Washington Hospital Center

# Bioabsorbable Stents

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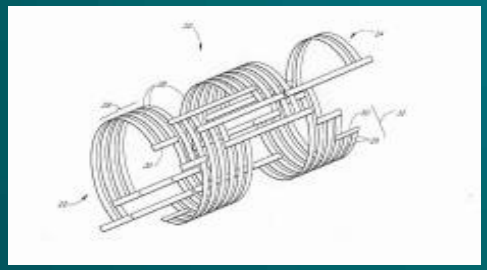
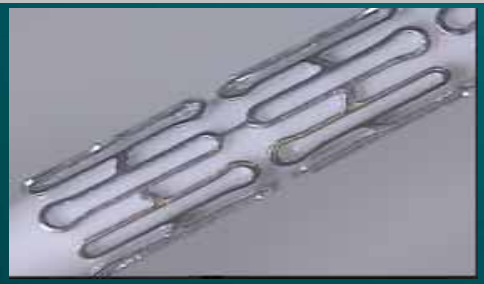
# Why absorbable stents?

**Why permanent stents?**

Vessel scaffolding is necessary only for a certain, limited time, than the permanent implant has no known advantage

- Short duration of Plavix post stenting
- **Avoid chronic** inflammatory processes
- **Problem of re-intervention with** traditional techniques
- **Ability of the vessel to perform** positive remodeling
- **Peripheral application: no longer** crushing **issue after absorption**
- CT and MR – **(follow up)** compatibility

# Bioabsorbable Stent Programs

| Company | Picture | Polymer/Drug | Features |
|---|---|---|---|
| **Bioabsorbable Vascular Solutions (BVS) [Guidant]** |  | All biodegradable polymers (PLLA) with everolimus | Self expanding and balloon expandable designs. |
| **Igaki-Tamai** |   | PLLA; Transilast | Zig-zag design which is deployed using a heated balloon FIH Trial with 50 patients |
| **Reva Medical** |  | Poly (DTE carbonate) with iodine on the backbone to make the stent radio opaque | Design do not require heat to expand the stent…by ratchet links |
| **Biotronik** |  | Mg Alloy | Balloon expanding stent with a delivery catheter |

# Igaki-Tamai PLLA Bioabsorbable Stent 4 Years Follow-up

- 63 lesions in 50 patients, 84 stents
- Non drug-eluting stent
- Four year follow-up data demonstrated no unusual findings

***Long Term (4-year results)***

| | |
|---|---|
| **Death** | **1/50 (2.0%)** |
| **QMI** | **1/50** (2.0%)** |
| **CABG** | **0** |
| **Stent Thrombosis** | **1/50** (2.0%)** |
| **TLR** | **9/50 (18.0%)** |

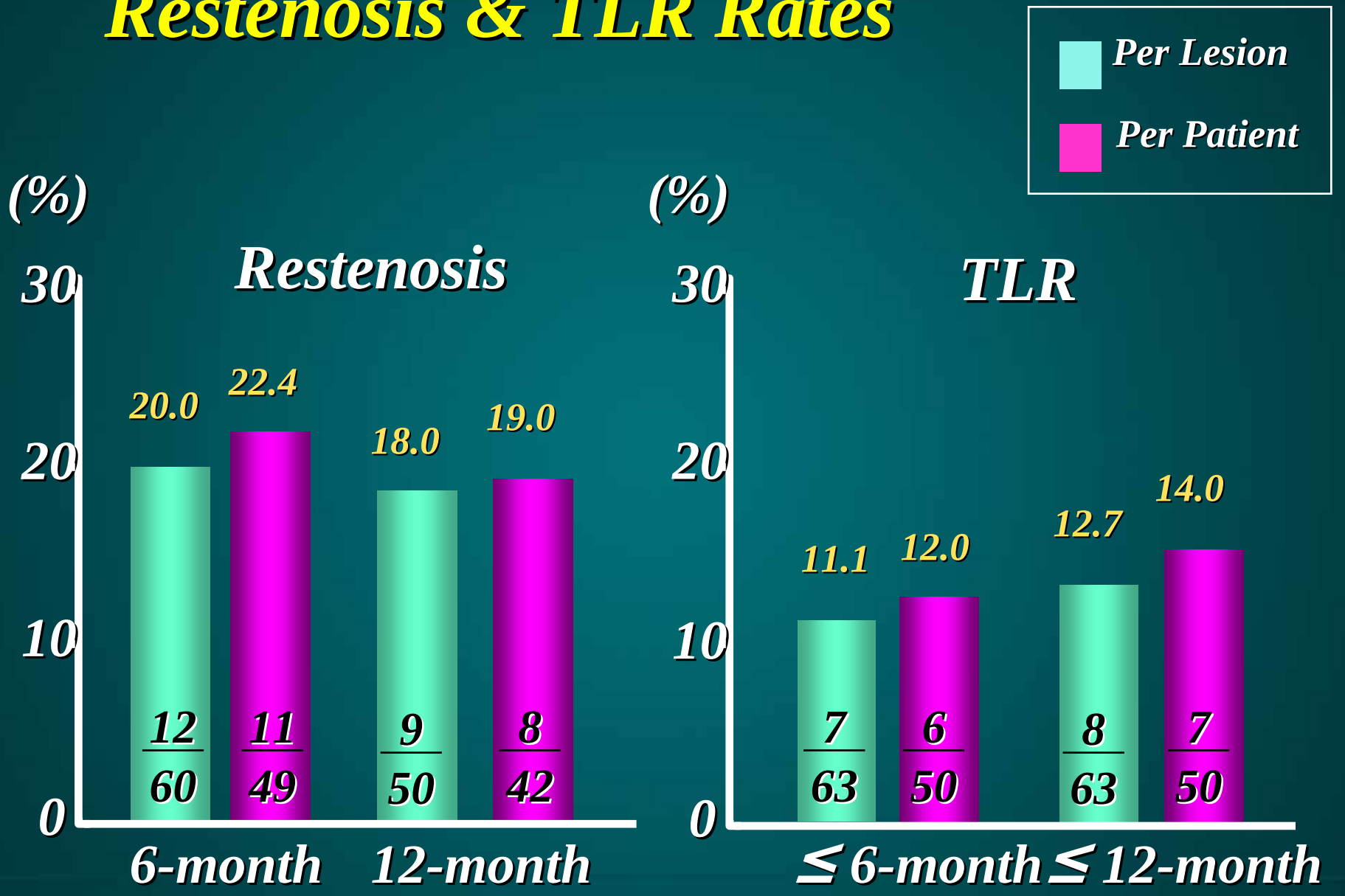
** = same patient

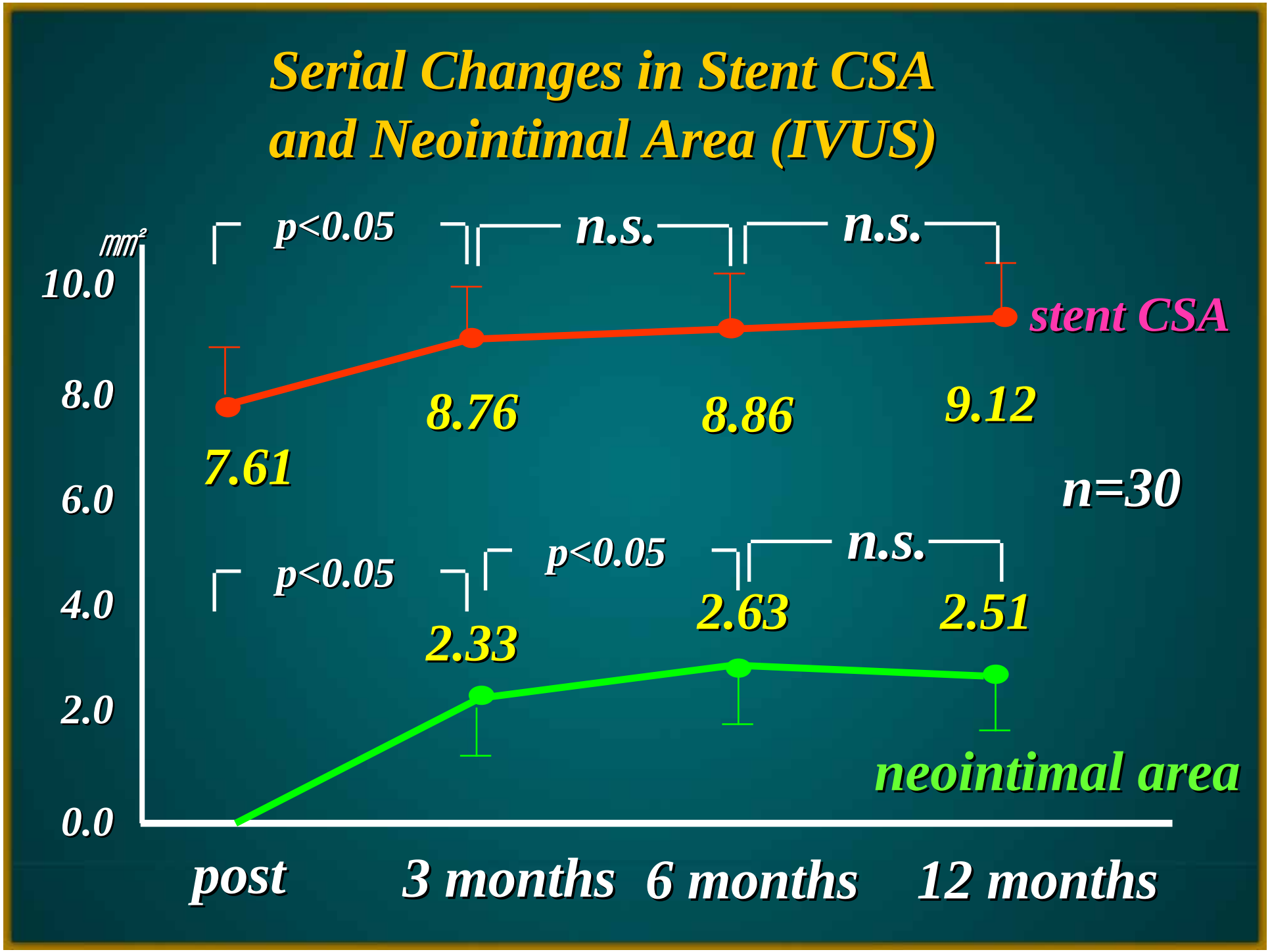
| | ABRR*** | Repeat PCI |
|---|---|---|
| 6 mo | 12/60 (20%) | 6/50 (12%) |
| 12 mo | 9/53 (17%) | 7/50 (14%) |
| 48 mo | | 9/50 (18%) |

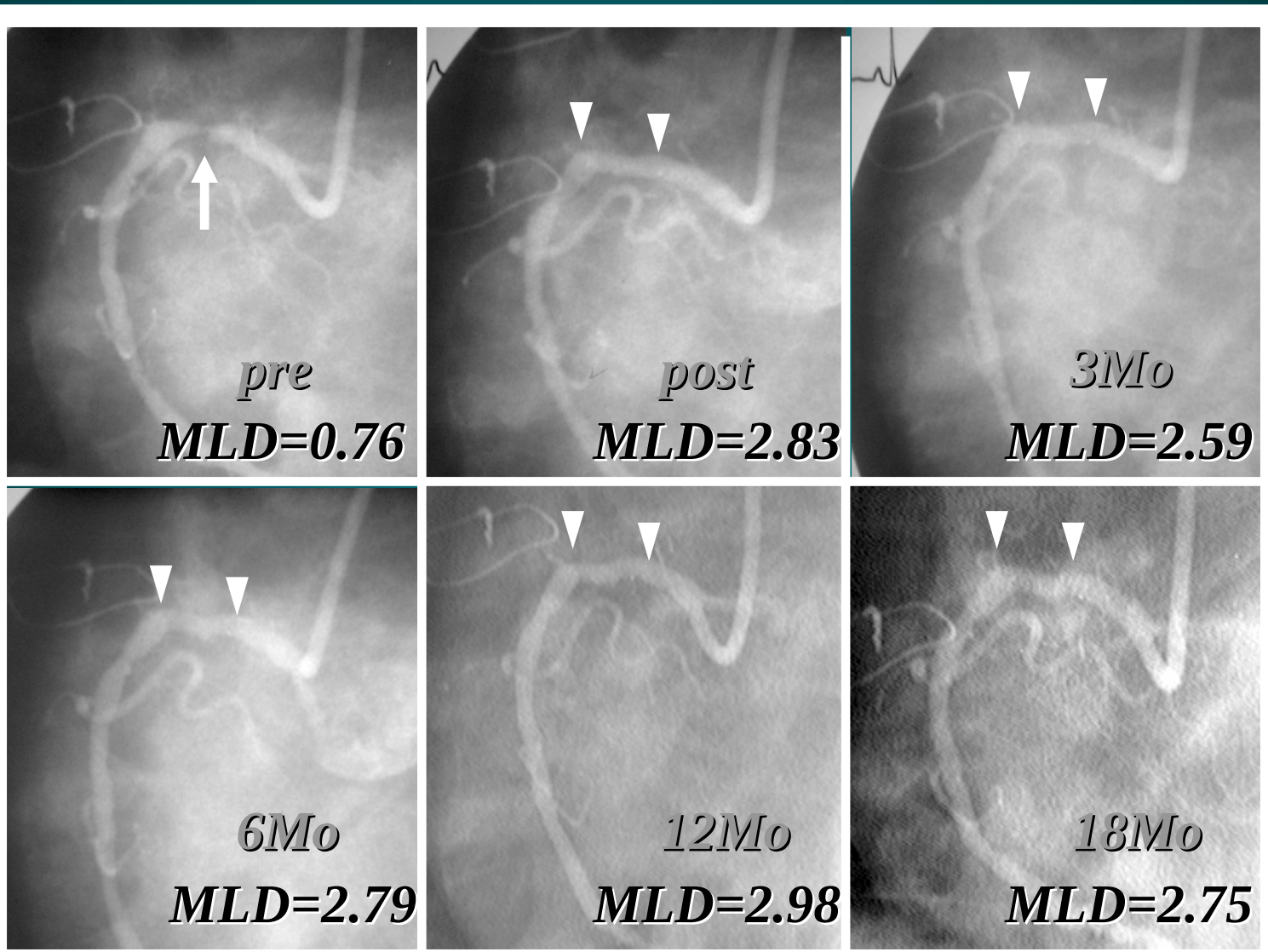
Hideo Tamai CCT 2004.

