

CT virtual intravascular endoscopy assessment of coronary artery plaques: A preliminary study

## **Abstract**

**Purpose:** The purpose of this study was to investigate the potential value of CT virtual intravascular endoscopy (VIE) in the visualization and assessment of coronary plaques in patients suspected of coronary artery disease.

**Materials and Methods:** 20 (13 men, 7 women, mean age 54 years) consecutive patients with suspected coronary artery disease undergoing 64-slice CT angiography were included in the study. Four main coronary artery branches were assessed with regard to the presence of coronary plaques based on 2D axial, multiplanar reformation, 3D volume rendering and VIE visualizations. The coronary plaques were characterized into calcified, noncalcified and mixed plaques. The intraluminal appearances of these coronary plaques were demonstrated with VIE images and correlated with 2D and 3D images to determine the diagnostic value of VIE for assessment of the plaques.

**Results:** VIE was able to identify and demonstrate the intraluminal appearances of coronary plaques in 18 patients involving 32 coronary artery branches which was shown as an irregularly intraluminal protruding sign in extensively calcified plaques and smooth protruding appearance in noncalcified or focally calcified plaques. An irregular intraluminal appearance was also noticed in the presence of mixed plaques due to variable components with different CT attenuation contained within the plaques. VIE accurately confirmed the degree of coronary stenosis or occlusion despite presence of heavy calcification.

**Conclusion:** VIE could be used as a complementary tool to conventional CT visualizations for analysis of luminal changes and assessment of disease extent caused by the coronary plaques.

**Key words:** coronary artery disease, coronary plaque, multislice computed tomography, virtual intravascular endoscopy, intraluminal appearance

## **Introduction**

The feasibility of multislice CT (MSCT) for diagnosis of coronary artery disease (CAD) was initially demonstrated with 4-slice MSCT [1, 2]. However, image evaluation was impaired in many cases due to limited spatial and temporal resolution. With the introduction of 16-slice CT, image quality in coronary MSCT has become more consistent with improved results achieved [3-6]. Shorter examination times are possible with further improved diagnostic accuracy with 64-slice MSCT due to improved spatial and temporal resolution compared with 16-slice MSCT [7-11]. Several meta-analyses of 64-slice CT studies reported sensitivities of 93% and specificities of 96% (in 6 studies) [9], sensitivities of 97% and specificities of 88% (in 15 studies) [10], and sensitivities of 86% and specificities of 96% (in 19 studies) [11]. These reports concluded that MSCT, especially with 64-or more slice CT has high diagnostic accuracy for detection of CAD and could be used as an effective alternative to invasive coronary angiography in selected patients.

Apart from the calcium detection, MSCT also allows non-invasive detection of plaque morphology and composition (calcified versus noncalcified atherosclerotic plaque), as well as the assessment of the extent of remodelling [12-14]. Atherosclerotic plaque size and geometry play an important role in the natural progression of the disease process and may have important clinical predictive value. Schmid et al [14] in their recent report concluded that a significant increase of the amount of noncalcified plaque was observed with 64-slice MSCT over a mean interval follow-up of 17 months, indicating that MSCT may be used as a tool to study the progression of coronary atherosclerosis. Recent emerging data support the idea of the prognostic value of MSCT. In two prospective studies comprising 1127 and 100 patients respectively, Min et al and Pundziute et al [13, 15] reported that MSCT provides

prognostic information over base-line clinical risk factors in patients with known or suspected CAD. However these studies were based on conventional 2D visualization to assess the coronary plaques, and no 3D, especially 3D intraluminal views were generated to demonstrate the intraluminal appearance of coronary plaques. Thus, the purpose of this study was to investigate the potential value of MSCT angiography in the visualization of coronary plaques using CT-generated virtual intravascular endoscopy (VIE). VIE has been previously reported to be valuable in the evaluation of aortic aneurysms and stent grafts [16, 17]. We expanded the application of VIE to the assessment of coronary artery disease and examined whether VIE could provide additional information about CAD, particularly the coronary plaques when compared to conventional 2D and 3D images.

