

# LEADERS

*Limus Eluted From A Durable vs ERodable Stent Coating*

## *OCT Substudy*

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***Consecutive patients in the Angiographic Substudy  
(1:4 randomization to Angiographic Follow-Up at 9  
months) were requested to perform an OCT  
examination during follow-up angiography***

***Primary endpoint: Presence neointimal coverage f-up***

***Secondary endpoints: Strut Apposition at f-up  
Neointimal Thickness  
% CSA Neointimal Obstruction***

***Independent Corelab: Cardialysis B.V.***



*LEADERS OCT  
Substudy*

# Introduction

## What Have We Learnt From LEADERS?

- ✓ A drug eluting stent with abluminal biodegradable polymer eluting biolimus is as good (in fact marginally better) than the first in class, the Cypher

## Why are People Excited About It?

- ✓ Because they hope that a biodegradable polymer will be better in terms of long term safety

## Definite Stent Thrombosis

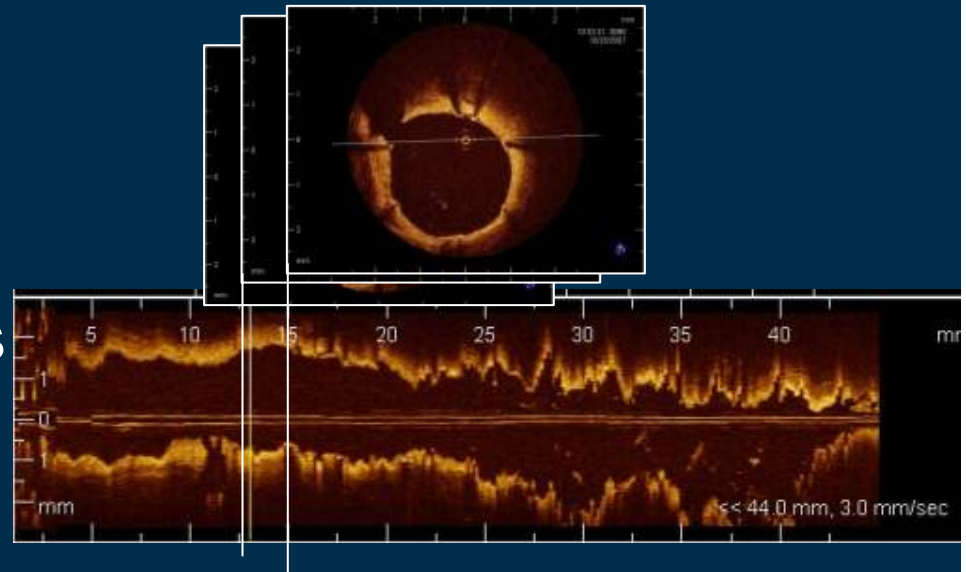
	<b>Biolimus Stent</b> <b>857 Patients</b>	<b>Sirolimus Stent</b> <b>850 Patients</b>	<b>P</b>
0-30 days	<b>1.6%</b>	<b>1.6%</b>	<b>0.98</b>
>30 days – 9 mo	<b>0.2%</b>	<b>0.5%</b>	<b>0.65</b>
0 mo – 12 mo	<b>2.0%</b>	<b>2.0%</b>	<b>0.99</b>
12 mo-24 mo	<b>?</b>	<b>?</b>	
24-36 mo	<b>?</b>	<b>?</b>	
36 – 48 mo	<b>?</b>	<b>?</b>	
48 – 60 mo	<b>?</b>	<b>?</b>	



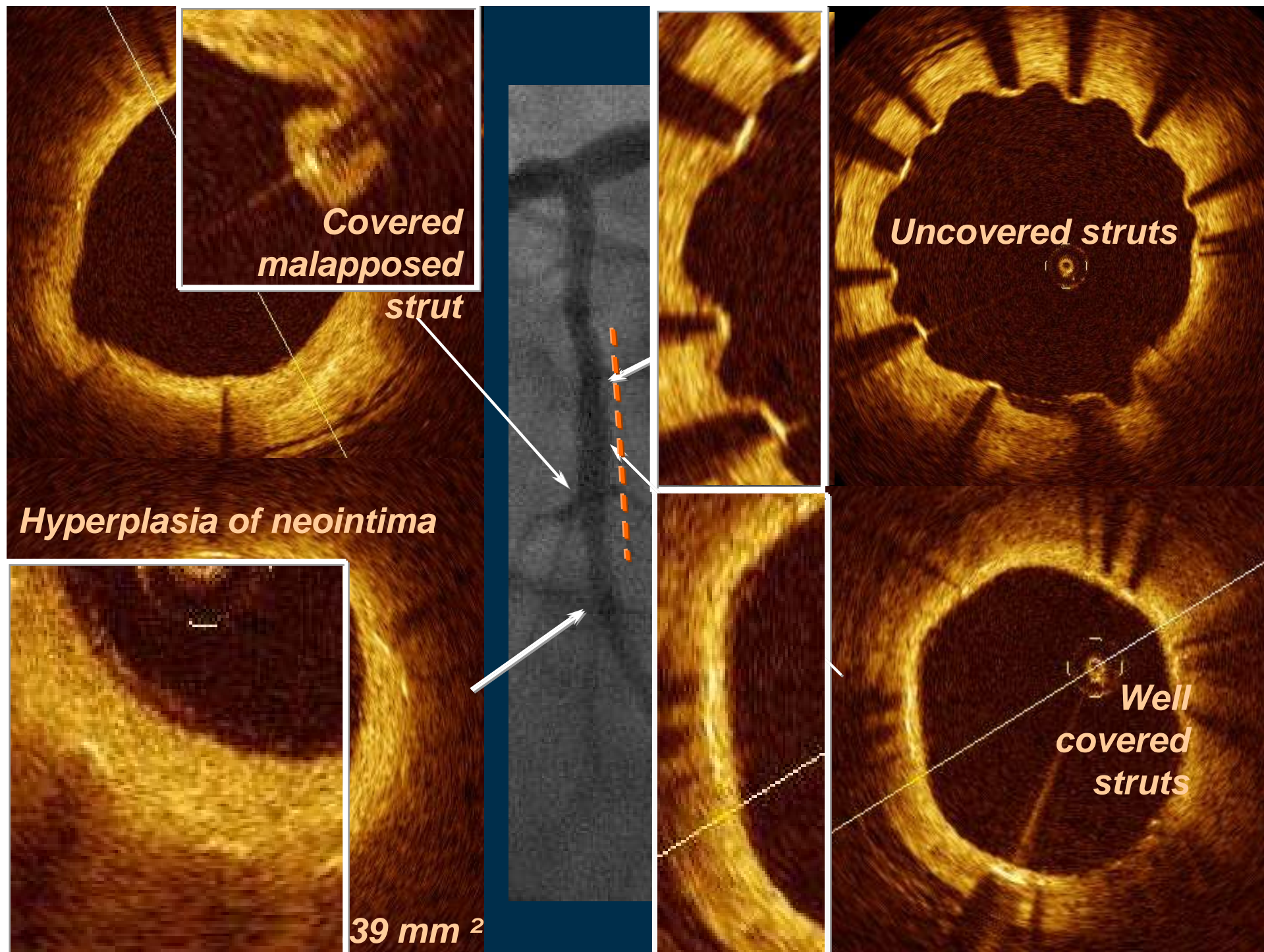
**LEADERS OCT Substudy**

# OCT Data Analysis

- Analysis of stented segment with computer-assisted contour detection at 450  $\mu\text{m}$  intervals
  - Lumen area
  - Stent area
  - Neointimal area
- Analysis of individual cross sections
  - Strut apposition
  - Strut coverage
  - Tissue appearance
  - Neointimal thickness
  - Intraluminal tissue/thrombus





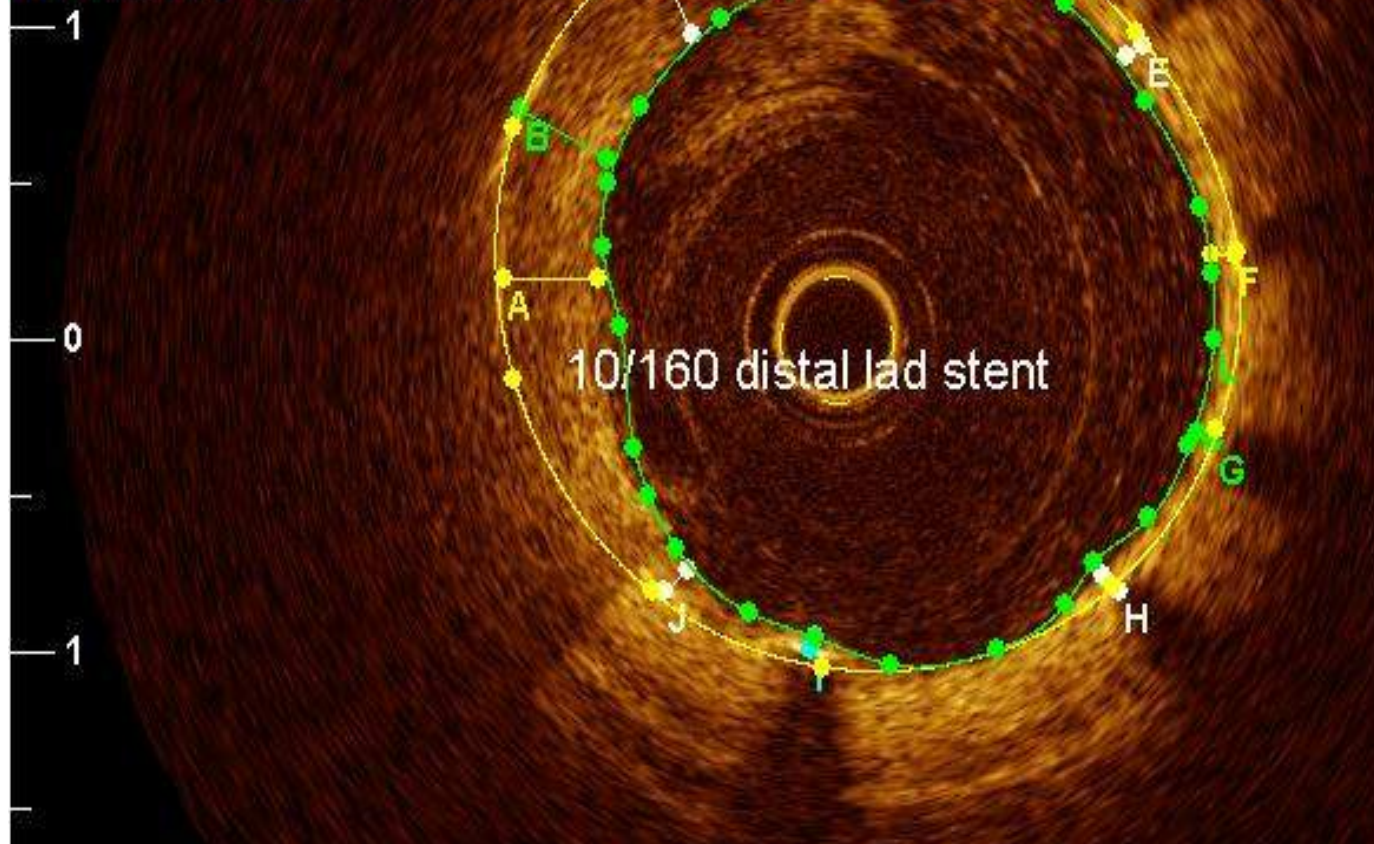




A Length: 0.33mm  
B Length: 0.35mm  
C Length: 0.32mm  
D Length: 0.22mm  
E Length: 0.07mm  
F Length: 0.08mm  
G Length: 0.07mm  
H Length: 0.08mm  
I Length: 0.04mm  
J Length: 0.10mm  
K Area: 5.25mm<sup>2</sup>  
L Area: 3.87mm<sup>2</sup>



