

The latest stent news

***Advances in cardiovascular
arrhythmias and great innovations in
cardiology***

Torino October 2011

F Prati

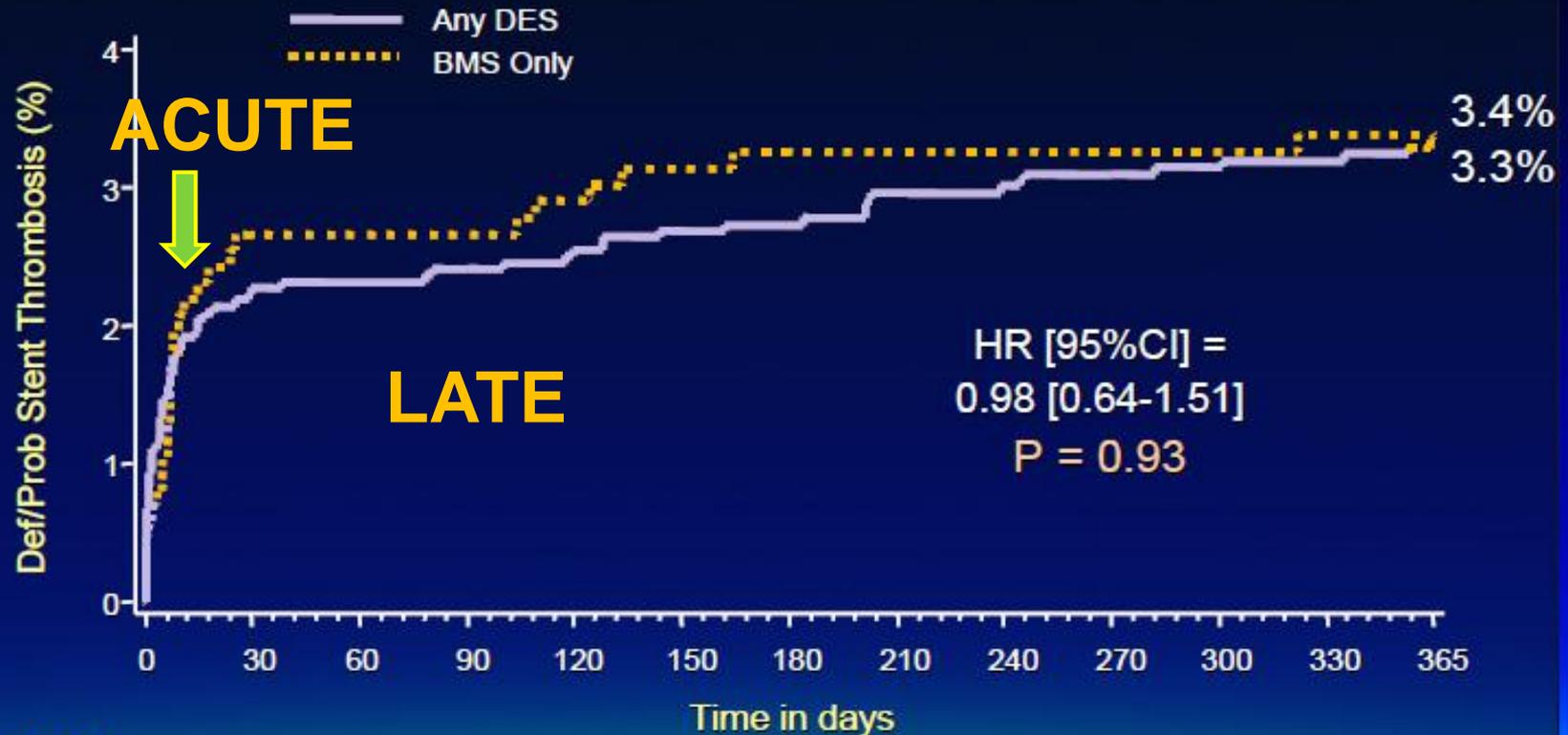
San Giovanni Hospital, Rome



Rome Heart Research

- **Stent thrombosis of first generation DES is still an issue**

1-Year Stent Thrombosis: Impact of Implanted Stent Type

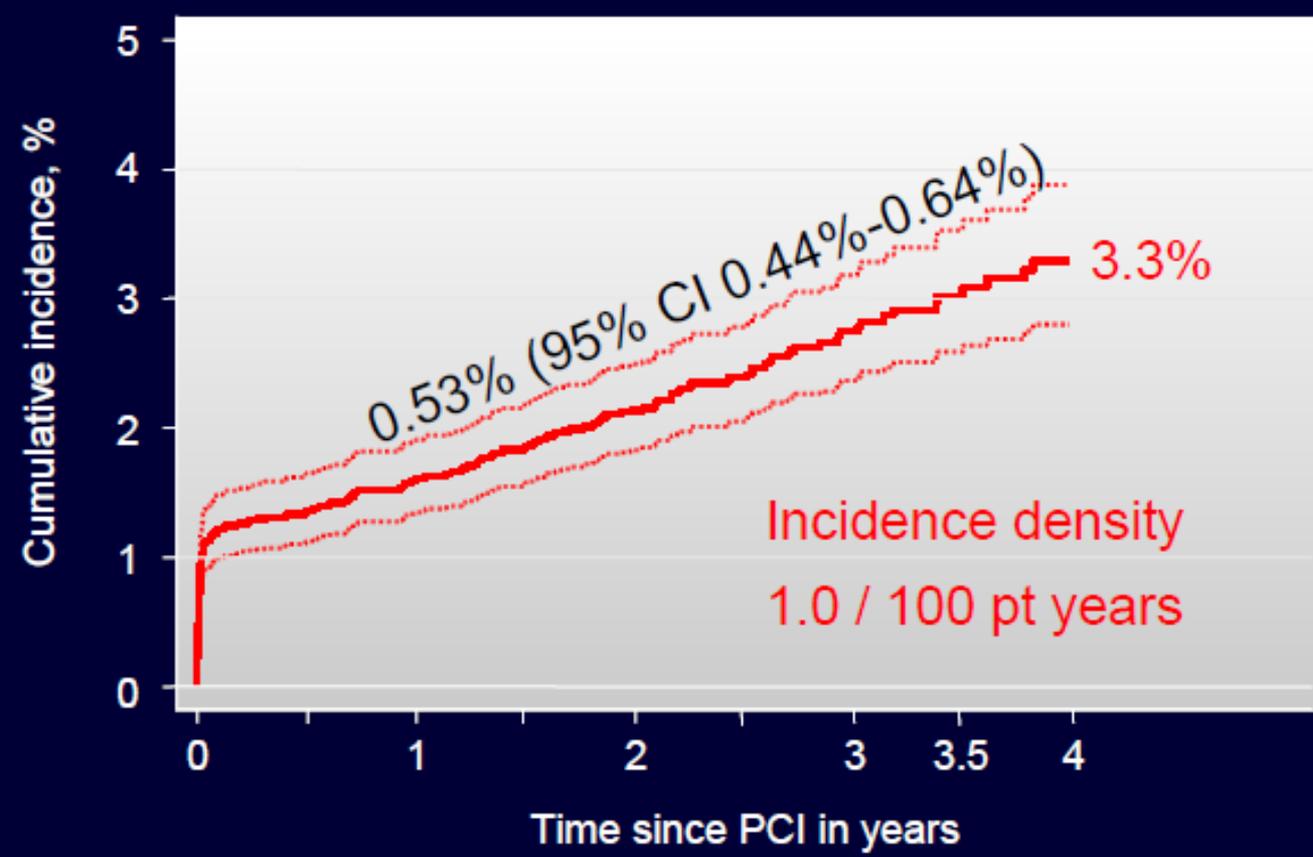


Number at risk

Any DES	2261	2171	2147	2123	2097	1900
BMS only	872	832	818	805	791	720

Definite Stent Thrombosis With DES: Bern - Rotterdam Cohort Study

Daemen J et al. *Lancet* 2007;369:667-78



Updated
Follow-up to
4 Years

192 ST cases
in a cohort
of 8.146 patients

Months	1	12	24	36	48
Cumulative incidence, %	1.2	1.6	2.1	2.7	3.3
Patients at risk	7538	7210	5164	2790	1051

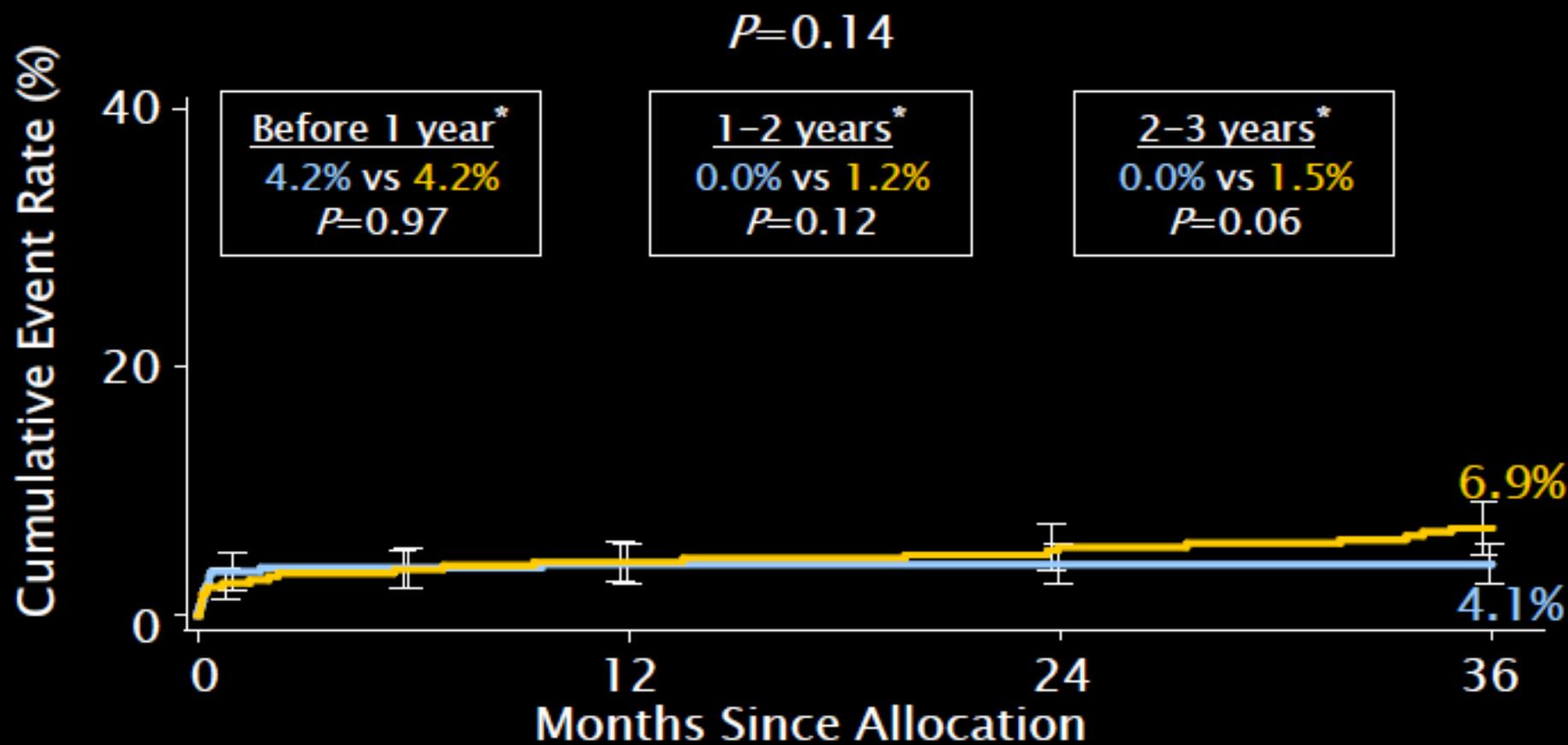
Myocardial Infarction to 3 Years

LM Subset



■ CABG (N=348)

■ TAXUS (N=357)



Cumulative KM Event Rate \pm 1.5 SE; log-rank P value; *Binary rates

ITT population

- **Stent restenosis of first generation DES in complex lesions is still an issue**

Three-year SYNTAX results extend CABG advantage to intermediate-risk patients

Cumulative event rate	CABG (%)	Taxus (%)	p
MACCE	20.2	28.0	<0.001
Death, stroke, MI	12.0	14.1	0.21
All-cause death	6.7	8.6	0.13
Stroke	3.4	2.0	0.07*
MI	3.6	7.1	0.002
Repeat revascularization	10.7	19.7	<0.001

•What is the mechanism of stent thrombosis ?

