PROGRESS-AMS

Clinical Performance and Angiographic Results of the Coronary Stenting with Absorbable Metal Stents
The PROGRESS-AMS Study

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For the PROGRESS-AMS investigators group

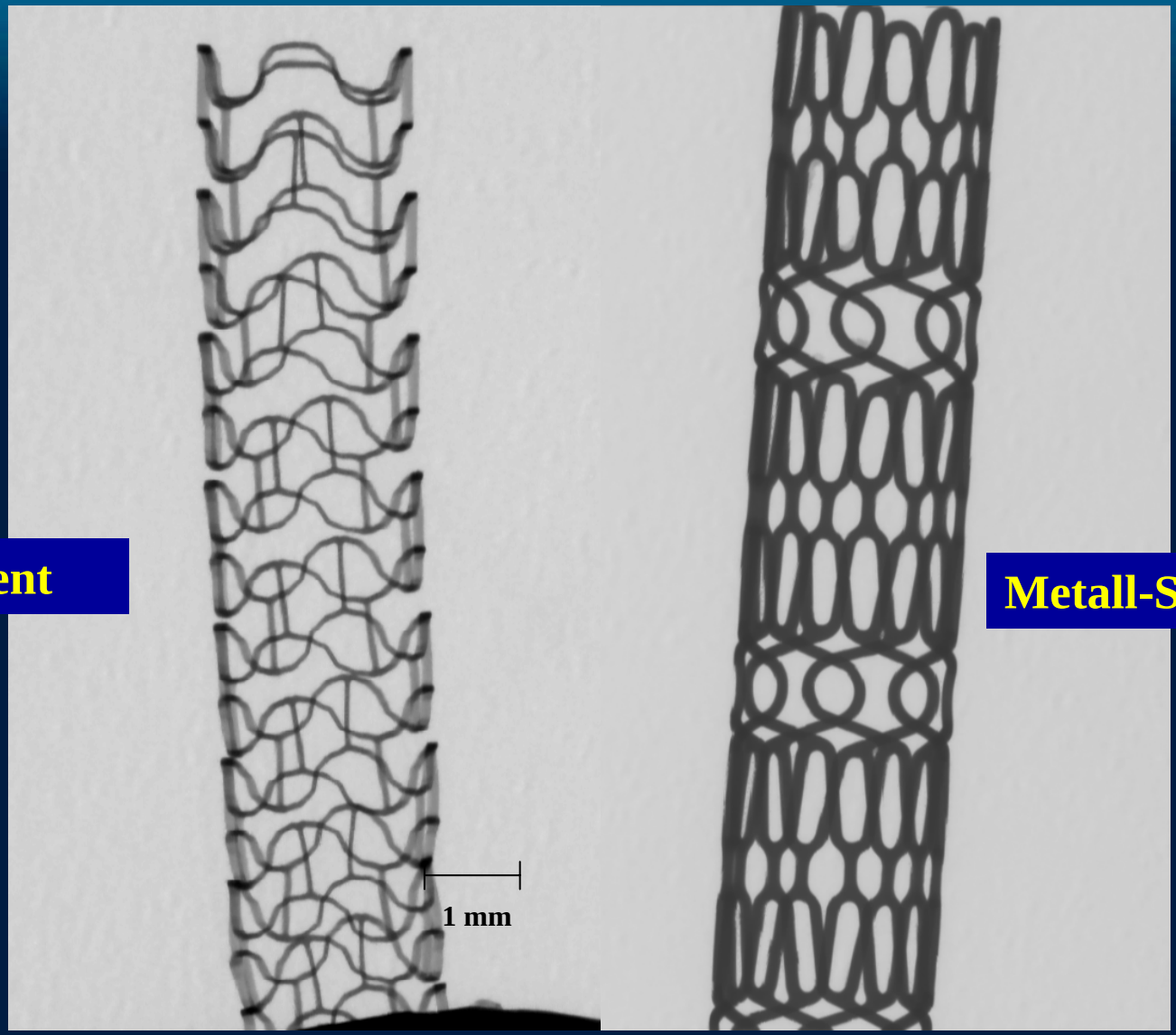
Background

- Coronary stent implantation provides
  - excellent vessel wall scaffolding
  - prevents coronary dissection
  - blocks elastic recoil
  - reduces restenosis rate

but

  - means permanent foreign body
  - limits further revascularization
  - reduces vasomotion with DES
  - limited use in children

Mikro CT of AMS and BMS



Clinical Performance and Angiographic Results of the Coronary Stenting with Absorbable Metal Stents The PROGRESS-AMS Study

- **Purpose**
  - To evaluate the clinical feasibility of an absorbable metal stent in the treatment of a single *de novo* lesion in a native coronary artery
- **Design**
  - Prospective, multi-center, consecutive, non-randomized FIM (First In Man – coronary) study
- **Hypothesis**
  - MACE rate after 4 months <30 % comparable to BMS efficacy

PROGRESS STUDY

Principal Investigator	Raimund Erbel, MD, Essen, Germany
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Steering Committee	Raimund Erbel, MD, Essen, Germany Ron Waksman, MD, Washington, USA Bernd Heublein † , MD, Hannover, Germany
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QCA Core laboratory	Cardialysis, The Netherlands
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Study Coordination	Stefan Wagner, PhD, Erlangen, Germany
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Australia	M Horrigan, Melbourne, AUS
Belgium	B de Bruyne & W Wijns, Aalst, BE
Germany	M Haude, S Sack, D Boese, R Erbel, DE
Netherlands	J Koolen, H Bonnier, Eindhoven
Switzerland	F Eberli & T Lüscher, Zurich, CH P Erne, Luzern, CH
UK	C Di Mario & C Ilsley, London, UK
USA	R Waksman, Washington, USA

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- **Primary Hypothesis**

  to demonstrate feasibility and safety being in the range of currently available stent systems with MACE rate after 4 months <30 % (max. 18 events) comparable to BMS efficacy

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primary endpoint

Major Adverse Cardiac Events at 4 M

defined as

- cardiac death
- nonfatal myocardial infarction
- ischemia driven TLR

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Inclusion Criteria

- patient ≥ 18 years of age
- ischemia (stable or unstable angina, or a positive stress test)
- single *de novo* lesion in native vessels
- 3.0 to 3.5 mm reference diameter
- < 15 mm lesion length
- ≥ 50% and < 100% diameter stenosis
- normal CK / CK-MB / troponin I

PROGRESS
Study Medication

- 75-100 mg of Aspirin
- 300 mg of clopidogrel
  75 mg for at least 6 months
- heparin
- GP-IIb/IIIa Inhibitor at the physician's discretion

Why magnesium as absorbable material?

