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Limited Applicability of Bioresorbable Stents for Complex Lesions

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Why bioresorbable stents seem to be atractive?

Advantage	Biodegradable stents	BMS	DES
Radial support	Transient	Permanent	Permanent
Need for prolonged double antiplatelet therapy	No	No	Yes
Late stent thrombosis	No	No	Yes
Expansive remodeling	Yes	No	No
Follow-up with noninvasive techniques	Yes	No	No
Permanent jailing of side Branches	No	Yes	Yes
Facilitate reintervention in the treated segment (CABG or PCI)	Yes	No	No
Potential recovery of the endothelial function	Yes	No	No

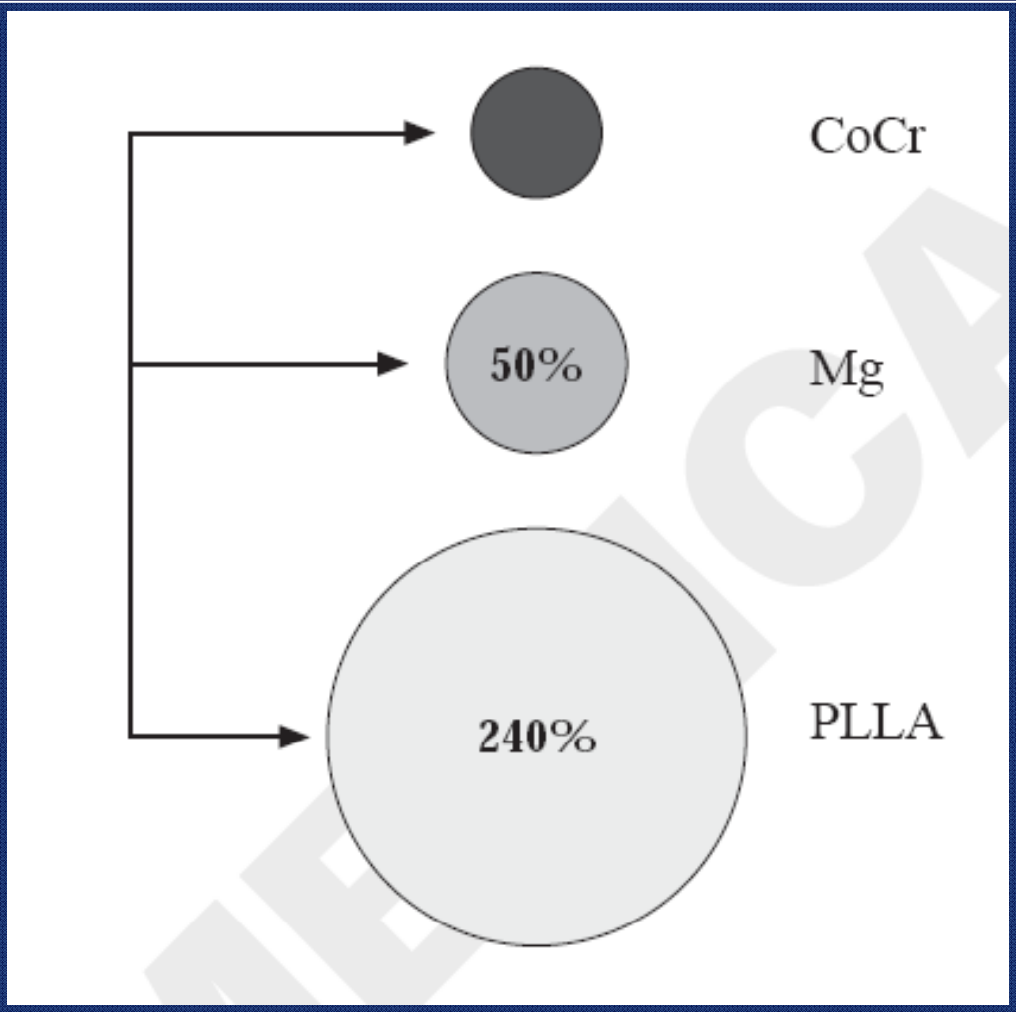
N. Gonzalo and C. Macaya; Vascular Health and Risk Management 2012:8

Potential Advantages and Downsides

Advantages	Downsides to Be Overcome
Mechanically functional for required healing period	Incompatibility due to poor polymer quality or processing (residual solvents, catalyst, monomer, etc)
Better physiologic healing of the artery upon degradation	Inadequate degradation and resorption profile
Permits positive remodelling of the artery	Inflammatory degradation residues
Allows repeated interventions	Insufficient mechanical properties
Disappears after healing is complete	Inadequate release profile when used with drug
Stent itself can be used as drug delivery system delivery system (i.e. larger loads)	

