Relationship between tissue characterization with 40 MHz intravascular ultrasound imaging and 64-slice computed tomography

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Abstract
Background: Identification of coronary plaque composition is important for selecting the treatment strategy, and 64-slice computed tomography (CT) is a noninvasive method of characterizing atherosclerotic plaques. However, the correlation between plaque characteristics detected by CT and intravascular ultrasound (IVUS) is not clear. A 40 MHz IVUS imaging system (iMap-IVUS) has recently been developed to evaluate plaque composition. The aim of this study was to compare iMap-IVUS with 64-slice CT angiography for the characterization of non-calcified coronary plaques.

Methods and results: Both 64-slice CT angiography and iMap-IVUS were performed in 19 patients (38 plaques). CT values were measured as Hounsfield units (HU) in circular regions of interest (ROI) drawn on the plaques. The iMap-IVUS system analyzed coronary plaques as fibrotic, lipidic, necrotic, or calcified tissue based on the radiofrequency spectrum.

A positive correlation was found between CT values and the percentage of fibrotic plaque ($r = 0.34, p = 0.036$) or calcified plaque ($r = 0.40, p = 0.011$). Conversely, a negative correlation was found between CT values and the percentage of lipidic plaque ($r = -0.41, p = 0.01$), or necrotic plaque ($r = -0.41, p = 0.01$).

Conclusions: Good correlations were observed between the characteristics of non-calcified plaque determined by iMap-IVUS and the CT values of plaque detected by 64-slice CT scanning.

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Introduction

Some reports have suggested that the characteristics of coronary atherosclerotic plaque have an important influence on the risk of coronary events [1–3], and that assessment of plaque composition before deciding the interventional
strategy is useful. Recent advances in 64-slice computed tomography (CT) have led to its use for the characterization of coronary atherosclerosis [4–9]. It has been shown that 64-slice CT can detect and classify coronary plaques and assess vascular remodeling [10–13]. The usefulness of tissue characterization by 64-slice CT for predicting post-procedural myocardial injury was also recently demonstrated [14]. Currently, intravascular ultrasound (IVUS) is recognized as the gold standard for quantitative measurement of coronary plaques and for characterization of plaque composition [9,15,16]. Although plaque morphology has an influence on major coronary events, grey-scale IVUS has some limitations for identifying plaque characteristics accurately [17,18]. Recently, spectral analysis of IVUS radiofrequency data (so-called virtual histology IVUS) has been introduced for the differentiation of plaque components [19,20]. However, the relations between CT density values and plaque components detected by virtual histology IVUS have not been determined [21,22]. The "iMap-IVUS" (Boston Scientific Corp., Fremont, CA, USA) is a new radiofrequency imaging system designed for tissue characterization. iMap technology converts the signal wave pattern into a frequency spectrum, and then compares it to specially selected autopsy spectra ("data library") to find the closest match. Since each tissue type (fibrotic, lipidic, necrotic, or calcified) has a distinct spectral pattern, the technology identifies the pattern that each spectrum most closely resembles [23]. However, there is limited information concerning the accuracy of coronary plaque characterization using iMap-IVUS. Therefore, the aim of this study was to compare iMap-IVUS with 64-slice CT angiography for the characterization of non-calced coronary plaques.

Materials and methods

Patient selection

In a single-center study, we enrolled 19 consecutive patients from July 2009 to January 2010. They had stable angina (13 men; mean age: 66.1 ± 11.8 years) and underwent 64-slice coronary CT before standard coronary angiography, with at least one coronary stenosis >50% being identified by quantitative coronary angiography. IVUS was performed for at least one vessel before percutaneous coronary intervention (PCI). Exclusion criteria were arrhythmias, heavily calcified lesions, restenosis, renal insufficiency (serum creatinine >1.5 mg/dl), a history of allergy to iodinated contrast media, and inability to breath-hold. In these 19 patients, 38 atherosclerotic lesions were selected for further investigation.

