

OCT Assessment of Post-DES Vascular Healing: Experimental Insights and Histology Correlates

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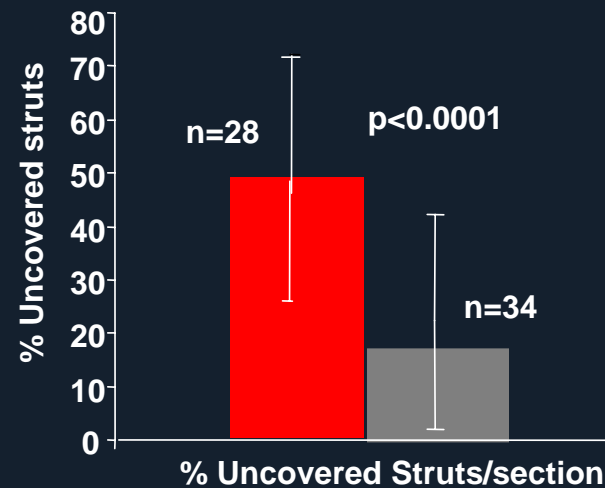
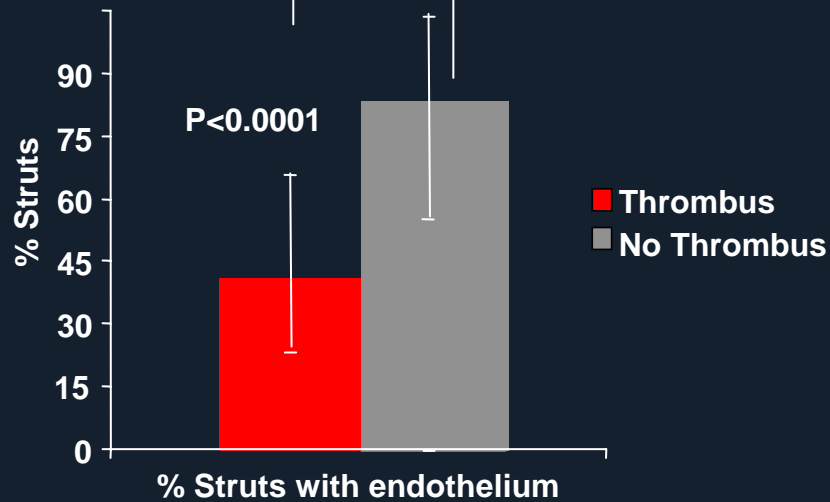
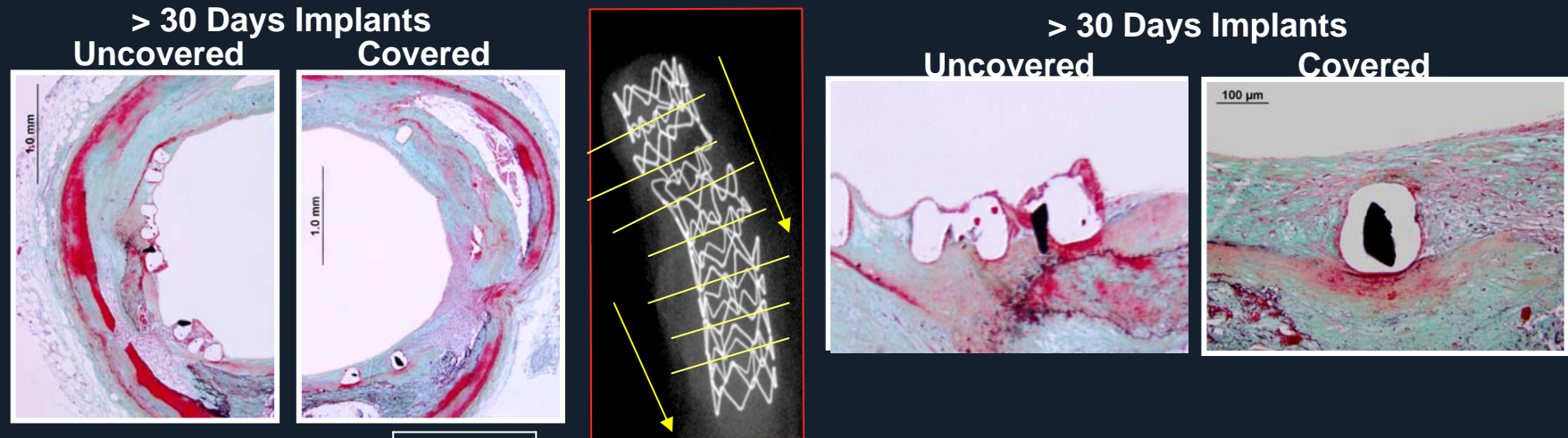
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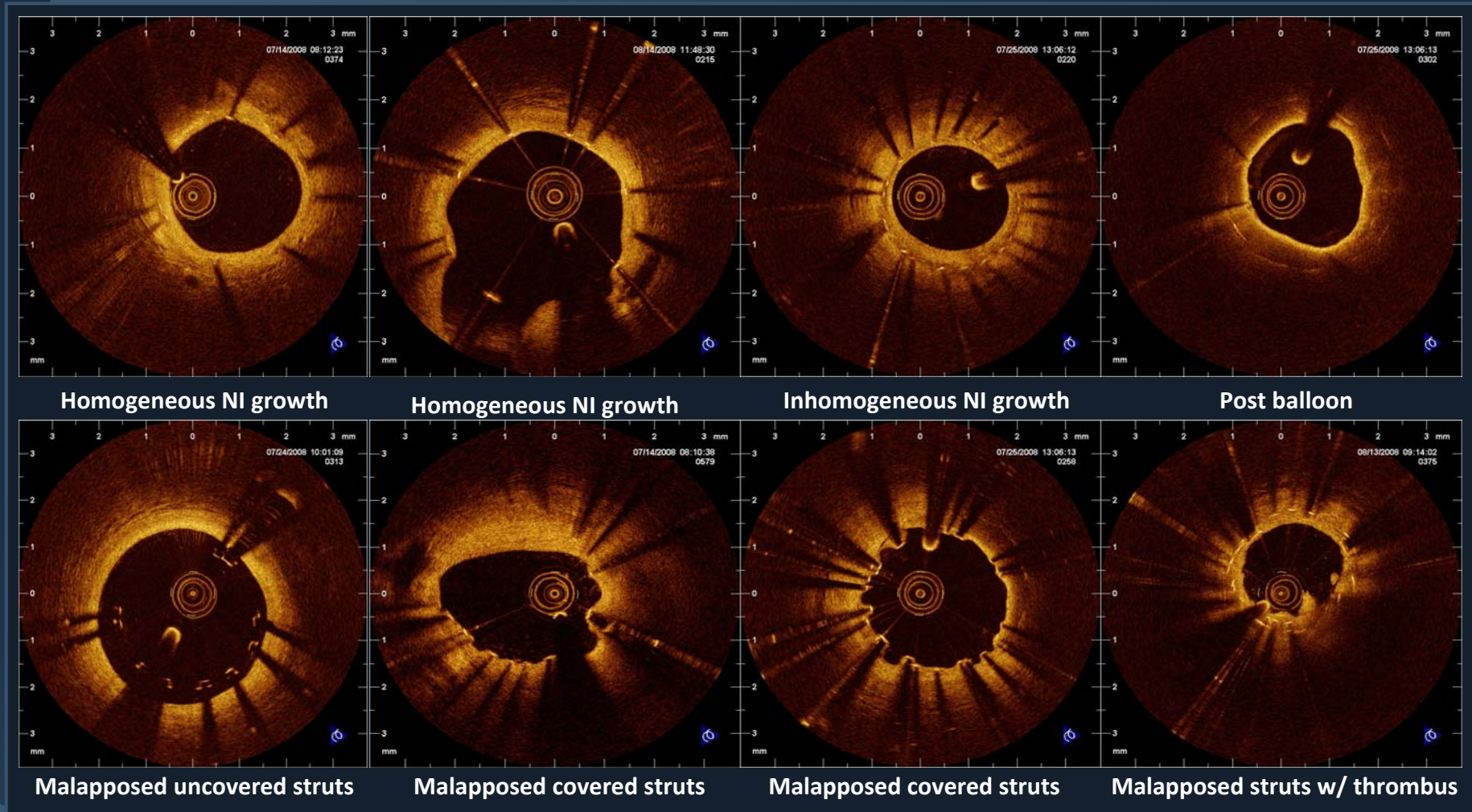
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Pathological Correlates of Late DES Thrombosis: Strut Coverage



Finn AV, et al., *Circulation* 2007;115:2435-2441

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



OCT and Vascular Healing Assessment Following DES Implantation

- Due to the high resolution, OCT is rapidly emerging as the “ideal” clinical tool for evaluating vascular healing following DES implantation:
 - *Visualization of intimal proliferation of drug-eluting stent and bare metal stent by use of optical coherence tomography. Chen et al. Zhonghua Yi Xue Za Zhi. 2006 Apr 25;86(16):1102-6.*
 - *Neointimal coverage of sirolimus-eluting stents at 6-month follow-up : evaluated by optical coherence tomography. Matsumoto et al. Eur Heart J. 2007 Apr;28(8):961-7.*
 - *Neointimal coverage of bare-metal and sirolimus-eluting stents evaluated with optical coherence tomography. Chen BX et al. Heart. 2008 May;94(5):566-70.*
 - *Neointimal coverage of sirolimus-eluting stents 6 months and 12 months after implantation: evaluation by optical coherence tomography. Yao ZH. Chin Med J (Engl). 2008 Mar 20;121(6):503-7.*
 - *Optical coherence tomography: high resolution intravascular imaging to evaluate vascular healing after coronary stenting. Guagliumi G et al. Catheter Cardiovasc Interv. 2008 Aug 1;72(2):237-47.*
- **However, the ability of OCT to make accurate measurements of stent strut coverage has not been validated in vivo.**



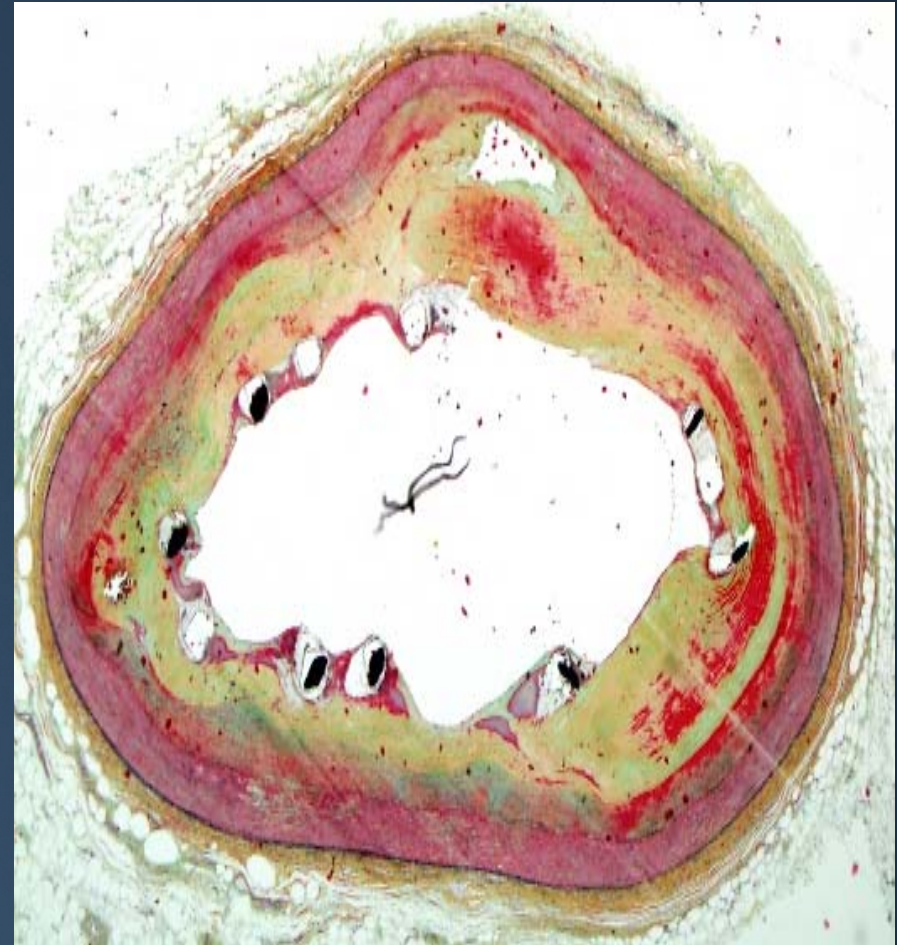
How Could OCT Evaluate Vascular Healing Following DES Implantation?

