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# Long-Term Durability and Safety of BRS: Lessons from Imaging and Clinical Data

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# Overview

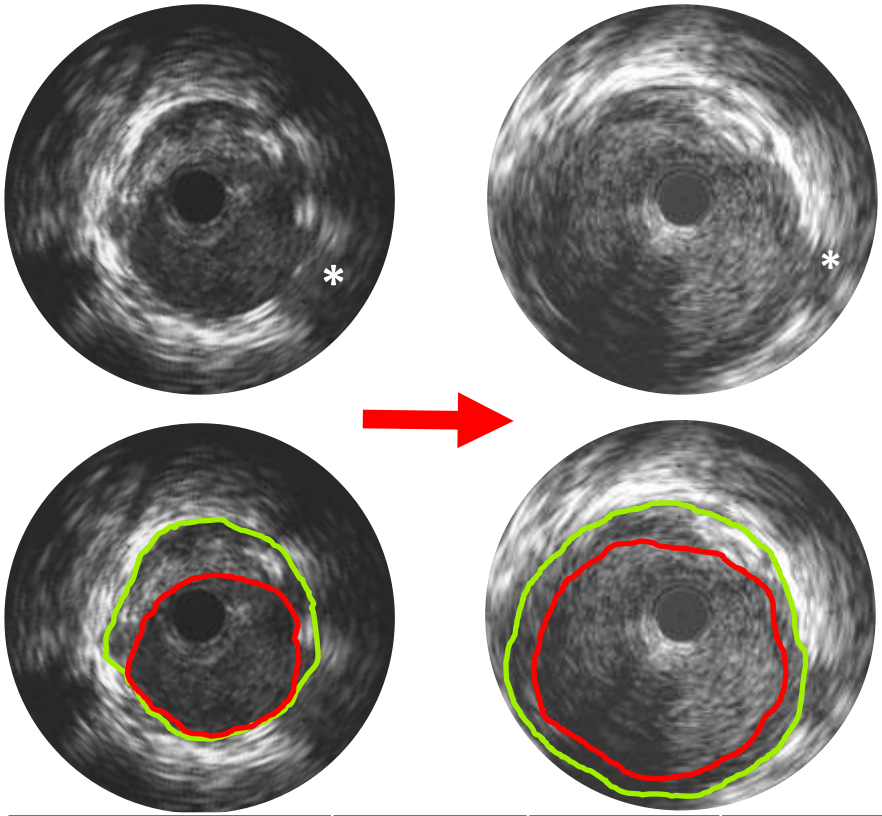
- **Long-term durability**
  - Remodeling on IVUS (Absorb II)
  - Long-term serial (18M and 6-7 year) MSCT FUP (Cohort B)
- **Long-term Safety**
  - Recent meta-analyses
  - Imaging correlates of VLST

# Representative cases of remodeling

Serruys et al. CRT 2017

## Expansive remodeling

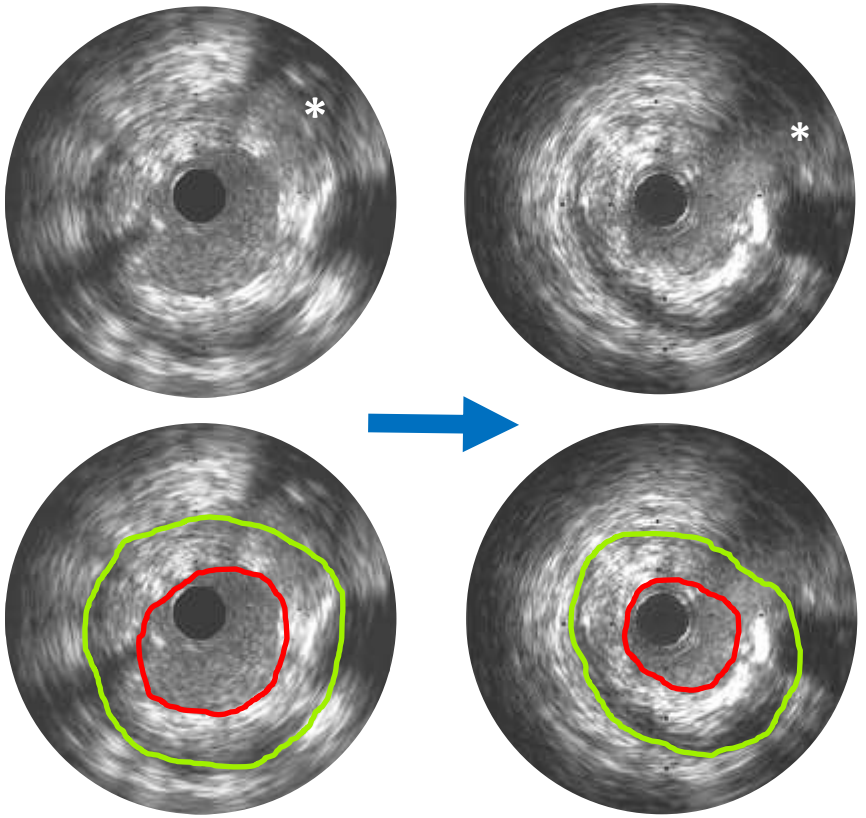
Post-procedure | 3-year follow-up



| | Post-procedure | At 3-year follow-up | Relative change (%) |
|---|---|---|---|
| Lumen area ($mm^2$) | 9.03 | 18.78 | +108% |
| Plaque area ($mm^2$) | 6.12 | 8.51 | +39.0% |
| Vessel area ($mm^2$) | 15.15 | 27.29 | +80.1% |

