Neoatherosclerosis and Mural Thrombus Detection After Sirolimus-Eluting Stent Implantation – Comparison of Angioscopy and Optical Coherence Tomography Assessment for Color-Based Tissue Characterization –

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Background: Although both optical coherence tomography (OCT) and angioscopy are robust tools for detecting intrastent thrombi and neoatherosclerosis in vivo, whether OCT findings are comparable with angioscopy findings remains unclear.

Methods and Results: 22 patients presenting with de novo lesions underwent 26 sirolimus-eluting stent (SES) implantations, with follow-up OCT and angioscopy at 10 months post-implantation for segmental assessment of the proximal, mid-, and distal SES segments (66 segments). The mean signal intensity index (signal intensity of the neointima/signal intensity of fibrous intimal hyperplasia) was quantified for angioscopically detected in-stent yellow and white segments. The detection rate for red thrombi was numerically higher with angioscopy than with OCT (17% vs. 9%; P=0.053). Angioscopically detected in-stent yellow segments were categorized into 3 OCT patterns: “high-attenuation tissue covering struts” (OCT-defined neoatherosclerosis), “high-attenuation tissue underneath struts,” and “low-attenuation and low-intensity tissue covering struts”; further, macrophage-like appearance was most frequently observed with OCT-defined neoatherosclerosis (56%, 6.3%, and 0%, respectively, P<0.001). The mean signal intensity index of neoatherosclerosis was significantly lower than that of angioscopically detected in-stent white segments (0.929 vs. 0.997, P=0.004).

Conclusions: Current OCT-based definitions for thrombus detection may underestimate the presence of subclinical red thrombi. Qualitative and quantitative OCT assessments of the neointima may enhance the detection of neoatherosclerosis over SES in vivo. (Circ J 2014; 78: 92 – 100)

Key Words: Angioscopy; Neoatherosclerosis; Optical coherence tomography; Sirolimus-eluting stent; Thrombus

In the present era of drug-eluting stents (DES), stent thrombosis poses a significant clinical problem. Although the underlying mechanisms are multifactorial, angioscopic studies have shown that newly formed yellow neointima (so-called neoatherosclerosis), as well as low-grade neointimal coverage (NC), are potentially thrombogenic. Angioscopy is considered the gold standard for detecting red thrombi and yellow neointima in vivo because of its full-color visualization.

Optical coherence tomography (OCT) can characterize important morphological features of atherosclerotic plaques or abnormally structured vessel wall associated with stent implantation, such as lipid, thrombus, NC, macrophage infiltration, and stent edge dissection at high axial resolutions of 10–20μm. However, whether OCT-based assessment is comparable to...
Neoatherosclerosis and Thrombi: OCT vs. Angioscopy

After performing coronary angiography at 10 months post-SES implantation, coronary angioscopy was performed using an occlusion balloon catheter (Vecmova NEO™, FiberTech, Tokyo, Japan) with lactated Ringer’s solution infusion for clearing red blood cells from the imaging site.

Angioscopic analysis aimed to assess the following: (1) the degree of segmental NC of the stent, (2) the presence of red and white thrombi, and (3) the color of the in-stent segment. We divided each SES-stented lesion into proximal, mid-, and distal SES segments, for the aforementioned reason. We used this method because we could definitely identify either the distal or proximal end of the SES in all cases; further, the number of strut-cells was determined according to the known length of the SES because each length of the SES has a unique cell–rink–cell pattern. NC of the stent was classified into 4 grades as previously described: grade 0: stent struts exposed; grade 1: struts bulging into the lumen, although covered; grade 2: struts embedded but seen translucently; and grade 3: struts fully embedded and invisible on angioscopy.

A segment with NC grade 0/1 indicated an incompletely covered segment, whereas a segment with NC grade 2/3 indicated a completely covered segment. A red thrombus was defined as red material with or without protrusion into the lumen or adherent to the luminal surface. Based on their location, red thrombi were classified as mural or peri-strut. Mural red thrombi were characterized by red material with or without protrusion into the lumen or adherent to the neointima over the struts. Peri-strut

Methods

Study Population and Protocol

We retrospectively enrolled 22 patients with de novo native coronary lesions treated with SES implantation (Cypher™, Cordis Corp, Miami Lakes, FL, USA) during February 2006–September 2010; these patients underwent follow-up OCT and angioscopy at 10 months post-implantation. All patients provided written informed consent for inclusion in the study and for follow-up OCT and angioscopic examinations at Kobe University Hospital, Japan.

