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Reduced iodine load with CT coronary angiography using dual-energy imaging: A prospective randomized trial compared with standard coronary CT angiography

Rekha Raju, MBChB^a, Angus G. Thompson, MBBS, PhD^a, Kristy Lee, MD^a, Bruce Precious, MD^a, Tae-Hyun Yang, MD^a, Adam Berger, MBBS^a, Carolyn Taylor, MD^a, Brett Heilbron, MD^a, Giang Nguyen, MD^a, James Earls, MD^b, James Min, MD^c, Patricia Carrascosa, MD^d, Darra Murphy, MD^a, Cameron Hague, MD^a, and Jonathon A. Leipsic, MD^{a,*}

^aDepartment of Radiology and Division of Cardiology, St Paul's Hospital, 1081 Burrard Street, Vancouver V6Z 1Y6, BC, Canada

^bFairfax Radiology, Virginia, USA

^cNew York Presbyterian/Weil Cornell Medical College, New York, NY, USA

^dDepartment of Radiology, Buenos Aires University School of Medicine, Buenos Aires, Argentina

Abstract

Background—There is concern regarding the administration of iodinated contrast to patients with impaired renal function because of the increased risk of contrast-induced nephropathy.

Objective—Evaluate image quality and feasibility of a protocol with a reduced volume of iodinated contrast and utilization of dual-energy coronary CT angiography (DECT) vs a standard iodinated contrast volume coronary CT angiography protocol (SCCTA).

Methods—A total of 102 consecutive patients were randomized to SCCTA (n = 53) or DECT with rapid kVp switching (n = 49). Eighty milliliters and 35 mL of iodinated contrast were administered in the SCCTA and DECT cohorts, respectively. Two readers measured signal and noise in the coronary arteries; signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated. A 5-point signal/noise Likert scale was used to evaluate image quality; scores of <3 were nondiagnostic. Agreement was assessed through kappa analyses.

Results—Demographics and radiation dose were not significantly different; there was no difference in CNR between both cohorts ($P = .95$). A significant difference in SNR between the groups ($P = .02$) lost significance ($P = .13$) when adjusted for body mass index. The median Likert score was inferior for DECT for reader 1 (3.6 ± 0.6 vs 4.3 ± 0.6 ; $P < .001$) but not reader 2 (4.1 ± 0.6 vs 4.3 ± 0.5 ; $P = .06$). Agreement in diagnostic interpretability in the DECT and SCCTA

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*Corresponding author.: jleipsic@providencehealth.bc.ca (J.A. Leipsic).

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groups was 91% (95% confidence interval, 86%–100%) and 96% (95% confidence interval, 90%–100%), respectively.

Conclusion—DECT resulted in inferior image quality scores but demonstrated comparable SNR, CNR, and rate of diagnostic interpretability without a radiation dose penalty while allowing for >50% reduction in contrast volume compared with SCCTA.

Keywords

Coronary CT angiography; Dual energy CT; Reduced iodinated contrast; Image quality; Diagnostic Efficacy

1. Introduction

Coronary CT angiography (coronary CTA) is now the accepted gold standard noninvasive imaging test to exclude coronary artery disease (CAD). Coronary CTA has been consistently shown to have a high negative predictive value to rule out significant CAD in intermediate-risk patients.^{1,2}

There does, however, remain a concern regarding the use of coronary CTA in patients with borderline renal function because of the potentially increased risk of contrast-induced nephropathy (CIN). Contrast administration to patients with CAD risk factors such as hypertension and diabetes may also predispose to a heightened risk of CIN.³ The CIN literature consistently reports a dose-effect relationship between administered contrast medium volume and renal toxicity. When the ratio of iodine to estimated glomerular filtration rate (GFR) is <1, the risk of developing CIN is 3%. This increases to 25% when the ratio of iodine to estimated GFR is ≥ 1 .⁴

As a result, multiple protocol adaptations and technological advancements have been developed to help reduce the volume of contrast and therefore iodine administered for coronary CTA.^{5,6}

One of these new technologies is single-source dual-energy CT with rapid tube voltage switching. In this approach, the tube voltage is switched between 80 kVp and 140 kVp in an alternating fashion. The system can switch between the low and high energies in <0.25 ms, minimizing misregistration between the 2 interleaved projection data sets. Because the data are nearly perfectly coregistered, a projection space processing technique can be used to align the projections corrected for Hounsfield unit (HU) shifts because of beam hardening and to mathematically transform the projections into the density of 2 basis materials (ie, water and iodine). Based on the materials' mass attenuation coefficient properties, a linear combination of these basis-pair material images is used to synthesize monochromatic CT images at any arbitrary energy between 40 and 140 keV. Attenuation in vascular structures is significantly increased in monochromatic images at low energies because of the closer proximity to the k-edge of iodine.⁶ This increased signal can potentially allow for a reduction in contrast medium administration during CTA.⁶ Although this technique has been validated for CT pulmonary angiography,⁶ this technology was not compatible with electrocardiography synchronization, limiting its applicability for coronary CTA until recently.

