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Original Research Article

Assessment of isotropic calcium using 0.5-mm reconstructions from 320-row CT data sets identifies more patients with non-zero Agatston score and more subclinical atherosclerosis than standard 3.0-mm coronary artery calcium scan and CT angiography

Anum Aslam MD, Usman S. Khokhar MD, Ammar Chaudhry MD, Alexander Abramowicz BS, Naveed Rajper MD, Michael Cortegiano BS, Michael Poon MD, Szilard Voros MD*

Division of Advanced Cardiovascular Imaging, Departments of Radiology and Cardiology, Stony Brook University Medical Center, Health Science Center, Level 4 Rm 120, Stony Brook, NY 11794, USA

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ABSTRACT

Background: The presence of calcified plaque in coronary arteries can be quantified by using 0.5-mm isotropic reconstructions from 320-row CT without increased radiation dose. Little is known about reclassification of patients with non-zero Agatston scores and quantitative measures of calcified plaque using 0.5-mm reconstructions.
Objective: The aim was to compare proportions of zero vs non-zero Agatston scores (subclinical atherosclerosis) in 0.5-mm isotropic reconstructions vs standard 3.0-mm and CT angiography (CTA) scans on 320-row CT.
Methods: Prospectively, we quantified calcified plaque in coronary arteries in 104 patients by using non–contrast-enhanced scans with 0.5 and 3.0 mm. Coronary calcium assessment was determined by 2 observers. Clinically indicated CTA was also performed; coronary calcium assessment findings were compared with CTA. Ranked Wilcoxon test and χ^2 test were performed for comparison. Reproducibility for proportion of zero vs non-zero was assessed by κ statistics.
Results: Median Agatston score (41.9 [interquartile range (IQR), 3.7–213.6] vs 5.2 [IQR, 0.0–128.5]), calcium volume (53.6 mm^3 [IQR, 8.1–202.3] vs 5.1 mm^3 [IQR, 0.0–96.8],), and lesion number (10.0 [IQR, 3.5–18.5] vs 1.0 [IQR, 0.0–6.0]) were significantly higher on 0.5-mm reconstruction ($P < .0001$) than on 3.0-mm reconstruction. More patients with subclinical

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* Corresponding author.
E-mail address: anum586@gmail.com (A. Aslam).

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atherosclerosis were detected on 0.5 mm than on 3.0 mm and CTA scans (76.9% vs 53.8% vs 54.8%; $P < .0001$). The κ values for inter-rater agreement were 0.94 and 0.52 on 3.0- and 0.5-mm data sets, respectively. However, when Agatston scores < 10 were excluded from analysis, the κ value rose to 0.83.

Conclusion: Isotropic 0.5-mm reconstruction detected 23.1% and 22.1% more patients with subclinical atherosclerosis than standard 3.0-mm scans and CTA, which may be more sensitive for the detection of subclinical atherosclerosis; its potential clinical utility needs to be validated in large, prospective studies.

1. Introduction

Coronary calcium scanning was developed to assess overall coronary arterial atherosclerotic burden. Although the Agatston score was developed to detect subclinical atherosclerosis, it has been shown to independently predict cardiovascular outcomes in asymptomatic subjects with no previous coronary artery disease (CAD).[1] Multidetector row CT (MDCT) is increasingly used for quantification of calcified plaque in coronary arteries and correlates well with electron-beam CT (EBCT).[2–6] Traditionally, 3-mm slice reconstructions are used for quantification, but they are limited by the presence of partial volume errors, leading to inaccuracy and underestimation of low attenuation small calcifications[7] with high interscan variability.[8] Recent guidelines from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging have laid great emphasis on zero Agatston score that clinically excludes CAD.[9]

With the advent of volumetric cardiac imaging that uses 320-row CT, the presence of calcified plaque in coronary arteries can now be quantified on 0.5-mm isotropic reconstructions without increased radiation. Little is known about the reproducibility and reclassification of patients with non-zero Agatston scores and quantitative measures of calcified plaque in coronary arteries with the use of 0.5-mm isotropic reconstructions compared with standard 3.0-mm coronary calcium and CT angiography (CTA) scans. A recent study showed greater sensitivity in depicting positive Agatston scores on 0.5-mm scans with zero Agatston score on 3.0-mm scans,[10] but none has compared them with CTA or has evaluated intra- and inter-rater reliability of coronary calcium scanning. We therefore hypothesized that isotropic coronary calcium scanning by using 0.5-mm slice thickness identifies more patients with non-zero Agatston score and hence more subclinical atherosclerosis than by using the standard 3.0-mm coronary calcium and CTA scans.

2. Methods

2.1. General study design

This was a prospective, single-center, observational study. The study protocol was approved by the institutional review board of Stony Brook University Medical Center. We prospectively enrolled 104 consecutive patients clinically referred for coronary calcium scanning and cardiac CTA on a 320-row CT scanner (Aquilion ONE; Toshiba Medical Systems, Otawara, Japan). Demographics and clinical information were extracted from the medical record. Patients with history of coronary artery bypass surgery, percutaneous coronary revascularization, pacemakers, and prosthetic heart valves were excluded.