PRESENT:

- Assessing the ***amount of neointimal tissue*** formed on the surface of the strut.
- Quantifying the ***number of stent struts*** that are properly covered.

FUTURE:

- Assessing the degree of ***functional stent coverage***.
- Characterizing the ***tissue type*** covering the struts (i.e., fibrin).

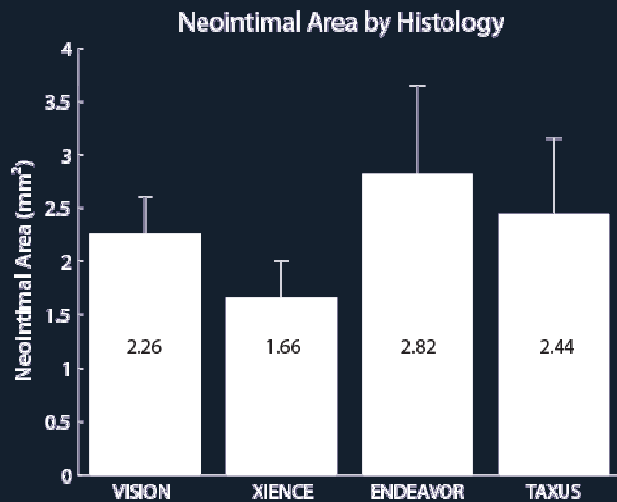
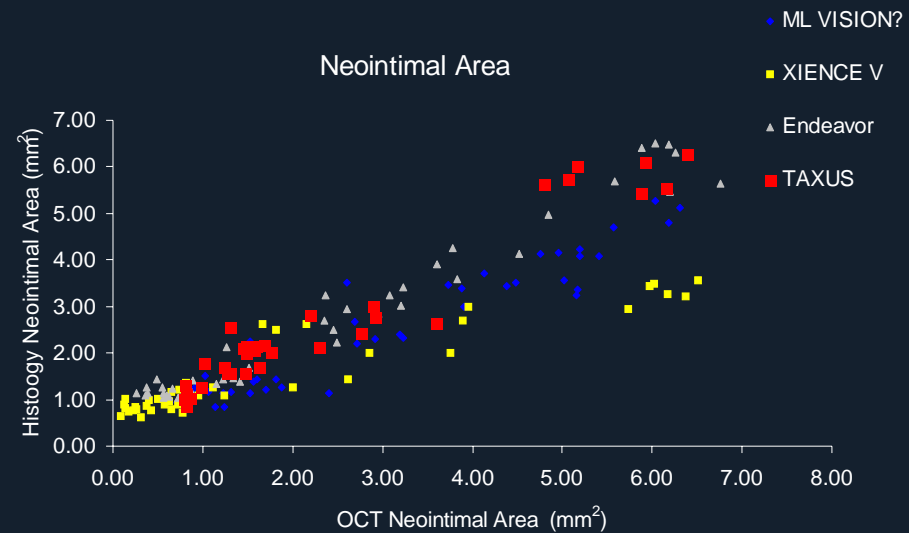
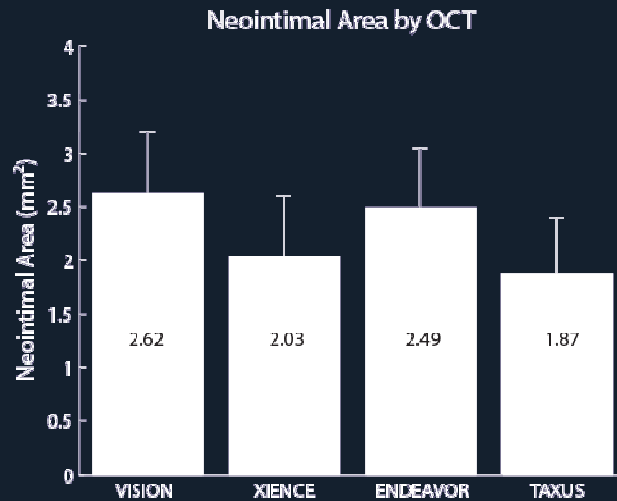


Validation of Several Morphometric Parameters Analyzed Following OCT: A Histology Correlation Study in Swine

- 14 Swine, Stents (11 Vision, 11 Xience, 10 Endeavor, 10 Taxus)
- OCT acquisition: LightLab Imaging, time domain OCT, 1300nm reported resolution of 15 μ m, pullbacks obtained at 1mm/sec, 15.6Hz frame rate:
 - *396 total frames were analyzed (143 matched with histology).*
 - Second observer for intra and inter observer 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



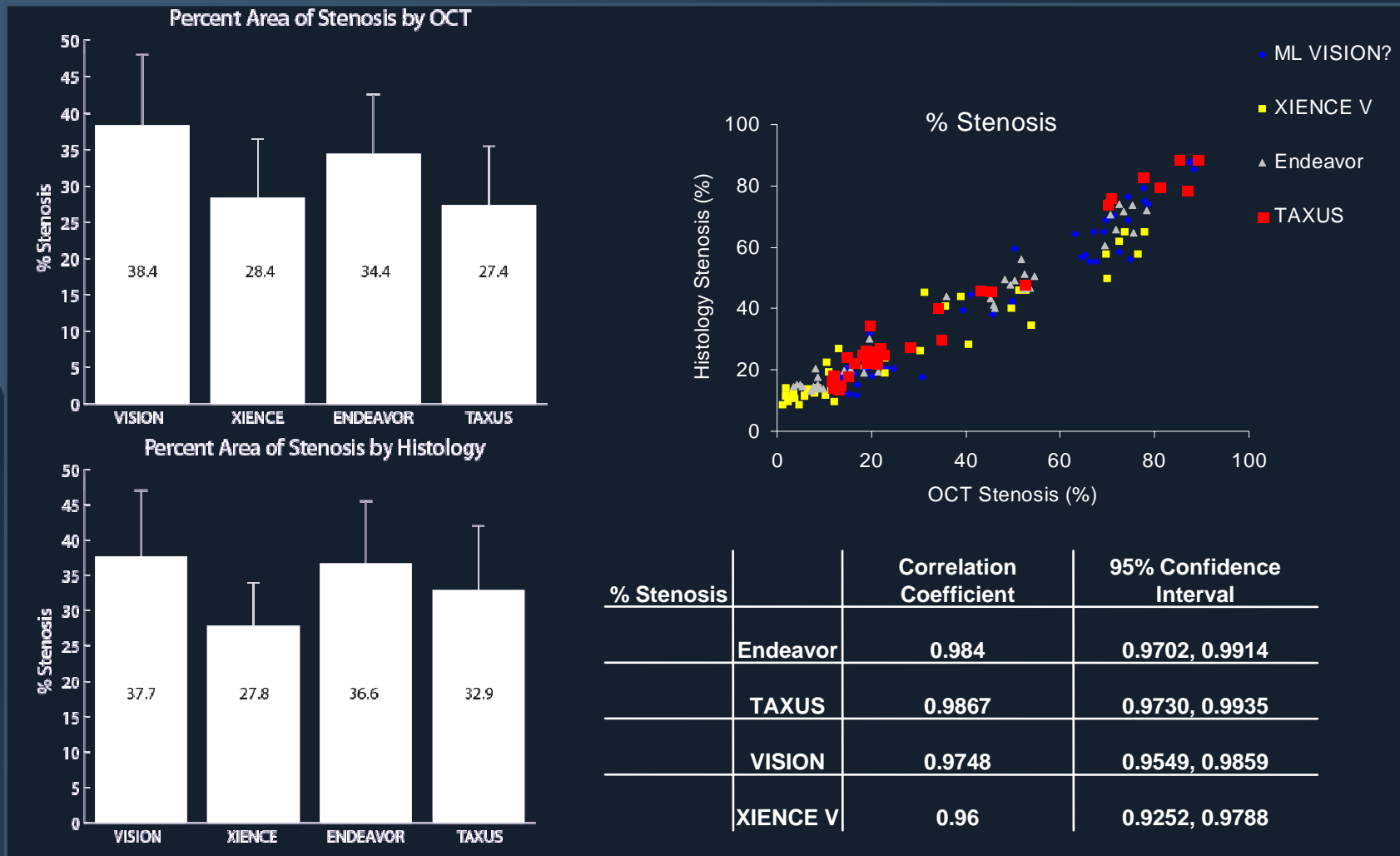
Analysis of Neointimal Area Using OCT in Different DES Types (28 Days)



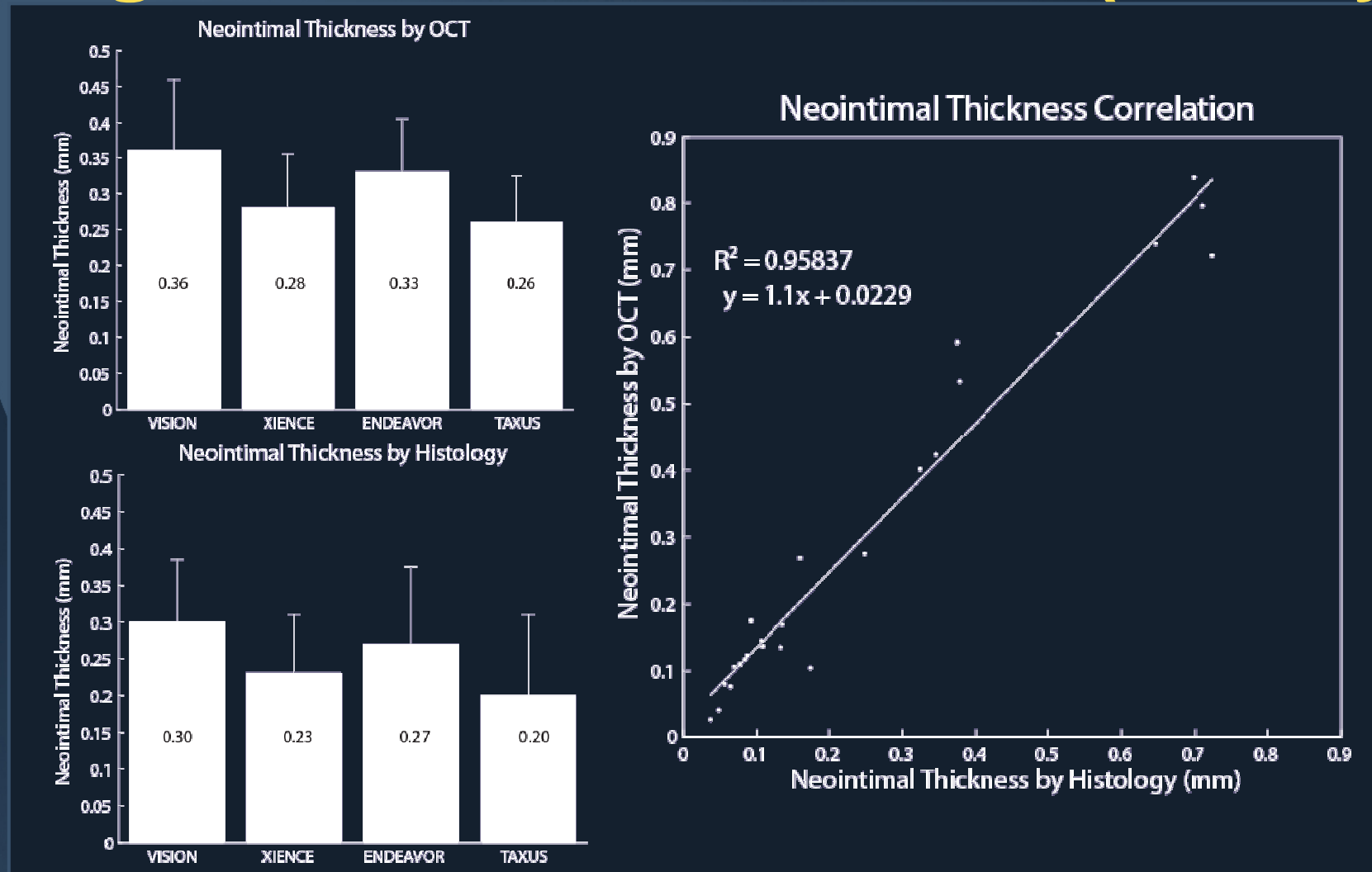
Neointima	Correlation Coefficient	95% Confidence Interval
Endeavor	0.9821	0.9667, 0.9904
TAXUS	0.9667	0.9339, 0.9834
ML VISION	0.9546	0.9190, 0.9748
XIENCE V	0.9302	0.8712, 0.9628



