23rd CARDIOVASCULAR SUMMIT TCTAP2018

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Rethinking All Mechanism of Scaffold Thrombosis and How to Fix It?

Yoshinobu Onuma MD, PhD
Erasmus MC, Rotterdam, the Netherlands
Cardialysis, Rotterdam, the Netherlands
Norihiro Kogame, MD, Yuki Katagiri, MD,
Taku Asano, MD, Kuniaki Takahashi, MD
Academic medical Centre, Amsterdam, the Netherlands
Patrick W. Serruys MD, PhD
Professor of Cardiology of Imperial College, UK
Dr. Honoris Causa in Biomedical Engineering, Melbourne university, Australia
Emeritus Professor of Cardiology, Erasmus MC, the Netherlands

CARDIALYSIS
Clinical Trial Management - Core Laboratories

Erasmus MC

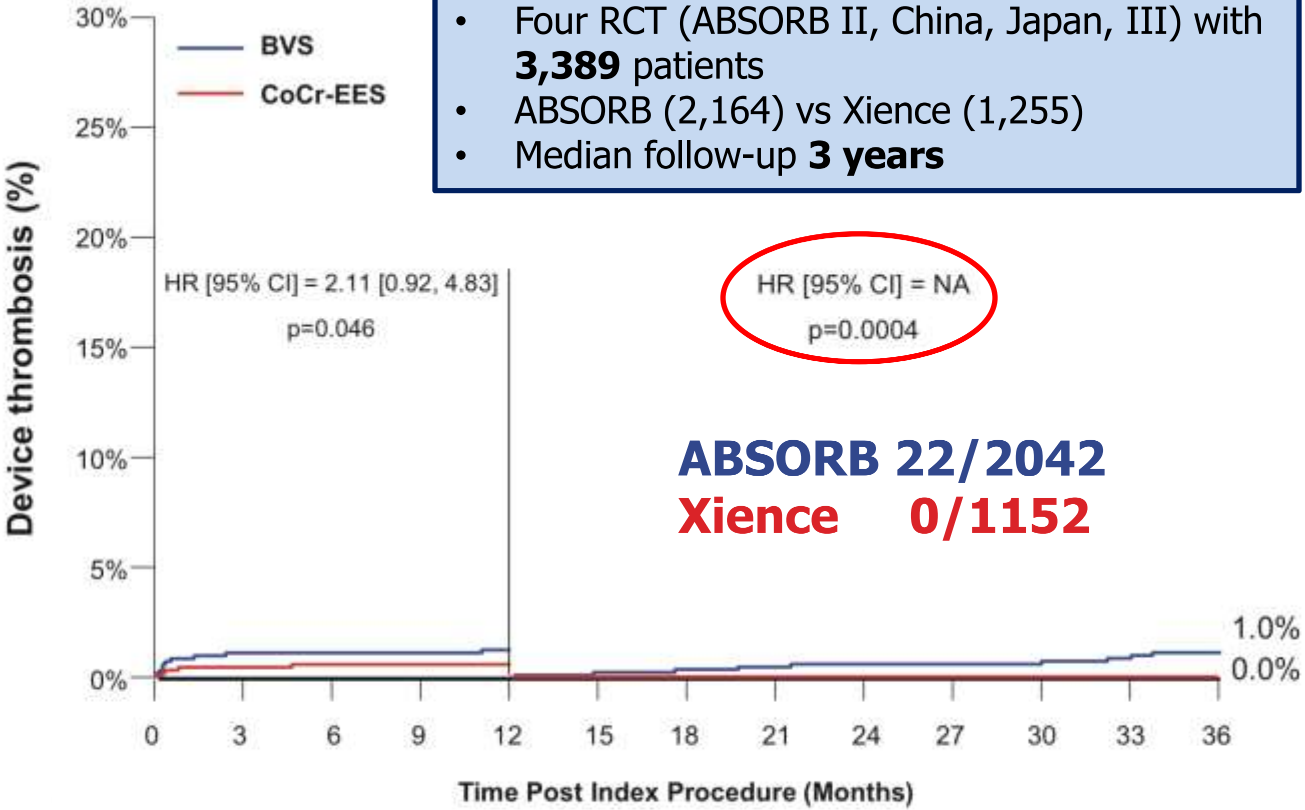
Disclosure Statement

Yoshinobu Onuma, MD. PhD.

Advisory board of Abbott Vascular

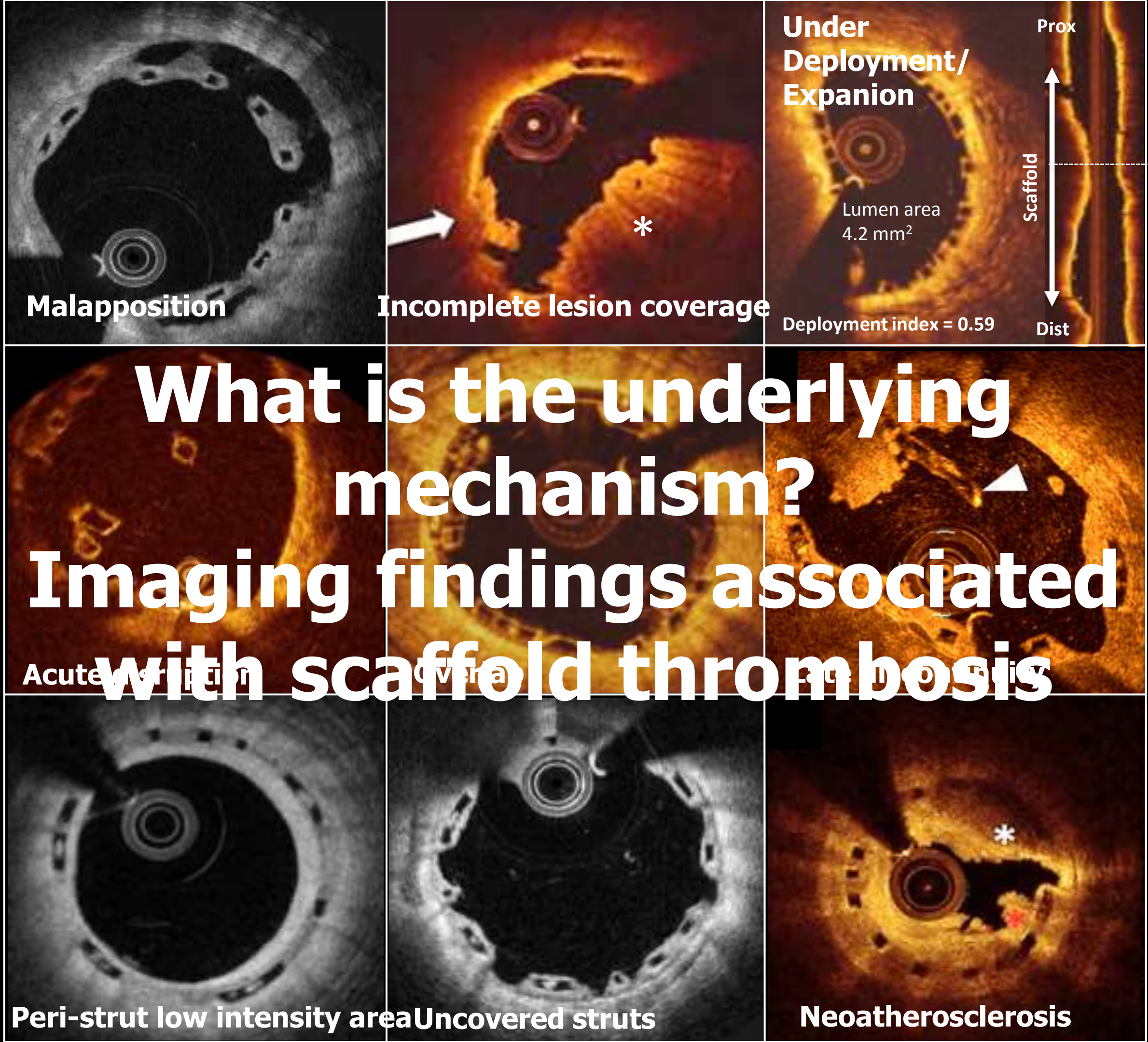
High incidence of very late scaffold thrombosis at 3 years

- Four RCT (ABSORB II, China, Japan, III) with **3,389** patients
- ABSORB (2,164) vs Xience (1,255)
- Median follow-up **3 years**



Ziad A. Circulation. 2018 Jan 30;137(5):464-479.

