Bioabsorbable Metallic Scaffolds

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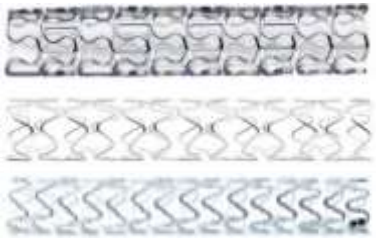
Conflicts of interest

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

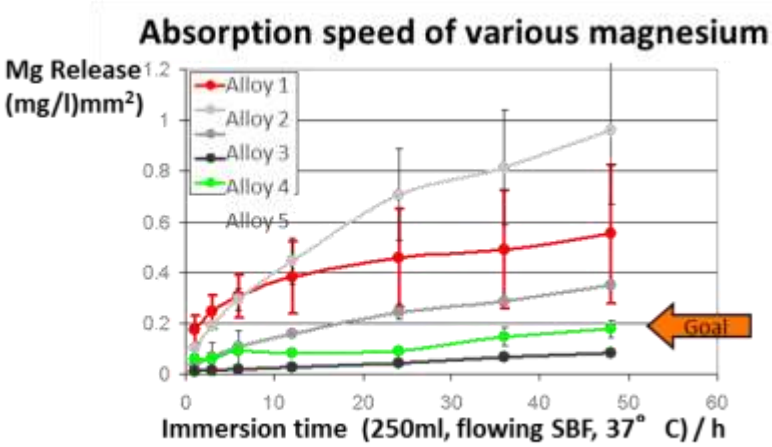
Metallic Bioresorbable Scaffolds



Scaffold	
Biotronik AMS	Mg-Alloy
Biotronik DREAMS I	Mg-Alloy + Paclitaxel
Biotronik DREAMS II	Mg-Alloy + Sirolimus
Medtronic	Mg-Alloy + Sirolimus
BSCI	Mg-Alloy
QualiMed UNITY	Mg-Alloy + Polymer (Hybrid)

Background

Different Mg alloys have different absorption speed

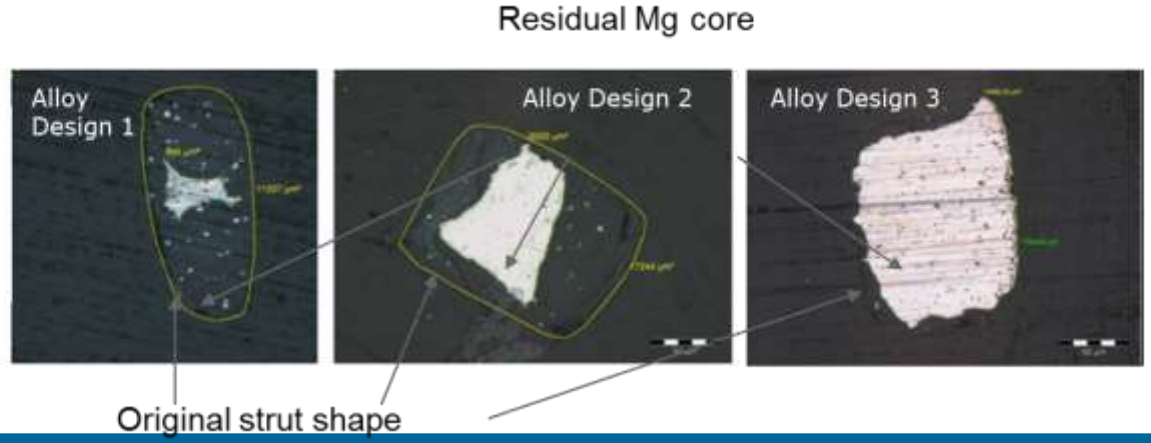


Adding <u>alloying elements</u> to magnesium can significantly alter the absorption speed

Impact of purity and processing (Alloy Design x) on degradation speed

28days

Porcine coronary model



Background

Evolution of the BIOTRONIK Magnesium Scaffold

		PROGRESS-AMS	BIOSOLVE-I	BIOSOLVE-II
	Device generation	AMS	DREAMS 1G	DREAMS 2G
Design	Sizes (mm)	Ø 3.0 & 3.5 Length: 15, 20	Ø3.25 & 3.5 Length: 15	Ø 2.5, 3.0 & 3.5 Length: 15, 20, 25
	Backbone	Mg alloy	Refined Mg alloy	Refined Mg alloy
	Strut thickness/width	165/80 µm	120/130 µm	120/120 µm (Ø 2.5) 150/150 µm (Ø 3.0 & 3.5)
	Markers	none	none	Ta-composite
	Coating - drug	none	PLGA/PTX	PLLA/SIR
	Crossing profile in mm	1.6	1.5	1.75
Kinetics	Drug elution kinetics	n.a.	like Taxus	like Orsiro
	Absorption period in month	1-2	3-4 (Mg)	≈12 (Mg)
Results	In-segment Late Lumen Loss (mm)	0.83±0.51	0.52±0.48	?
	In-scaffold Late Lumen Loss (mm)	1.08±0.49	0.65±0.50	?
	TLF* (%)	23.8	4.3	?
	Definite or Probable Scaffold Thrombosis (%)	0.0	0.0	?

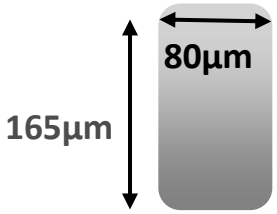
*Composite of cardiac death, target vessel myocardial infarction, clinically driven target lesion revascularization and CABG

Device evolution - from AMS to DREAMS G1

AMS

(Absorbable Magnesium Scaffold)

No drug/polymer coating

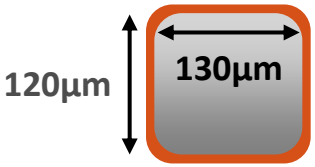


PROGRESS-AMS

DREAMS 1st generation

(Drug Eluting AMS 3.0)

Paclitaxel + PLGA



- Refined Mg-alloy with slower absorption rate
- Optimized scaffold design (6 crown)
- Reduced strut thickness
- **PLGA polymer carrier**
- **Paclitaxel drug elution**
- Used in BIOSOLVE-I study

BIOSOLVE-I

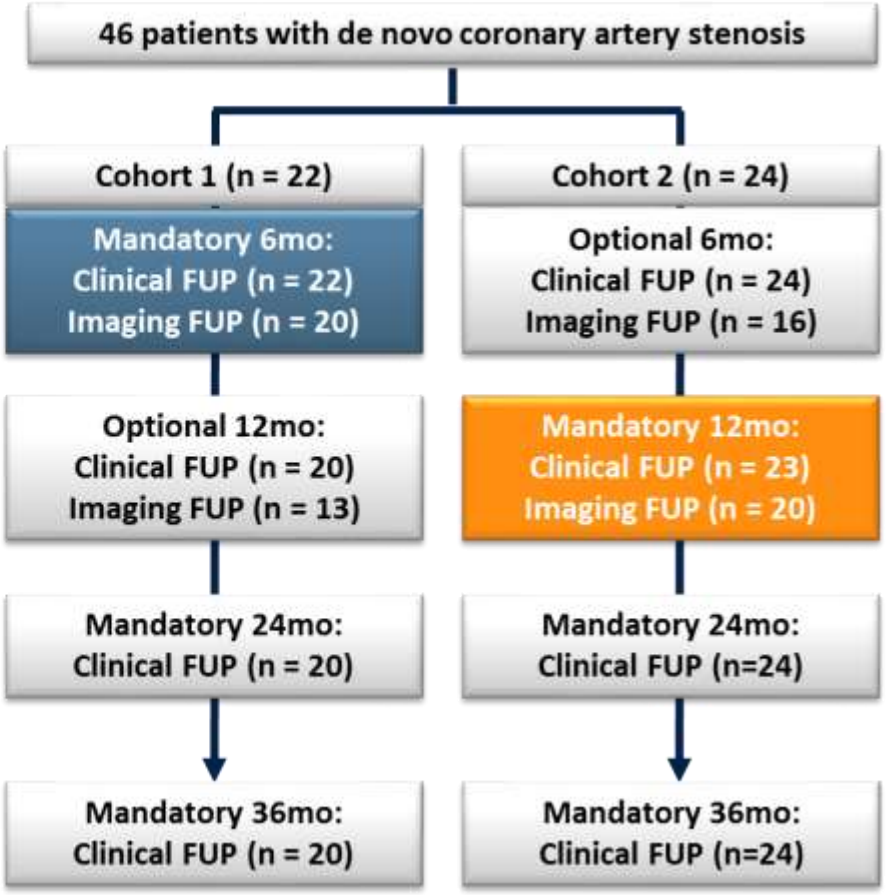
BIOSOLVE-I study results

6-and 12-month late lumen loss (LLL)