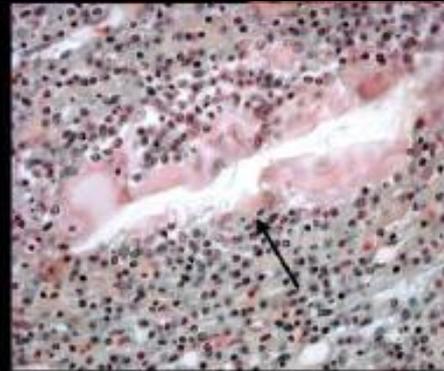
•What do IC imaging modalities tell us?



Localized Hypersensitivity and Late Coronary Thrombosis



18 Months FU



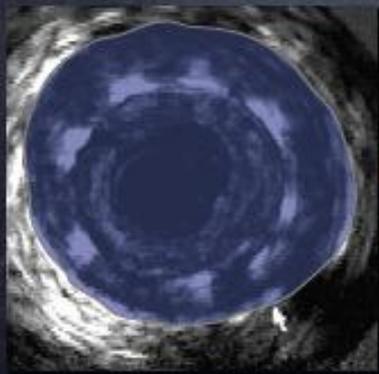
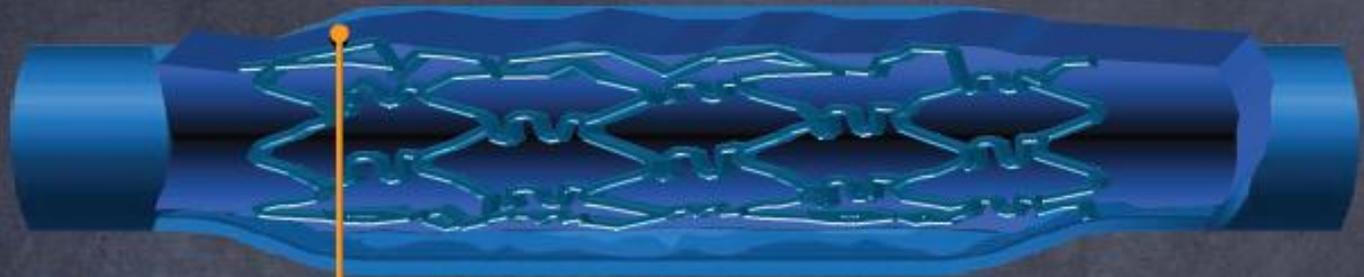
Giant cells surrounding foreign material in aneurysm (arrow)



Eosinophils (red stain)

FIM Study: Vessel Area Behind Struts

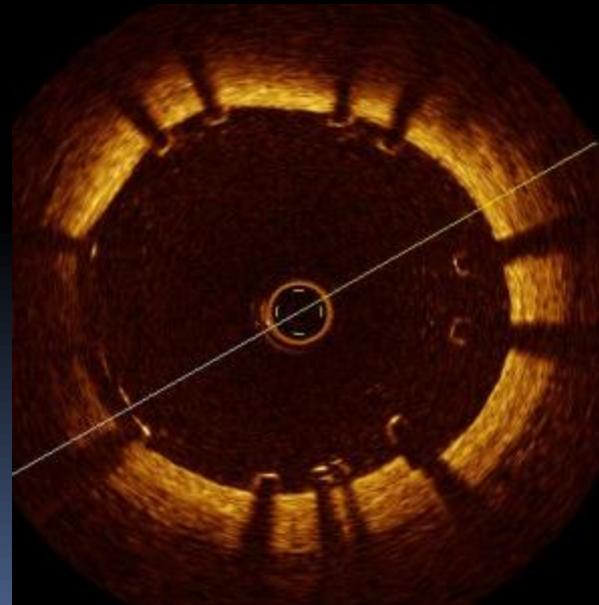
IVUS Analysis



vessel area
(mm²)



- **Is strut uncoverage and malapposition an issue?**



The MOST study: OCT findings in stent thrombosis

Parodi G, Prati F et al.

Final results: 7 DES with subacute thrombosis analysed and matched

	MOST	MOST Thromb. site	Matched group	p
Uncovered struts	16,09	24,43	7,51	p< 0,001 for all
Malapposed struts	8,13	13,96	8,20	p< 0,001 for all

Accepted TCT 2011

2nd generation DES

Xience, Endeavour

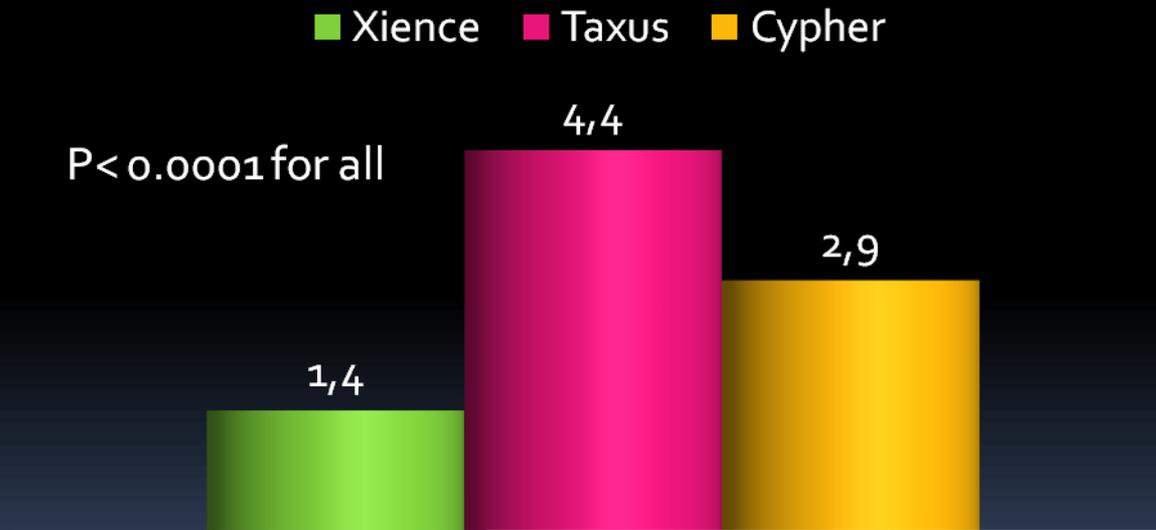


CYPHER®	TAXUS®	ENDEAVOR	XIENCE V
			
Strut Thickness: 157 µm	Strut Thickness: 132 µm	Strut Thickness: 91 µm	Strut Thickness: 81 µm
Polymer Thickness: 12.6 µm	Polymer Thickness: 16 µm	Polymer Thickness: 5.3 µm	Polymer Thickness: 7.6 µm
Total: 169.6 µm	Total: 148 µm	Total: 96.3 µm	Total: 88.6 µm

Chromium cobaltumt thin struts, releasing Everolimus

12,339 consecutive patients treated with:

- Xience V everolimus-eluting stents n = 4,212;
- Cypher sirolimus-eluting stents n = 3,819;
- Taxus Express paclitaxel-eluting stents n = 4,308



