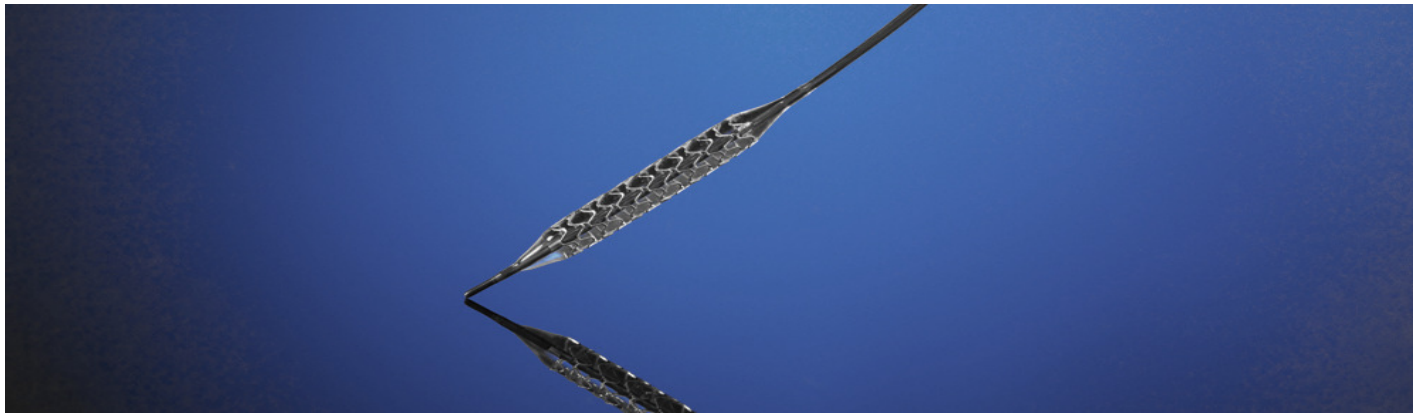
Vascular Intervention

Marseille

May 6 2010

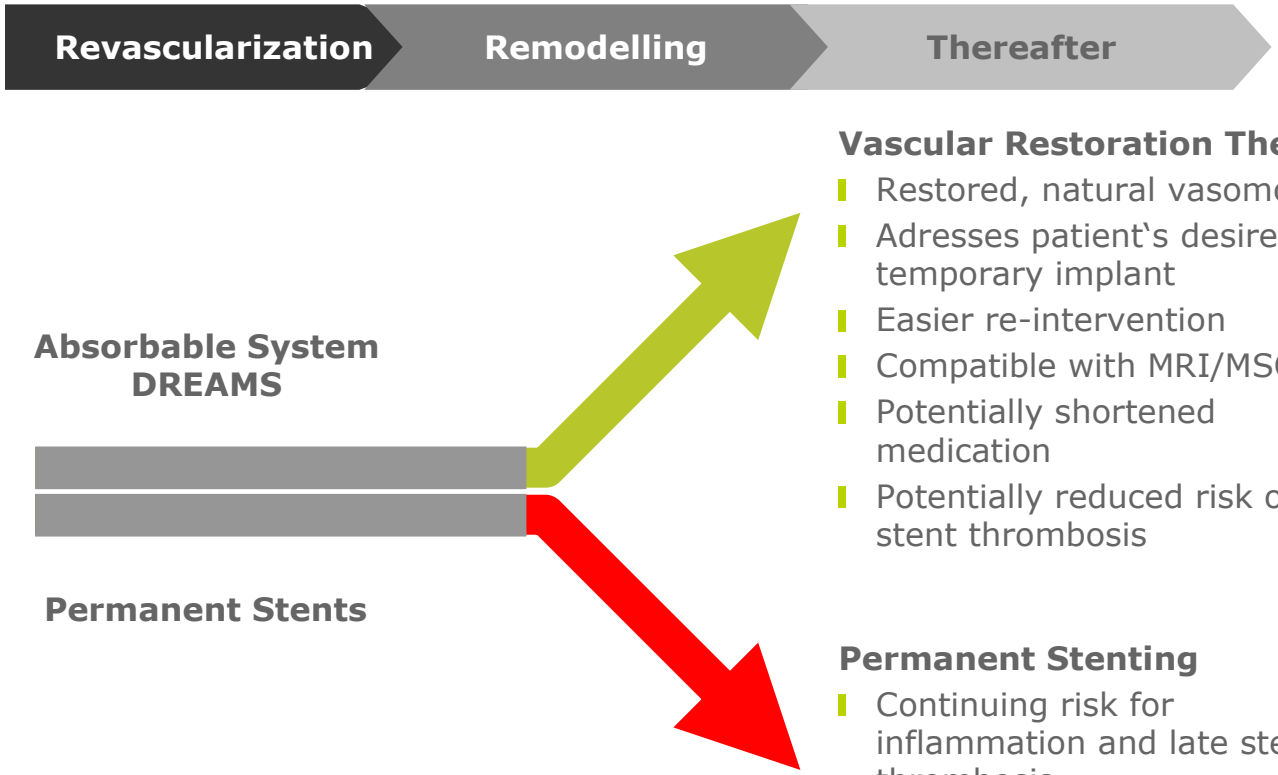
Endocardiac Biomechanics Research
Update on Absorbable Metallic Stent