2.2. Coronary artery calcium image acquisition and reconstruction

Non–contrast-enhanced CT images were acquired with prospective electrocardiographic (ECG) triggering on a 320-row CT scanner with the use of a volumetric mode and were reconstructed with either standard 3.0-mm or 0.5-mm axial slices. Acquisition parameters included a gantry rotation time of 0.35 seconds, collimation of 0.5 mm × 280, tube voltage of 120 kV, and tube current between 200 and 500 mA, tailored to patients' size.

2.3. Contrast-enhanced CTA image acquisition

Contrast-enhanced coronary CTA was performed during end-expiratory breathhold with the use of prospective ECG gating. Oral and intravenous metoprolol were given to keep the heart rate < 60 beats/min, and 0.4 mg of sublingual nitroglycerin was administered for maximal vasodilatation. A power injection of 70 mL of intravenous contrast (Ultravist 370) was then administered at a rate of 5 mL/s, followed by 40 mL of normal saline flush. ECG-triggered volumetric scanning was performed from the tracheal bifurcation to 2 cm below the diaphragm during a single breathhold. Acquisition parameters included a gantry rotation time of 0.35 seconds, collimation of 0.5 mm × 280/320 with scan length of 140 to 160 mm, tube voltage of 80 to 120 kV, and tube current between 200 and 500 mA, tailored to patients' size.

2.4. Image processing

Calcified plaque in coronary arteries was quantified with both 0.5- and 3.0-mm reconstructions on a commercial image processing workstation (Aquarius version 4.4.7.85.5213; TeraRecon, Foster City, CA) by 2 independent, blinded observers. Agatston scores were calculated according to the method described by Agatston et al.[11] Calcium volume and lesion number were also determined. These parameters were measured in all major epicardial arterial segments such as the left main coronary artery (LMCA), left anterior descending artery (LAD), left circumflex artery (LCx), and right coronary artery (RCA). The Agatston scores were summed to determine the total Agatston score. Calcium volume (in mm^3) was calculated

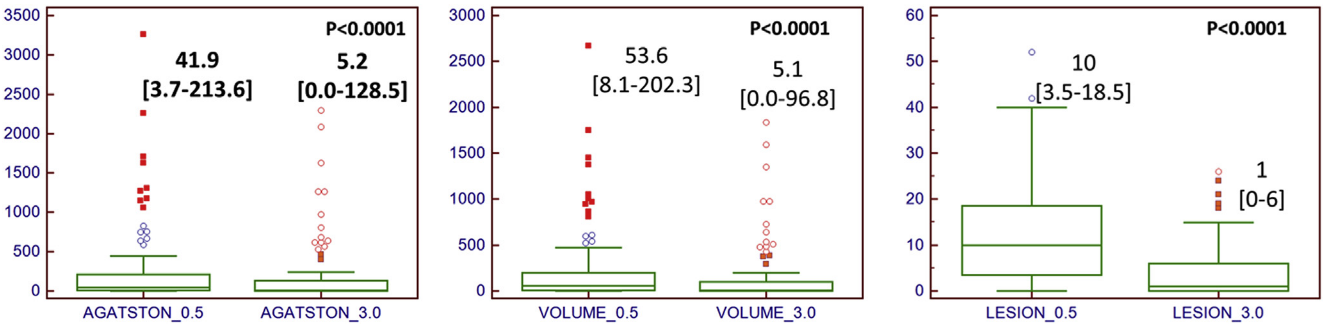

Fig. 1 – Bar graph shows higher (statistically significant) total Agatston score, calcium volume (in mm^3), and lesion number on 0.5-mm vs 3.0-mm reconstructions. Values are expressed as median (interquartile range).

as the total volume of the calcification in the major epicardial arteries, where calcification was identified as voxels with attenuation values of at least 130 Hounsfield unit (HU). For a lesion that covered 2 or more arterial segments, the arterial segment closest to the aorta was the designated arterial segment for the lesion. For example, if a lesion was located at the ostium of the LAD and LCx and covered all 3 arterial segments, LMCA, LAD, and LCx, the lesion was labeled as LMCA.

Noise was measured as the standard deviation of attenuation values in a circular region of interest in the ascending aorta at the level of the LMCA. The extended dose-length product (DLPe) for each coronary calcium examination on the 320-row CT was also recorded and converted into the effective radiation dose by multiplying the DLPe with the standard dose conversion factor 0.014 mSv · mGy^{-1} · cm^{-1}.

2.5. *Intra- and inter-rater agreement*

The analysis was performed by 2 independent, blinded observers on all 104 patients by using both 0.5- and 3.0-mm reconstructions to quantify the total Agatston score, calcium volume, and number of lesions. Reader 1 evaluated the data set twice with an interval of 1 week, and reader 2 evaluated the data set once. Intra- and inter-rater agreement was then determined. Clinically indicated coronary CTA was also performed on the same 104 patients and used as the reference standard to semiquantitatively compare the percentage of patients with subclinical atherosclerosis at 3.0- vs 0.5-mm reconstruction.

Table 1 – Per-vessel Agatston score, calcium volume, and lesion number on 3.0-mm vs 0.5-mm reconstruction on 320-row CT.

