

OCT Technology: Differences between Biodegradable and Durable Polymers: Insights from the LEADERS Trial



LEADERS OCT Substudy

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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

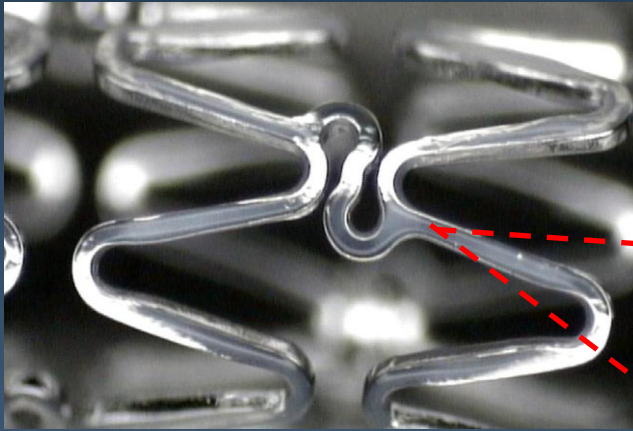
Why are People Excited About It?

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

BioMatrix Flex™ Stent Platform

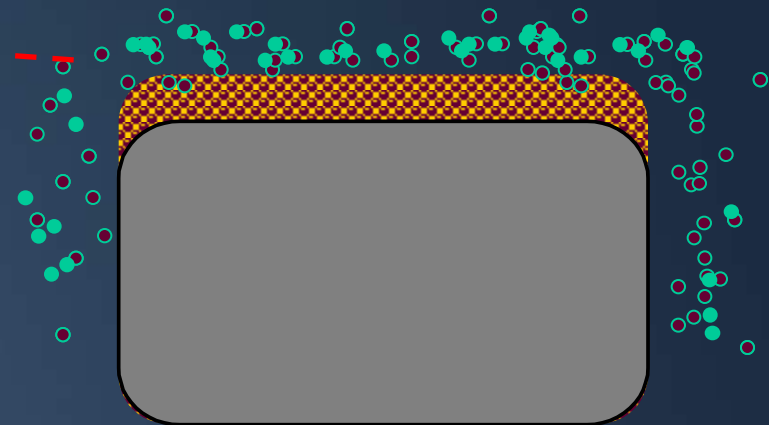
Drug: Biolimus A9™
15.6 µg/ mm stent

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



Stent platform:

- stainless steel (112 µm)
- corrugated ring, quadrature-link design for improved flexibility



**Cross-section sketch
of Biolimus A9-eluting stent**
-asymmetric, abluminal coating

| | Biolimus Stent | Sirolimus Stent | <i>P</i> |
|--|-----------------------|------------------------|----------|
| | 857 Patients | 850 Patients | |

| | | | |
|-----------------|-------------|-------------|-------------|
| 0-30 days | 1.6% | 1.6% | 0.98 |
| >30 days – 9 mo | 0.2% | 0.5% | 0.65 |
| 0 mo – 12 mo | 2.0% | 2.0% | 0.99 |
| 12 mo-24 mo | ? | ? | |
| 24-36 mo | ? | ? | |
| 36 – 48 mo | ? | ? | |
| 48 – 60 mo | ? | ? | |

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***

Baseline Clinical Characteristics



| | Sirolimus | Biolimus | P |
|--|------------------|-----------------|--------------|
| | n = 26 | n = 20 | Value |

| | | | |
|------------------------------|------------------|------------------|-------------|
| Age (years) | 65±10 | 66±10 | 0.98 |
| Male (%) | 69.2 | 70.0 | 0.99 |
| Hypertension (%) | 65.4 | 50.0 | 0.37 |
| Diabetes Mellitus (%) | 19.2 | 20.0 | 1.0 |
| Smoker (%) | 32.6 | 38.5 | 0.36 |
| Dyslipidaemia (%) | 73.1 | 50.0 | 0.13 |
| Family History (%) | 61.5 | 55.0 | 0.77 |
| Prior MI (%) | 34.6 | 25.0 | 0.54 |
| Prior PCI (%) | 23.1 | 15.0 | 0.71 |
| Prior CABG (%) | 15.4 | 5.0 | 0.37 |
| LVEF (%) | 54.9±16.7 | 64.5±6.36 | 0.60 |
| Primary PCI STEMI (%) | 15.4 | 25.0 | 0.47 |





| | ALL (n=64) | Sirolimus (n=35) | Biolimus (n=29) | P value |
|-----------------------|---------------|---------------------|--------------------|---------|
| Target vessel | | | | 0.15 |
| Left main | 0 | 0 | 0 | |
| LAD | 27 | 12 | 15 | |
| Left circumflex | 13 | 10 | 3 | |
| RCA | 24 | 13 | 11 | |
| Bypass graft | 0 | 0 | 0 | |
| Reference VD (mm) | 2.5±0.6 | 2.4±0.5 | 2.7±0.6 | 0.02 |
| Lesion length (mm) | 13.8±11.9 | 13.3±9.1 | 14.3±14.5 | 0.80 |
| MLD (mm) | 0.76±0.58 | 0.63±0.53 | 0.93±0.60 | 0.04 |
| DS, % | 70.8±20.8 | 73.4±21.0 | 66.9±20.3 | 0.20 |

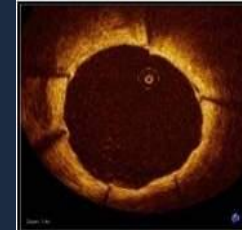


QCA After Procedure



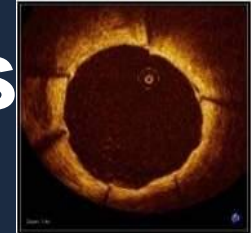
| | ALL (n=64) | Cypher Select (n=35) | BioMatrix (n=29) | P value |
|------------------------|------------|----------------------|------------------|---------|
| MLD (mm) | | | | |
| In-stent | 2.30±0.46 | 2.22±0.43 | 2.40±0.47 | 0.13 |
| In-segment | 2.00±0.50 | 1.95±0.45 | 2.06±0.55 | 0.49 |
| DS (%) | | | | |
| In-stent | 14.3±6.7 | 15.2±7.0 | 13.1±6.4 | 0.25 |
| In-segment | 23.2±8.3 | 22.9±7.7 | 23.2±8.3 | 0.76 |
| Acute gain (mm) | | | | |
| In-stent | 1.54±0.51 | 1.58±0.45 | 1.50±0.57 | 0.73 |
| In-segment | 1.24±0.53 | 1.31±0.44 | 1.15±0.63 | 0.30 |

QCA at F/U



| | ALL (n=64) | Sirolimus (n=35) | Biolimus (n=29) | P value |
|-------------------|-----------------|------------------|-----------------|---------|
| Reference VD (mm) | 2.71±0.53 | 2.60±0.57 | 2.84±0.44 | 0.11 |
| MLD (mm) | | | | |
| In-stent | 2.13±0.63 | 2.03±0.57 | 2.24±0.69 | 0.27 |
| In-segment | 1.91±0.59 | 1.83±0.54 | 2.01±0.63 | 0.37 |
| DS (%) | | | | |
| In-stent | 21.73±16.4 7 | 21.89±13.56 | 21.54±19.5 1 | 0.98 |
| In-segment | 27.69±15.0 5 | 27.55±12.33 | 27.85±17.8 7 | 0.87 |
| Late loss | | | | |
| In-stent | 0.17±0.40 | 0.18±0.39 | 0.16±0.41 | 0.99 |
| In-segment | 0.08±0.35 | 0.09±0.36 | 0.06±0.35 | 0.77 |

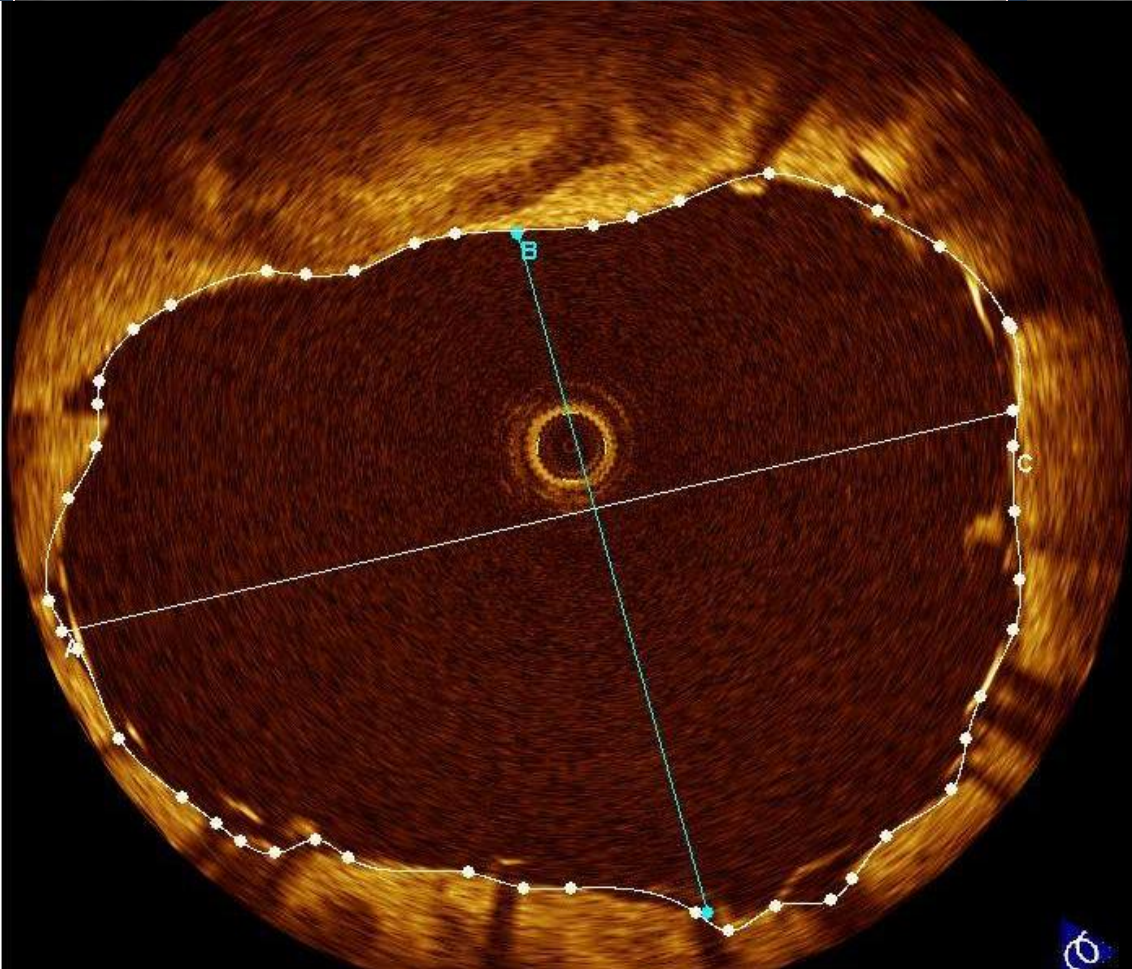
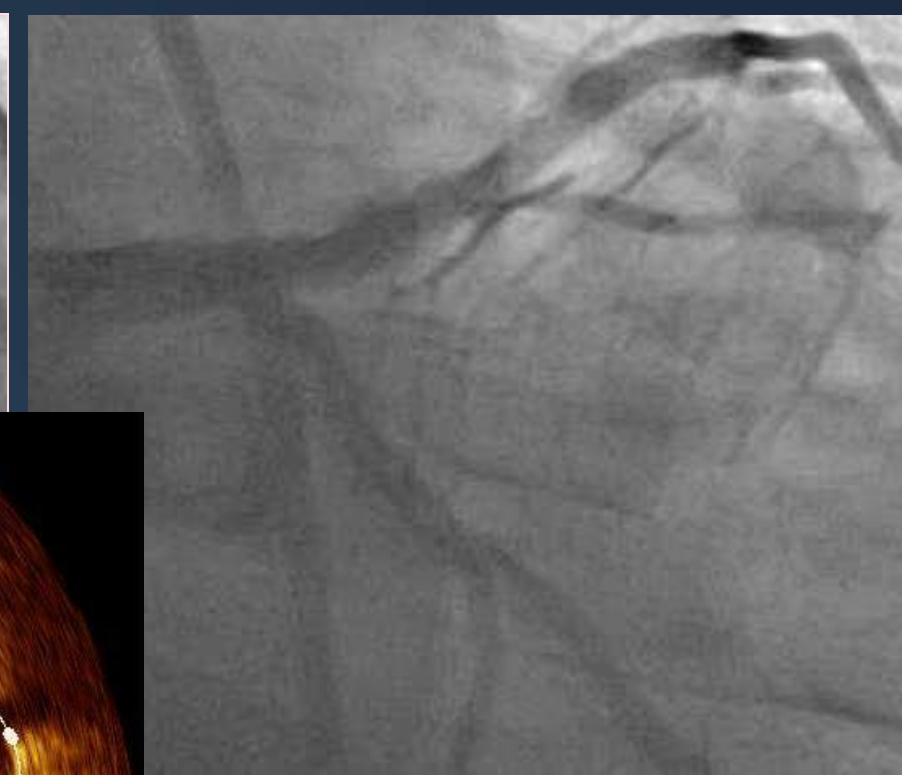




