TCT-AP 2011

ABSORB: Evaluation of 2nd generation of a Drug-eluting Vascular Scaffold for Treatment of De Novo Native Coronary Artery Lesions:

1 Year Angiographic, IVUS, IVUS-VH and OCT Results of Cohort B

Patrick W. Serruys, MD, PhD

On behalf of the ABSORB B investigators

Erasmus MC, the Netherlands

Tutorial Arena, Level 4

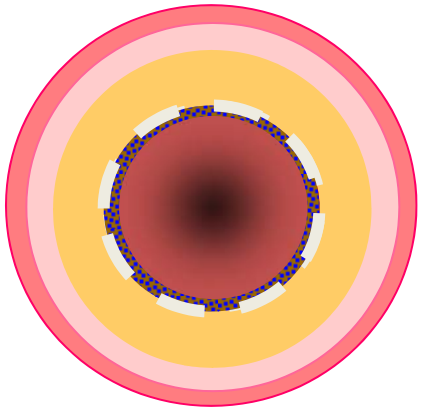
8:50-9:00, April 28

The ABSORB trial was sponsored and funded by Abbott Vascular, Santa Clara, California

Background I: The first generation of everolimus-eluting bioresorbable scaffold (BVS1.0) showed signs of shrinkage at 6 months (dubbed "late recoil") that contributed to the late luminal loss.

6 months

ABSORB
BVS 1.0



Late Loss = 0.43mm

Δ Vessel Area = ***+0.3%***

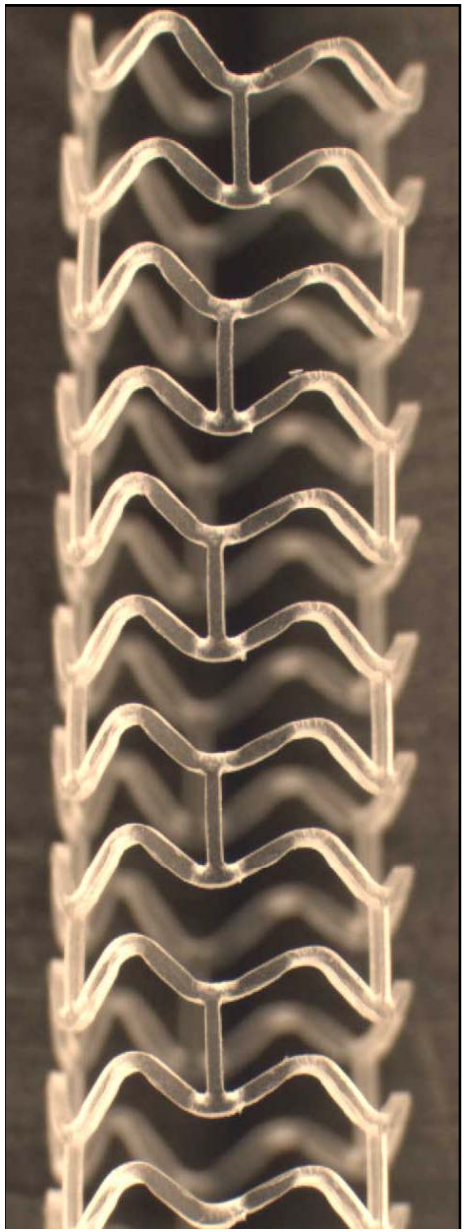
Δ scaffold Area = ***-11.8%***

% Scaffold Obstruction = 5.3%

Δ Lumen Area = ***-16.8%***

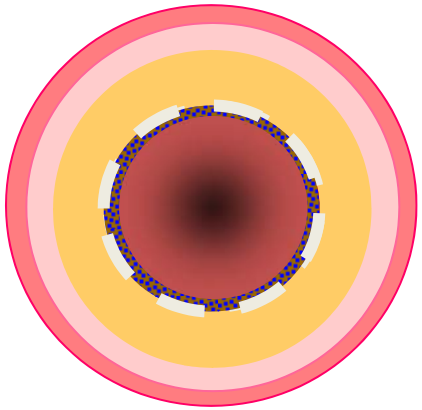
Lancet 2008, Circulation 2010

Background I: The second generation (BVS1.1) has a modified platform design and a different manufacturing process of the polymer.



6 months

ABSORB
BVS 1.0



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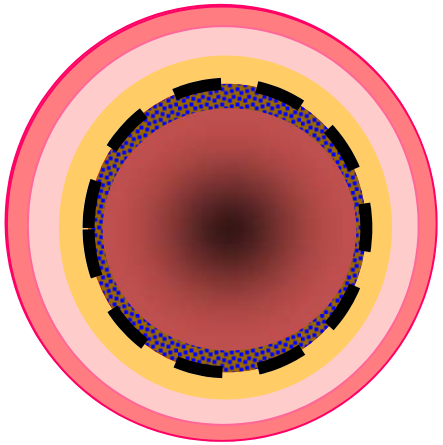
6 months

ABSORB
BVS 1.1



Late Loss = 0.19mm

Δ Vessel Area = ***+2.4%***
Δ Scaffold Area = ***-2.0%***
% Scaffold Obstruction = 1.2%
Δ Lumen Area = ***-3.1%***

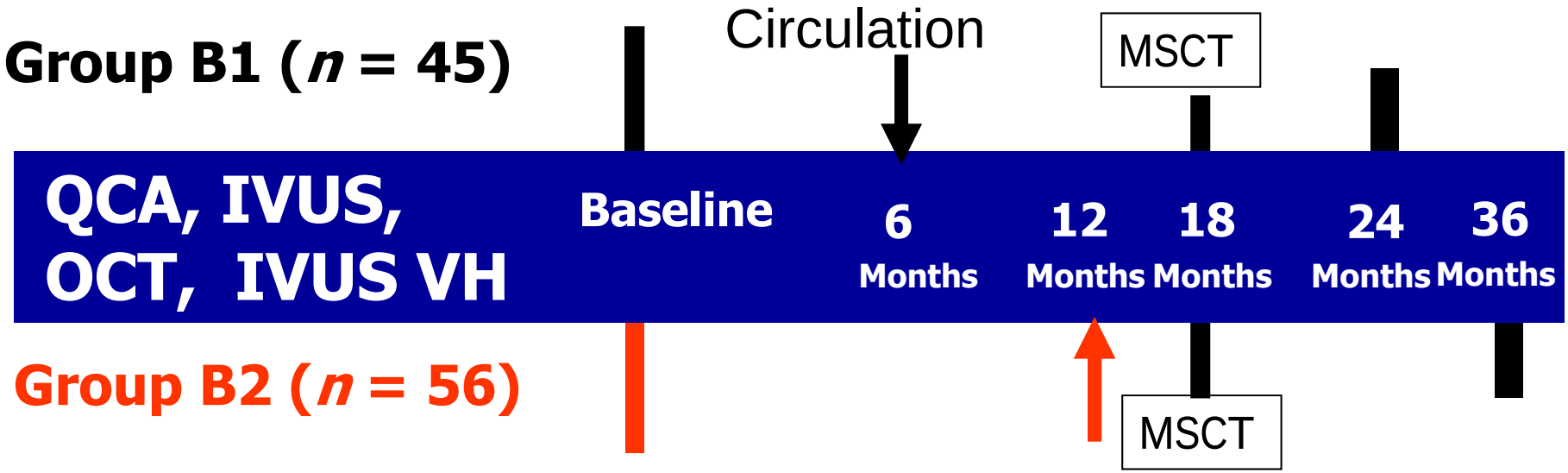
Lancet 2008, Circulation 2010

However, in the first cohort of BVS 1.1, between baseline and 6 months, there were

- **No signs of bioresorption on OCT**
- **No signs of bioresorption on IVUS-VH**
- **No signs of vasomotion induced by Ergonovine/ Ach**

Critical minds have suggested that

- **Late recoil (prevented at 6 months) was just postponed to 12 months**
- **Neointimal hyperplasia would become manifest during bioresorption between 6 and 12 months**



- Sponsor/ Funding: Abbott Vascular
- Primary Investigators:
  - PW Serruys MD, PhD
  - J Ormiston MD
- DSMB: J Tijssen PhD, M Wiemer MD, P Urban MD
- CEC: C Hanet MD, R Tölg MD, V Umans MD
- Angiographic, IVUS and OCT Corelab: Cardialysis
- Prospective, open label, FIM
- 3.0 x 18mm devices to treat up to 2 lesions ≤ 14mm in length

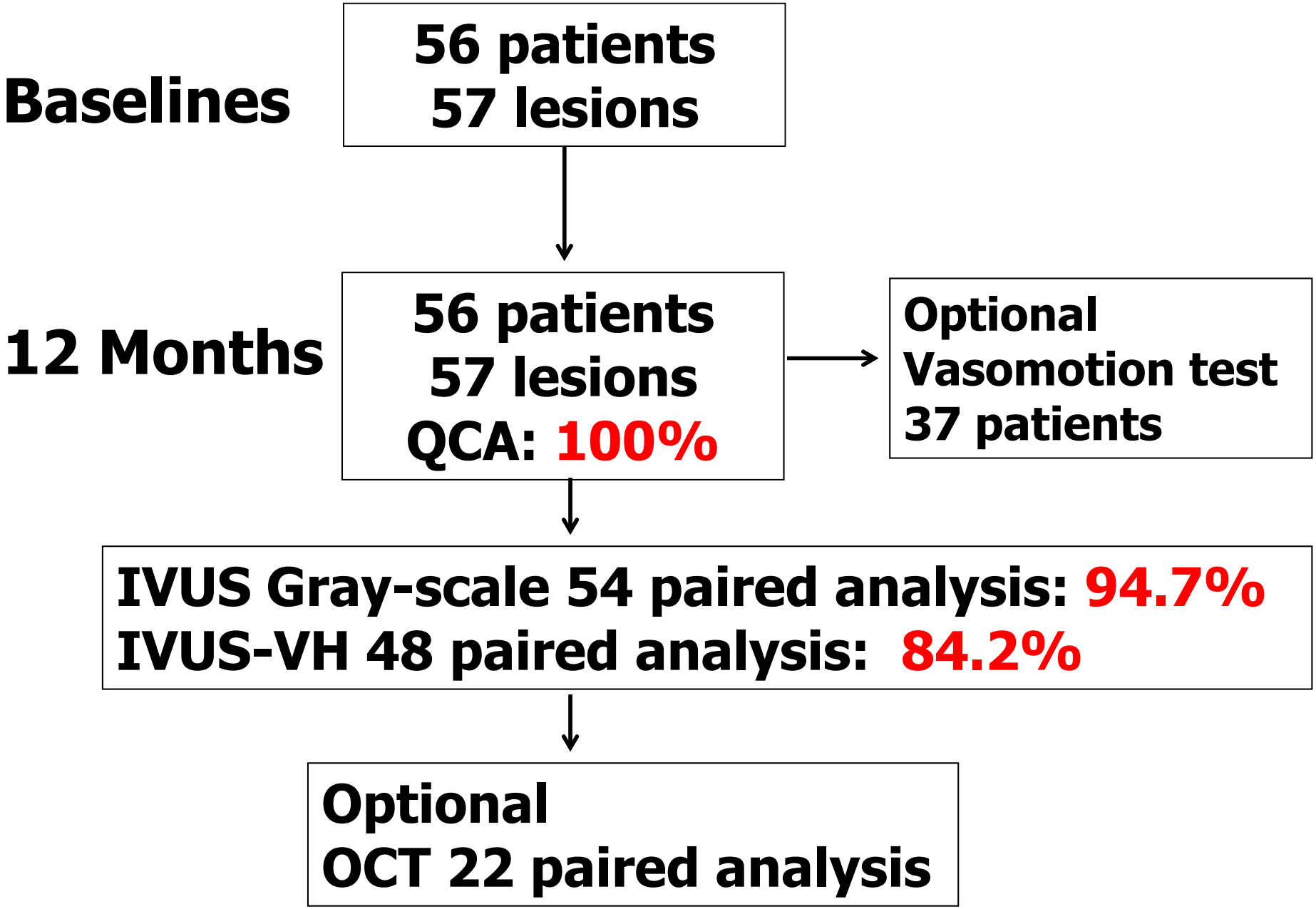
- 12 sites Europe, Australia, New Zealand
- B de Bruyne, MD, PhD
- D Dudek, MD
- L Thuesen, MD
- P Smits, MD, PhD
- B Chevalier, MD
- D McClean, MD
- J Koolen, MD, PhD
- S Windecker, MD
- R Whitbourn, MD
- I Meredith, MD, PhD
- 101 patients enrolled between 19 March and 6 November 2009