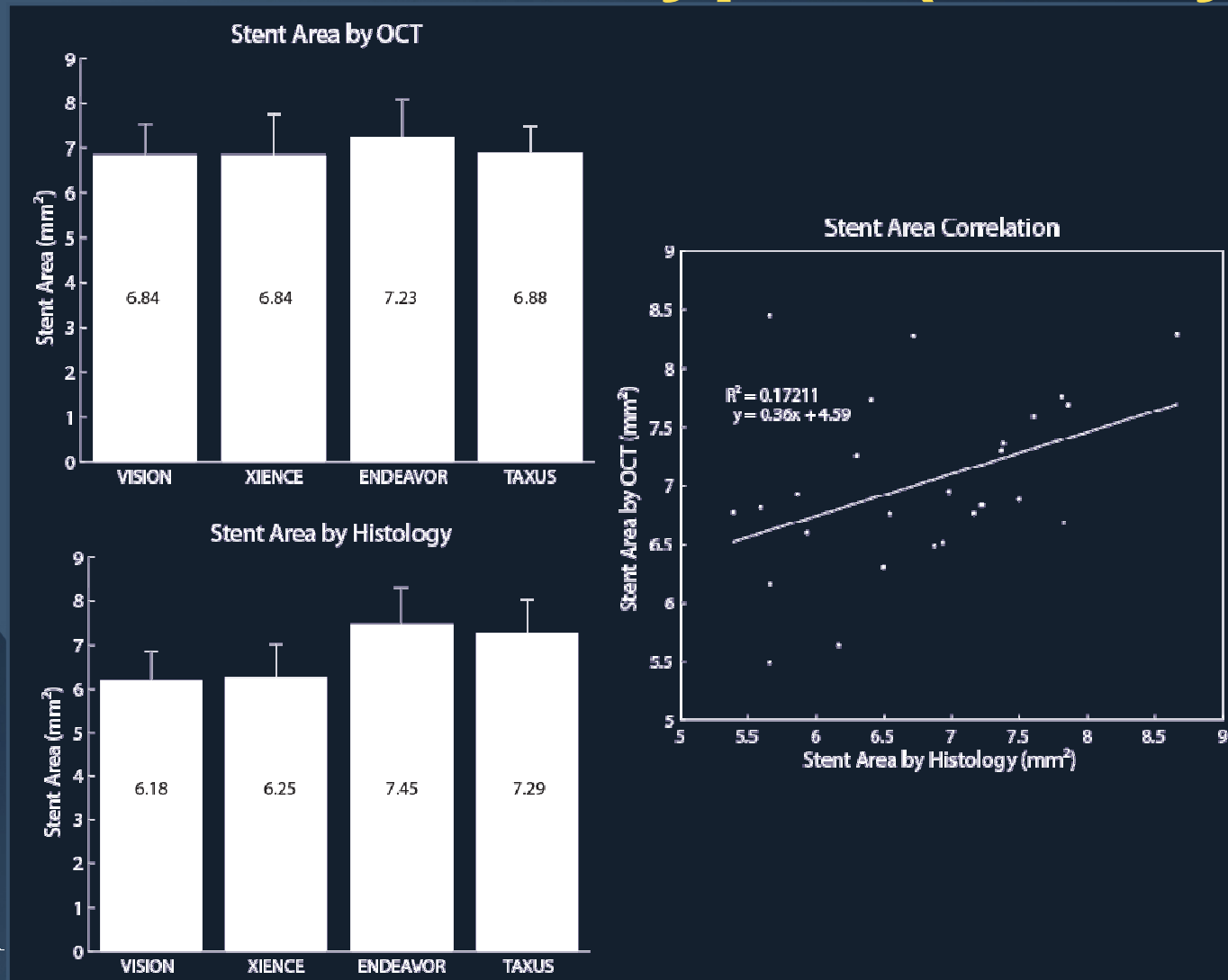
Analysis of %AS Using OCT in Different DES Types (28 Days)



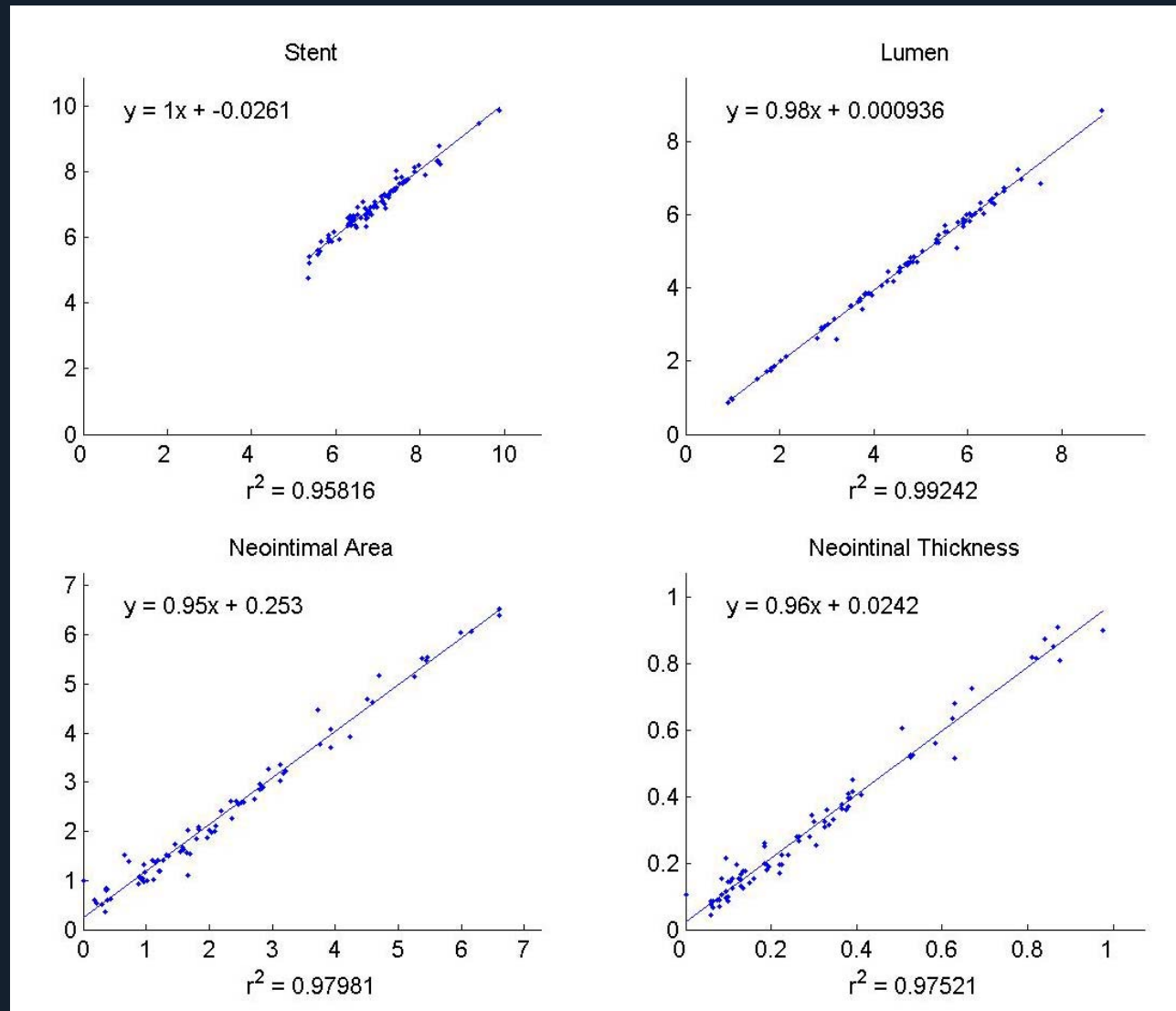
Analysis of Neointimal Thickness Using OCT in Different DES (28 Days)



