Absorbable Metal Stent, Clinical Update and DREAMS: Concept and preclinical Data

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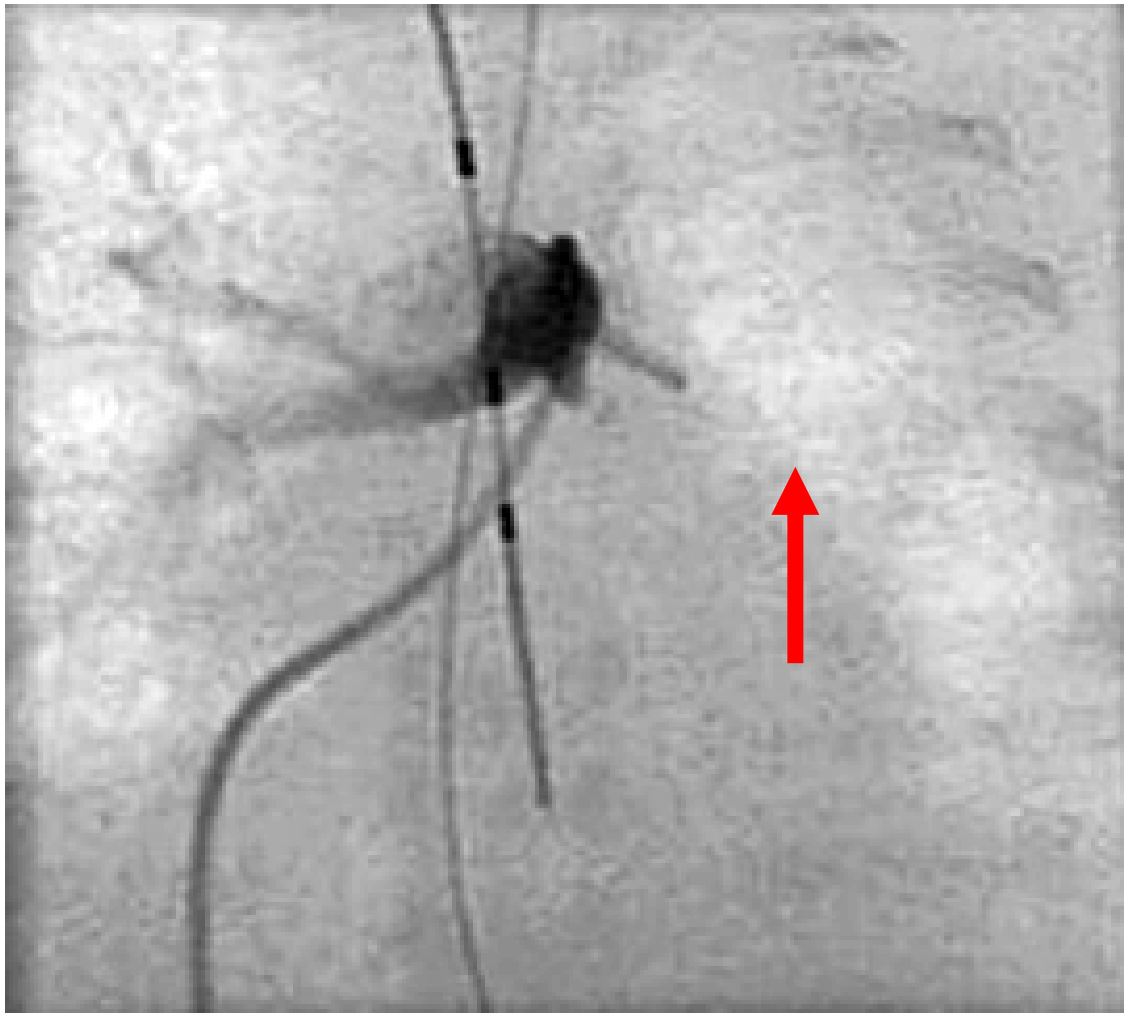
Washington Hospital Center Washington DC

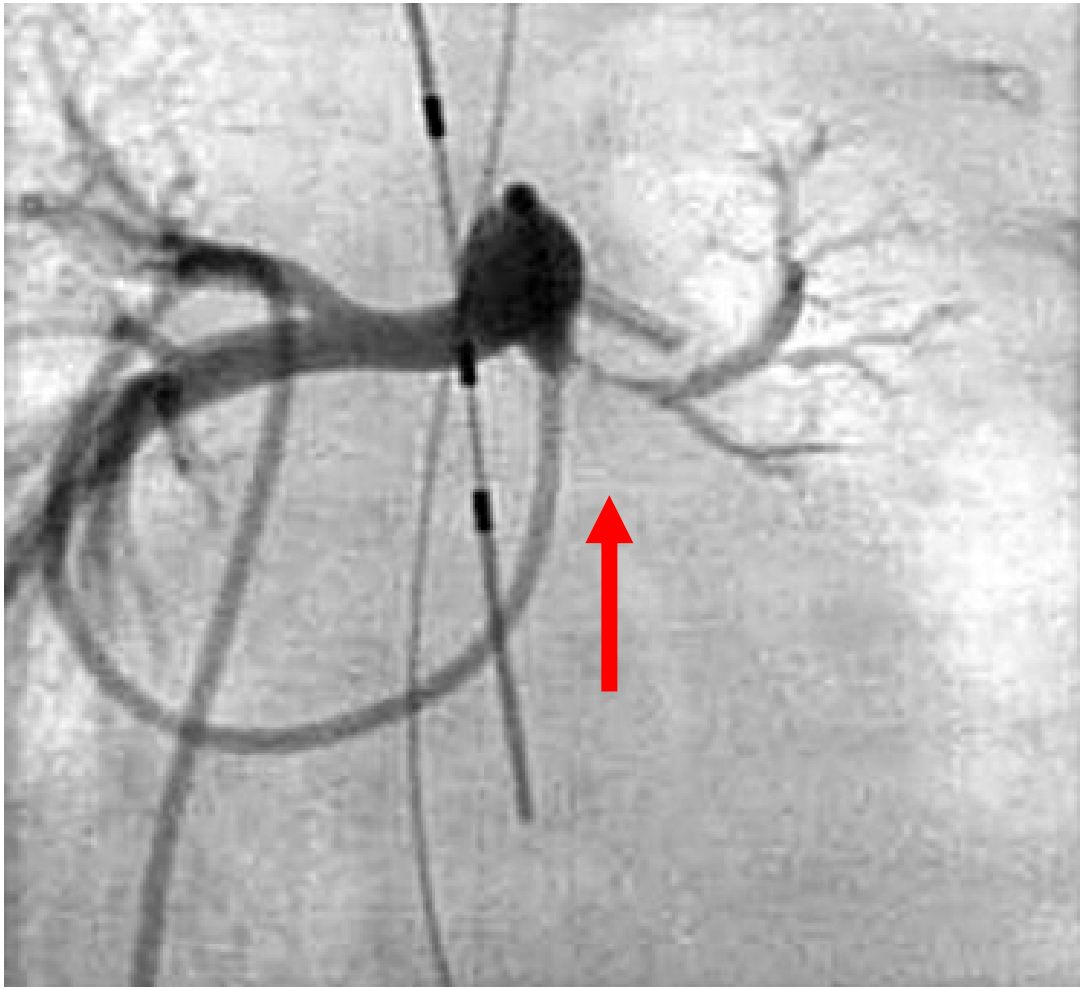
Washington Hospital Center

Complete occlusion of the left pulmonary artery after de-banding and closure of the arterial duct with a clip (the device with three markers is for calibration purposes)



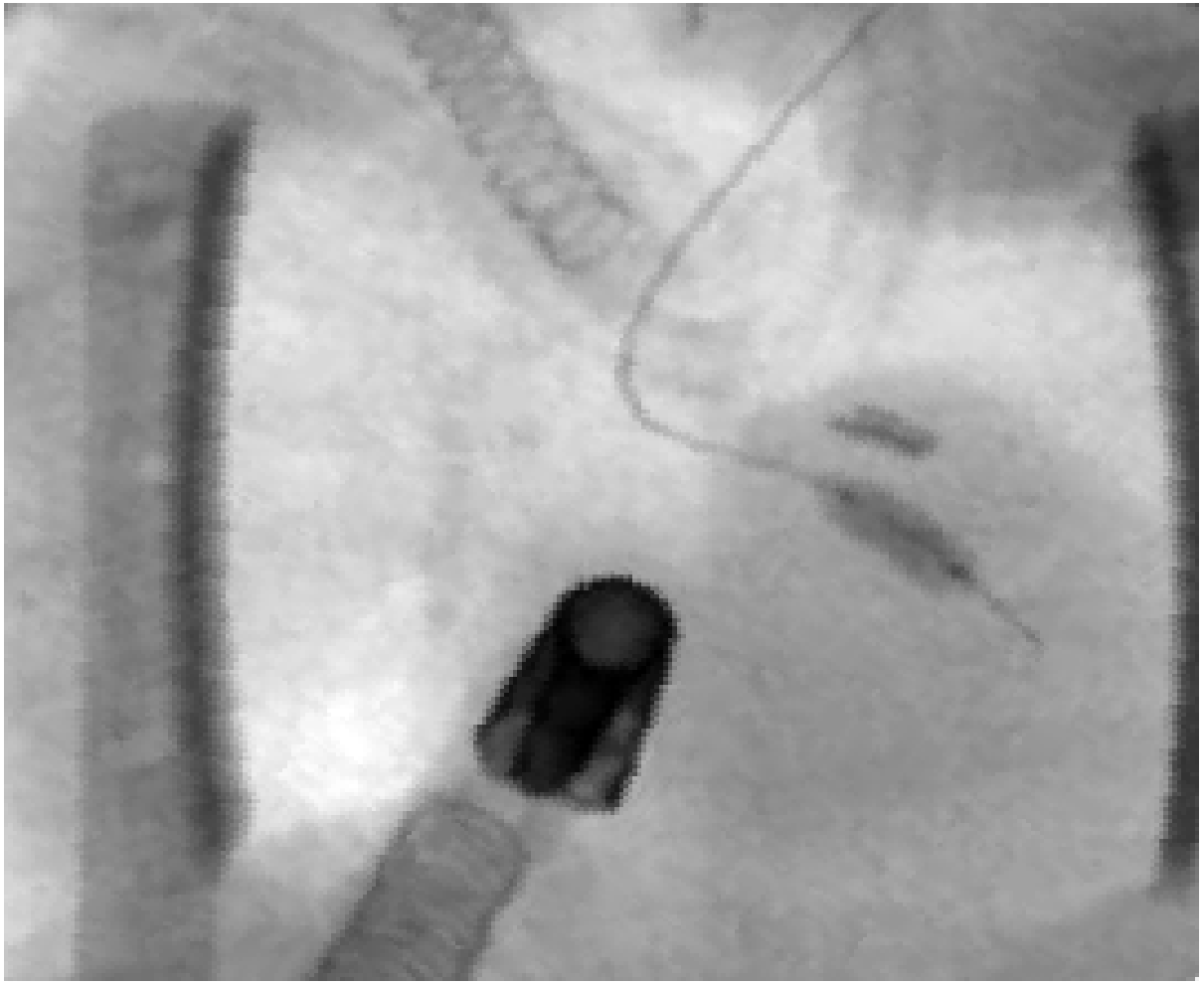
Peter Zartner, M. D., Pediatric CardiologyUniversity of Erlangen-Nuremberg, Germany

Crossing the stenosis with a guide wire angiography revealed reperfusion



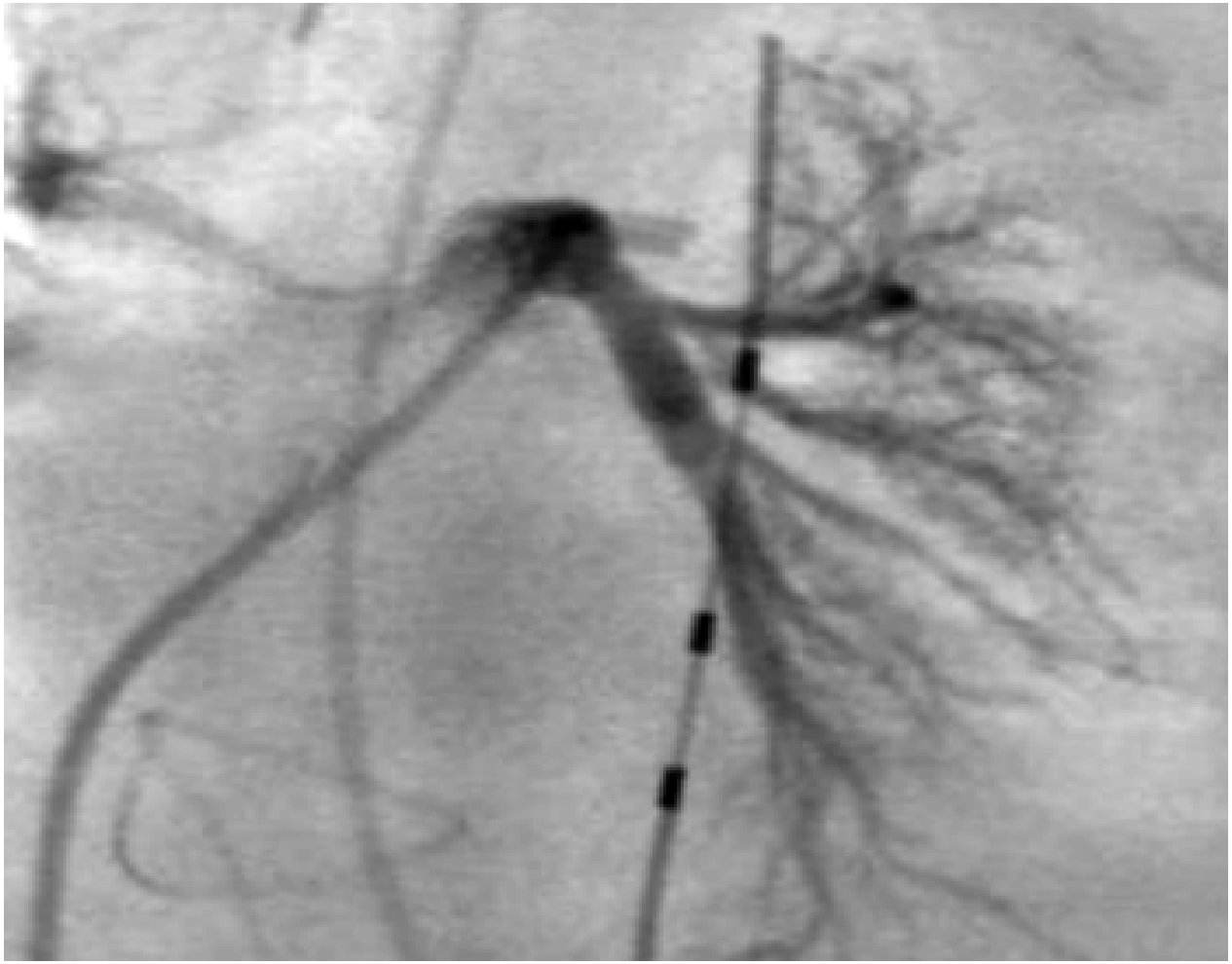
Peter Zartner, M. D., Pediatric CardiologyUniversity of Erlangen-Nuremberg, Germany

Implantation procedure of Mg Stent 3.0/10mm with a contrast filled balloon catheter



Peter Zartner, M. D., Pediatric CardiologyUniversity of Erlangen-Nuremberg, Germany

At one week follow up after Mg Stent the left lung was reperfused



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Why bio-absorbable stents?

