

Intravenous contrast material administration in multislice computed tomography coronary angiography

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Abstract. Rationale and objectives: to compare contrast material (CM) administration protocols in non-invasive coronary angiography (CA) using a 16-row multislice CT (16-MSCT). Methods: 45 patients undergoing CA with 16-MSCT were divided into three CM protocols: group 1 (140 ml@4ml/s), group 2 (140 ml = 60 ml@5ml/s + 80 ml@3ml/s), and group 3 (100 ml@4ml/s). The attenuation at the origin of the coronary vessels was assessed. Three regions of interest were evaluated: 1) ascending aorta (ROI1); 2) descending aorta (ROI2); 3) pulmonary artery (ROI3). The resulting time-density curves generated the average attenuation and the slope of bolus geometry. Results: the attenuation at the origin of the coronary vessels, and the average attenuation of bolus geometry were not significantly different ($p>0.05$). The slope of bolus geometry was in ROI1 and ROI2 significantly lower for group 2, in ROI3 significantly lower for group 3 ($p<0.05$). Conclusion: 100 ml of CM provide the same attenuation in 16-MSCT CA as mono- or multi-phasic 140 ml protocols.

Key words: 16-row MSCT; bolus tracking; contrast material; non-invasive coronary angiography

Introduction

Four-row retrospectively ECG-gated multislice CT (4-MSCT) has been investigated for the detection of atherosclerotic coronary artery disease (1-3). A substantial volume of contrast material is required (4): 140-180 ml (1-3, 5, 6). Moreover, due to the long data acquisition time (~40 s), a hyperventilation manoeuvre of 8s to 10s may be required to maintain a complete motionless breath hold (1-3, 5, 6).

Manufacturers have recently introduced MSCT scanners with up to 16 arrays of detector-rows (16-MSCT), and increased spatial and temporal resolution (7-12). These improvements impact the protocol for contrast material (CM) administration (4). In fact, the time needed to scan the entire heart has been re-

duced below 20 s and therefore the CM administration parameters should be modified accordingly (9, 13). Also synchronization techniques have been reported to improve the optimization of vascular attenuation in CT angiography (4). Fixed delay and test bolus techniques were used to synchronize the passage of contrast material and the scan with 4-MSCT coronary angiography (1-3, 5, 6), while real time bolus tracking technique has only recently been applied after the introduction of 16-MSCT (13).

Three different intravenous CM administration protocols were compared: two with high volume (140 ml monophasic and biphasic) and one with a low-volume (100 ml), using a bolus tracking technique and a 16-MSCT scanner for the purpose of non-invasive coronary angiography. Aim of the study was to de-

monstrate that 16-MSCT coronary angiography can be performed with a lower volume of CM without affecting the vascular attenuation.

Materials and methods

Study population

Between September and October 2002, forty-five patients, 39 males and 6 females (mean age: 58; range 28-79), who underwent CT coronary angiography because of stable angina or undetermined chest pain, were prospectively enrolled in the study. Exclusion criteria for coronary CT angiography were: irregular heart rates, contraindications for intravenous iodinated contrast material (e.g. previous allergic reaction, serum creatinine >120 mmol/L), contraindications to RX exposure (e.g. pregnancy), inability to maintain a 20 s breath-hold (e.g. COPD, unstable clinical condition, or heart failure). The Institutional Review Board approved the study and all patients gave their informed consent.

Patients were randomly divided into three groups with different contrast material administration protocols (Table 1). Previously described CM administration protocols have been applied in group 1 and 2, while in group 3 a low-volume protocol (14), based on a volume providing an injection time slightly longer than acquisition time, was used (1-6). Patients' age, body weight, heart rate, scan delay and scan time were recorded.

Scan protocol

Prior to the examination the patients' heart rate (HR) was measured. Patients with a pre-scan HR equal or above 65 bpm and in the absence of con-

traindications were given a single oral dose of 100mg of metoprolol one hour before the scan. Patients were thoroughly instructed with respect to the examination and breath-hold procedure in order to avoid Valsalva manoeuvre and breathing artefacts during the scan.

The contrast material (Iodixanol 320 mgI/ml, Visipaque, Amersham Health, Little Chalfont, UK) was injected using an automatic power injector (En-Vision, MedRAD, Pittsburgh, PN, USA) through a 18-20 G IV cannula in an antecubital vein. Three different protocols were applied (Table 1).