## Constrictive remodeling

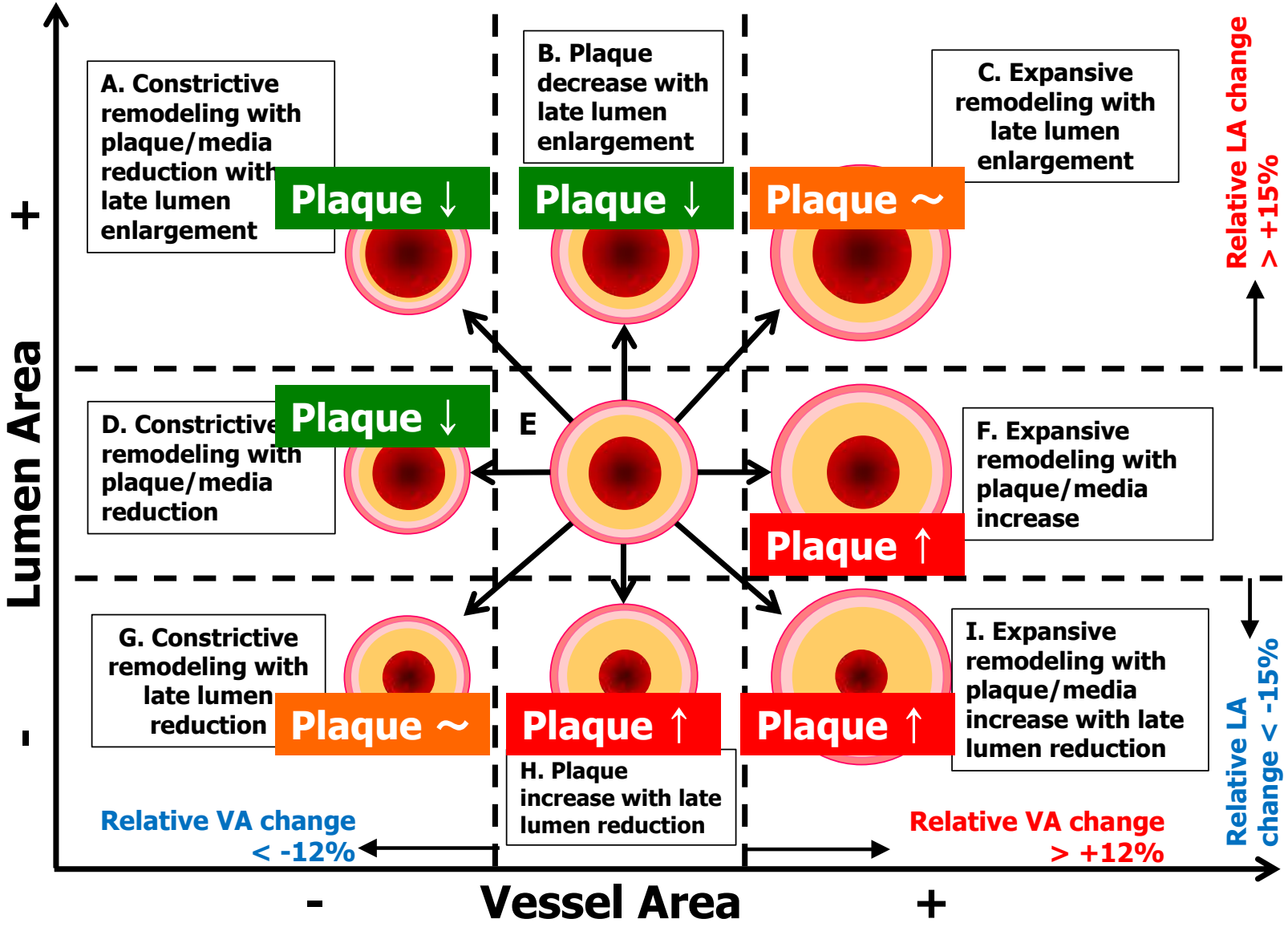
Post-procedure | 3-year follow-up



| | Post-procedure | At 3-year follow-up | Relative change (%) |
|---|---|---|---|
| Lumen area ($mm^2$) | 6.36 | 3.93 | -38.2% |
| Plaque area ($mm^2$) | 14.80 | 12.13 | -18.0% |
| Vessel area ($mm^2$) | 21.16 | 16.06 | -24.1% |

Both cross sections were matched with the side branch (*)

# Glagovian approach

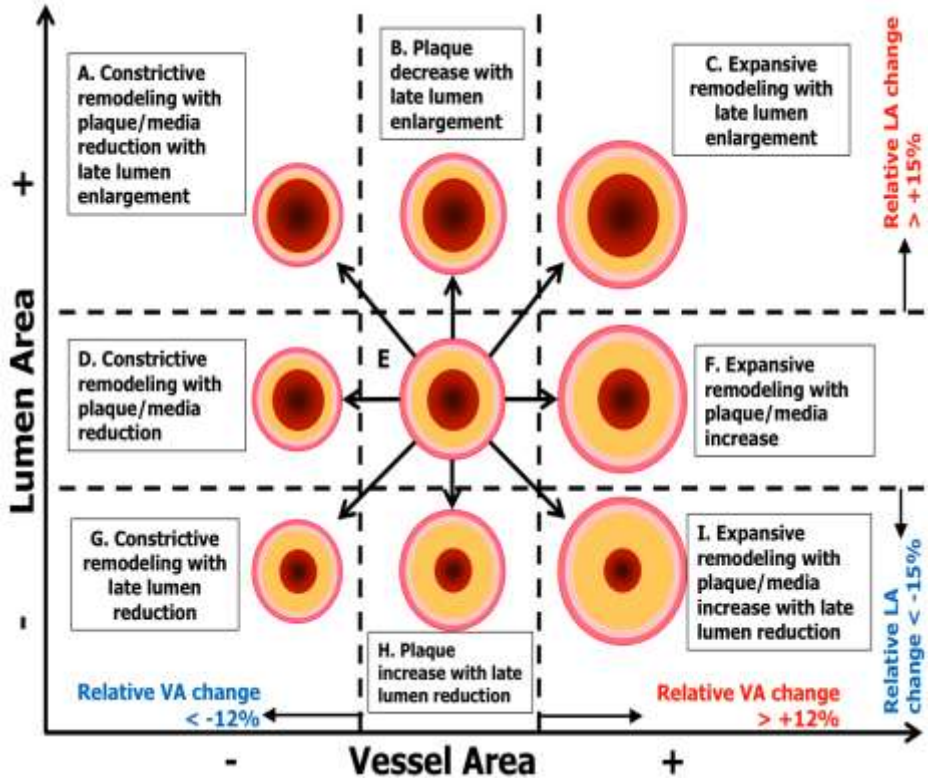


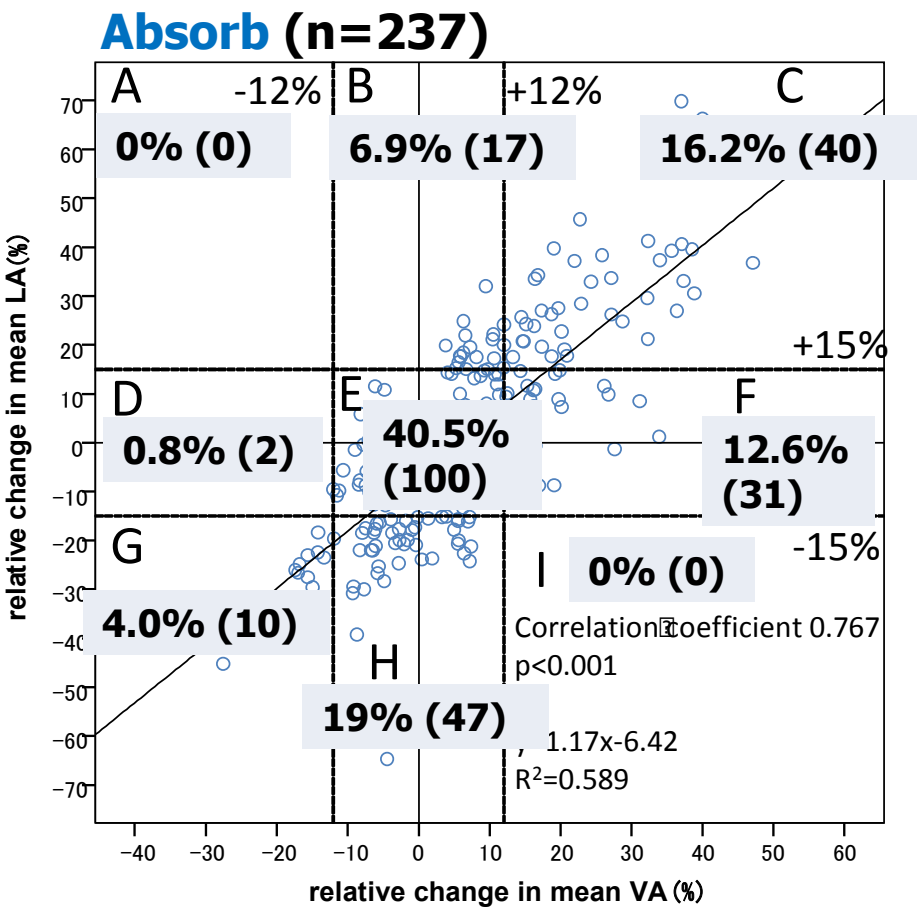

Van Mieghem, Serruys et al. *Int J Cardiovasc Imaging* 2005

# Relationship between relative change in mean lumen area, vessel area over 3 years

Serruys et al. CRT 2017

| | |
|---|---|
| 0% | A. Constrictive remodeling with late lumen enlargement |
| 6.9% | **B. Plaque media decrease with late lumen enlargement** |
| 16.2% | **C. Expansive remodeling with late lumen enlargement** |
| 0.8% | D. Constrictive remodeling with plaque/media reduction |
| 40.5% | **E. Within the reproducibility of the measurement** |
| 12.6% | **F. Expansive remodeling with plaque/media increase** |
| 4.0% | **G. Constrictive remodeling with late lumen reduction** |
| 19% | **H. Plaque/media increase with late lumen reduction** |
| 0% | I. Expansive remodeling with late lumen reduction |



