



TCTAP 2017:

Seoul, April 27th , 2017: 7.24 am to 7.32 am



Drug Eluting Bioresorbable Mg Scaffold

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Conflicts of interest



Grant support:

Biotronik, Orbus Neich, Abbott, Medtronic, Cardiac Dimensions

Speaker's bureau:

Biotronik, Orbus Neich, Abbott, Medtronic, Lilly, Volcano, Cardiac Dimensions (Proctor)

Consultancy:

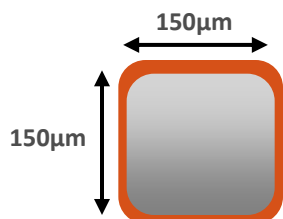
Biotronik, Orbus Neich, Abbott



DREAMS 2G (Magmaris) Basics



Sirolimus + PLLA (BIOLute)



90-Day Faxitron, porcine explant

- 6-crown 2-link design,
- 150µm strut thickness
- 150µm strut width
- Optimized scaffold design for
 - Higher bending flexibility
 - Higher acute radial force
 - Slower absorption rate: 95% at 12 months
- **Sirolimus drug elution & PLLA (ORSIRO BIOLute coating)**
- Tantalum radiopaque markers
- Gained CE mark in June 2016

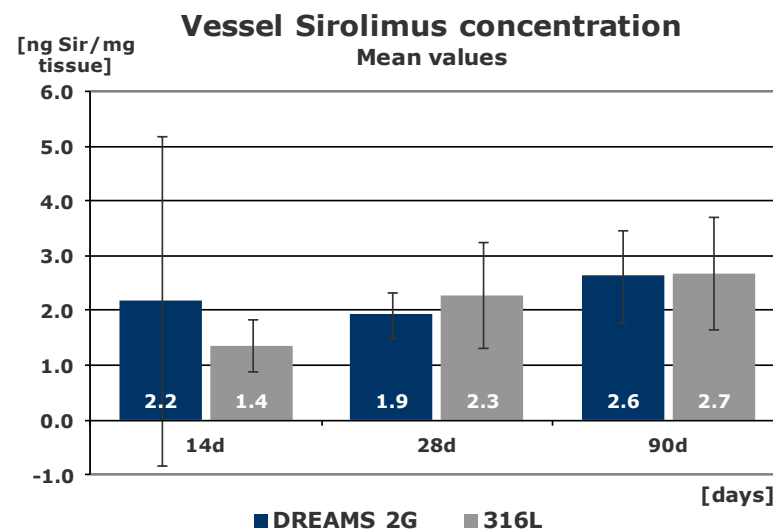
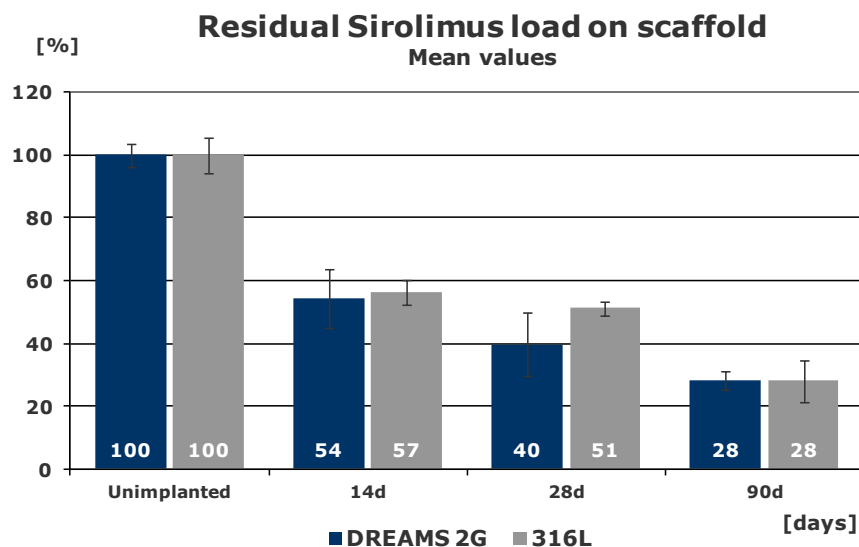


DREAMS 2G (Magmaris) Basics

Sirolimus elution kinetics



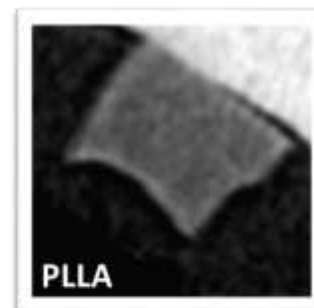
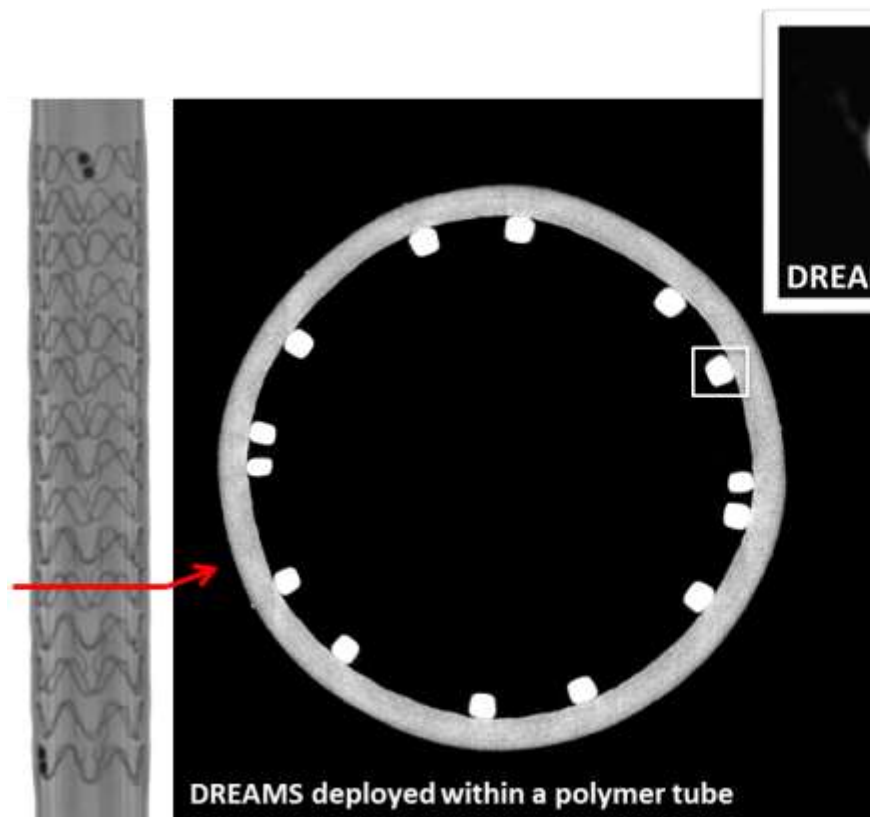
Comparison of DREAMS 2nd Generation to an identical scaffold made from stainless steel in a porcine coronary artery model.