LEADERS OCT Substudy



# Neointimal & Stent Areas + Thickness

*Independent Core*

*Laboratory*

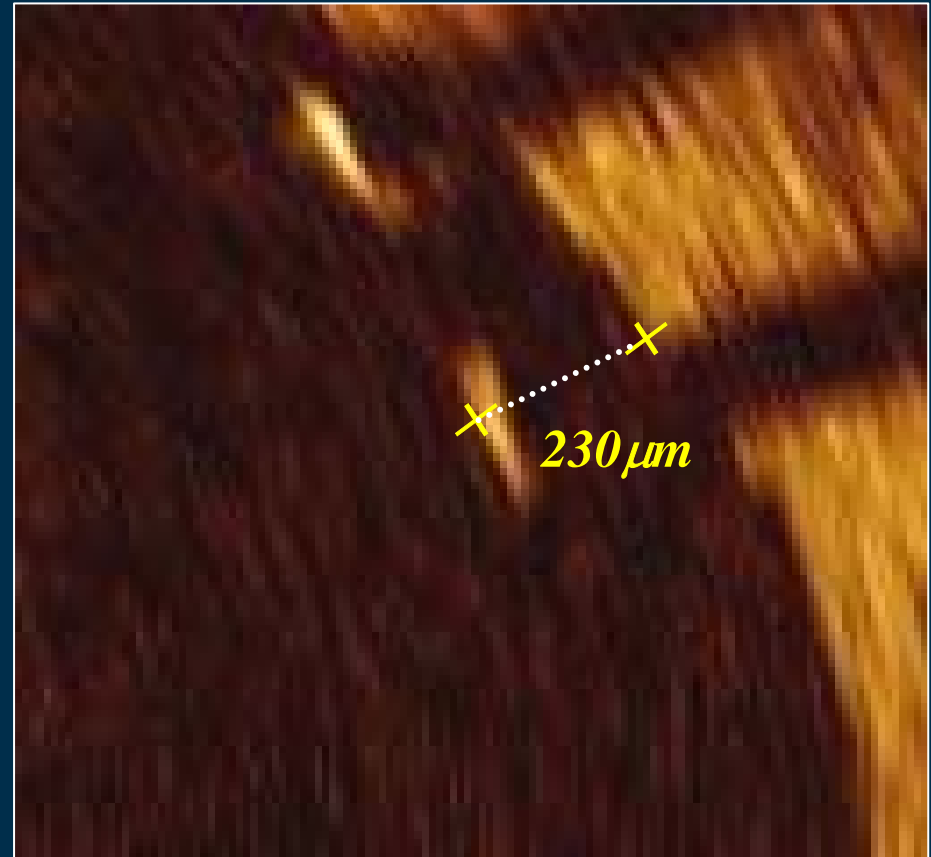
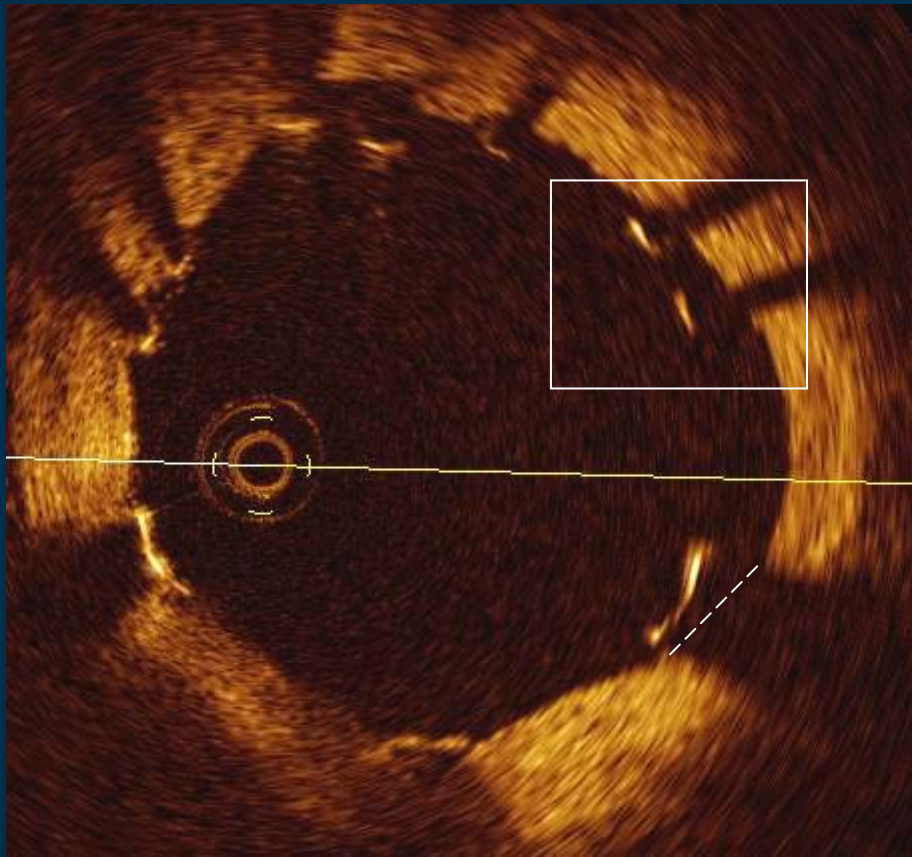
*(Cardialysis) with*

*Analysts Blinded*

*To Randomisation*

# ***Minimal Distance between mid-point Leading Edge Stent Strut and Intimal Contour***

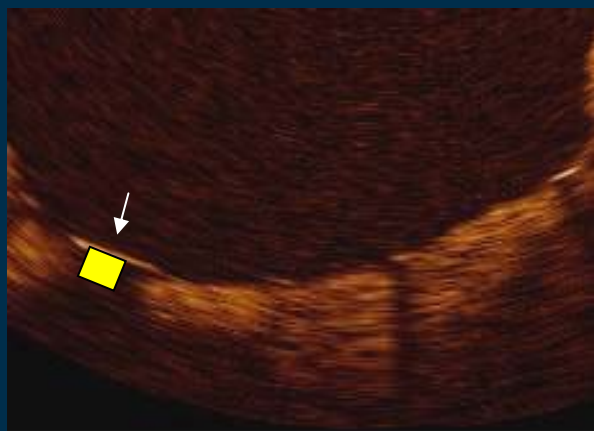
*If the intimal contour is shadowed behind strut, draw a line  
connecting adjacent visible intimal contours*



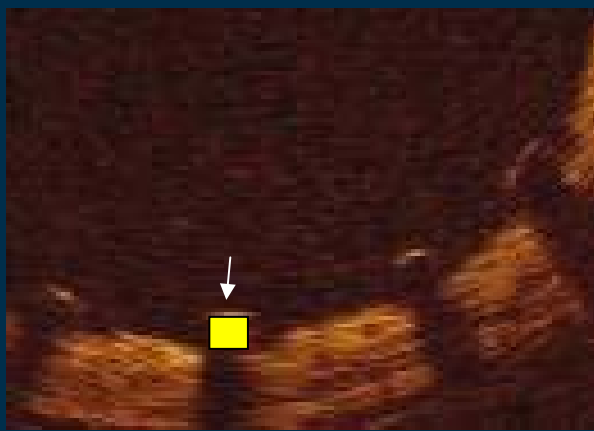


# ***Classification of Stent Strut Malapposition***

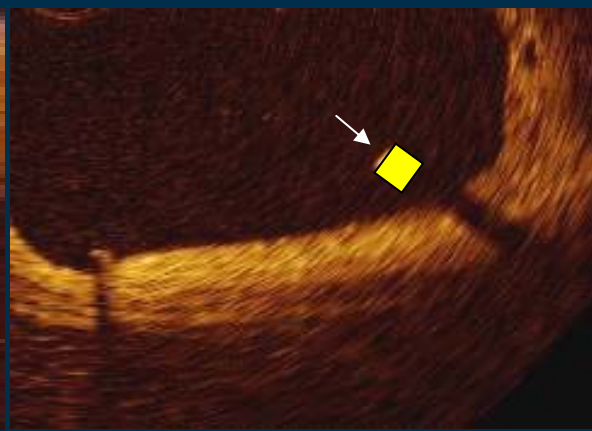
	<b>Apposed</b>		<b>Malapposed</b>
	<b>Embedded</b>	<b>Protruding</b>	<b>Malapposed</b>
<b>Cypher Select</b>	$< 80\mu\text{m}$	$80 - 160\mu\text{m}$	$\geq 160\mu\text{m}$
<b>BioMatrix</b>	$< 56\mu\text{m}$	$56 - 112\mu\text{m}$	$\geq 112\mu\text{m}$



***Embedded***



***Protruding***



***Malapposed***

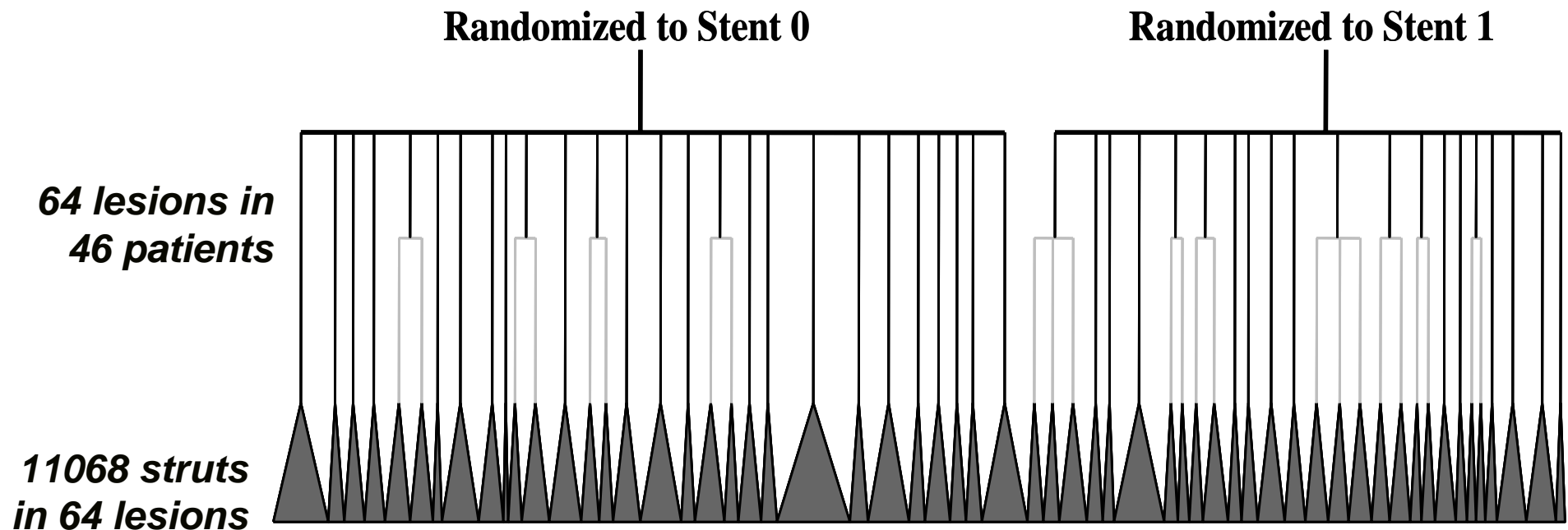




**LEADERS OCT Substudy**

# OCT Analysable Data

**11068 struts in 64 lesions (triangles) in 46 patients belonging to the two groups were examined. Triangle base reflects the number of struts in each lesion.**