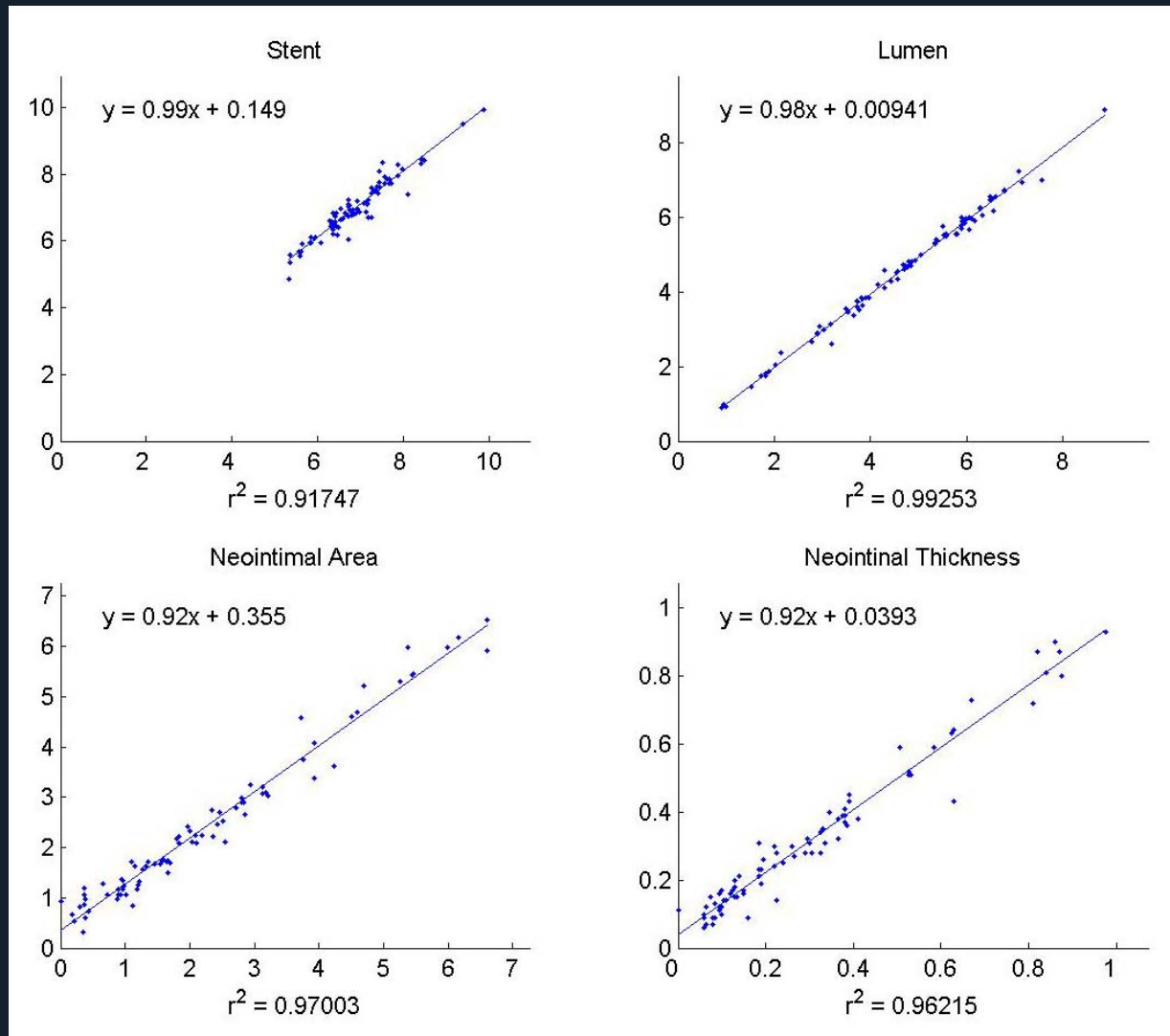
Analysis of Stent Area Using OCT in Different DES Types (28 Days)



OCT Intra-Observer Variability

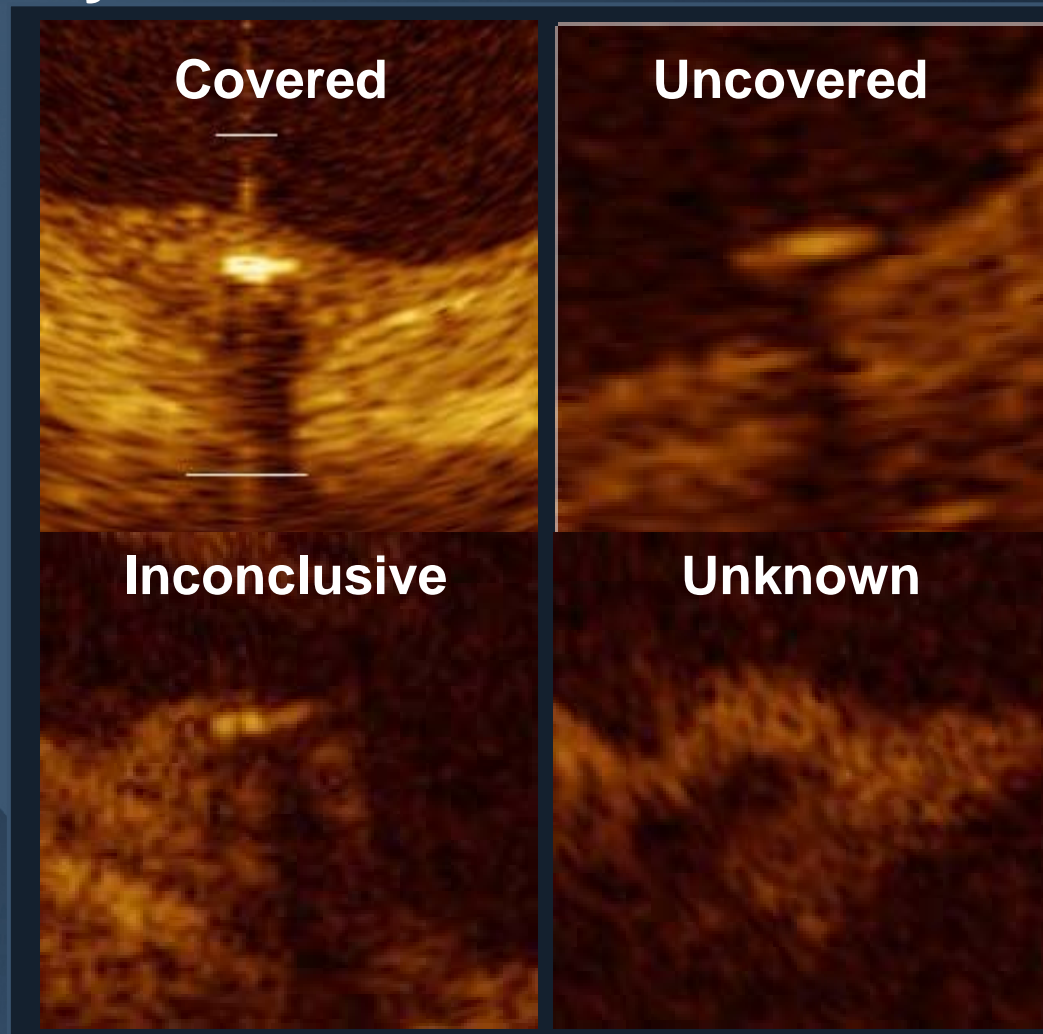


OCT Inter-Observer Variability

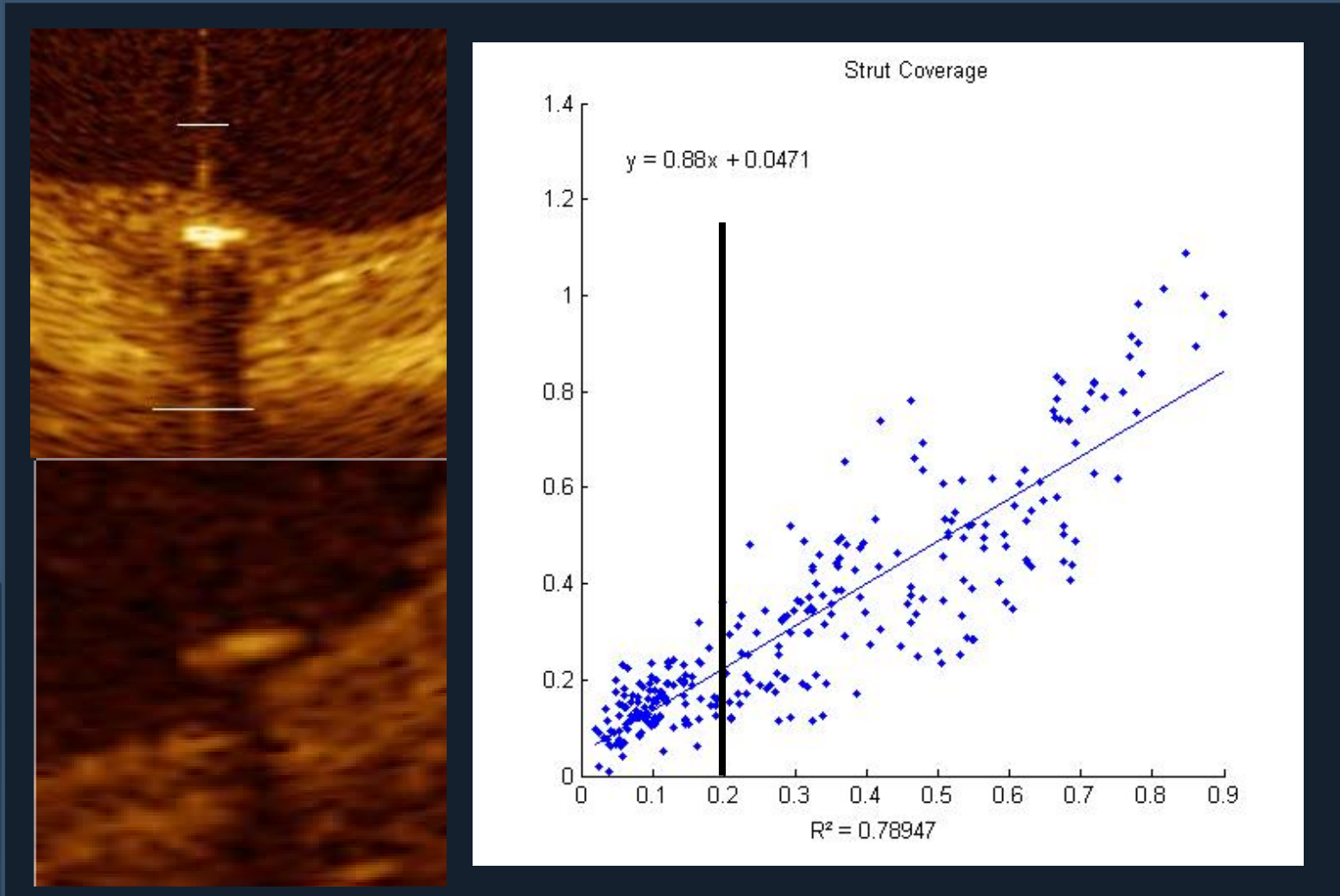


Validation Study of Strut Coverage Analyzed Following OCT Imaging

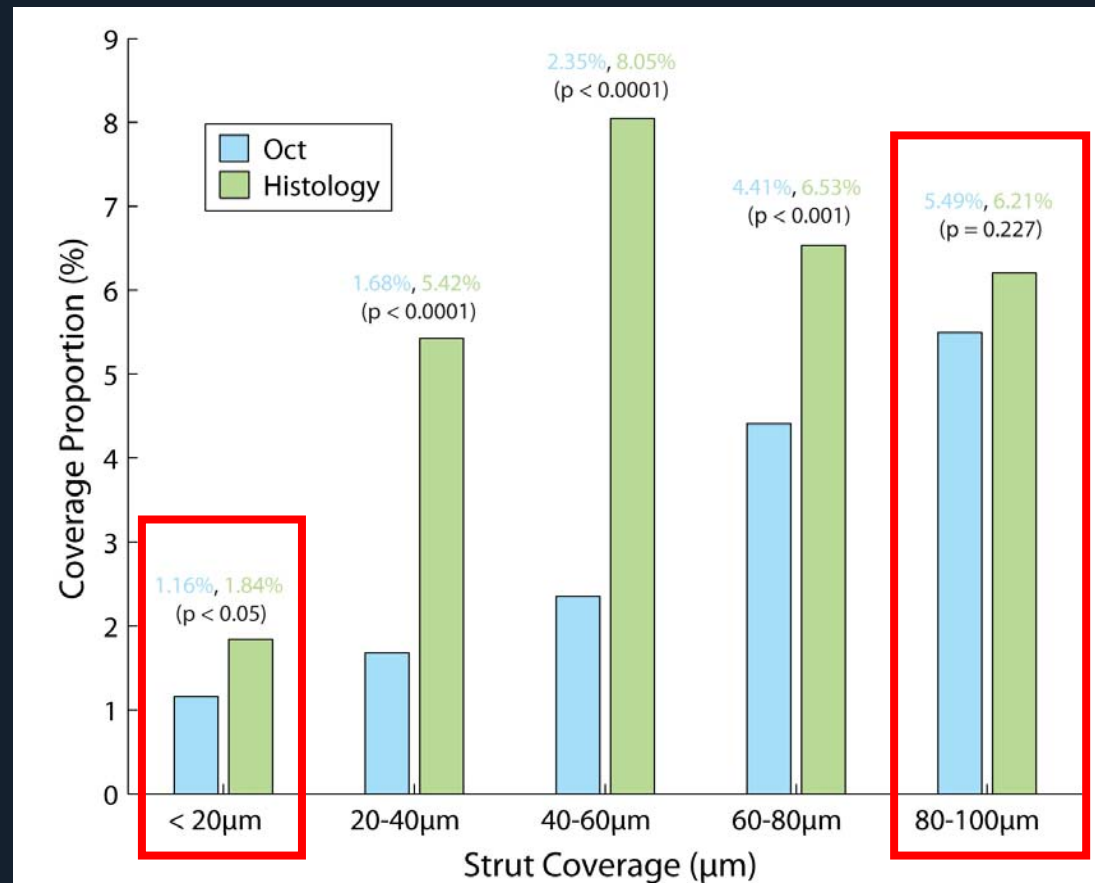
Accuracy for the Evaluation of Strut Coverage