Provides stent scaffolding and radial strength properties as long as needed to ensure an open lumen - same as a permanent stent

AND

Different to permanent stents:

- Leaves no stent behind long-term (no chronic inflammation, no long-term impact on local vasomotion)
- No “Full metal jacket” makes later treatments of the same segment easier (e.g., surgical bypass)
- MRI / CT compatibility (allows non-invasive follow-ups)
- Potentially: no late stent thrombosis and no need for prolonged antiplatelet therapy

Absorbable Metal Stent

Biocompatibility – BIOTRONIK Magnesium Alloy

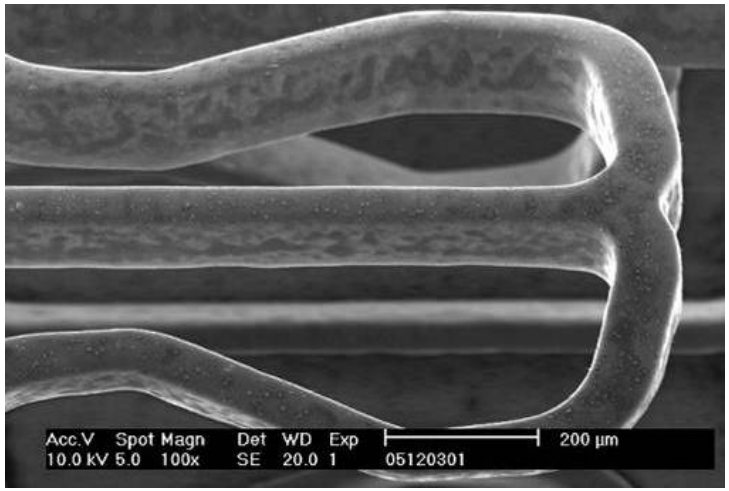
Magnesium and the human body

- Essential element for human body, involved in the synthesis of more than 300 enzymes
- Physiologically occurrence: 4th most common mineral
- Quantity in human body: ~ 20 g
- Daily need (adult): ~ 350 mg
- Quantity in the intracellular space: > 40%

BIOTRONIK AMS features

- Weight of a 3.0x10mm stent: ~ 3 mg
- Complete absorption: ≈ 12 weeks

First generation AMS device (AMS 1)



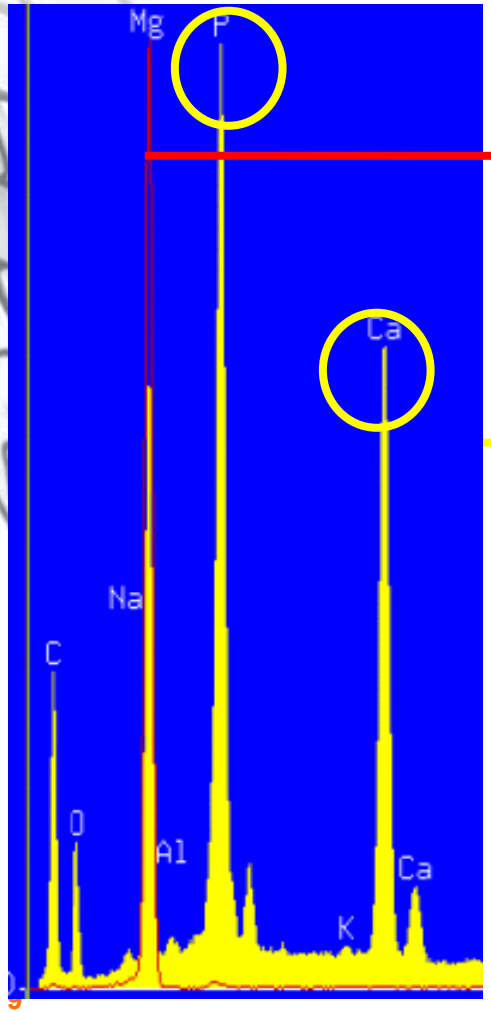
Available sizes

- Diameter: 3.0 and 3.5mm
- Length: 10mm and 15 mm

Magnesium alloy device

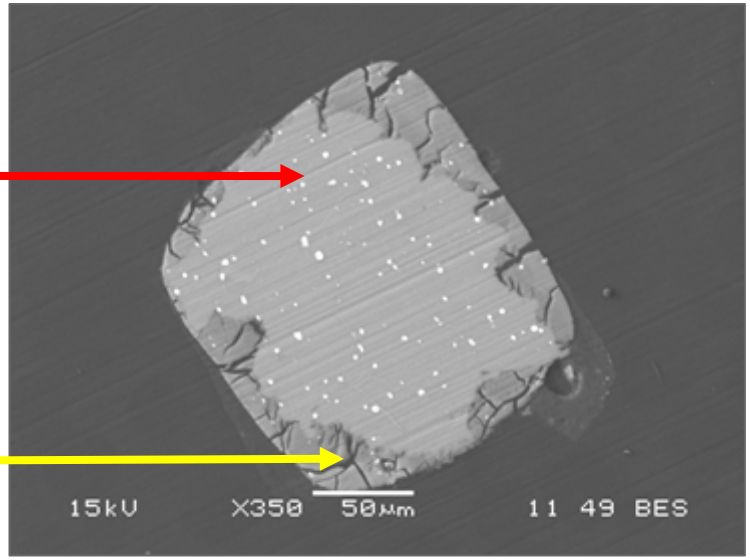
- Weight of a magnesium stent: ~ 3 mg
- Complete absorption: several months
- High collapse pressures

Analysis of degradation products by EDX analysis



Mg alloy <u>before</u> degradation

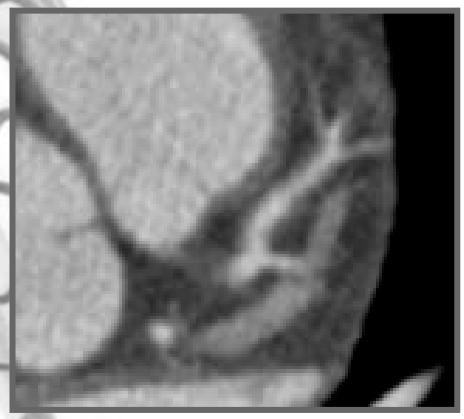
Conversion layer: soft shell of $Ca(PO_4)_2$

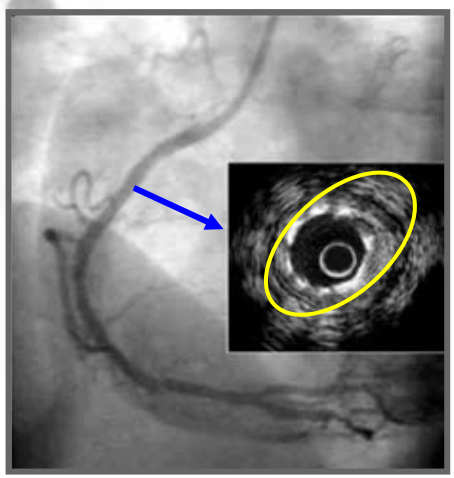


Mg alloy after 13 days in porcine blood

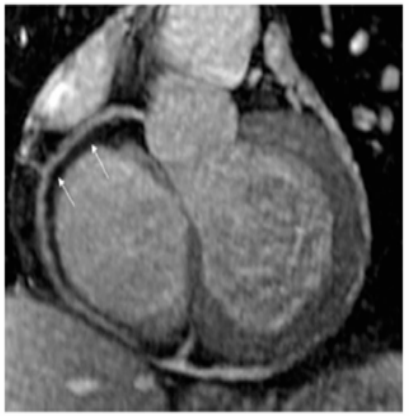
Compatibility of AMS in MRI and multi-slice CT

16 Multi Slice CT



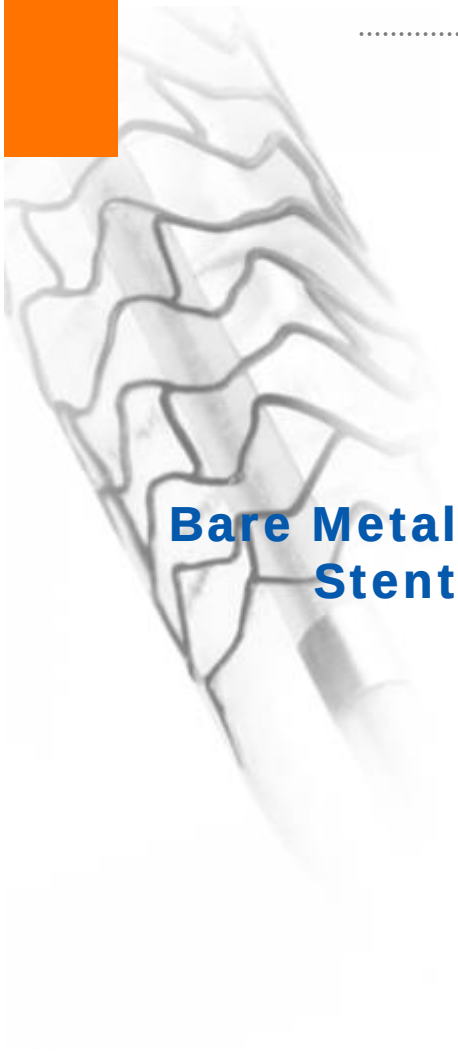


Magnetom (Sonata, 1.5 T, Siemens)

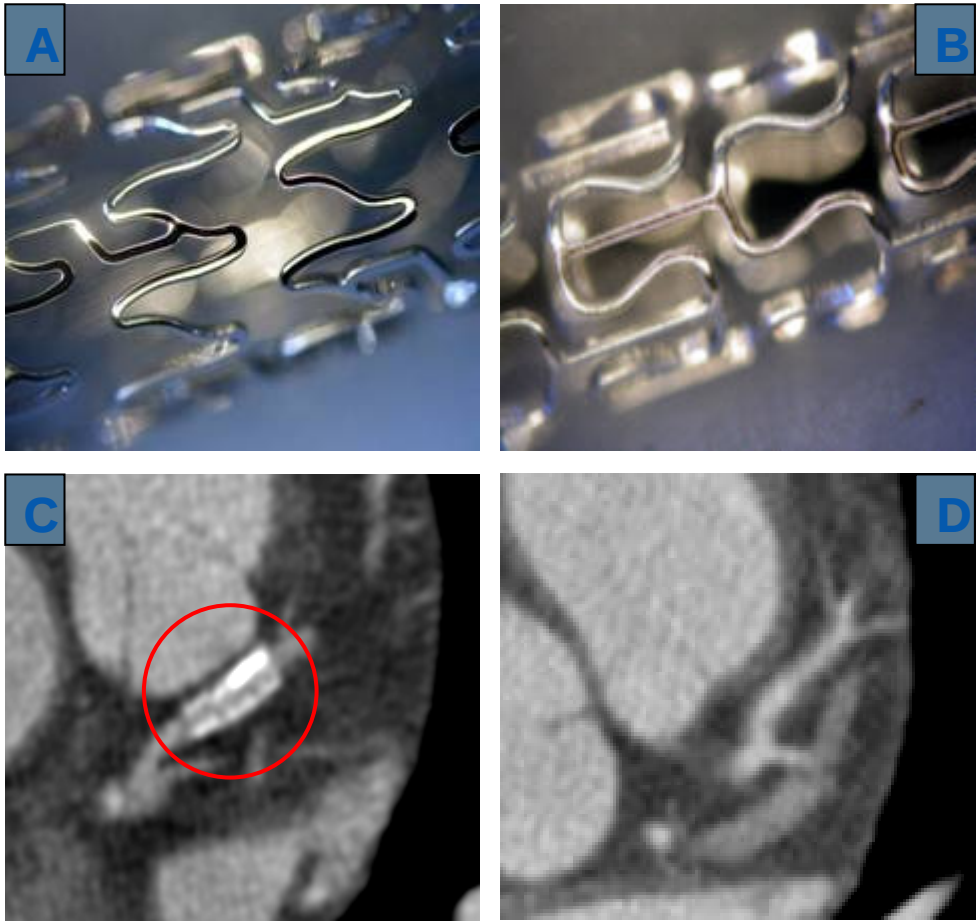


- No stent artefact
- Optimal vessel lumen imaging

CT compatibility of AMS

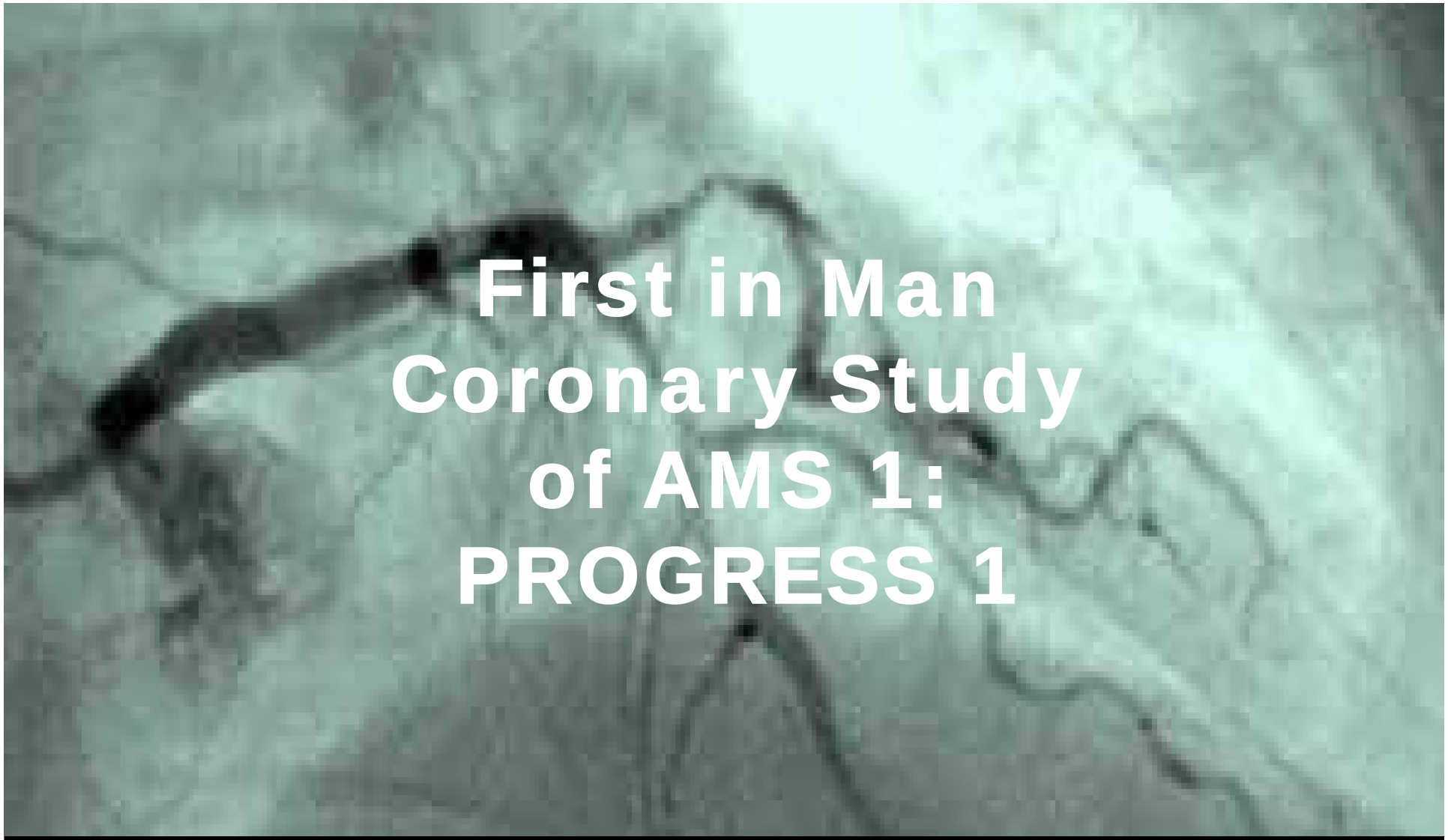


Bare Metal Stent



Absorbable Metal Stent

16-row MSCT



First in Man Coronary Study of AMS 1: PROGRESS 1

Clinical Performance and Angiographic Results of the Coronary Stenting with Absorbable Metal Stents