## Multilevel structure of stent-related OCT data

- Struts and stents clustered in lesions
- Lesions clustered in patients

Principle of data independence

***violated***

**CANNOT USE CLASSIC STATS:**

t-test

chi-square

linear regression

logistic regression

***Patient***  
***Lesion***  
***Stent***  
***Strut***



## *Stent-related OCT data: Multilevel analysis*

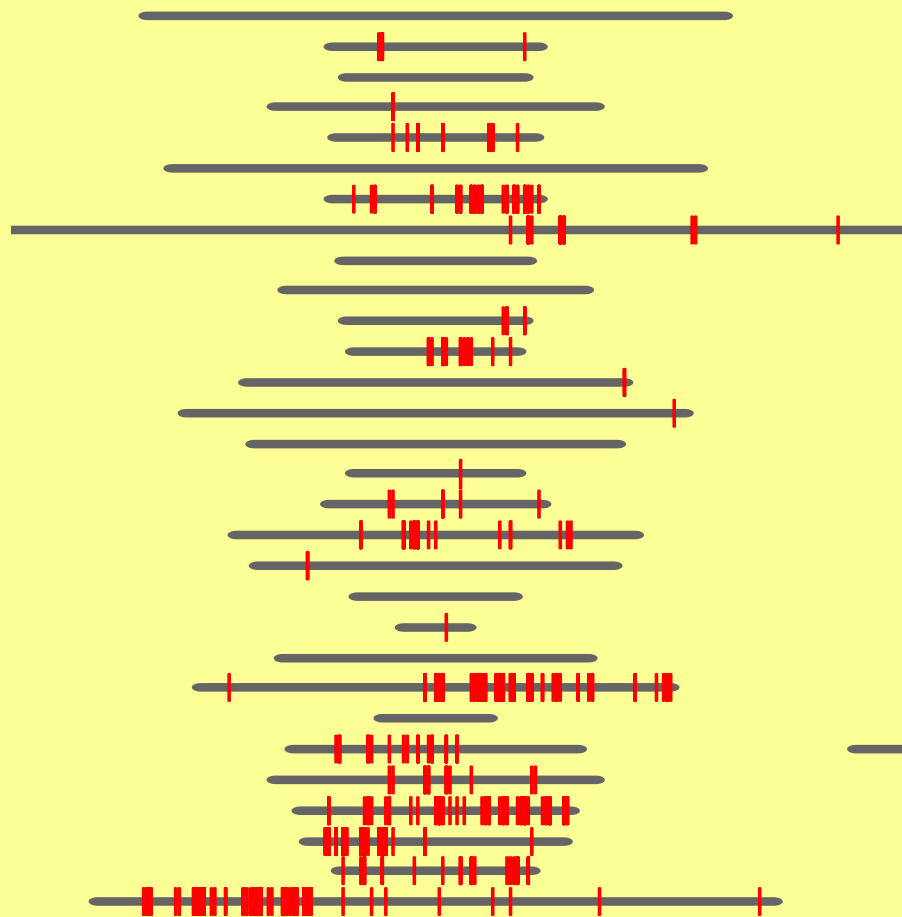
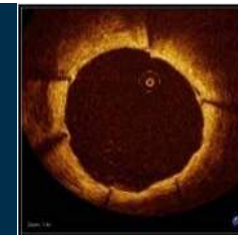


### ***WEIGHTED MULTILEVEL ANALYSIS IN WINBUGS***

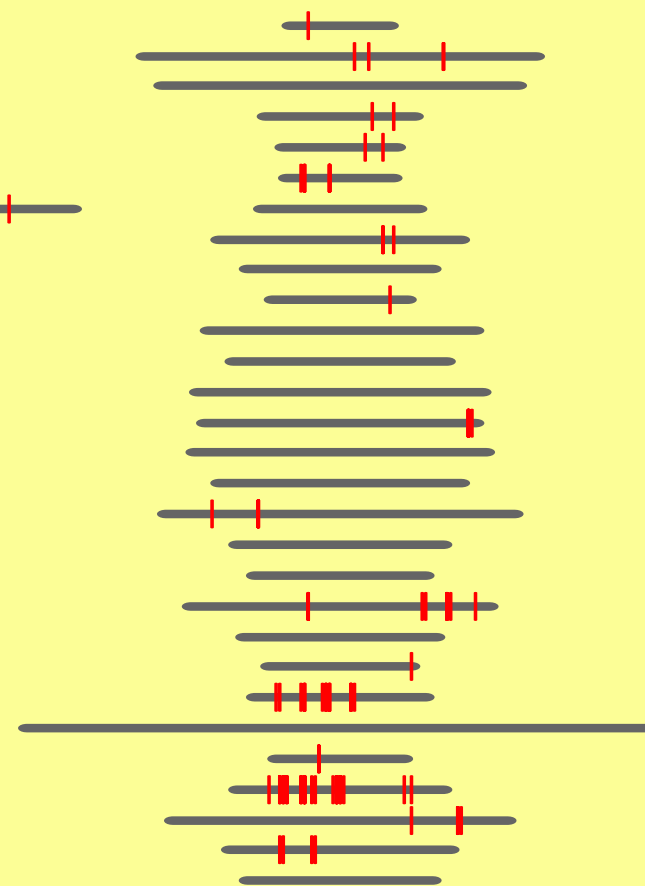
- *Two levels:*
  - *Patients* *Lesions*
- *Includes random effects at the level of patients*
- *Accounts for correlation of lesion characteristics within patients*
- *Implicitly assigns analytical weights proportional to numbers of struts observed within each lesion*



