Intriguing Peri-Strut Low-Intensity Area Detected by Optical Coherence Tomography After Coronary Stent Deployment

Tomohiko Teramoto, MD, PhD; Fumiaki Ikeno, MD; Hiromasa Otake, MD, PhD; Jennifer K. Lyons; Heleen M. M. van Beusekom, PhD*; William F. Fearon, MD; Alan C. Yeung, MD

Background: Although peri-strut low-intensity area (PLIA) is frequently observed on post-stenting optical coherence tomography (OCT) images, the histology associated with PLIA is undocumented.

Methods and Results: The 36 porcine coronary lesions treated with bare-metal (BMS: n=16) or drug-eluting (DES: n=20) stents were assessed by OCT and histology at 28 days. DES showed a significantly higher incidence of PLIA than BMS. Also, +PLIA stents had greater neointima than −PLIA stents. Histological analysis revealed the existence of fibrinoid and proteoglycans at the site of PLIA.

Conclusions: PLIA might be represented by the presence of fibrinoid and proteoglycans, and associated with neointimal proliferation after stenting. (Circ J 2010; 74: 1257–1259)

Key Words: Drug-eluting stent (DES); Optical coherence tomography (OCT); Restenosis

The use of optical coherence tomography (OCT) in the clinical filed is a recent development. Although peri-strut low-backscattering, a low intensity area, is often detected by OCT after stent deployment, published remarks about the corresponding histology are absent. Therefore, in this study, we termed this characteristic image as peri-strut low-intensity area (PLIA: Figure 1A) and compared it with histology.

Methods

Animals
Six Juvenile Yorkshire pigs were used. Animal protocols were approved by the Stanford University Administrative Panel on Laboratory Animal Care.

OCT Procedure and Assessment
We deployed 16 bare-metal stents (BMS) and 20 drug-eluting stents (DES) (11 sirolimus-eluting stents (SES) Cypher™, Cordis Corp, 9 paclitaxel-eluting stents (PES) TAXUS™, Boston Scientific) in each coronary artery. At 28 days, OCT imaging was performed with the M2 OCT system (LightLab Imaging Inc, Westford, MA, USA) as previously reported. Motorized OCT pullback was performed at a rate of 1.0 mm/s with 15 frames/s.

The area of both the lumen and stent was measured every 1 mm and the percent neointimal area (%NIA) was calculated as the lumen/stent×100. To quantify the prevalence of struts with PLIA, the percentage of stent struts with PLIA (%PLIA struts) was calculated as the number of struts with PLIA divided by the number of visible struts×100.

Definition of PLIA
PLIA was defined as a region around stent struts with a homogeneous, lower intensity appearance than the surrounding tissue on OCT images without significant signal attenuation behind the area (Figure 1A). We judged the existence of PLIA only when we obtained clear stent strut images, and by the agreement of 2 independent experienced investigators blinded to the results of histology.

Histology
At 28 days, all pigs were killed humanely. The stented coronary arteries were dissected and serial cross-sections were obtained at 0.6-mm intervals. These sections were surface-stained with hematoxylin–eosin (HE). A subset of sections was stained with and Alcian blue. OCT images and HE-stained cross-sections were matched within ±0.2 mm by the distance from the proximal end of the stent strut, as previously described. Each histological specimen was oriented to

Received March 2, 2010; revised manuscript received April 16, 2010; accepted April 18, 2010; released online April 29, 2010  Time for primary review: 15 days  
Department of Cardiovascular Medicine, Stanford University, Stanford, CA, USA, *Department of Experimental Cardiology, Erasmus MC, Rotterdam, the Netherlands  
Mailing address: Fumiaki Ikeno, MD, Division of Cardiovascular Medicine, Falk Cardiovascular Research Building, 300 Pasteur Drive, CV-007, Stanford, CA 94305-5406, USA  
E-mail: fiken@cvmed.stanford.edu  
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the OCT image by the morphology of the stented lumen.

**Statistical Analysis**

Statistical analyses were performed with JMP 7 (SAS institute Inc, Cary, NC, USA). Unpaired t-test was used for the analysis of continuous variables. A P-value <0.05 was considered statistically significant.

