Triphasic Contrast Agent Injection in 64-MDCT Coronary Artery Angiography

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Abstract

Purpose: To evaluate image quality and cardiovascular enhancement after triphasic injection in 64-slice-CT coronary angiography (c-CTA). **Methods:** c-CTA of twenty-two asymptomatic patients following triphasic injection (65ml-contrast bolus + mixed 30ml-contrast and 20ml-saline bolus + 50ml-saline chaser) were retrospectively reviewed. Attenuation in the great vessels, cardiac chambers, and coronary arteries in 13 places were measured by region of interest. Also, differences in enhancement between the right coronary artery (RCA) and the right cardiac chambers (RCA versus right atrium or RA; RCA versus right ventricle or RV) were analyzed. Quality of images and contrast-related streak artifacts were subjectively assessed by 2 radiologists in consensus on a 4-point scale. **Results:** There was excellent enhancement in the coronary arteries (mean range 395.84-429.90 Hounsfield Units or HU), ascending aorta (mean 448.58 HU), descending aorta (mean 433.49 HU), and pulmonary artery (mean 385.45 HU). There was adequate difference in attenuation between RCA versus RA (mean range 126.12-148.43 HU) and RCA versus RV (mean range 50.34-72.66 HU). There was high and inhomogeneous attenuation in the superior vena cava (mean 509.23 HU). The quality of images was considered good (mean 1.6; 1 = excellent, 2 = good, 3 = moderate, 4 = low) and contrast-related streak artifacts were considered low (mean 2.9; 1 = severe, 2 = moderate, 3 = low, 4 = absent) by two radiologists. **Conclusions:** Our triphasic contrast injection provides excellent cardiovascular enhancement with minimal contrast-related streak artifacts, particularly in the right cardiac chambers while adequately differentiating the right coronary artery.

Keywords: Coronary artery, Triphasic injection, Computed tomography, Enhancement, ROI

Introduction

The first non-invasive cardiac-specific device with ECG synchronization was the electron-beam CT (EBCT), introduced in 1984. Since then, rapid advances in CT technology have led to the development of

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multi-detector CT scans, and introduction of 64-slice CT scanner has dramatically improved diagnostic ability of cardiac imaging[1]. Simultaneously, new protocols have been developed for obtaining images of progressively improving quality. In particular, developing an adequate contrast injection protocol is an important step. The single bolus injection protocol (pure contrast agent) and double bolus injection protocol (contrast bolus with saline chaser) have been used in the last few years[1-8]. The double bolus injection protocol is performed in many ways, generally consisting of 80-140ml of contrast at 3-5 ml/sec flow rate followed by a 20-50 ml saline chaser[1,9].

There have been several studies [10-13] performed with triphasic injection protocol, which consists of two contrast boluses at different flow rates followed by a saline chaser. In general, the aim of any injection protocol is to achieve an adequate, consistent, and homogeneous contrast enhancement in the coronary arteries and the cardiac chambers, in order to facilitate depiction of anatomy and pathology[1].

The aim of this study was to objectively assess cardiovascular enhancement following a triphasic contrast agent injection protocol on a 64-slice computed tomography coronary angiography (c-CTA). Also, image quality and contrast-related streak artifacts were evaluated subjectively.

Our hypothesis was that our triphasic protocol provides excellent cardiovascular enhancement with minimal contrast-related streak artifacts, particularly in the right cardiac chambers while adequately differentiating the right coronary artery.

Material And Methods

Patients

A retrospective review of consecutive patients who underwent CT coronary angiography was performed. Included in the study were 22 asymptomatic and volunteer patients who underwent a c-CTA. There were 12 males and 10 females between the ages of 32 and 58 and with a mean age of 44. Each patient's informed consent was obtained at the time the CT scan was performed. Institutional review board was not required as the patient cohort was recruited for an alternate study.