# Distribution of Uncovered Struts within Lesions



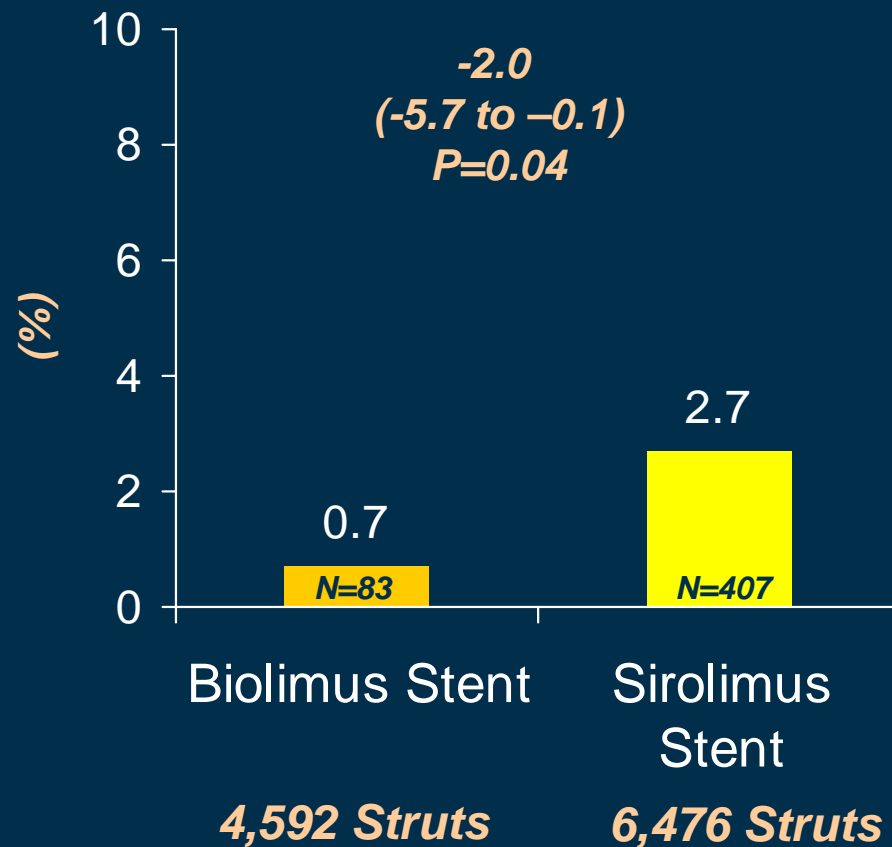
*Sirolimus*



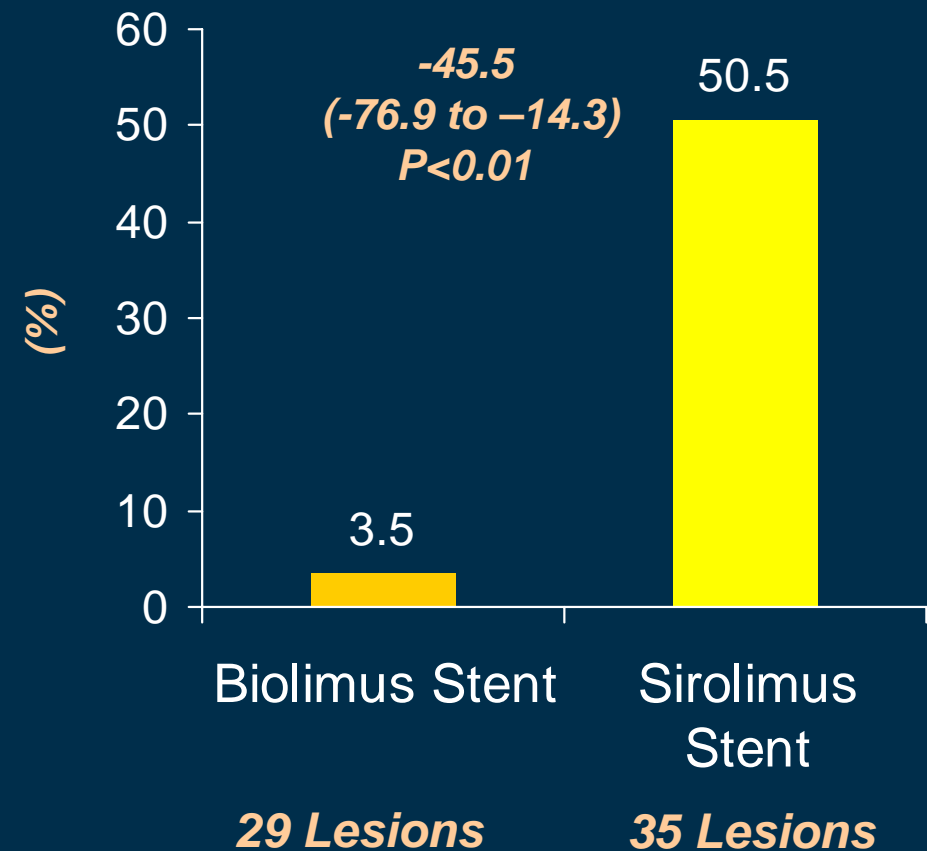
*Biolimus*

# LEADERS - OCT Substudy

## Uncovered Struts



## Lesions With At Least 5% Uncovered Struts

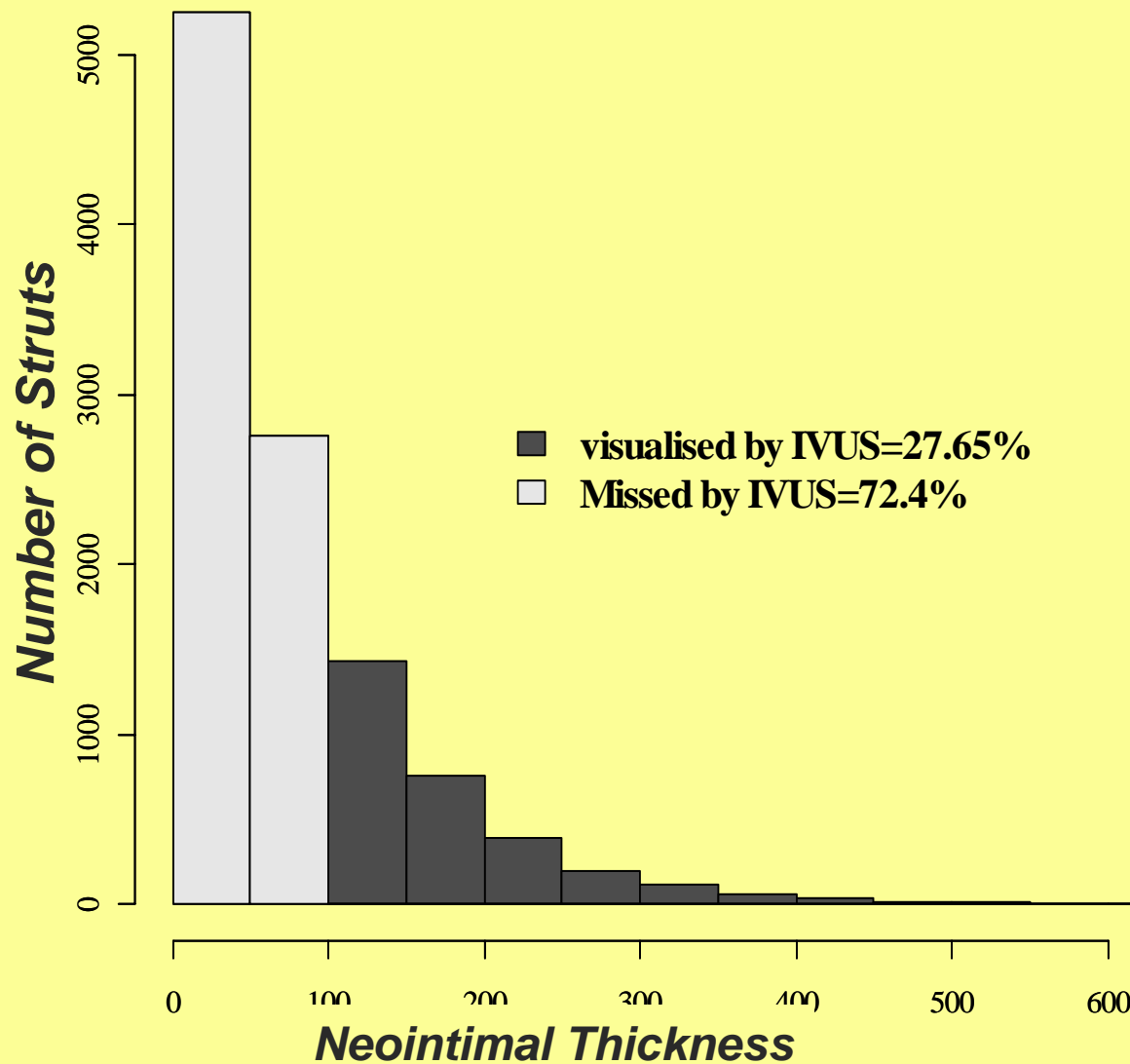


**Sensitivity Analysis: adjusted for lesion length, RVD, N of implanted stents, stent overlap**



**LEADERS OCT Substudy**

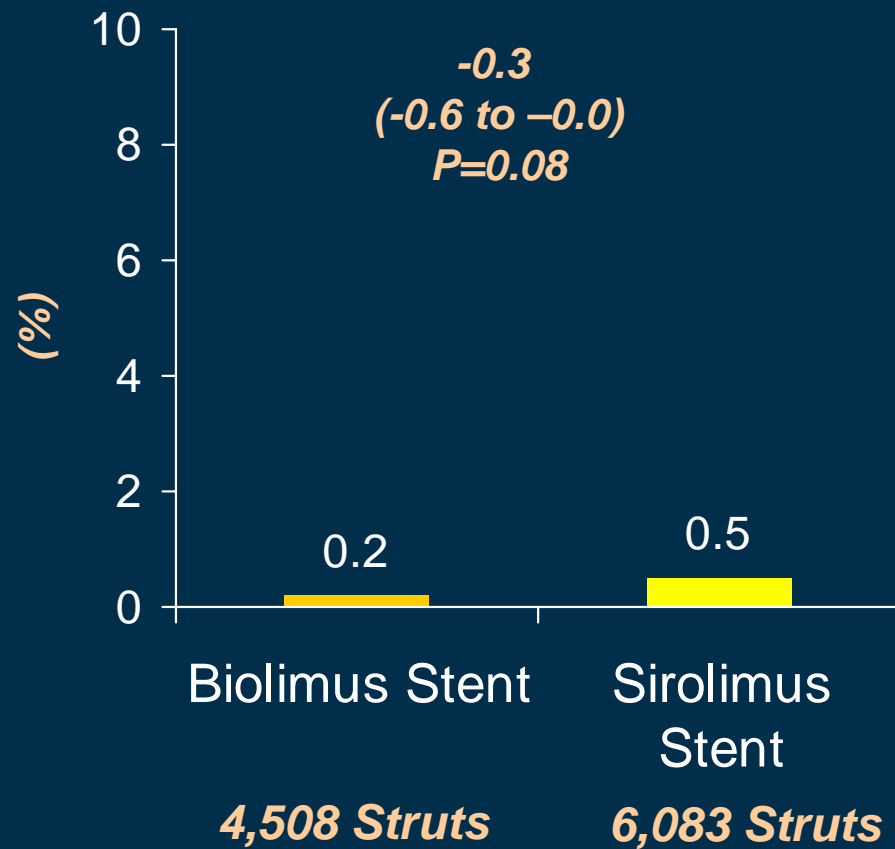
# Neointimal Thickness Distribution



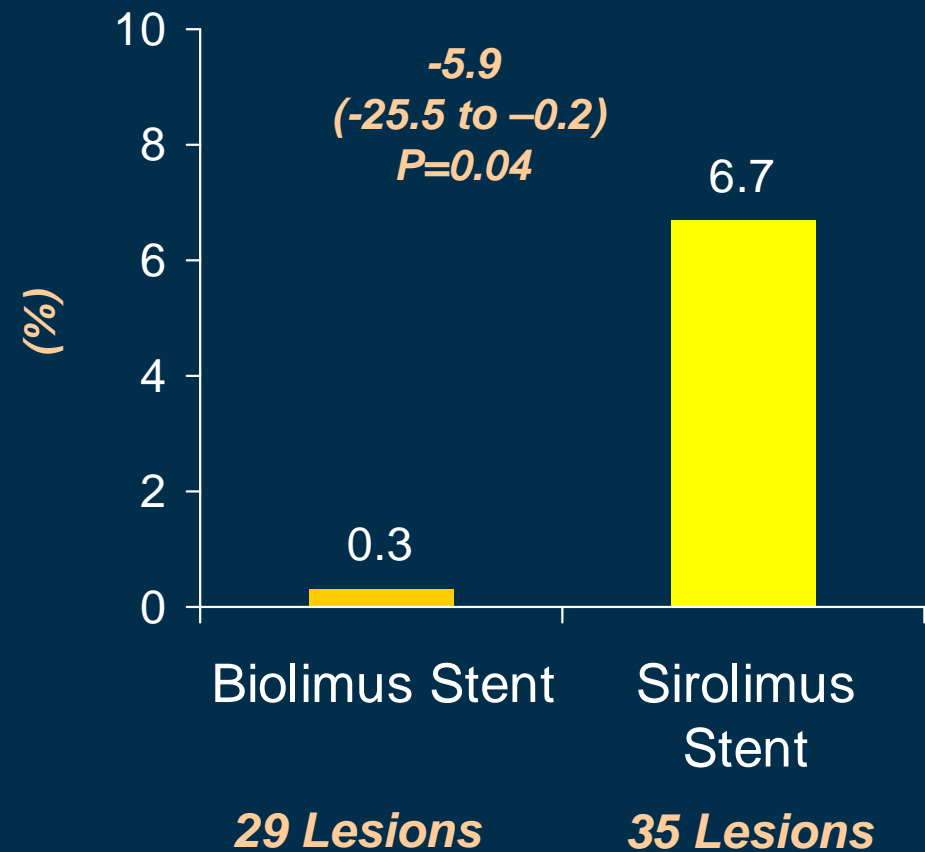


# LEADERS - OCT Substudy

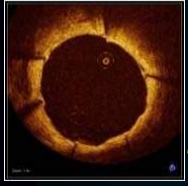
## Malapposed Struts



## Lesions With At Least 5% Malapposed Struts



**Sensitivity Analysis:** adjusted for lesion length, RVD, N of implanted stents, stent overlap



**LEADERS OCT Substudy**

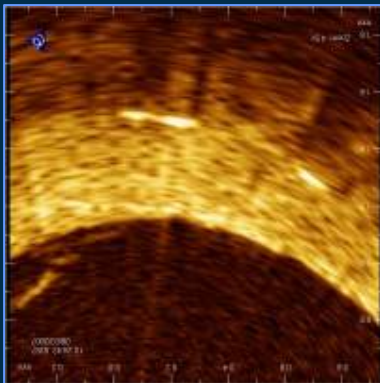
# Conclusions

- ✓ In a consecutive group of patients/lesions from the randomised LEADERS trial the biolimus eluting stent struts are more frequently apposed and have more frequently neointimal coverage visualised with OCT than sirolimus eluting stents
- ✓ The clinical relevance of these findings require further scrutiny
- ✓ Neointimal thickness in covered struts is similar in sirolimus and biolimus struts and below 100  $\mu\text{m}$  (IVUS threshold) in the majority of cases (72.4%)