N. Gonzalo and C. Macaya; Vascular Health and Risk Management 2012:8

Relative size of stent struts required in stents made of magnesium and PLLA to ensure they have the same mechanical strength as CoCr



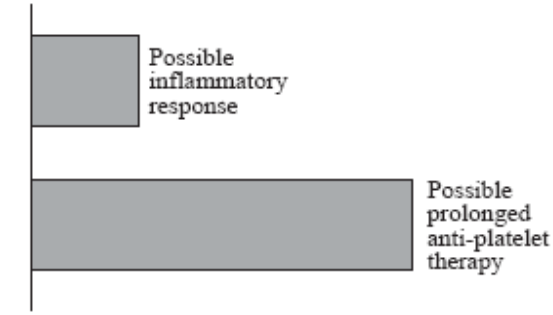
S. Garg, P. Serruys; Minerva Cardiolangiol 2009; 57; 537; 65

Challenges facing biodegradable stent technology

Chalenges for biodegradable stent technology

Biodegradation

Ideally stent degradation should occur within one year



Biomechanics

The stent ideally shoud maintain:

- Mechanical strength to support the vessel and provide radial strength
- Maintain deliverability (stent must be flexibile, with low crossing profile)
- Appear no different to the end user
  - Room storage
  - 6 month shelf life
  - Easy visualisation
  - Standard deployment

Biocompatibility

- The stent must not cause any significant inflammatory response as it degrades
- Inflammation is influenced by:
  - Chemistry of degradation
  - Rate of degradation
  - Amount of material to be absorbed
  - Potentially artherosclerotic environment

S. Garg, P. Serruys; Minerva Cardiolangiol 2009; 57; 537; 65

A comparison of the properties of biodegradable stents

Stent	Strut material	Drug elution	Stent radio-opacity	Total strut thickness (μm)	Crossing profile (mm)
Igaki- Tamai	Poly-L-lactic acid	Nil	Gold markers	170	Covered sheath ≥8F
BVS					
Revision 1.0	Poly-L-lactide	Everolimus	Platinum markers	156	1.4
Revision 1.1	Poly-L-lactide	Everolimus	Platinum markers	156	1.4
OrbusNeich	3x Lactide polymers	Yes	Tantalum markers	—	1.1
REVA stent	Polymer-tyrosine-derived polycarbonate	Nil	Iodine impregnated	200	1.7
BTI					
Generation I	Polymer+ Salicylate	Sirolimus Salicylate	Nil	200	2.0
Generation II	Polymer + Salicylate	Sirolimus Salicylate	Nil	175	1.5
AMS					
AMS-1	Magnesium alloy	Nil	Nil	165	1.2
AMS-2	Magnesium alloy	Nil	Nil	125	—
AMS-3	Magnesium alloy	Yes	Nil	125	—

BVS: bioabsorbable vascular solutions; BTI: Bioabsorbable Therapeutics Inc; AMS: absorbable metallic stent; FIM: First in Man.

