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Variability of Repeated Coronary Artery Calcium Scoring and Radiation
Dose on 64-slice and 16-slice CT by Prospective
Electrocardiograph-triggered Axial and Retrospective
Electrocardiograph-gated Spiral CT - A Phantom Study

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Short running head:

Variability of CACS on 64- and 16-slice CT

Title

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Abstract

Rationale and Objectives: To compare coronary artery calcium scores, the variability and radiation doses on 64-slice and 16-slice CT scanners by both prospective electrocardiograph (ECG)-triggered and retrospective ECG-gated scans.

Materials and Methods: Coronary artery models (n=3) with different plaque CT densities (~240 HU, ~600 HU and ~1000 HU) of four sizes (1 mm, 3 mm, 5 mm and 10 mm in length) on a cardiac phantom were scanned three times in 5 heart rate sequences. The tube current-time-products were set to almost the same on all four protocols (32.7 mAs for 64-slice prospective and retrospective scans, 33.3 mAs for 16-slice prospective and retrospective scans). Slice-thickness was set to 2.5 mm in order to keep the radiation dose low. Overlapping reconstruction with 1.25 mm increment was applied on the retrospective ECG-gated scan.

Results: The coronary artery calcium scores were not different between the four protocols (one-factor ANOVA, Agatston; $p=0.32$, volume; $p=0.19$ and mass; $p=0.09$). Two-factor factorial ANOVA test revealed that the interscan variability was different between protocols ($p<0.01$) and scoring algorithms ($p<0.01$). The average variability of Agatston/volume/mass scoring and effective doses were 64-slice prospective scan: 16%/15%/11% and 0.5 mSv, 64-slice retrospective scan: 11%/11%/8% and 3.7 mSv, 16-slice prospective scan: 20%/18%/13% and 0.6 mSv & 16-slice retrospective scan: 16%/15%/11% and 2.9 to 3.5 mSv (depending on the pitch).

Conclusions: Retrospective ECG-gated 64-slice CT showed the lowest variability. Prospective ECG-triggered 64-slice CT, with low radiation dose, shows low variability

on coronary artery calcium scoring comparable to retrospective ECG-gated 16-slice CT.

Key Words

CT, coronary artery, calcium, radiation dose

Introduction

Coronary artery calcium (CAC) scoring is performed to evaluate the presence of coronary atherosclerosis or to assess the progression and regression of coronary atherosclerosis [1]. Therefore, low variability and low radiation exposure are both key requirements on CAC scoring. Interscan variability of Agatston score [2] on electron beam CT however, yielding 20% to 37% [3-6] is high, considering that normal progression of CAC score per year is 14-27% (average 24%) [7] and is accelerated up to 33-48% with significant coronary disease [8,9]. To reduce the variability, the volumetric approach [3] and the calcium mass [4] were devised as alternative CAC scoring algorithms. Also, on multidetector CT (MDCT), CAC scoring using the conventional Agatston method on non-overlapping reconstruction, yields high interscan variability; 23% to 43% [10-12] on 4-slice spiral CT and 22% [13] on 16-slice CT. Through retrospective ECG-gated overlapping scan, a considerable reduction of interscan variability of Agatston scores can be achieved; 23% to 12% [10] and 22% to 13% [13], however with the expense of increased radiation exposure compared with ECG-triggered scan. Thin-slice images (1.25 mm or 1.5 mm) are shown to also reduce variability of CAC in both electron beam CT [14,15] and 64-slice CT [16]. It does however, require increased radiation dose to maintain required image quality. In these circumstances, CAC scoring is preferably performed with a standard image thickness (2.5 mm or 3 mm), offering the best balance of low scoring variability and low radiation dose. The purpose of this study is, using a pulsating cardiac phantom, to assess the variability of CAC scoring on 64- and 16-slice CT scanners by both prospective

ECG-triggered and retrospective ECG-gated scans.

Materials and Methods

Cardiac Phantom

A prototype cardiac phantom is commercially available (ALPHA 2, Fuyo corp. Tokyo, Japan). The phantom consists of five components: driver, control, support, rubber balloon and ECG. A controller with an ECG-synchronizer drives the balloon. The main characteristics of this phantom are programmable variable heart rate sequences and mimicking of natural heart movements. The detail of the phantom is described elsewhere [17,18].

In this study, 5 types of heart rate sequences were programmed (Fig. 1). Two were stable heart rate sequences, two were 'shift' sequences and the remaining one was arrhythmia. The 'shift' sequence was defined as heart rate with small variation, i.e. the sequence '55 bpm shift' repeat a cycle of 55 bpm, 60 bpm, 55 bpm and 50 bpm. The volumes of the balloon phantom at the systolic and diastolic phases were approximately 100ml and 200 ml, respectively. The main motion of the coronary artery models was in in-plane direction. Deformity of the balloon however, resulted in some through-plane motion.