- essential mineral ~ 350 mg/day
- Mg body content 20 g
- antiarrhythmic properties
- calcium antagonist properties

- positive effects in AMI (meta analysis)
- reduction of restenosis (single study)
- no allergy

3 – 4.5 mg Mg

B Heublein, et al.
EHJ 21: 286, 2000

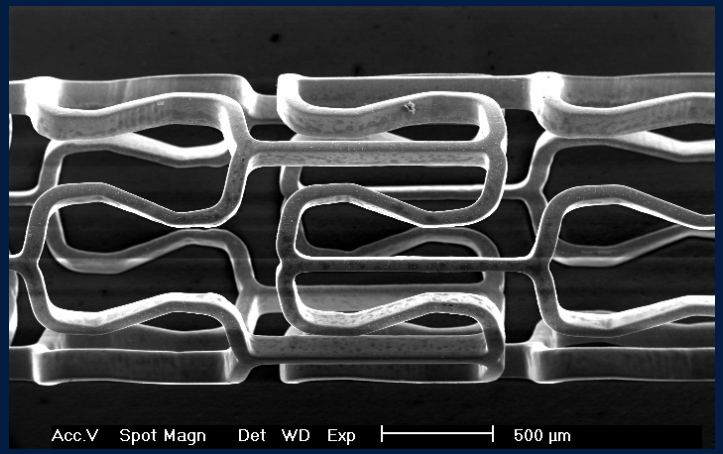
Heublein B et al

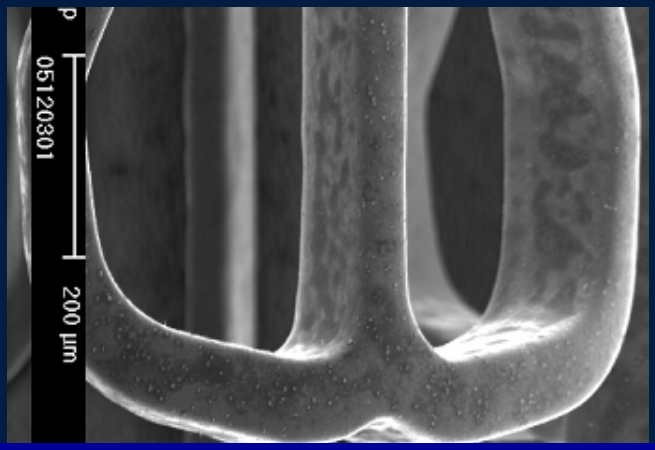
Heart 89: 651 – 6, 2003

Absorbable Metal Stent

Mg Alloy
~ 93 % magnesium,
and 7 % rare earths
rapid neoendothelialisation
low thrombogeneity
2 months degradation time

Light Microscopy





Scanning Electron Microscopy

Heublein B et al **Heart 89: 651 – 6, 2003**

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Procedure Details

- 2.5 mm x 15 mm pre PTCA
- < 16 atm AMS implantation

  3.0 mm 3.5 mm
- **AMS size**

  10 mm 15 mm

- < 16 atm post dilatation if necessary
- double marker balloon, because the AMS fluoroscopically not visible
- angiogram/IVUS before and after implantation

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Study Protocol

	Screening	Treatment	1 d post	1 m post ± 7 d	4 m post ± 1 w	6 m post ± 2 w	12 m post ± 4 w
Clinical follow-up	X		X	X	X	X	X
CK (CK-MB)/ Troponin I	X		X				
QCA		X			X		
IVUS		X			X		
MRI (subgr.)*			X	X	X		

*MRI for analysis of degradation kinetics

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N = 63

• Age, yrs	61.3 ± 9.5	
• Males, % (n)	69.8	44/63
• Diabetes, % (n)	17.4	11/63
• Insulin dependent, % (n)	4.8	3/63
• Smoking History, % (n)	47.6	30/63
• Hypercholesterolemia, % (n)	61.9	39/63
• Hypertension , % (n)	65.1	41/63
• Prior MI, % (n)	41.3	26/63
• Unstable Angina, % (n)	9.5	6/63
• Prior CVA, % (n)	1.6	1/63
• Prior PCI, % (n)	23.8	15/63

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Lesion Location	%	n
Left Main	0	0/63
RCA	36.5	23/63
LAD	34.9	22/63
LCX	28.6	18/63
Discrete* (<10mm in length)	36.5	23/63
Tubular* (10 -15 mm)	63.5	40/63
Diffuse* (>20 mm in length)	0	0/63