DESIGN:
Prospective, multi-center FIM.
Single, *de novo* lesions 3.0-3.5mm and ≤ 12mm long

PRIMARY ENDPOINT:
Cohort 1: TLF at 6 months
Cohort 2: TLF at 12 months

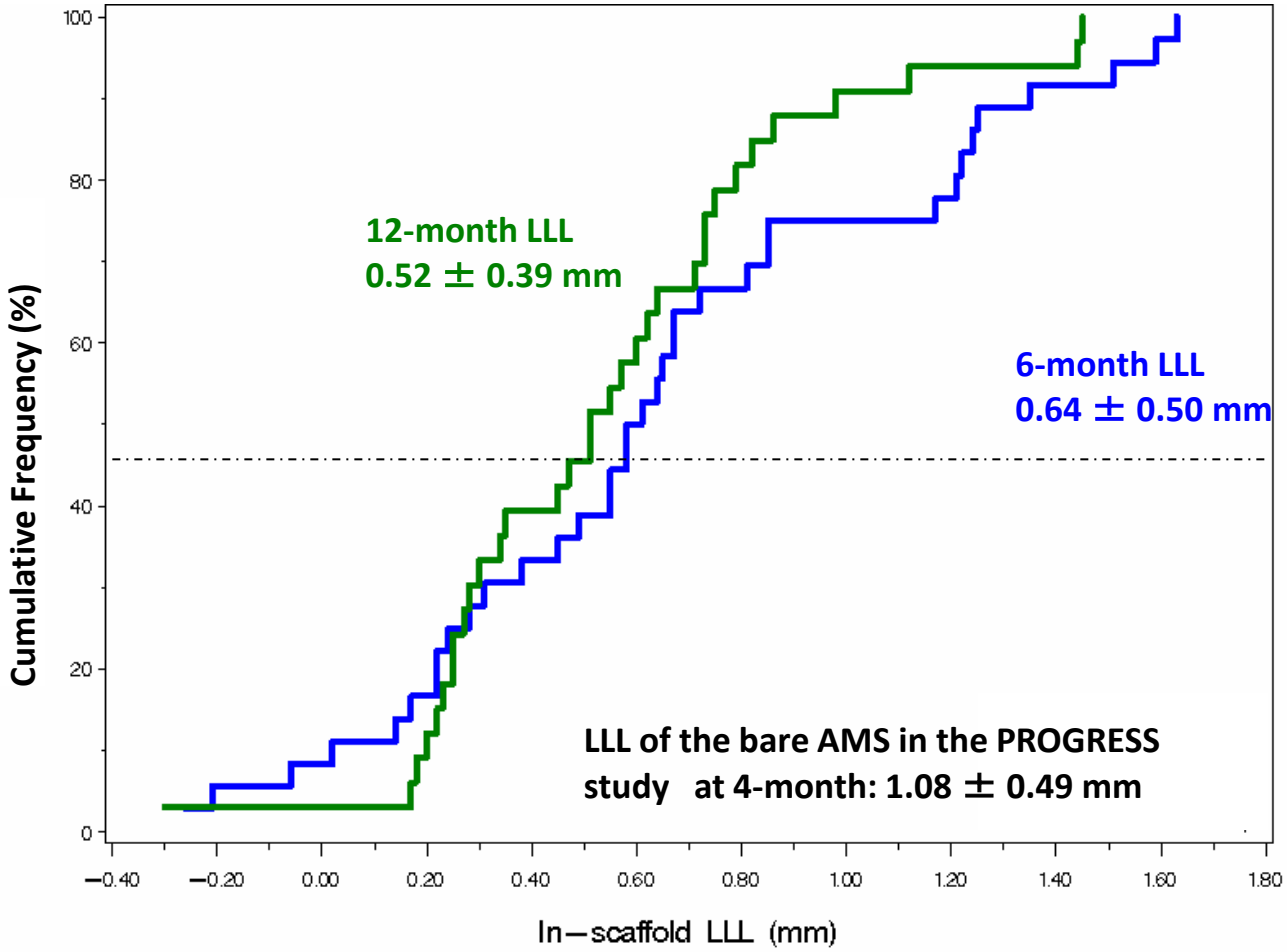
PRIMARY INVESTIGATOR:
J. Koolen. MD. Catharina Ziekenhuis, Eindhoven, Netherlands



Haude et al. Lancet 2013; 381:836-44.

BIOSOLVE-I study results

6-and 12-month late lumen loss (LLL)



Haude et al. Lancet 2013; 381:836-44.