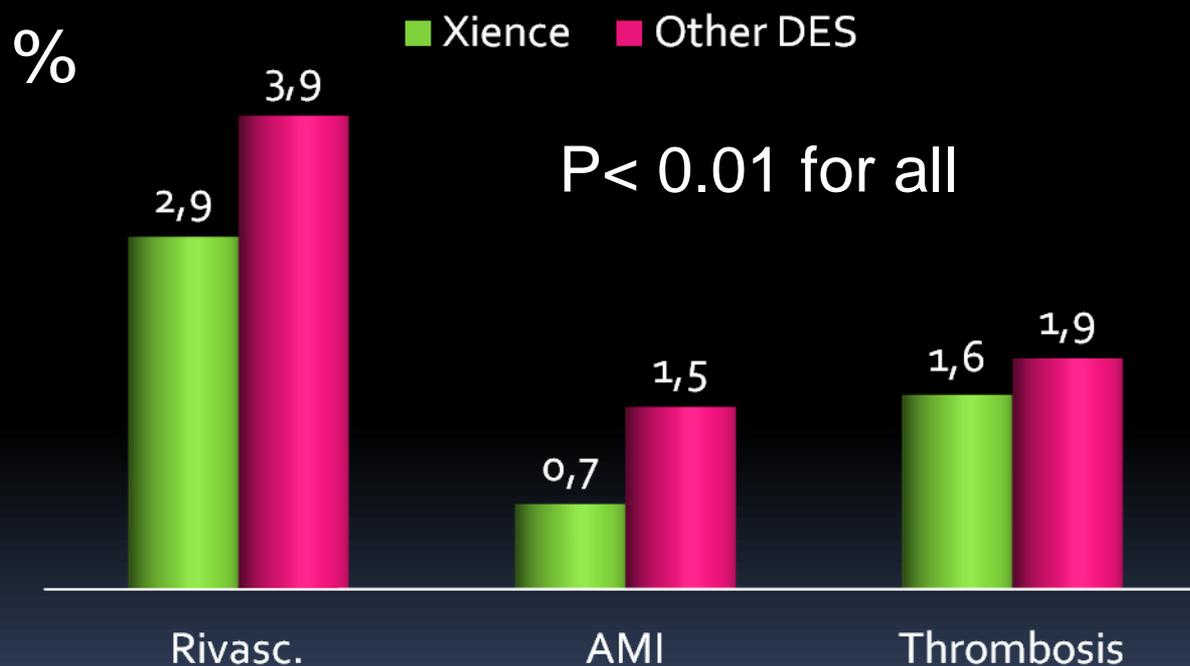
DES Thrombosis



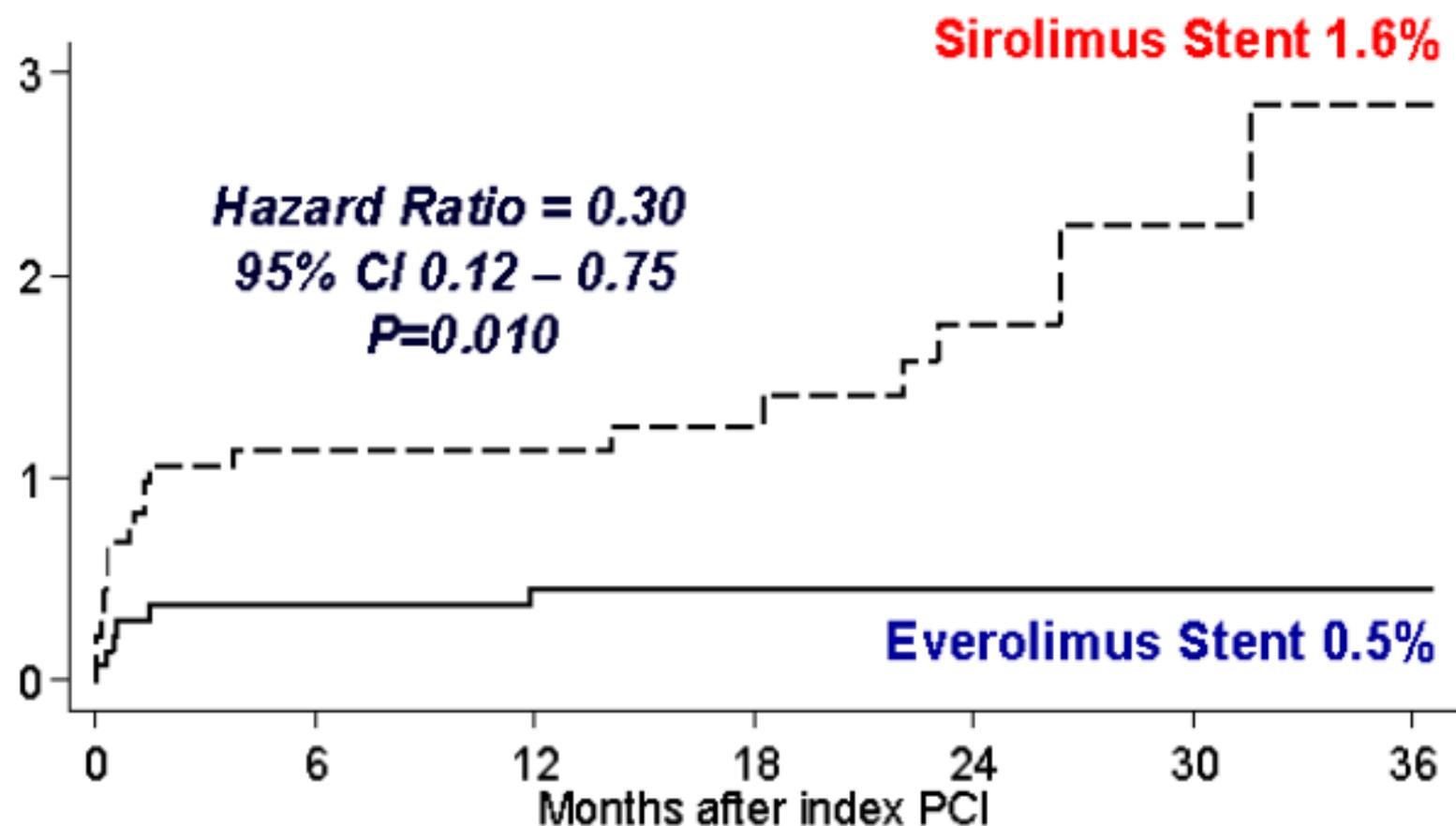
ESC 2011

Meta-analysis on 13 randomized trials involving 17,101 patients.

EES vs other DES (excluding those with nonpermanent polymers)



Lesson I – Definite Stent Thrombosis @ 3 Years



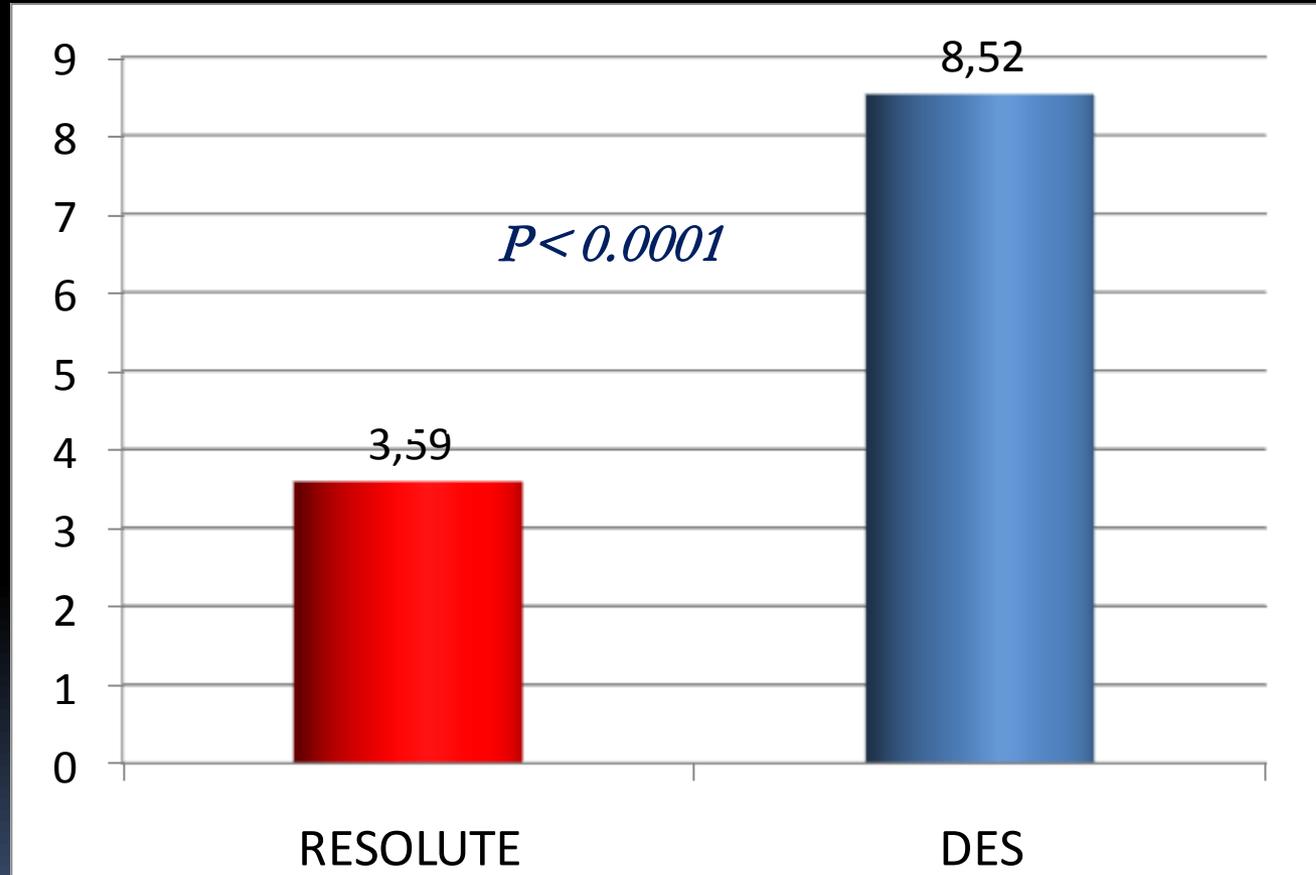
No. at risk

EES	1342	1296	1234	620	543	226	29
SES	1342	1271	1216	619	527	223	28

RESORT study

Primary End Point

Uncovered stent struts (%)



26 Pts

13 RESOLUTE

14 First gen. DES

Tot N of
analyzed struts

RESOLUTE: 18112

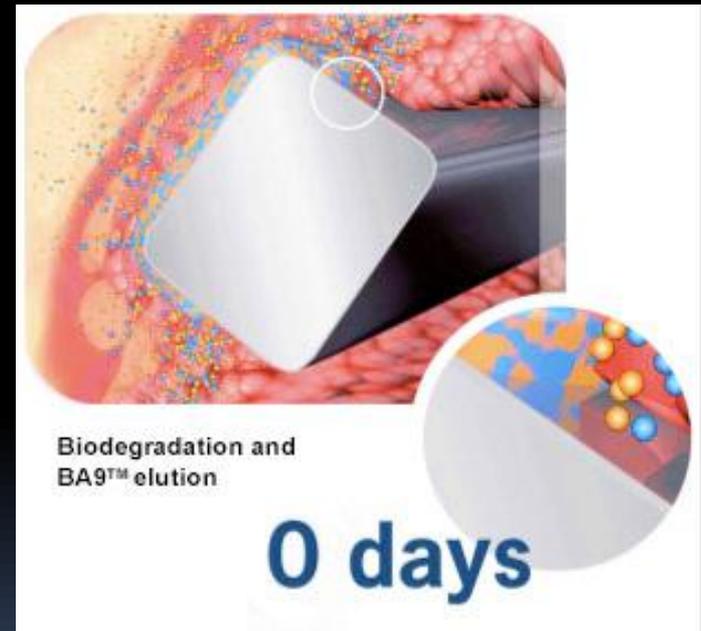
DES: 16642

PCR

2009

Prati F et al.

Bio-absorbable polymer



Biolimus-A9™ Eluting Stent



- Biolimus is a semi-synthetic sirolimus analogue with **10x higher lipophilicity** and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 $\mu\text{g}/\text{mm}$ into a biodegradable polymer, polylactic acid, and applied solely to the **abluminal stent surface** by a fully automated process.
- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after **a 6-9 months period**.
- The stainless steel stent platform has a strut thickness of 120 μm with a **quadrature link** design.

3-Year Safety Endpoints

■ BES (N=857) ■ SES (N=850)

