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TECHNOLOGICAL INNOVATION FOR CORONARY STENTS

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Erice, 1 maggio 2015

International School of Cardiac Surgery

Introduction

Patent search -

Heart valve

Stent

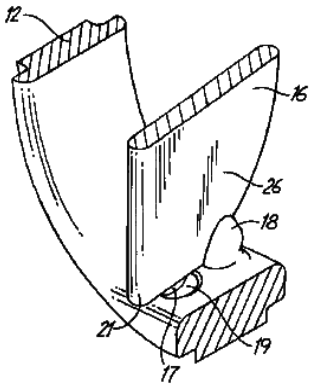
Mechanical cardiac valves

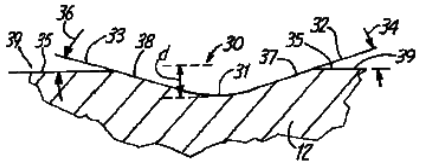
US006395025B1

(12) **United States Patent**
Fordenbacher et al.

(10) **Patent No.: US 6,395,025 B1**
(45) **Date of Patent: May 28, 2002**

(54) **MECHANICAL HEART VALVE PROSTHESIS**

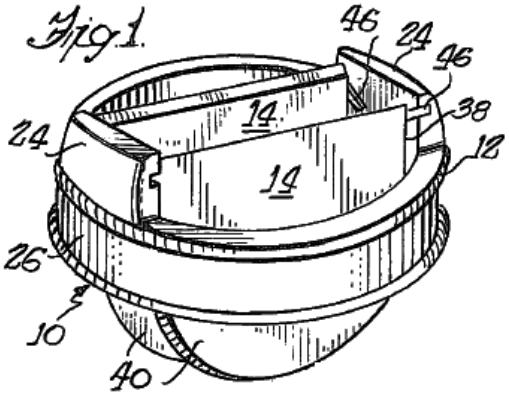




United States Patent [19]
Bokros

[11] **4,272,854**
[45] **Jun. 16, 1981**

[54] **BI-LEAFLET HEART VALVE**



US005882335A

United States Patent [19]

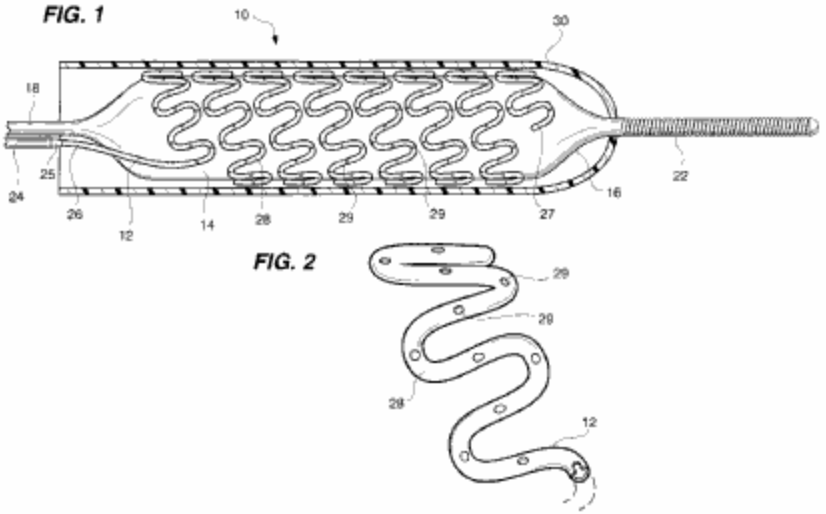
Leone et al.

[11] **Patent Number: 5,882,335**

[45] **Date of Patent: Mar. 16, 1999**

[54] **RETRIEVABLE DRUG DELIVERY STENT**

5,306,250 4/1994 March et al. 604/104



US005810872A

United States Patent [19]

Kanesaka et al.