## **Materials and Methods**

### *Study Patients*

The study population consisted of 25 consecutive patients who presented to the cardiac clinic at Ramsay Health-Rumah Sakit Surabaya International, Surabaya, Indonesia, and were referred for further evaluation of suspected CAD (chest pain complains, or abnormal test results). Exclusion criteria were renal insufficiency (serum creatinine level  $>1.5$  mg/mL) or known allergic reaction to iodinated contrast medium, atrial fibrillation or other arrhythmias or inability to follow breath-hold commands. Patients who had undergone bypass surgery or coronary stents were also excluded from the study. Based on the above criteria, 20 patients comprised the study (13 men, 7 women, mean age, 54 years  $\pm$  8). All patients gave written informed consent to the study protocol, which was approved by the local ethics committee.

### *Scan protocols of MSCT coronary angiography*

Multislice CT scans were performed with a 64-slice scanner (GE Medical Systems, Lightspeed VCT, 64x0.625 mm) with the following protocols: beam collimation 0.625 mm, pitch 0.2-0.26, reconstruction interval of 0.4 mm, with tube voltage of 120 kVp and tube current ranging from 300 to 650 mAs (tube current modulation). Contrast medium (iopamiro 370, 60 ml) was injected onto the ante-cubital vein at 5ml/s followed by 50 ml of saline chasing at 4 ml/s, and the scan was performed with a bolus tracking technique with a CT attenuation of 220 HU as the triggering threshold at the ascending aorta to initiate the scan.

Axial images were reconstructed with a slice thickness of 0.625 mm in 0.4 mm increment resulting in isotropic volume data with a voxel size of 0.4 x 0.4 x 0.4 mm<sup>3</sup>. Retrospective electrocardiographic-gating protocol was used to acquire the volume data achieving a temporal resolution of 165 ms in the centre of the gantry rotation. Volume data were reconstructed at 70-80% RR interval to minimize the artifacts. For patients with a heart rate more than 70 bpm, a beta-blocker was used to slow down the heart rate.

#### *Generation of virtual intravascular endoscopy images*

Original DICOM data (digital imaging and communication in medicine) were transferred to a workstation equipped with Analyze V 7.0 (AnalyzeDirect, Inc., Lexana, KS, USA) for generation of 3D virtual intravascular endoscopy (VIE) images. Post-processing of CT data was performed with a CT number thresholding technique, which was described before [16, 17]. In summary, the first step was to measure the CT attenuation at the 4 main coronary arteries, namely right coronary artery (RCA), left main stem, left anterior descending (LAD) and left circumflex (LCX) and determine the threshold that was used to remove the contrast-enhanced blood from the coronary artery. Then the CT threshold value which was measured

between 150 HU and 250 HU in the first step was applied in these cases to generate the intraluminal views of coronary artery ostium, lumen surface and coronary plaques.

#### *Characterization of coronary plaques*

Coronary artery plaque was characterized into the following three types based on the CT attenuation [15]: 1) noncalcified plaques refer to plaques having lower density compared with the contrast-enhanced vessel lumen; 2) calcified plaques indicate plaques with high density; 3) mixed plaques refer to plaques with noncalcified and calcified elements within a single plaque or within a segment of the coronary artery. In addition, we also further characterized the calcified plaques into focal and extensive types according to the distribution of the plaques along the coronary artery. This aims to identify if there is any difference of intraluminal appearance visualized on VIE between the focally and extensively calcified plaques, or whether the focally calcified plaques can be accurately identified with VIE when compared to conventional 2D images in terms of the luminal stenosis or occlusion.

2D axial images were used to define the type of coronary artery plaques supplemented by multiplanar reformatted views (coronal, sagittal and curved planar reformation), and 3D volume rendering. VIE images were correlated with 2D/3D images regarding the intraluminal appearance and location corresponding with each type of plaque, and the degree of stenosis or occlusion in the coronary arteries.