Claus Harder



BIOTRONIK
excellence for life

DREAMS opens new horizons in the treatment of vascular disease



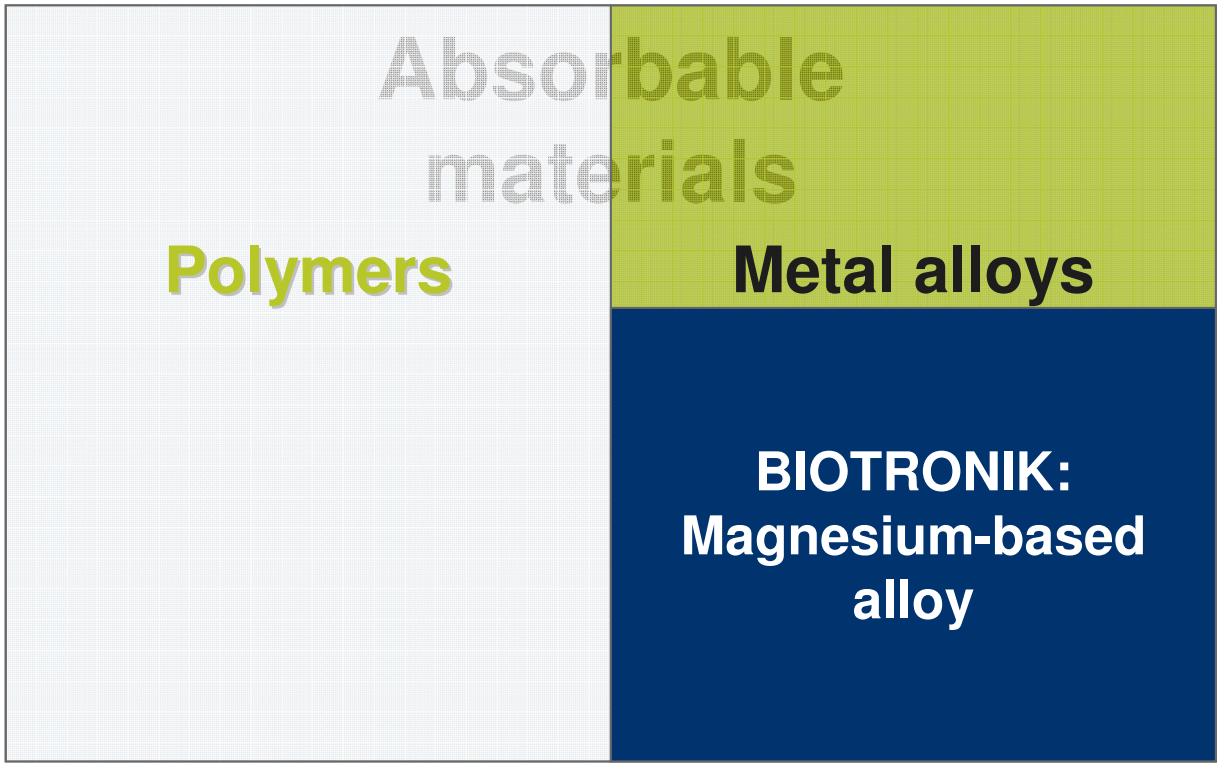
Vascular Restoration Therapy

- Restored, natural vasomotion
- Adresses patient‘s desire for a temporary implant
- Easier re-intervention
- Compatible with MRI/MSCT
- Potentially shortened medication
- Potentially reduced risk of late stent thrombosis

Permanent Stenting

- Continuing risk for inflammation and late stent thrombosis
- Long-lasting medication necessary, especially for DES

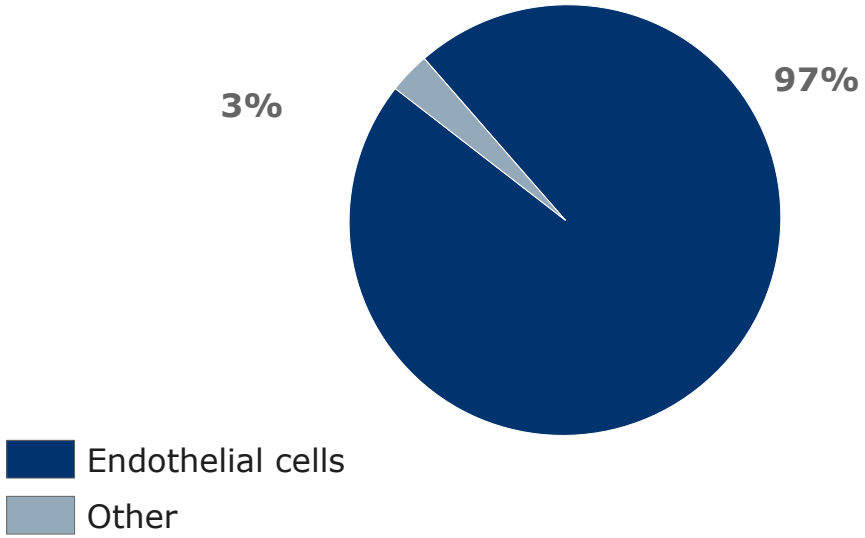
There are two main classes of materials for absorbable stents



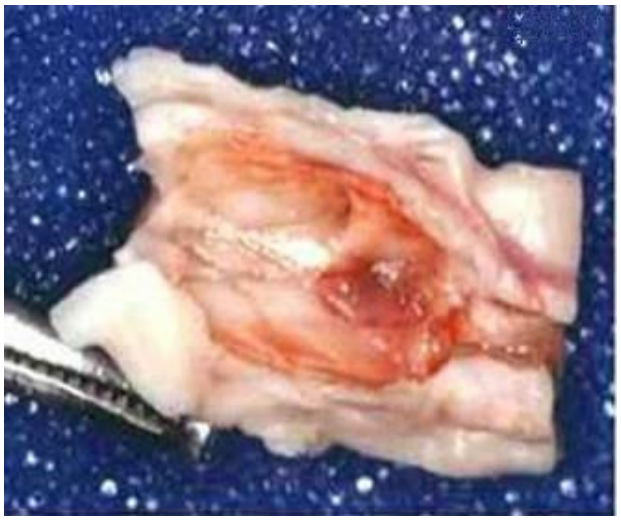
BIOTRONIK believes that tailor-made Magnesium alloys provide the best balance between biocompatibility, mechanical properties and absorption characteristics for coronary stents

As expected for Magnesium, AMS shows excellent biocompatibility

Magnesium Alloy: Quick Endothelialisation



Endothelialisation after
3 days: 97%[1]



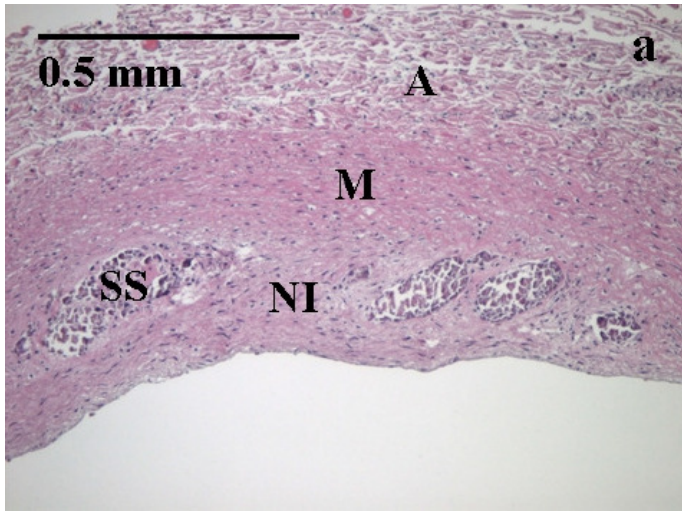
Endothelialisation after
10 days: complete coverage[2]