Target lesions fulfilled the following inclusion criteria: reference vessel diameter of 2.5–3.5 mm by visual estimation, visually estimated stenosis of more than 75% of the luminal diameter or chronic total occlusion. At the follow-up examinations, we segmentally assessed the SES-stented lesions in the proximal, mid-, and distal SES segments by both angioscopy and OCT, because the extent of NC and the distribution of in-stent yellow lesion were so heterogeneous that stent-based analysis may have lacked the precision to adequately evaluate the tissue characteristics of the SES-stented lesions.
red thrombi were characterized by red lining material limited to location along the stent struts. A white thrombus was defined as white material with or without protrusion into the lumen or adherent to the neointima over the struts, with a shaggy, irregular, and cotton-wool-like appearance. The color of the in-stent segment was classified as white or yellow, as previously reported (Figure 1).\(^\text{11}\)

**OCT Examination and Analysis**

Because frequency-domain OCT had not been approved for clinical use in Japan at the beginning of the study period, time-domain OCT was used in this study, as previously reported.\(^\text{5}\)

Cross-sectional OCT analysis was performed every 1 mm to (1) measure neointimal thickness (NIT) over the SES struts, (2) assess the presence of mural red or white thrombi, and (3) evaluate macrophage-like appearance. The cell–rind pattern of SES was recognized by OCT images; further, each SES-stented lesion could be divided into the proximal, mid-, and distal SES segments using OCT. NIT was measured from the neointimal surface to the central reflection of the strut.\(^\text{12}\) A mural red thrombus was defined as a mass protruding beyond the stent strut into the lumen with significant attenuation behind the mass. A mural white thrombus was defined as a mass protruding beyond the stent strut into the lumen without significant attenuation behind the mass (Figures 1a,b).\(^\text{6}\) Macrophage-like appearance was defined as linear, strong OCT images on plaque surface accompanied by high attenuation (Figure 1c).\(^\text{13}\)

For in-stent segments with complete NC, we calculated the mean signal intensity index, defined as the average signal intensity of fibrous intimal hyperplasia at 5 consecutive cross-sections using the same method (Figure 1e).\(^\text{15}\)

**Comparison of Angioscopic and OCT Images**

To compare the angioscopy and OCT images, we located landmarks such as side branches by both angioscopy and OCT, as well as dividing each SES-stented lesion into the proximal, mid-, and distal SES segments. Moreover, we compared the OCT and angioscopic images based on the angioscopically detected landmarks, and the OCT findings of red or white thrombi and in-stent white or yellow segments were identified from the corresponding angioscopic images.

**Statistical Analysis**

Qualitative data are presented as frequencies and quantitative data as medians (25th and 75th percentiles) or mean value ± SD. Categorical data were compared using either the chi-square test or Fisher’s exact test. Continuous data for NIT were tested by 1-way analysis of variance among the different categories (NC grade), and the post-hoc Fisher’s test was performed in case of significant differences. Receiver-operating characteristics analysis was used to assess the diagnostic accuracy of the optical intensity analysis in completely covered segments for detecting in-stent yellow segments. Other quantitative data were analyzed using an unpaired t-test. A 2-sided P-value <0.05 was considered statistically significant. Statistical analyses were performed

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**Table 1. Patients’ Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>22</td>
</tr>
<tr>
<td>No. of SES</td>
<td>26</td>
</tr>
<tr>
<td>Male</td>
<td>18 (82)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70.5±8.6</td>
</tr>
<tr>
<td>Follow-up (days)</td>
<td>306±182</td>
</tr>
<tr>
<td>Coronary risk factors</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 (50)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20 (91)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>18 (82)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>8 (36)</td>
</tr>
<tr>
<td>LAD/LCX/RCA</td>
<td>8 (31)/8 (31)/10 (38)</td>
</tr>
<tr>
<td>Type B2/C lesions*</td>
<td>22 (85)</td>
</tr>
<tr>
<td>CTO</td>
<td>5 (19)</td>
</tr>
<tr>
<td>Stent diameter (mm)</td>
<td>2.86±0.34</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>23.8±6.8</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). *Based on American College of Cardiology/American Heart Association classification. CTO, chronic total occlusion; LAD, left anterior descending artery; LCX, left circumflex artery; MI, myocardial infarction; RCA, right coronary artery; SES, sirolimus-eluting stent(s).