BIOSOLVE-I study results

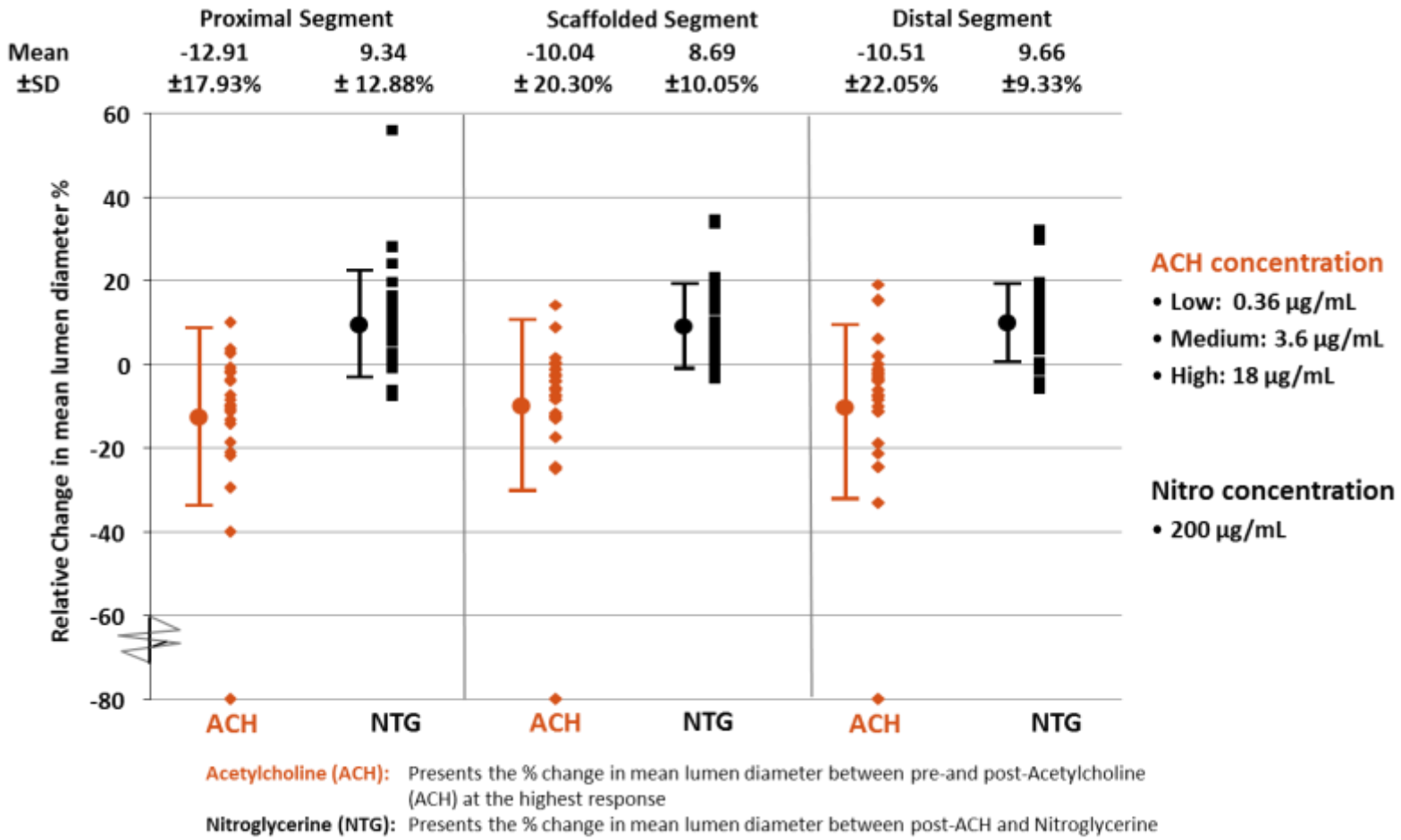
clinical results up to 3 years

	6-month[1] N=26	12-month[1] N=44	24-month[2] N=44	36-month[3] N=44
TLF % (n)	4.3% (2)	6.8% (3)	6.8% (3)	6.8% (3)
Cardiac death % (n)	0.0%	0.0%	0.0%	0.0%
MI % (n)	0.0%	2.3% (1)	2.3% (1)	2.3% (1)
Scaffold thrombosis % (n)	0.0%	0.0%	0.0%	0.0%
Clinical TLR % (n)	4.3% (2)	4.5% (2)	4.5% (2)	4.5% (2)

[1] Haude et al. Lancet 2013; 381:836-44.
[2] Haude et al, oral presentation EuroPCR 2013,
[3] Haude et al Eurointervention 2016 in press

BIOSOLVE-I study results

Vasomotion results at 6-month (N=26)



Acetylcholine (ACH): Presents the % change in mean lumen diameter between pre-and post-Acetylcholine (ACH) at the highest response

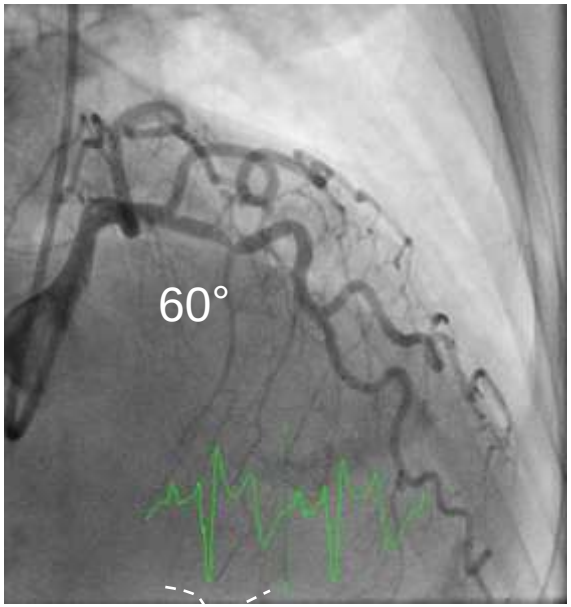
Nitroglycerine (NTG): Presents the % change in mean lumen diameter between post-ACH and Nitroglycerine

Haude et al. Lancet 2013; 381:836-44.

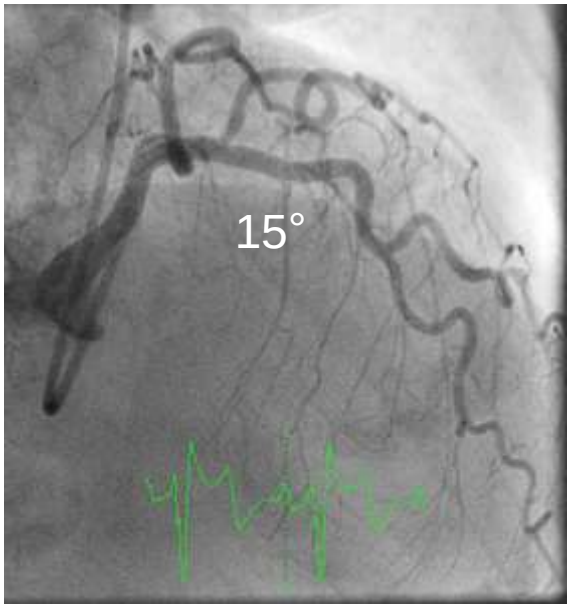
BIOSOLVE-I Results

- Change in vessel angulations at 6 months -

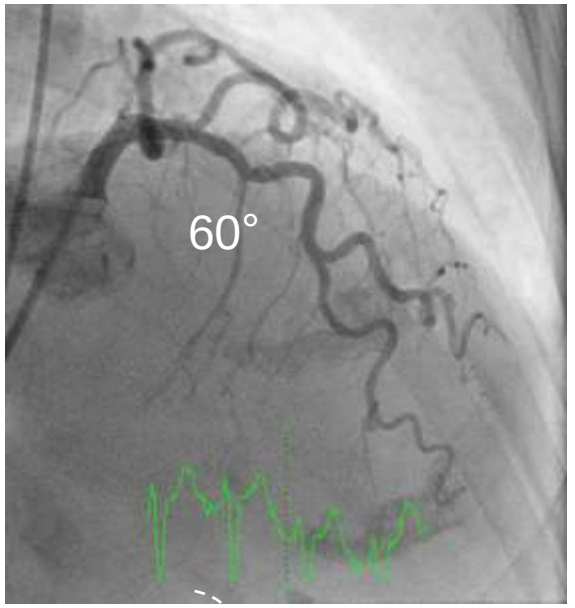
Pre-Procedure



Post-Procedure



6-month FUP



	Pre-Procedure N=47	Post-Procedure N=47	6-Month FUP N=36
Lesion Angulation (°)	31.38 ± 21.23	14.89 ± 12.00	26.11 ± 15.91

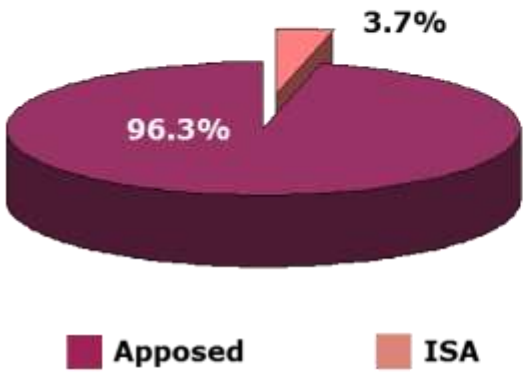
Data are presented in mean ± SD

Haude et al. Lancet 2013; 381:836-44.