All patients underwent CT coronary angiography with a 16-row MSCT scanner (Sensation 16, Siemens, Forchheim, Germany). Scan parameters were: number of detector rows 16, individual detector width 0.75 mm, gantry rotation time 420 ms, kV 120, mAs 400-500, table feed/rotation 3.0 mm, scan direction cranio-caudal, scan time ~16-21 s (depending on individual patient's size and anatomy). For the purpose of the study, iso-cardio-phasic (e.g. data from the same phase of the cardiac cycle) data-set were reconstructed using retrospective ECG gating with a time window starting at 400 ms before the next R wave.

Two data-set have been reconstructed: one for the analysis of coronary artery attenuation with 1mm effective slice width and 0.5 mm increment, and the other for the analysis of the great vessels of the thorax with 3 mm effective slice width and 3 mm increment. Images were sent to a stand-alone workstation (Leonardo, Siemens, Forchheim, Germany).

Bolus Tracking technique (Fig. 1)

The arrival of the injected IV CM bolus, was monitored in real time using a series of dynamic axial low-dose monitoring scans (120 kV, 20 mAs) at the level ascending aorta level at intervals of 1.25s. The

Table 1. Contrast material administration protocols

	Group 1	Group 2	Group 3
CM volume	140 ml	140 ml	100 ml
Administration	Mono-phasic	Bi-phasic	Mono-phasic
CM rate	4 ml/s	50 ml at 5 ml/s and 80 ml at 3 ml/s	4 ml/s
Total injection time	35 s	39 s	25 s

Abbreviations: CM=Contrast material; ml/s=millilitres per second; s=seconds

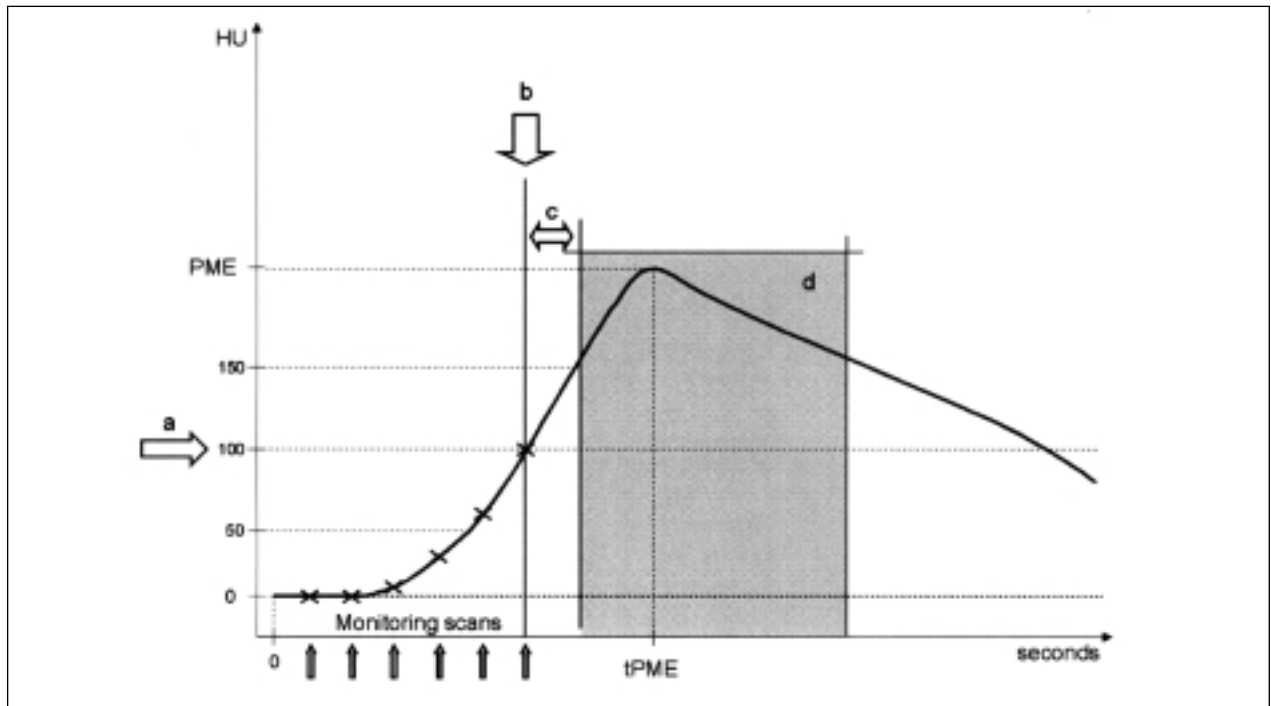


Figure 1. Bolus Tracking technique.