**Results**

Of 36 stents, PLIA was observed in 16 (SES 9, PES 4, BMS 3). The incidence of PLIA was significantly higher in DES than in BMS (65% (13/20) vs 19% (3/16), P<0.001). Among stents with PLIA, no significant difference was observed in %PLIA struts between DES and BMS (44.0±23.7% vs 40.0±21.8%, P=0.89). Overall, stents with PLIA showed significantly greater %NIA than stents without PLIA (47.8±18.9% vs 34.6±18.7%, P=0.04). This difference still existed in each stent group (BMS: 63.0±14.5% vs 35.0±16.5%, P<0.01; DES: 45.5±18.3% vs 27.6±18.9%, P=0.05).

Among the DES, SES showed a numerically higher incidence of PLIA than PES (73% (8/11) vs 56% (5/9), P=0.15). The %NIA was numerically but nonsignificantly greater with SES than with PES (40.7±22.1% vs 31.4±18.6%, P=0.30). Similarly, among stents with PLIA, a numerically greater %PLIA struts was observed with SES than with PES (43.2±26.3% vs 31.3±10.9%, P=0.26).

Histological analysis showed a neointima typically consisting of an innermost neointimal layer with concentric orientation of smooth muscle cells (Figure 1B). The regions corresponding with PLIA were distinguished as hypocellular (stained pink, hematoxylin–eosin), suggesting the presence of fibrinoid and/or hyaline extracellular protein (arrow: corresponding site with PLIA on OCT). (C) Histological specimen corresponding to PLIA on OCT imaging (medium magnification). The region corresponding to PLIA is distinguished as hypocellular (stained pink, hematoxylin–eosin), suggesting the presence of fibrinoid and/or hyaline extracellular protein (arrow: corresponding site with PLIA on OCT). (D) Histological specimen corresponding to PLIA on OCT imaging (high magnification). Some macrophages (arrowhead) and lymphocytes (arrows) can be seen. Inflammatory cell infiltrate implies chronic inflammation, and there is a small amount of fibrosis. (Bars, B: 1 mm, C: 500 μm, D: 20 μm.)

**Discussion**

To the best of our knowledge, this is the first report of the...
histological changes corresponding with PLIA seen on OCT images. After stent deployment, it is generally considered that neointimal formation involves the replacement of fibrin by extracellular matrix. Judging from the pathological findings of the present study, PLIA might represent the existence of fibrinoid. Neither eosinophilic cell infiltration nor proteoglycans was observed in direct association with the struts in these regions.

In a recent human pathological study, Beusekom et al clearly showed the presence of acellular areas after DES implantation, but not with BMS, which appears to support our finding that PLIA was observed more frequently with DES than BMS. In a study assessing the relationship between sirolimus dose and pathological findings, fibrinoid tissue surrounding SES struts was observed in a sirolimus-dose-dependent manner. Considered together, drug eluted from DES might contribute to the process of PLIA formation. The presence of PLIA might reflect a difference between DES and BMS for arterial healing.

According to previous studies, extracellular matrix remodeling plays an essential role in neointimal formation and excessive matrix formation is a determinant of failure of radiation therapy. Our findings are in accordance with those reports, showing greater neointimal proliferation in stents with PLIA than in stents without PLIA, for both DES and BMS. In contrast to a human study, SES showed numerically greater %NIA than PES in this porcine model. Interestingly, SES also showed a numerically higher incidence of PLIA than PES, with a greater prevalence of struts with PLIA. These findings might represent different healing processes with SES and PES, which may be associated with different neointimal proliferation during follow-up. Further evaluation might be needed for the better understanding of the possible role of PLIA in the process of arterial healing after stenting.

Study Limitations
First, porcine vascular reactivity to intravascular intervention may differ from that of humans. Second, despite our endeavors for precision, the judgment of the existence of PLIA might include some intuition. Finally, technical limitations include the difficulty in exactly matching the histologic cross-sections with the OCT images.

Disclosures
Conflict of Interest: none declared.

Acknowledgment
We appreciate the assistance of Heidi N Bonneau, RN, MS, CCA.

References