XXII Jornadas SOLACI
7° Región Cono Sur
21 / 22 de Noviembre 2013

SOLACI
SOCIEDAD LATINOAMERICANA DE CARDIOLOGIA INTERVENCIONISTA

Stents Coronarios
Pasado, Presente y Futuro

HOSPITAL ITALIANO
de Buenos Aires
Instituto de Medicina Cardiovascular

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Jefe de Cardiologia Intervencionista
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LA PAZ
BOLIVIA

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- ***Conferencista***
  Biosensors, Boston Scientific, Terumo
- ***Fondos para investigación***
  Abbot, Eurocor
- ***Programas de entrenamiento y educación***
  Biosensors, Terumo

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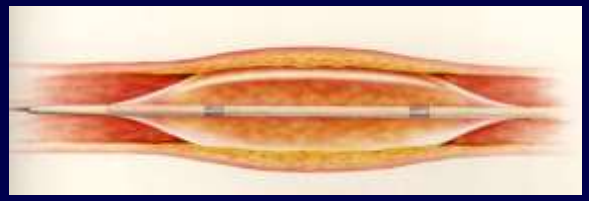
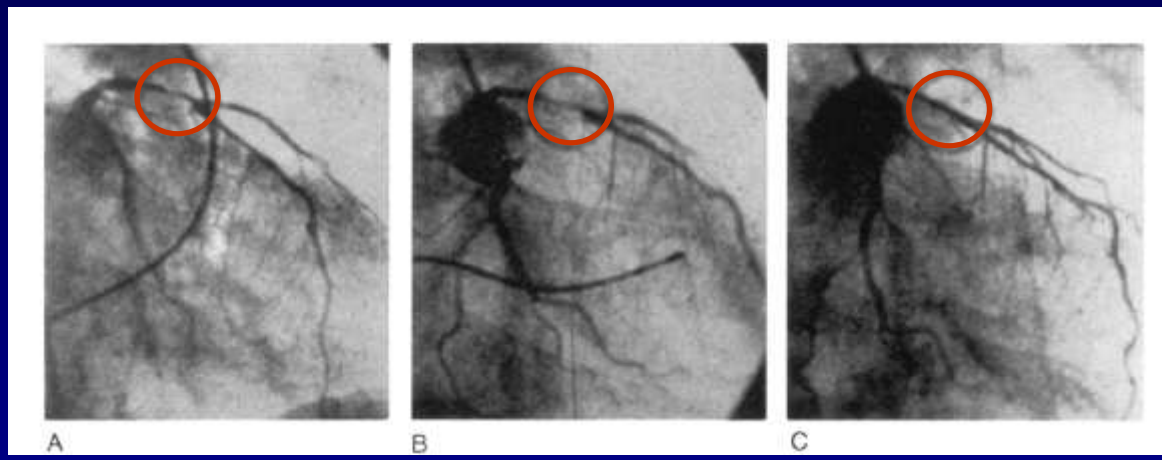
LA PAZ
BOLIVIA

Andreas Gruentzig
September 1977

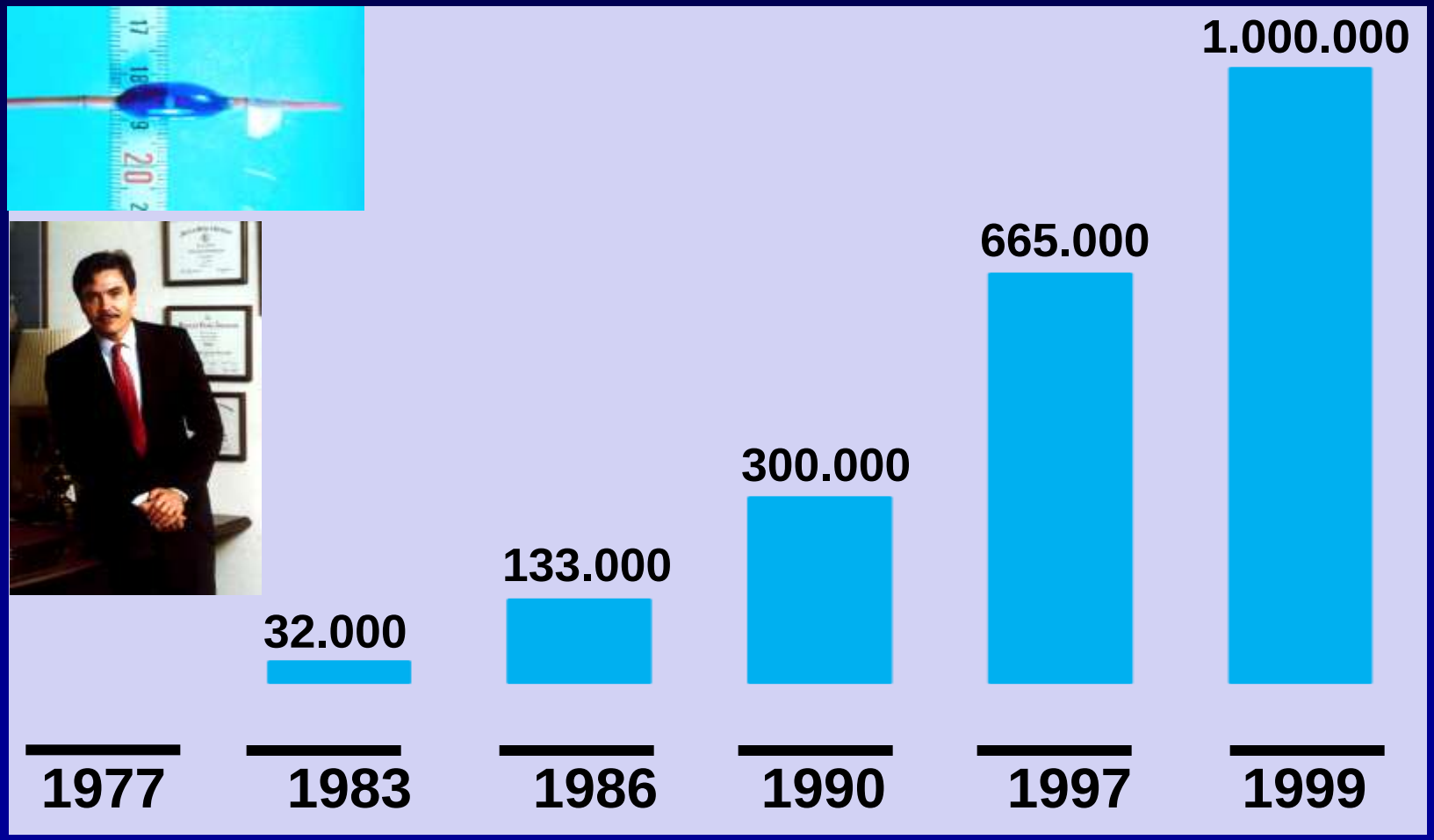


Balloon angioplasty



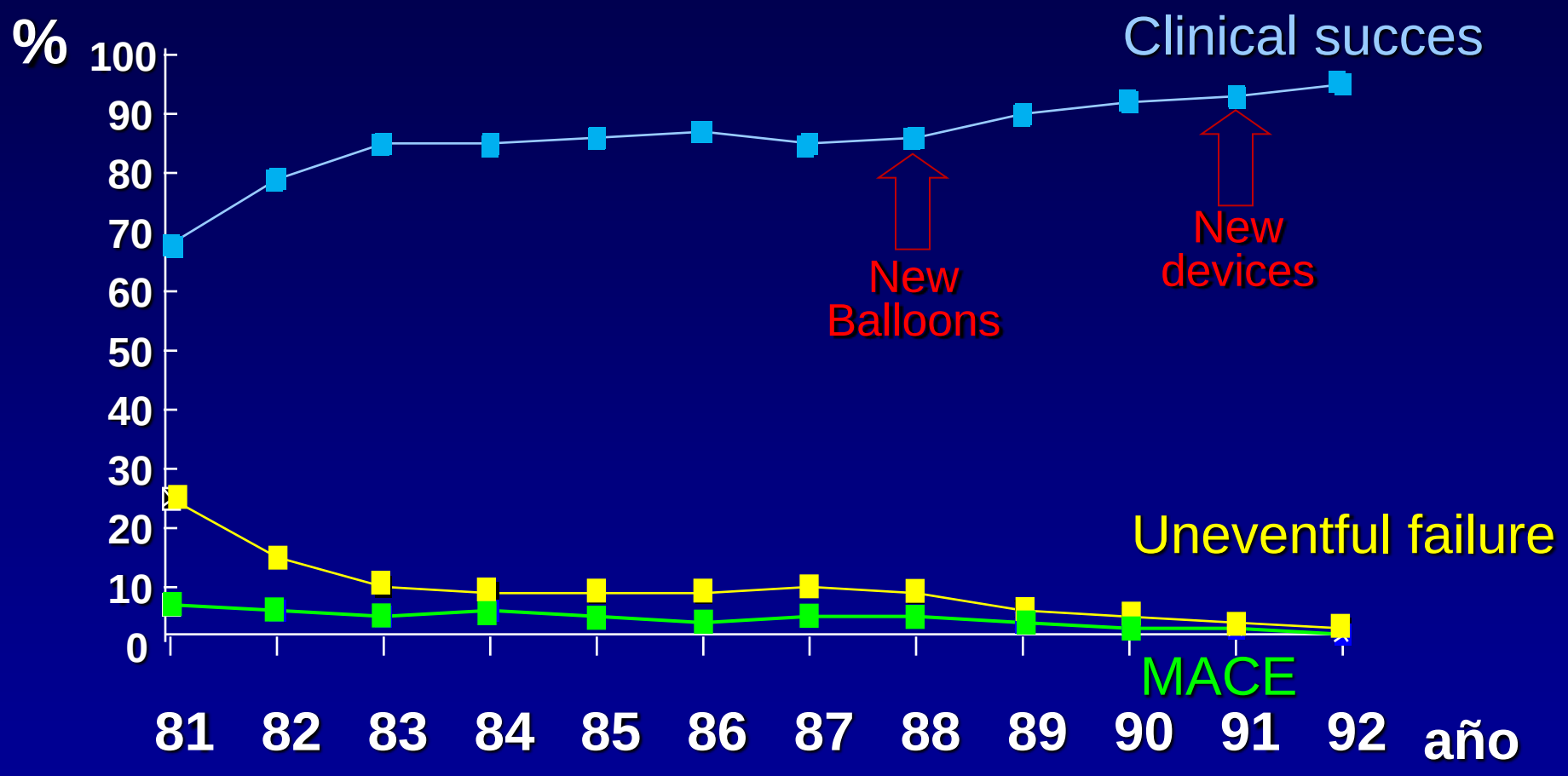
Roads opened by “insane”
will be later traveled by the “wise man”
C. Dossi

Evolución de la angioplastia en sus comienzos



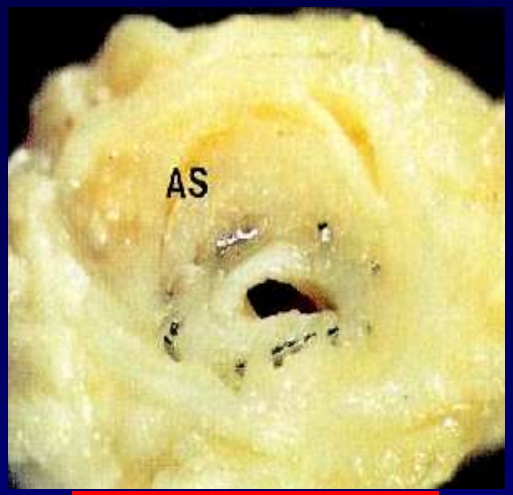
Modified from
ACC/AHA TASK FORCE,1988/1993
HFMA February 1998