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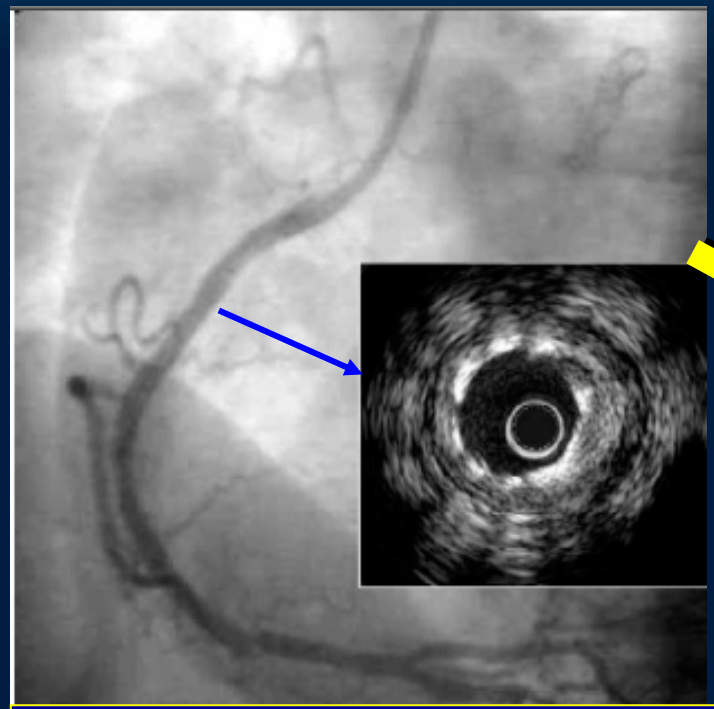
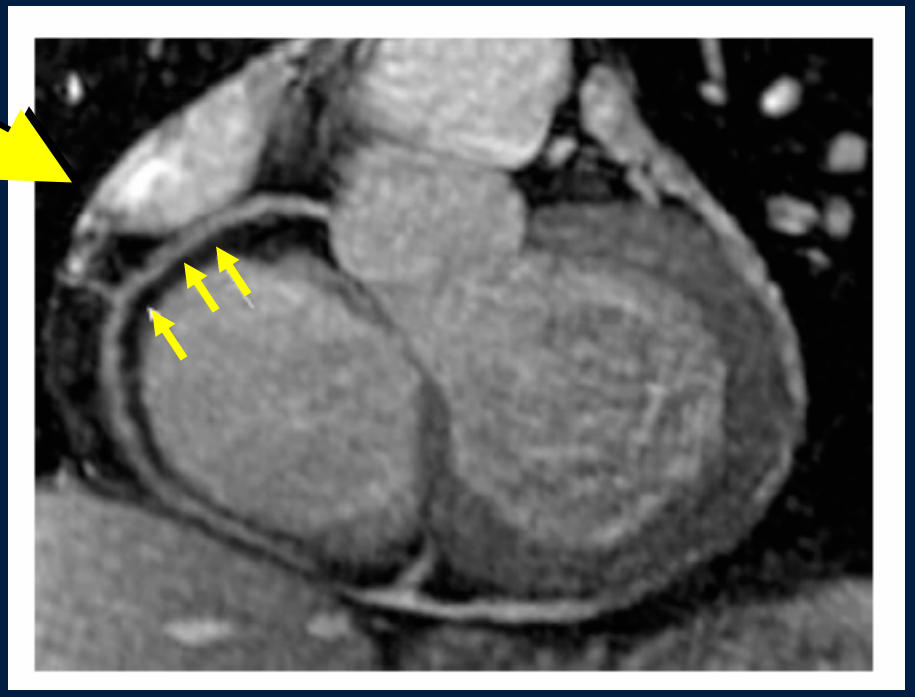
PCI Procedure Characteristics		n
- pre dilatation	100 %	63/63
– pressure (8 atm, 20 sec)	9 ± 2.1	
- AMS pressure, atm	16 ± 0.9	
- post dilatation	67 %	42/63
- post dilatation pressure, atm	16 ± 3.9	
- 2nd stent	13 %	8/63
- average stent number	1.1 ± 0.3	

Magnetic Resonance Imaging of AMS the MRI compatible stent



Magnetom,
(Sonata, 1.5 T, Siemens)



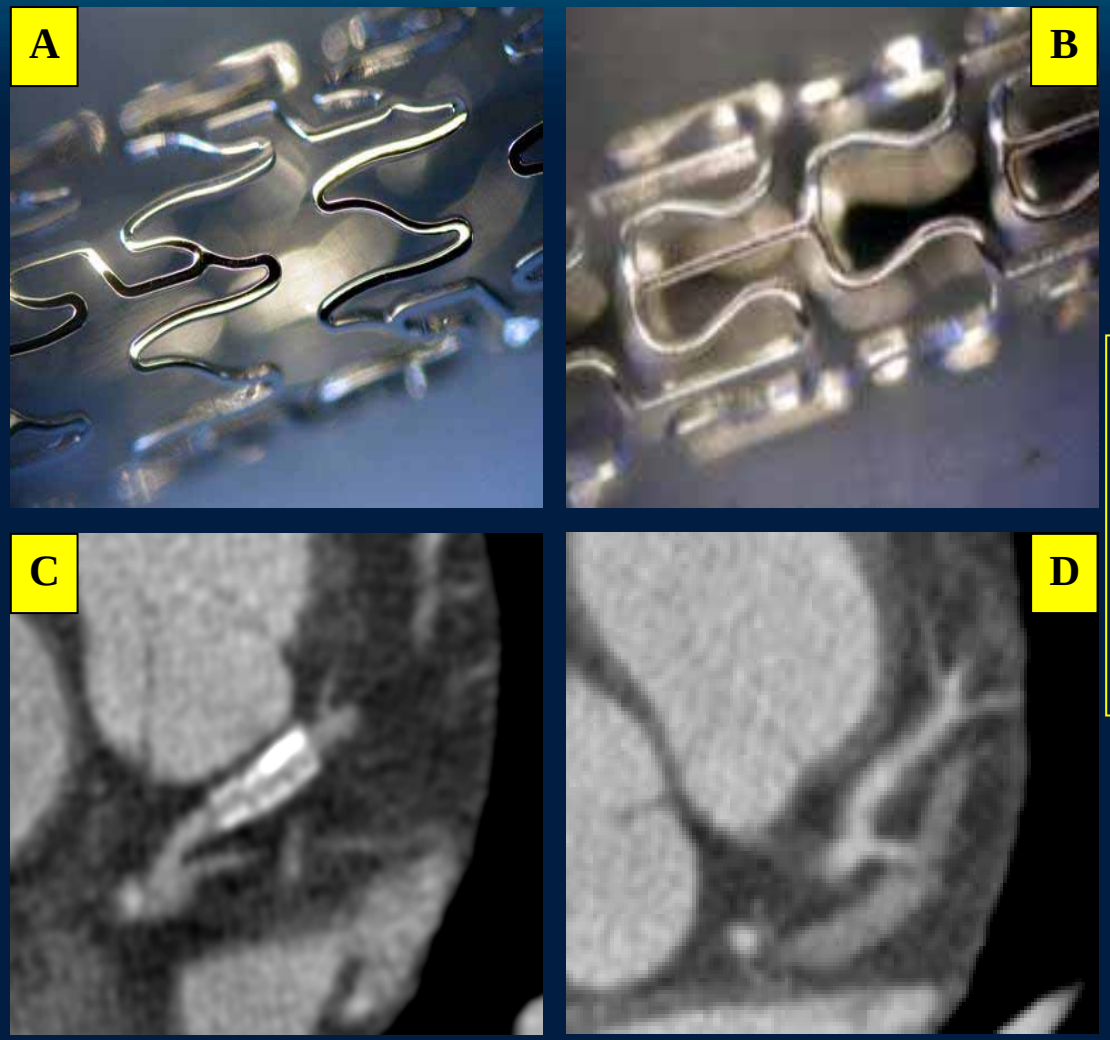
- **no stent artifact,**
- **AMS not visible**
- **optimal vessel lumen imaging**