As coronary artery is a small vessel with a diameter of 3 mm, it is not unusual to encounter the situation where it is difficult to confirm the location of coronary plaques or stenosis on VIE visualization. Our solution to resolve this issue is to correlate virtual endoscopic views/measurements with the orthogonal views, which allows the user to determine the exact position of the normal artery branch or lesions. As shown in Figure 1, a VIE image inside the proximal part of left coronary artery viewing the

left anterior descending (square box) and left circumflex (arrows). These two coronary ostia were confirmed by correlating VIE views with the corresponding multiplanar views.

Generation and analysis of VIE images with correlation to 2D/3D views was performed by one reviewer (Z.S) with 10 years of experience in 3D image processing and visualization in cardiovascular disease.

## **Results**

### *Patient characteristics and distribution of CAD*

Baseline characteristics are provided in Table 1. Our small group consisted of relatively young age patients, as 25% of them were less than 50 years old, and one of the patients was only 38 years old. All of the patients presented with suspected CAD at the time of MSCT scans, whereas in two patients, all of the four main coronary arteries were normal without any abnormality being detected on MSCT images.

Distribution and CT attenuation of the coronary plaques are provided in Table 2. There were altogether 80 coronary arteries included for visualization and analysis in the study. We only focused on the visualization of proximal, middle and distal segments of each main coronary branch. As the left main stem was normal and free of involvement in all of the patients, thus our analysis included the RCA, LAD and LCX branches. 33 coronary arteries were affected with coronary plaques to variable extents. 21% of the coronary plaques were found to involve only one coronary artery, and all of the plaques were located in the left coronary artery branches (LAD and LCX). 42% of them involved two coronary arteries with most of them located at the RCA and LAD, while the remaining 36% of the coronary plaques were found to distribute in the three main coronary branches.



### *2D visualization and measurement of coronary plaques*

Plaque density was measured in all of the patients on 2D axial images, as shown in Table 2. Calcified plaques were measured with a mean CT attenuation of 577 HU (range: 316-942 HU). The distribution of the calcified plaques is generally related to the patient's age and clinical symptoms, as focal plaques were found in a relatively younger age group with less than 50% luminal stenosis observed in 60% of the coronary branches, while extensive plaques were seen in relatively older group with more than 50% luminal stenosis observed in 60% of the coronary branches. 13 mixed plaques were found in 11 patients involving 13 coronary arteries. Of these 13 mixed plaques, 6 of them had CT attenuation lower than 0 HU.

Multiplanar reformatted, especially curved planar reformatted (CVR) images best demonstrated the coronary plaques in these artery branches since coronary artery is not a straight branch and it follows a circular path. Figures 2A is an example showing mixed plaques with extensive calcification in the proximal LAD with more than 70% stenosis, while figure 2B is a CVR view with LAD being straightened in the same case, and corresponding VIE demonstrates the irregular appearance in the artery wall.

### *3D virtual intravascular endoscopy findings*

VIE was successfully generated in all of the patients with clearly showing the intraluminal appearances of normal coronary wall, coronary plaques and luminal changes. In the presence of calcified plaques, the intraluminal appearance is typically demonstrated as either a focal protrusion appearance for focally calcified plaques (Fig 3) and noncalcified plaques (Fig 4), or circular protrusion appearance on the coronary wall for extensively calcified plaques (Fig 5).

VIE appearance of the mixed plaques was dependent on the components within the plaques, and in most of the cases as observed in our group, it is similar to what was

seen in the extensively calcified plaques, which was shown as irregular intraluminal protruding sign in the artery wall (Fig 2C). Figure 6 is an example showing a mixed plaque in the LAD with the noncalcified component representing the majority of the component with more than 90% luminal stenosis on 2D axial view, and VIE confirms the severe stenosis of the artery lumen. In summary, the intraluminal appearance of focally calcified and noncalcified coronary plaques was relatively smooth on VIE visualization, while the extensively calcified and mixed plaques presented with irregular intraluminal appearance. Table 3 shows VIE visualization of the coronary plaques in the major coronary arteries. As shown in the table, smooth appearance was noticed in most of the right coronary and left circumflex arteries, while irregular appearance was found in 40% of the left anterior descending artery due to the presence of extensively calcified plaques.