Baseline Demographics and Lesion Characteristics of the ABSORB Cohort B2

	No. of Patients = 56
Age (years)	60
Male gender	71%
Current Smokers	21%
Diabetes	20%
Hypertension Requiring Medication	64%
Hyperlipidemia Requiring Medication	66%
Prior target vessel Intervention	4%

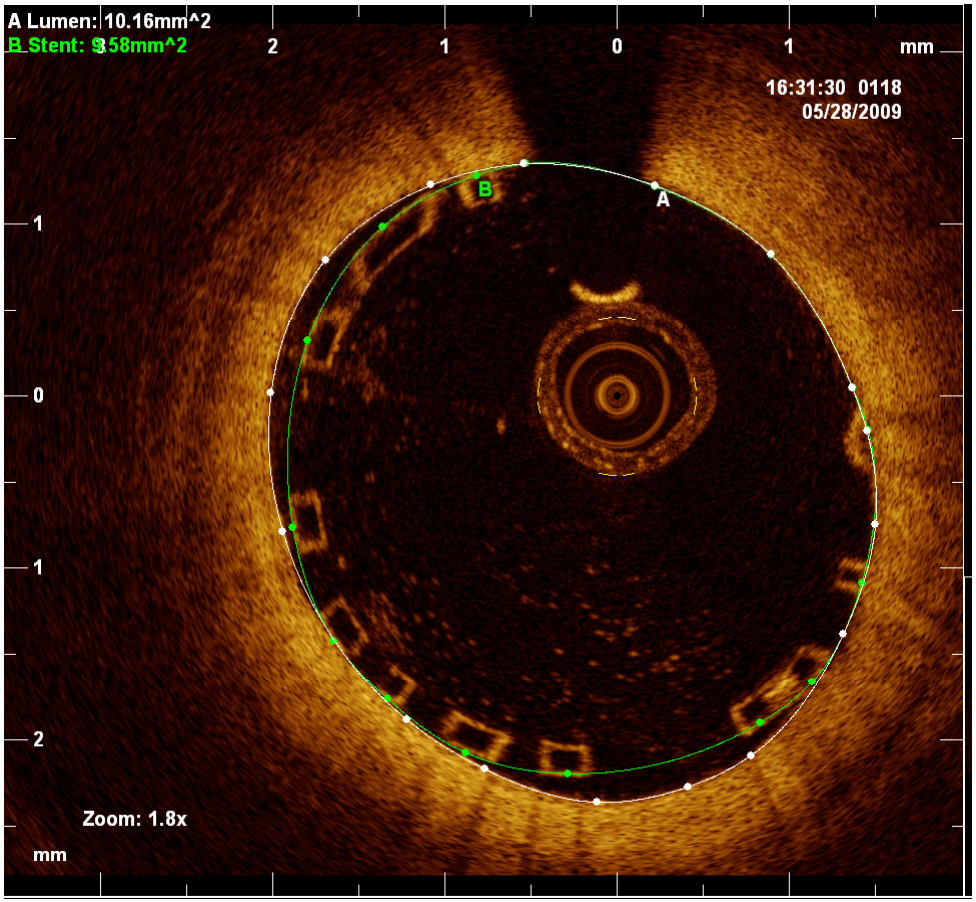
	No. of Lesions = 57
Target Vessel (%)	
Left Anterior Descending	47
Left Circumflex	21
Right Coronary Artery	32
AHA / ACC Lesion Classification (%)	
A	0
B1	63
B2	32
C	5
Clinical Device success (%)	100
Clinical Procedure success (%)	98

ABSORB Cohort B2 Invasive Follow-up

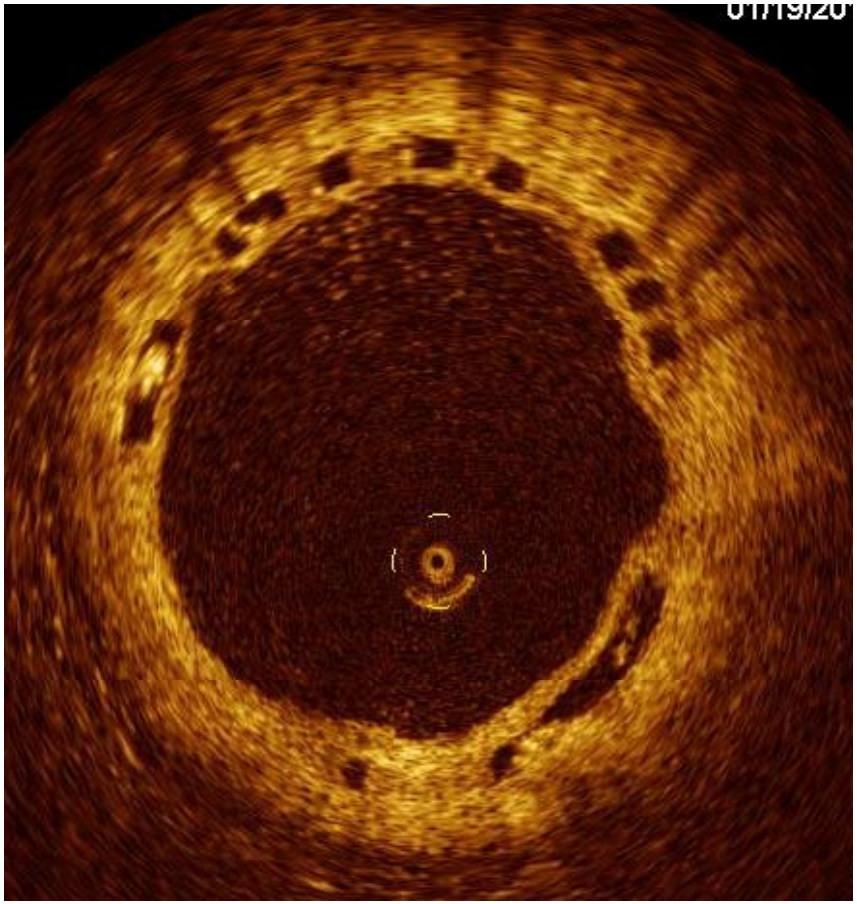


Quantitative OCT Assessment of BVS 1.1

Baseline



Follow-up



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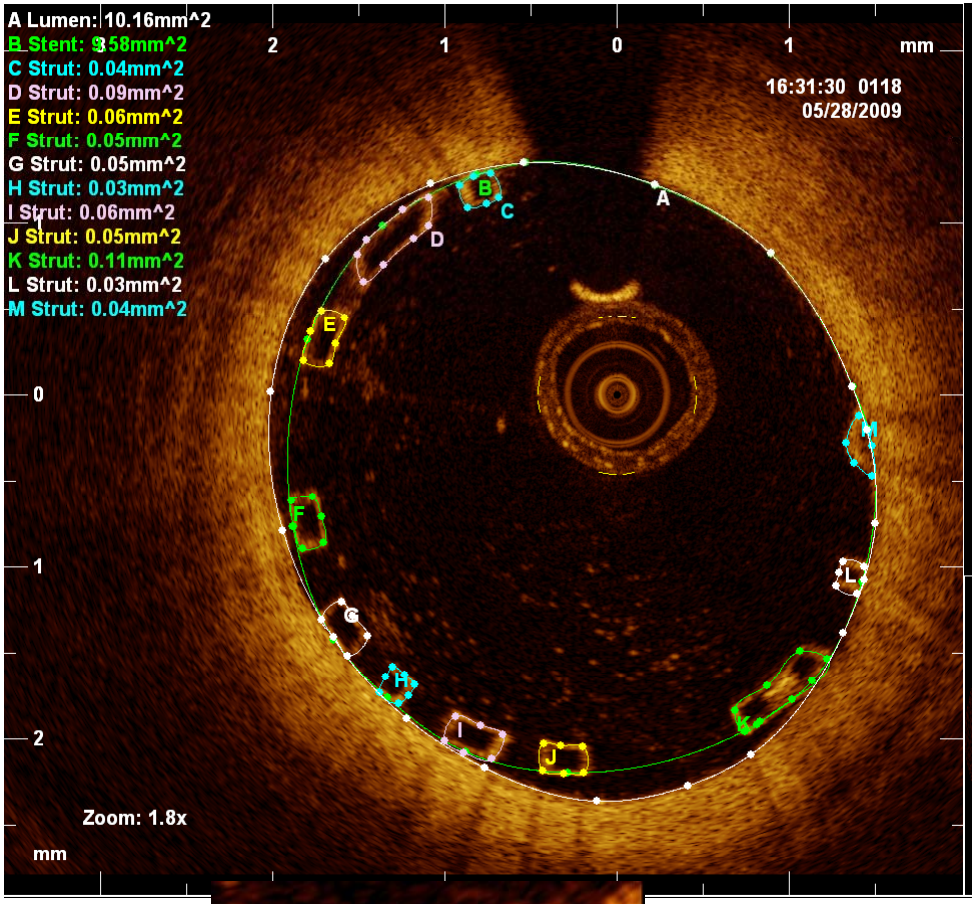
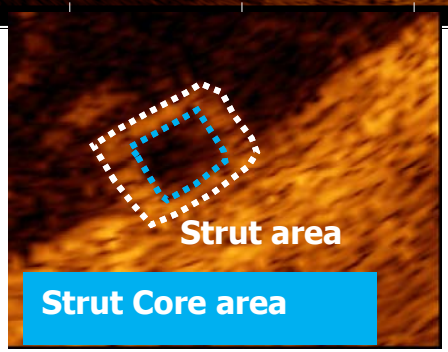
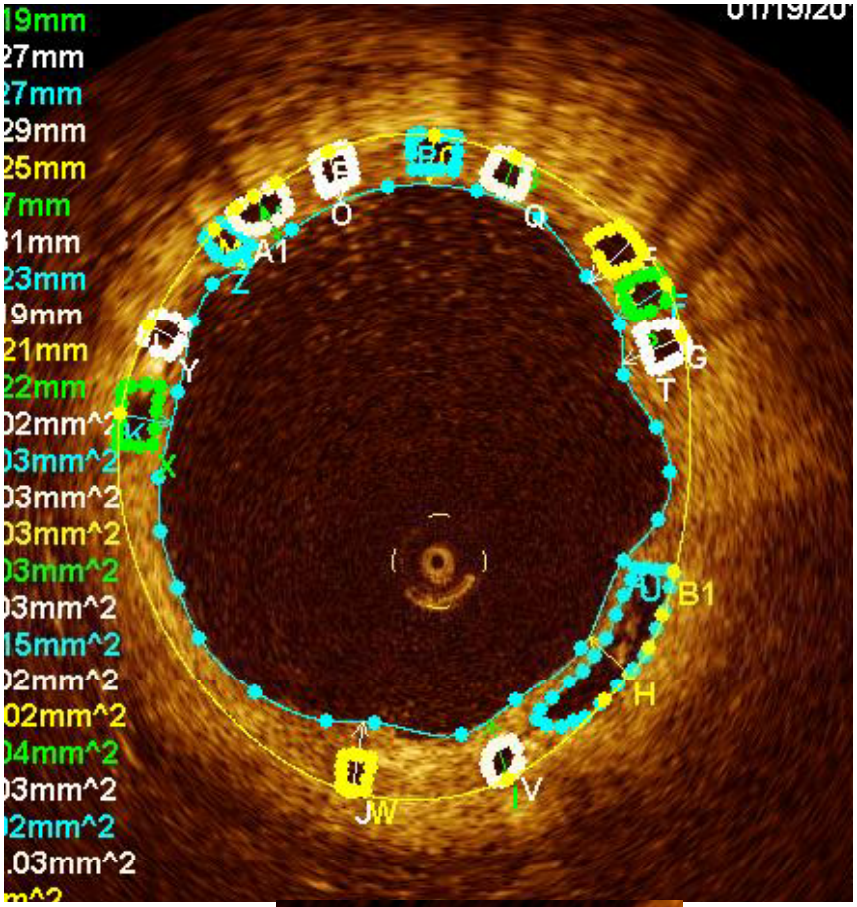
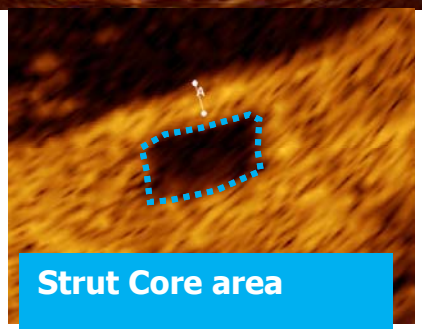