Eggebrecht et al

Circulation 112, 303 – 4, 2005

Computed Tomography
16 MSCT AMS: the invisible stent

Bare Metal Stent



Ab-sorbable Metal Stent

Lind et al

Heart 91:1604, 2005

PROGRESS STUDY

Lesion Classification	%	n
Type A, %	49.2	31/63
Type B1, %	42.9	27/63
Type B2, %	7.9	5/63
Type C, %	0	0/63

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Indication for Second Stent Implantation

- dissection of type A or B	0/8 (0)
- dissection of type D, E or F	2/8 (25.0)
- lesion not covered 1st stent	3/8 (37.5)
- suboptimal result	1/8 (12.5)
- others	2/8 (25.0)

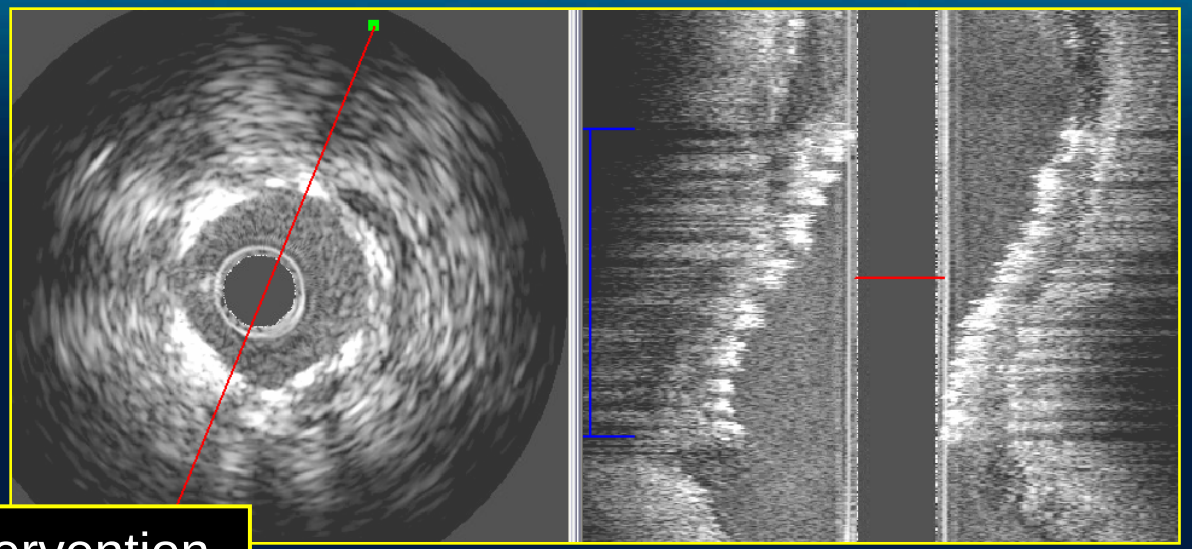
QCA Analysis

Parameter	before	after	4 - month FU
Ref MLD/mm	2.76 ± 0.47		2.66 ± 0.46
MLD/mm	1.05 ± 0.38	2.46 0.37	1.37 0.52
Acute Gain/mm	1.45 ± 0.45		
Late loss/mm		1.09 ± 0.51	
D % Stenosis	62 ± 13	12 6	48 17