Principal Investigator: Prof. Raimund Erbel

PROGRESS AMS 1

Purpose

- To evaluate the clinical feasibility of the Absorbable Metal Stent in the treatment of a single de novo lesion in a native coronary artery

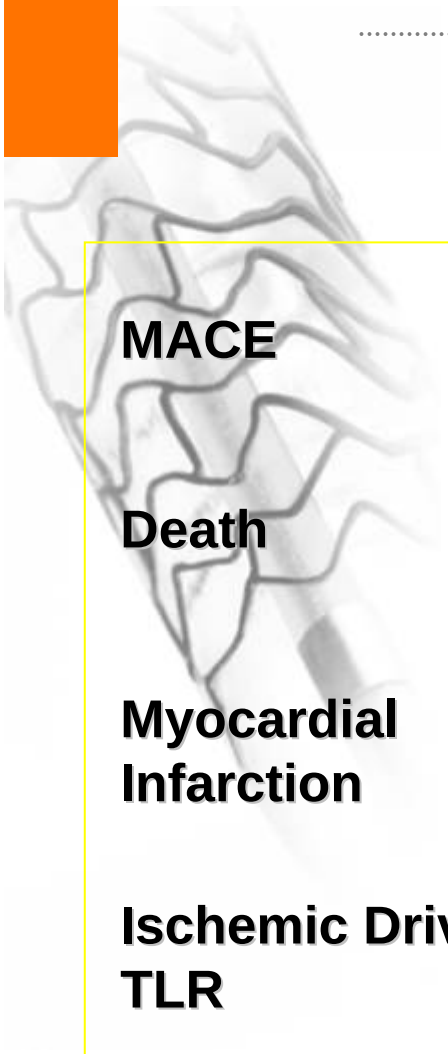
Design

- Prospective, multi-center, consecutive, non-randomized FIM (First In Man – coronary) study

Patients

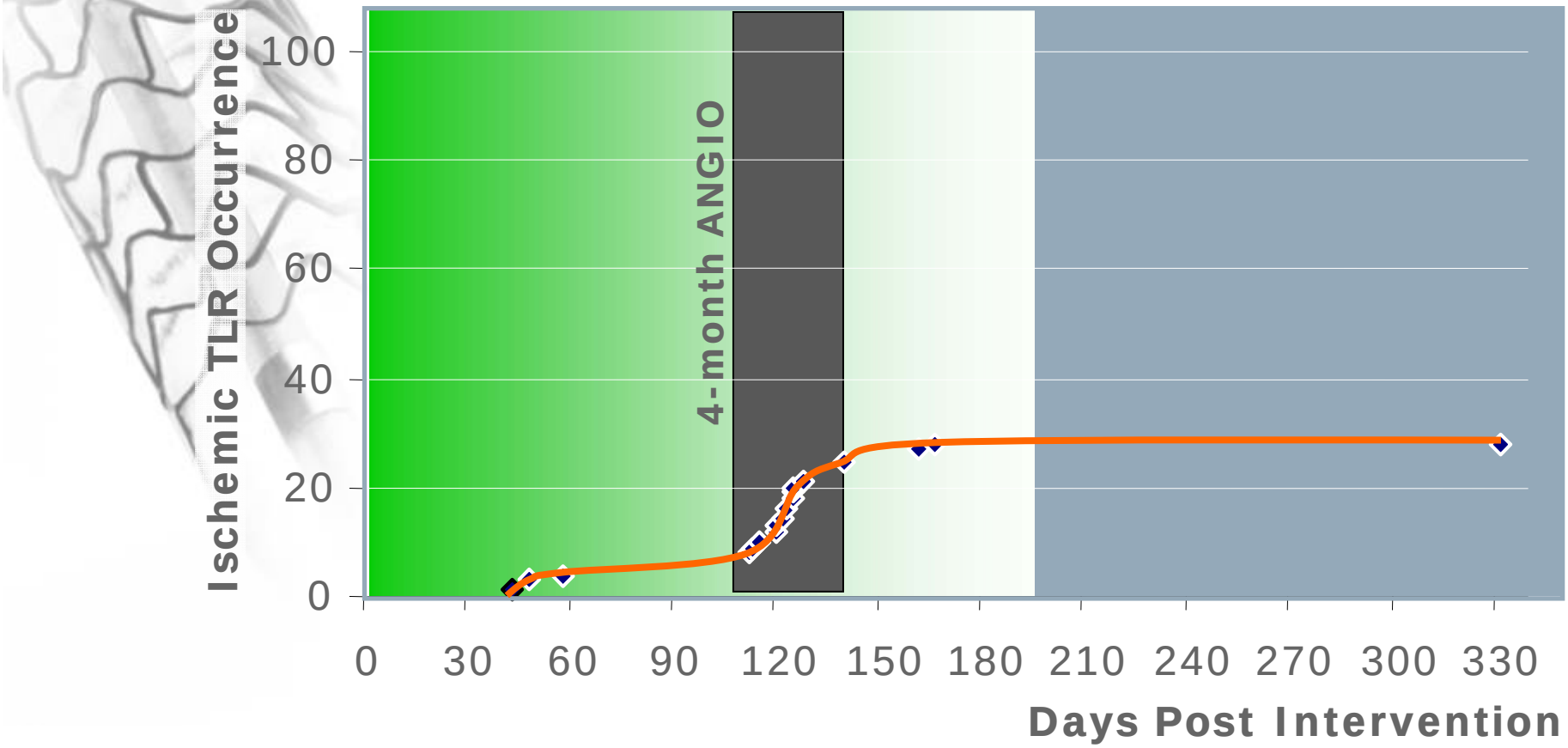
- The study included 63 patients at 8 international clinical sites

PROGRESS: Clinical Results

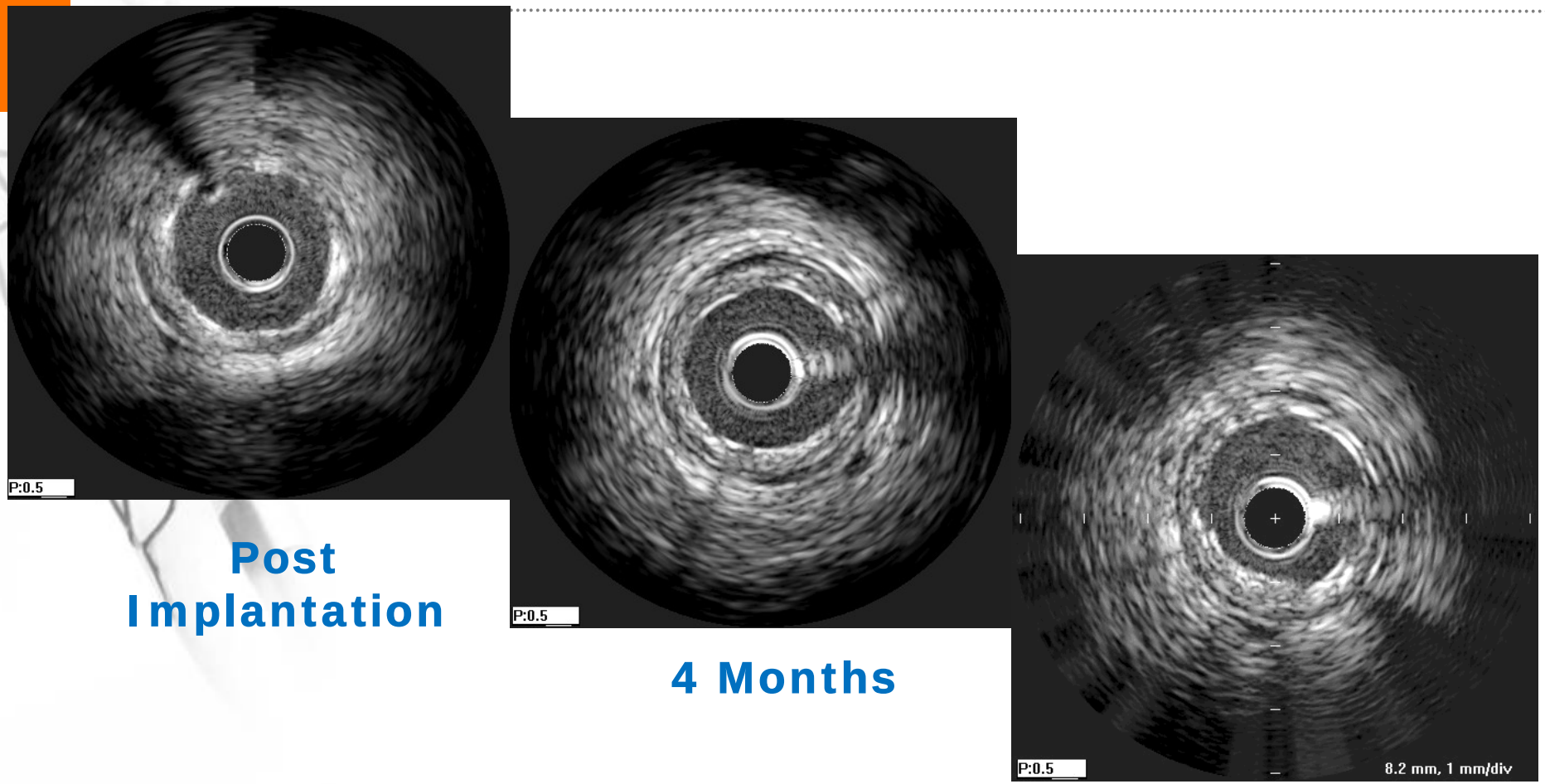


	In Hospital		4 Months		4-12 Months		12 Months	
	N	%	N	%	N	%	N	%
MACE	0	0	15	23.8	2	3.3	17	27.9
Death	0	0	0	0	0	0	0	0
Myocardial Infarction	0	0	0	0	0	0	0	0
Ischemic Driven TLR	0	0	15	23.8	2	3.3	17	27.9