DREAMS 2G (Magmaris) Basics

Strut shape

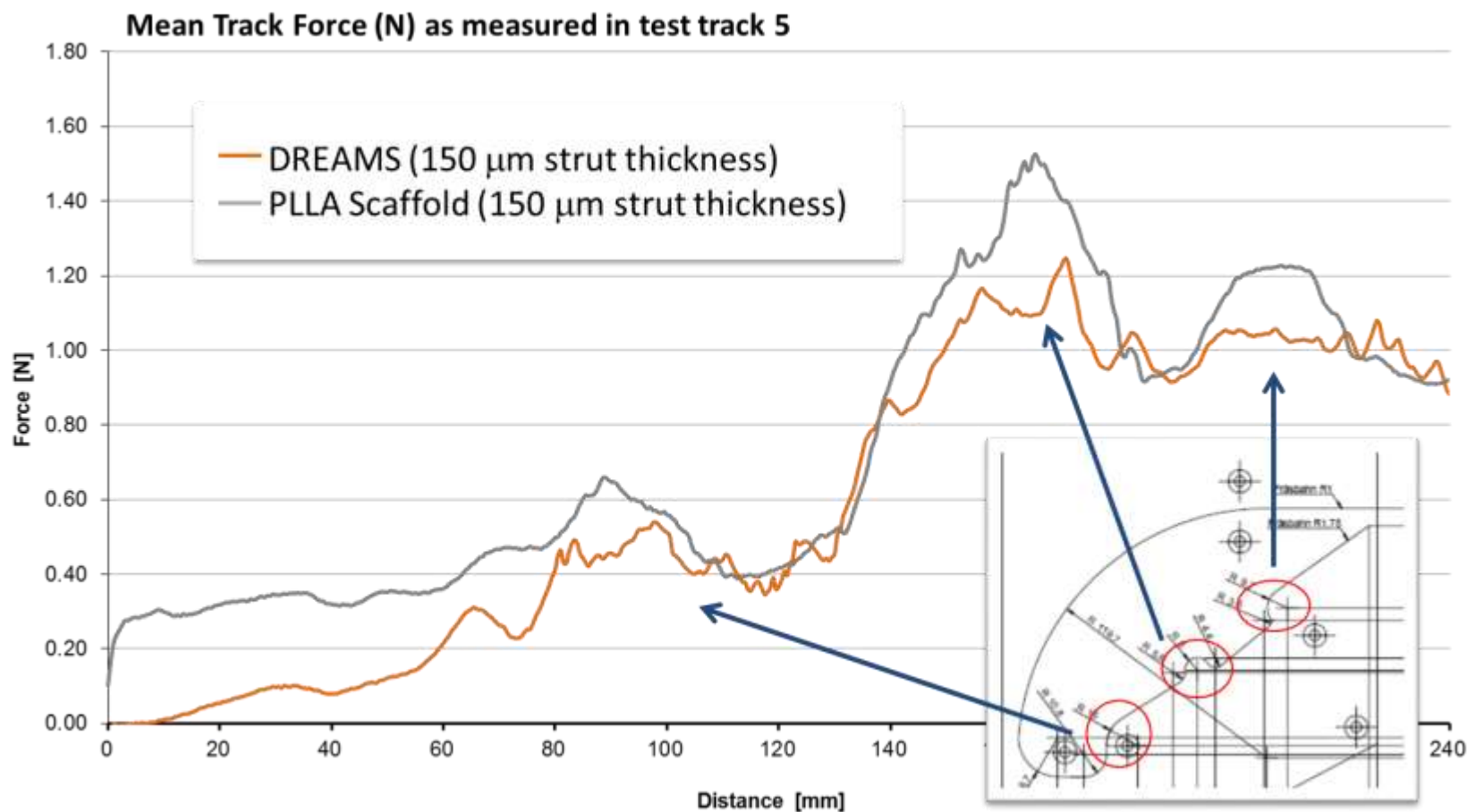


- Electropolished surface result in rounded struts
- Rounded Mg struts may better embedding into the vessel wall and allow improved peri-strut flow



DREAMS 2G (Magmaris) Basics

Benchmark trackability test vs Absorb BVS



Source: Data on file at BIOTRONIK AG.

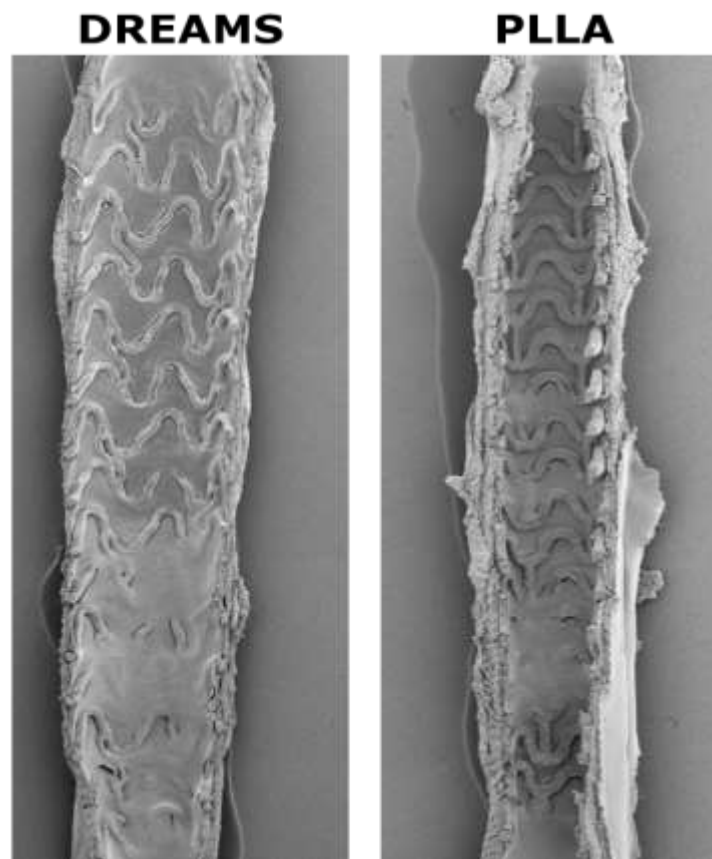
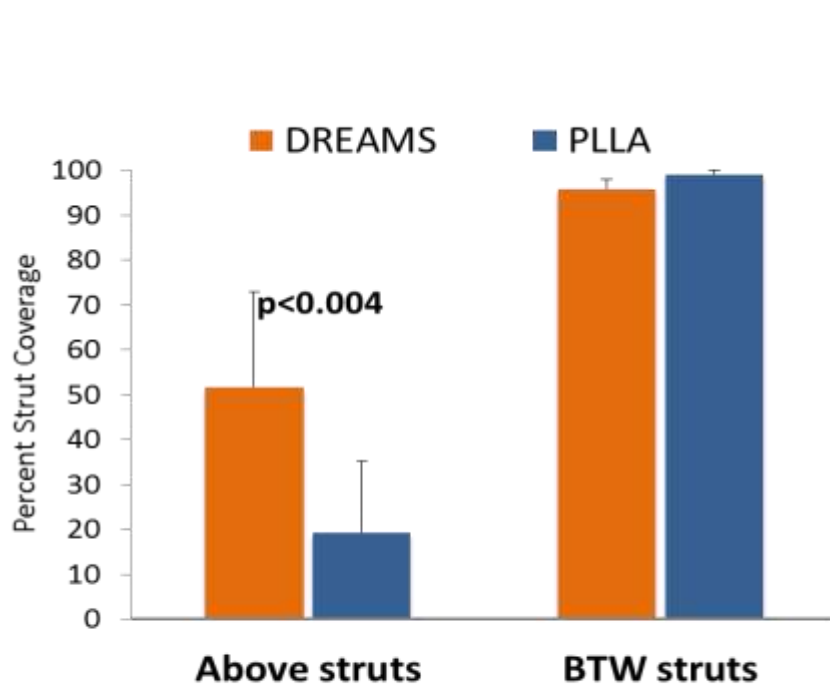


DREAMS 2G (MAGMARIS)

Endothelialization vs Absorb BVS:



Endothelialization in New Zealand white rabbits at 28 days



Source: Adapted from M. Joner, oral presentation, CRT 2015.