Vessel segments	3.0-mm reconstruction	0.5-mm reconstruction	*P* value
Left main			
Agatston score	0.0 (0.0–3.3)	0.0 (0.0–19.8)	<.0001
Calcium volume	0.0 (0.0–3.4)	0.0 (0.0–21.8)	<.0001
Lesion number	0.0 (0.0–1.0)	0.0 (0.0–2.0)	<.0001
Left anterior descending			
Agatston score	0.0 (0.0–35.1)	4.7 (0.0–82.4)	<.0001
Calcium volume	0.0 (0.0–30.9)	8.9 (0.0–69.8)	<.0001
Lesion number	0.0 (0.0–2.0)	2.0 (0.0–5.0)	<.0001
Left circumflex			
Agatston score	0.0 (0.0–1.9)	0.5 (0.0–12.6)	<.0001
Calcium volume	0.0 (0.0–1.9)	1.2 (0.0–18.7)	<.0001
Lesion number	0.0 (0.0–1.0)	1.0 (0.0–3.0)	<.0001
Right coronary artery			
Agatston score	0.0 (0.0–18.2)	11.0 (0.6–68.1)	<.0001
Calcium volume	0.0 (0.0–21.7)	19.2 (1.5–77.5)	<.0001
Lesion number	0.0 (0.0–2.0)	4.0 (1.0–9.5)	<.0001

Calcium volume in mm^3; median and interquartile range in brackets.

2.6. *Statistical analysis*

Medcalc software version 12.3.0.0 (Mariakerke, Belgium) was used for all statistical analyses. Ranked Wilcoxon test was used for analyses because the variables were non-normally distributed in the population and expressed as median (interquartile range [IQR]). Relationship between continuous variables (noise and body mass index [BMI; calculated as weight divided by height squared; kg/m^2]) was tested with linear regression. The total and per-vessel proportions of zero vs non-zero Agatston scores in 3.0- vs 0.5-mm reconstruction were calculated to determine the percentage reclassification at 0.5-mm isotropic reconstruction. For semiquantitative analyses, inter-rater agreement for the proportion of zero vs non-zero at 3.0 vs 0.5 mm for total Agatston score was determined by weighted κ statistics. χ^2 test was used to compare the proportions of patients with subclinical atherosclerosis in standard coronary CTA, 3.0-mm reconstruction, and 0.5-mm reconstruction.

For the quantitative analysis, intra- and inter-observer agreement was assessed with the concordance correlation coefficient with 95% CI, Pearsons precision P (R value) with 95% CI, and Bland-Altman analysis with 95% limits of agreement. *P* value <.05 was considered significant.

3. Results

3.1. *General demographics*

Mean age was 54 ± 12 years; 52 patients were men (50%). Mean BMI was 29.1 ± 5.5. For coronary calcium scanning, DLPe and effective radiation dose were 94 mGy · cm (94–103.6 mGy · cm), and 1.31 mSv (1.31–1.45 mSv), respectively.

Table 2 – Inter-rater agreement between total AG, CV, and LN on 3.0-mm and 0.5-mm reconstructions.

Inter-rater agreement

	r (PPP)	CCC	95% CI	R1, median (IQR)	R2, median (IQR)	R1, mean ± SD	R2, mean ± SD	Mean difference, absolute	Mean difference, %	Limits of agreement, absolute	Limits of agreement, %
AG-3.0	0.95	0.95	0.93–0.97	5.2 (0–128.5)	5.2 (0–108.8)	178.9 ± 405.1	161.3 ± 387.7	14.6	9.1	±236.2	±146.4
AG-0.5	0.95	0.95	0.92–0.96	41.9 (3.7–213.6)	38.0 (0.6–207.7)	256.4 ± 507.6	227.5 ± 438.2	28.9	12.7	±316.3	±139.0
CV-3.0	0.96	0.95	0.93–0.97	5.06 (0–96.8)	5.57 (0–88.6)	138.2 ± 319.1	126.9 ± 305.1	11.2	8.8	±183	±144.1
CV-0.5	0.95	0.94	0.91–0.95	53.6 (8.1–202.3)	42 (1.4–170.9)	224.9 ± 413.4	197.2 ± 361.2	27.8	14.1	±267.6	±135.7
LN-3.0	0.95	0.95	0.93–0.97	1 (0–6)	1 (0–5)	3.8 ± 5.6	3.4 ± 5.3	0.4	11.9	±3.1	±91.9
LN-0.5	0.76	0.65	0.55–0.74	10 (3.5–18.5)	5 (1–11)	12.9 ± 11.5	7.9 ± 8.8	4.9	61.4	±14.7	±184.2

AG, Agatston score; CCC, concordance correlation coefficient; CV, calcium volume; IQR, interquartile range; LN, lesion number; PPP, Pearson's precision P; R1, reader 1; R2, reader 2.

3.2. *Coronary calcium scanning with 3.0-mm vs 0.5-mm reconstruction*

Total Agatston score, calcium volume, and lesion number were significantly higher on 0.5-mm reconstructions (all $P < .0001$; Fig. 1). Similarly per-vessel Agatston score, calcium volume, and lesion number were higher on 0.5 mm with the maximum score seen in the RCA (all $P < .0001$; Table 1).

3.3. *Quantitative analysis and reproducibility of quantitative measures of calcified plaque in coronary arteries on 3.0-mm and 0.5-mm reconstruction*

Intra-observer agreement for total Agatston score, calcium volume, and lesion number on 3.0- and 0.5-mm data sets was excellent for all parameters except for lesion number at 0.5-mm reconstruction. Concordance correlation coefficient for Agatston score, calcium volume, and lesion number at 3.0 and 0.5 mm were 0.95, 0.95, 0.95, 0.95, 0.96 and 0.79 (95% CI, 0.93–0.97), respectively.

