22nd CARDIOVASCULAR SUMMIT
TCTAP 2017

# BRS Failure Analysis: Lessons from Serial Imaging Studies

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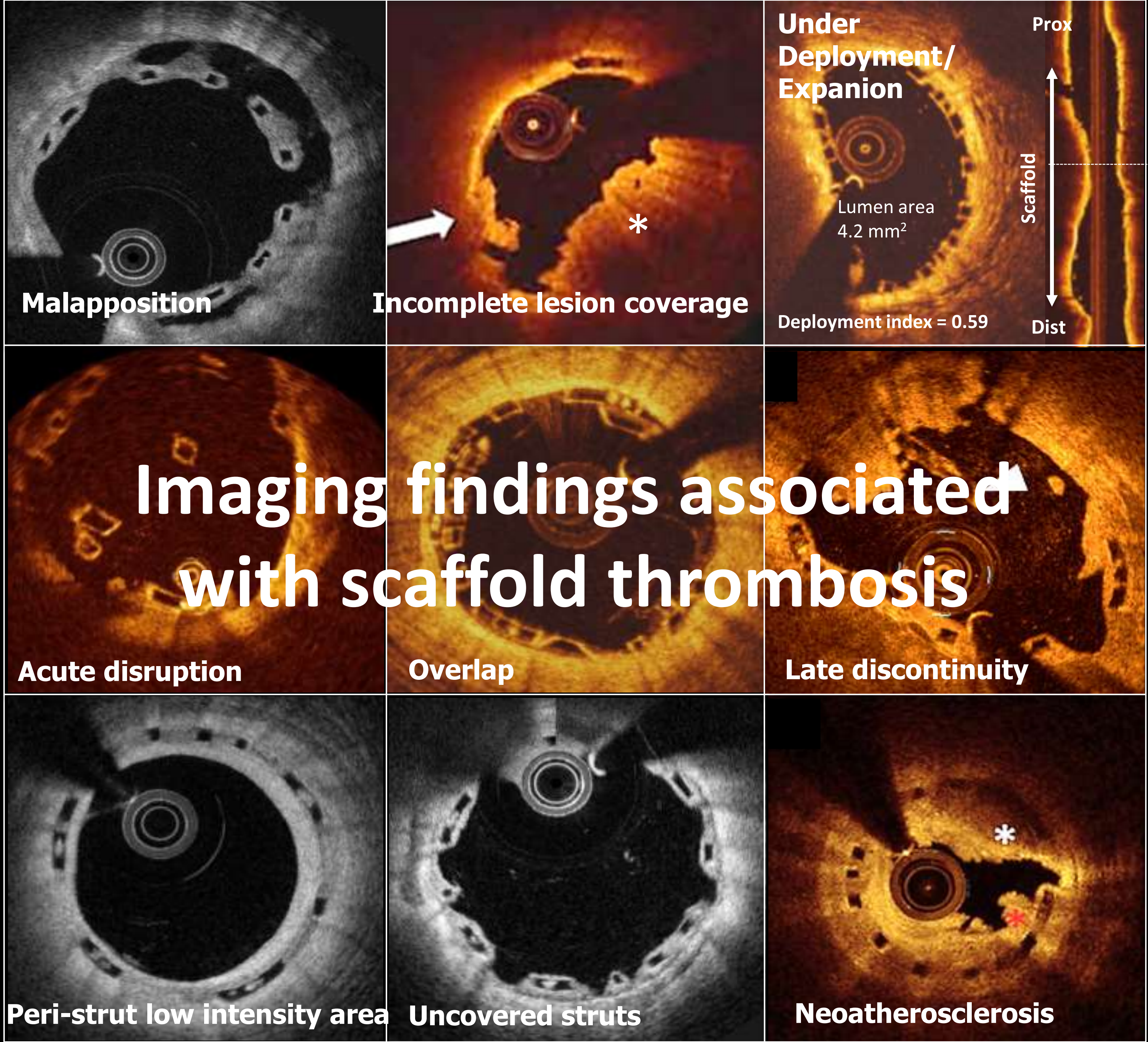
# Meta-analysis of long-term outcomes after the ABSORB implantation

| Study | Number of included patients | Included study | follow-up year | TLF rate (BVS vs EES) OR (95%CI) | TV-MI (BVS vs EES) OR (95%CI) | ID-TLR rate (BVS vs EES) OR (95%CI) | Definite/ probable ST rate (BVS vs EES) OR (95%CI) | Very late ST rate (BVS vs EES) OR (95%CI) |
|---|---|---|---|---|---|---|---|---|
| **Collet et al.[1]** | 1,730 (1,015 vs. 715) | ABSORB II<br>ABSORB JAPAN<br>ABSORB CHINA<br>TROFI II<br>EVERBIO II | 3Y<br>2Y<br>2Y<br>2Y<br>2Y | 9.3% vs. 6.6%<br>**OR 1.48 (0.90-2.42)** | 4.5% vs. 1.6%<br>**OR 2.25 (0.81-6.19)** | 5.6% vs. 3.0%<br>**OR 1.89 (1.15-3.13)** | 2.4% vs. 0.9%<br>**OR 2.95 (1.37-6.26)** | 1.4% vs. 0.5%<br>**OR 3.04 (1.20-7.68)** |
| **Ha et al.[3]** | 2,582 (1,407 vs. 1,095) | ABSORB II<br>ABSORB JAPAN<br>ABSORB CHINA<br>ABSORB EXAMINATIO N<br>ABSORB EXTEND | 3Y<br>2Y<br>2Y<br>2Y<br>3Y | **OR 1.31 (0.93-1.83)** | **OR 2.59 (1.17-5.70)** | **OR 1.70 (1.02-2.83)** | **OR 2.35 (1.14-4.86)** | Not reported |
| **Sorrentino et al.[2]** | 5,583 (3,261 vs. 2,322) | ABSORB II<br>ABSORB III<br>ABSORB JAPAN<br>ABSORB CHINA<br>AIDA<br>TROFI II<br>EVERBIO II | 3Y<br>2Y<br>2Y<br>2Y<br>2Y<br>2Y<br>2Y | 9.6% vs. 7.2%<br>**OR 1.32 (1.1-1.59)** | 5.8% vs. 3.2%<br>**OR: 1.62 (1.24 to 2.12)** | 5.7% vs. 4.1%<br>**OR 1.40 (1.10-1.79)** | 2.4% vs. 0.7%<br>**OR 3.15 (1.87-5.30)** | 0.84% vs. 0.13%<br>**OR 3.96 (1.47-10.66)** |

*1; EHJ. 2017, 2; JACC 2017, 3; JACC Cardiovasc Interv. 2017.*

# BRS Failure Analysis: Lessons from Serial Imaging Studies

1. **What are the imaging findings at the time of acute, subacute and late/very late Scaffold Thrombosis?**
2. **What are post-procedural imaging findings correlating to very late scaffold thrombosis?**
3. **What is the relationship of scaffold discontinuities and very late scaffold thrombosis?**




Sotomi et al. EI 2016

**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[3], MD, PhD

# Systematic review

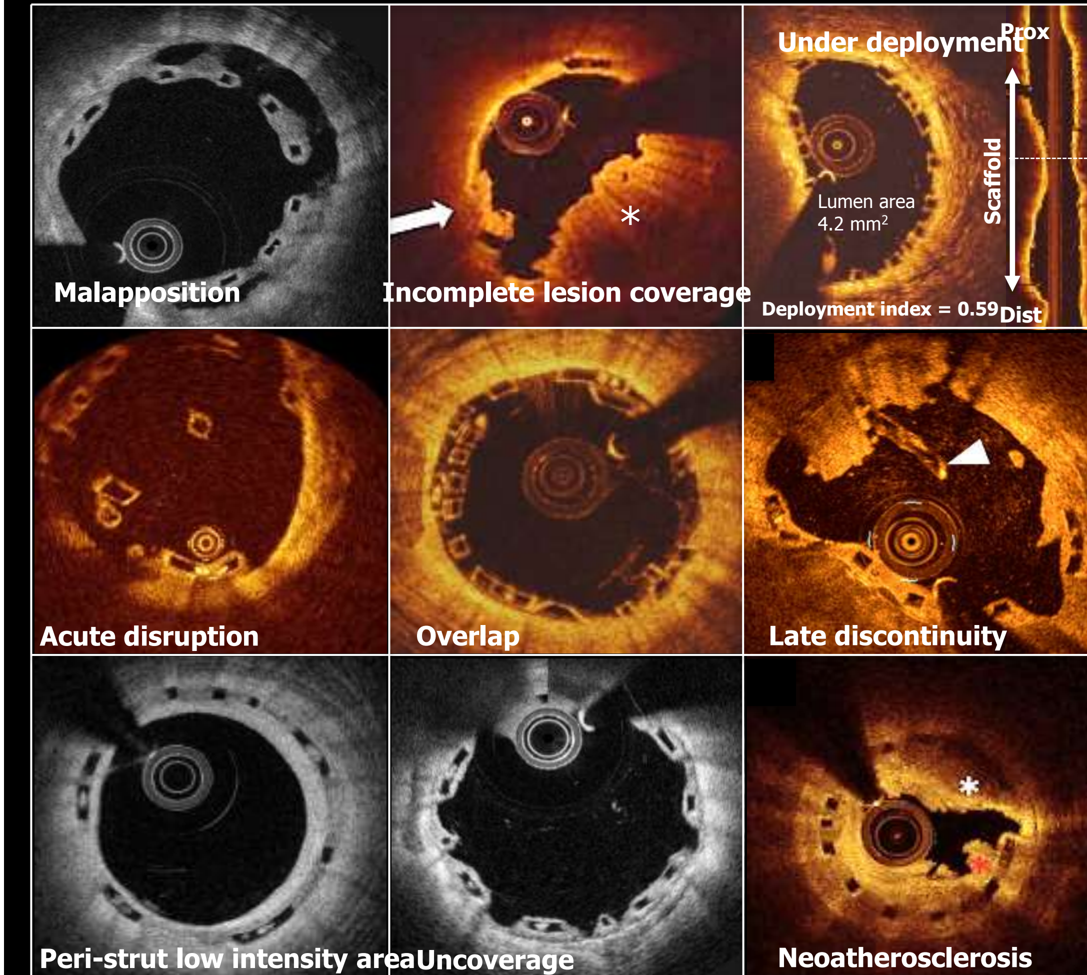
# Imaging findings in ScT cases

- **Early ScT (N=17)**

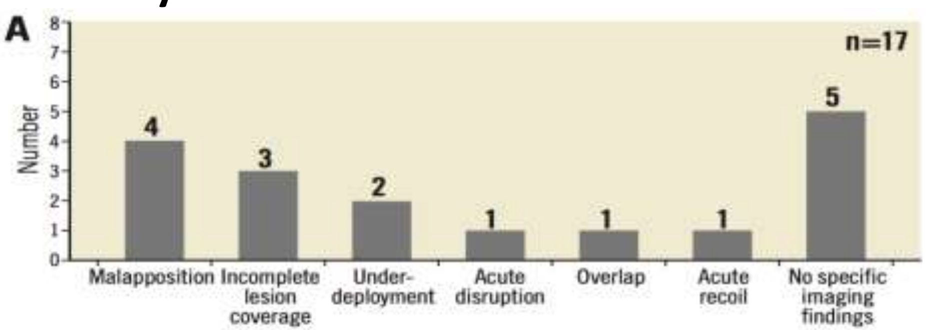
malapposition (24%), incomplete lesion coverage (18%), and underdeployment (12%)