Clinical Study: BIOSOLVE-II



Study design

Prospective, multi-center FIM. Single de novo coronary artery lesions in up to two coronary arteries

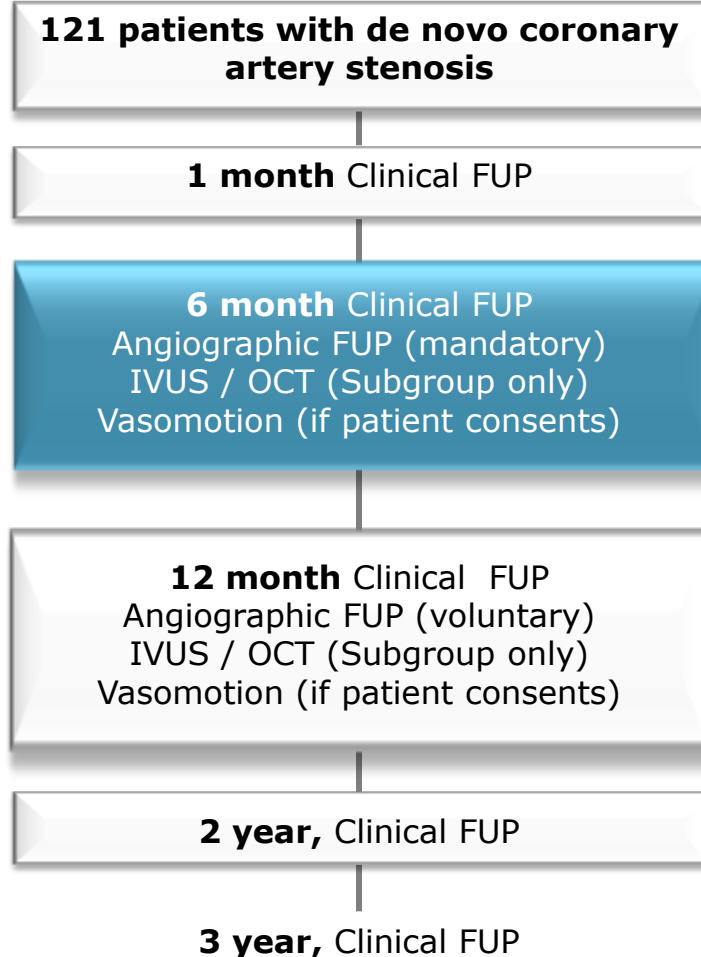
Primary endpoints

In-segment late lumen loss @ 6-month

Coordinating Clinical Investigator

M.Haude, Lukaskrankenhaus GmbH, Neuss, Germany

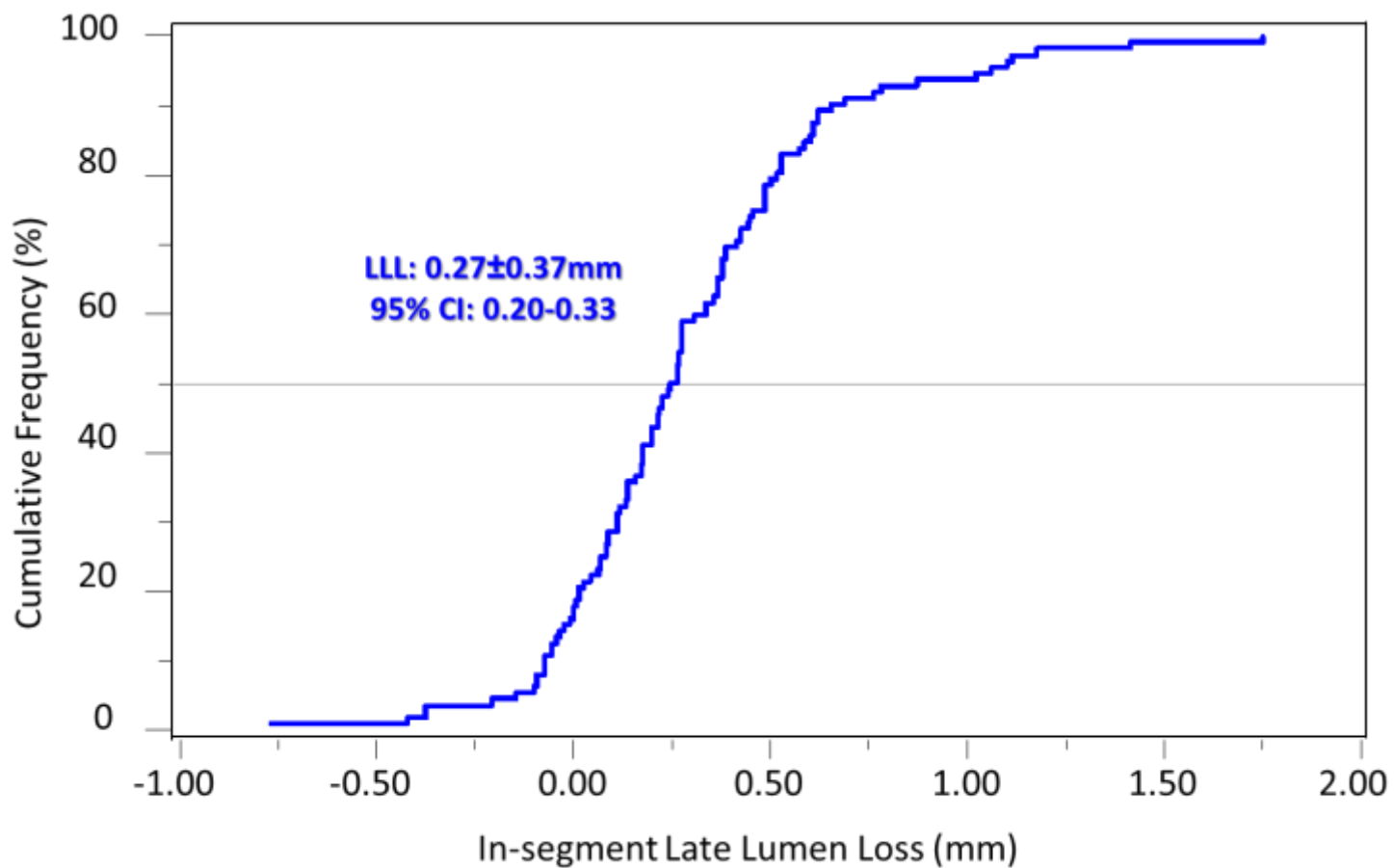
First patient enrolled Oct 8, 2013