[1]6 Minipigs. Light microscopy after coloring of Endothelial cells. Data on file

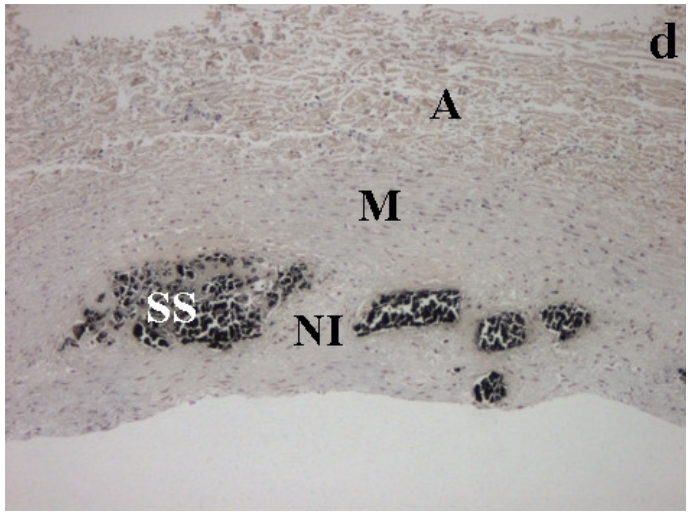
[2]Alloy 1 in domestic pig RCA after 10 d. Heublein, et al., MHH

A pediatric case proves advanced absorption at 5 months

Hematoxylin/Eosin stain



von Kossa's stain



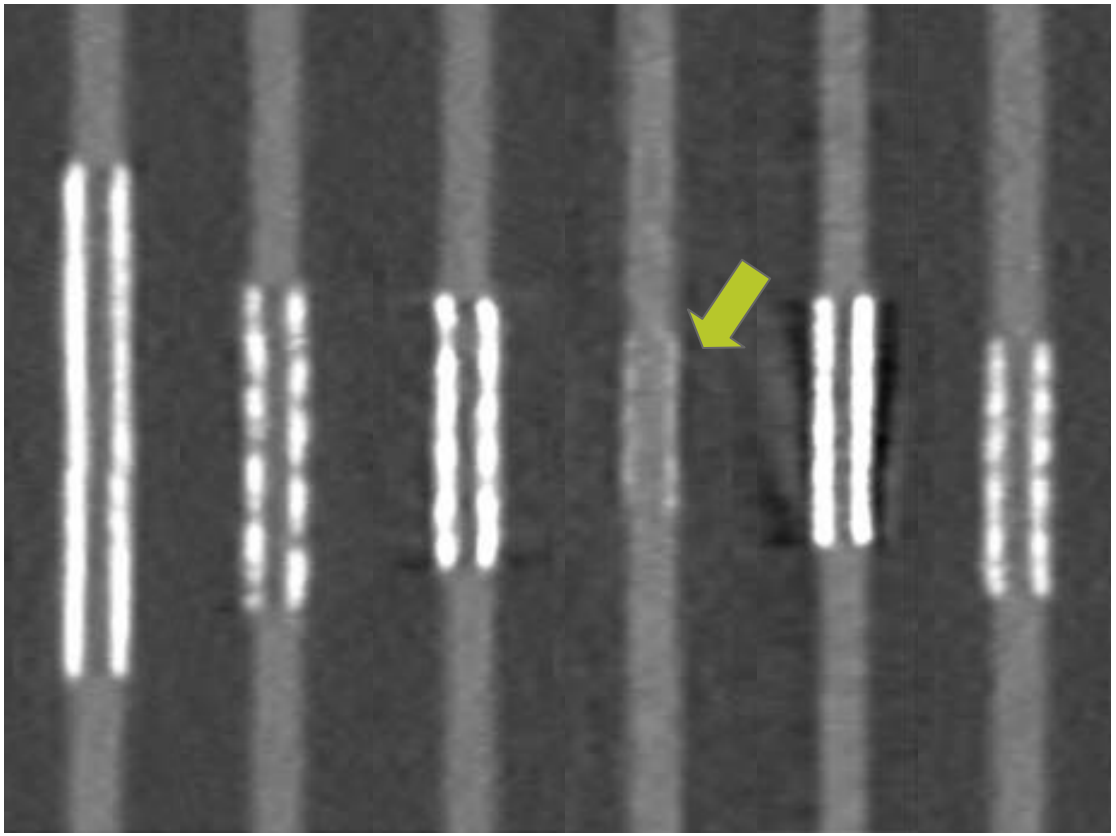
NI: Neointima
M: Media
A: Adventitia
SS: Stent strut

- Low concentration of inflammatory cells
- Thin coverage with neointima
- Beginning cell penetration into former stent struts

Preterm baby with pulmonary artery stenosis / stent implantation at 2 months resulting in adequate lung perfusion
Patient died at 7 months due to multiple organ failure (non stent-related)
Zartner et al., Catheder Cardiovasc Interv. 2007 Feb-15; 69(3): 443-6

AMS allows non-invasive imaging of the stented vessel

Endeavor | Coroflex Please | Costar | AMS-1 | ZoMaxx | Pro-Kinetic



Dual source 64-slice CT images (Siemens)

Source: Maintz et al, Eur Radiol (2009) 19: 42-49

First in Man Coronary Study of AMS-1: PROGRESS-1

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

PROGRESS-1 was set-up as a multi-center, coronary FIM study

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

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

Primary Endpoints
Major Adverse Cardiac Events (MACE) at 4 months (defined as cardiac death, nonfatal myocardial infarction, and ischemia driven TLR) <30 %