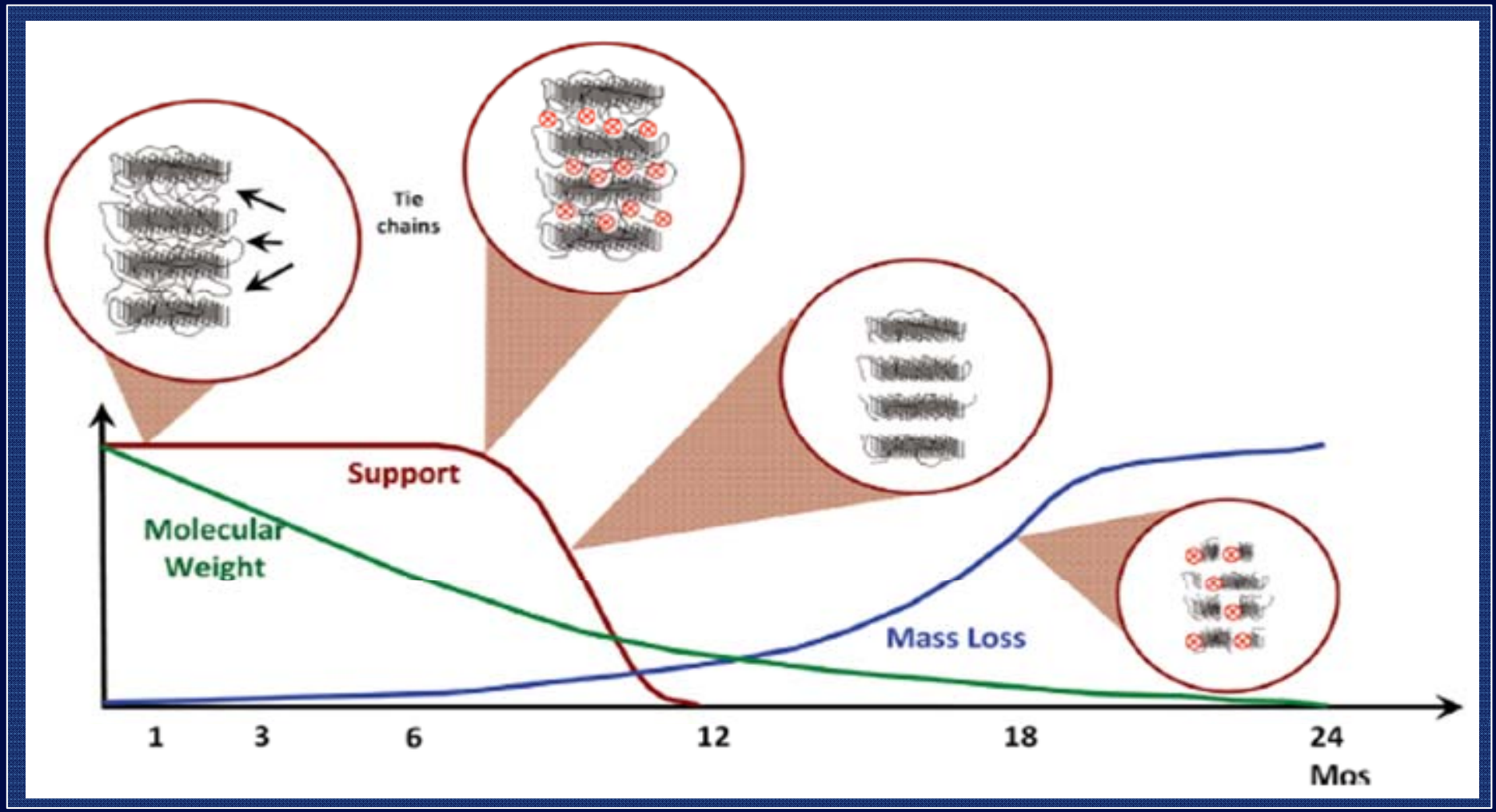
S. Garg, P. Serruys; Minerva Cardiolangiol 2009; 57; 537; 65

Mechanical Properties and Degradation Time for Different Polymers and Metals

Polymer composition	Tensile modulus of elasticity (Gpa)	Tensile strength (Mpa)	Elongation at break (%)	Degradation time (months)
Poly (L-lactide)	3.1–3.7	60–70	2–6	>24
Poly (DL-lactide)	3.1–3.7	45–55	2–6	12–6
Poly (glycolide)	6.5–7.0	90–110	1–2	6–12
50/50 DL-lactide/glycolide	3.4–3.8	40–50	1–4	1–2
82/18 L-lactide/glycolide	3.3–3.5	60–70	2–6	12–18
70/30 L-lactide/ε-caprolactone	0.02–0.04	18–22	>100	12–24
Cobalt chromium	210–235	1,449	~40	Biostable
Stainless steel 316L	193	668	40+	Biostable
Nitinol	45	700–1,100	10–20	Biostable
Magnesium alloy	40–45	220–330	2–20	1–3