P=0.25*

P=0.36*

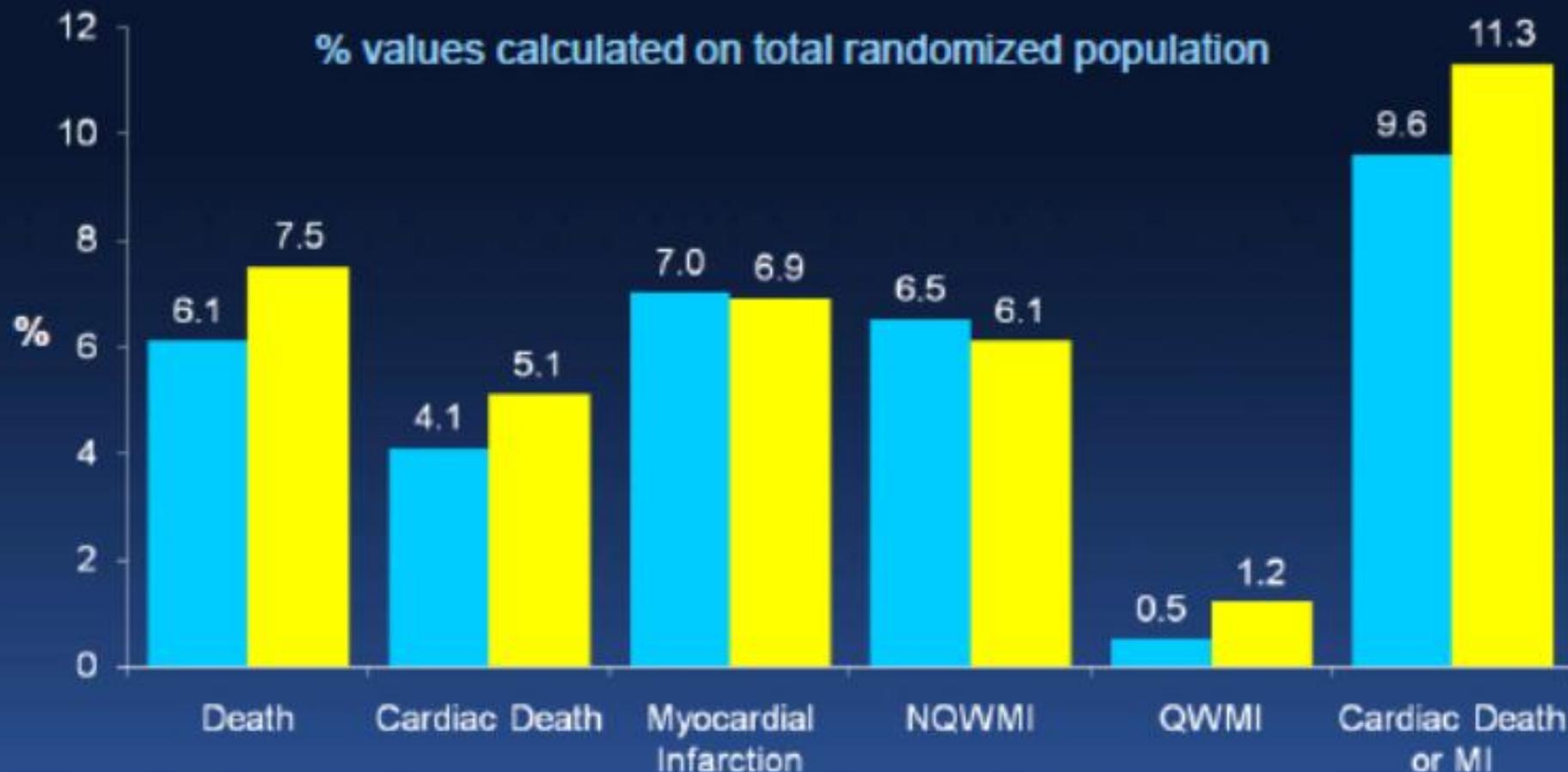
P=1.00*

P=0.77*

P=0.12*

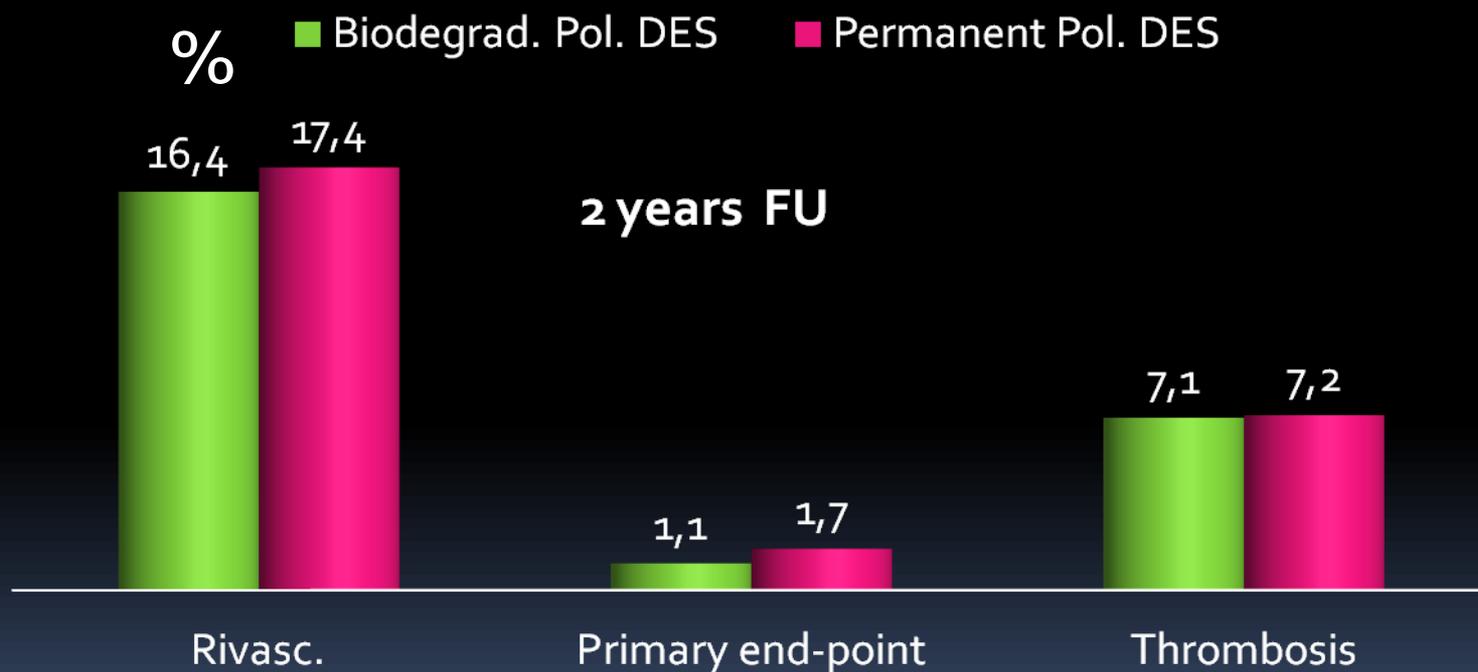
P=0.27*

% values calculated on total randomized population



*P values for superiority (Fisher Exact Test)

ISAR-TEST-4 . Randomized study on 2,603 patients with stable CAD or ACS. Biodegradable sirolimus-eluting stent (n = 1,299) Vs permanent polymer DES (n = 1,304) (Cypher n or Xience)
The biodegradable stent: stainless steel microporous, thin-strut platform coated with a mixture of rapamycin, biodegradable polymer, and a biocompatible resin.



Biodegradable Polymer vs. Permanent Polymer DES and Everolimus- vs. Sirolimus-Eluting Stents in Patients with CAD

2,603 all-comer randomized pts from ISAR-TEST 4.

3-Year Follow-up	Biodegradable Polymer (n = 1,299)	Permanent Polymer (n = 1,304)	P Value
Cardiac Death, Target-Vessel MI, TLR	20.1%	20.9%	0.59
Definite/Probable Stent Thrombosis	1.2%	1.7%	0.32

Comparison of EES with SES also showed no difference in outcomes.

Conclusion: At 3 years, biodegradable- and permanent-polymer DES are associated with similar outcomes.

Byrne RA, et al. *J Am Coll Cardiol.*
2011;58:1325-1331.

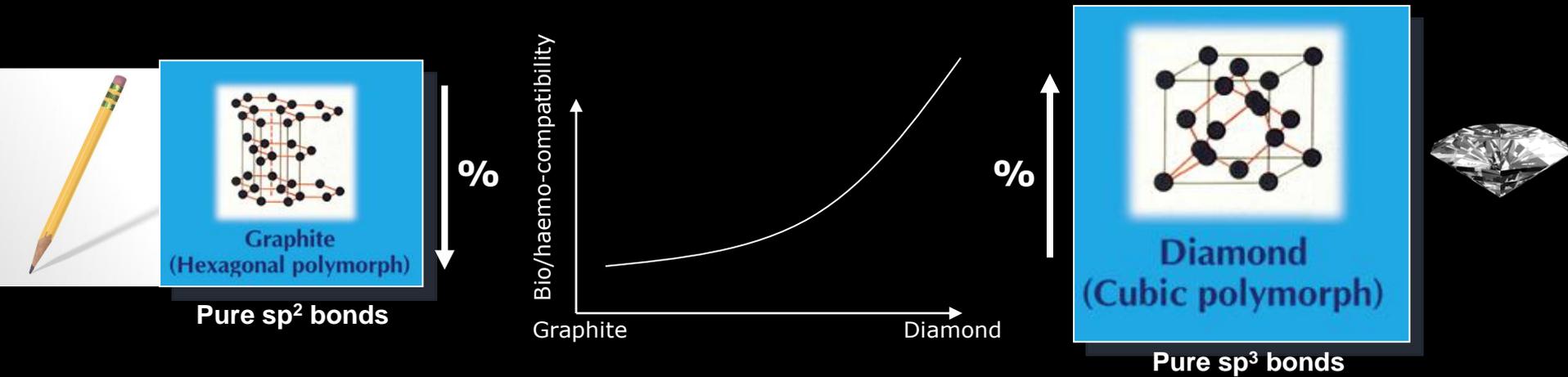
Patients with STEMI

How to promote vessel healing and reduce malapposition?

1) Stents with endoluminal biocompatible surface

CID Bio Inducer Surface

The Bio Inducer Surface (BIS) is made of pure carbon atoms



The Bio Inducer Surface ($\leq 0.3 \mu\text{m}$) is a 2nd generation pure carbon coating that has a cristalline structure extremely close to that of diamond, with a further improvement of its bio/haemo compatibility