Enrollment
The study included 63 patients at 8 international clinical sites

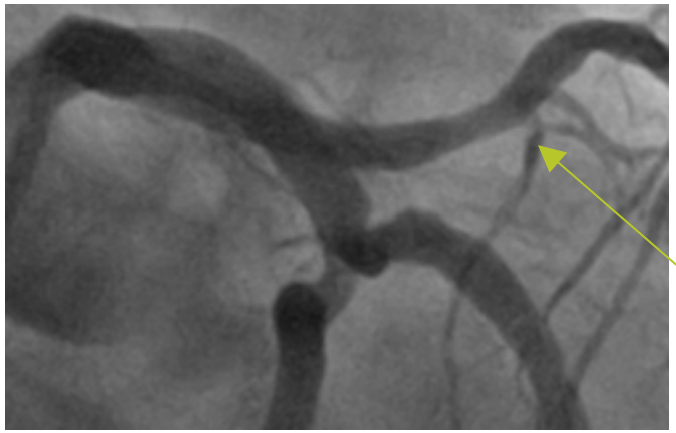
Source: Erbel et al. Lancet 2007; 369: 1869–75

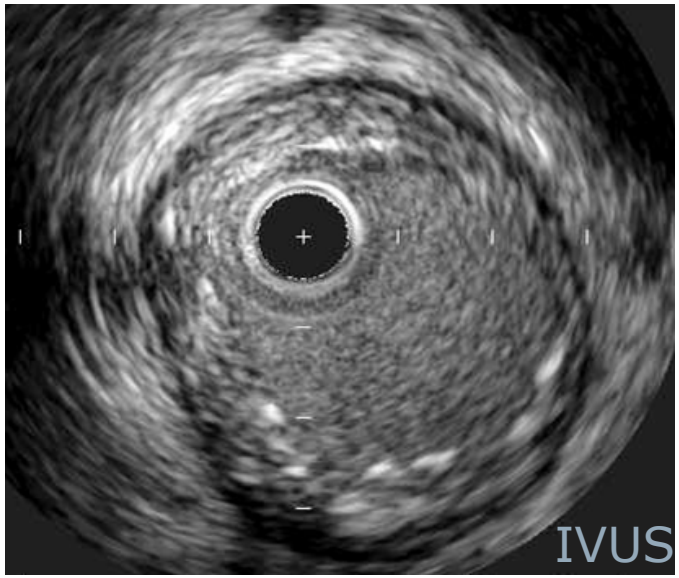
PROGRESS-1 confirmed safety in coronary arteries - but moderate TLR

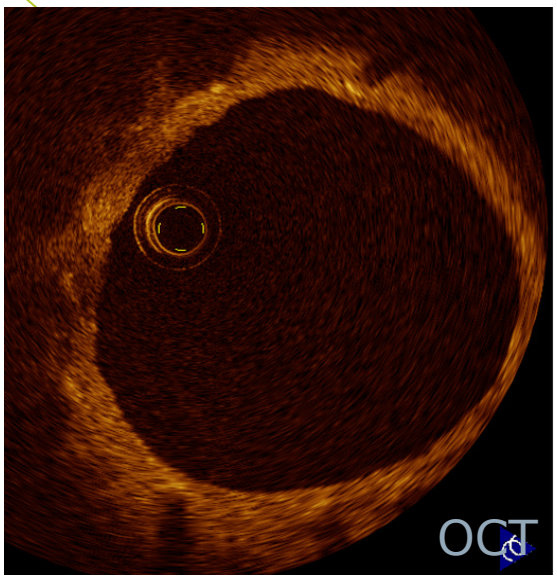
	In Hospital N = 63		4 Months N = 63		12 Months N = 60	
	n	%	n	%	n	%
MACE (Cardiac death, nonfatal MI, ischemia driven TLR)	0	0	15	23.8	16	26.7
Death	0	0	0	0	0	0
Q-wave MI (new pathol. Q-waves w/ CK or CK-MB elevated)	0	0	0	0	0	0
Non Q wave MI (CK 2x above normal with CK-MB elevated)	0	0	0	0	0	0
Ischemic Driven TLR	0	0	15	23.8	16	26.7

Source: Erbel et al. Lancet 2007; 369: 1869–75

PROGRESS AMS-1 long term results (15 months) showed perfect ingrowth





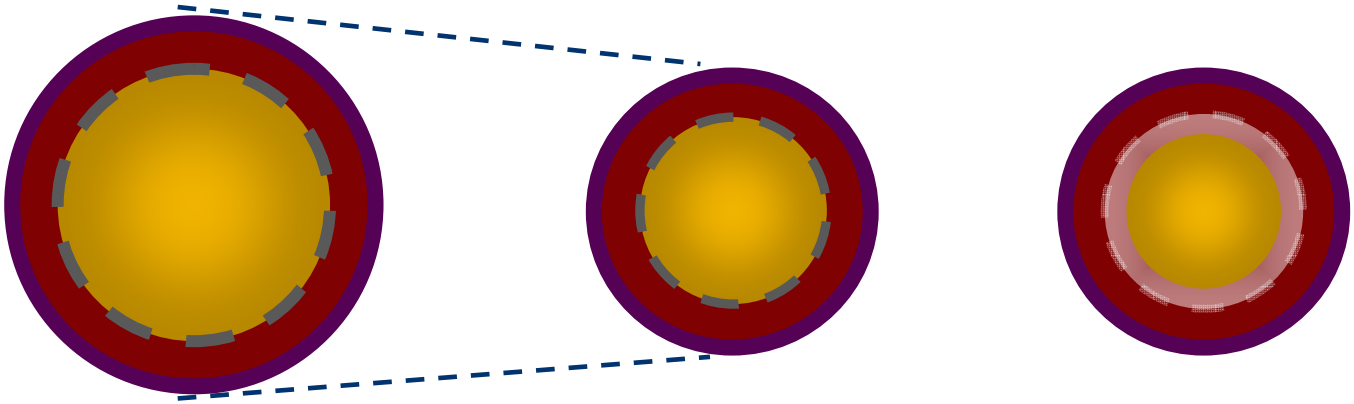


- Very thin neointima
- Perfect ingrowth of AMS
- Completed healing of the stented vessel