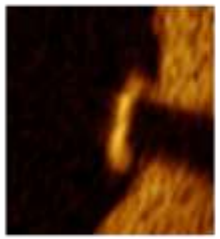
BIOSOLVE-I Results

- OCT evaluation: post-procedure and at 6 months -

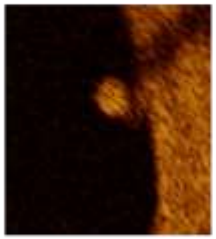
Scaffold Strut Apposition – Baseline



N=8 scaffolds, 6,574 struts

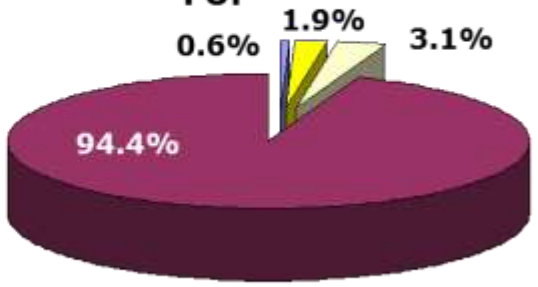


Apposed

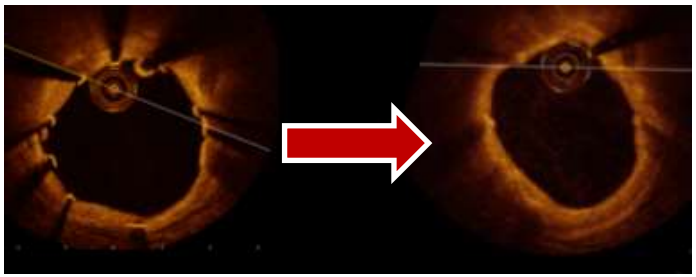


ISA – Incomplete Strut Apposition

Apposition of Strut Remnants – 6 Mo FUP



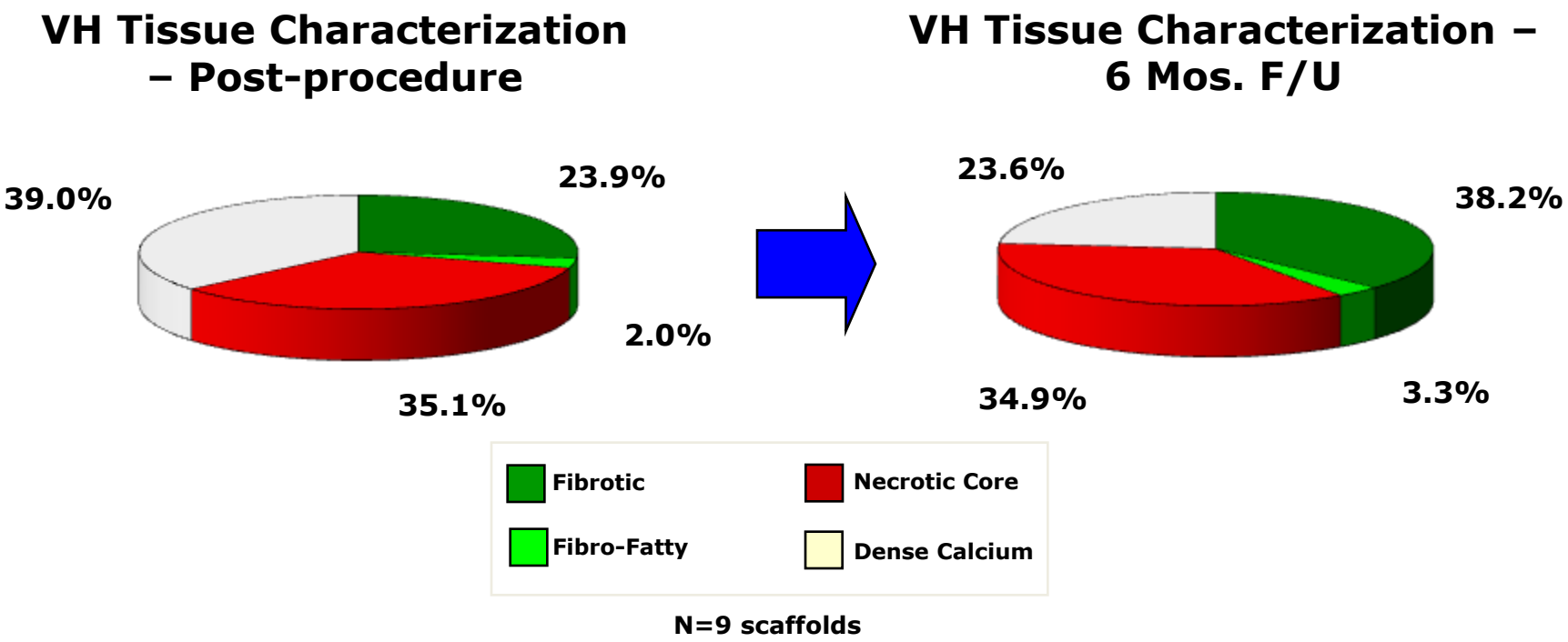
N=8 scaffolds, 6,574 struts



Haude et al. Lancet 2013; 381:836-44.

BIOSOLVE-I Results

- IVUS-VH evaluation: post-procedure and at 6 months -



Reduction in dense calcium by 39.5%

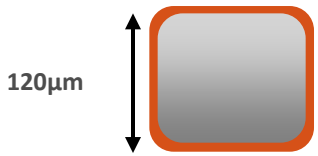
Haude et al. Lancet 2013; 381:836-44.

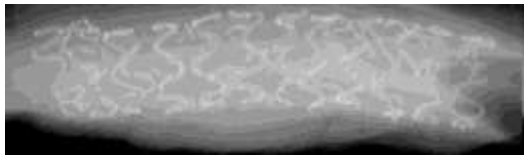
Device evolution - from DREAMS G1 to G2

DREAMS 1st generation

(Drug Eluting AMS 3.0)

Paclitaxel + PLGA





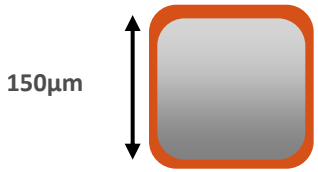
90-Day Faxitron, porcine explant

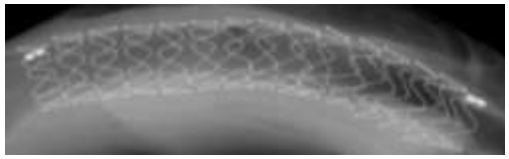
BIOSOLVE-I

DREAMS 2nd generation

(Drug Eluting AMS 3.5)

Sirolimus + PLLA (BIOlute)





90-Day Faxitron, porcine explant

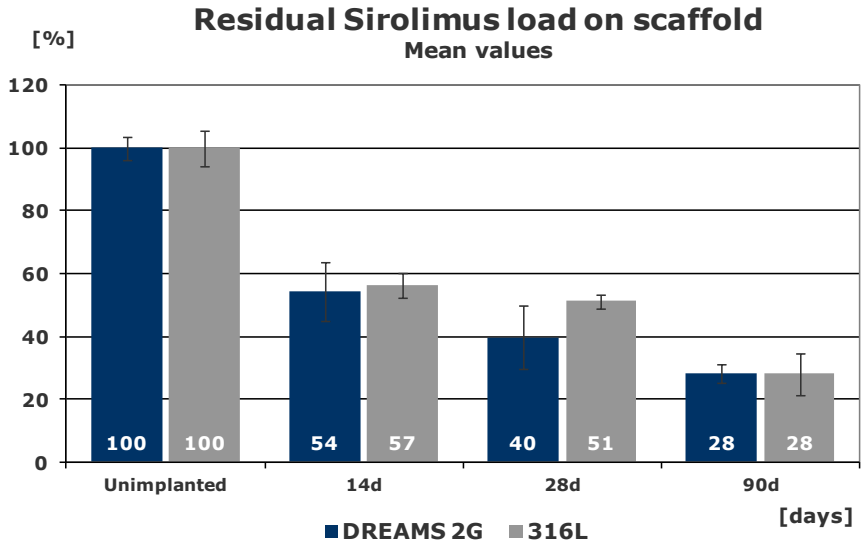
- 6-crown 2-link design, 150µm strut thickness
- Optimized scaffold design for
  - Higher bending flexibility
  - Higher acute radial force
  - Slower absorption rate
- Sirolimus drug elution & PLLA (ORSIRO BIOlute coating)
- Tantalum radiopaque markers