- **Late/very late ScT (N=26)**

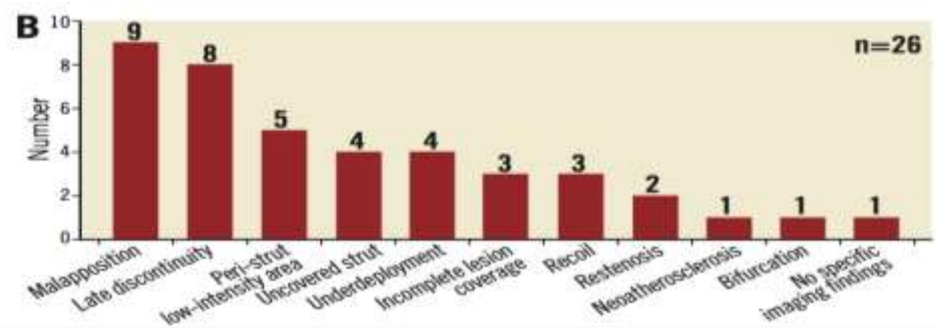
malapposition (35%), late discontinuity (31%) and peri-strut low-intensity area (19%)




## Early scaffold thrombosis




## Late/very late scaffold thrombosis



# BRS Failure Analysis: Lessons from Serial Imaging Studies

1. What are the imaging findings at the time of acute, subacute and late/very late Scaffold Thrombosis?

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# Scaffold or stent thrombosis in ABSORB II trial

**2 : 1 randomization**

| | Absorb 335 patients | Xience 166 patients | p value |
|---|---|---|---|
| **Definite** | **2.5% (8)** | **0.0% (0)** | **0.06** |
| **Acute (0–1 day)** | **0.3% (1)** | **0.0% (0)** | **1.0** |
| **Sub-acute (2–30 days)** | **0.3% (1)** | **0.0% (0)** | **1.0** |
| **Late (31–365 days)** | **0.0% (0)** | **0.0% (0)** | **1.0** |
| **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 mechanism of very late complications.

**Serruys et al. 2017 CRT**

# Prospective analysis by core laboratory blind for events

**Impacts of pre-procedure, device sizing and post-dilatation related parameters on VLScT**

**QCA parameter**
- Reference vessel diameter pre-device implantation
- Device sizing with reference to pre-reference vessel diameter

**IVUS parameter**
- Reference lumen diameter pre-device implantation
- Device sizing with reference to pre-reference lumen diameter

**Procedure**
- Final balloon (nominal)/device ratio
- Maximal final-dilatation balloon pressure

**Impacts of post-procedural parameters on VLScT**

**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

**Serruys et al. 2017 CRT**

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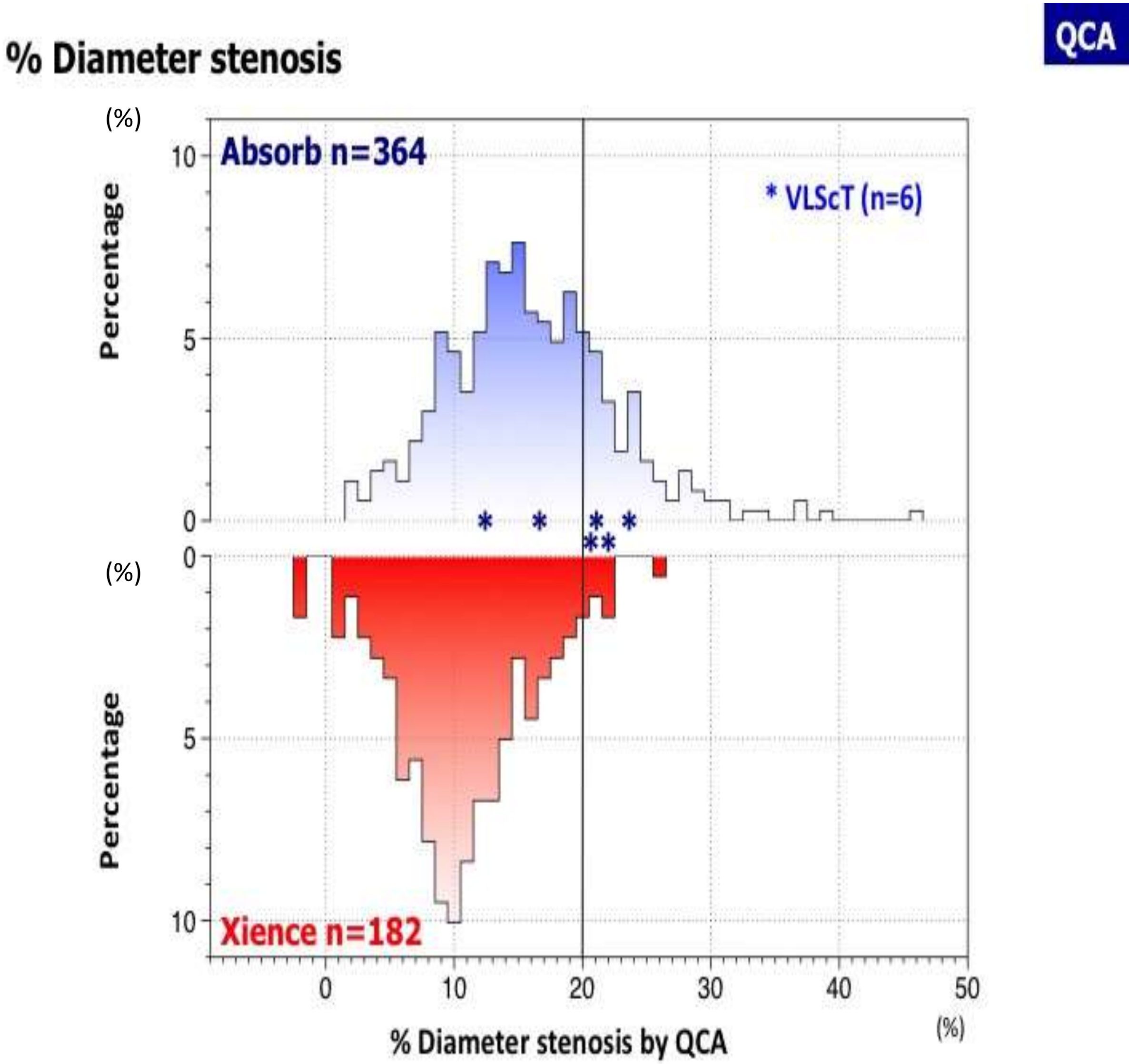


**Serruys et al. 2017 CRT**

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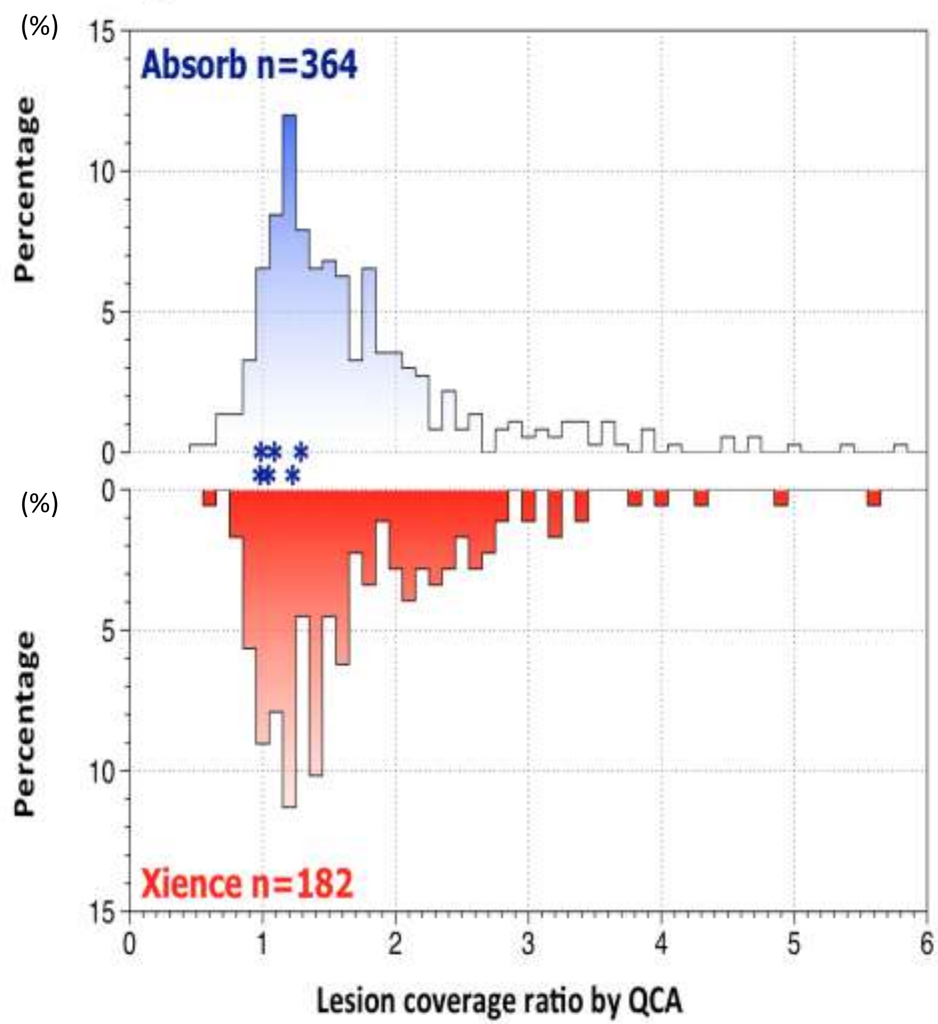
**Lesion coverage ratio = Stent length / pre-lesion length**
**(both measured by QCA)**