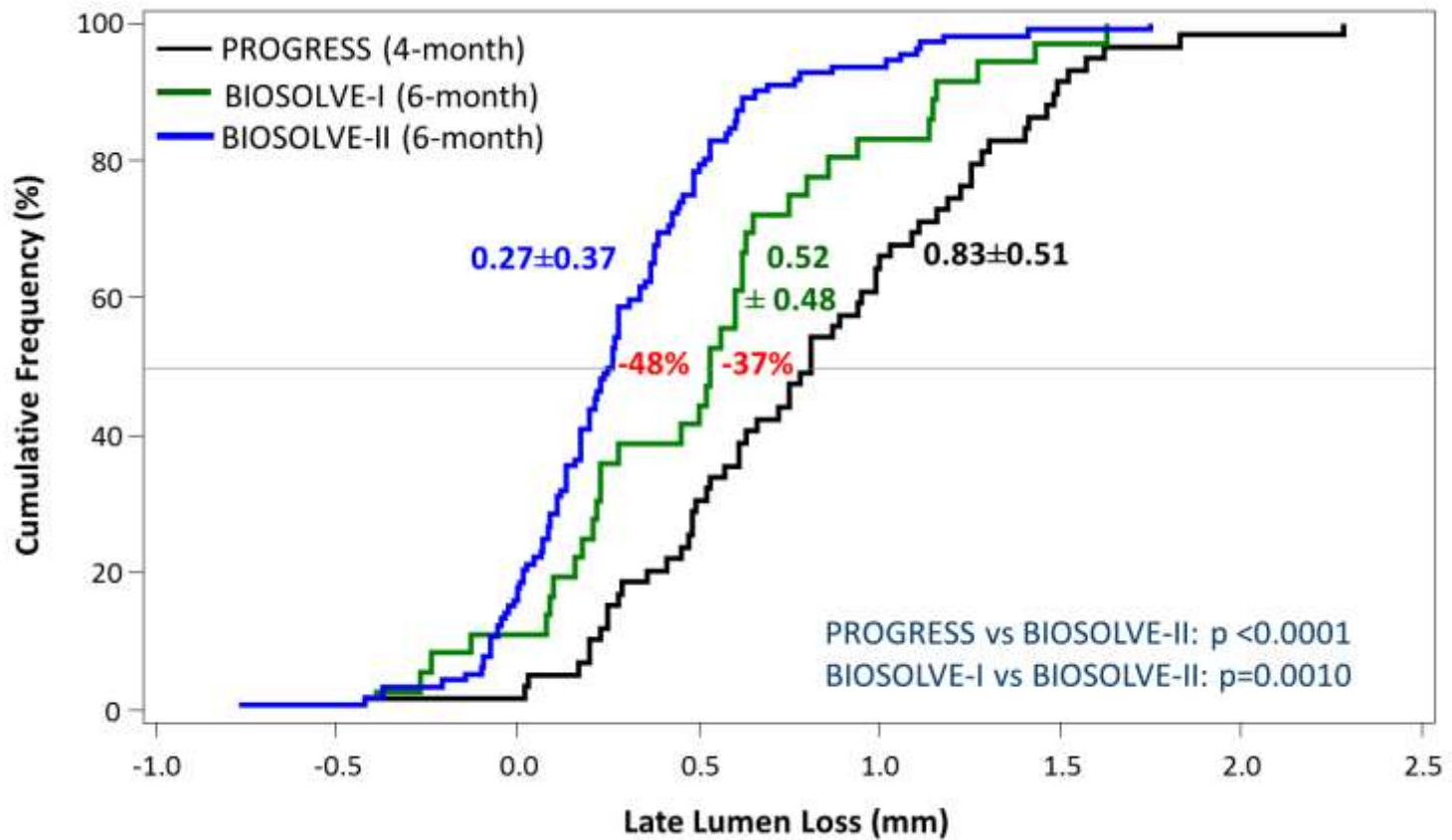


Primary Endpoint

In-segment Late Lumen Loss at 6-month



Comparison of in-segment LLL in PROGRESS, BIOSOLVE-I and BIOSOLVE-II

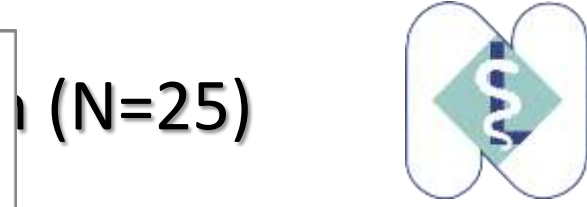
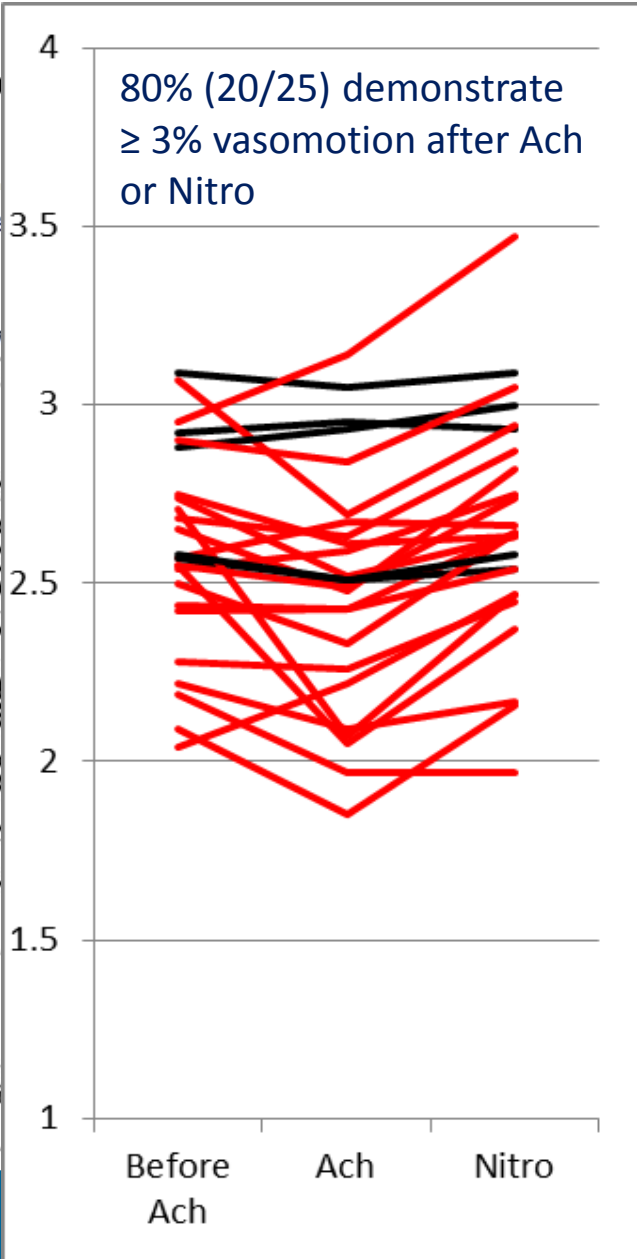
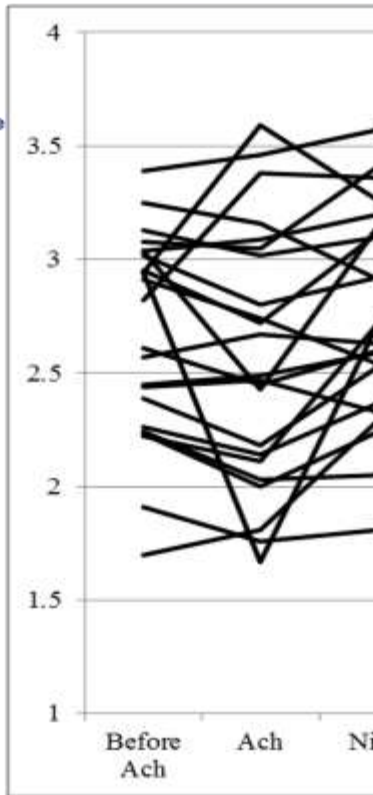




Vasomotility

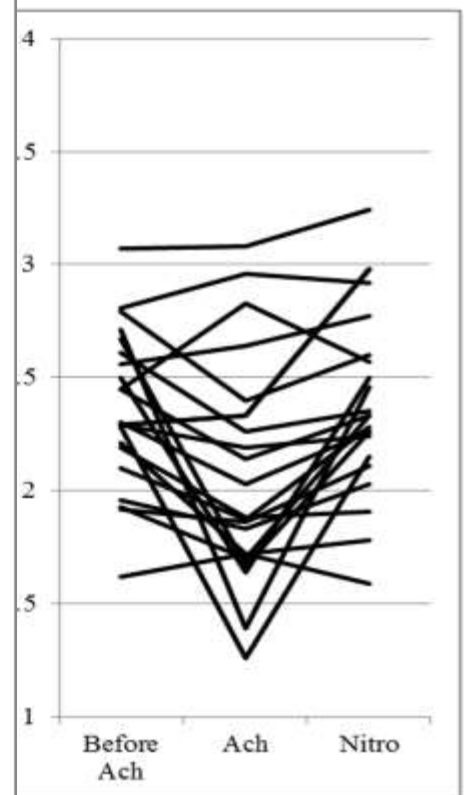
Mean Lumen Diameter Proximal (mm ± SD)
2.68 ± 0.45 2.57 ± 0.56 2.7