Table 2 shows quantitative measures of calcified plaque in coronary arteries for reader 1 and reader 2 on both reconstructions. Inter-observer agreement for total Agatston score and calcium volume were excellent. Lesion number at 3.0 mm had excellent agreement, whereas 0.5 mm had good inter-rater agreement. On the basis of Bland-Altman analysis, absolute mean differences were small, and limits of agreement were narrow at 3.0 mm vs 0.5 mm, especially for absolute measurements (Table 2 and Fig. 2).

3.4. *Agatston score: Classification of patients*

The proportion of patients with non-zero Agatston score, calcium volume, and lesion number were significantly higher on the 0.5-mm data sets than on the 3.0-mm data sets. Of 104 total patients, 56 (53.8%) on 3.0-mm and 80 (76.9%) on 0.5-mm reconstruction had a non-zero Agatston score. Of 48 patients with a zero Agatston score on 3.0 mm, 24 had a non-zero Agatston score on 0.5 mm with a net reclassification of 23.1% ($P = .0008$). Absolute non-zero median Agatston scores for total calcified plaque in coronary arteries, calcium volume, and lesion number were 6.89 (IQR, 1.49–27.9), 15.59 mm^3 (IQR, 3.34–44.68), and 5 (IQR, 2–10.5), respectively. Similar findings were seen in the proportions in all epicardial vessel segments as shown in Fig. 3. The greatest difference was seen in the RCA with 63 patients (60.6%) having non-zero Agatston score on 0.5-mm reconstruction compared with 40 patients (38.5%) on 3.0-mm reconstruction, resulting in reclassification of 23 more patients (22.1%) into the non-zero 0.5-mm Agatston score group ($P = .0023$). In the RCA, the absolute non-zero 0.5-mm Agatston score, calcium volume, and lesion number were found to be the highest compared with other vessels (4.36 [0.89–8.76], 8.19 mm^3 [1.52–13.95], and 2 [1–4], respectively; $P < .05$).

3.5. *Reproducibility of semiquantitative analysis*

Inter-rater agreement for the proportion of non-zero Agatston score by using 3.0- and 0.5-mm data sets were excellent and good, respectively (weighted κ, 0.94 and 0.52, respectively). We

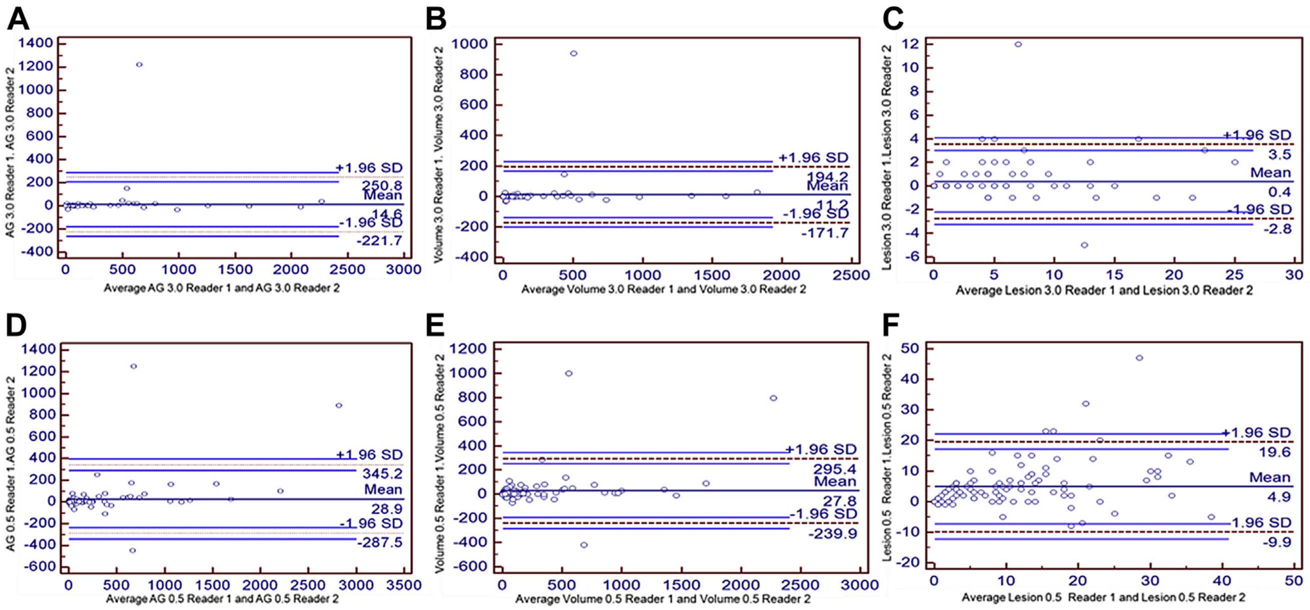

Fig. 2 – Inter-observer agreement between READER 1 and READER 2 for quantitative measures of calcified plaque in coronary arteries as follows: average AG at 3.0-mm reconstructions (A), average calcium volume (mm^3) at 3.0-mm reconstructions (B), average lesion number at 3.0-mm reconstructions (C), average AG at 0.5-mm reconstructions (D), average calcium volume (mm^3) at 0.5-mm reconstructions (E), and average lesion number at 0.5-mm reconstructions (F). Quantitative parameters for Bland-Altman analysis are shown in detail in Table 2. AG, Agatston score.

further divided the Agatston score into 2 groups as follows: Agatston score < 10 and Agatston score ≥ 10. All scores < 10 were assigned a value of zero and scores ≥ 10 were assigned a value of 1. With the use of this criterion, we found excellent inter-rater agreement on both 3.0- and 0.5-mm reconstructions (weighted κ, 0.96 and 0.83, respectively).