What is the underlying mechanism? Imaging findings associated with scaffold thrombosis



Sotomi et al. EI 2016

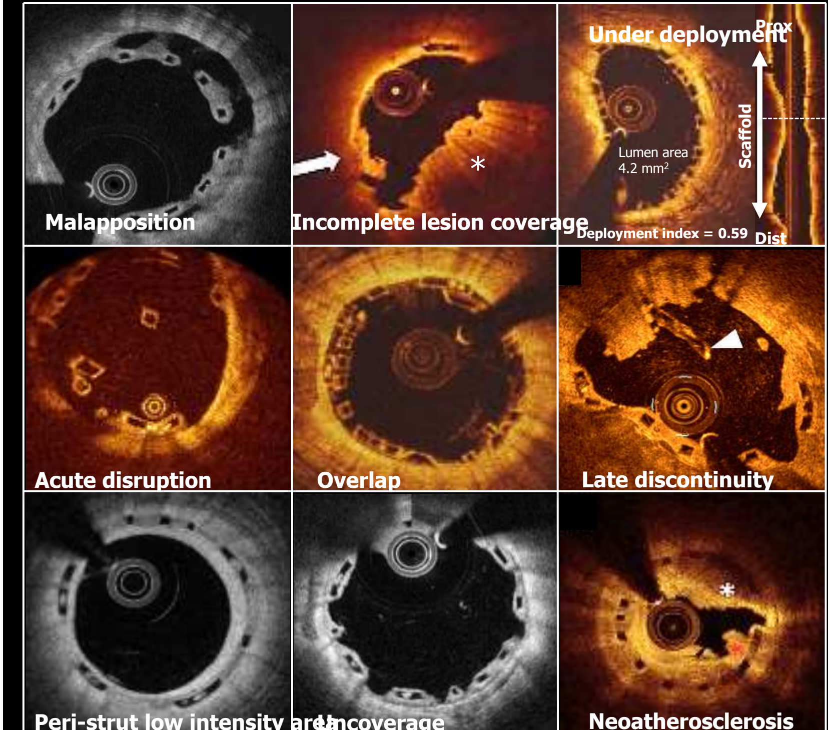
Possible mechanical causes of scaffold thrombosis: insights from case reports with intracoronary imaging

Systematic review

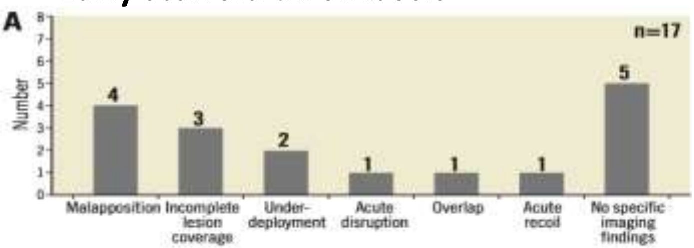
Imaging findings in ScT cases

- **Early ScT (N=17)**
malapposition (24%), incomplete lesion coverage (18%), and underdeployment (12%)

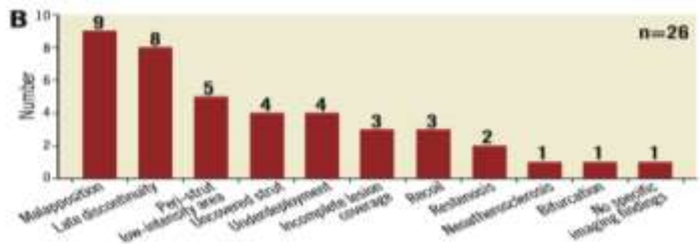
- **Late/very late ScT (N=26)**
malapposition (35%), late discontinuity (31%) and peri-strut low-intensity area (19%)



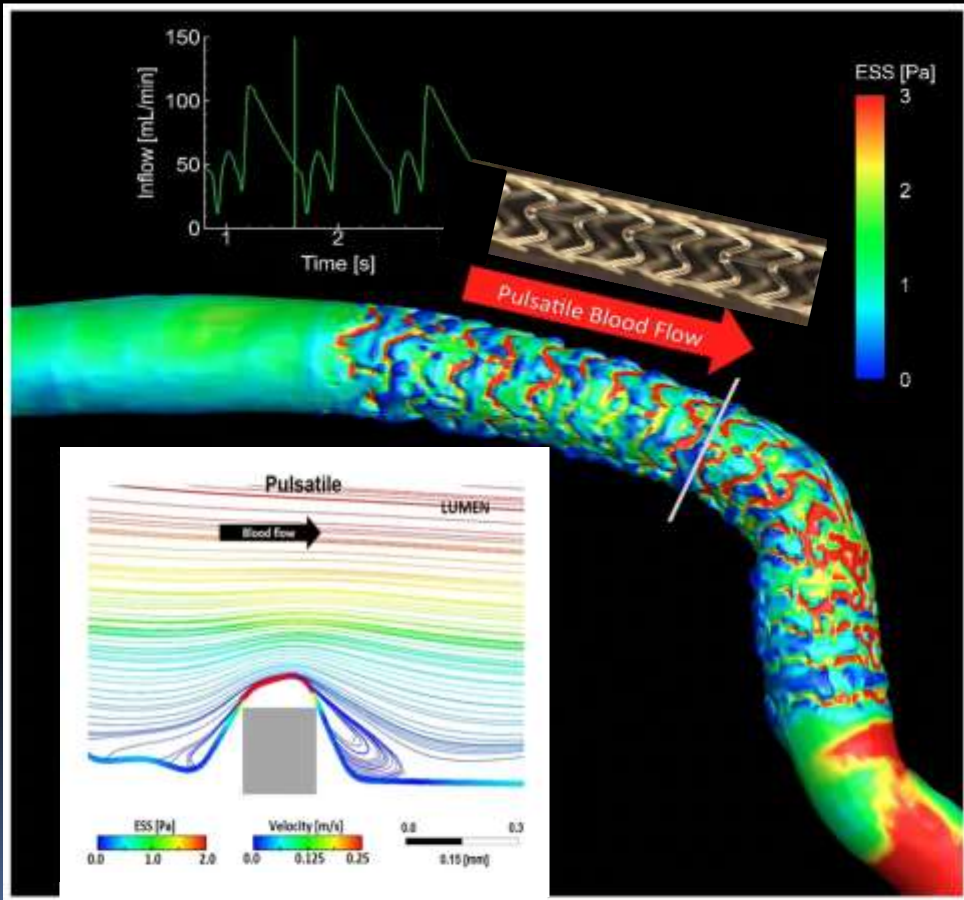
Early scaffold thrombosis



Late/very late scaffold thrombosis



Fusion of Angio and OCT, pulsatile flow, non-Newtonian fluid and shear stress immediately after Absorb implantation in a human being



THE UNIVERSITY OF MELBOURNE

Tenekecioglu E, Poon E, et al. Serruys PW.

The Nidus for Possible Thrombus Formation: Insight From the Microenvironment of Bioresorbable Vascular Scaffold.

JACC Cardiovasc Interv. 2016 Oct 24;9(20): 2167-2168.

Tenekecioglu et al.

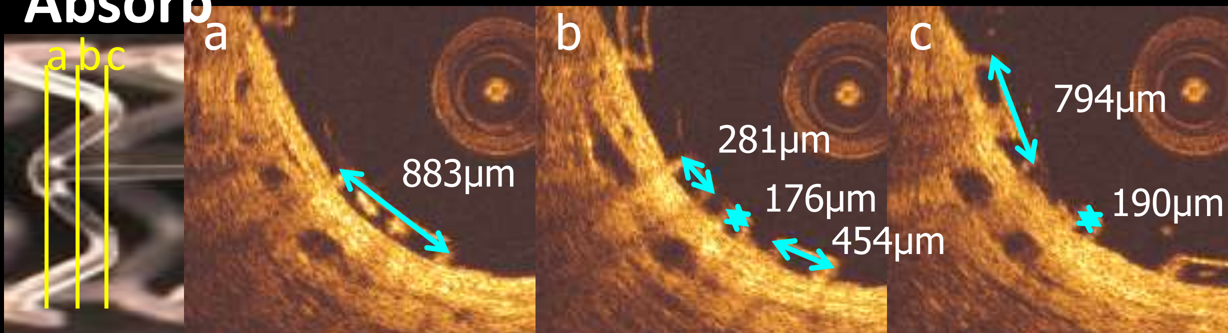
Int J Cardiol. 2017 Jan 15; 227:467-473.