Ach = Acetylcholine
Nitro = Nitroglycerine



(N=25)

Mean Lumen Diameter Distal (mm ± SD)
2.39 ± 0.35 2.09 ± 0.50 2.39 ± 0.40





IVUS Analysis

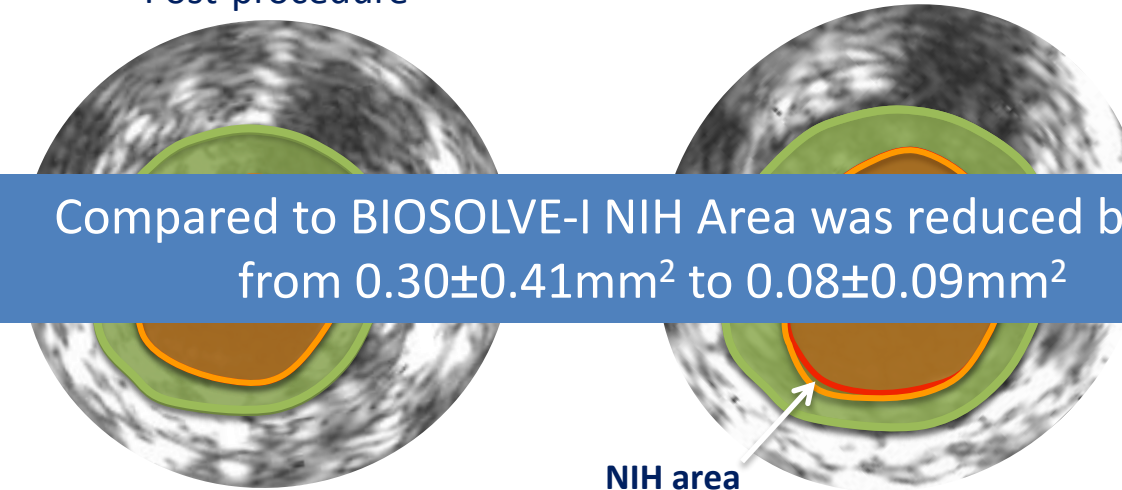
Subgroup N=30




Post-procedure

6-month

Compared to BIOSOLVE-I NIH Area was reduced by 73%
from $0.30 \pm 0.41 \text{ mm}^2$ to $0.08 \pm 0.09 \text{ mm}^2$



Lumen area 
Scaffold Area 

Vessel area 
Plaque area 

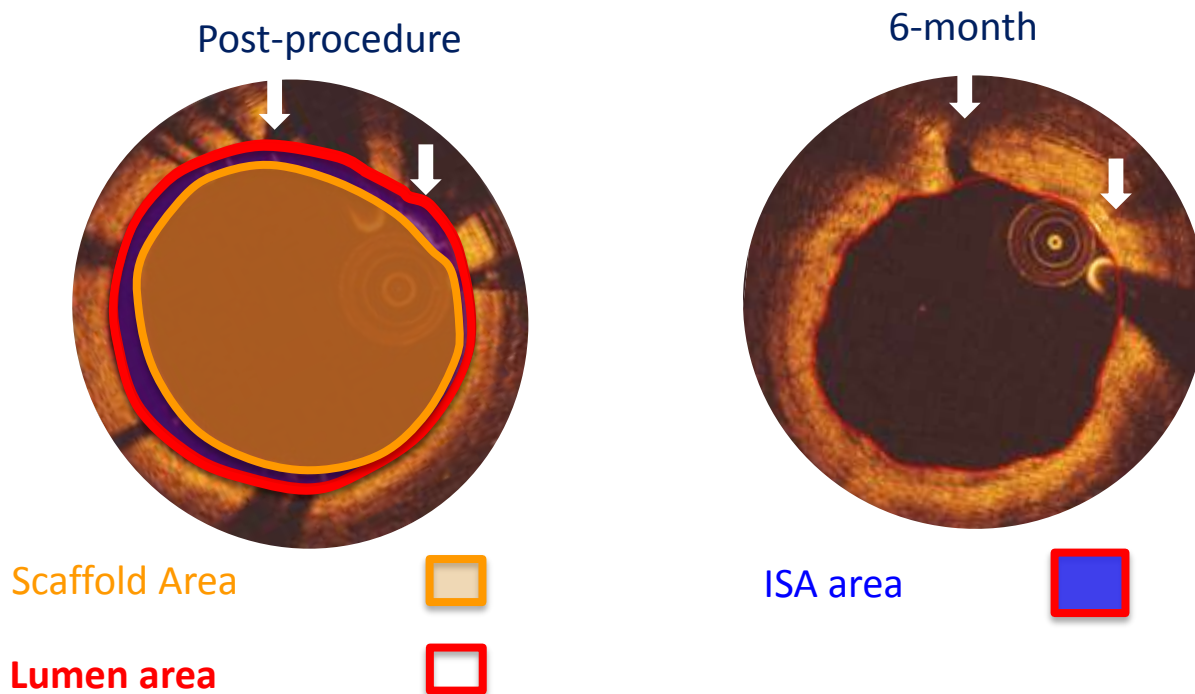
NIH= Neointimal Hyperplasia

NA = Not Applicable	Post-procedure	6-month	Δ 6-month vs post [95% CI]	p-value
Vessel area (mm ²)	14.06 \pm 3.17	14.21 \pm 3.14	0.15[-0.13-0.42]	0.289
Scaffold area (mm ²)	6.24 \pm 1.15	6.21 \pm 1.22	-0.03[-0.29-0.23]	0.803
Plaque area (mm ²)	7.76 \pm 2.41	8.06 \pm 2.23	0.29[0.11-0.47]	0.002
NIH area (mm ²)	NA	0.08 \pm 0.09	NA	NA



OCT Analysis

Subgroup Analysis



ISA = Incomplete Strut Apposition	Post-procedure
Mean ISA area (mm ²)	0.16±0.16
Mean intraluminal mass area (mm ²)*	0.00±0.00