Imaging protocol

In all patients, an ECG-gated contrast-enhanced cardiac computed tomography was performed, in accordance with our institutional protocol. A 64-slice CT scan (Brilliance 64®, Philips, Eindhoven, The Netherlands) was used and the protocol included the following scan parameters: tube rotation time 0.4 ms, detector collimation 64 x 0.625 mm, pitch 0.2, tube voltage 120 kV, and current 600 mAs. Patients were scanned in supine position in the craniocaudal direction from 2 cm superior to the carina to 2 cm inferior to the heart, while maintaining an inspiratory breath-hold. Standard ECG-gated images were reconstructed with 0.67 mm slice thickness and 0.33 mm reconstruction interval every 10% of the cardiac cycle interval. The end-diastolic dataset at 75% of cardiac cycle was evaluated. Patients with heart rate higher than 65 beats per minute (BPM) received 5mg of metoprolol by intravenous injection before entering the CT room: the target heart rate was 65 BPM. All patients received 0.4 mg sublingual nitrate immediately before

scanning. Angiographic data acquisition was performed after injection of a triphasic contrast and saline bolus. We first injected 65 ml of a non-ionic iodine contrast agent (Isovue 370®, Bracco Diagnostics Inc., Princeton, NJ) at a 5 ml/sec flow rate. The first bolus was followed by a mixed contrast and saline bolus (30 ml contrast and 20 ml saline) and then by a 50 ml saline chaser bolus, both at the same flow rate as the first one. The saline agent was a sterile isotonic 0.9% saline solution. Bolus-tracking technique was used to determine the scanning delay, with the ROI in the descending aorta, just superior to the heart. The scan automatically started at a threshold of 110 Hounsfield Units (HU).

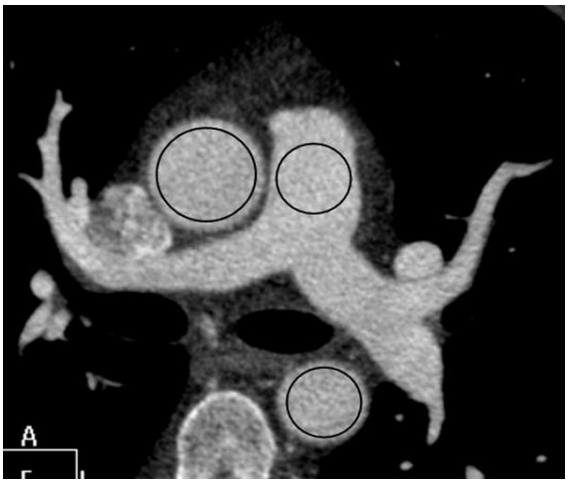

Fig 1: Contrast-enhanced axial CT at the level of the subcarina shows regions of interest drawn in the ascending aorta, main pulmonary artery, and descending aorta (clockwise) to measure the intraluminal attenuation.

Images analysis

Cardiovascular enhancement measurements:
In accordance with the literature and the American Heart Association segmentation guidelines, attenuation was measured as Hounsfield units (HU) mean and standard

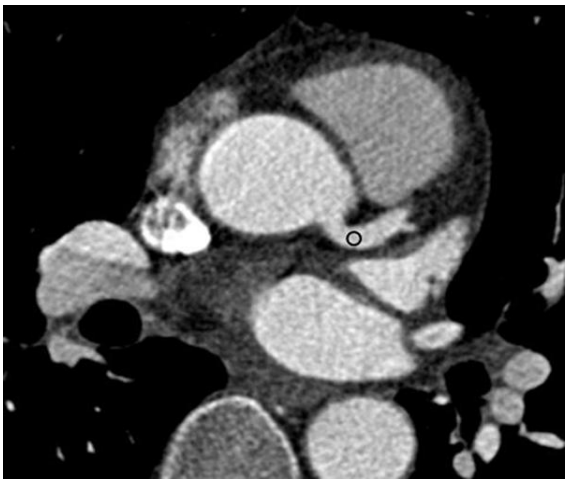

Fig 2: Contrast-enhanced axial CT at the origin of the left coronary artery shows the region of interest in the lumen of the left main artery.

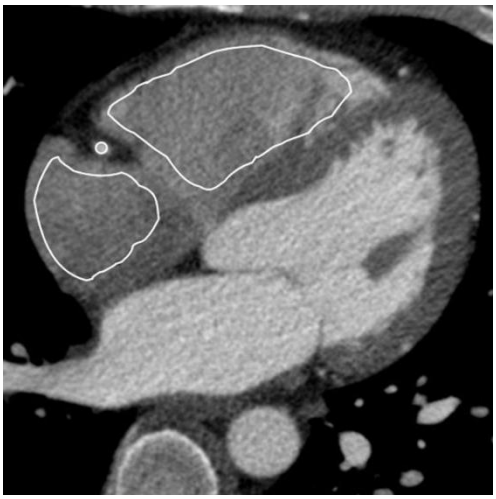

Fig 3: Contrast-enhanced axial CT shows the region of interest (ROI) in the lumen of the middle segment of the right coronary artery. Also, ROI has been drawn as large as possible in the right atrium and right ventricle.