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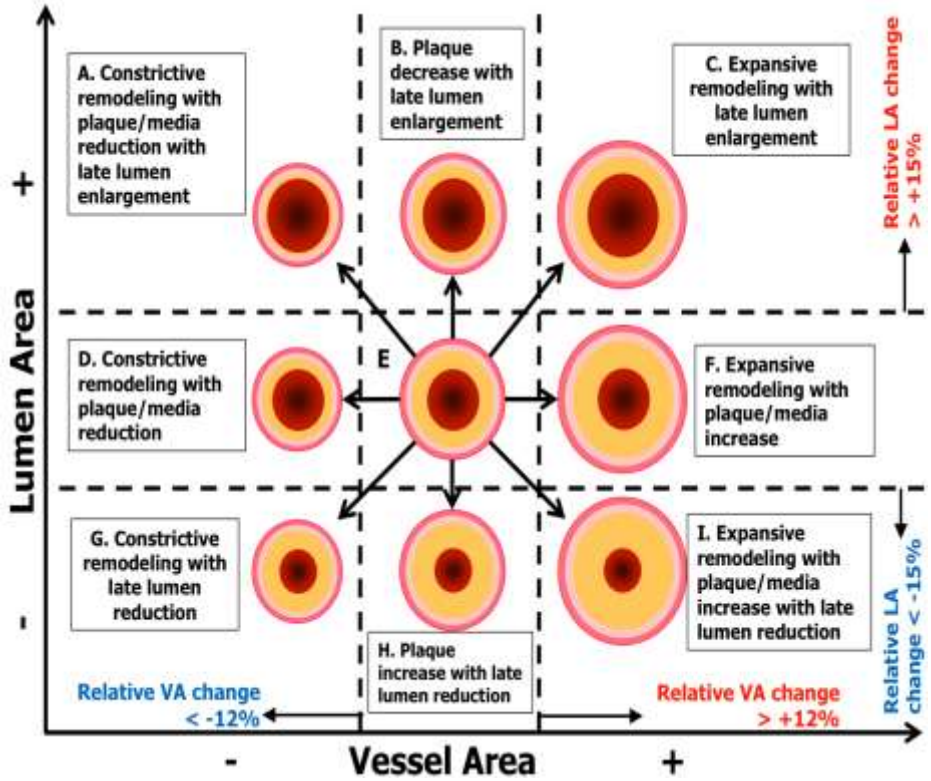


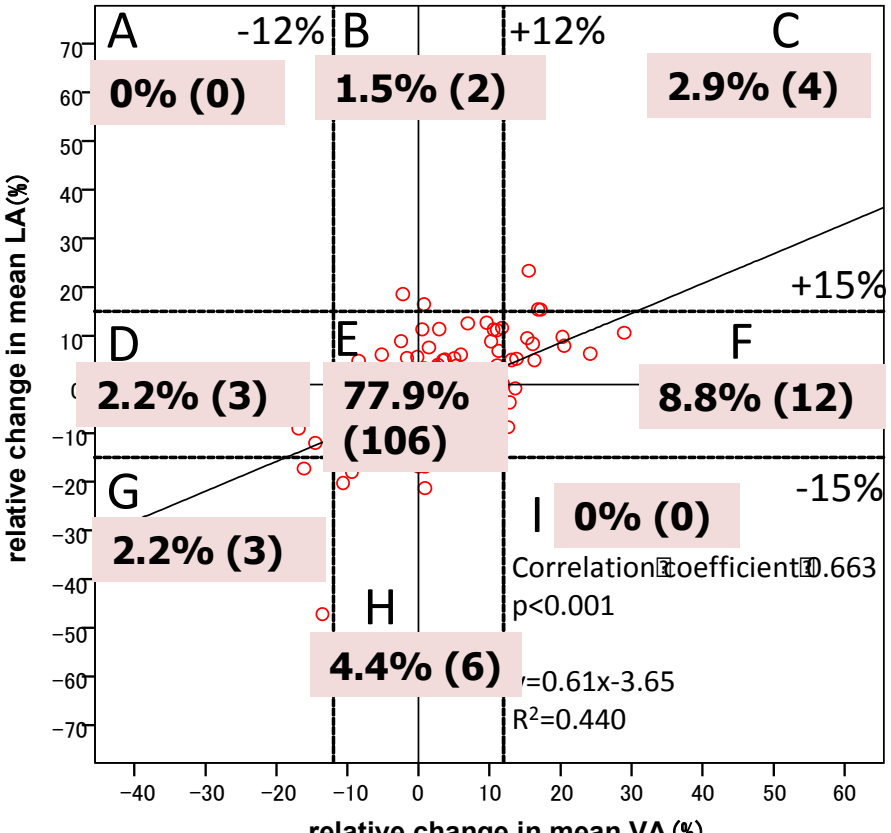

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Serruys et al. CRT 2017

A. Constrictive remodeling with late lumen enlargement
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D. Constrictive remodeling with plaque/media reduction
**E. Within the reproducibility of the measurement**
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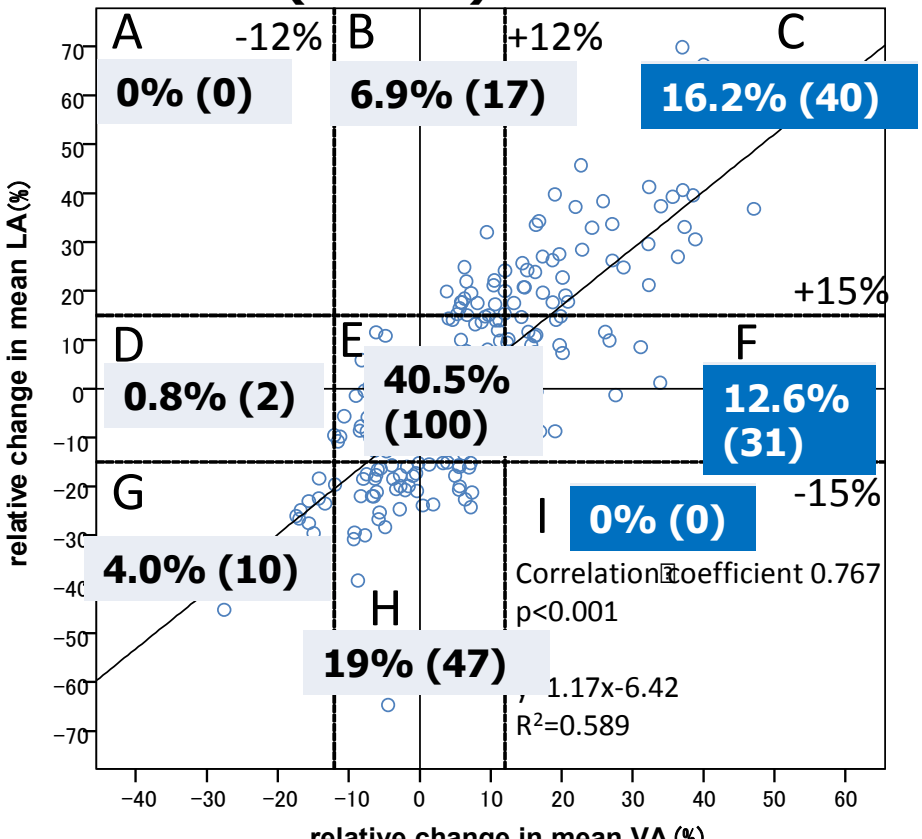
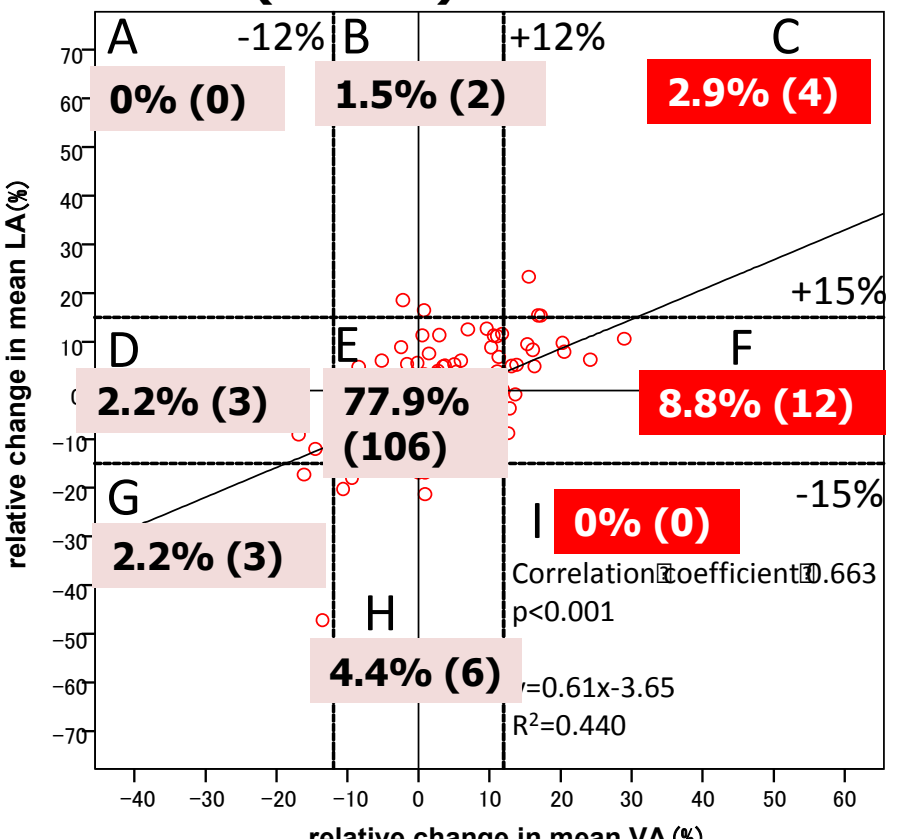
**H. Plaque/media increase with late lumen reduction**
I. Expansive remodeling with late lumen reduction