Snowshoe Versus Ice Skate for Scaffolding of Disrupted Vessel Wall*

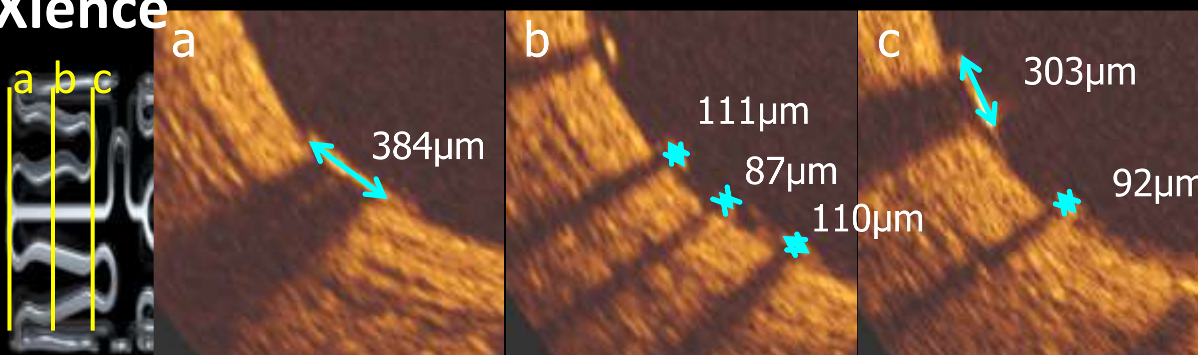
Patrick W. Serruys, MD, PhD,† Pannipa Suwannasom, MD,‡ Shimpei Nakatani, MD,‡ Yoshinobu Onuma, MD, PhD‡

Difference of Strut Width in each part (Hinge, Link, Ring)

Absorb

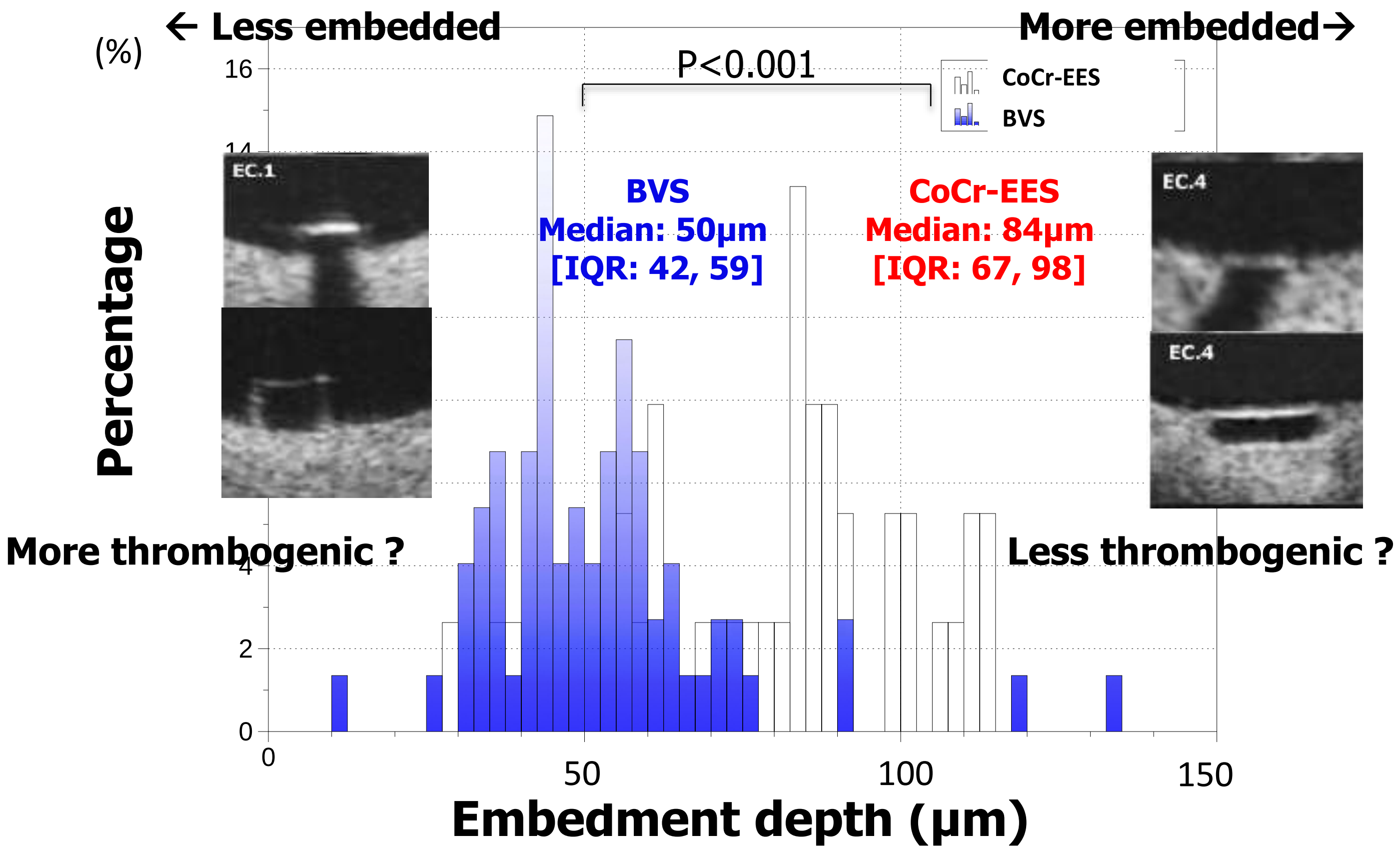


Xience



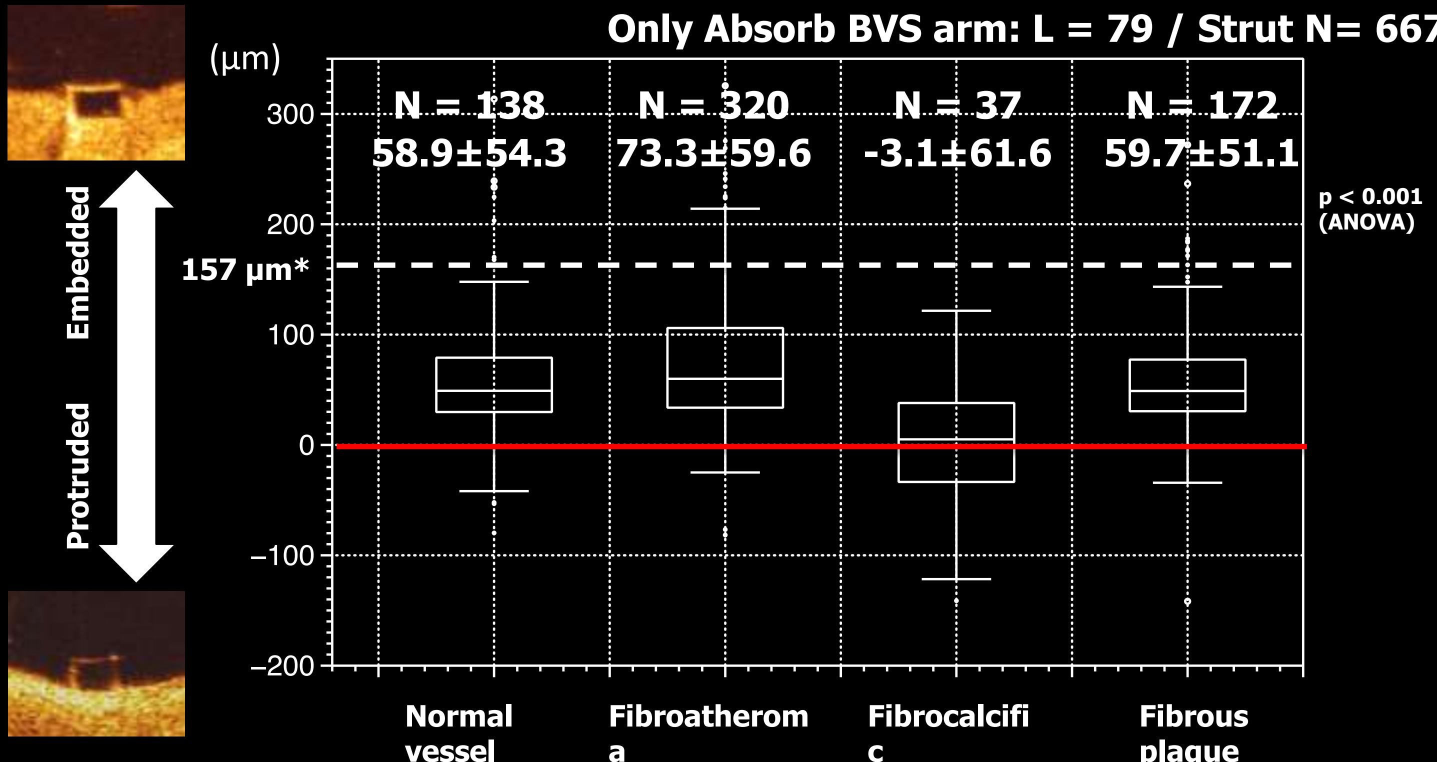
ABSORB Japan OCT-1 Subgroup

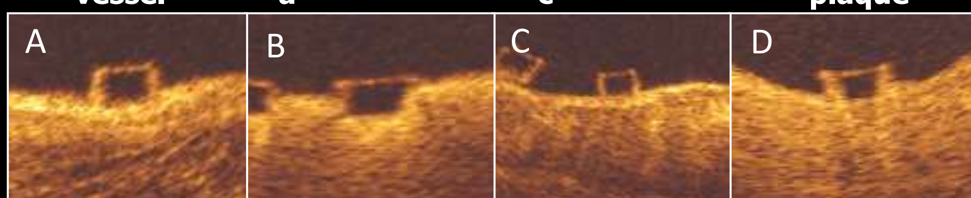
Distribution of embedment depth of BVS and CoCr-EES



Onuma et al. EuroIntervention 2016

Embedment depth stratified by underlying plaque type





Int J Cardiovasc Imaging. 2016;32(6):871-83.