deviation in the lumen of the most important anatomical structures, namely, right coronary artery in proximal (pRCA) and middle (mRCA) segments, left main coronary artery (LM), proximal circumflex coronary artery (CF), proximal left anterior descending coronary artery (LAD); ascending aorta (aAO), descending aorta (dAO) and pulmonary artery trunk (PA) at the level of

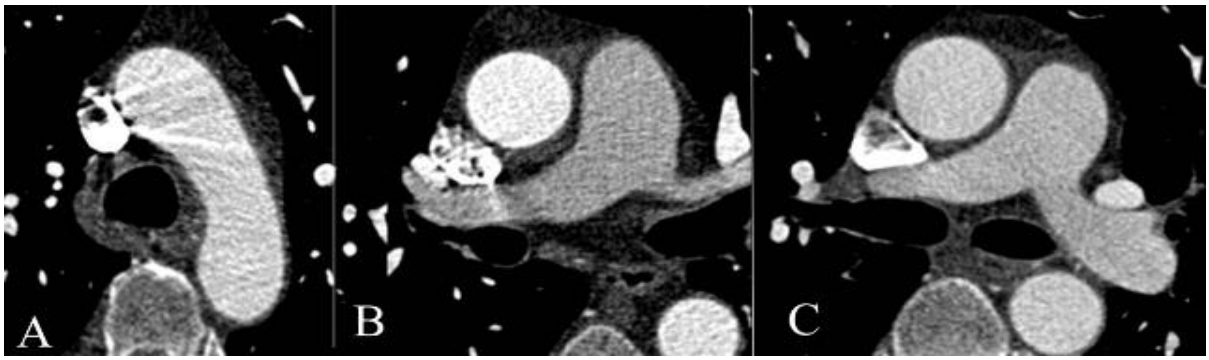

Fig 4: 4A. Contrast-enhanced axial CT shows contrast-related streak artifacts in the superior vena cava (SVC) obscuring the pulmonary artery, classified as score 2. 4B. Contrast-enhanced axial CT shows a few streak artifacts in the SVC with good visualization of the anatomical structures, classified as score 3 - the most common score regarding artifacts in our study. 4C. Contrast-enhanced axial CT shows high and inhomogeneous attenuation in the SVC but no contrast-related streak artifacts, classified as score 4.

the carina; superior vena cava (SVC) 1 cm superior to the right atrium; right atrium (RA); left atrium (LA); right ventricle (RV) and left ventricle (LV). All enhancement measurements were obtained on axial images by region of interest (ROI). Each ROI was drawn as large as possible inside the vessels and cardiac chambers while avoiding their walls, calcifications, and plaques (figure 1-3).

Enhancement of greater than 250 HU in the coronary arteries, left cardiac chambers, and great vessels was considered significant. Enhancement of 150-250 HU in the SVC and in the right cardiac chambers was considered sufficient. We also calculated the difference in enhancement between different segments of RCA versus the right cardiac chambers (pRCA versus RA; pRCA versus RV; mRCA versus RA; mRCA versus RV). A difference of >50 HU was considered adequate.

Image quality evaluation

For evaluating the quality of the images, we considered two parameters: presence of contrast-related streak artifacts and subjective consideration on quality by two radiologists in consensus.

The presence and the degree of contrast-related streak artifacts related to high concentration of contrast passing through SVC and the right cardiac chambers were determined on a 4-point subjective scale: 1 = severe, when artifacts did not allow good visualization of anatomic structures; 2 = moderate, when artifacts were moderate and allowed structural evaluation; 3 = low, when some artifacts were present, but all structures were visible; 4 = absent, when no artifacts were visualized (figure 4). Two radiologists were also asked to note their subjective impression about the quality of the images on a 4-point score scale (1 = excellent, 2 = good, 3 = moderate, 4 = low) (figure 5).