**Table 2. Angioscopic Assessment and Optical Coherence Tomographic Measurement**

<table>
<thead>
<tr>
<th>Angioscopic assessment</th>
<th>No. of segments</th>
<th>66</th>
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<tbody>
<tr>
<td>NC grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0/1</td>
<td></td>
<td>3 (4)/35 (53)</td>
</tr>
<tr>
<td>2/3</td>
<td></td>
<td>13 (20)/15 (23)</td>
</tr>
<tr>
<td>In-stent yellow segment</td>
<td></td>
<td>42 (64)</td>
</tr>
<tr>
<td>Red thrombus</td>
<td></td>
<td>11 (17)</td>
</tr>
<tr>
<td>Mural red thrombus</td>
<td></td>
<td>5 (8)</td>
</tr>
<tr>
<td>Peri-strut red thrombus</td>
<td></td>
<td>6 (9)</td>
</tr>
<tr>
<td>White thrombus</td>
<td></td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Optical coherence tomographic measurement</th>
<th>No. of segments</th>
<th>66</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cross-sections</td>
<td></td>
<td>420</td>
</tr>
<tr>
<td>Total no. of stent struts</td>
<td></td>
<td>3,199</td>
</tr>
<tr>
<td>Median NIT (μm)</td>
<td>60 (25th: 40; 75th: 130)</td>
<td></td>
</tr>
<tr>
<td>Average NIT (μm)</td>
<td>101±118</td>
<td></td>
</tr>
<tr>
<td>OCT mural thrombus</td>
<td>7 (11)</td>
<td></td>
</tr>
<tr>
<td>Mural red thrombus</td>
<td>6 (9)</td>
<td></td>
</tr>
<tr>
<td>Mural white thrombus</td>
<td>1 (2)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). NC grade, neointimal coverage grade; NIT, neointimal thickness.
Neoatherosclerosis and Thrombi: OCT vs. Angioscopy

Comparisons of Angioscopic Findings With OCT Findings

**NIT** The mean NIT on OCT increased in correspondence with increased NC grade on angioscopy in a stepwise fashion (NC grade 0: 5.6±3.9 µm; NC grade 1: 54±25 µm; NC grade 2: 114±68 µm; NC grade 3: 210±136 µm; P=0.28 for NC grade 0 vs. NC grade 1, P=0.02 for NC grade 1 vs. NC grade 2 and P=0.001 for NC grade 2 vs. NC grade 3). All the angiographic peri-strut thrombi occurred in segments classified as NC grade 1. Further, of the 5 angioscopic mural thrombi, 4 occurred in NC grade 1 segments and 1 occurred in an NC grade 2 segment.

**Red Thrombus** The OCT images of angioscopically detected peri-strut red thrombi were characterized by isointense material near protruding struts (Figure 3a), none of which could be determined as mural red thrombi based on the current OCT-based definitions. Among the 5 angioscopically detected mural red thrombi, 3 corresponded to the OCT-detected mural red thrombi (Figure 3c). However, the remaining 2 did not fulfill the definitions, instead resembling “peri-strut low-intensity area (PLIA)” on OCT images, as previously reported (Figure 3d). Some of these PLIA-like OCT images, however, demonstrated the presence of in-stent yellow segments without mural red thrombi (Figure 3e).

In contrast, among the 6 mural red thrombi diagnosed by OCT analysis were performed for the same 66 segments.

Mural thrombi were detected in 7 segments by OCT and of them, 1 was a mural white thrombus and the other 6 were mural red thrombi (Table 2).

**Results**

Overall, we enrolled 22 patients (18 males; age, 70.5±8.6 years) treated with 26 SES (66 segments); 12 segments were excluded from the analysis because of incomplete angioscopic or OCT image acquisition or inability to measure the signal intensity index because of strong signal attenuation. The average interval of follow-up angiography was 306±182 days (Table 1).

**Angioscopic and OCT Findings**

Among the 66 segments examined by angioscopy, NC grade 1 was most frequently observed, and 64% of all segments contained in-stent yellow segments (Table 2). Overall, red thrombi were detected in 11 segments (17%) and were more frequently observed in incompletely covered segments than in completely covered segments (10 [26%] vs. 1 [3%], P=0.02). Peri-strut red thrombi were also more frequently found in incompletely covered segments than in completely covered segments. Mural red thrombi, however, were observed only over in-stent yellow segments (Figure 2). On the other hand, a tiny white thrombus was detected in 1 segment, which was characterized as a completely covered, in-stent yellow segment.