MACE (46 Pts, 100%) & QCA (65 Lesions, 98%)

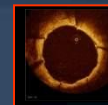
| Major Adverse Events | Sirolimus n = 26 | Biolimus n = 20 | P Value |
|----------------------|---------------------|--------------------|---------|
| Q-Wave MI | 0 | 0 | |
| Non-Q wave MI | 2 | 1 | |
| TVR | 2 | 0 | |



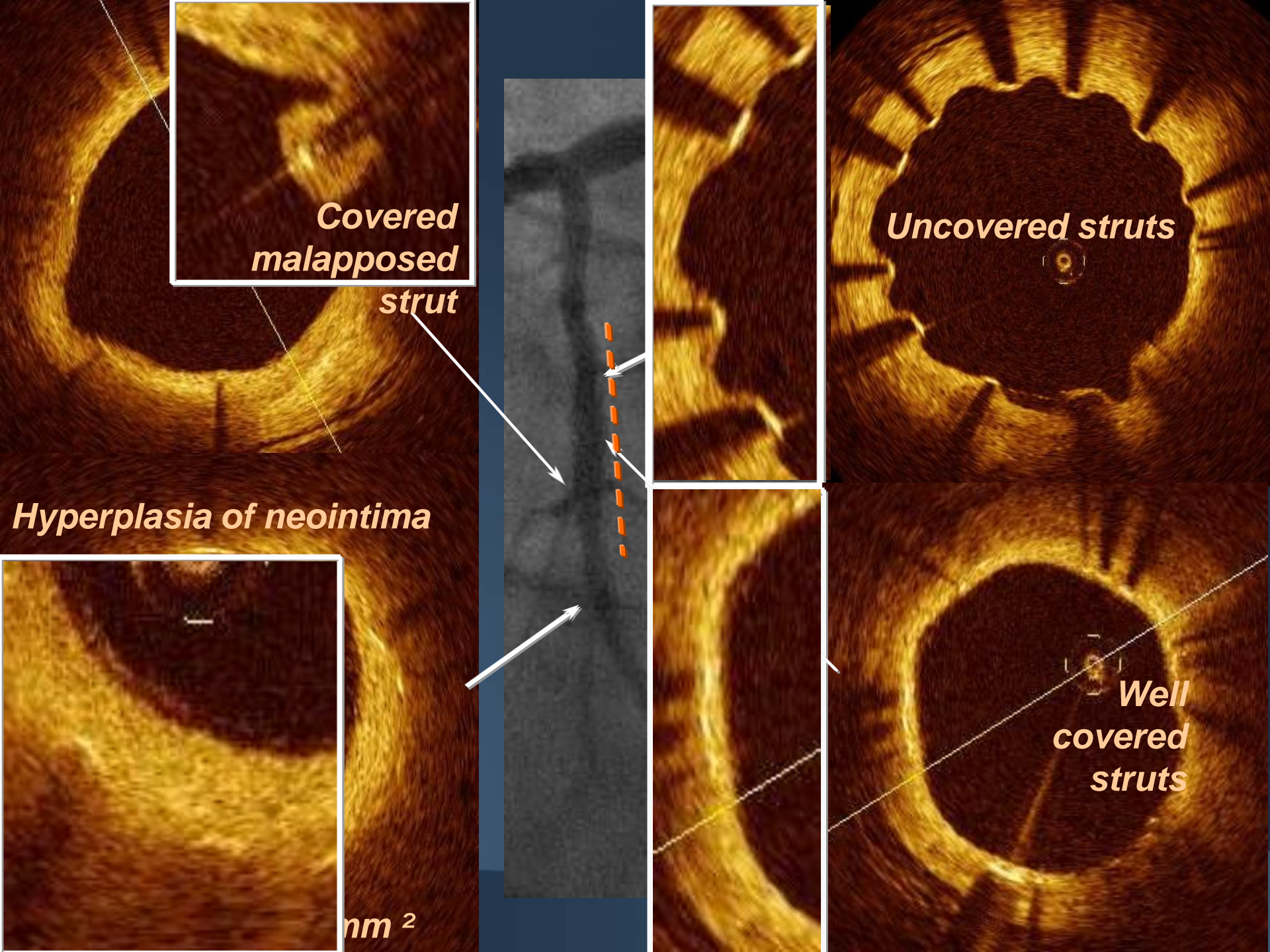


***A Typical LEADERS
Case from Rotterdam***

***2 Biolimus Eluting
Stents***

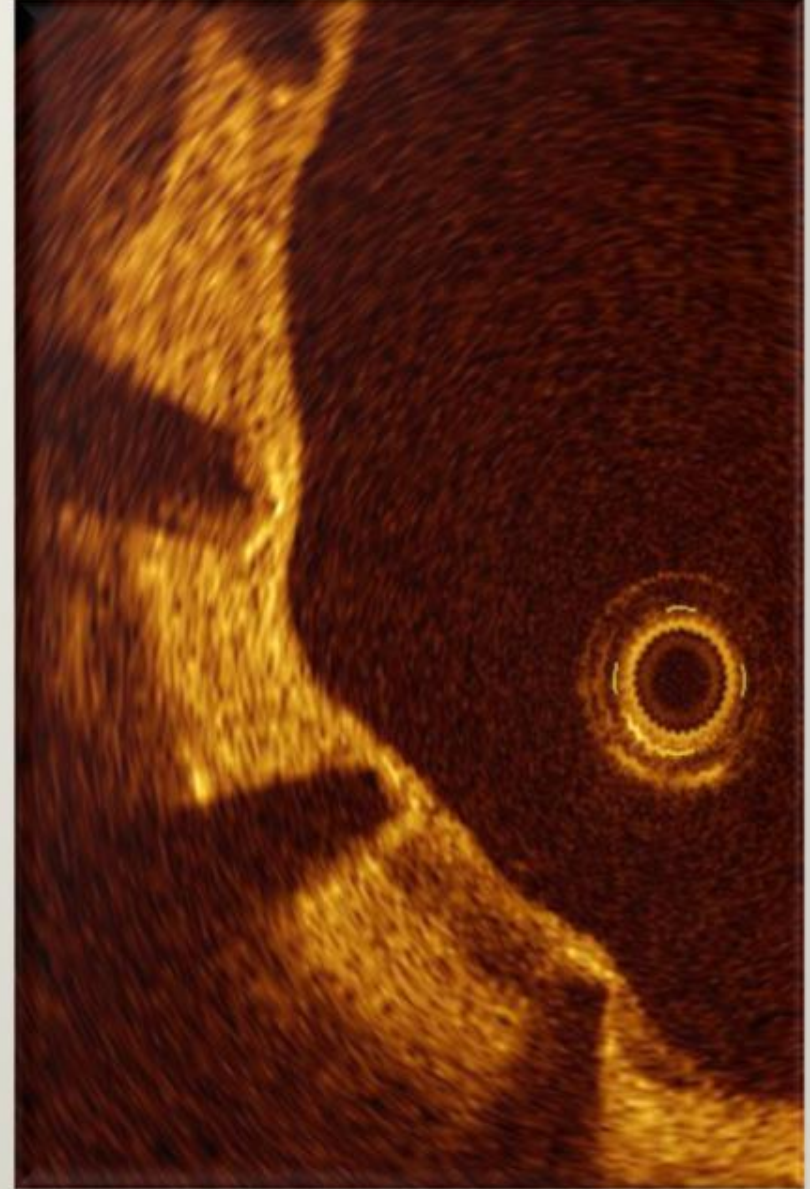
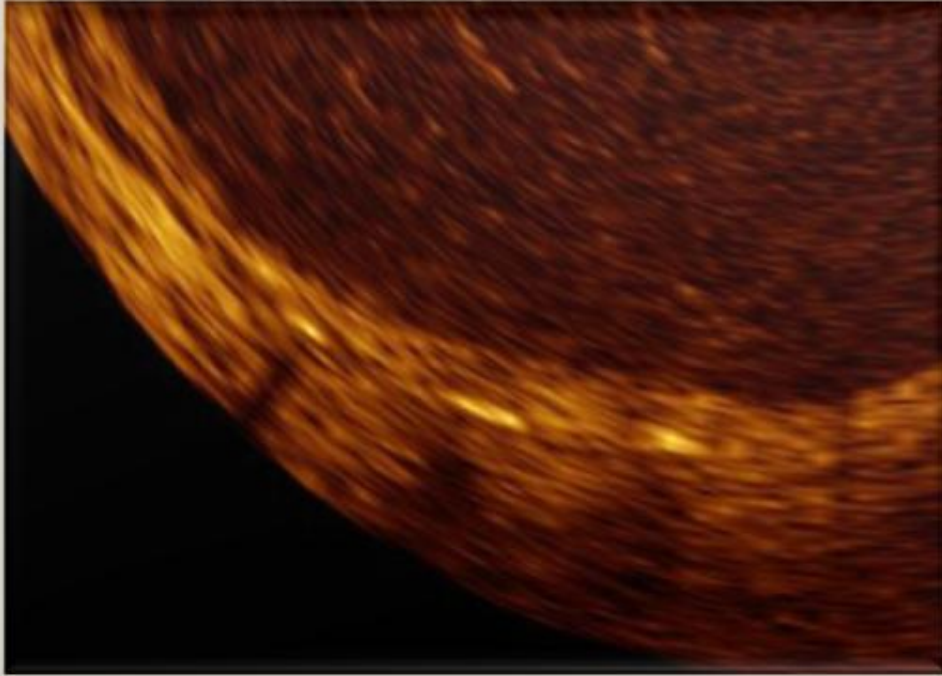