The geometry of the main bolus is displayed on a time-attenuation graph. The level of the axial low dose dynamic monitoring scan is chosen on the topogram, and a pre-monitoring test scan is performed. Then a region of interest is plotted inside the ascending aorta and a threshold (a) is set at +100 HU above the baseline attenuation. The contrast material administration and the monitoring sequence are started together. Monitoring scans are displayed on the screen in real time and the attenuation inside the ROI too. When the attenuation in the ROI reaches the value of 100HU or more (b), the scan is automatically triggered and after 4s (c), needed to give breath-hold instructions to the patient, the main scan is performed (d). The ideal overlapping between actual bolus geometry and scan period is also displayed. The peak of maximum enhancement in fact should fall in the first half of the scan

monitoring sequence was started 10 s after the beginning of the administration of contrast material. The scan was triggered automatically by means of a threshold measured in a ROI set into the ascending aorta. The trigger threshold inside the ROI was set at +100 HU above the baseline attenuation (~150 HU in absolute HU value). When the threshold was reached, the table moved to the cranial start position while the patient was instructed to maintain deep inspiratory breath-hold. Four seconds after the trigger value was reached, during which the contrast enhancement reached the optimal attenuation level, the main angiographic scan automatically started.

Data collection

One operator (F.C.) processed all the main scans at the workstation. Two data-set were used for the at-

tenuation measurement: 1) the attenuation at the origin of the coronary arteries and their branches, in order to monitor the effect of the different protocols on coronary arteries enhancement; and 2) the attenuation at the level of the main vessels of the thorax, in order to assess the bolus geometry.

The operator scrolled axial images to find the origin of the coronary arteries and their main branches (e.g. left main=LM, left anterior descending=LAD, circumflex=CX, right coronary artery=RCA) were detected and a ROI was positioned in order to measure the attenuation (Fig. 2).

The DICOM layout of the slices provides information on the exact acquisition time (down to sec⁻²) of the scan in each reconstructed slice. Using this information, the attenuation in HU was measured, at intervals of 1 s, drawing a ROI in each slice, throughout the entire data-set (along the *z-axis* in contiguous sli-