Follow-up





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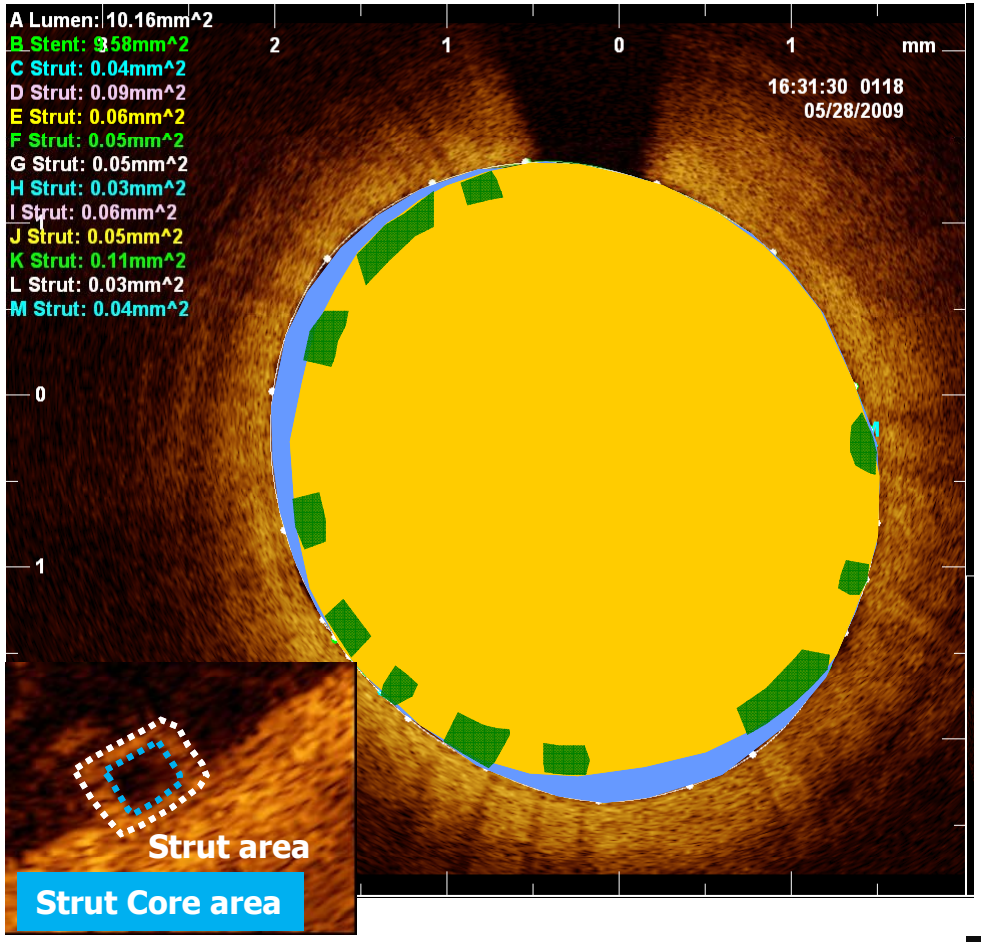
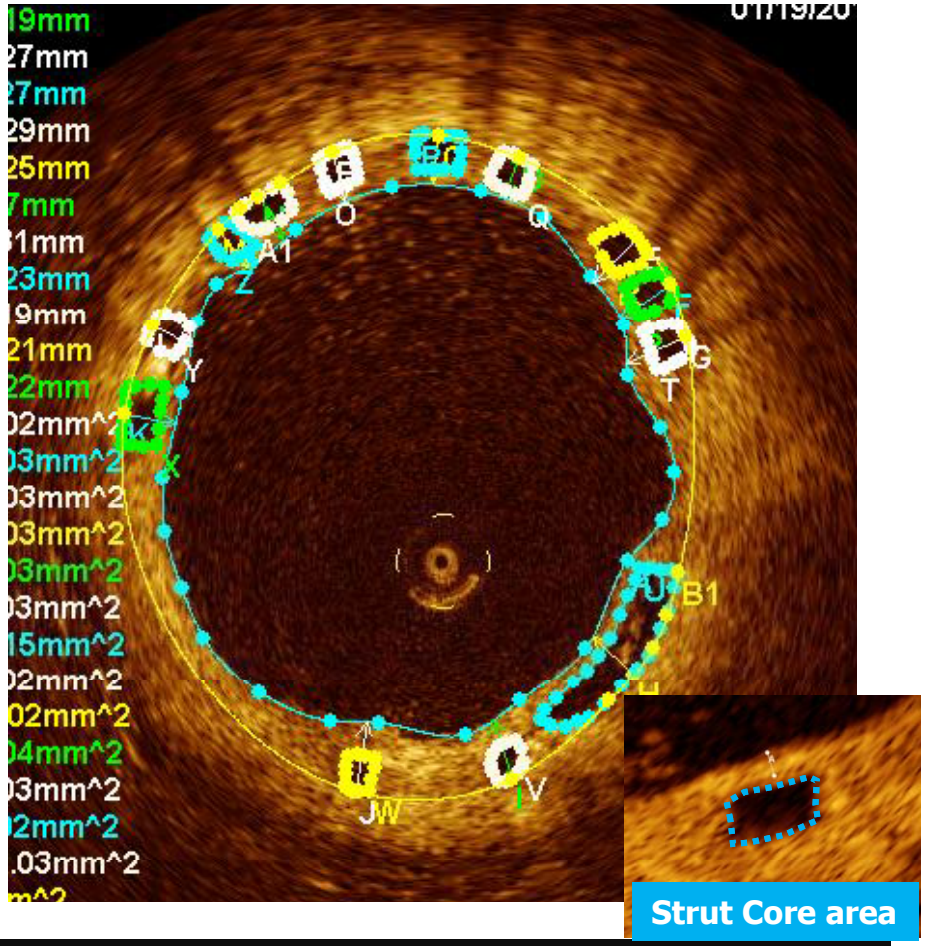


Follow-up

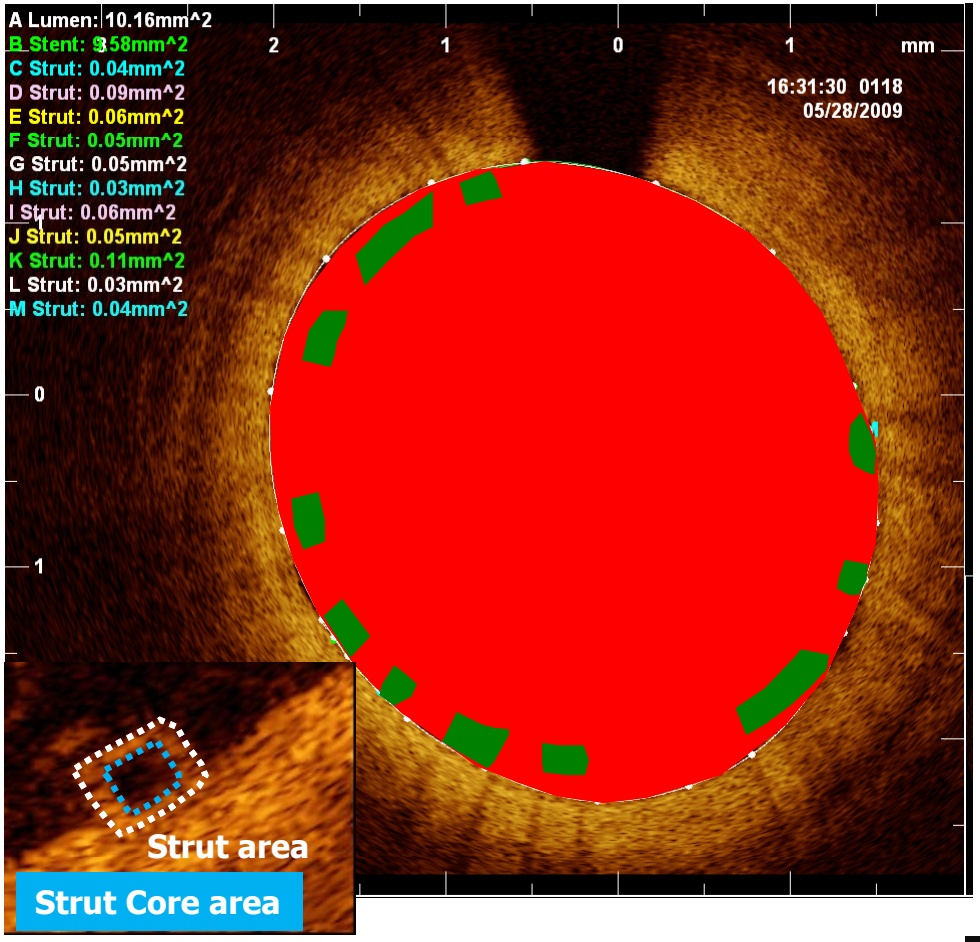


Lumen Area
Scaffold Area
Strut Core area

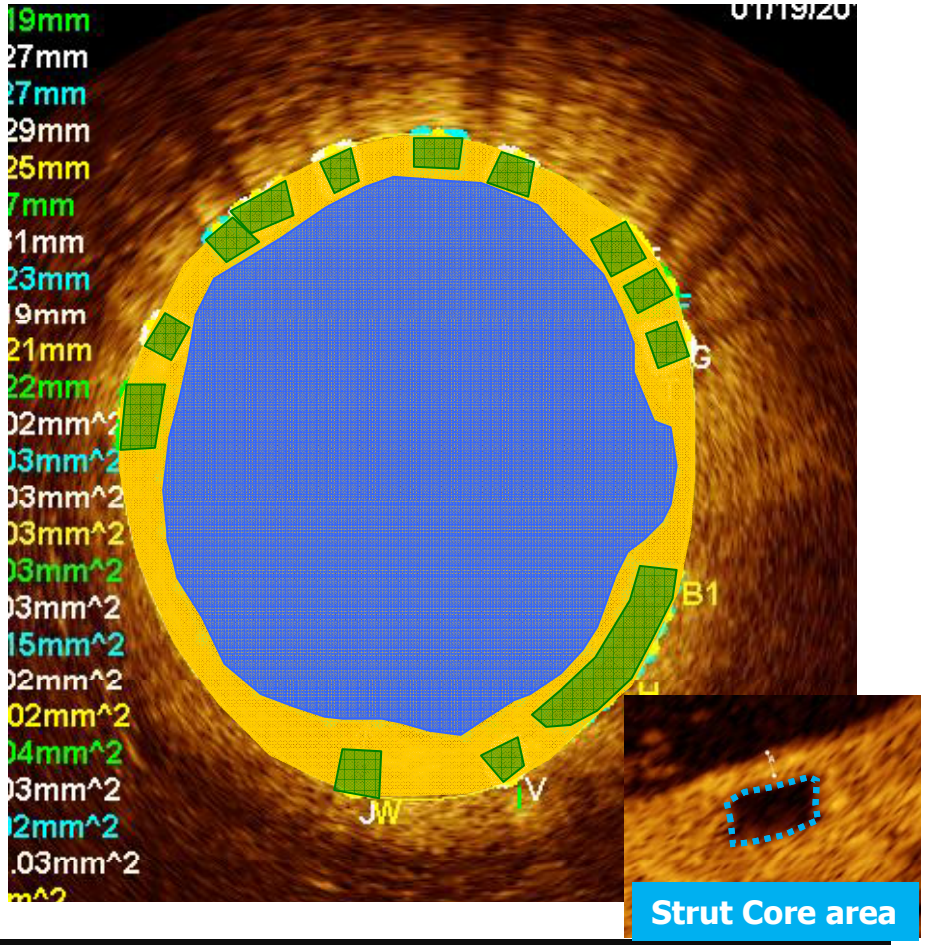
Neointimal area = Scaffold area – Lumen area – Strut core area