QCA

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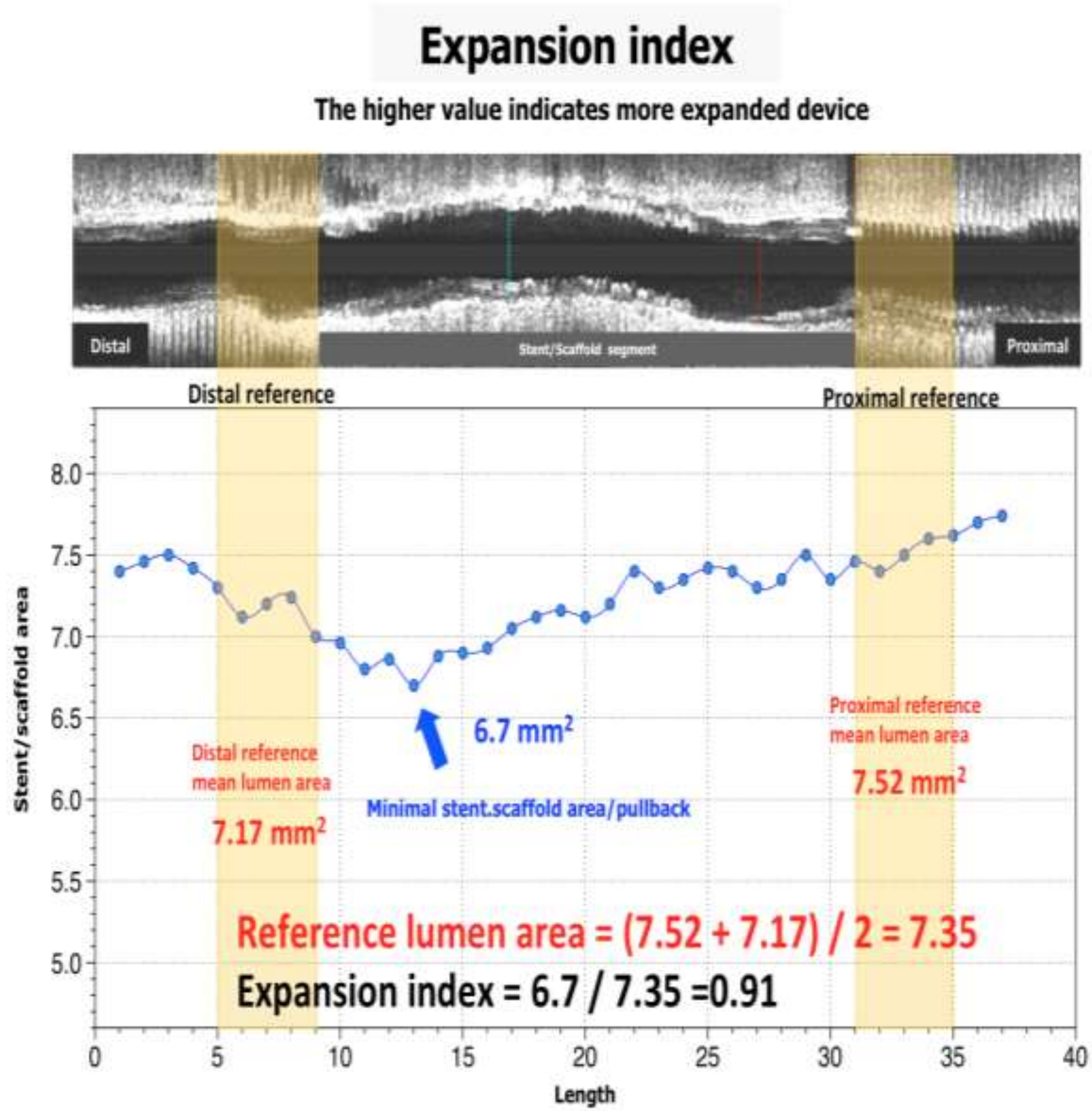


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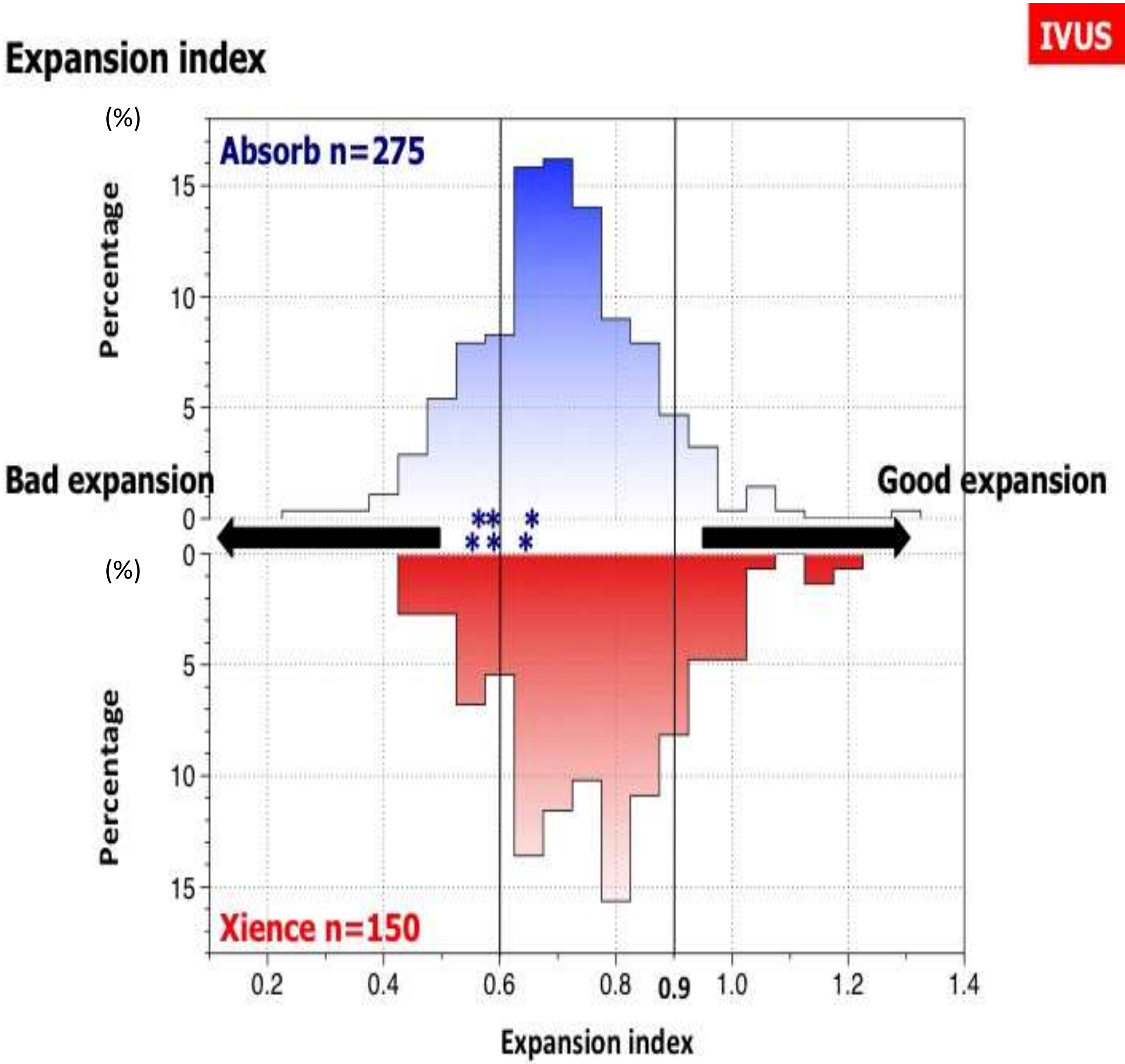


Serruys et al. 2017 CRT

# 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** |

**Serruys et al. 2017 CRT**

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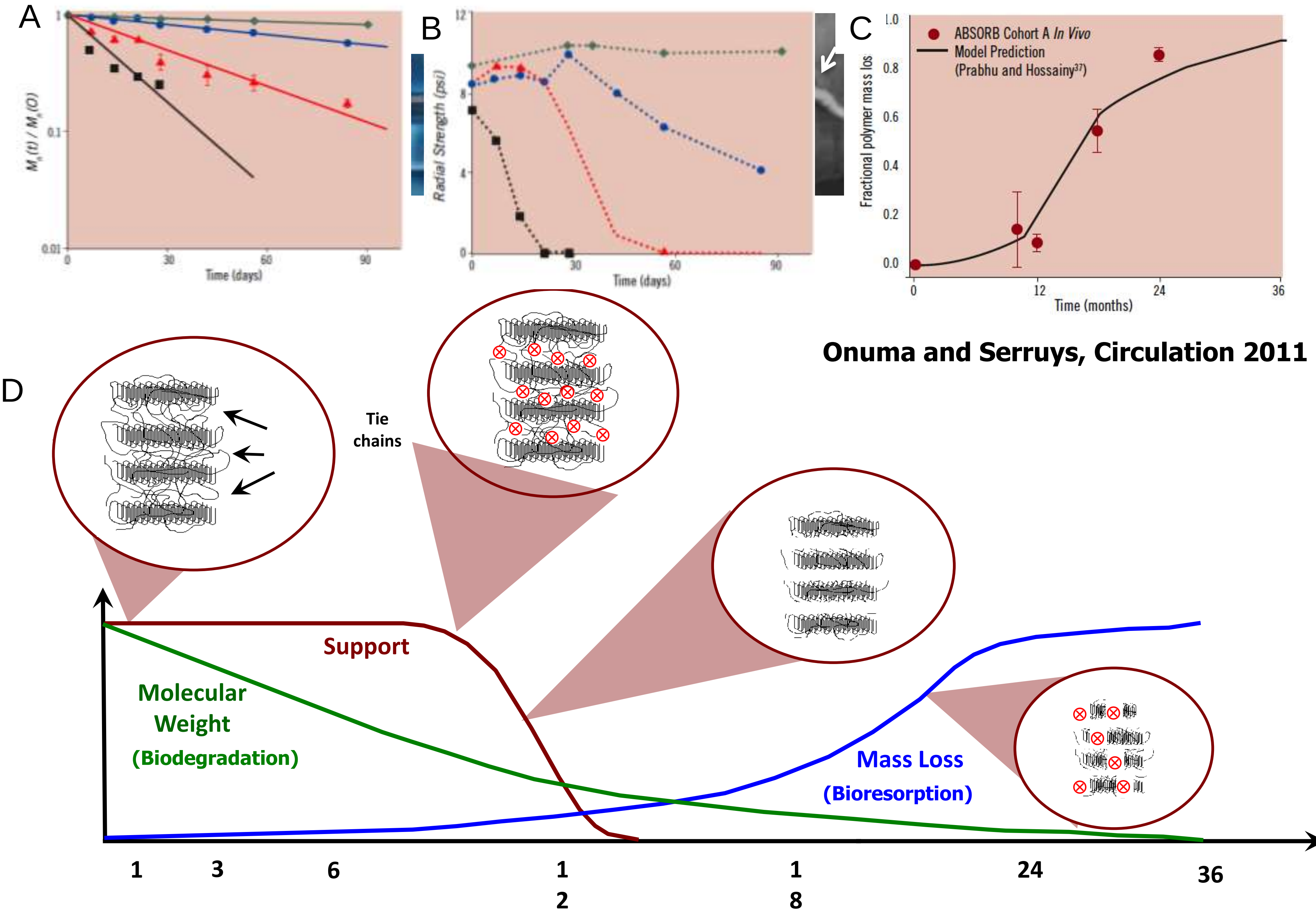
# Molecular weight, Mechanical support and Mass loss