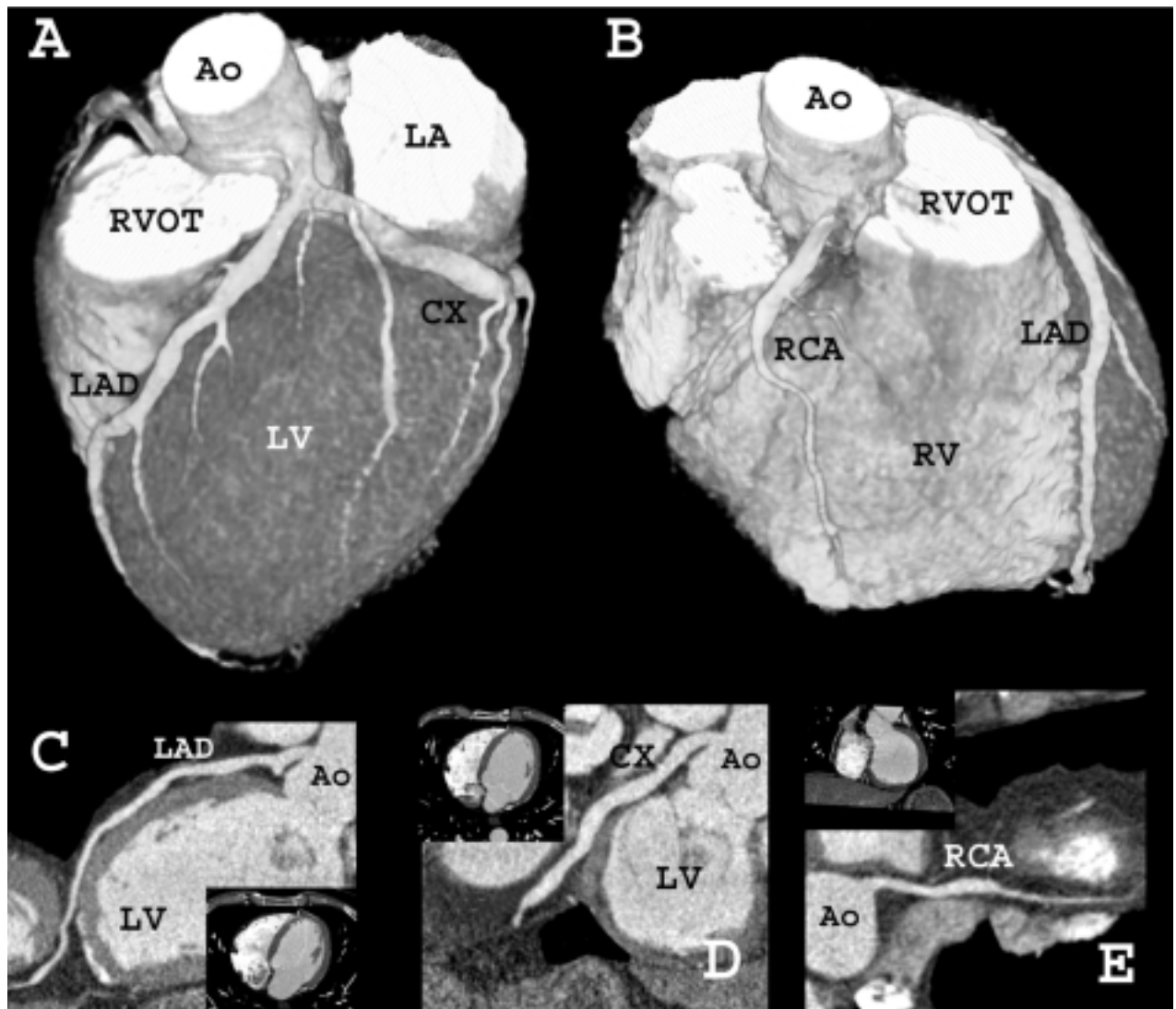


Figure 2. Example of coronary angiography with 16-row MSCT.

A young patient was enrolled in group 1 (100 ml of 320 mgI/ml administered at 4 ml/s) and showed no evidence of coronary artery disease. In A and B three-dimensional volume rendering reconstructions while in C, D, and E, curved MPR are performed along the lumen of LAD, CX, and RCA. The size of the coronary arteries is larger than average (A and B). Atherosclerotic lesions are absent and the patency of all 4 vessels and main branches is preserved (C, D, and E). An anatomical variant is present. In fact the anatomy shows a CX dominant with RCA ending with one thin middle tract (AHA segment 2) and a ventricular branch (B). *Abbreviations: Ao=aortic root; CX=circumflex; LA; left atrium; LAD=left anterior descending; LV=left ventricle; RCA=right coronary artery; RV=right ventricle; RVOT=right ventricle outflow tract*

ces) into three main regions (Fig. 3): 1) the ascending aorta (ROI1); 2) the descending aorta (ROI2); and 3) the pulmonary artery (ROI3). All the ROIs were drawn as large as the anatomic configuration of the vessel allowed in the axial slice, carefully avoiding area of stenosis, soft plaque and calcification.

Data analysis

To rule out significant differences among the three sample populations, an ANOVA test was applied to the following parameters: age, weight, and mean heart rate (HR) during the scan.