Behaves similar to bare metal stents

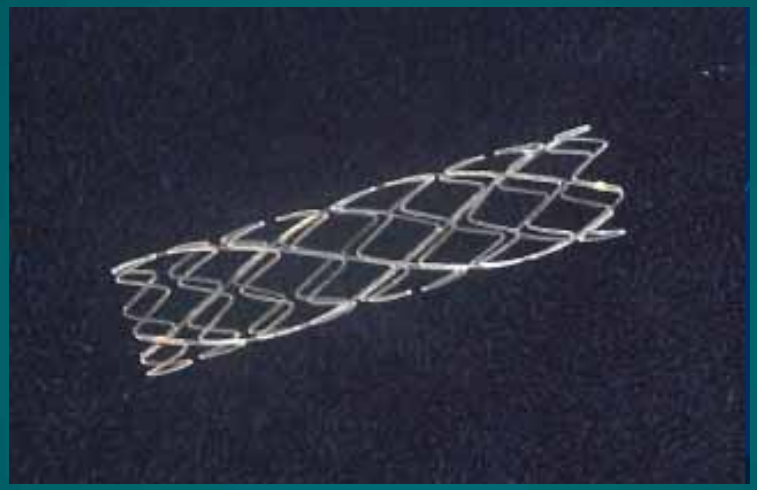
# Restenosis & TLR Rates




Serial Changes in Stent CSA
and Neointimal Area (IVUS)
mm²
10.0
8.0
6.0
4.0
2.0
0.0
p<0.05
n.s.
n.s.
stent CSA
7.61
8.76
8.86
9.12
n=30
p<0.05
p<0.05
n.s.
2.33
2.63
2.51
neointimal area
post
3 months
6 months
12 months


pre
MLD=0.76
post
MLD=2.83
3Mo
MLD=2.59
6Mo
MLD=2.79
12Mo
MLD=2.98
18Mo
MLD=2.75

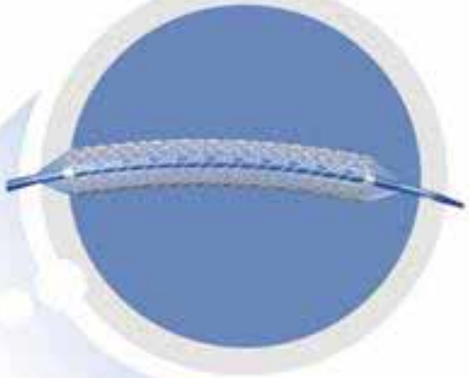
# Igaki-Tamai PLLA Bioabsorbable Self expanding stent for the SFA



| | |
|---|---|
| Material composition : | PLLA(poly-L-lactic acid) medical grade |
| Stent design : | Zig zag helical coil |
| Strut thickness : | 0.009 inch (0.24 mm) |
| Radio-opaque markers : | 2 gold markers |
| Currently available diameters : | 5, 6, 7, 8 mm |
| Currently available length : | 36 mm |

# BVS Fully Bioabsorbable Drug Eluting Stent

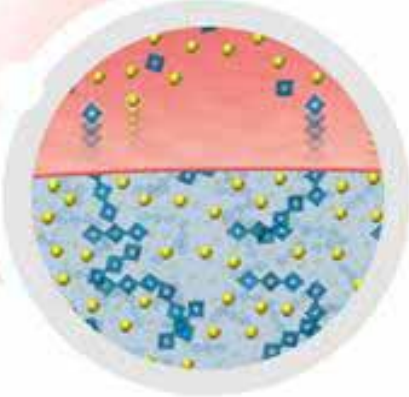
**BVS Bioabsorbable Stent Platform**



**ML VISION® Balloon SDS**

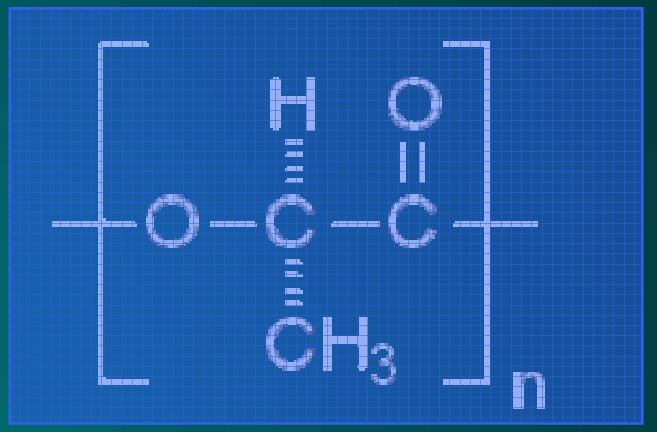
**Everolimus**

**Champion™ Bioabsorbable Polymeric Drug Release**



# Poly Lactic Acid Bioabsorbable Polymer

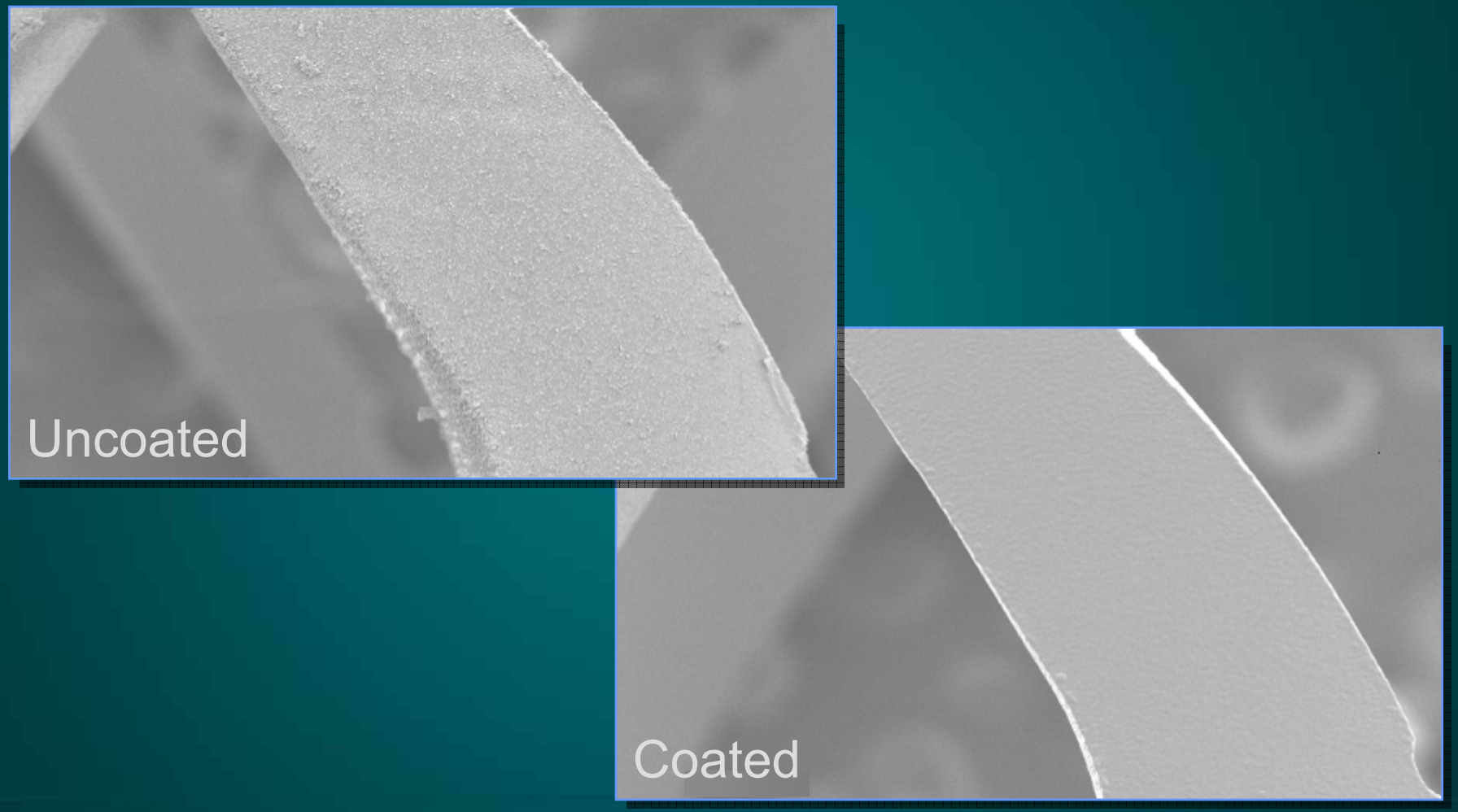
## Poly Lactic Acid (PLA)




- PLA safely used in numerous medical applications since the 1960s
  - Approx. 200 products made from PLA or co-polymer containing PLA
- Breaks down to lactic acid, a natural metabolite
- BVS stent has a tailored bioabsorption rate
- Fully bioabsorbed – no drug left behind

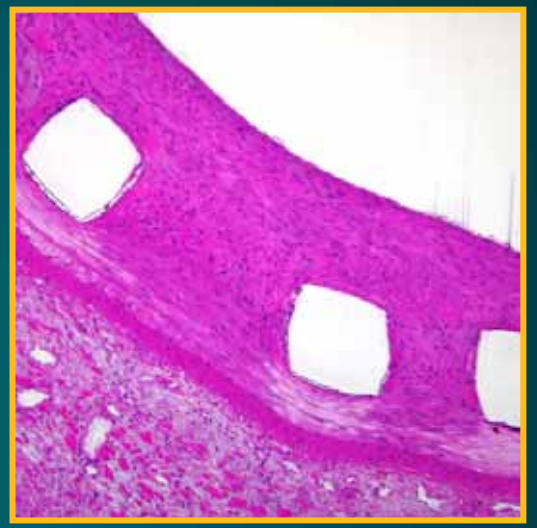
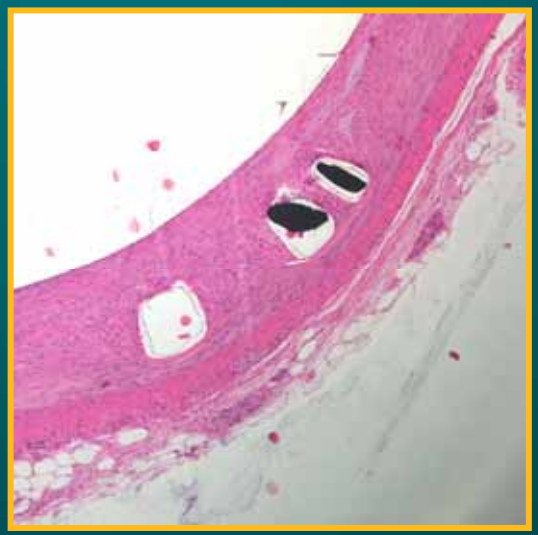
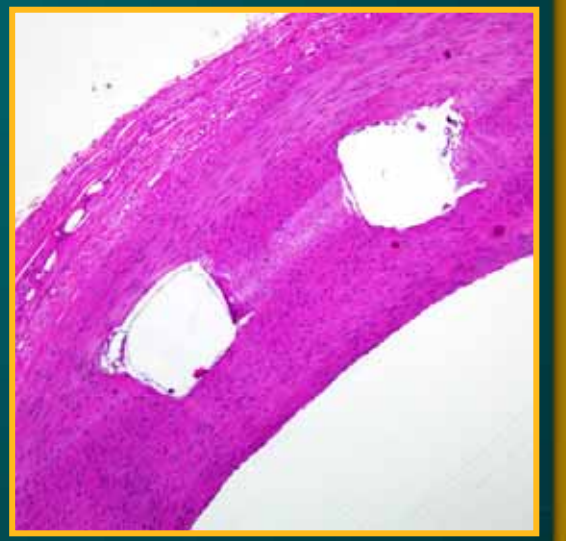
Data on file at Guidant.

# Bioabsorbable Everolimus Eluting Coronary Stent Surface




Photos on file at Guidant.

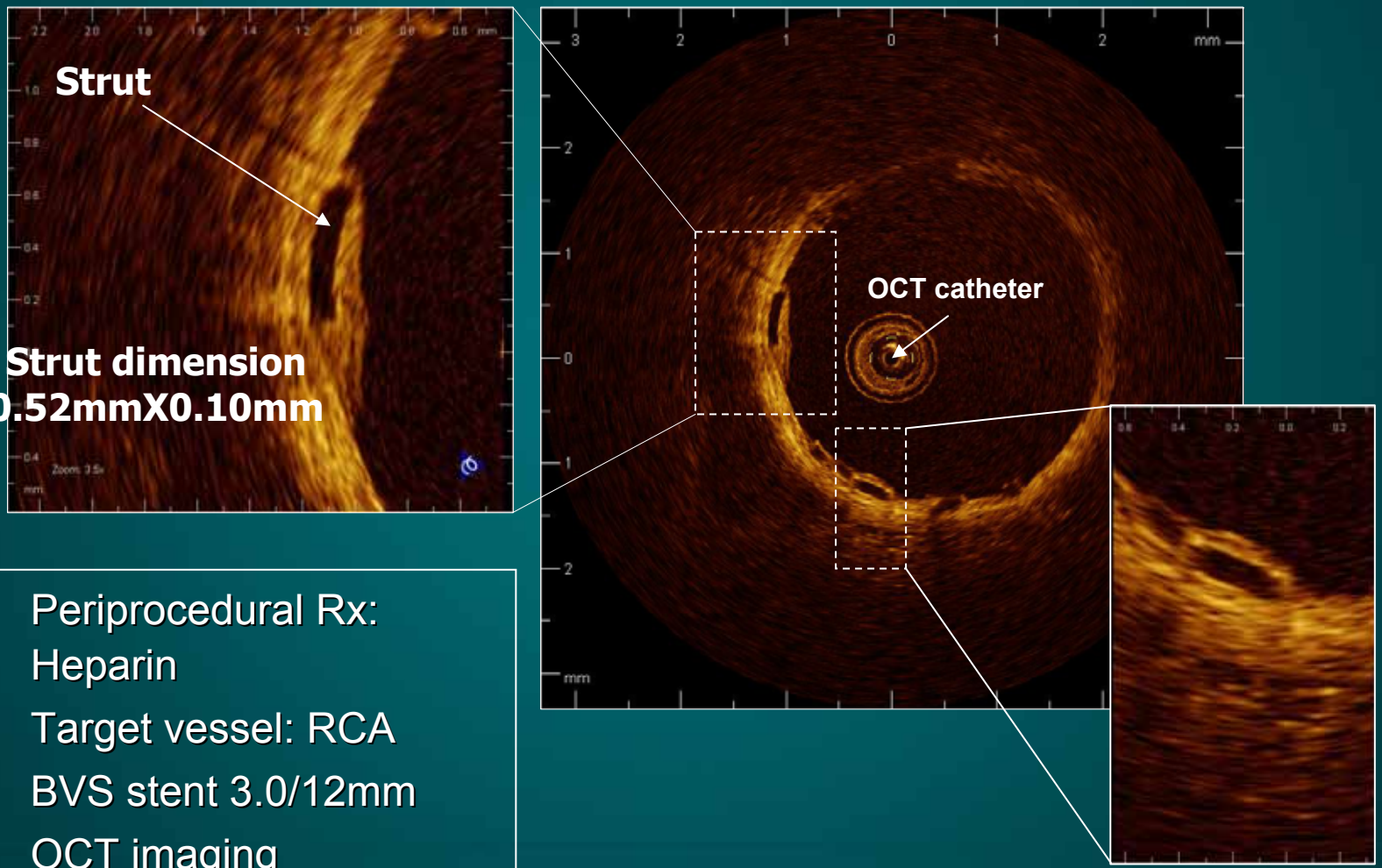
# Representative Photomicrographs (10x): Porcine Coronary Studies

| | 28 Day | 90 Day | 180 Day |
|---|---|---|---|
| BVS |  |  |  |
| **CYPHER®** |  |  |  |

Photos on file at Guidant.