Source: Courtesy Dr Di Mario

PROGRESS-1 IVUS analysis identified two main drivers for restenosis

Post implantation **Degradation** **4 month follow-up**

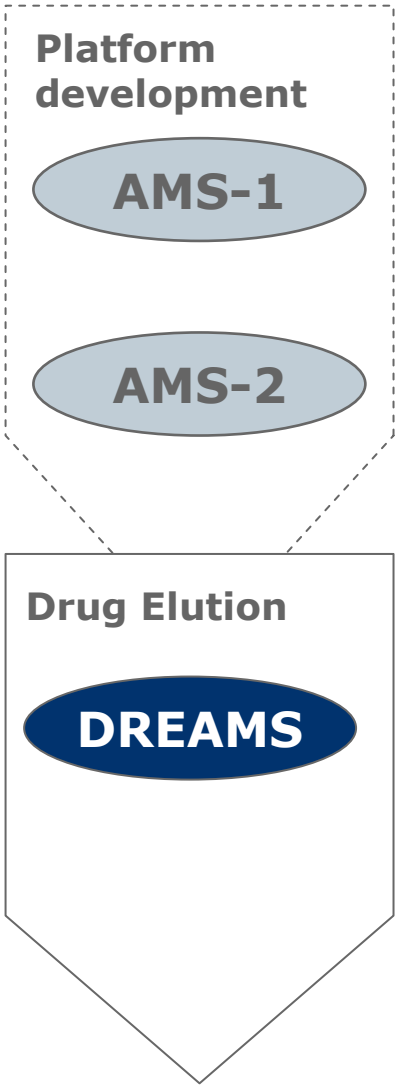


Contribution to lumen loss		Loss of scaffolding		In-stent neointima
1.1mm	=	***0.6mm***	+	***0.5mm***

Ischemic driven TLR of 23.8%

Source: PROGRESS AMS-1 IVUS

DREAMS evolves as a new therapy concept from previous experience with bare Magnesium stents



First generation device

- 4-crown design with 165µm strut thickness

Enhanced platform with prolonged stability

- Alloy with slower degradation
- 6-crown design with 120µm strut thickness

Drug eluting system for vascular restoration

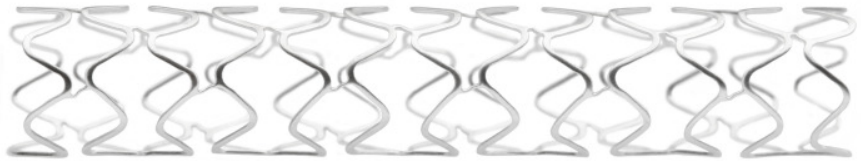
- Fast degradable drug carrier
- Proven anti-proliferative drug