LEADERS OCT Substudy



20 YEARS OF INNOVATION

Thin Intimal Coverage of Stent Struts

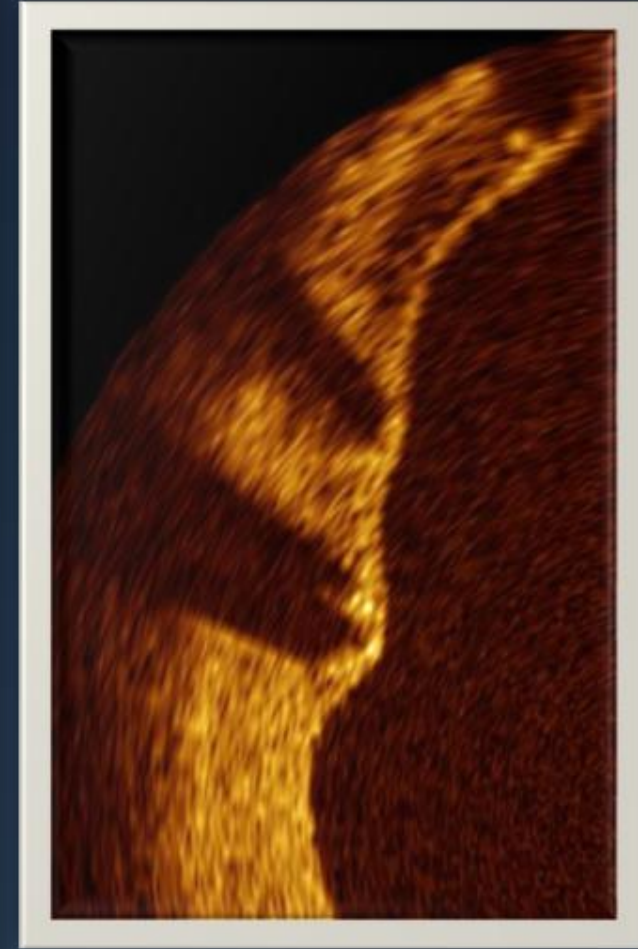
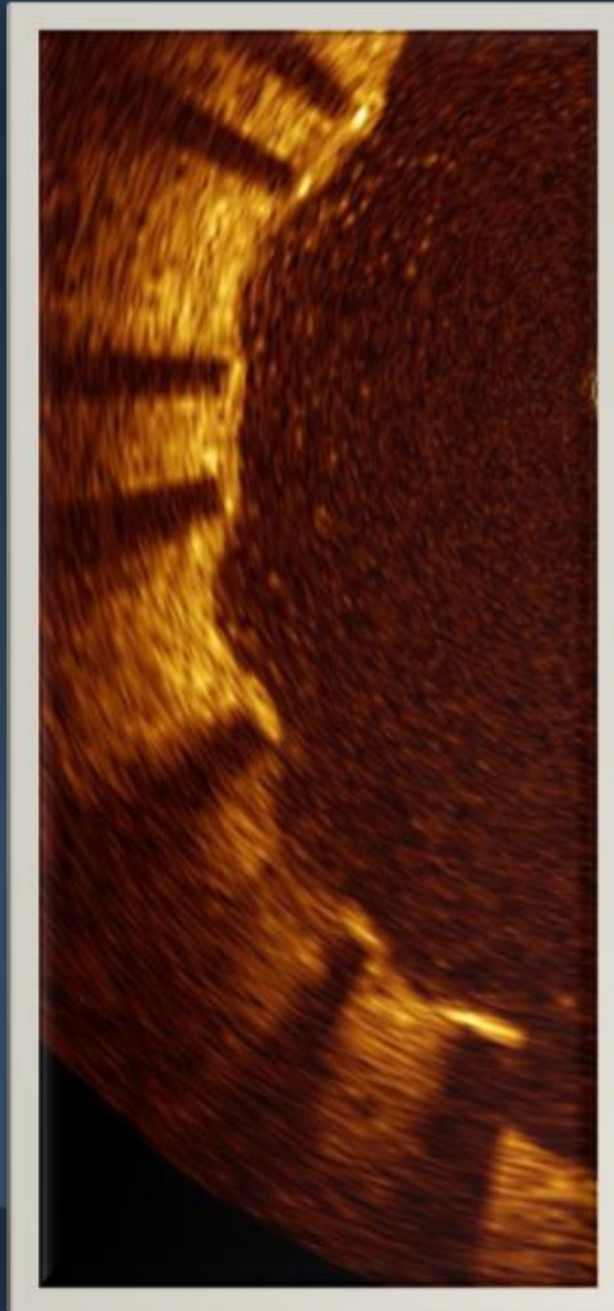


BioMatrix Stent 7 Months post Implantation

Incomplete Coverage of Stent Struts

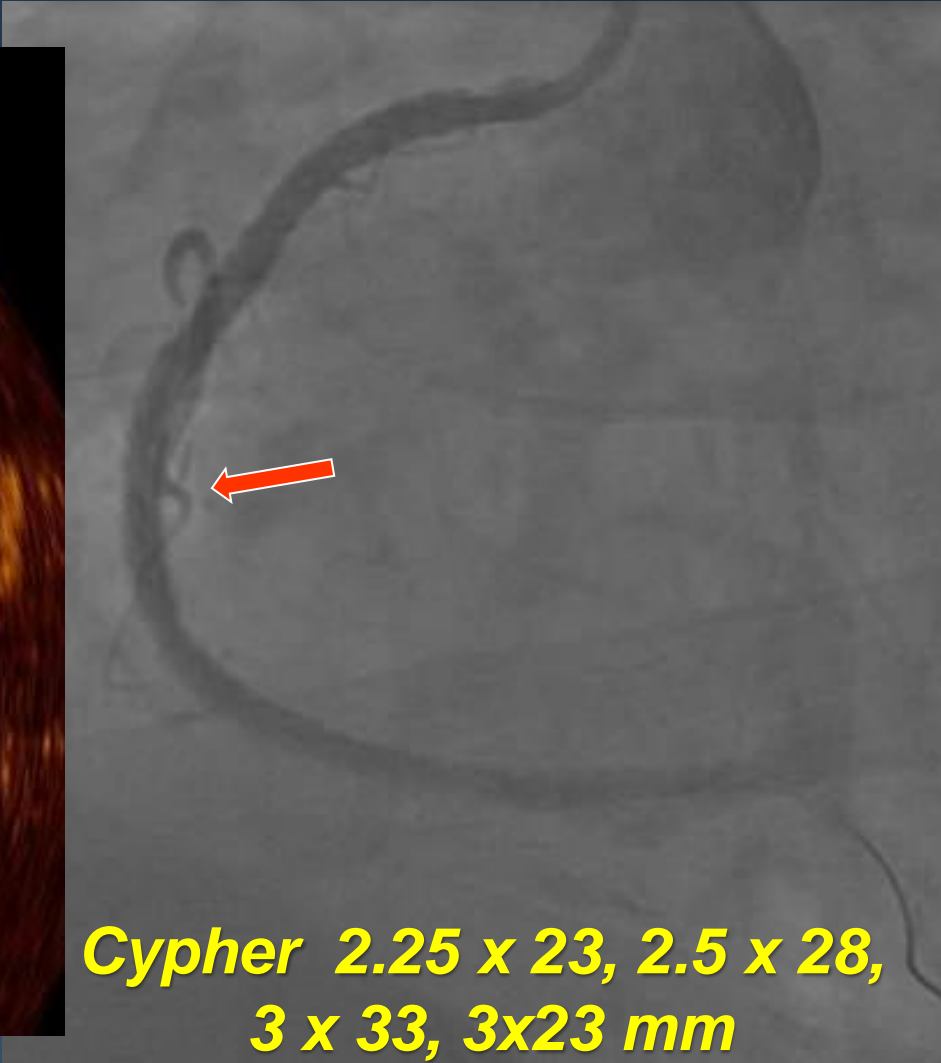
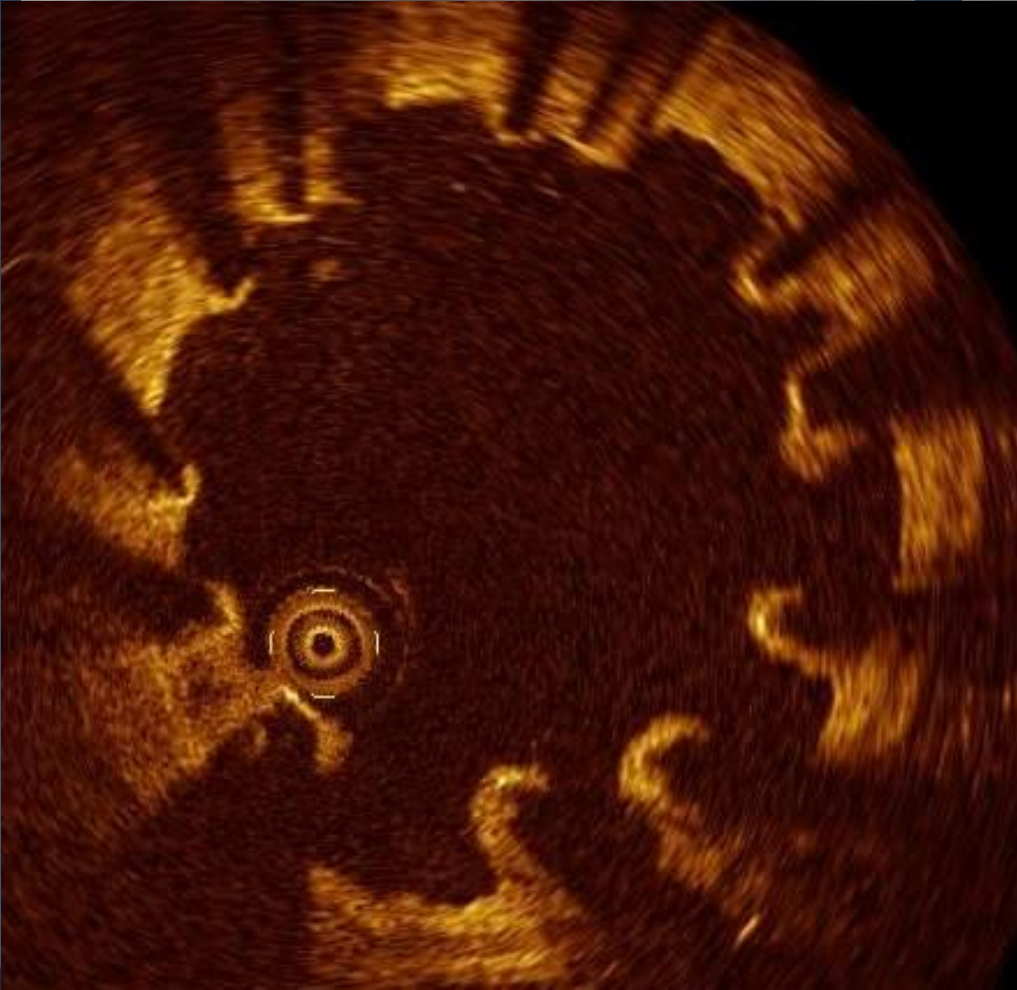