## Absorb (n=237)




## Xience (n=136)



# Multivariate analysis for predicting expansive remodeling over 3 years

| | Overall | | |
|---|---|---|---|
| | OR | [95% CI] | p value |
| Absorb implantation | 2.85 | [1.16-6.96] | 0.022 |
| Female | 2.84 | [1.35-5.96] | 0.006 |
| Expected balloon-artery ratio > 1.25 | 2.45 | [1.11-5.41] | 0.026 |
| Post-procedural IVUS: expansion index ≥ 0.8 | 2.44 | [1.11-5.36] | 0.026 |
| Previous PCI | 2.13 | [1.04-4.34] | 0.038 |
| mean LDL cholesterol over 3 years (per mmol/L) | 2.10 | [1.20-3.65] | 0.009 |
| Pre-procedural IVUS-VH: necrotic core > 16.7% | 1.64 | [0.81-3.31] | 0.166 |
| Post-procedural IVUS: asymmetry index > 0.3 | 1.49 | [0.64-3.44] | 0.352 |
| Post-procedural IVUS: eccentricity index < 0.7 | 1.21 | [0.49-2.99] | 0.686 |
| Pre-procedural IVUS: mean lumen area (per $mm^2$) | 0.97 | [0.63-1.50] | 0.896 |
| Pre-procedural IVUS: mean vessel area (per $mm^2$) | 0.90 | [0.75-1.08] | 0.236 |

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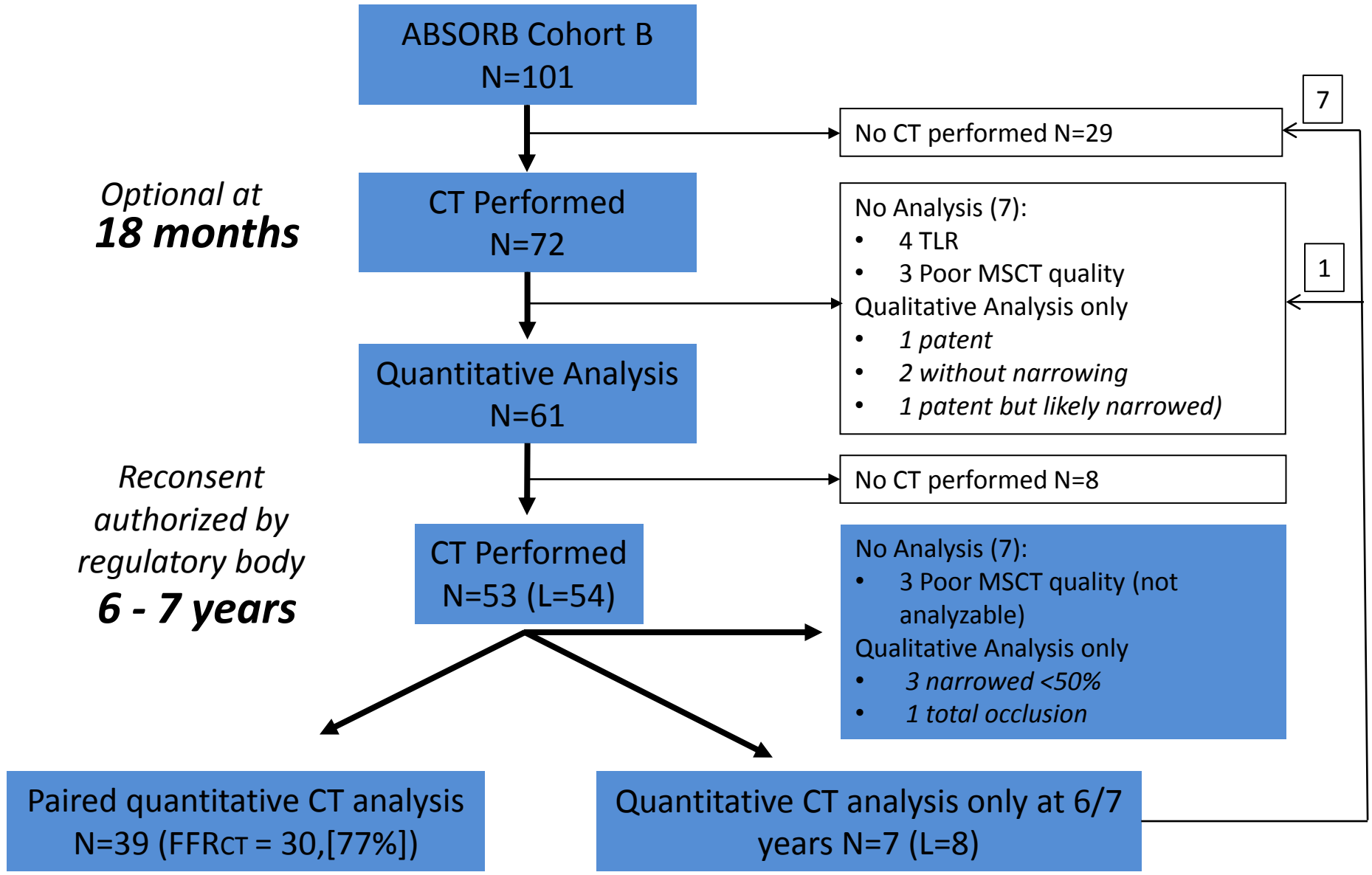
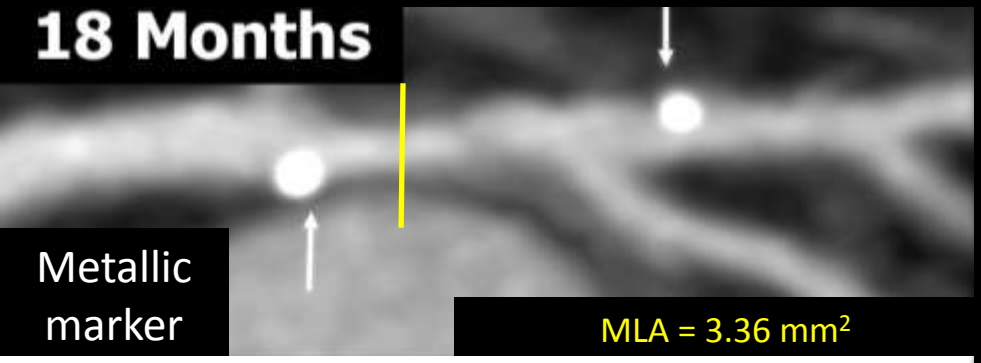
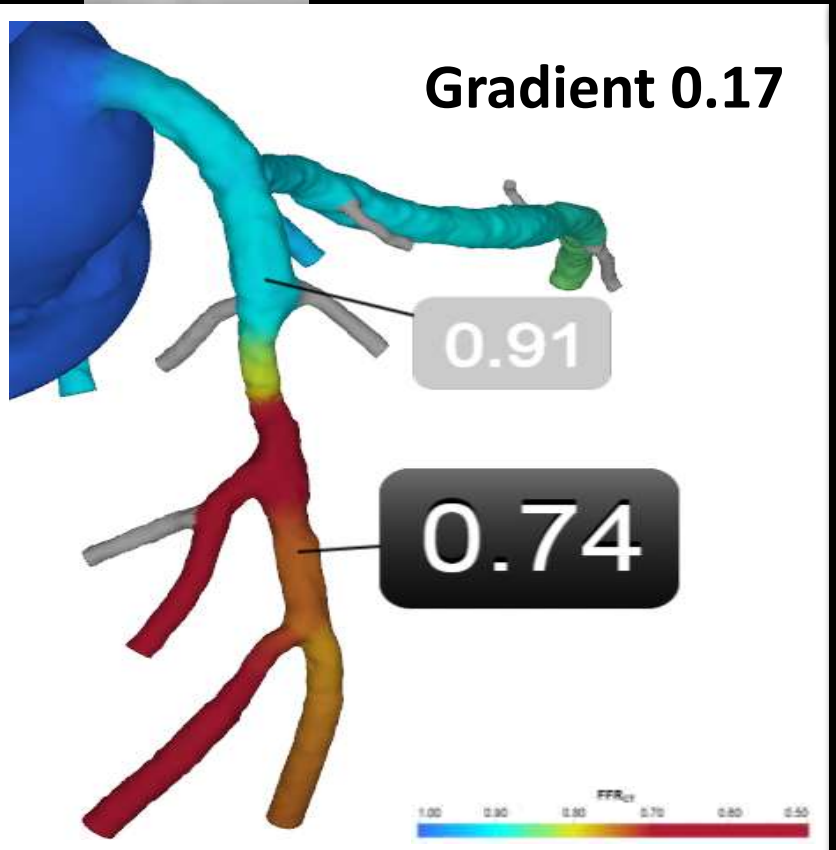
# ABSORB B MSCT Flowchart