Analysis of Strut Coverage Using OCT in Different DES Types (28 Days)



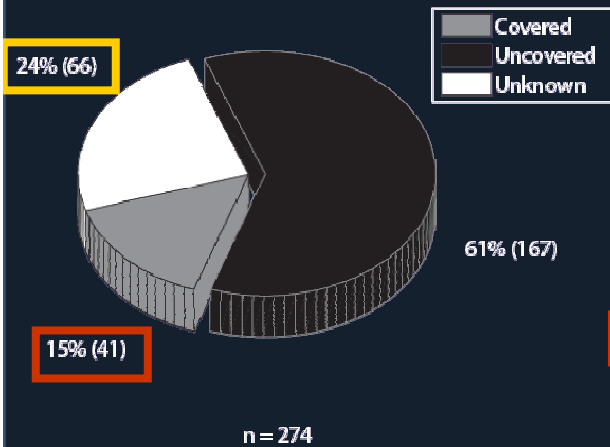
Proportion of Neointimal Thickness by OCT & Histology in DES: Implications for Individual Strut Coverage Analysis



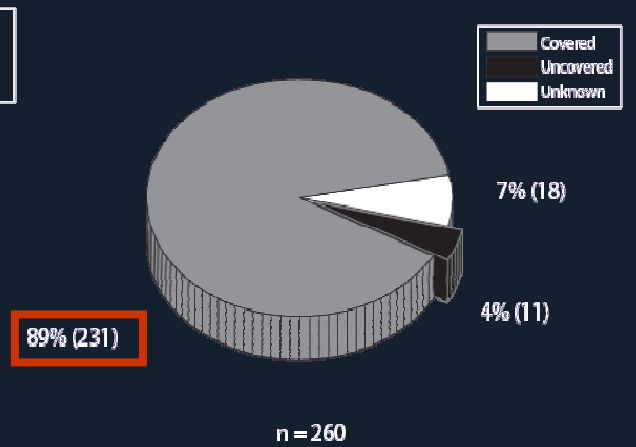
Strut Coverage by OCT

BMS versus DES at Different Time Points

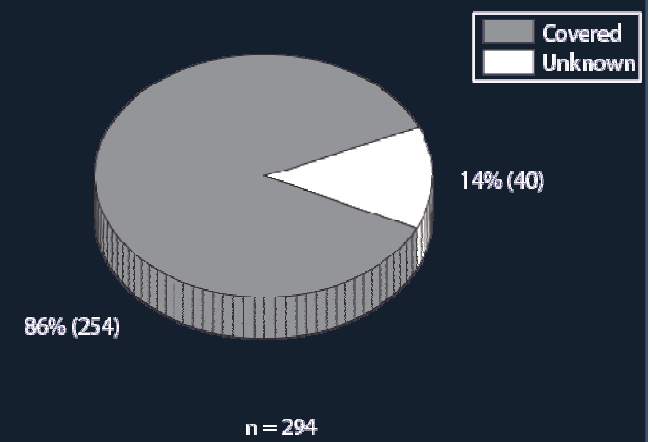
Stent Strut Coverage (BMS at 4 days)



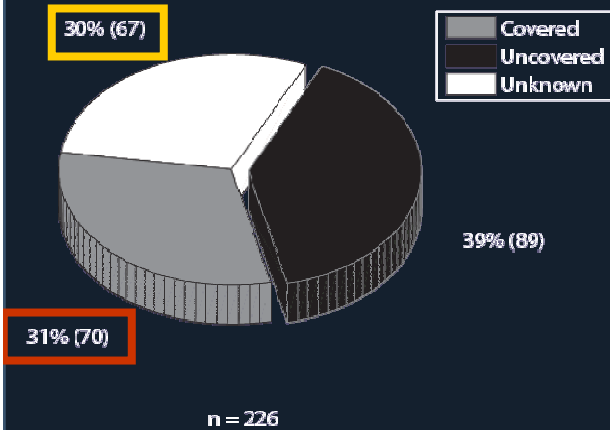
Stent Strut Coverage (BMS at 10 days)



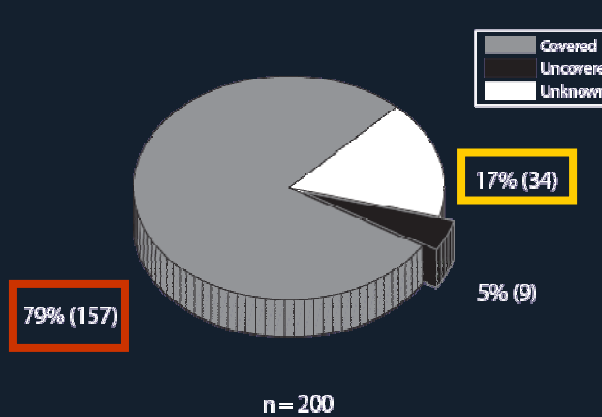
Stent Strut Coverage (BMS at 28 days)



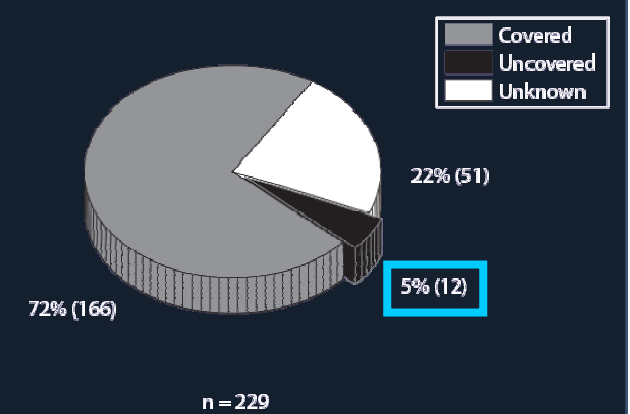
Stent Strut Coverage (DES at 4 days)



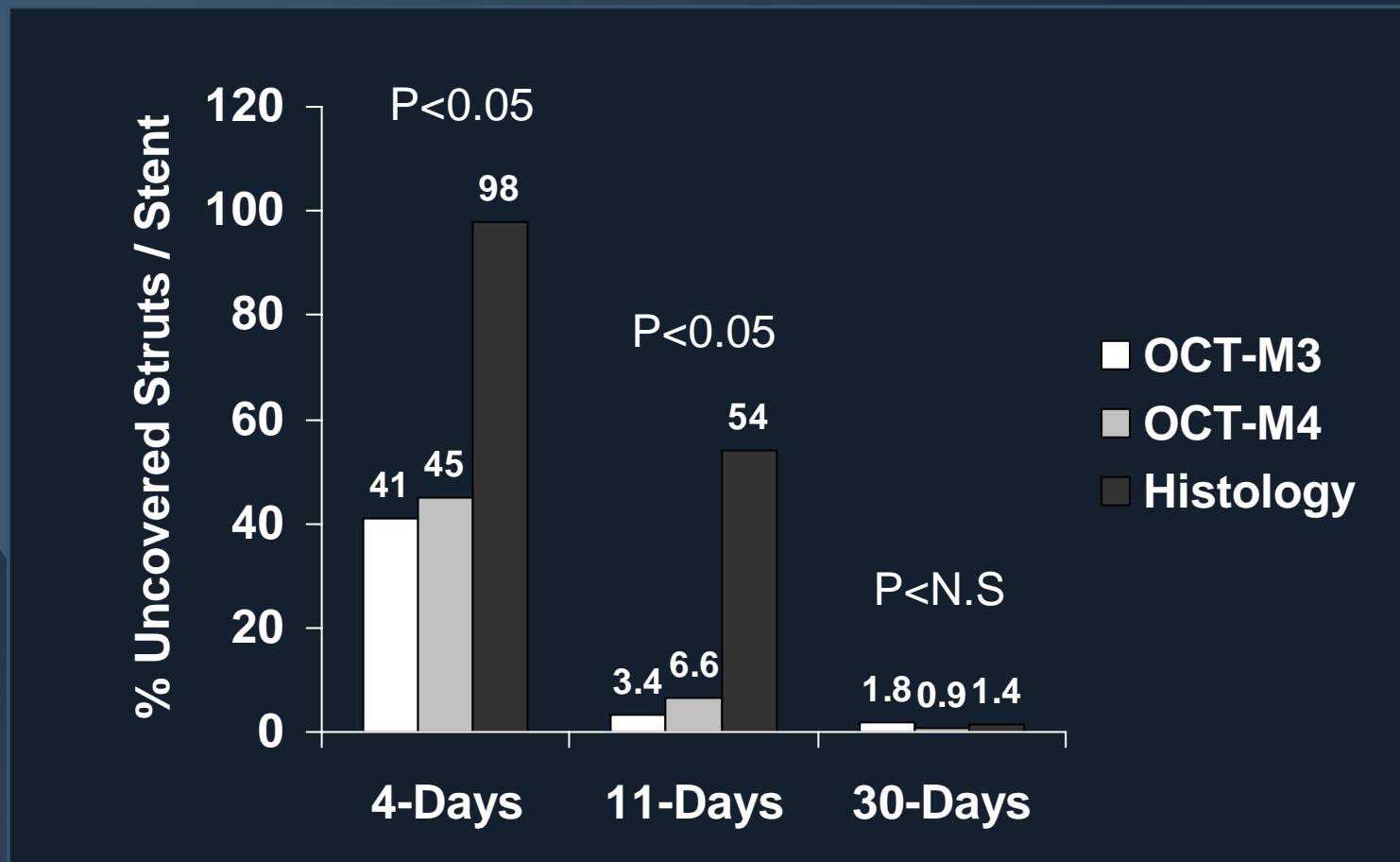
Stent Strut Coverage (DES at 10 days)



Stent Strut Coverage (DES at 28 days)