Quantitative OCT Assessment of BVS 1.1

Baseline



Follow-up

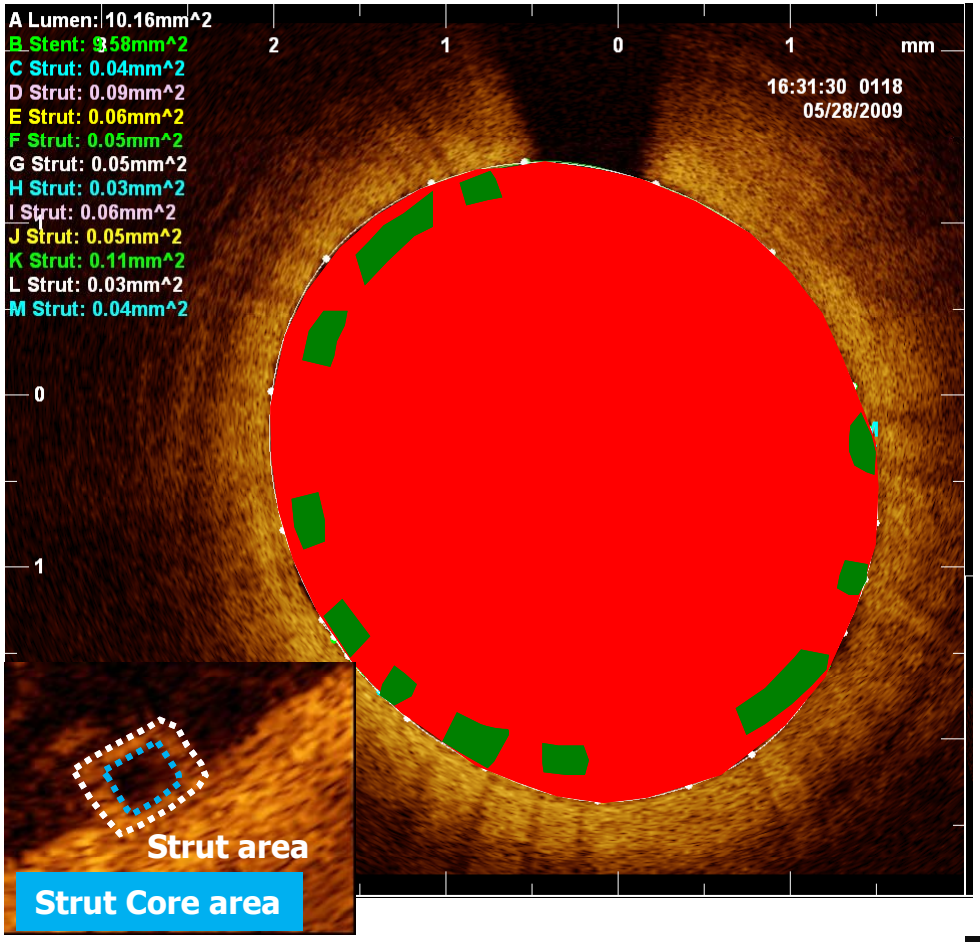


Flow area = Lumen area – strut core area

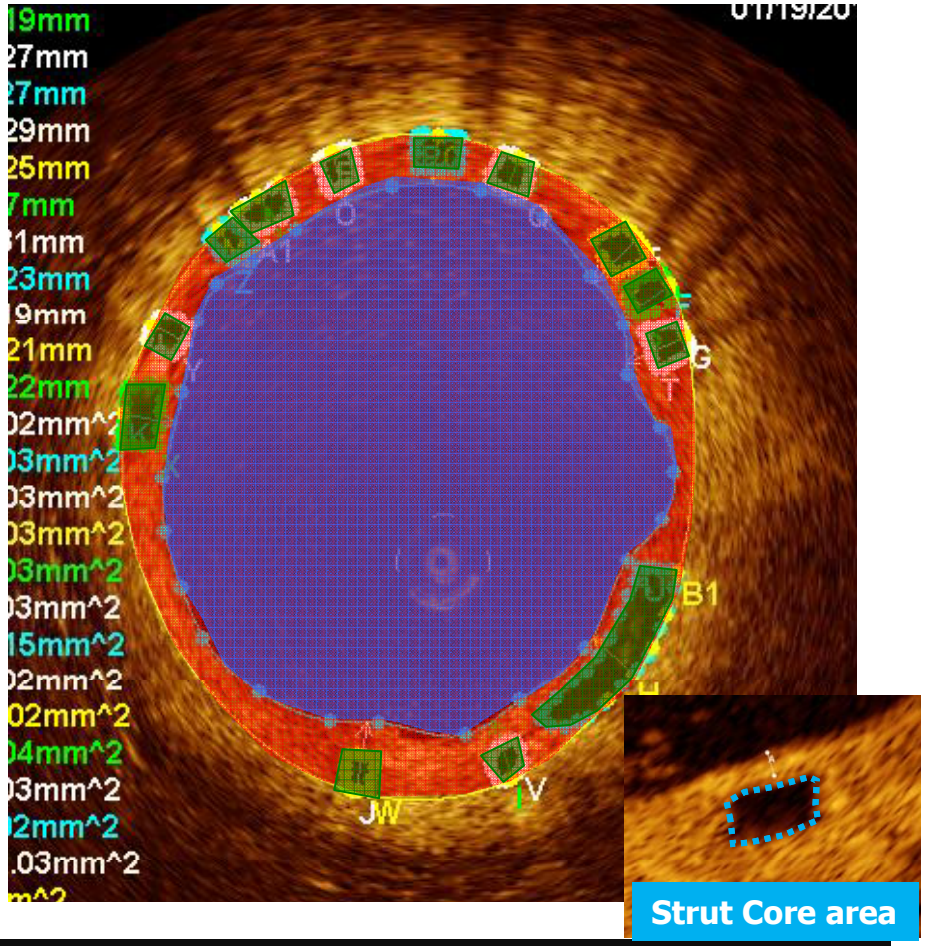
Neointimal area = Scaffold area – Lumen area – Strut core area

Quantitative OCT Assessment of BVS 1.1

Baseline



Follow-up



Flow area = Lumen area – strut core area

Neointimal area =Scaffold area – Lumen area –Strut core area

Results of Quantitative OCT Analysis

22 Paired OCT in 21 pts	Post procedure	12 month	% Difference	P values
Mean scaffold area, mm^2	**7.66**	**7.59**	**-0.66**	**0.30**
Minimal scaffold area, mm^2	**6.23**	**6.08**	**-2.05**	**0.33**
Mean prolapse area, mm^2	**0.14**	**na**	**-**	**-**
Mean strut core area, mm^2	**0.19**	**0.16**	**-11.4**	**0.003**
Mean Neointimal area, mm^2	**-**	**1.34**	**-**	**-**
Mean flow area, mm^2	**7.51**	**6.13**	**-18.1**	**<0.001**
Minimal flow area, mm^2	**5.95**	**4.51**	**-23.4**	**< 0.001**
Lumen area stenosis, %	**20.2**	**26.9**		**0.02**
Uncovered struts, %	**na**	**3.11**		
ISA area, mm^2 (for patients with ISA)	**0.41 (n=18)**	**2.94 (n=4)**		**-**

Results of Quantitative OCT Analysis

22 Paired OCT in 21 pts	Post procedure	12 month	% Difference	P values
Mean scaffold area, mm^2	**No late scaffold shrinkage**			
Minimal scaffold area, mm^2				
Mean prolapse area, mm^2	**0.14**	**na**	**-**	**-**
Mean strut core area, mm^2	**0.19**	**0.16**	**-11.4**	**0.003**
Mean Neointimal area, mm^2	**-**	**1.34**	**-**	**-**
Mean flow area, mm^2	**7.51**	**6.13**	**-18.1**	**<0.001**
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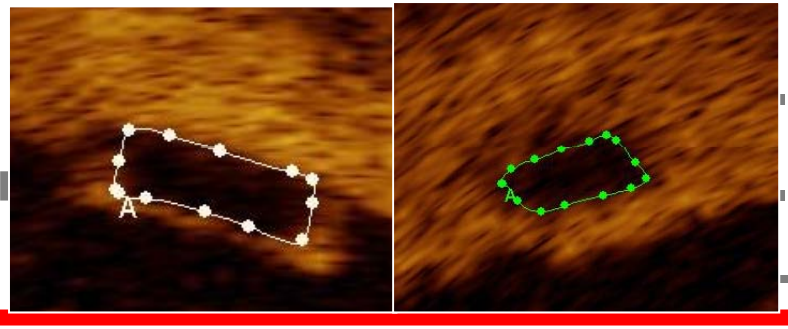
Mean scaffold area, mm^2			.66	0.30
Minimal scaffold area, m			.05	0.33
Mean prolapse area, mm^2			-	-
Mean strut core area, mm^2	**First signs of bioresorption**			
Mean Neointimal area, mm^2	-	1.34	-	-
Mean flow area, mm^2	7.51	6.13	-18.1	<0.001
Minimal flow area, mm^2	5.95	4.51	-23.4	< 0.001
Lumen area stenosis, %	20.2	26.9		0.02
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Mean prolapse area, mm^2	0.14	na	-	-
Mean strut core area, mm^2	0.19	0.16	-11.4	0.003
Mean Neointimal area, mm^2	**Well controlled inhibition of neointima**			
Mean flow area, mm^2	7.51	6.13	-18.1	<0.001
Minimal flow area, mm^2	5.95	4.51	-23.4	< 0.001
Lumen area stenosis, %	20.2	26.9		0.02
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Mean strut core area, mm^2	0.19	0.16	-11.4	0.003
Mean Neointimal area, mm^2	-	1.34	-	-
Mean flow area, mm^2				
Minimal flow area, mm^2	**Minimal reduction in functional lumen area**			
Lumen area stenosis, %				
Uncovered struts, %	na	3.11		
ISA area, mm^2 (for patients with ISA)	0.41 (n=18)	2.94 (n=4)		-