Pipeline DES products are currently in development at Guidant. Not available for sale.

# BVS Intracoronary, *In-vivo* OCT Imaging




- Periprocedural Rx: Heparin
- Target vessel: RCA
- BVS stent 3.0/12mm
- OCT imaging

# REVA Bioresorbable Stent

- Fully bioresorbable coronary stent system
- Integral bioresorbable drug-elution coating
- Paclitaxel-eluting

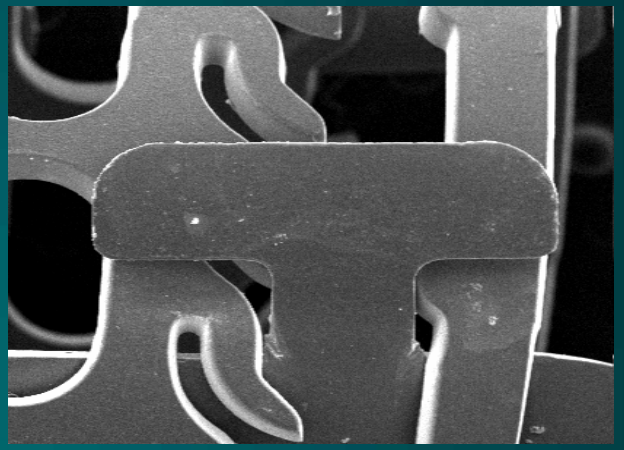
# Slide & Lock Design

## Design Enables Material

- Expansion based upon sliding, locking parts rather than material deformation
  - Facilitates the use of polymers

## Enables Performance

- Negligible recoil
- Comparable radial strength & flexibility
- Equivalent sizing to current metal stents
- Standard balloon deployment

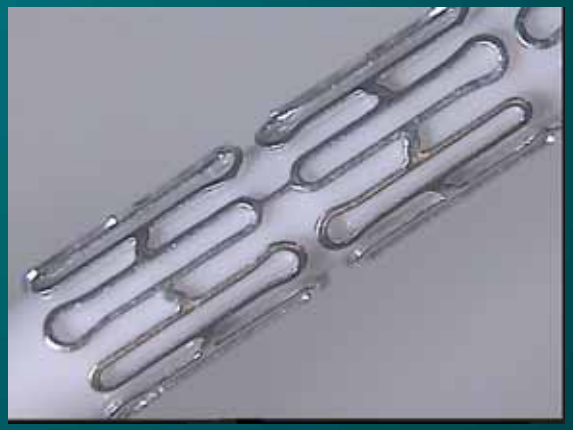


Close-up of Slide & Lock Mechanism

7.35 mm Bend Radius

# *Mg Alloy Bioabsorbable Stent*

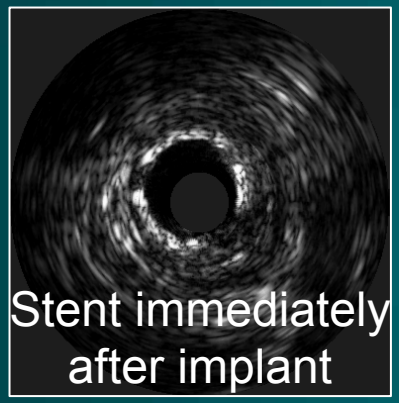
Metalic **stents provide temporary scaffolding, that will *Disappear* *at 60-90 days* *a*fter deployment and may reduce restenosis! and will be compatible with cardiac imaging MRI or CT**



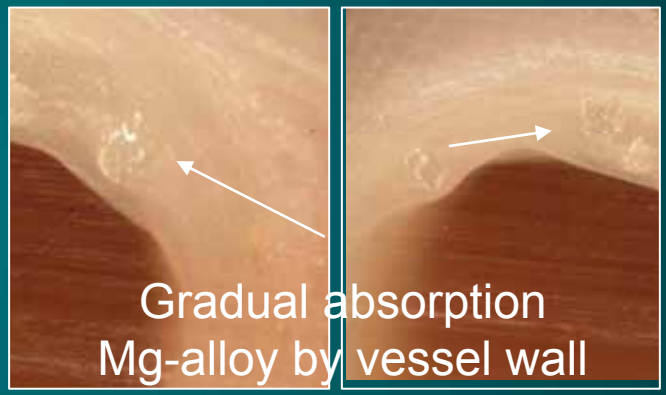
***Magnesium Based Alloys – Bioabsorbable Stents***