Coronary Artery Calcium Models

Three coronary artery models (plastic cylinders with a diameter of 4 mm) and different calcified plaque CT densities (silicone: ~240 HU, putty: ~600 HU, Teflon: ~1000 HU) were manufactured for this experiment (Fuyo corp. Tokyo, Japan). Each coronary artery model had four sizes of plaques; 1 mm, 3 mm, 5 mm and 10 mm in length. These plaques resulted in an 82% area of stenosis. The coronary artery models were attached to the balloon phantom (mimicking the heart) with the long axis of the model corresponding to the z-axis and were surrounded by oil (-112 HU), simulating epicardial fat (Fig. 2).

Prospective ECG-triggered Axial 64-slice CT Protocol

Three repeated scans with a table advancement of 1mm during the scans were performed using a 64-slice MDCT scanner (LightSpeed VCT; GE Healthcare, Waukesha, WI, USA). Prospective ECG-triggered axial scan was performed using 2.5 mm collimation width x 16 detectors so that the center of the temporal window corresponded to 80% of the R-R interval (diastole of the phantom). The scanning parameters were a gantry rotation speed of 0.35 sec/rotation, 120 kV and 140 mA. The matrix size was 512 x 512 pixels and the display field of view was 26 cm. The reconstruction kernel for soft tissue, which is routinely used in abdominal imaging, was used. The temporal resolution was 175 msec.

Retrospective ECG-gated Spiral 64-slice CT Protocol

Retrospective ECG-gated spiral scan was performed with 1.25 mm collimation width x 32 detectors. The tube current was controlled using the ECG modulation technique. The maximal current was set to 140 mA during the cardiac phase 70-90%, and was reduced in the other phase to a minimum of 30 mA. CT pitch factor was set to 0.20 by the heart rate, according to the manufacturer's recommendations for coronary CT angiography protocol. Images of 2.5 mm thickness were retrospectively reconstructed with 1.25 mm spacing to reduce partial volume averaging. Multisector reconstruction was used on the heart rate sequences of 85 beats per minute (bpm) and 85 bpm shift. The temporal resolution was 134 msec on 85 bpm and varied on 85 bpm shift, depending on the combination of adjacent heart rates used for image reconstruction. Other scanning parameters were the same as prospective ECG-triggered 64-slice CT protocol.

Prospective ECG-triggered Axial 16-slice CT Protocol

A 16-slice MDCT scanner (LightSpeed Ultrafast 16, GE Healthcare, Waukesha, WI, USA) was used. Scan was performed using with 2.5 mm collimation width x 8 detectors. Gantry rotation speed was 0.5 sec/rotation. The tube current of 100 mA, which is a standard level on CAC scoring using 0.5 sec/rotation scanners [19], was used. The temporal resolution was 250 msec. Other scanning parameters were the same as the prospective ECG-triggered 64-slice CT protocol.

Retrospective ECG-Gated Spiral 16-slice CT Protocol

The scan was performed with 1.25 mm collimation width x 16 detectors. The ECG modulation technique was not available and the current was set to 100 mA. CT pitch factors varied from 0.275 to 0.325 by the heart rate, according to the manufacturer's recommendations for coronary CT angiography protocol. Images of 2.5 mm thickness with 1.25 mm spacing were reconstructed. Multisector reconstruction was used on the heart rate sequences of 85 bpm and 85 bpm shift. The temporal resolution was 158 msec on 85 bpm and varied on 85 bpm shift, depending on the combination of adjacent heart rates used for image reconstruction. Other scanning parameters were the same as the prospective ECG-triggered 16-slice CT protocol.

Calcium Scoring

The Agatston [2], calcium volume and mass [4], summing over all slices corresponding to each CAC model, were determined on a commercially available external workstation (Advantage Windows Version 4.2, GE Healthcare, Waukesha, WI, USA), CAC-scoring software (Smartscore Version 3.5) and a calibrating anthropomorphic phantom (Anthropomorphic Cardio Phantom, Institute of Medical Physics, and QRM GmbH) according to the following equations:

1. Agatston score= slice increment / slice thickness x   (area x cofactor)

2. Volume=   (area x slice increment)

3. Mass=   (area x slice increment x mean CT density) x calibration factor [19]

The calcium phantom was scanned on the 4 protocols to enable calibration for

determining calcium mass. All CT scans were scored by one radiologist with 8 year's experience of CAC measurement. Interobserver variability was not investigated as CAC scoring in this phantom study was very simple.

