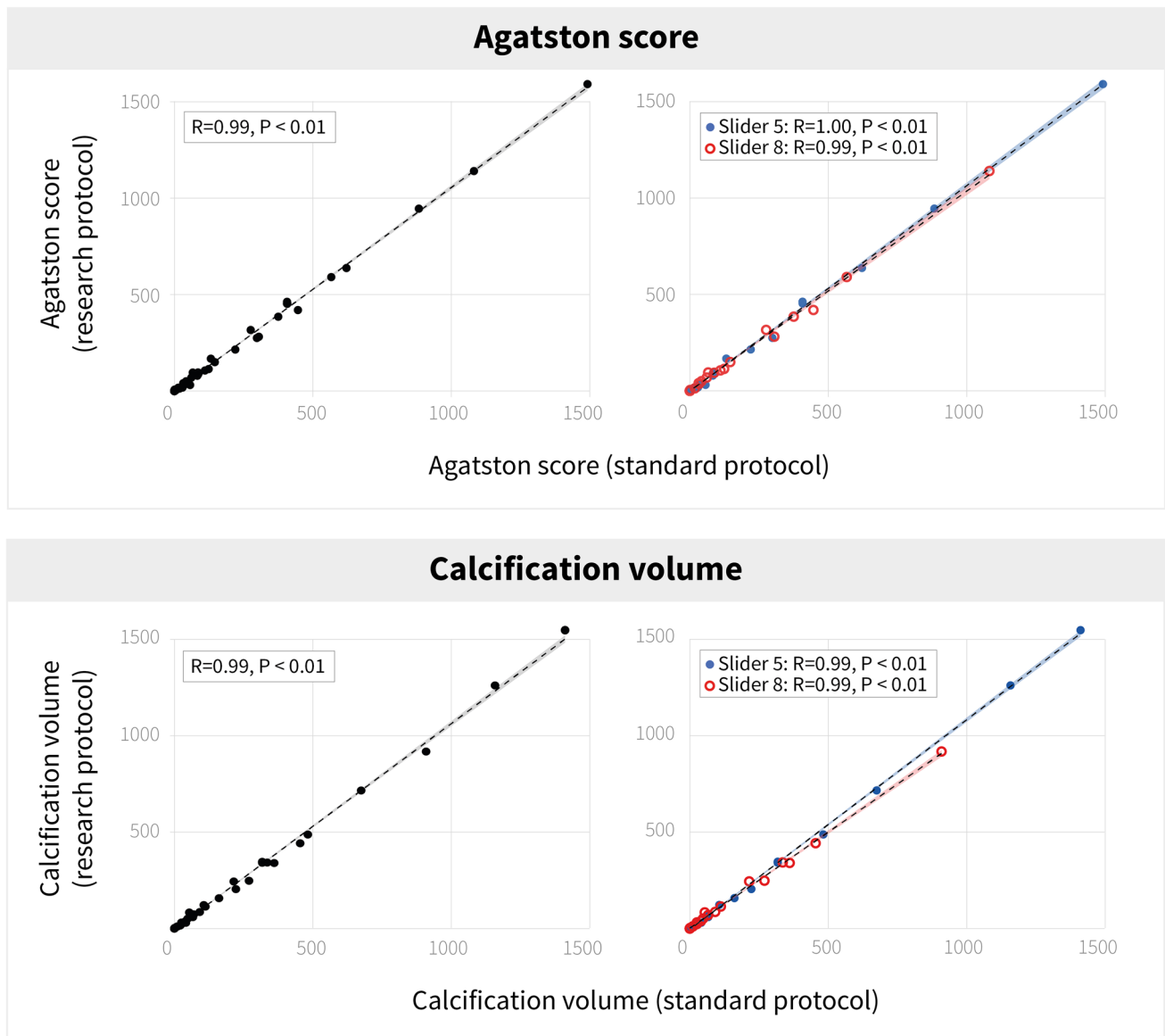
**Fig. 4** Correlation of the Agatston (upper row) and calcium volumes (lower row) between the standard and research scans

may further establish the performance of the Sa36f kernel in patients with a high calcium score.

The research protocol resulted in a substantial reduction in radiation exposure with a mean reduction of 22% in DLP and 25% in CTDI$_{vol}$. Setting the slider bar at position 8 (low target CNR) resulted in a greater radiation exposure reduction, while maintaining an excellent correlation in Agatston scores with standard scans. However, the Agatston mean relative difference between research and standard scans trended higher when the slider position was set on position 8 compared to position 5.

Our study had a few limitations. First, this was a single-center study including a relatively low number of patients.

The results may not apply to patients with a BMI > 35 kg/m$^2$. Larger studies are warranted to confirm our results and to establish the dose saving potential further. Second, our results are vendor-specific, and it might be challenging to translate our settings on other CT platforms. The effect of the Sa36f kernel on other materials requires further investigation.