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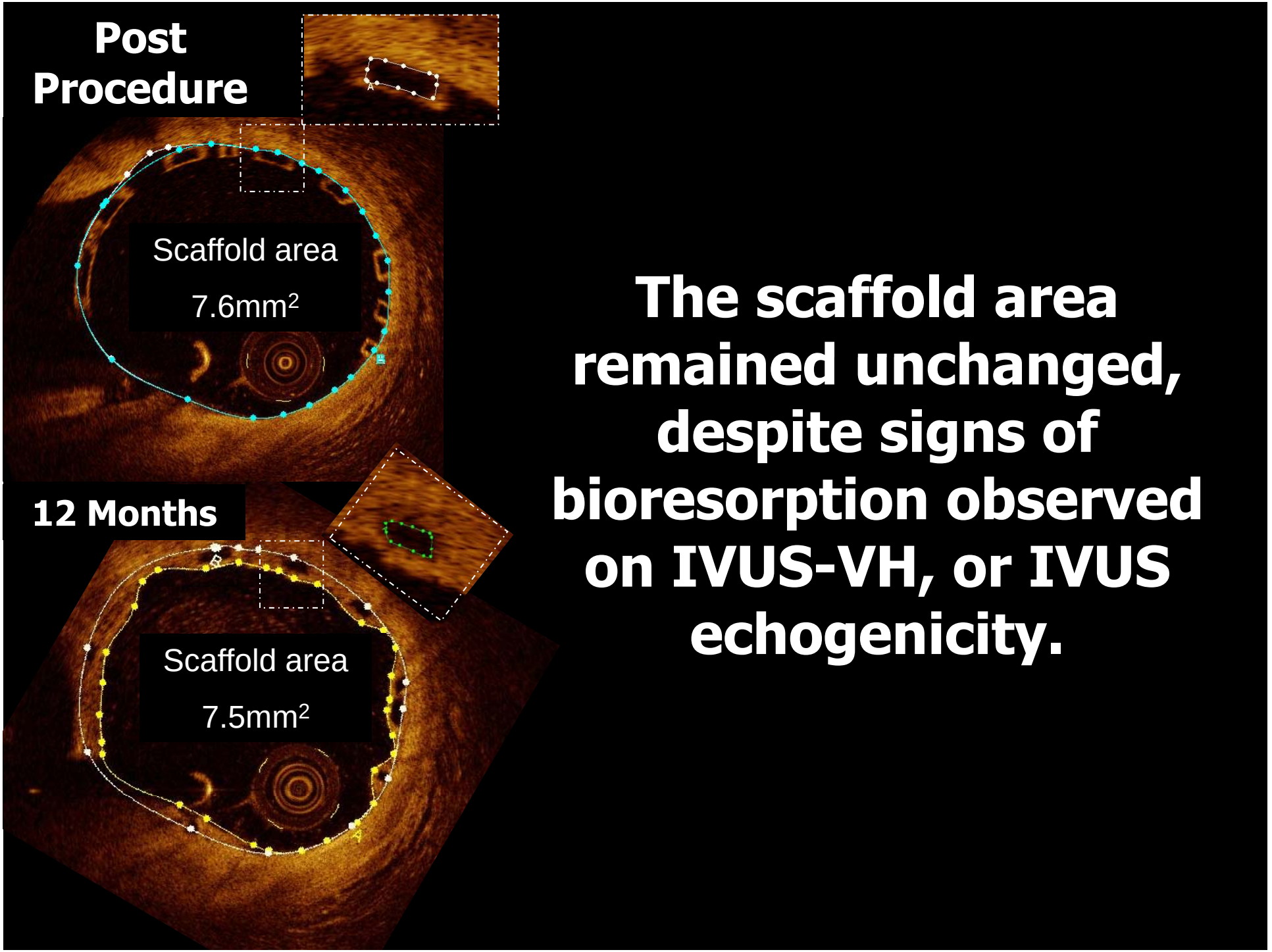
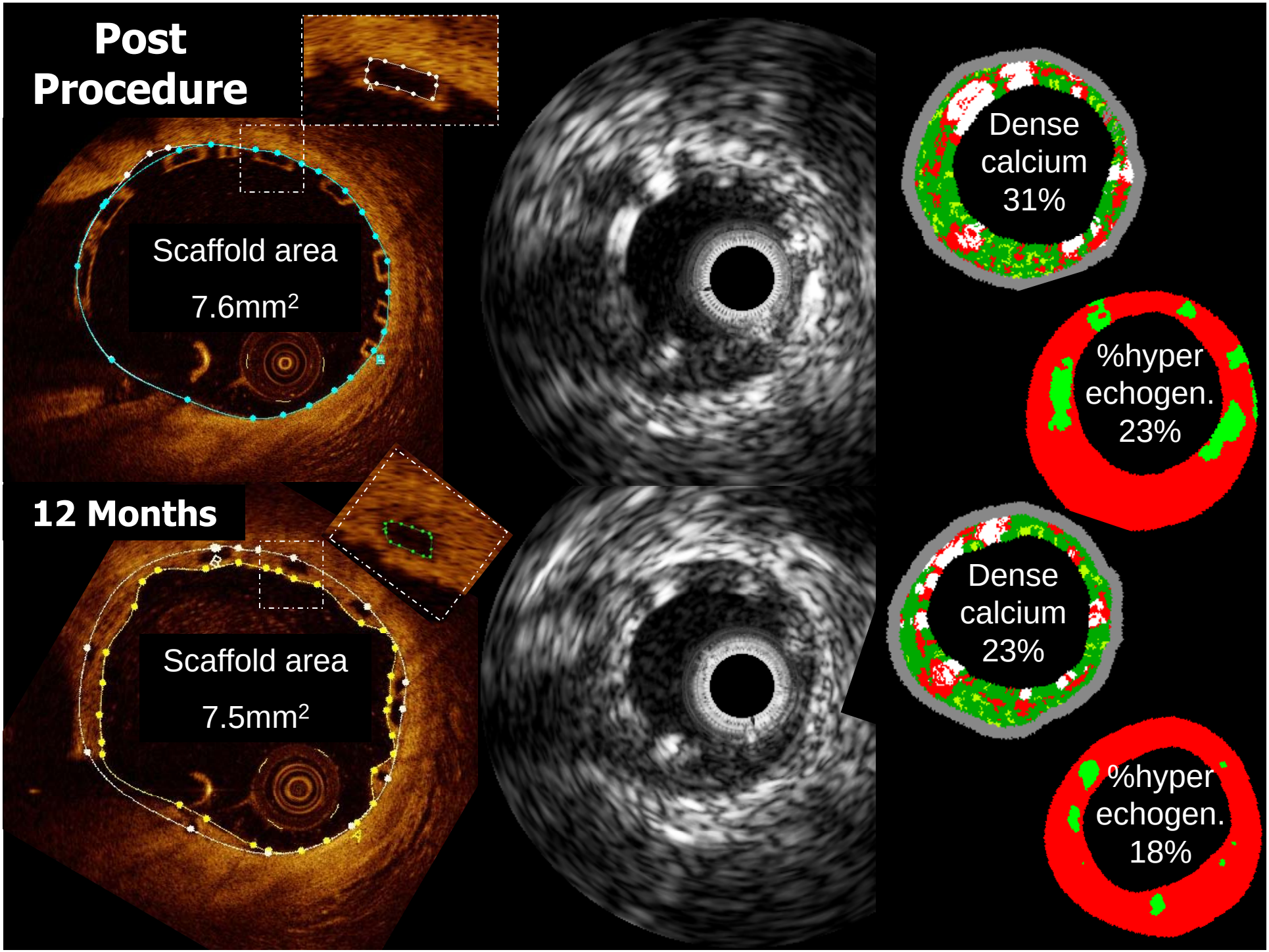
Mean flow area, mm^2	7.51	6.13	-18.1	<0.001
Minimal flow area, mm^2	5.95	4.51	-23.4	< 0.001
Lumen area stenosis, %	20.2	26.9		0.02
Uncovered struts, %	**Almost complete coverage of the struts with resolution of incomplete apposition**			
ISA area, mm^2 (for patients with ISA)				



The scaffold area remained unchanged, despite signs of bioresorption observed on IVUS-VH, or IVUS echogenicity.


Post Procedure
Scaffold area
7.6mm2
Dense calcium 31%
%hyper echogen. 23%
12 Months
Scaffold area
7.5mm2
Dense calcium 23%
%hyper echogen. 18%

Results of Quantitative IVUS Analysis
(Paired analysis from Intent-to-treat population)

	Paired Intent-to-treat (n=54)			
IVUS Grayscale	**Post PCI**	**12 Months**	**Difference %**	**P value**
Mean Vessel area, mm^2	**14.03**	**14.63**	**4.82**	**0.012**
Mean Scaffold area, mm^2	**6.29**	**6.33**	**0.90**	**0.66**
Minimum scaffold area, mm^2	**5.11**	**5.07**	**-0.18**	**0.38**
Neointimal hyperplasia area, mm^2	**-**	**0.09**	**-**	**-**
Minimum lumen area, mm^2	**5.11**	**4.98**	**-1.94**	**0.12**
Plaque area, mm^2	**7.72**	**8.30**	**8.94**	**<0.001**

IVUS VH (n=48) Echogenicity (n=35)	**Post PCI**	**12 Months**	**Difference %,**	**P value**
Dense calcium area, %	**30.9**	**23.1**	**-17.7**	**<0.001**
Hyper-Echogenicity , %	**23.5**	**18.3**	**-20**	**<0.001**

Results of Quantitative IVUS Analysis
(Paired analysis from Intent-to-treat population)

	Paired Intent-to-treat (n=54)			
IVUS Grayscale	**Post PCI**	**12 Months**	**Difference %**	**P value**
Mean Vessel area, mm^2	14.03	14.63	4.82	0.012
Mean Scaffold area, mm^2	**No scaffold area reduction**			
Minimum scaffold area, mm^2				
Neointimal hyperplasia area, mm^2	-	0.09	-	-
Minimum lumen area, mm^2	5.11	4.98	-1.94	0.12
Plaque area, mm^2	7.72	8.30	8.94	<0.001

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Mean Scaffold area, mm^2	6.29	6.33	0.90	0.66
Minimum scaffold area, mm^2	5.11	5.07	-0.18	0.38
Neointimal hyperplasia area, mm^2	**Minimal hyperplasia**			
Minimum lumen area, mm^2	**Non-significant Lumen reduction**			
Plaque area, mm^2	7.72	8.30	8.94	<0.001

IVUS VH (n=48) Echogenicity (n=35)	Post PCI	12 Months	Difference %,	P value
Dense calcium area, %	30.9	23.1	-17.7	<0.001
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Minimum scaffold area, mm^2				
Neointimal hyperplasia area, mm^2				
Minimum lumen area, mm^2				
Plaque area, mm^2	**7.72**	**8.30**	**8.94**	**<0.001**

Slight positive remodeling with plaque area increase

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Neointimal hyperplasia area, mm^2	-	0.09	-	-
Minimum lumen area, mm^2	5.11	4.98	-1.94	0.12
Plaque area, mm^2	7.72	8.30	8.94	<0.001

IVUS VH (n=48) Echogenicity (n=35)	**Post PCI**	**12 Months**	**Difference %,**	**P value**
Dense calcium area, %	**Signs of dissolution of polymeric struts**			
Hyper-Echogenicity , %				