Coronary Artery Calcium Score

Each of the Agatston, volume and mass scores, in logarithmic scale in order to reduce skewness, were compared between the protocols using one-factor ANOVA test. Sixty scans (4 protocols, 5 heart rate sequences, 3 repeated scans) were performed on 12 CAC materials.

Interscan Variability of Repeated Coronary Artery Calcium Scoring

The percentage variability was determined by calculating the mean numeric difference between each of the three score values and dividing this by the mean score as follows:

$$1/3 \times [abs\ (S1 - S2) + abs\ (S2 - S3) + abs\ (S3 - S1)] / [1/3 \times (S1 + S2 + S3)]$$

where abs is absolute value, S1 is CAC score on the first scan, and S2 and S3 are the CAC scores on the second and third scans, respectively. From the sixty scans (4 protocols, 5 heart rate sequences and 3 scans), 720 sets of variability (12 CAC materials, 3 scoring algorithms) data were obtained. The interscan variability was compared between the protocols and scoring algorithms using two-factor factorial ANOVA.

Interprotocol Variability of Coronary Artery Calcium Scoring

The percentage variability was determined by calculating the mean numeric difference between each of the four score values and dividing this by the mean score as follows:

1/6 x [abs (S1 – S2) + abs (S1 – S3) + abs (S1 – S4) + abs (S2 – S3) + abs (S2 – S4) + abs (S3 – S4)] / [1/4 x (S1 + S2 + S3+ S4)]

where abs is absolute value, S1, S2, S3 and S4 is CAC score on the 64-slice prospective, 64-slice retrospective, 16-slice prospective and 16-slice retrospective, respectively. From the sixty scans, 540 sets of variability (12 CAC materials, 3 scoring algorithms) data were obtained. The interprotocol variability was compared between the repeated scans and scoring algorithms using two-factor factorial ANOVA.

Image Noise

Image noise, defined as standard deviation of CT value of the cardiac phantom was measured 15 times (5 heart rate sequences, 3 repeated scans). These values were compared between the 4 protocols using one-factor ANOVA test.

Statistical Analyses

All statistical analyses were performed using a commercially available software package (Statcel2, oms-publishing, Saitama, Japan). For statistical analyses, one-factor and two-factor factorial ANOVA (multivariate calculations) tests were used to determine

differences. When statistical significance was observed by two-factor factorial ANOVA, the results were made post hoc by Scheffé test for multiple pairwise comparisons. P-values < 0.05 were considered to identify significant differences.

Radiation Dose

Volume computed tomography dose index (CTDIvol) displayed on Dose Report on the CT scanner was recorded on each protocol. As dose-length product (DLP) on the phantom is not suited for simulating DLP on patients' scan, DLP is defined with the assumption that the heart ranges 12 cm in the z-axis.

DLP (mGy x cm) = CTDIvol (Gy) x 12 cm

A reasonable approximation of the effective dose (E) can be obtained using the equation [20].

E=k x DLP

where E is Effective dose estimate and k = 0.017 mSv x mGy^{-1}x cm^{-1}. This value is applicable to chest scans and is the average between the male and female models.

Results

Coronary Artery Calcium Scores

The Agatston, volume and mass scores on the protocols are summarized in Table 1. All calcium scores were positive. The minimal score was 1, 3 and 0.4 on Agatston,

12

volume and mass scores, respectively. One-factor ANOVA revealed that there was no statistical significance of log transformed CAC scores between protocols (Agatston; p=0.52, volume; p=0.26 and mass; p=0.25).

Interscan Variability of Repeated Coronary Artery Calcium Scoring

The interscan variability in Agatston, volume and mass scores on the protocols are shown in Figure 3. Two-factor factorial ANOVA test revealed that there were significant differences between protocols (p<0.01) and scoring algorithms (p<0.01). The Scheffé test revealed that the interscan variability on 64-slice retrospective protocol was lower than that on 64-slice prospective (p<0.01), 16-slice retrospective (p<0.01) or 16-slice prospective (p<0.01) protocols. The interscan variability in mass score was lower than that in Agatston (p<0.01) or volume (p<0.01).

Interprotocol Variability of Coronary Artery Calcium Scoring

The interprotocol variability of CAC Score on Agatston, volume and mass scoring algorithms is shown in Figure 4. Two-factor factorial ANOVA test revealed that there were not significant differences between scans (p=0.13), however there were between scoring algorithms (p<0.05). The Scheffé test revealed that the interprotocol variability in mass score was lower than that in Agatston (p<0.05) or volume (p<0.05).