BioMatrix



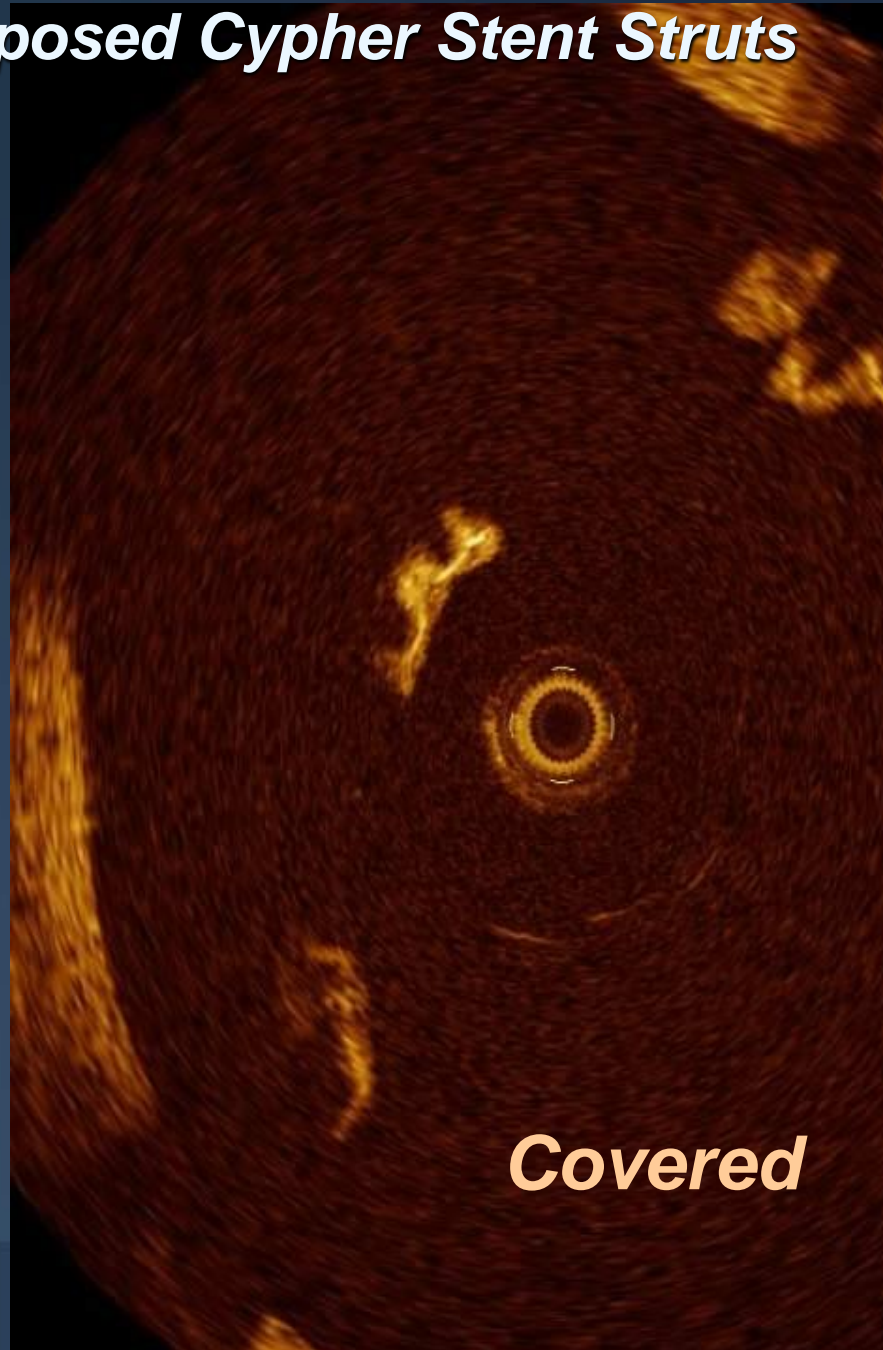
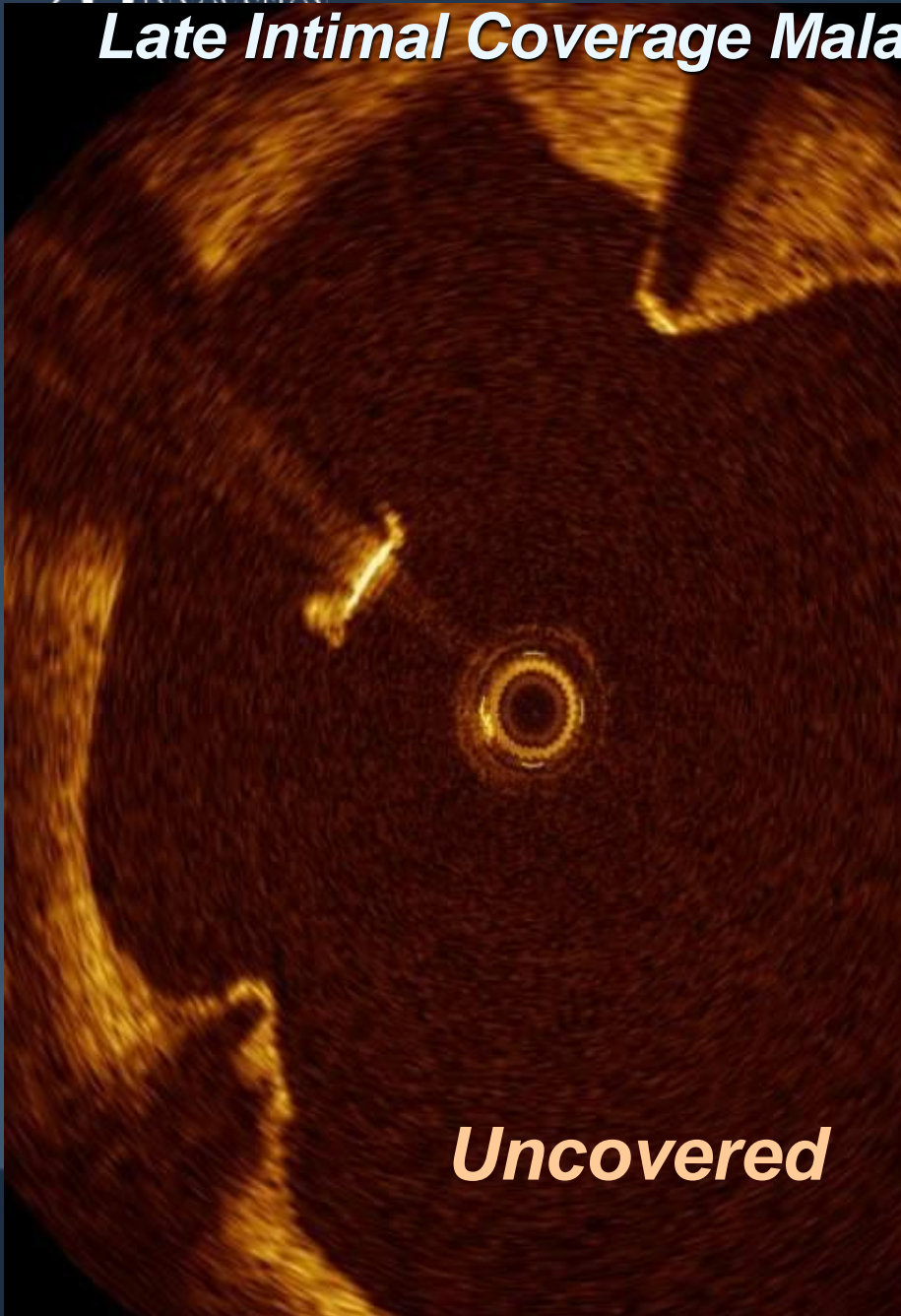
Cypher