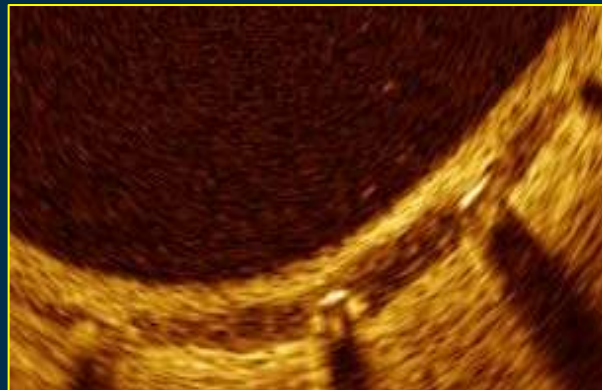
# OCT – Qualitative Analysis

## *Tissue Appearance*

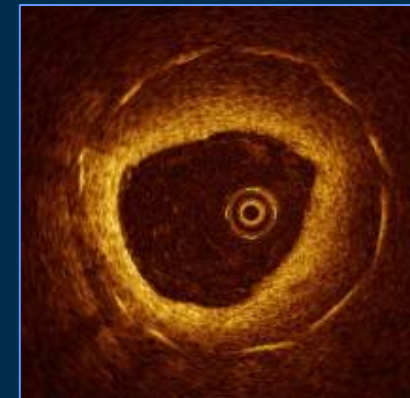
**A**



**B**



**C**



### ***Homogenous***

*Strut is covered on luminal side with tissue, that is homogenous, dense and signal-rich*

### ***Inhomogenous***

*Strut is covered on luminal side with tissue, that is not homogenous but shows signal-rich and sharply Delineated, focal signal-poor areas*

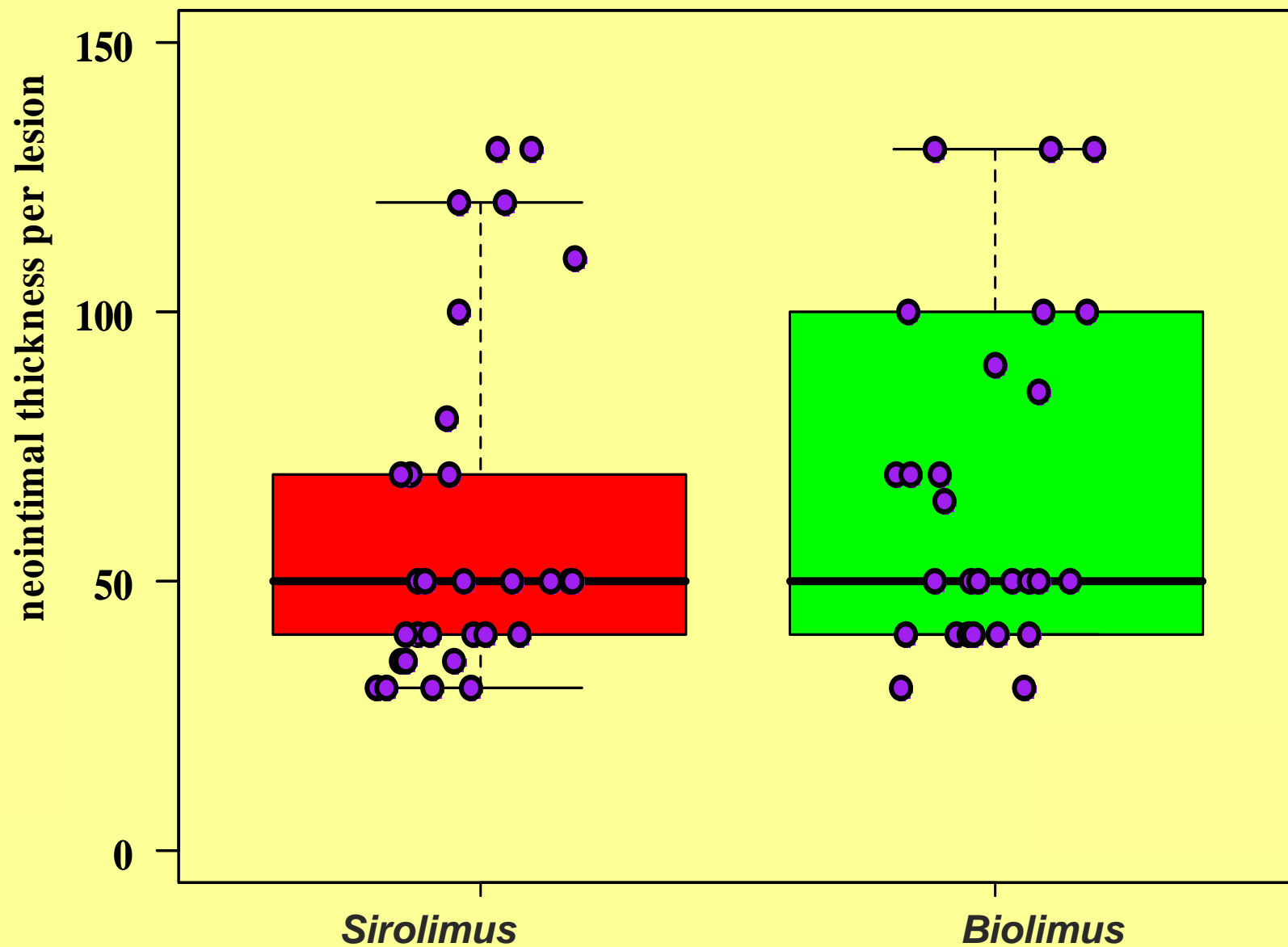
### ***Layered***

*Strut is covered on luminal side with tissue, that shows a concentric, layered appearance with transition from signal-rich to signal poor tissue*

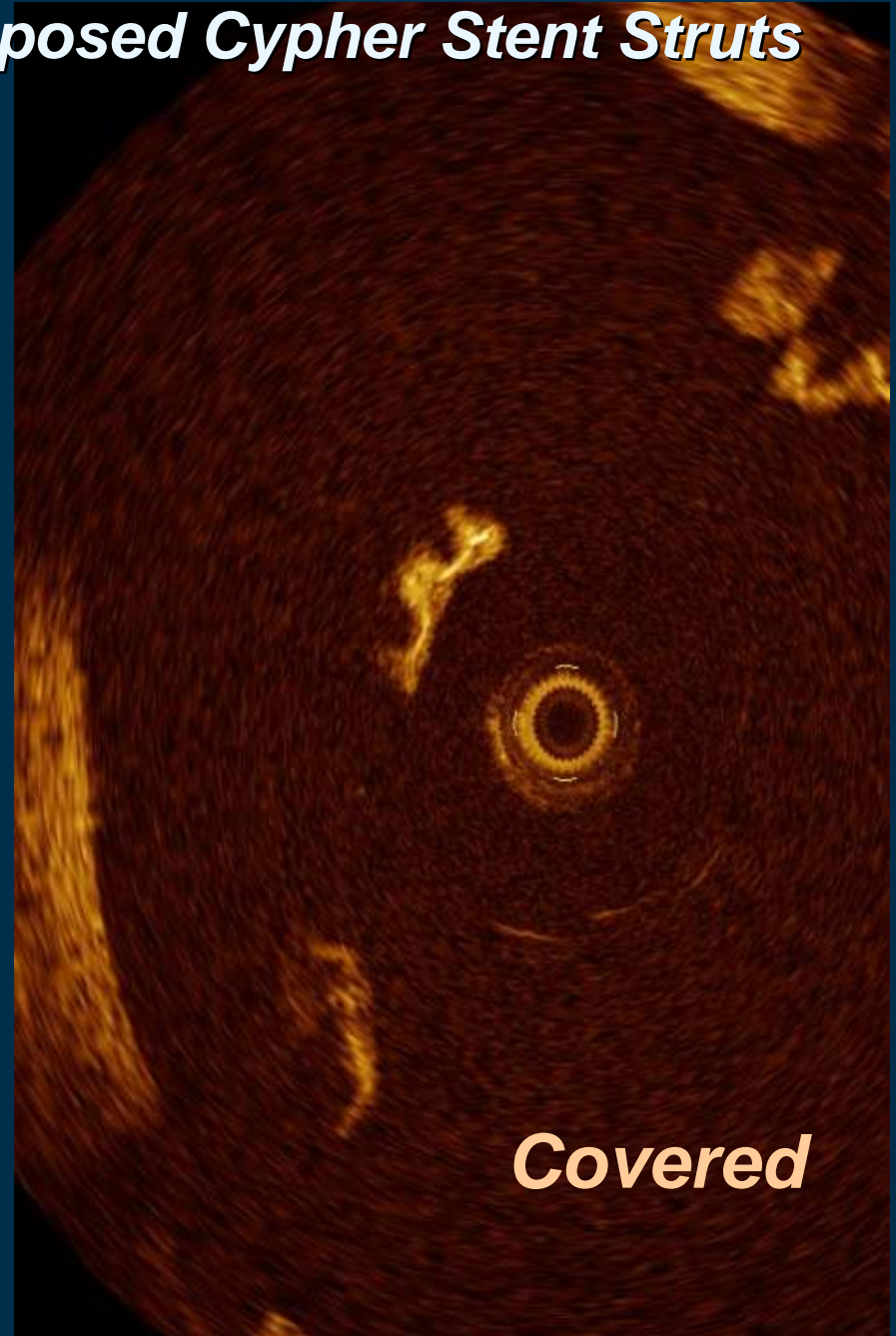
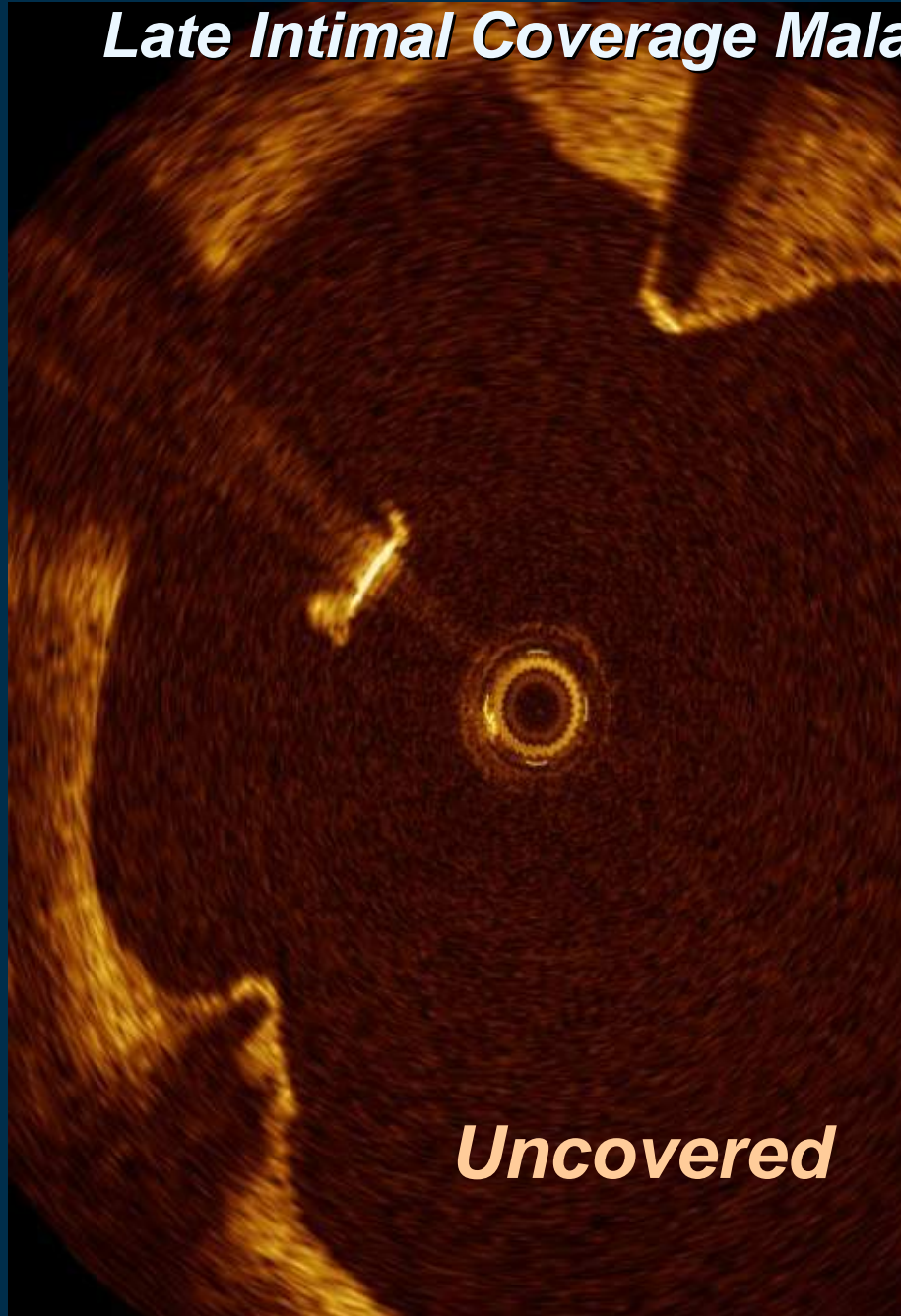
***Courtesy of Dr E. Regar, Rotterdam, NL***