3.6. *Coronary calcium assessment by using 3.0- or 0.5-mm reconstruction vs CTA for detection of subclinical atherosclerosis*

Coronary calcium scans that used either 3.0-mm or 0.5-mm reconstruction were compared with findings from coronary CTA by using the χ^2 test. Subclinical atherosclerosis was detected on CTA in 57 patients (54.8%) compared with 56 patients (53.8%) by using 3.0-mm coronary calcium scans and 80 patients (76.9%) by using 0.5-mm coronary calcium scans ($P < .0001$; Table 3).

3.7. *Image quality (image noise)*

Image noise was non-normally distributed. Fig. 4 shows that image noise was significantly higher on 0.5-mm than on 3.0-mm reconstruction ($P < .0001$). To avoid false-positive depiction of image noise as calcium, we used direct lesion comparison between reconstructions. The calcified lesion had to be larger than spots of image noise on the same slice level and the lesion had to be present in 2 adjacent slices (Fig. 5).

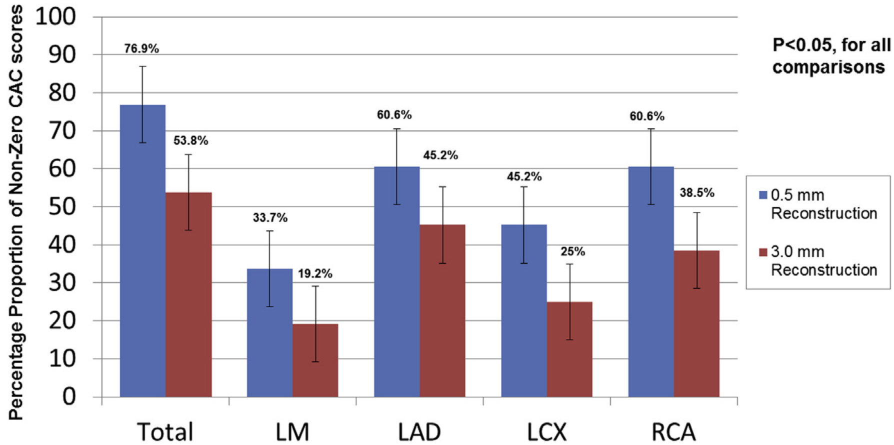

Fig. 3 – Percentage proportions of non-zero Agatston scores according to epicardial arterial segments. LAD, left anterior descending; LCx, left circumflex; LM, left main; RCA, right coronary artery.

Table 3 – Proportion of patients with subclinical atherosclerosis on 0.5-mm coronary calcium scanning, 3.0-mm coronary calcium scanning, and CTA scanning.

	Negative for subclinical atherosclerosis, n (%)	Positive for subclinical atherosclerosis, n (%)	χ^2 test	P value
Coronary calcium scanning 0.5-mm reconstruction	24 (23.1)	80 (76.9)		
Agatston score ≥ 10 Reconstruction	40 (38.5)	64 (61.5)	46.56	<.0001
Coronary calcium scanning 3.0-mm reconstruction	48 (46.1)	56 (53.8)	33.64	<.0001
Coronary CTA	47 (45.2)	57 (54.8)	35.02	<.0001

CTA, CT angiography.

BMI was associated with noise with both reconstructions ($P < .0001$; Fig. 6), whereas Agatston score, calcium volume, and lesion number had no to minimal association with noise with both reconstructions (Fig. 7).

4. Discussion

Our study has 3 important findings. First, 0.5-mm isotropic coronary calcium scanning was more sensitive in detecting the proportion of patients with non-zero Agatston score compared with traditional 3.0-mm scans and coronary CTA. Second, as body size increased, despite the use of higher tube current, significantly more noise was seen at thinner slice reconstruction. However, no relationship was found between noise and whole heart Agatston score. Finally, the intra- and inter-rater reproducibility was similar for all measures of coronary calcium scanning on both 0.5- and 3.0-mm data sets, except for lower agreement of zero vs non-zero Agatston scores at 0.5 mm for patients with low scores (weighted κ, 0.94 vs 0.52). However, when comparing Agatston score < 10 and Agatston score ≥ 10, excellent agreement was observed on both data sets (weighted κ, 0.96 and 0.83).

