Coronary Artery Calcium:

0.5 mm Slice-Thickness Reconstruction with Adjusted Attenuation Threshold Outperforms 3.0 mm by Validating Against Spatially Registered Intravascular Ultrasound with Radiofrequency Backscatter

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Rationale and Objectives: Coronary artery calcium (CAC) images can be reconstructed with thinner slice thickness on some modern multidetector-row computed tomography scanners without additional radiation. We hypothesized that the isotropic 0.5-mm CAC reconstruction outperforms the conventional 3.0-mm reconstruction in detecting and quantifying coronary calcium, and we proposed to compare them by validating against spatially registered intravascular ultrasound with radiofrequency backscatter-virtual histology (IVUS-VH).

Materials and Methods: Twenty-seven patients were enrolled, and 5976 mm of coronary arteries were analyzed. A semiautomatic software was developed to coregister CAC and IVUS-VH on a detailed slice-by-slice basis. Calcium detection and calcium volume quantification were evaluated and compared using varying calcium attenuation thresholds. Algorithms for deriving individualized optimal threshold and comparable Agatston score on the 0.5-mm reconstruction were developed.

Results: The isotropic 0.5-mm reconstruction achieved significantly higher area under receiver-operating curve than the conventional 3.0-mm reconstruction (0.9 vs. 0.74, $P < .001$). Using the optimal threshold, the 0.5-mm reconstruction had higher sensitivity (0.79 vs. 0.65), specificity (0.85 vs. 0.77), positive predictive value (0.42 vs. 0.29), and negative predictive value (0.97 vs. 0.94) than the 3.0 mm. Individualized optimal threshold was significantly correlated with the image noise ($r = 0.66$, $P < .001$) in the 0.5-mm reconstruction.

Conclusions: By optimizing the calcium threshold, the 0.5-mm reconstruction is superior to the conventional 3.0-mm in detecting and quantifying calcium, which may improve the clinical value of CAC without additional radiation.

Key Words: Coronary artery calcium; CT reconstruction; IVUS; registration.

Coronary artery calcium (CAC) scoring is a noninvasive, low-radiation computed tomography (CT)-based imaging technique that quantifies the calcium in the coronary vasculature (1,2). It provides a well-validated risk stratification scheme for future cardiovascular events (1,3). CAC studies were originally developed and validated on the electron-beam CT scanner (EBCT) (4,5), and were quantified by calculating the Agatston score (6) and/or the volume score (7), in which a minimum attenuation value of 130 Hounsfield unit (HU) is typically used as the threshold to detect coronary calcium. Recent studies have shown that the fixed 130-HU threshold may not be optimal for detecting calcium (8), and a scanner-specific and individualized attenuation threshold is more desirable (9,10).

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With the increasing popularity and accessibility of multidetector-row CT (MDCT), CAC studies are now typically performed on MDCT scanners. To make the CAC quantification on the MDCT comparable to the original EBCT, current MDCT-based CACs are reconstructed with a 3.0-mm slice thickness, which is the typical collimation thickness on the EBCT scanners. However, CAC volumes acquired on most MDCT scanners can be reconstructed with thinner slice thickness because of MDCT's smaller detector size. For example, CAC images can be acquired volumetrically using a prospective single-rotation protocol on a 320-detector-row CT scanner. Because of the 0.5-mm collimation thickness, CAC images can be reconstructed with the 0.5-mm slice thickness to achieve an isotropic resolution without increasing the radiation dose. Compared to 3.0 mm, thinner slice thickness potentially reduces partial volume artifact and may improve the sensitivity/specificity and accuracy in quantifying calcium. Some studies (11,12) reported that the thinner-slice reconstruction resulted in significantly higher Agatston and volume scores and was able to identify more subclinical calcification lesions. On the other hand, some researchers (12,13) found that the image noise level was significantly higher in the thinner-slice reconstructions, and the conventional threshold of 130 HU leads to more false positives. Mühlenbruch et al. (14) empirically used the threshold of 350 HU in the 1.0-mm reconstruction. However, little is known about the optimal calcium threshold in thinner-slice reconstructions.

Coronary calcification only represents approximately 20% of the total plaque burden. Any minimal calcification may have important prognostic value. In essence, in young patients, any burden of atherosclerosis would place them in the >90th percentile for their age, gender, and race. If small amounts of calcium (<1 by Agatston method) are not detected, the patients may not return for a follow-up scan for up to 7 years, and without necessary medical therapy, it would make a large clinical impact downstream.