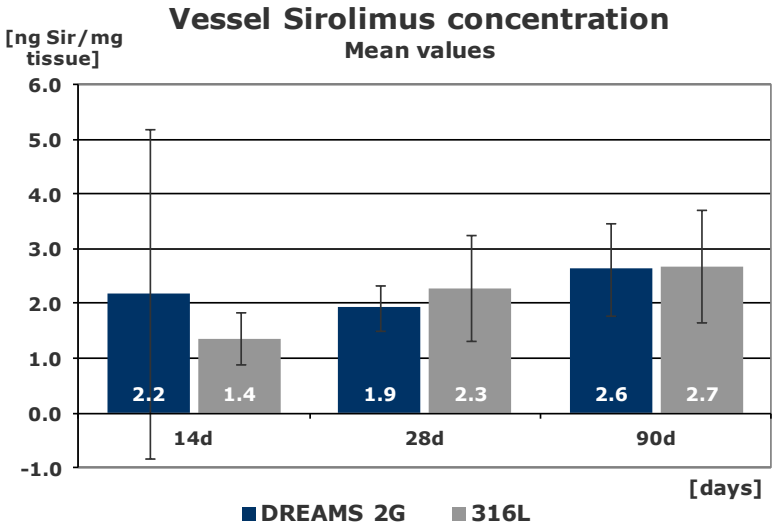
BIOSOLVE-II

Background

DREAMS 2G: Sirolimus elution kinetics

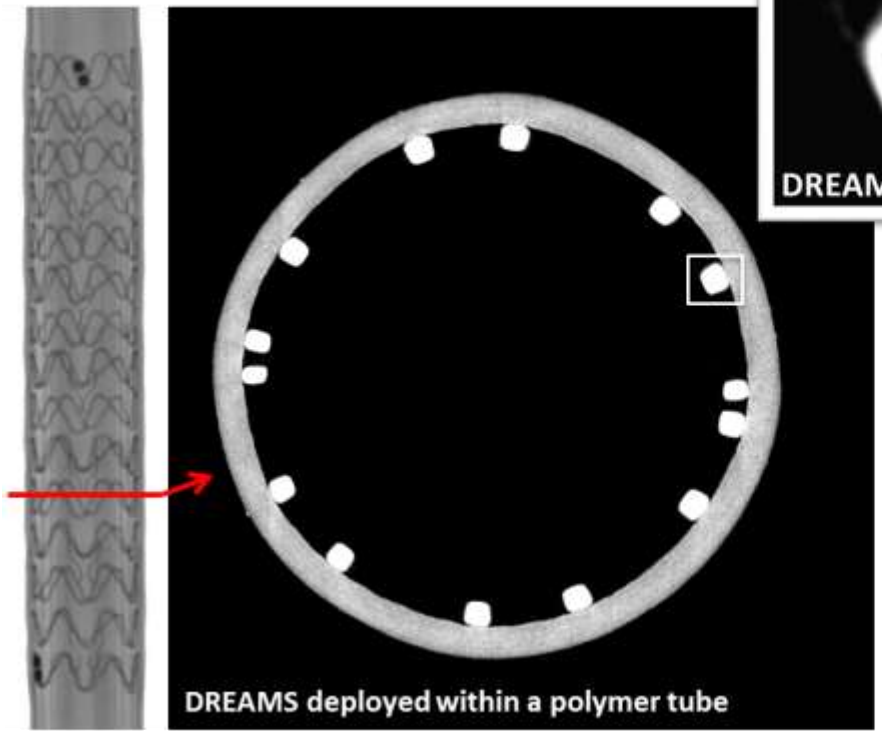
Comparison of DREAMS 2nd Generation to an identical scaffold made from stainless steel in a porcine coronary artery model.

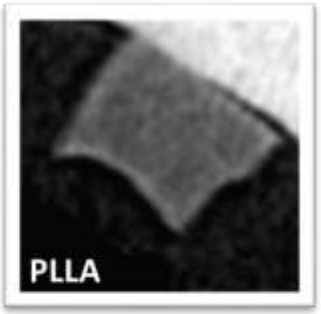




Background

DREAMS 2G: Strut shape

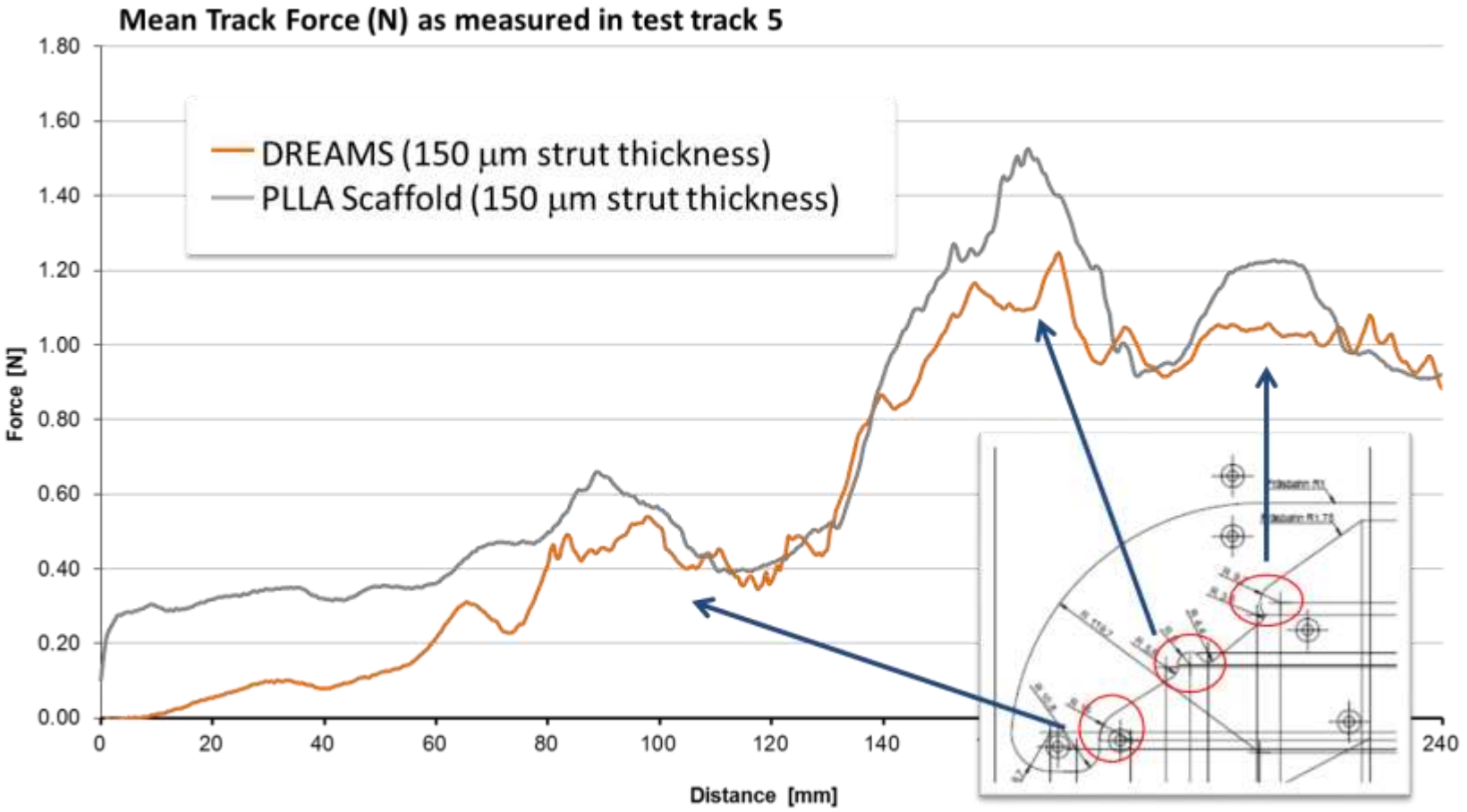




- Electropolished surface result in rounded struts
- Rounded Mg struts may better embedding into the vessel wall and allow improved peri-strut flow