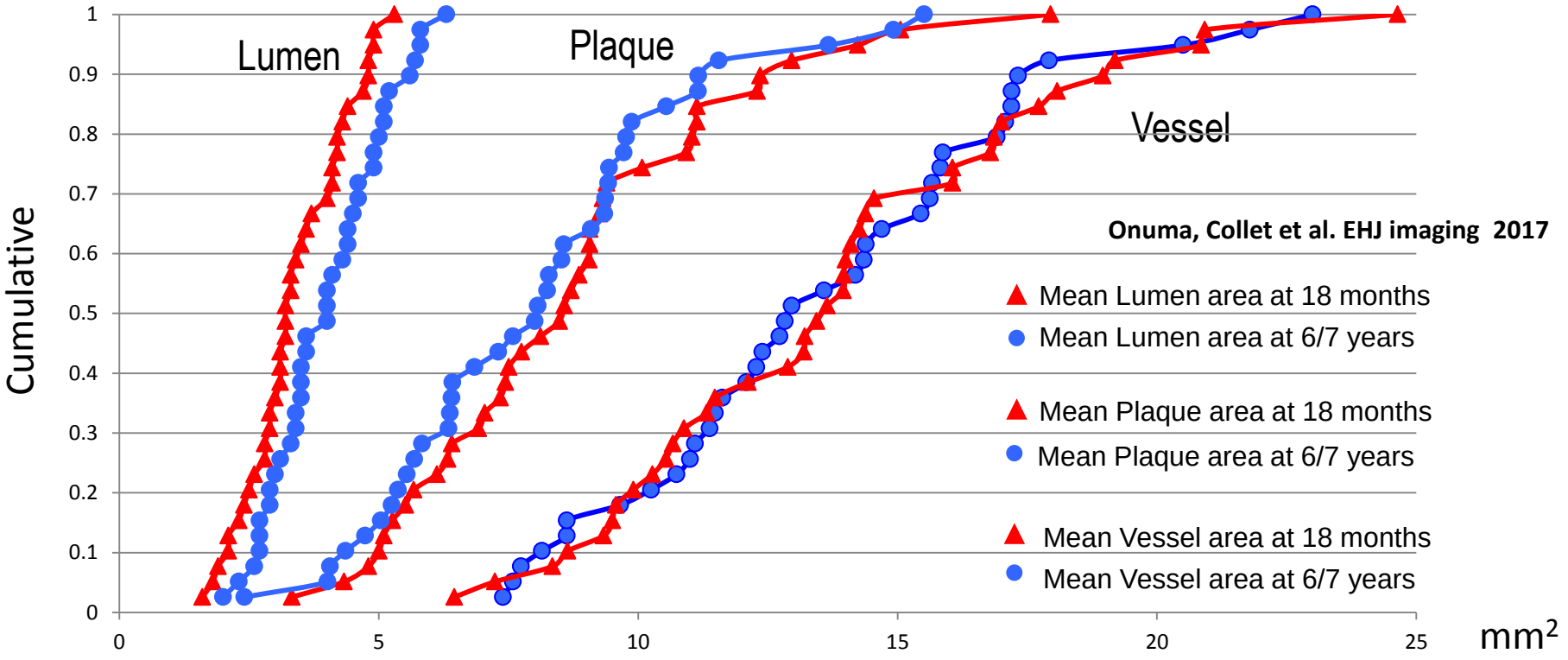
# A case of a improved lumen and non-invasive FFR (18M and 60M follow-up)

Onuma, Collet et al. EHJ Imaging 2017



# Cumulative frequency distribution curves of mean vessel, plaque and lumen area at 18 and 6/7 years




| | 18 months n=39 | 6/7 years n=39 | Δ | P-value |
|---|---|---|---|---|
| **Mean lumen area, $mm^2$** | **5.02 ± 1.36** | **5.52 ± 1.27** | **+0.49** | **0.019** |
| **Minimum Lumen area, $mm^2$** | **3.38 ± 0.96** | **4.02 ± 1.09** | **+0.64** | **0.002** |
| **Mean plaque area, $mm^2$** | **8.68 ± 3.15** | **8.04 ± 2.96** | **-0.64** | **0.451** |
| **Mean vessel area, $mm^2$** | **13.71 ± 4.06** | **13.56 ± 3.85** | **-0.15** | **0.717** |

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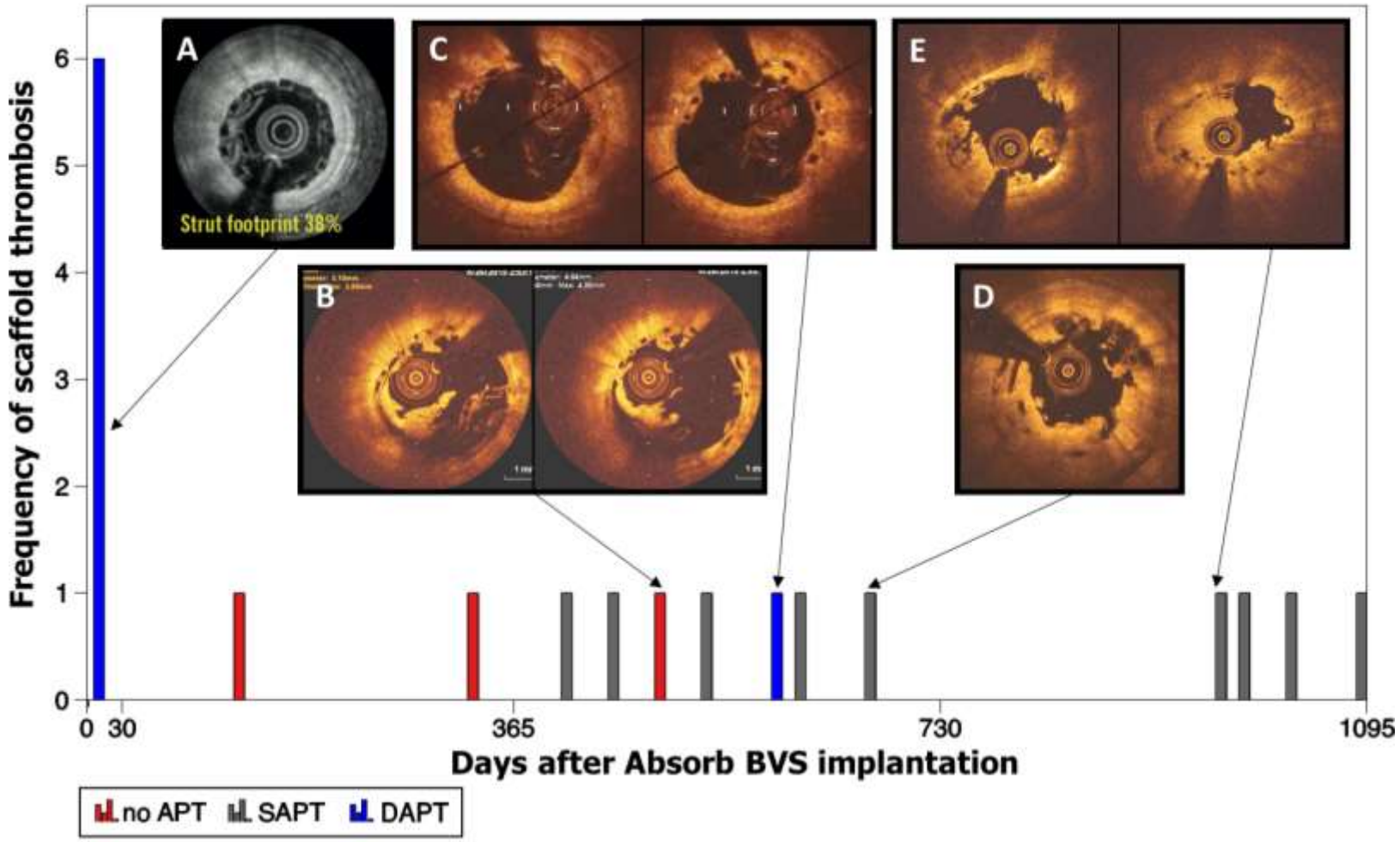
# Meta-analysis of long-term outcomes after the ABSORB implantation