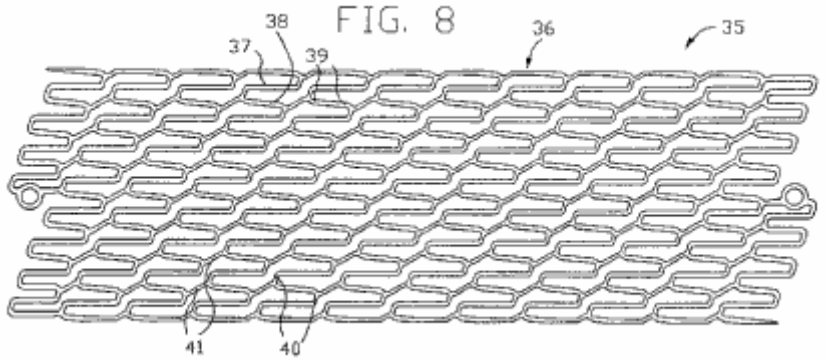
[11] **Patent Number: 5,810,872**

[45] **Date of Patent: Sep. 22, 1998**

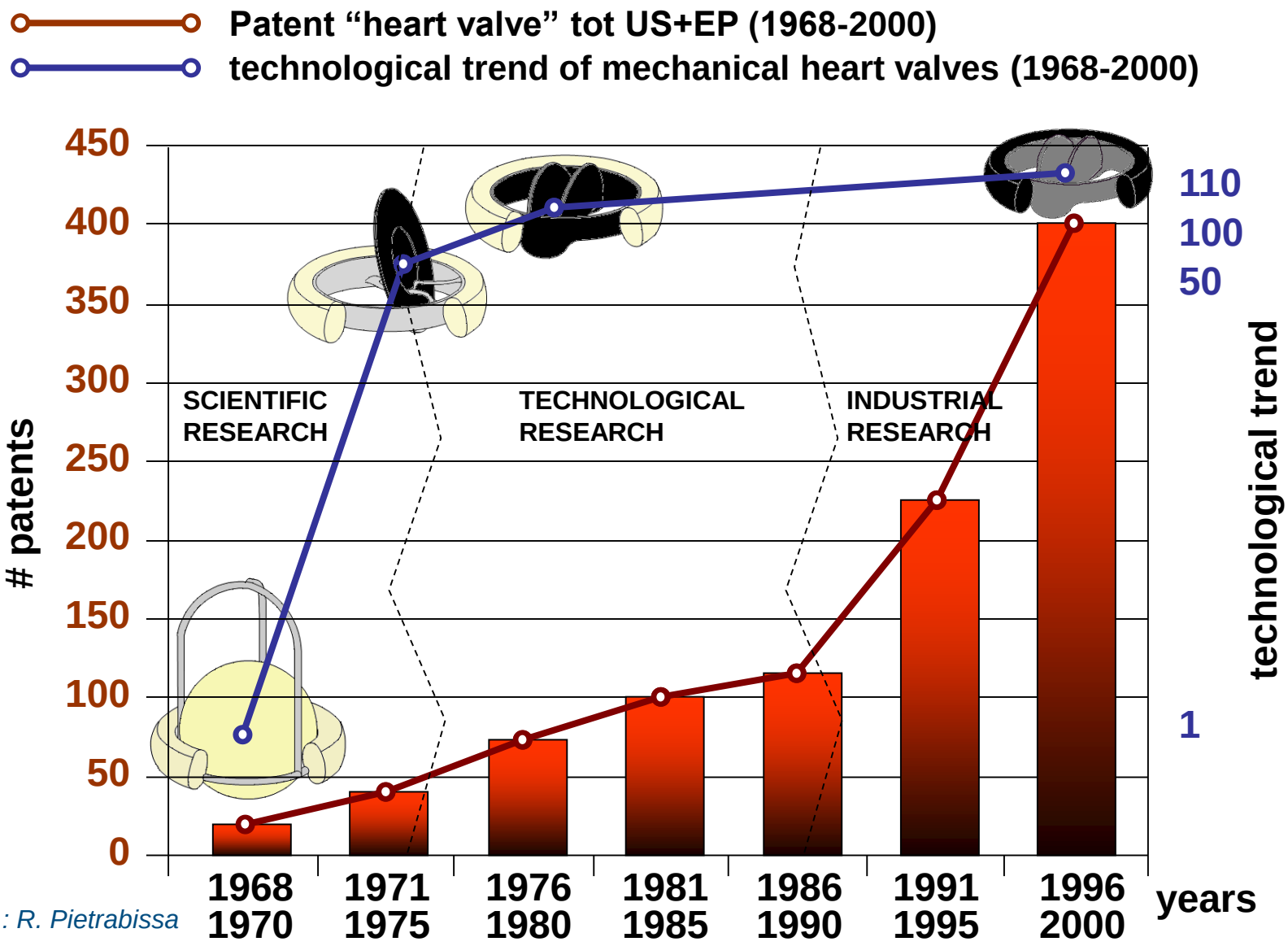
[54] **FLEXIBLE STENT**

FOREIGN PATENT DOCUMENTS

0679372 A2 11/1994 European Pat. Off. .

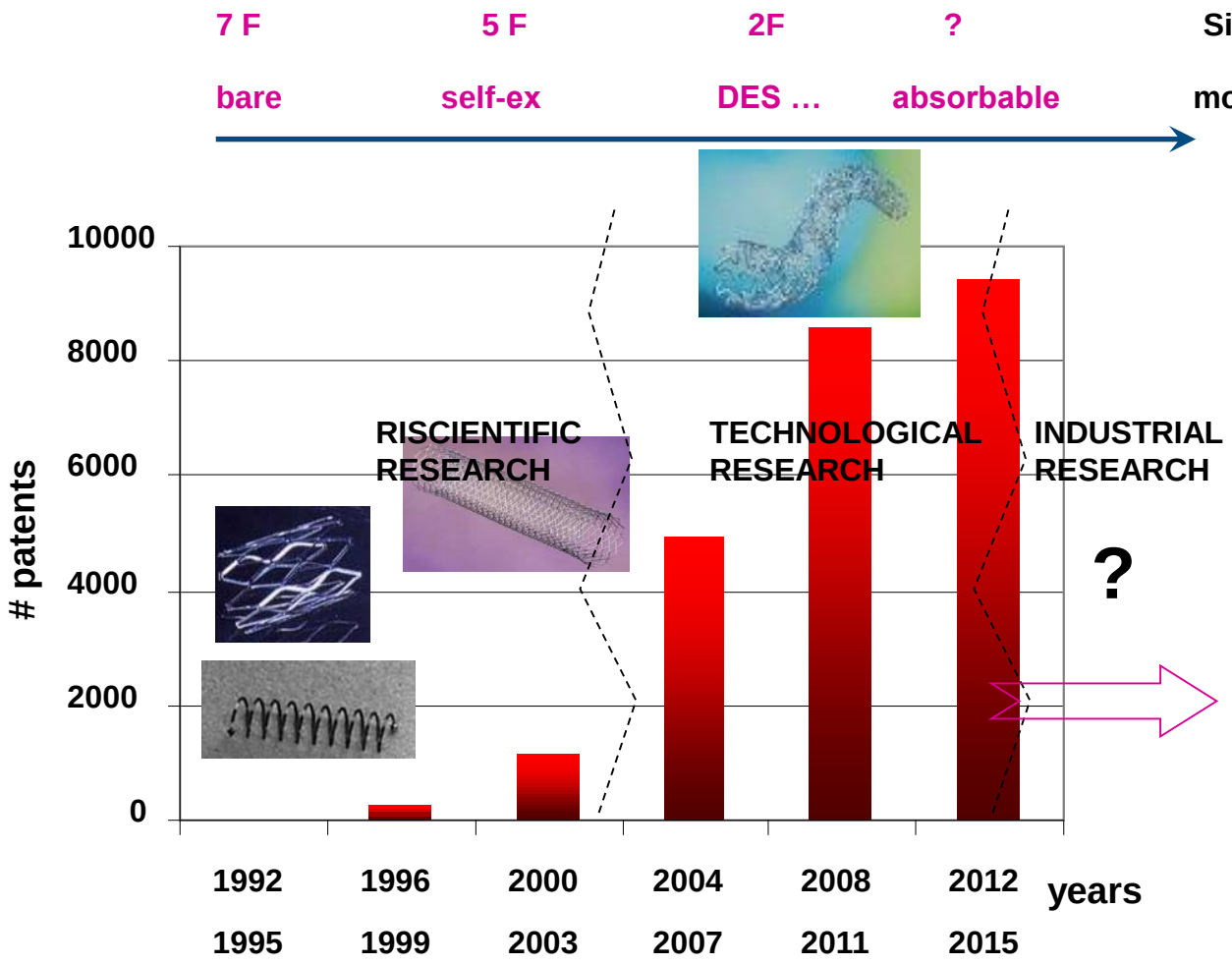


Mechanical heart valves

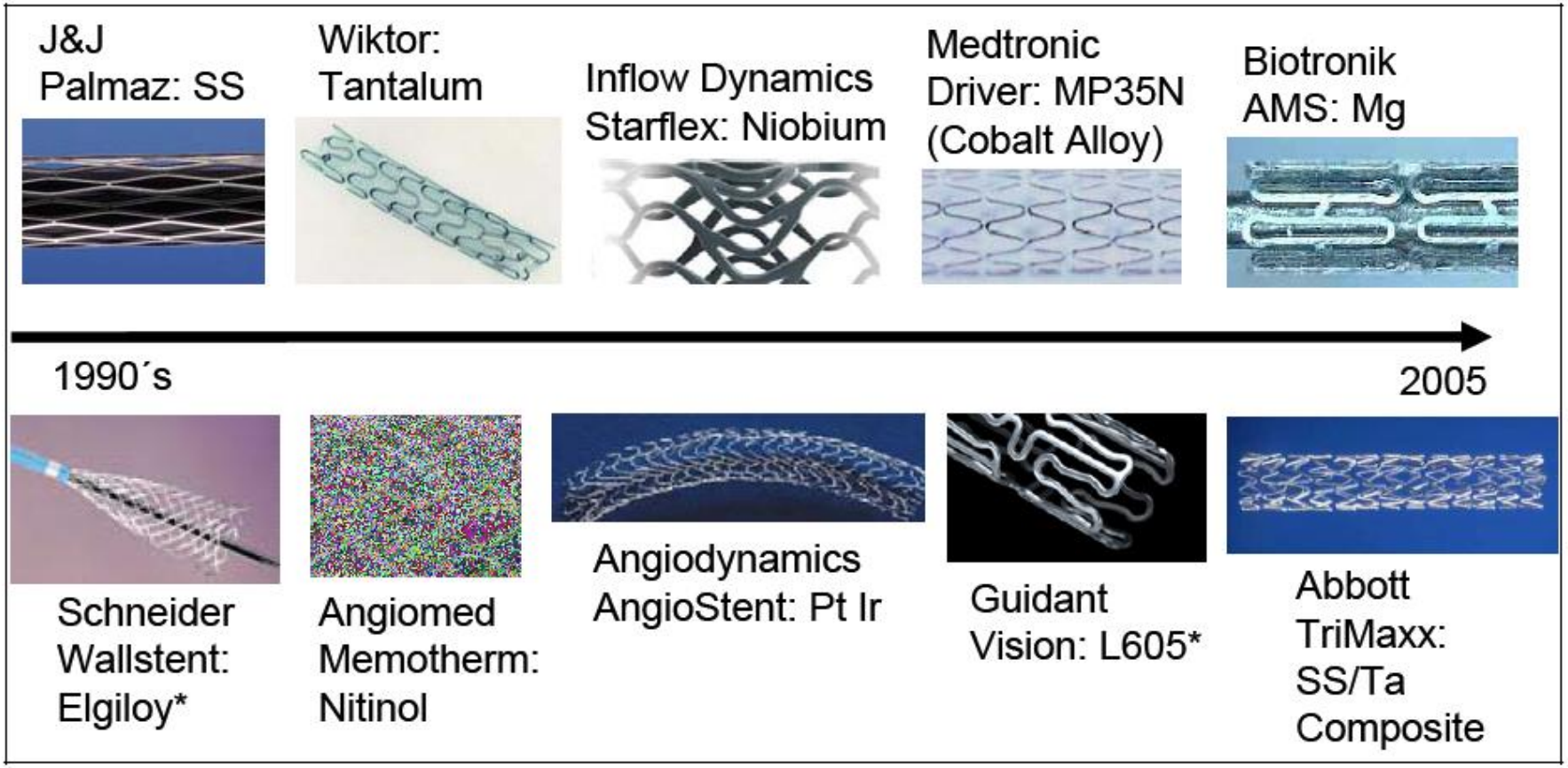


Courtesy of : R. Pietrabissa

Stent patents

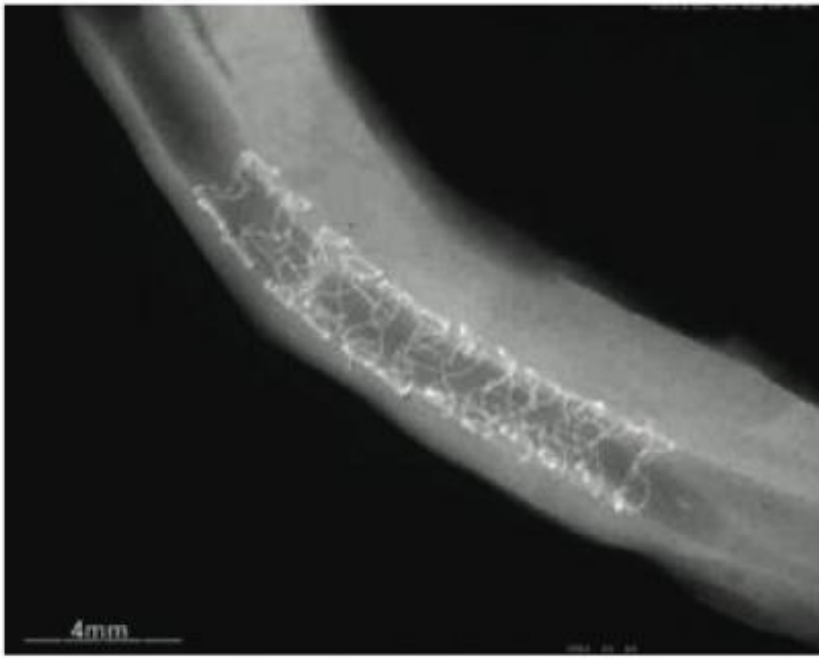


stent history

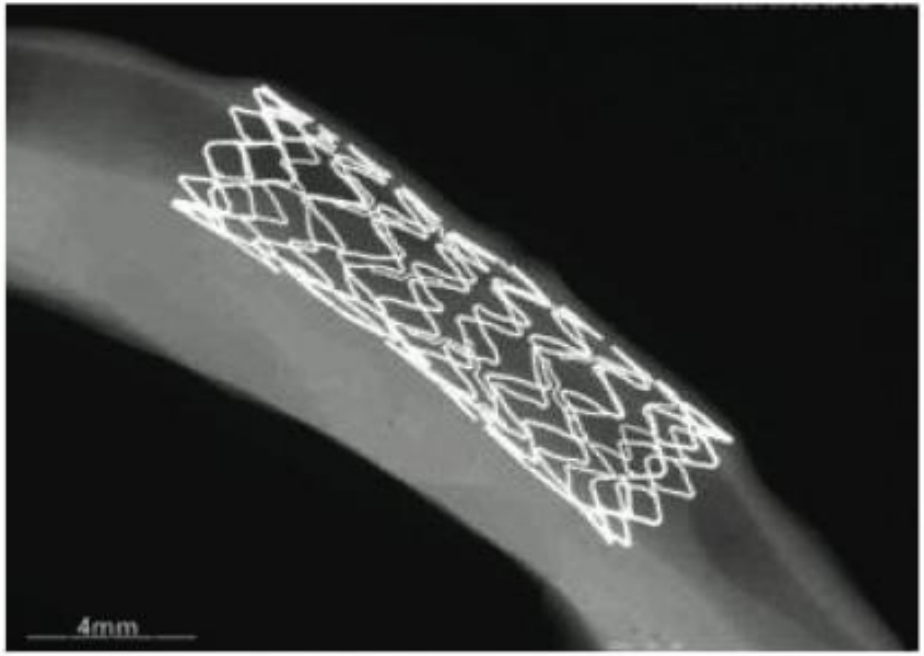


http://www.admedes.com/literature

30 days after implant in porcine coronaries



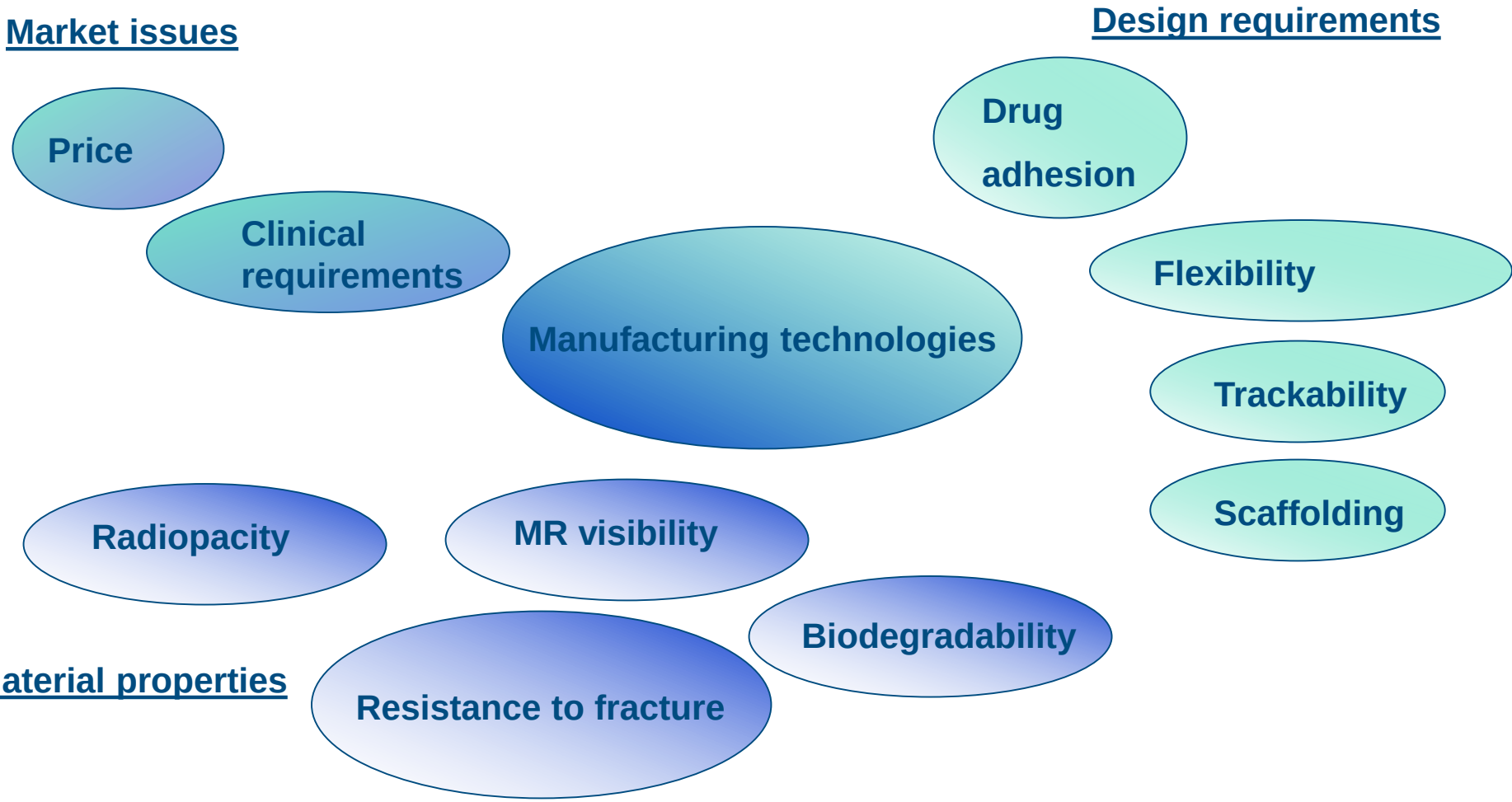
Mg stent



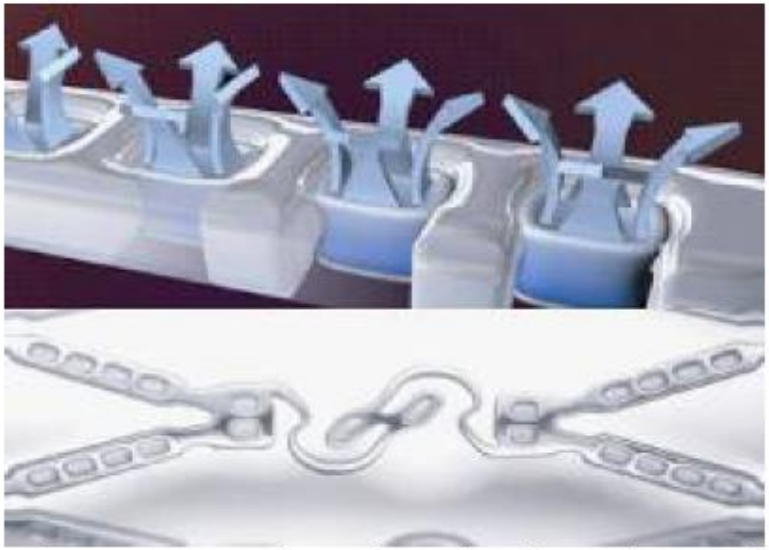
SS stent

Waksman R. Adjunctive therapy: Biodegradable stents: They do their job and disappear. *J Invas Cardiol 2006;* 18: 70)74.

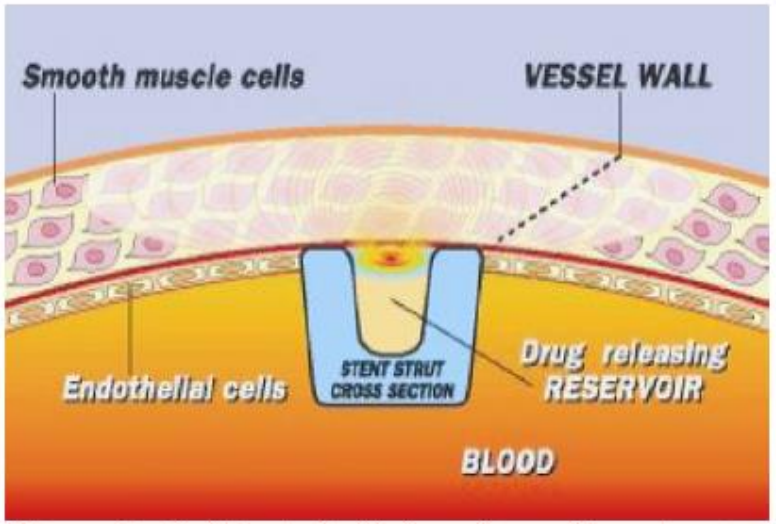
Stent requirements



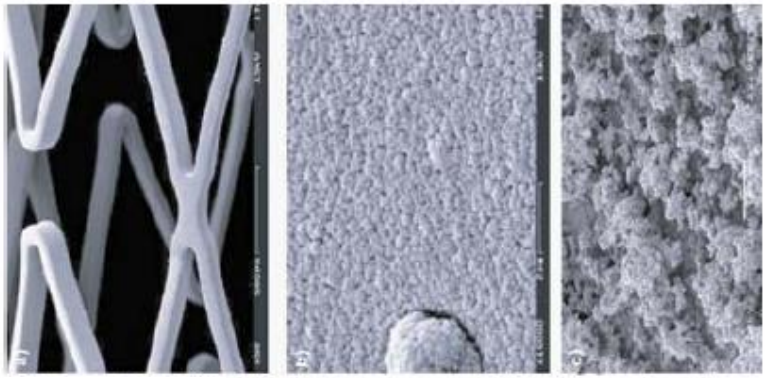
Drug eluting stents



Drug release through polymer drug pads which are embedded e.g. by laser cutting cavities (Source: Conor Medsystems Inc.).



Cavities to hold drugs by surface structuring (Source: Sorin Biomedical)



Stent structure with micro structure, porous surface from oxides, porous surface from metal

Drug eluting stents

Drug carrier

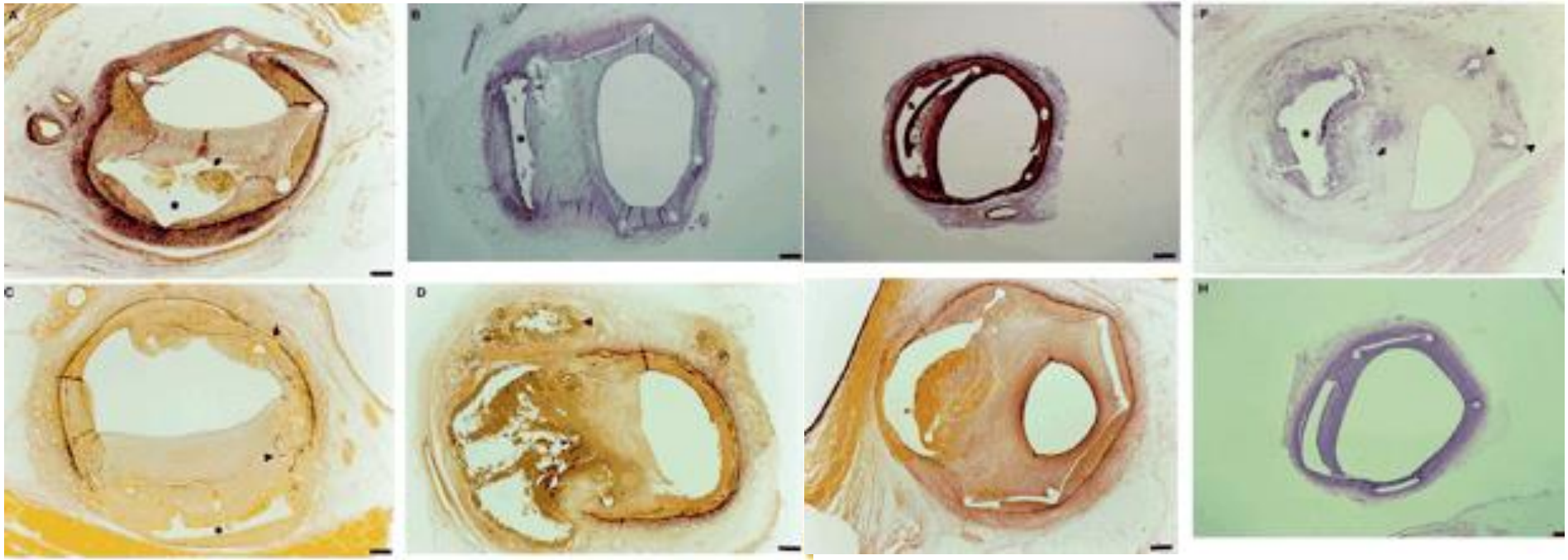
Polymer (biodegradable or not biodegradable)

Inflammatory reaction

Stent

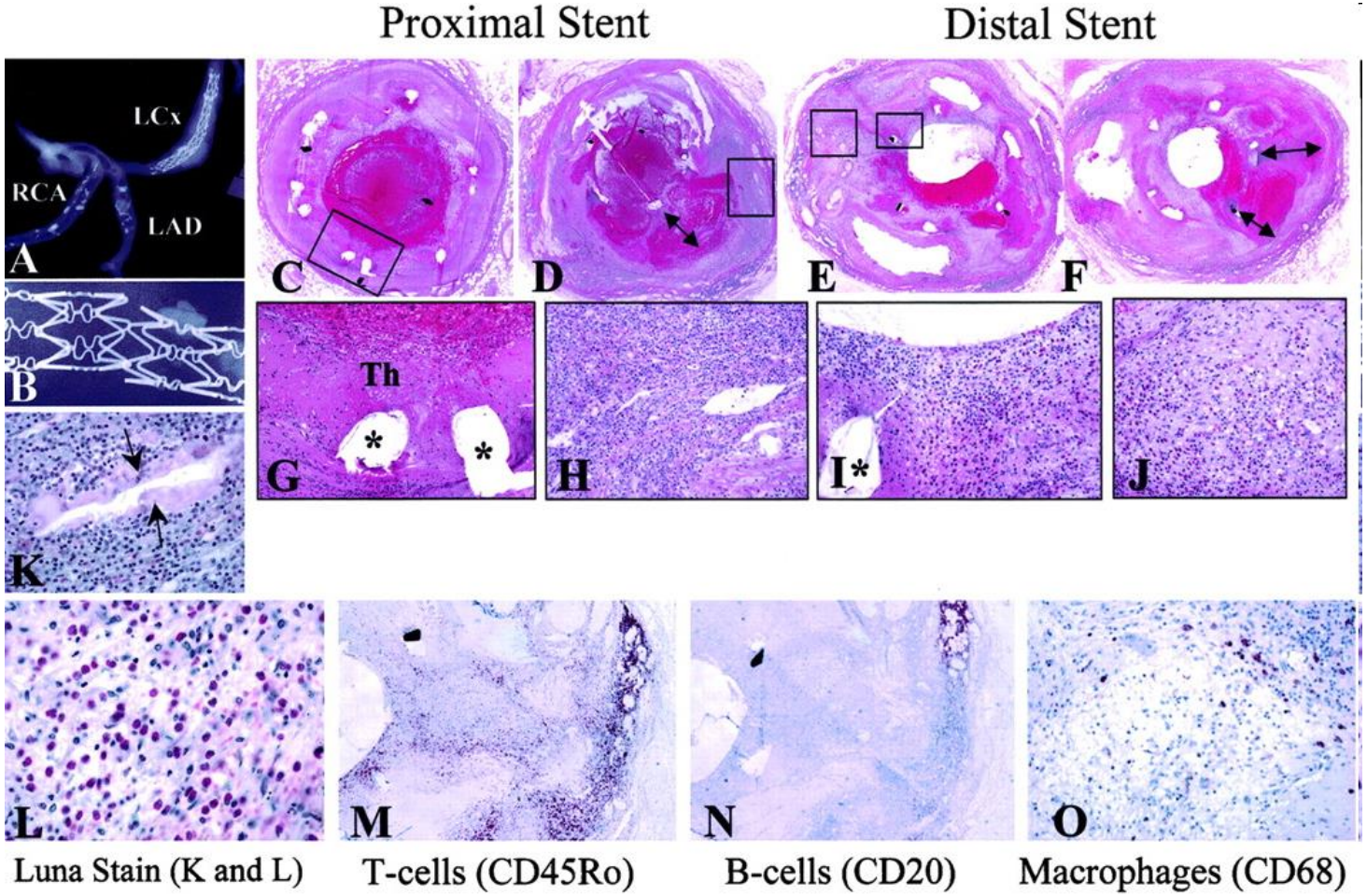
Drug

Drug eluting stents



van der Giessen, et al. Marked Inflammatory Sequelae to Implantation of Biodegradable and Nonbiodegradable Polymers in Porcine Coronary Arteries *Circulation*. 1996;94:1690-1697

