Visualization of Coronary Atherosclerotic Plaques in Patients Using Optical Coherence Tomography: Comparison With Intravascular Ultrasound

Ik-Kyung Jang, MD, Ph.D, FACC,* Brett E. Bouma, Ph.D,† Dong-Heon Kang, MD,*§ Seung-Jung Park, MD, FACC,‖ Seong-Wook Park, MD, FACC,‖ Ki-Bae Seung, MD,§ Kyu-Bo Choi, MD, FACC,§ Milen Shishkov, Ph.D,† Kelly Schlendorf, BS,† Eugene Pomerantsev, MD, Ph.D,* Stuart L. Houser, MD,‡ H. Thomas Aretz, MD,‡ Guillermo J. Tearney, MD, Ph.D†‡

Boston, Massachusetts and Seoul, Korea

OBJECTIVES

The aim of this study was to evaluate the feasibility and the ability of intravascular optical coherence tomography (OCT) to visualize the components of coronary plaques in living patients.

BACKGROUND

Disruption of a vulnerable coronary plaque with subsequent thrombosis is currently recognized as the primary mechanism for acute myocardial infarction. Although such plaques are considered to have a thin fibrous cap overlying a lipid pool, imaging modalities in current clinical practice do not have sufficient resolution to identify thin (<65 μm) fibrous caps. Optical coherence tomography is a new imaging modality capable of obtaining cross-sectional images of coronary vessels at a resolution of approximately 10 μm.

METHODS

The OCT images and corresponding histology of 42 coronary plaques were compared to establish OCT criteria for different types of plaques. Atherosclerotic lesions with mild to moderate stenosis were identified on angiograms in 10 patients undergoing cardiac catheterization. Optical coherence tomography and intravascular ultrasound (IVUS) images of these sites were obtained in all patients without complication.

RESULTS

Comparison between OCT and histology demonstrated that lipid-rich plaques and fibrous plaques have distinct OCT characteristics. A total of 17 IVUS and OCT image pairs obtained from patients were compared. Axial resolution measured 13 ± 3 μm with OCT and 98 ± 19 μm with IVUS. All fibrous plaques, macrocalcifications and echolucent regions identified by IVUS were visualized in corresponding OCT images. Intimal hyperplasia and echolucent regions, which may correspond to lipid pools, were identified more frequently by OCT than by IVUS.

CONCLUSIONS

Intracoronary OCT appears to be feasible and safe. Optical coherence tomography identified most architectural features detected by IVUS and may provide additional detailed structural information. (J Am Coll Cardiol 2002;39:604–9) © 2002 by the American College of Cardiology

Autopsy studies have identified several histologic characteristics of plaques that are prone to rupture and cause acute coronary events. These vulnerable plaques possess: 1) a thin fibrous cap (<65 μm); 2) a large lipid pool; and 3) activated macrophages near the fibrous cap (1–4). Because many of the determinants of plaque vulnerability are structural abnormalities, a high-resolution imaging technique may offer promise as a method of detecting vulnerable plaques. Presently, however, a reliable method of identifying such plaques is not available.

Non-invasive imaging modalities such as magnetic resonance and computerized tomography are currently under intense investigation. Catheter-based diagnostic techniques, however, can provide structural information with higher resolution than non-invasive methods. Intravascular magnetic resonance is being actively investigated for plaque detection and characterization (5). Intravascular ultrasound (IVUS) is widely used in interventional cardiology. A recent publication suggests a correlation between the presence of echolucent zones in coronary plaques on IVUS images and acute coronary events (6). Preliminary angioscopic studies have suggested that the presence of yellow plaques with a glistening surface correlates with acute events (7). More quantitative approaches (8,9), which measure molecular absorption overtones of lipid or the Raman shift of cholesterol, may provide unique signals from vessel walls to identify large lipid pools. Based on the hypothesis that local
inflammation within vulnerable plaques may lead to local elevations in temperature, a temperature-sensing catheter has been used to study temperature heterogeneity and temperature differences between atherosclerotic plaque and healthy vessel walls (10,11).

Intravascular optical coherence tomography (OCT) has recently been proposed as a high-resolution imaging method for plaque characterization (12). Optical coherence tomography is an optical analog of ultrasound imaging because it measures the amplitude of backscattered light (optical echoes) returning from a sample as a function of delay. In vitro studies have shown that the resolution of OCT (10 \( \mu \text{m} \) to 20 \( \mu \text{m} \)) can resolve the thin fibrous caps thought to be responsible for plaque vulnerability. Additionally, the intrinsic optical properties of typical plaque constituents have provided sufficient contrast in these studies for OCT to differentiate between lipid, calcium and fibrous tissue. Recent experiments performed in vivo have demonstrated intravascular OCT imaging of normal rabbit aortas (13) and swine coronary arteries (14). Here we present the first application, to our knowledge, of intracoronary OCT in living patients. The goals of this study were: 1) to demonstrate the feasibility and safety of OCT imaging in patients; and 2) to assess OCT images of human coronary pathology acquired in vivo by comparison with IVUS images obtained from corresponding locations.