*strut thickness of BVS

Possible mechanical causes of scaffold thrombosis: insights from case reports with intracoronary imaging

Yohei Sotomi[1], MD; Pannipa Suwannasom[1,2,3], MD; Patrick W. Serruys[4*], MD, PhD; Yoshinobu Onuma[2], MD, PhD

Systematic review

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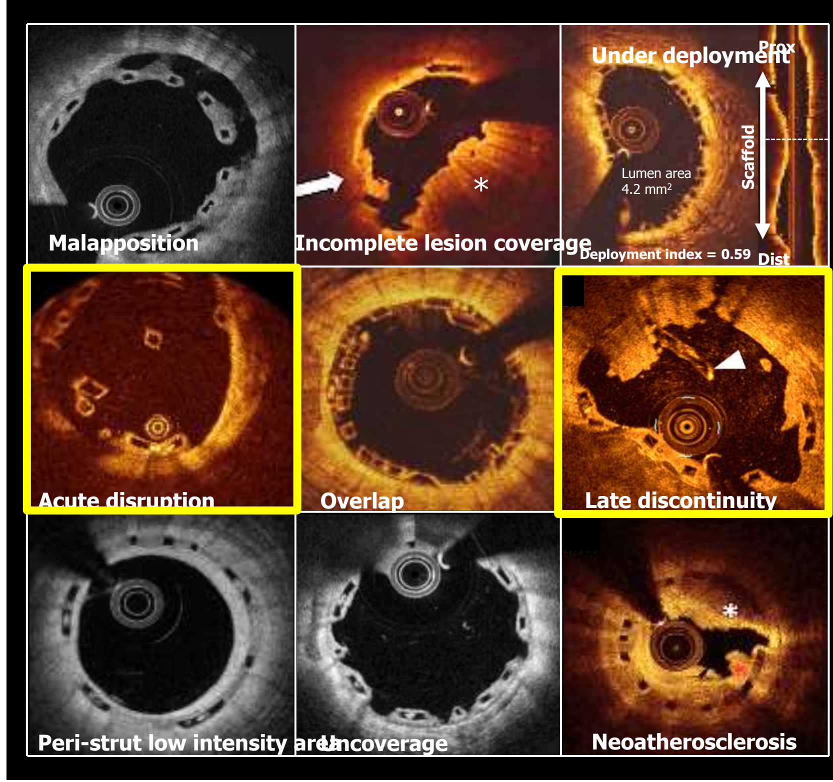
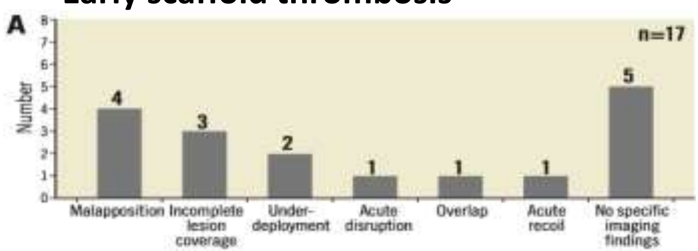
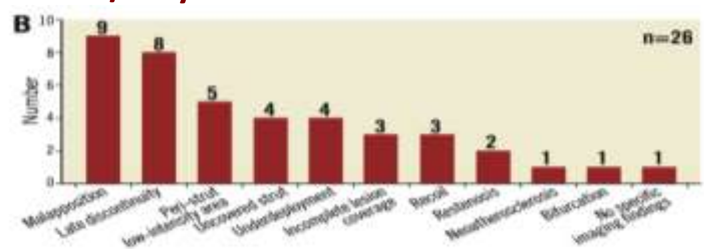


Early scaffold thrombosis

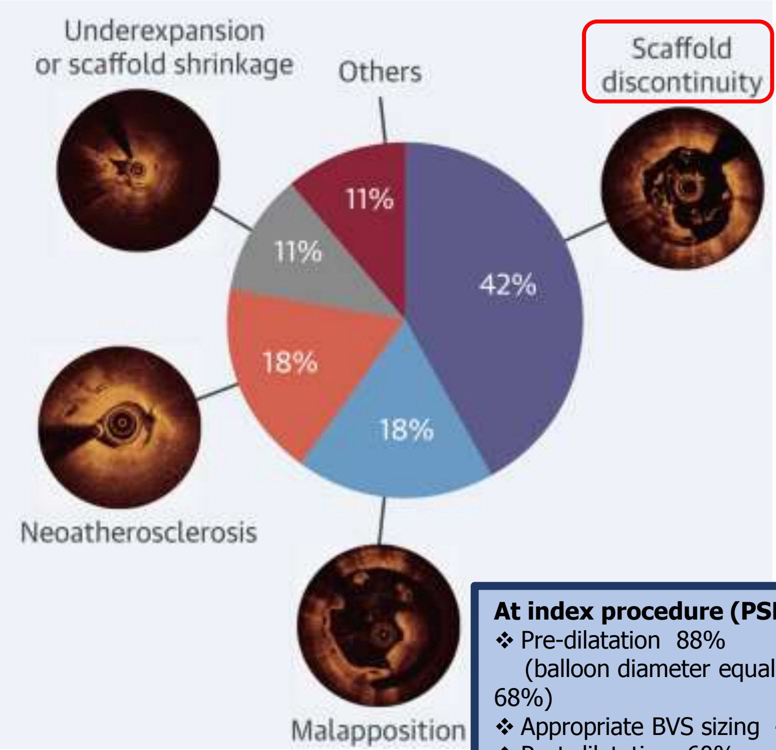


Late/very late scaffold thrombosis



Mechanisms of Very Late Scaffold Thrombosis: The INVEST Registry

- **Multicenter registry**
- **Total 36 patients (38 lesions)** with **VLScT** underwent **OCT**
- VLScT occurred at a median of **20 months**
- At the time of VLScT, **83%** of patients received **aspirin monotherapy**, **17%** received **DAPT**
- The leading mechanism of underlying VLScT was **scaffold discontinuity (42.1 %)**

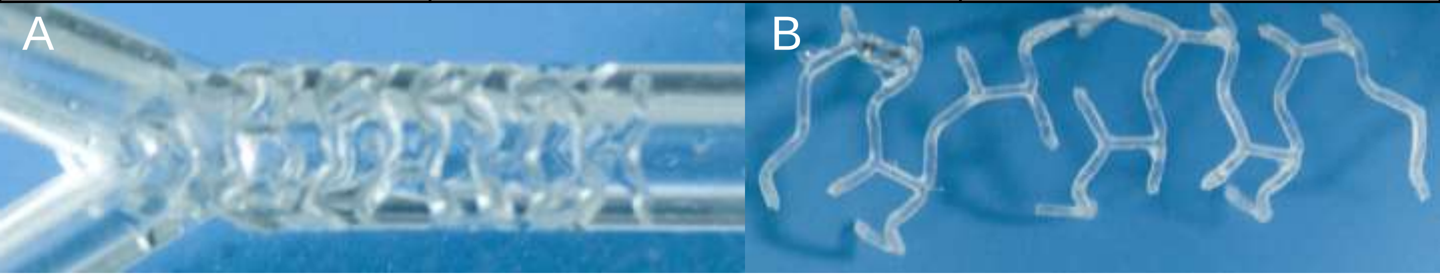


At index procedure (PSP)
❖ Pre-dilatation 88%
(balloon diameter equal to RVD 68%)
❖ Appropriate BVS sizing 44%
❖ Post-dilatation 60%
(high pressure (≥16atm) 34%)
❖ Post in-segment %DS<30% 84%

Yamaji, K. et al. J Am Coll Cardiol.201

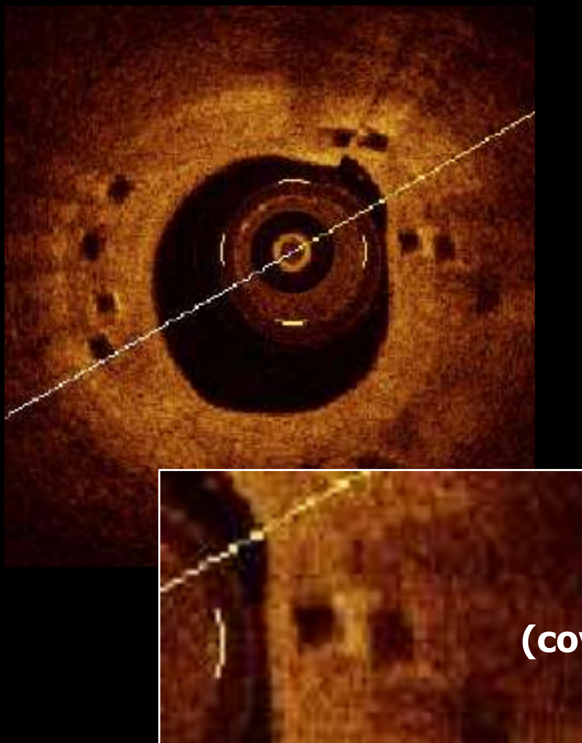
3 criteria to judge acute disruption/late discontinuities on OCT