NHLBI Coronary Angioplsty Registry

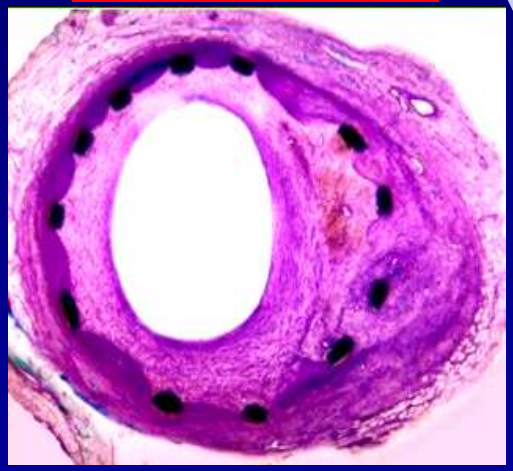


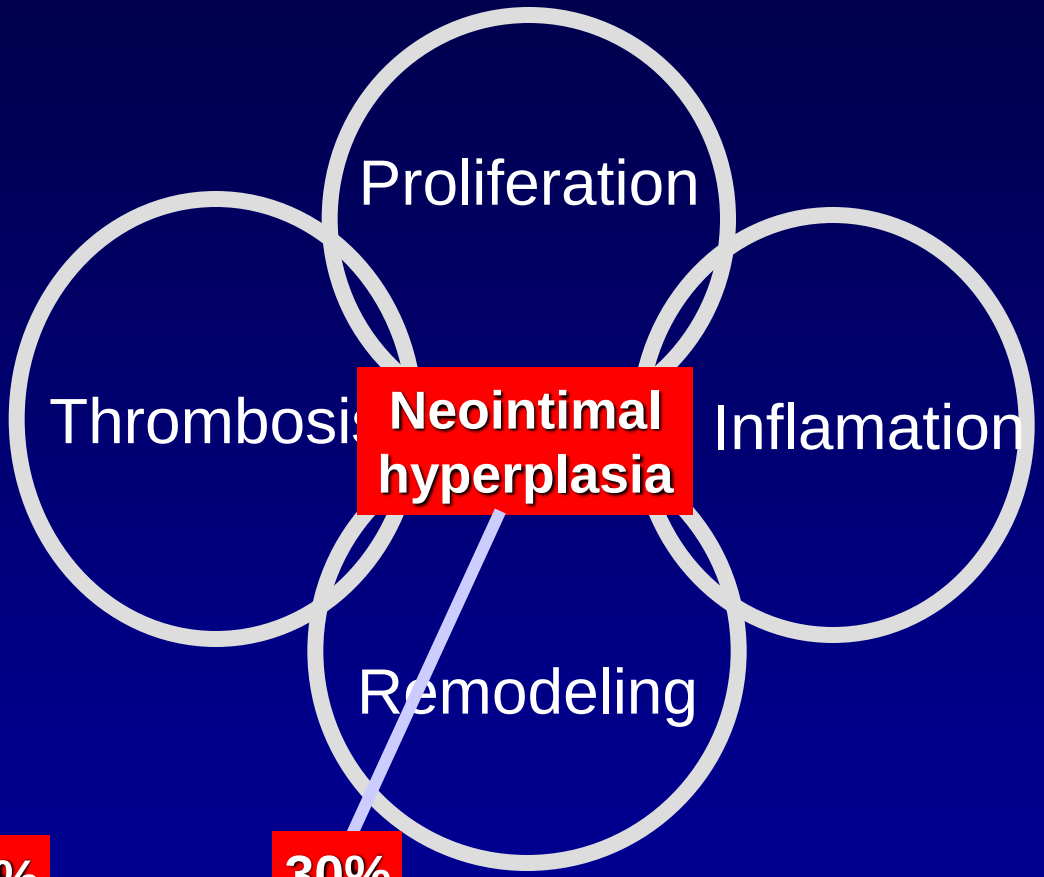
1977: Balloon Angioplsty → **1981 (NHBLI Registry)**

Response to vascular injury



Elastic recoil





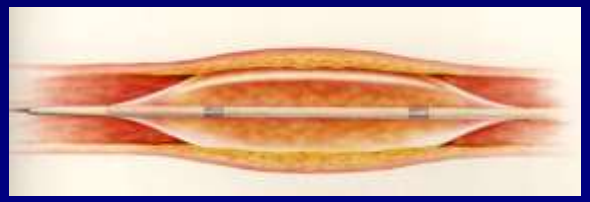
70%

30%

RESTENOSIS

Palmaz balloon expandable stent

Balloon expanded stent



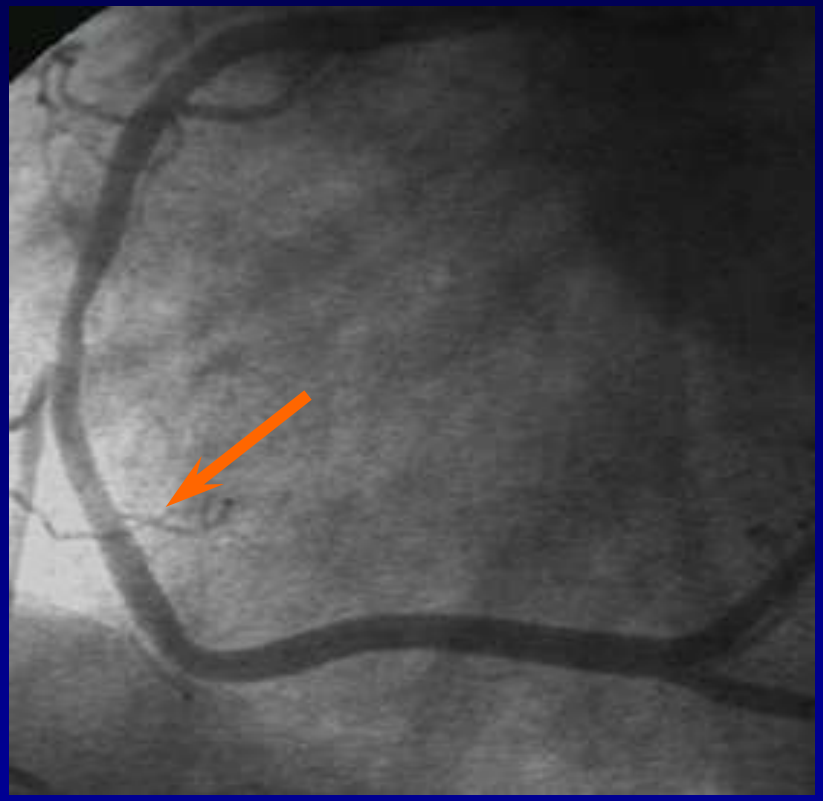
Balloon angioplasty

Stent implanted

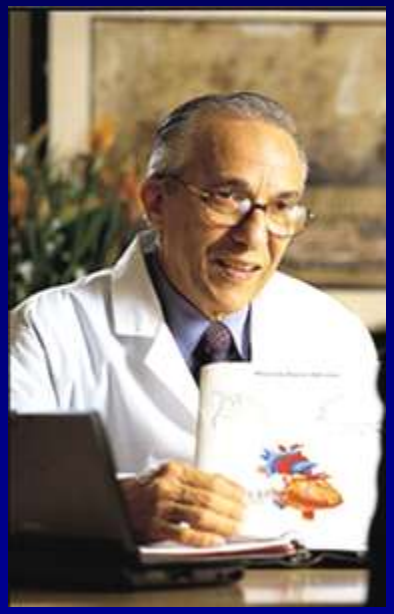
Balloon result

Stent result

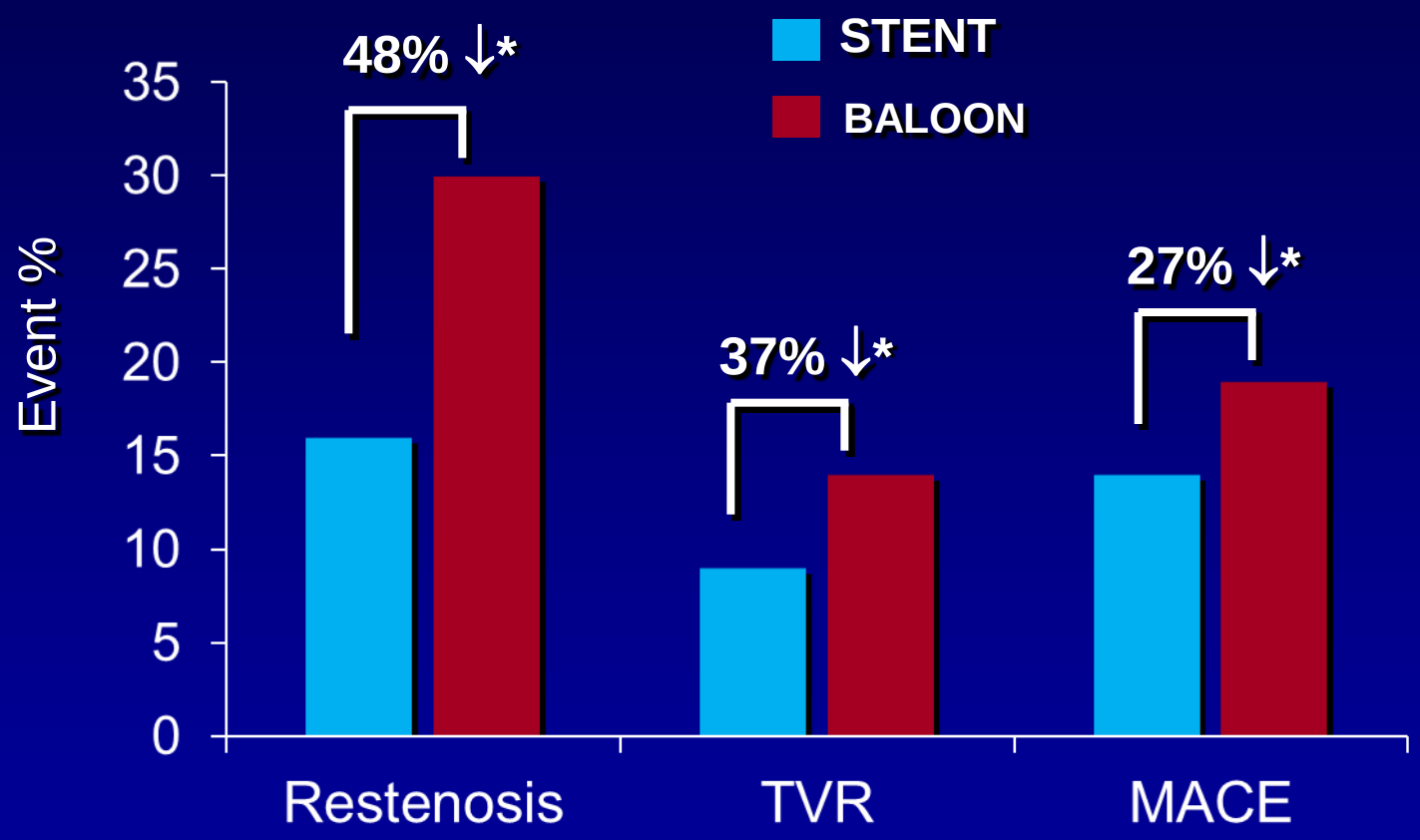
First Palmaz-Schatz™ (1986)



