OCT in the Evaluation of Vascular Healing Following DES Implantation: Will It Be a Helpful Tool to Reduce Stent Thrombosis?

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Why Do We Need to Perform Advanced Endovascular Imaging in Contemporaneous PCI?
### Issue #1: Clinical Evidence (OCT) of Delayed Healing in Humans

<table>
<thead>
<tr>
<th>Normal Healing in a Human in a <strong>Bare Metal Stent</strong> at 13 Months Follow Up</th>
<th>Abnormal Healing in a Human in a <strong>Cypher™ Stent</strong> at 6 Months Follow Up</th>
</tr>
</thead>
</table>

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G. Guagliumi MD, Ospedali Riuniti di Bergamo
Issue #2: Pathological Correlates of Late DES Thrombosis

> 30 Days Implants
Covered

Uncovered

P<0.0001

% Struts with endothelium

Thrombus
No Thrombus

% Uncovered struts

n=28
p<0.0001

n=34

Finn AV, et al., Circulation 2007;115:2435-2441
**Issue #3: Late Loss by QCA: Threshold for Detecting OCT-NT**

Segment 7

**Late Loss by QCA: Threshold for Detecting OCT Neointimal Thickness**

- $R = 0.604$
- OCT Neointimal Thickness = 0.415 mm

High Resolution Near Field Imaging of Stent and Peri-Stent Areas

- Homogeneous NI growth
- Homogeneous NI growth
- Inhomogeneous NI growth
- Post balloon

- Malapposed uncovered struts
- Malapposed covered struts
- Malapposed covered struts
- Malapposed struts w/ thrombus
Comparison of neointimal coverage of sirolimus-eluting stents and Paclitaxel eluting stents using optical coherence tomography at 9 months after implantation.

Evaluation in 3 months duration of neointimal coverage after zotarolimus-eluting stent implantation by optical coherence tomography: the ENDEAVOR OCT trial.

An optical coherence tomography study of a biodegradable vs. durable polymer-coated limus-eluting stent: a LEADERS trial sub-study.

Incomplete stent apposition and delayed tissue coverage are more frequent in drug-eluting stents implanted during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction than in drug-eluting stents implanted for stable/unstable angina: insights from optical coherence tomography.
How Could OCT Evaluate Vascular Healing Following DES Implantation?

1. Assessing the **amount of neointimal tissue** formed on the surface of the strut.
2. Quantifying the **number of stent struts** that are properly covered.
3. Assessing the degree of **functional stent coverage**.
4. Characterizing the **tissue type** covering the struts (i.e., fibrin).

*Picture courtesy of Renu Virmani*
Evaluation of Vascular Healing Using OCT Following DES Implantation
A Histology Correlation Study in Swine

- 14 Swine, 42 Stents (11 Vision, 11 Xience, 10 Endeavor, 10 Taxus)
- OCT acquisition: LightLab Imaging, time domain OCT, 1300nm, reported resolution of 15 um, pullbacks obtained at 1mm/sec, 15.6Hz frame rate:
  - 396 total frames analyzed (143 matched with histology)
  - Second observer for intra- and interobserver variability
  - Measured: NA, %AS, NT, uncovered and covered struts
- Histology analysis:
  - Sectioned to correspond with OCT, stained with H&E and van Gieson’s
  - Histomorphometry: Neointimal area, %AS, NT, uncovered and covered struts
  - SEM: overall assessment of lumen coverage and endothelialization

Analysis of **Neointimal Area** Using OCT in Different DES (28 Days)

<table>
<thead>
<tr>
<th>Neointima</th>
<th>Correlation Coefficient</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endeavor</td>
<td>0.9821</td>
<td>0.9667, 0.9904</td>
</tr>
<tr>
<td>TAXUS</td>
<td>0.9667</td>
<td>0.9339, 0.9834</td>
</tr>
<tr>
<td>ML VISION</td>
<td>0.9546</td>
<td>0.9190, 0.9748</td>
</tr>
<tr>
<td>XIENCE V</td>
<td>0.9302</td>
<td>0.8712, 0.9628</td>
</tr>
</tbody>
</table>

Analysis of %AS Using OCT in Different DES Types (28 Days)

<table>
<thead>
<tr>
<th>% Stenosis</th>
<th>Correlation Coefficient</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endeavor</td>
<td>0.984</td>
<td>0.9702, 0.9914</td>
</tr>
<tr>
<td>TAXUS</td>
<td>0.9867</td>
<td>0.9730, 0.9935</td>
</tr>
<tr>
<td>VISION</td>
<td>0.9748</td>
<td>0.9549, 0.9859</td>
</tr>
<tr>
<td>XIENCE V</td>
<td>0.96</td>
<td>0.9252, 0.9788</td>
</tr>
</tbody>
</table>