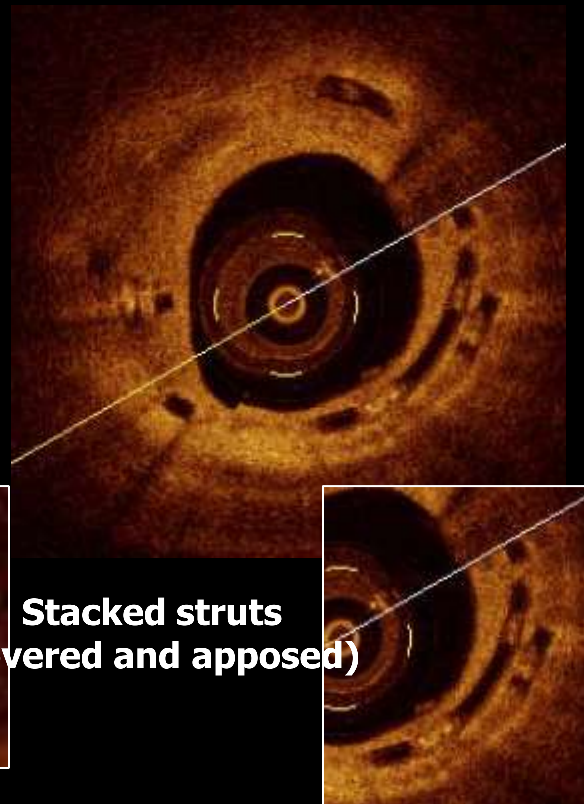
	Time of OCT observation	
	Post procedure	**Late**
Acute Scaffold disruption	•Stacked struts	Persistent
	•Overhung struts	
	•Isolated intra-luminal strut(s)	
Late Scaffold discontinuities	No disruption	•Stacked/ overhung / isolated or intraluminal strut (s)



Onuma et al. JACC int 2014

Late discontinuities observed in porcine coronary artery





Stacked struts
(covered and apposed)

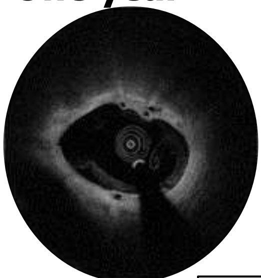
#3. Mechanism of ST/VLST

Late discontinuities of a s[...]
Carpet view of the scaffold

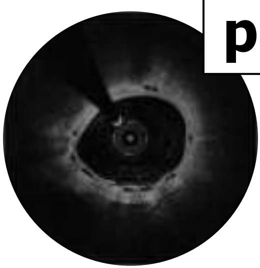
Onuma et al. JACC int 2014

Post Procedure

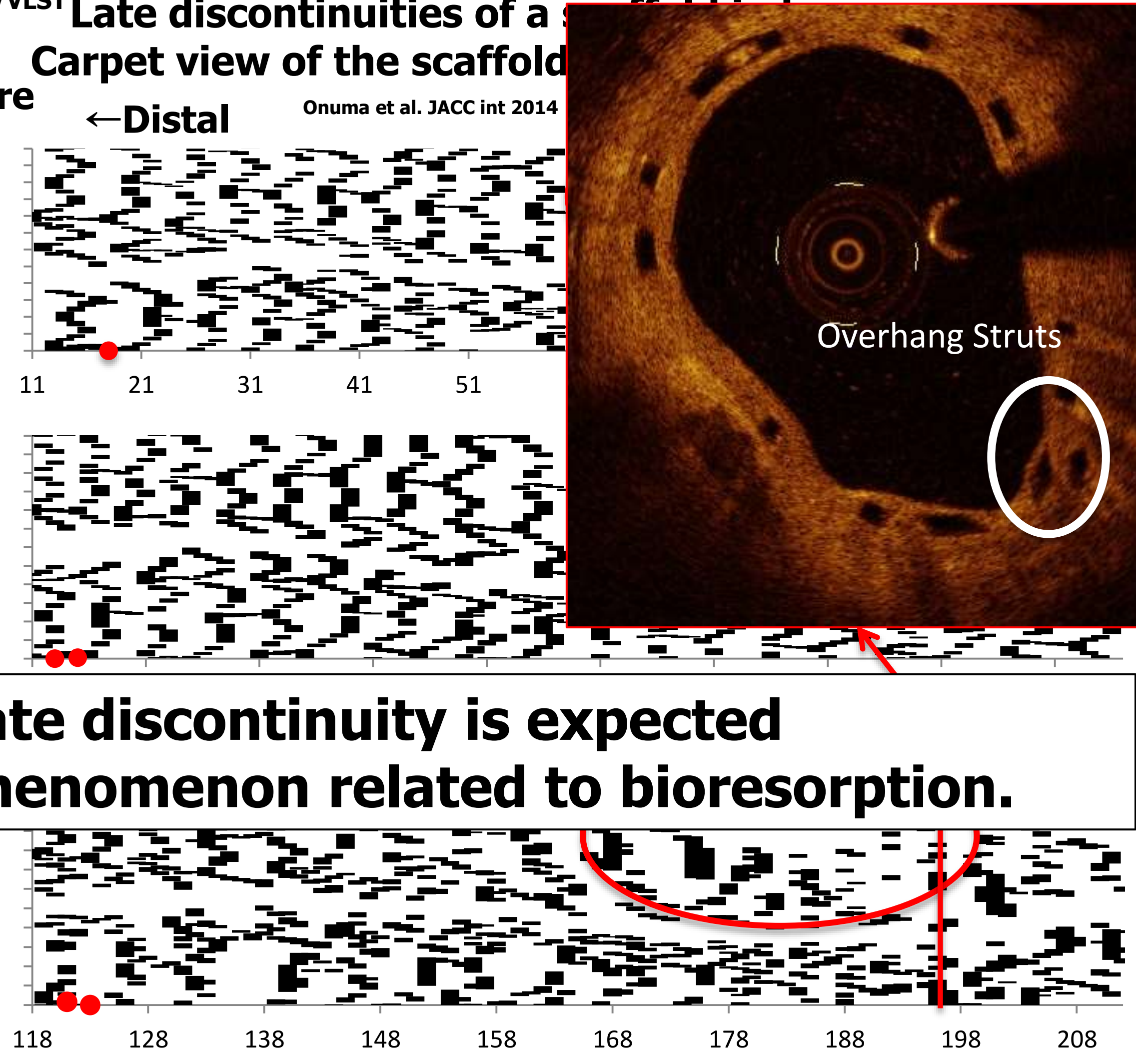
One year



Three yea[rs]



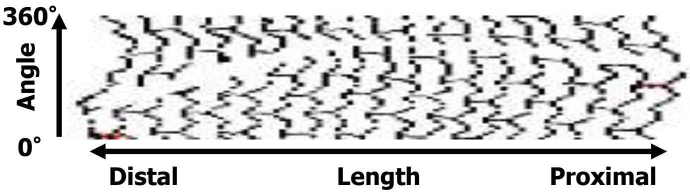
←Distal



Late discontinuity is expected phenomenon related to bioresorption.