13-years post stent



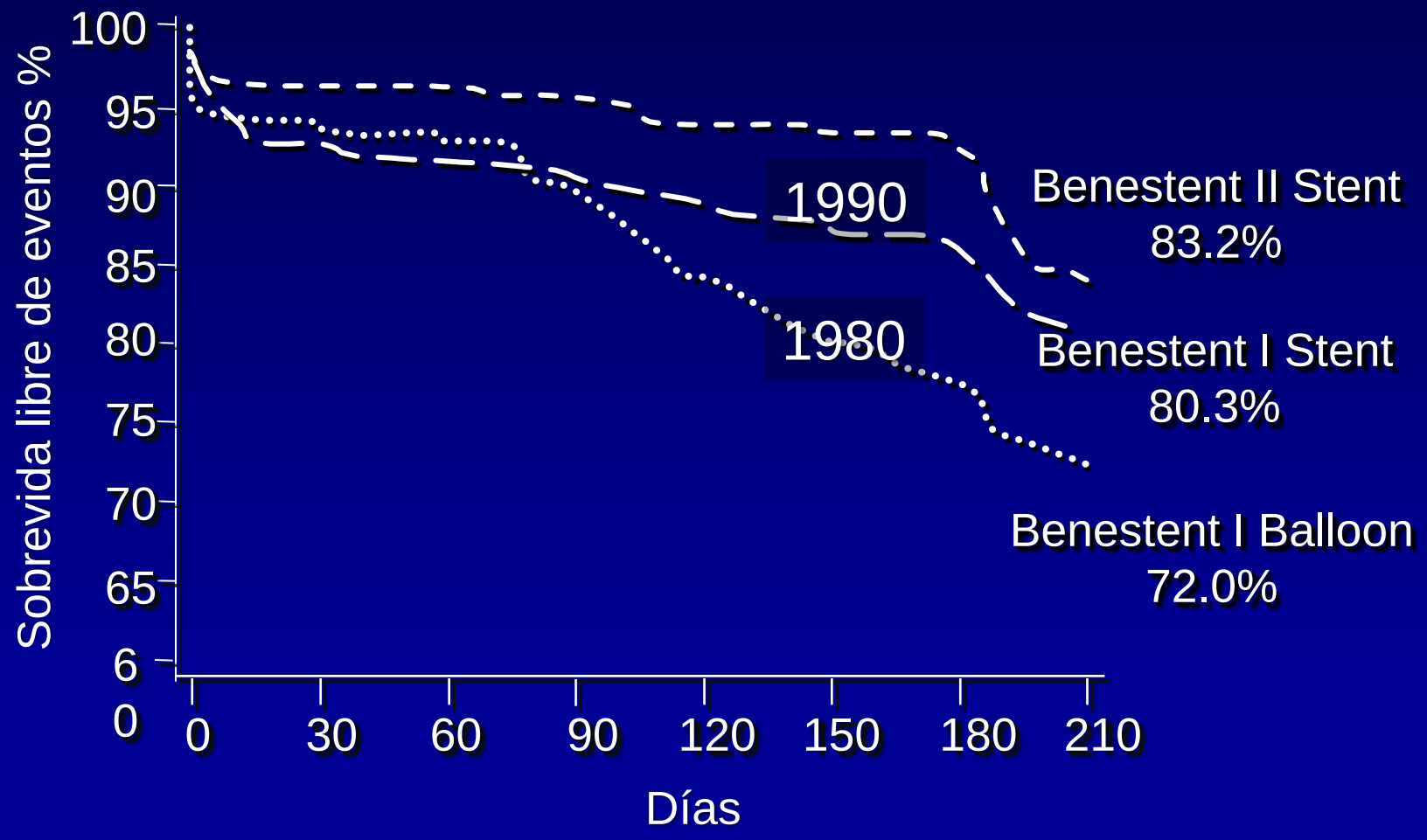
BENESTENT II study trial



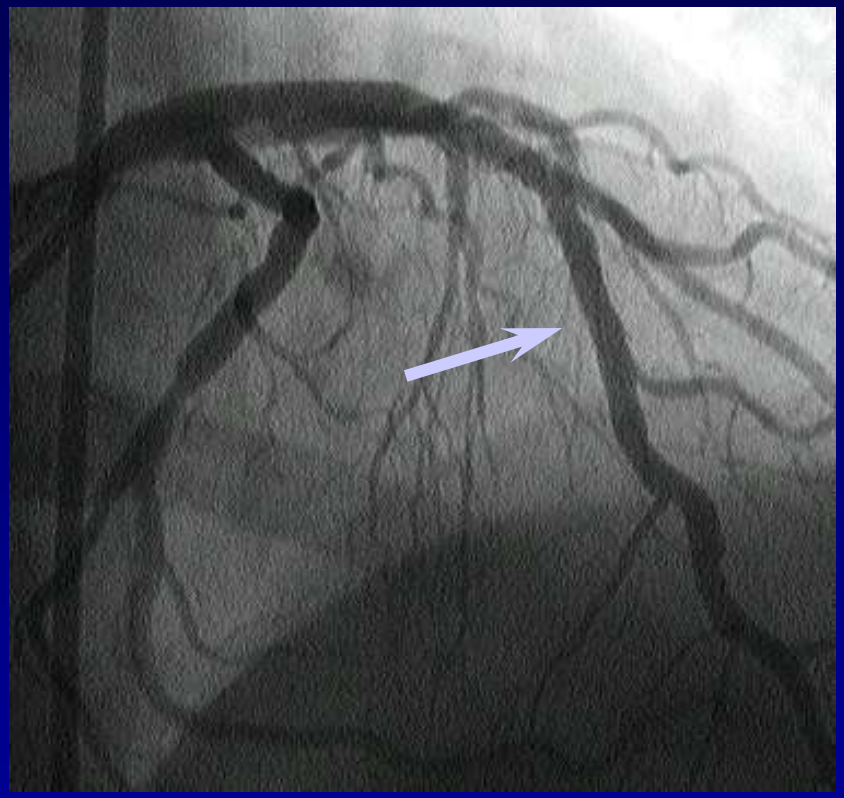
1986: Stent angioplasty → **1994 (BENESTENT)**

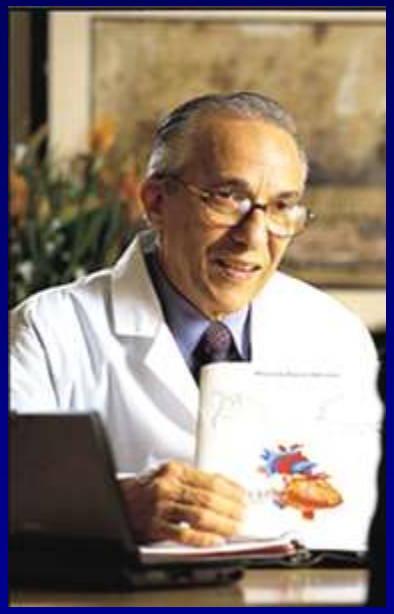
IMPACTO CLÍNICO DE LOS STENTS

Sobrevida libre de eventos: Muerte, Infarto, CRM o Re-ATC



First Cypher™ (1999)