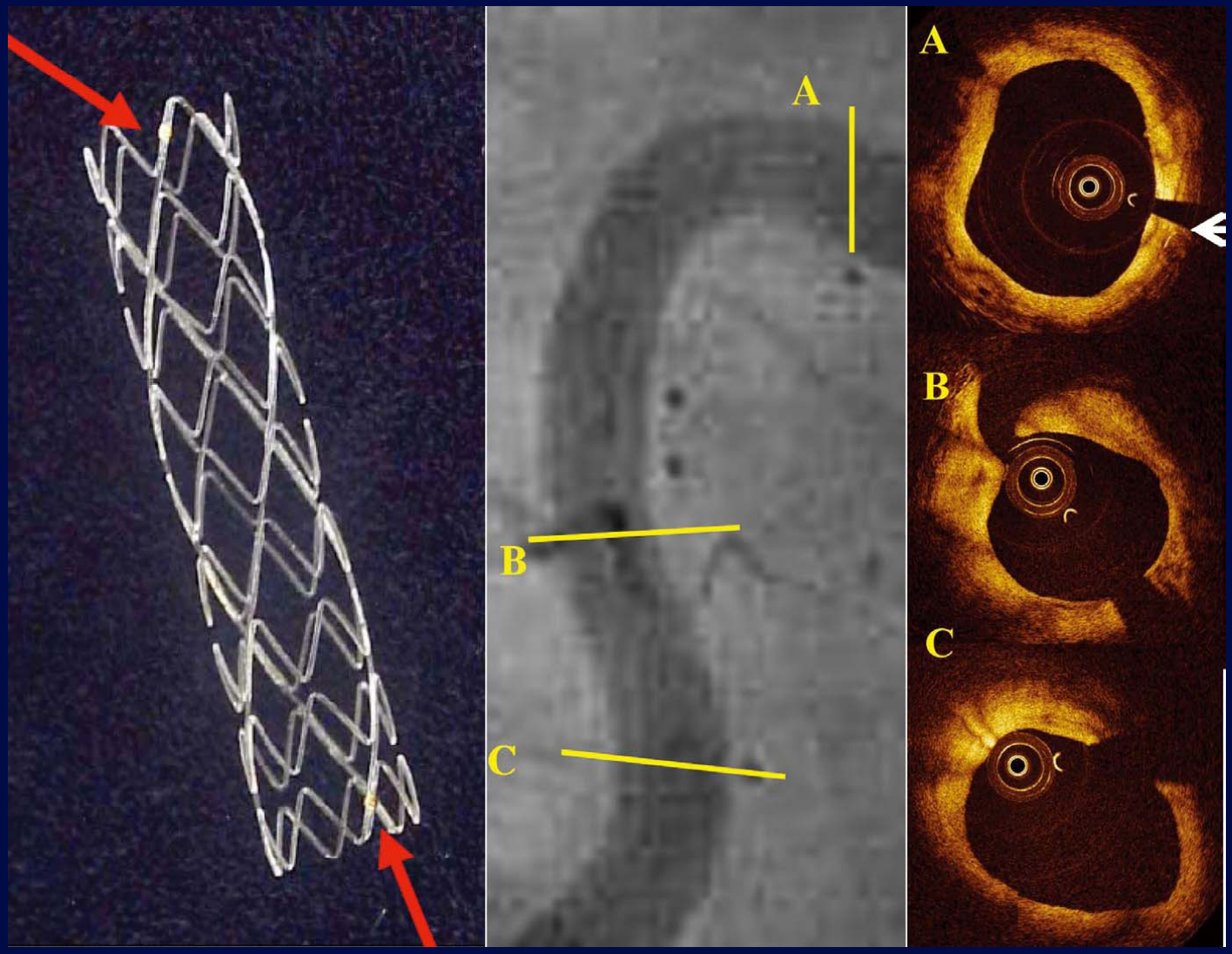
Source: Y. Onuma,; Circulation Journal Vol.75, March 2011

Initial reduction in molecular weight, the decrease in radial support around 6 months