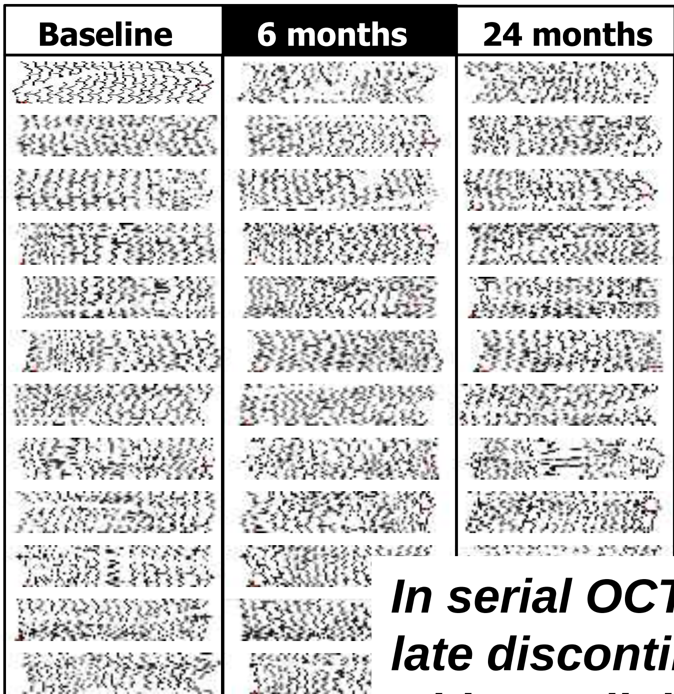
Serial changes of strut distribution

BRS textbook

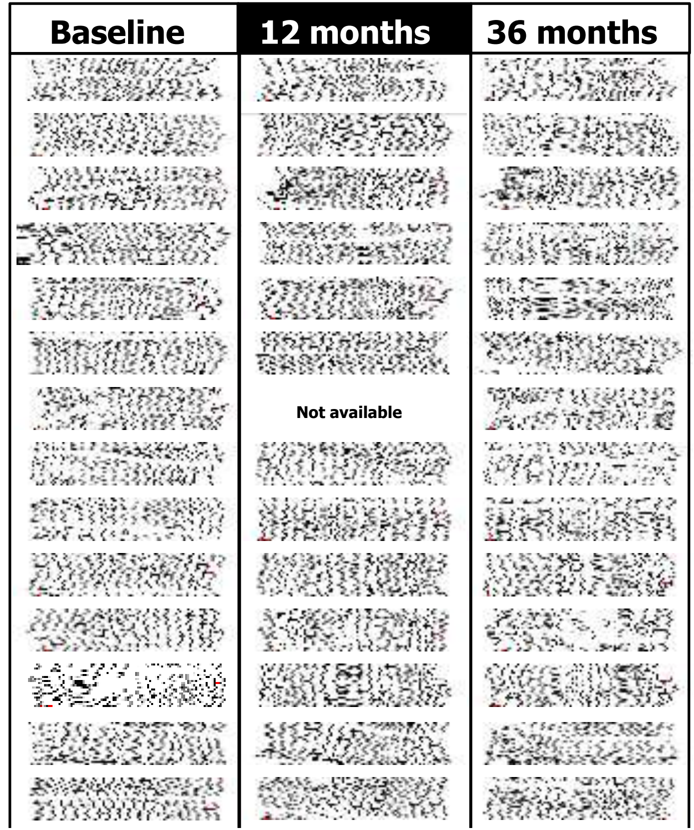


Absorb Strut
Metallic marker

ABSORB Cohort B1



ABSORB Cohort B2



Onuma et al. JACC int 2014

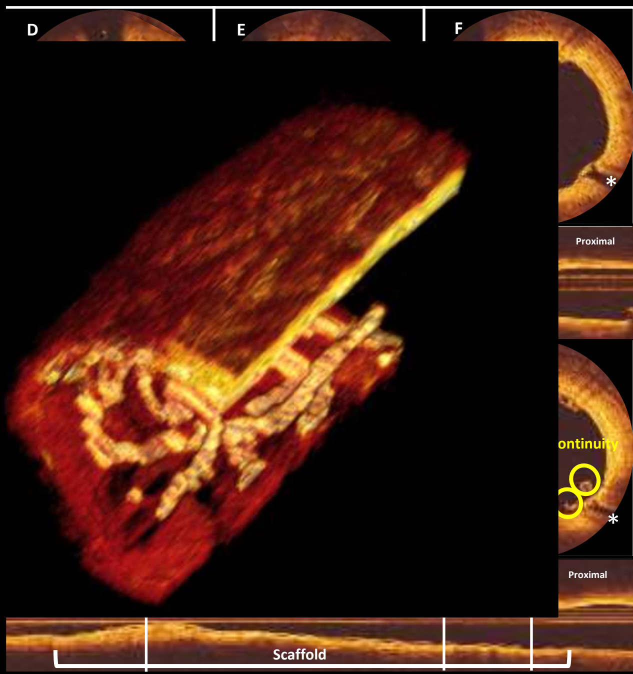
In serial OCT observation up to 36 months, late discontinuities were observed in 43%, without clinical events

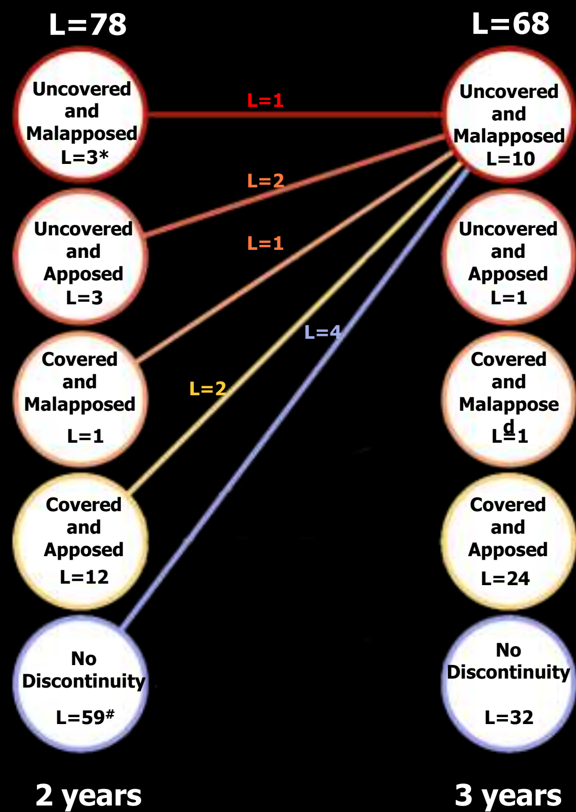
Frequency of late discontinuities between 2 and 3 years (truly serial analysis at lesion level)

-by courtesy of Prof. Kimura

2-year Follow-Up

3-year Follow-Up

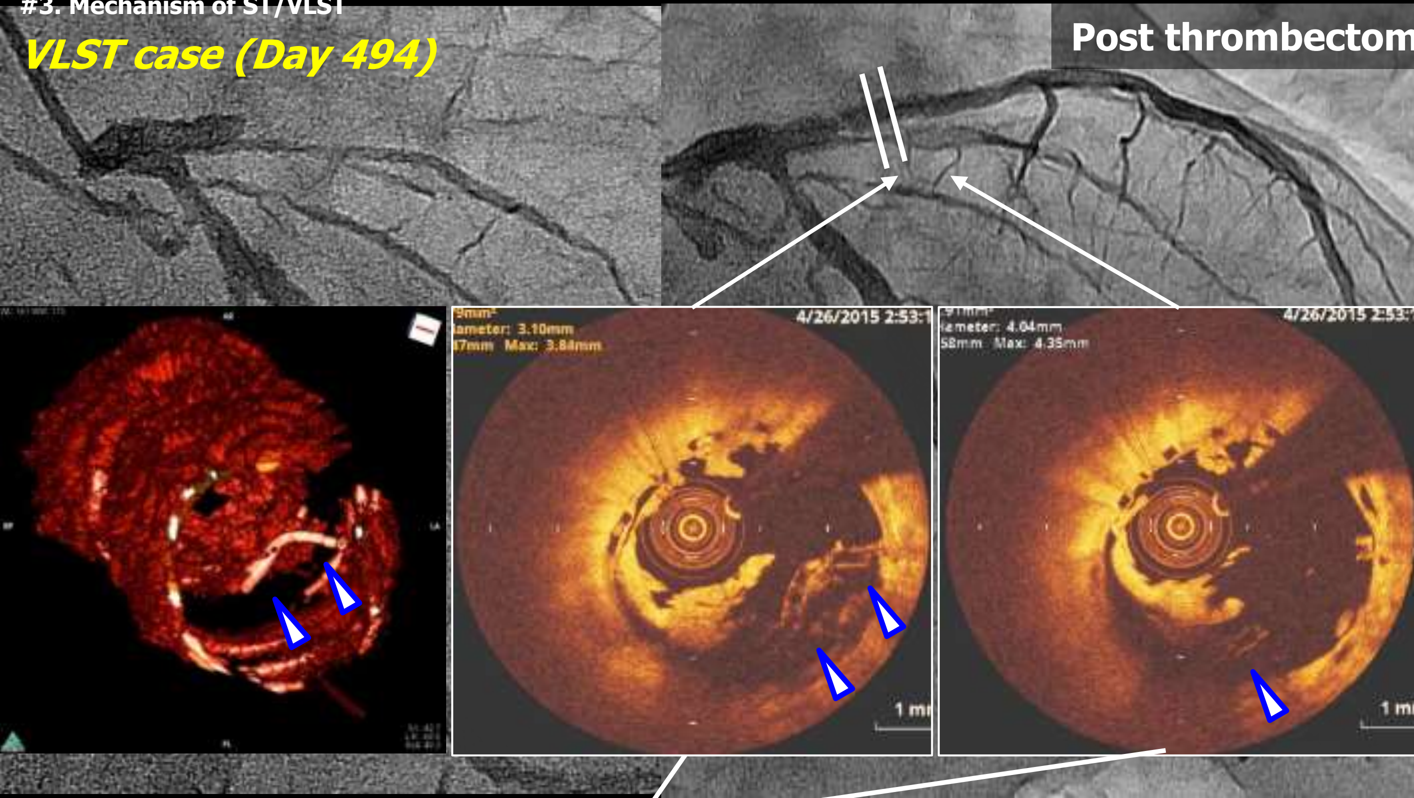




* Two lesions were not analyzable at 3 years. # Eight lesions were not analyzable at 3 years.