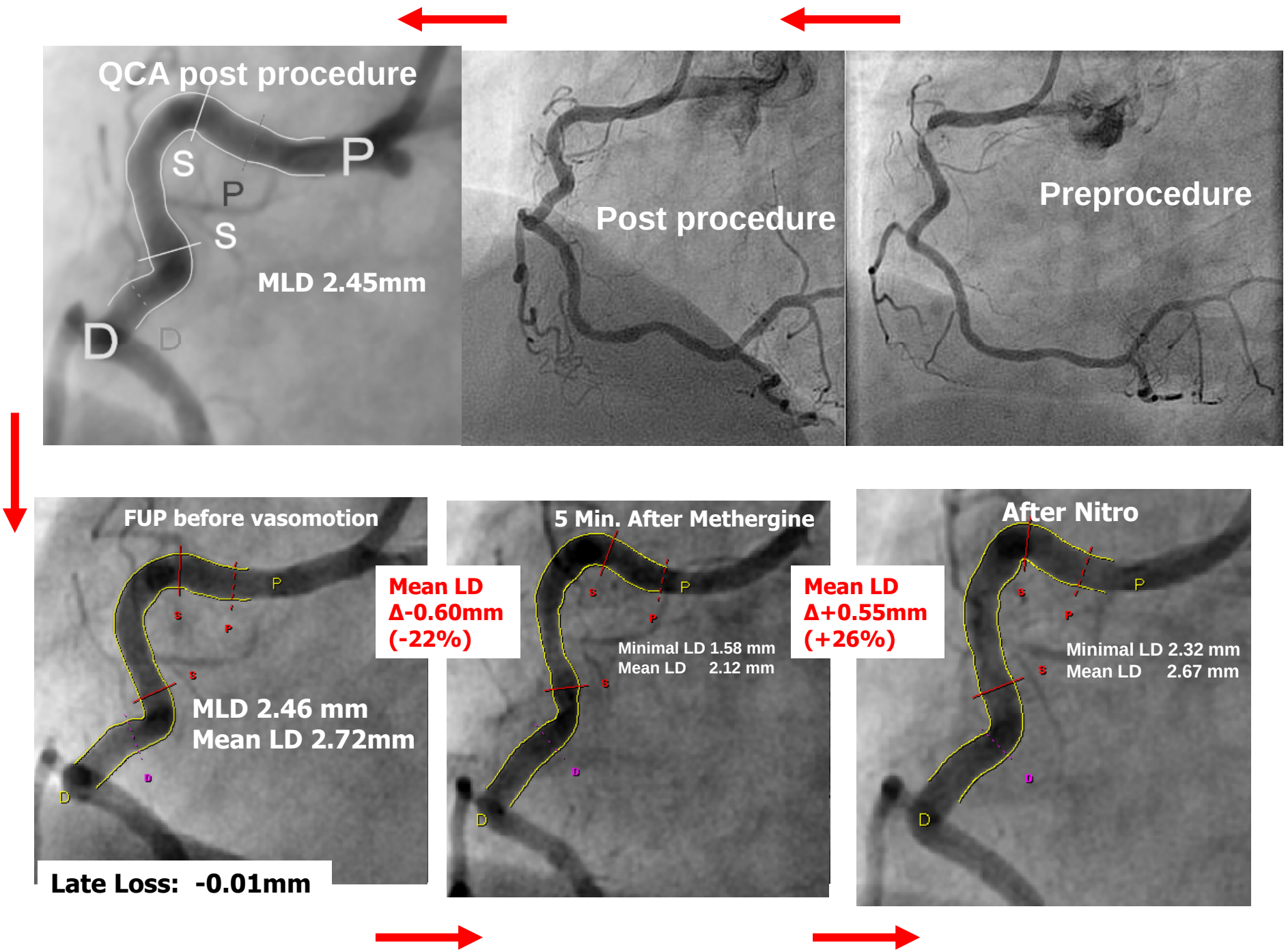
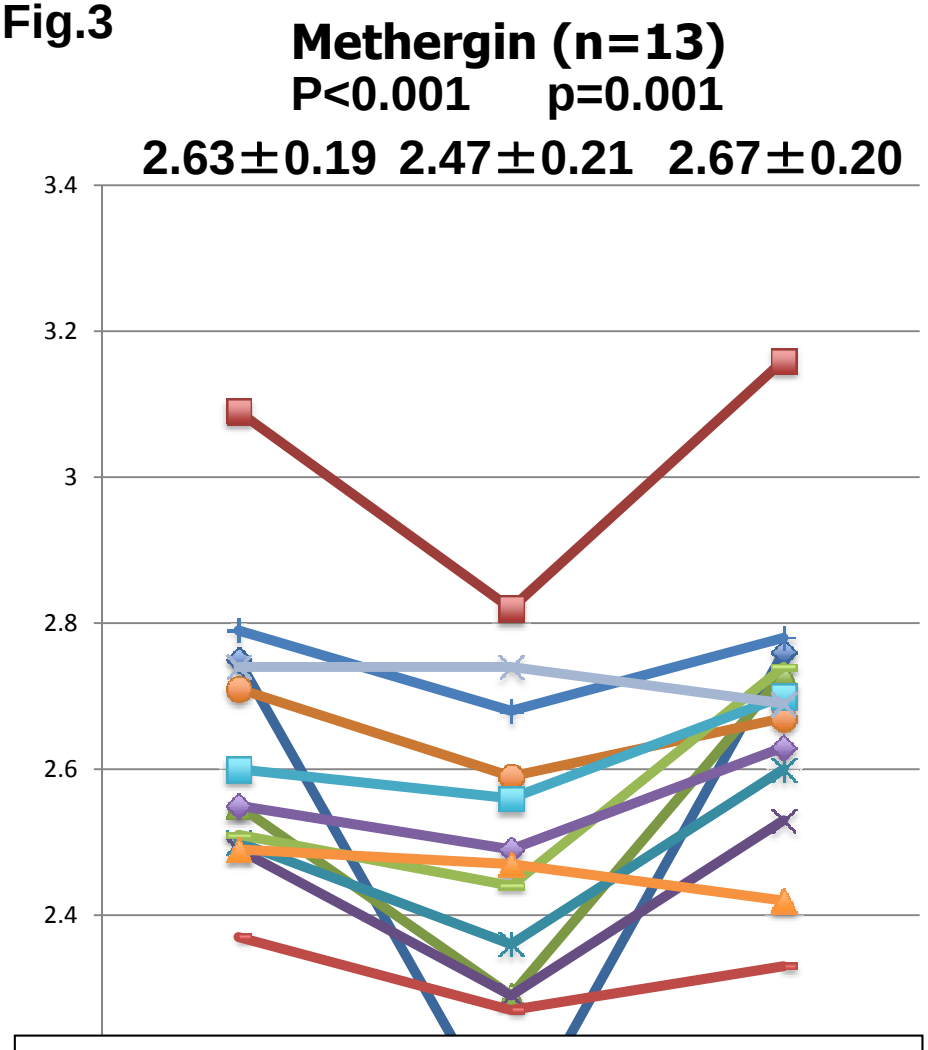
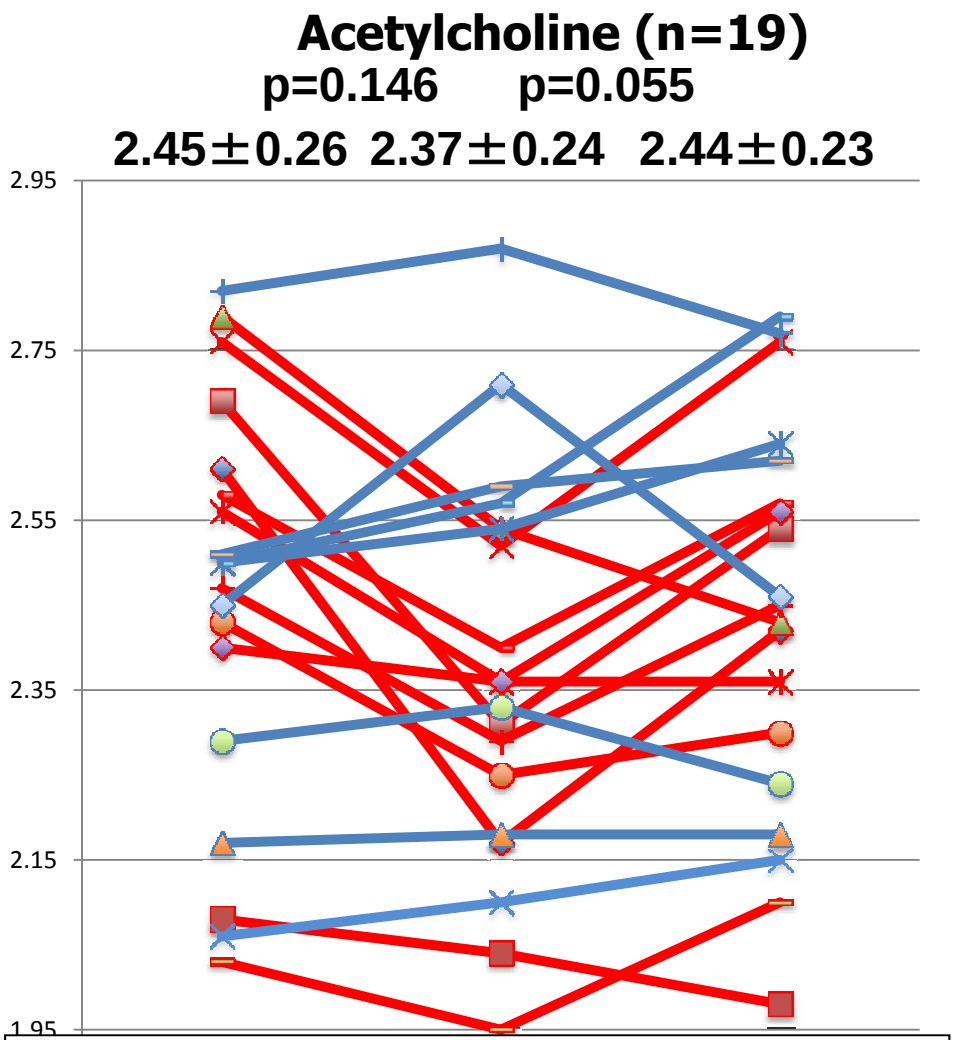

QCA post procedure
S
P
P
S
MLD 2.45mm
D
D
Post procedure
Preprocedure
FUP before vasomotion
MLD 2.46 mm
Mean LD 2.72mm
Late Loss: -0.01mm
Mean LD
Δ-0.60mm
(-22%)
5 Min. After Methergine
Minimal LD 1.58 mm
Mean LD 2.12 mm
Mean LD
Δ+0.55mm
(+26%)
After Nitro
Minimal LD 2.32 mm
Mean LD 2.67 mm

Fig.3

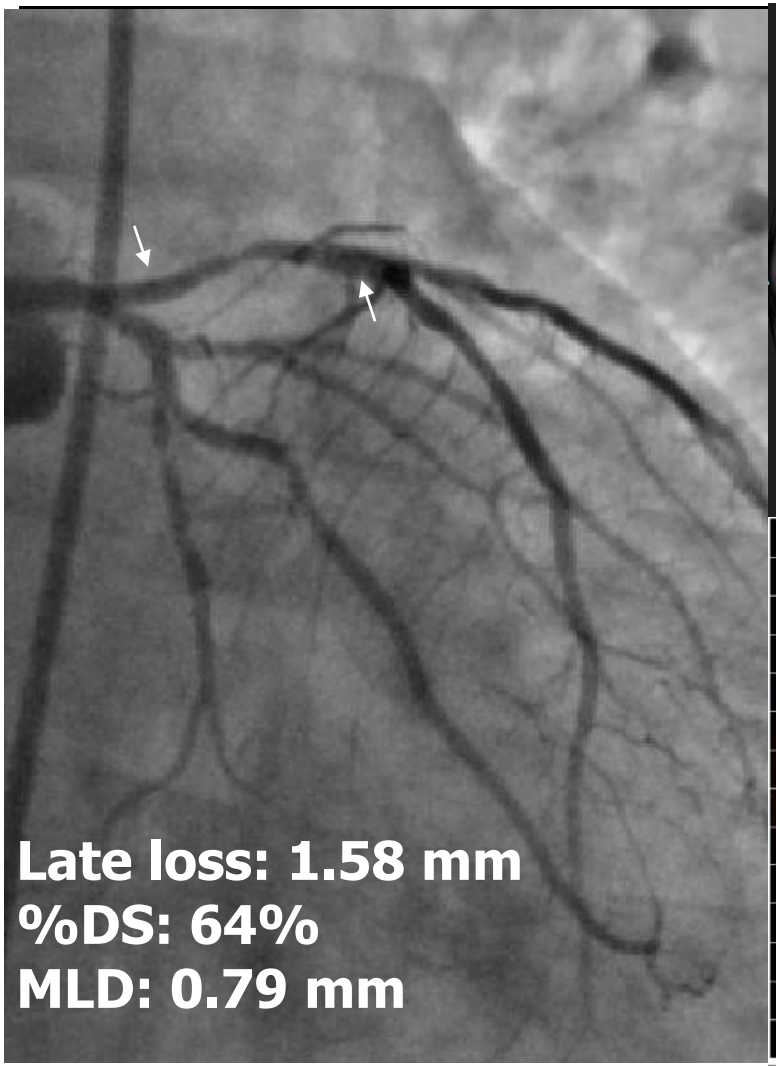


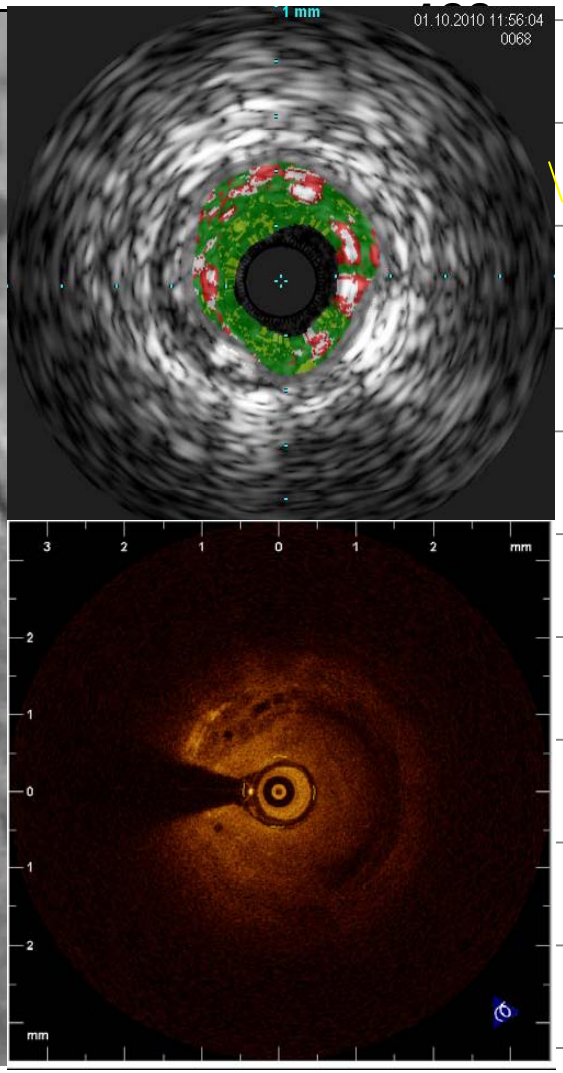


Methergine test showed significant vasoconstriction in the scaffolded segment, suggesting restoration of vasomotor tone.