Onuma and Serruys, Circulation 2011

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

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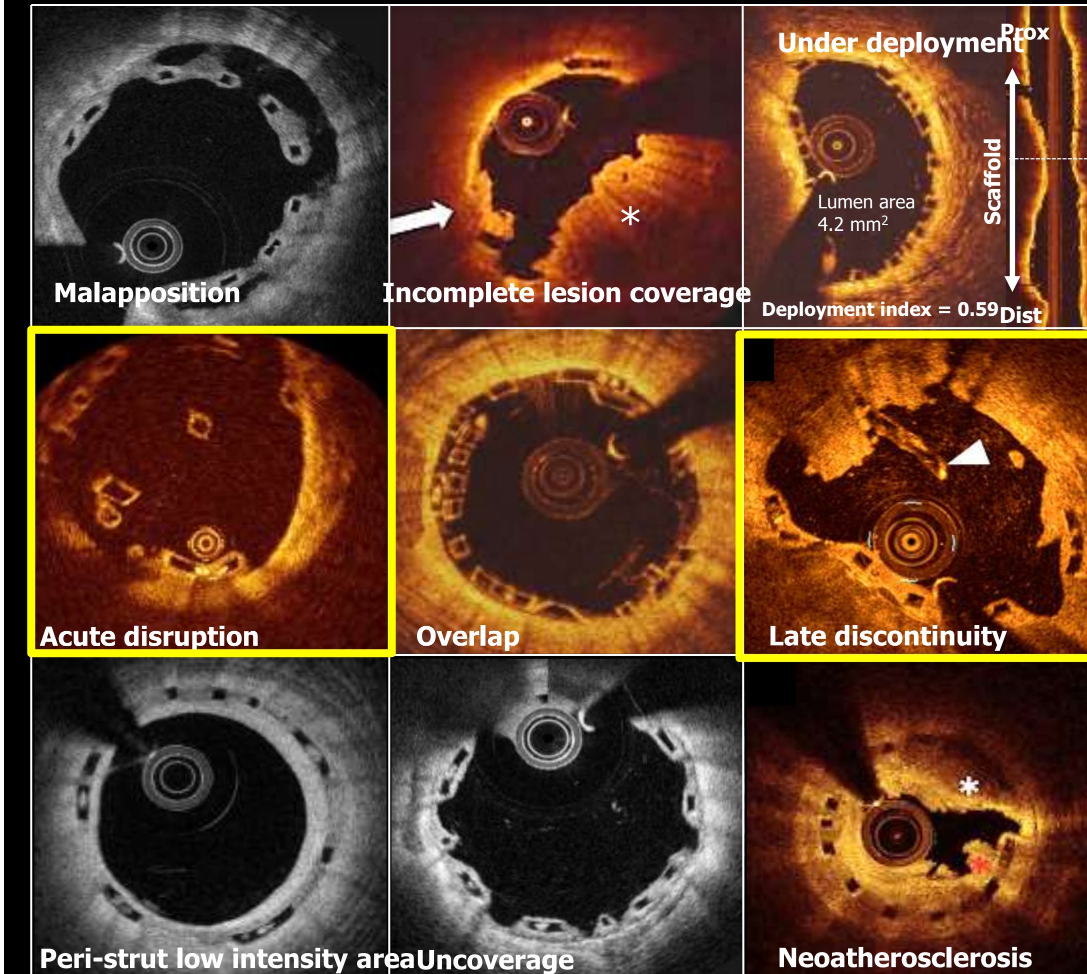
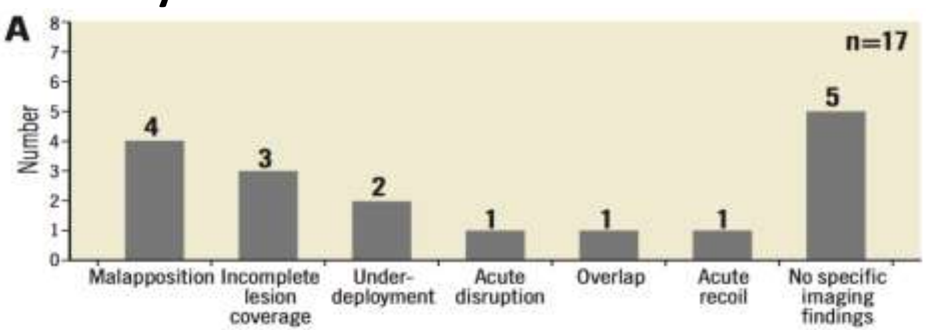
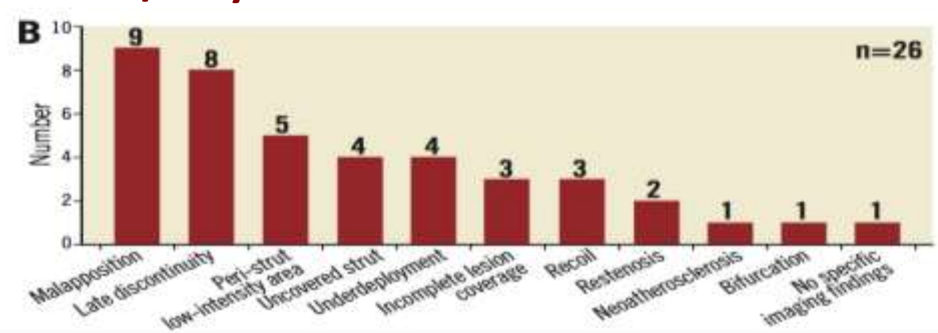