Coronary CT angiography

Patients with a resting heart rate of >60 beats/min received atenolol (1 mg/kg orally) at 60 min before imaging, and all patients received nitroglycerin (0.3 mg sublingually) at 5 min before imaging. A 64-slice CT scanner (Aquilion 64, Toshiba, Otowara, Japan) was used with 64 × 0.5 mm collimation, a detector pitch of 9.8–11.2, pixel size of 0.39 mm × 0.39 mm, gantry rotation time of 350 ms, tube current of 400 mA, and voltage of 120 kV. Contrast medium (370 ml/ml-1 iopamido; Bayer Schering Pharma, Osaka, Japan) was injected at a rate of 0.06 ml/kg/s throughout the entire scanning time plus 2 s, followed by 0.15 ml/kg of contrast medium plus 0.15 ml/kg of saline solution with a dual injector. Acquisition of CT data and the electrocardiogram (ECG) was started as soon as the CT density of the ascending aorta reached a predefined threshold of 250 HU. The effective radiation dose was 15–18 mSv. Acquisition time was reduced to 175 ms by applying a half-scan algorithm (data from gantry rotation of only 180° was used for image reconstruction) in all patients.

CT image reconstruction

Raw CT data were reconstructed using a half-scan algorithm optimized for retrograde ECG-gated reconstruction. The reconstruction period was terminated at the peak of the P wave on the monitoring ECG. Reconstructed CT images were transferred to a computer workstation (Ziostation, Amin, Tokyo, Japan) for post-processing and analysis. After visual inspection of volume-rendered images to assess the configuration of the coronary artery lumen, coronary plaques were carefully inspected on both axial and curved multiplanar reformatted images, which were used to visually classify each lesion.

Images were reconstructed with the optimal setting to detect plaques and vessel boundaries. This was done with an average width representing 155% (range: 395–809 HU) of the mean intraluminal intensity and at a level representing 65% of the mean intensity (range: 165–339 HU), as previously reported [6]. Coronary plaques were outlined by manual tracing and the coronary plaque area was calculated as the difference between the vessel area (inside the external elastic lamina) and the luminal area at the site of maximum luminal narrowing observed on cross-sectional 64-slice CT images. Coronary plaques were defined as structures with an area >1 mm² within and/or adjacent to the coronary artery lumen and surrounding pericardium. For plaque analysis and tissue characterization, CT images were evaluated with a window level of 83 HU and a width of 230 HU. Regions of interest (ROIs) with an area of 1.0 mm² were placed inside each plaque, and tissue density (in HU) was measured at 3 randomly selected points independently by 2 cardiologists.

IVUS

Before stenting, IVUS was performed after the intracoronary administration of nitroglycerin (125–250 μg). Data were acquired with a 40 MHz IVUS catheter (Atlantis SR Pro, Boston Scientific Corp.). The catheter was advanced beyond the target lesion, and imaging was performed retrogradely during automatic pullback at a speed of 0.5 mm/s. The IVUS data were stored on a hard disk for offline analysis, which was performed independently by experienced analysts who were unaware of the angiographic findings or the baseline clinical and lesional characteristics. Qualitative analysis of each plaque was done with iMap software. The lumen and the media–adventitia interface were outlined manually for the entire culprit lesion. Then the iMap IVUS system classified each plaque into 4 color-coded components as previously described (green for fibrous plaque, yellow for lipidic plaque, red for necrotic plaque, and blue for calcification).
Relationship between tissue characterization with 40 MHz intravascular ultrasound imaging and 64-slice computed tomography

Figure 1  Plaque characterization with 64-slice computed tomography (CT) and iMap-intravascular ultrasound (IVUS). (a) Curved multiplanner reconstructions of non-calcified plaque in proximal right coronary artery (RCA). (b) Measurement of CT attenuation in cross-sectional image. The CT attenuation determined based on the mean value in different three sites. (c) Color-coded IVUS image at the same location of proximal RCA. Plaque composition is analyzed by iMap-IVUS. Plaque areas were manually outlined and plaque components were evaluated. Plaque locations determined by CT and IVUS were carefully harmonized.

CT versus IVUS

Coronary plaques were viewed on CT scans and the locations of each one in the coronary arteries were noted. An experienced analyst evaluated the CT scans and corresponding IVUS images side-by-side to detect non-calcified plaques. Anatomical cross-correlation between CT and IVUS was achieved by using side branches as landmarks and measuring the distance between branches on the CT and IVUS images, as well as by comparing the plaque area and shape.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) for Windows version 15.0 (Chicago, IL, USA) was used for all analyses. Continuous variables were expressed as the mean ± standard deviation, while discrete variables are presented as the number and percentage. Correlations between CT and IVUS findings were assessed by Pearson’s correlation analysis. The reproducibility of CT values for coronary plaque was assessed by calculating the intra-observer and inter-observer variability, which was defined as the difference between the corresponding measurements expressed as a percentage of their mean. A p-value of less than 0.05 was taken to indicate statistical significance in these analyses.