Statistical analysis

The mean attenuation value of each ROI was compared at each place. The differences in attenuation between different segments of RCA (pRCA and mRCA) versus the right

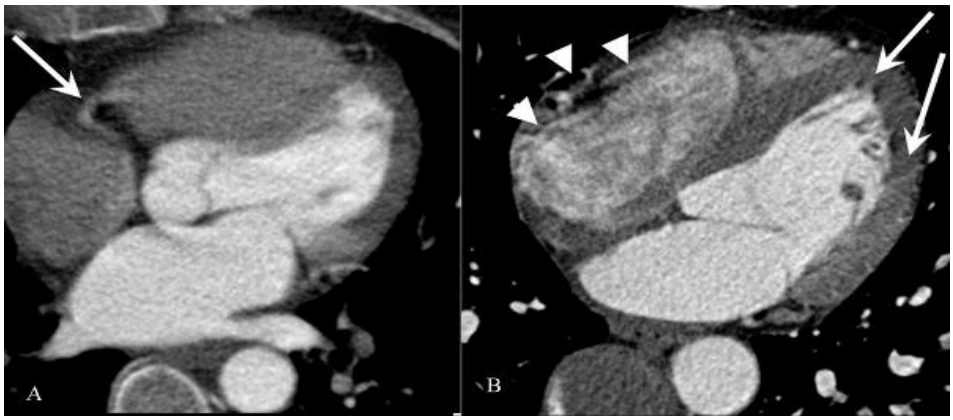

Fig 5: Contrast-enhanced axial CT shows the presence of artifacts generated both by right coronary artery motion (5A, arrow), by cardiac motion (5B, arrowheads), and beam hardening (5B, arrows). These artifacts caused the image quality to be classified as low (score 4).

cardiac chambers (RA and RV) were also calculated. To evaluate the differences among segments within each coronary artery we used the paired T-test for RCA (preliminary analysis revealed the data were normally distributed) and the analysis of variance for repeated measurements of the LCA (sphericity assumed test). A two-tailed one-sample T-test with mean of 250 was done to find the significance of the attenuation value measured within the lumen of vessels and cardiac chambers versus 250 HU. P value < .05 was considered as significant. We also calculated the mean values of radiologist's impression on artifact and image quality.

Results

Coronary arteries

Mean coronary arterial enhancement values for RCA and LCA segments are shown in table 1. Attenuation values for all coronary segments were significantly higher than 250 HU (P<.05) (table 2). The differences in attenuation between segments of the same coronary artery were not significant (RCA: mean difference 22.3±82 HU, P=0.942; LCA: P=0.845). We always found a difference higher than 50 HU between the RCA segments and the right cardiac chambers (table 3).

Great vessels

The mean attenuation values in the aorta, pulmonary artery, and SVC are shown in table 1. All attenuation values of great vessels except that of SVC (P = 0.30) were significantly higher than 250 HU (P<.05) (table 2).

Cardiac chambers

The mean attenuation values in the right and left cardiac chambers are shown in table 1. The values in the left cardiac chambers were significantly higher than 250 HU (P<.05). The values in the right cardiac chambers were not significant (p=0.40 in RA and p=0.10 in RV) (table 2), although the mean values were higher than 250 HU (table 1).

Artifacts and image quality

The mean value for the presence of contrast-related streak artifacts was 2.9 (3=low), with a median of 3. Seventy-seven percent of patients had low (15/22) or no (2/22) artifact

Table 1: Mean Attenuation Values

	Great vessels				Cardiac chambers				Coronary arteries				
	SVC	**aAO**	**dAO**	**PA**	**RA**	**RV**	**LA**	**LV**	**pRCA**	**mRCA**	**LM**	**CF**	**LAD**
Mean	489.44	448.58	433.49	385.45	278.36	300.55	409.83	419.81	429.90	398.27	405.43	408.38	395.84
SD (±)	335.25	71.52	53.55	94.23	128.31	151.03	60.22	60.07	129.38	113.48	84.95	75.09	93.09
Max	1357.40	526.30	506.60	549.30	495.14	665.40	511.72	508.62	558.20	545.10	502.10	505.10	506.40
Min	145.60	313.60	325.60	265.60	112.64	146.52	285.4	290.26	138.50	171.50	246.40	264.90	200.50

The attenuation values for the great vessels, cardiac chambers, and coronary arteries are shown above.

SVC=superior vena cava; aAO=ascending aorta; dAO=descending aorta; PA=pulmonary artery; RA=right atrium; RV=right ventricle; LA=left atrium; LV=left ventricle; pRCA=proximal right coronary artery; mRCA=middle right coronary artery; LM=left main; CF=circumflex; LAD=left anterior descending; SD=standard deviation; Max=maximum attenuation value; Min=minimum attenuation value.