## Early scaffold thrombosis

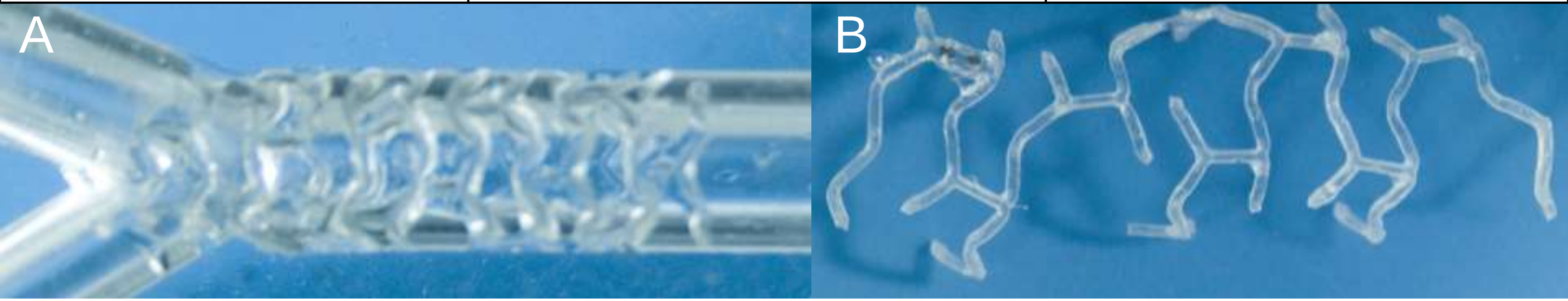



## Late/very late scaffold thrombosis

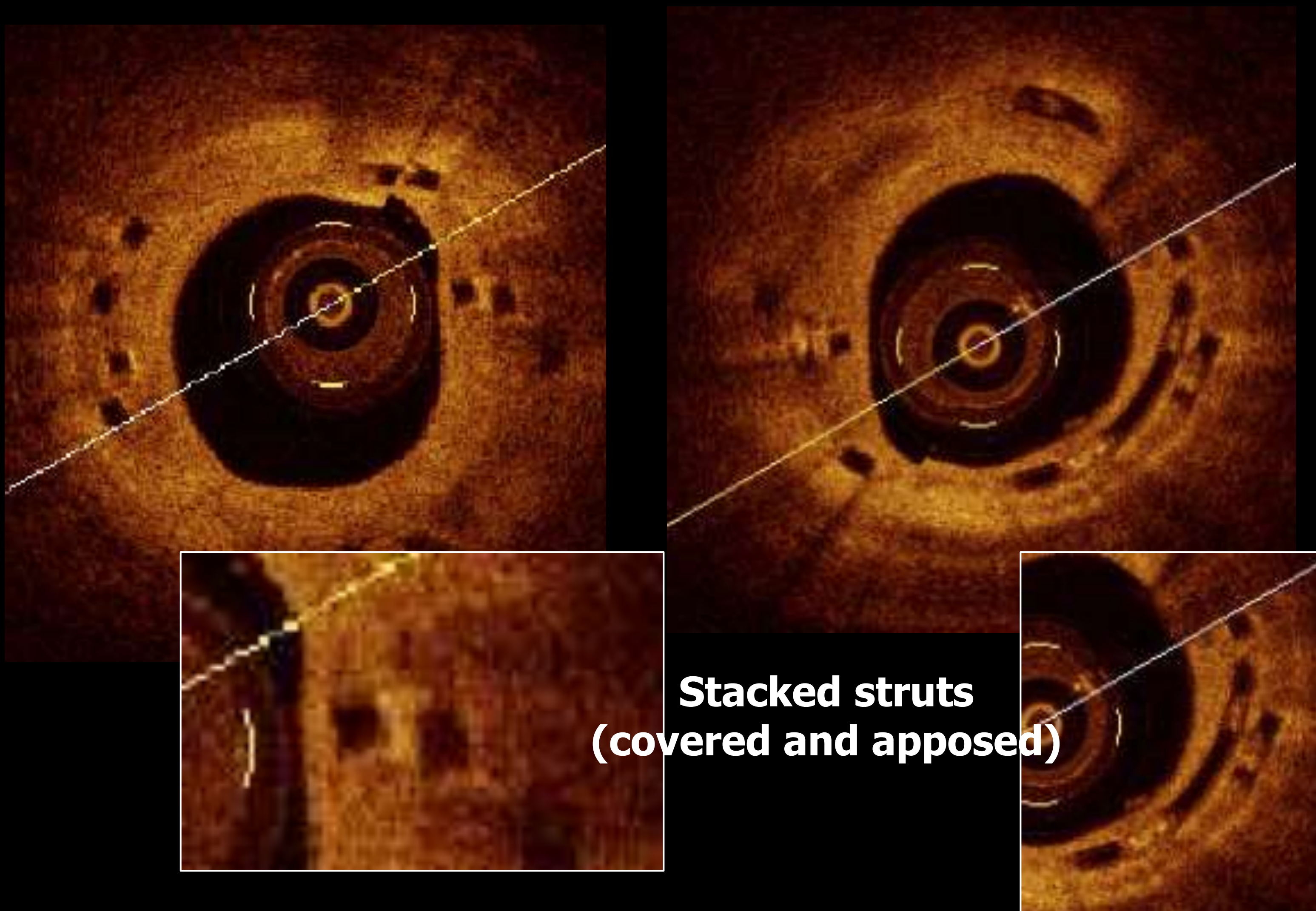


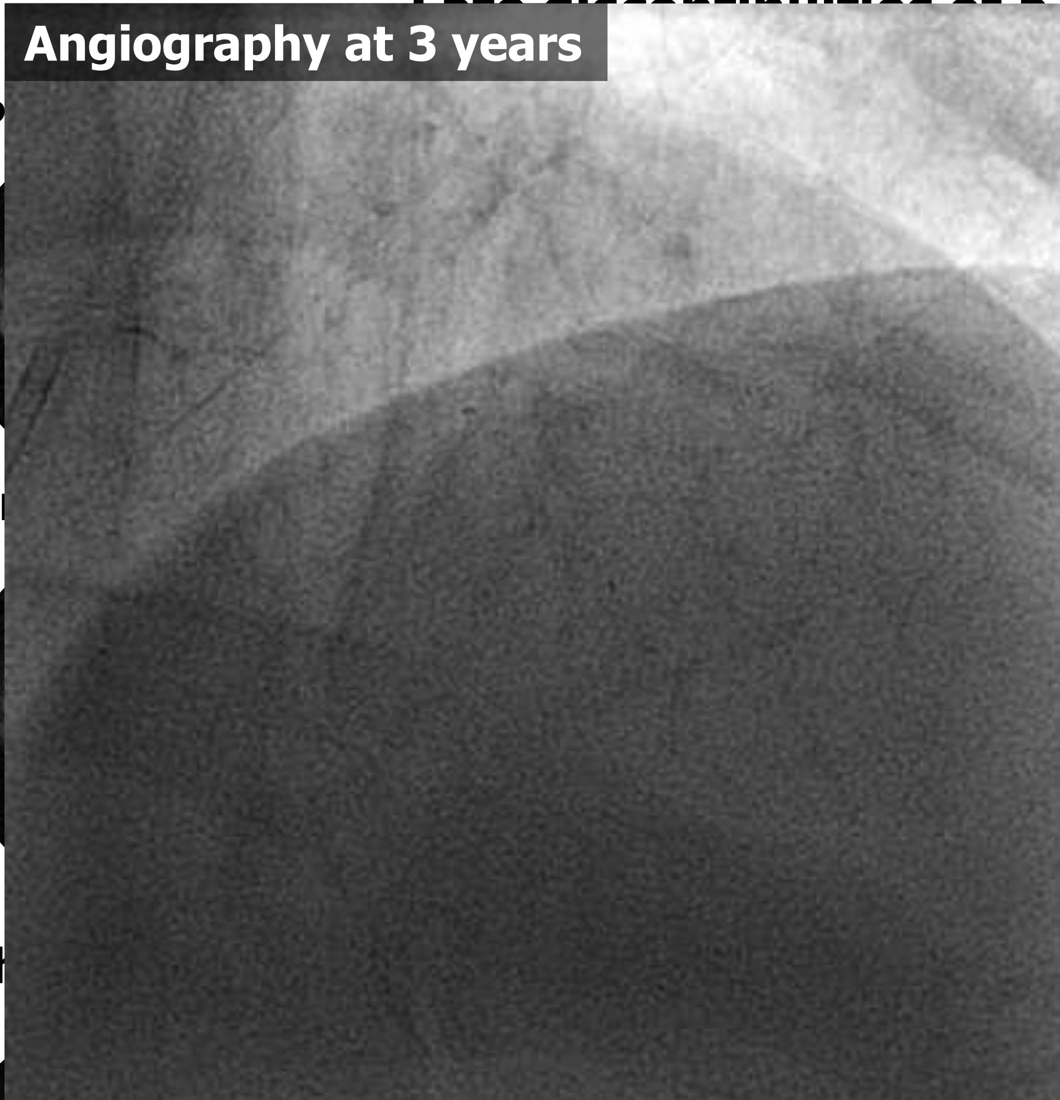
# 3 criteria to judge acute disruption/late discontinuities on OCT

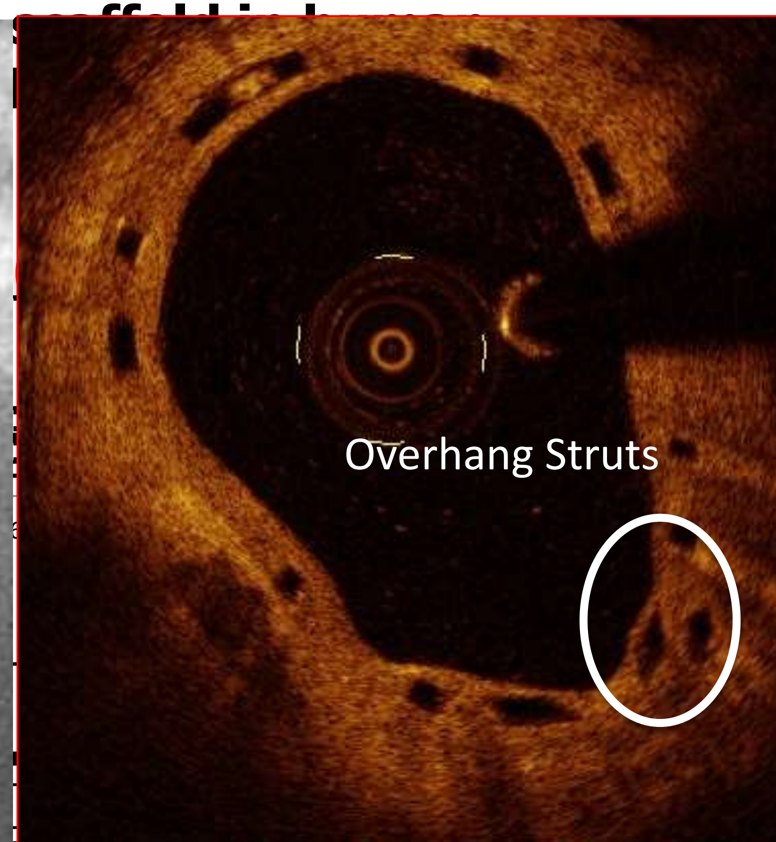
| | Time of OCT observation | |
|---|---|---|
| | **Post procedure** | **Late** |
| **Acute Scaffold disruption** | •Stacked struts | Persistent |
| | •Overhung struts | |
| | •Isolated intra-luminal strut(s) | |
| **Late Scaffold discontinuities** | No disruption | •Stacked/ overhung / isolated or intraluminal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