METHODS

The OCT system used in this study has been described previously (15). Optical coherence tomography images were acquired at either 8 (250 angular pixels \( \times \) 250 radial pixels) or 4 frames per second (500 angular pixels \( \times \) 250 radial pixels), displayed using a gray-scale lookup table and digitally archived. Optical coherence tomography catheters were constructed using modified 3.2F IVUS catheters. Key modifications included the insertion of a single mode optical fiber through the IVUS core and distal termination of the optical fiber by a miniature gradient index lens and a micro prism.

Before performing OCT in living patients, 42 human cadaveric coronary artery segments were imaged using both 7F and 3.2F OCT catheters in order to determine the OCT characteristics of different plaque types. Histologic sections were obtained every 50 \( \mu \text{m} \) and stained with Movat’s Pentachrome. Corresponding OCT images and histologic sections were compared.

Patients (n = 10, 8 men/2 women, mean age of 59) undergoing percutaneous coronary intervention were enrolled after written informed consent was obtained. The study protocol was approved by the institutional review board of the individual institutions. After stent deployment for more severely stenotic plaques, adjacent atherosclerotic lesions (n = 17) with mild to moderate stenosis in the same vessel were evaluated using IVUS (3.2F, 30-MHz, Boston Scientific, Natick, Massachusetts) and OCT. Intravascular ultrasound was performed with an automatic pullback device at a rate of 0.5 mm/s, and an OCT catheter was advanced to a previously identified site. The exact locations of the IVUS and OCT catheters were identified using different landmarks, such as side branches and angles of the vessel as well as the tip of the guide catheter and the stent edges.

In order to remove blood from the field of view and allow clear visualization of the vessel wall, OCT images were recorded during intermittent 8 to 10 cc saline flushes through the guide catheter. The total time that was added to the procedure for OCT imaging was approximately 5 to 10 min.

After the procedure, corresponding OCT and IVUS images were selected. For each OCT imaging site, the longitudinal distances along the vessel between the image plane and at least two landmarks were measured using digitally recorded angiograms and commercially available image processing software (IPLab Spectrum 3.1, Signal Analytics, Vienna, Virginia). Single IVUS frames were extracted and digitized for direct comparison with the corresponding OCT images.

The resolutions for each modality were determined by measuring the full-width-half-maximum (FWHM) of the first derivative of a single axial reflectance scan at the surface of the tissue. A total of 10 FWHM measurements were used to compute the mean and standard deviation of the axial resolution for the two modalities. This method provides the true “image resolution” and differs from previously published methods for determining the system axial point-spread function using a phantom.

An experienced observer, blinded to the OCT data set, reviewed the IVUS data using established criteria (16–19) to classify plaque type and identify image features including the presence of a plaque, echolucent regions and intimal hyperplasia. The plaque type was classified as fibrous, calcific or lipid-rich. An OCT observer, blinded to all IVUS information, reviewed all OCT images and evaluated the images with respect to the features described above, as well as the presence of the internal and external elastic laminae. The OCT observer’s interpretation of the images was based on the results of in vitro studies (criteria in Table 1).

RESULTS

Representative OCT images and corresponding histology of different coronary plaques from 42 human coronary artery segments are shown in Figure 1. The layered structure of the normal coronary wall was absent in all OCT images of atherosclerotic plaques. Calcifications within plaques were
Table 1. OCT Image Features of Vessel Wall Structure by Histopathologic Finding (11–13)

<table>
<thead>
<tr>
<th>Histopathologic Finding</th>
<th>OCT Finding</th>
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<tbody>
<tr>
<td>Intimal hyperplasia</td>
<td>Signal-rich layer nearest lumen</td>
</tr>
<tr>
<td>Media</td>
<td>Signal-poor middle layer</td>
</tr>
<tr>
<td>Adventitia</td>
<td>Signal-rich, heterogeneous outer layer</td>
</tr>
<tr>
<td>Internal elastic lamina</td>
<td>Signal-rich band (20 μm) between the intima and media</td>
</tr>
<tr>
<td>External elastic lamina</td>
<td>Signal-rich band (20 μm) between the media and adventitia</td>
</tr>
<tr>
<td>Plaque</td>
<td>Loss of layered appearance, narrowing of lumen</td>
</tr>
<tr>
<td>Fibrous plaque</td>
<td>Homogeneous, signal-rich region</td>
</tr>
<tr>
<td>Macrolcalcification</td>
<td>Large, heterogeneous, sharply delineated, signal-poor or signal-rich region or alternating signal-poor and signal-rich region</td>
</tr>
<tr>
<td>Lipid pool</td>
<td>Large, homogeneous, poorly delineated, signal-poor (echolucent) region</td>
</tr>
<tr>
<td>Fibrous cap</td>
<td>Signal-rich band overlying signal-poor region</td>
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OCT = optical coherence tomography.