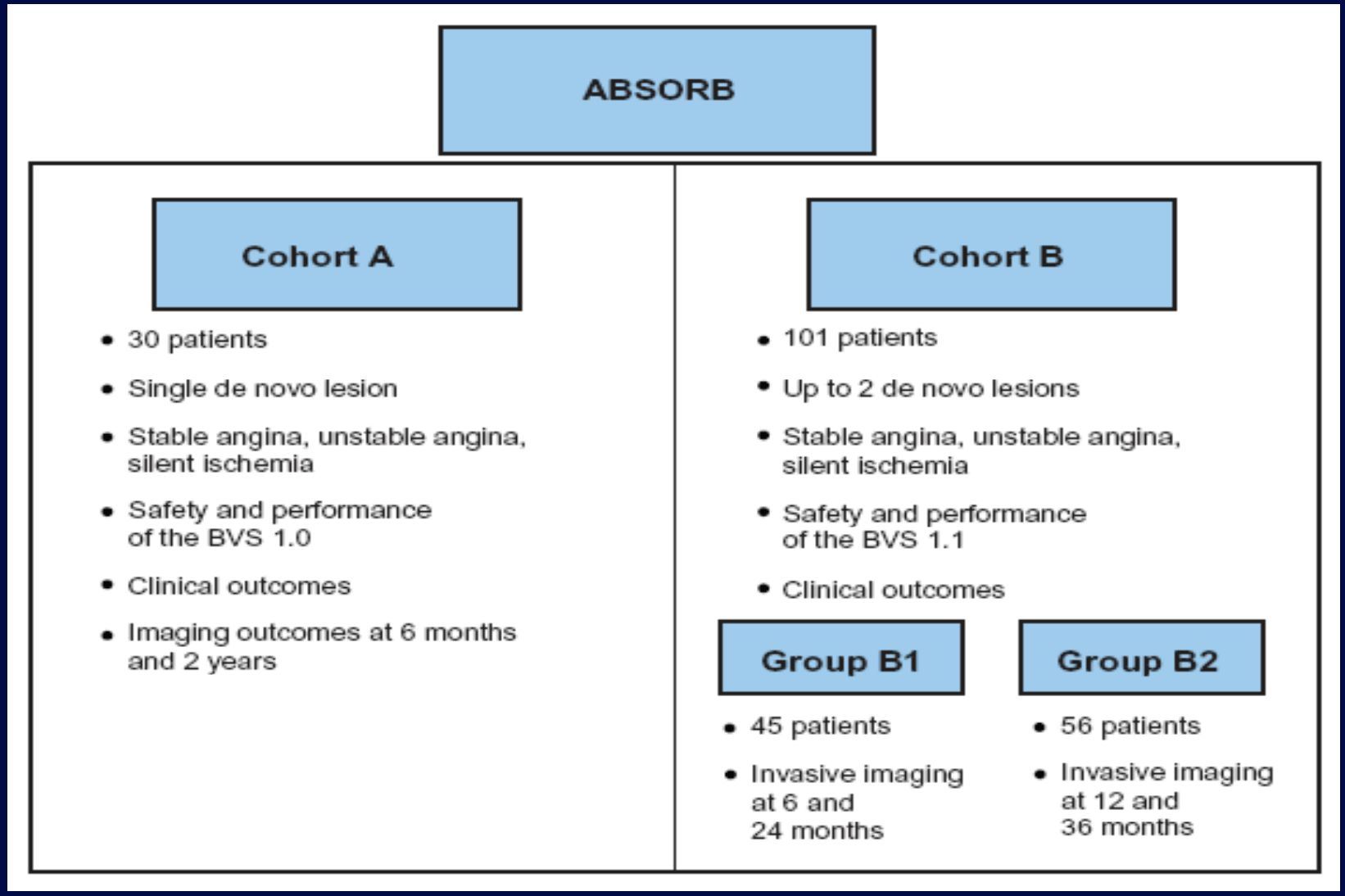


Source: Y. Onuma,; Circulation Journal Vol.75, March 2011

Igaki-Tamai PLLA stent



Overview of the ABSORB Trial