Complete coronary occlusion was noticed with 2D views in two patients involving four coronary arteries due to presence of noncalcified plaques, and this was confirmed by VIE visualization in all branches except in one case which the occlusion of left circumflex was found to be severely stenosed instead of complete occlusion (Fig 7). Figure 8 is an example in a patient with total occlusion of the right coronary artery visualized on CVR and volume rendering images, and corresponding VIE confirms the occlusion of the artery lumen.

Invasive coronary angiography confirmed the total occlusion of these four artery branches, however, it fails to show spotty calcifications in the right coronary artery in one patient, and another noncalcified plaque in the proximal right coronary artery. These two abnormalities were all clearly demonstrated on CVR images, and the noncalcified plaque was visualized on VIE views (Fig 4).

## **Discussion**

The study was designed to investigate the potential value of CT VIE in the visualization and assessment of coronary plaques. Our preliminary findings are two-fold: first, the intraluminal appearance of coronary plaques was clearly visualized and assessed with VIE images; VIE was more accurate than 2D images in the demonstration of intraluminal changes caused by plaques as VIE viewing is not affected by the blooming artefacts resulting from severe or extensive calcification. Heavy calcification interferes with accurate assessment of coronary artery disease as it is noticed to result in overestimation of the luminal stenosis, thus decreasing lumen visualization, leading to decreased diagnostic accuracy [18, 19]. However, this is not the case for VIE visualization as VIE focuses on intraluminal views of the coronary artery instead of the external vessel lumen. Second, VIE is able to confirm or exclude the presence of total occlusion caused by coronary plaques and is more accurate than 2D views. Although based on a small number of patients, our study provides insight into the potential diagnostic value of 3D VIE visualization for quantification of coronary plaques and assessment of disease extent.

With the rapid development of multislice CT technique, especially the recent emergence of 64-slice or dual source CT [8, 10, 11, 20], researchers concluded that multislice CT angiography provides high diagnostic value for detection of coronary artery disease, thus it could be used as a reliable alternative to invasive coronary angiography in selected patients. Almost all of these studies so far focused on the diagnostic accuracy of multislice CT compared to the gold standard technique, invasive coronary angiography, however, few studies addressed the important issue of coronary plaques in terms of volume measurement or quantification [14, 15]. Although intravascular ultrasound was regarded as the method of choice for visualization of coronary plaque intraluminally and performance of quantitative

analysis of plaque volume, it is an invasive procedure, thus is not widely available in many centers. We believe VIE visualization offers potential value in this aspect.

In this study, we presented our experience of using VIE visualization for assessment of coronary plaques. To the best of our knowledge, this is the first report to characterize and assess the coronary plaques with aid of VIE. Our initial results showed that the intraluminal appearance of different types of plaques was clearly demonstrated, however, VIE is unable to accurately characterize these plaques intraluminally since the calcified and noncalcified plaques have similar protruding appearance on the coronary artery wall. Correlation of VIE with 2D axial views is always necessary to confirm the identity of plaques. However, VIE does provide useful information about the luminal changes in relation to the type of plaques, such as extensively calcified or mixed type of plaques which are associated with irregular wall changes. Moreover, VIE presents accurate information about the degree of stenosis or occlusion as confirmed in one case with a total artery occlusion when compared to conventional 2D or 3D views. Thus, we believe VIE could be used as a complementary tool to conventional CT imaging for assessment of coronary artery disease, especially for monitoring the intraluminal changes caused by the plaques.

In addition to the diagnostic value of CAD, cardiac CT can provide objective estimates of calcified and noncalcified atherosclerosis burden. The presence and amount of calcium, as measured in Hounsfield unit, has been shown to be strongly associated with the amount of atherosclerotic plaque present in autopsy studies [21, 22]. We observed this phenomenon in our small group as high CT attenuation was correlated to the extent of the calcified plaques, consequently this was correlated to the subsequent intraluminal appearance visualized on VIE. Coronary artery calcification scoring has been shown to provide incremental value over conventional

risk factors and biochemical markers for the prediction of both significant and insignificant luminal narrowing on angiography [23, 24]. Moreover, it has been reported that the risk of adverse cardiovascular events increases as a function of coronary artery calcification in both asymptomatic individuals and symptomatic patients [25, 26]. To correlate VIE visualization of the coronary wall changes with the identity of plaques will offer additional information for assessing the extent of coronary artery disease, predict the prognosis and monitor the treatment outcomes, although this requires further studies for confirmation.