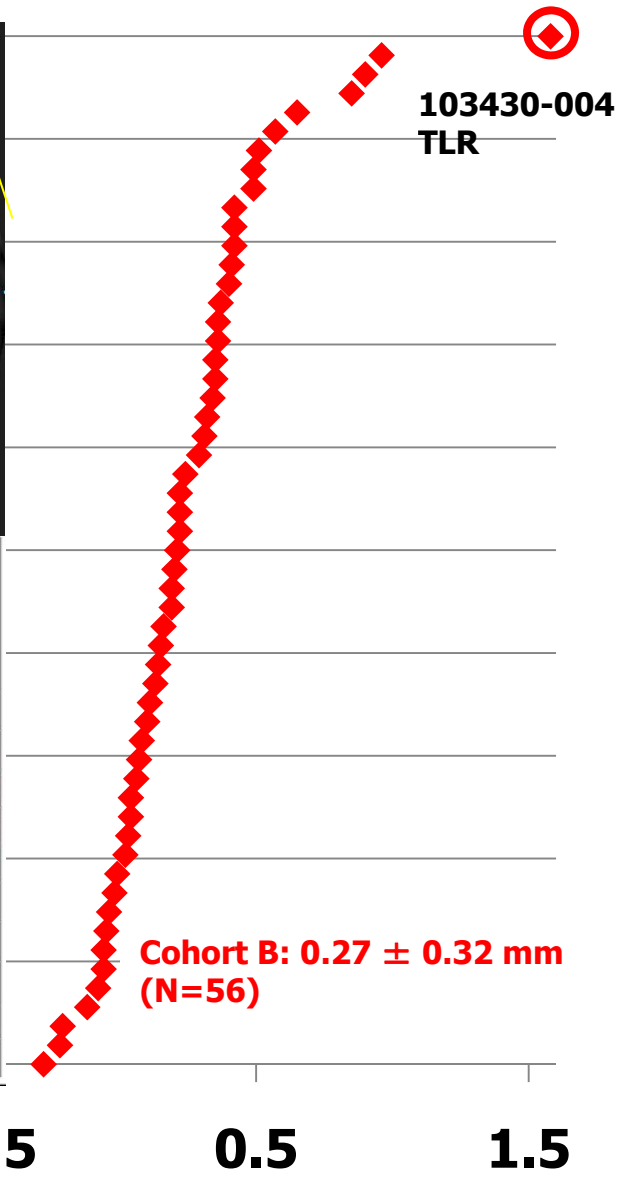
Out of 19 patients who underwent ach test, eight patients showed vasodilatation, and one had unchanged luminal dimension, and 10 patients showed vasoconstriction.

QCA results at 12 months



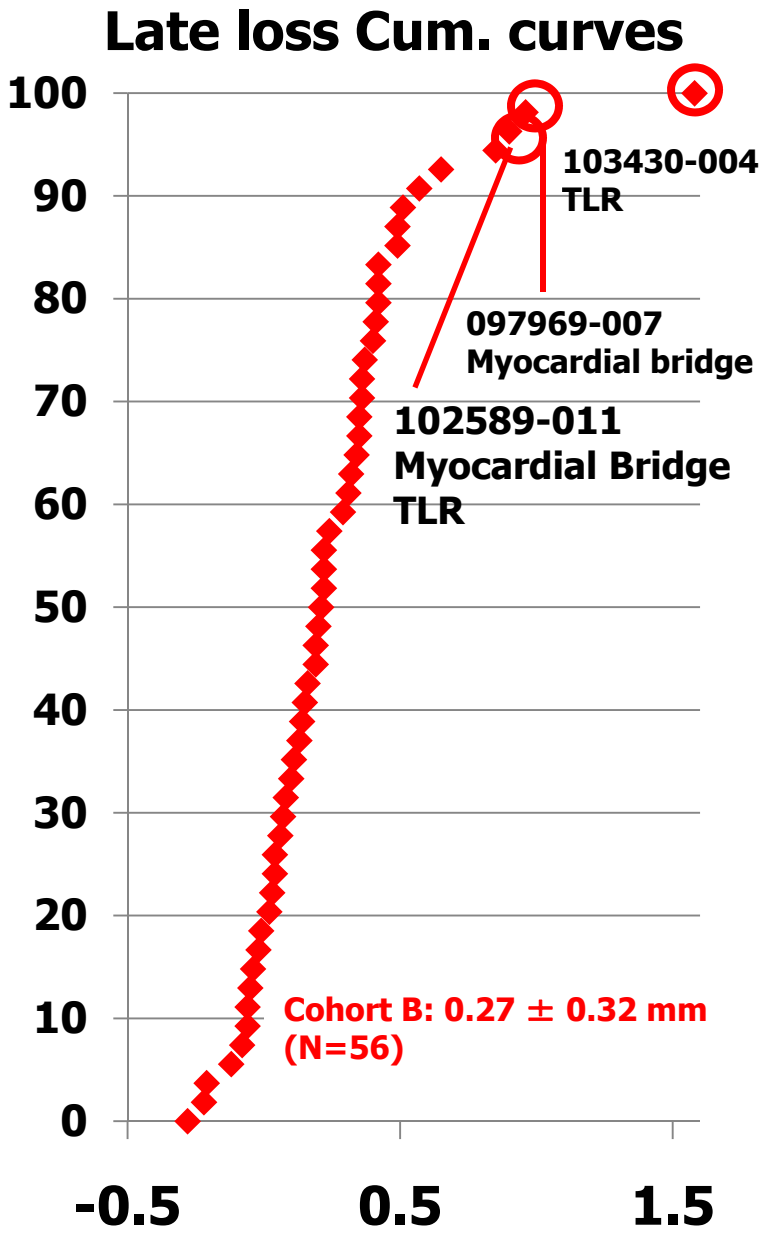


Late loss Cum. curves



QCA results at 12 months

N=56	Proximal	In-scaffold	Distal
Minimal Luminal Diameter			
Post procedure	2.43	2.27	2.18
At 12 months	2.30	2.00	2.10
P value	0.003	<0.001	0.047
Late Loss, mm	0.12	0.27	0.07
Diameter Stenosis, %			
Post procedure	13	15	15
At 12 months	12	21	13
P value	0.75	<0.001	0.10
Binary restenosis	0%	3.57%	0%



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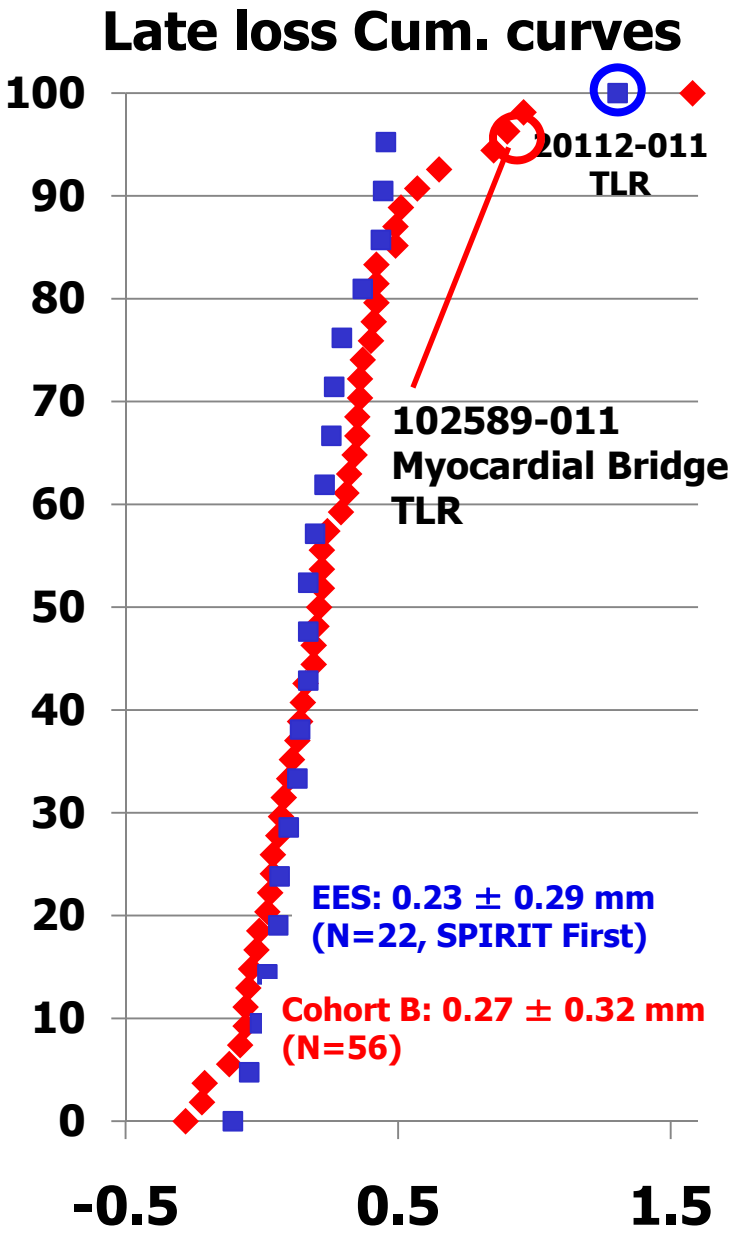
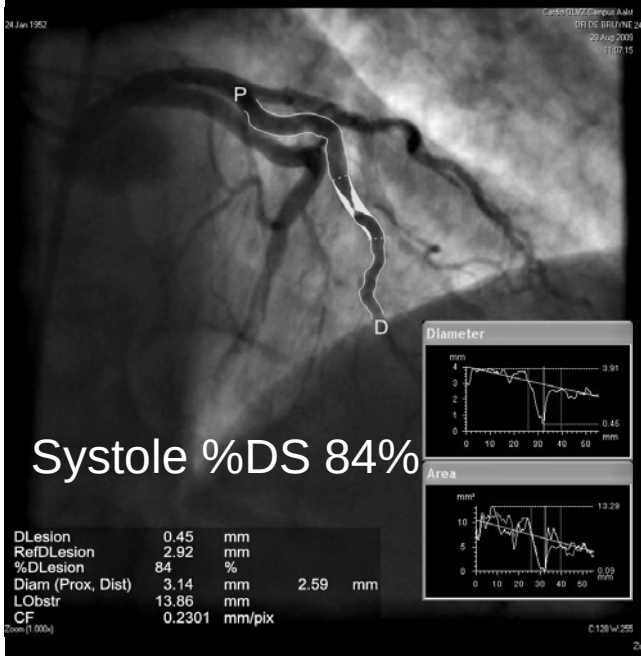