Drug eluting stents

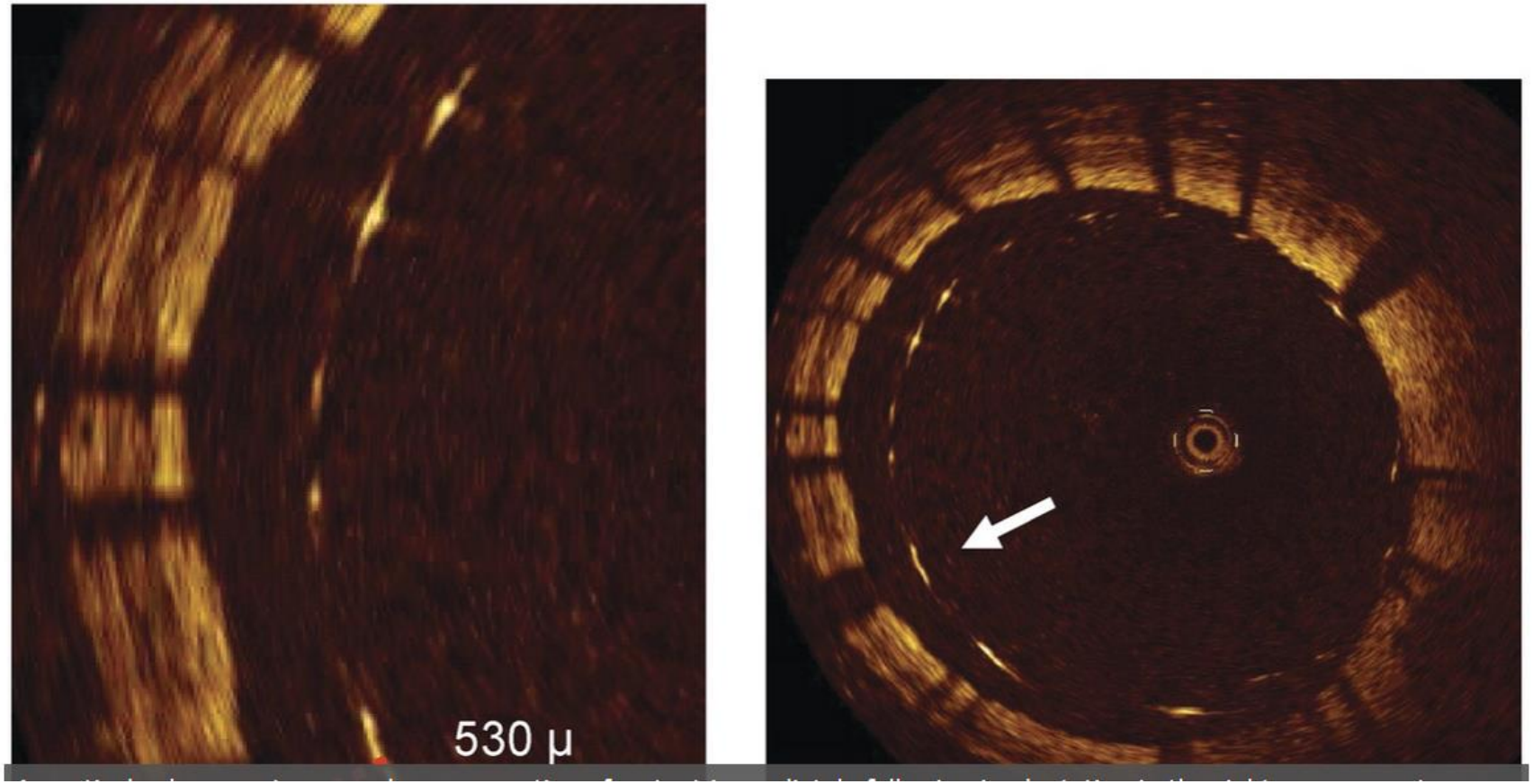


Virmani, et al. Localized Hypersensitivity and Late Coronary Thrombosis Secondary to a Sirolimus-Eluting Stent. Should We Be Cautious? *Circulation*. 2004;109:701-705

Drug eluting stents

Drug carrier	Polymer (biodegradable or not biodegradable)	Inflammatory reaction
Stent	Regular “Spacing” between struts	Uniform and controlled drug release
	Conformability (minimal struts malapposition)	More drug in the blood stream than in the arterial wall
Drug		

OCT

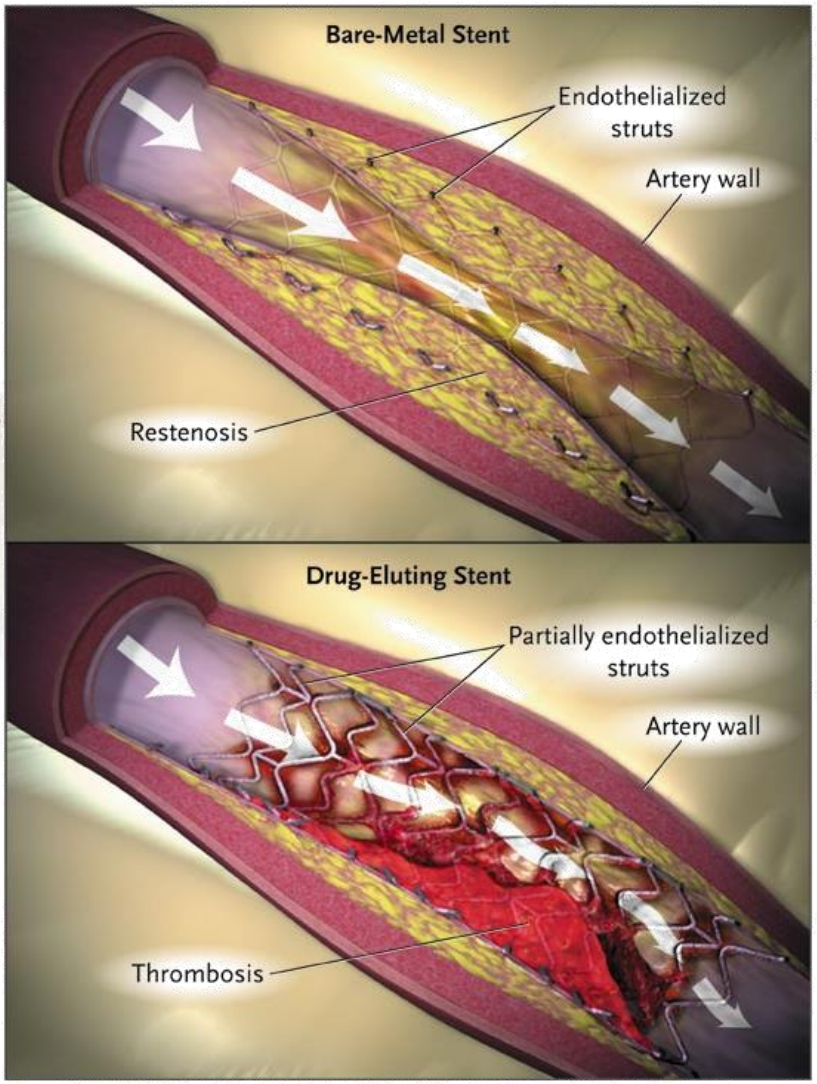


Prati et al. European Heart Journal
doi:10.1093/eurheartj/ehs095

Drug eluting stents

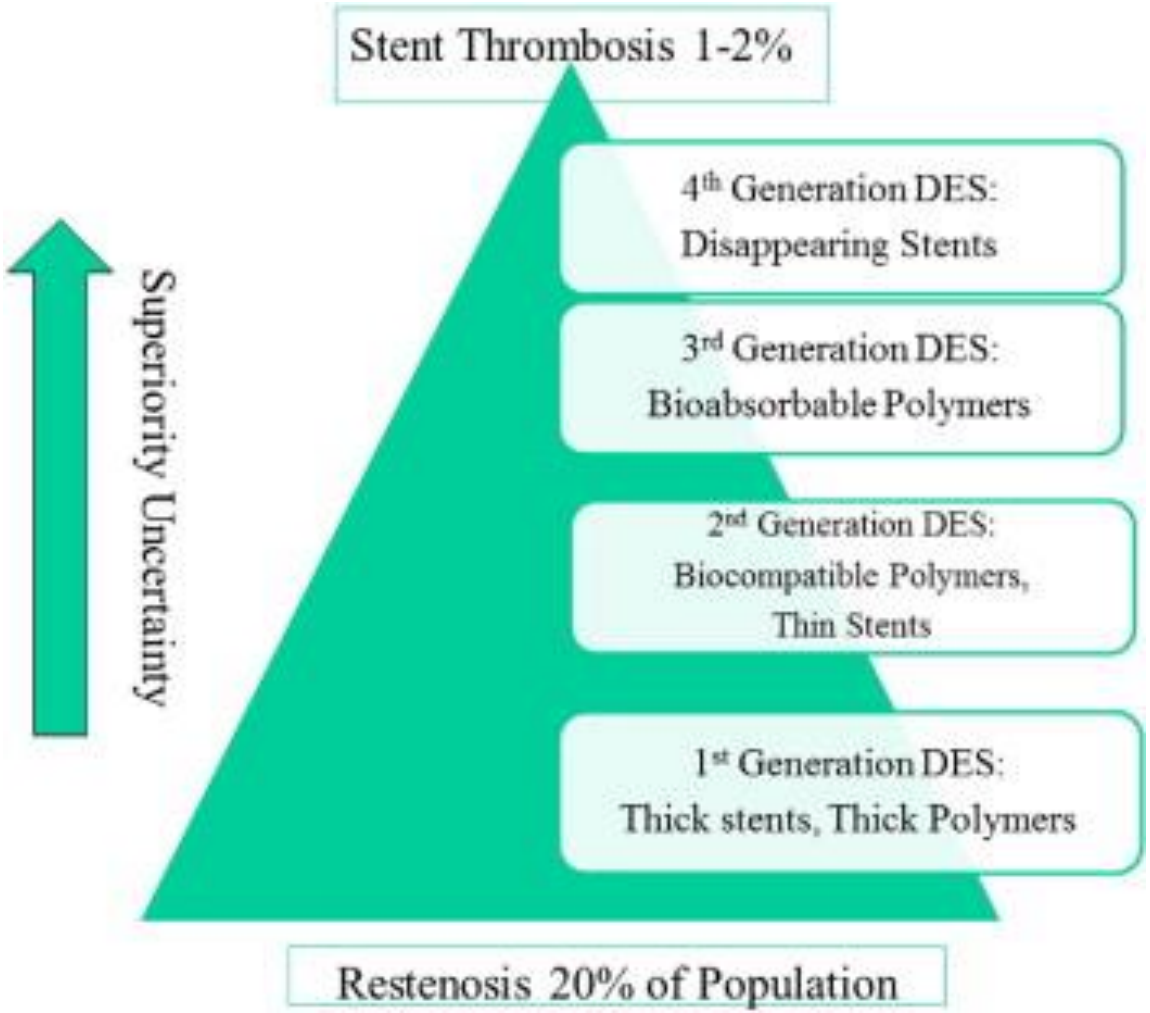
Drug carrier	Polymer (biodegradable or not biodegradable)	Inflammatory reaction
Stent	Regular “Spacing” between struts	Uniform and controlled drug release
	Conformability (minimal struts malapposition)	More drug in the blood stream than in the arterial wall
		Toxicity
Drug	Uniform and controlled drug release	

Drug eluting stents



LATE STENT THROMBOSIS

Drug eluting stents



Dauerman H, The Magic of Disappearing Stents
J Am Coll Cardiol. 2011;58(15):1589-1591.