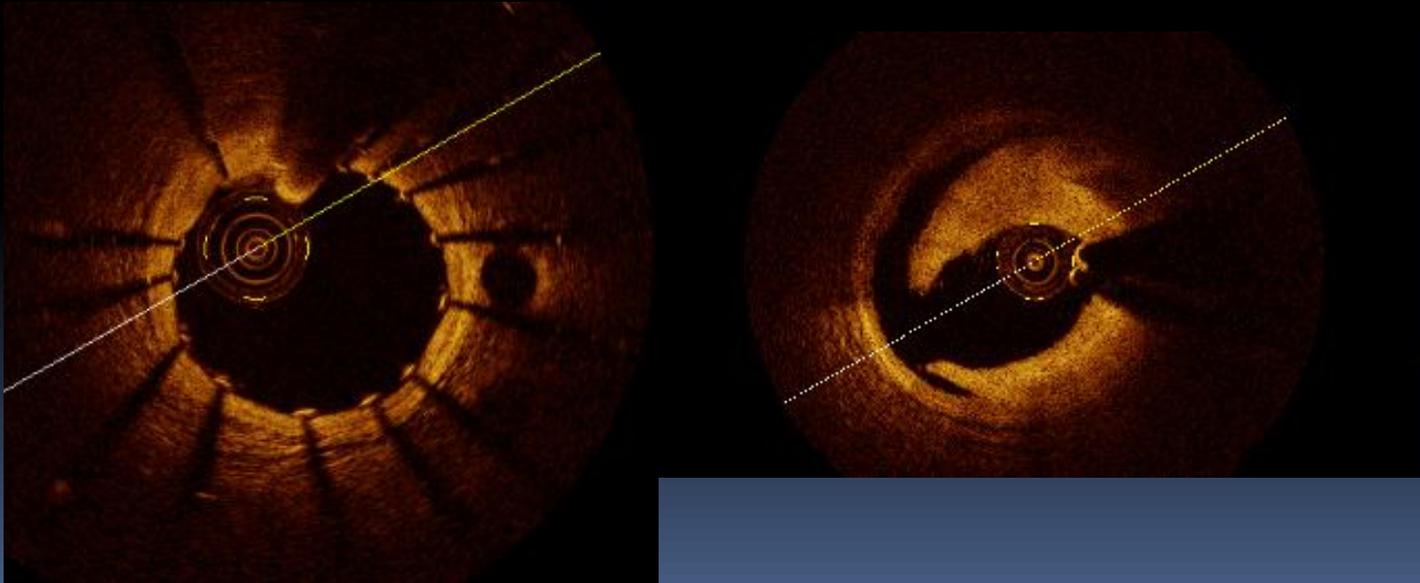
Patients with STEMI

**How to address stent efficacy:
clinical outcome vs
assessment of stent coverage**

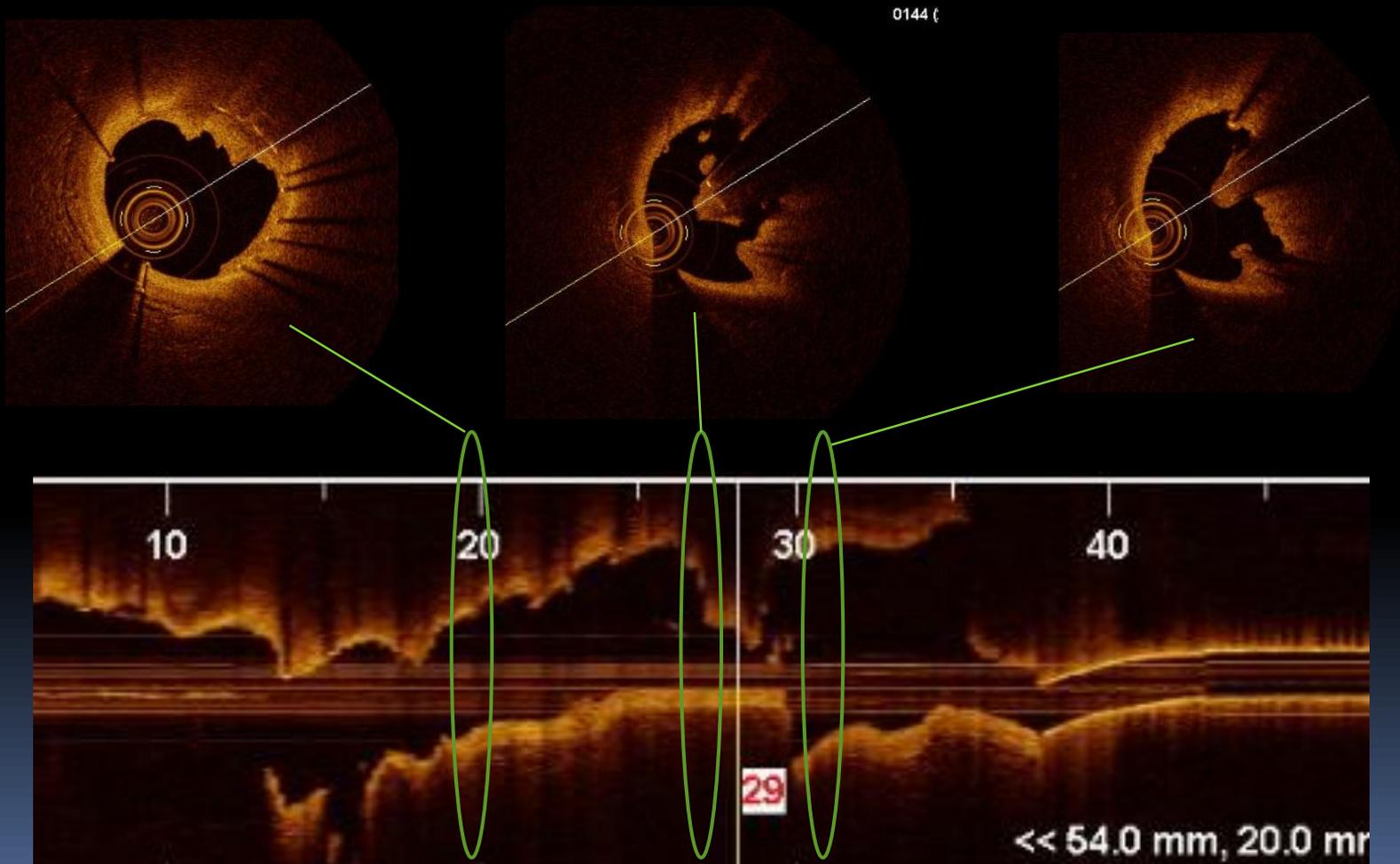
The MOST study: OCT findings in stent thrombosis

Parodi G, Prati F et al.

Interim results: Acute dissections is frequently observed in pts with acute/subacute



MOST registry. Marked stent underexpansion causing subacute thrombosis

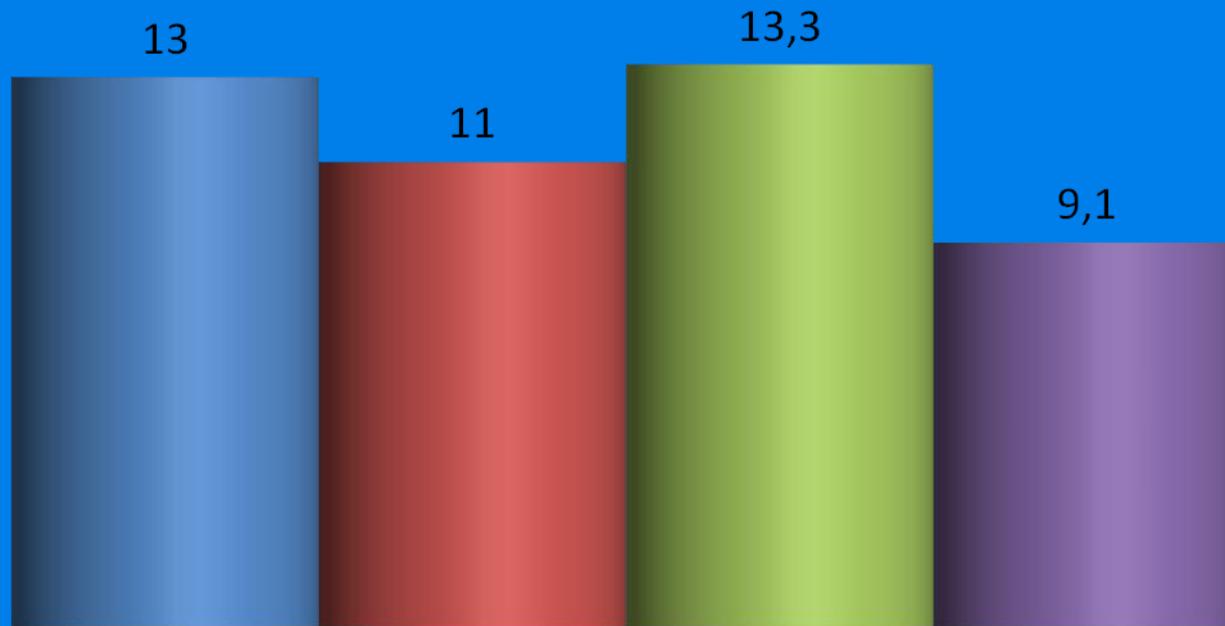


**What is the amount and timing
of stent struts coverage?**

The DETECTIVE registry

Strut Uncoverage

■ First gen.DES ■ CCS ■ Culprit STEMI lesions ■ Non culprit



Uncoverage %

Prati et al. In press Heart

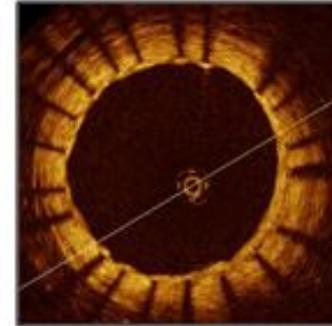


Bio Inducer Surface: OCT Results



Results

FU OCT data @ 4-7
days



Stent struts coverage in 96.1% of struts

only 3.9% of struts were uncovered

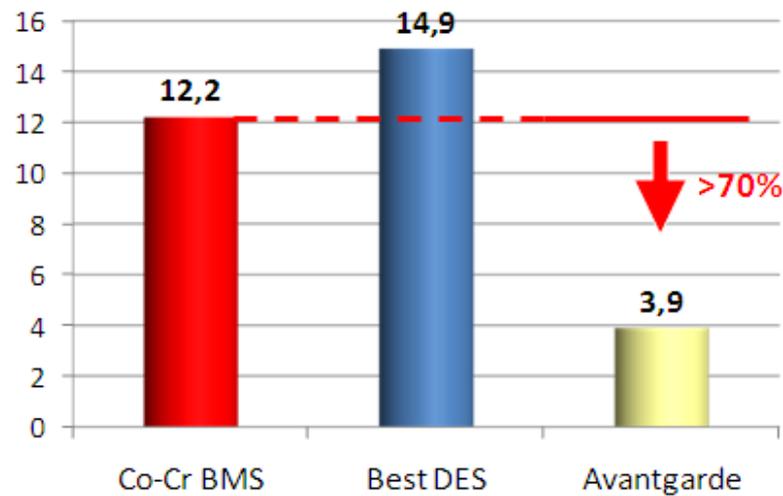


Bio Inducer Surface: OCT Results



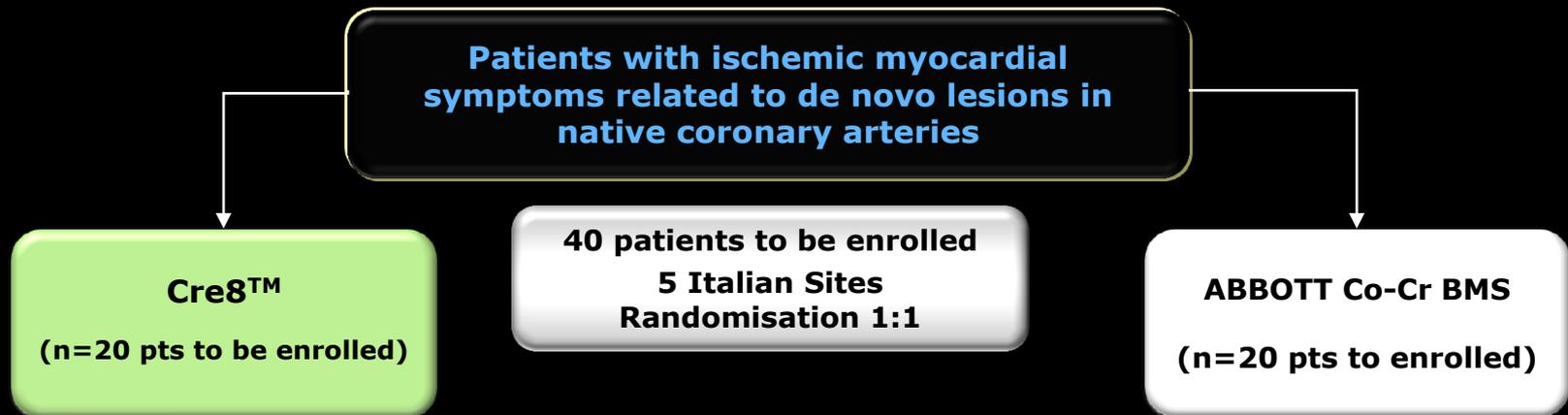
Comparison vs other RHR data

Uncovered stent struts (%)



Demonstr8 Clinical Trial

Randomized comparison between a DES and a BMS to assess neointimal coverage by OCT evaluation



OBJECTIVE: demonstrate non-inferiority in terms of neointimal coverage, assessed by OCT, of Cre8 DES, evaluated at 3 months after index procedure, compared to Vision/Multilink 8 BMS (Abbott) evaluated at 1 month.