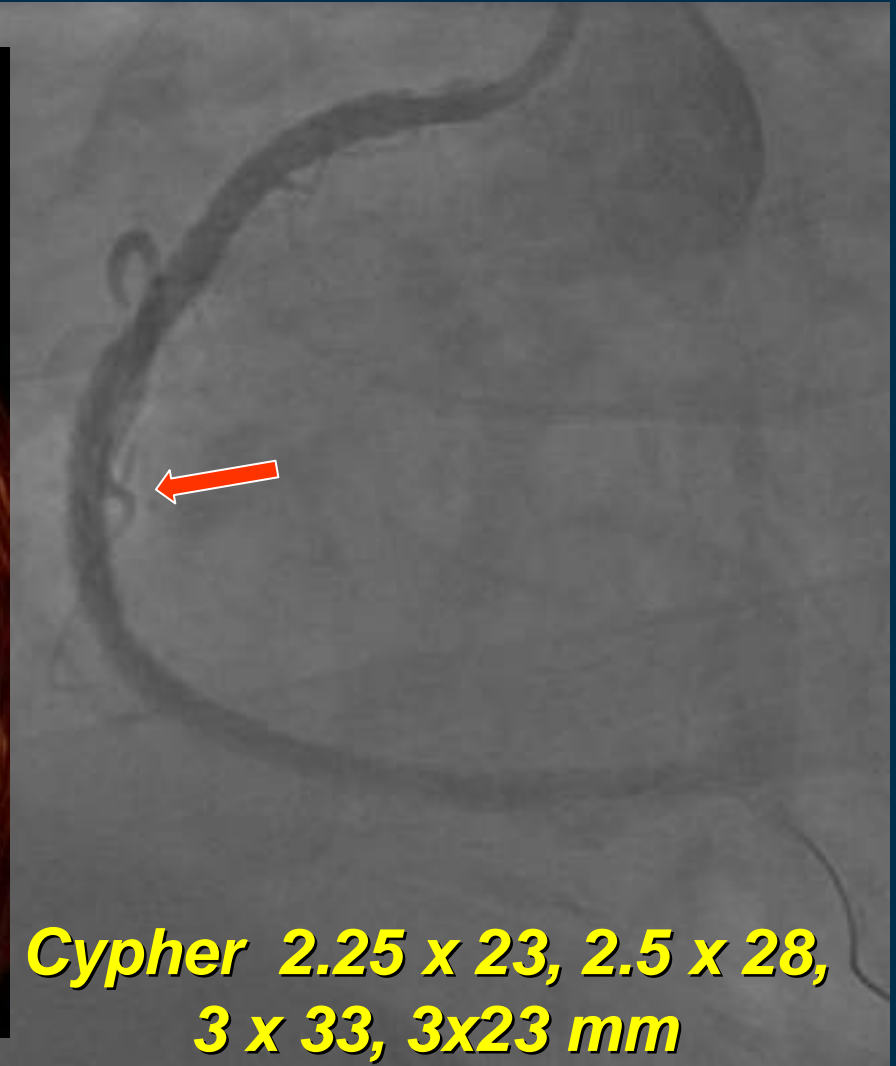
# Neointimal Coverage per Lesion



***Late Intimal Coverage Malapposed Cypher Stent Struts***



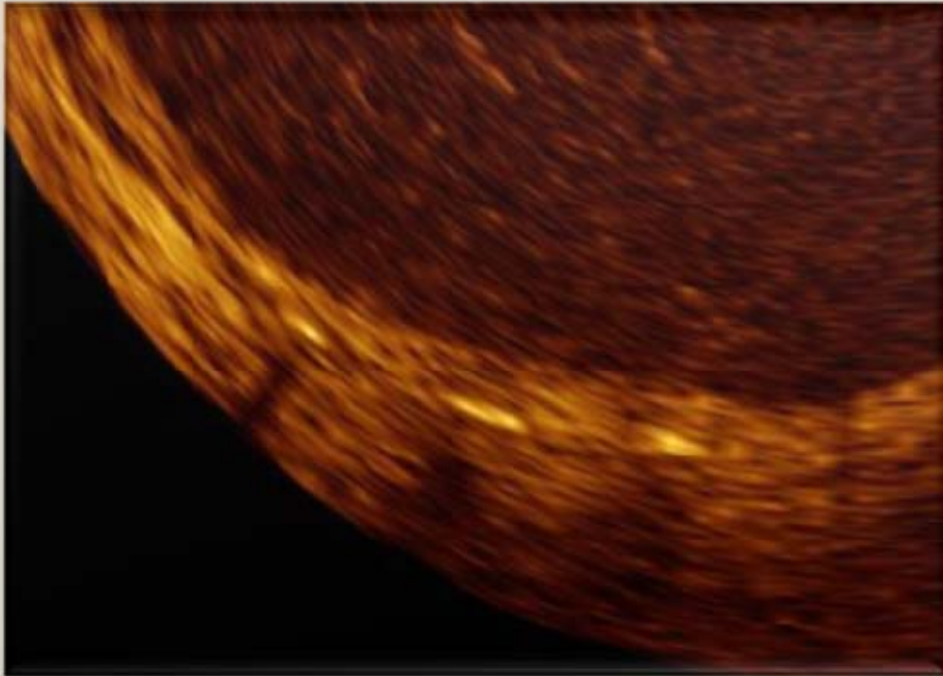
# ***Coverage of Overlapping Stents***



***Cypher 2.25 x 23, 2.5 x 28,  
3 x 33, 3x23 mm***

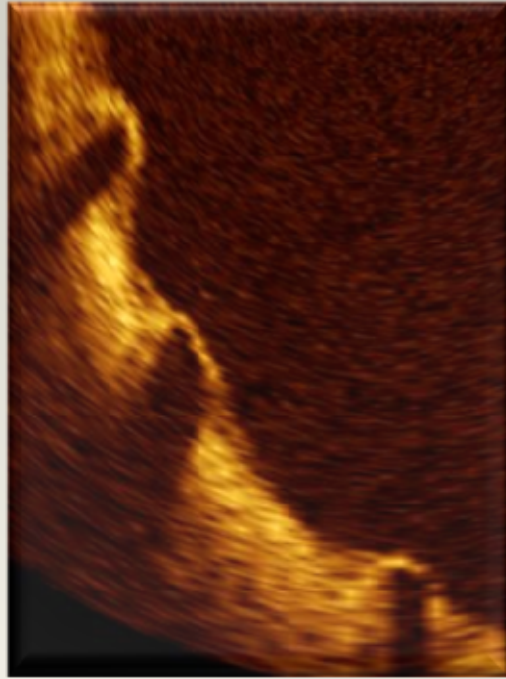


## *Thin Intimal Coverage of Stent Struts*

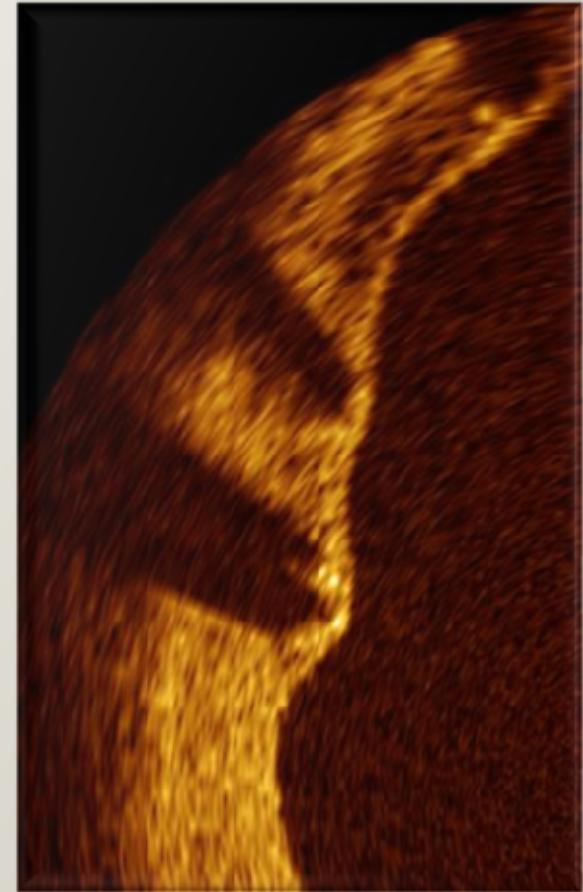
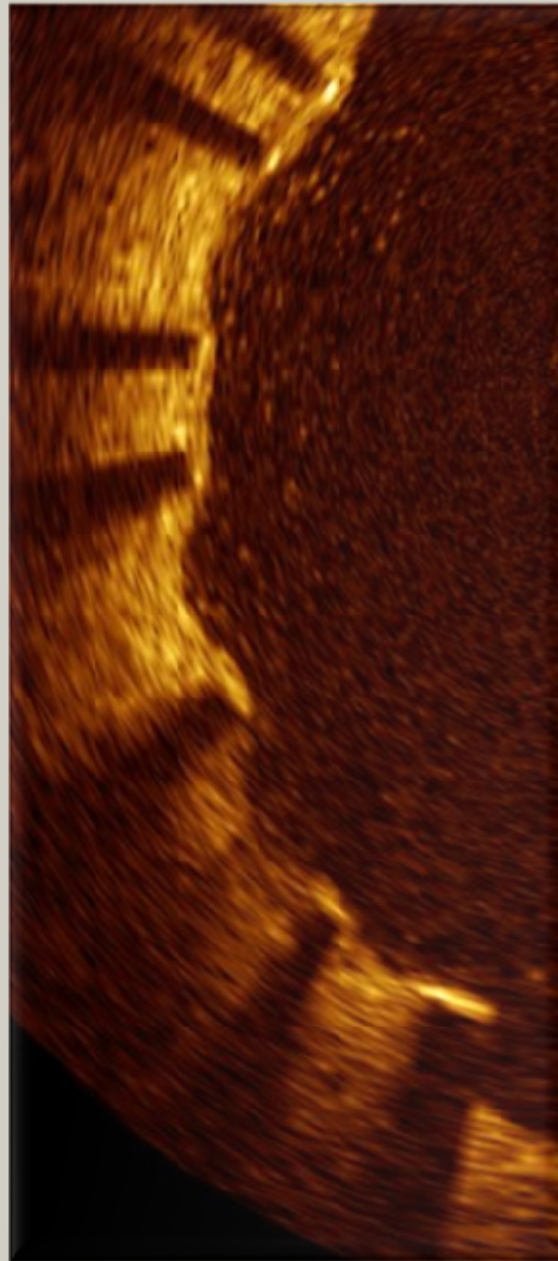