Drug eluting stents

Strut thickness of only ≤ 50/60 μm

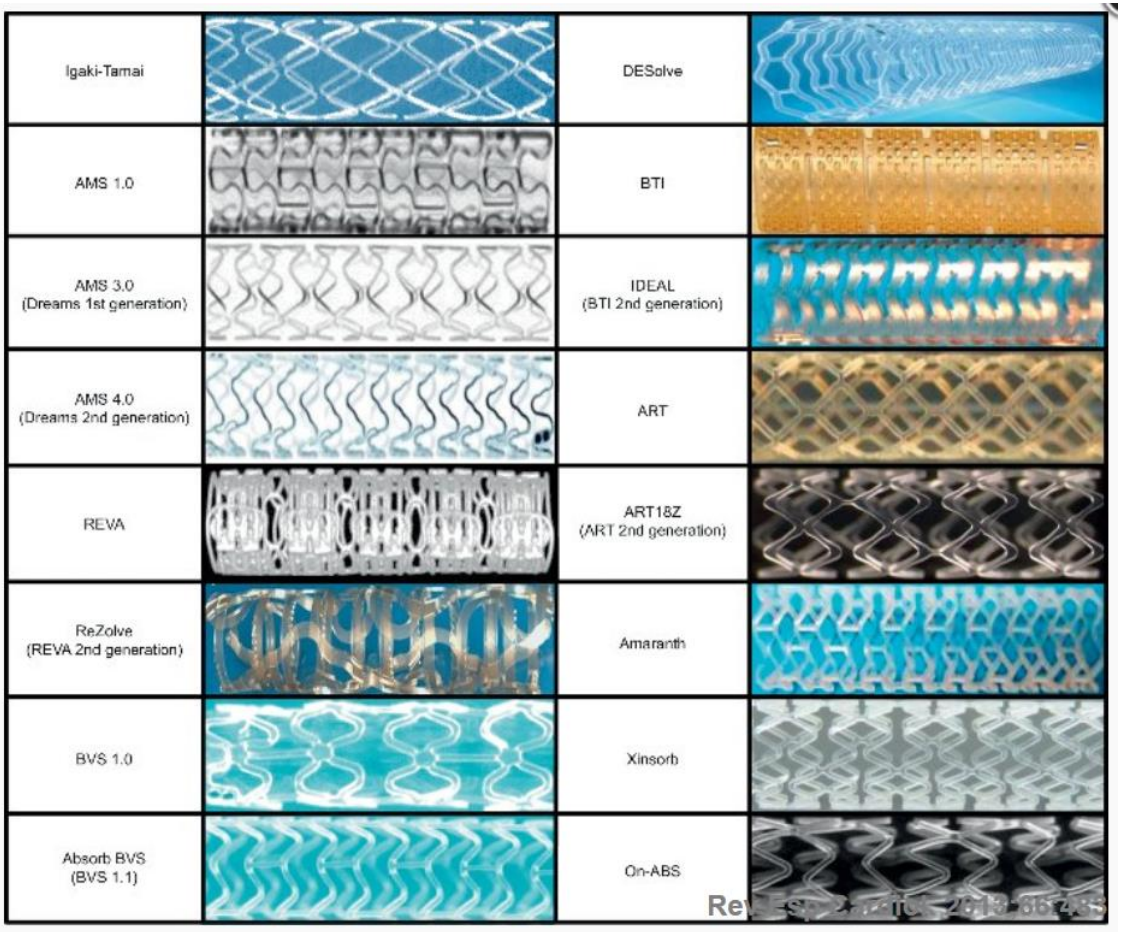
100% Polymer-Free Drug Delivery

Bio-resorbable Drug Matrix

Sirolimus - Matrix Excipient: Probucol

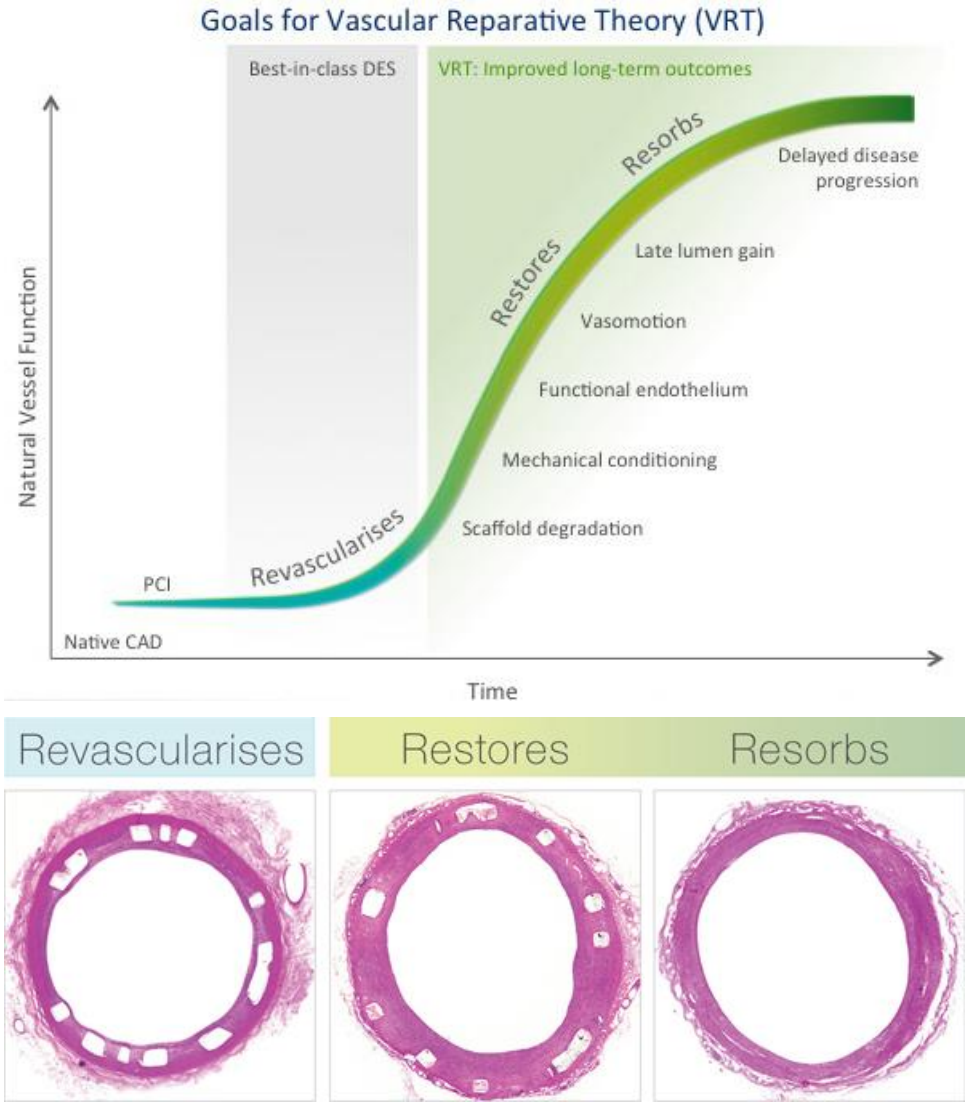
Source: www.bbraun.com

Bioabsorbable stents: a crowded field



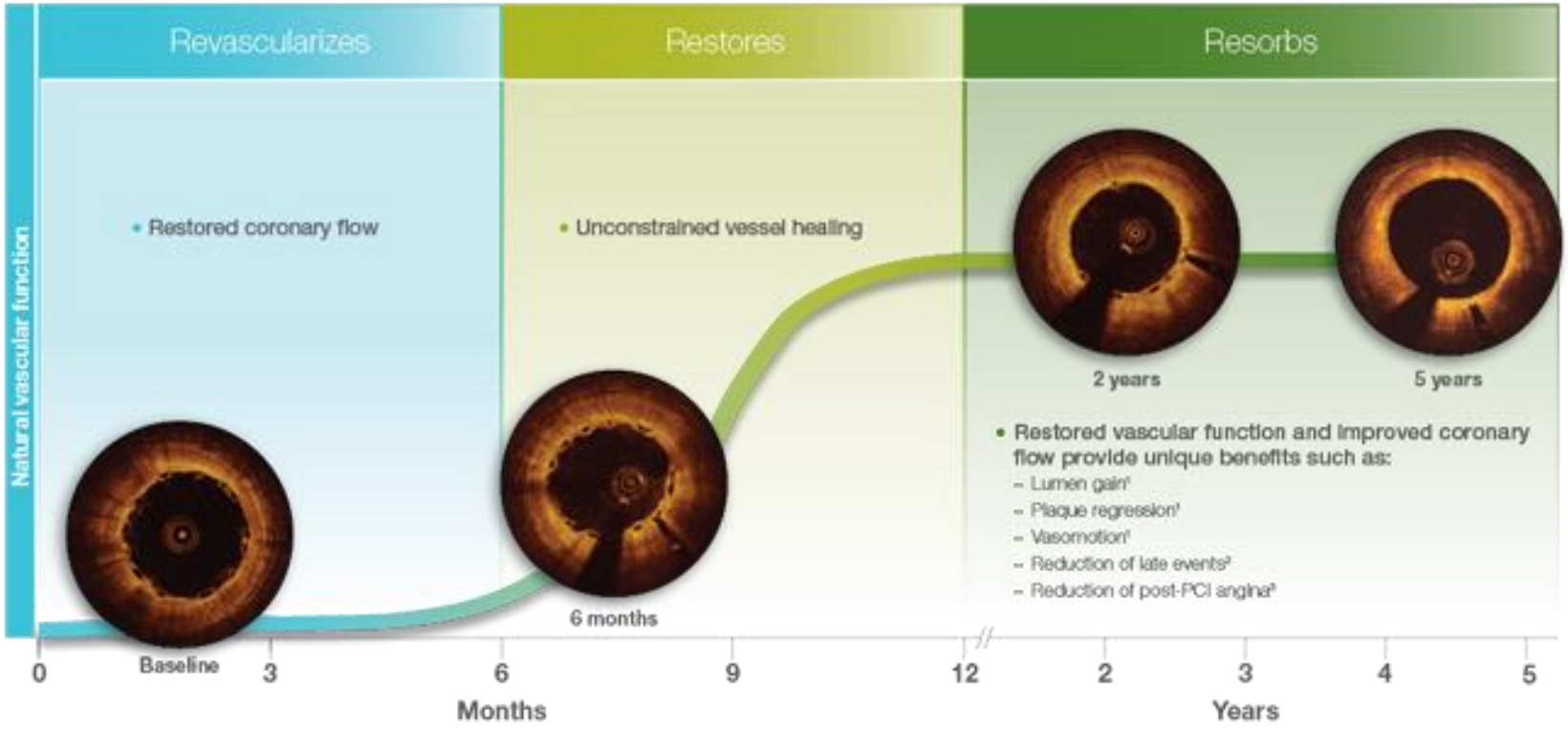
Muramatsu et al. Progress in Treatment by Percutaneous Coronary Intervention: The Stent of the Future. Rev Esp Cardiol. 2013;66:483-96.

bioresorbable stents



Source: www.abbottvascular.com

bioresorbable stents



Source: www.abbottvascular.com

BACKGROUND

Use of simulations for bioabsorbable stent

- to predict the mechanical behaviour of stent (recoil, radial strength, flexibility, …)
- to predict the degradation behaviour
- to optimise the design for a prolonged/shortened degradation resistance

DEGRADABLE MATERIALS FOR STENTING

Metals:

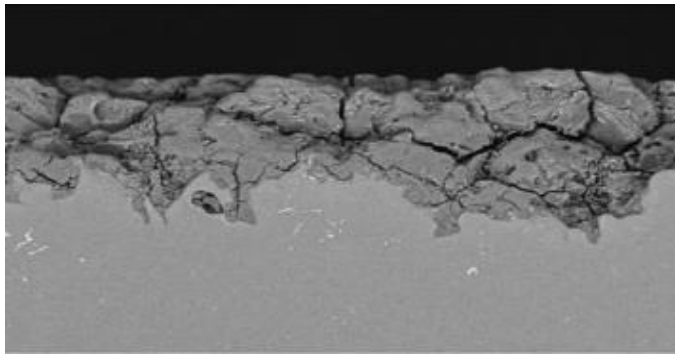
- **Magnesium alloys**
- Iron alloys

Polymers:

- **PLLA**
- polycarbonate
- PLGA/PCL-PGA
- salicyclic acid polymer

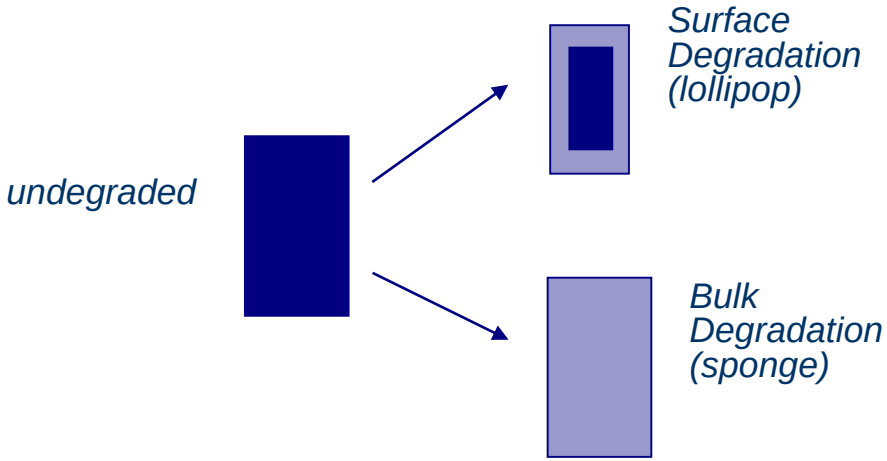
Degradation mechanisms

Corrosion



[Levesque et al 2008]

Bulk vs surface degradation



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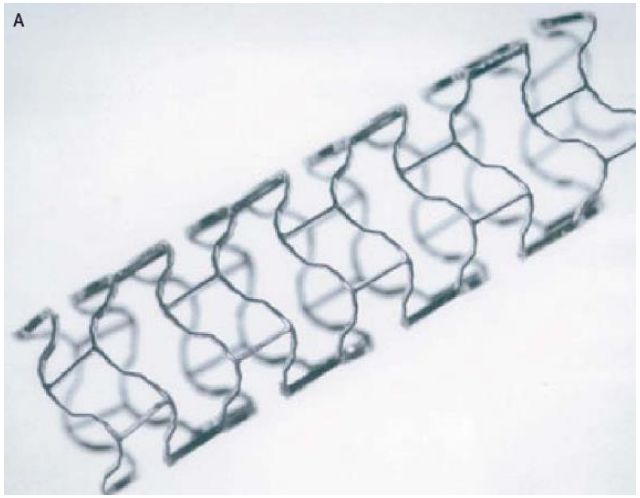
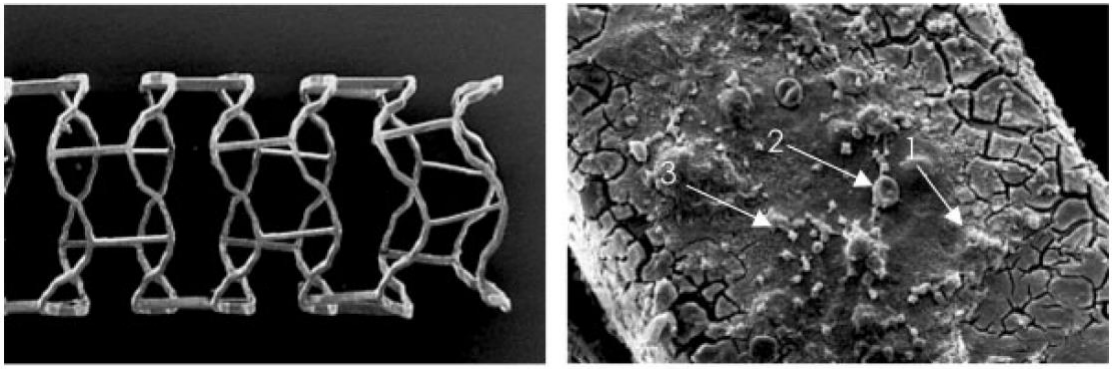
Biodegradable stents

MAGNESIUM ALLOYS STENTS



Bioresorbable Magnesium stent (BIOTRONIK, Berlin, Germany) [Erbel et al 2007]



Hansi et al, Cath Cardiovasc Interv, 73:488-496, 2009.

Degradation rate too fast!!!

To improve corrosion resistance:

- **alloying**
- **mechanical/heat treatments**
- **surface modifications and coatings**

TARGET:
Degradation rate has to be reduced to ensure mechanical support to the vessel for a longer time

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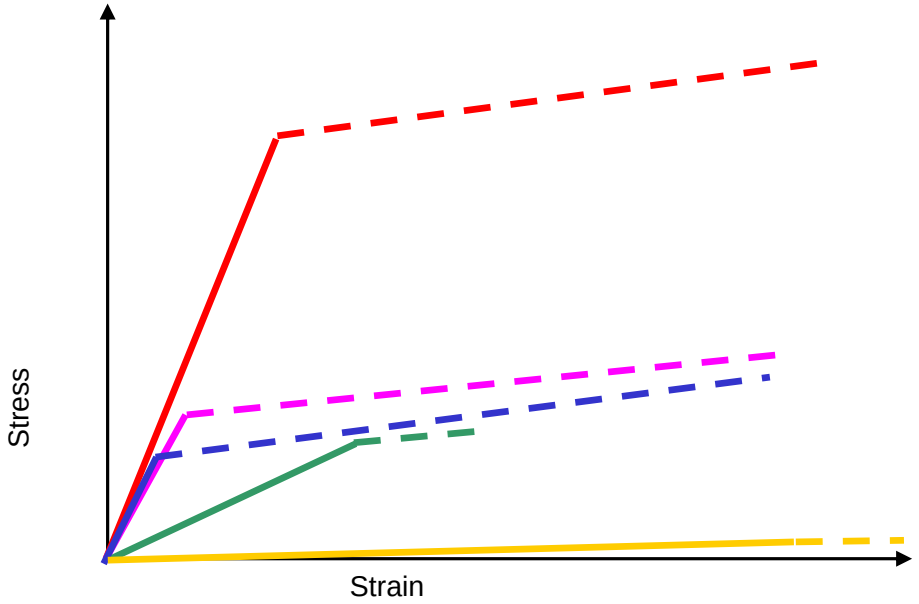
MECHANICAL PROPERTIES OF MATERIALS FOR STENTS

Material	Stiffness E [GPa]	yield stress σ_y [MP]	ultimate stress σ_u[MP]
Co-Cr	240	600	1100
Fe	210	150	210
SS 316L	200	190	490
WE43	44	150	210
PLLA	2	-	45



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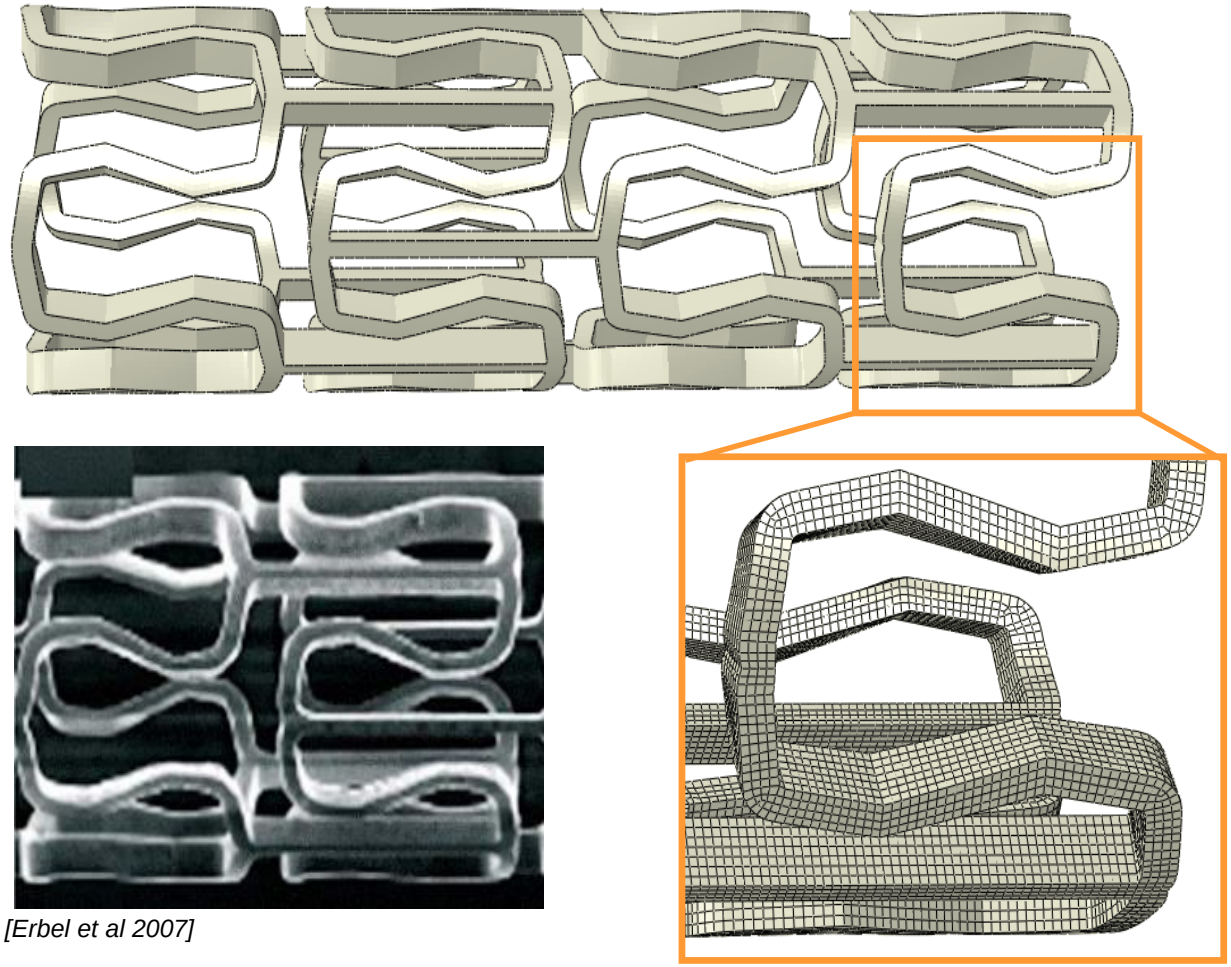
MG - GEOMETRY

AMS (Biotronik, Germany): 4 struts with links

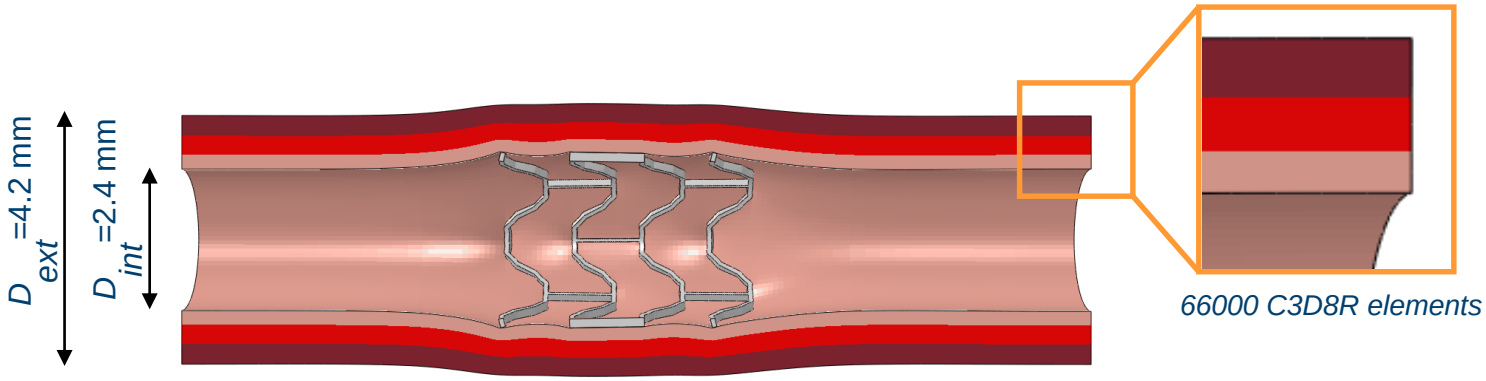


[Erbel et al 2007]

84476 elements C3D8R

MODEL OF STENTING PROCEDURE

- *coronary vessel*



66000 C3D8R elements

3 hyperelastic layers:

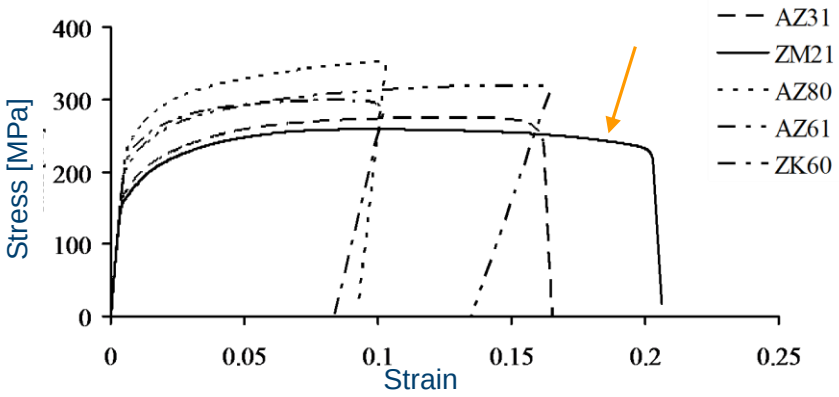
$s_{adventitia}$ =0.34 mm

s_{media} =0.32 mm

s_{intima} =0.24 mm

[Holzapfel et al 2005]

- *stent material*



Alloy	E [GPa]	$\sigma_{0.2\%}$ [MPa]	σ_p [MPa]	ϵ_b [%]
AZ31	45.1	174	278	16
AZ61	45.2	212	324	17
AZ80	45.2	243	361	13
ZM21	44.2	165	262	19
ZK60	45.4	239	317	11

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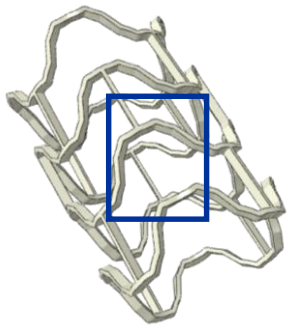
Biodegradable stents

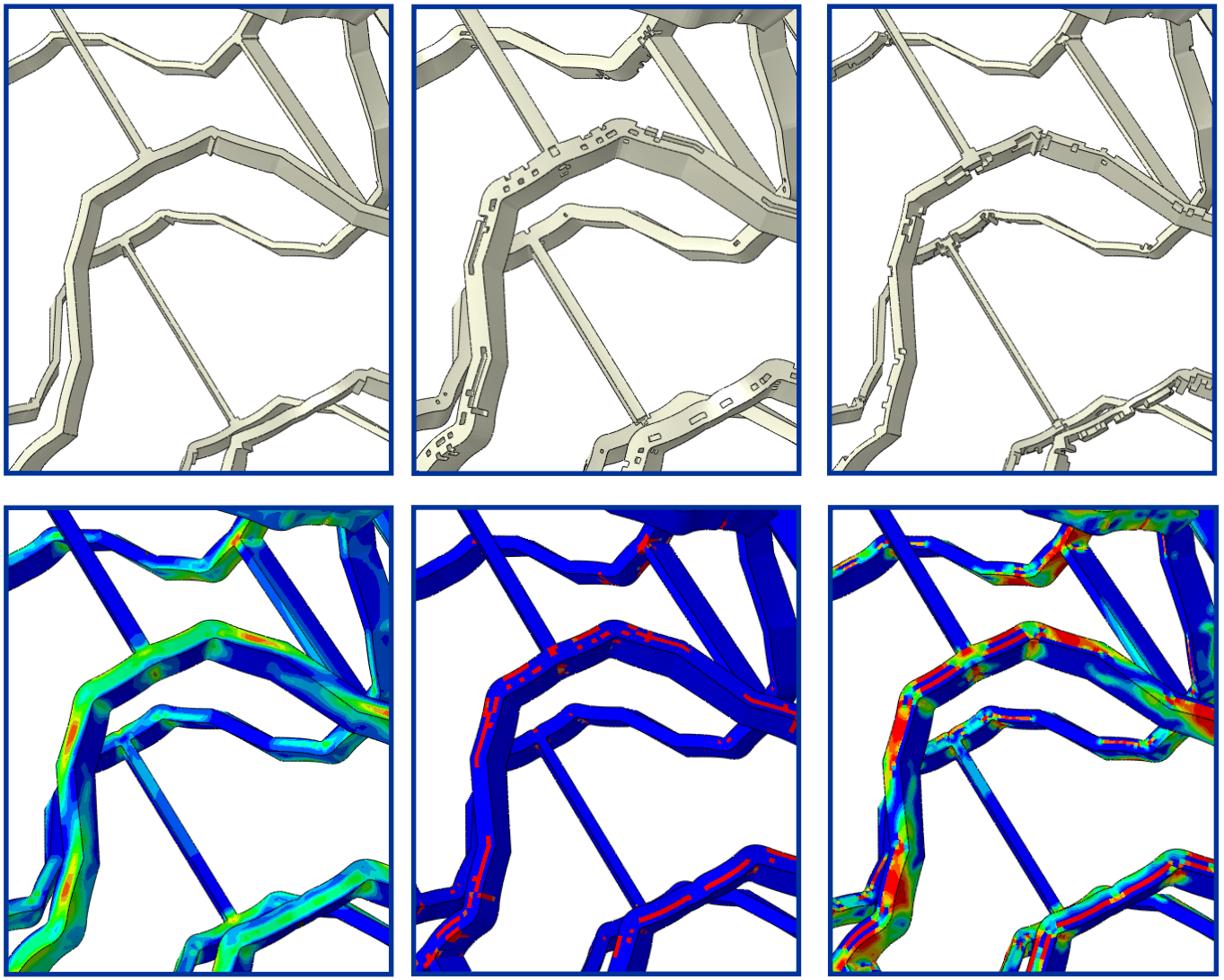
RESULTS: DEGRADATION OF STENT STRUCTURE



Uniform Corrosion: 48 t

Stress Corrosion: 48 t

Combined Corrosion: 48 t



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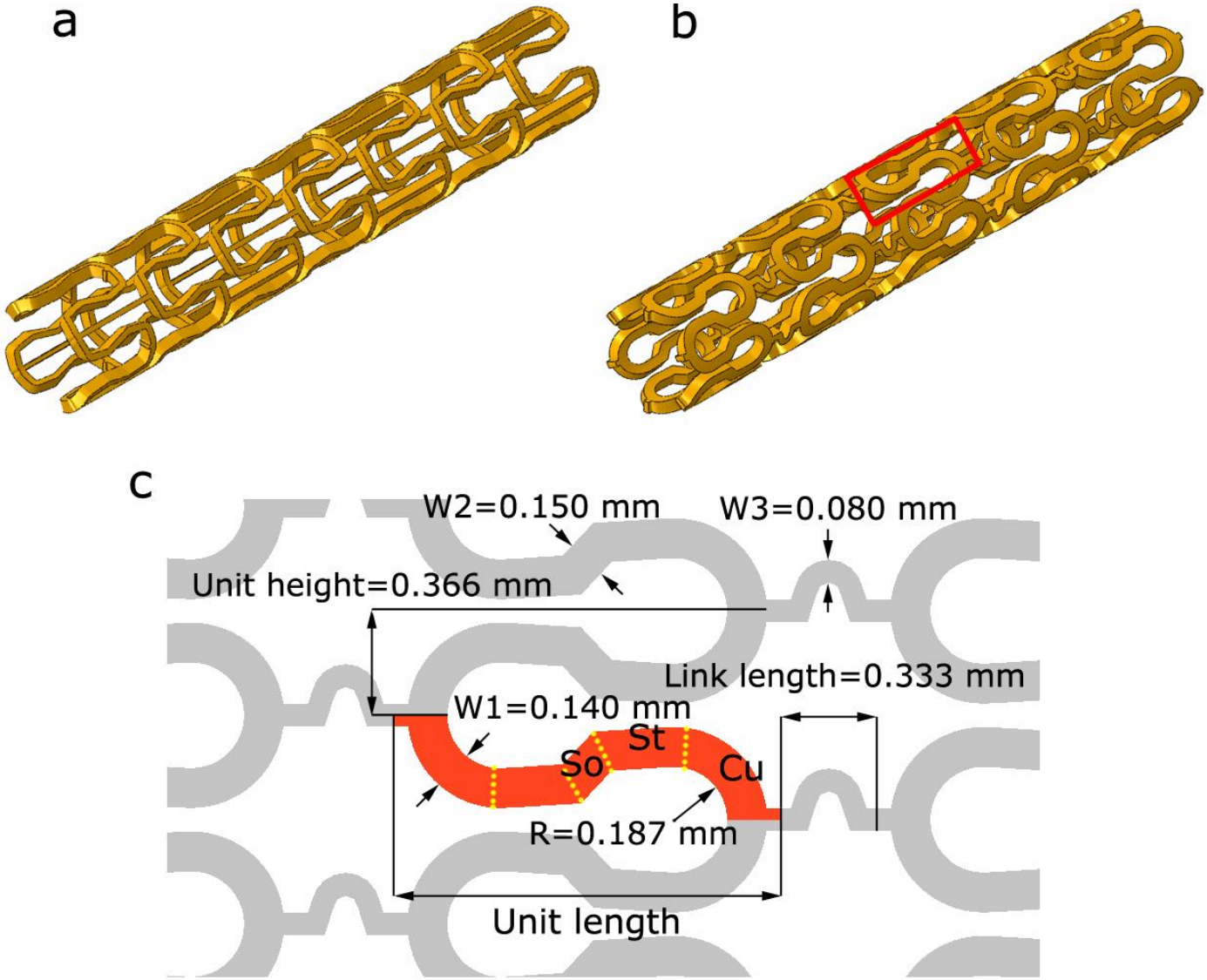
Biodegradable stents

OPTIMISATION PROCEDURE



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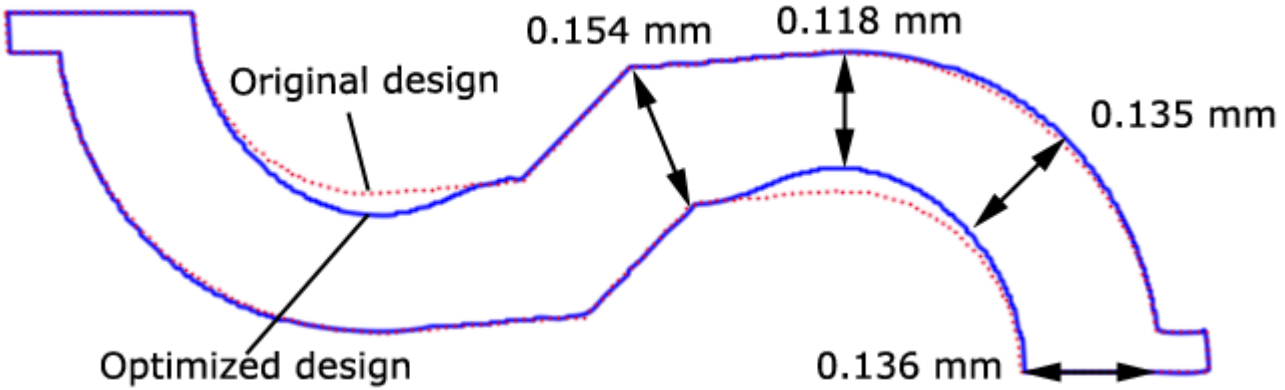
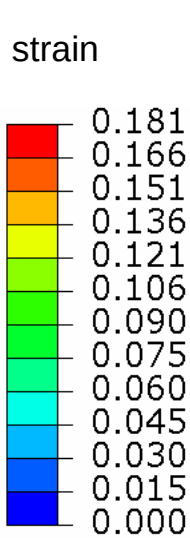
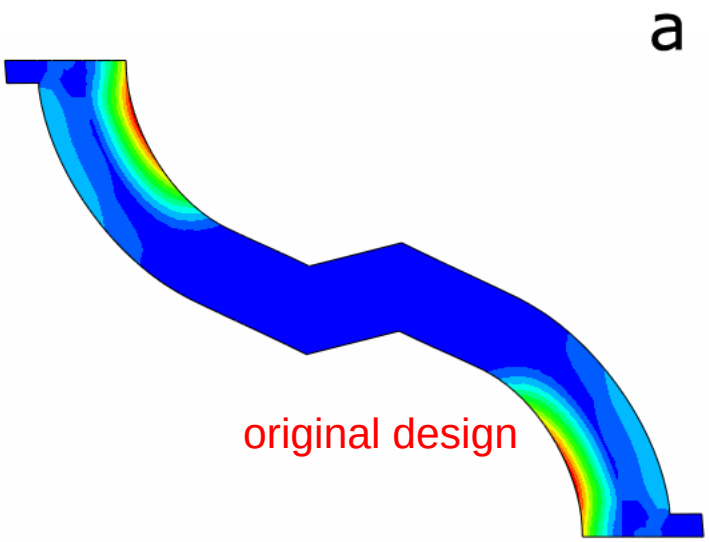
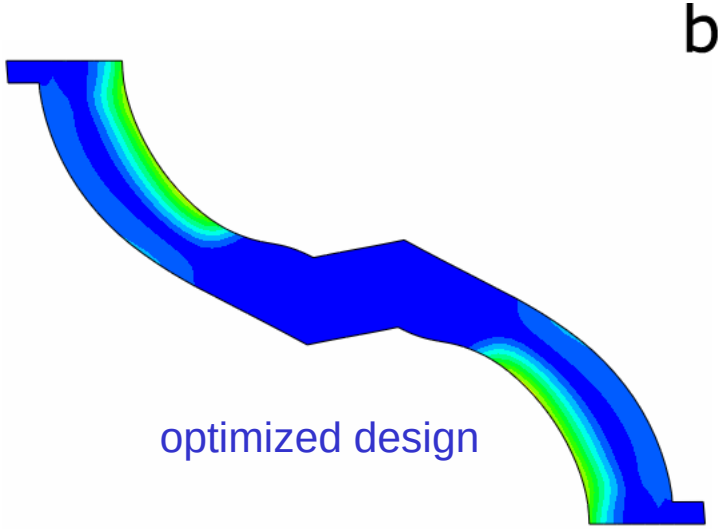
Biodegradable stents

OPTIMISATION PROCEDURE









Wu et al: 'FE shape optimization for biodegradable magnesium alloy stents' Ann Biomed Eng, 2010.

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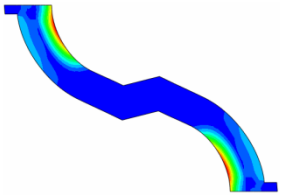
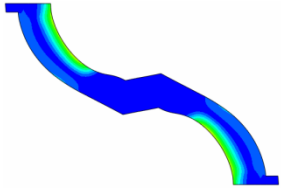
OPTIMISATION PROCEDURE

ZM21





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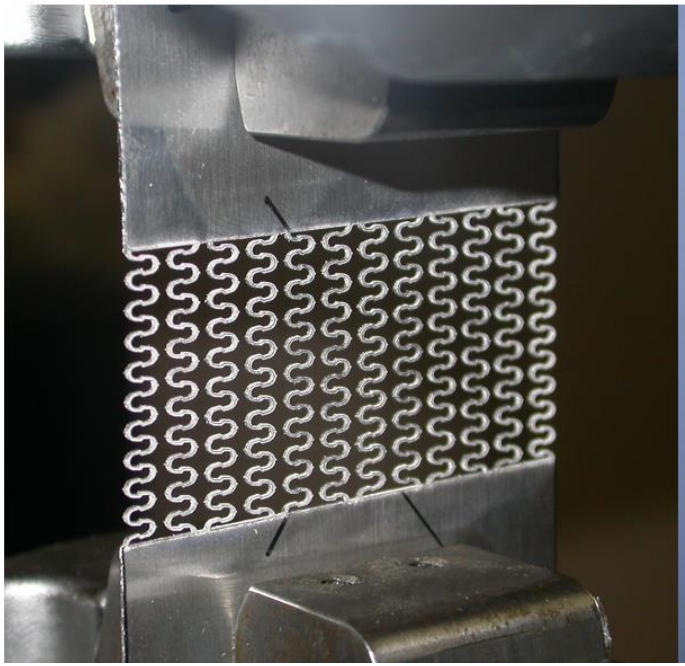