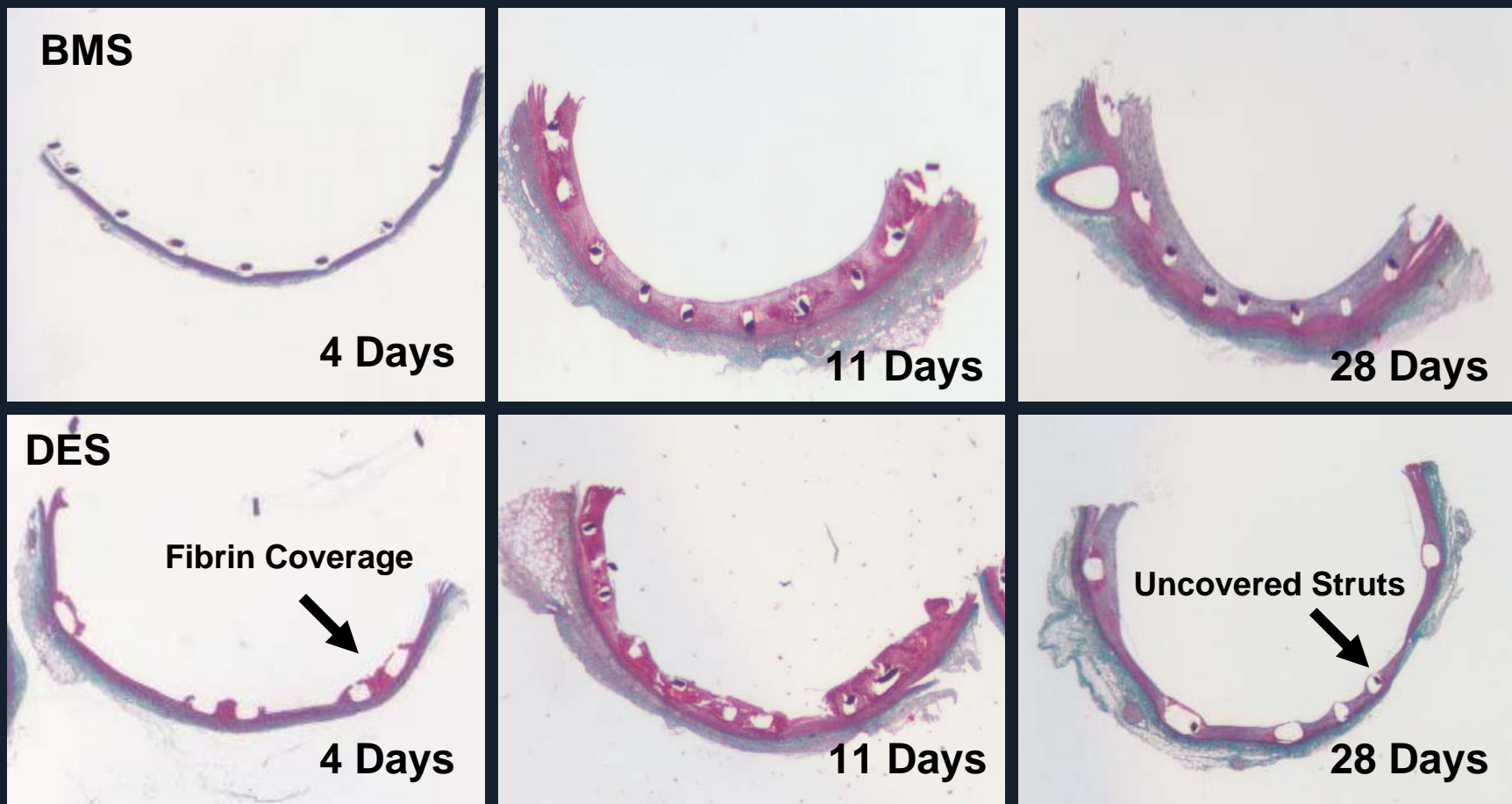


Percentage of Uncovered Stent Struts as Assessed by OCT (M3 and M4) and Histology at Different Time Points