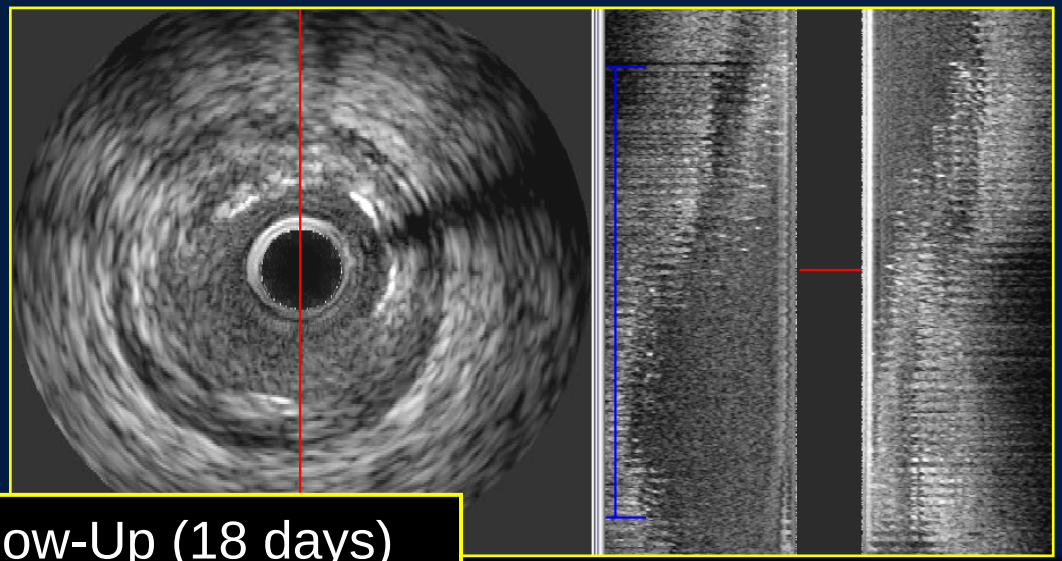
PROGRESS STUDY

QCA Parameters	N = 60 lesions
- % D stenosis post AMS	12.4 ± 5.6
- MLD POST (mm)	2.5 ± 0.4
FOLLOW-UP at 4 months	N = 57 lesions
- % D stenosis	48.2 ± 17.2
- binary restenosis (%)	31//57 (54.4%)
- MLD, mm	1.4 ± 0.5
- late lumen loss, mm	1.1 ± 0.5

GIRO 065-001 C-R



Post Intervention



Follow-Up (18 days)

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	In Hospital		30-days		4-months	
	%	n	%	n	%	n
MACE						
Death	0	0	0	0	0	0
Q-wave MI (Q-waves with CK or CK-MB)	0	0	0	0	0	0
Non Q wave MI (CK 2 times UNL)	0	0	0	0	0	0
Ischemic Driven TLR	0	0	0	0	23.8	15

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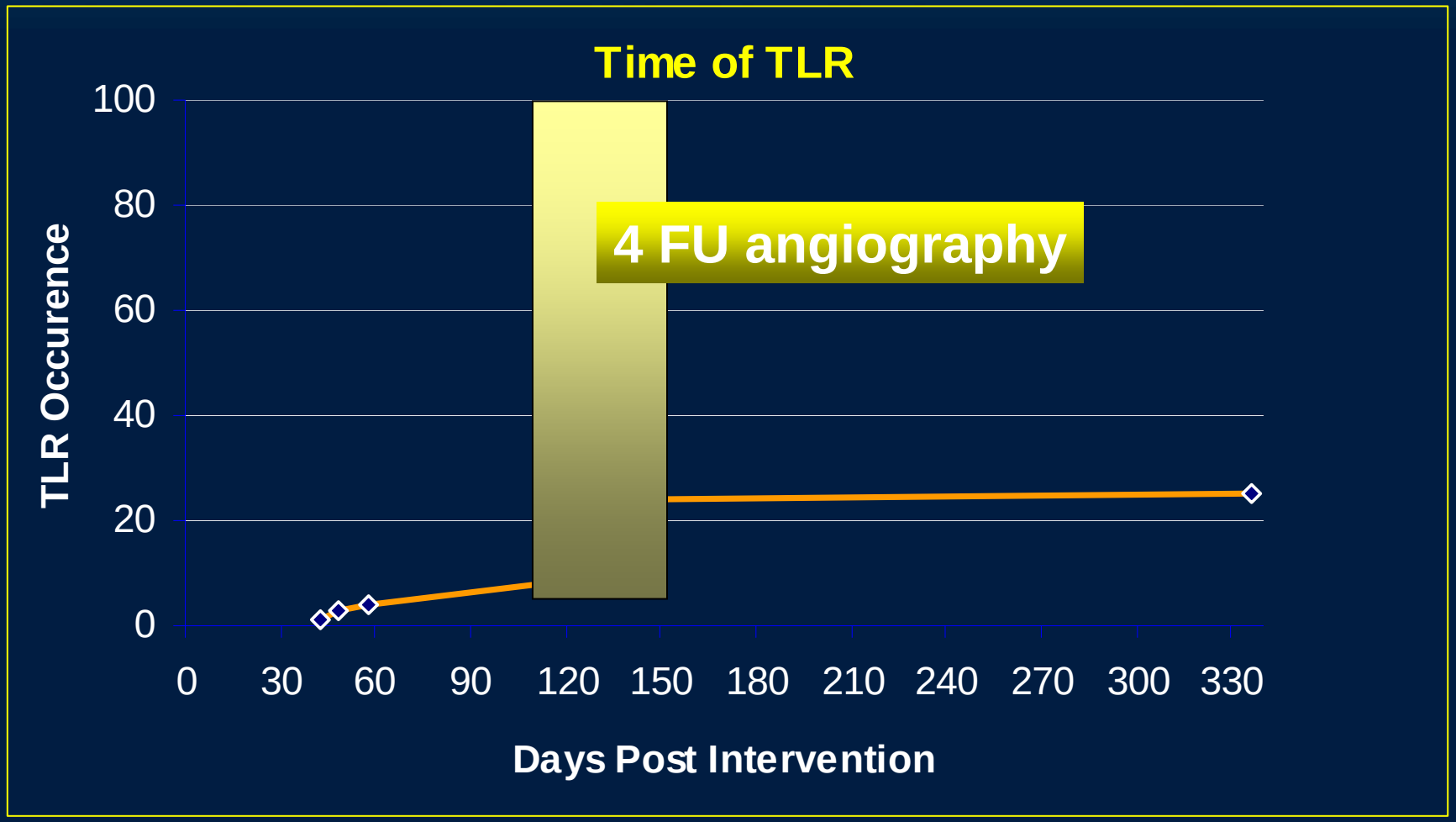