*Intraluminal mass is defined as a defect free from the vessel wall



Comparison of clinical results in PROGRESS, BIOSOLVE-I and BIOSOLVE-II

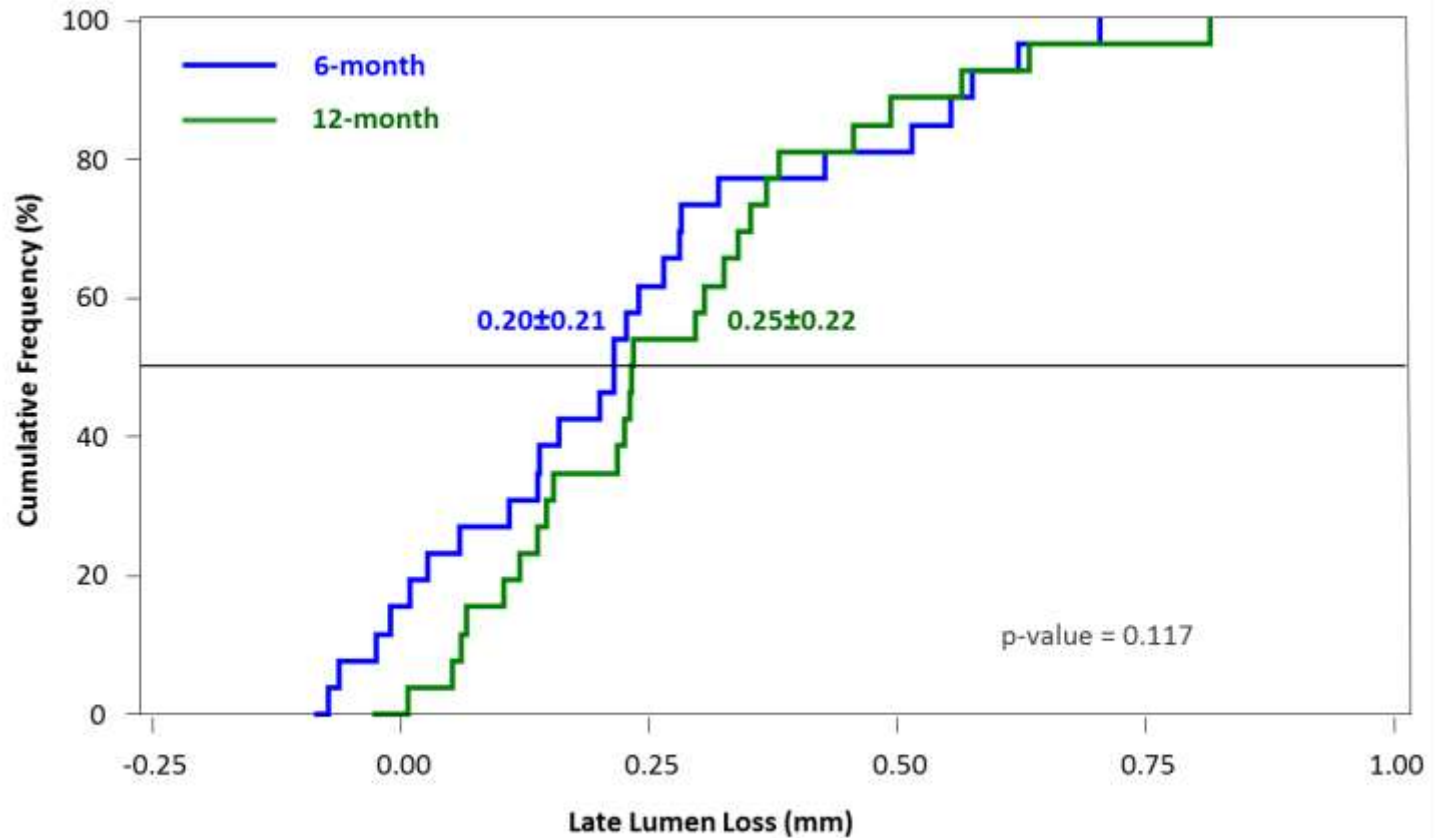


Clinical results at 6-month (4-month for PROGRESS)

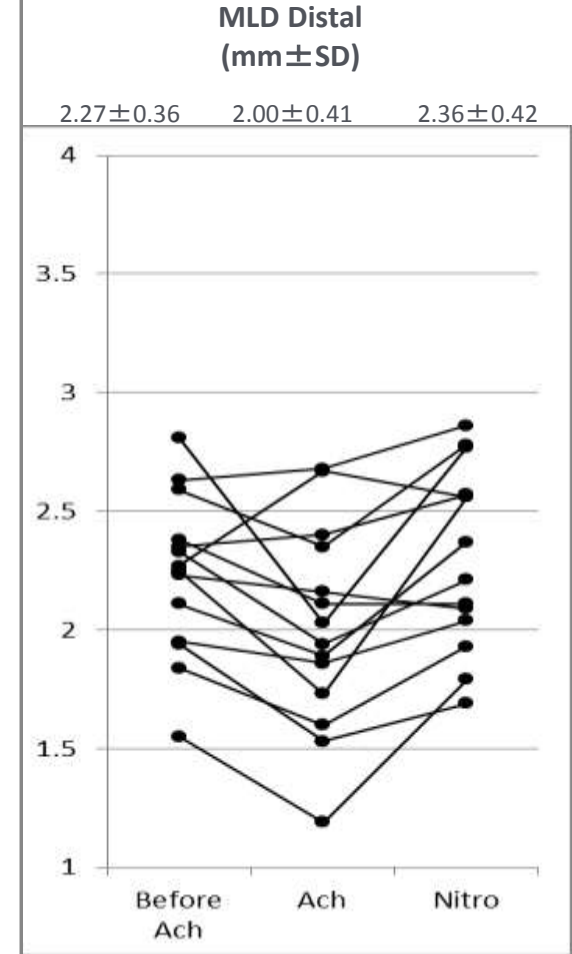
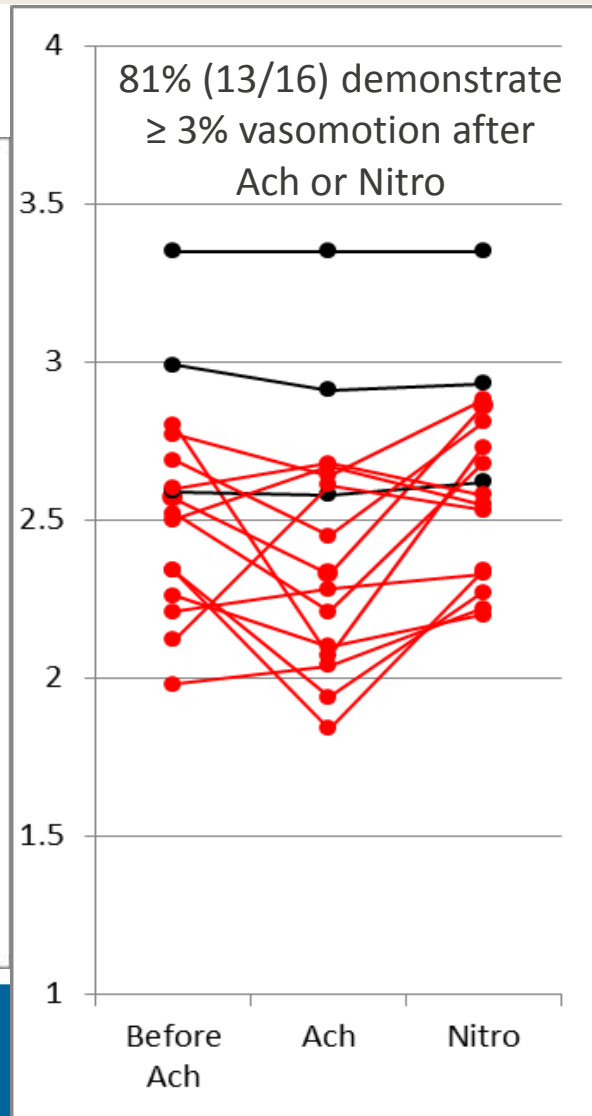
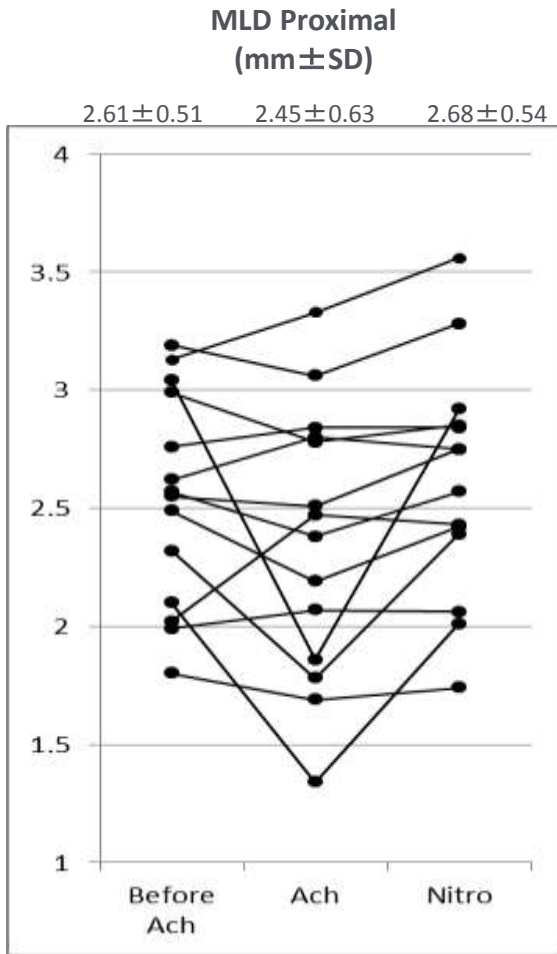
	PROGRESS N=63	BIOSOLVE-I N=46	BIOSOLVE-II N=123
TLF¹ (%)	23.8	4.3	3.3
Cardiac Death (%)	0.0	0.0	0.8
Target Vessel MI (%)	0.0	0.0	0.8
Clinically driven TLR (%)	23.8	4.3	1.7
CABG	0.0	0.0	0.0
Scaffold Thrombosis Definite or probable	0.0	0.0	0.0