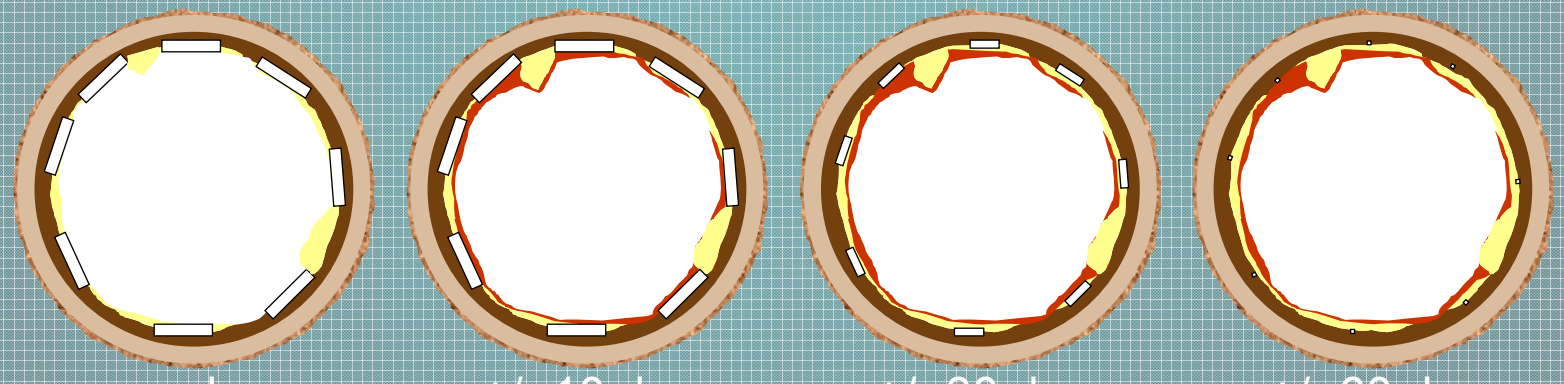
# In-vivo results animal trials

Quick endotheliasation and gradual absorption



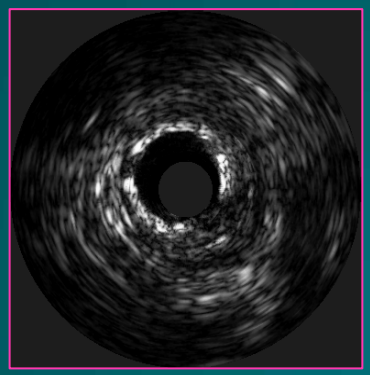


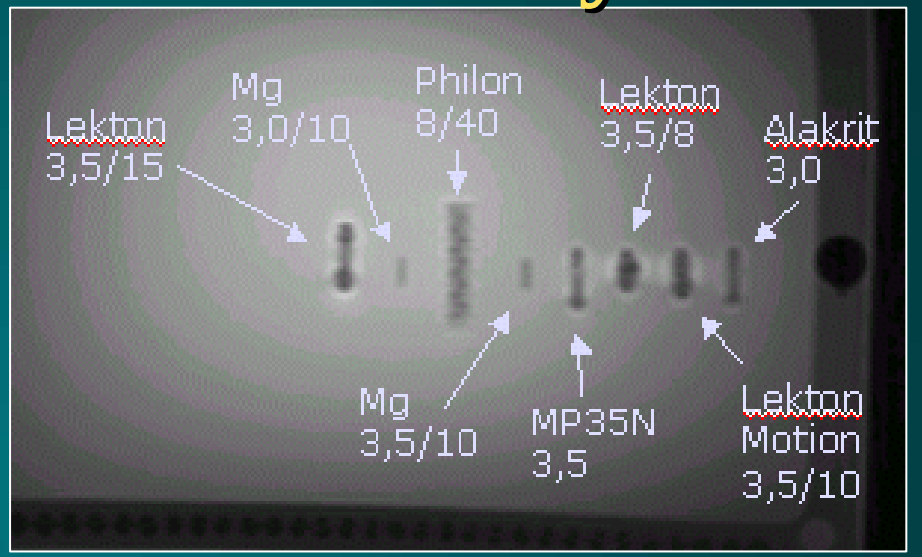


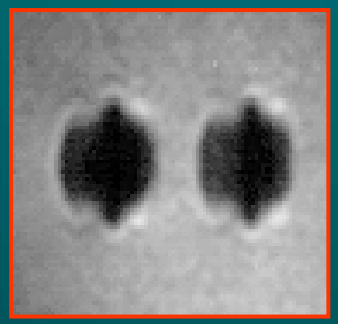
# Magnesium Stent: Visibility

- IVUS

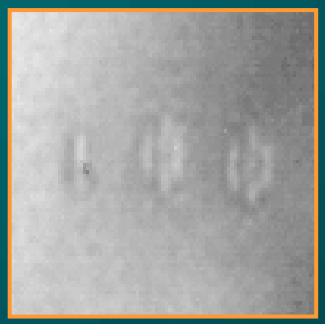





- MR



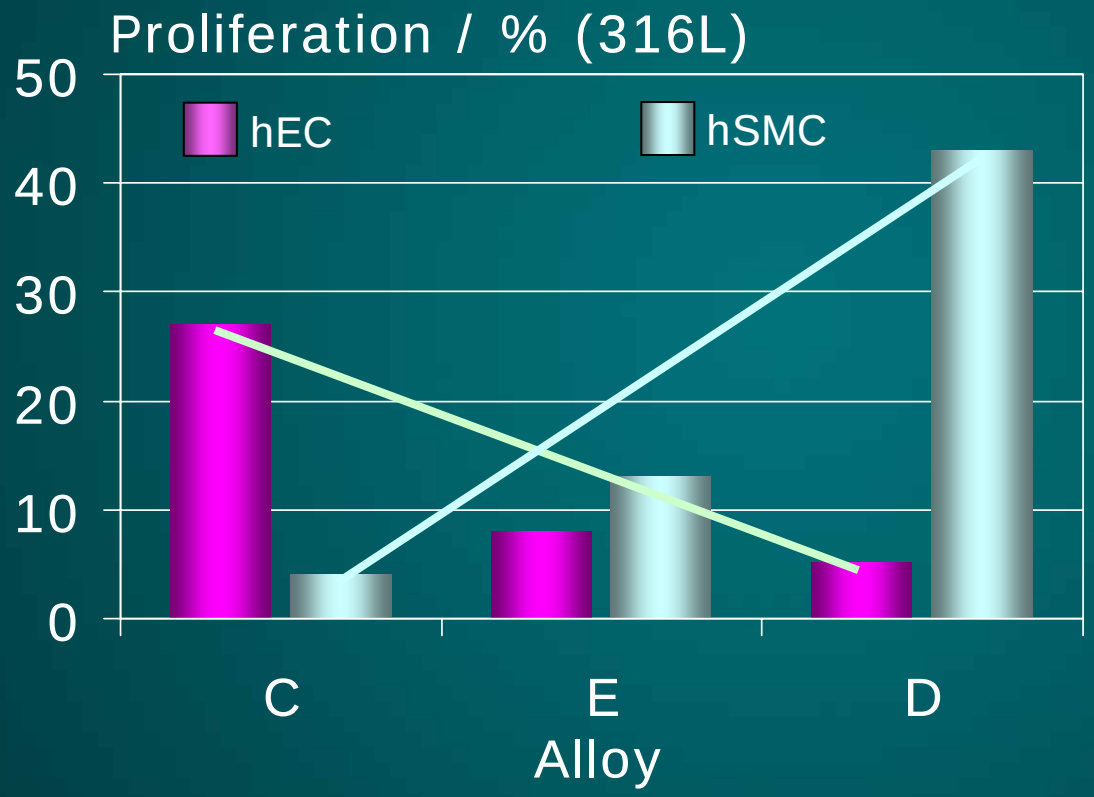
316L

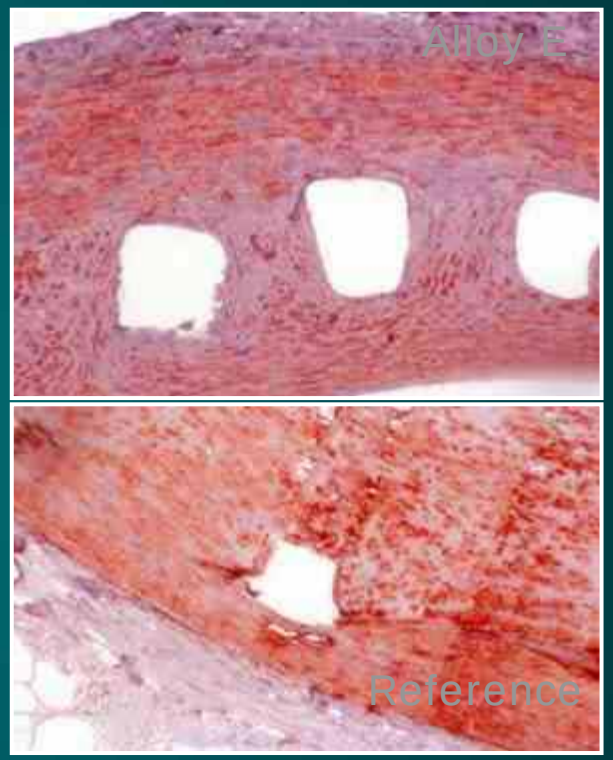


Mg alloy

# Properties Biocompatibility

Reduced Proliferation of SMCs & ECs




α-actin straining after 35d
Heublein, et al., MHH

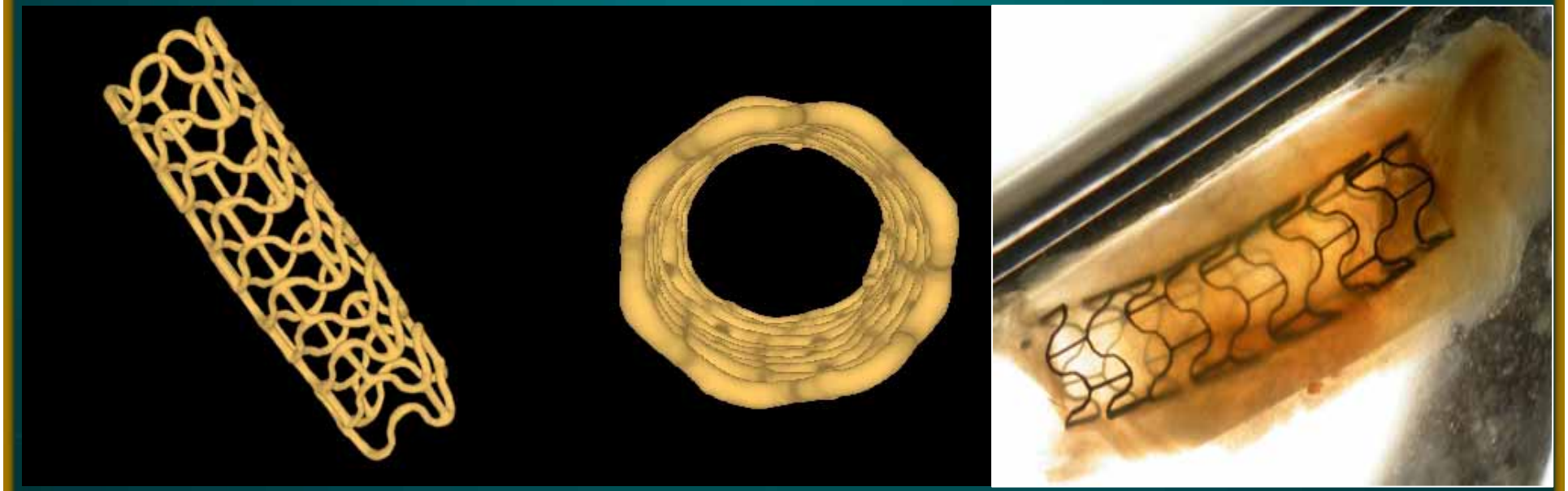
Proliferation (BrdU) test of aterial hSMC and hEC in eluates.
Heublein, et al., MHH

# Structural Integrity

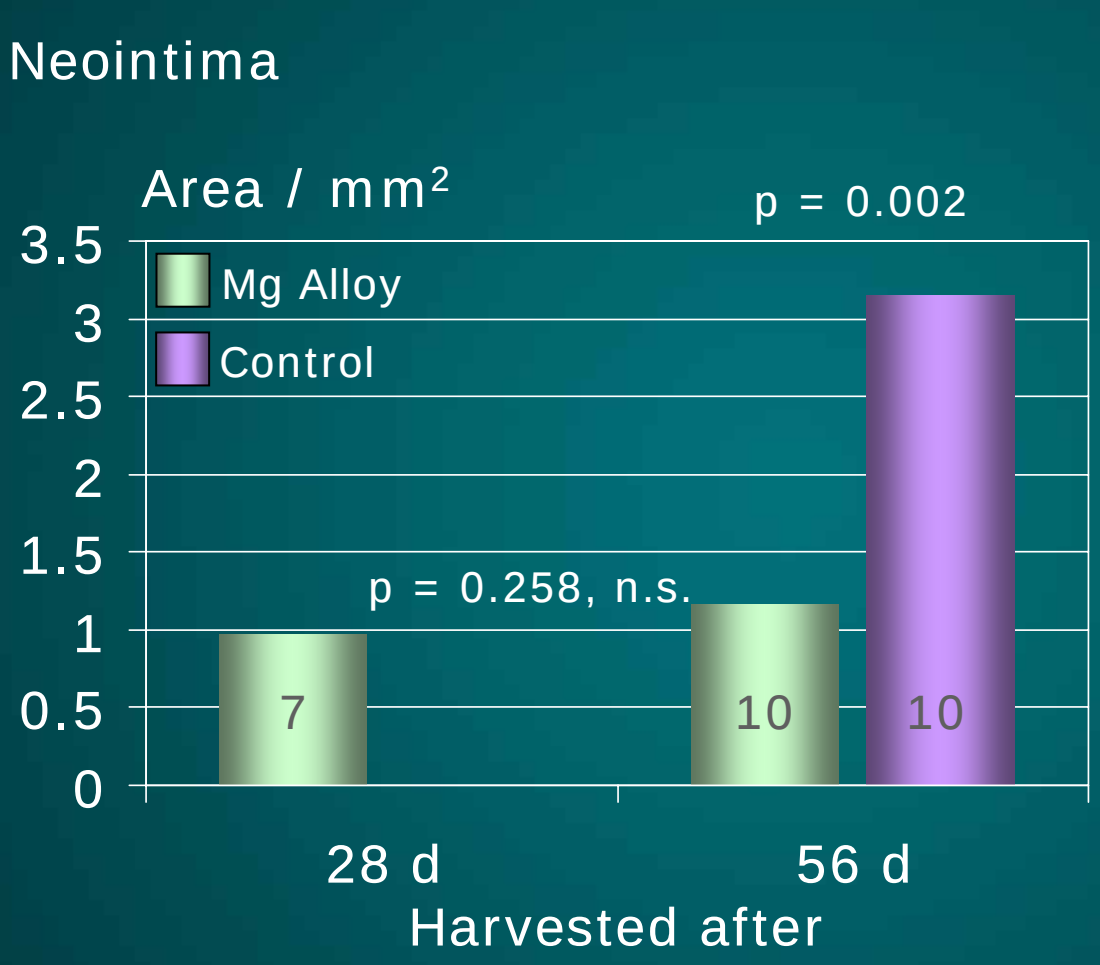
**Testing after 3 days of implantation (minipig)**

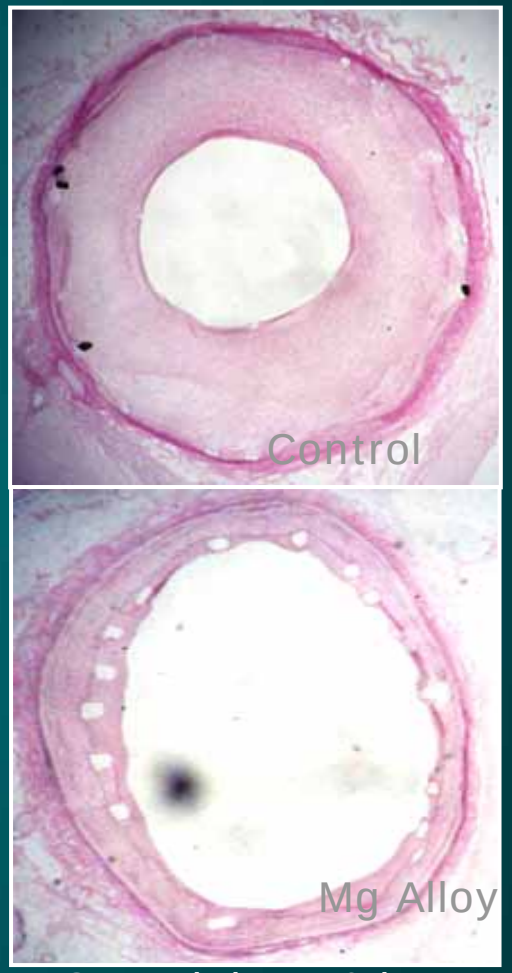
**Stent structure is completely intact**

Micro CT and Light optical microscope images of Mg-stents 3 days after implantation



# Histology & Morphometry



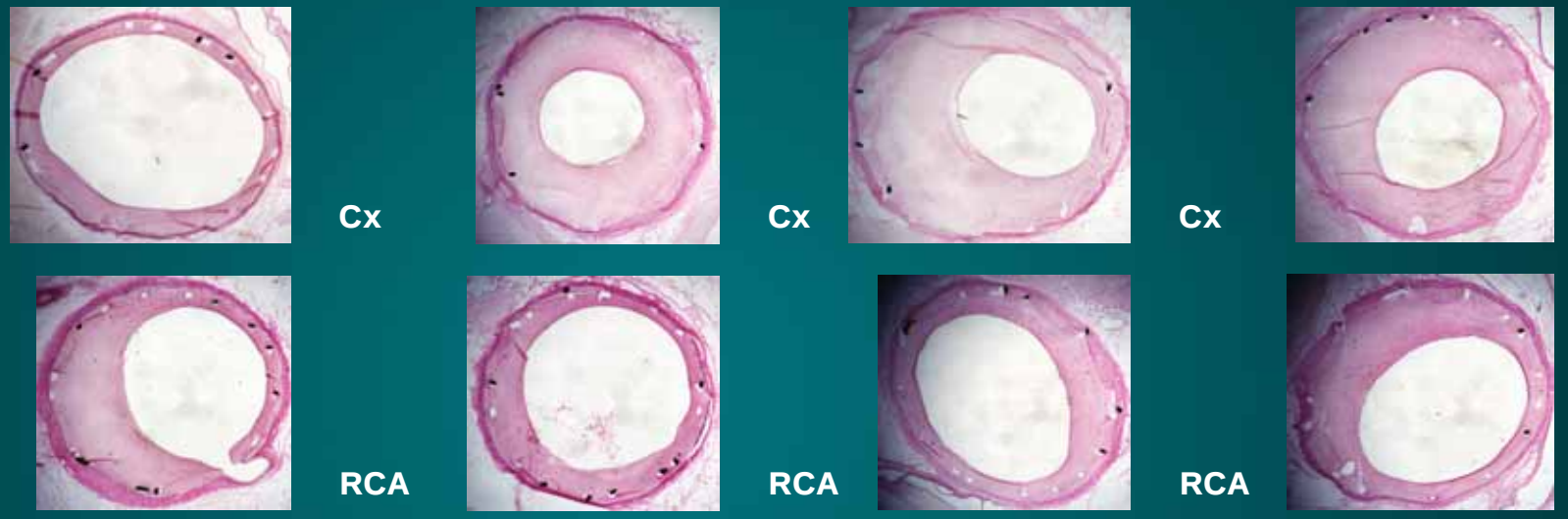




EvG straining 56d
Heublein, et al., MHH

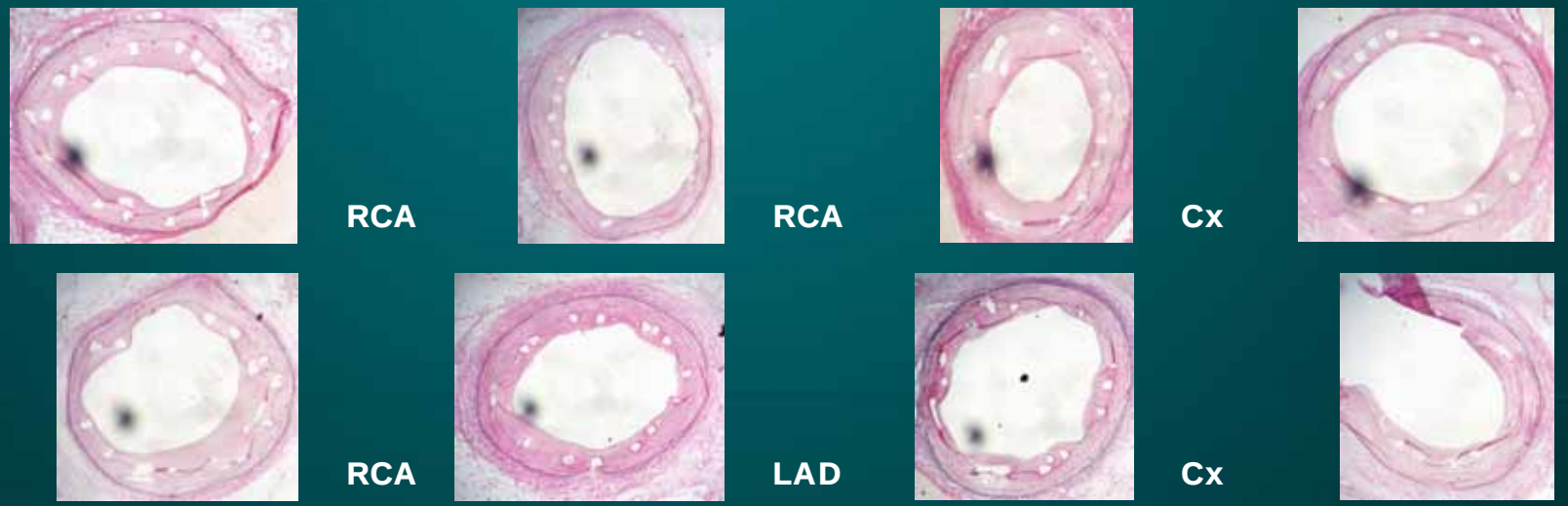
Mean neointima in minipig coronary arteries
adjusted for injury score and media reference (ANCOVA)
Heublein, et al., MHH