| 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) | 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 (1,012 vs. 713) | ABSORB II | 3Y | 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)** | 2.5% vs. 0.9%<br>**OR 2.95 (1.37-6.26)** | 1.4% vs. 0.5%<br>**OR 3.04 (1.20-7.68)** |
| | | ABSORB JAPAN | 2Y | | | | |
| | | ABSORB CHINA | 2Y | | | | |
| | | TROFI II | 2Y | | | | |
| | | EVERBIO II | 2Y | | | | |
| **Ha et al.[3]** | 2,582 (1,407 vs. 1,095) | ABSORB II | 3Y | **OR 1.31 (0.93-1.83)** | **OR 2.59 (1.17-5.70)** | **OR 2.35 (1.14-4.86)** | Not reported |
| | | ABSORB JAPAN | 2Y | | | | |
| | | ABSORB CHINA | 2Y | | | | |
| | | ABSORB EXAMINATION | 2Y | | | | |
| | | ABSORB EXTEND | 3Y | | | | |
| **Sorrentino et al.[2]** | 5,583 (3,261 vs. 2,322) | ABSORB II | 3Y | 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)** | 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)** |
| | | ABSORB III | 2Y | | | | |
| | | ABSORB JAPAN | 2Y | | | | |
| | | ABSORB CHINA | 2Y | | | | |
| | | AIDA | 2Y | | | | |
| | | TROFI II | 2Y | | | | |
| | | EVERBIO II | 2Y | | | | |

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

# 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

# What are the imaging correlates with very late scaffold thromboses?

# 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.

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

QCA

**QCA parameter**

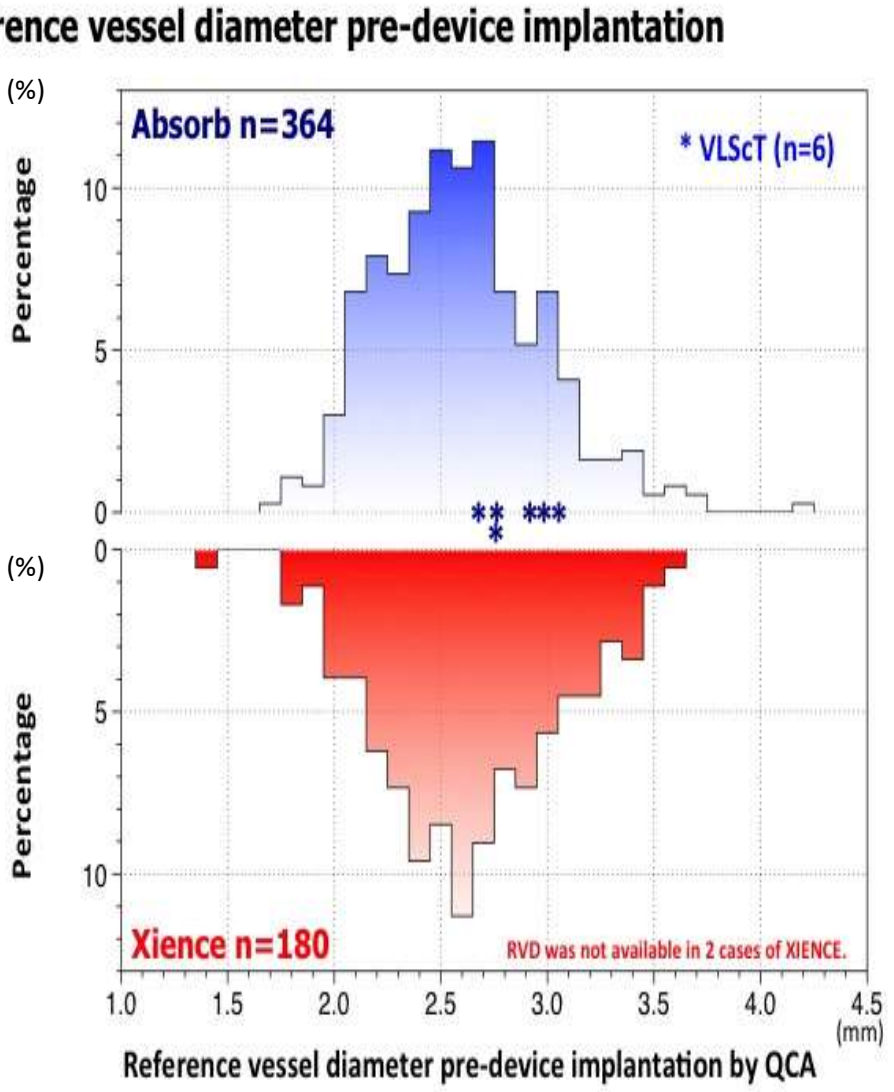
- Reference vessel diameter pre-device implantation
- Device sizing with reference to pre-reference vessel diameter

**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




Serruys et al. 2017 CRT

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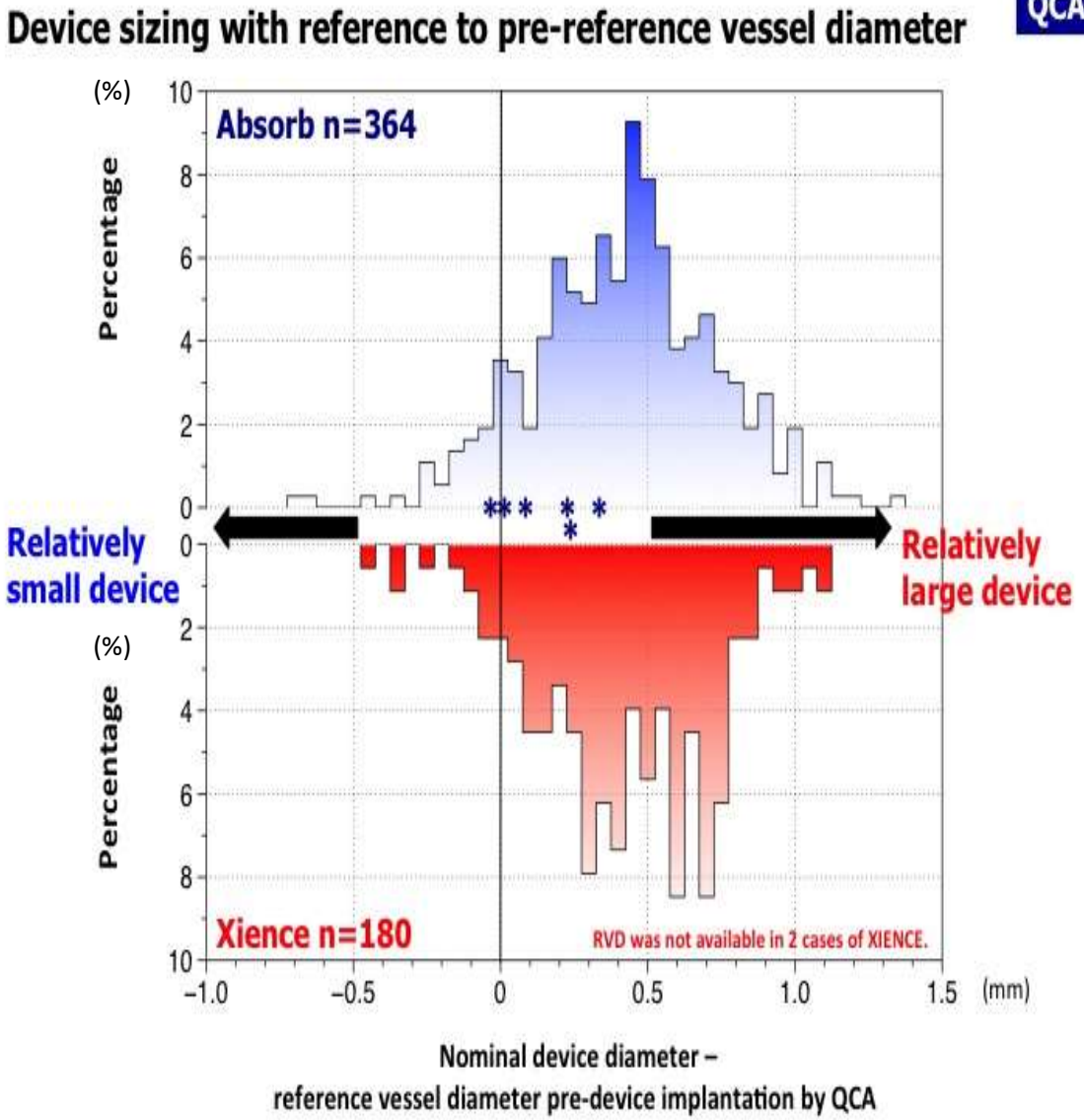