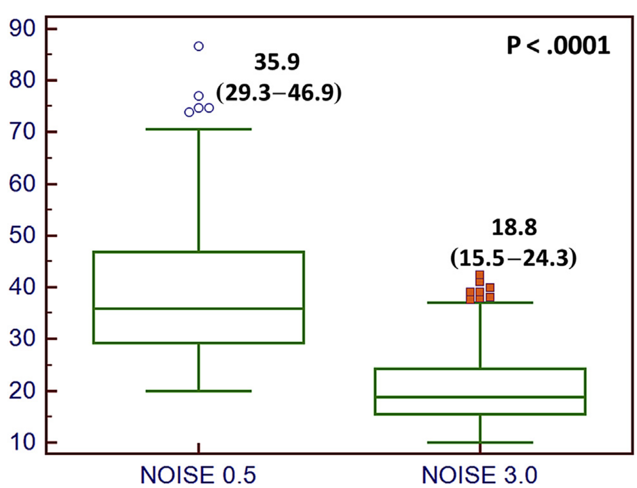

Fig. 4 – Image noise at 0.5-mm vs 3.0-mm reconstruction. Values are expressed as median (interquartile range). Orange boxes represent outliers.

It has been described that standard 3-mm reconstructions may underestimate subclinical CAD.[9] Prior studies that used multislice CT and EBCT that compared different slice thickness reconstructions indicated mixed results. Vliegenthart et al[12] observed decreased accuracy in assessing calcium volume on 3.0-mm compared with 1.5-mm EBCT scans in a phantom and a patient study. Our study showed increased sensitivity in detecting calcified plaques on isotropic scans compared with the standard 3-mm scan. This may be due to the partial volume effect in which a smaller slice thickness yields improved detection of calcified plaque in coronary arteries because of a smaller voxel size. This finding was consistent with the results of a study by Mühlenbruch et al.[13] Although the in vitro data showed higher Agatston scores on thinner slices with the same number of lesions being depicted as larger lesions on the phantom study, the in vivo data indicated more lesions on 1-mm slice thickness than on 3-mm slice thickness for the same reason.[13] The clinical relevance of our findings need to be validated in further studies because the detection of even the smallest amount of calcified plaque could provide an opportunity for risk factor modification and thus prevent coronary heart disease events.[14]

Slice thickness of 0.5 mm reclassified 23.1% and 22.1% of patients with zero Agatston score on 3.0-mm coronary calcium and CTA scans to the non-zero category. These findings were consistent with a recent study by van der Bijl et al[10] who compared 100 patients with positive and 100 patients with negative Agatston scores and reclassified 21% patients with a zero score at 3.0 mm to a non-zero score at 0.5-mm reconstruction. Similarly another study compared Agatston scores on 3.0-mm slices with nonoverlapping 1.0-mm slices in 50 patients and found 4 patients with positive Agatston scores at thinner slice reconstruction with a zero score at 3.0-mm slice reconstruction.[13] However, they discriminated image noise from true calcified lesion by increasing the detection threshold from 130 to 350 HU, contrary to our study. As a result of this, 6 of 33 patients (18%) with calcified lesions on 3.0 mm were excluded from further evaluation. We used the same threshold value of 130 HU[11] for both reconstructions to increase sensitivity and to prevent false-negative results in depicting low attenuation calcifications.

Another important finding of our study was finding 0.5-mm coronary calcium scans to be more sensitive in detecting subclinical atherosclerosis than the CTA scans. To our knowledge, no prior comparison has been studied. Hou et al[15] noted increased prognostic value of CTA with zero

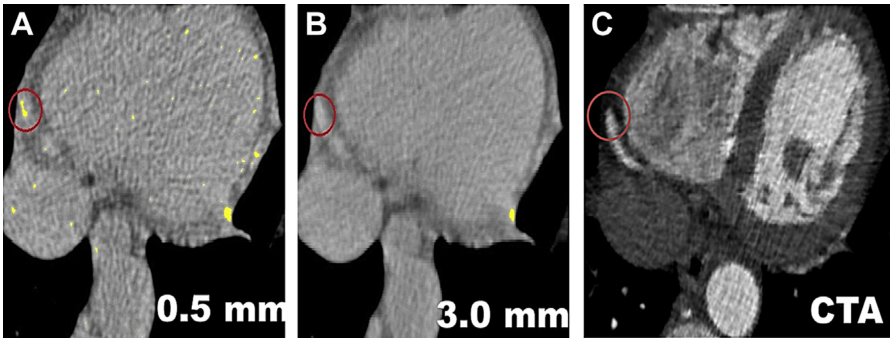

Fig. 5 – (A) Noncontrast CT in a 54-year-old woman with positive calcium (*circled area*) in the right coronary artery at 0.5-mm reconstruction. (B) No calcium is seen (*circled area*) on the same slice level at 3.0-mm reconstruction. (C) No calcified plaque (*circled area*) detected on CTA. CTA, CT angiography.

Agatston score compared with standard coronary calcium scan with zero Agatston score, for predicting major adverse cardiac events at 3 years.

Importantly, on 0.5-mm reconstruction, the proportion of patients with non-zero Agatston score were also increased in all the vessels, with the largest difference in the RCA compared with LMCA and LAD (22.1% vs 16% vs 15%; $P = .0023$). This finding may be explained by the through-plane resolution effect. Although the in-plane resolution is identical for all vessels, the RCA anatomically courses through the image acquisition plane more so than the LM and LAD; hence, it has the largest through-plane resolution at 0.5-mm reconstruction. In addition, small calcified lesions may not be detectable on CTA scans, especially in scans with high iodine content.