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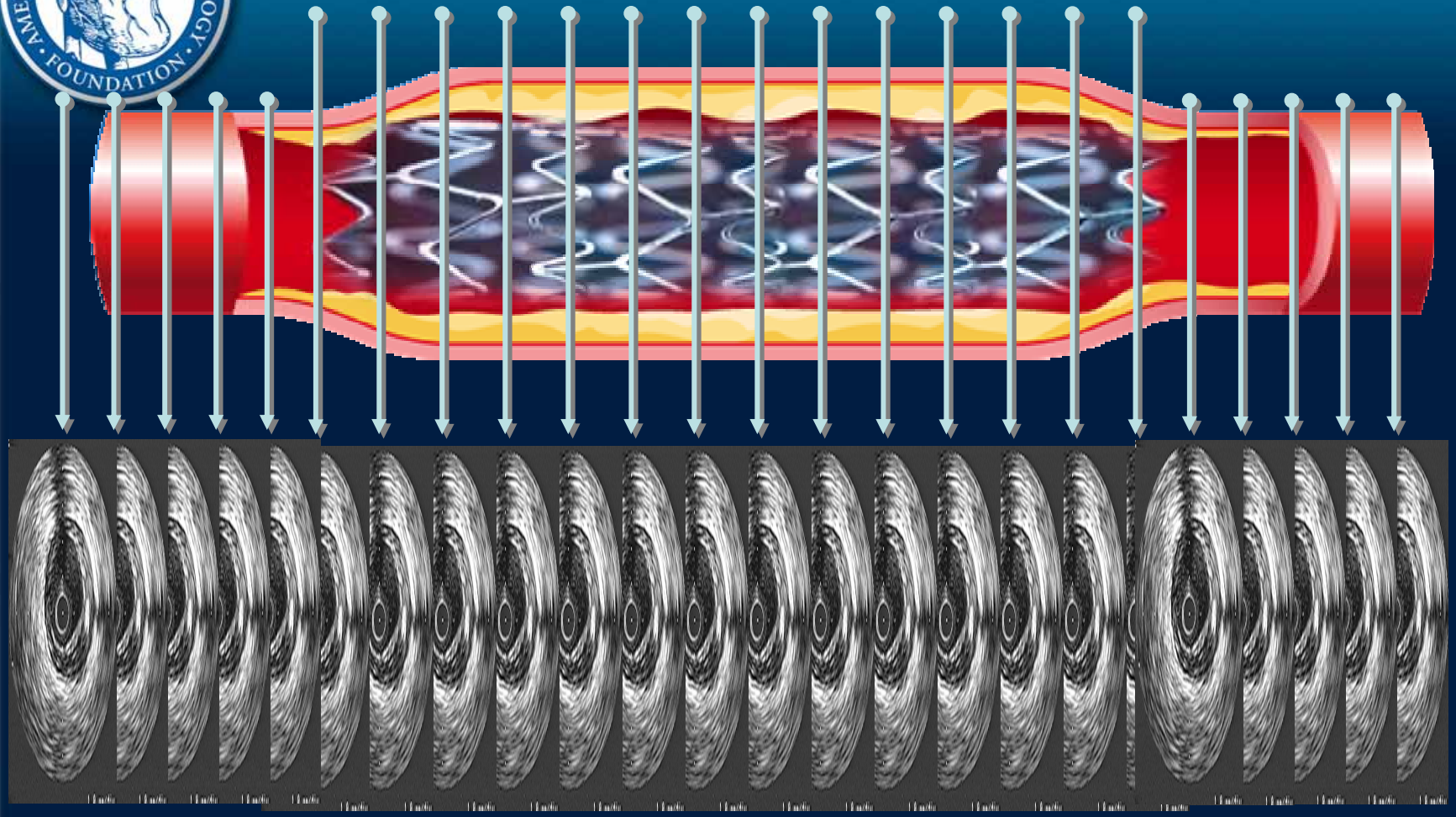
Primary Endpoint

MACE at 4 months	**23.8% (15/63)**

Secondary Endpoints

• Device Success	100%
• Procedural Success	100%
• Late Loss (stent) at 4 months	1.1 ± 0.5
• % D stenosis at 4 months	48.2 ± 17.2
• Binary Restenosis	54.4%
• TLR at 4 months	38.1%
• TVR at 4 months	38.1%