PRIMARY ENDPOINT: rate of cross-sections with RUTTS score of ≤ 0.3 , determined by OCT, at 1 or 3 months, according to the randomization group





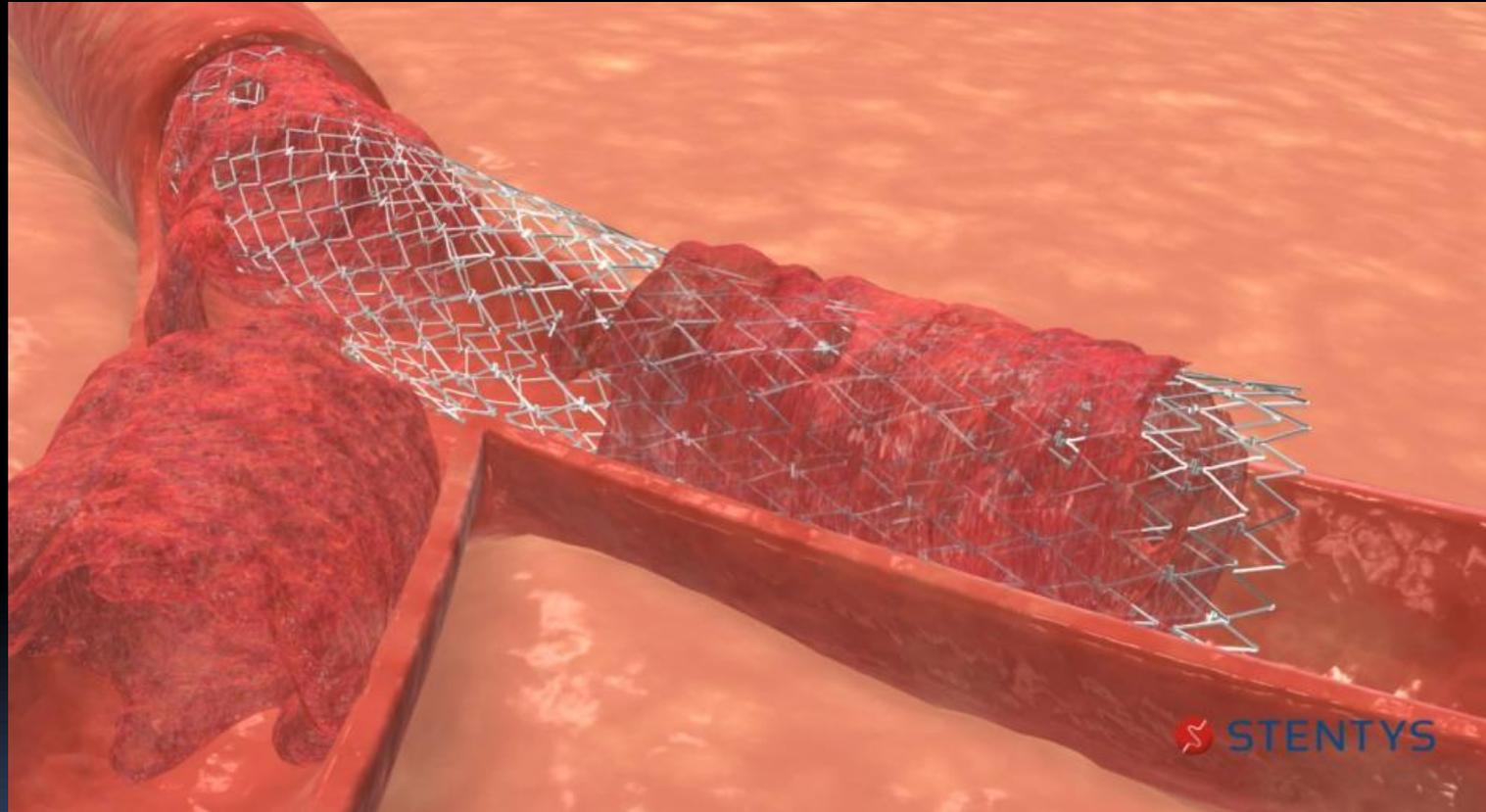
Patients with STEMI

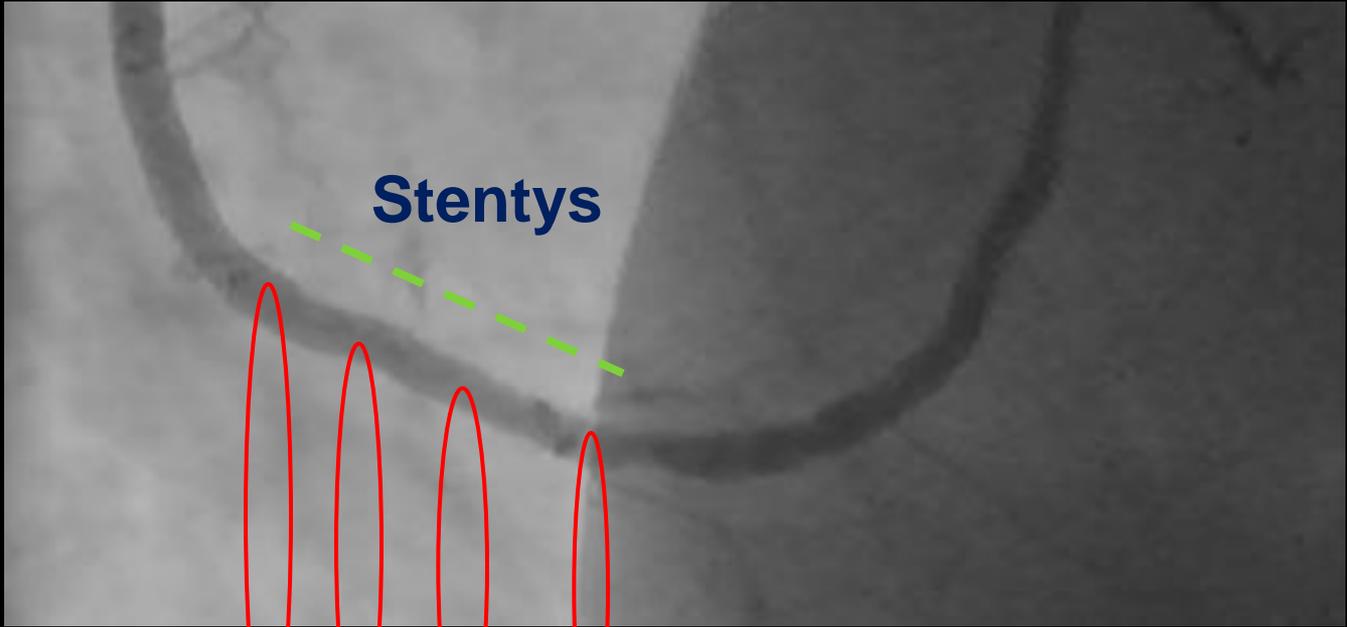
How to promote vessel healing and reduce malapposition?



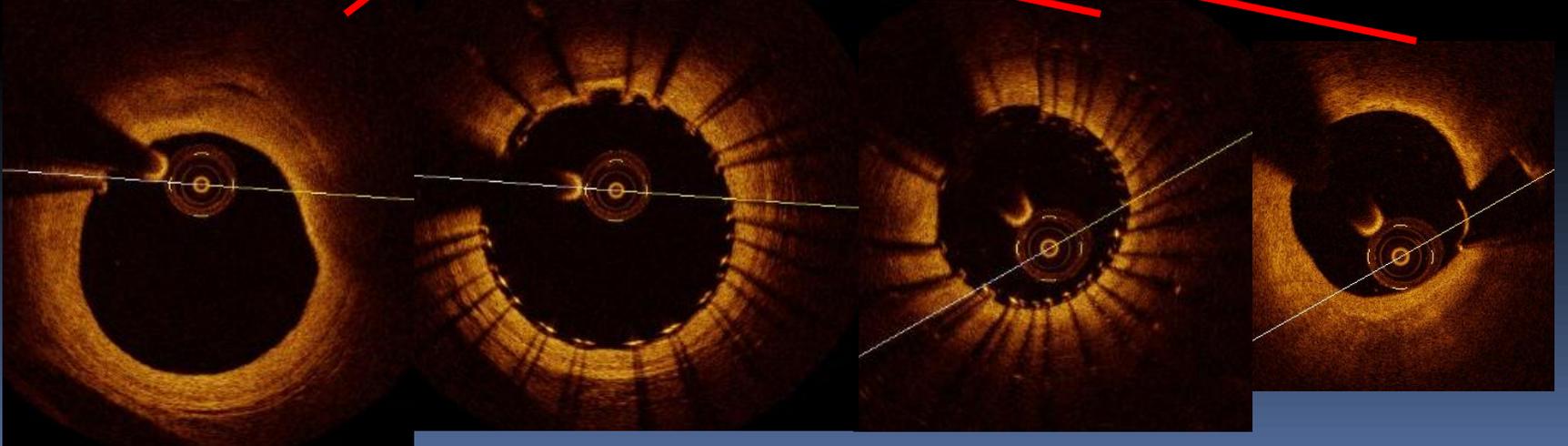
1) Self expanding stent to reduce malapposition

STENTYS Approach





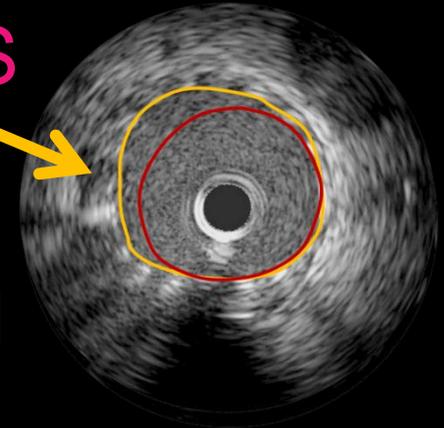
RHR



APPOSITION I Results

RESULTS AT 30 DAYS

20% lumen
area increase



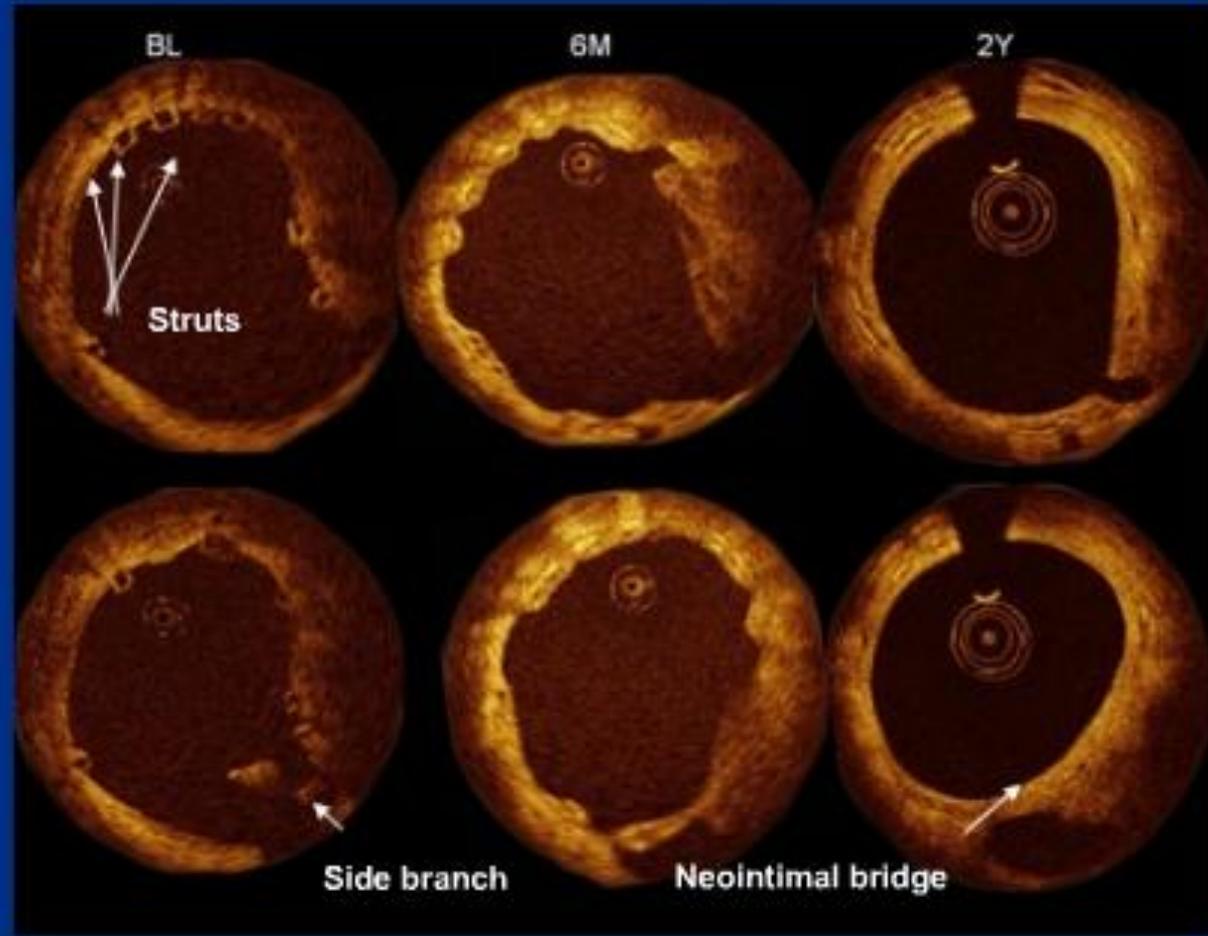
- No MACE
- 100% procedural success
- 24/25 final TIMI 3 flow
- Excellent apposition with significant 20% minimum lumen area increase at 3 days
- Accommodation to early changes in anatomy (thrombus dissolution and vasodilation)