In conclusion, in this pilot study, we demonstrated the feasibility of a kV-independent coronary artery calcium scoring CT scan protocol with a novel image reconstruction kernel. Our protocol was tested in patients and resulted in lower radiation exposure while maintaining an excellent correlation with the standard protocol Agatston and volume results.

**Table 4** Comparison of CT scanning protocol and results between cohort A (slider 5) and cohort B (slider 8)

| | Cohort A (Slider 5) | | Cohort B (Slider 8) | | p value | |
|---|---|---|---|---|---|---|
| N | 31 | | 30 | | | |
| Male | 16 (52%) | | 21 (70%) | | 0.142* | |
| Age (years) | 63 (56–73) | | 60 (52–68.25) | | 0.639 | |
| BMI | 24.7 (22.4–28.6) | | 23.7 (22.6–27.1) | | 0.678 | |
| | Standard | Research | Standard | Research | Standard | Research |
| Tube voltage (kVp) | 120 (120–120) | 100 (90–100) | 120 (120–120) | 80 (80–90) | 1.000 | **< 0.001** |
| 70 kVp | | 1 (3%) | | 5 (17%) | | |
| 80 kVp | | 2 (6%) | | 16 (53%) | | |
| 90 kVp | | 7 (23%) | | 8 (27%) | | |
| 100 kVp | | 15 (48%) | | 1 (3%) | | |
| 110 kVp | | 6 (19%) | | 0 (0%) | | |
| 120 kVp | 31 (100%) | 0 (0%) | 30 (100%) | 0 (0%) | | |
| Tube current (mAs) | 170.0 (108.0–192.0) | 238.0 (192.0–304.0) | 129.0 (99.5–158.8) | 296.0 (257.5–366.0) | 0.135 | **0.001** |
| CTDI$_{vol}$ (mGy) | 6.4 (4.1–7.4) | 6.0 (4.1–7.2) | 4.9 (3.8–6.1) | 3.7 (2.7–4.8) | 0.157 | **0.002** |
| DLP (mGy·cm) | 78.5 (55.5–99.3) | 75.9 (53.5–93.4) | 71.0 (54.6–87.2) | 52.7 (39.2–69.3) | 0.411 | **0.008** |
| Calcium quantification | | | | | | |
| Lesions | 2 (0–6) | 3 (0–6) | 2 (0–7) | 2 (0–8) | 0.841 | 0.603 |
| Agatston Score | 29.4 (0.0–220.0) | 17.4 (0.0–214.6) | 25.1 (0.0–129.5) | 24.3 (0.0–122.4) | 0.842 | 0.789 |
| Volume (mm$^3$) | 21.0 (0.0–161.2) | 15.6 (0.0–157.5) | 11.5 (0.0–96.7) | 11.1 (0.0–92.9) | 0.722 | 0.635 |

Values are reported as median (interquartile range) or *n* (%). All *p* values are based on Mann–Whitney *U* test, except for * (Pearson's chi-square test). Significant *p* values are indicated in bold

*CTDI$_{vol}$* volume computed tomography dose index; *DLP* dose-length product; *kVp* kilovoltage peak; *mAs* milliampere-second; *mGy* milligray; *Qr36d* conventional, medium sharp kernel; *Sa36f* novel kernel

## Declarations

**Guarantor** The scientific guarantor of this publication is Dr. Koen Nieman, MD, PhD.

**Conflict of interest** The authors of this manuscript declare relationships with the following companies:

D. M.: Activities related to the present article—none. Activities not related to the present article—research grant from the National Institute of Biomedical Imaging and Bioengineering (5T32EB009035). Shareholder of Segmed, Inc. Consultant for Segmed, Inc. Other relationships—no relevant relationships.

Gv. P.: Institution received an unconditional grant from PUSH (a collaboration between Siemens Healthineers and the University Medical Center Groningen) to hire a doctoral candidate to investigate automatic quantification of inflammatory and infectious diseases in (PET/)CT. Other relationships—no relevant relationships.

M. J. W.: Activities related to the present article—none. Activities not related to the present article—research grants from American Heart Association (18POST34030192), Philips Healthcare, and Stanford University, consulting for Arterys, Inc., and co-founder/shareholder of Segmed, Inc. Other relationships—no relevant relationships.

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K. N.: unrestricted institutional research support from Siemens Healthineers, Bayer, HeartFlow Inc.; Consulting for Siemens Medical Solutions USA.

The other authors have no conflict of interest to disclose.

**Statistics and biometry** One of the authors has significant statistical expertise.

**Informed consent** Written informed consent was obtained from all subjects (patients) in this study.

**Ethical approval** Institutional Review Board approval was obtained.

**Methodology**
- Prospective
- Experimental
- Performed at one institution

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