DREAMS
Drug Eluting Absorbable Metal System

Drug carrier
- Fast degrading Polymer

Backbone
- Speciality Mg-alloy
- Good biocompatibility

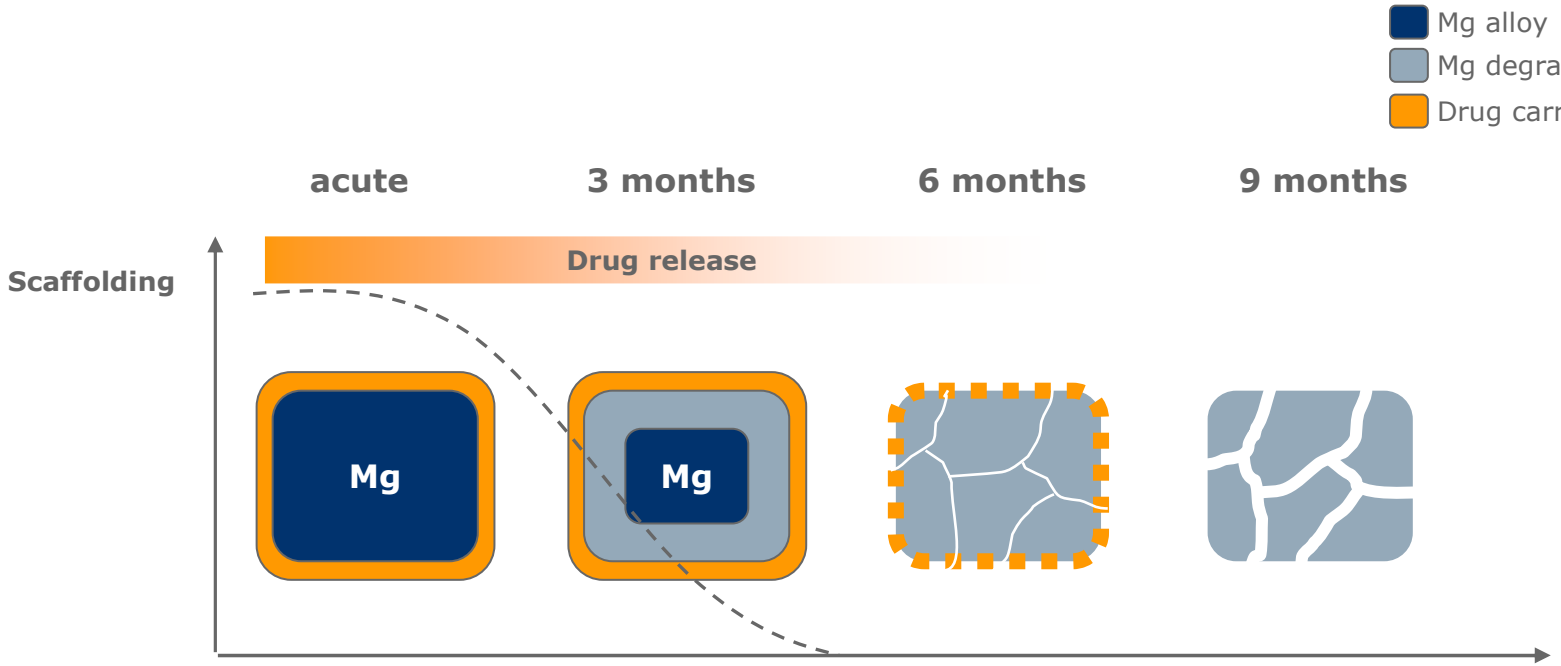
Drug
- Proven anti-proliferative drug



Delivery system
- BIOTRONIK Pantera

Size range
- 3.0/3.25/3.5 x 16/20
- 6F profile

DREAMS provides scaffolding and drug release up to 3 months



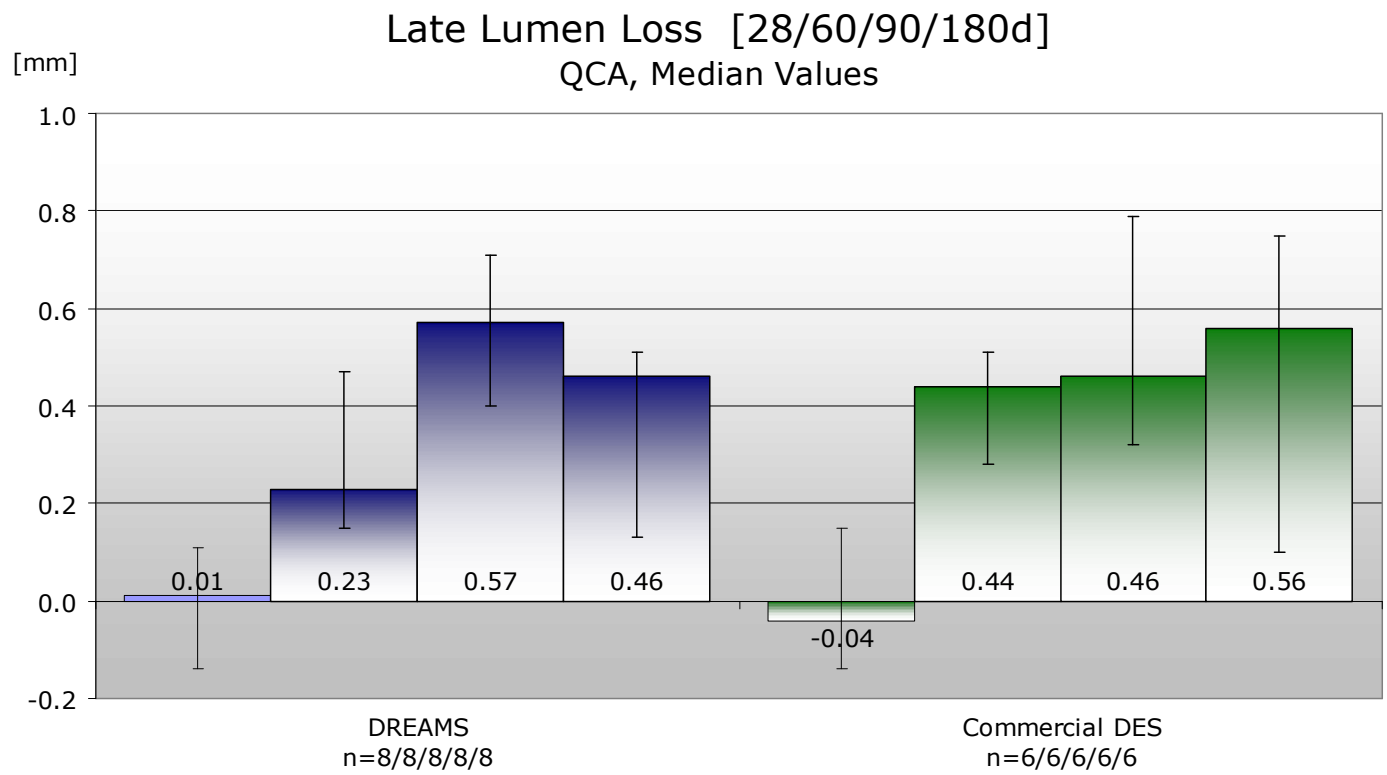
- Mg degradation (conversion)
- Stable drug carrier layer
- Diffusion controlled drug release

- Mg degradation completed
- Beginning degradation of drug carrier layer
- Drug release completed

- Drug carrier layer degradation completed
- Beginning disintegration of Mg degradation product

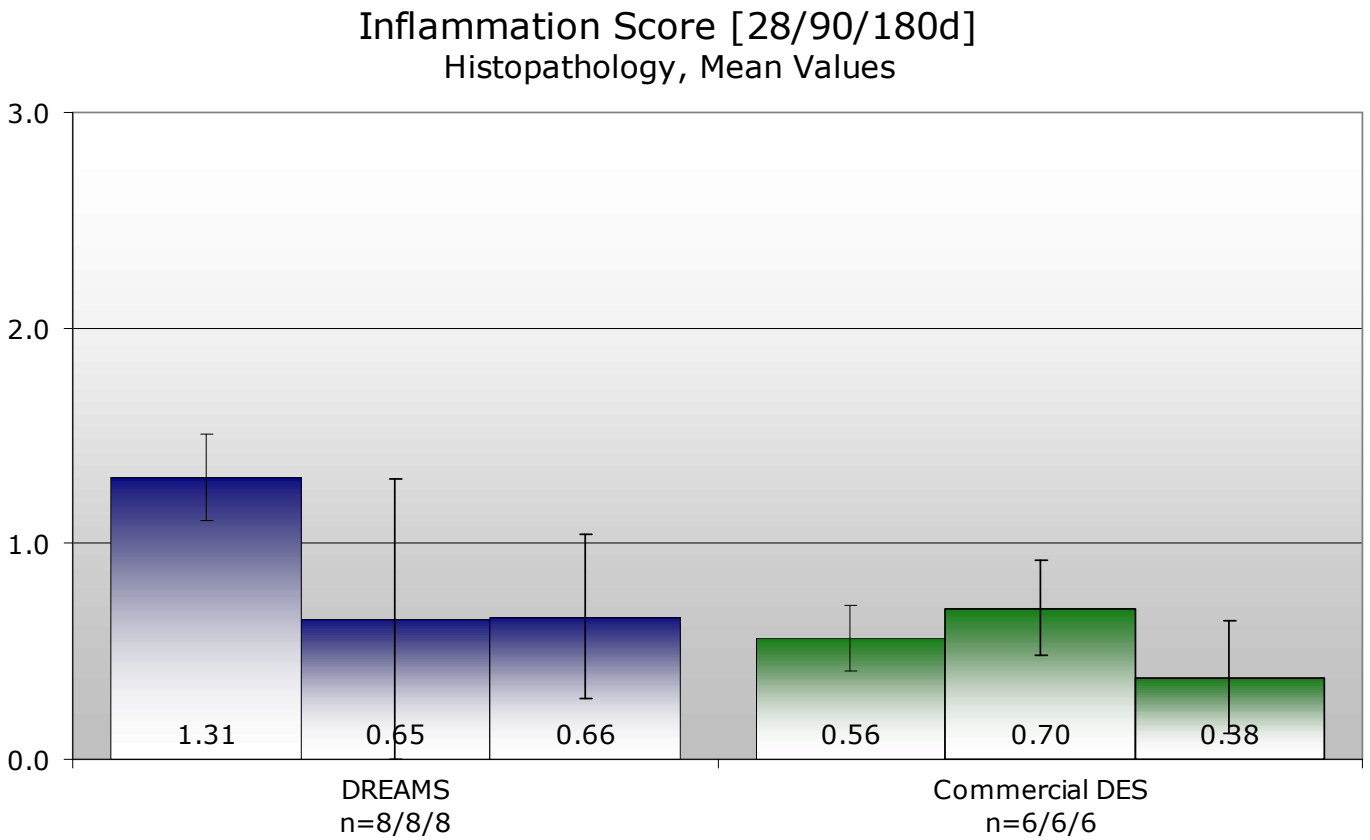
Source: preclinical studies, data on file