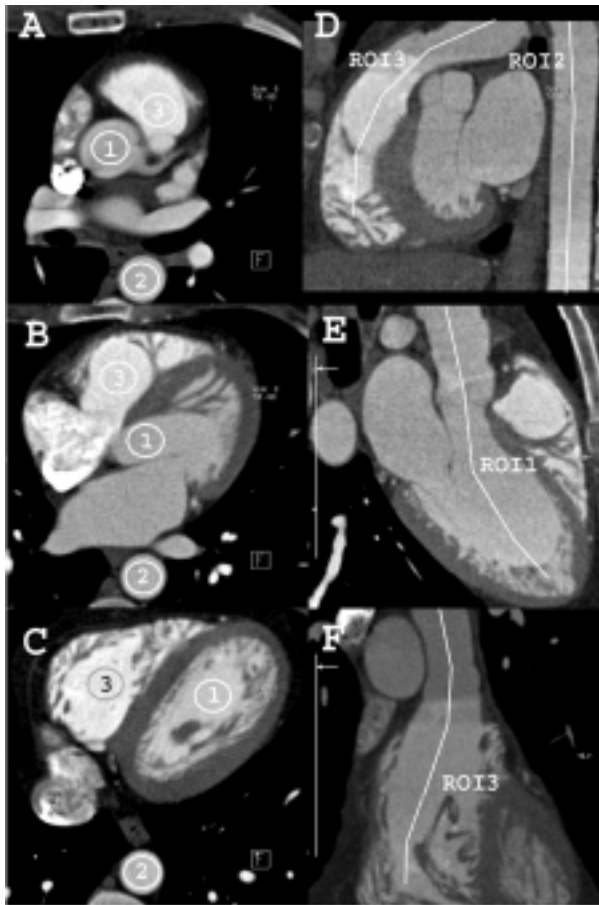


Figure 3. Settings of the regions of interest throughout the data-set.

In A, B, and C, three different axial slices at the origin level of the left anterior descending (A), the mitral valve (B), and the orifice of the inferior vena cava inside the right atrium (C). In D, a sagittal multiplanar (MPR) reformats is performed through the pulmonary artery and descending aorta. In E, a curved MPR is performed through the ascending aorta and the left ventricle. In F, a curved MPR is performed along the pulmonary artery and right ventricle. The three ROIs are positioned in the ascending aorta (ROI1=1) and in the left ventricle (A, B, C, and E), in the descending aorta (ROI2=2; A, B, C, and D), and in pulmonary artery and right ventricle (ROI3=3; A, B, C, D, and F)

The mean scan delays were calculated from the bolus tracking dynamic series using the following algorithm: 10 s (delay for the monitoring sequence) + 4 s (automatic patient instruction and table repositioning) + (number of monitoring slices x 1.25 s).

The attenuation value detected at the origin of LM, LAD, CX, and RCA, were averaged.

The beginning (e.g. first image/slice of the data-set) of the scan was considered as time 0 in each ROI. From this point, a time-density curve was generated in each ROI with intervals of one second. The values obtained at each time interval (e.g. *time 0, time 1, time 2,...*) in each patient and each ROI were used to plot a resulting "average time-density curve" for each ROI and each group.

Because of the individual anatomy and size, the duration and the longitudinal length (*z-axis*) of the scan were different in each patient (in our series between 14 s and 21 s, meaning between 94 mm and 141 mm). In the same way, the anatomical configuration and size of the main vessels were different in each patient. In order to acquire consistent results (i.e. use the information from all patients) only time intervals during which measurements were available in all patients were considered for evaluation. In other words, the longest duration of the scan (ROI2) or the largest longitudinal extension of the vessel measured (ROI1 and ROI3) in all patients were included in all groups (Fig. 4). For this reason the time ranges considered for evaluation have been limited to $t=0$ to $t=8s$, $t=0$ to $t=14s$, and $t=0$ to $t=8s$, for ROI1, ROI2, and ROI3, respectively. The mean value of attenuation (HU value) at time 0, the maximum enhancement value (MEV), and the time to reach the MEV were calculated (15, 16).

The results have been compared with an ANOVA test to detect significant differences among the three groups. When differences were detected, a Student's t test was applied between two different groups at a time.

Results

Patients groups were not significantly different regarding age, weight, heart rate, scan delay and scan time ($p>0.05$) (Table 2). Results are summarized in table 3 and 4.

Coronary artery

No significant differences ($P>0.05$) were observed in the attenuation at the origin of all four coronary vessels (Tab. 3 - Figs. 3 and 5A).