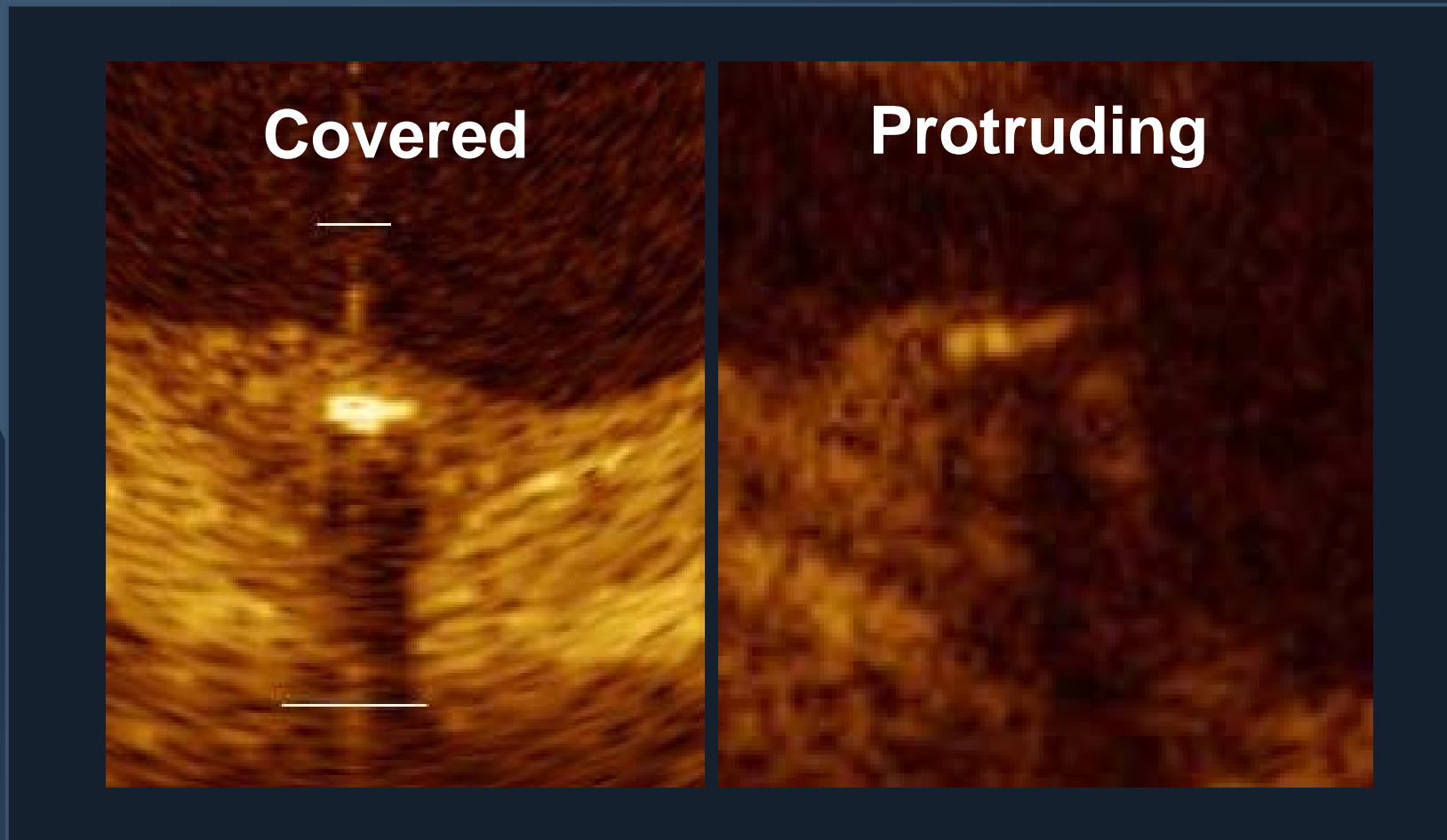


Strut Coverage by OCT

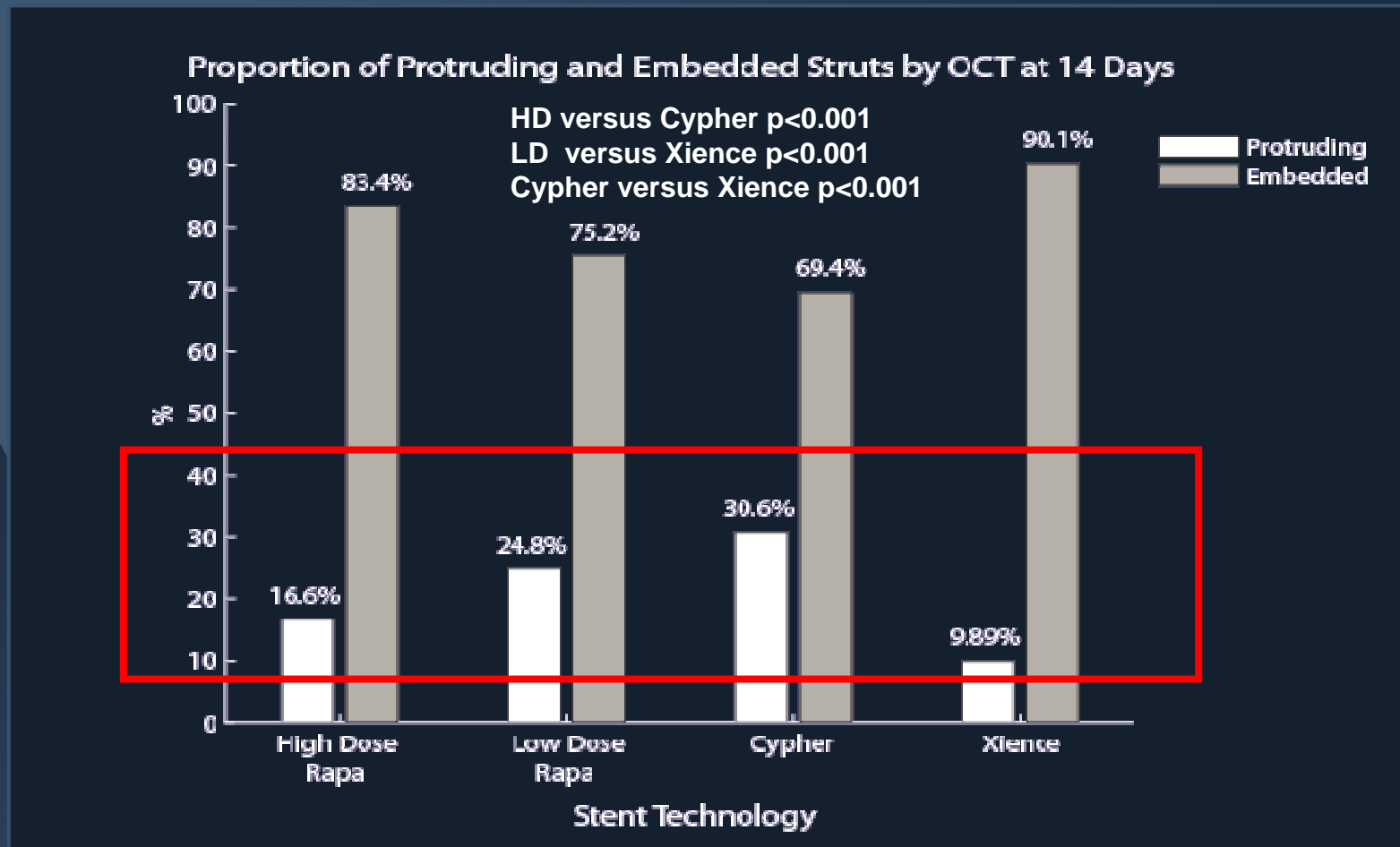
BMS versus DES at Different Time Points



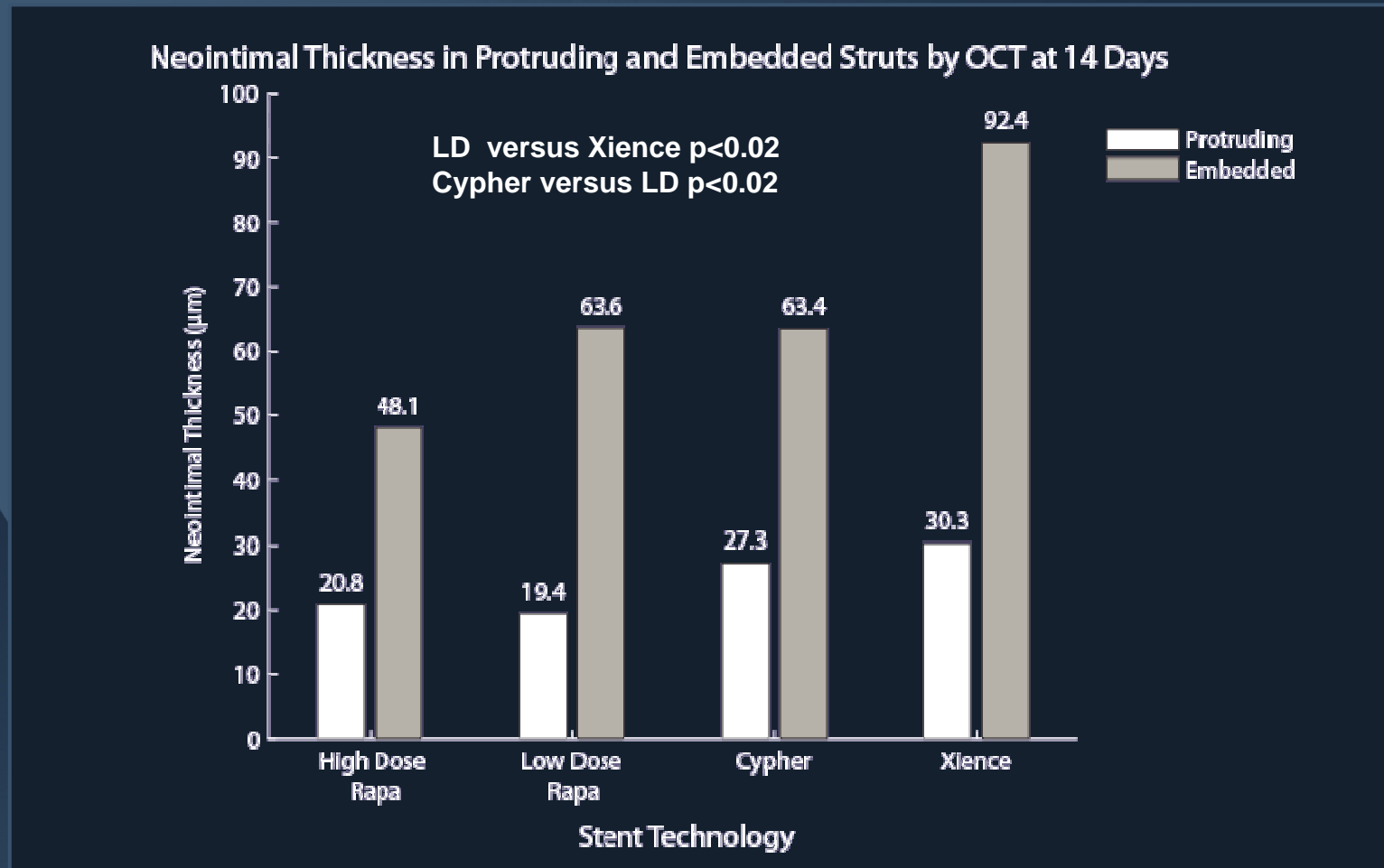
“The Protruding Strut”: Implications for Healing and Coverage



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

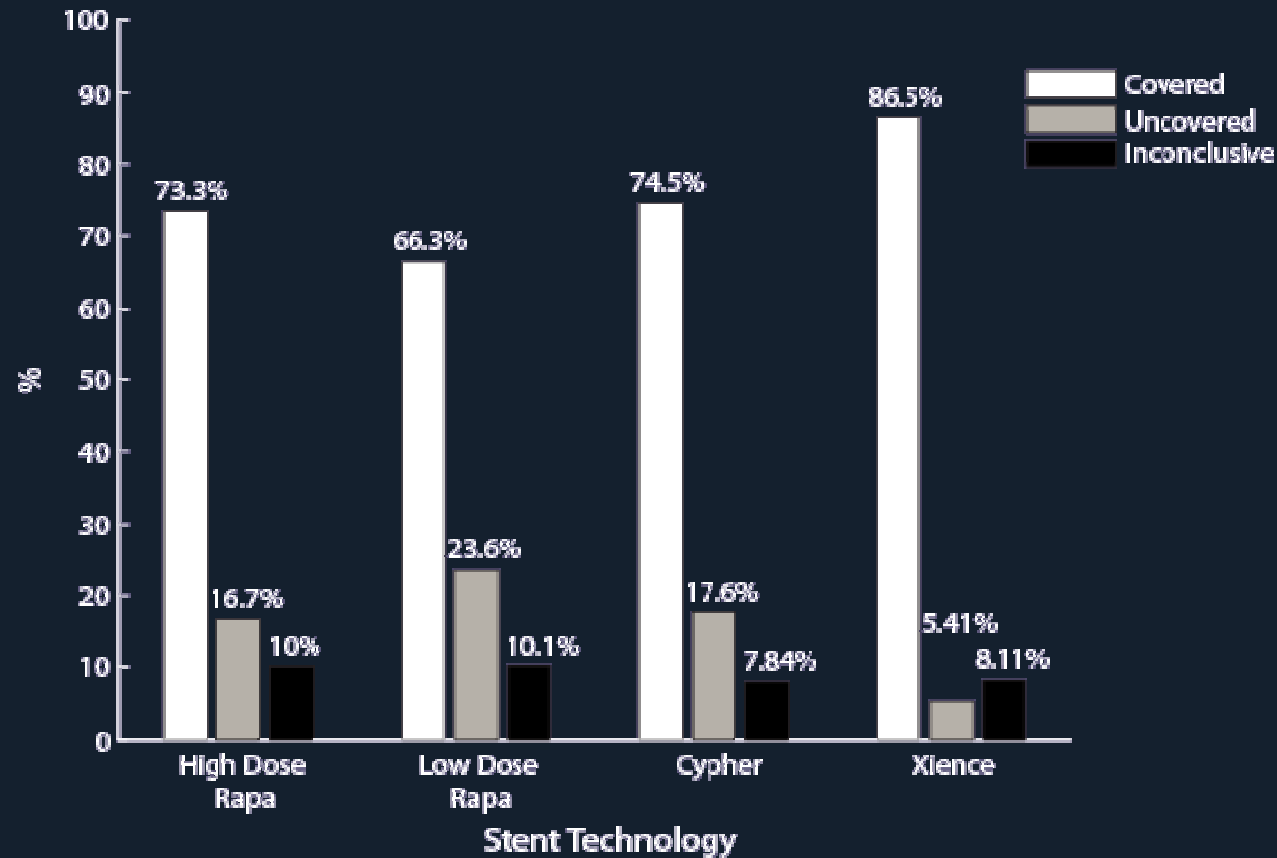


The Protruding Strut and Neointimal Thickness at 14 Days

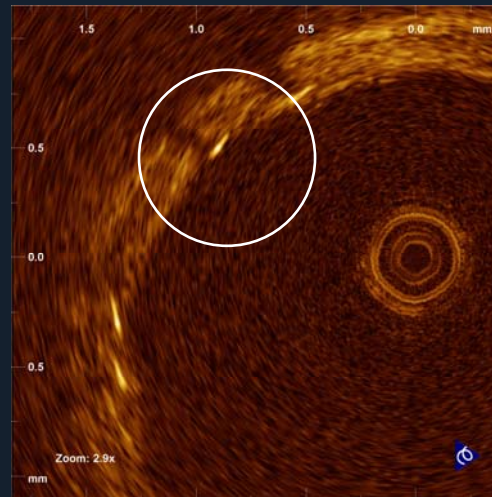
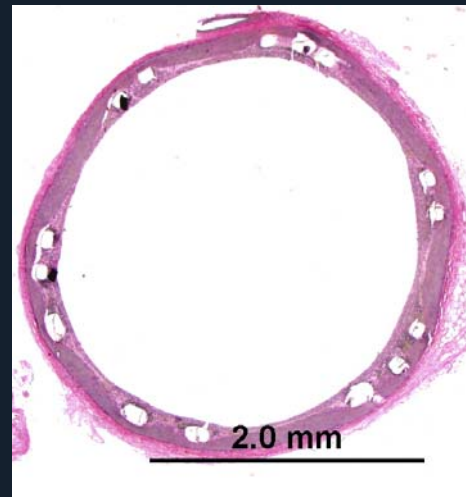
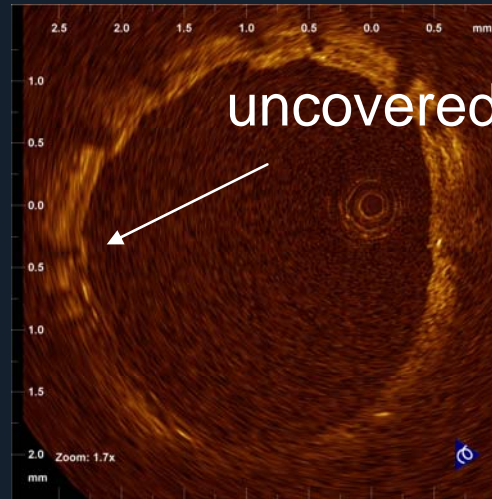
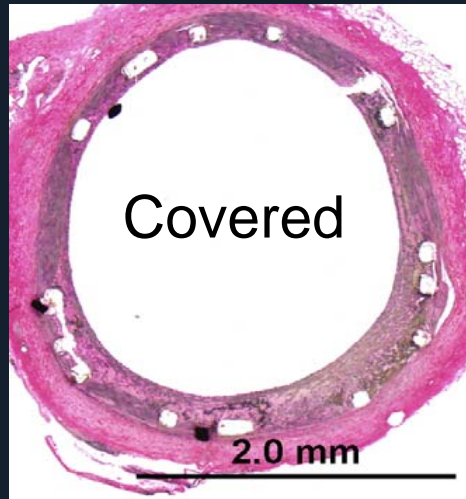


The Protruding Strut and Strut Coverage at 14 Days

Qualitative Stent Coverage in Protruding Struts by OCT at 14 Days



Limitations: Insufficient Resolution to Detect Thin Neointima



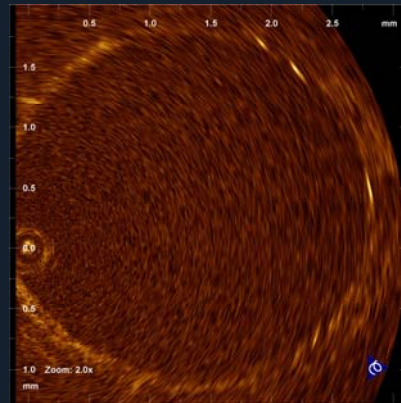
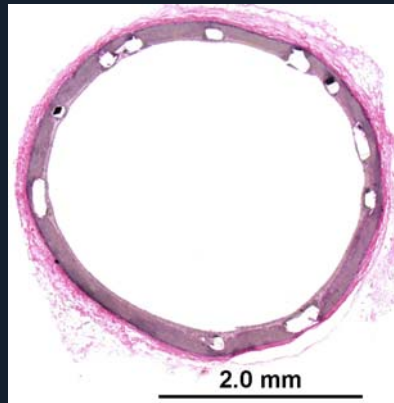
**Histological
NT: 0.04mm**

Histological NT (mean):