Coverage of Overlapping Stents



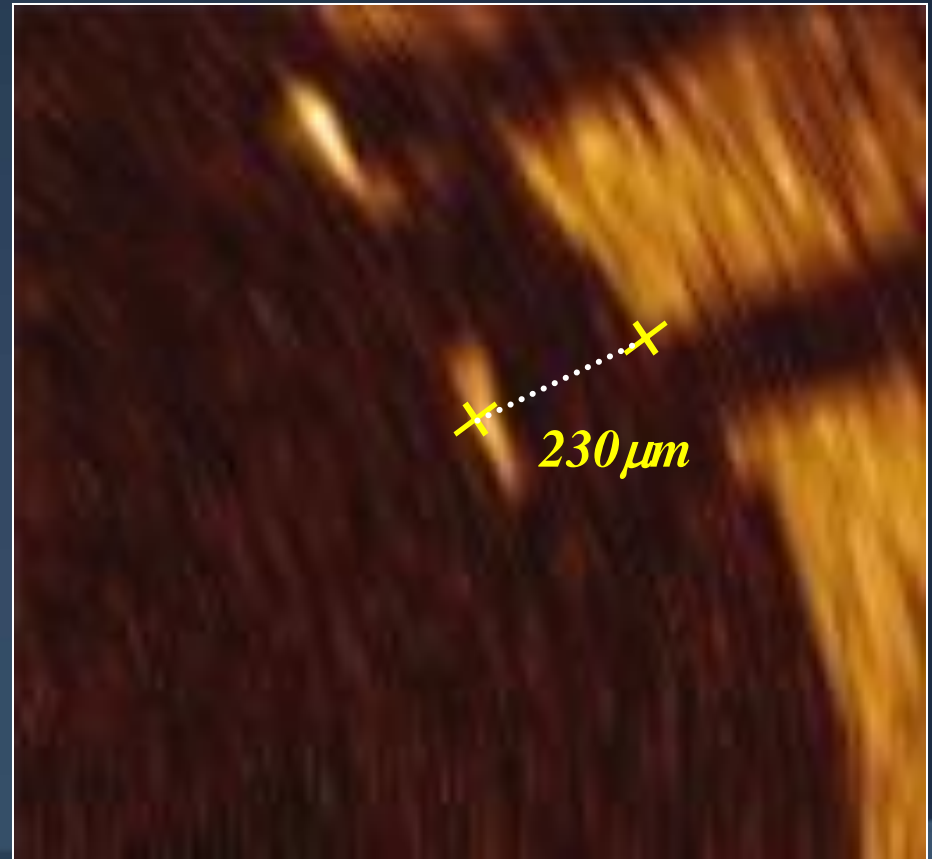
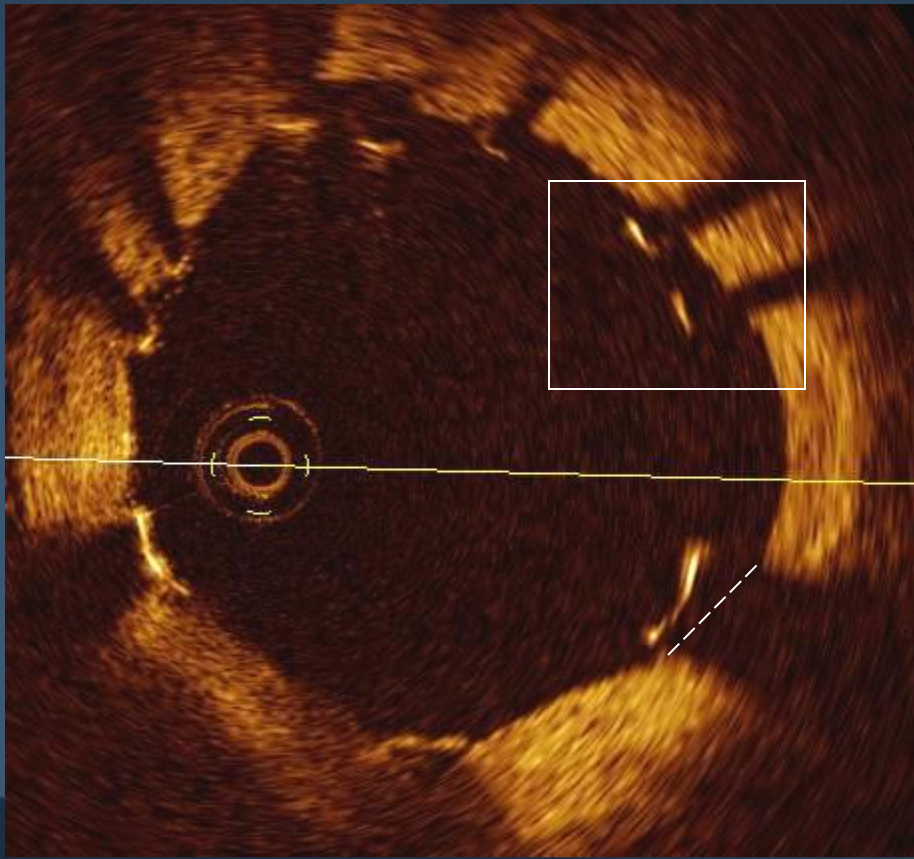
**Cypher 2.25 x 23, 2.5 x 28,
3 x 33, 3x23 mm**

Late Intimal Coverage Malapposed Cypher Stent Struts



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

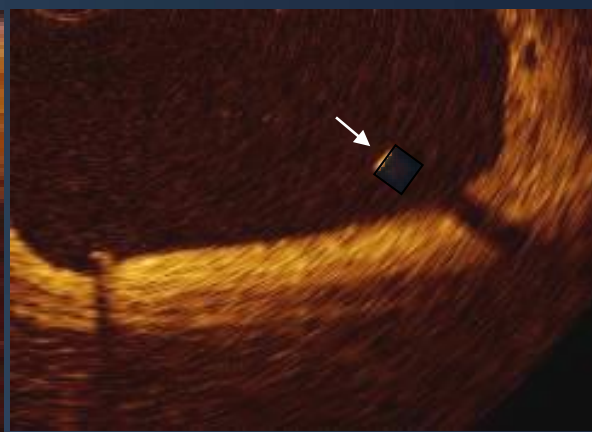
| | Apposed | | Malapposed |
|--------------------------|--------------|------------------|--------------------|
| | Embedded | Protruding | Malapposed |
| Cypher Select | < 80 μ m | 80 - 160 μ m | \geq 160 μ m |
| Taxus Liberte | < 65 μ m | 65 - 130 μ m | \geq 130 μ m |
| Endeavor/Resolute | < 55 μ m | 55 - 110 μ m | \geq 110 μ m |
| BioMatrix | < 56 μ m | 56 - 112 μ m | \geq 112 μ m |



Embedded

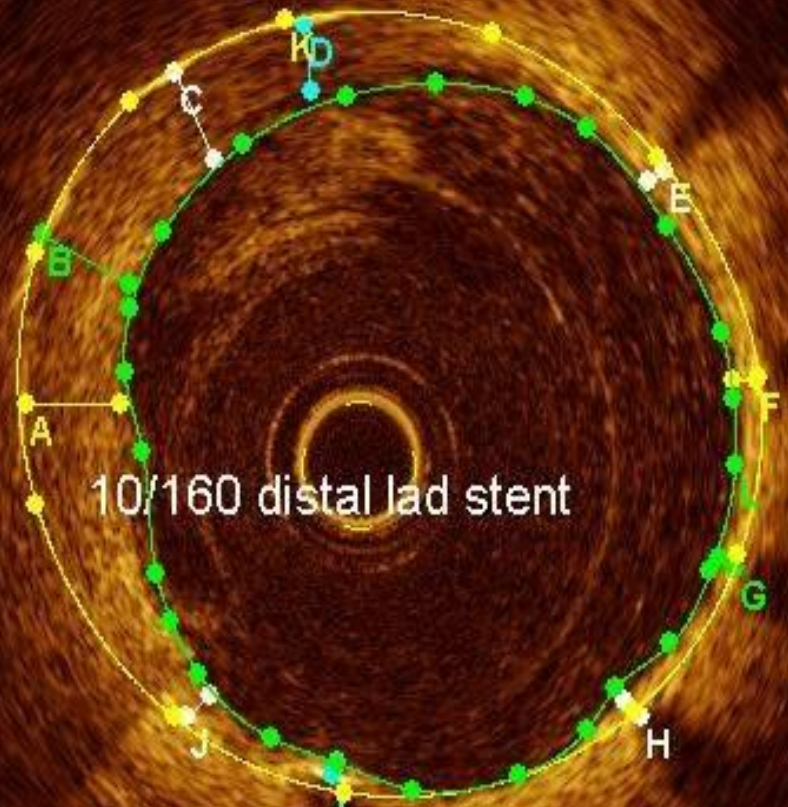


Protruding



Malapposed

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: 5.25mm²
L Area: 3.87mm²



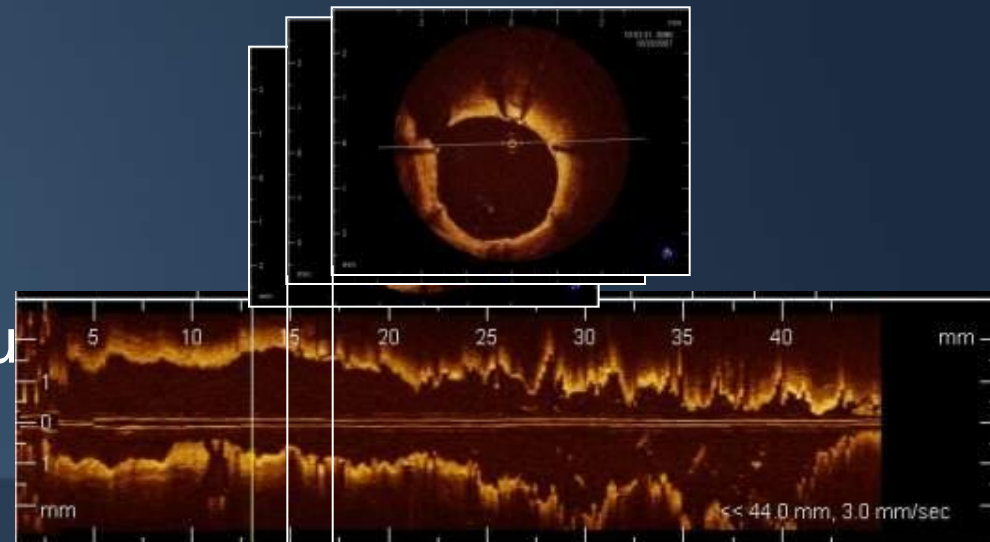
Neointimal & Stent Areas + Thickness

*Independent Core
Laboratory
(Cardialysis) with
Analysts Blinded
To Randomisation*



OCT Data Analysis

- Analysis of stented segment with computer-assisted contour detection at 450 μm intervals
 - Lumen area
 - Stent area
 - Neointimal area
- Analysis of individual cross sections
 - Strut apposition
 - Strut coverage
 - Tissue appearance
 - Neointimal thickness
 - Intraluminal tissue/thrombus