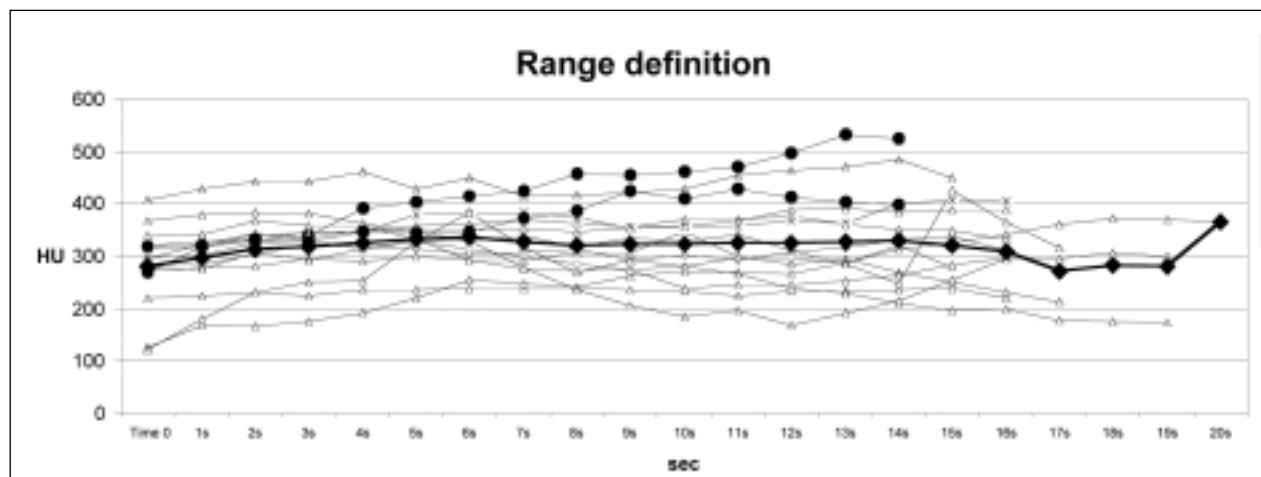


Figure 4. Definition of evaluation ranges for the average time-density curve.

The example shows the time-density curves of the descending aorta in group 1. Even though the resulting average time-density curve (thick black line - ♦) can be observed until *time 20s*, several scans are shorter and in particular two of them reaches *time 14s* (thin black lines - •). Therefore, to consider an average time-density curve that has all the time-density curve of each patient, the average time-density curve must be cut at *time 14s*

Table 2. Patients data.

	Overall	Group 1	Group 2	Group 3
Number of patients	45	15	15	15
Male/Female	39/6	11/4	14/1	14/1
Mean age (range) yrs	58 (28-79)	58 (34-74)	58 (28-73)	59 (45-79)
Mean weight (range) kg	72 (55-95)	71 (55-90)	72 (60-88)	73 (60-95)
Mean heart rate (range) bpm	57 (45-72)	58 (46-72)	56 (45-65)	56 (45-68)
Mean scan delay (SD) s	20.8±2.2	21.7±1.8	20.5±2.7	20.3±1.9
Mean scan time (SD) s	17.2±1.6	17.6±1.3	17.5±1.6	16.4±1.8

Abbreviations: yrs= years; kg= kilograms; bpm= beat per minute; s= seconds

Table 3. Coronary arteries attenuation.

	Group 1	Group 2	Group 3
LM (HU)	321±51	314±54	321±55
LAD (HU)	316±52	310±53	314±54
CX (HU)	309±52	299±49	307±53
RCA (HU)	298±50	290±46	304±55

The average density and standard deviation measured at the origin of the coronary arteries and their main branches are displayed. No significant differences have been detected in the attenuation at the origin of the main coronary vessels.

Abbreviations: LM=left main; LAD=left anterior descending; CX= circumflex; RCA=right coronary artery; HU=Hounsfield Units

Ascending aorta-left ventricle (Fig. 5B)

The attenuation values at t=0 were not significantly different among the three groups. The average

time-density curves of group 1, group 2 and group 3 were not significantly different ($p>0.05$). The MEV was higher ($p>0.05$) and earlier in group 2 ($348±61$ HU at +1s). In group 1 and 3 attenuation >300 HU was achieved throughout the scan while in group 2 only between time 0s and time 6s.

Descending aorta (Fig. 5C)

The attenuation values at t=0 and the average time-density curves were not significantly different among the three groups ($p>0.05$). The average time-density curve in group 2 showed a biphasic configuration. The MEV was higher ($p>0.05$) and earlier in group 2 ($341±63$ HU at +3 s). In group 1 and 3 attenuation >300 HU was achieved after time 1 s and time 2 s, respectively.