# **Control and Mg** – minipig coronary arteries; 8 weeks fu

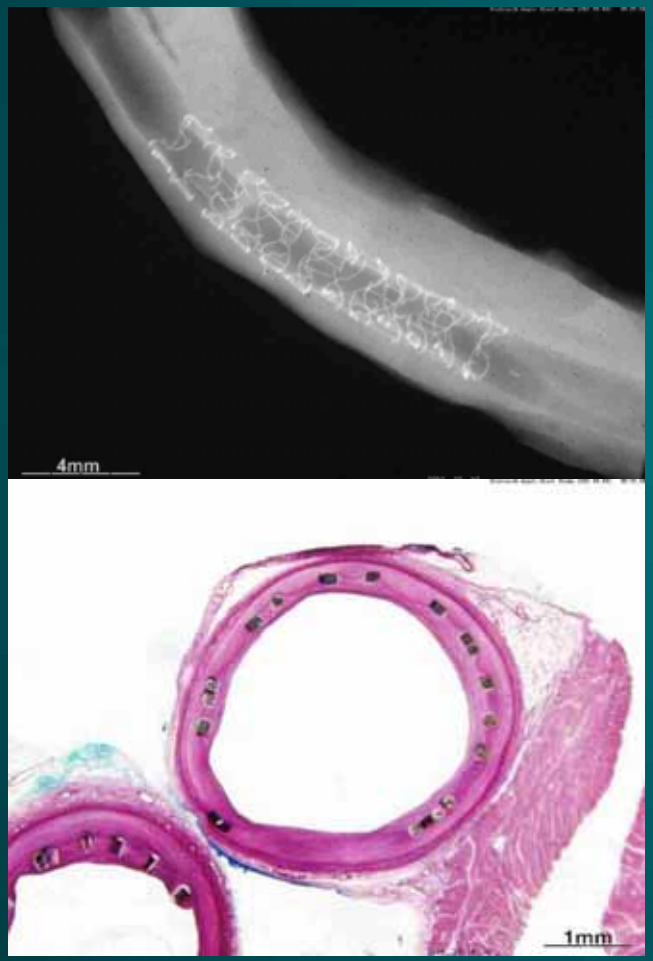
**Control**



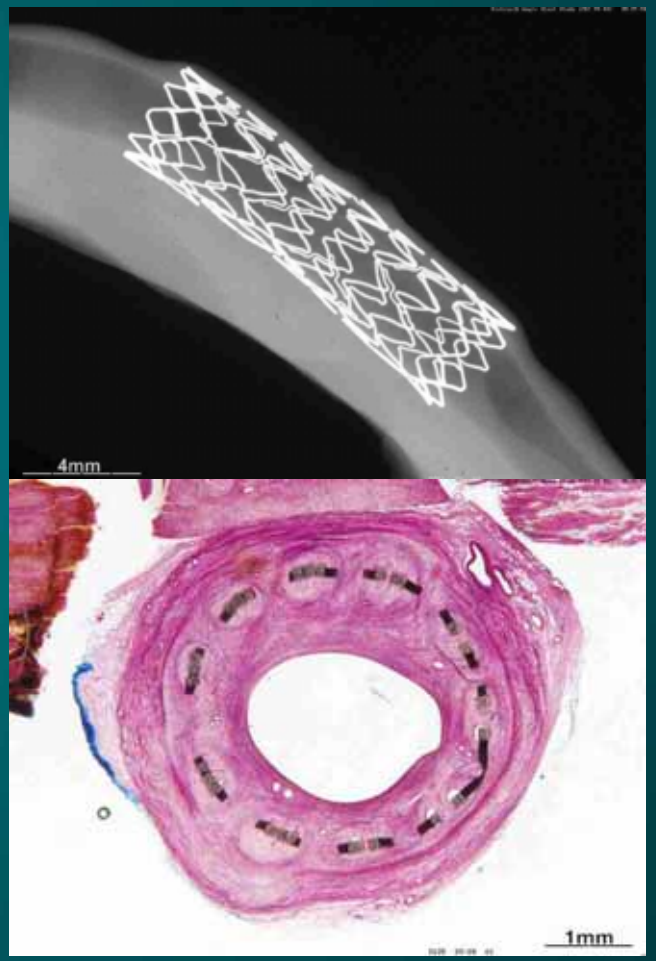

**Mg Alloy**



# Mg versus Control at 30 days

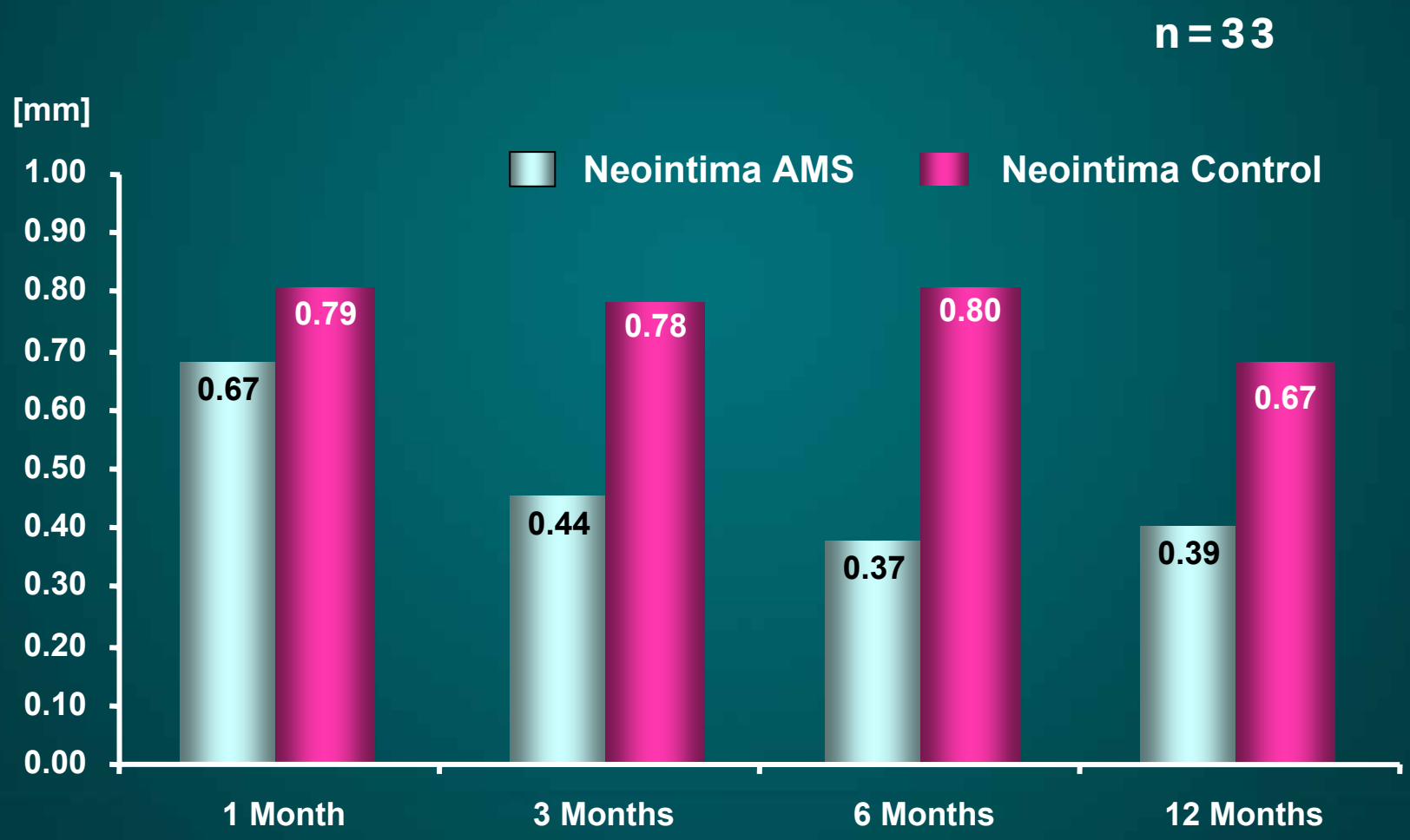



Mg

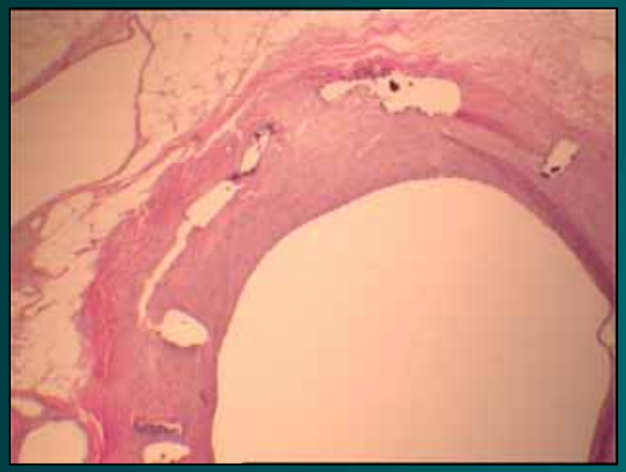



Conrtol L316

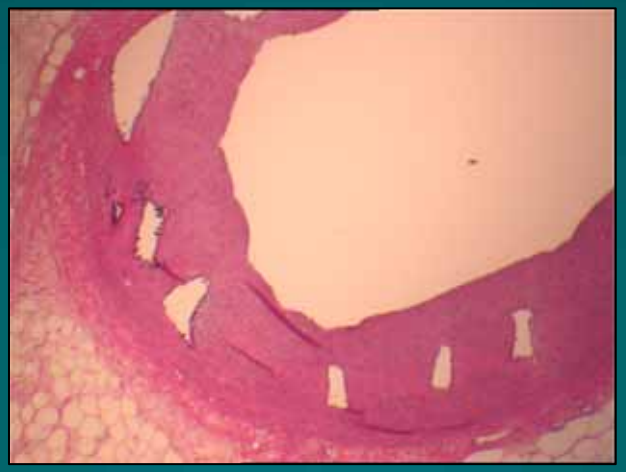
# Neointimal Thickness of AMS Decreases in Minipig



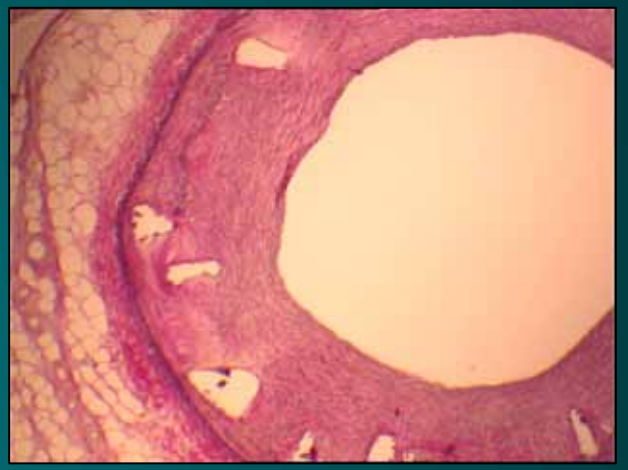
# AMS-Animal Study, 6 months follow up Histological Findings



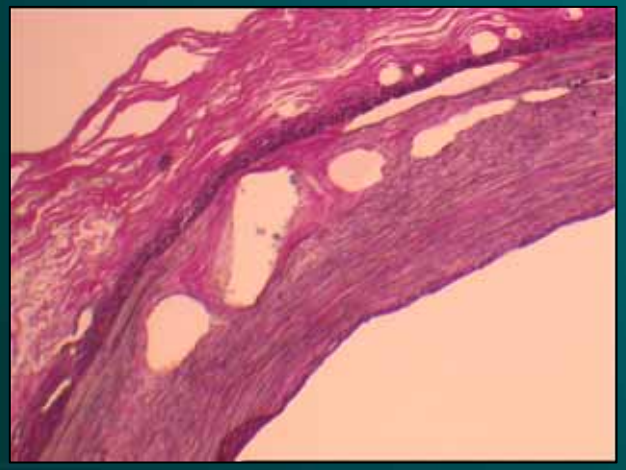
Animal 1, RCA pos.2, (HE 25x magnification)



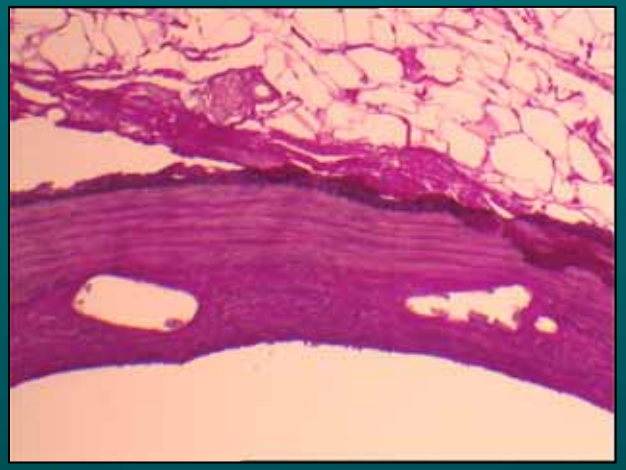
Animal 1, RCA pos.4, (HE 25x magnification)



Animal 26, RCA pos.2 (EvG 25x magnification)



Animal 15, LAD pos.2, (EvG 63x magnification)



Animal 15, RCA pos.2, (EvG 63x magnification)

Animal 1, RCA pos.4, (EvG 63x magnification)

*HE = hematoxylin-eosin staining; EvG = Elastica van Giesson staining*

# PROGRESS AMS I Clinical Study

**Preliminary Data Analysis**

***March 2006***

***Late Breaking Trials ACC***

# PROGRESS AMS – Overview

**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 AMS – Hypothesis

The PROGRESS-AMS study designed to yield first data on the clinical safety and efficacy of the absorbable metal stent in the coronary artery application

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)

# PROGRESS AMS – Primary Endpoint

**The primary endpoint of PROGRESS-AMS is**

Major Adverse Cardiac Events (MACE)
at 4 months **defined as**

**Cardiac death**

**Nonfatal myocardial infarction**

**Ischemia driven TLR**

Early primary endpoint as basis for starting subsequent clinical trials with Absorbable Metal Stent