Image Noise

One-factor ANOVA revealed that image noise was different between the protocols ($p < 0.01$). The standard deviation of CT value on 64-slice prospective, 64-slice retrospective, 16-slice prospective and 16-slice retrospective scans was 17.4±0.5 HU, 16.9±0.7 HU, 20.2±0.7 HU and 22.8±0.8 HU, respectively.

Radiation Dose

CTDIvol displayed on Dose Report on the CT scanner and the effective doses, estimated for a typical patient were 64-slice prospective: 2.3 mGy/ 0.5 mSv, 64-slice retrospective: 18.3 mGy/ 3.7 mSv, 16-slice prospective: 3.1 mGy/ 0.6 mSv and 16-slice retrospective: 14.4 to 17.0 mGy/ 2.9 to 3.5 mSv (depending on the pitch).

Discussion

The present study is the first to compare variability of repeated CAC scoring and radiation doses on 64-slice and 16-slice CT scanners by both prospective ECG-triggered and retrospective ECG-gated scans. The results show that retrospective ECG-gated 64-slice CT shows the lowest variability and that prospective ECG-triggered 64-slice CT, with low radiation dose, shows low variability on repeated measurement comparable to retrospective ECG-gated 16-slice CT.

The partial volume averaging is known to be a major contributor influencing

interscan variability on CAC. The use of thin-slice images [14-16] or overlapping image reconstruction [10,13,22] has been suggested to reduce partial volume averaging. Some studies however, show that thin-slice images lead to significantly increased CAC scores, due to increased noise and improved detection of subtle CAC [23,24]. This indicates that thin-slice images need increased radiation dose in order to maintain desirable image quality. We, therefore, decided on a slice thickness of 2.5 mm in all CT protocols. Since the purpose of CAC scoring is screening of coronary atherosclerosis or tracing its progression and regression, radiation exposure needs to be kept "as low as reasonably achievable (ALARA)". In this respect, the effective doses of prospective ECG-triggered CT in the current study (64-slice CT; 0.5 mSv, 16-slice CT; 0.6 mSv), which are comparable to that of electron beam CT (0.7 mSv) [21], have a definite advantage over retrospective ECG-gated scan.

CAC scores in three scoring algorithms were not significantly different. The finding suggests that, in the CT scanner we used, CAC score does not depend on either prospective/ retrospective protocol or 64-slice / 16-slice CT. Concerning interscan variability of repeated CAC score, 64-slice retrospective scan showed the least interscan variability, implicating that this can most reliably assess the progression and regression of coronary atherosclerosis. The interscan variability on 64-slice prospective scan also seems to be promising, as being almost the same level of the 16-slice retrospective scan. We believe that this finding is related to substantial reduction of motion artifacts, which is also one of the most important factors in increasing interscan variability on CAC. This is achieved by improved temporal resolution of 64-slice CT (175msec for

prospective ECG-triggered scan) with acceleration of gantry rotation speed. Apart from improved temporal resolution, we must also address reducing scan time, achieved by wide detector coverage. Two breath-holds, increasing variability of CAC scoring [6], are no longer necessary in most patients. Changes of heart rate and body posture are also reduced. These two factors, increasing variability, are not simulated in the current phantom study. Thus, as mentioned above, irrespective of prospective or retrospective, 64-slice CT is considered to have advantages over 16-slice CT.

Among CAC scoring algorithms, the mass showed the least variability in all CT protocols and the effect of decreasing the variability was prominent on prospective ECG-triggered scans both on 64-slice and 16-slice CT. As regards interprotocol variability of CAC score, the mass showed the least variability, which best optimizes the monitoring of CAC over different CT scanners and scan protocols due to its intrinsic calibration function ability [25]. The facts support the very important value of mass among CAC scoring algorithms.

High image quality on 64-slice CT suggested from the current study also enhances its value. It reduces the chances of hyperdense noise being erroneously judged as calcium [26]. The noise level on 16-slice CT in the study (20HU, 23HU) is concordant with that suggested in standardization of CAC; i.e. a noise level target of 20 HU for small and medium-size patients and a noise level target of 23 HU for large patients [25]. The noise level on 64-slice CT in the study (17HU) is below the recommendation (20-23 HU). These findings indicate further reduction of radiation dose in CAC imaging is possible,

while still maintaining image quality.

The study has some limitations. We used smooth calcium models with homogeneous CT values, different from the actual calcium plaques; i.e. irregular and inhomogeneous. The heart rate sequences set were also different from those in patients. The cardiac phantom only had some through-plane motion, thus limited the simulation of true motion of the coronary arteries. We however, do not consider these issues important, because our purpose is not to predict variability values of the four protocols, but to compare them and thereby suggest an optimal protocol. The level of variability in real patients should be further studied. The other limitation is that we did not reproduce the optimal cardiac cycle for 0.35-sec rotation speed 64-slice CT. This should be verified in clinical studies by comparing between multiple cardiac phase reconstruction images.