OCT analysis was performed for the same 66 segments.

using MedCalc version 12.1.3.0 (MedCalc Software, Mariakerke, Belgium).
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"high-attenuation tissue underneath struts", and "low-attenuation and low-intensity tissue covering struts" (Figures 4c–e).

OCT images of in-stent yellow segments in completely covered segments were characterized by "high-attenuation tissue covering struts", whereas those of in-stent yellow segments in incompletely covered segments were characterized by "high-attenuation tissue underneath struts" or "low-attenuation and low-intensity tissue covering struts". Macrophage-like appearance was more frequently observed with OCT-defined neoatherosclerosis than with the other 2 OCT patterns of in-stent yellow segments (Figure 5).

**Figure 3.** Angioscopy and optical coherence tomography (OCT) images of intrastent thrombi. (A–D) Angioscopic images at the incompletely covered segment. (C–F) Angioscopic images at an in-stent yellow segment. (a–f) Corresponding OCT images: (a) peri-strut red thrombus, (b) without peri-strut red thrombus, (c, d) mural red thrombus, (e) in-stent yellow segment without red thrombus, (f) mural white thrombus. Red arrow indicates a mural red thrombus. White arrow shows a mural white thrombus.

**In-Stent White and Yellow Segments** In-stent white segments were categorized into 2 patterns by OCT: “high- and homogeneous-intensity tissue” or “high-intensity tissue underneath struts” (Figures 4a,b). Similarly, in-stent yellow segments were categorized into 3 patterns by OCT based on the presence of strut coverage and the intensity: “high-attenuation tissue covering struts” (OCT-defined neoatherosclerosis), “high-attenuation tissue underneath struts”, and “low-attenuation and low-intensity tissue covering struts” (Figures 4c–e). OCT images of in-stent yellow segments in completely covered segments were characterized by “high-attenuation tissue covering struts”, whereas those of in-stent yellow segments in incompletely covered segments were characterized by “high-attenuation tissue underneath struts” or “low-attenuation and low-intensity tissue covering struts”. Macrophage-like appearance was more frequently observed with OCT-defined neoatherosclerosis than with the other 2 OCT patterns of in-stent yellow segments (Figure 5).

**Relationship Between Angioscopically Detected Red Thrombi and OCT Patterns of In-Stent Yellow Segments** Among the 5 mural thrombi detected by angioscopy, 1 was located on “high-attenuation tissue covering struts”; 2 on
Figure 4. Comparisons of the angioscopy and optical coherence tomography (OCT) findings. (A) In-stent white segment with complete coverage. (B) In-stent white segment with incomplete coverage. (C) In-stent yellow segment with complete coverage. (D, E) In-stent yellow segment with incomplete coverage. (a–e) Corresponding OCT images.

Figure 5. Frequency of macrophage-like appearance at angioscopically detected in-stent yellow segments. It most frequently occurred with the “high-attenuation tissue covering struts” OCT pattern (OCT-defined neoatherosclerosis).
The OCT-measured NIT strongly correlated with the angioscopic NC grade. In terms of the relationship between the presence of angioscopically detected red thrombi, the angioscopic NC grade, and the NIT on OCT, all except 1 of the angioscopically detected red thrombi occurred in incompletely covered segments.

**Red and White Thrombi**

We observed 2 types of angioscopically detected red thrombi (peri-strut and mural), which differed distinctly in their angioscopic appearance. The detection rate of red thrombi by angioscopy was numerically higher than that by OCT; moreover, some angioscopic findings for red thrombi disagreed with those diagnosed as mural thrombi by OCT. All of the peri-strut red thrombi plus 2 of the 5 mural red thrombi identified on angioscopy could not be recognized as red thrombi on OCT (Figures 3a, d). The reason for this discrepancy is the difference between the definitions used for the angioscopic and OCT parameters for the detection of red thrombi. The OCT-defined mural red thrombus is a mass protruding into the lumen with significant attenuation, whereas red material can be categorized as red thrombi by angioscopy regardless of its morphology.