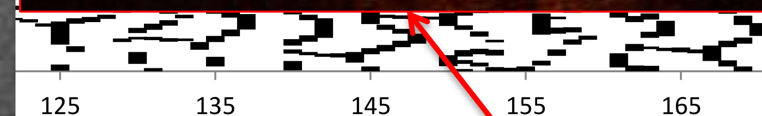


# Late discontinuities observed in porcine coronary artery





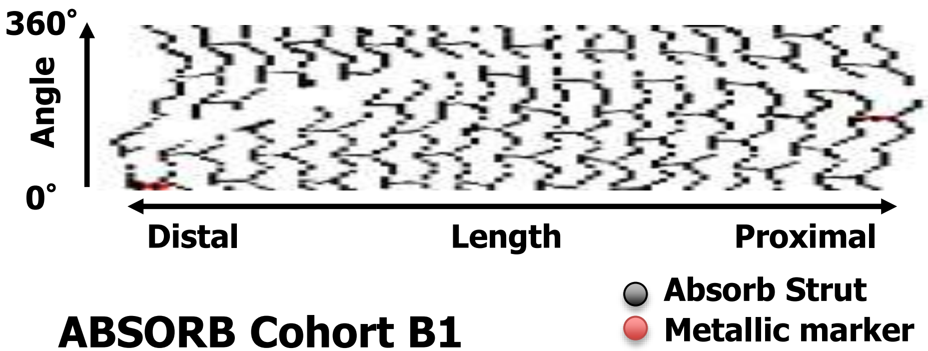



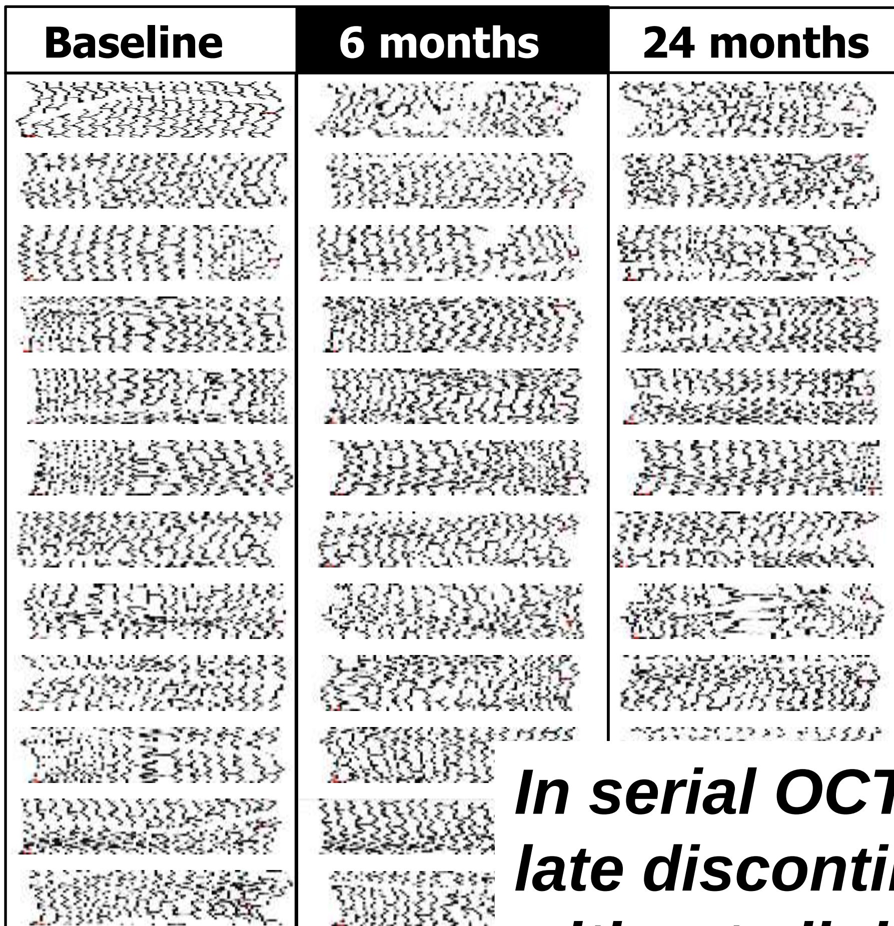


**Late discontinuity is expected phenomenon related to bioresorption.**

# Serial changes of strut distribution




## ABSORB Cohort B1



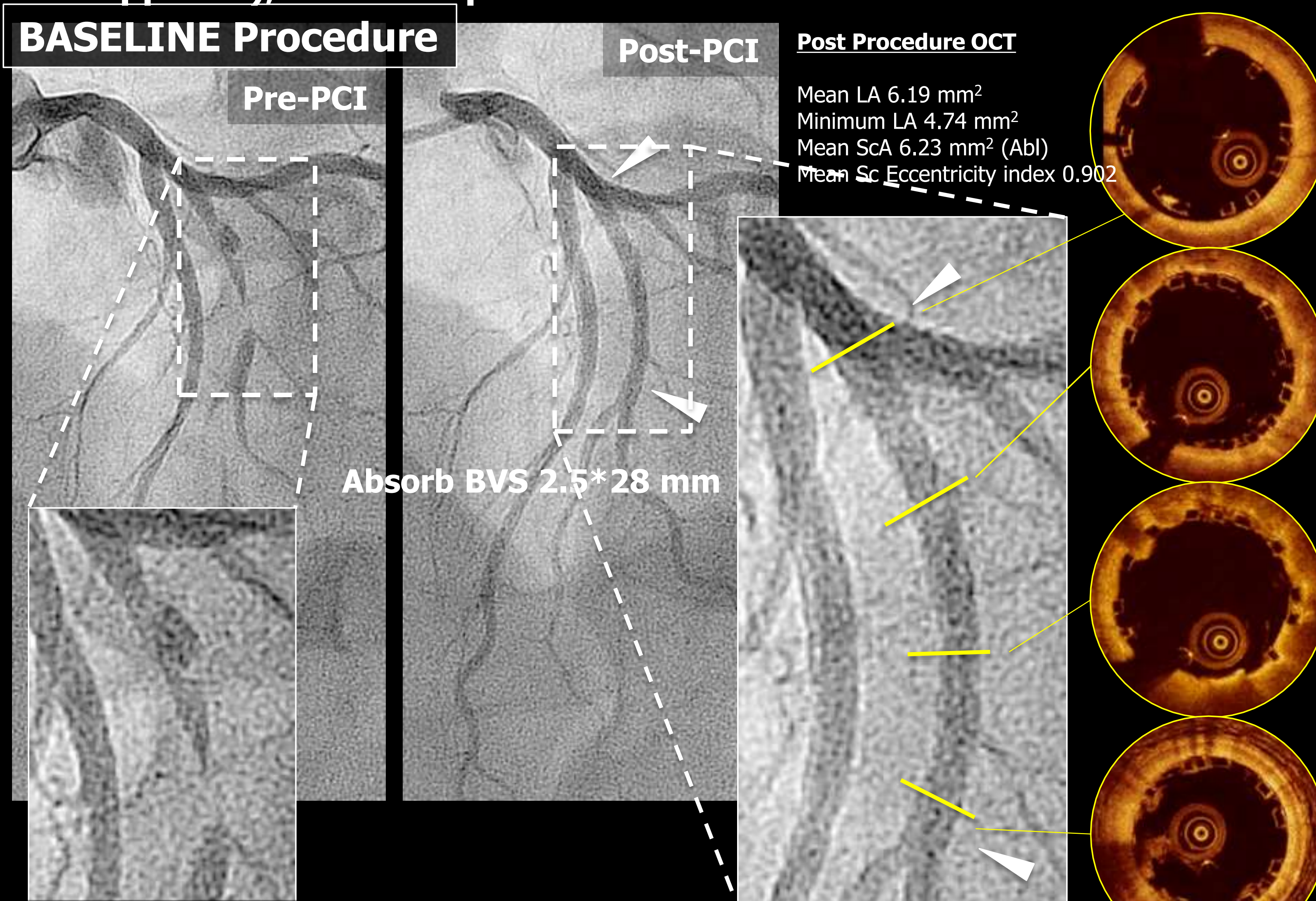

## ABSORB Cohort B2


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

*Onuma et al. JACC int 2014,*

# Case 3: Late Discontinuities observed at 2-year planned FUP OCT (Uncovered and malapposed), Absorb Japan

Onuma et al. EuroIntervention. 2016