*BioMatrix Stent 7 Months post Implantation*

## ***Incomplete Coverage of Stent Struts***

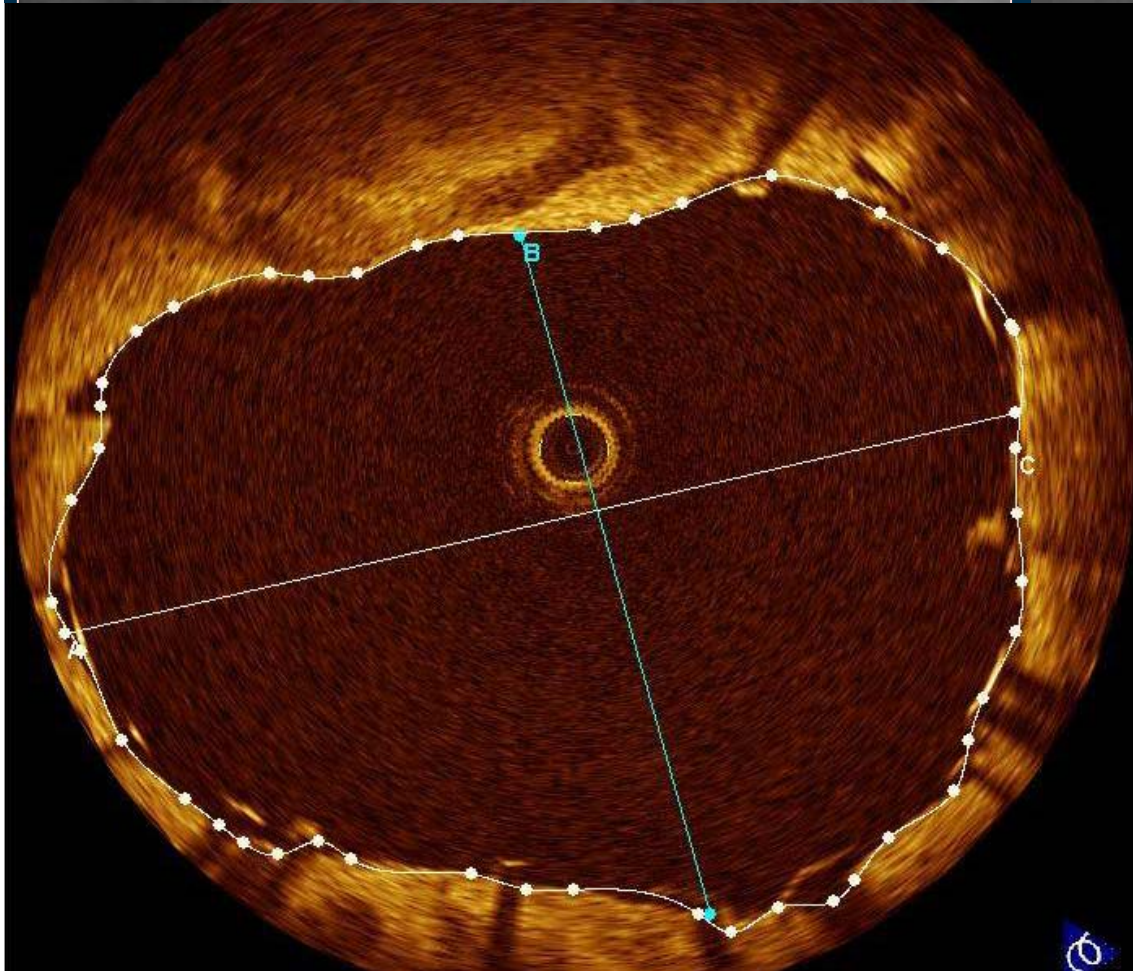


***BioMatrix***



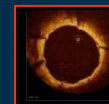
***Cypher***





***A Typical LEADERS  
Case from Rotterdam***

***2 Biolimus Eluting  
Stents***

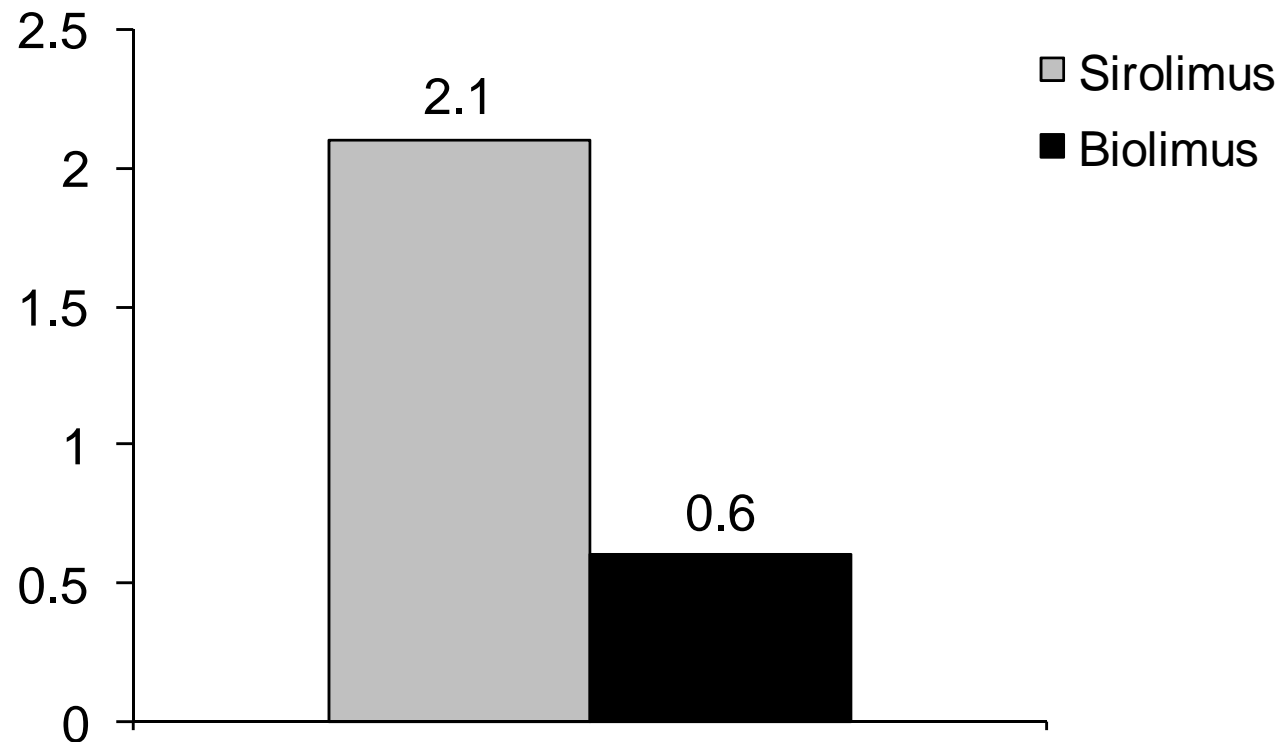


***LEADERS OCT Substudy***

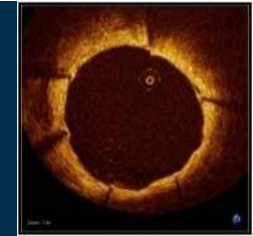
# Percentage of Uncovered Struts



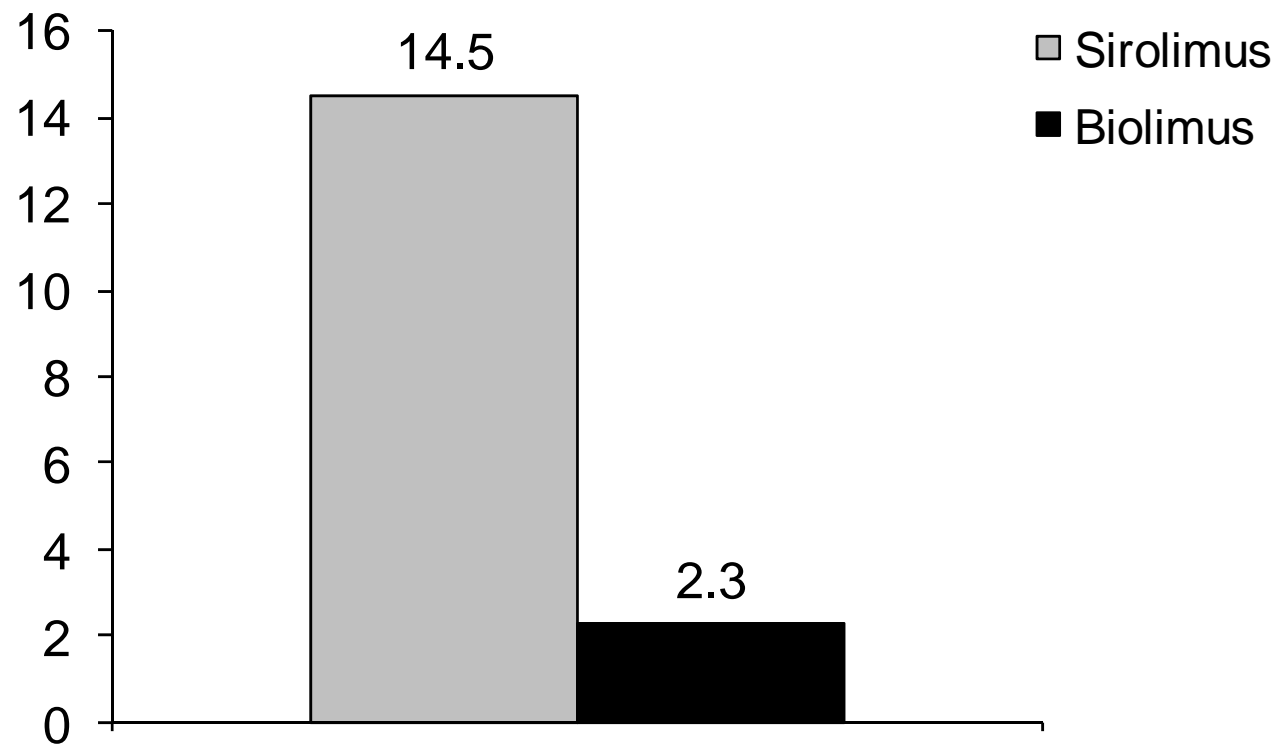
***Difference 1.4%, 95% CI 0.0 to 3.7%,  $p=0.06$***