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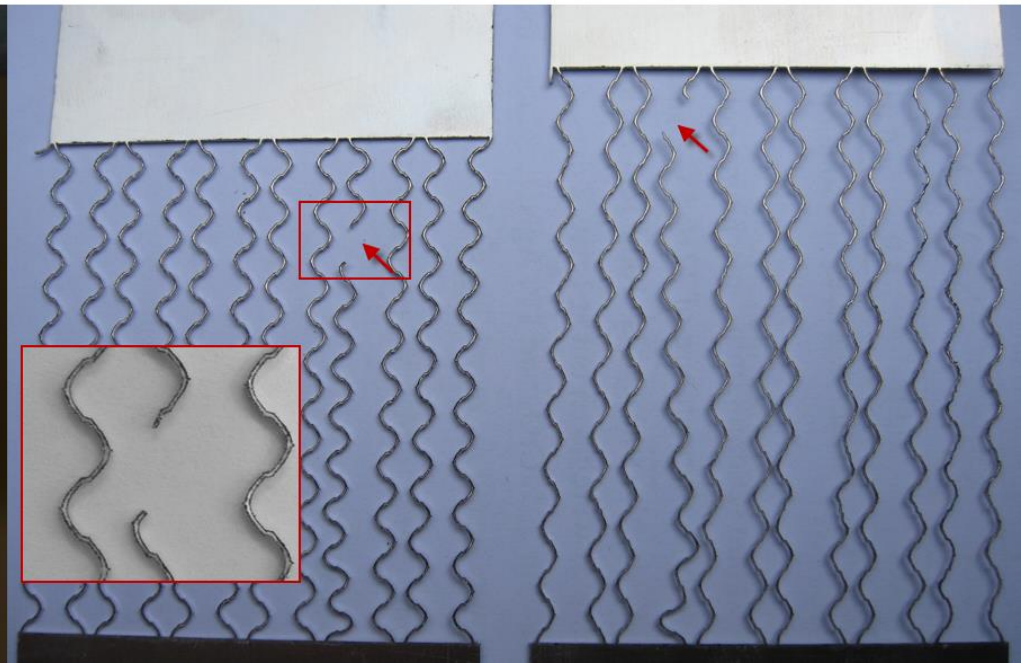

original design

optimized design

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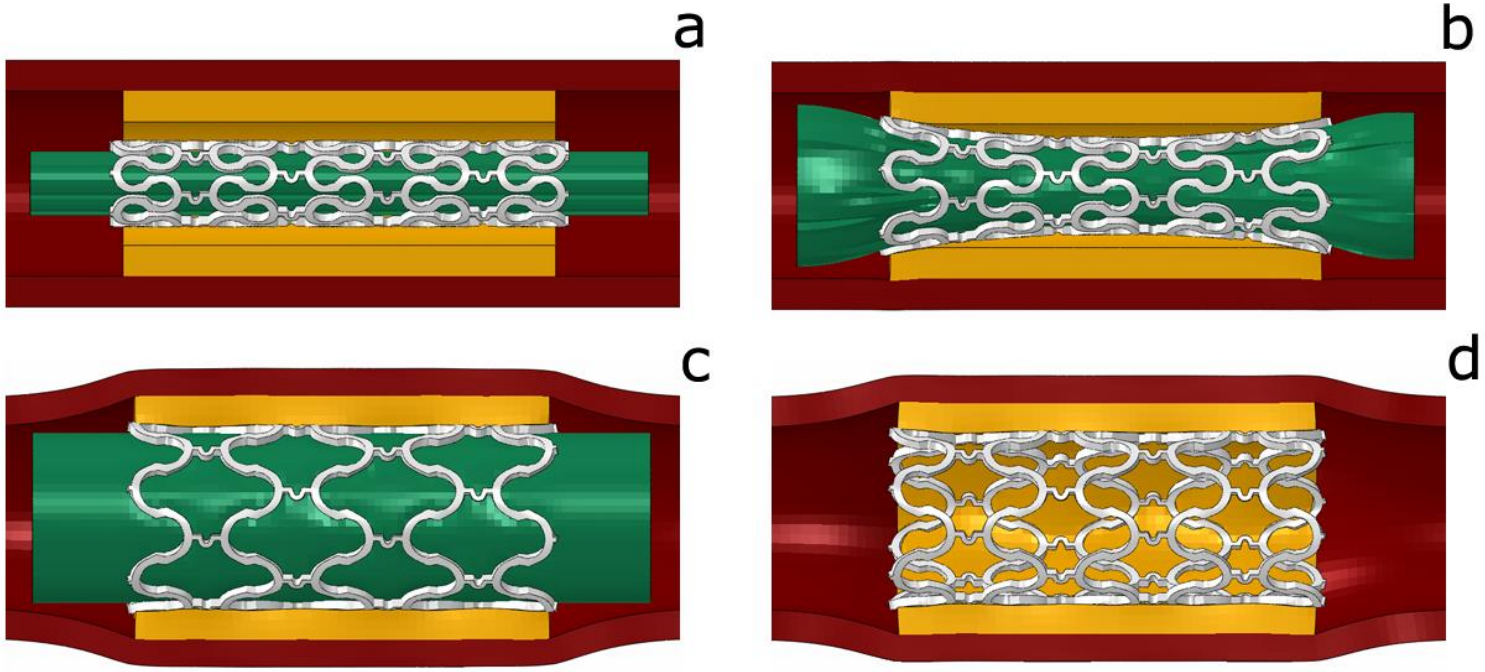
OPTIMISATION PROCEDURE



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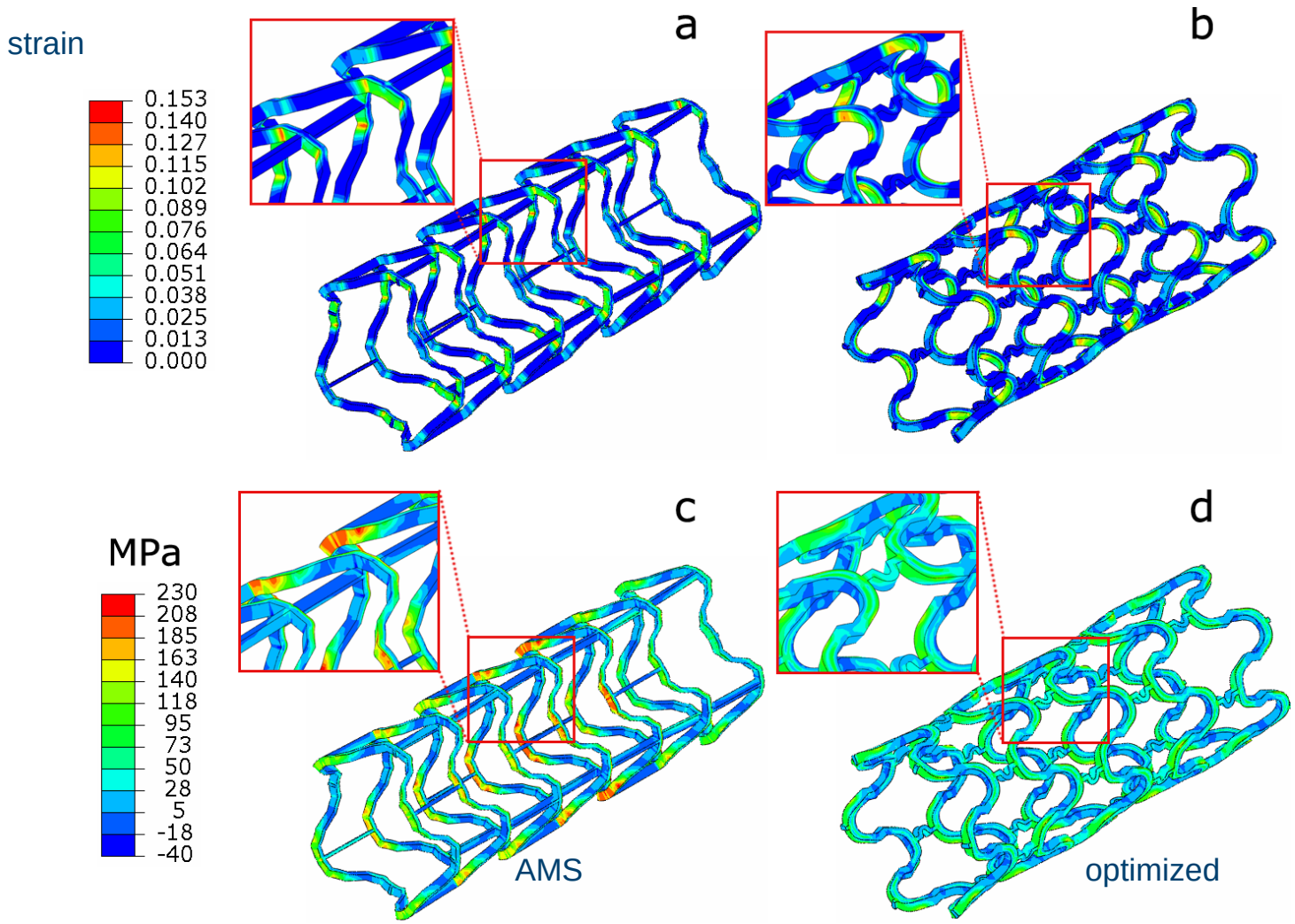
Biodegradable stents

OPTIMISATION PROCEDURE



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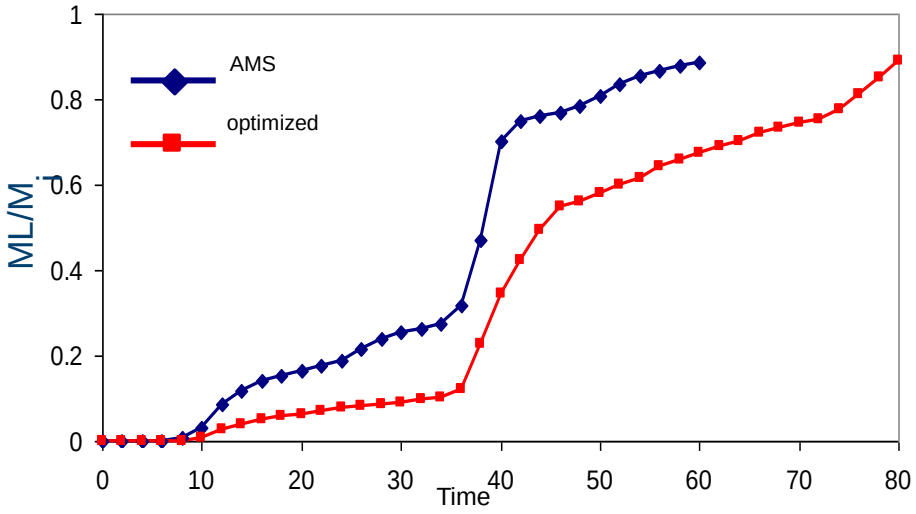
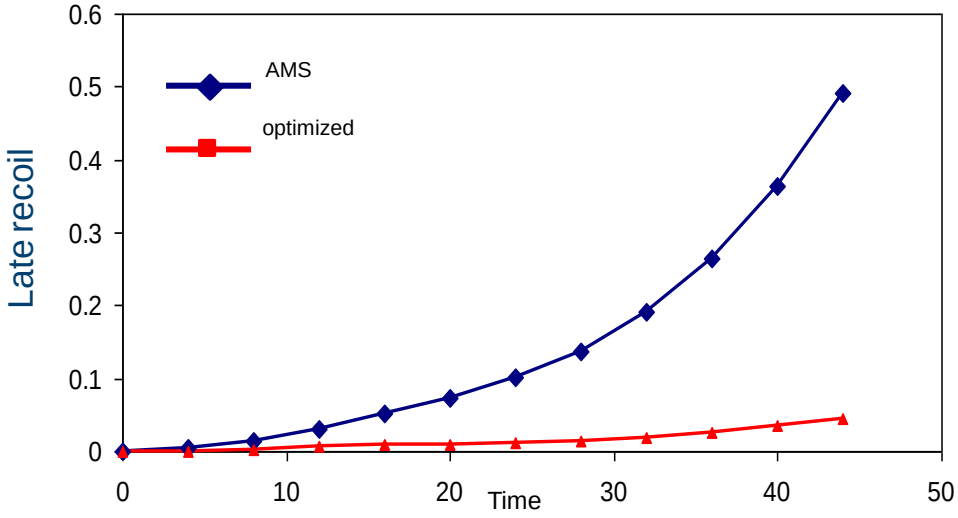
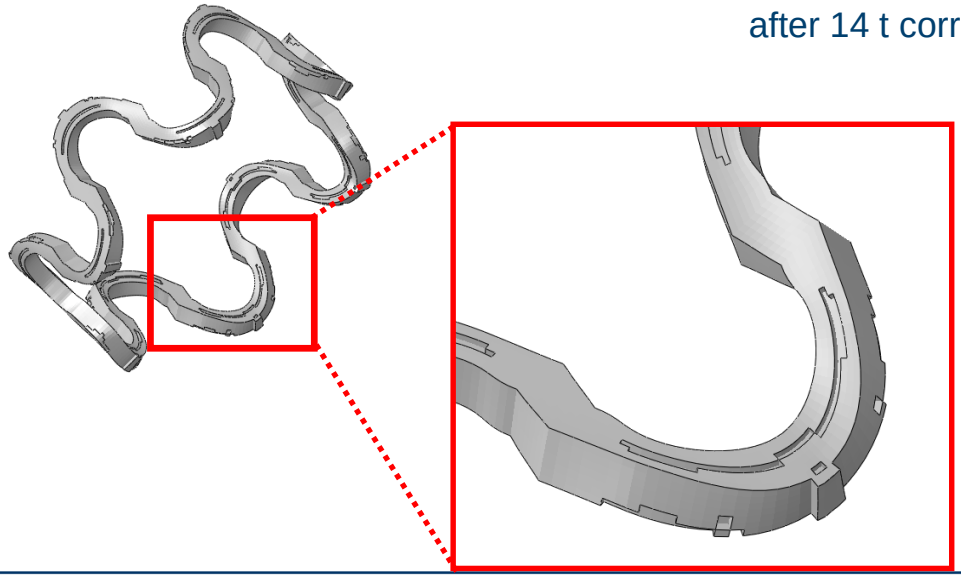
Biodegradable stents

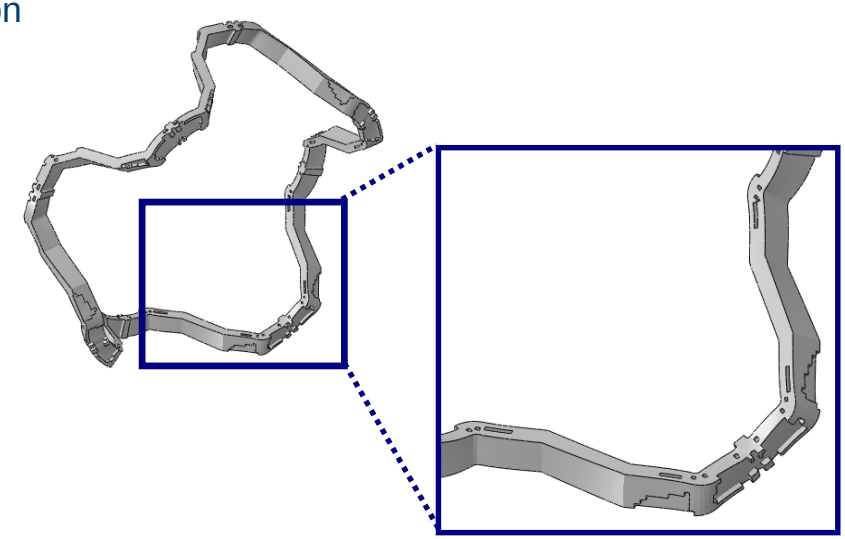
DEGRADATION RESULTS





after 14 t corrosion





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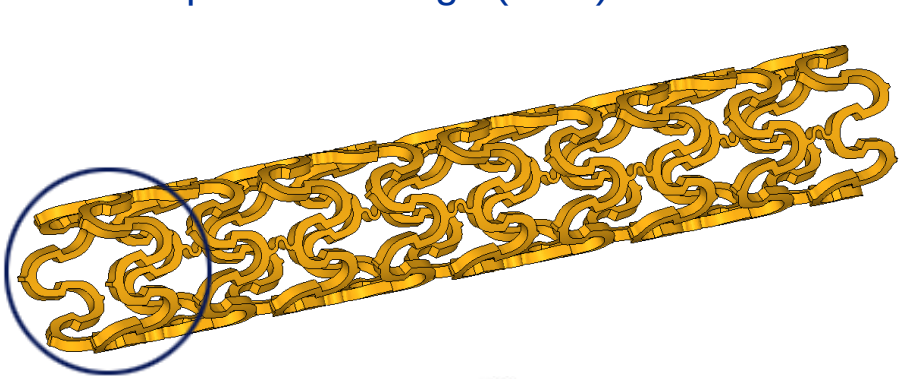
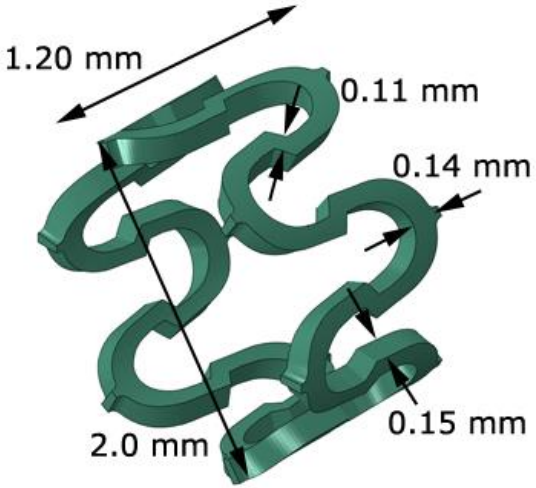
Biodegradable stents

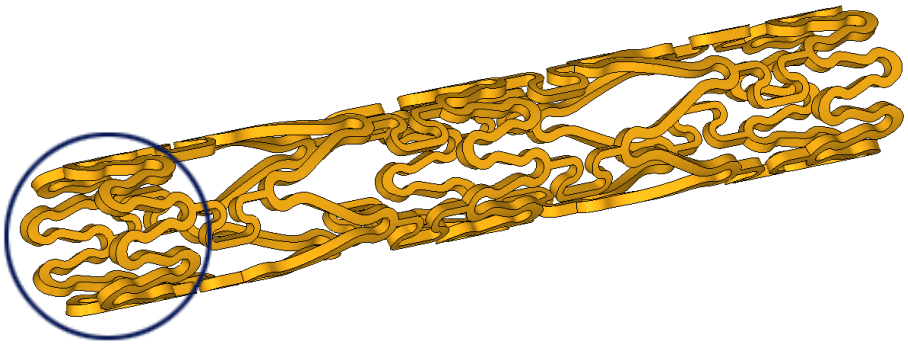
Two FEA models of MAS in the simulation of degradation

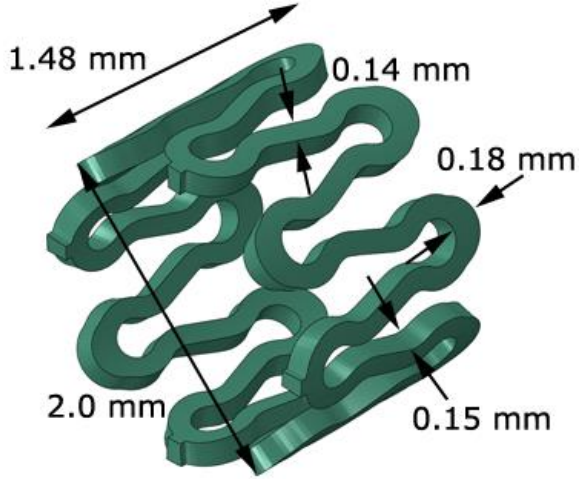
Optimized design (OPT)