In conclusion, retrospective ECG-gated 64-slice CT has the least interscan variability in repeated CAC scoring, showing to have the best advantage of tracking CAC amount over time. Prospective ECG-triggered 64-slice CT, with radiation dose equivalent to that of electron beam CT, shows low variability in repeated CAC scoring comparable to retrospective ECG-gated 16-slice CT. CAC scoring with prospective ECG-triggered 64-slice CT, especially when combined with mass algorithm, provides a balance between radiation and variability and would seem optimal for clinical purposes.

Acknowledgements

Abbreviations

CT: computed tomography

CAC: coronary artery calcium

ECG: electrocardiograph

HU: Hounsfield unit

DLP: dose-length product

CTDIvol: volume computed tomography dose index

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Figure legends
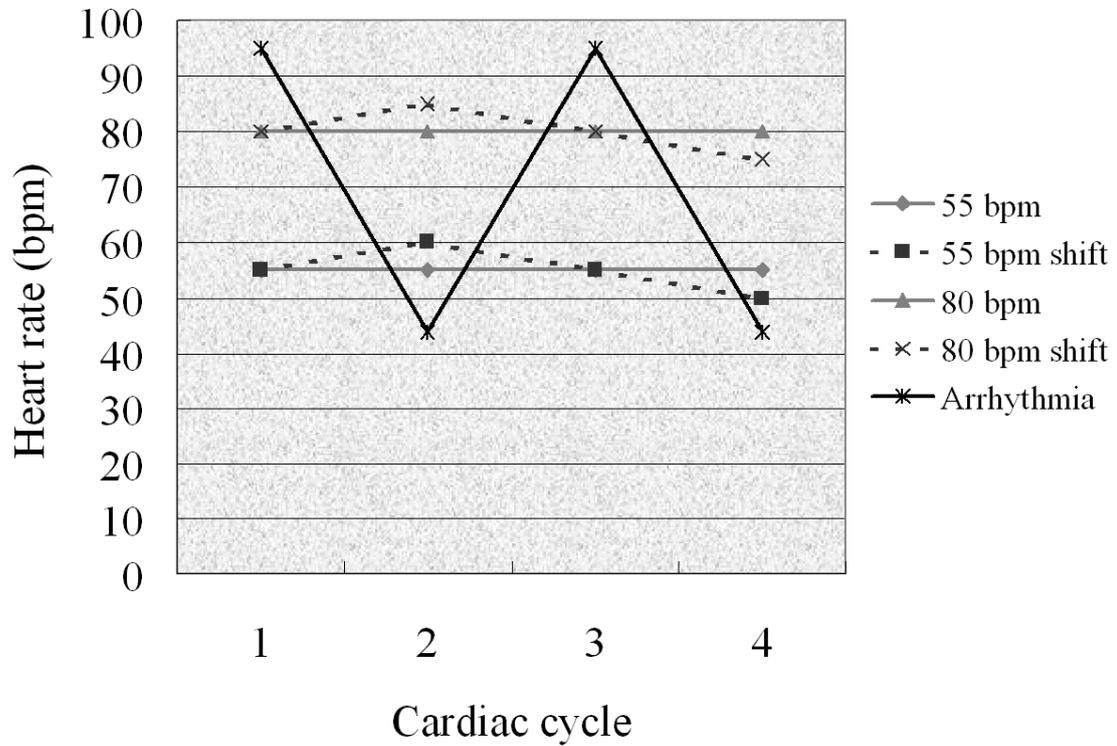
Fig. 1   Heart Rate Sequences