# Percentage of lesions with >10% uncovered struts



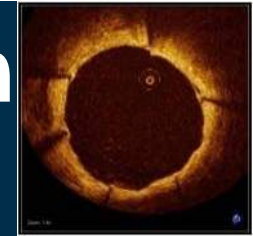
***Difference 11.2%, 95% CI -0.5 to 32.5%,  $p=0.06$***



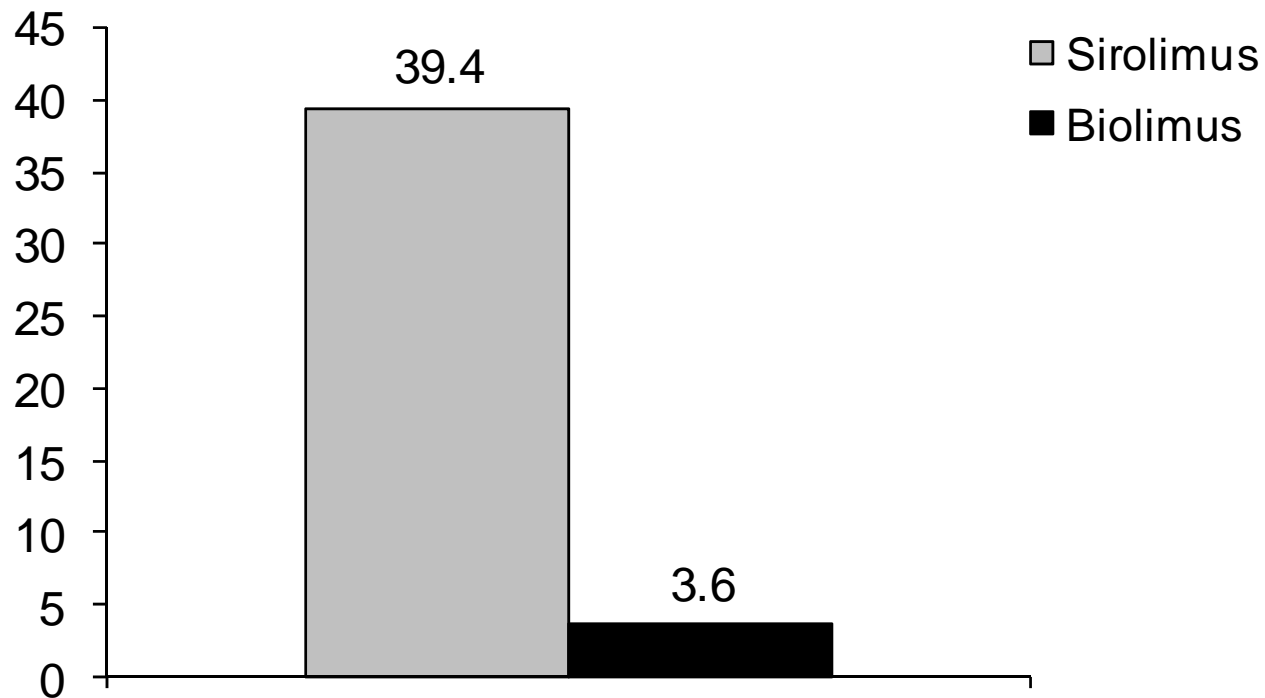
LEADERS



# Percentage of lesions with >5% uncovered struts



***Difference 34.5%, 95% CI 10.4 to 62.7%,  $p=0.005$***

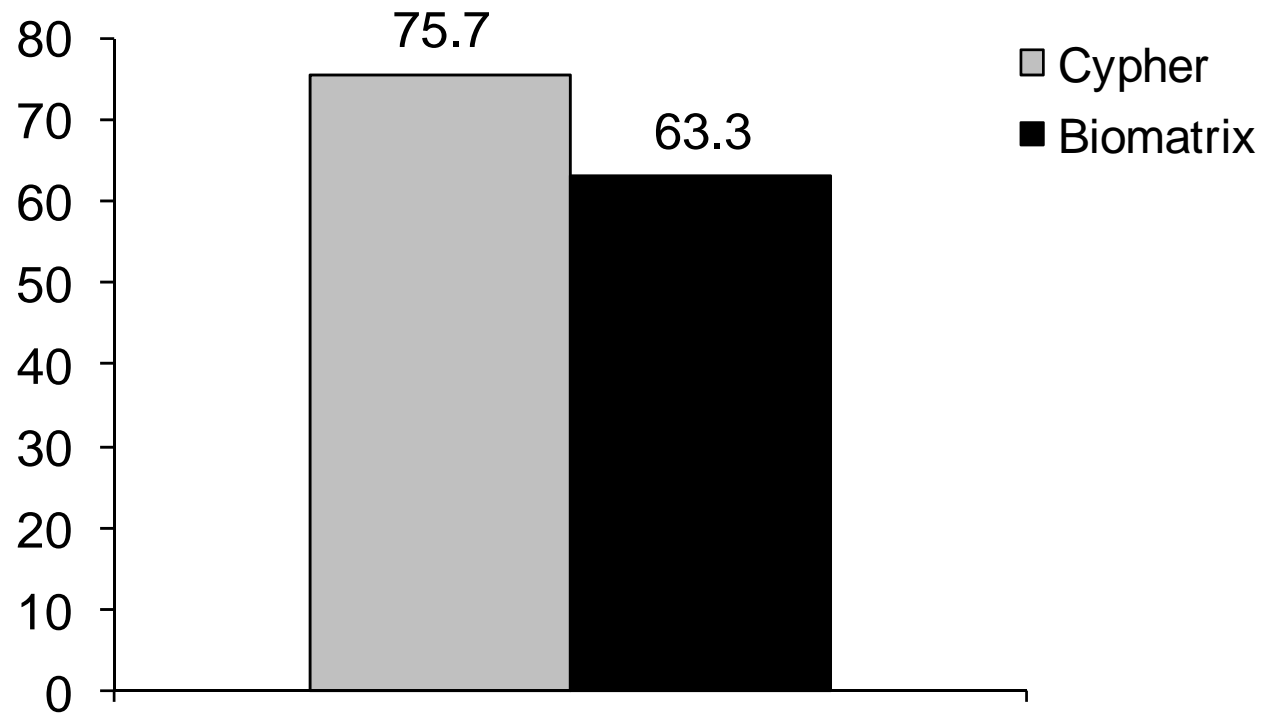




# Percentage of lesions with any uncovered struts



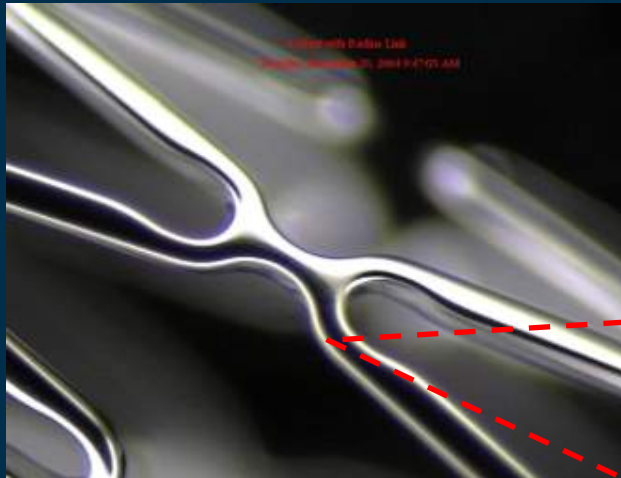
***Difference 11.7%, 95% CI -17.8 to 46.2%,***



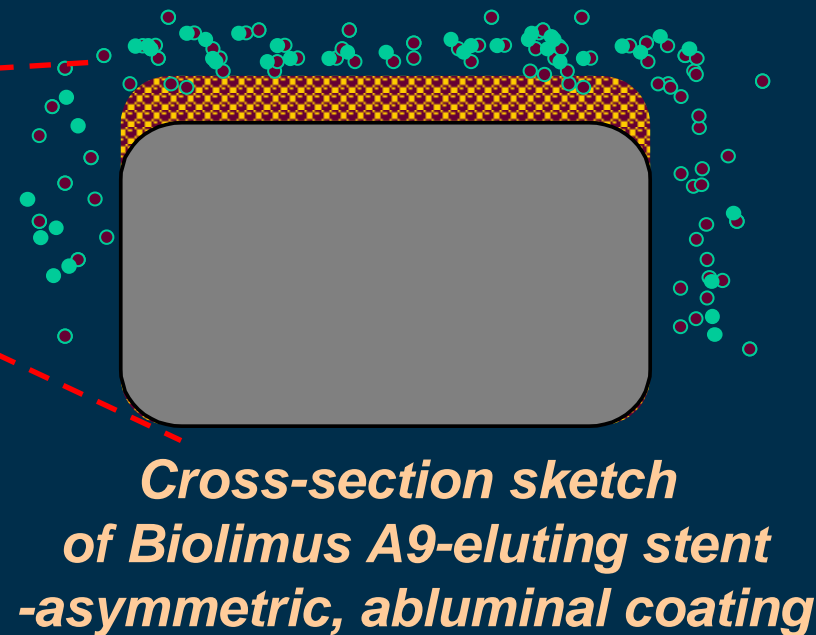
# BioMatrix™ Stent Platform

**Drug: Biolimus A9™**  
**15.6  $\mu\text{g}/\text{mm}$  stent**

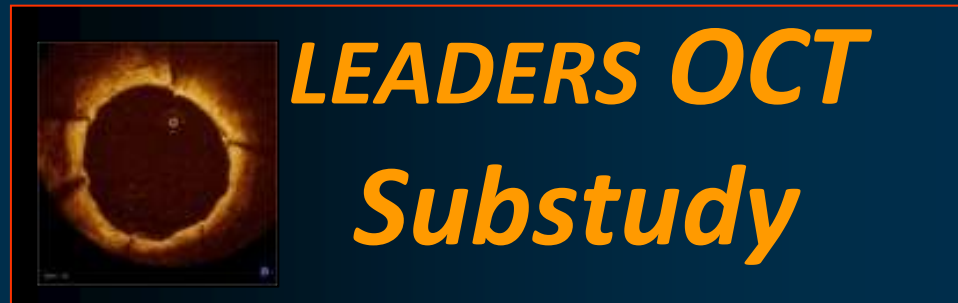
**Drug carrier: Poly(Lactic Acid)**  
**PLA:BA9=50:50**



**Stent platform:**  
**-stainless steel (112  $\mu\text{m}$ )**  
**-corrugated ring, quadrature-link**  
**design for improved flexibility**



# LEADERS: Analysis of 9-month OCT Results



*Patrick Serruys, MD*

*Carlo Di Mario, MD*

*Peter Barlis, MD*

*Evelyn Regar, MD*

*Peter Juni, MD*

*13:15-25, April 22, 2009*

*Asian Pacific TCT*