Table 4. Resume of bolus geometry in the great vessels of the thorax

	Ascending Aorta			Descending Aorta			Pulmonary Artery		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
Average (HU)	314±46	317±46	324±55	316.5±48.2	311±47.5	320.9±61.2	336±84	314±49	320±67
Slope	-2.3	-7.4*	2	1.4	-3.6*	2.0	6.5	7.3	-10.3*
Time 0 (HU)	311±40	338±57	311±70	289±33	319±51	282±78	313±69	305±53	350±105
MEV (HU)	339±44	361±57	363±60	349±56	353±59	377±70	405±77	364±59	403±83
tMEV (sec)	3.2±1.3	2.3±1.8	5.7±3.5*	9.6±4	5.8±5.1*	9.9±4.4	4.2±2.8	5.1±3.2	3.1±2.9

The quantitative parameters of the bolus geometry of the main vessels of the thorax are displayed. The values significantly different from the others are highlighted by *

Abbreviations: MEV= Maximum enhancement Value; tMEV= time to reach the MEV; HU= Hounsfield Units

Pulmonary artery-right ventricle (Figure 5D)

The attenuation values at t=0 were not significantly different among the three groups ($p>0.05$). The average time-density curves of group 1 and group 2 were significantly different ($p<0.05$). In group 1 and group 2 the average time-density curves showed a tendency to increase during the scan, while group 3 showed the opposite behaviour.

Discussion

Three protocols for the intravenous administration of contrast material were compared: the first two protocols, similar to those previously described in 4-MSCT and 16-MSCT coronary angiography (group 1 and group 2), were compared to a low volume protocol, similar to a protocol described in 16-MSCT coronary angiography (group 3), allowed by reduced scan time and bolus tracking synchronization technique provided by 16-MSCT scanners (1, 2, 13, 14, 17). The study was aimed at identifying the minimal volume of contrast material that provides the highest intra-vascular attenuation, assuming that a higher intra-vascular attenuation provides a better visualization of the coronary lumen with MSCT.

The attenuation resulting from the different contrast material administration protocols was measured at the origin of the coronary vessels (LM, LAD, CX, and RCA), while the geometry of the contrast material bolus has been evaluated by means of three ROIs positioned inside the three main vessels of the thorax.

The results showed no significant differences among the three protocols in terms of attenuation at the origin of the coronary arteries. The average attenuation resulted not significantly different in all three groups in all three main thoracic vessels, while the slope resulted significantly lower in ascending aorta and descending aorta in group 2 (-7.4 and -3.6, respectively) compared to group 1 and 3. This means that in group 2 the pattern of enhancement was decreasing during the scan, while in group 1 and 3 it was approximately a plateau. The slope in pulmonary artery was instead significantly lower (-10.3) in group 3 compared to the other two groups. This means that the pattern of attenuation in pulmonary artery for group 3 was a steep decrease in enhancement.

The attenuation at *time 0* and the MEV were not significantly different in all three thoracic vessels for all groups. Instead, the tMEV was significantly longer in group 3 in ascending aorta (5.7 s), and significantly shorter in group 2 in ROI2 (5.8 s). This observation can be hardly addressed.

The performance of the three protocols resulted comparable and the small differences did not significantly affected the attenuation at the level of the coronary arteries. The biphasic protocol (group 2) did not show significant advantages over the others. In particular there was no evidence of a more sustained and homogeneous plateau of attenuation, as expected from previous literature (18-20).

Therefore, despite a lower volume of contrast material (group 3) similar results are achieved as compared to protocols with 40% more contrast material (13). Moreover, if the comparison is performed with previously cited protocols using test bolus and 4-