1. Composite of cardiac death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG

Comparison of in-scaffold Late Lumen Loss in 42 serial subjects at 6 (Primary Endpoint) and 12-month Follow-up



Vasomotion results at 12 months in 16 subjects





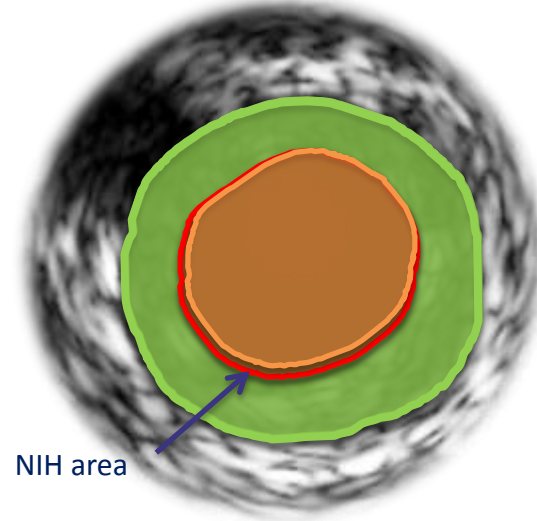
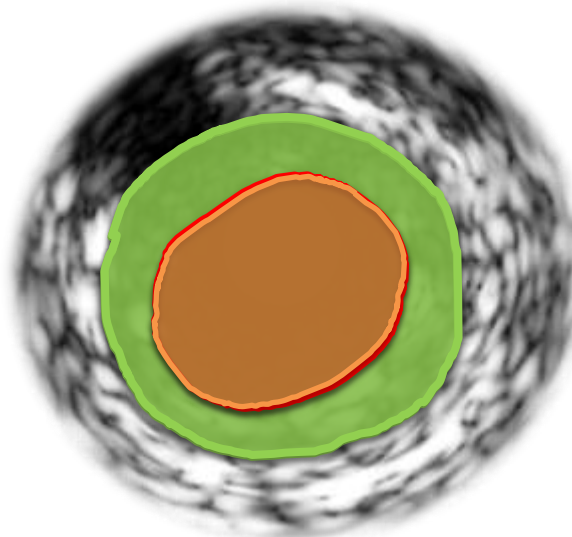
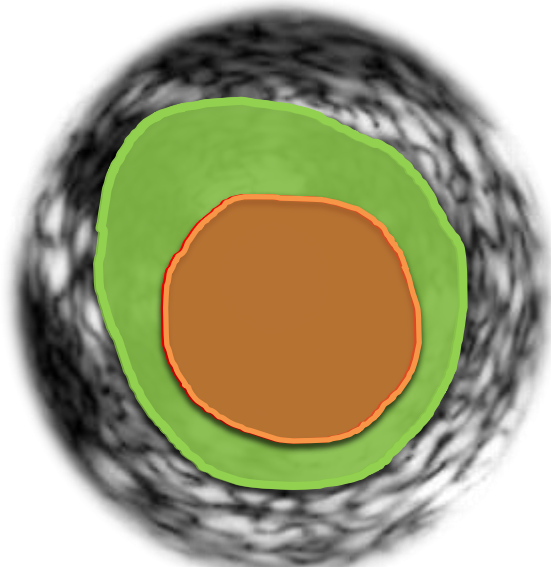
Serial IVUS analysis in 11 subjects at baseline, 6- and 12-month



Post-procedure

6-month

12-month



NIH area

Lumen area



Scaffold Area



Vessel area



Plaque area



NIH= Neointimal Hyperplasia

	Post-procedure [95% CI]	6-month [95% CI]	12-month [95% CI]	Δ 12-month vs post [95% CI]	Δ 6- vs 12-month [95% CI]
Vessel area, mm ²	15.38 [13.40-16.40]	14.72 [13.38-16.67]	14.98 [13.17-15.79]	-0.61 [-0.88-0.32]	0.43[-0.82-0.42]
Scaffold area, mm ²	6.58 [6.33-6.76]	6.29 [5.46-7.11]	6.09 [5.55-6.67]	-0.34 [-0.92-0.07]	-0.14[-0.46-0.31]
Plaque area, mm ²	8.59 [6.61-9.25]	8.54 [7.47-9.81]	9.07 [7.22-9.58]	-0.33 [-0.45-0.84]	0.05[-0.41-0.25]
NIH area, mm ²	na	0.05 [0.00-0.13]	0.13 [0.03-0.19]	na	0.05[-0.02-0.13]



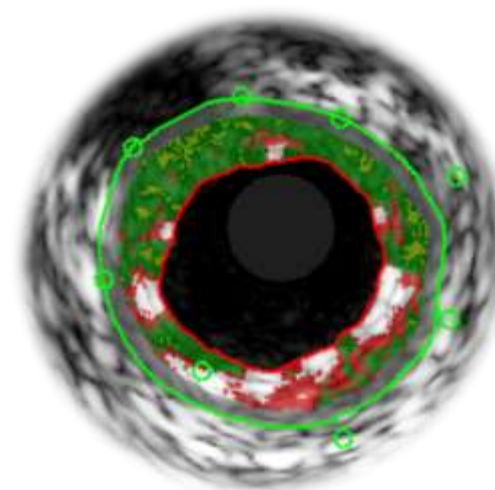
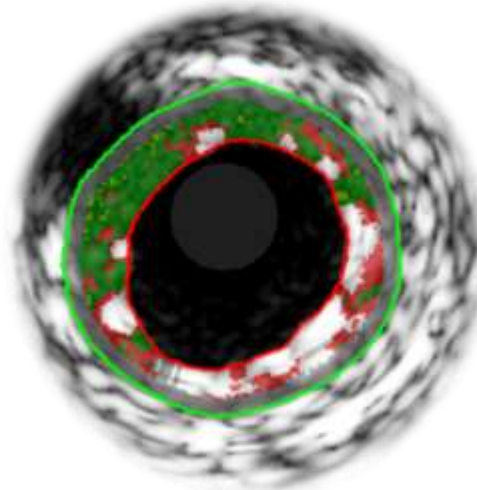
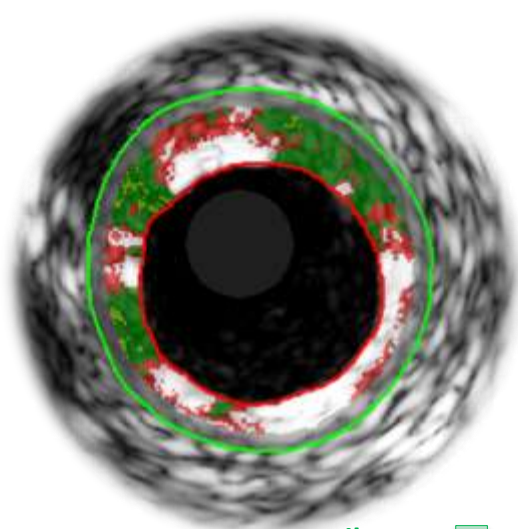
Serial IVUS VH analyses in 11 subjects at post-procedure, 6-and 12-month