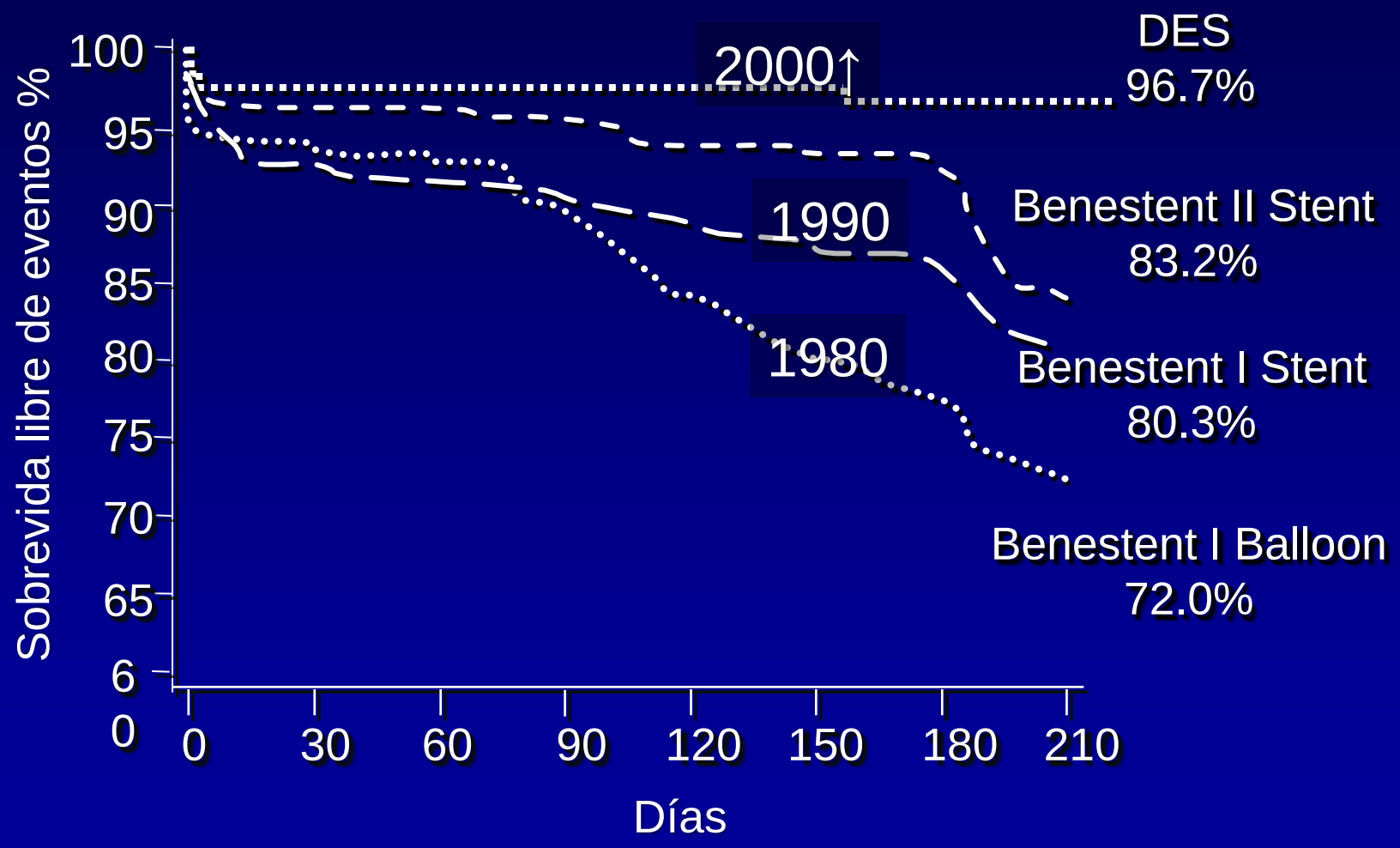




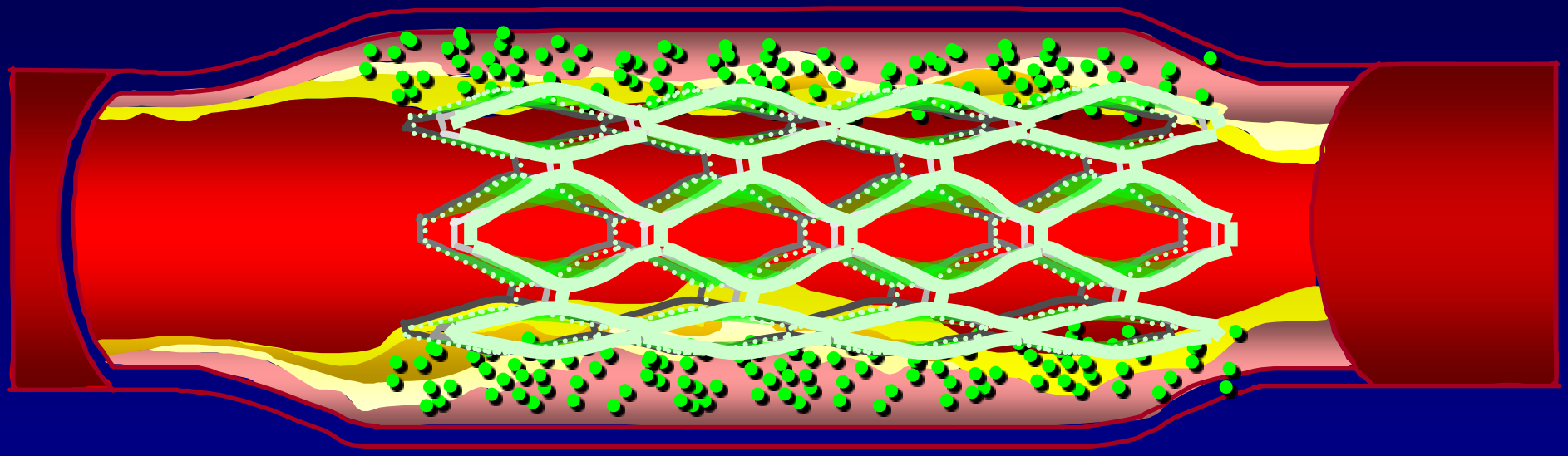
2-years post DES stenting

IMPACTO CLÍNICO DE LOS STENTS

Sobrevida libre de eventos: Muerte, Infarto, CRM o Re-ATC



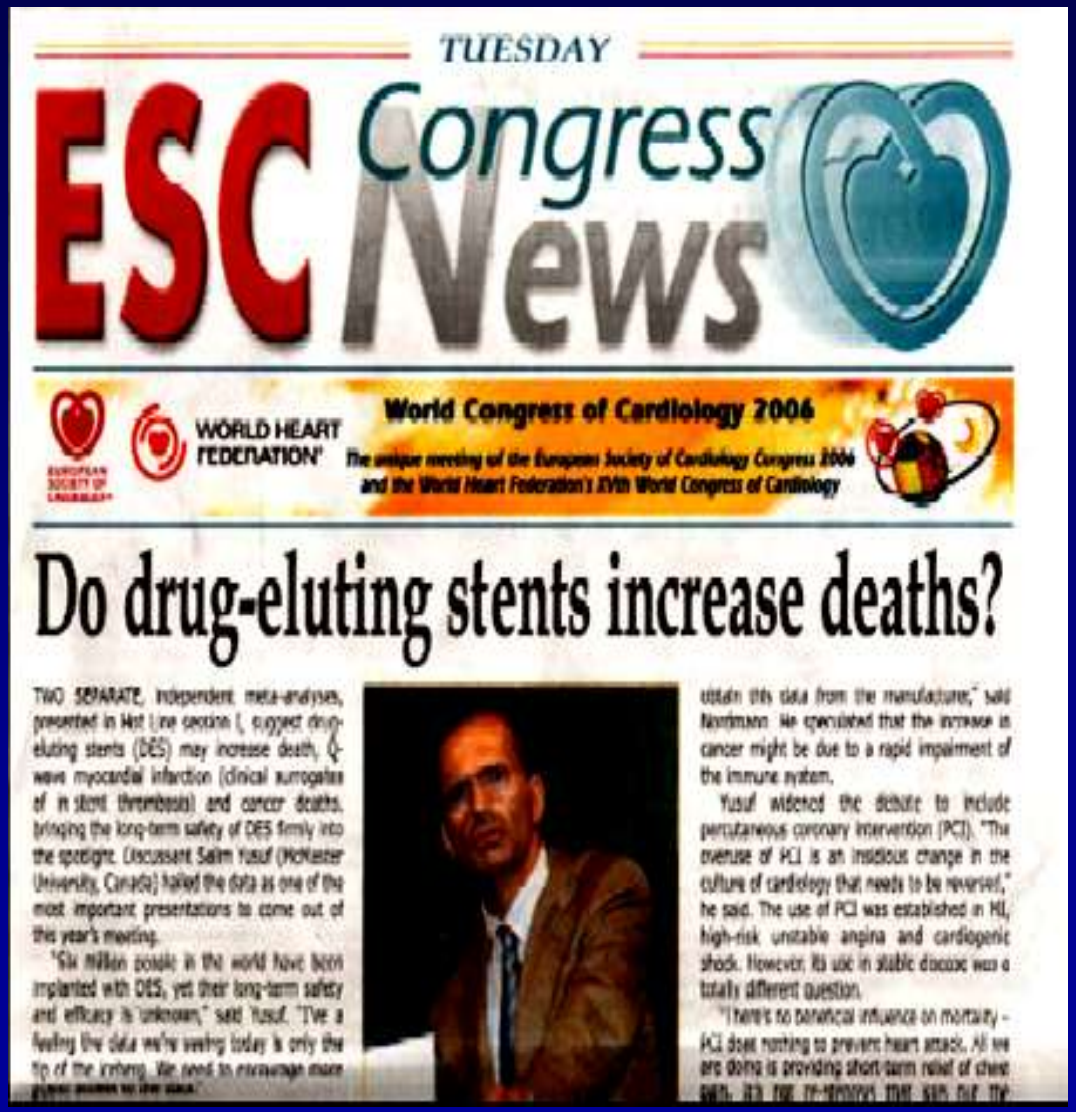
Stent con liberación de drogas



Plataforma **Droga** **Polímero**

Inflamación Trombosis Migración Proliferación

WCC Congress 2006



TUESDAY

ESC Congress News

WORLD HEART FEDERATION

World Congress of Cardiology 2006

The unique meeting of the European Society of Cardiology Congress 2006 and the World Heart Federation's XVth World Congress of Cardiology

Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year's meeting.

"Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is 'unknown,' said Yusuf. "I've a feeling the data we're seeing today is only the tip of the iceberg. We need to encourage more groups [illegible] to the data."

obtain this data from the manufacturer," said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

Yusuf widened the debate to include percutaneous coronary intervention (PCI). "The overuse of PCI is an insidious change in the culture of cardiology that needs to be reversed," he said. The use of PCI was established in MI, high-risk unstable angina and cardiogenic shock. However, its use in stable disease was a totally different question.

"There's no beneficial influence on mortality - PCI does nothing to prevent heart attacks. All we are doing is providing short term relief of chest pain. It's not [illegible] that sign out the

Concerns Prompt Some Hospitals To Pare Use of Drug-Coated Stents

By Sylvia Pagán Westphal

Rising concern over potentially deadly blood clots has led some cardiac centers to cut back on use of drug-coated stents—tiny, wire-mesh tubes that have propped open the arteries of more than three million heart patients since their introduction in 2003.

The moves come as a growing number of studies question the effectiveness and safety of the stents, which are coated by drugs to prevent arterial scarring. They have quickly become by far the most common form of stent in use, generating $5.3 billion in sales last year in a field dominated by Boston Scientific Corp. and Johnson & Johnson.

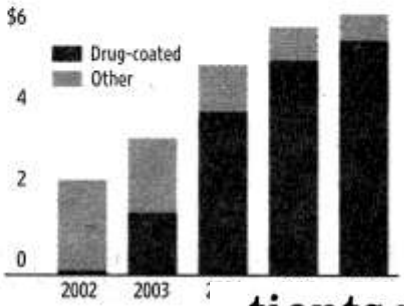
Hospitals aren't drastically curbing use of coated stents, and there's no indication yet of an overall decline in sales of them. But some leading hospitals have started substituting uncoated, bare-metal stents in some patients.

Moreover, the debate over the safety of drug-coated stents could signal turmoil in the booming industry. Drug-coated stents, which cost about $2,300 apiece, are far more profitable than the uncoated variety, which sell for about $700.

The new research also raises questions of long-term safety risks for patients who already have the devices. Comparing drug-coated stents and uncoated, bare-metal stents, a recent Swiss study found 3.3 more heart attacks and deaths per 100 patients with the drug-coated variety, beginning six months after implantation and ending a year later. The heart attacks and deaths were mostly attributed to blood clots.

Expanding Pipeline

World-wide stent revenue, in billions



Source: Bank of America

Stents are small n
to keep arteries op
cleared of fatty depo
prevent a future he
risky heart-bypass s
heart patients have r
they won federal ap
1990s.

But stents can trigger the growth of scar tissue that gradually re-narrows the artery, a condition called restenosis. The condition rarely leads to deaths from heart attacks, but can affect a patient's quality of life by causing chest pain. If restenosis progresses, a patient must get the area opened up again—a process called "revascularization."

Drug-coated stents were designed to

Please Turn to Page A15, Column 1

The Wall Street Journal
Thursday ,June 22, 2006

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paring drug-coated stents and uncoated
bare-metal stents, a recent Swiss study
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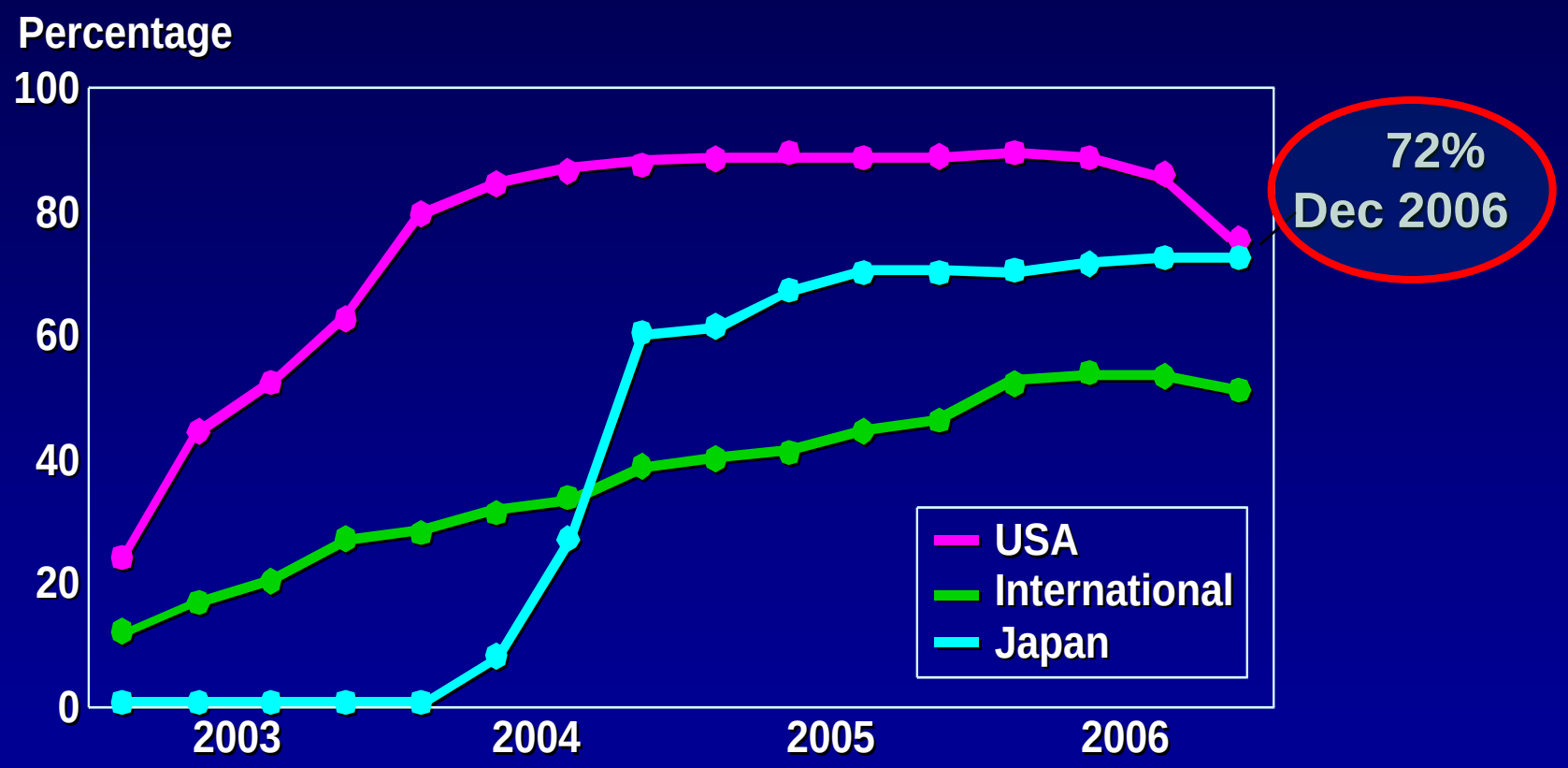
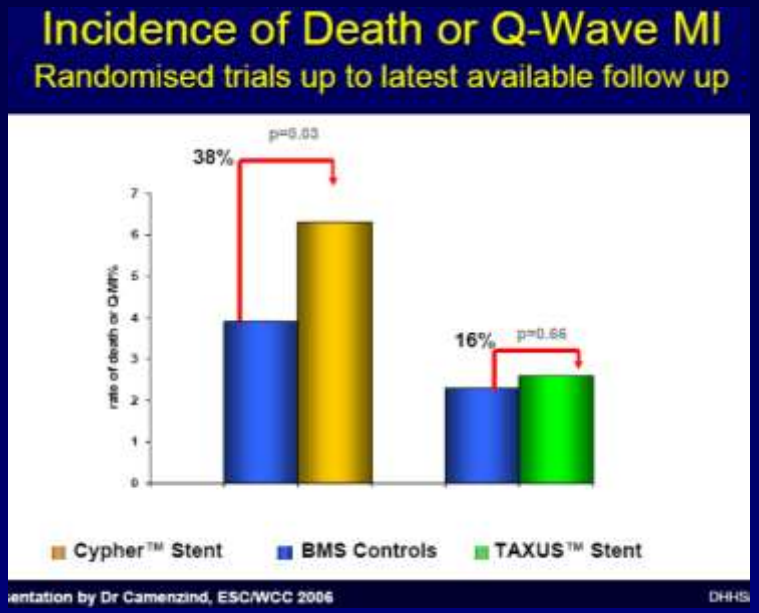
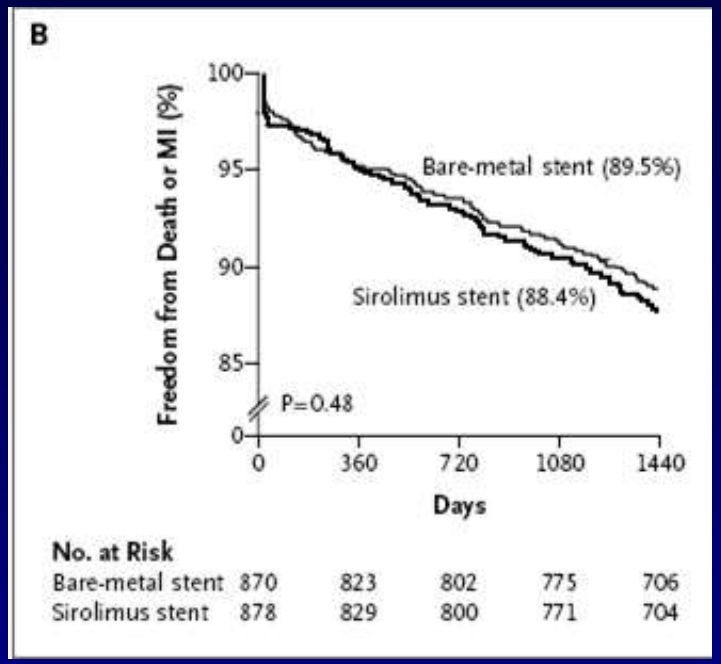
per 100 patients with the drug-coated vari
ety, beginning six months after implanta