Recently, rapid kVp switching dual-energy imaging has been introduced for coronary imaging but to date has not been validated as an effective contrast medium dose-reduction tool. We therefore sought to assess the feasibility and diagnostic interpretability of coronary CTA using a dual-energy low monochromatic energy reduced-contrast scan protocol by performing a head-to-head prospective randomized clinical trial comparing reduced-contrast volume dual-energy coronary CTA (DECT) with standard contrast volume single-energy coronary CTA (SCCTA).

2. Methods

2.1. Study groups

This single-center, double-blinded, prospective study received institutional board ethics approval from the University of British Columbia. Each participant provided informed consent. None of the authors or research participants received funding or remuneration for this project.

Consecutive patients were recruited from November 2012 until April 2013. Patients who were referred for nonurgent outpatient coronary CTA were included in this study. Exclusion criteria were known allergy to CT contrast, pregnancy, age <35 years, body mass index (BMI) >35 kg/m², estimated GFR <45 mL/kg/m², baseline heart rate >65 beats/min, and inpatient and emergency department referrals.

A total of 320 outpatients underwent coronary CTA during the recruitment period. One hundred eight patients declined to take part in this study. After exclusion of patients with elevated BMI (34), impaired GFR (2), elevated heart rate (62), language barrier to consent (11), and age (1), 102 patients were enrolled and randomly assigned to 1 of the 2 coronary CTA protocols using a research randomizer tool: standard coronary CTA (n = 53) or dual-energy coronary CTA (n = 49).

2.2. Coronary CTA scan protocols

All coronary CTA studies were acquired with a multidetector CT scanner (Discovery HD 750; Gemstone Spectral Imaging, GE Healthcare, Milwaukee, WI) at suspended full inspiration using a prospectively electrocardiography-triggered technique if the heart rate was stable and <60 beats/min. The tube-on time was expanded when heart rates were >60 beats/min, with an additional 75 ms padding applied.

As per standard practice at our institution, the test bolus technique was applied using 20 mL of contrast medium (Visipaque 320 [iodixanol 320 mgI/mL]; GE Healthcare, Mississauga, Ontario, Canada) to synchronize data acquisition with the arrival of contrast material in the aorta. The bolus tracking technique was not used as all variables apart from the contrast volume in the injection protocol were left unchanged. The contrast injection was performed using a power injector (Stellant; Medrad, Warrendale, PA) through an antecubital vein at a rate of 5.5 mL/s.

A triple-bolus injection protocol was used for both cohorts, with the concentration of iodine but not total injected volume differing between the 2 groups. Patients on the standard

protocol (SCCTA) were given an injection of 50 mL of undiluted iodine contrast medium. This was immediately followed by a dilute mixture of 50 mL of iodine contrast medium and normal saline. This dilution composed of 60% iodine contrast medium and 40% normal saline (30 mL:20 mL). Patients were administered a lower iodine contrast concentration in the DECT group. They were administered a 50% dilute mixture of iodine contrast medium and normal saline (25 mL:25 mL). This was then followed with 20% concentration of iodine contrast medium and 80% normal saline (10 mL:40 mL). Both protocols were followed by a 40-mL normal saline chasing bolus at 5.5 mL/s. The absolute volume of contrast administered was 80 mL and 35 mL in the SCCTA and DECT cohorts, respectively, therefore resulting in a 56% reduction in the iodine load, whereas the total injected volume (140 mL) remained unchanged. Parameters of CT scanning and contrast medium administration are summarized in Table 1.

Effective radiation dose was calculated by multiplying dose-length product with the conversion factor for cardiac CT examinations (0.014 mSv/mGy·cm).⁷

2.3. Image reconstruction

Images were reconstructed with a standard iterative reconstruction algorithm at 40% adaptive statistical iterative reconstruction in the standard coronary CTA cohort. Dual-energy coronary CTA scans were reconstructed at a monochromatic energy of 60 keV as that is the lowest monochromatic energy level available that can be reconstructed with an iterative reconstruction algorithm. Images were then reviewed and analyzed on a dedicated off-line workstation (AW 4.3–4.4 Advantage Workstations; GE Healthcare).