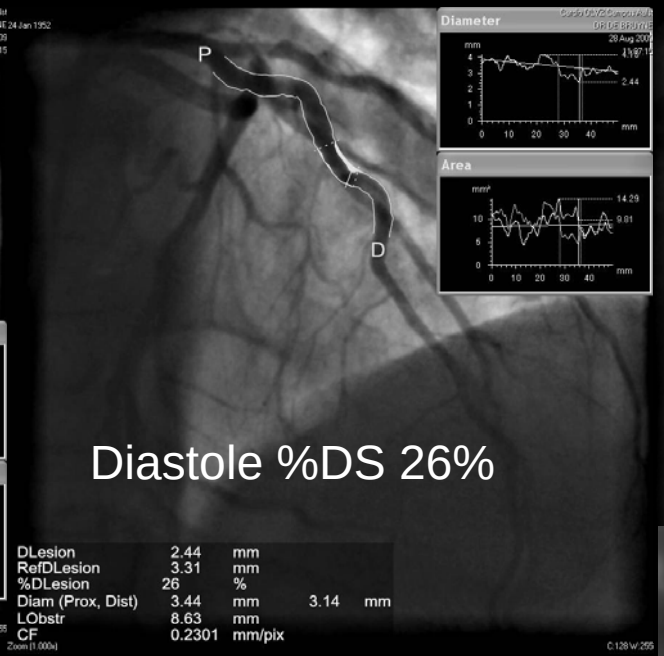
Before scaffolding

Post scaffolding



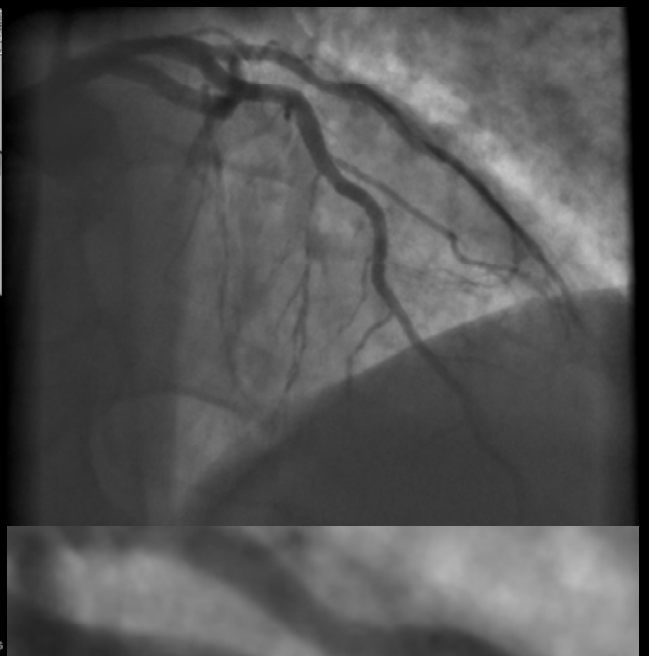
Systole %DS 84%

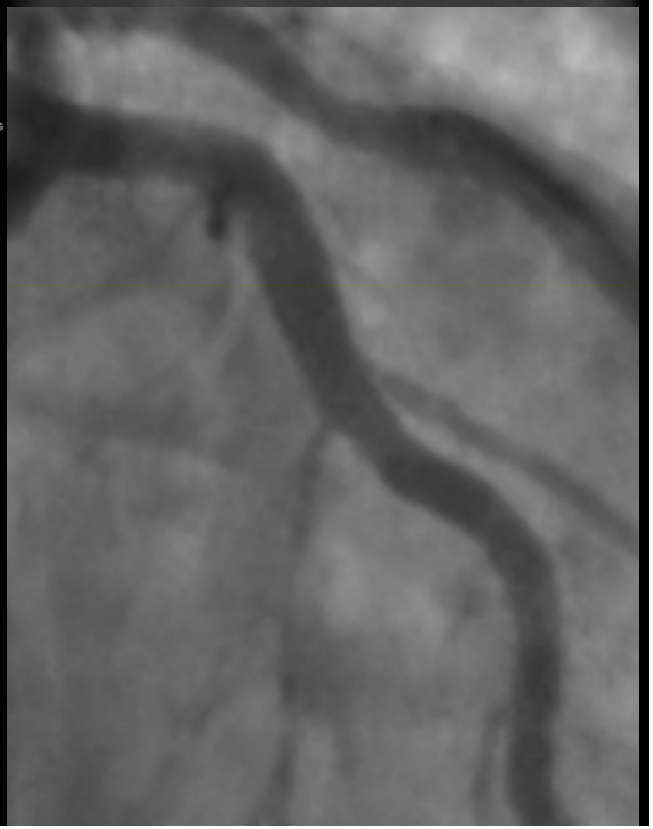
DLesion	0.45	mm		
RefDLesion	2.92	mm		
%DLesion	84	%		
Diam (Prox, Dist)	3.14	mm	2.59	mm
LObstr	13.86	mm		
CF	0.2301	mm/pix		



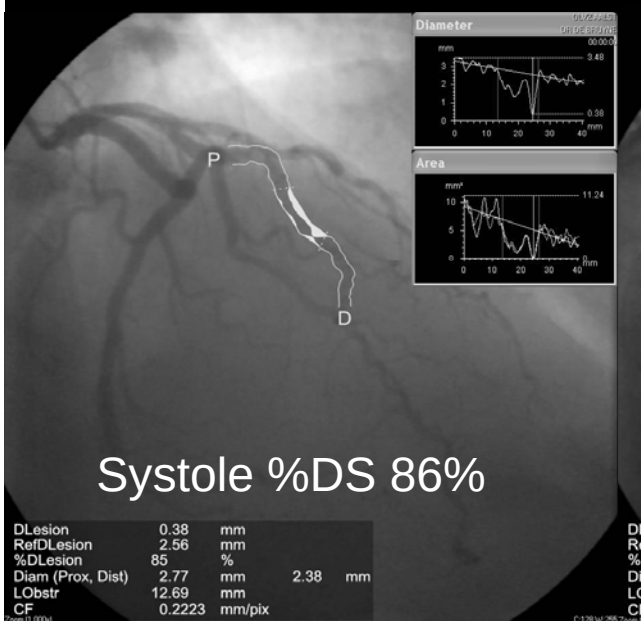
Diastole %DS 26%

DLesion	2.44	mm		
RefDLesion	3.31	mm		
%DLesion	26	%		
Diam (Prox, Dist)	3.44	mm	3.14	mm
LObstr	8.63	mm		
CF	0.2301	mm/pix		



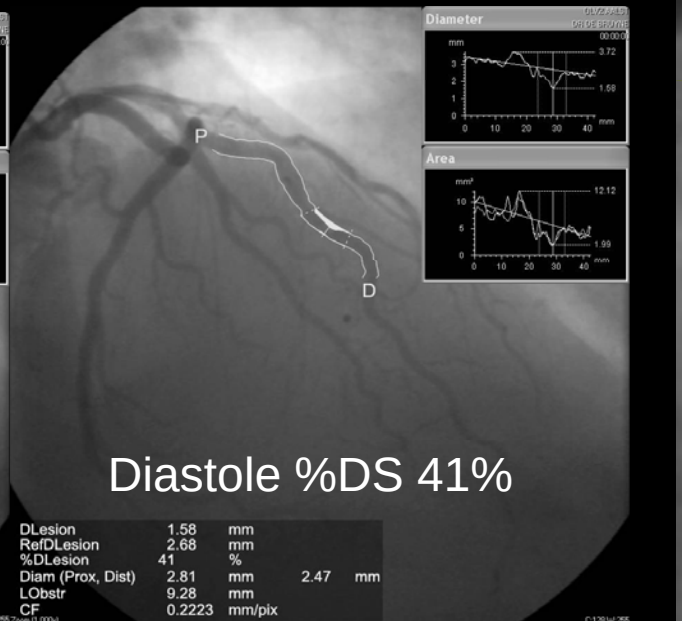


3 months later



Systole %DS 86%

DLesion	0.38	mm		
RefDLesion	2.56	mm		
%DLesion	85	%		
Diam (Prox, Dist)	2.77	mm	2.38	mm
LObstr	12.69	mm		
CF	0.2223	mm/pix		



Diastole %DS 41%

DLesion	1.58	mm		
RefDLesion	2.68	mm		
%DLesion	41	%		
Diam (Prox, Dist)	2.81	mm	2.47	mm
LObstr	9.28	mm		
CF	0.2223	mm/pix		

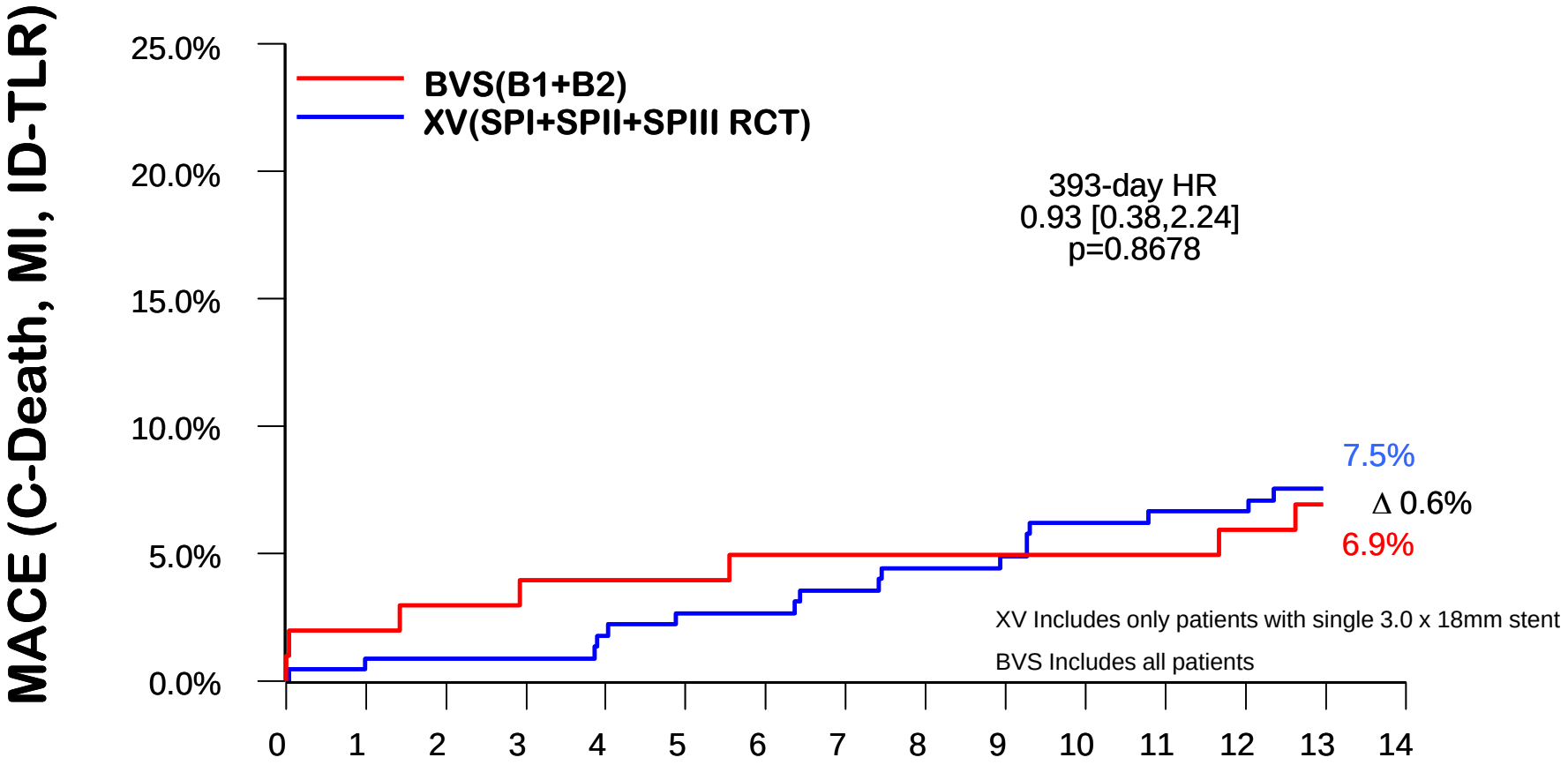
Clinical Results up to 12 Months

Non-Hierarchical	12 Months N = 56
Cardiac Death %	**0**
Myocardial Infarction % (n)	**3.6 (2)**
Q-wave MI	**0**
Non Q-wave MI	**3.6 (2)**
Ischemia driven TLR %	**3.6 (2)**
CABG	**0**
PCI	**3.6 (2)**
Hierarchical MACE % (n)	**7.1 (4)**

No scaffold thrombosis by ARC or Protocol

MACE: Cardiac death, MI, ischemia-driven TLR
TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

KM estimate of MACE rate in patients treated with BVS (Absorb Cohort B, n=101) vs. patients treated with a single 3x 18 mm metallic EES (Spirit I+II+III, n=227)



Patients at risk	0 days	37 days	194 days	284 days	365 days	393 days
BVS(B1+B2)	101	99	96	96	95	94
XV(SPI+SPII+SPIII RCT)	227	224	219	211	209	208

Summary

- Despite early ultrasound and optical signs of bioresorption, both IVUS and OCT confirmed the total absence of late reduction in scaffold area
- However, the mechanical integrity and radial force of the scaffold must have substantially subsided since the scaffolded segments exhibit clear signs of pharmacologically induced vasomotion.
- These observations substantiate the concept of restenosis as a time limited process, and thereby validate the principle of a transient need for a scaffold.
- The late lumen loss (0.27mm) and MACE rate at one year (7.1%) are comparable to those observed in a historical series of metallic everolimus-eluting stents.