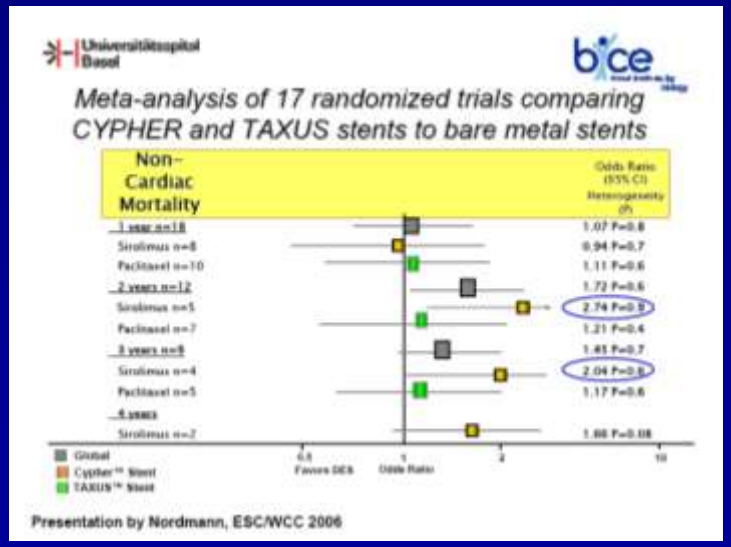
Use of DES world wide





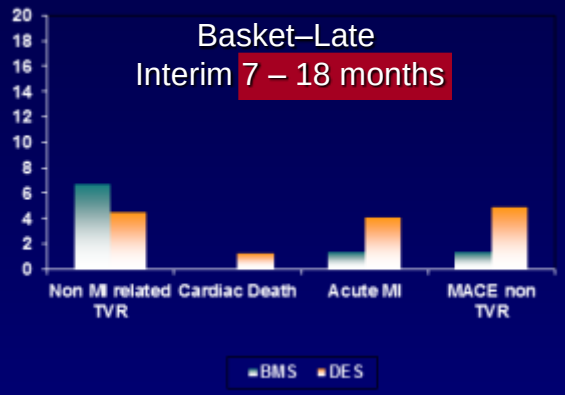


Spaulding C, et al. N Engl J of Med. March 2007

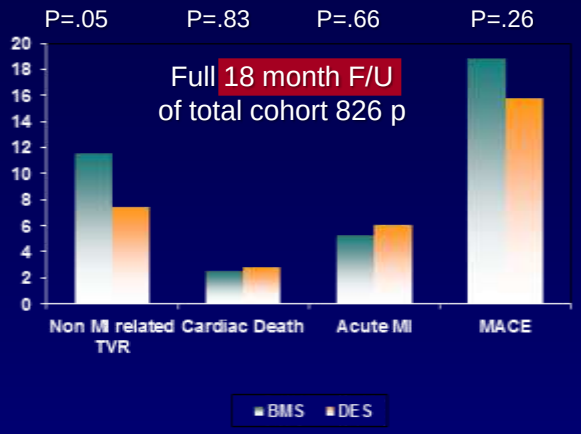


?

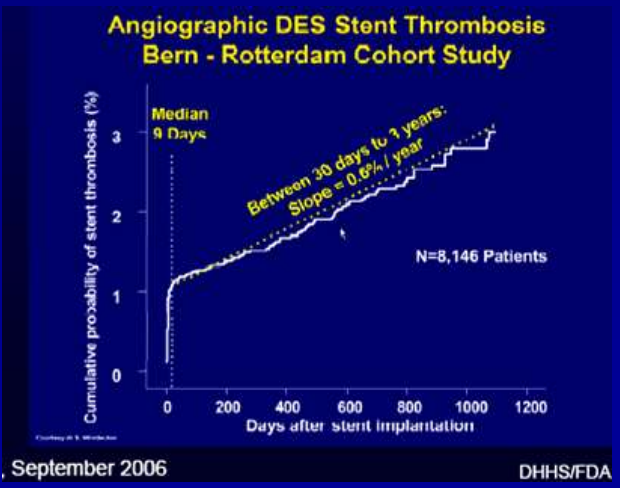
Complete FU



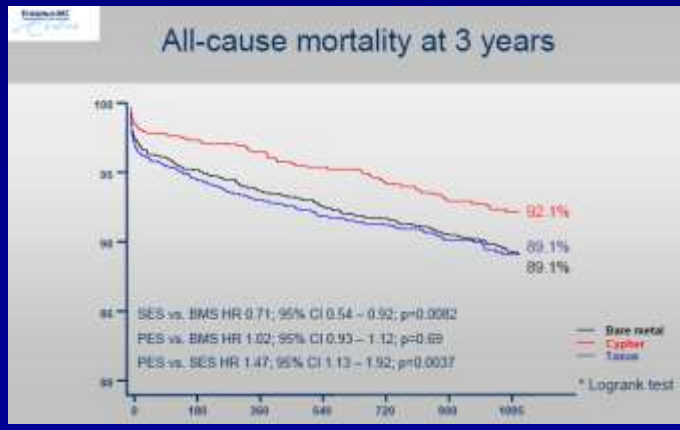
Pfisterer et al. J Am Coll Cardiol 2006; 48:



Kaiser C. World Congress of Cardiology
September 2006; Barcelona, Spain



3 Years Follow-up Comparision with BMS



Internal Medicine World Report January 2007

FDA Panel Discourages Off-Label Use of Drug-Eluting Stents

Continuing Antiplatelet Therapy Emphasized

BY WAYNE KUZNAR

GAITHERSBURG, Md—After 2 days of testimony, a uncertainty hung over advisory panel hearing to examine the safety eluting stents (DESs). I DESs were deemed to additional risk to pati used for simple ster called on-label use, with bare-metal stents

But when used off-l as for bifurcation lesio tiple stenoses, the ben ratio of DESs was not a at least 60% of DESs are used off-label, and some estimate this

The one certainty is that when used outside the indicated patient populations, DESs are associated with an increased risk of stent thrombosis, death, and myocardial infarction (MI) compared with on-label use, but the

Continued on page 10

“Off – label” uses = Not always bad

ISIS 2 published in 1988
Aspirin reduced Mortality in AMI

FDA approved Aspirin for this indication in 1998

There was a 10 years delay !!!!!!!!!!

Courtesy Conrad Simpfendorfer

Thanks a lot Dr. Camenzind! Because of your “metanalysis”…..

……we have learnt that evidences are not always obvious

…... industry and physicians will look for deeper pathophysiological understanding of new developments

…... we are moving faster towards “true” new generations of DES

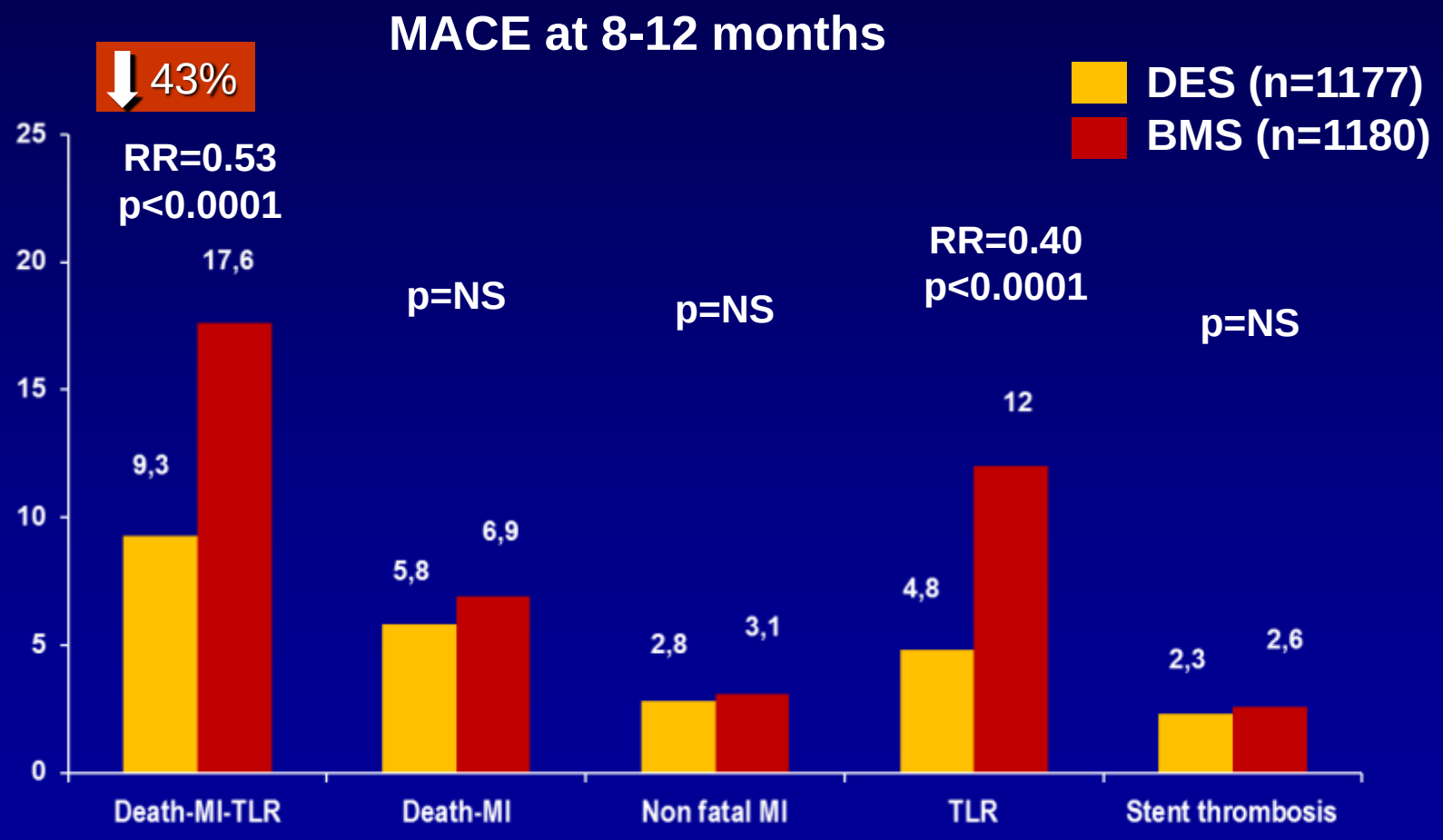
…... the debate about “off label” indications and Regulatory Agencies is now wide open

…... we understood that we were right extending the use of DES to more complex patients, improving quality of life and MACE.

…... we “ALL” have learnt that medical evidences should be addressed in scientific forums and peer-review Journals but NOT in newspaper Headlines.

