Measurement of Stent healing by OCT.

Key Points:

- Optical coherence tomography is superior to other imaging modalities in gauging the degree of stent tissue coverage
- Study results show that at 3 months, bare-metal stents are well covered,while sirolimus-eluting stents remain poorly covered
- Longer follow-up is needed to track changes in coverage of sirolimus-eluting stents and to determine whether coverage is a reliable predictor of decreased thrombosis risk

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By Kim Dalton

Optical coherence tomography (OCT) shows that at 3 months postimplantation, bare-metal stents (BMS) are well covered with neointimal tissue, suggesting that patients with such devices may no longer need dual antiplatelet therapy. On the other hand, sirolimus-eluting stents (SES) remain uncovered or poorly covered over the same time period.

Despite this finding, reported in a study published online April 28, 2008, ahead of print in the *American Journal of Cardiology,* there was no significant difference in the incidence of stent thrombosis within the 3-month time frame.

The investigators, led by Masamichi Takano, MD, PhD, of Nippon Medical School (Tokyo, Japan), used high-resolution OCT to compare coverage of BMS vs. SES. Pathologic research has demonstrated that incomplete neointimal coverage of stent struts is the strongest morphometric predictor of late stent thrombosis.

According to the researchers, earlier angioscopic studies suggested that complete coverage of BMS required 3 to 6 months. Angioscopy, however, cannot quantify the proportion and thickness of neointimal coverage. And intravascular ultrasound (IVUS) may not provide detailed information about the neointima. OCT yields axial resolution of about 10 to 20 µm, 10 times greater than that of IVUS. This enables visualization of neointima formation and stent malapposition—which plays a significant role in late stent thrombosis.

For the study, the researchers performed OCT on 40 patients, 16 of whom had received BMS (1 of 3 designs) and 24 of whom received SES (Cypher, Cordis/Johnson & Johnson, Miami Lakes, FL). The BMS group had larger reference vessel diameters and thus larger stent diameters than the SES group. The BMS group also had shorter stent lengths.

Neointimal thickness on each strut and the percentage of neointimal area per OCT cross section were greater in the BMS group, while the frequency of uncovered struts was higher in the SES group. In addition, malapposed struts were more common in the SES group, and a higher percentage of uncovered struts showed malapposition (table 1).

Table 1. OCT Analysis of Stent Struts at 30 Days

	SES (5,076 struts)	**BMS** (2,875 struts)	***P* Value**
NIH* Thickness (µm)	31 ± 39	351 ± 248	<0.0001
Uncovered Struts	741 (15%)	3 (0.1%)	<0.0001
Malapposed Struts	777 (15%)	33 (1.1%)	<0.0001
Uncovered Struts with Malapposition	320 (6%)	3 (0.1%)	<0.0001

**NIH = Neointimal hyperplasia*

Several hypotheses have been put forward to explain the connection between malapposition and poor stent coverage, the researchers note, including:

- The antiproliferative effects of sirolimus may inhibit the growth of tissue in the space between the struts and the vessel wall.
- Local artery hypersensitivity reactions to the polymer and drug may induce positive vessel remodeling out of proportion to the increase in intimal hyperplasia.

The Two Faces of SES

The researchers observed that while SES had a larger lumen area than BMS, most SES struts were poorly covered (<50 µm thickness). They concluded, "These findings verified the premise that SES not only inhibited hyperproliferation of neointima [that leads to] restenosis but also suppressed the endothelial healing process over the struts, thus leaving the metallic struts and polymer exposed to the lumen as thrombogenic components."

In the study, uncovered stent struts were found in both groups, although the incidence was much higher in SES patients. Yet even in the SES group, thrombi were found in only 14% of patients (no BMS patients experienced thrombosis). The researchers say this implies that late stent thrombosis is a multifactorial process and that uncovered struts may only provide an underlying substrate for thrombi formation.

In an e-mail communication with TCTMD, Dr. Takano wrote, "Our serial OCT observation shows that uncovered stent struts decreased from 3-month to 6-month follow-up . . . . However, some of the uncovered [SES] struts persist for up to 2 years, and potential risk may remain."

What Does Stent "Coverage" Cover?

Dr. Takano acknowledged that OCT has significant limitations. "A thin fibrin layer or thrombus may be recognized as neointima," he wrote. Moreover, structures identified as neointima may not have "mature endothelial functions."

In a telephone interview with TCTMD, Juan F. Granada, MD, of The Jack H. Skirball Center for Cardiovascular Research (Orangeburg, NY), agreed, cautioning that "it's important not to take ["coverage"] as a surrogate of endothelialization—or the risk of thrombosis in the future."

Dr. Takano suggested that "confirming complete stent coverage by coronary imaging modalities such as OCT may become an index of medical management [with] aspirin monotherapy." Dr. Granada concurred that in the future, researchers will likely correlate the number of exposed struts with stent thrombosis risk, using that information to define when clopidogrel therapy may be safely stopped. But for now, he emphasized, it is too early to make any assumptions.

Dr. Granada concluded that although this is a small, short-term study, it represents a "good first effort" and "the beginning of a new era" of using OCT to assess stent coverage.

Note:
The Jack H. Skirball Center for Cardiovascular Research is the preclinical facility of the Cardiovascular Research Foundation, which owns and operates TCTMD.