Absorbable stents

PLLA or magnesium



ABSORB Cohort A OCT Images – Baseline, 6 months and 2 years



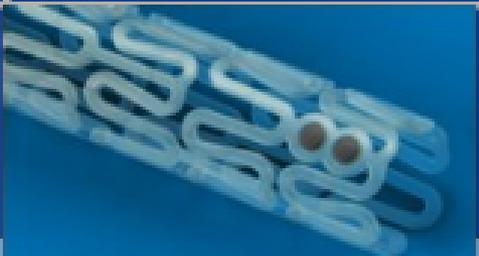
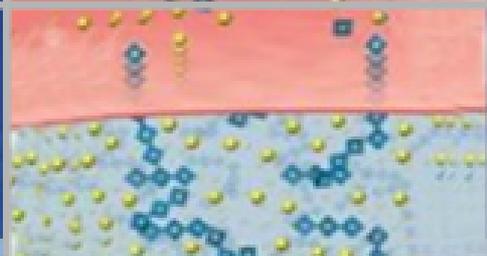
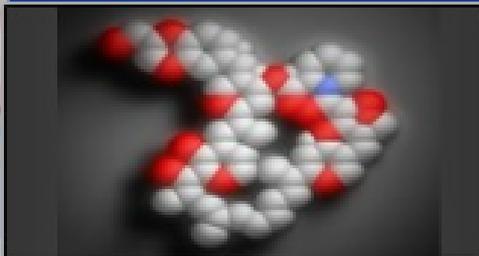
Serruys, PW., ESC 2008.

© 2010 Abbott Laboratories

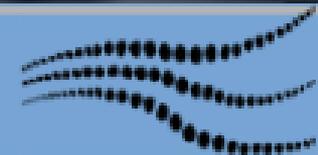
Pipeline product. Currently in development at Abbott Vascular. Not available for sale.



Abbott Vascular Everolimus-Eluting Bioresorbable Vascular Scaffold Components

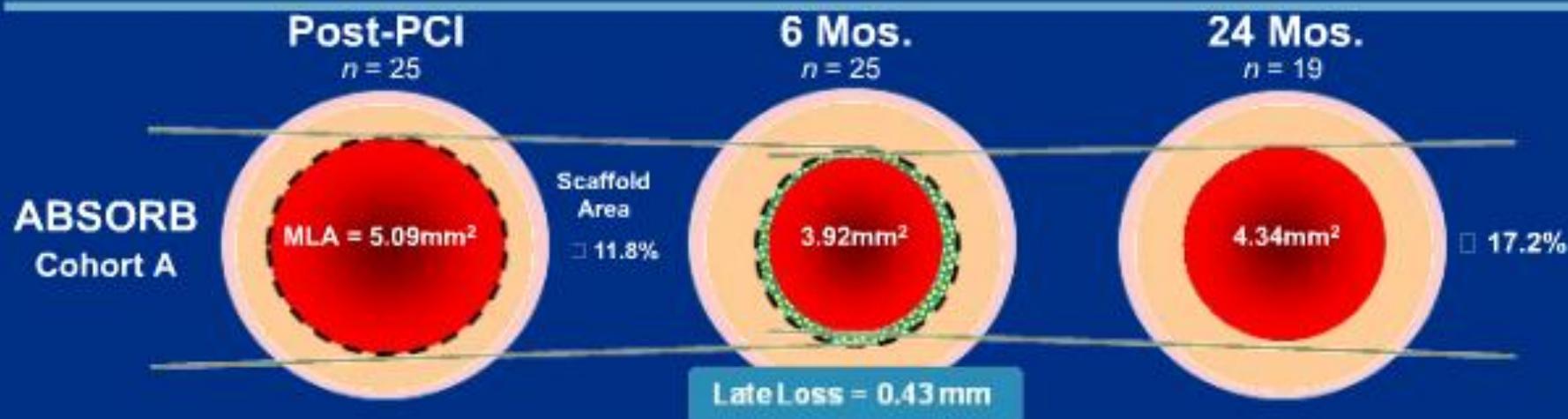
ML VISION Delivery System	Bioresorbable Scaffold	Bioresorbable Coating	Everolimus
<ul style="list-style-type: none">• Seven generations of MULTI-LINK success• World-class deliverability	<ul style="list-style-type: none">• Polylactide (PLLA)• Naturally resorbed, fully metabolized	<ul style="list-style-type: none">• Polylactide (PDLLA) coating• Fully biodegradable	<ul style="list-style-type: none">• Similar dose density and release rate to XIENCE V
			

All illustrations are artists' renditions



ABSORB Cohort A

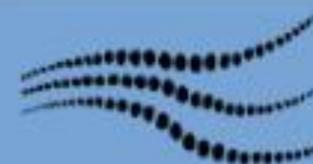
Temporal Lumen Dimensional Changes, Per Treatment



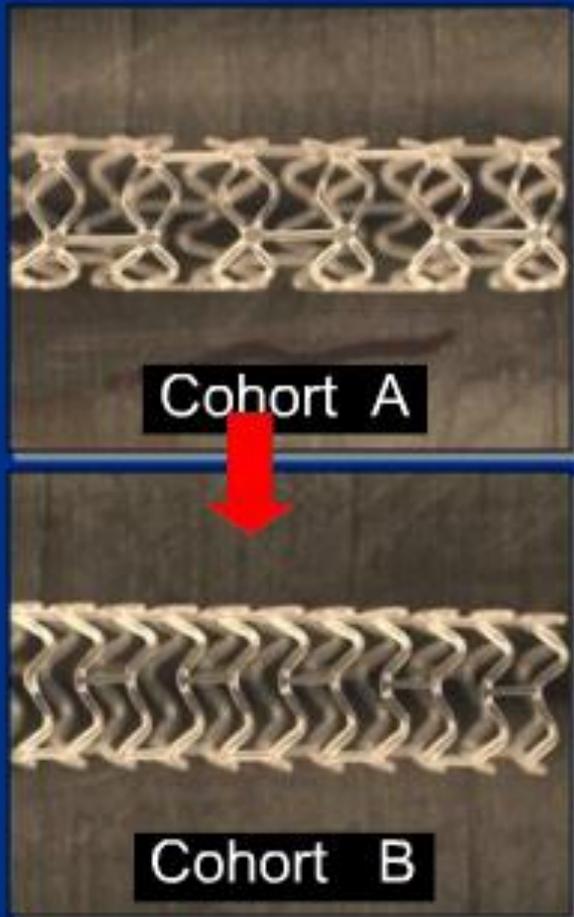
Late lumen loss at 6 months mainly due to reduction in scaffold area

Very late lumen enlargement noted from 6 months to 2 years

Serruys, PW, et al. *Lancet* 2009; 373: 897-910.

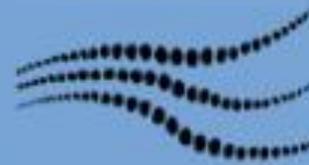


BVS Device Optimization Objectives



- More uniform strut distribution
- More even support of arterial wall
- Lower late scaffold area loss
 - Maintain radial strength for at least 3 months
- Storage at room temperature
- Improved device retention
- Unchanged:
 - Material, coating and backbone
 - Strut thickness
 - Drug release profile
 - Total degradation Time

Photos taken by and on file at Abbott Vascular.



ABSORB A - 4 Year Clinical Results

Hierarchical	6 Months 30 Patients	12 Months 29 Patients*	3 Years 29 Patients*	4 Years 29 Patients*
Ischemia Driven MACE, %(n)	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Cardiac Death, %	0.0%	0.0%	0.0%	0.0%
MI, %(n)				
Q-Wave MI	0.0%	0.0%	0.0%	0.0%
Non Q-Wave MI	3.3% (1)**	3.4% (1)**	3.4% (1)**	3.4% (1)**
Ischemia Driven TLR, %				
by PCI	0.0%	0.0%	0.0%	0.0%
by CABG	0.0%	0.0%	0.0%	0.0%

No new MACE events between 6 months and 4 years

No scaffold thrombosis up to 4 years (All patients off clopidogrel)

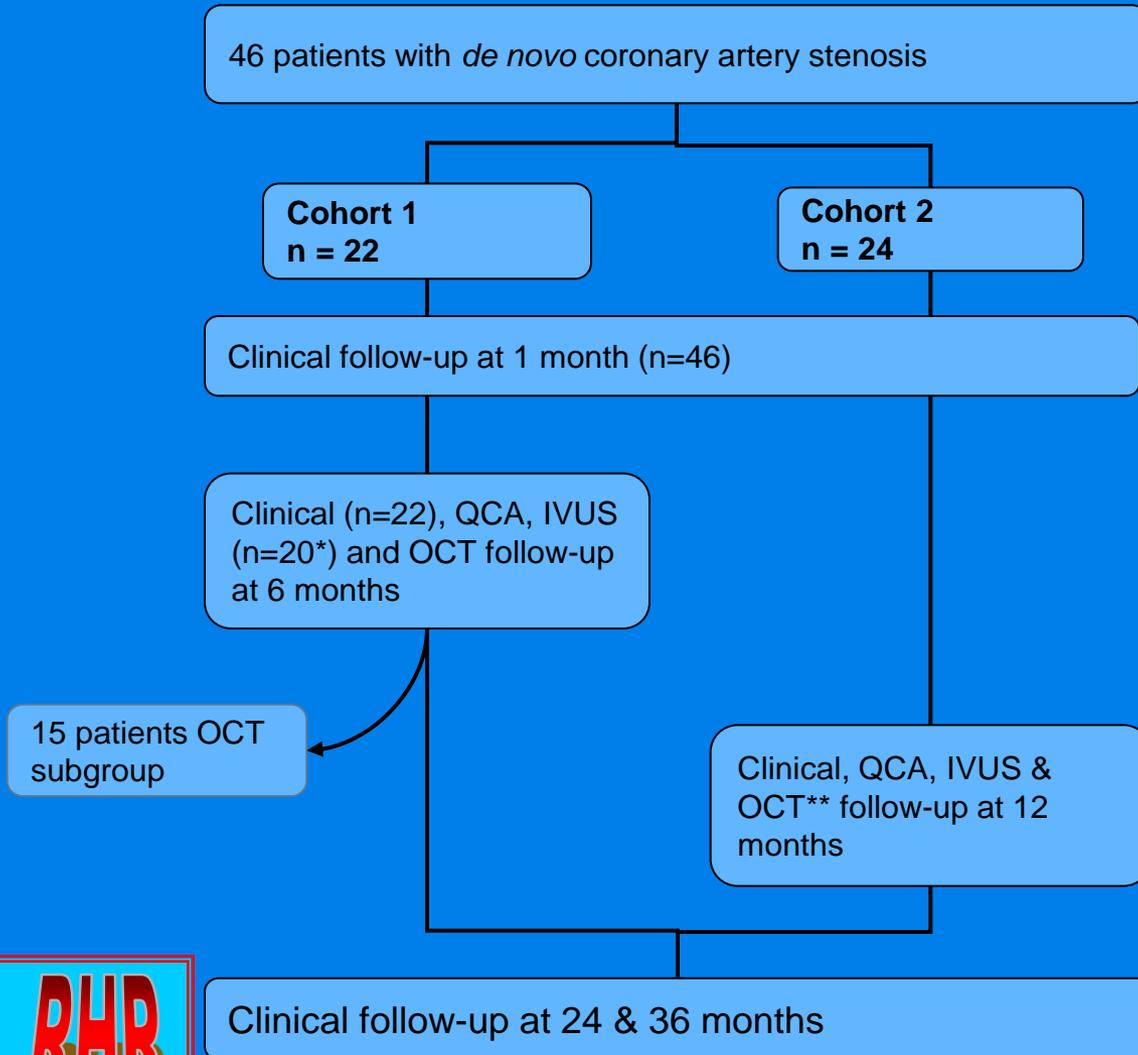
*One patient withdrew consent after 6 months but the vital status of the patients and absence of cardiac event is known through the referring physician.