Patent design as control (CON)





The ratio of mass per length unit is 1.93 : 2.64

Ren et al., An Absorbable Implantation Stent of Magnesium Metal, Chinese patent, 2006

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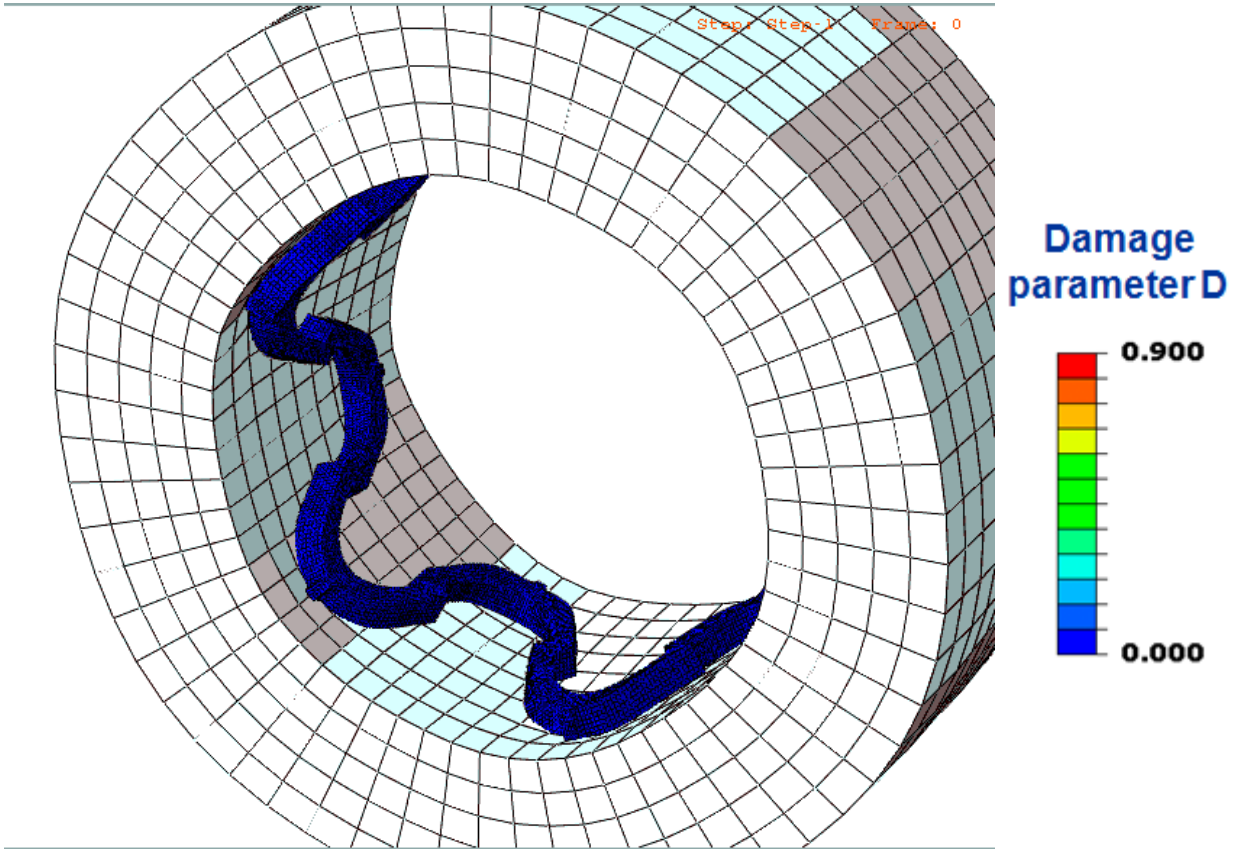
INTERACTION BETWEEN OPT MODEL AND VESSEL DURING DEGRADATION



When the stent degraded the vessel recoiled until then stent broke

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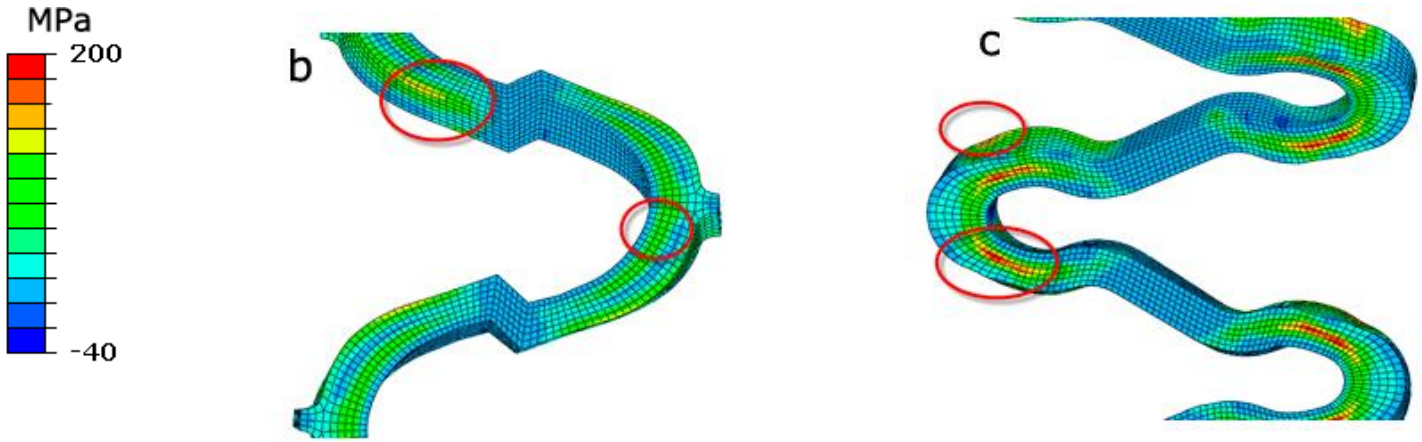
RESULTS AFTER STENT IMPLANTATION

Result of the stent models after implanting procedure

Stent	Max. principal strain after expansion	Stent recoil (%)	Max. principal stress after recoil [MPa]
OPT	0.076	7.0	163
CON	0.138	12.6	230

OPT CON



The distribution of residual stress

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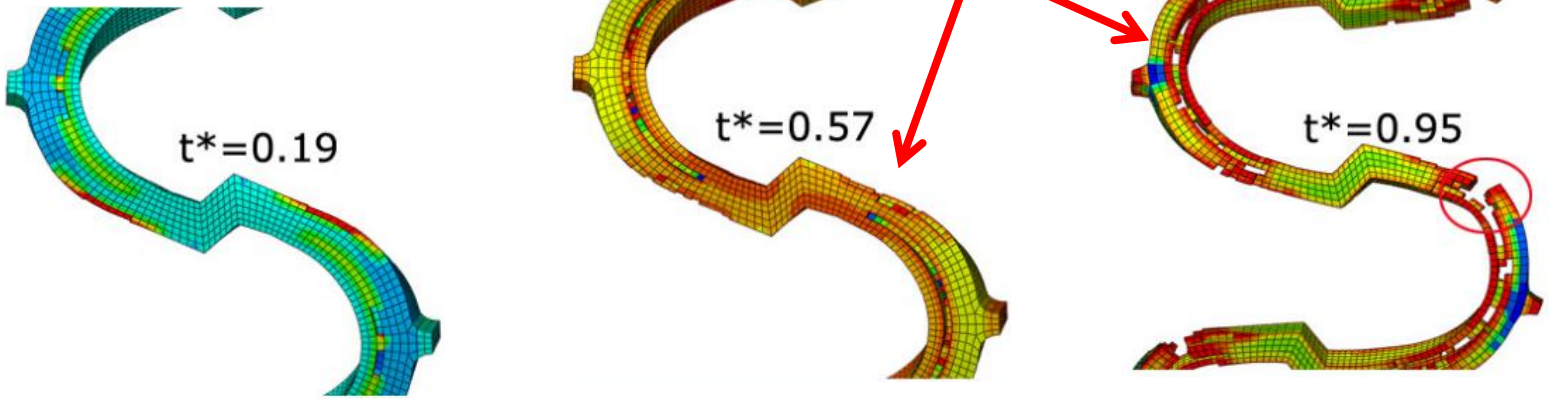
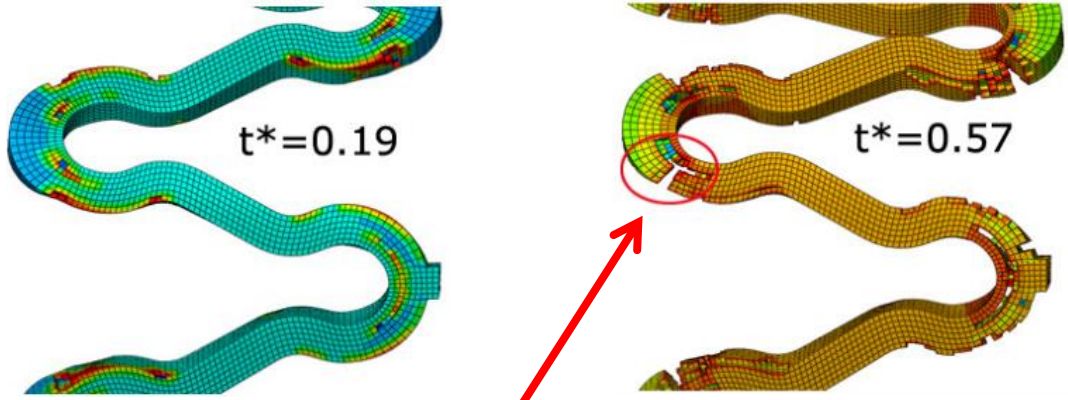
UNIFORM AND STRESS CORROSION EVLUTION

Uniform corrosion

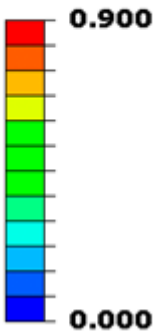
OPT



CON



Damage parameter D

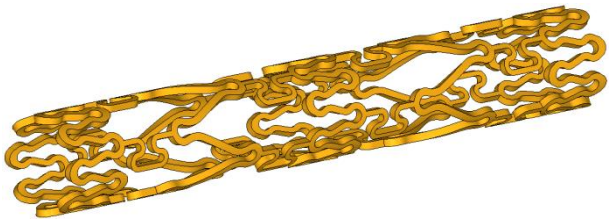


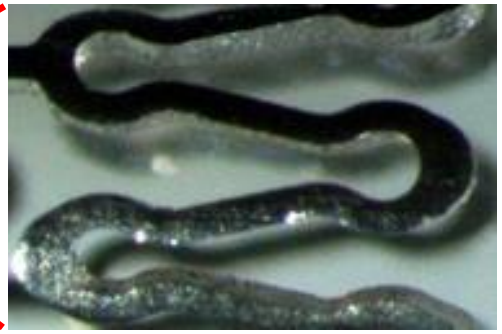
Faster stress corrosion evolution

Biodegradable stents

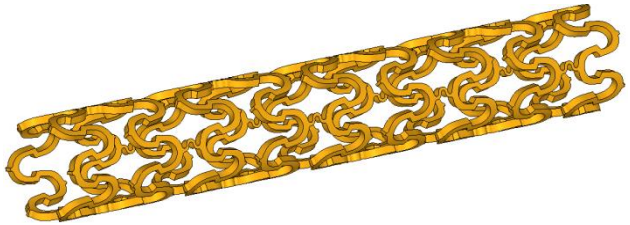
LASER CUTTING AND ELECTRO-POLISHING OF THE MAS SAMPLES

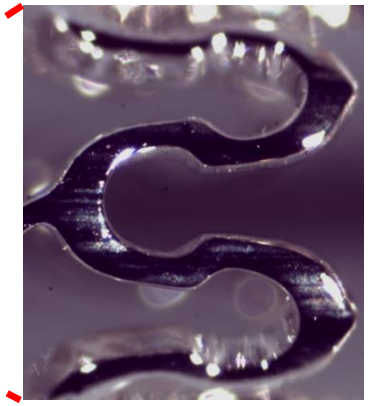
OPT





CON





Material: AZ31 tube

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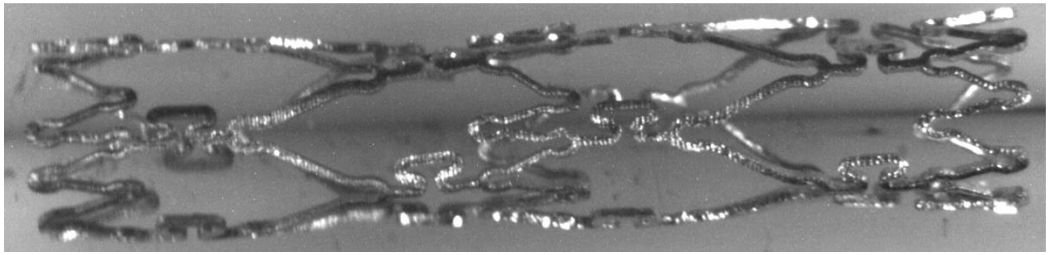
DEGRADATION EXPERIMENT OF THE TWO SAMPLES

- The two samples were crimped to 1.2 mm of outer diameter and expanded to 3.0 mm then recoiled freely. The expanded CON sample is shown below.



- The two expanded samples were immersed in the D-Hank's solution for 7 days, with pH 7.5 and and temperature 37°C.

Composition of D-Hank's solution (g/L)

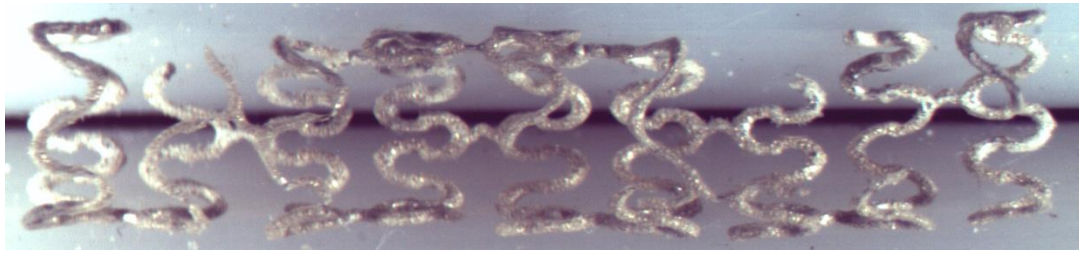
KCl	KH_2PO_4	NaCl	$NaHCO_3$	$Na_2HPO_4 \cdot 7H_2O$	Phenol red
0.4	0.06	8.0	0.35	0.06	0.02

- The two samples were observed with unaided eyes to check structural integrity when immersed in solution. Then they were taken out for the observation with stereo or scanning electron microscope (SEM) after 7 days of corrosion.

EXPERIMENTAL RESULTS: STRUCTURAL INTEGRITY

- After the first day of immersion, the CON sample had several broken points on the strut while the OPT sample kept the structural integrity until the third day of immersion.
- After 7 days of corrosion, the CON sample has scattered into pieces, while the OPT has not scattered even though it had several broken points. The result is compatible with simulation that the OPT model has better property to resist corrosion.