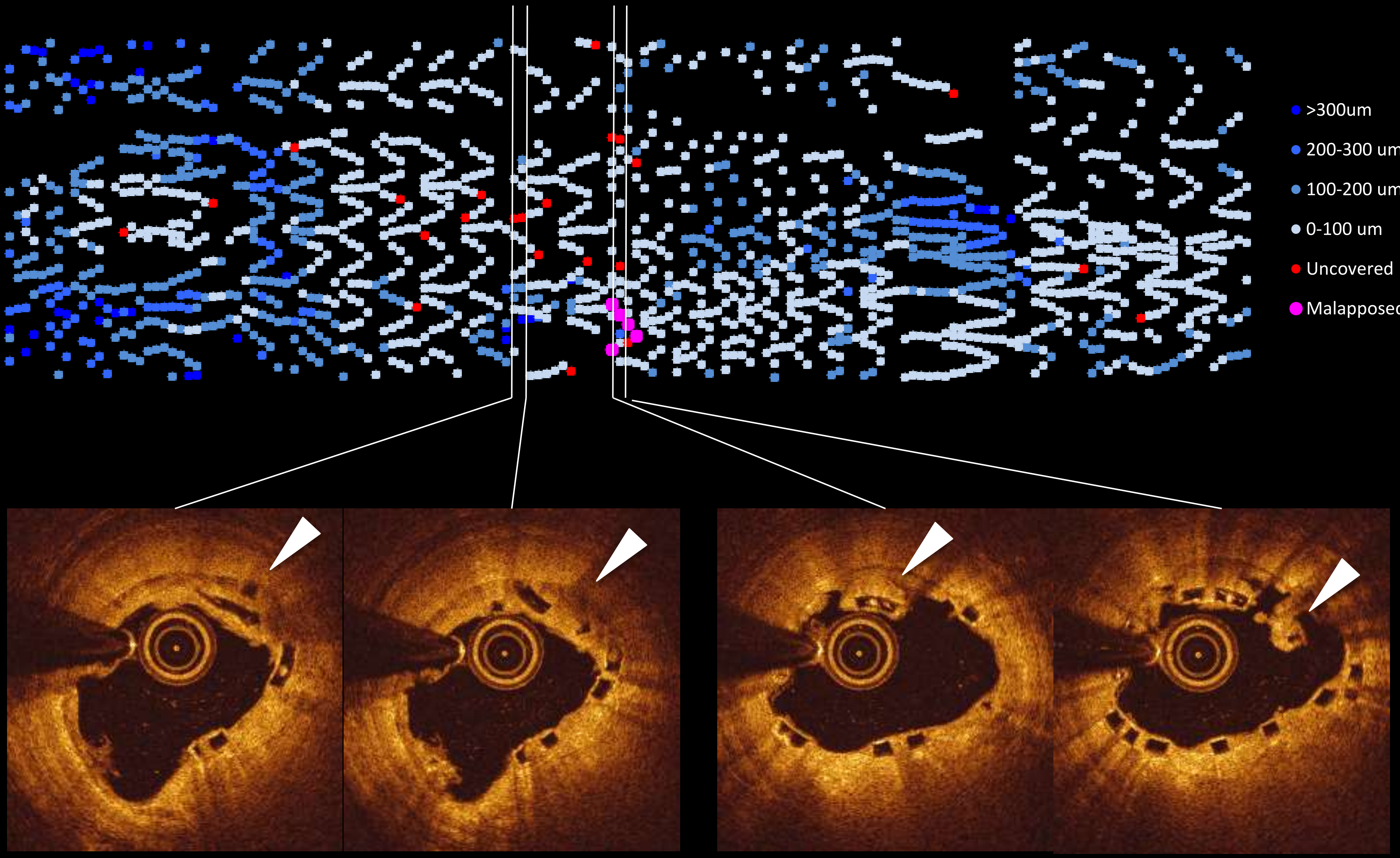

Reference diameter 1.82 mm
Minimum lumen diameter 0.67 mm
%DS 67%

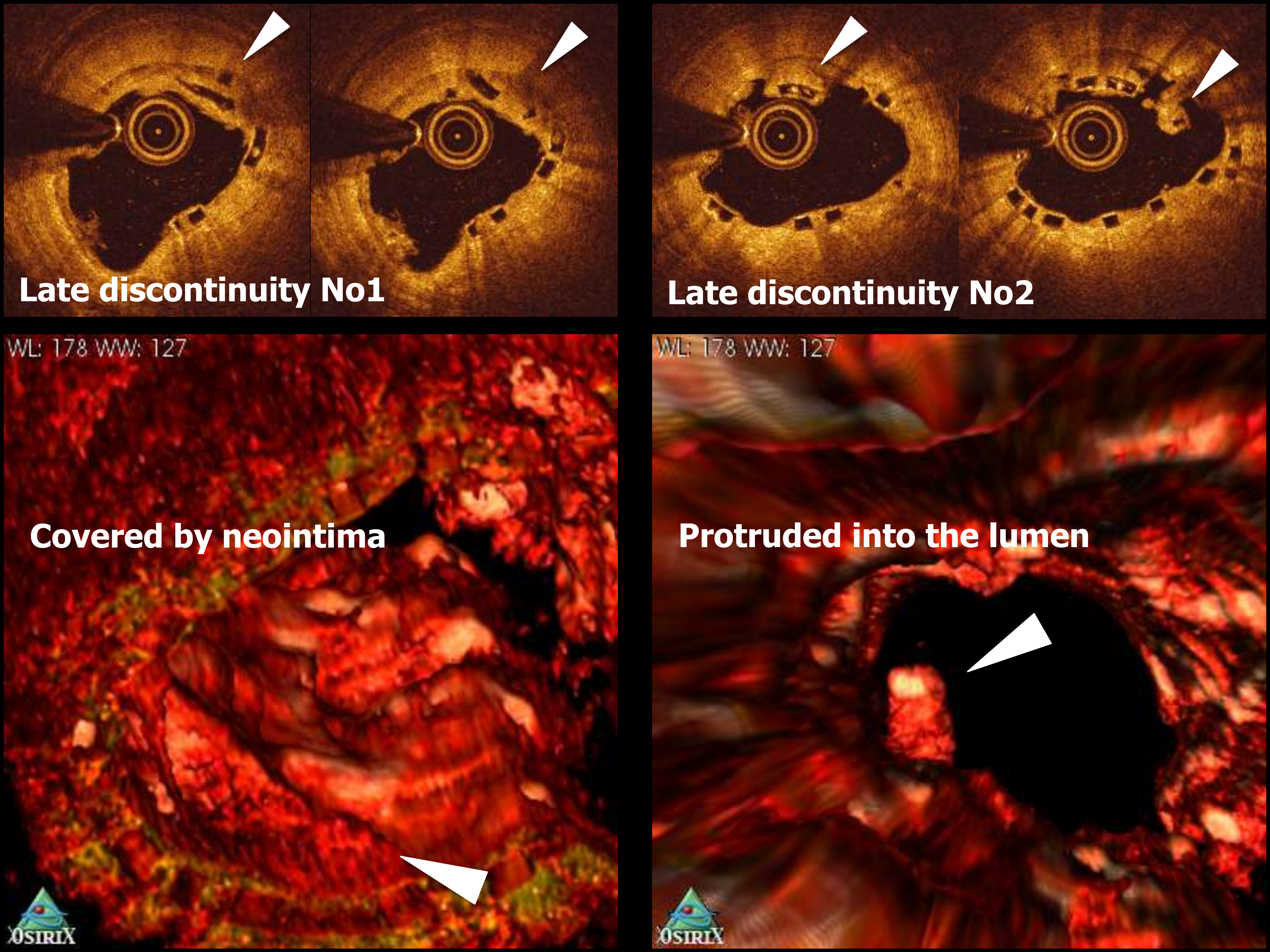
**Pre-dilatation 2.5mm x 14 atm**
**>>> BVS 2.5 x 28 mm >>>Post-dilatation 2.75 x 22 atm**

# Case 3: Late Discontinuities observed at 2-year planned FUP OCT (Uncovered and malapposed), Absorb Japan

Onuma et al. EuroIntervention. 2016

## Neointimal coverage

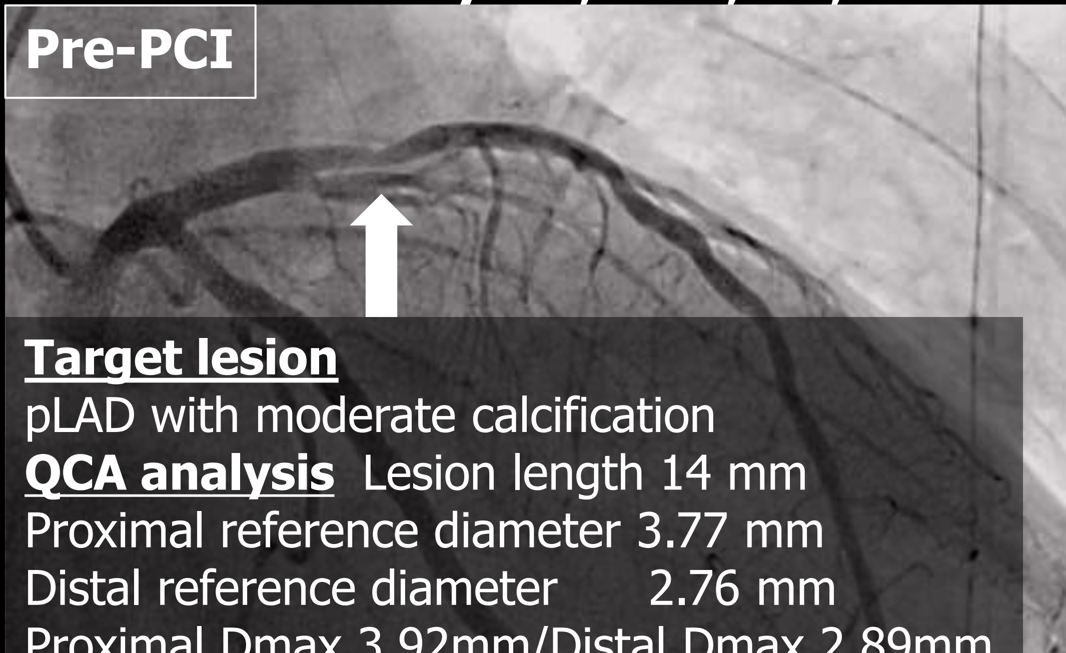


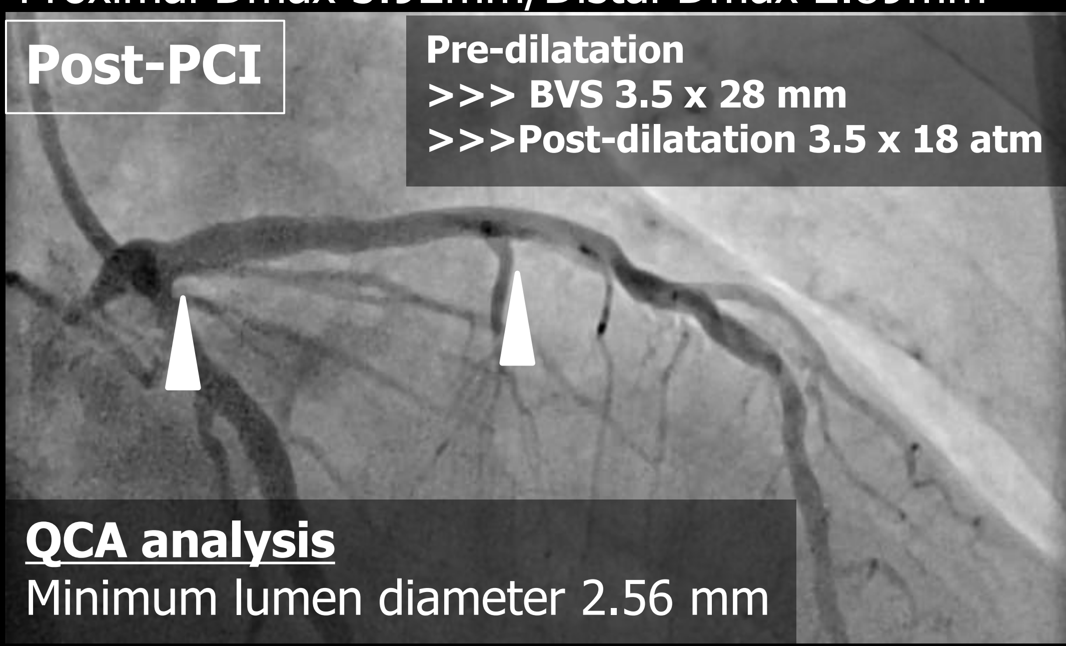

Late discontinuity No1
Late discontinuity No2
WL: 178 WW: 127
Covered by neointima
WL: 178 WW: 127
Protruded into the lumen
OSIRIX
OSIRIX