**This patient also underwent a TLR, not qualified as ID-TLR (DS = 42%) followed by post-procedural troponin qualified as non-Q MI and died from his Hodgkin's disease at 888 days post-procedure.

Magnesium absorbable stent

Biotronik

Biosolve study



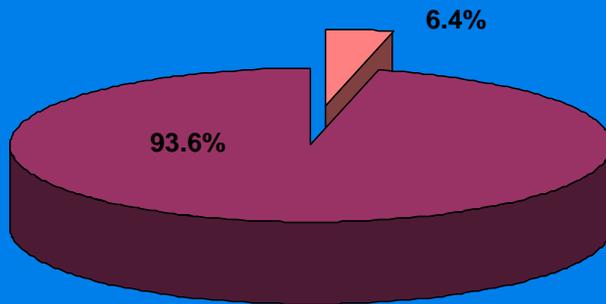
To be presented
at TCT 2011



*2 patients withdrew consent for imaging FUP

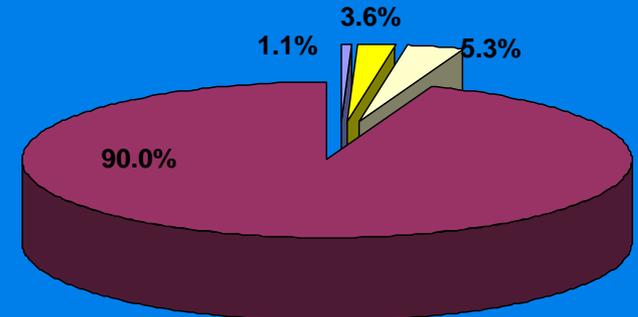
OCT evaluation shows little malapposition post-procedure and at 6 months

Scaffold Strut Apposition – Baseline

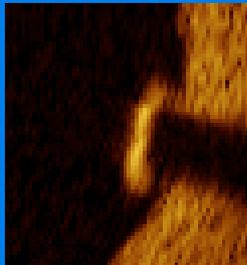


N=4 scaffolds, 3226 struts

Scaffold Strut Apposition – 6 Mo FUP



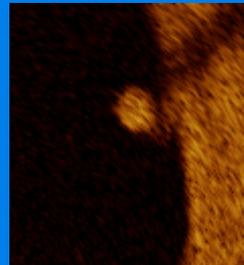
N=4 scaffolds, 3226 struts



Apposed



ISA



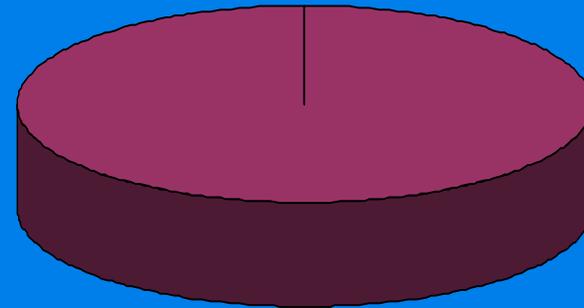
ISA at follow-up

To be presented at
TCT 2011

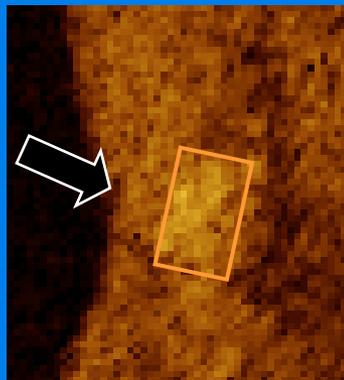


Complete strut coverage

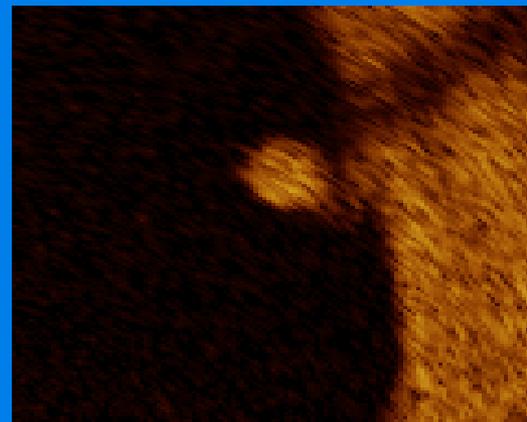
Scaffold Strut Coverage – 6 Mo FUP



To be presented
at TCT 2011



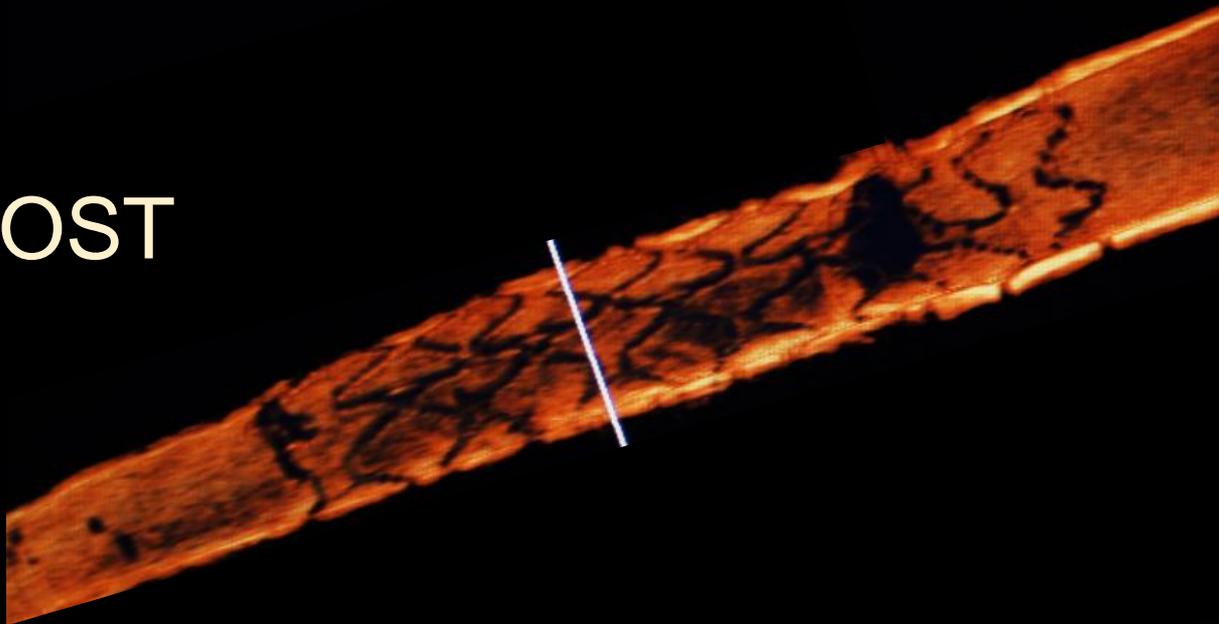
Complete



ISA at follow-up

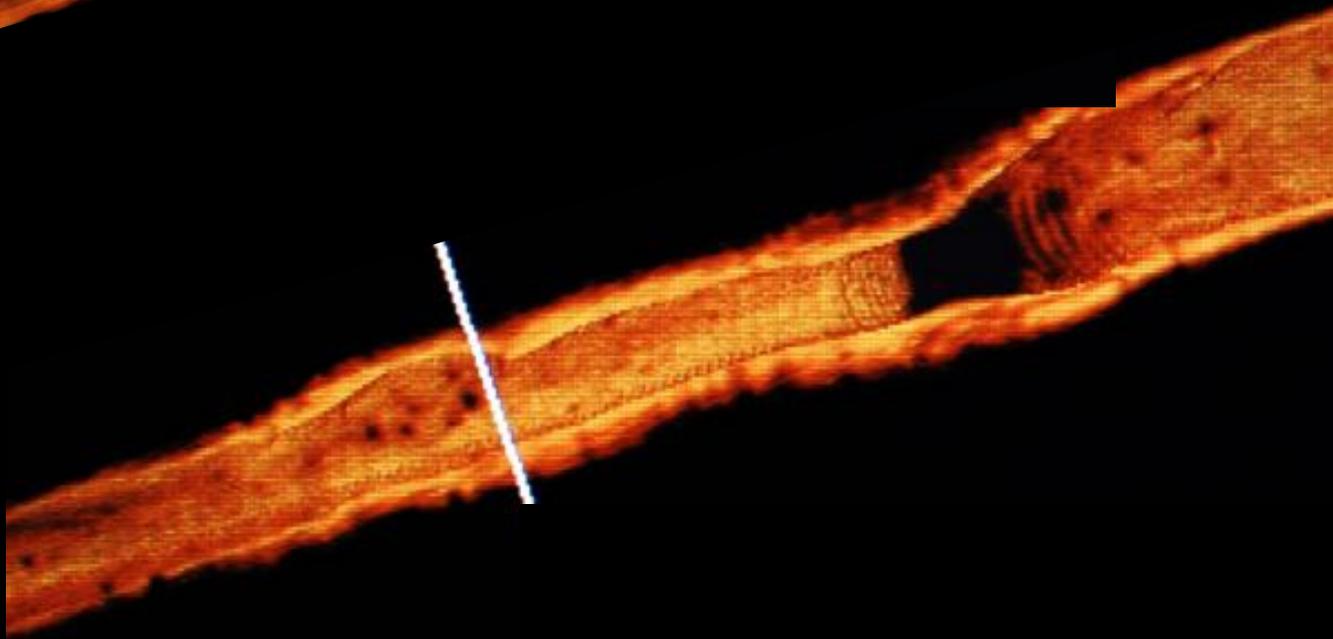


POST



Ger
443-12

FU



Conclusions



Late thrombosis of first gen.
DES occurs in about 0.5%
cases per year

Stent thrombosis is more rare in
second generation DES

New stent designs and
particularly fully bio-absorbable
DES may be a valid solution to
improve clinical outcome after
stenting



Stent positioning on proximal LAD

Advance and deploy main vessel stent