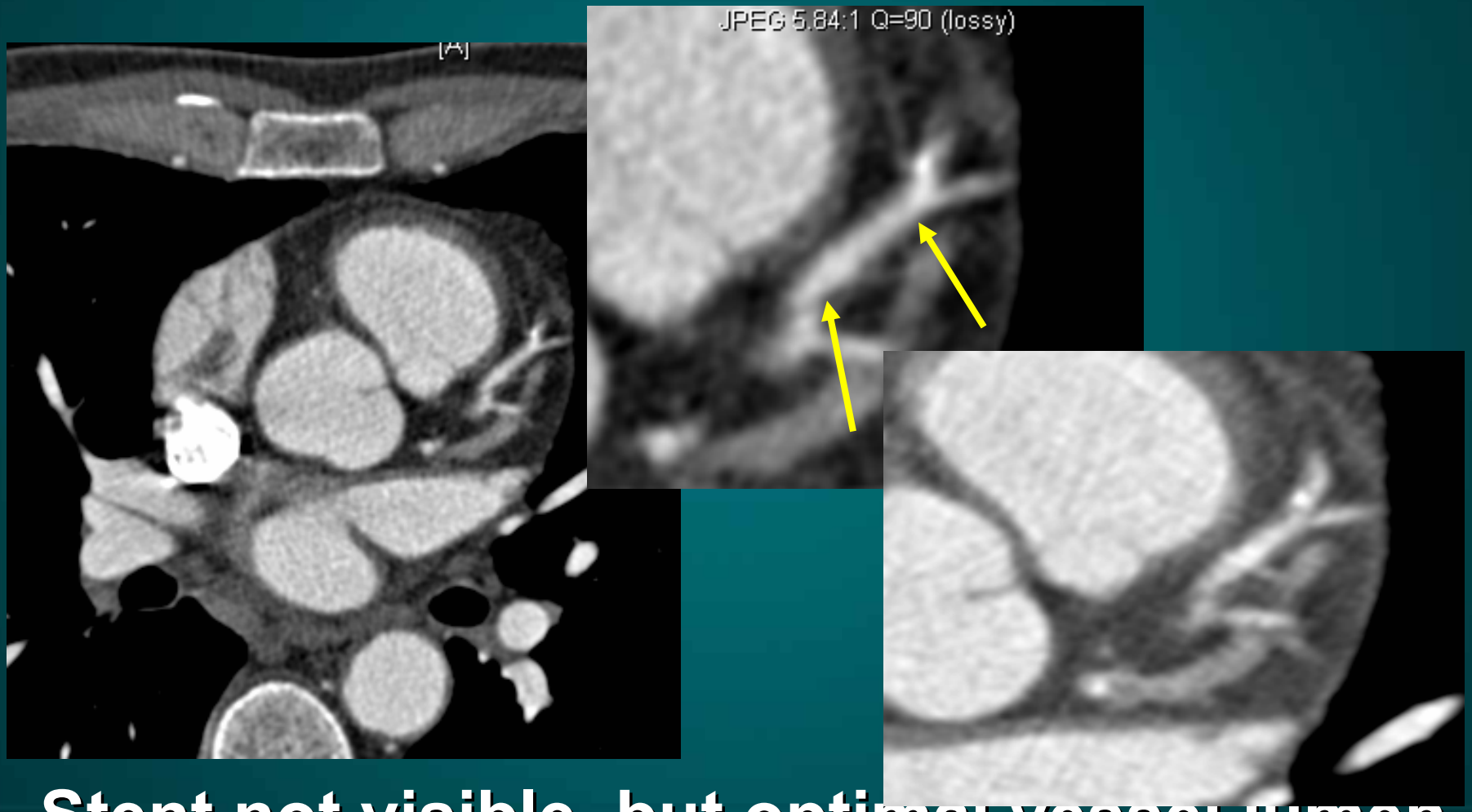
# PRELIMINARY RESULTS
## Demographics

| | | |
|---|---|---|
| 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 |

# PRELIMINARY RESULTS

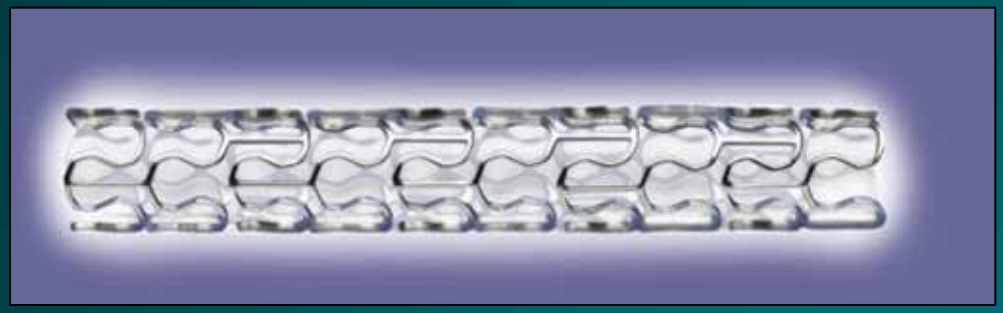
| | In Hospital Events | | 30-Day Events | | 4-Month Events | |
|---|---|---|---|---|---|---|
| | % | n | % | n | % | n |
| MACE (Cardiac death, nonfatal MI, ischemia driven TLR) | 0 | 0 | 0 | 0 | 23.8 | 15 |
| Death | 0 | 0 | 0 | 0 | 0 | 0 |
| Q-wave MI (new pathol. Q-waves with CK or CK-MB elevated) | 0 | 0 | 0 | 0 | 0 | 0 |
| Non Q wave MI (CK 2 times above normal with CK-MB elevated) | 0 | 0 | 0 | 0 | 0 | 0 |
| Ischemic Driven TLR | 0 | 0 | 0 | 0 | 23.8 | 15 |
| TLR (Any) | 0 | 0 | 0 | 0 | 38.1 | 24 |

# Multislice CT (16 row) imaging of coronary arteries



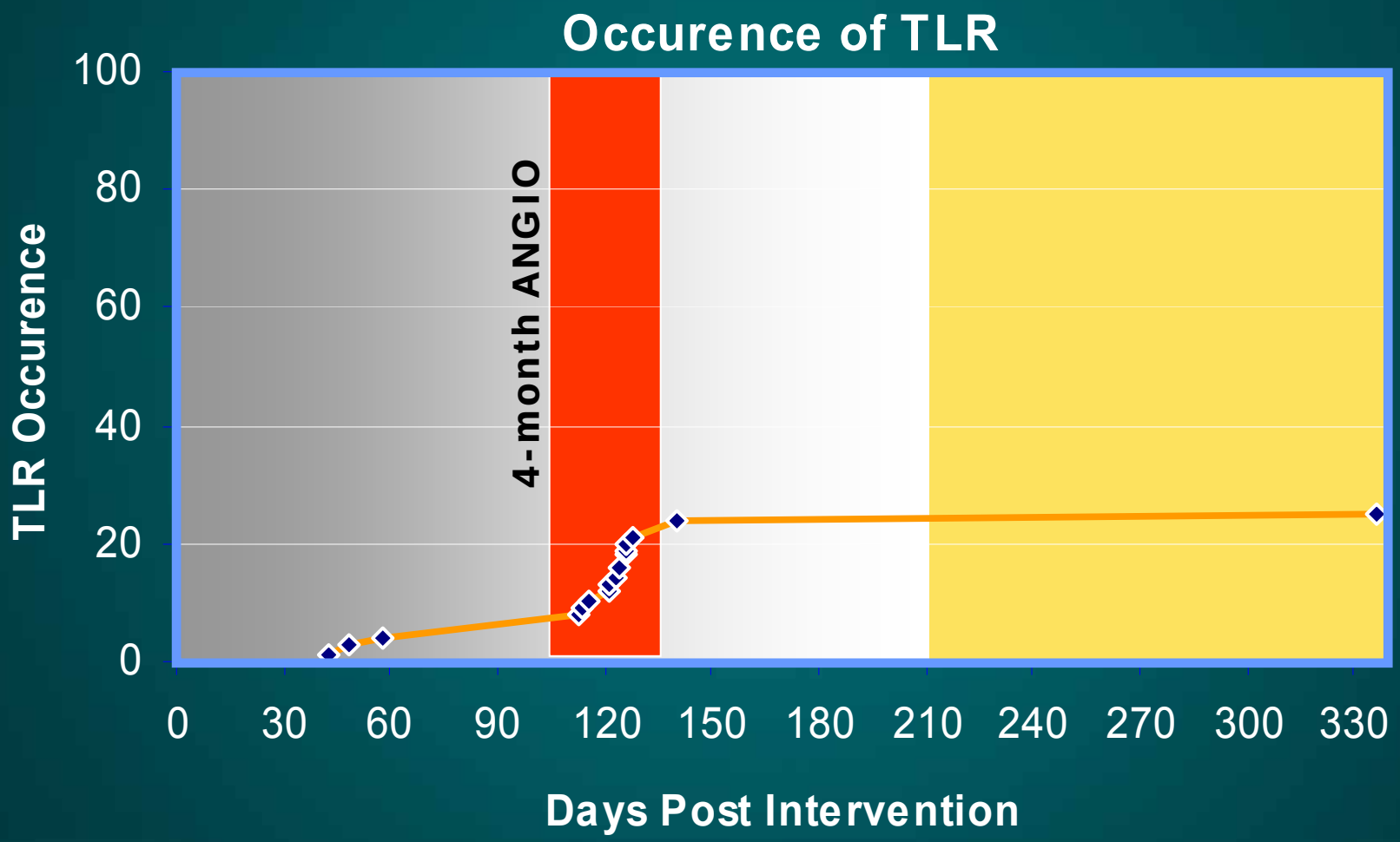

**Stent not visible, but optimal vessel lumen opacification**

# PRELIMINARY RESULTS – QCA Brief Summary

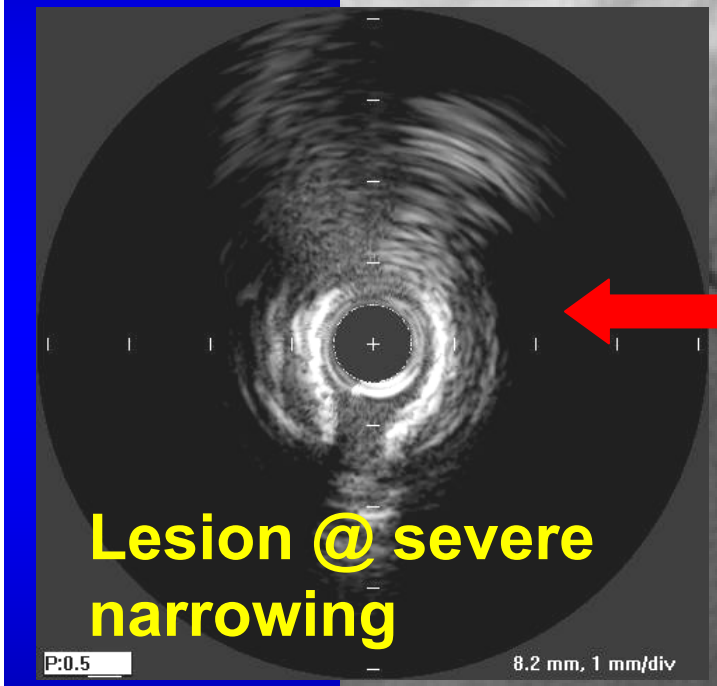


| | N = 60 lesions |
|---|---|
| Diameter Stenosis (%) Post | 12.4 ± 5.6 |
| MLD POST, mm | 2.46 ± 0.37 |
| **FOLLOW-UP QCA at 4 months** | **N = 57 lesions** |
| Diameter Stenosis (%) | 48.2 ± 17.2 |
| Binary Restenosis (%) | 31//57 (54.4%) |
| MLD, mm | 1.37 ± 0.52 |
| Late Loss, mm | 1.09 ± 0.51 |

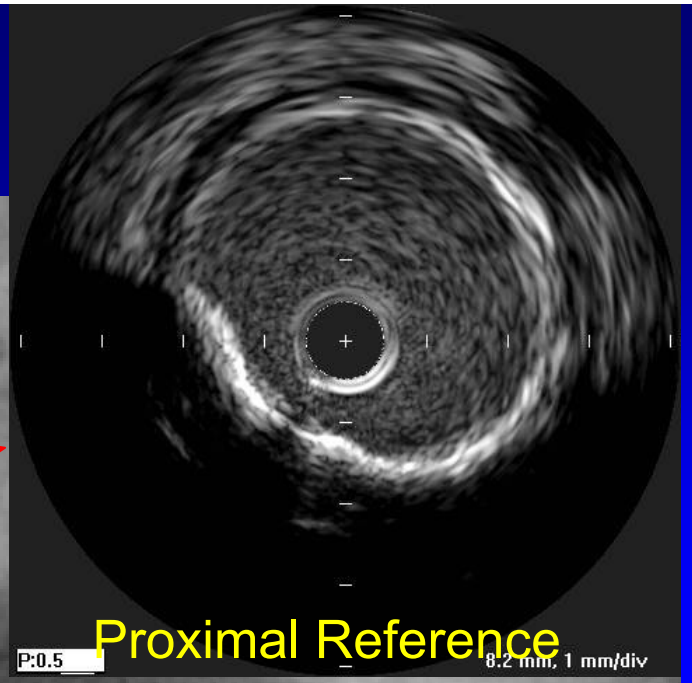
# All TLR Preliminary Summary



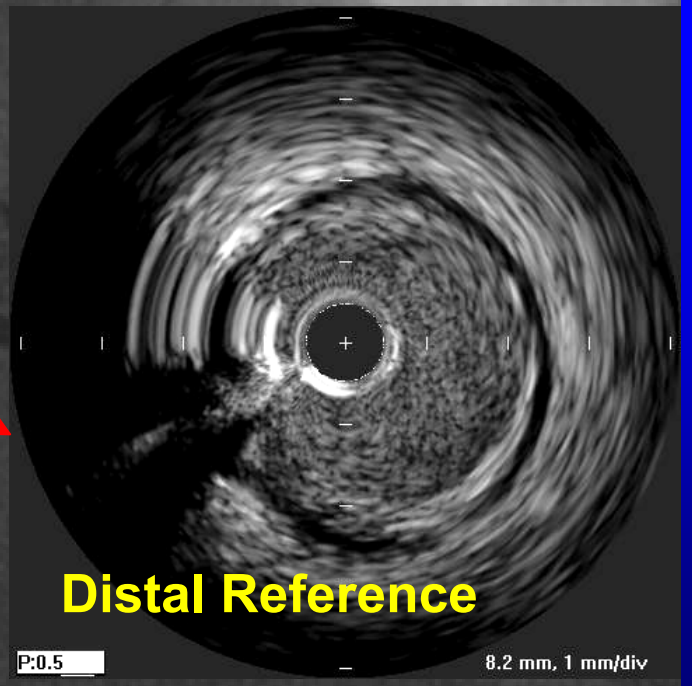
# IVUS of Heavily Calcified RCA (Pre)