Graph shows 5 types of heart rate sequences programmed to the ECG generator. Heart rates in the sequence '55 bpm shift' repeat a cycle of 55 bpm, 60 bpm, 55 bpm and 50 bpm.
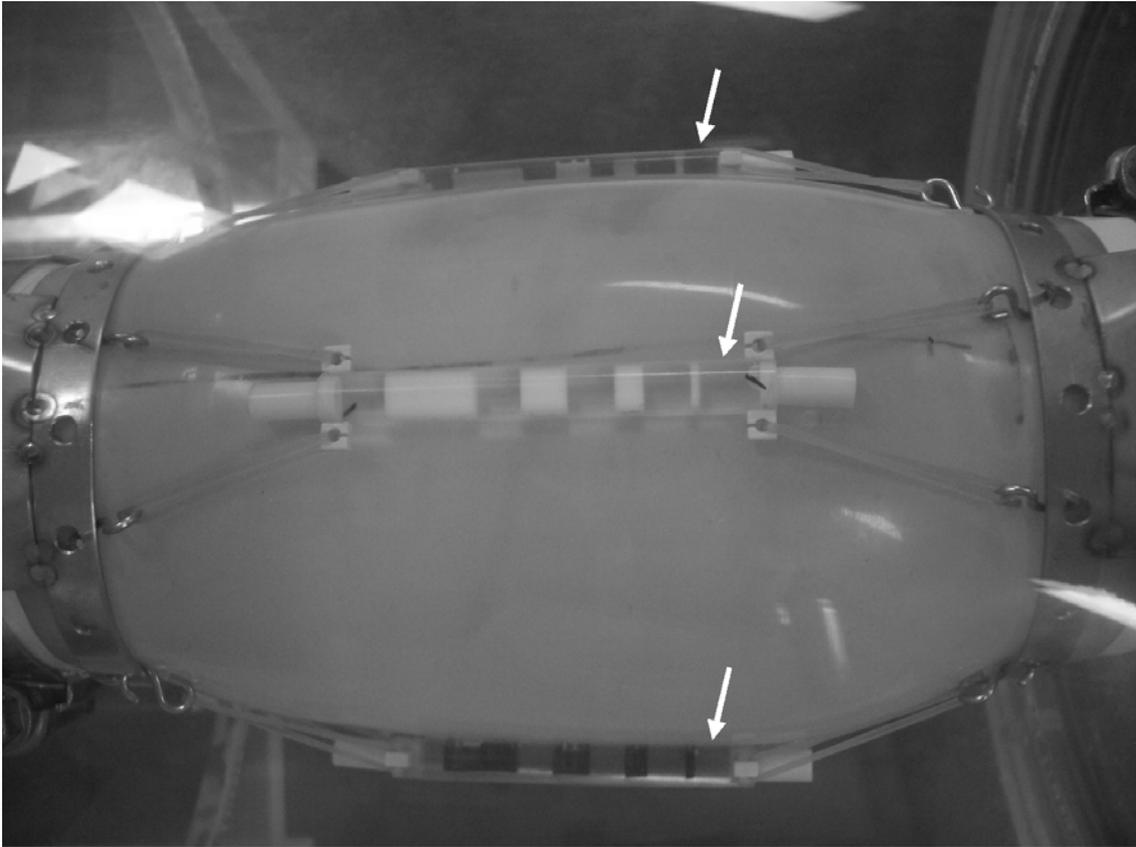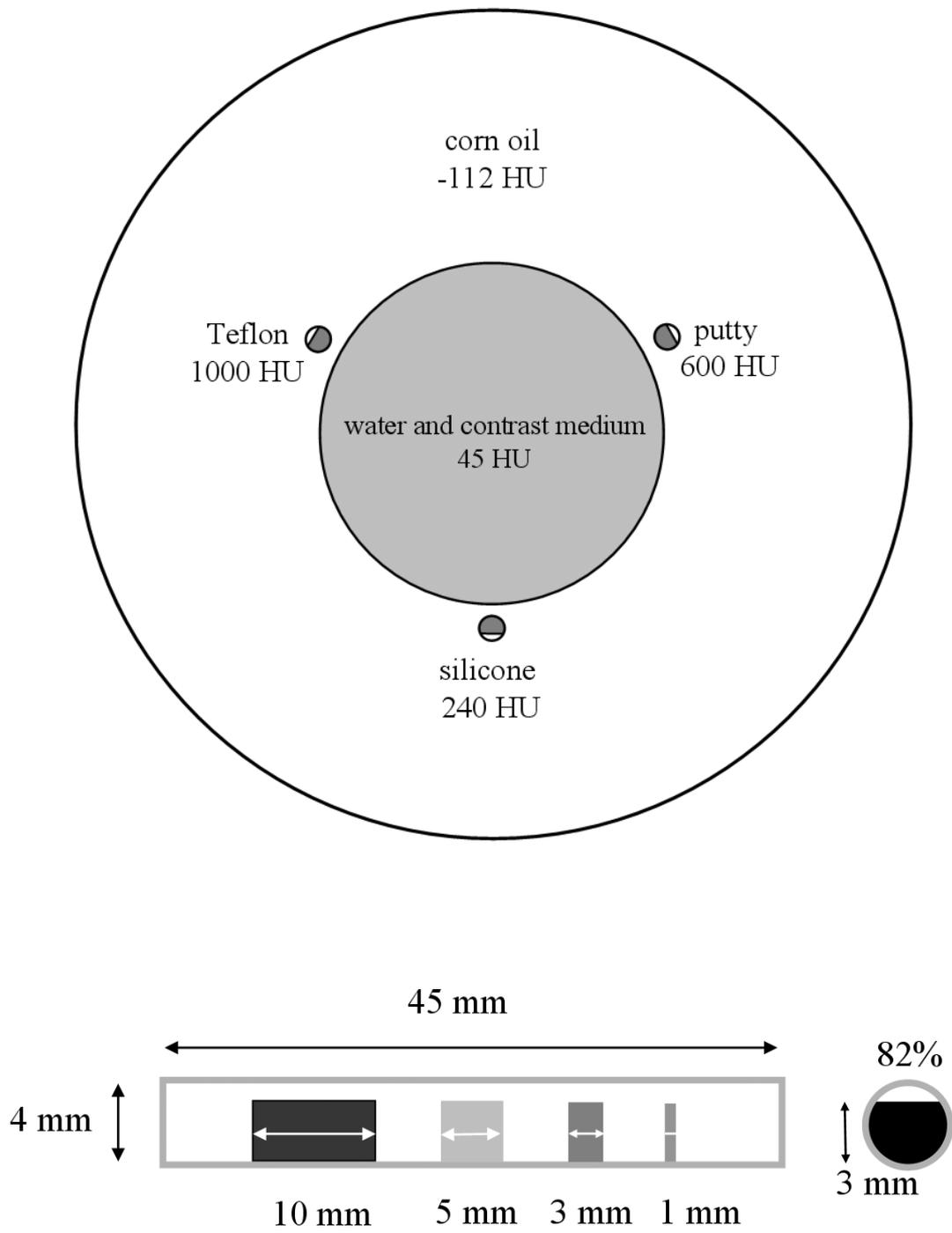
Fig. 2   Cardiac Balloon Phantom