Results

Representative examples of iMap-IVUS image and CT images are shown in Fig. 1.

Baseline patient characteristics are summarized in Table 1. Coronary CT angiography was performed in all 19 patients, and none of them were excluded because of problems with CT image quality. Thirty-eight non-calcified plaques were analyzed by both CT and iMap-IVUS. The distribution of these plaques is shown in Table 2. The iMap-IVUS provided good images in all cases. In these, 24 plaques were in culprit lesion and in all cases IVUS catheter could cross

Table 1  Characteristics of the patients.

<table>
<thead>
<tr>
<th>Variables</th>
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<tbody>
<tr>
<td>Total patients (n)</td>
<td>19</td>
</tr>
<tr>
<td>Male (%)</td>
<td>13  (68.4)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.1 ± 11.8</td>
</tr>
<tr>
<td>Risk factors (%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>6   (31.6)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13  (68.4)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>9   (47.4)</td>
</tr>
<tr>
<td>Family history</td>
<td>2   (10.5)</td>
</tr>
<tr>
<td>Smoking</td>
<td>9   (47.4)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>0   (0)</td>
</tr>
<tr>
<td>Statin use (%)</td>
<td>12  (63.2)</td>
</tr>
<tr>
<td>EF</td>
<td>66.1 ± 7.8</td>
</tr>
</tbody>
</table>

MI, myocardial infarctio; EF, ejection fraction.
Figure 2  Linear regression analysis for non-calcified plaque attenuation determined by computed tomography (CT) and plaque composition detected by iMap-intravascular ultrasound. Percentage of fibrous plaque and calcified plaque has positive correlation with CT attenuation, and percentage of lipidic plaque and necrotic plaque has negative correlation with CT attenuation.

d-the lesion before ballooning. The intra-observer and inter-observer variability of the HU values of plaques detected by 64-slice coronary CT was 8 ± 6% and 10 ± 8%, respectively. The mean CT value was 73.7 ± 36.1 HU. There was no significant difference in CT density values between plaques in different coronary arteries. There was a good correlation between 64-slice coronary CT findings and the plaque components detected by iMap-IVUS. A positive correlation was noted between the CT values and the percentage of fibrotic plaque ($r = 0.34, p = 0.036$) or the percentage of calcified plaque ($r = 0.40, p = 0.011$). Conversely, a negative correlation was found between the CT values and the percentage of lipidic plaque ($r = -0.41, p = 0.01$) or the percentage of necrotic plaque ($r = -0.41, p = 0.01$) (Fig. 2).

**Table 2** Distribution of non-calcified coronary plaques.

<table>
<thead>
<tr>
<th>Coronary segment (%)</th>
<th>N = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main</td>
<td>2 (5.3)</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>20 (52.6)</td>
</tr>
<tr>
<td>Proximal</td>
<td>8 (21.1)</td>
</tr>
<tr>
<td>Middle</td>
<td>11 (28.9)</td>
</tr>
<tr>
<td>Distal</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Proximal</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Middle</td>
<td>2 (5.3)</td>
</tr>
<tr>
<td>Distal</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Right</td>
<td>13 (34.2)</td>
</tr>
<tr>
<td>Proximal</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Middle</td>
<td>9 (23.7)</td>
</tr>
<tr>
<td>Distal</td>
<td>3 (7.9)</td>
</tr>
</tbody>
</table>

**Discussion**

The main objective of this study was to compare the characterization of non-calcified plaques by using color-coded 40 MHz IVUS radiofrequency data (iMap-IVUS) with 64-slice coronary CT. Various studies have demonstrated that grey-scale IVUS cannot assess plaque composition accurately when compared with the histopathology of atherectomy samples [24]. On the other hand, it has been reported that multidetector-row CT has the potential to identify soft, fibrous, and calcified plaques [25,26]. Furthermore, previous studies have shown a significant difference between the CT density of hypoechoic, hyperechoic, and calcified lesions, suggesting that CT values closely reflect plaque composi-
Conclusion

Good correlations were observed between the composition of non-calcified plaque as determined by iMap-IVUS and the CT values of plaque on 64-slice CT images. The iMap-IVUS system may be reliable for characterization of non-calcified plaque.

Acknowledgment

This study was performed at Toho Ohashi Medical Center, Tokyo, Japan.

References