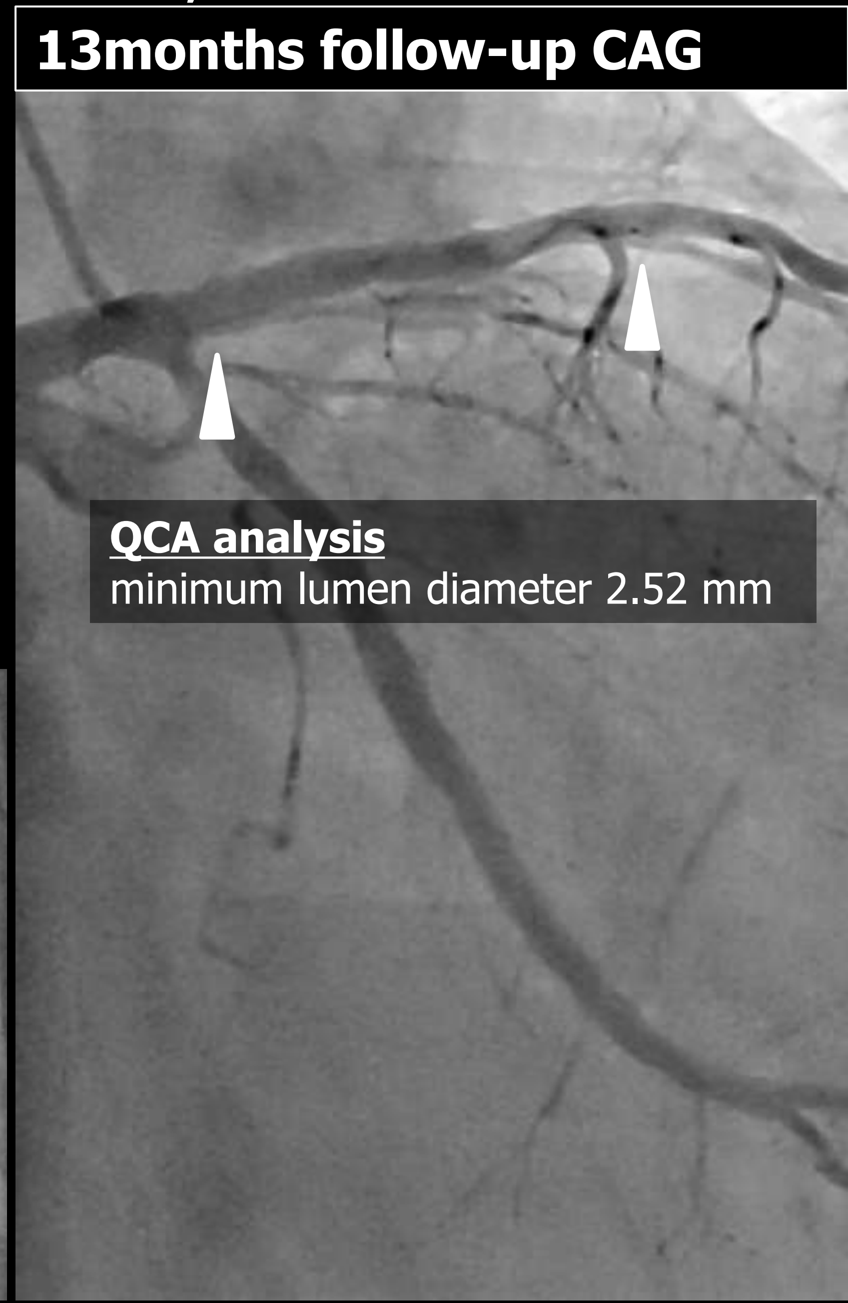
***#4. VLST case 1 (Day 494)***

*Onuma et al. Eurointervention 2016*

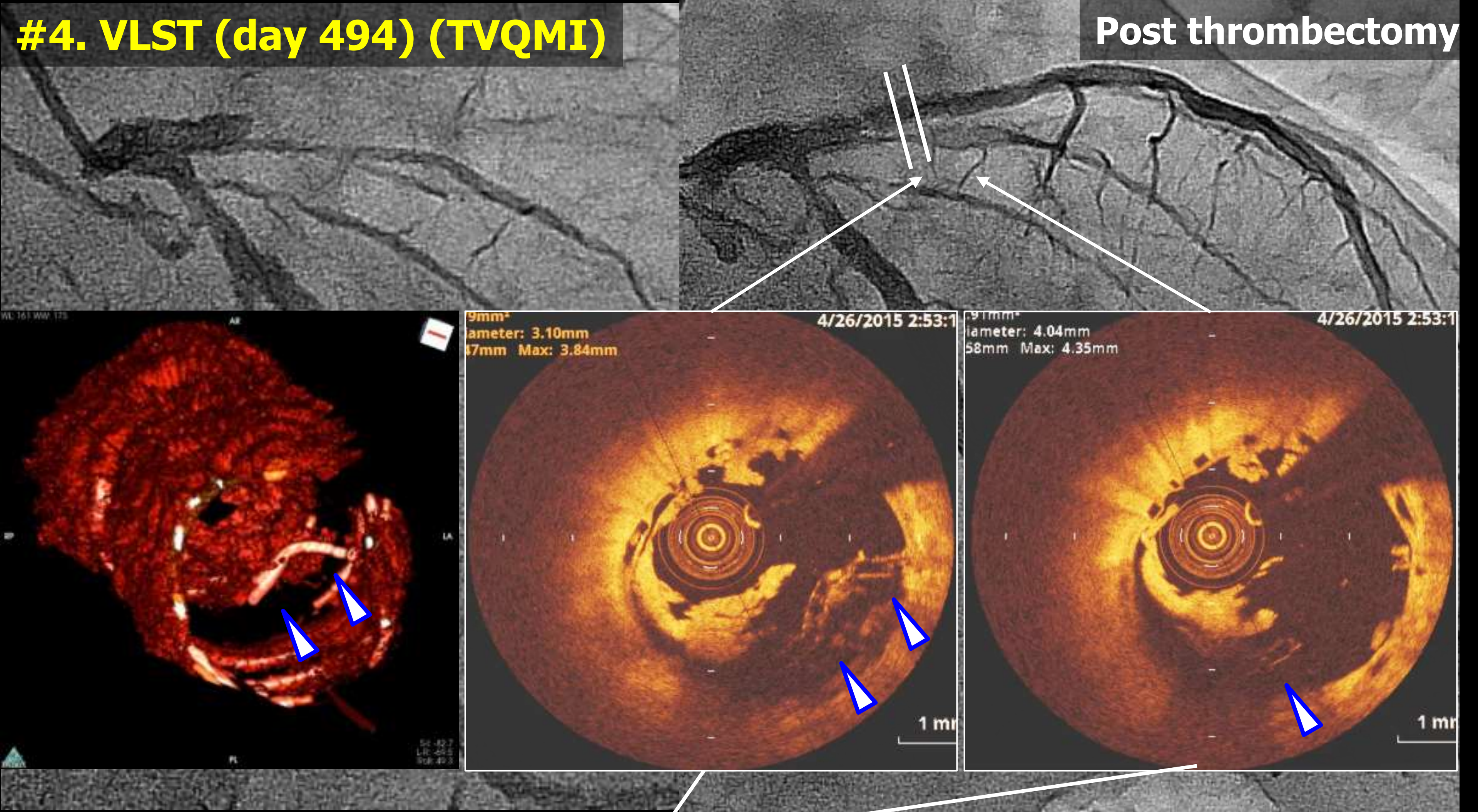
**Risk factors: 79 yo M, HTN, HL, former smoker, DM II**



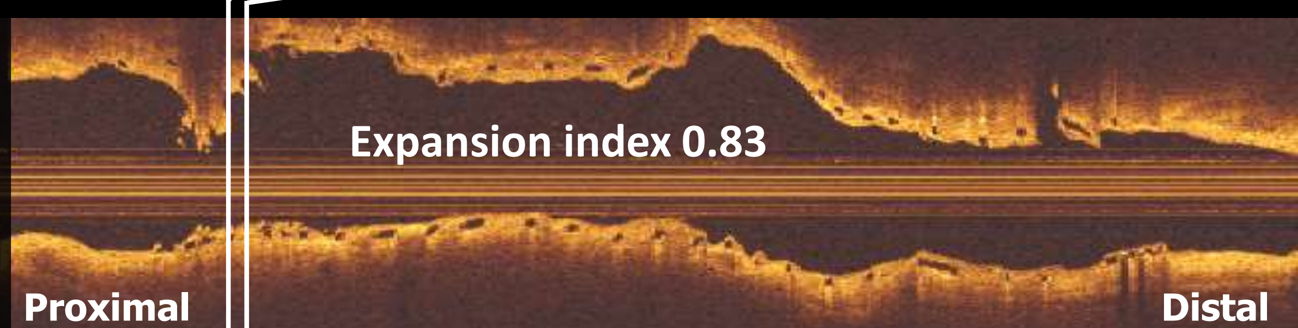



# #4. VLST (day 494) (TVQMI)

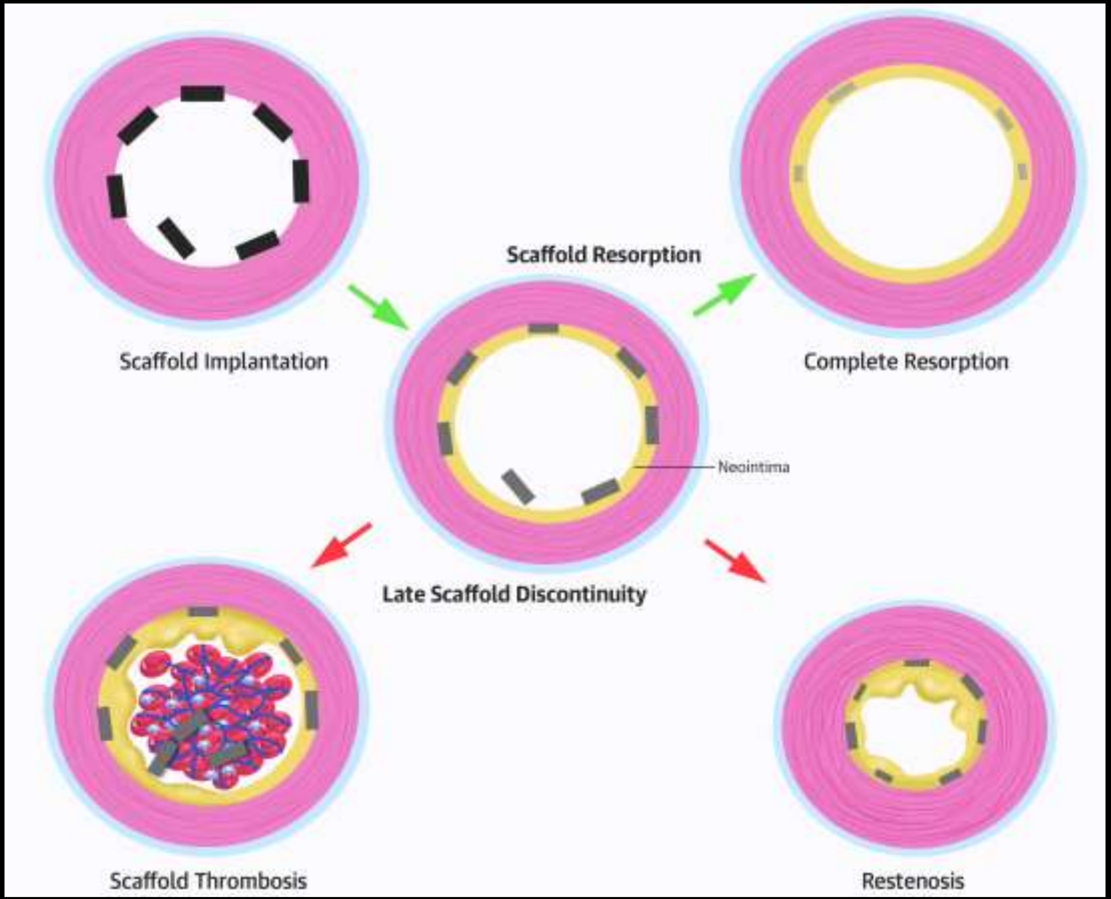



**Status of antiplatelet therapy**

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

# Conclusion

- Malapposition, incomplete plaque coverage, overlap and underexpansion are frequently observed in intracoronary imaging at the time of early scaffold thrombosis, whereas malapposition, late discontinuity and peri-strut low-intensity were reported by imaging at the time of late/very late scaffold thrombosis.

- Despite the small number of patients and events, Absorb II imaging analysis suggested a correlation between the **under-expansion** and the occurrence of VLScT after implantation of Absorb scaffold.

- Late discontinuity is in general a benign change during the bioresorption process and does not cause any problems if struts are well covered. However, in case struts are not covered by neointima and late discontinuity lets protrude part of the struts into the lumen, late discontinuity could be a malignant potential cause of ScT. Enhancement of neointimal coverage would be a key to prevent ScT associated with late discontinuity. Further research is needed to investigate what triggers VLST.