2.4. Quantitative analysis (signal intensity, noise, and contrast)

Quantitative measures of image quality were performed by measuring the signal and noise properties in the aorta, left main coronary artery, left anterior descending, left circumflex and right coronary artery, and the epicardial fat.

Signal intensity (SI) was defined as the mean CT number in HUs and noise was the standard deviation of the CT number in HUs. The mean SI and noise were calculated in each patient by averaging the values obtained from the 4 coronary arteries. The signal-to-noise ratio (SNR) was calculated as the mean SI of the coronary arteries divided by the mean noise: $SNR = \text{mean SI} / \text{mean noise}$.

Contrast refers to the difference in the SI between 2 structures. The contrast-to-noise ratio (CNR) was defined as the difference between the mean SI of the coronary arteries and the SI of the epicardial fat divided by the mean noise. $CNR = (\text{mean SI of the coronary arteries} - \text{SI of epicardial fat}) / \text{mean noise}$.

These measurements were obtained in 1 session by a single radiologist (R.R.; 2 years of post-fellowship experience), manually placing a circular region of interest at each anatomic site mentioned previously. The region of interest was 1.0 cm² for the aorta at the level of the left main coronary artery. This was adapted to 0.2 to 0.4 cm² for the coronary arteries (left main, left anterior descending, left circumflex, and right coronary artery) and epicardial fat.

2.5. Qualitative analysis (subjective evaluation of image quality)

All SCCTA and DECT scans were independently subjectively evaluated by 2 experienced level-3 coronary CTA readers (C.T. and B.H.) with 4 and 18 years of post-fellowship experience, respectively, on an off-line workstation (AW 4.3–4.4 Advantage Workstations; GE Healthcare). The CT readers were blinded to the image acquisition protocols. All scans were graded using a modified Likert scale.³

All scans were graded on a per-patient (SCCTA, $n = 53$; DECT, $n = 49$) and a per-vessel (SCCT, $n = 212$; DECT, $n = 196$) basis. An overall image quality score was assigned to each coronary CTA examination, which took into account the degree of contrast enhancement in the coronary arteries and the presence of image noise and motion artifact. A separate image quality score was assigned to the coronary arteries on a per-vessel basis, which excluded presence of motion artifact but assessed the degree of vascular enhancement and presence of image noise. Dichotomization of the 5-point Likert scoring system was performed by grouping scores of 1 and 2 into the “nondiagnostic” category and scores of 3, 4, and 5 into the “diagnostic” category (Fig. 1). In addition, both readers independently assessed all scans for the presence of obstructive CAD, which was defined as the presence of a $>50\%$ stenosis.

A third coronary CTA reader (C.H.; 4 years of post-fellowship experience) provided consensus when there was discordance between the 2 primary readers as to whether there was evidence of obstructive disease or whether a study was of diagnostic quality. Obstructive disease was not validated because of the absence of the gold standard angiographic correlation.

2.6. Statistical analysis

Analyses were performed using statistical software (SAS, version 9.1; SAS Institute, Cary, NC). A statistically significant difference was defined as a P value $< .05$. Continuous variables were expressed as median $\pm$ standard deviation.

Differences in patient characteristics, scanning parameters, and quantitative measures of image quality (SI, noise, SNR, and CNR) between the 2 groups were tested for significance. A 2-sided t test was applied when the distribution of data from both groups was of equal variance, and Welch-Satterthwaite t test was used when unequal variance was found. A univariate model was initially applied to both cohorts to determine if there was any link between patient characteristics and SNR. A multivariate linear mixed-effect model was then performed to eliminate any potential bias from continuous variables such as BMI.

To measure the inter-reader agreement of “diagnostic” and “nondiagnostic” studies, a total agreement rate (defined as the sum of agreed count of nondiagnostic and diagnostic cases over the total cases) was used. A similar calculation was performed to test the inter-reader agreement of “obstructive” and “nonobstructive” studies. A bootstrap method⁸ was used to construct the 95% confidence interval for such measurements.

3. Results

3.1. Patient demographics

A total of 102 consecutive eligible outpatients referred for nonurgent coronary CTA (57 male and 45 female) were enrolled. The median age was 55 years $\pm$ 9.2 years (standard deviation) for the entire cohort (53 years $\pm$ 9.6 years for females and 57 years $\pm$ 8.7 years for males). There was no significant difference in sex distribution, age, or BMI between the 2 groups (all $P > .05$; Table 1).