Background

DREAMS 2G vs Absorb BVS: Benchmark trackability test

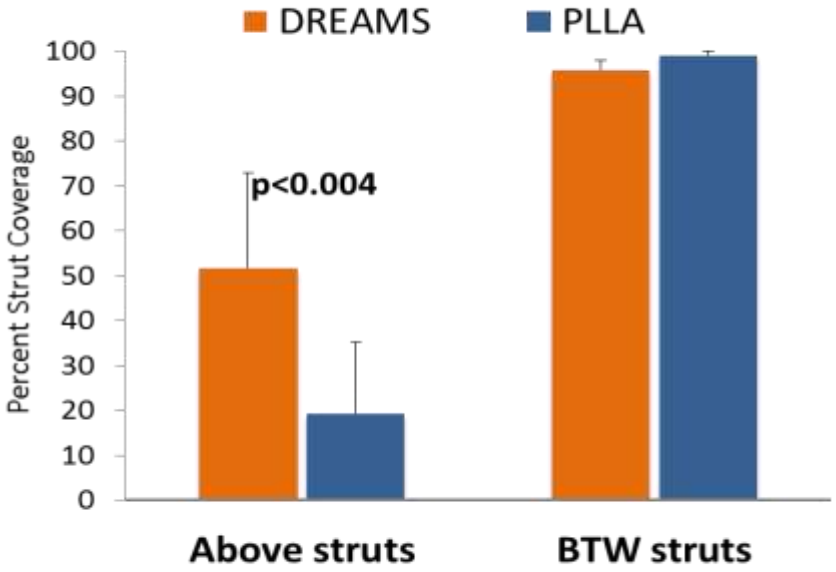


Source: Data on file at BIOTRONIK AG.