TLR occurrence in PROGRESS 1



NLD 014-002

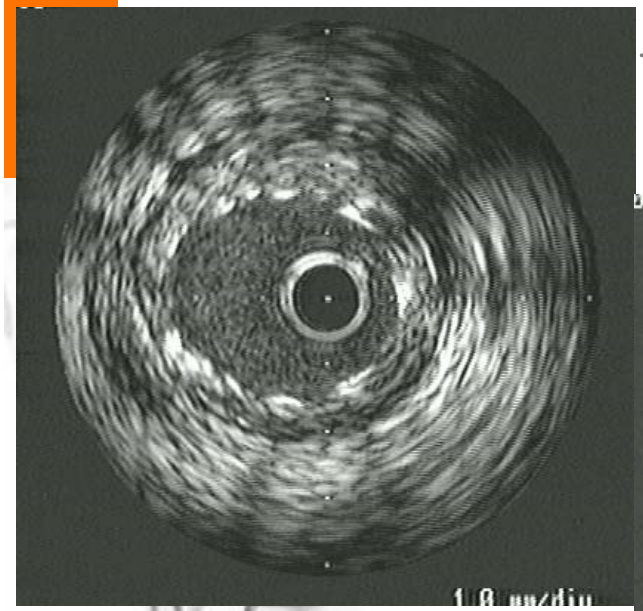


Post Implantation

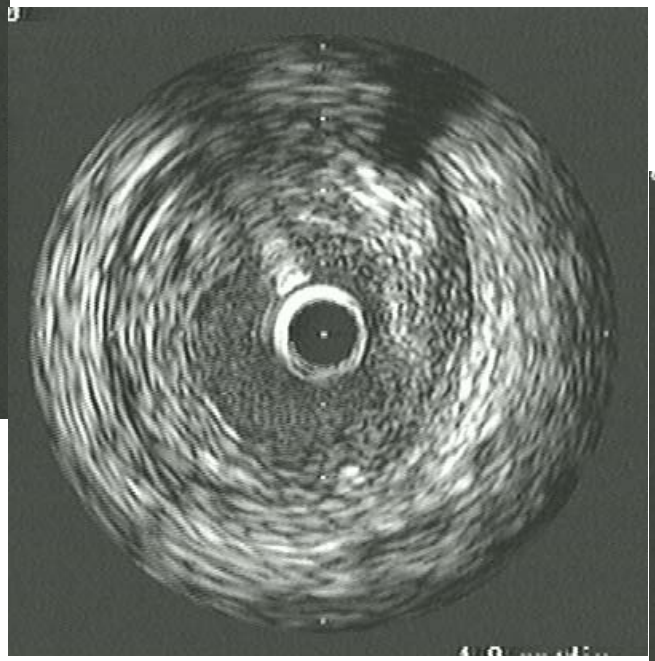
4 Months

28 Months

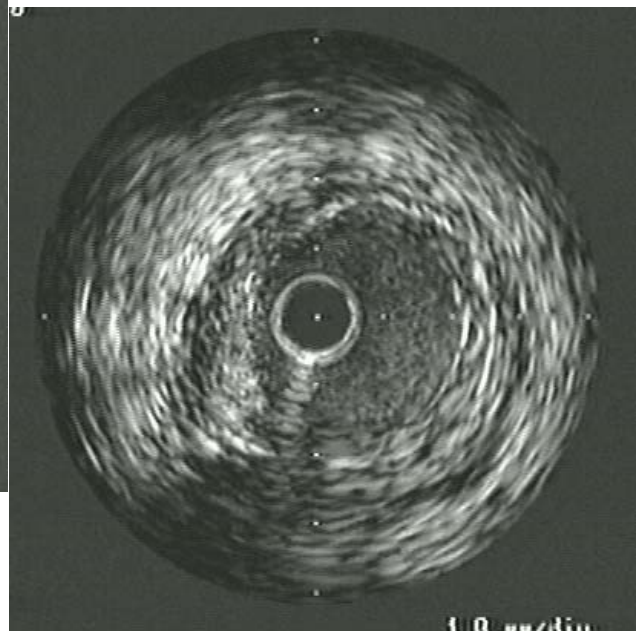
AUS 004-001



Post Implantation



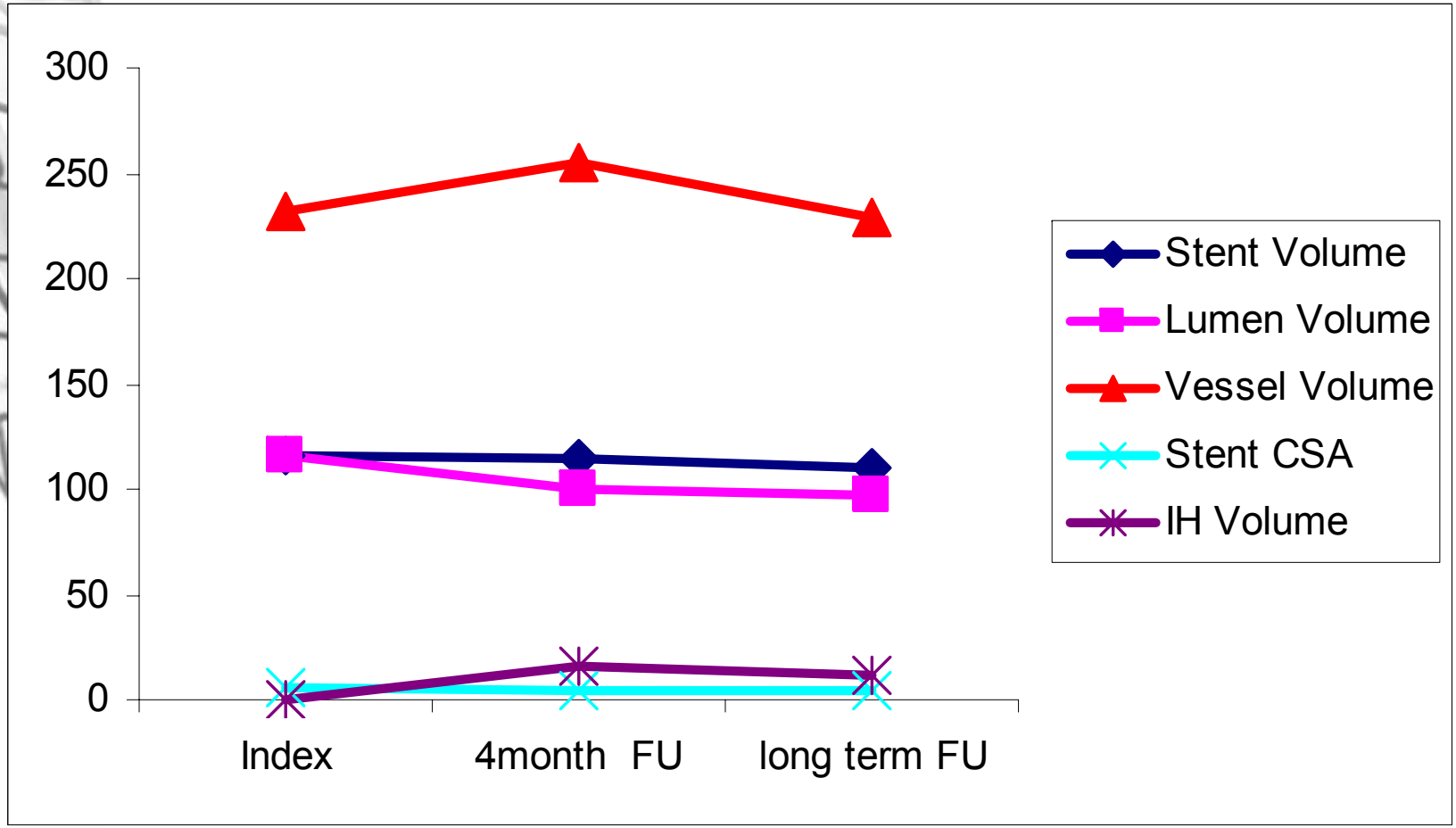
4 Months



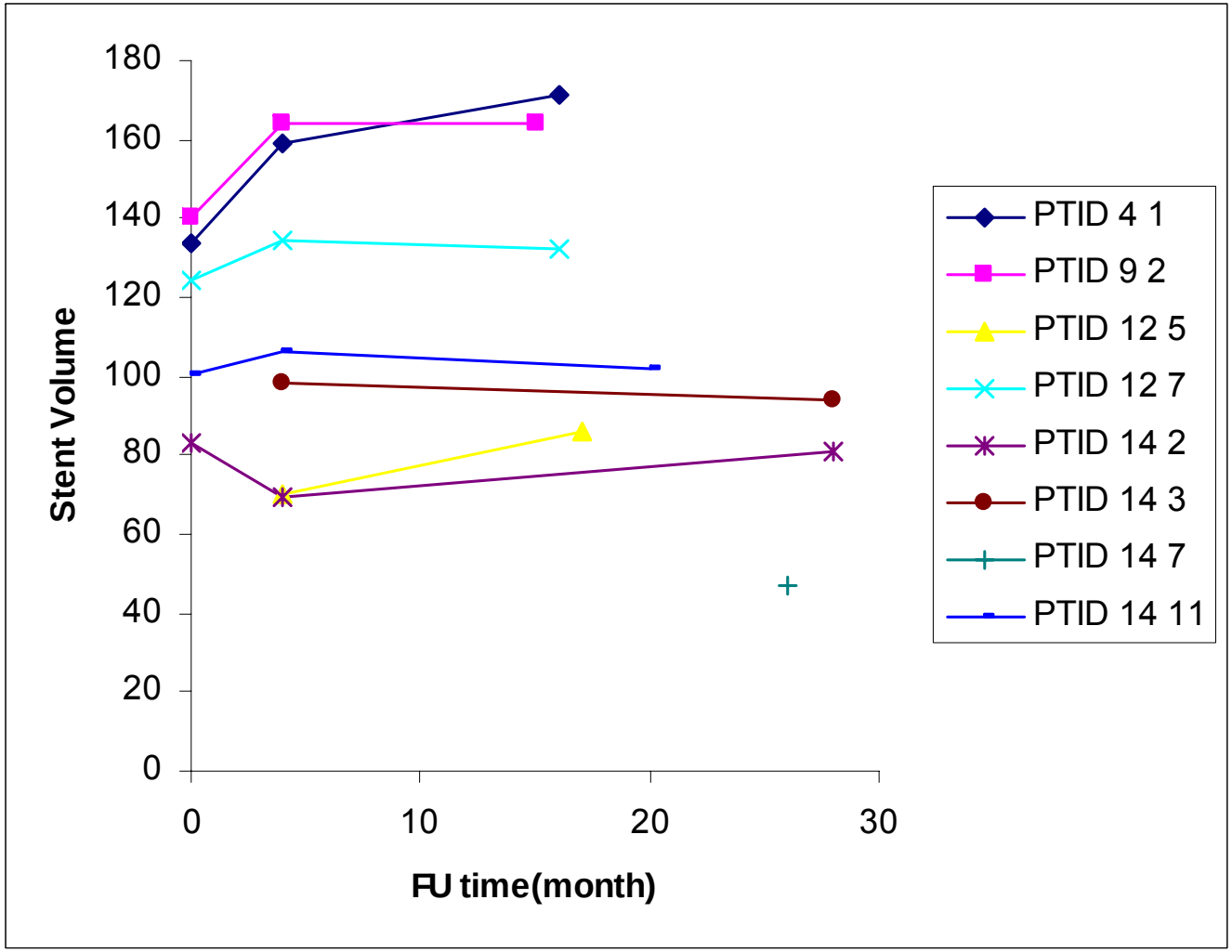
16 Months

17

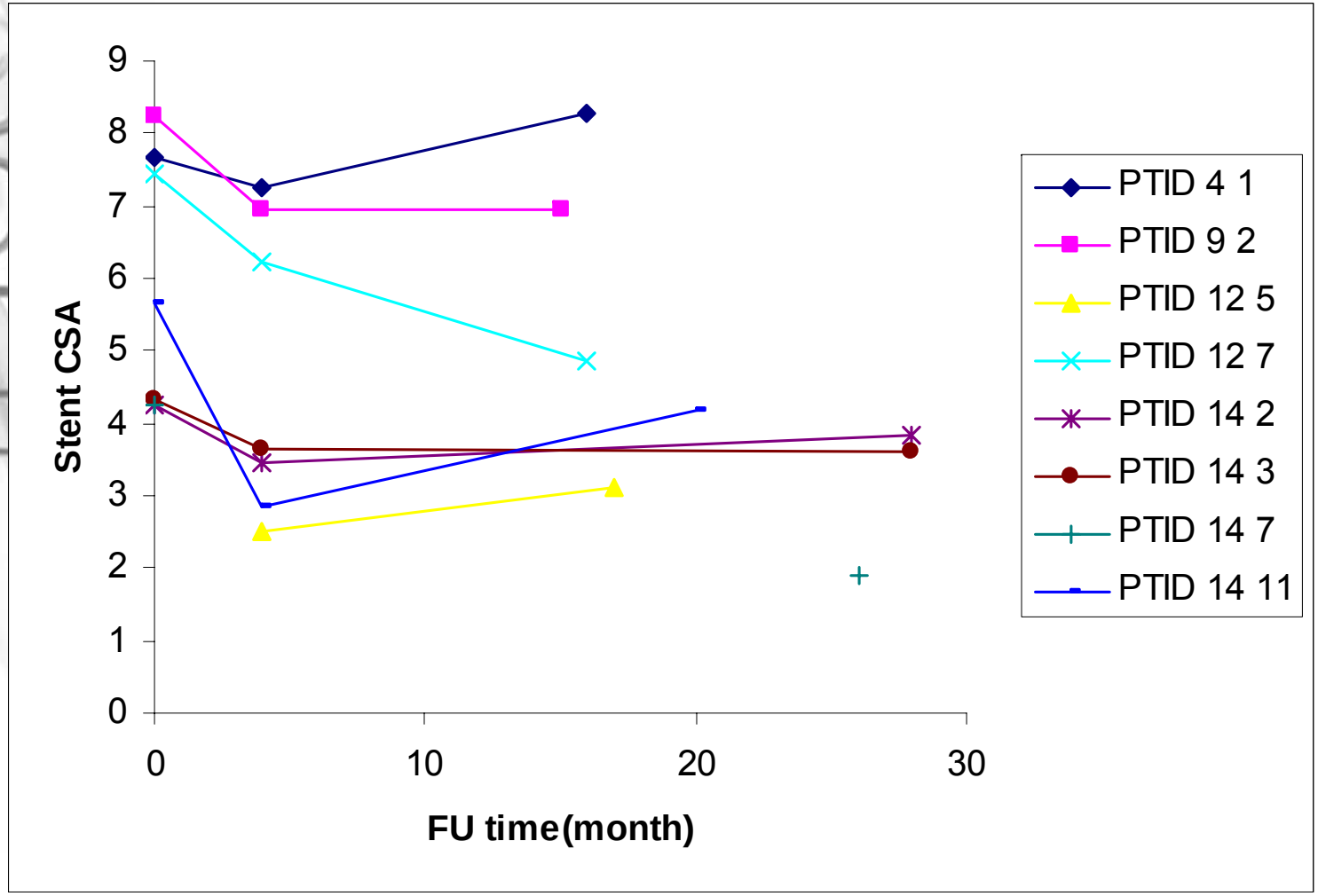
IVUS Analysis



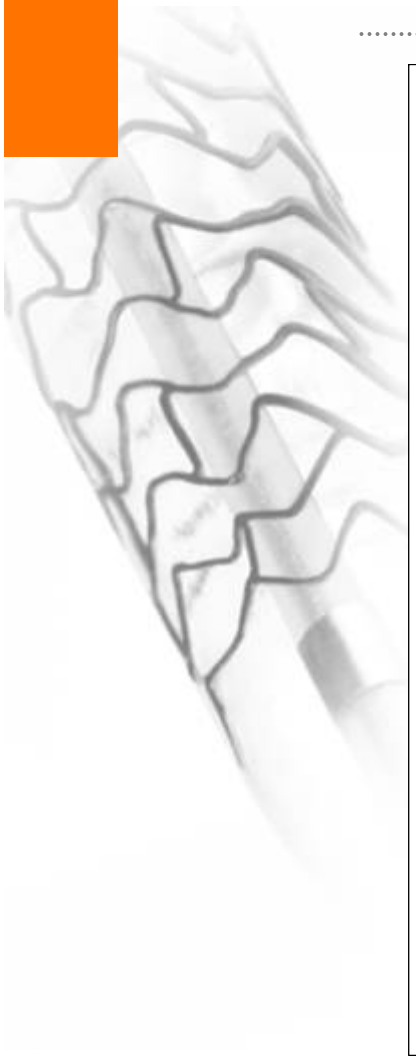
IVUS Stent Volume

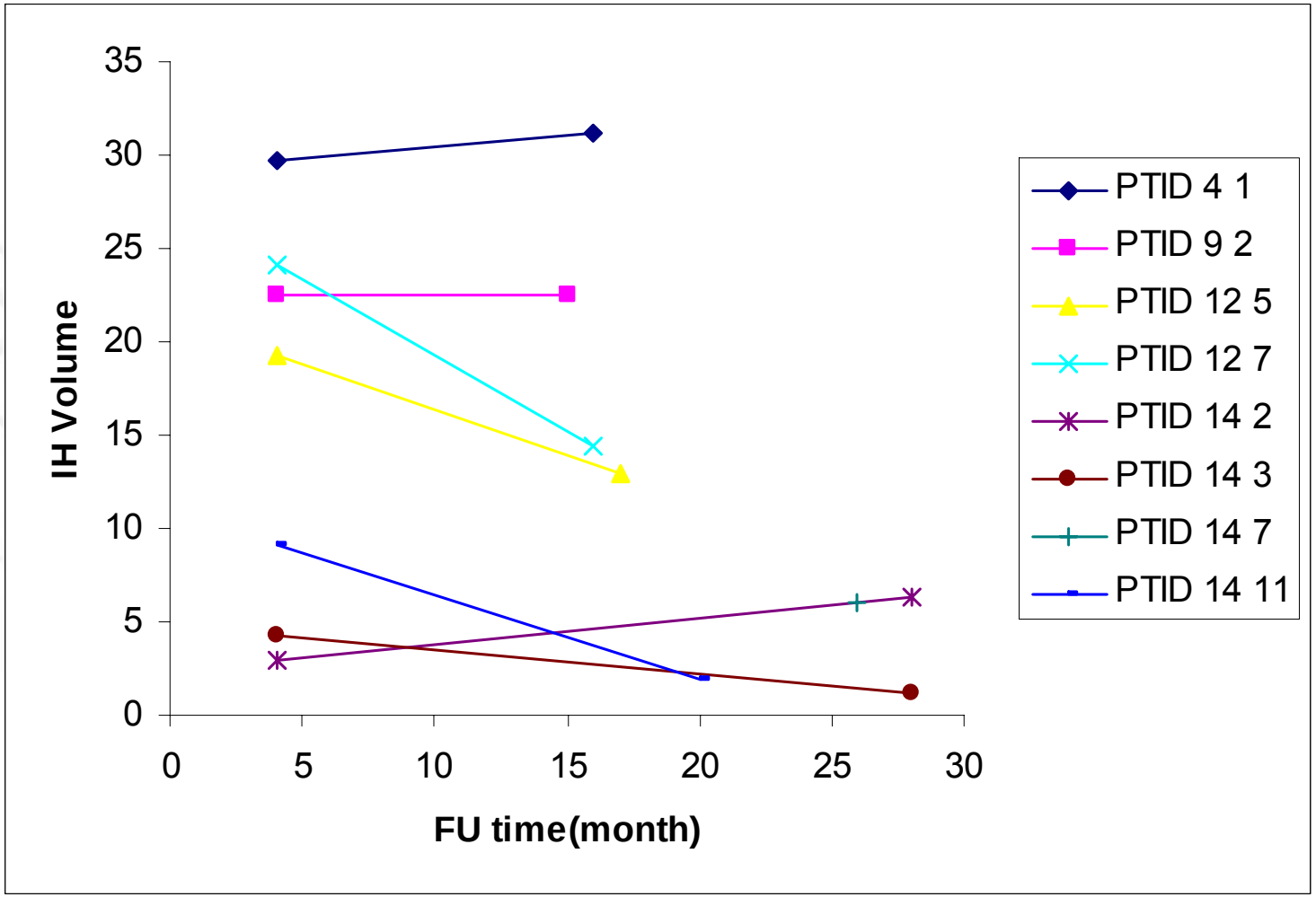


IVUS CSA

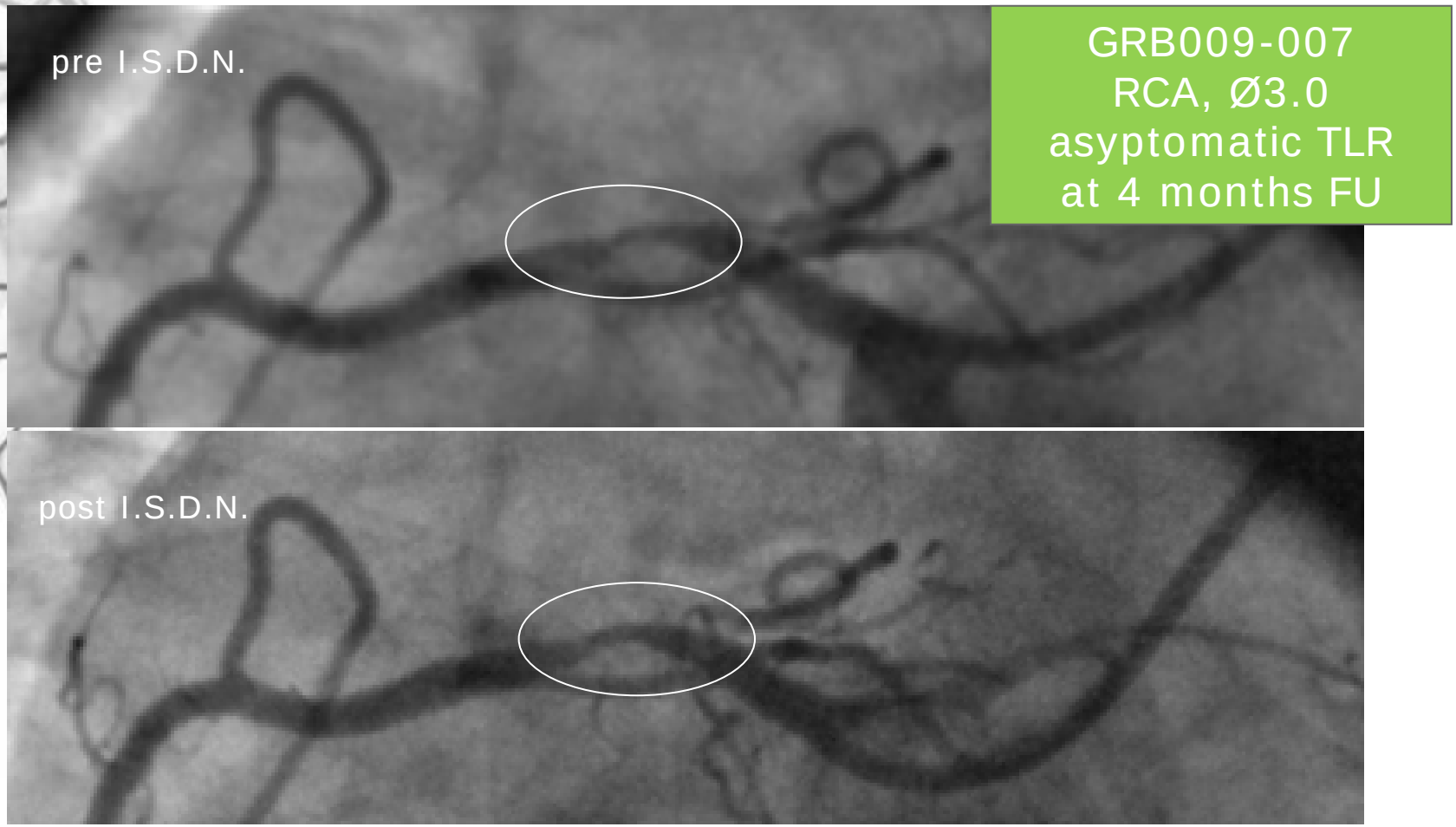

Stent CSA
9
8
7
6
5
4
3
2
1
0
0
10
20
30
FU time(month)
PTID 4 1
PTID 9 2
PTID 12 5
PTID 12 7
PTID 14 2
PTID 14 3
PTID 14 7
PTID 14 11

IVUS Intimal Hyperplasia Volume





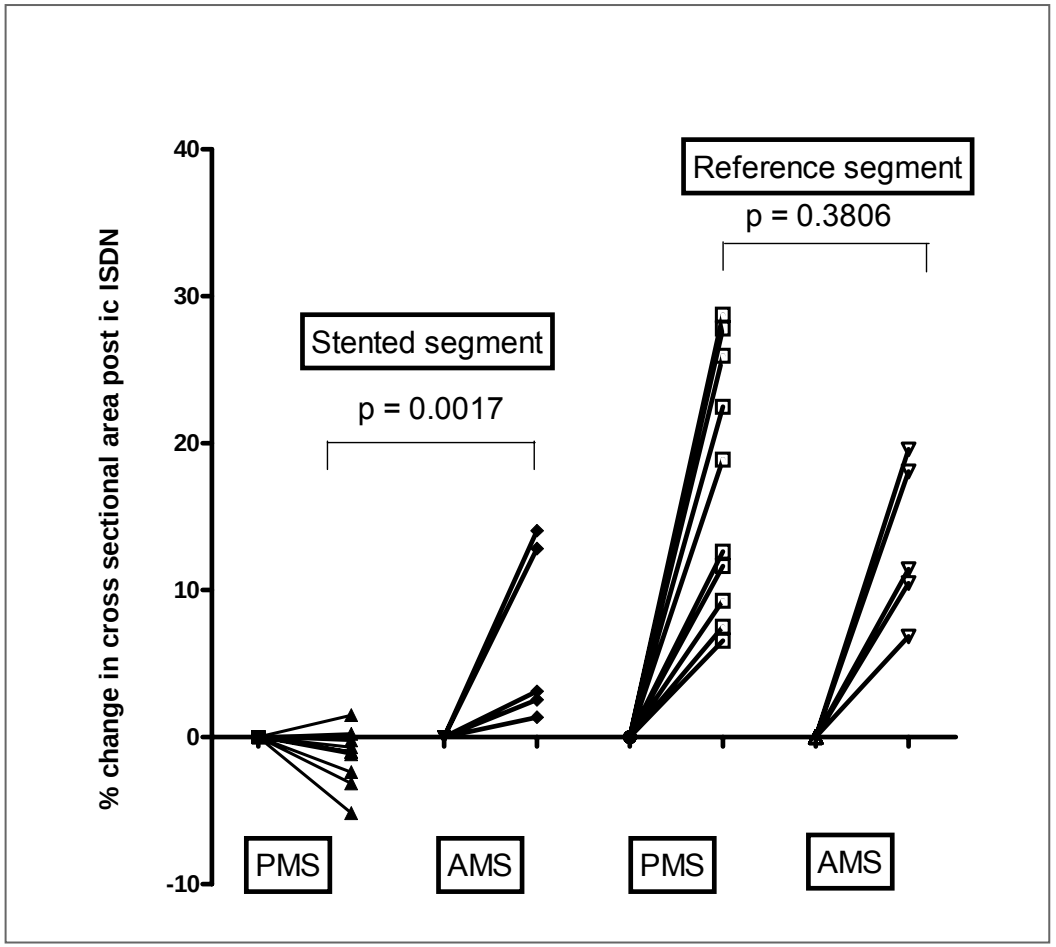
First evidence of vessel flexibility in AMS stented area by angio pre / post nitroglycerin



GRB009-007
RCA, Ø3.0
asyptomatic TLR
at 4 months FU

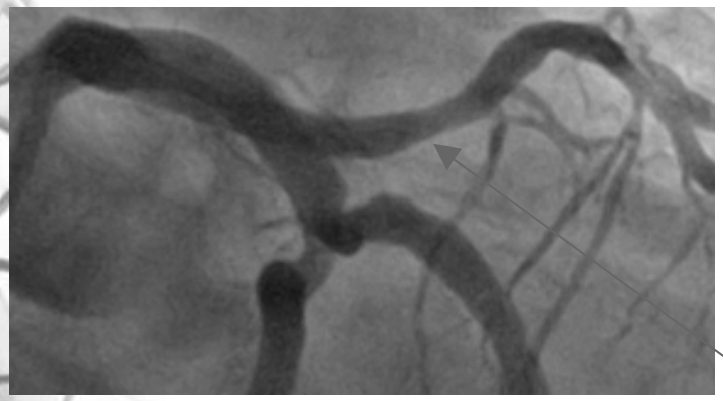
Vessel Reactivity

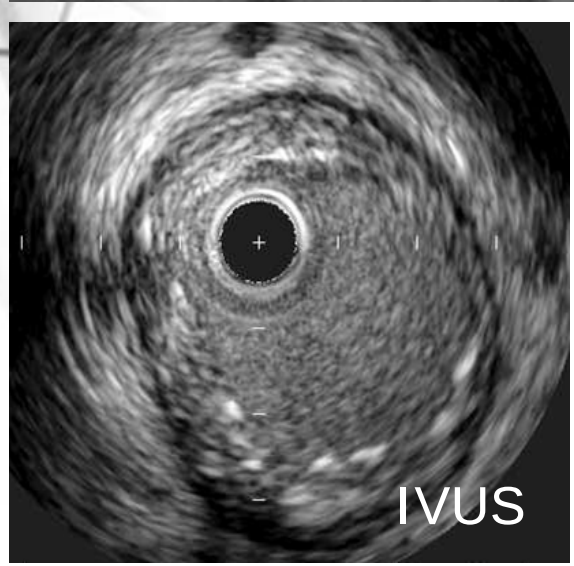