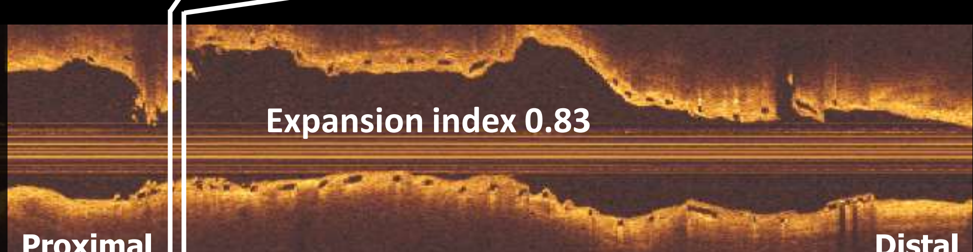
#3. Mechanism of ST/VLST

VLST case (Day 494)

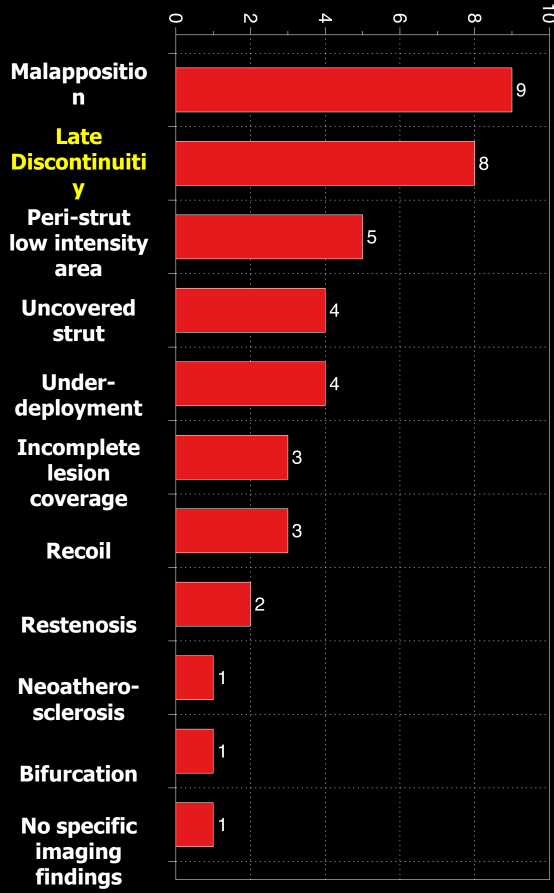


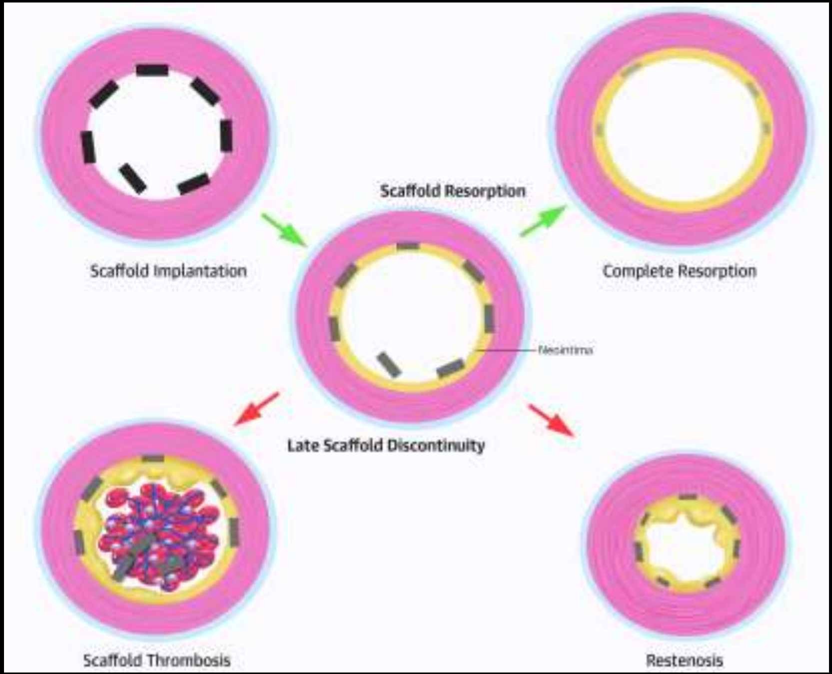
Status of antiplatelet therapy

ASA: quit at 487 days
(1 week before event)
Clopidogrel: quit at 1 year
Ciostazol: quit at 3 weeks



Imaging findings associated with Late/ Very Late scaffold thrombosis reported in literature





- ***What is triggering VLST?***

Lorenz Räber et al. JACC 2015, Onuma et al. JACC interv 2014, Sotomi et al. Submitted

Can operator improve the outcomes ?

Scaffold or stent thrombosis in ABSORB II trial

2 : 1 randomization

	Absorb 335 patients	Xience 166 patients	p value
Definite ST	**2.5% (8)**	**0.0% (0)**	**0.06**
Acute (0–1 day)	**0.3% (1)**	**0.0% (0)**	**1**
Sub-acute (2–30 days)	**0.3% (1)**	**0.0% (0)**	**1**
Late (31–365 days)	**0.0% (0)**	**0.0% (0)**	**1**
Very late (>365 days)	**1.8% (6)**	**0.0% (0)**	**0.19**

- The ABSORB II trial was plagued by the unexpected occurrence of very late scaffold thromboses, although the observation did not reach statistical significance when compared to the non-occurrence of VLST in the Xience arm.

- It is hypothesized that these late and very late events (up to 3 years) are related to the acute suboptimal implantation results such as under-expansion and malapposition.

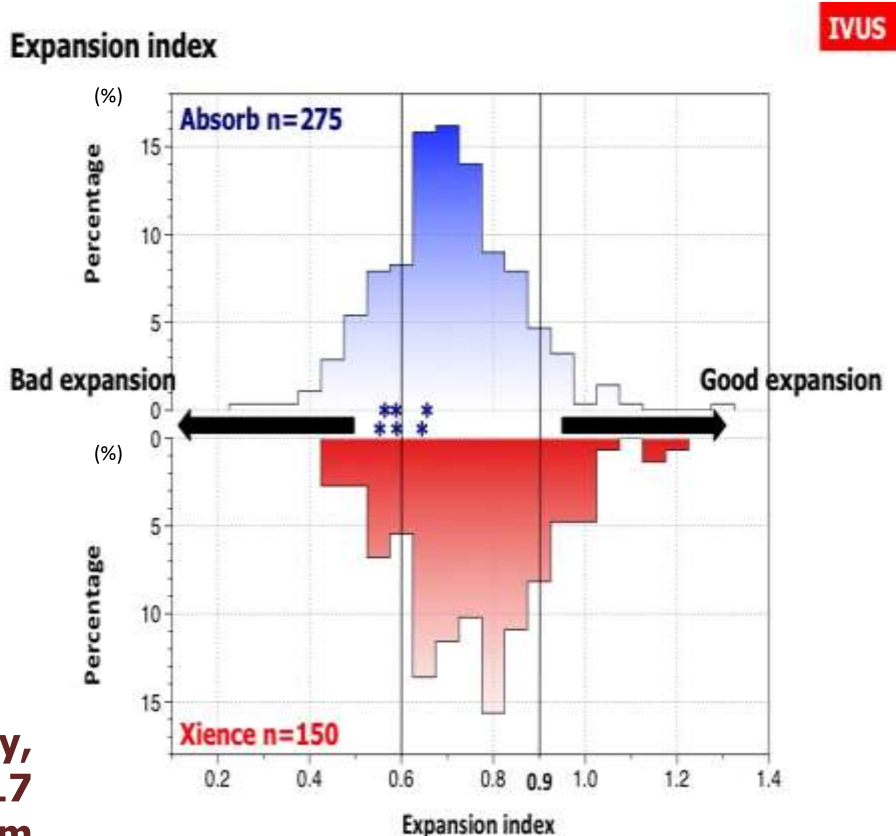
- The objective of the current study is to investigate the possible relationship of baseline demographics, post-procedural angiographic and ultrasound imaging results with the occurrence of definite very late scaffold thromboses in the Absorb II trial, in order to unravel potential **predictors of very late complications**.

Serruys et al. 2017 CRT

In-Depth Analysis of ABSORB II: Poor Expansion Index Might Be Responsible For Very Late Scaffold Thrombosis? True or Not True?

QCA parameter
- Percent diameter stenosis
- Minimum lumen diameter
- Lesion coverage ratio

IVUS parameter
- Minimum lumen diameter
- Expansion index
- Minimum eccentricity index
- Asymmetry index
- Deployment index
- Maximal ISA distance



Full presentation:
1:55-2:05 PM, Tuesday, February 21, 2017
Palladian Ballroom

In-Depth Analysis of ABSORB II: Poor Expansion Index Might Be Responsible For Very Late Scaffold Thrombosis? True or Not True?