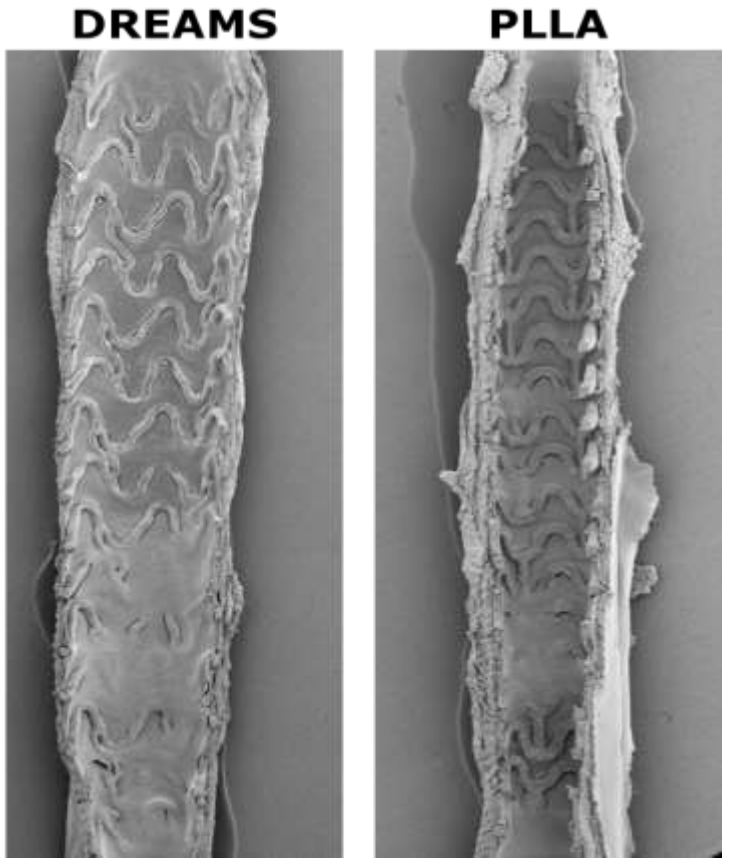
Background

DREAMS 2G 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

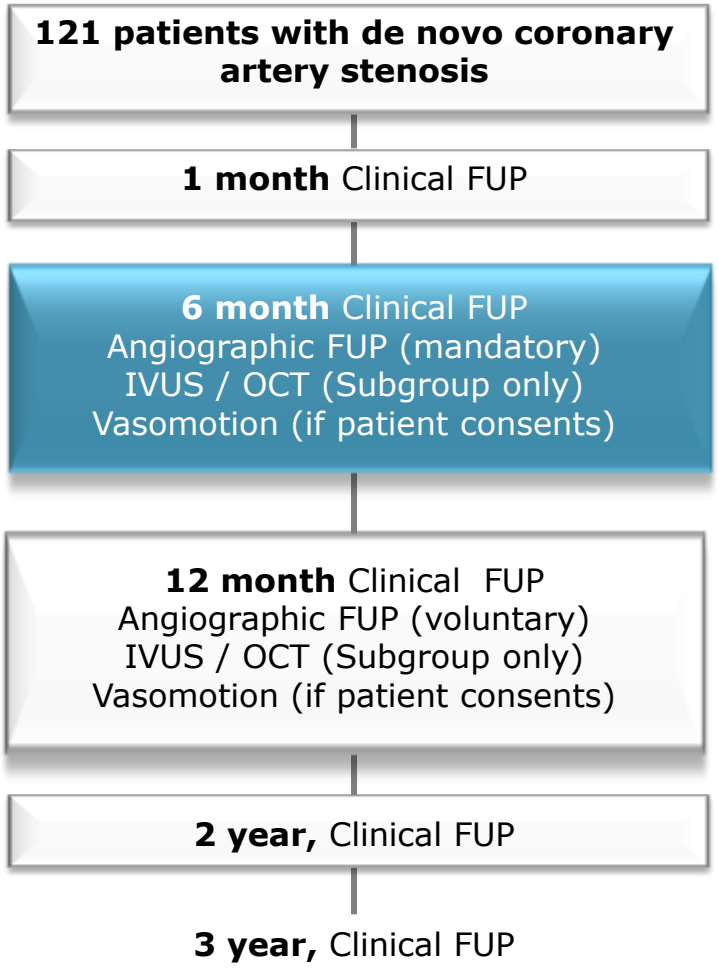
Primary endpoints

In-segment late lumen loss @ 6-month

Coordinating Clinical Investigator

M.Haude, Lukaskrankenhaus GmbH, Neuss, Germany

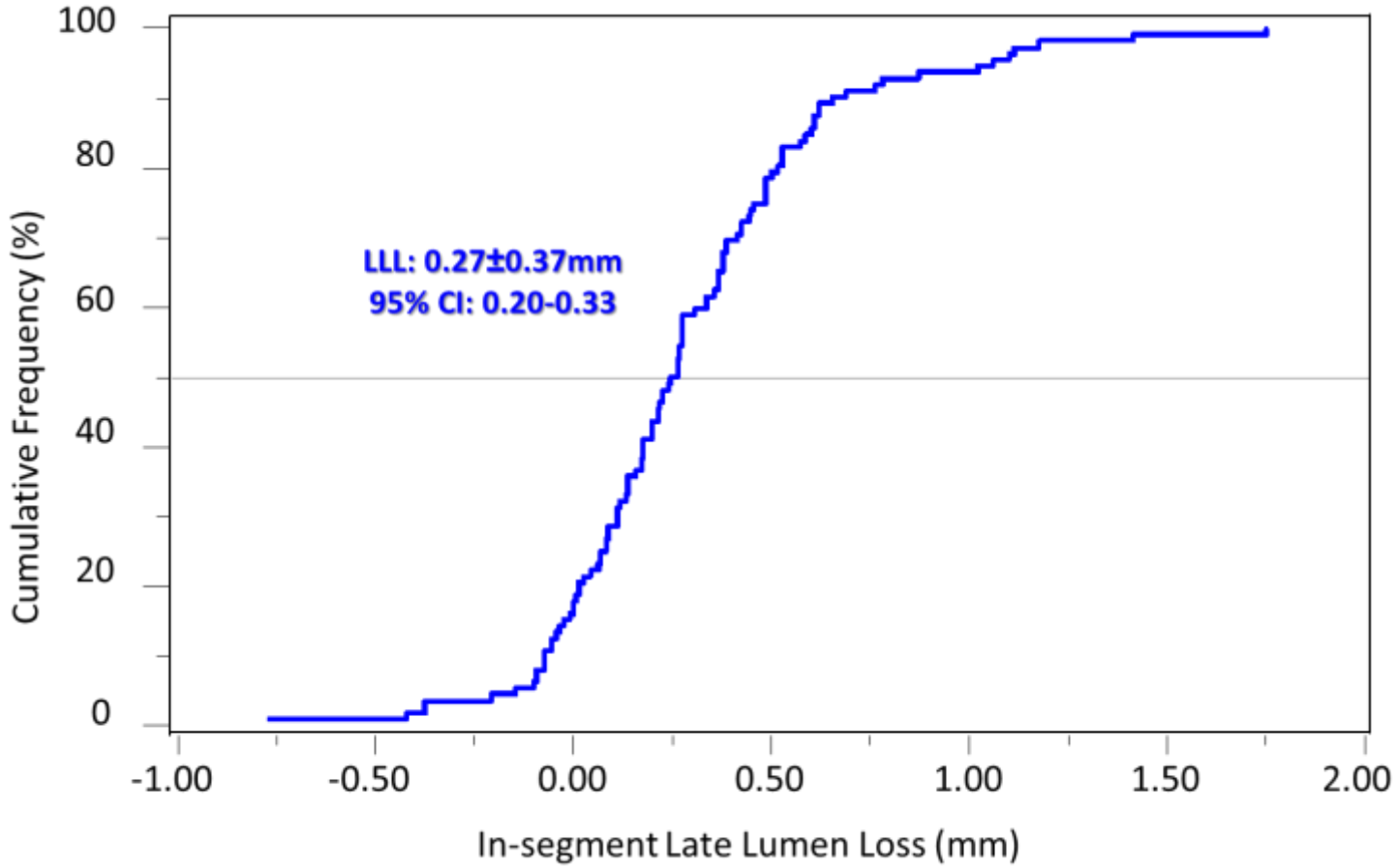
First patient enrolled Oct 8, 2013



M Haude et al, Lancet 2016; 387:31-39.

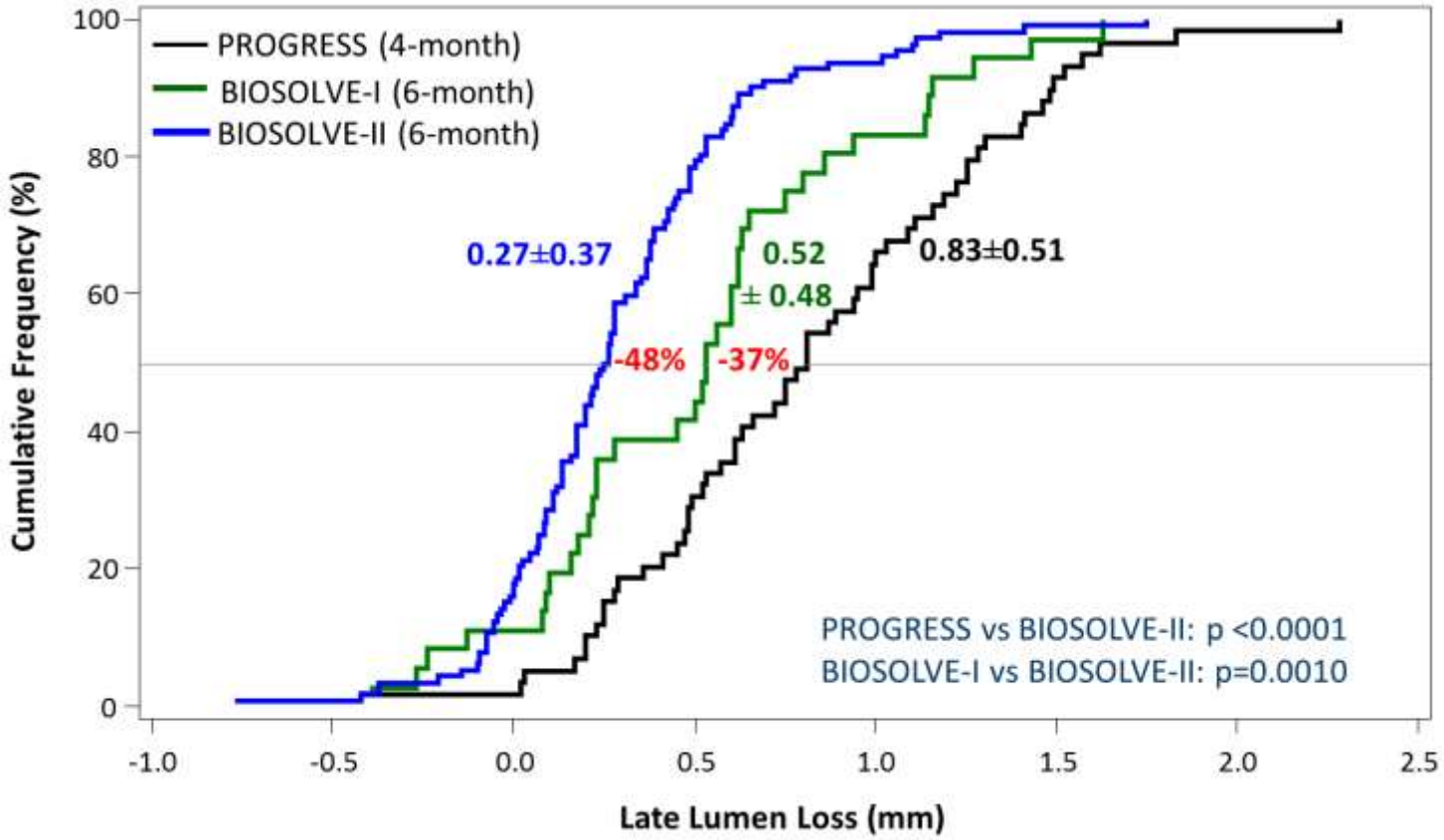
Primary Endpoint

In-segment Late Lumen Loss at 6-month



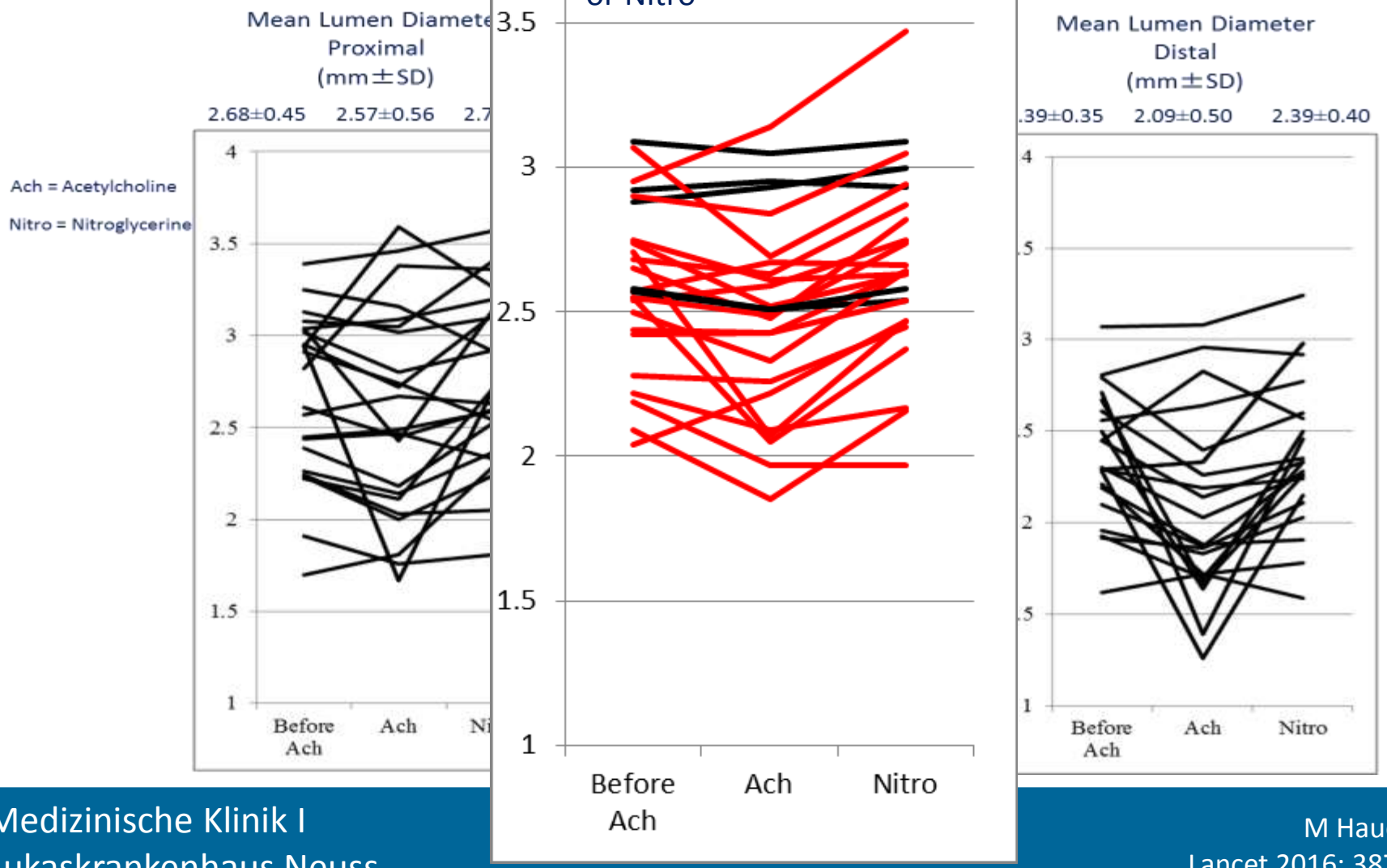
M Haude et al, Lancet 2016; 387:31-39.