Intracoronary nitrate induced vasodilatation in Permanent Metal Stent (PMS) control patients and Absorbable Metal Stent (AMS) patients within stent and in proximal reference segments at 4 months post implant.

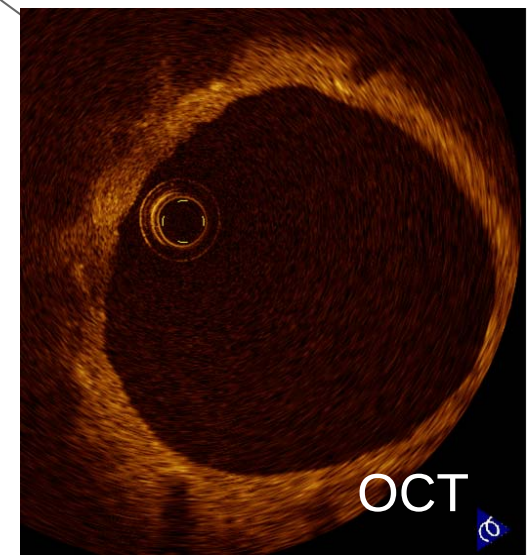


Courtesy of Dr Miles Dalby
Royal Brompton & Harefield

15 months after AMS implantation in human







- Very thin neointima
- Perfect ingrowth of AMS
- Completed healing of the stented vessel

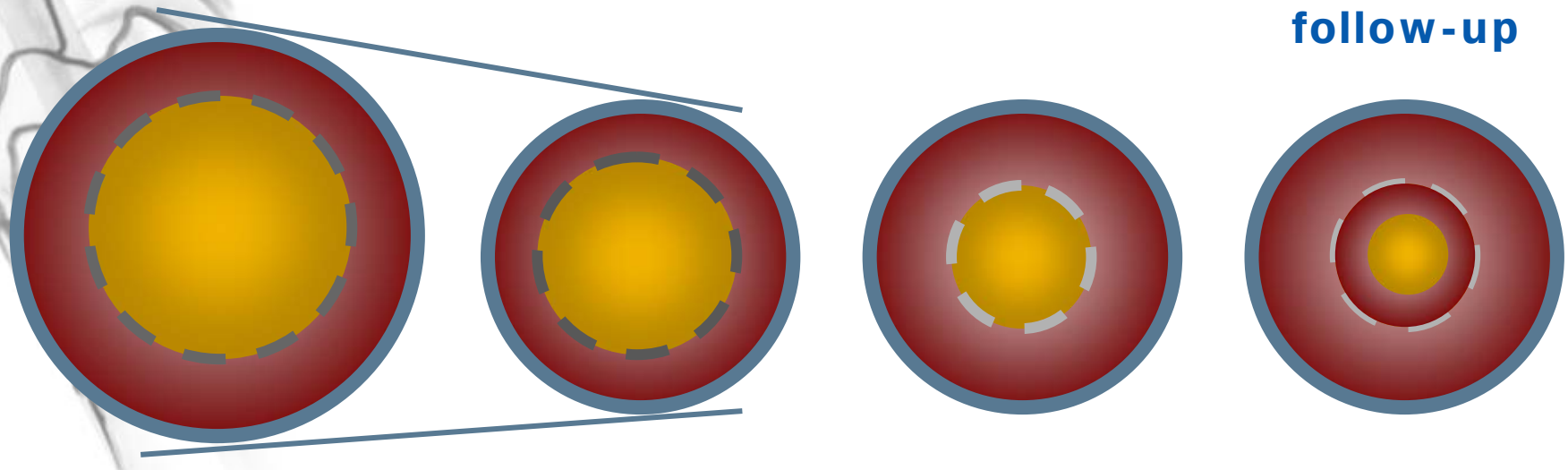
Conclusions - PROGRESS 1

- The AMS technology is feasible (high technical and procedural success), absorption of the device as intended
- The AMS provided safety (no death, no MI, no stent thrombosis)
- The study met the primary endpoint (MACE <30%)
- Further improvement of the AMS 1 technology are needed to improve efficacy for coronary use

Results PROGRESS 1 - IVUS

Post implantation

4 months follow-up



Contribution to lumen loss	Negative remodeling/ recoil	Thickening of extra-stent tissue	In-stent neointima
	42%	13.5%	41%

Improvement of AMS 1

AMS 1 is currently improved by ...