**Mean Signal Intensity Index of Completely Covered Neointima**

To quantitatively assess the presence of neoatherosclerotic changes in the neointima by OCT, we compared the mean signal intensity index of 18 segments showing in-stent yellow segments with “high-attenuation tissue covering struts” (OCT-defined neatherosclerosis) with that of 9 segments showing “high- and homogeneous-intensity tissue” (in-stent white segments with complete coverage). The mean signal intensity index of OCT-defined neoatherosclerosis was significantly lower than that of in-stent white segments with complete coverage (Figure 6A). The optimal cutoff value of the mean signal intensity index for identifying OCT-defined neoatherosclerosis was 0.9461 (sensitivity: 72.2%, specificity: 100%, area under the curve: 0.90) (Figure 6B).

**Discussion**

This is the first report describing the OCT characteristics of intrastent thrombi and in-stent yellow segments within SES by simultaneous application of OCT and angioscopy 10 months after stent implantation. Our primary findings are as follows. Red thrombi were more frequently detected by angioscopy than by OCT. Using the current OCT definitions, OCT failed to detect all of the angioscopically detected red thrombi. When in-stent yellow segments were classified into 3 OCT patterns, most cases of the macrophage-like appearance (91%) were observed for in-stent segments with the “high-attenuation tissue covering struts” OCT pattern (OCT-defined neoatherosclerosis). Mean signal intensity index analysis with a cutoff value of 0.9461 was clinically useful for in vivo detection of OCT-defined neoatherosclerosis.

**NIT**

The OCT-measured NIT strongly correlated with the angioscopic NC grade. In terms of the relationship between the presence of angioscopically detected red thrombi, the angioscopic NC grade, and the NIT on OCT, all except 1 of the angioscopically detected red thrombi occurred in incompletely covered segments.

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We observed 2 types of angioscopically detected red thrombi (peri-strut and mural), which differed distinctly in their angioscopic appearance. The detection rate of red thrombi by angioscopy was numerically higher than that by OCT; moreover, some angioscopic findings for red thrombi disagreed with those diagnosed as mural thrombi by OCT. All of the peri-strut red thrombi plus 2 of the 5 mural red thrombi identified on angioscopy could not be recognized as red thrombi on OCT (Figures 3a, d). The reason for this discrepancy is the difference between the definitions used for the angioscopic and OCT parameters for the detection of red thrombi. The OCT-defined mural red thrombus is a mass protruding into the lumen with significant attenuation, whereas red material can be categorized as red thrombi by angioscopy regardless of its morphology.

Two mural red thrombi detected only by angioscopy were characterized as “low-attenuation and low-intensity tissue covering struts” (so-called PLIA-like OCT image, Figure 3d), some of which demonstrated the presence of in-stent yellow segments without mural red thrombi (Figure 3e). This OCT image suggested the presence of hypocellular material on the SES-stented vessel wall; angioscopically, this red material suggested the presence of fibrin or red blood cells. In the process of arterial healing after stent implantation, adherence of red blood cells and inflammatory cells followed by transformation into fibrin deposition on the struts is required. Taking
these phenomena together, we speculate that angioscopically detected red material in stented segments may result from fibrin deposition with red blood cells on the SES-stented vessel wall through arterial healing after stent implantation. In contrast, of the 6 OCT-detected mural red thrombi, 3 corresponded with the angioscopically detected mural red thrombi; however, the remaining 3 were not confirmed as mural red thrombi by angioscopy. This may be because (1) angioscopy cannot always examine the whole surface of the surveyed vessel wall, whereas OCT can visualize the whole vessel surface, and because (2) OCT-based mural thrombi may not be identified as red thrombi by angioscopy because of the absence of red material. Taking these limitations together, we consider that the current OCT criteria for the detection of mural red thrombi sometimes fail to detect red thrombi. Therefore, physicians need to consider these limitations when using OCT in the clinical setting.

In-Stent Yellow Segments
In this study, we precisely examined in-stent yellow segments by simultaneous application of angioscopy and OCT, and characterized the angioscopically detected in-stent yellow segments into 3 OCT patterns. Neoatherosclerosis can occur within 1–2 years after implantation of first-generation DES.8,9 Angioscopy is considered the gold standard for detecting yellow plaques because of its full-color visualization; however, it has an inherent limitation in differentiating yellow neointima from yellow plaques underneath stent struts because of its lack of cross-sectional vessel wall analysis. In this study, we demonstrated that OCT could differentiate between yellow neointima and yellow plaques underneath stent struts by recognizing “high-attenuation tissue covering struts.” Moreover, the presence of this pattern was associated with a high rate of macrophage-like appearance, which is a known feature of vulnerable plaques.10 Owing to its ability to perform cross-sectional analysis, OCT can distinguish neoatherosclerosis from a plaque underneath the struts and provide valuable information on macrophage-like appearance.