identified by the presence of well-delineated, low backscattering heterogeneous regions (Figs. 1A and 1B). Fibrous plaques consisted of homogeneous high backscattering areas (Figs. 1C and 1D). Lipid pools were less well-delineated than calcifications and demonstrated decreased signal density and more heterogeneous backscattering than fibrous plaques (Figs. 1E and 1F). The strong contrast between lipid-rich cores and fibrous regions in OCT images allowed fibrous caps to be easily identified. The information obtained from the cadaveric coronary artery study allowed the identification of similar morphologic features in living patients.

All patients tolerated the procedure well without complications. The duration of clear OCT imaging after each saline purge was approximately 2 s. The maximum penetration depth of OCT imaging measured 1.25 mm versus 5 mm for IVUS. Optical coherence tomography and IVUS axial resolutions measured 13 ± 3 μm and 98 ± 19 μm, respectively. The superior resolution of OCT can be readily appreciated by comparing corresponding OCT and IVUS images showing regions of intimal hyperplasia (Figs. 2A and 2B).

Table 2 summarizes the correlation between OCT and IVUS findings. In 10 patients, 17 distinct vessel locations were evaluated by OCT and IVUS. An OCT image consistent with an eccentric fibrous plaque is presented in Figure 2A, with the IVUS image from the same location in Figure 2B. All plaques identified by OCT were characterized by the loss of the layered structure observed in normal vessels or vessels with intimal hyperplasia (Fig. 2A, inset). A total of 13 imaging locations were identified as fibrous plaques by IVUS. All of these sites were also identified as fibrous plaques by OCT.

Macrolcalcifications were identified in four plaques by OCT (Figs. 3A and 3C) and IVUS (Figs. 3B and 3D). The contrast between calcifications and the surrounding vessel wall was often higher in IVUS images (Figs. 3B and 3D). However, the bright IVUS signal from calcifications made assessment of neighboring tissue difficult due to saturation artifact. Moreover, the attenuation of ultrasound by calcifications caused shadowing, which impaired visualization of deeper vessel wall structures and prevented accurate measurement of the depth of calcification. In contrast, OCT images allowed improved evaluation of the extent of calcifications within plaques and visualization of plaque microstructure adjacent to calcifications.

Echolucent regions, possibly representing large lipid pools, were identified in two corresponding OCT and IVUS image pairs (Figs. 4 and 5). Comparison of the OCT and IVUS images of the signal-rich band overlying the echolu-
cent regions demonstrates the potential for OCT to measure cap thickness with a greater degree of precision than IVUS. Optical coherence tomography also identified two additional plaques with similar characteristics that were not definitely identified by IVUS.

**DISCUSSION**

Corresponding OCT and IVUS image pairs form a basis for validating OCT findings and comparison of the two modalities. All fibrous plaques, calcifications and echolucent regions identified by IVUS were seen in OCT images. Moreover, as compared with IVUS, OCT images provided additional morphologic information, which could be used to improve plaque characterization (Table 2). The high resolution of OCT facilitated the identification of intimal hyperplasia, the internal and external elastic laminae, and echolucent regions, architecture that can be difficult to discern by IVUS. In addition, the lack of saturation and shadowing artifacts in OCT images of calcium deposits allowed calcium within the vessel wall to be located and enabled visualization of adjacent tissues. Most importantly, the high resolution of OCT permits the measurement of thin fibrous caps (<65 μm), thought to be present in a majority of vulnerable coronary plaques (4).

**Table 2. IVUS and OCT Findings for Corresponding Image Pairs (n = 17)**

<table>
<thead>
<tr>
<th>Feature</th>
<th>A. Identified by Both OCT and IVUS</th>
<th>B. Identified by OCT Alone</th>
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<tr>
<td>Intimal hyperplasia</td>
<td>3 (3 patients)</td>
<td>8 (7 patients)</td>
</tr>
<tr>
<td>Internal elastic lamina</td>
<td>NE</td>
<td>11 (8 patients)</td>
</tr>
<tr>
<td>External elastic lamina</td>
<td>NE</td>
<td>10 (7 patients)</td>
</tr>
<tr>
<td>Plaque</td>
<td>17 (10 patients)</td>
<td>0</td>
</tr>
<tr>
<td>Fibrous plaque</td>
<td>13 (10 patients)</td>
<td>0</td>
</tr>
<tr>
<td>Calcific plaque</td>
<td>4 (4 patients)</td>
<td>0</td>
</tr>
<tr>
<td>Echolucent region</td>
<td>2 (2 patients)</td>
<td>2 (2 patients)</td>
</tr>
</tbody>
</table>

All features of the vessel wall structure identified by the IVUS reader were seen in the corresponding OCT image (column A). Additional findings by OCT that were not identified by the IVUS reader are enumerated in column B.