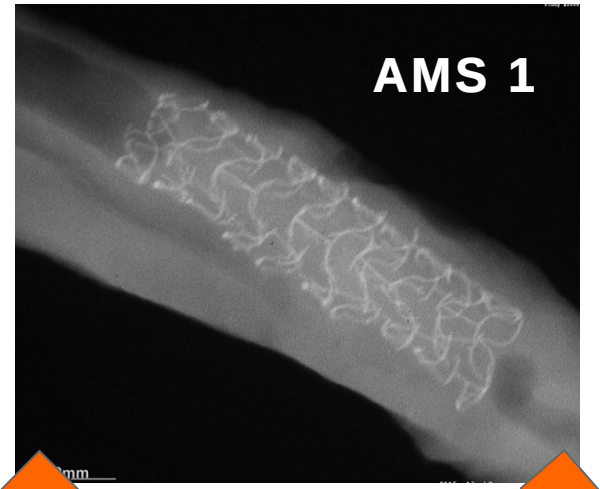
... prolonged mechanical stability

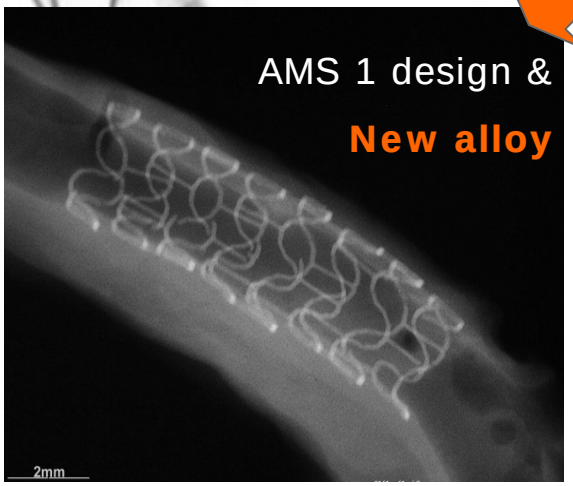
- Improved stent design
- Surface passivation
- Modified Alloy

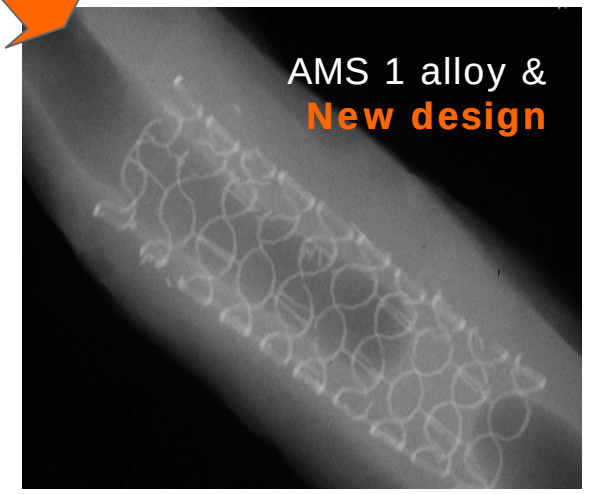
... reduction of neointima hyperplasia

- “DREAMS” = Drug elution

Selection trial - Stent structure after 4 weeks



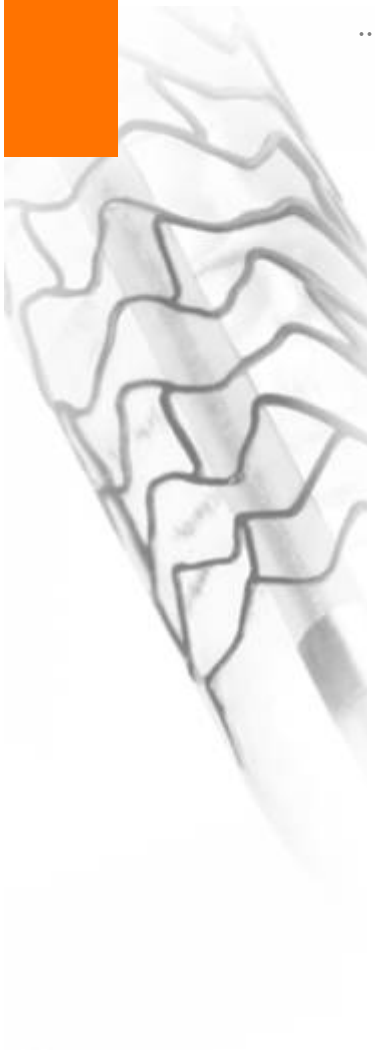


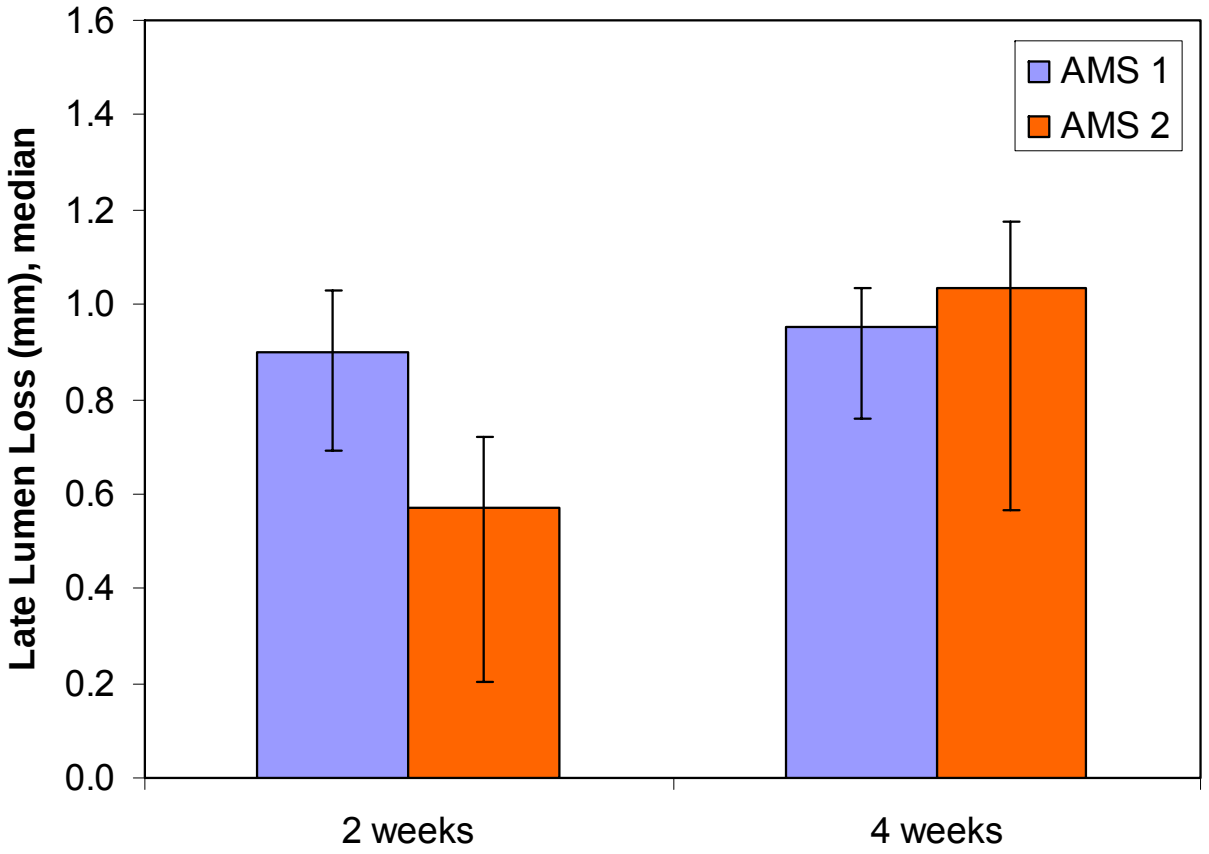


Description of new AMS 2 device

- Bare stent (no coating)
- Special Magnesium alloy
- Refined stent design
- Stent range
  - Diameters: 3.0 and 3.5mm
  - Lengths: 10 and 15 mm
- 6F compatible system, RX catheter

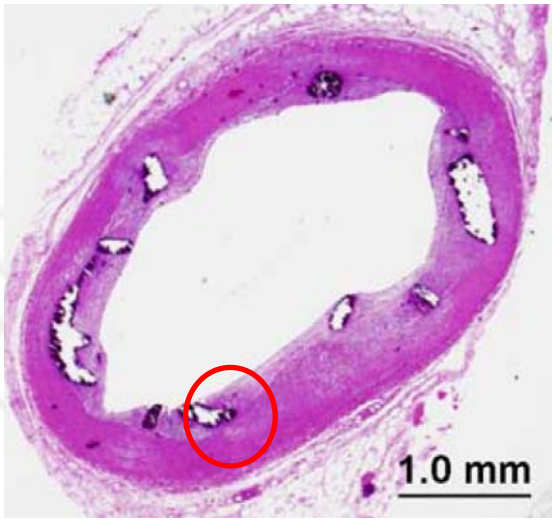
Combination trial - Angiography

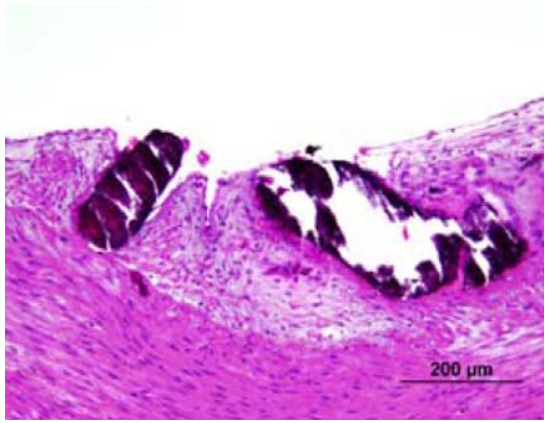




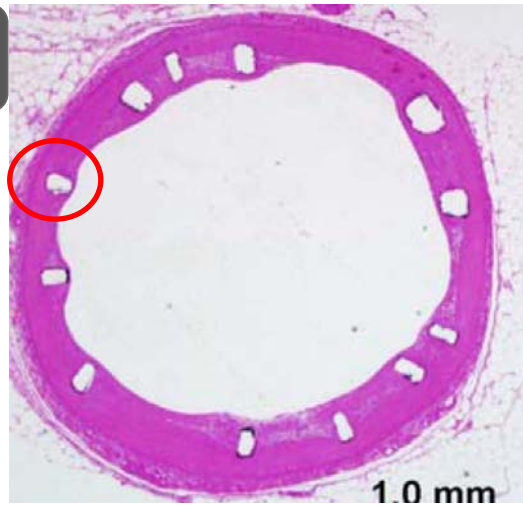
Combination trial- Representative histology 4 weeks