Predictors for VLScT: Univariate Cox regression analysis

Variable	Odds ratio [95% confidence interval]	p value
Procedure		
Post-dilatation performed	0.55 [0.11-2.78]	0.471
Post-dilatation maximal pressure (atm)	0.76 [0.51-1.13]	0.176
QCA		
In-device % diameter stenosis (%)	1.07 [0.96-1.19]	0.218
In-device minimum lumen diameter (mm)	2.58 [0.25-26.08]	0.422
Lesion coverage ratio per 0.1 increase	**0.74 [0.56-0.98]**	**0.032**
IVUS		
Minimum lumen diameter (mm)	1.80 [0.18-17.74]	0.613
Asymmetry index per 0.1 increase	0.34 [0.10-1.18]	0.088
Expansion index per 0.1 increase	0.58 [0.32-1.04]	0.066
Minimum eccentricity index per 0.1 increase	2.29 [0.63-8.35]	0.208
Deployment index per 0.1 increase	1.78 [0.75-4.22]	0.188
Expansion index <0.6	**6.93 [1.24-38.82]**	**0.028**

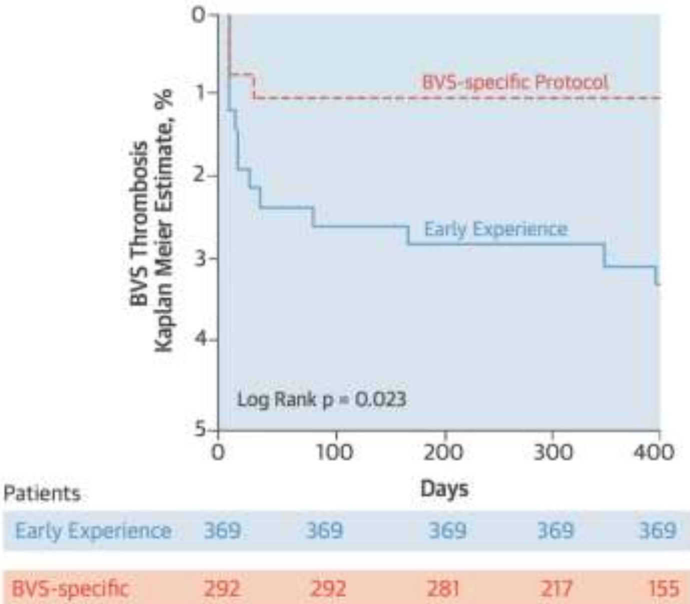
Full presentation: 1:55-2:05 PM, Tuesday, February 21, 2017, Palladian Ballroom

Impact of PSP strategy studied in registries

Bioresorbable Coronary Scaffold Thrombosis

Multicenter Comprehensive Analysis of Clinical Presentation, Mechanisms, and Predictors

Puricel et al. *J Am Coll Cardiol*. 2016;67:921-31

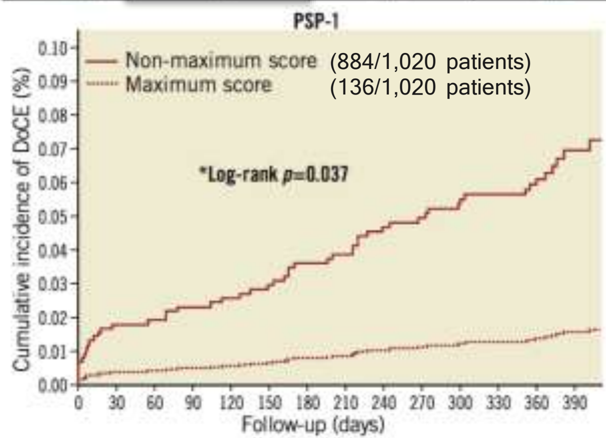


Predilation, sizing and post-dilation scoring in patients undergoing everolimus-eluting bioresorbable scaffold implantation for prediction of cardiac adverse events: development and internal validation of the PSP score

Ortega-Paz et al. *EuroIntervention* 2017;12:2110-211

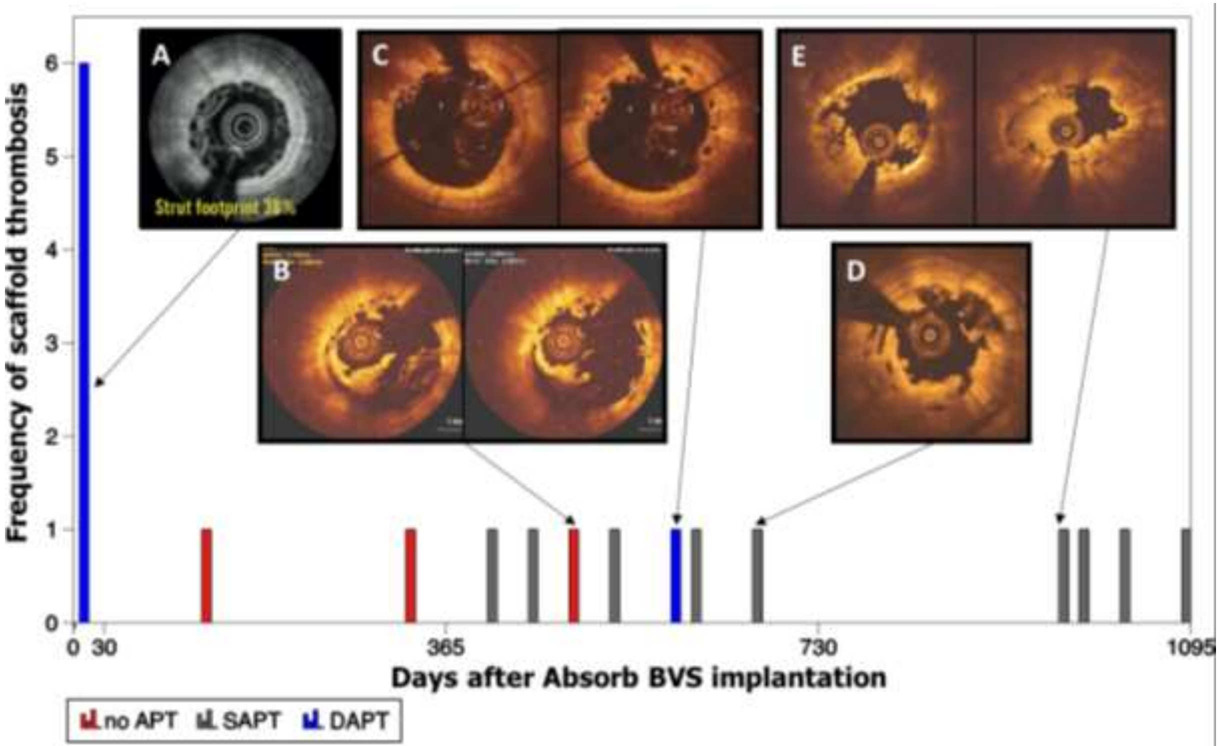
A — PSP score models estimation

	PSP-1	PSP-2	PSP-3
Predilation	Not performed=0 Performed=0.63	Not performed or residual stenosis ≥30%=0 Residual stenosis <30%=1.56	Not performed=0 Performed=0.63
Scaffold sizing	Incorrect=0 Correct*=1.96		
Post-dilation	Not performed, over-expanded† or performed with a 1:1 NC balloon‡=0 Performed with a NC balloon >1:1§=1.93	Not performed, over-expanded† or performed with a 1:1 NC balloon‡=0 Performed with a NC balloon >1:1§=1.93	Not performed, over-expanded†, or performed with a 1:1 NC balloon pressure <16 atm=0 Performed with a NC balloon pressure ≥16 atm=1.06
Maximum score	4.52	5.45	3.65



Late thrombotic events after bioresorbable scaffold implantation: a systematic review and meta-analysis of randomized clinical trials

Carlos Collet[1], Taku Asano[1], Yosuke Miyazaki[2], Erhan Tenekecioglu[2], Yuki Katagiri[1], Yohei Sotomi[1], Rafael Cavalcante[2], Robert J. de Winter[1], Takeshi Kimura[3], Runlin Gao[4], Serban Puricel[5], Stéphane Cook[5], Davide Capodanno[6], Yoshinobu Onuma[2], and Patrick W. Serruys[7]*



Collet et al. EHJ. 2017

Conclusion

- Recent meta-analyses of mid-term outcomes (2-3 years) demonstrated increased rates of scaffold thrombosis as well as very late scaffold thrombosis after implantation of the Absorb scaffold in comparison with the Xience stent.
- Malapposition and protruding struts resulting in recirculation behind struts are the important mechanisms for early scaffold thrombosis. This could be prevented by applying better procedural technique and reducing strut thickness with better embedment.
- Late discontinuity seems to be one of major mechanisms of VLScT. Late discontinuities is in general a benign change during the bioresorption process, occurring in 40% up to 3 years. However, in case struts are not covered by neointima, late discontinuity could be a malignant potential cause of ScT. Under-expansion might also play a role the occurrence of VLScT; hypothetically when discontinuities occurs in underexpanded segment, this could cause a collapse of scaffold.
- Enhancement of neointimal coverage before the scaffold lose its mechanical integrity would be a key to prevent ScT associated with late discontinuity. This could be achieved by improving techniques, tuning bioresorption profile and drug elution.