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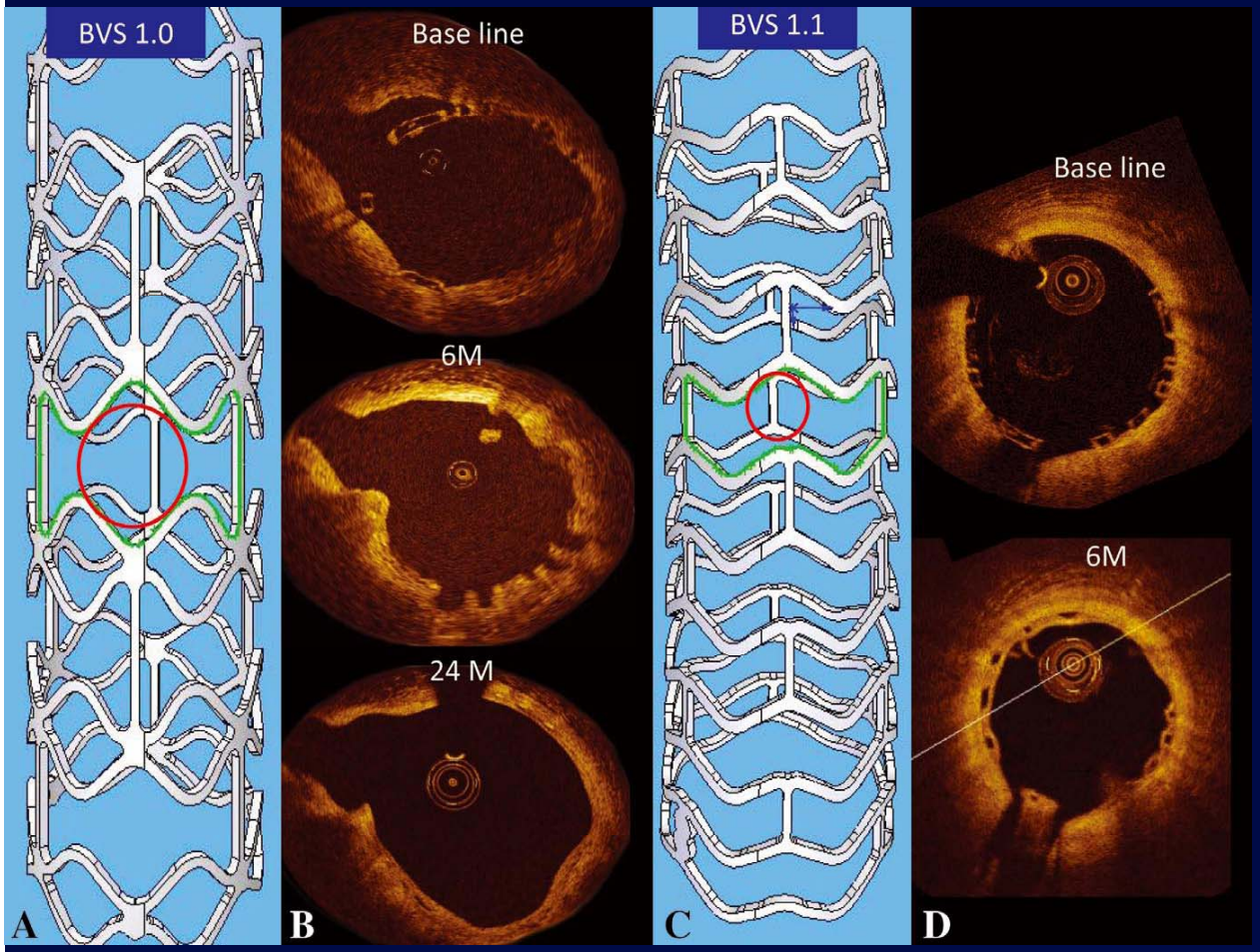
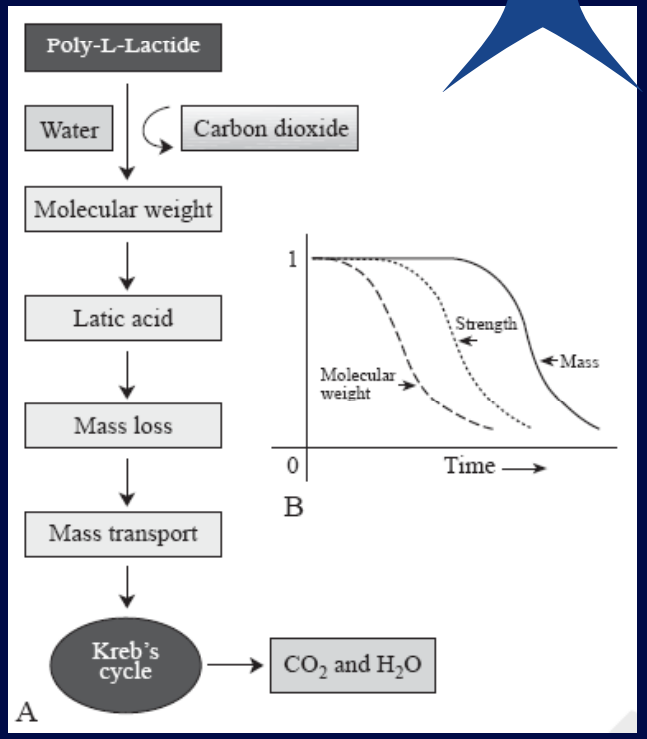
BVS (Abbott)