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



R Erbel et al, Lancet 2007; 369:1869-75,
M Haude. et al. Lancet 2013; 381:836-44,
M Haude et al, Lancet 2016; 387:31-39.

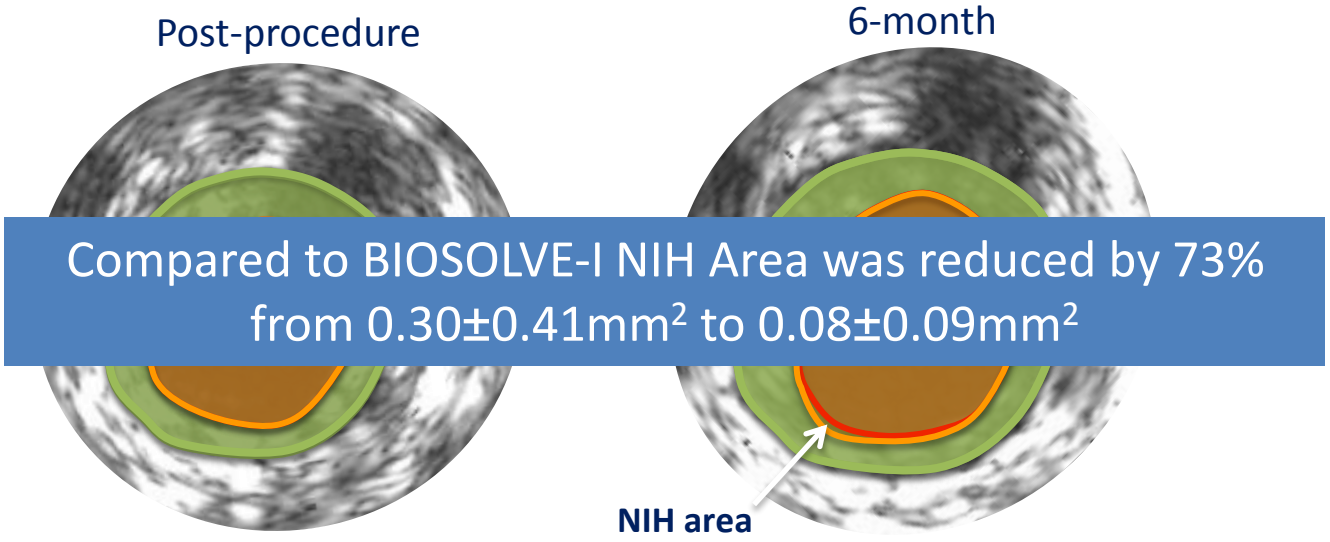
Vasomoti (N=25)



M Haude et al,
Lancet 2016; 387:31-39.

IVUS Analysis

Subgroup N=30



Compared to BIOSOLVE-I NIH Area was reduced by 73% from 0.30±0.41mm² to 0.08±0.09mm²

Lumen area

Scaffold Area

Vessel area

Plaque area

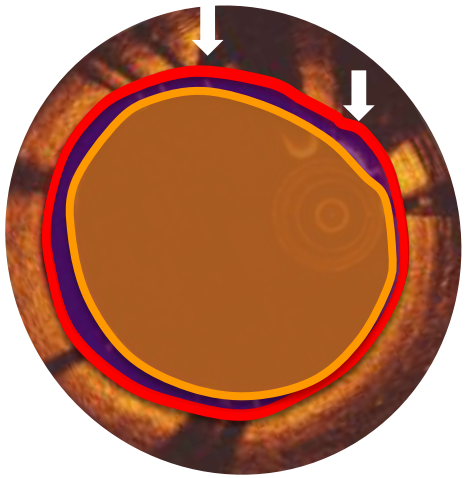
NIH= Neointimal Hyperplasia

NA = Not Applicable	Post-procedure	6-month	Δ6-month vs post [95% CI]	p-value
Vessel area (mm²)	14.06±3.17	14.21±3.14	0.15[-0.13-0.42]	0.289
Scaffold area (mm²)	6.24±1.15	6.21±1.22	-0.03[-0.29-023]	0.803
Plaque area (mm²)	7.76±2.41	8.06±2.23	0.29[0.11-0.47]	0.002
NIH area (mm²)	NA	0.08±0.09	NA	NA

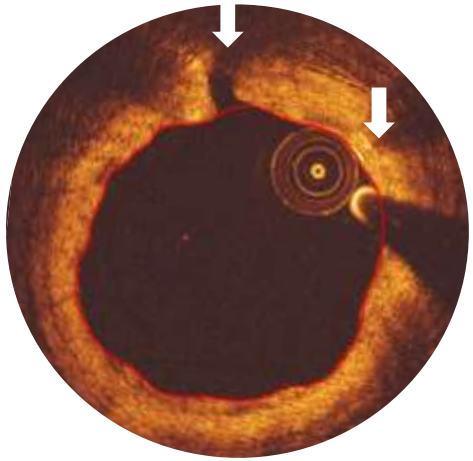
OCT Analysis

Subgroup Analysis

Post-procedure



6-month



Scaffold Area

ISA area

Lumen area

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

M Haude et al, Lancet 2016; 387:31-39.

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
TLF[1] (%)	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

R Erbel et al, Lancet 2007; 369:1869-75,
M Haude. et al. Lancet 2013; 381:836-44,
M Haude et al, Lancet 2016; 387:31-39.

Conclusion

- DREAMS 2G in BIOSOLVE-II demonstrates significantly improved **in-segment LLL (0.27±0.37mm)** compared to it`s precursor devices tested in the PROGRESS (0.83±0.37mm) and the BIOSOLVE-I study (0.52±0.48mm)
- Vasomotion of the scaffolded vessel segment was demonstrated at 6 months
- IVUS results in a subgroup of 30 subjects demonstrate a **preservation of the scaffold area with a low neo-intimal area at 6-month**
- **No intra-luminal masses** were observed by OCT at any time in a subgroup of 30 subjects
- DREAMS 2G in BIOSOLVE-II demonstrates a **low TLF (3.3%) and TLR (1.7%) rate** at 6-month, which is comparable to other absorbable scaffolds and permanent drug eluting stents
- **No definite or probable scaffold thrombosis** was observed with DREAMS 2G tested in BIOSOLVE-II or any of its precursor devices tested in PROGRESS and BIOSOLVE-I in a total of 232 subjects