Table 2: Attenuation Value Versus 250 HU

	Great vessels				Cardiac chambers				Coronary arteries				
	SVC	**aAO**	**dAO**	**PA**	**RA**	**RV**	**LA**	**LV**	**pRCA**	**mRCA**	**LM**	**CF**	**LAD**
P	0.30	<0.001	<0.001	<0.001	0.40	0.10	0.005	0.006	<0.001	<0.001	<0.001	<0.001	<0.001
Min Diff	26.43	153.14	149.47	75.58	-47.20	-25.57	44.29	47.48	97.70	99.84	103.89	102.11	86.70
Max Diff	452.45	244.01	217.52	195.318	110.13	240.06	202.92	215.77	262.10	215.33	208.15	207.13	204.97

The attenuation values were compared with 250 HU. Attenuation values of all great vessels except that of SVC (P = 0.30) were significantly higher than 250 HU (P<.05). Attenuation values of the left cardiac chambers were significantly higher than 250 HU (P<.05) while those of the right cardiac chambers were not significantly higher. Attenuation values for all coronary segments were significantly higher than 250 HU (P<.05).

SVC=superior vena cava; aAO=ascending aorta; dAO=descending aorta; PA=pulmonary artery; RA=right atrium; RV=right ventricle; LA=left atrium; LV=left ventricle; pRCA=proximal right coronary artery; mRCA=middle right coronary artery; LM=left main; CF=circumflex; LAD=left anterior descending; P=T-test vale of significance; Min Diff=lowest difference from 250 HU; Max Diff=highest difference from 250 HU.

visualized. 5 patients had moderate artifacts and none had severe artifacts (total 5/22, 23%). The mean value for subjective image quality evaluation was 2 (2=good), with a median of 2. Seventy-three percent of patients had a "positive" quality of the images, which include excellent (8/22) or good (8/22). In twenty-seven percent of patients with "negative" image quality (moderate=4/22; low=2/22), findings were mostly attributable to patient-related motion

Table 3: Attenuation Difference in the Right Heart

	RA-pRCA	RV-pRCA	RA-mRCA	RV-mRCA
Mean	148.43	72.66	126.12	50.34
Max Diff	251.80	342.70	233.70	405.70
Min Diff	0.70	4.20	4.10	35.8

Regarding the difference in attenuation between the right coronary artery (RCA) segments and the right cardiac chambers, we always found a difference higher than 50 HU, allowing for good visualization of RCA.

RA-pRCA=difference in attenuation between right atrium and proximal right coronary artery; RV-pRCA=difference in attenuation between right ventricle and proximal right coronary artery; RA-mRCA=difference in attenuation between right atrium and middle right coronary artery; RV-mRCA=difference in attenuation between right ventricle and middle right coronary artery; Mean=mean of the differences; Max Diff=maximum difference between values; Min=Minimum difference between values.

artifacts rather than contrast-related streak artifacts.

Discussion

Multidetector computed tomography angiography of coronary arteries is a proven method to investigate coronary artery disease (CAD) in both elective [14-16] and emergency patients [17], and a technique in continuous evolution. It is a method of non-invasive detection and grading of CAD, with the ultimate aim of replacing conventional angiography as the gold standard in diagnostic imaging of the coronary arteries [1]. Therefore, contrast injection protocol is one of the most important tools to obtain diagnostically adequate images with consistent and homogeneous attenuation in the coronary arteries and cardiac chambers [1]. In the past, many authors have studied different injection protocols, including single bolus (contrast agent only) [18,19] and double bolus (contrast agent and saline chaser) [5,7,20,21].

Monophasic injection protocol provides good coronary artery enhancement, but has many flow-related artifacts. Also, there is no significant difference in enhancement between the cardiac structures, particularly between the right cardiac chambers and right coronary artery, which is often more difficult to detect. The biphasic injection protocol was developed to overcome some of these shortcomings. Studies on the efficacy of biphasic injection protocol have demonstrated substantial improvement in image quality over the monophasic protocol, providing excellent coronary artery enhancement with less contrast-related streak artifacts in the SVC [22,23]. However, in many patients, the saline chaser bolus flushes contrast in the right cardiac chambers so effectively that it is unable to discern the internal structures (valve, papillary muscles,

etc.) and to distinguish the wall from the lumen [24].

The aim of this study was to demonstrate that our triphasic protocol provides excellent cardiovascular enhancement with minimal contrast-related streak artifacts, particularly in the right cardiac chambers while adequately differentiating the right coronary artery. Two studies [12,13] with contrast injection protocols similar to ours have demonstrated the utility of a triphasic protocol as a multipurpose technique for patients with acute non-specific chest pain. However, neither of these two studies measured the difference between the right cardiac chambers and right coronary artery, which offers insight into the adequacy of evaluation of right coronary artery. Other studies have used the triphasic protocol but examined the image quality based on heart rate [10] or adequacy for detecting aortic valvular pathology [11].