Picture shows a pulsating phantom with three coronary artery models, indicated with arrows. (Figure 2A). The coronary artery models with different CT densities were attached to a balloon filled with a mixture of water and contrast medium (45 HU) to simulate noncontrast blood. The balloon was submerged in corn oil (-112 HU), simulating epicardial and pericardial fat (Figure 2B). The drawing shows four coronary artery calcium models (1 mm, 3 mm, 5 mm and 10 mm in length) resulting in 75% area stenosis were inserted into a coronary artery model with a diameter of 4 mm (Figure 2C).
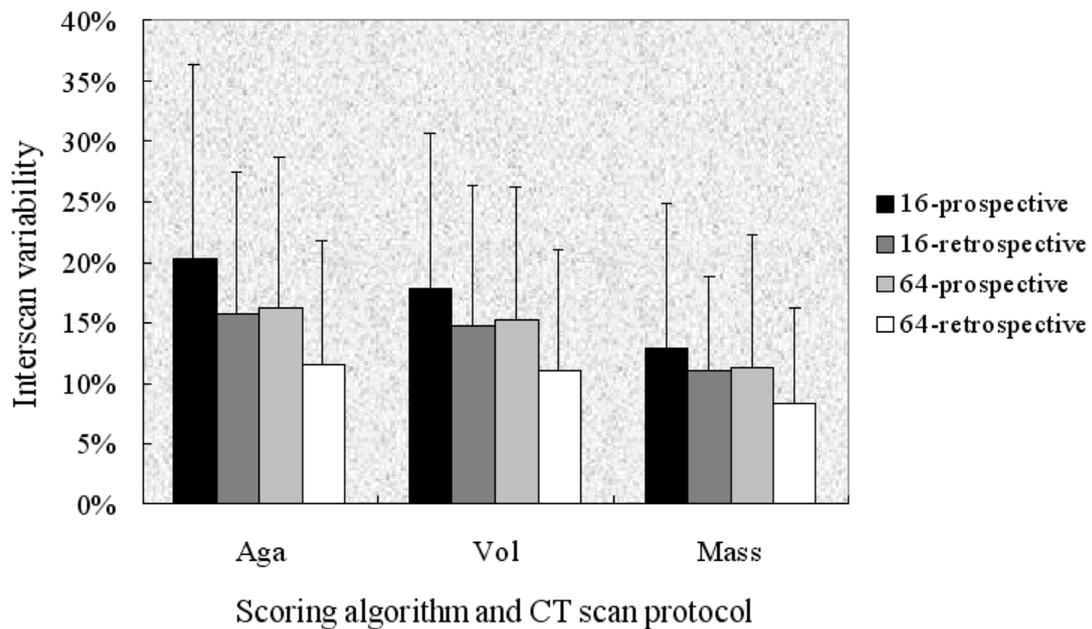
Fig. 3   Interscan Variability of Repeated Coronary Artery Calcium Score

Graph shows the interscan variability in Agatston, volume and mass scoring algorithms on 4 protocols (16-slice prospective; black, 16-slice retrospective; dark gray,