Lesion @ severe narrowing



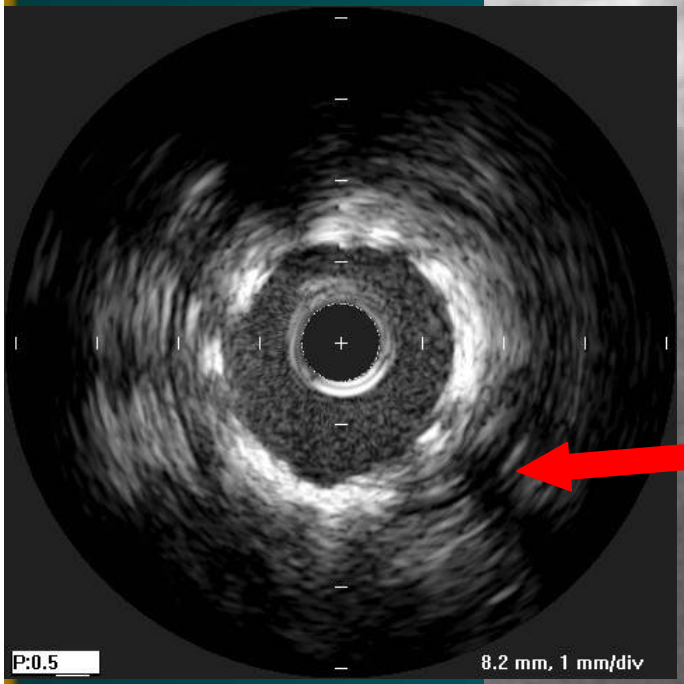

Proximal Reference

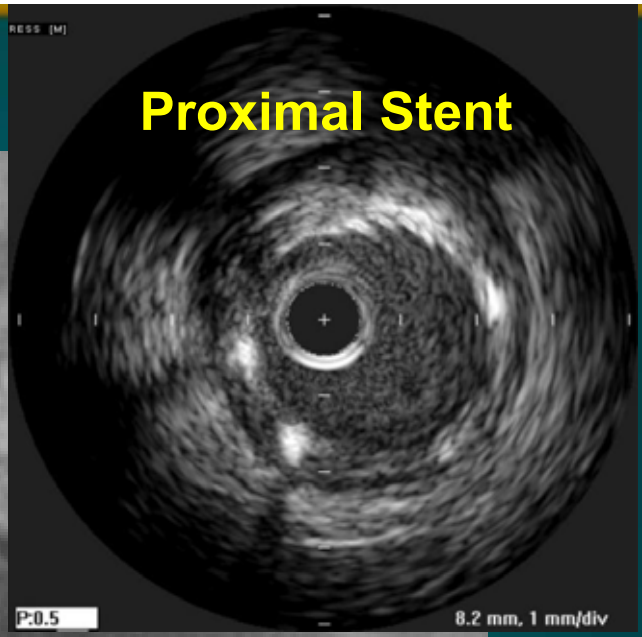


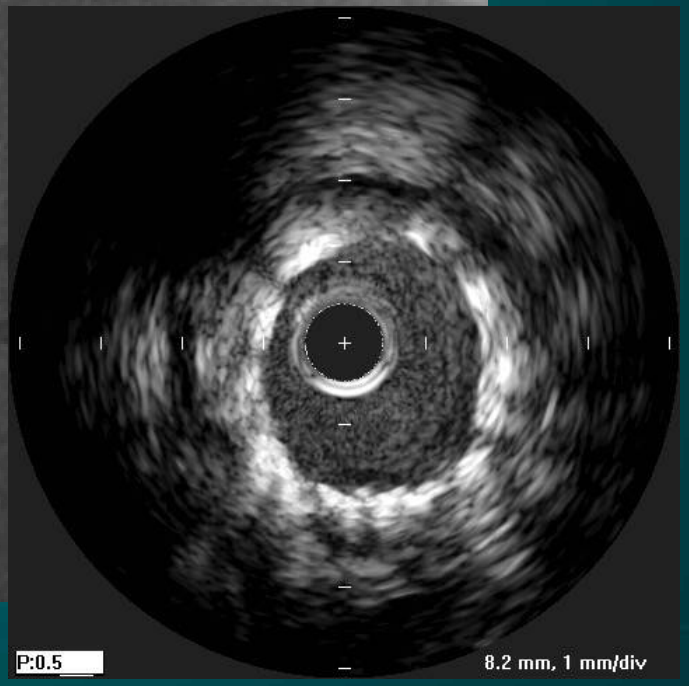

Distal Reference

Bonnier Waksman, Eindhoven May 21, 2004

# Full expansion after second proximal stent

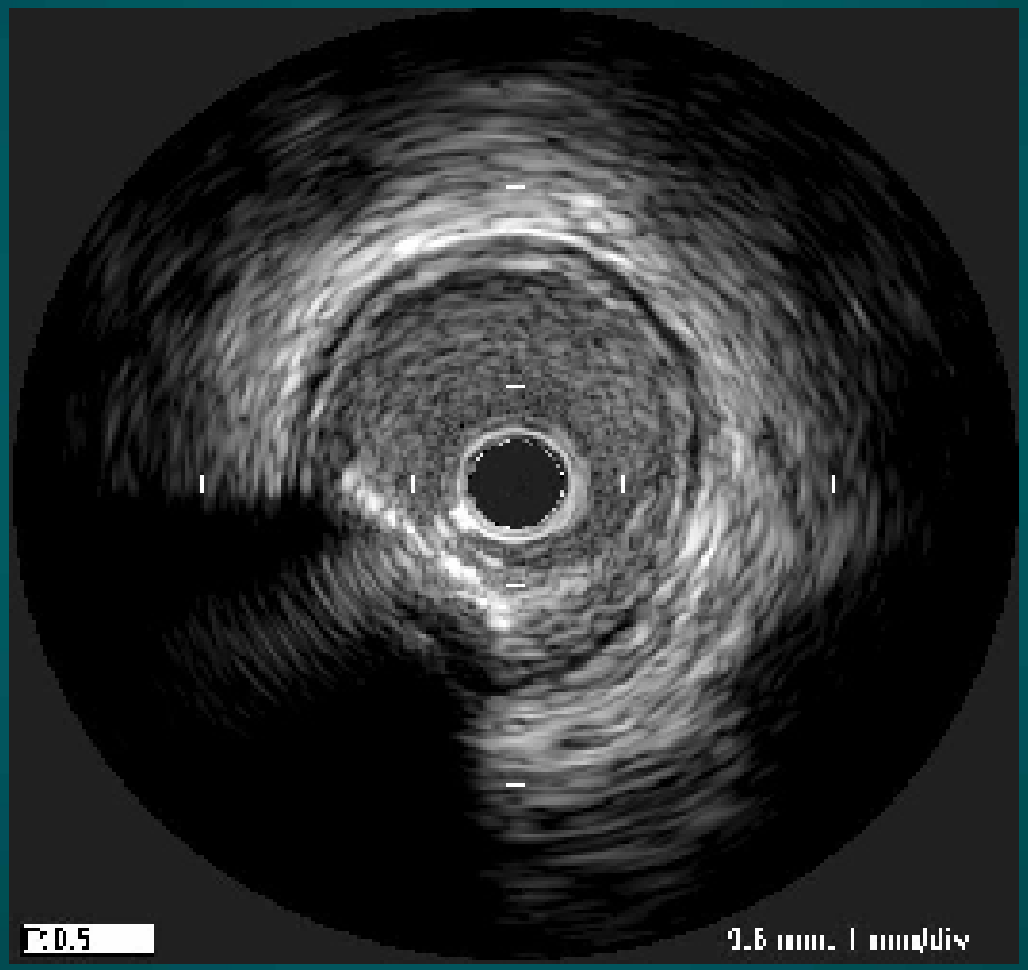



Bonnier Waksman, Eindhoven May 21, 2004

# IVUS at Follow-up



# Conclusions

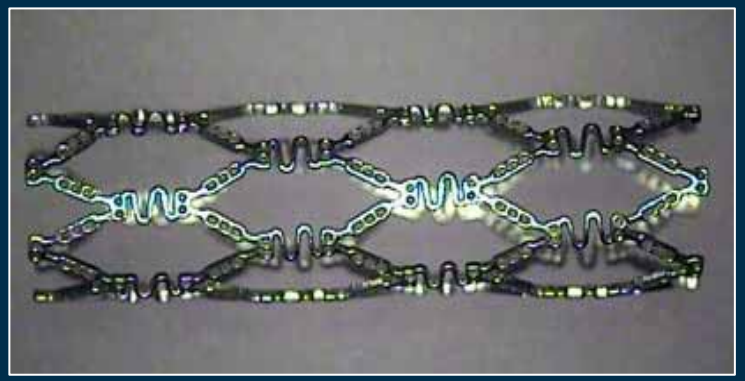
The FIM coronary study showed:

- **Feasibility**
- **Safety: no death, no MI, no stent thrombosis**
- **The study met the primary endpoint < 30% of MACE**
- The Absorbable Metal Stent (AMS):
- **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**

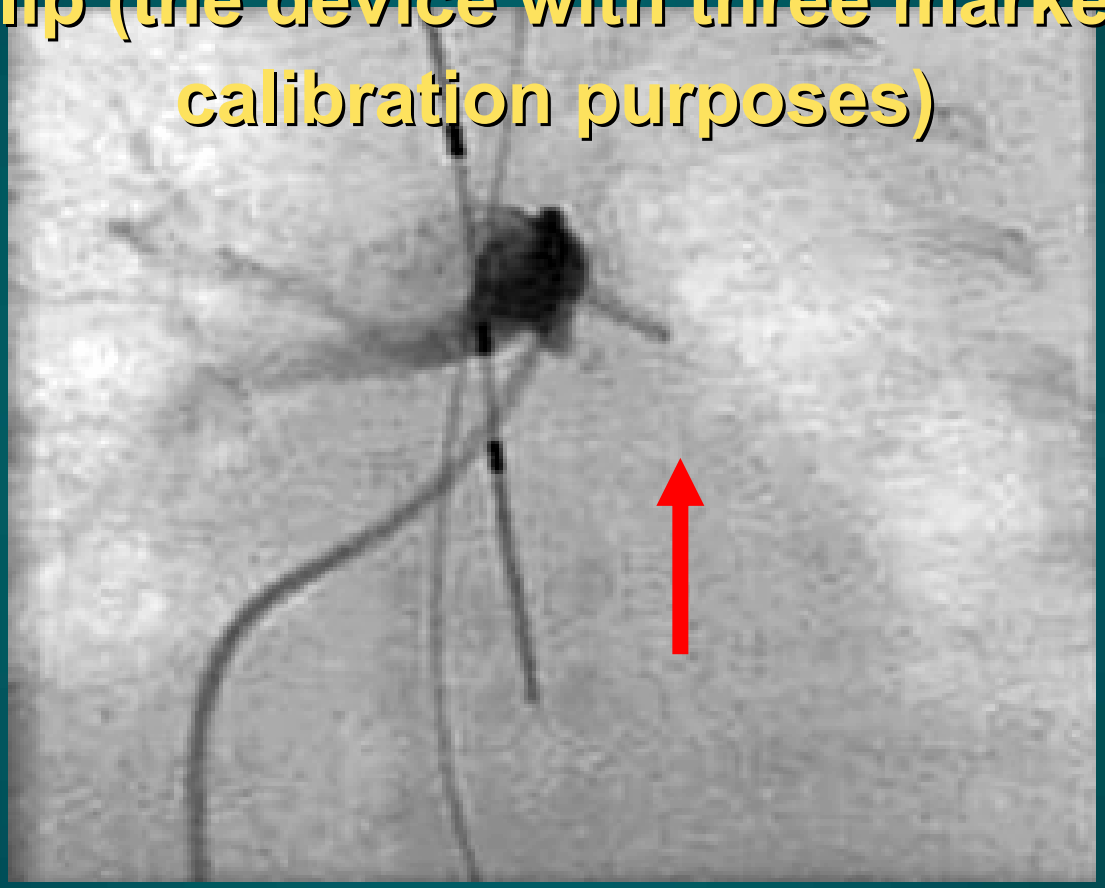


**Controlled Drug Eluting Stent Design**:

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

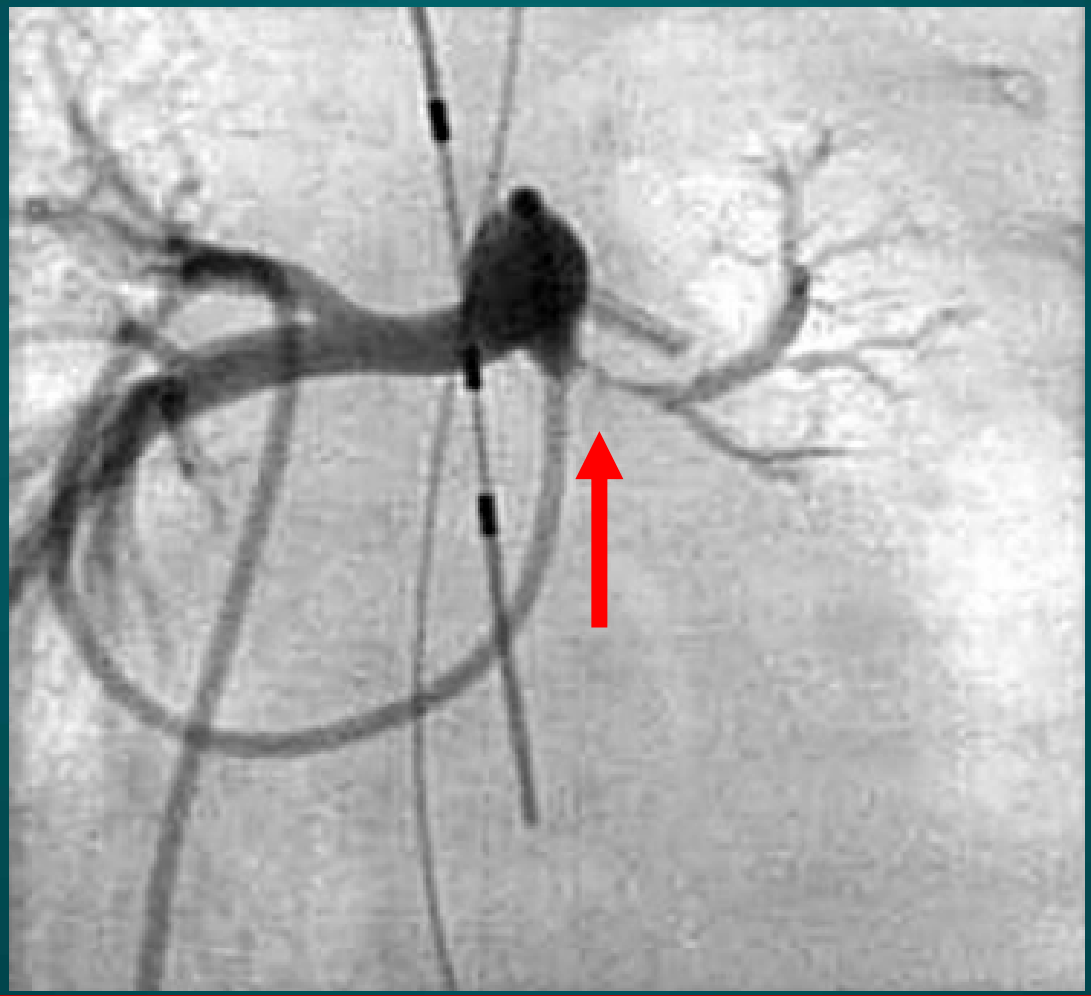
* = Animal data available at Biotronik / ** = In vitro data available at Biotronik