Noise and BMI are 2 main factors that affect the Agatston score. In our study, significantly more noise was seen at lesser slice thickness. To differentiate increased calcified plaque from image noise at 0.5 mm, we performed linear regression test and found no direct relation between noise, Agatston score, calcium volume, and lesion number ($P > .05$). Hence, the increase in calcified plaque at 0.5 mm was independent of noise. Higher BMI produced worse image noise and quality at 0.5-mm reconstruction than at 3.0-mm reconstruction.[16] However, the overall effect of increased image noise on detecting a true calcified lesion is minimized because the signal intensity also increases at a smaller slice thickness. This is a result of the reduced partial volume effect that does not decrease the signal-to-noise ratio.[10]

The potential for using any modality for assessing disease progression depends on the reproducibility of the technology.[17] Previously, studies have shown excellent interscan and inter-observer reproducibility of coronary calcium measurements with the use of 4-row CT and EBCT[12,17,18] but none with the use of 320-row CT. Kopp et al[4] demonstrated excellent MDCT reproducibility through the use of cardiac phantom, and Ohnesorge et al[19] demonstrated repeat examination reproducibility with the use of retrospectively gated ECG MDCT. To our knowledge, we are the first to determine inter- and intra-observer reproducibility of total Agatston score, calcium volume, and lesion number on both reconstructions with the use of 320-row CT. Our results suggest that both intra- and inter-observer agreements were excellent at both reconstructions in the 0.91 to 0.97 range.

4.1. *Limitations*

This was a single-center study, and its applicability to other centers is unknown. Furthermore, although we found that isotropic coronary calcium scanning detected more patients with subclinical atherosclerosis than traditional 3.0-mm reconstructions and CTA, no external reference standard is available. However, it is unlikely that a study could be conducted with an external reference standard, because these

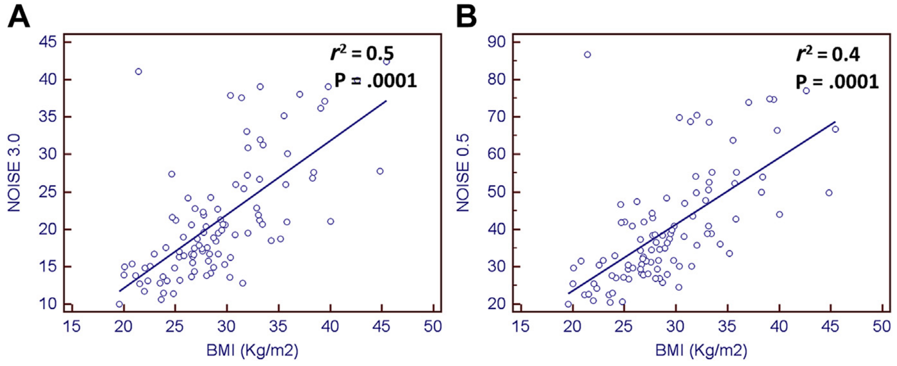

Fig. 6 – Relationship between BMI and noise at 3.0-mm (A) and 0.5-mm (B) reconstructions. BMI, body mass index.