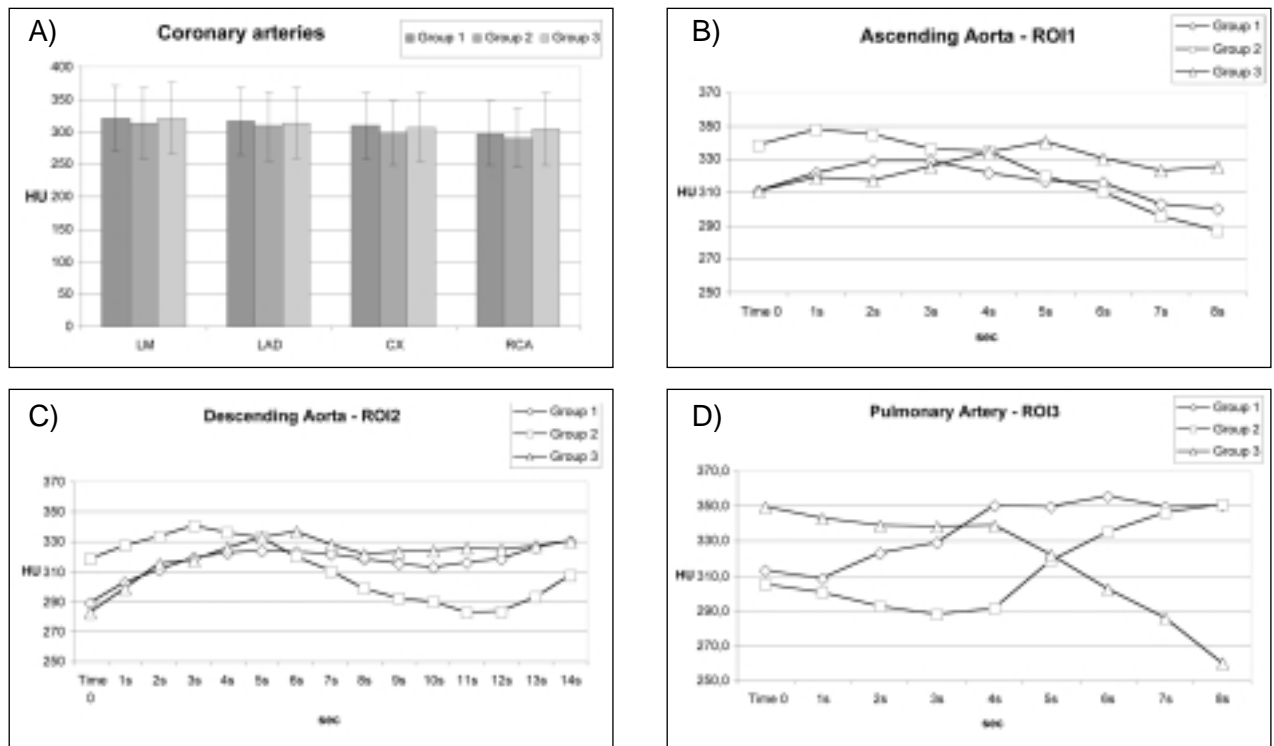


Figure 5. Coronary artery attenuation and average time-density curves. The attenuation at the origin of the 4 main coronary vessels shows no significant differences among the three different protocols (A). In the ascending aorta (B), the average time-density curves show a similar attenuation value and a similar pattern of enhancement. In the descending aorta (C), the average time-density curves are again not significantly different but the pattern of group 2 is more biphasic with a peak in the first half and a slight decrease in the second half. In the pulmonary artery (D), the slope of group 3 is significantly different than the ones of group 1 and 2 ($p < 0.05$). This due to the reduced contrast material pooling in the right section of the heart, a significant difference between the curve of group 1 and group 2 is shown. *Abbreviations: LM=left main; LAD=left anterior descending; CX=circumflex; RCA=right coronary artery.*

MSCT, the volume reduction could be as much as 60% (1, 2, 21).

The importance of bolus timing in CT angiography (CTA) has been extensively studied for single detector CT and even more for MSCT (4, 22). To obtain an optimal synchronization between contrast material administration and data acquisition different approaches are possible: fixed delay, test bolus technique and bolus tracking technique (4). In our protocols we applied bolus tracking because it represents the standard in our institution

A limitation of the study concerns the evaluation of attenuation that was not performed on the number and length of coronary artery visualization. This is because the coronary arteries size, the heart rate, and va-

rious degree of vessels diseases (soft and calcified lesions, stenosis, and occlusions) severely affects the visualization capability regardless the protocol performance for contrast material administration. Moreover, the patient population is too small to account for these variables.

Another limitation is related to the sub-optimal methodology used for the measurement of bolus geometry in the great vessels of the thorax. Measurements should be performed in the same position during contrast material administration (4). Even though this can be a limitation, the same inaccuracy occurs in each patient in each ROI. Therefore each position in time corresponds to the same distance from the cranial starting position.

Conclusion

A volume of one-hundred ml of contrast material administered at 4 ml/s provided the same results in terms of vascular attenuation, as previously reported protocols with higher volumes. Sixteen-row MSCT coronary angiography paired with an optimized contrast material protocol, allow to use 40–60% less contrast material with a resulting reduced nephrotoxicity for the patient and increased cost-effectiveness. The implementation of a bolus chaser might further improve the opacification obtained with a reduced CM volume (23).

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