Late lumen loss is comparable to commercial DES reference



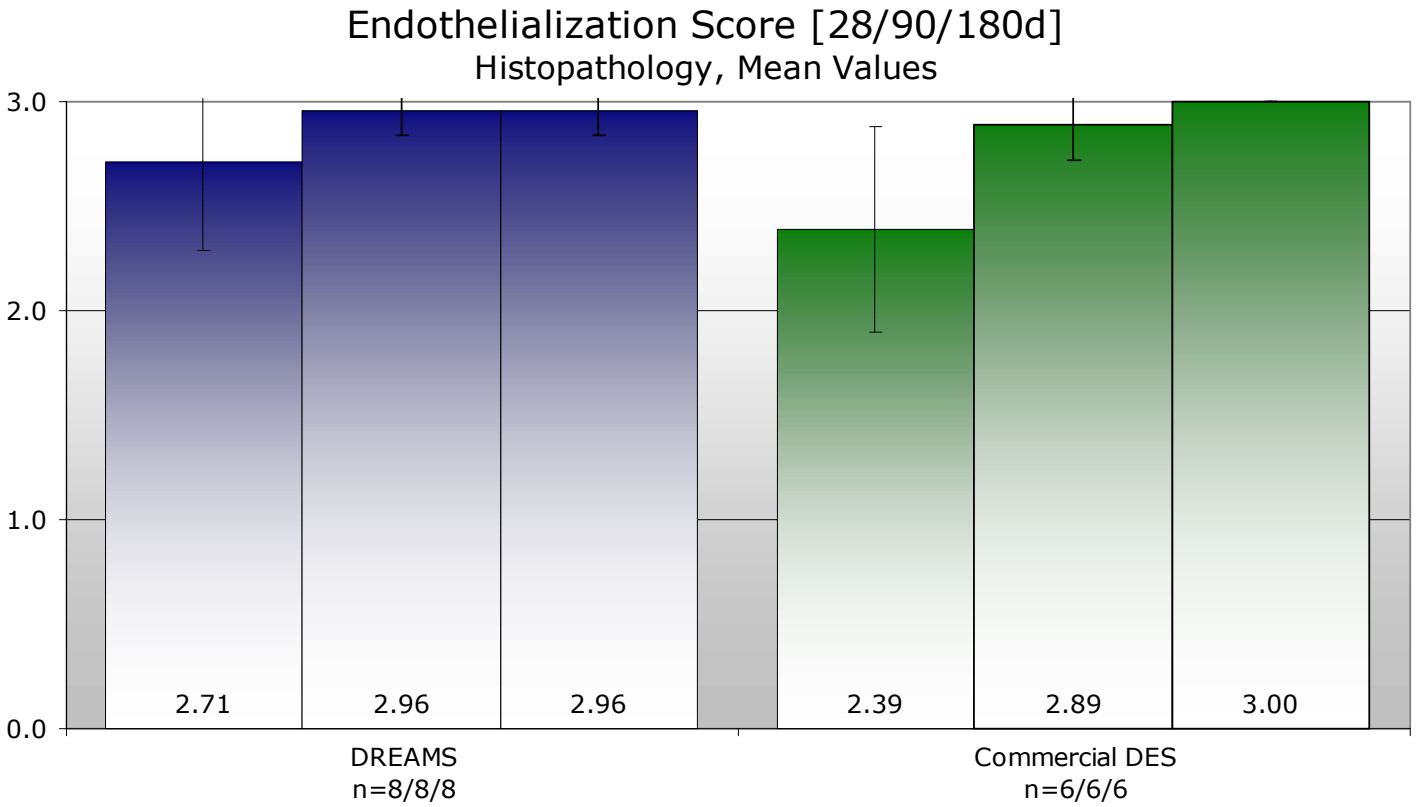
Source: preclinical studies, data on file

DREAMS shows increased but uncritical inflammation at 28 days due to degradation of base material



Source: preclinical studies, data on file

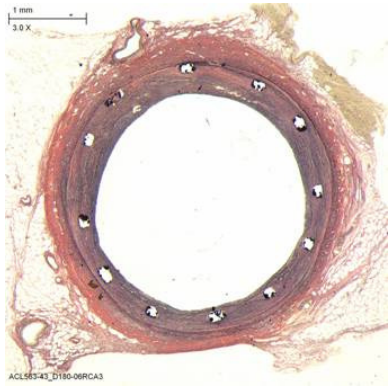
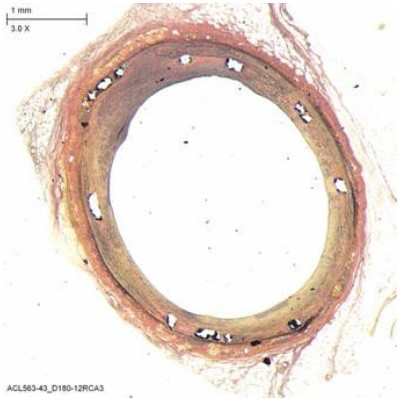
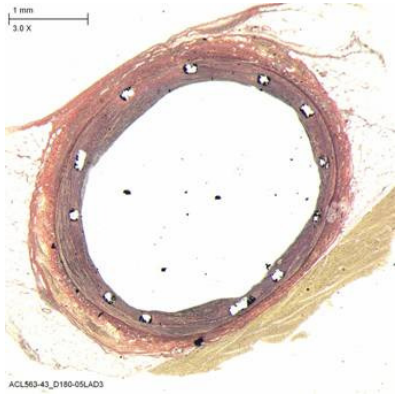
DREAMS shows slightly faster endothelialization