IVUS = intravascular ultrasound; NE = not evaluated; OCT = optical coherence tomography.

**Figure 2.** Fibrous coronary plaque imaged in vivo by optical coherence tomography (OCT) (A) and intravascular ultrasound (IVUS) (B). (A) From 9 o’clock to 2 o’clock, this OCT image demonstrates visualization of the intima (with intimal hyperplasia [i]), media (m) and adventitia (a). The internal and external elastic laminae are visible as signal-rich lines bordering the media (inset). A plaque extending from 2 o’clock to 9 o’clock contains a homogeneous, signal-rich region consistent with a fibrous plaque (f) that is partially obscured by a guidewire shadow artifact (*). (B) In the corresponding IVUS image, the fibrous plaque (f) is also visualized. Tick marks, 1 mm.

**Figure 3.** Calcific coronary plaques imaged in vivo by optical coherence tomography (OCT) (A, C) and intravascular ultrasound (IVUS) (B, D). (A) This OCT image shows a well delineated, heterogeneous, signal-poor region corresponding to a macrocalcification (A, arrow), also seen in the corresponding IVUS image (B, arrow). A thin layer of circumferential calcification (A, two arrowheads) overlying the calcification is easily identified in the OCT image but is obscured by a saturation artifact in the IVUS image. (C) A thin layer of circumferential calcification is seen in this OCT image (arrows) as a well-defined, heterogeneous, signal-poor region within the vessel wall. A side-branch (arrowhead) can be seen adjacent to the guidewire artifact (*). (D) The extent of the calcifications (arrows) and their relation to the surrounding fibrous components of the plaque are not as clearly seen in the corresponding IVUS image. The borders of the guidewire (*) artifact are marked by dotted lines in A, C. Tick marks, 1 mm.
Limitations of OCT. Clear visualization of the entire vessel lumen by OCT was possible only by displacing blood with saline. Because the maximum duration of optimal imaging after a single purge was only approximately 2 s, screening long vessel segments with OCT would be difficult. One possible solution to this problem is the proximal occlusion with an occluding balloon or the placement of the flushing catheter inside the guiding catheter with subsequent continuous saline flush, a technique commonly practiced in angioscopy (7). For an accurate measurement of a total lipid pool or for the evaluation of a vessel remodeling process, the limited depth of penetration of OCT could indeed pose a problem. However, the current capabilities of OCT are well suited for the identification and study of vulnerable plaques, where the relevant morphologic features are primarily localized to within 500 μm of the luminal surface (1–4). One way to overcome this limitation of penetration is to combine OCT with other modalities capable of imaging through blood. Other techniques such as angioscopy and thermography have been shown to provide additional information that may be related to plaque vulnerability (7,10,11). Combining these modalities with OCT may render a device with improved sensitivity for detecting vulnerable coronary plaques. Finally, although the relatively slow frame rates (4 to 8 frames per second) can potentially give rise to motion artifacts, these effects were surprisingly minimal in our study.

Future role of OCT. Identification of vulnerable plaques might lead to a therapeutic strategy specifically designed for a given patient, such as balloon angioplasty, stenting, local delivery therapy or radiation brachytherapy to prevent acute coronary syndromes (20,21). In situ OCT imaging could also advance our understanding of the intrinsic morphologic features that determine plaque vulnerability. In addition,
OCT could be used to monitor structural changes that occur with plaque regression after genetic or pharmacologic intervention (22,23).

**Conclusions.** Our study demonstrates the feasibility of intracoronary OCT to visualize coronary plaque microstructure in patients. The OCT images of human coronary atherosclerotic plaques obtained in vivo provide additional, more detailed structural information than IVUS. The unique capability of OCT to resolve micrometer-scale features of coronary plaques in patients suggests that this new technique holds promise for identifying features of coronary plaques at risk for rupture. The findings of this initial experience should be supported by a prospective clinical trial to test the ability of OCT to identify vulnerable plaques. Once the predictive capability of OCT is established, a trial demonstrating effective treatment could potentially contribute to the prevention of acute myocardial infarction and sudden cardiac death.

Reprint requests and correspondence: Dr. Ik-Kyung Jang, Cardiology Division, Bulfinch 105, Massachusetts General Hospital, 55 Fruit Street, Boston, Massachusetts 02114. E-mail: jang.ik@mgh.harvard.edu.

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