# 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)



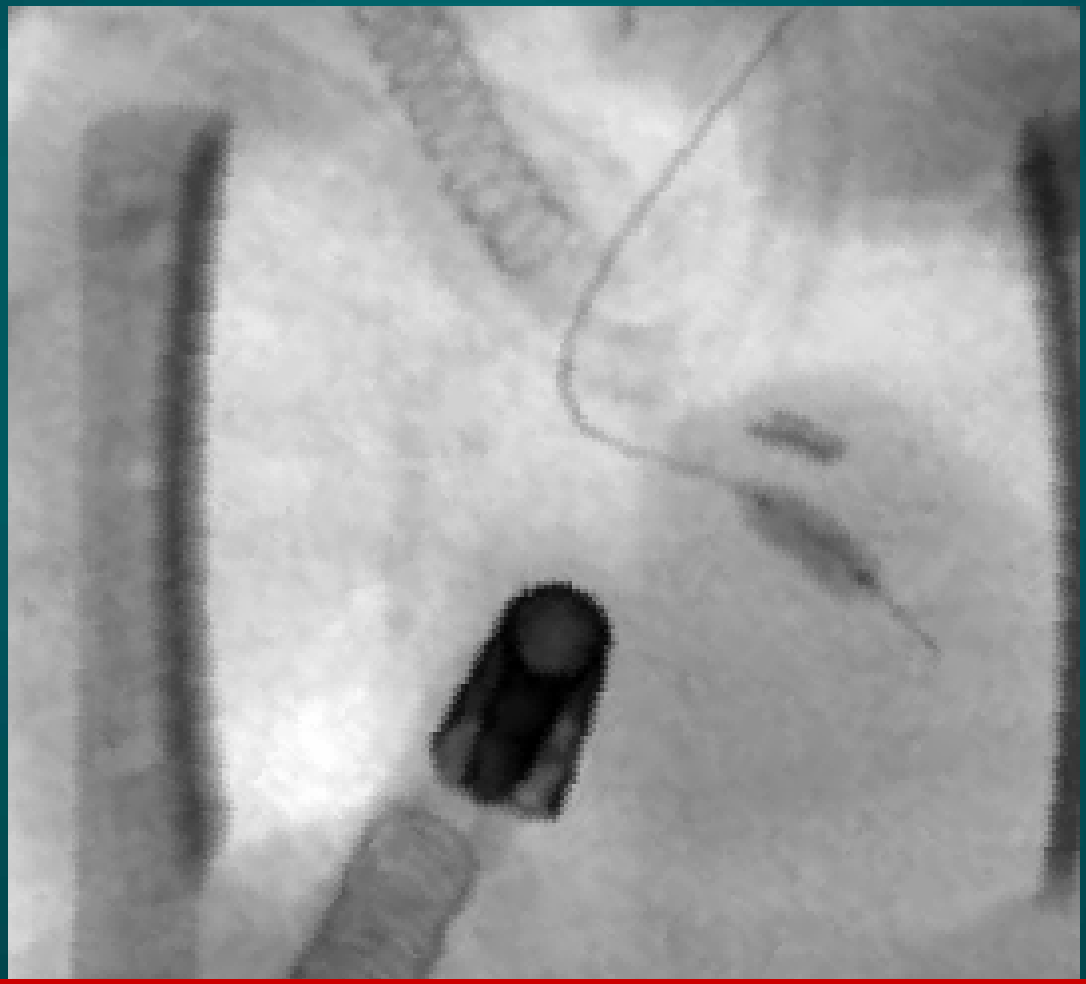
Peter Zartner, M. D., Pediatric CardiologyUniversity of Erlangen-Nuremberg, Germany

# 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

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

# FIM details Below The Knee

- 20 CLI patients (Rutherford 4-5) with BTK pathology

  1. Improving inflow limiting ATK lesions

  2. Lekton Mg implant if short (max 30mm) BTK stenoses
     - Suboptimal angiographic result after PTA
       - ≥50% stenosis post-treatment
     - At the physician's discretion
       - flow-limiting dissection
       - threatened or acute closure

- Implants performed between December '03 – January '04

# Patient demographics (N=20)

- Male 10 50%
- Female 10 50%
- Average age 76 yrs (59 - 96)
- Clinical vascular status
  - Rutherford Class IV 9 45%
  - Rutherford Class V 11 55%

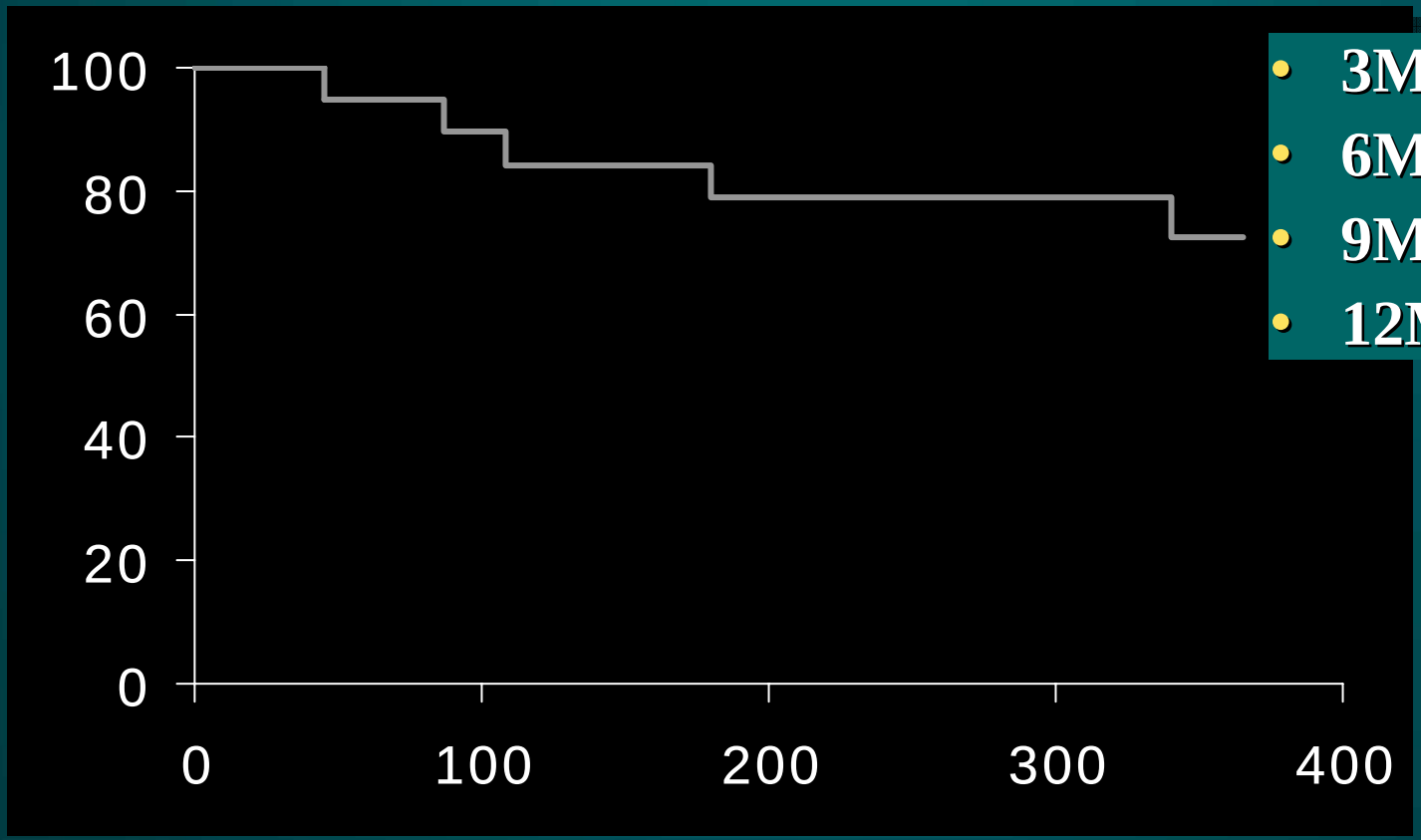
# Lesion description (N=20)

- Average lesion length 11 mm (2 mm – 20 mm)
- Average vessel diameter 2.7mm (2.5 mm – 3 mm)
- Average stenosis 84 % (75% – 95%)

| | | |
|---|---|---|
| • Dissection | 0 | 0% |
| • Ulceration | 1 | 5% |
| • Thrombus | 3 | 15% |
| • Calcification | 14 | 70% |

# High Patency Rate Below The Knee

- Primary Clinical Patency



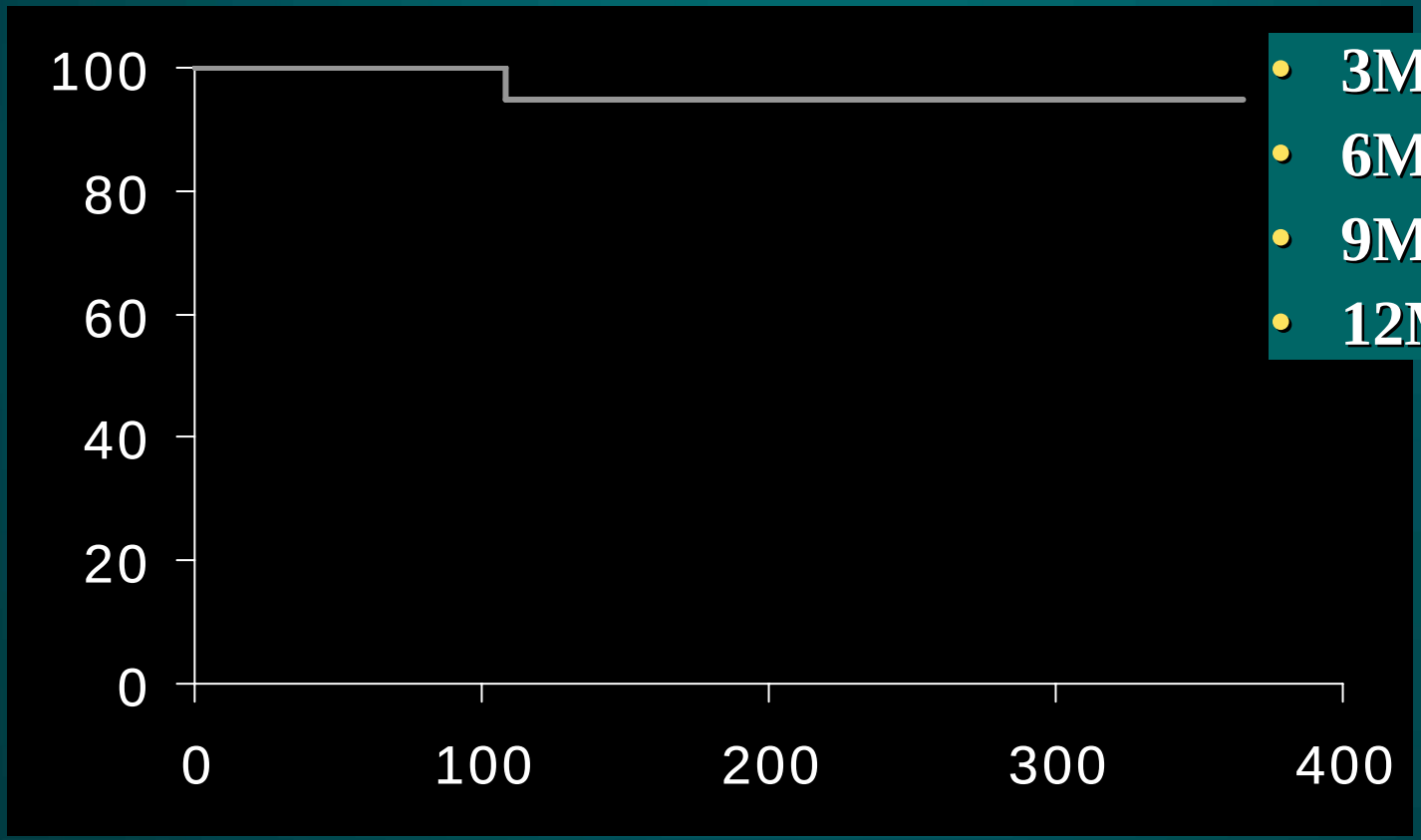

- 3M 89.5%
- 6M 84.2%
- 9M 78.9%
- 12M 72.4%

- Time
- (Days)

Bosiers M, Dendermonde, Belgium; Peeters P, Bonheiden, Belgium

# 94.7% Limb Salvage After One Year

- Limb Salvage Rate




- 3M 100.0%
- 6M 94.7%
- 9M 94.7%
- 12M 94.7%

- Time
- (Days)

Bosiers M, Dendermonde, Belgium; Peeters P, Bonheiden, Belgium

# 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.