3.2. Radiation dose

The difference in radiation dose was not statistically significant (dose-length product and effective radiation dose) in the SCCTA and DECT cohorts: 164.79 mGy·cm $\pm$ 84.49 mGy·cm and 2.31 mSv $\pm$ 1.18 mSv for SCCTA vs 159.41 mGy·cm $\pm$ 46.73 mGy·cm and 2.23 mSv $\pm$ 0.65 mSv for DECT (both $P > .05$; Table 1).

3.3. Quantitative analysis

There was lower SI in the individual coronary arteries in the DECT protocol (all $P < .05$). Noise was significantly higher in the left circumflex and right coronary artery in the DECT compared with the standard coronary CTA protocol ($P < .05$). The overall mean SI and mean noise for all arteries was significantly lower for DECT compared with SCCTA ($P < .05$). There was no significant difference in CNR between both cohorts ($P = .95$). Initial univariate analysis demonstrated a significant difference in SNR between both cohorts ($P = .02$), which was then found not to be statistically significant after performing a multivariate linear mixed-effect model adjusting for BMI ($P = .13$; Table 2).

3.4. Qualitative analysis

The median signal/noise Likert score was 3.6 ± 0.6 for DECT and 4.3 ± 0.6 for the SCCTA protocol from reader 1 ($P < .001$) and 4.1 ± 0.6 and 4.3 ± 0.5 , respectively, from reader 2 ($P = .06$; Fig. 2).

When being assessed strictly for signal and noise, 192 of the 196 vessels (97.9%) in the DECT and 211 of the 212 vessels (99.5%) in the SCCTA groups were classified as diagnostic ($P = .20$).

The total agreement rate in the diagnostic interpretability of scans in the DECT and SCCTA groups was 91% (95% confidence interval, 86%–100%) and 96% (95% confidence interval, 90%–100%), respectively. This improved to 99% (95% confidence interval, 98%–100%) in both cohorts on a per-vessel basis.

3.5. Stenosis assessment

There was discordance with regard to obstructive and non-obstructive disease in 13 cases. The total agreement rate for the presence of obstructive disease was similar between the 2 groups: 86% (95% confidence interval, 76%–94%) for the DECT compared with 89% (95% confidence interval, 80%–96%) for the SCCTA protocol. Figure 1 and 2 illustrate representative multiplanar reconstructed images of obstructive and non-obstructive plaque in

the coronary arteries from a standard coronary CTA (Fig. 1) and a dual-energy coronary CTA (Fig. 2), respectively.

After consensus reads, obstructive CAD was diagnosed in 9 of 53 patients (17%) in the SCCTA and 3 of 49 patients (6%) in the DECT groups ($P = .13$).

4. Discussion

In our prospective randomized trial, low monochromatic energy coronary CTA allowed for >50% reduction in iodine administration while maintaining diagnostic interpretability, SNR, and CNR with slight compromise on subjective image quality scores. Importantly, comparable inter-reader agreement regarding the presence of obstructive disease was confirmed.

Our study suggests that diagnostically comparable images may be acquired using a dual-energy low-iodine contrast dose protocol. In patients in whom CIN is a concern and yet there is clinical indication for coronary CTA, a low-dose iodine contrast protocol may be a viable alternative. The reduction in iodine load using dual-energy imaging is advantageous as it offers a direct benefit to patients in terms of renal protection. This technique may enable patients previously considered unsuitable for coronary CTA to undergo this noninvasive imaging test.

Although our data suggest equipoise in SNR, CNR, and diagnostic interpretability, we did identify a reduction in overall image quality and an increase in noise properties. For image reconstruction, we chose 60 keV because our initial experiences suggest that this monochromatic energy level afforded the best balance between increased image SI and image noise. This decision though was significantly impacted by the inability to integrate iterative reconstruction at lower energy levels, which rendered scans heavily degraded by image noise. In the future, there is the potential to realize further improvements in signal and SNR by reconstructing images closer to the k-edge of iodine (33 keV) when iterative reconstruction becomes available for use with energy levels < 60keV.