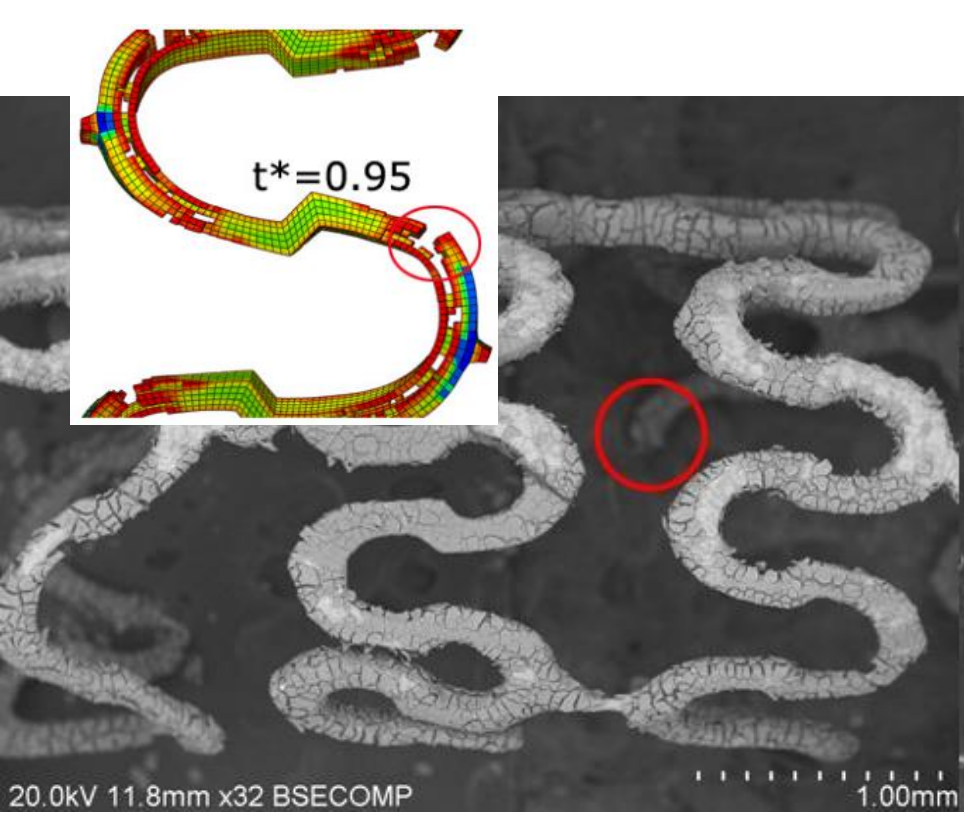
OPT

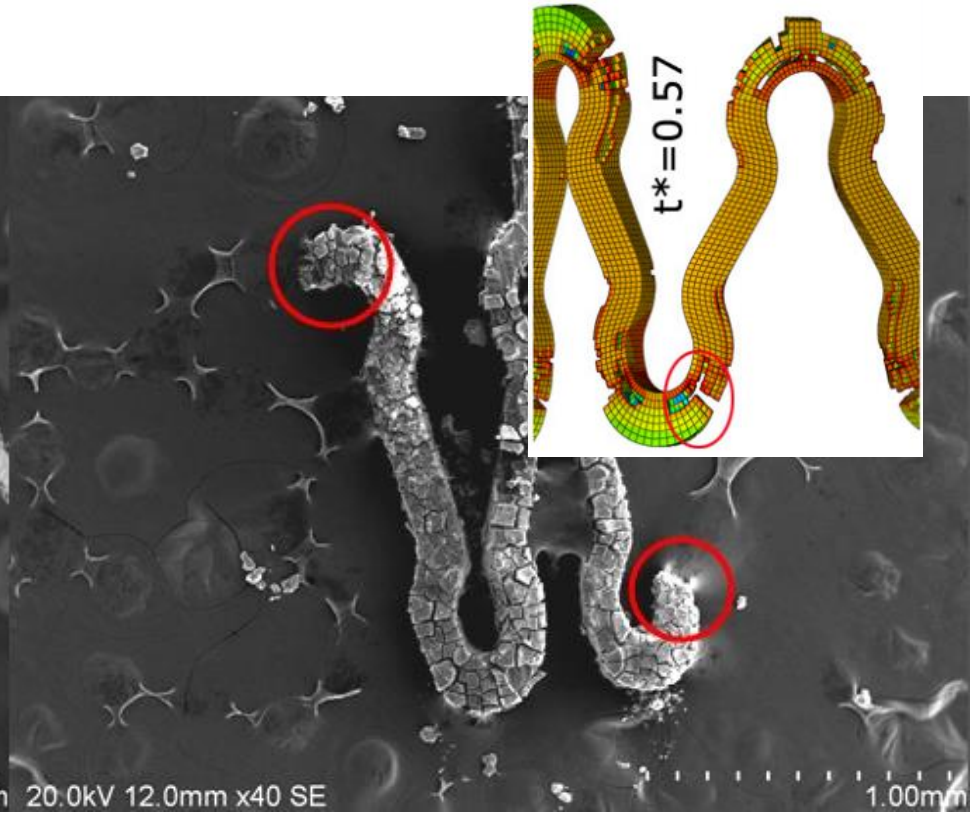


CON

EXPERIMENTAL RESULTS: UNIFORM AND STRESS CORROSION

- The SEM observation shows that corrosion layers caused by uniform corrosion, which were shedding from the stent matrix. The early broken points caused by stress corrosion can also be observed and are compatible with the expected location in simulation.





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CONCLUSIONS FROM MATHEMATICAL MODELLING

- Both simulation and experiment indicated that the optimized MAS design can yield better property to resist corrosion.

- Both simulation and experiment showed that the degradation of MAS consists of uniform and stress corrosion.

- The experiment preliminarily verified that the proposed numerical approach can be an effective tool for novel MAS design and property comparisons.

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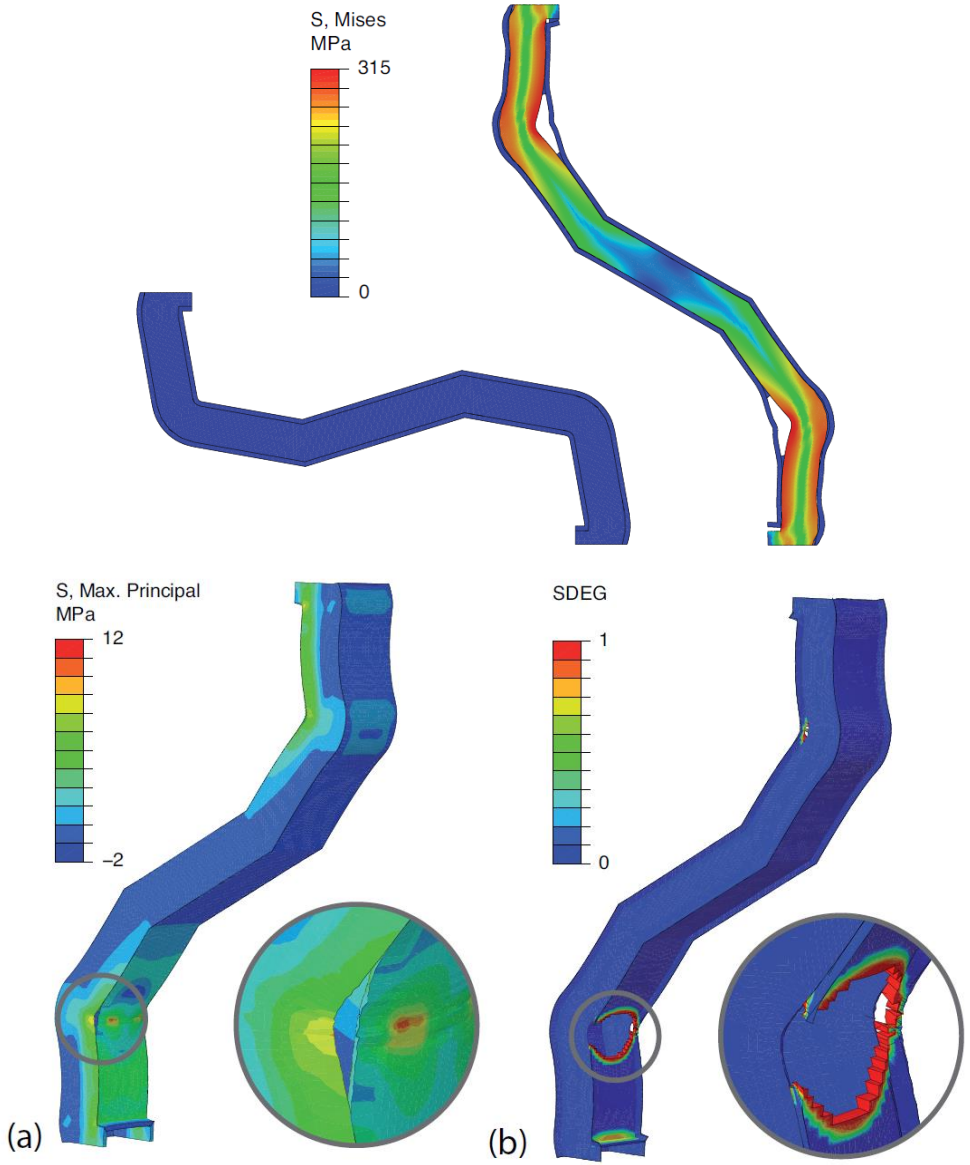
In progress



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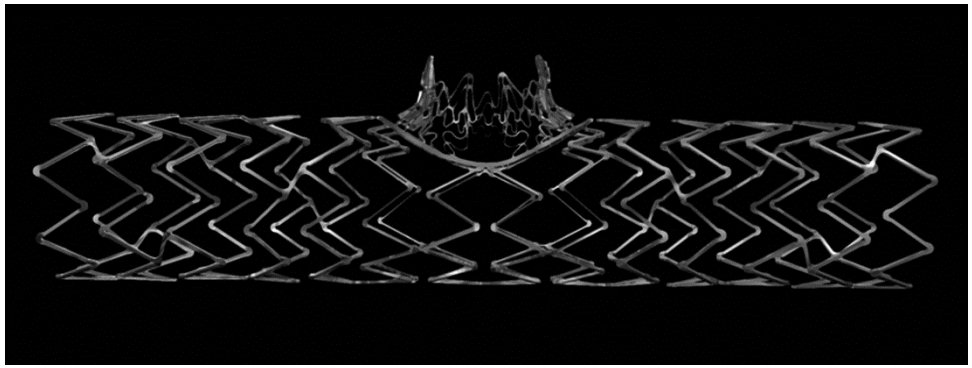
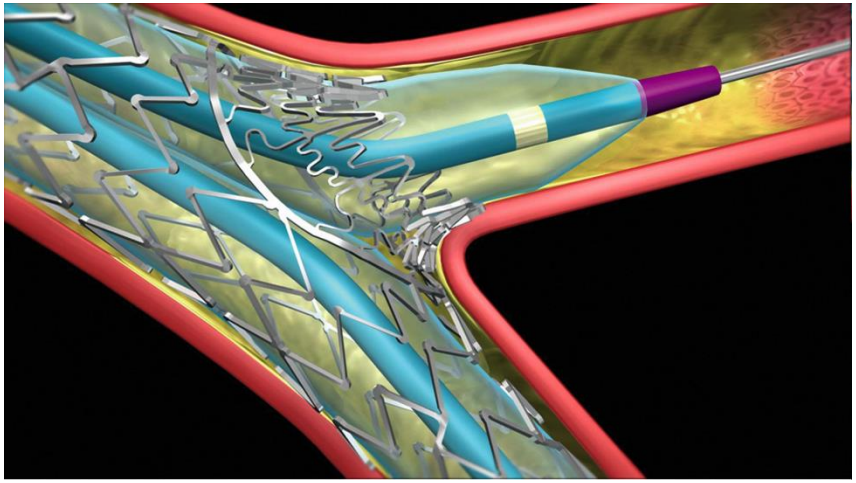
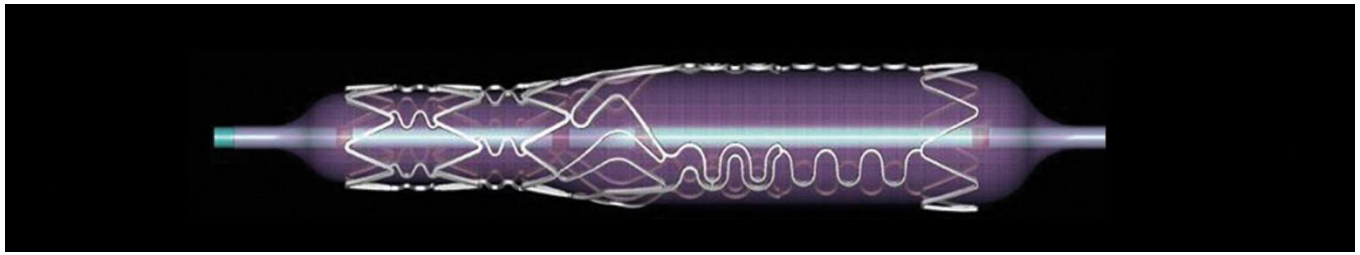
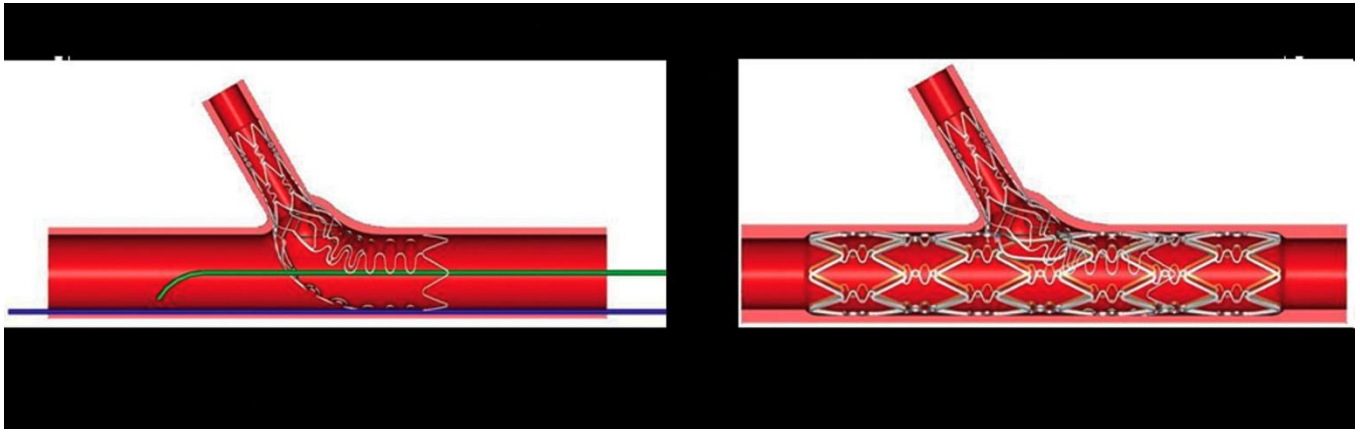
Coronary bifurcation

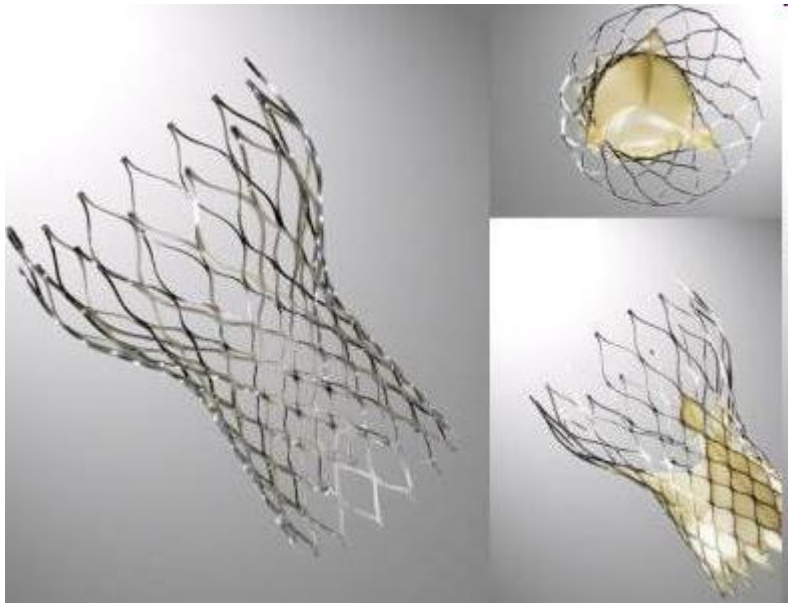


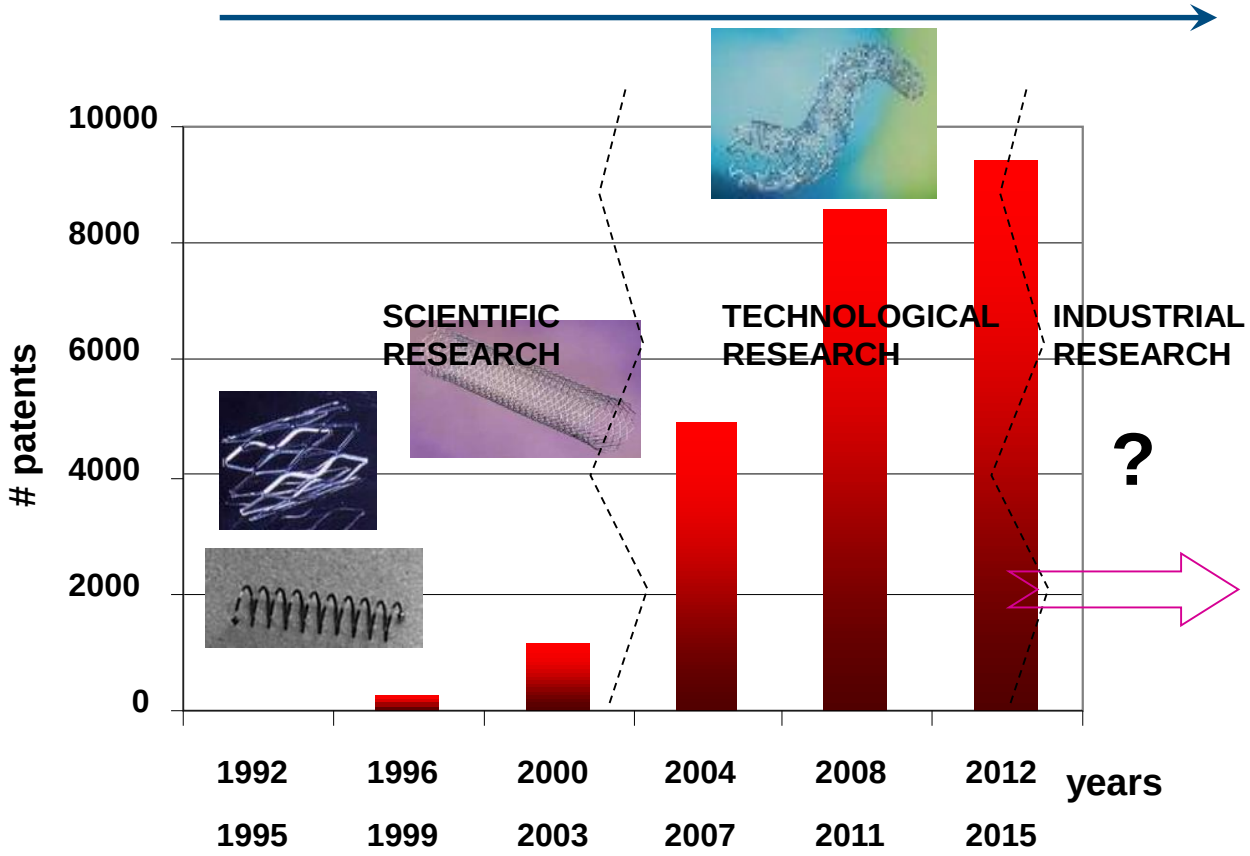






different stent applications





The optimal design, however, of scaffolds, polymers, antiproliferative drugs and their degradation/release kinetics is still under investigation.

Thank you

Computational models presented here are carried out with the help of:

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Dario Gastaldi

Lorenza Petrini

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