In this context, OCT can also classify angioscopically detected in-stent yellow segments in incompletely covered (visible struts) segments into 2 groups: “high-attenuation tissue underneath struts” and “low-attenuation and low-intensity tissue covering struts” (Figures 4d,e). We speculate that these OCT patterns reflect the delayed process of arterial healing after SES implantation. “High-attenuation tissue underneath struts” might represent inhibited neointimal proliferation of SES implanted on underlying lipid-rich plaques. The angioscopic image of “low-attenuation and low-intensity tissue covering struts” was characterized by struts covered by a yellowish translucent membrane, which enabled us to delineate these plaques in the vessel wall underneath the struts. In contrast to the yellow appearance of atheromatous plaques induced by deposition of β-carotene,18,19 the corresponding OCT image suggested that this translucent membrane is in fact loose hypocellular material; however, this has not been validated by histopathologic examination.

Relationship Between Angioscopically Detected Red Thrombi and OCT Patterns of In-Stent Yellow Segments
Of the 3 mural red thrombi that were detected on both angioscopy and OCT, 2 were located at the “high-attenuation tissue underneath struts” OCT pattern and 1 was located at the “high-attenuation tissue covering struts” (so-called neoatherosclerosis) OCT pattern. In their angioscopic study, Higo et al used mid-term angioscopic follow-up and reported similar findings, wherein the prevalence of red thrombi was higher in newly formed yellow neointima and in poor-coverage neointima.20 Recent clinical studies have also suggested that SES implantation can induce coronary artery endothelial dysfunction with impaired vasomotor function in adjacent stent segments even if the SES struts are completely covered by neointima.20 Therefore, we consider that the occurrence of mural thrombi within SES may be related to such endothelial dysfunction derived from neoatherosclerosis as well as incomplete NC.

Mean Signal Intensity Index of Completely Covered Neointima
OCT tissue characterization is typically based upon qualitative assessments, resulting in confusion in borderline cases. A recent study demonstrated that the ratio of the optical intensity of the surrounding tissue to that of the area of stent struts provided information on fibrin- or neointima-covered struts that was validated by electron and light microscopy analyses.17 Therefore, in this study, we used a mean signal intensity index to examine whether this was a useful technique for accurately detecting OCT-defined neoatherosclerosis and our results indicated that it was indeed useful (Figure 6). Although our results were not validated by pathological analysis, the overall incidence of OCT-defined neoatherosclerosis in patients with DES in-stent restenosis appears to correspond with that reported by previous pathological, intravascular ultrasonographic, and OCT studies.8,12 In addition, the majority of cases of macrophage-like appearance (a marker of unstable plaque) occurred at segments with OCT-defined neoatherosclerosis. Therefore, we hypothesize that a mean signal intensity index may be useful for detecting neoatherosclerosis after SES implantation in vivo. A large-scale pathology-controlled study is warranted to validate our present findings.

Study Limitations
Our study has certain limitations. First, the current angioscopic and OCT observations were performed retrospectively in a relatively small number of patients at a single center, with widely varying lesion characteristics; this inevitably resulted in selection bias. Second, angioscopy cannot always visualize the same location of the tissue visualized by OCT. Third, our findings were not validated by pathological analysis; therefore, we do not accurately know whether OCT-defined neoatherosclerotic tissue truly contains atherogenic changes and whether all OCT images with macrophage-like appearance reflect the presence of a high concentration of macrophages. Finally, the status of plaque color at the stenotic lesion before SES implantation was unknown because no angioscopic study was performed immediately after SES implantation. Therefore, we cannot confirm whether the angioscopically detected in-stent yellow segments in incompletely covered segments were newly formed or had persisted from before SES implantation.

Conclusions
Although the current OCT-based definitions for thrombus detection may underestimate the presence of subclinical red thrombi, detailed OCT assessment combined with qualitative and quantitative evaluation of the neointima may enhance the detection of neoatherosclerosis over SES in vivo.

Disclosures
Financial Support: No conflicts of interest.
References