Other techniques have been previously proposed to enable contrast volume reduction in CTA. In 2004, Sigal-Cinqualbre et al⁹ proposed low-kilovoltage scanning as a technique which allows for reduced iodine contrast load because of the lower effective energy which is closer to the k-edge of iodine (33 keV), resulting in a greater photoelectric effect¹⁰ and consequently increasing the degree of vascular attenuation. An additional advantage of the dual-energy technique over a single-energy low tube voltage technique is the ability to reconstruct images at varied monochromatic energy levels, allowing for greater flexibility when reviewing the image data set. It has been recently proposed that higher monochromatic energy levels may be more appropriate for stent evaluation where lower energy imaging results in attenuation values too high for appropriate edge detection.¹⁰ Furthermore, standard low tube potential imaging is limited to patients with smaller body habitus.^{11,12} This is a particular limitation when it comes to evaluating pulmonary pathology in patients with undifferentiated chest pain.

There has been concern regarding the potential dose implications of the integration of dual-energy scan protocols that would be perceived as a step backward with regard to the steady progression toward lower-dose coronary CTA scanning.¹³ Importantly, there was no statistically significant difference in the estimated dose exposure in both arms ($P = .28$) suggesting that this protocol adaptation has only modest dose implications, if any. There is a misconception that dual-energy protocols result in doubling of the overall tube potential used for acquisition. With rapid kVp acquisition, the mean tube potential during the acquisition is approximately 110 kVp, resulting in a reduction in the tube energy as compared with standard 120 kVp coronary CTA. The slightly higher dose in our cohort reflects the broad adoption of dose-reduction strategies at our site, with 36% of patients in the standard arm undergoing coronary CTA with a tube potential of 100 kVp. In addition, in the patient at risk for CIN the potential benefit of a 56% reduction in iodine load administration confers a much more substantive potential benefit⁴ likely outweighing the nominal increase in radiation dose.

4.1. Limitations

Our study is not without limitations. Our evaluation focused on quantitative and qualitative measures of image quality without an evaluation of diagnostic accuracy as compared with current gold standard techniques for detecting coronary artery stenosis such as invasive coronary angiography. We do, however, note stable reader confidence and agreement with regard to the diagnosis of obstructive CAD in both arms. In addition, many other protocol adaptations such as low tube potential scanning have largely been integrated on the basis of studies documenting preserved image quality and interpretability.

Furthermore, the coronary CTA scans in our study were evaluated by highly experienced level-3 coronary CTA readers. We cannot exclude that the extensive experience and comfort level of the readers may have contributed to the non-inferiority of image quality in dual-energy coronary CTA arm. Although we did not detect a significant difference in the diagnostic interpretability of the studies between the 2 cohorts, we recognize that we lack the power to evaluate per-subject interpretability. To help mitigate this limitation, we performed our analysis on a per-vessel basis giving us more than 400 data points for evaluation. That being said, our data are meant to serve as a proof of concept and are exploratory in nature, which suggests that low-contrast dual-energy coronary CTA may be a reasonable alternative to standard coronary CTA in patients at risk of CIN.

Furthermore, the cohort examined in our trial had a relatively high median BMI with a higher BMI in the DECT cohort. Although the applicability of our findings on patients with lower BMI cannot be definitely stated, we feel that the cohort assessed in our study is, if anything, a more difficult cohort to evaluate with a reduced-contrast technique because of inherently higher image noise properties negatively impacting image quality. We cannot comment on the applicability of our findings in a higher-risk cohort; however, we felt the population evaluated compares well with a typical coronary CTA laboratory cohort.

Finally, although it is accepted that reducing iodine volume is the best mechanism for reducing CIN risk, we did not test our protocol in at-risk patients nor did we evaluate postscan serum creatinine levels. We can therefore not comment on the rate of CIN in either

of our arms nor comment on the safety or the ability to reduce the rate of CIN in an at-risk population.

5. Conclusion

In summary, reduced-contrast dual-energy coronary CTA allows for >50% reduction in iodine administration while maintaining SNR, CNR, and diagnostic interpretability with slight compromise on qualitative measures of image quality. Reduced-contrast dual-energy coronary CTA technique may be a viable option in a select group of patients with already significantly impaired renal function, who are at a higher risk of CIN but in whom coronary CTA is indicated.

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Fig. 1.

Representative images of the coronary arterial tree from a patient randomized to standard coronary CT angiography protocol, which demonstrates a long segment of occlusive partially calcified plaque in the proximal LAD (A), mild partially calcified plaque in the circumflex artery (B), and scattered foci of minimal nonobstructive calcified plaque in the RCA (C). Images of the coronary arteries are optimal with image quality Likert scores of 4 to 5/5. LAD, left anterior descending; RCA, right coronary artery.