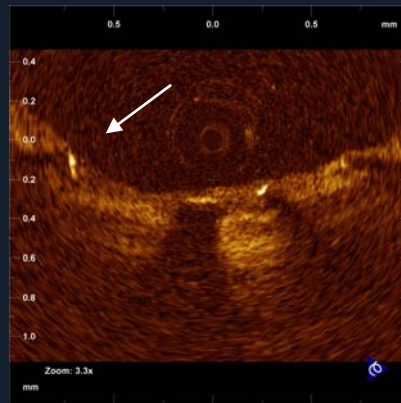
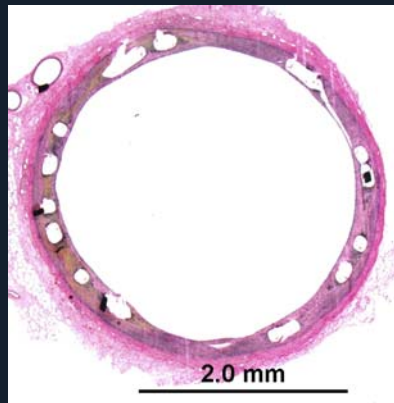
- Xience 0.040 mm
- Taxus 0.038 mm
- Endeavor 0.042 mm



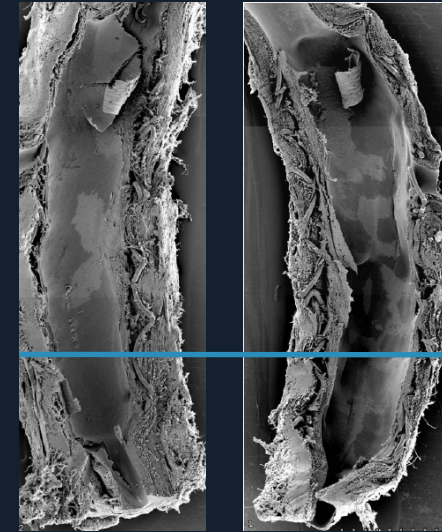
Limitations: Areas of Difficult Interpretation



Poor Image quality



Out of plane stent



Poor tissue/stent contrast



The Challenges of the Qualitative Assessment of Strut Coverage by OCT

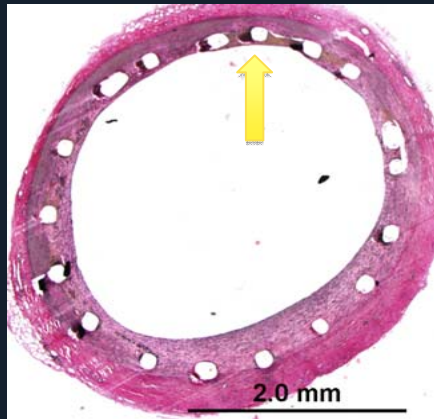
Strut Coverage versus Endothelialization

- The mean cross sectional diameter of an individual EC is out of the range of resolution of OCT.
- Therefore, strut coverage by OCT must be seen as a marker of the amount of tissue deposited on the surface of the stent and not as a marker of stent endothelialization.
- Strut coverage occurs early after stent implantation, occurring earlier and in a higher proportion in DES.
- In addition, the amount of strut coverage identified in vivo by OCT must be interpreted with caution as the strut may be covered by tissue other than healthy ECs (i.e., fibrin).

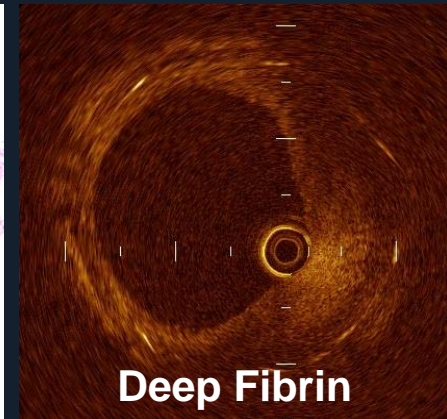


OCT Histological Correlates

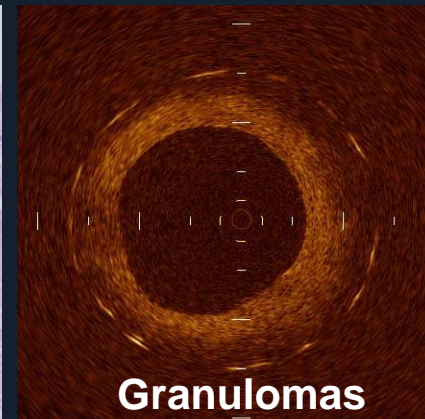
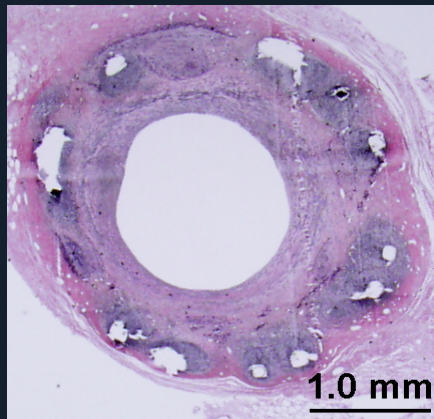
Drug Eluting Stents at 28 Days



Superficial Fibrin



Deep Fibrin

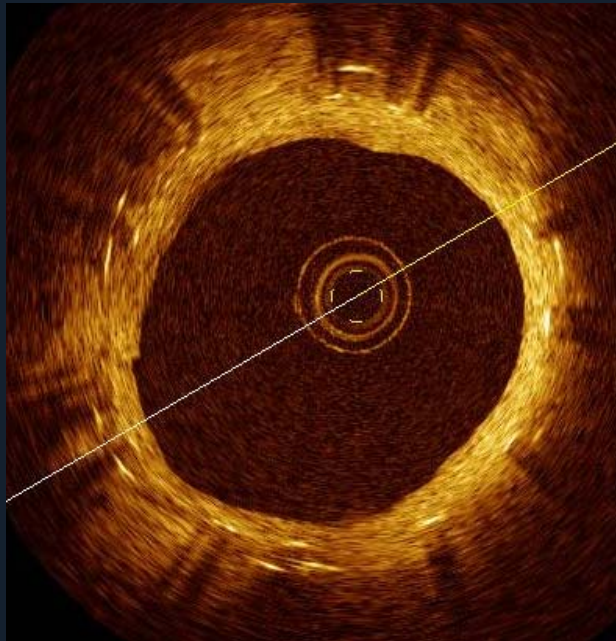


Granulomas

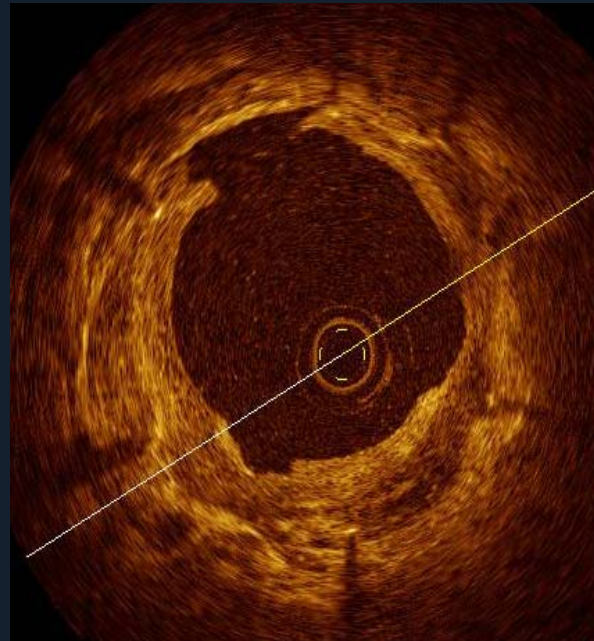
Therefore, several OCT imaging patterns may be the result of the deposition of different tissue types carrying different biological consequences.



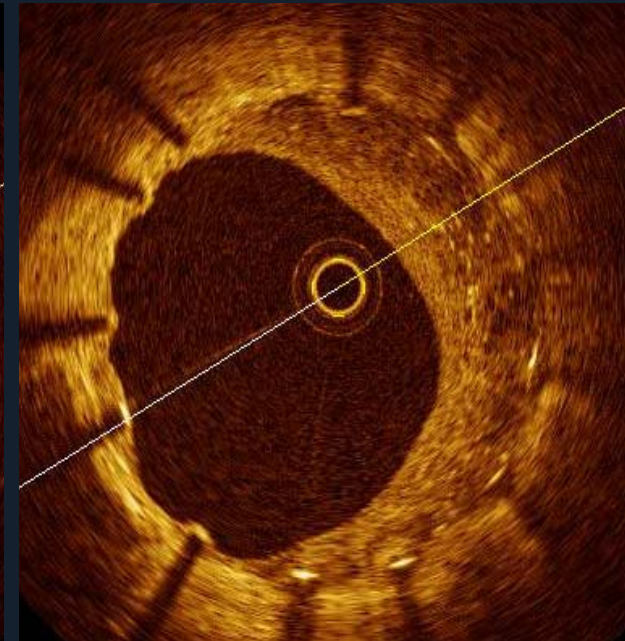
Different Neointimal Patterns Seen in OCT Following DES Implantation



Cypher - 6 Months

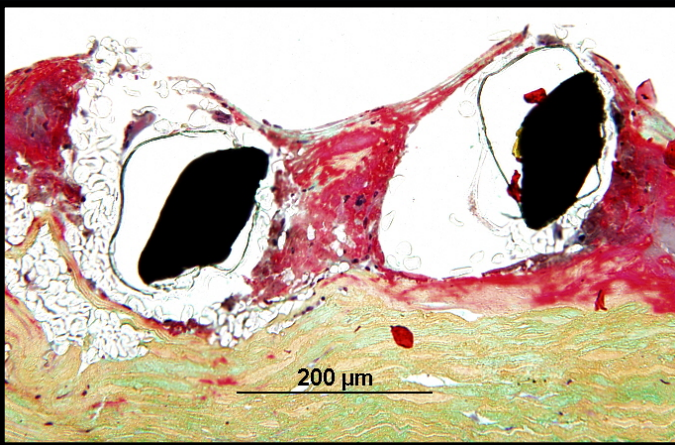
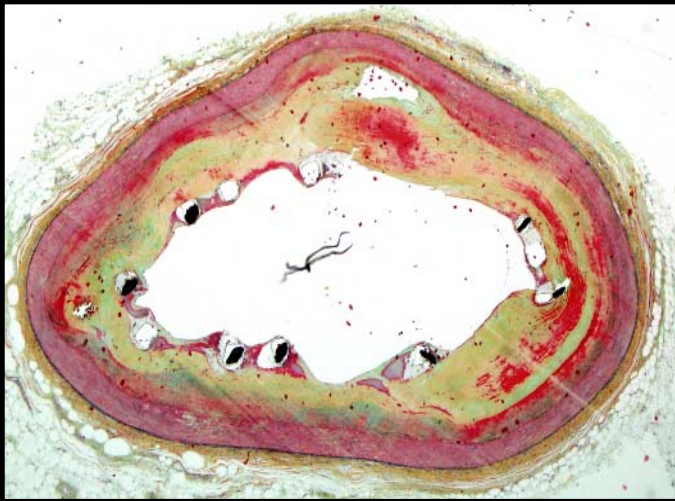


Cypher - 6 Months



Taxus - 13 Months

Endovascular Imaging and Vascular Healing: “Stent Coverage Risk Score”



- Degree of strut coverage:
 - Endothelial Cells.
 - Others.
- Fibrin deposition:
 - Superficial (peri-strut).
 - Deep (vessel wall).
- Vessel wall inflammation.
- Overall vessel wall “assessment”:
 - Pro-thrombogenic surface *versus*
 - Anti-thrombogenic surface.

OCT Imaging and Vascular Healing Assessment Following DES Implantation

- Today, due to significant improvements in OCT technology, the 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 using different DES technologies are essential.
- Due to its technical limitations in the far field, IVUS-OCT combination techniques will be required...and developed.
- In the future, it is possible that lessons learned from prospective clinical trials using this technology, will provide the basis to enhance the safety profile of DES.