Serruys et al. 2017 CRT

# Impacts of post-procedural parameters on VLScT

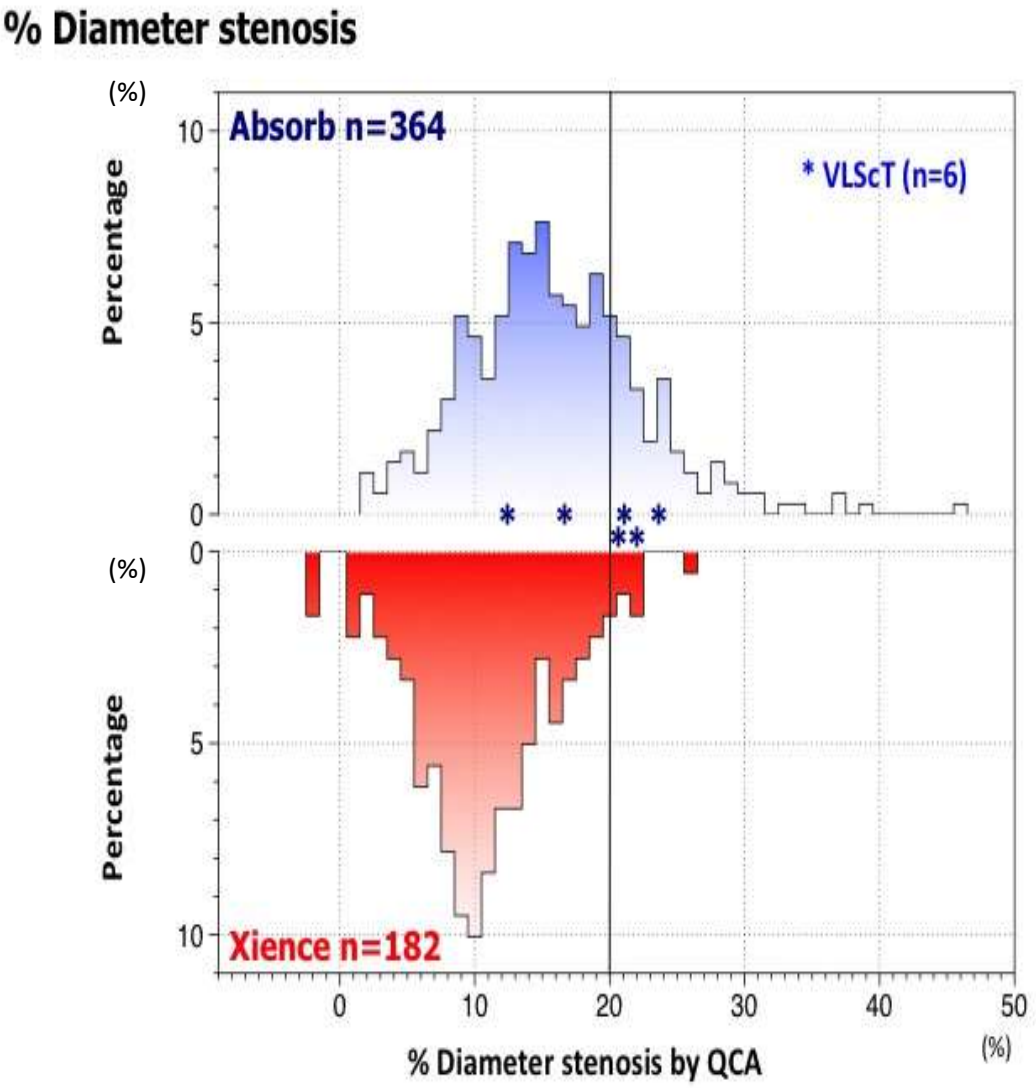
QCA

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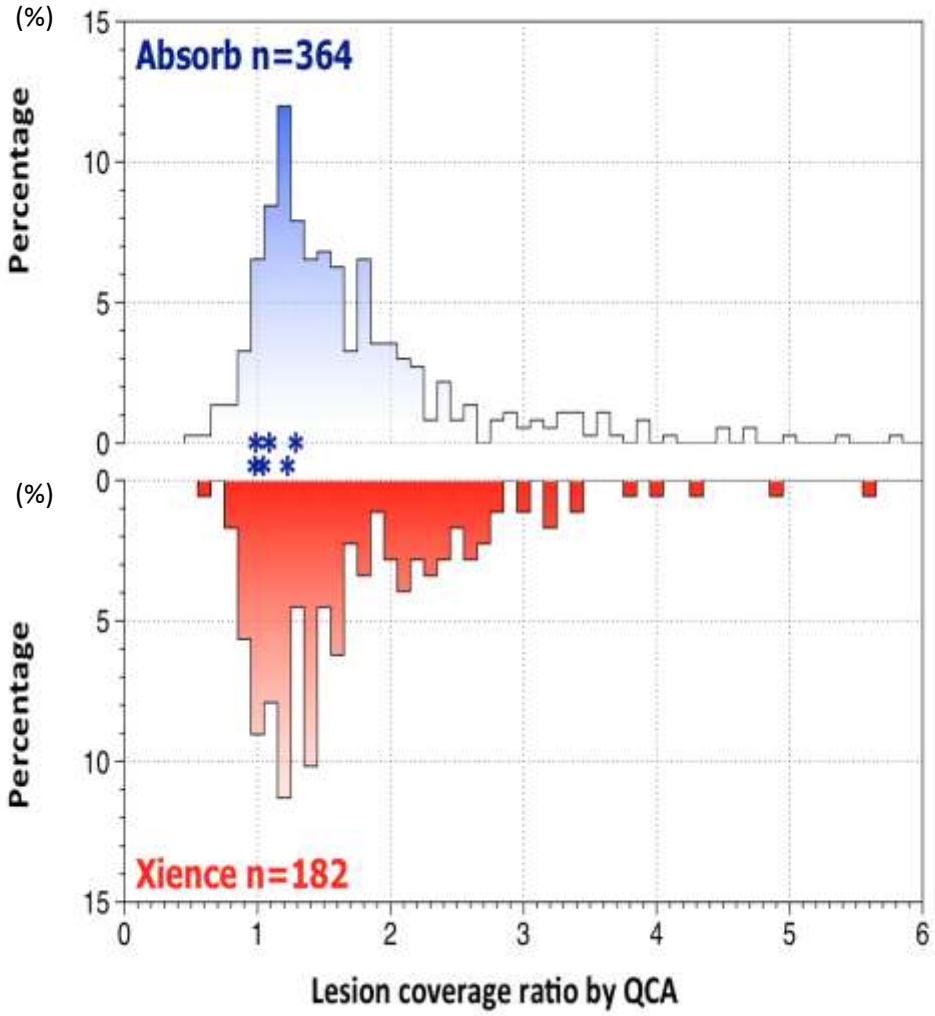
**Lesion coverage ratio = Stent length / pre-lesion length**
**(both measured by QCA)**