Post-procedure

6-month

12-month



Fibrous 

Fibrous Fatty 

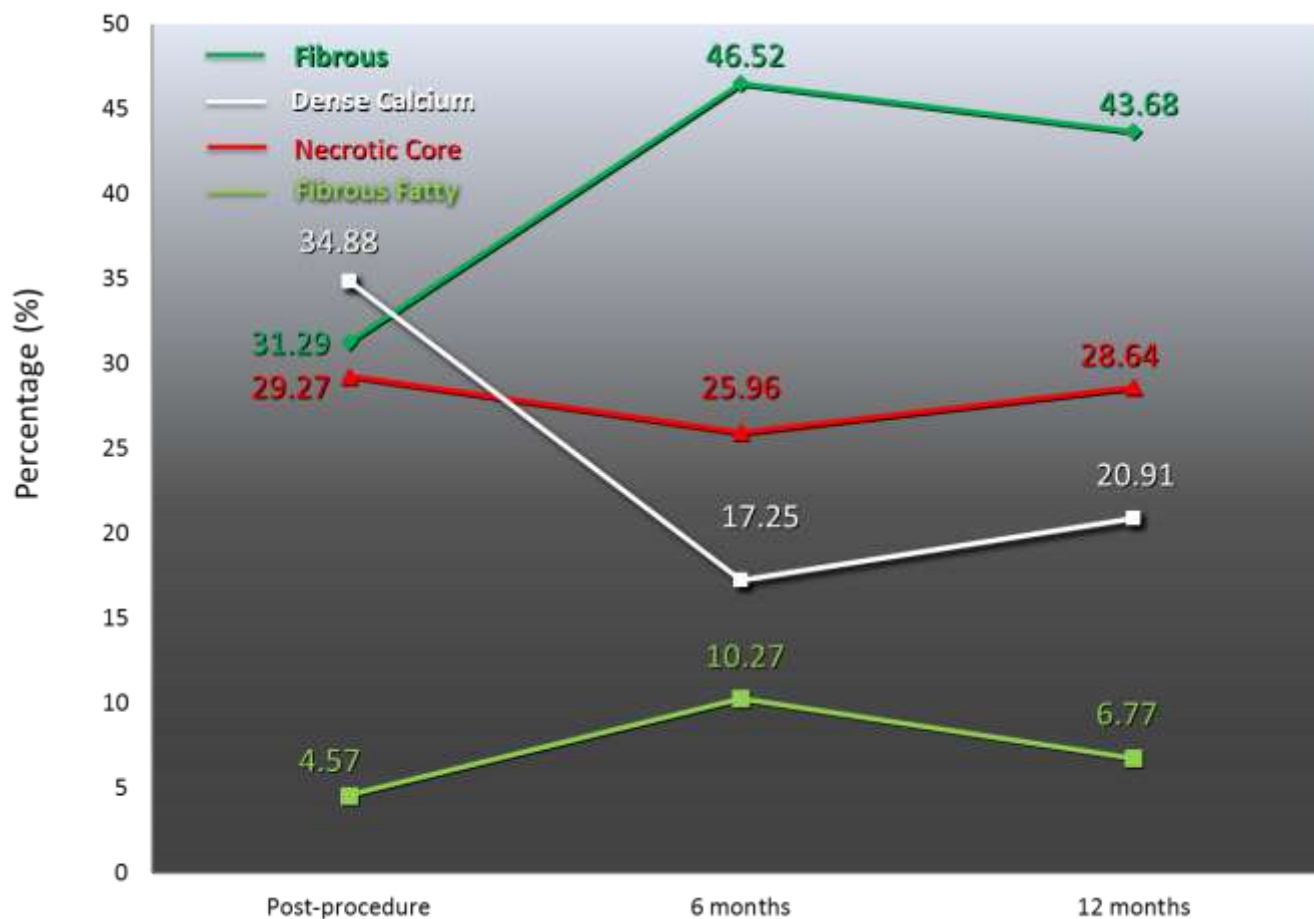
Necrotic core 

Calcium 

	Post-procedure	6-month	12-month	Δ 12-month vs post (P Value)	Δ 6- vs 12-month (P Value)
Fibrous , %	31.29	46.52	43.68	12.39 (<.0001)	-2.84 (0.2409)
Fibrous Fatty , %	4.57	10.27	6.77	2.2 (0.2245)	5.7 (0.0041)
Necrotic core , %	29.27	25.96	28.64	-0.63 (0.7556)	2.68 (0.1951)
Calcium , %	34.88	17.25	20.91	-13.97 (<.0001)	3.66 (0.1212)



Serial IVUS Virtual Histology analysis in 11 subjects at post-procedure, 6-and 12-month





Clinical Results until 12-month follow-up



	6-month		12-month	
	N=120	%	N=118	%
TLF¹	4	3.3	4	3.4
Cardiac Death	1 ²	0.8	1 ²	0.8
Target Vessel MI	1	0.8	1	0.8
Clinically driven TLR	2	1.7	2	1.7
CABG	0	0.0	0	0
Scaffold Thrombosis Definite or probable	0	0.0	0	0.0

1. Composite of cardiac death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG

2. 58 old smoker, CV RF: hypertension and hyperlipidemia, stable angina CCS Class II, treated with a DREAMS 2G 3.0x20mm in the distal RCA. Patient experienced an unwitnessed death 134 days post procedure. Since a cardiac cause could not be ruled out, patient was adjudicated as cardiac death by the Clinical Event Committee



Conclusion



- DREAMS 2G (Magmaris) in BIOSOLVE-II demonstrates **significantly improved in-segment LLL ($0.27\pm 0.37\text{mm}$) at 6-month** compared to its precursor devices tested in the PROGRESS ($0.83\pm 0.37\text{mm}$) and the BIOSOLVE-I study ($0.52\pm 0.48\text{mm}$), which **remained stable between 6- and 12-month**
- **Clinical outcomes remained stable between 6- and 12-month FUP** with low TLF (3.4%) and TLR (1.7%) rates, comparable to other absorbable scaffolds and permanent drug-eluting stents
- There was **no definite or probable scaffold thrombosis until 12-month FUP**
- **Vasomotion** of the scaffolded coronary segment **was already demonstrated after 6 months** and showed no significant change from 6 to 12-month FUP
- **Serial IVUS** in a subgroup of 11 patients **demonstrated preservation of the scaffold area with a small neo-intimal areal until 12-month FUP**
- **Serial Virtual Histology IVUS** showed a **decrease in dense calcium** content over time, a surrogate endpoint for scaffold absorption
- OCT showed **good scaffold strut apposition** and **no intraluminal masses** during the absorption up to 12 months