64-slice prospective; light gray and 64-slice retrospective; white). Bars and vertical

lines indicate mean and standard deviation, respectively.
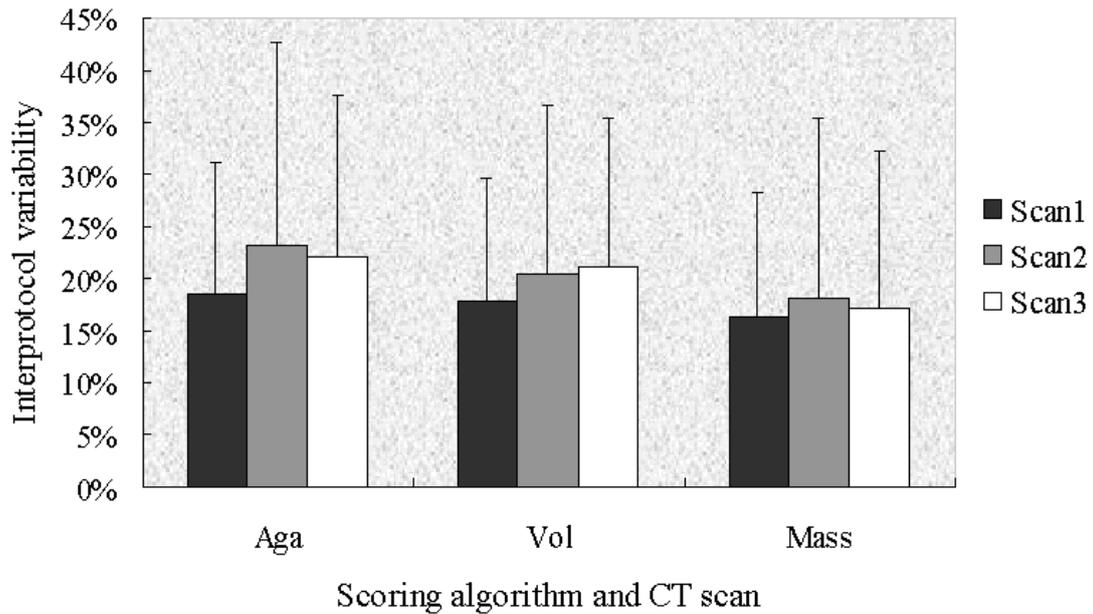
Fig. 4   Interprotocol Variability of Coronary Artery Calcium Score

Graph shows the interprotocol variability of CAC Score on Agatston, volume and

mass scoring algorithms. Bars and vertical lines indicate mean and standard deviation,

respectively.

Tables

Table 1: Agatston, volume and mass scores on 64-slice prospective, 64-slice

retrospective, 16-slice prospective and 16-slice retrospective scans

	64-prospective	64-retrospective	16-prospective	16-retrospective
1 mm				
Agatston	27 (37), 1-55	26 (34), 3-47	29 (37), 3-61	25 (31), 1-55
volume	32 (37), 4-65	35 (45), 9-54	35 (39), 8-61	36 (45), 4-65
mass	5 (6), 0-8	5 (7), 1-9	6 (7), 1-10	5 (7), 0-10
3 mm				
Agatston	79 (89), 25-121	80 (97), 22-169	92 (106), 24-187	84 (101), 19-191
volume	75 (84), 34-106	76 (84), 37-146	87 (93), 35-172	81 (90), 31-170
mass	15 (18), 5-23	16 (20), 5-24	19 (23), 5-33	16 (18), 4-26
5 mm				
Agatston	109 (123), 52-161	125 (140), 56-253	143 (159), 49-275	135 (150), 42-273
volume	97 (96), 62-129	112 (115), 73-216	125 (129), 70-234	125 (129), 66-212
mass	22 (24), 9-35	26 (30), 11-49	29 (35), 12-53	27 (32), 9-45
10 mm				
Agatston	242 (263), 120-413	233 (264), 129-395	269 (304), 107-524	260 (295), 93-441
volume	204 (212), 139-309	199 (210), 141-288	229 (234), 145-422	223 (231), 139-342
mass	52 (60), 21-76	53 (61), 24-77	59 (68), 24-90	55 (62), 21-85
Overall				
Agatston	114 (108), 1-413	116 (102), 3-395	133 (117), 3-524	126 (108), 1-411
volume	102 (87), 1-441	105 (87), 9-288	119 (101), 8-422	116 (96), 4-342
mass	24 (21), 0-76	25 (22), 1-77	28 (24), 1-90	26 (22), 0-85

64-prospective: prospective ECG-triggering scan on 64-slice CT
1 mm: 1 mm-sized coronary artery calcium models (silicone, putty and Teflon)
data are expressed as mean (median), range