Volumetric IVUS analysis

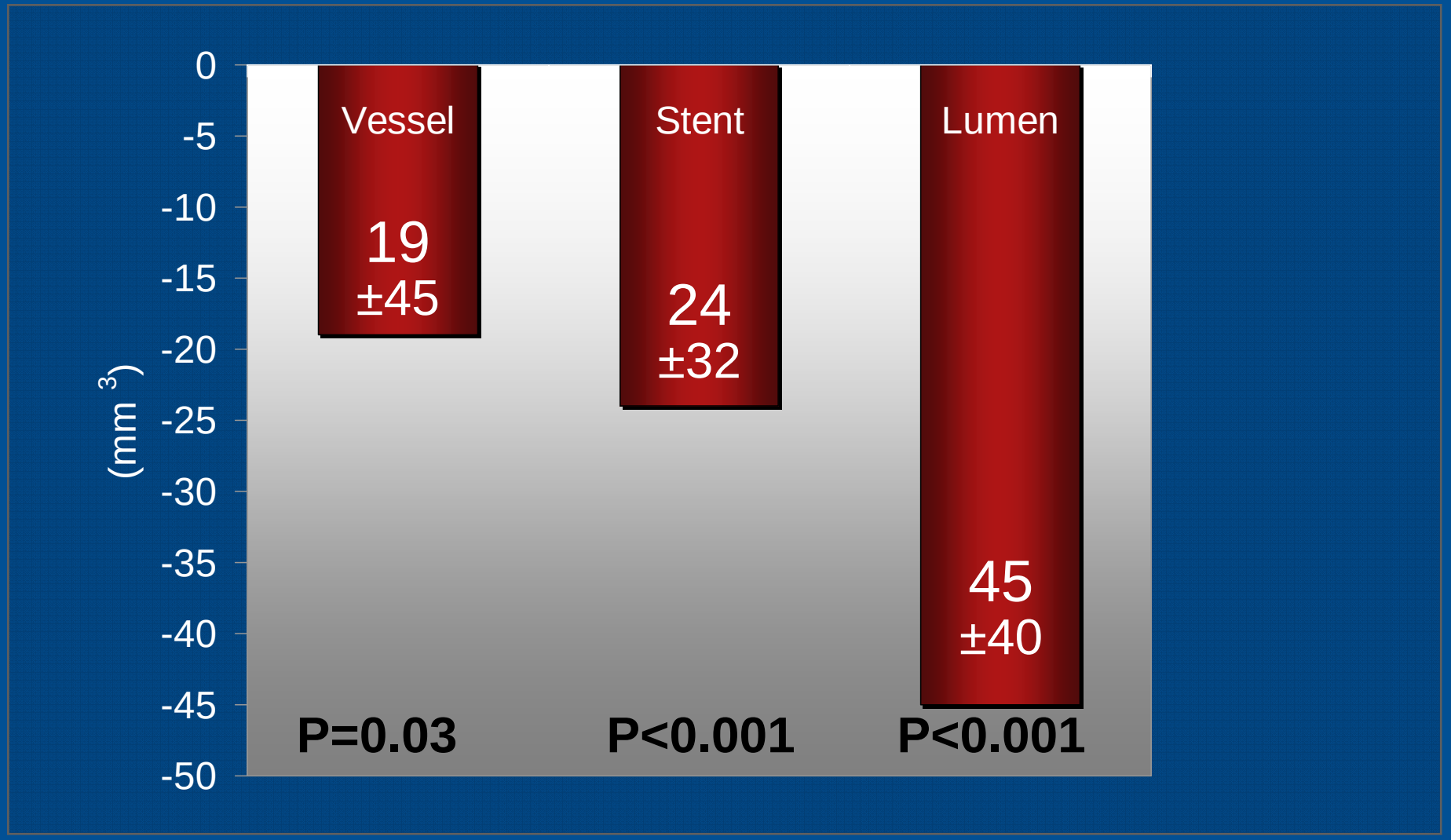


analysis of proximal edge

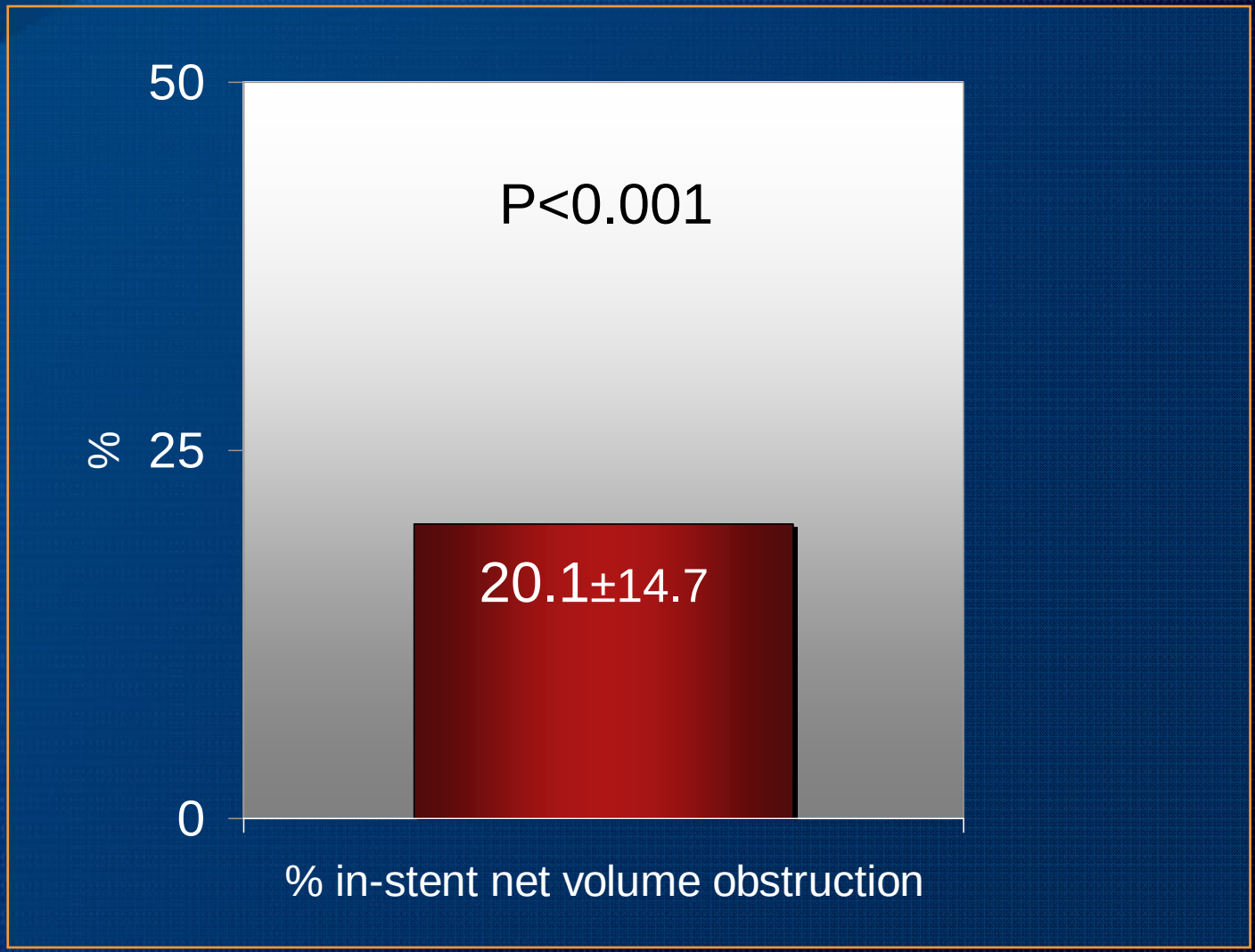
analysis in-stent

analysis of distal edge

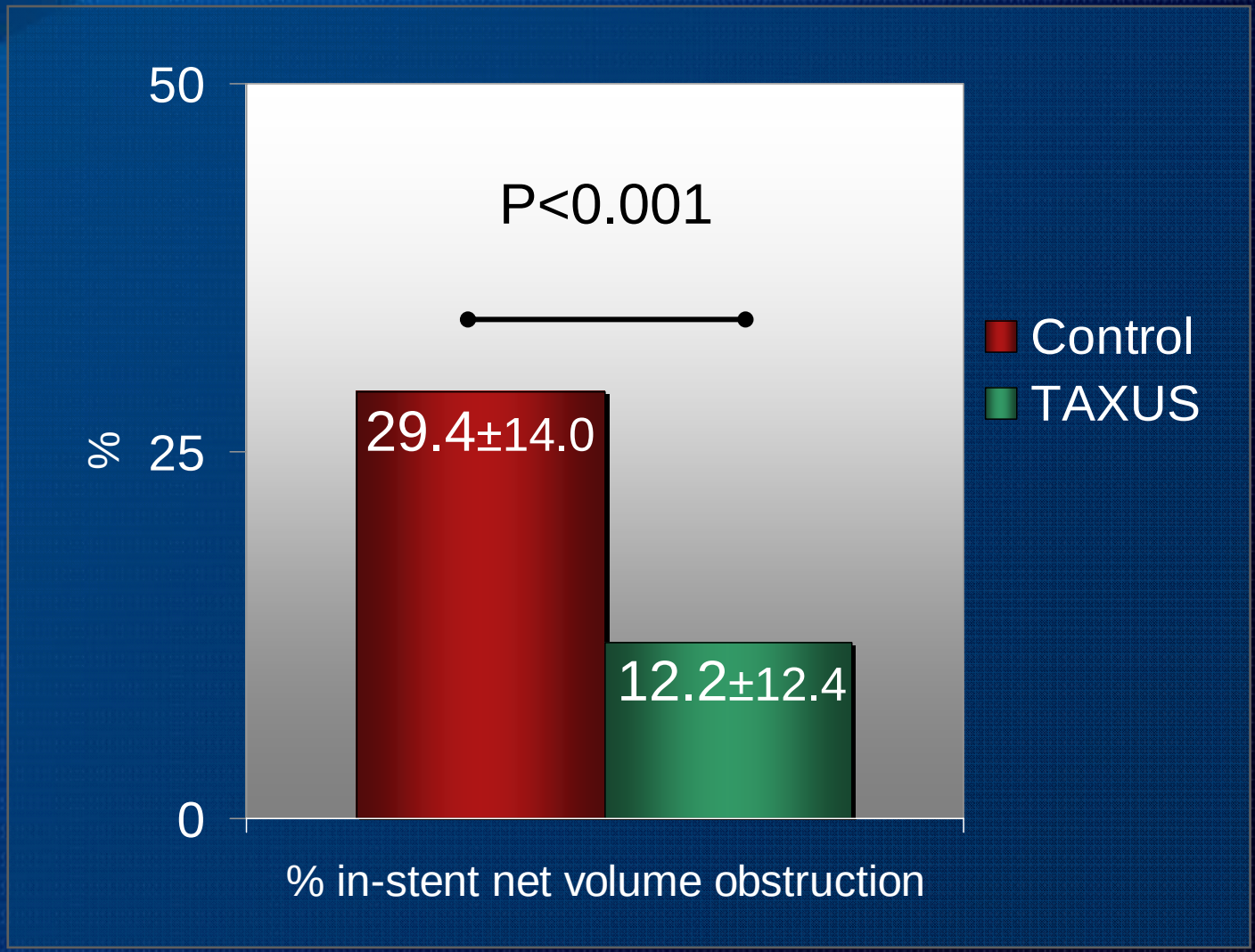
Change in Volumetric IVUS parameters (Paired analysis)



% In-stent net volume obstruction



% In-stent net volume obstruction Reduced in TAXUS



PROGRESS STUDY

Conclusions:

- PROGRESS met the primary endpoint
- high technical and procedural success
- AMS compatible for MRT and CT for FU
- No stent thrombosis
- IVUS detected degradation at 4 months
- iTLR rate comparable to BMS

→ DES properties and/ or more delayed degradation necessary

PROGRESS: conclusions

The FIM coronary study showed:

- Feasibility
- Safety: no death, no MI, no stent thrombosis
- The study met the primary endpoint < 30% of MACE
- The AMS technology platform is proven
- Was successfully delivered to the lesion (100% device success)
- Was MRI / CT compatible
- Was absorbed as intended

Outlook - Drug eluting absorbable metal stent

Absorbable Metal Stent Platform:

- Fully absorbable platform
- Proven biocompatibility throughout the entire absorption process*
- Effective scaffolding properties**

Controlled Drug Eluting Stent Design:

- Precise drug release kinetic and direction
- Resorbable polymer with minimal tissue/polymer contact area
- Protected non-deforming reservoirs

* = Animal data available at Biotronik / ** = In vitro data available at Biotronik

Bioabsorbable Stents
Future Directions

Main challenges

- Rate of degradation
- Time to complete degradation
- Radial force and elimination of recoil
- Bioabsorbable DES

Future Applications

- Coronary, Workhorse stent Vulnerable Plaque
- Peripheral, SFA, tibial
- Pediatric pulmonary coarctation of aorta biliary, etc.