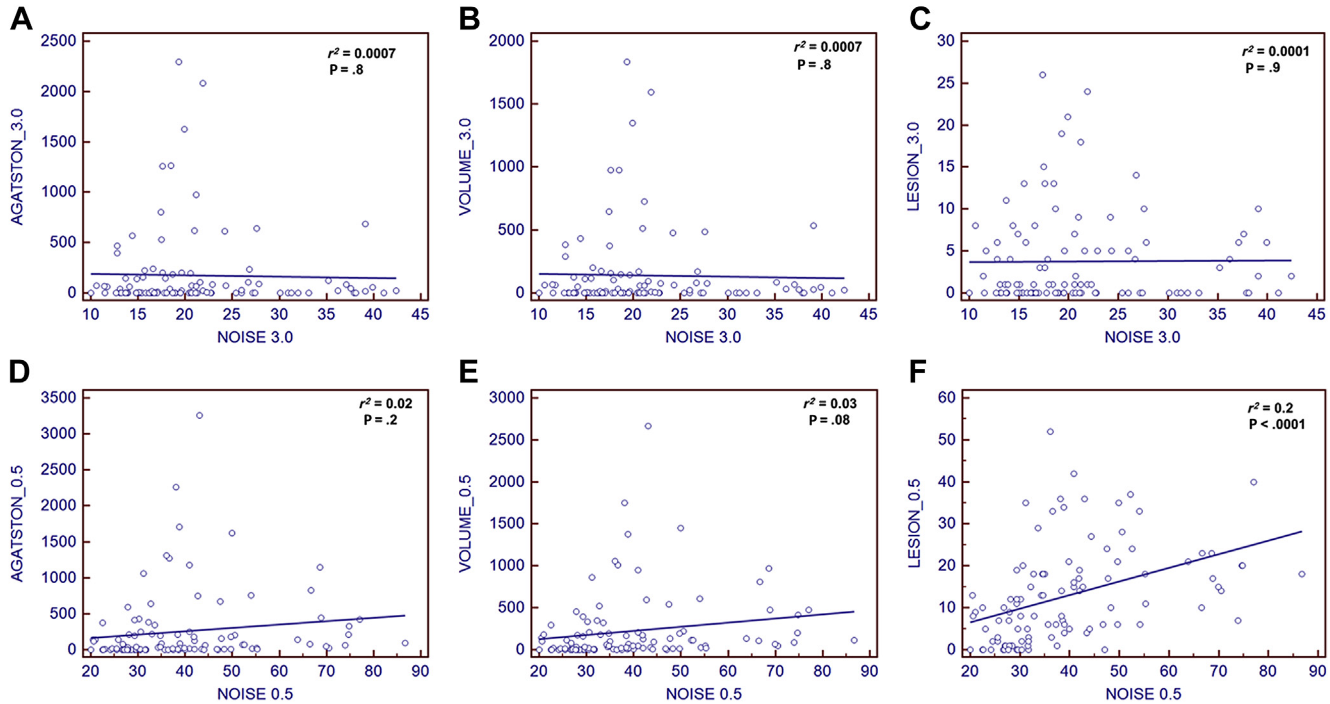

Fig. 7 – No to minimal association of Agatston score, calcium volume (in mm^3), and lesion number to noise at 3.0- (A, B, and C, respectively) and 0.5 -mm (D, E, and F, respectively) reconstructions.

low-risk, low-likelihood patients are not candidates for invasive imaging.

5. Conclusion

Our study suggests that 0.5-mm isotropic calcium scanning is more sensitive in detecting subclinical atherosclerosis than 3.0-mm coronary calcium and CTA scans that use 320-row CT in low-risk patients. Furthermore, the reproducibility of quantification of calcified plaque in coronary arteries was similar at both reconstructions except for lower agreement for the proportion of zero vs non-zero at 0.5 mm, which corrected when Agatston scores < 10 were excluded from analysis. The clinical utility of this finding needs to be validated in large, prospective, population-based longitudinal studies that include the potential effects of optimal medical therapy and other risk factor modification on long-term cardiovascular outcomes in patients with subclinical disease.

REFERENCES

1. Budoff MJ, Hokanson JE, Nasir K, et al. Progression of coronary artery calcium predicts all-cause mortality. *JACC Cardiovasc Imaging*. 2010;3:1229–1236.
2. Carr JJ, Crouse 3rd JR, Goff Jr DC, D'Agostino Jr RB, Peterson NP, Burke GL. Evaluation of subsecond gated helical CT for quantification of coronary artery calcium and comparison with electron beam CT. *AJR Am J Roentgenol*. 2000;174:915–921.
3. Becker CR, Kleffel T, Crispin A, et al. Coronary artery calcium measurement: agreement of multirow detector and electron beam CT. *AJR Am J Roentgenol*. 2001;176:1295–1298.
4. Kopp AF, Ohnesorge B, Becker C, et al. Reproducibility and accuracy of coronary calcium measurements with multi-detector row versus electron-beam CT. *Radiology*. 2002;225:113–119.
5. Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. *J Am Coll Cardiol*. 2000;36:1253–1260.
6. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. *Circulation*. 1995;92:2157–2162.
7. Mühlenbruch G, Klotz E, Wildberger JE, et al. The accuracy of 1- and 3-mm slices in coronary calcium scoring using multi-slice CT in vitro and in vivo. *Eur Radiol*. 2007;17:321–329.
8. Yoon HC, Goldin JG, Greaser 3rd LE, Sayre J, Fonarow GC. Interscan variation in coronary artery calcium quantification in a large asymptomatic patient population. *AJR Am J Roentgenol*. 2000;174:803–809.
9. Oudkerk M, Stillman AE, Halliburton SS, et al. Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging. *Int J Cardiovasc Imaging*. 2008;24:645–671.
10. van der Bijl N, de Bruin PW, Geleijns J, et al. Assessment of coronary artery calcium by using volumetric 320-row multi-detector computed tomography: comparison of 0.5 mm with 3.0 mm slice reconstructions. *Int J Cardiovasc Imaging*. 2010;26:473–482.
11. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte Jr M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15:827–832.

12. Vliegenthart R, Song B, Hofman A, Witteman JC, Oudkerk M. Coronary calcification at electron-beam CT: effect of section thickness on calcium scoring in vitro and in vivo. *Radiology*. 2003;229:520–525.
13. Mühlenbruch G, Thomas C, Wildberger JE, et al. Effect of varying slice thickness on coronary calcium scoring with multislice computed tomography in vitro and in vivo. *Invest Radiol*. 2005;40:695–699.
14. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA*. 2004;291:210–215.
15. Hou ZH, Lu B, Gao Y, et al. Prognostic value of coronary CT angiography and calcium score for major adverse cardiac events in outpatients. *JACC Cardiovasc Imaging*. 2012;5:990–999.
16. Qian Z, Joshi PH, Shaukat AF, et al. Relationship between chest lateral width, tube current, image noise, and radiation exposure associated with coronary artery calcium scanning on 320-detector row CT. *J Cardiovasc Comput Tomogr*. 2011;5:231–239.
17. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation*. 2006;114:1761–1791.
18. Sabour S, Rutten A, van der Schouw YT, et al. Inter-scan reproducibility of coronary calcium measurement using Multi Detector-Row Computed Tomography (MDCT). *Eur J Epidemiol*. 2007;22:235–243.
19. Ohnesorge B, Flohr T, Fischbach R, et al. Reproducibility of coronary calcium quantification in repeat examinations with retrospectively ECG-gated multisection spiral CT. *Eur Radiol*. 2002;12:1532–1540.