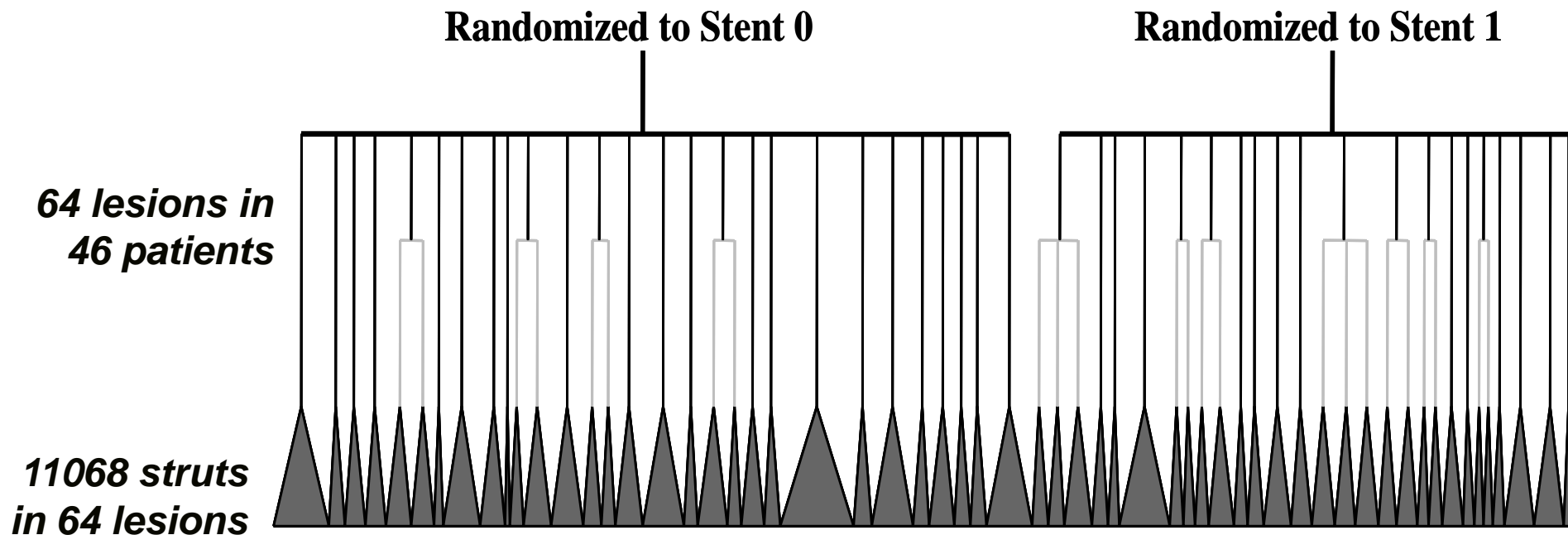




LEADERS OCT Substudy

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

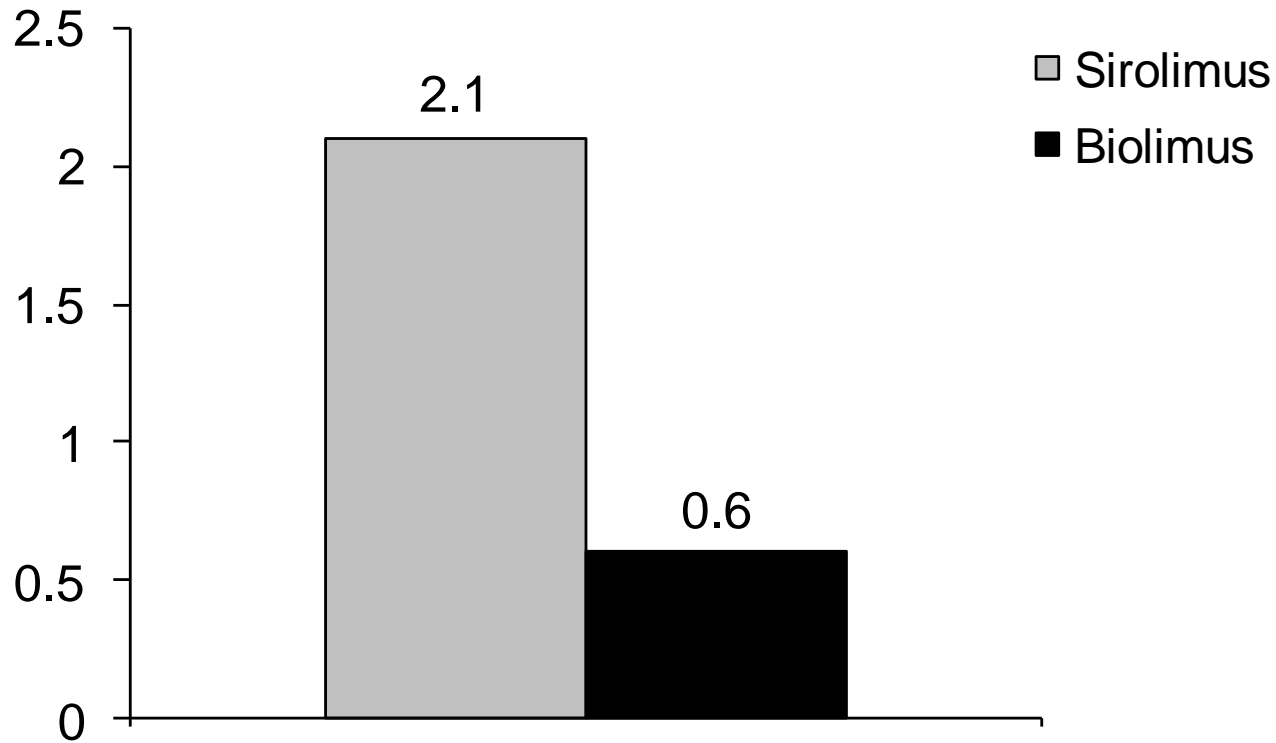
- Implicitly assigns analytical weights proportional to numbers of struts observed within each lesion



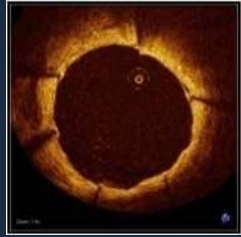
Percentage of Uncovered Struts



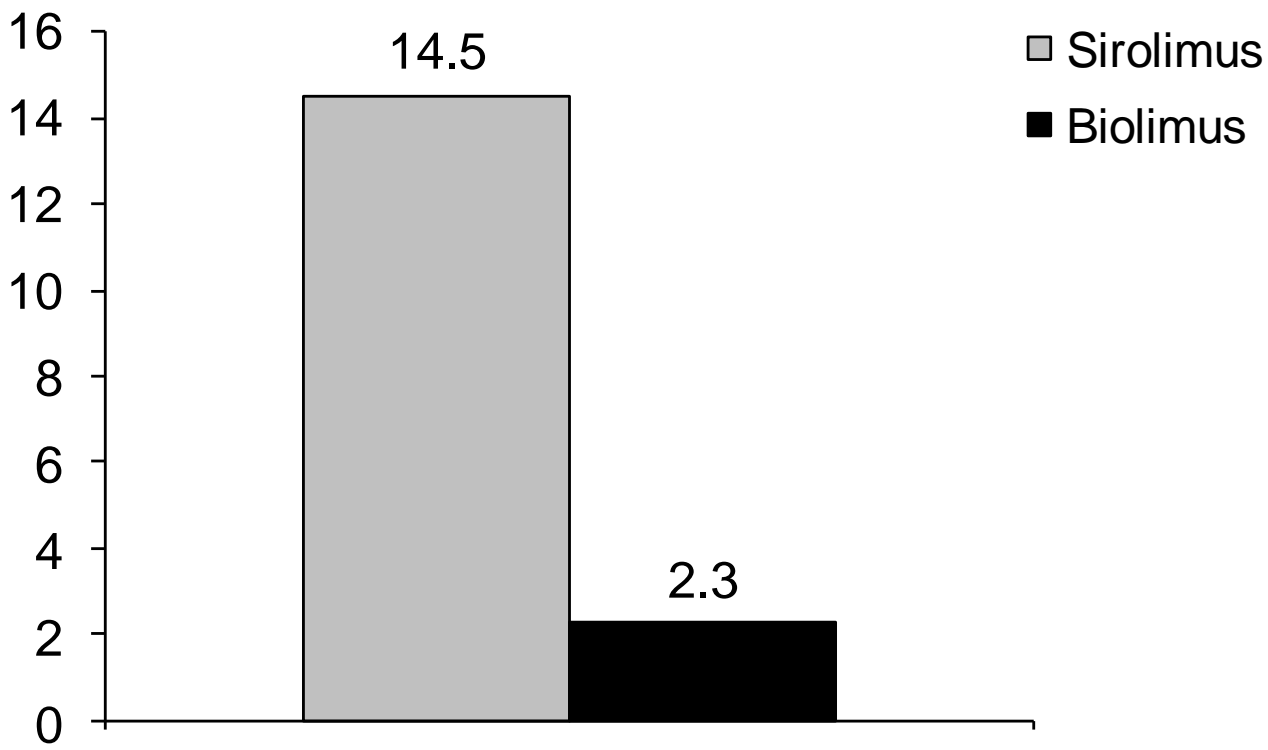
Difference 1.4%, 95% CI 0.0 to 3.7%, p=0.06



Percentage of lesions with >10% uncovered struts



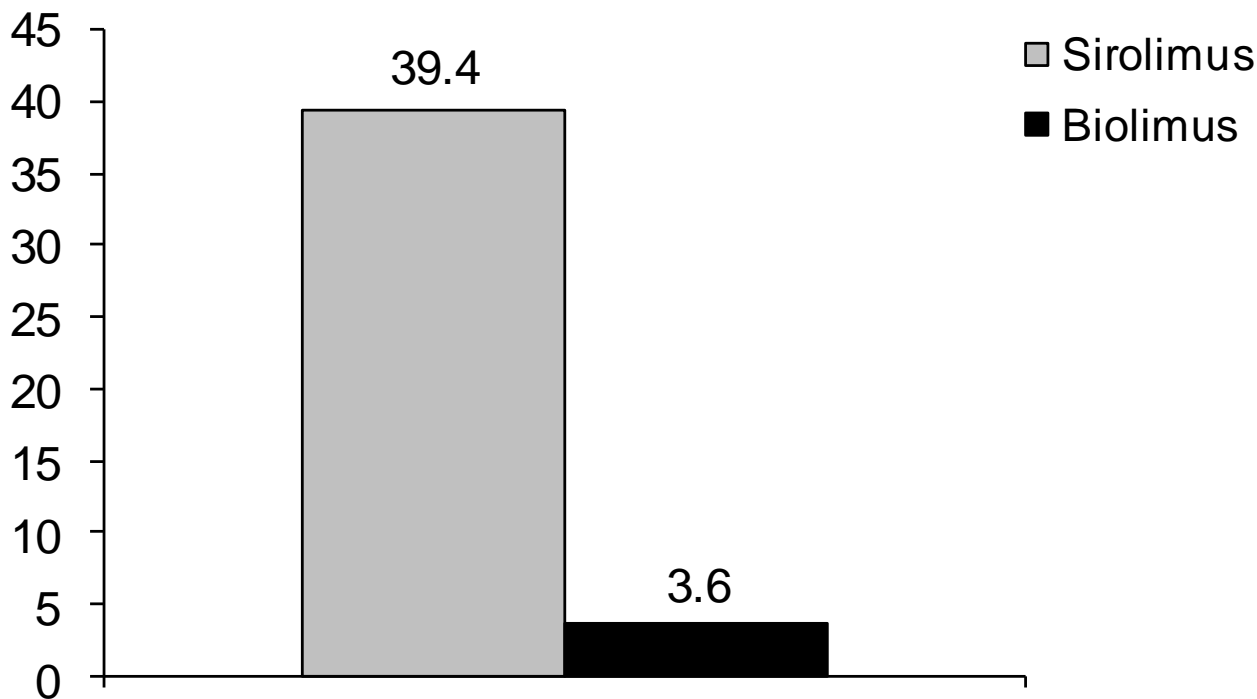
Difference 11.2%, 95% CI -0.5 to 32.5%, p=0.06