Fig. 2.

Representative images of the coronary arterial tree from a patient randomized to low-iodine contrast volume dual-energy coronary CT angiography protocol. Images of the coronary arteries are not inferior to that of a standard iodine contrast volume coronary CT angiography protocol as seen in Figure 1. There is a short segment occlusive plaque in the proximal LAD (A). The circumflex artery (B) and RCA (C) are normal in appearance with no plaque identified. Assessment of the coronary artery vasculature is optimal with image quality Likert scores of 4 to 5/5. LAD, left anterior descending; RCA, right coronary artery.

Table 1

Patient characteristics, CT scanning parameters, and iodine contrast administration protocol.

Parameter	Dual-energy CCTA (n = 49)	Standard CCTA (n = 53)
Patient characteristics		
Female:Male	22:27	23:30 ($P = 1.00$)
Age (y) *	56 $\pm$ 8.9	54 $\pm$ 9.5 ($P = .67$)
Height (cm) *	170 $\pm$ 10.3	175 $\pm$ 11.8 ($P = .57$)
Weight (kg) *	77 $\pm$ 13.3	79 $\pm$ 15.5 ($P = .70$)
BMI (kg/m ²) *	27 $\pm$ 3.1	27 $\pm$ 3.5 ($P = .31$)
Radiation dose		
Dose-length product (mGy-cm)	164.8 $\pm$ 84.5	168.2 $\pm$ 119.5 ($P = .28$)
Effective radiation dose (mSv)	2.31 $\pm$ 1.18	2.35 $\pm$ 1.67 ($P = .28$)
Conversion factor for cardiac CT = 0.014 mSv/mGy-cm		
Scanning parameters		
Tube voltage (kVp)	Rapid switching between 140 and 80	120 if BMI >30, 100 if BMI <30
Tube current (mA)	600	Dose modulation with noise index 28
Rotation time (s)	0.5	0.5
Table feed/rotation (mm)	0.984	0.984
Section collimation (mm)	1.25	1.25
ASIR [†]	—	40%
Contrast medium (iodine [‡] :normal saline)		
Injection volume (mL)	25:25	50:0
	10:40	30:20
Chasing bolus (mL)	0:40	0:40
Absolute iodine volume (mL)	35	80
Injection rate (mL/s)	5.5	5.5

BMI, body mass index; CCTA, coronary CT angiography; SD, standard deviation.

P values are included in brackets. $P < .05$ defined as statistically significant.

* Data are median $\pm$ standard deviation.

[†] ASIR: adaptive statistical iterative reconstruction.

[‡] Ioversol 320 (320 mgI/mL).

Table 2

Quantitative image analysis (signal intensity, noise, CNR, and SNR).

Parameter	Dual-energy CCTA (n = 49), mean $\pm$ SD	Standard CCTA (n = 53), mean $\pm$ SD	P value
Signal intensity (HU)			
Left main	324.8 $\pm$ 94.2	429.4 $\pm$ 130.3	<.001
Left anterior descending	307.3 $\pm$ 85.9	420.2 $\pm$ 120.5	<.001
Left circumflex	301.9 $\pm$ 84.6	430.1 $\pm$ 118.6	<.001
Right coronary	301.4 $\pm$ 90.2	436.3 $\pm$ 123.8	<.001
Noise (HU)			
Left main	25.5 $\pm$ 9.5	28.7 $\pm$ 12.7	.15
Left anterior descending	29.4 $\pm$ 15.5	32.2 $\pm$ 18.9	.42
Left circumflex	28.8 $\pm$ 13.0	38.0 $\pm$ 20.7	<.05
Right coronary	26.3 $\pm$ 11.8	35.2 $\pm$ 20.9	<.05
SI and noise measurements			
Mean signal intensity (HU)	308.4 $\pm$ 84.4	429.0 $\pm$ 119.5	<.001
Mean noise (HU)	27.5 $\pm$ 8.9	33.5 $\pm$ 14.0	<.05
CNR	16.8 $\pm$ 5.2	16.9 $\pm$ 4.8	.95
SNR	12.0 $\pm$ 3.9	13.8 $\pm$ 3.9	.02
SNR (after multivariate analysis)	12.0 $\pm$ 3.9	13.8 $\pm$ 3.9	.13

CCTA, coronary CT angiography; CNR, contrast-to-noise ratio; HU, Hounsfield units; SD, standard deviation; SNR, signal-to-noise ratio.