Source: preclinical studies, data on file

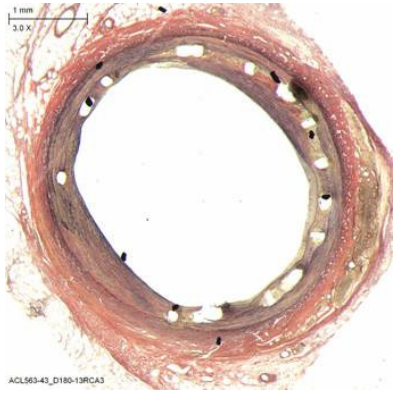
At 180 days there is no catch-up after complete drug release of DREAMS

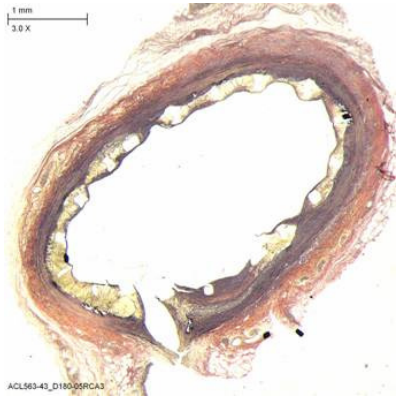
DREAMS

Black spots above represent Mg degradation product (Calcium-Apatite)

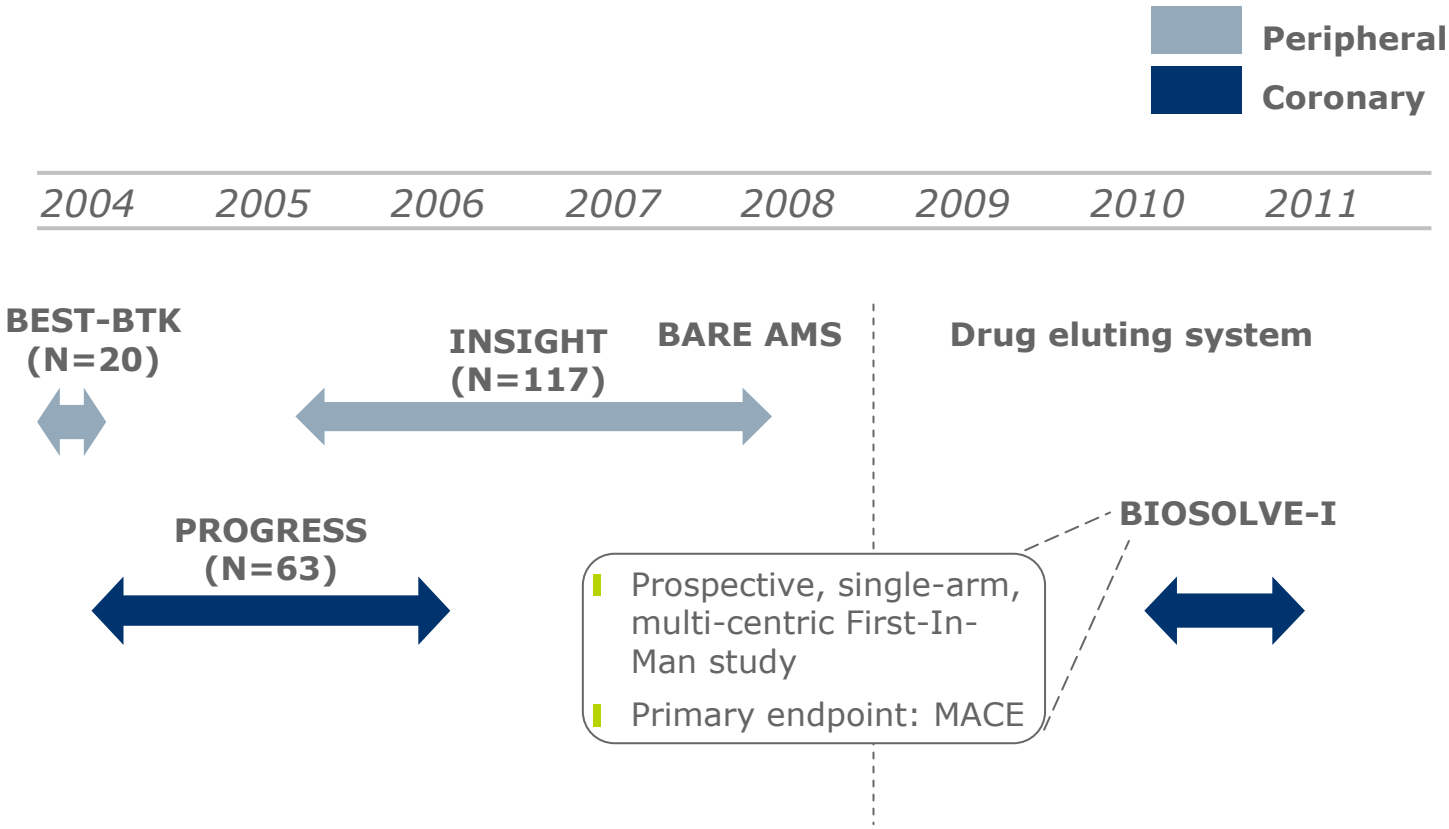
DES Reference





Source: preclinical studies, data on file

The clinical program will continue this year with the drug eluting AMS (DREAMS)



BEST-BTK: Bosiers et al. Vascular Disease Management 2005;2(4):86-91
PROGRESS: Erbel et al. Lancet 2007; 369: 1869–75
INSIGHT: Bosiers et al. Cardiovascular and Interventional Radiology 2008

Summary

- BIOTRONIK's Absorbable Metal System is based on a specialty Magnesium alloy that offers superior mechanics and biocompatibility
- Previous generations of bare AMS have demonstrated safety in several human applications (150 cases) but lacked sufficient efficacy
- DREAMS is a drug eluting device optimized to match the specific needs of an absorbable vascular scaffold
- DREAMS will be investigated in the BIOSOLVE-I first-in-man trial later in 2010