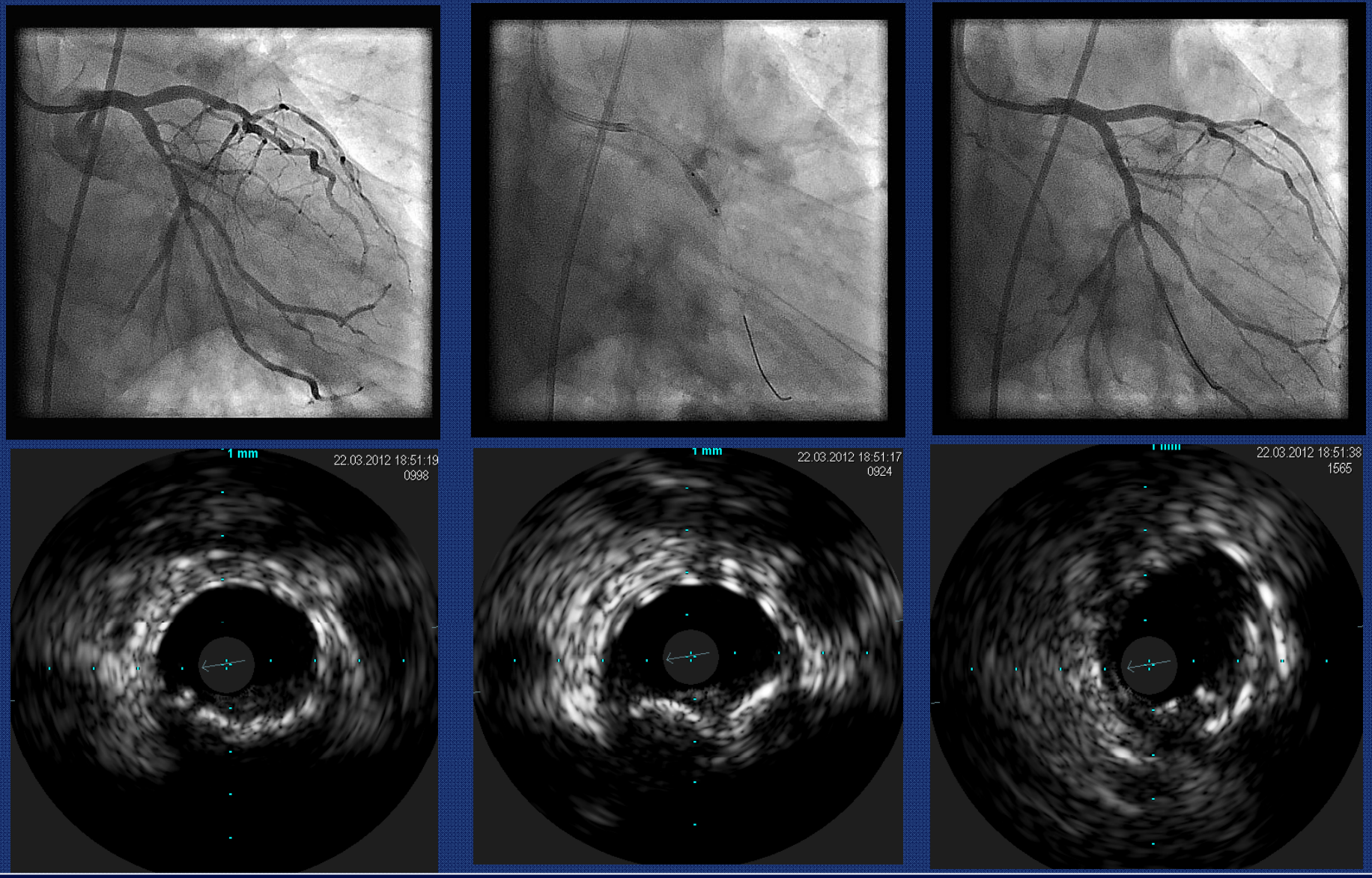




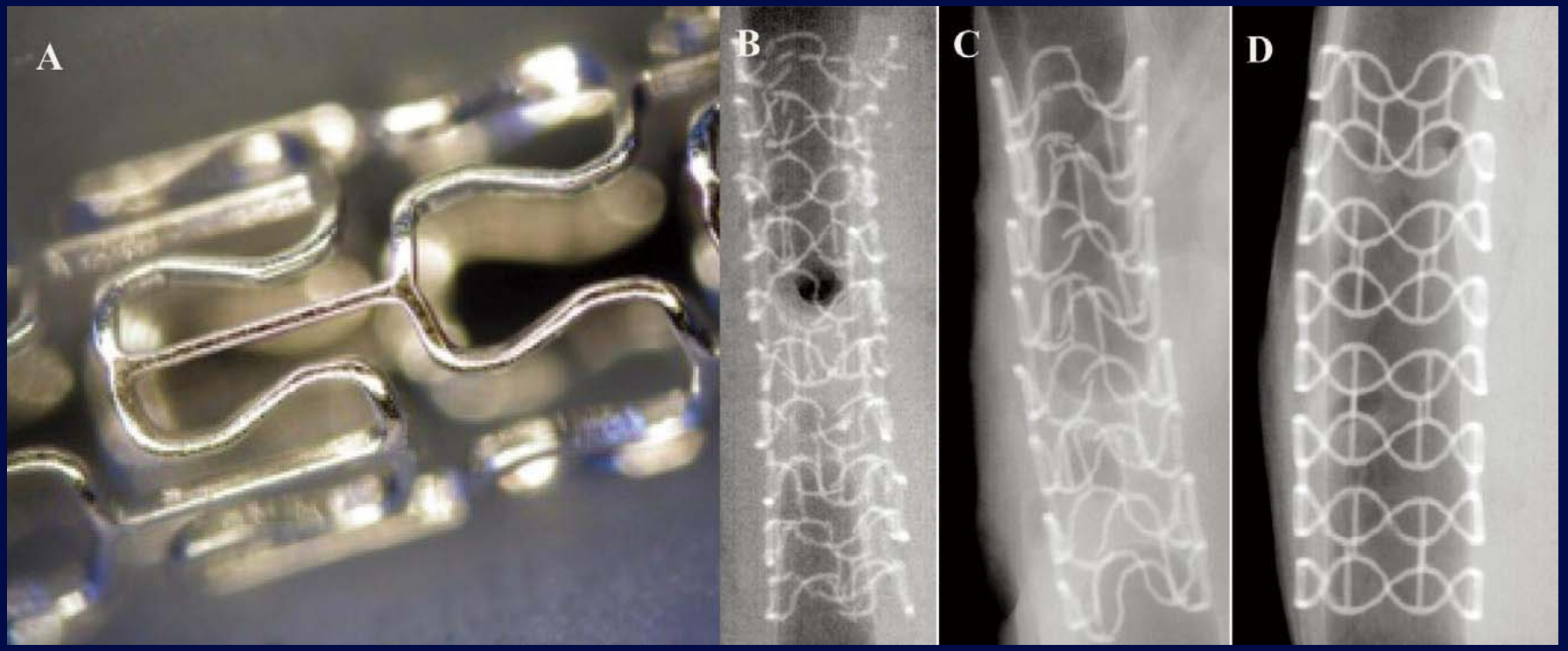
In Cohort A, 2-year angiography showed an in-stent late loss of 0.48 ± 0.28 mm, similar to the results at 6 months.

In Cohort B, the late loss was 0.19 ± 0.18 mm at 6 months and 0.27 ± 0.32 mm at 12 months

Suboptimal stent expansion / underdeployment



AMS-1 magnesium



Balloon-expandable AMS-1 BRS (Biotronik) is composed of 93% magnesium and 7% rare earth metals.
PROGRESS AMS I Clinical study:
Late loss 1.09mm, Binary restenosis 54,4%

Complex lesions

- Lesion characteristics

-calcified and fibrotic

-small vessels

-long lesions

-tortous vessels

-distal localization

- Stent requirements:
  - High radial strenght
  - Good pushibility
  - Low profile

Bioabsorbable stents

- Stent characteristics:

-high profile

-bulky and stiff

-breakable

- Good for

-proximal lesions

-large vessel

-straight segments

-non-calcfied

Very expensive toy in cath lab!

CONCLUSIONS

- Bioabsorbable stents limitations:

-profile and mechanic characteristics

-rate of degradation and time to complete degradation

-loss of radial force and late recoil

-inflammation and luminal late loss catch-up

- Current application:

-coronary single, type A or B1 de novo lesions

-PAD (UTK)

-pediatric

Specifications and Requirements

Criteria	Specification
Crimping on traditional angioplasty balloon and deployed with minimal recoil	Deformable material with minimal elasticity
Specific Mechanical properties	Sufficient to maintain artery open Weak enough to allow stent deformation during navigation and minimal artery tonicity
Biostable	No release of toxic agents (except drug release)
Hemocompatible	Nonthrombogenic surface
Endothelialisation	Cell compatible surface
Sterility	Properties insignificantly changed after sterilisation
Eliminated after accomplishing function	Bioresorbable material

T. SHARKAWI et al. JOURNAL OF PHARMACEUTICAL SCIENCES, VOL. 96, NO. 11, NOVEMBER 2007