Percentage of lesions with >5% uncovered struts



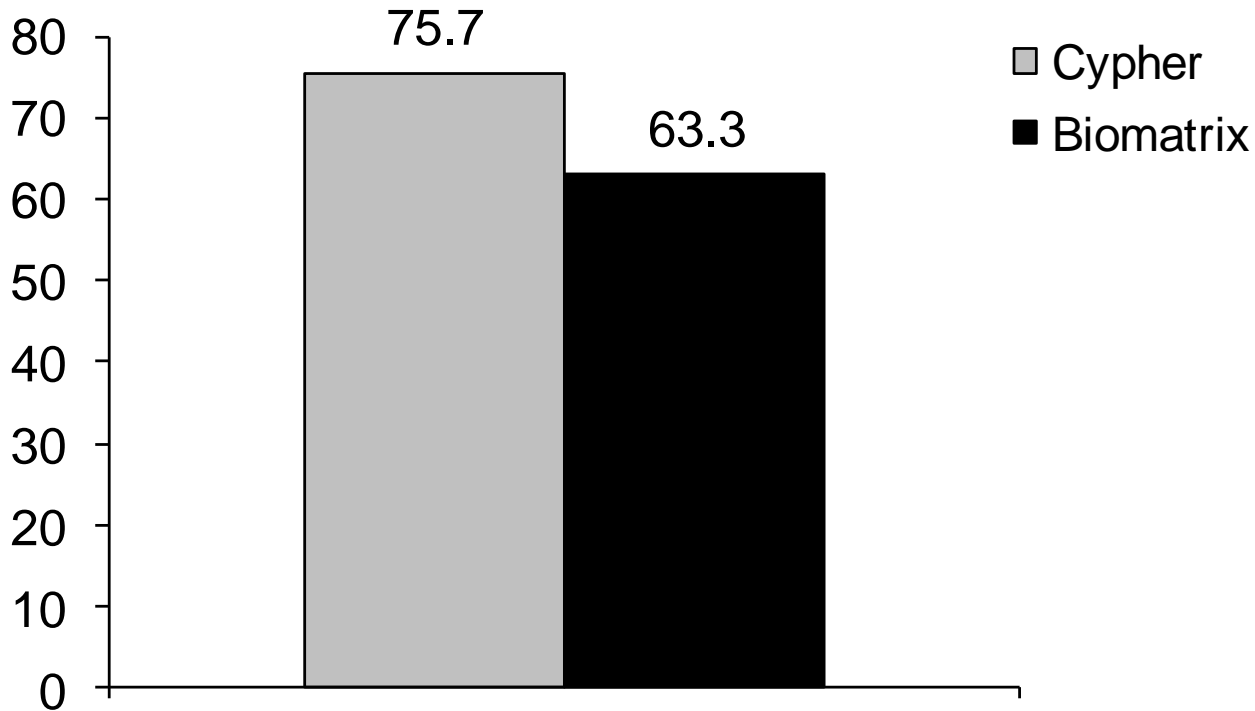
Difference 34.5%, 95% CI 10.4 to 62.7%, p=0.005



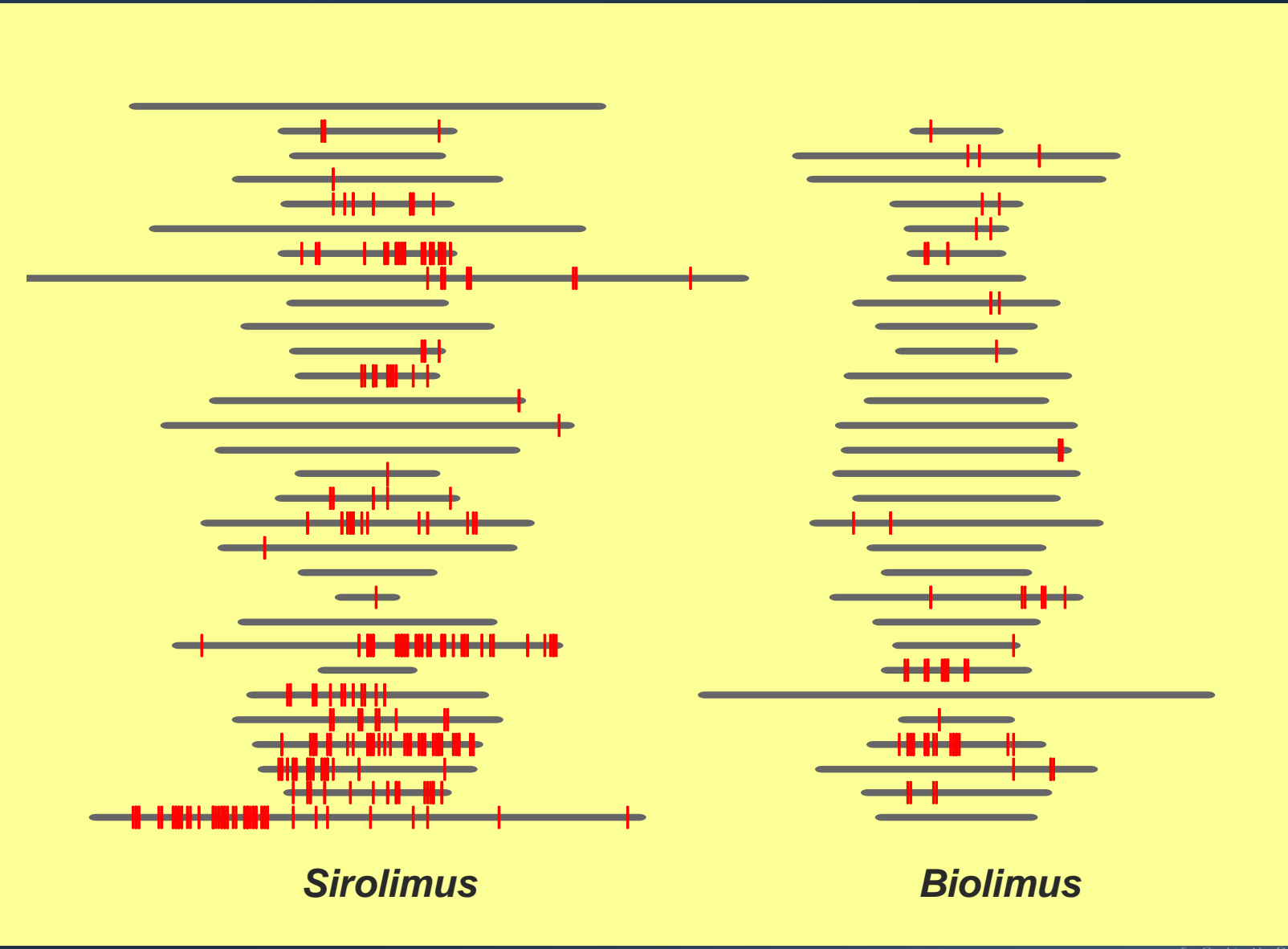
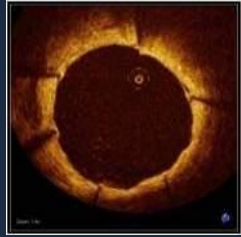
Percentage of lesions with any uncovered struts



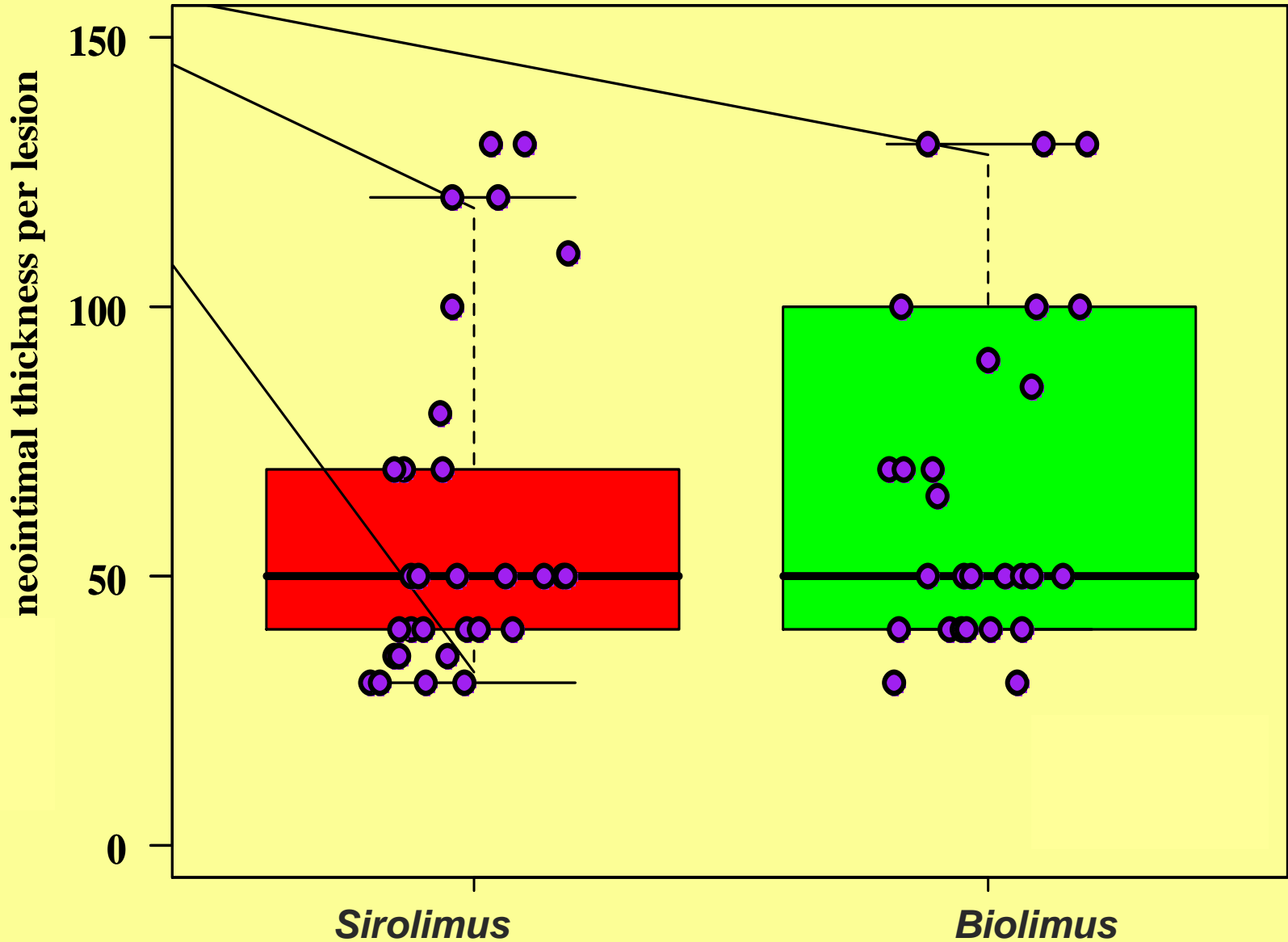
Difference 11.7%, 95% CI -17.8 to 46.2%,