DES for AMI

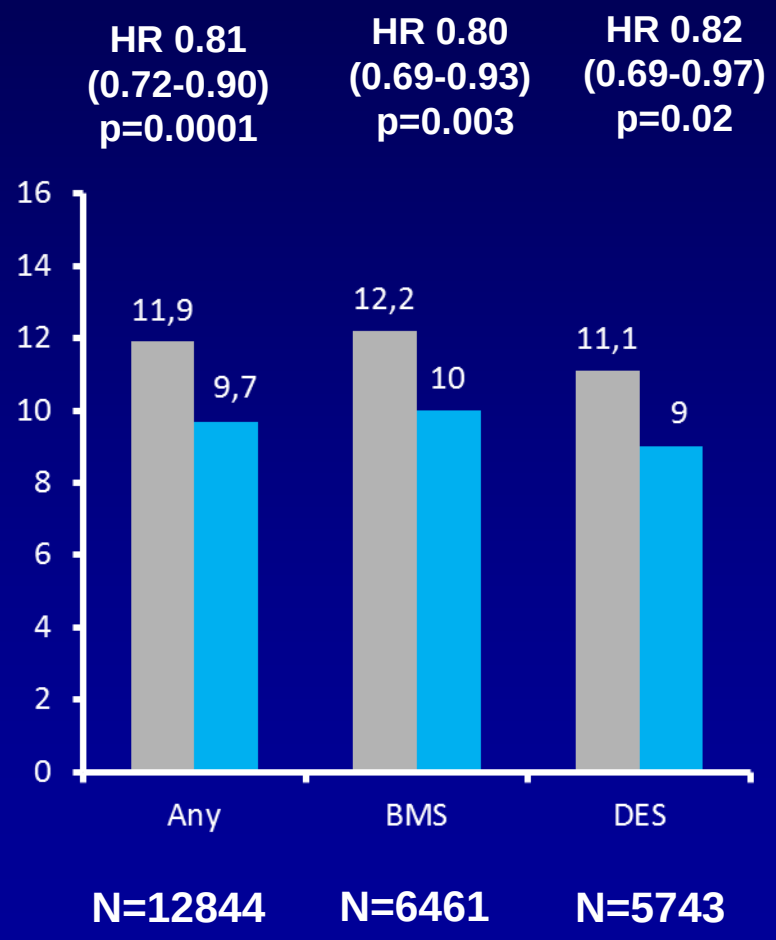
Metanalysis (n= 2357 p)



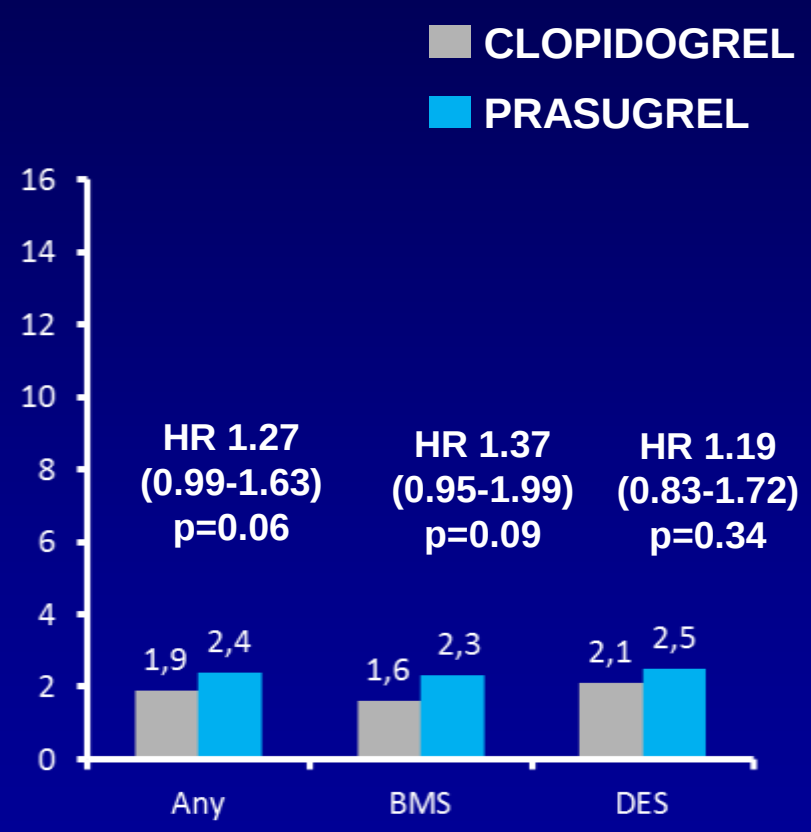
Pasceri V. Am Heart J 2007;153:749-754.

DES vs. BMS in NSTEMI

CVD/MI/CVA



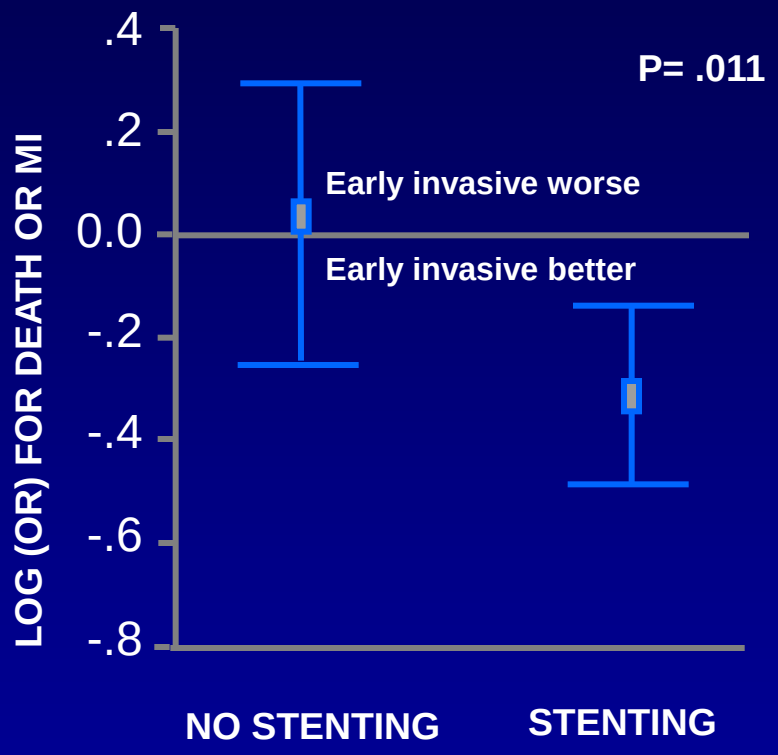
Major Bleeding

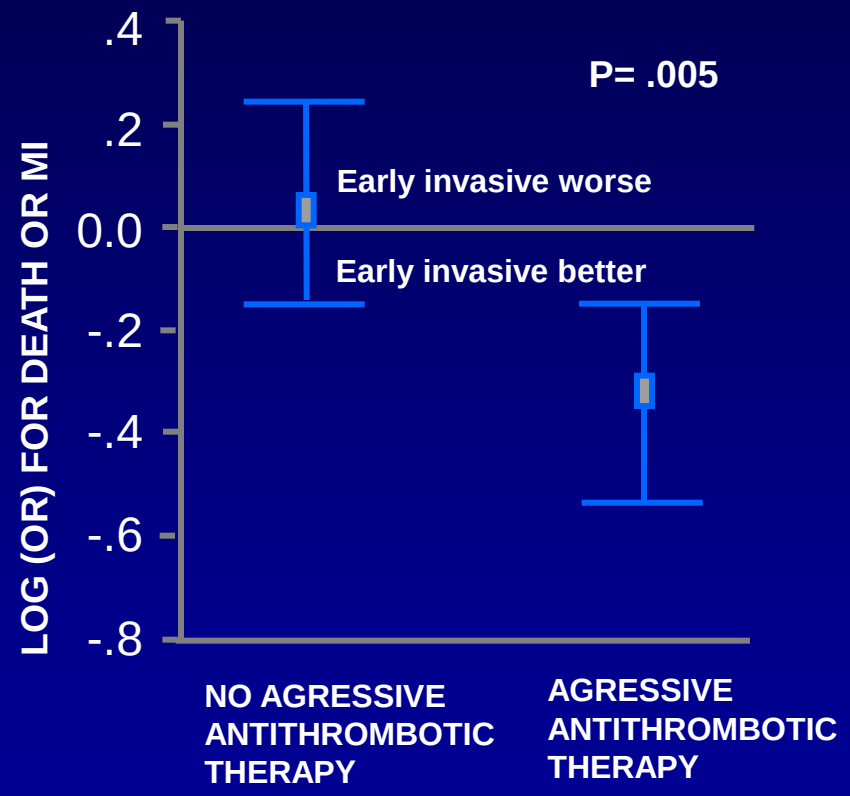


TRITON/TIMI 38 **Key Efficacy, Safety EP: Stratified by Stent Type**

Invasive vs. Conservative in NSTEMI

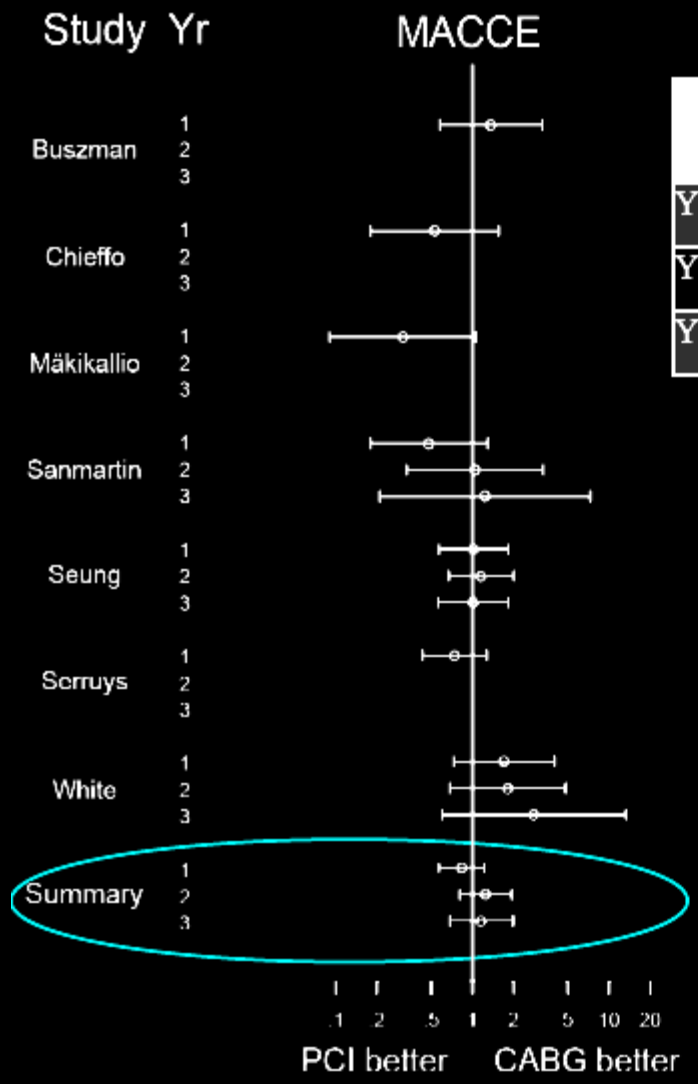
Very early PCI in ACS





Meta-regression. Am Heart J 2005

Meta-Análisis
(3773 pacientes)



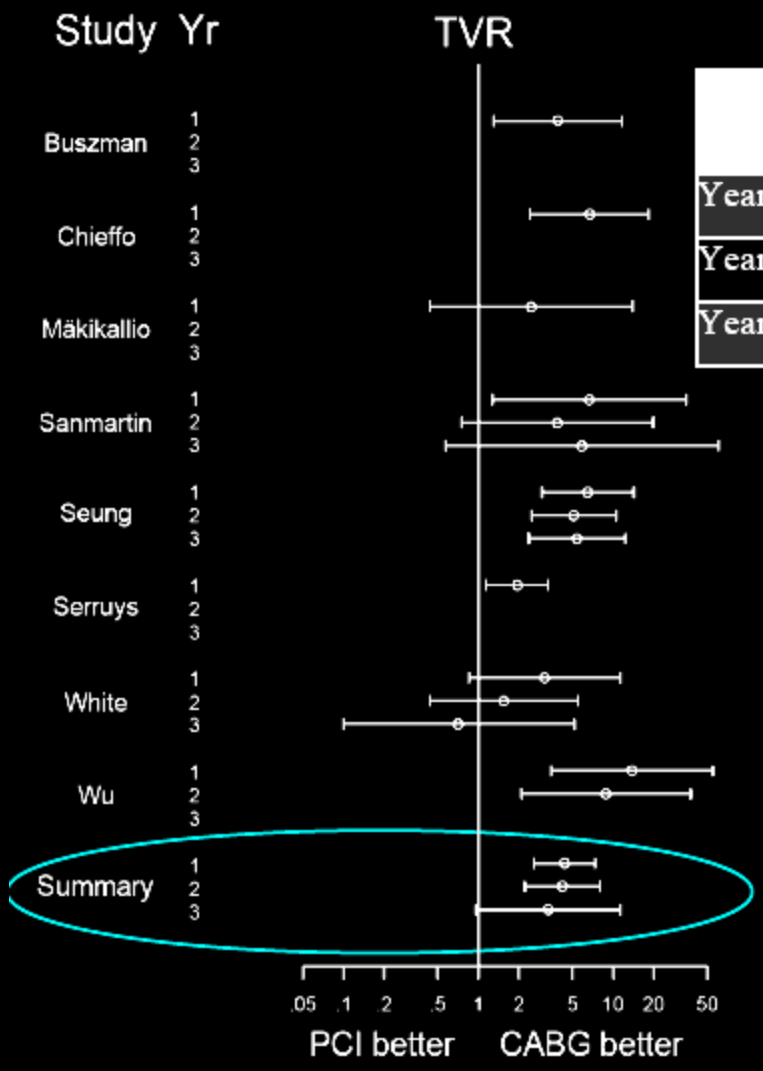
	CABG n	PCI n	Summary OR	95% CI
Year 1	1614	1239	**0.84**	0.57-1.22
Year 2	652	432	**1.25**	0.81-1.94
Year 3	451	236	**1.16**	0.68-1.98

Death, MI and Stroke

No differences up to 3 years

Naik H et al. JACC Intervention 2009; 2: 730-747

Meta-Análisis
(3773 pacientes)