Analysis of Neointimal Thickness Using OCT in Different DES (28 Days)

Analysis of **Stent Area** Using OCT in Different DES Types (28 Days)

Challenges of Evaluation of Stent Area: OCT versus Histology

PROXIMAL

MID

DISTAL
OCT Intra-Observer Variability

Stent

\[ y = 1x - 0.0261 \]

\[ r^2 = 0.95816 \]

Lumen

\[ y = 0.98x + 0.000936 \]

\[ r^2 = 0.99242 \]

Neointimal Area

\[ y = 0.95x + 0.253 \]

\[ r^2 = 0.97981 \]

Neointimal Thickness

\[ y = 0.96x + 0.0242 \]

\[ r^2 = 0.97521 \]

OCT Inter-Observer Variability

Stent

\[ y = 0.99x + 0.149 \]

\[ r^2 = 0.91747 \]

Lumen

\[ y = 0.98x + 0.00941 \]

\[ r^2 = 0.99253 \]

Neointimal Area

\[ y = 0.92x + 0.355 \]

\[ r^2 = 0.97003 \]

Neointimal Thickness

\[ y = 0.92x + 0.0393 \]

\[ r^2 = 0.96215 \]

Evaluation of Peri-Strut Coverage: OCT versus Histology
OCT Evaluation of **Strut Coverage** Following DES Implantation

- **Covered**
- **Uncovered**
- **Inconclusive**
- **Unknown**
Analysis of **Strut Coverage** Using OCT in Different DES Types (28 Days)

Uncovered (<20 microns)

\[ y = 0.98x + 0.0471 \]

\[ R^2 = 0.78947 \]
Proportion of Neointimal Thickness by OCT & Histology in DES: Implications for Individual Strut Coverage Analysis

Patterns of Strut Coverage Overtime

OCT Analysis BMS vs. DES at 4 Days

DES had twice as many covered struts compared to BMS
Patterns of Strut Coverage Overtime

OCT Analysis BMS vs. DES at 10 Days

- BMS has more covered struts than DES
- Increased number of “difficult to analyze” struts in DES
Patterns of Strut Coverage Overtime
OCT Analysis BMS vs. DES at 28 Days

Stent Strut Coverage (BMS at 28 days)
N= 294
- Covered: 86% (254)
- Uncovered: 14% (40)

Stent Strut Coverage (DES at 28 days)
N= 229
- Covered: 72% (166)
- Uncovered: 22% (51)

Uncovered struts by OCT persist only in the DES group
Strut Coverage Analysis
OCT versus Histology

4 Days

Unknown: 0, 19
Inconclusive: 0, 4.7
Uncovered: 3.87, 57.2
Covered: 19.15

28 Days

Unknown: 0, 14.45
Inconclusive: 0, 0.37
Uncovered: 2.5, 1.74
Covered: 19.15, 83.4

Percentage (%)
Strut Coverage Analysis
OCT versus Histology

10 Days

- Unknown: 9.52%
- Inconclusive: 2.98%
- Uncovered: 40%
- Covered: 60%

28 Days

- Unknown: 14.45%
- Inconclusive: 0.37%
- Uncovered: 2.5%
- Covered: 97.5%
“The Protruding Strut”: Implications for Healing and Coverage

Covered

Protruding
The Protruding Strut: Is It an OCT Surrogate of Vascular Healing?

HD versus Cypher p<0.001
LD versus Xience p<0.001
Cypher versus Xience p<0.001

Protruding Struts by OCT Display Lower Degrees of Neointimal Thickness at 14 Days

Uncovered Struts Are Frequently Seen on Protruding Strut Evaluated by OCT at 14 Days

1427 stent struts were analyzed

Different Neointimal Patterns Seen in OCT Following DES Implantation

Cypher - 6 Months  Cypher - 6 Months  Taxus - 13 Months
Therefore, several OCT imaging patterns may be the result of the deposition of different tissue types carrying different biological consequences.
Assessment of Strut Coverage: Volumetric Stent Analysis

Strut Coverage Map

3-D reconstruction – In-vivo Fresh Stent Implantation, Helios Heart Center

Tissue Characterization
Today, due to significant improvements in OCT technology, the \textit{in vivo} assessment of vascular healing following stent implantation is possible.

OCT can accurately and reproducibly measure subtle changes in neointimal area, thickness, and percent area of stenosis.

The assessment of strut coverage is feasible and reproducible. However, its clinical significance is still unknown and further research is required to elucidate the importance of this finding.

As these biological changes may be technology-specific, tissue characterization studies of different DES technologies are essential.

Due to its technical limitations in the far field, OCT combination technologies may be required.

In the future, it is possible that lessons learned from prospective clinical trials using this technology will provide the basis of DES safety profile enhancement.