Distribution of Uncovered Struts within Lesions

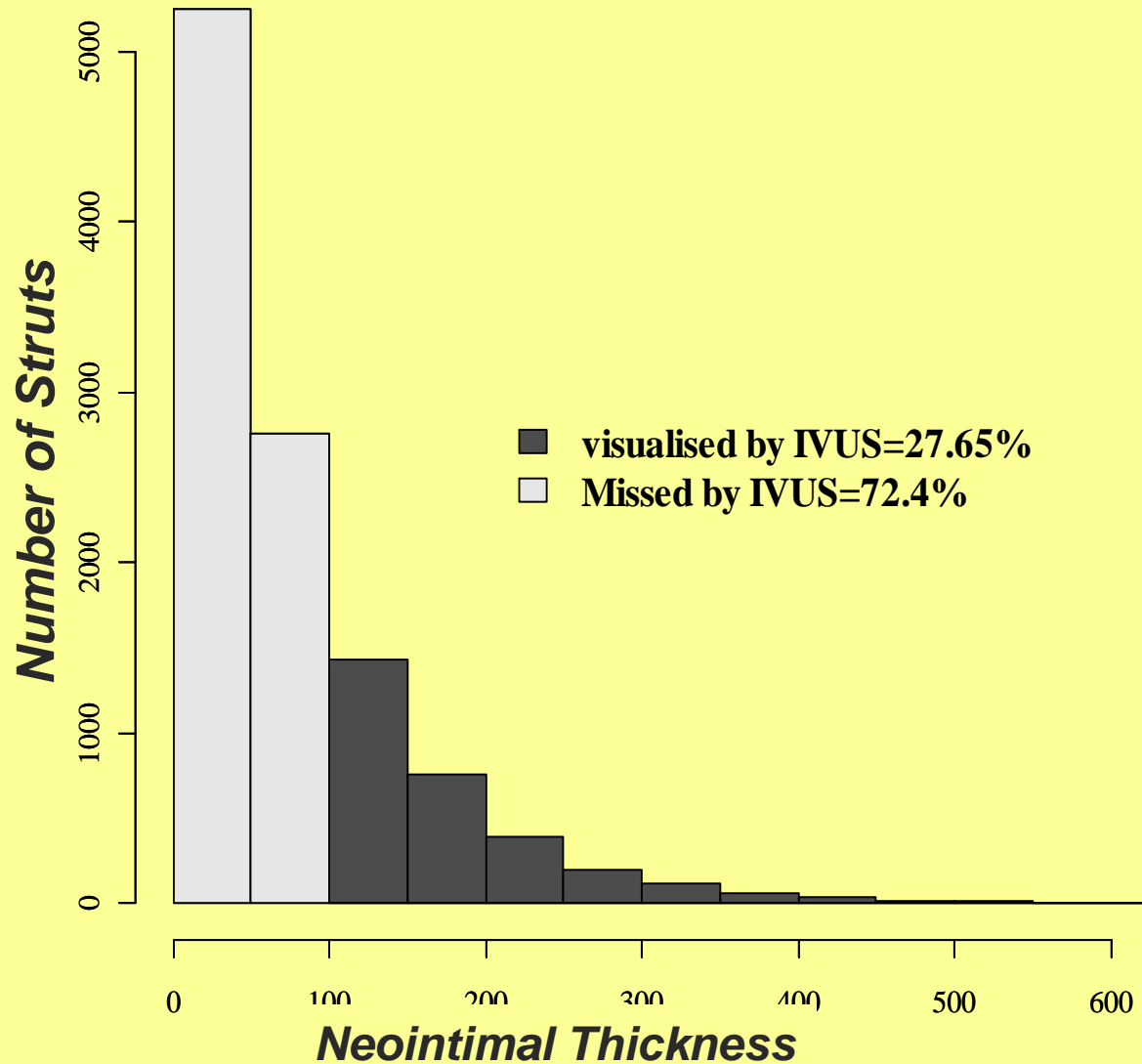


Neointimal Coverage per Lesion





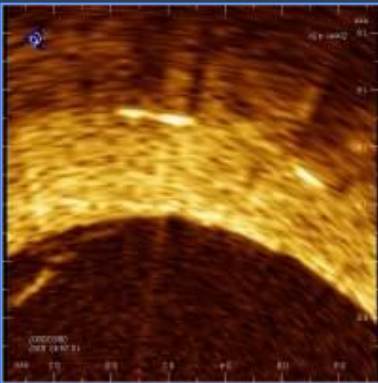
Neointimal Thickness Distribution



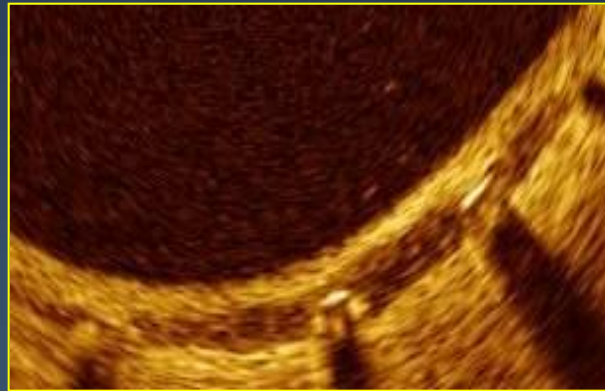
OCT – Qualitative Analysis

Tissue Appearance

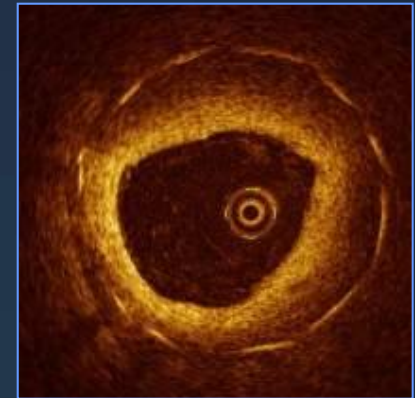
A



B



C



Homogenous

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

Inhomogenous

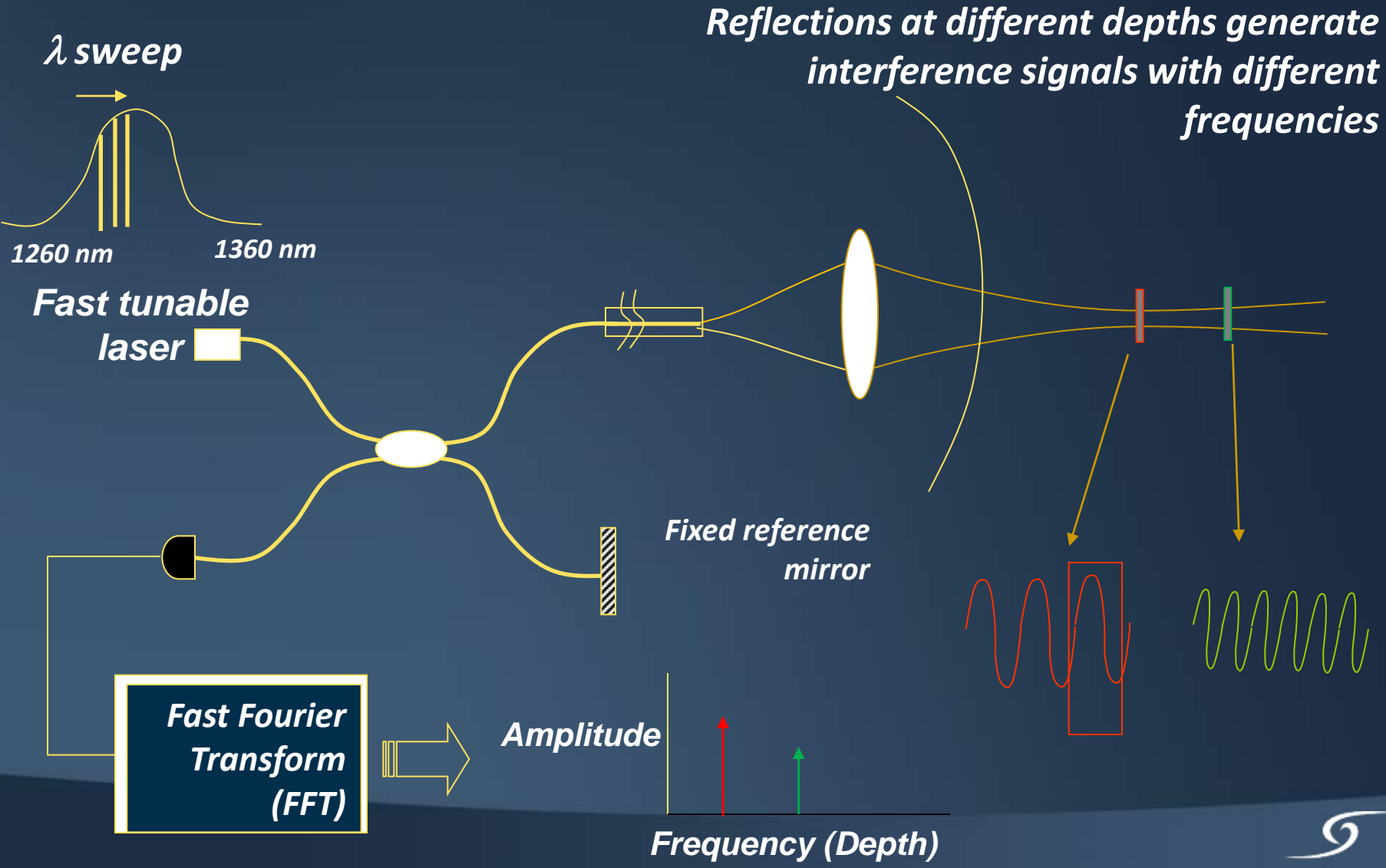
Strut is covered on luminal side with tissue, that is not homogenous but shows signal-rich and sharply delineated, focal signal-poor areas

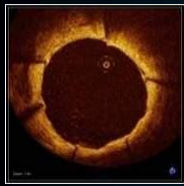
Layered

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

Fourier-Domain OCT Imaging





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 μm (IVUS threshold) in the majority of cases (72.4%)