Our hypothesis is that, with optimized attenuation threshold, the 0.5-mm reconstruction achieves better sensitivity/specificity and accuracy in detecting and quantifying CAC compared to the conventional 3.0-mm reconstruction. In contrast to most previous studies that were based on phantom or ex vivo experiments (8,10,13,15), this study aimed to improve the clinical significance by using in vivo intravascular ultrasound with radiofrequency backscatter-virtual histology (IVUS-VH) as the reference standard for calcium quantification. IVUS-VH is a clinically established method for atherosclerosis characterization, which has been shown to detect different plaque compositions with very good accuracies (16). Studies reported that IVUS-VH had predictive accuracies of more than 96% for dense calcium both in vivo (17) and ex vivo (18). The present study was designed to study the performances of calcium volume quantification on the 0.5-mm isotropic CAC scans versus the conventional 3.0-mm reconstructions by validating against spatially registered IVUS-VH on a very detailed slice-by-slice basis. In addition, we studied the effect of varying the CAC attenuation threshold on the accuracy of calcium quantification.

MATERIALS AND METHODS

General Study Design

This study was approved by the institutional review board. Informed consents were obtained from the patients on enrollment. A total of 27 symptomatic patients were studied, 14 of whom were prospectively enrolled and underwent CAC, coronary CT angiography (CTA), and IVUS-VH. They were confirmed to have moderate-to-severe coronary artery disease (CAD) with partially calcified plaques in selected arteries by both CTA and IVUS-VH. The other 13 patients were retrospectively reviewed as control patients, who had clinical CAC and CTA, and were confirmed by CTA to have completely normal coronary arteries. IVUS-VH was not available in the control group because it is an invasive procedure and because of the associated risk, it was unethical to perform IVUS on normal subjects. Coronary calcification is the product of the natural healing process of atherosclerotic injury. The presence of coronary calcification is always accompanied by CAD.

TABLE 1. CT Imaging Parameters of the CAC Scan

Image Acquisition Parameters	Values
Detector width, mm	0.5
No. of detectors	320
Gantry rotation time, milliseconds	350
Scan mode	Volumetric
EKG synchronization	Prospectively triggered
Tube voltage, kVp	120
Tube current, mA	100–550
Reconstruction slice thickness, mm	3.0 and 0.5
Reconstruction kernel	FC12

CAC, coronary artery calcium; CT, computed tomography; EKG, electrocardiogram.

Based on the high sensitivity and high negative predictive value of CTA in detecting CAD (24,25), we assumed that the coronary vasculatures in those 13 CTA-indicated control patients were calcium free.

CAC Image Acquisition and Analysis

CAC images were acquired on a 320-MDCT scanner (Aquilion ONE; Toshiba Medical Systems, Otawara, Japan) with a conventional CAC imaging protocol. General imaging parameters were summarized in Table 1. Tube voltage was maintained at 120 kV for all patients, and the manufacturer-recommended default tube current was adjusted on the basis of patient size and body mass index, to reduce the radiation dose and ensure clinically adequate image quality. The image volume was reconstructed with both 0.5-mm and 3.0-mm slice thicknesses, without additional radiation exposure to the patients.

Because the volume of dense calcification can be quantified in the cross-sectional slices in IVUS-VH, to compare CAC with IVUS-VH, similarly, we quantified the calcium volumes on a slice-by-slice basis along the coronary arteries in the CAC image. We first manually extracted the coronary artery centerlines, and then, adapted the three-dimensional (3D) morphologic dilation operation (19) to derive a neighborhood of 3.5-mm radius along the centerline. The choice of 3.5-mm was made experimentally to cover all possible calcified voxels in the artery, but avoid including any nonarterial calcification. The conventional threshold of 130 HU was implemented to derive the initial slice-by-slice calcium volumes in both 3.0 and 0.5-mm reconstructions. Furthermore, we tested the cutoffs ranging from 50 HU to 400 HU and attempted to derive the optimal calcium thresholds for 3.0-mm and 0.5-mm reconstructions.

IVUS Image Acquisition and Analysis

The IVUS-VH images were acquired on an IVUS-VH console using a phased array catheter (20 MHz, Eagle Eye, Volcano Corporation, Rancho Cordova, CA). Automated pullback of the catheter was performed at a rate of 0.5 mm/s. IVUS-VH images were recorded at the R wave peaks of the