QCA




Serruys et al. 2017 CRT

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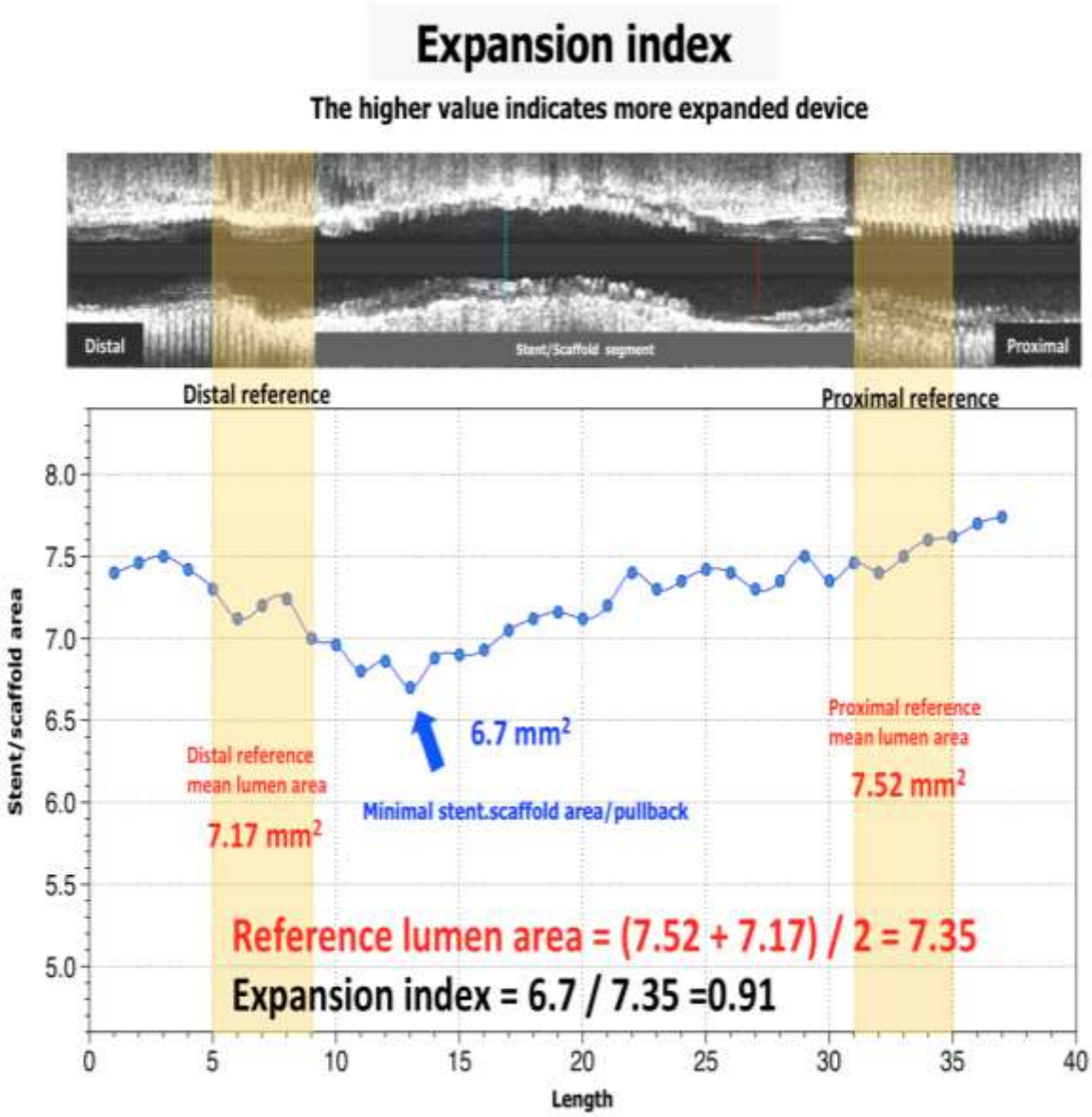

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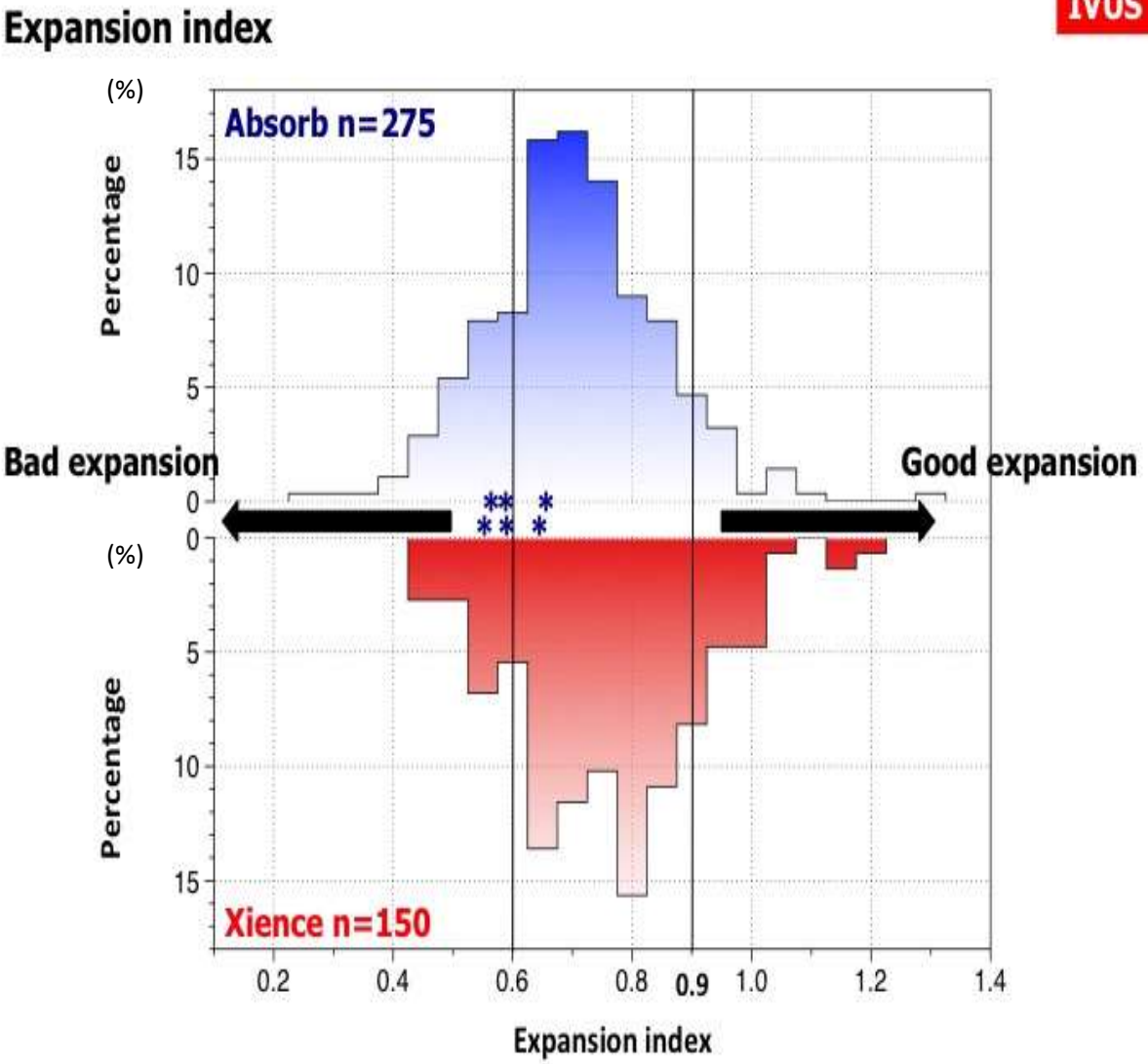
IVUS



# 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**

# Summary

- Serial IVUS assessment at BL and 3Y showed:
  - Lesions treated with Absorb exhibited frequently larger increase in mean vessel area and lumen area than lesions treated with Xience.
  - Absorb implantation, female gender, expected balloon-artery ratio ≥ 1.25, expansion index ≥ 0.8, previous PCI, and higher mean level of LDL cholesterol (average over 3 years) were independent factors predicting expansive remodeling.
- Serial MSCT assessment at 18 and 72 months demonstrated an enlargement of lumen.
- However, recent meta-analyses of mid-term outcomes (2-3 years) demonstrated increased rates of TV-MI, scaffold thrombosis and very late scaffold thrombosis of Absorb scaffold in comparison with Xience stent.
- 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. It remains to be proven that the improvement of device expansion by intensive technique could decrease the VLScT.