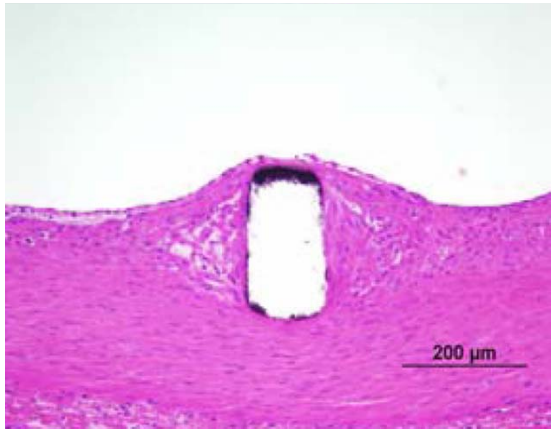
AMS 1





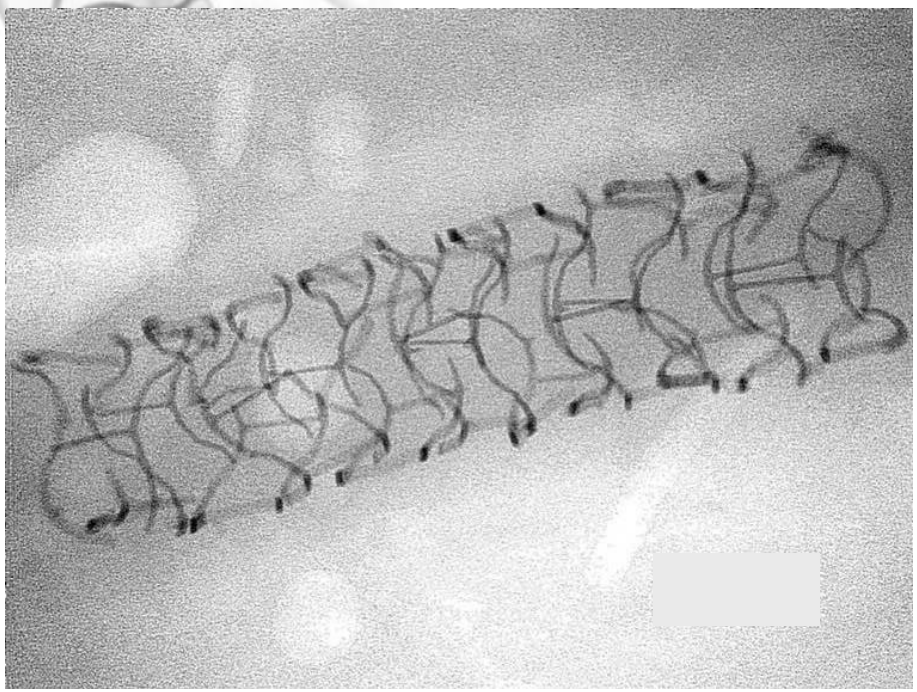
AMS 2



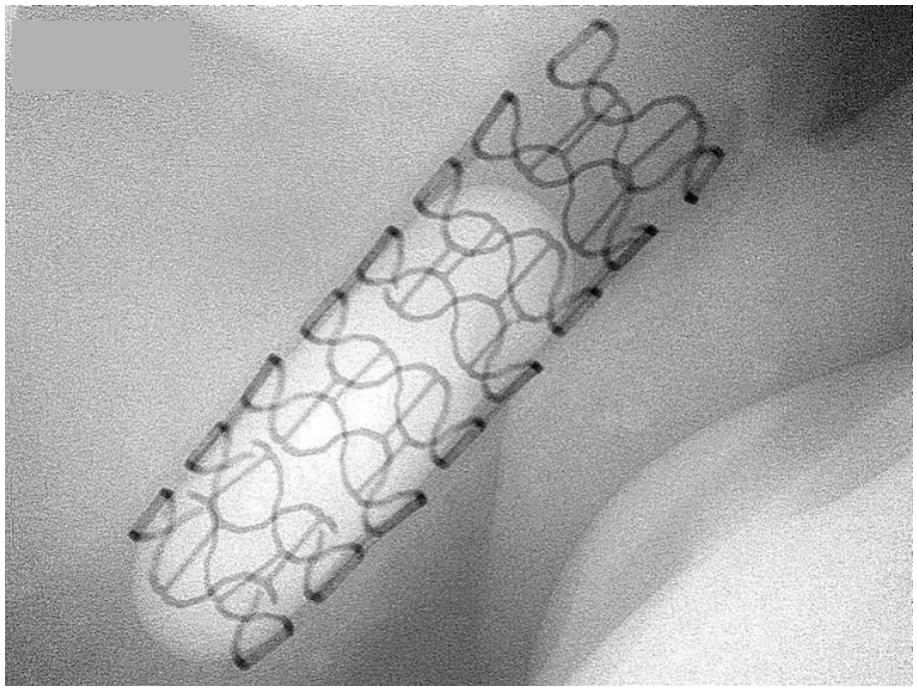


Combination trial - Representative stent structure at 2 weeks

AMS 1



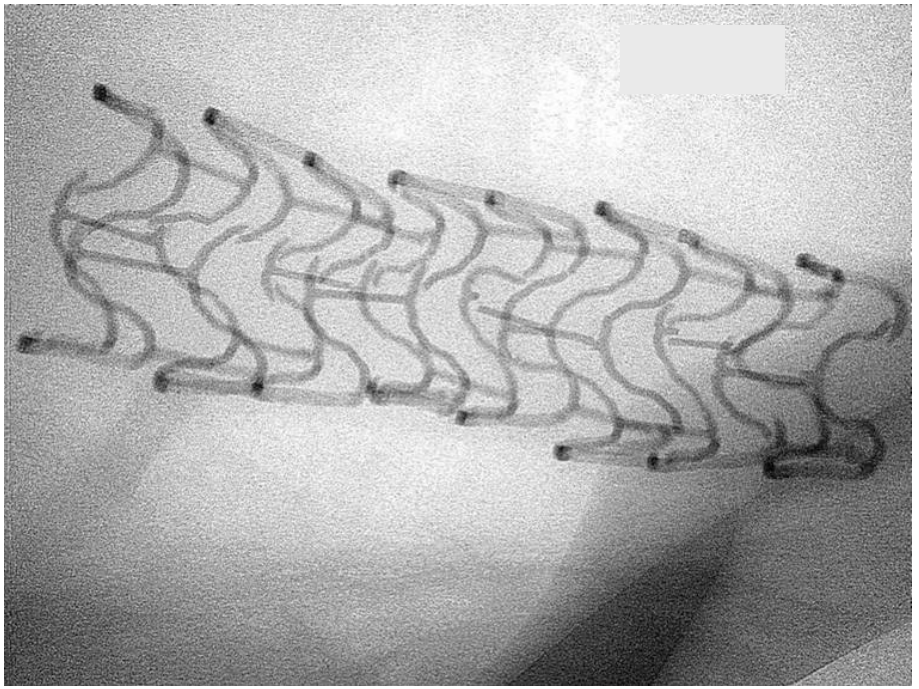
AMS 2



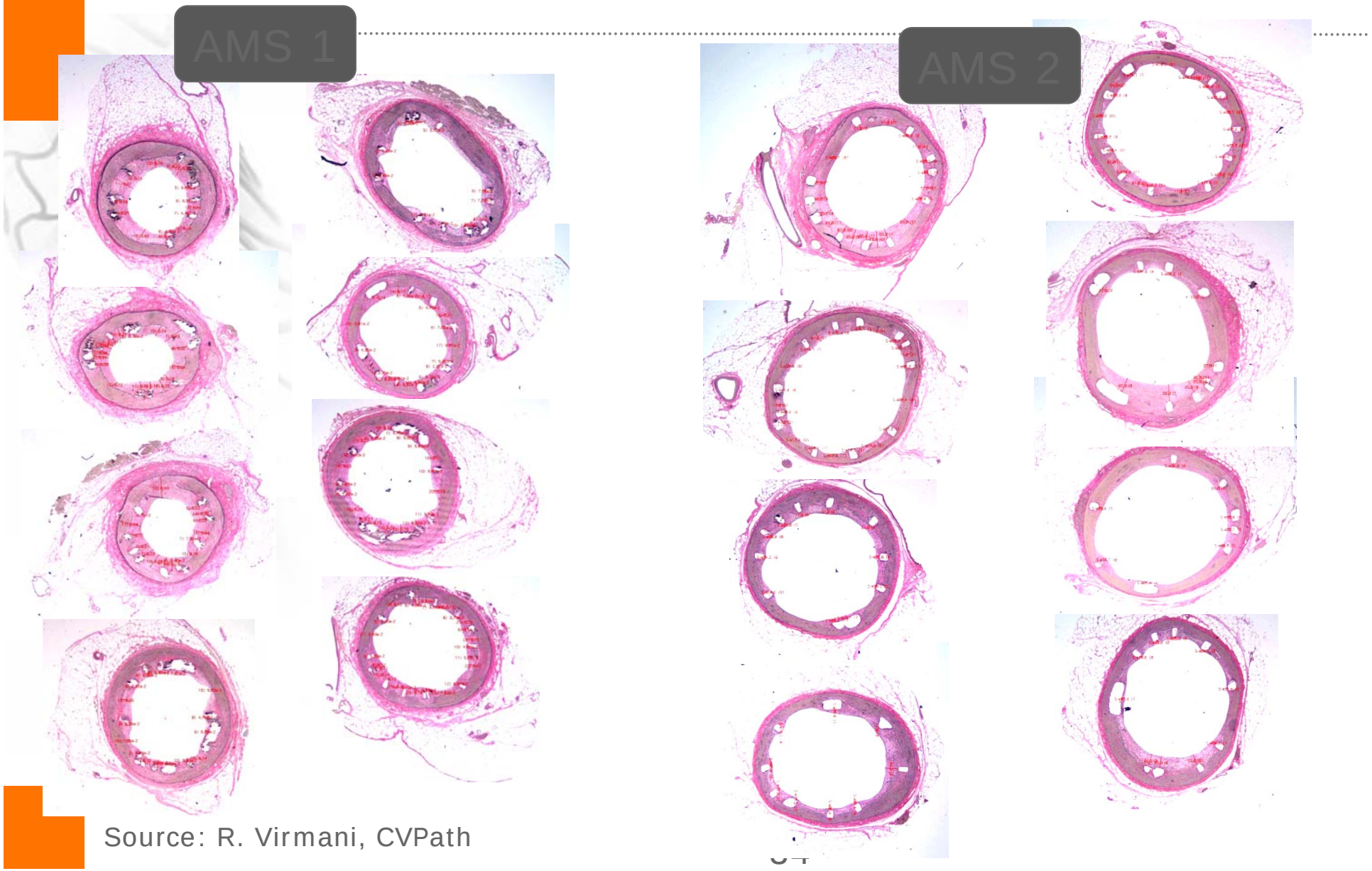
Combination trial - Representative stent structure at 4 weeks

AMS 1

AMS 2



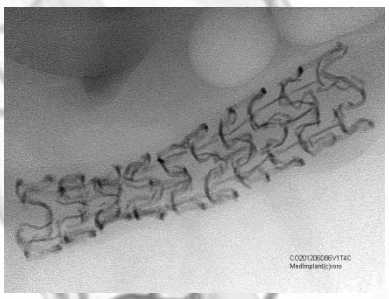
Histology 4 weeks

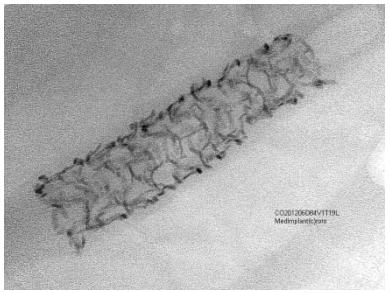


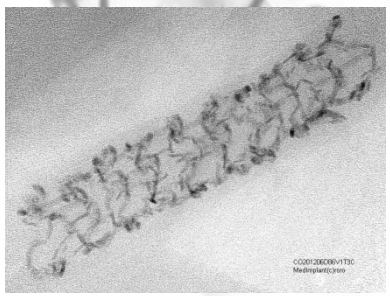
Source: R. Virmani, CVPath

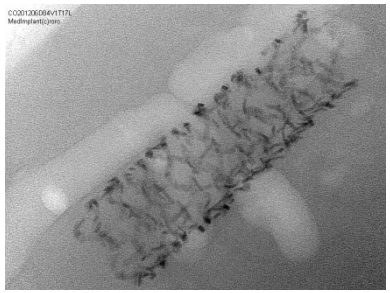
Stent structure at 3 month

AMS 1

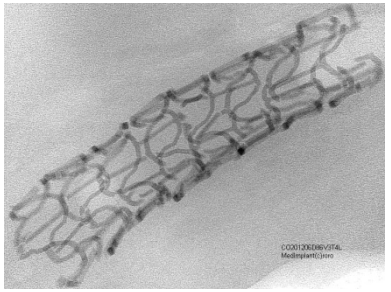


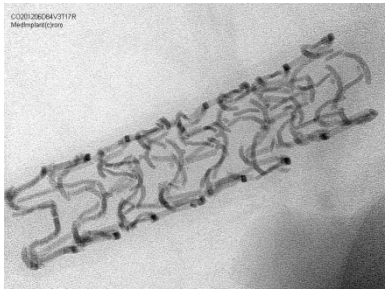


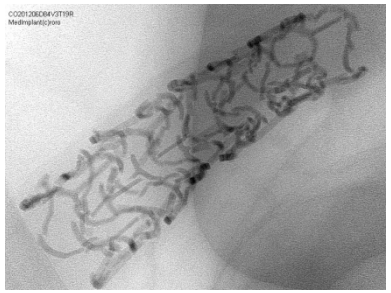


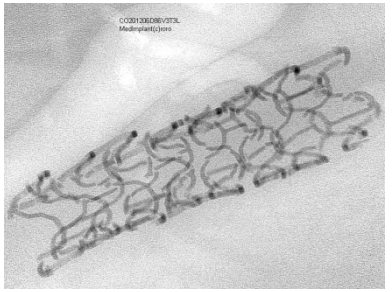


AMS 2



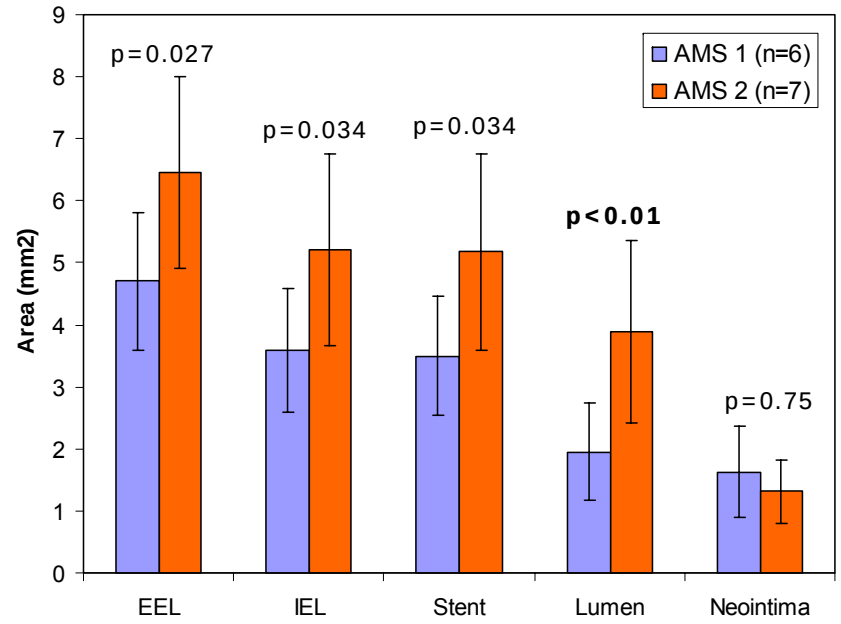




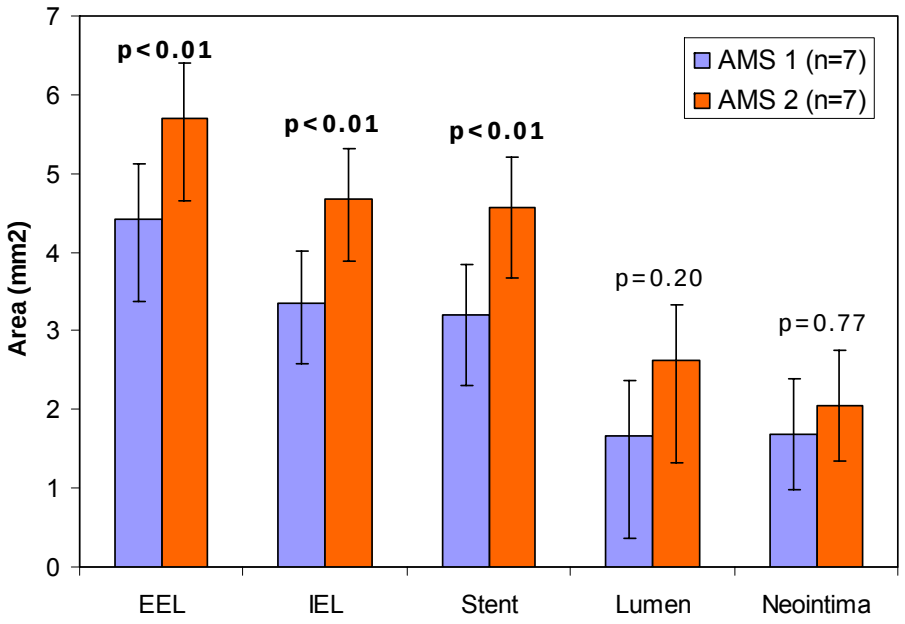


Combination trial - Histomorphometry

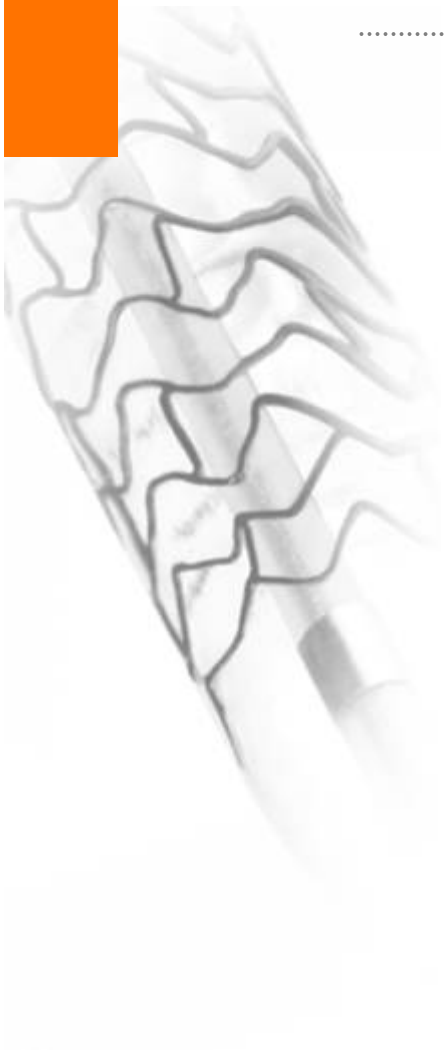
2 weeks



4 weeks



Status AMS 2 - Summary



- The optimization of both the Magnesium alloy and the stent design contribute to a longer stent integrity in animal
- The new AMS generation with increased integrity shows significantly improved efficacy in animal

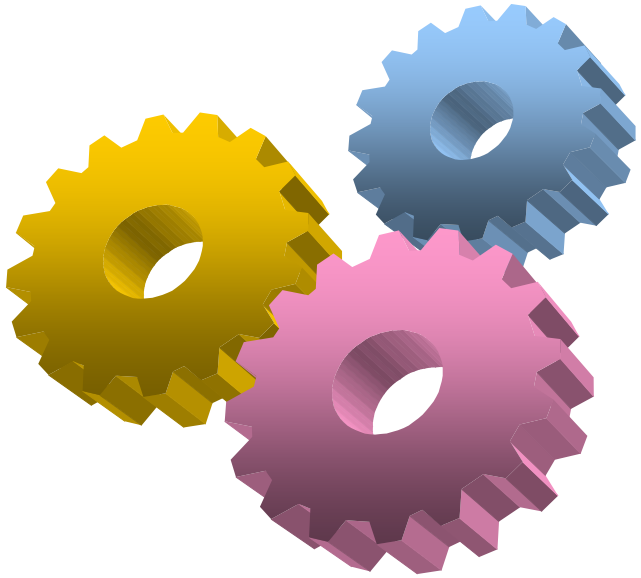
DREAMS concept

DREAMS
=
DRug Eluting AMS

- Degradable carrier from Magnesium alloy
- Effective anti-proliferativ drug
- Specialized proprietary matrix to cope with degradation of Magnesium alloy
  - Non-permanent polymer
  - Optimized rate of drug elution

DREAMS DRUG-Eluting Stent System

Drug:



Stent:

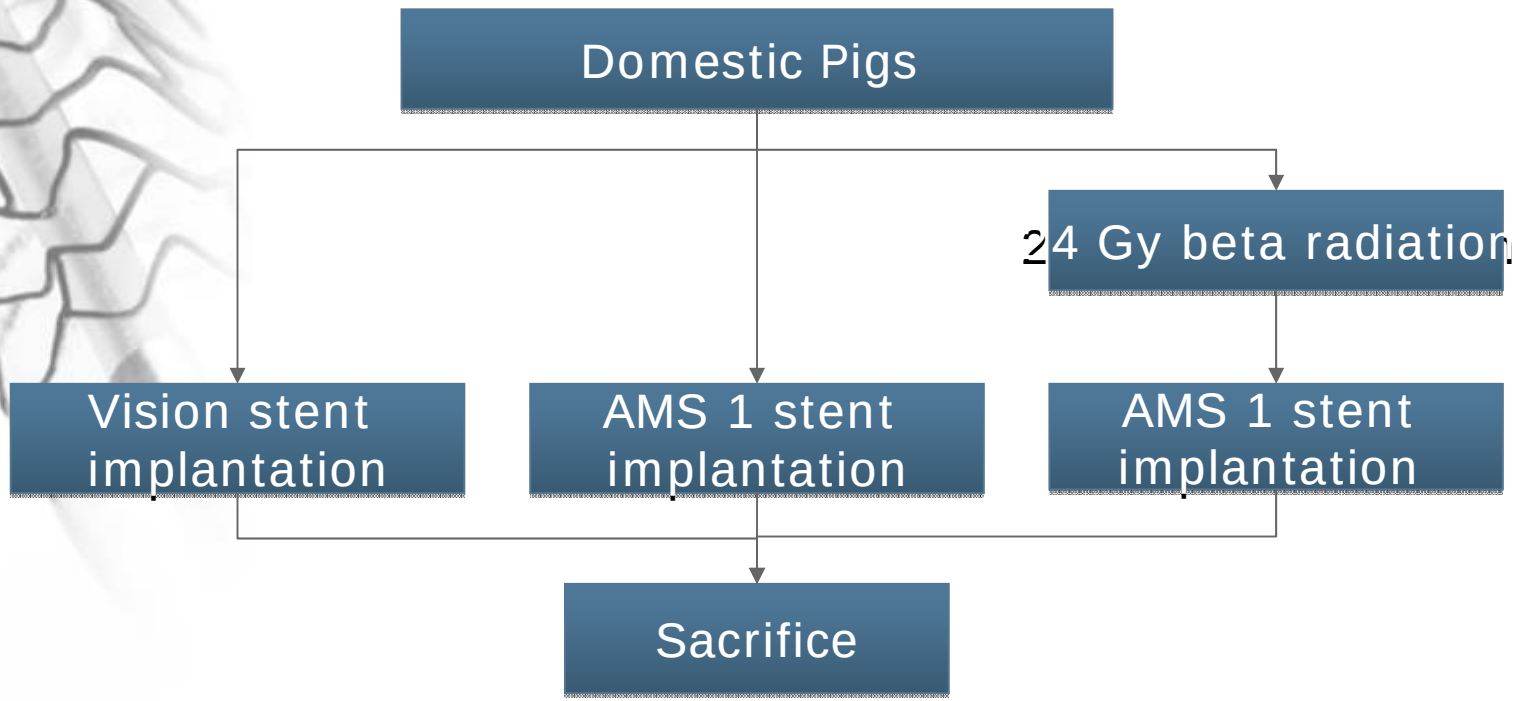
Bioabsorbable
Magnesium Alloy

Discrete Drug
Delivery Reservoirs

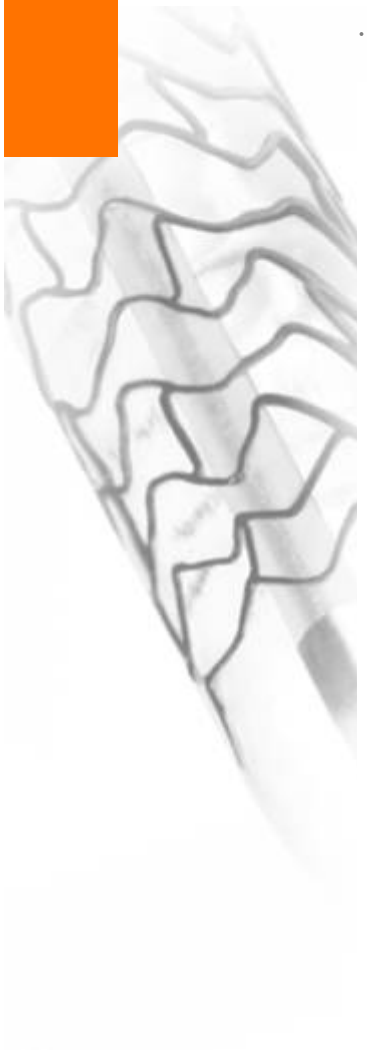
Carrier:

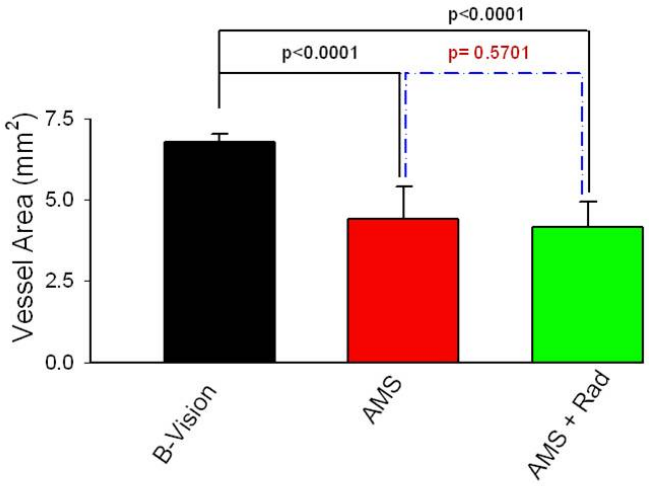
Bioresorbable Matrix

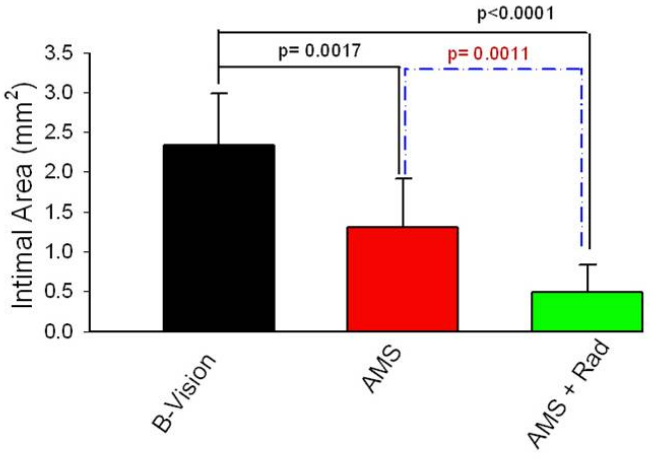
Brachytherapy and AMS - Study design

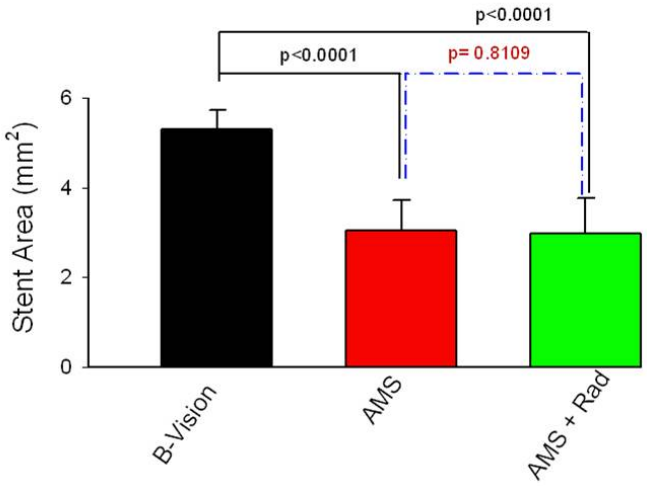


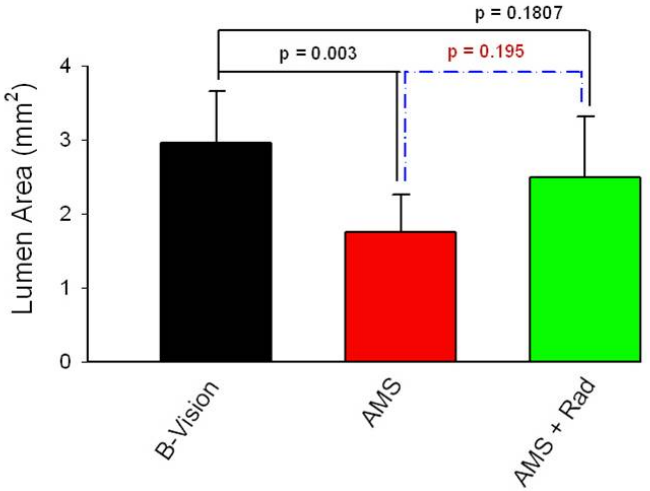
Brachytherapy and AMS - Histopathology





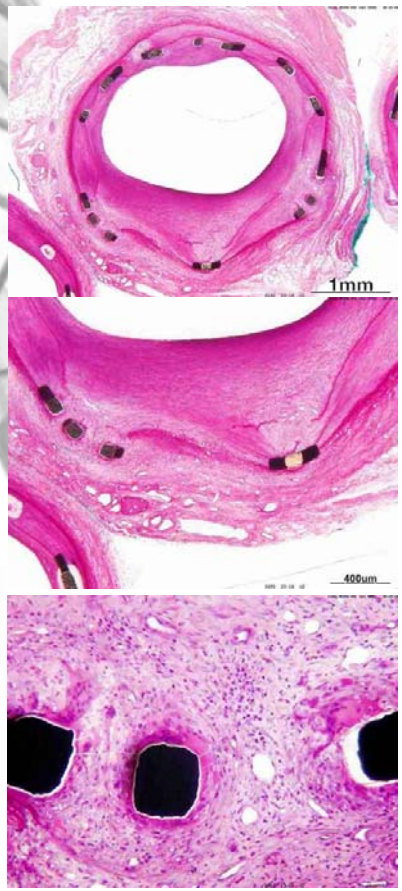




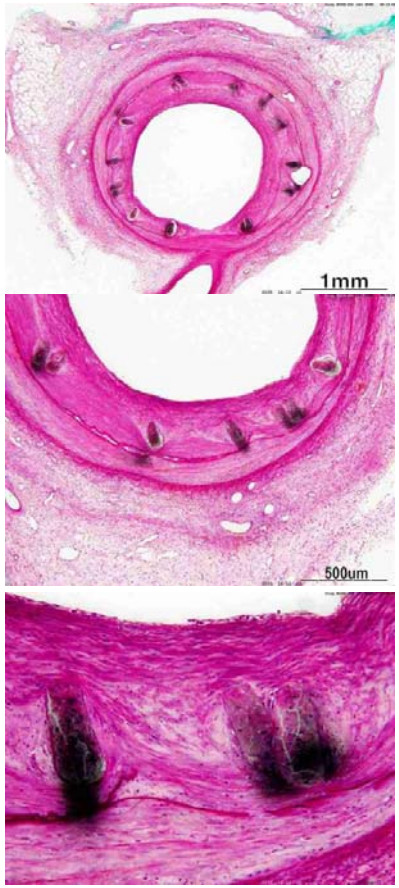


Brachytherapy and AMS - representative images

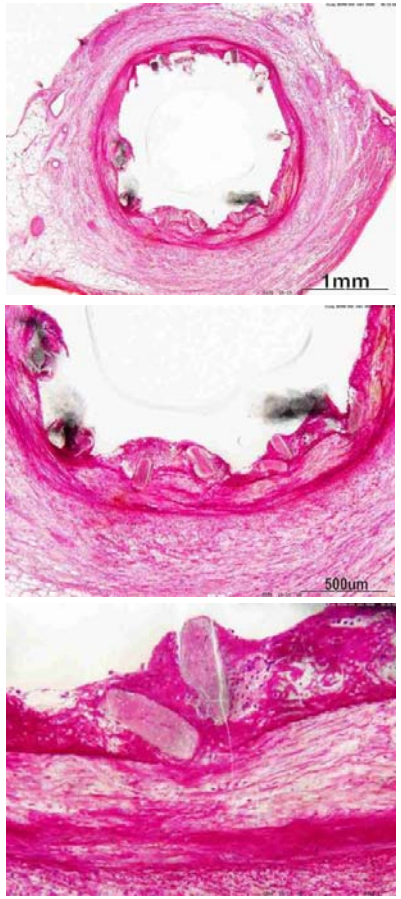
Vision



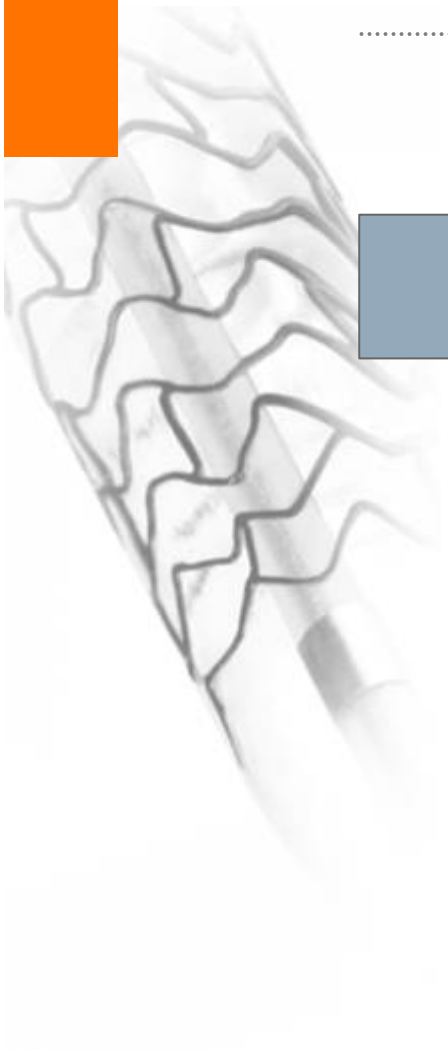
AMS 1



AMS 1 + VBT



AMS program

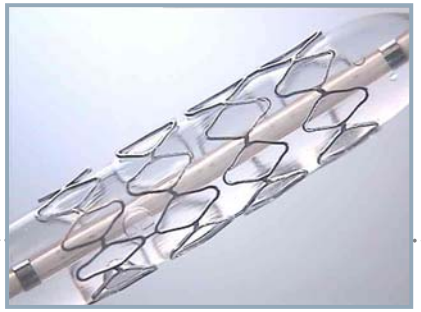


AMS 1 — First clinical experience: AMS is “safe”

AMS 2 — Improved mechanical integrity by modified alloy and improved stent design

AMS 3 — Drug-eluting AMS (DREAMS) incl. surface passivation and X-ray markers

Status of AMS 2007



- Safe in human coronaries
- Safe in peripheral arteries (tibial)
- Absorbed as intended < 90 days
- Fully compatible with CT or MRI angiography
- Restenosis mainly due to early recoil and neointima formation
- New Generations AMS under preclinical testing
- Resume Clinical testing to be announces

Thank You