Our study suffers from some limitations. We only compared VIE with 2D and 3D reconstructed images, without comparing with invasive angiography, which is one of the limitations. The purpose of the study is to assess the potential value of VIE in the visualization of coronary plaques rather than evaluate the diagnostic accuracy of VIE for detection of CAD. Moreover, the invasive coronary angiography can only reveal luminal changes and fails to provide information of the plaque characteristics. Second, our study consists of a very small number of patients, and no follow-up results were provided. Further studies with focus on predictors of cardiac events based on different types of coronary plaques are essential to verify the prognostic value of MSCT with inclusion of VIE in patients suspected of CAD. Last, only one reviewer was responsible for generation and assessment of VIE images, which could introduce biased opinion. Two or more reviewers are preferable to be involved in the subjective analysis of these images.

In conclusion, our preliminary study shows that VIE images clearly demonstrate the intraluminal appearance of coronary plaques and accurately localize and confirm the stenosis or occlusion caused by the plaques in patients suspected of CAD. VIE could be used as a complementary tool to conventional CT imaging for quantitative analysis

of plaques, in terms of corresponding luminal changes, disease extent and risk stratification of CAD. Further studies are needed to verify our initial results.

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## **Figure legends**

Figure 1 Virtual intravascular endoscopy view of the left anterior descending (square box) and left circumflex (arrows), and this is confirmed by the corresponding orthogonal views (axial image on the top right, coronary and sagittal views on the bottom row).

Figure 2A shows extensive calcified plaques in the LAD observed on CVR view with more than 70% luminal stenosis in a 52-year-old man with chest discomfort. Figure 2B is a multiplanar reformatted view with the LAD being straightened. This was confirmed on VIE visualization (Fig 2C) which demonstrates irregular intraluminal appearance with significant stenosis of the coronary artery.

Figure 3A is an example of a focal calcified plaque present in the LAD with more than 90% lumen stenosis in a 51 year-old man suffering from chest pain. Corresponding VIE (Fig 3B) shows intraluminal protrusion caused by the plaque, however, the luminal stenosis is less than 70%

Figure 4 is an example of a noncalcified plaque in the proximal segment of RCA (arrow on axial image) in a 69-year-old man, and VIE shows the protruding appearance arising from the inferior wall of RCA (arrows).

Figure 5 shows the type of extensive calcified plaques observed on 2D axial image in the LAD with more than 70% luminal stenosis in a 52-year-old man with chest discomfort. This was confirmed on VIE visualization which demonstrates significant stenosis of the coronary artery with an irregular intraluminal appearance (arrows).

Figure 6 shows a mixed plaque in LAD in a 69-year-old man with chest pain and the noncalcified component comprises the majority of the plaque on axial image. VIE reveals significant luminal stenosis (arrows).

Figure 7. Extensive calcified plaques were found in the LAD and LCX with total occlusion of mid-LCX observed on CVR (Fig 7A) in a 52-year old man with atypical chest pain. Corresponding VIE images show the significant stenosis of proximal and middle LCX (Fig 7B, C) without evidence of complete luminal occlusion.

Figure 8. A total occlusion of the middle RCA was observed in a 61-year old man presented with angina pectoris. CVR with RCA being straightened (Fig 8 A) and 3D volume rendering (Fig 8B) demonstrated the occlusion of mid RCA, and this was confirmed by VIE which shows total luminal occlusion (Fig 8C).

Figure 9 A mixed plaque was found in the proximal LAD in a 38-year-old man suffering from atypical chest pain. More than 50% stenosis of proximal LAD was noticed on the 2D axial image, and this was confirmed by VIE showing the intraluminal protrusion caused by the plaque (arrows).