	CABG n	PCI n	Summary OR	95% CI
Year 1	1692	1240	**4.36**	2.60-7.32
Year 2	699	417	**4.20**	2.21-7.97
Year 3	447	211	**3.30**	0.96-11.33

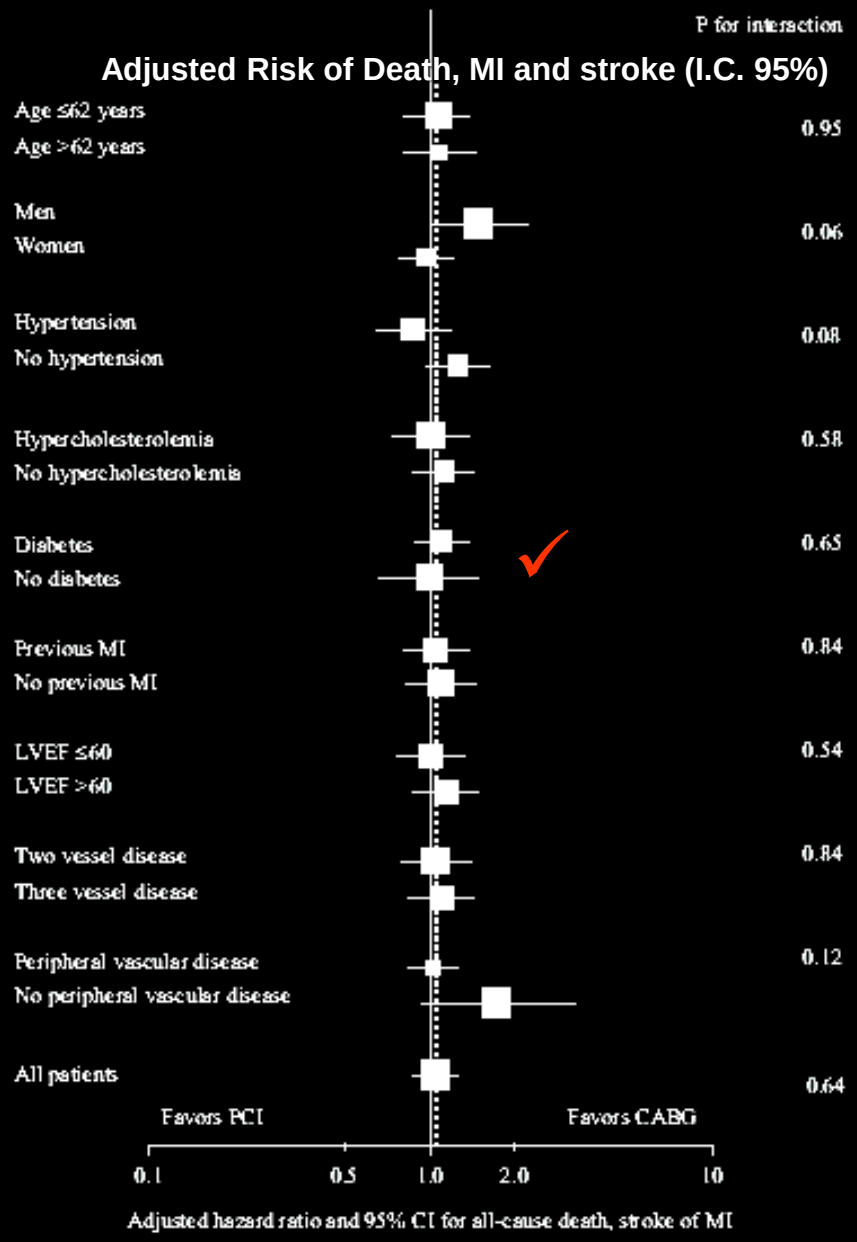
TVR

Increased up to 3 years

Naik H et al. JACC Intervention 2009; 2: 730-747

Metánalisis DES vs. CABG

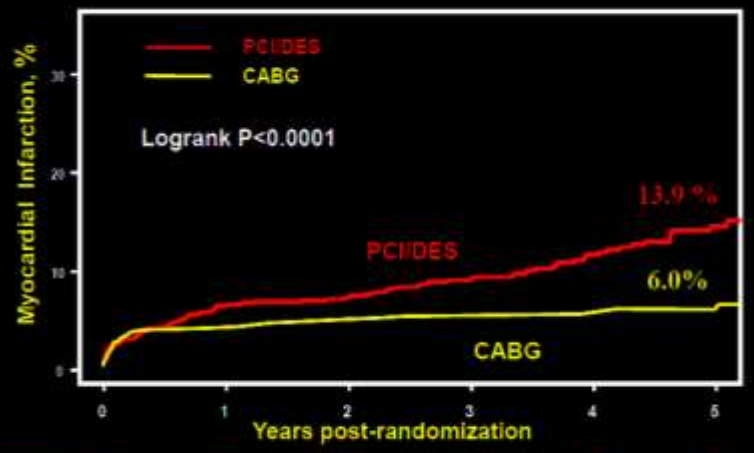
Diabetes



Daemen J et al. Circulation 2008;118;1146-1154

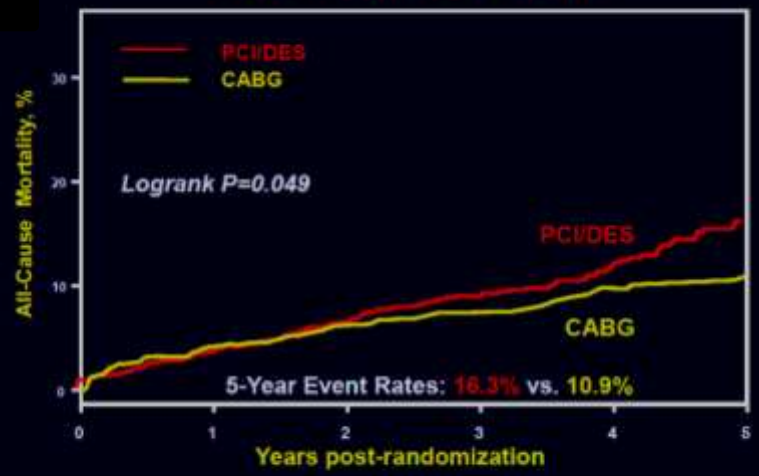
FREEDOM

MYOCARDIAL INFARCTION



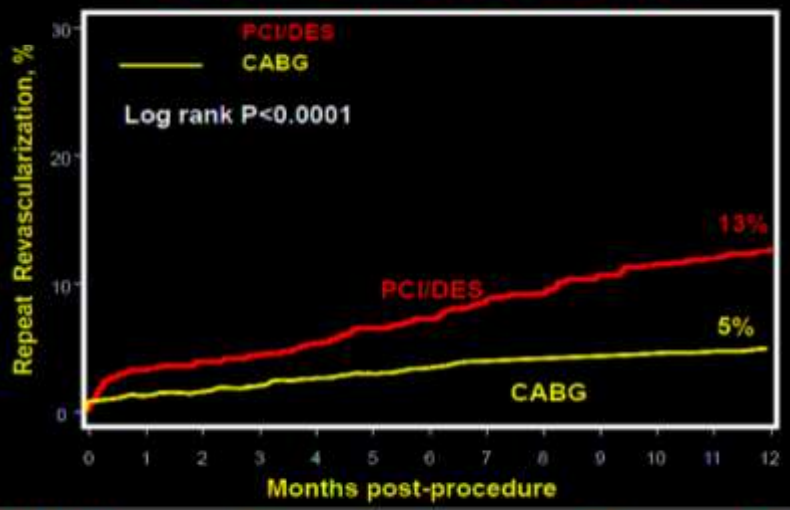
PCI/DES N	953	853	798	636	422	220
CABG N	947	824	772	629	432	229

ALL-CAUSE MORTALITY



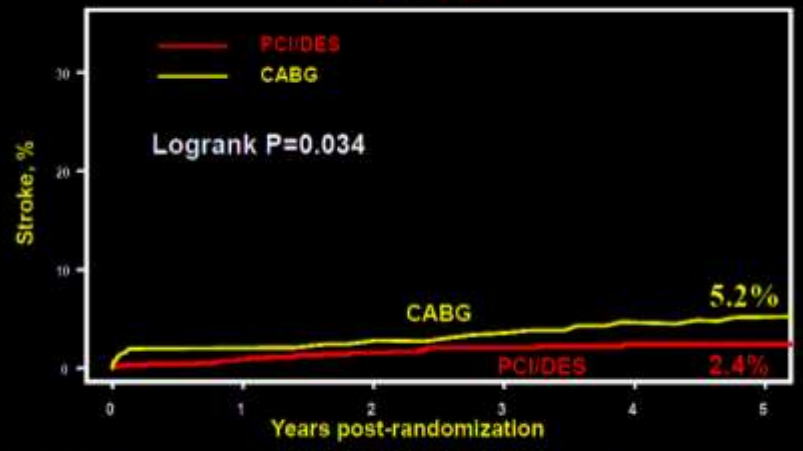
PCI/DES N	953	897	845	665	466	243
CABG N	947	855	806	655	449	238

REPEAT REVASCULARIZATION



PCI/DES N	944	887	856	818	792
CABG N	911	858	836	825	806

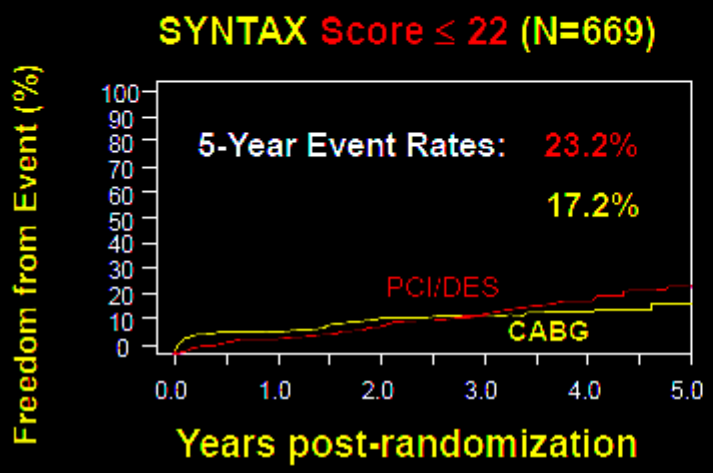
STROKE

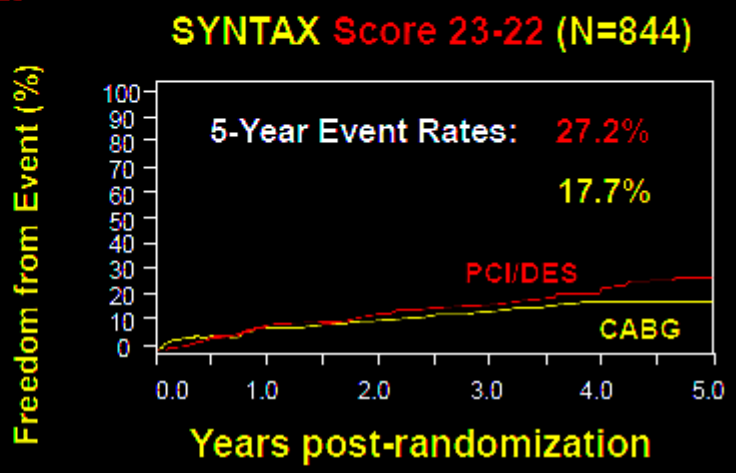


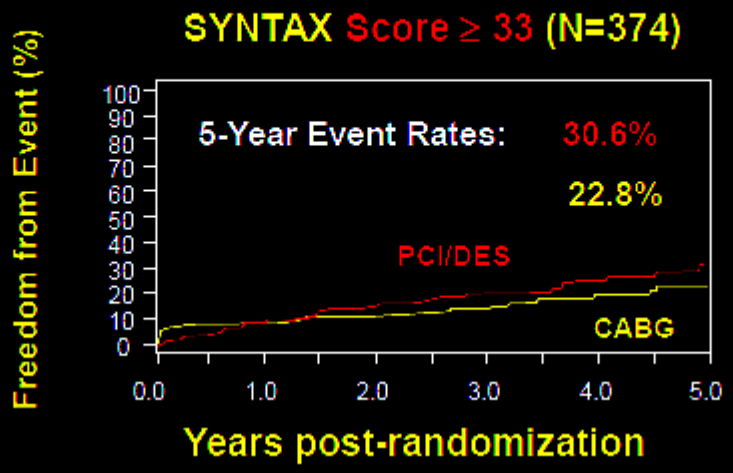
PCI/DES N	953	891	833	673	460	241
CABG N	947	844	791	640	439	230

Fuster V. AHA Nov. 3–7, 2012

PRIMARY ENDPOINT – DEATH / STROKE / MI
TREATMENT / SYNTAX INTERACTION - p=0.58







Fuster V. AHA Nov. 3–7, 2012

BASELINE CHARACTERISTICS BY TREATMENT ASSIGNMENT

Characteristic	PCI/DES	CABG	P-value*
HDL cholesterol – mg/dL	38.9±10.9	39.4±11.4	0.34
Angina			0.25
Stable	68%	71%	
Unstable	32%	30%	
LV Ejection Fraction (<30%)	0.8%	0.3%	0.28
LV Ejection Fraction (< 40%)	3%	2%	0.07
EuroSCORE ✔ [Median (IQR)]	2.7±2.4 [1.9 (1.3, 3.1)]	2.8±2.5 [2.0 (1.3, 3.3)]	0.52
SYNTAX score ✔	26.2±8.4	26.1±8.8	0.77
No. of lesions	5.7±2.2	5.7±2.2	0.33
Chronic total occlusion	6%	6%	0.99
Bifurcation	22%	21%	0.06

Fuster V. AHA Nov. 3–7, 2012

IMPACTO CLÍNICO DE LOS STENTS

Revascularización del vaso culpable (Megametanálisis)

Tipo de estudio	N de Pacientes	N de Estudios	Riesgo Relativo	Valor de P
RCT: Todos	7291	16	0.45	<0.001
RCT: “on-label”	4618	9	0.53	<0.001
RCT: “off-label”	2673	8	0.38	<0.001
Registros	73 819	17	0.53	<0.001

*Modelo de efecto randomizado

RCT= Estudios Randomizados

⬇ 47 to 62%

Kirtane AJ, Stone GW. Comprehensive meta-analysis of DES vs BMS randomized trials and registries; ACC 2008; Chicago, IL.