Cademartiri et al [9] found that an attenuation value in the coronary artery was optimal at 250-300 HU, and this was confirmed by Johnson et al [4] and Yamamuro et al [5]. Our attenuation values were significantly higher than 250 HU in all coronary segments of all patients. As demonstrated by Mitsumori et al [12] using a triphasic protocol similar to ours, we found no significant difference in attenuation between the coronary arteries (pRCA and mRCA; LM, CF, and LAD). Thus, our triphasic injection protocol provides excellent homogeneous enhancement in the coronary arteries. Cademartiri et al [9] demonstrated that good enhancement is the most important tool in establishing the diagnosis of CAD.

We found excellent attenuation in all great vessels. Attenuation values in the aorta and the pulmonary artery were significantly higher than 250 HU (table 2). The mean attenuation value was >250 HU but without statistical significance in the SVC.

We found excellent attenuation in the left cardiac chambers. This is important in order to detect intra-cardiac structures. We did not specifically analyze how the internal structures (valves, papillary muscles, etc.) are visualized, but good enhancement is the first step to identify anatomical anomalies according to Bouvier et al [11]. We found mean attenuation slightly above 250 HU without statistical significance in the right cardiac chambers, but less than that of all other structures (RA=278.36 HU; RV=300.55 HU; all other structures ranged from 385.45 to 489.44 HU). In particular, we specifically compared the attenuation values of the right cardiac chambers with multiple segments of the RCA (pRCA and mRCA) and always found 50 HU less attenuation in the right cardiac chambers. This allowed good visualization of the RCA, which is often more difficult to detect.

Our triphasic protocol also minimized contrast-related streak artifacts in the SVC while preserving optimal enhancement of coronary arteries and cardiac chambers. We found the degree of contrast-related streak artifacts was low (mean = 2.9) and the image quality was good (mean = 1.6). In other words, despite the presence of contrast-related streak artifacts in the SVC, there was good visualization of anatomy. Contrast-related streak artifact is one of the most important limitations of image quality in c-CTA. As Haage et al [22] demonstrated streak artifacts may mask anatomy (particularly

RCA) and make the evaluation more difficult. They found that injection of a small amount of contrast followed by a saline bolus provided good enhancement with reduced artifact.

We found that our protocol achieved the same goals, avoiding significant contrast-related streak artifacts. Johnson et al [4] confirmed that using a saline chaser was an appropriate method to avoid the artifact in the venous system. They demonstrated that the contrast passage in SVC is quite different from other great vessels, which may explain the high and inhomogeneous enhancement in the SVC we found despite the low degree of contrast-related streak artifacts. Continued research should be performed by reducing the amount of contrast agent in the second bolus and increasing the amount of saline bolus to improve the dilution of the mixed bolus.

In conclusion, our study demonstrates that our triphasic contrast injection provides excellent cardiovascular enhancement with minimal contrast-related streak artifacts, particularly in the right cardiac chambers while adequately differentiating the right coronary artery.

Limitation of the study

Our population consisted of only 22 patients. Our results could be better evaluated by studies with a larger number of patients. Also, our patients were volunteers who were asymptomatic. We did not correlate the patients' BMI with our results. We did not compare the new triphasic protocol with the older biphasic protocol. A direct comparison between the two protocols may be appropriate but difficult to perform practically. We focused our assessment on the proximal segments of the coronary arteries, which are generally the most clinically and interventionally relevant segments. We only analyzed the 75% cardiac phase. This is the phase where most of the anatomical structures are better visualized and clinical diagnosis is made [19]. Although not specifically assessed, we noticed artifacts related to atrial contraction in end-diastole. 50% phase may offer better analysis of CF and RCA compared to 75% phase [15,16,19]. We did not assess the visualization of internal structures such as valves and papillary muscles. Our measurements were obtained only on axial images without obtaining true transverse sections of vessels and chambers. We believe this does not affect our data adversely because axial images are the "cornerstone" in which all other reconstructed images are built [7] and isotropic voxels and thin sections make the results closer to other-plane analysis. Finally, our assessment of artifacts and image quality was subjective. Assessment of signal-to-noise ratio and contrast-to-noise ratio may offer a more objective evaluation.

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