IMPACTO CLÍNICO DE LOS STENTS

Mortalidad de cualquier causa (Megametanálisis)

Tipo de estudio	N de Pacientes	N de Estudios	Riesgo Relativo	Valor de P
RCT: Todos	8867	21	0.97	0.72[a]
RCT: “on-label”	4818	10	1.05	0.69[a]
RCT: “off-label”	4049	12	0.84	0.24[a]
Registros	161 232	28	0.80	<0.001[b]

a. Modelo de efecto fijo

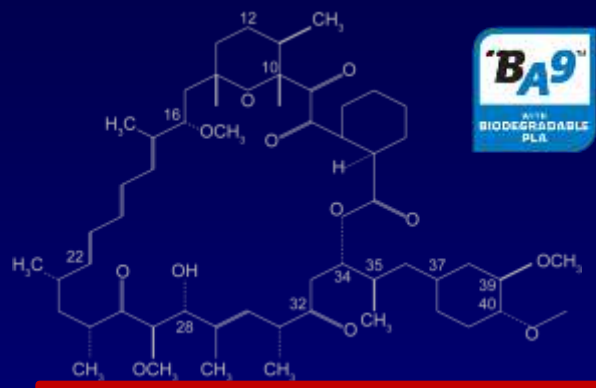
b. Modelo de efecto randomizado

RCT= Estudios Randomizados

⬇ 20%

Kirtane AJ, Stone GW. Comprehensive meta-analysis of DES vs BMS randomized trials and registries; ACC 2008; Chicago, IL.

Biolimus-A9™ Eluting Stent



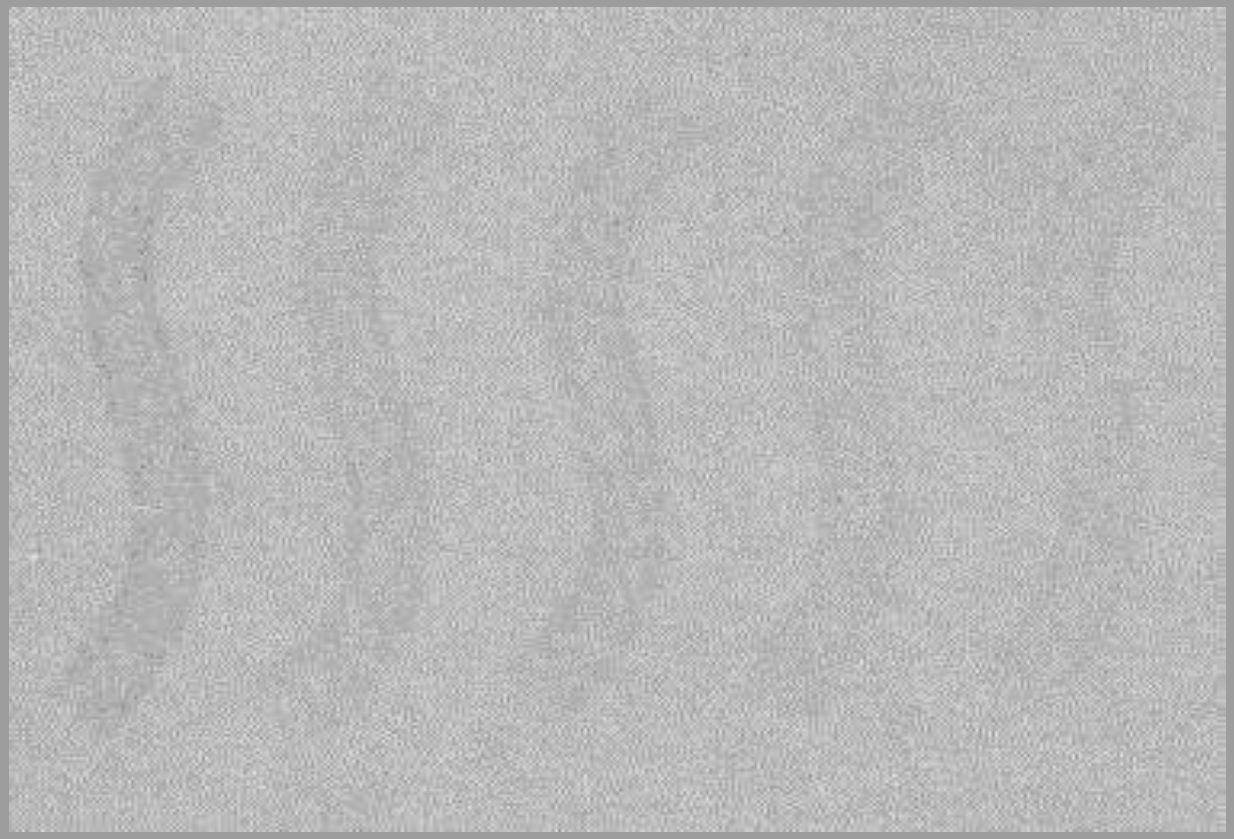
- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency as sirolimus.
- Biolimus 15.6 μg/mm applied solely to the abluminal stent surface.

- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after a 6-9 months period.

Turns into a BMS!!!

- Stainless steel stent platform has a strut thickness of 120 μm with a quadrature link design.

Visibility Bench Test Comparison



PtCr Promus Element™ Stent **0.0032”** (0.0813mm)	CoCr Xience V™ Stent **0.0032”** (0.0813mm)	CoCr Xience Prime™ Stent **0.0032”** (0.0813mm)	CoNi Endeavor™ Stent **0.0036”** (0.0914mm)	CoNi Resolute Integrity™ Stent **0.0035”** (0.0889mm)

Data on file. Based on 2.50 mm stents. Copper phantom to simulate body mass. Photographs taken by Boston Scientific. Bench test results may not necessarily be indicative of clinical performance.

Radiopacidad

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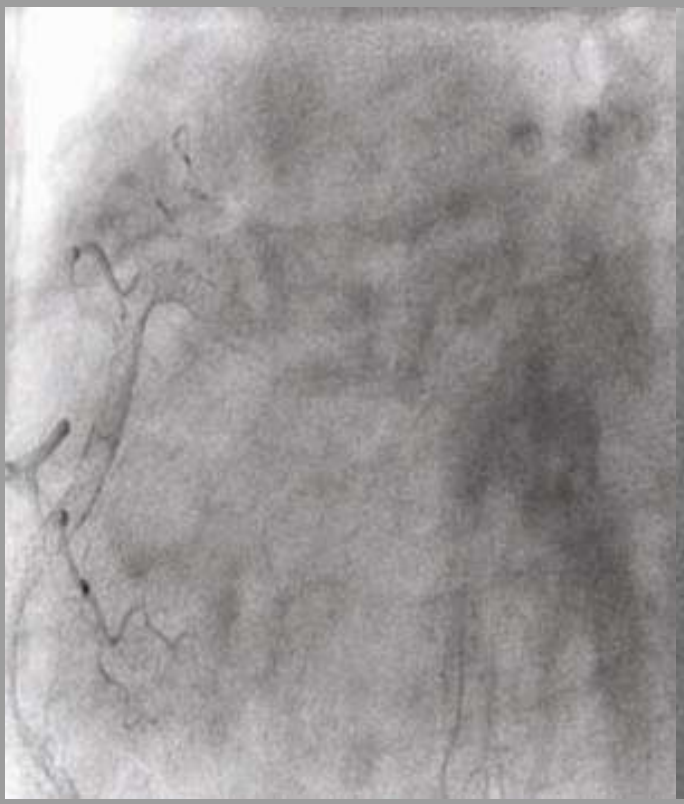
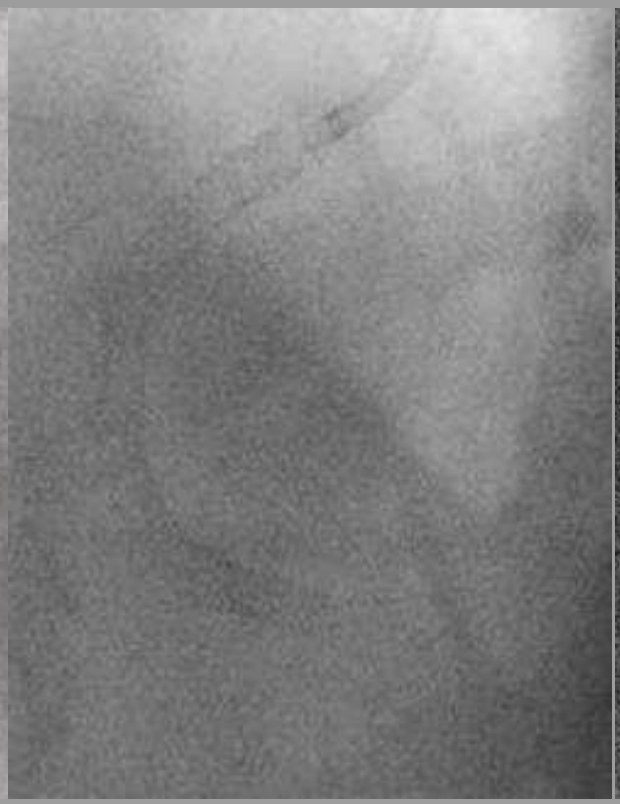
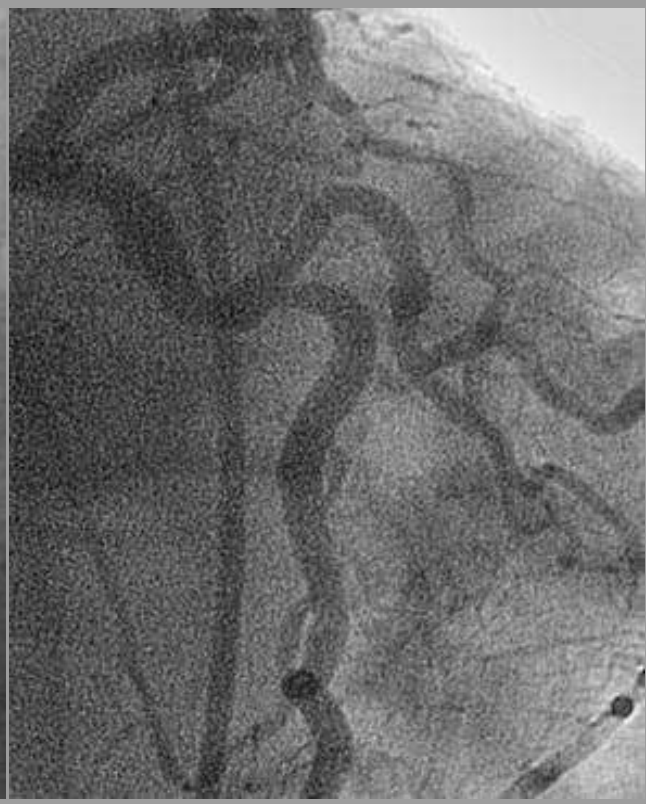
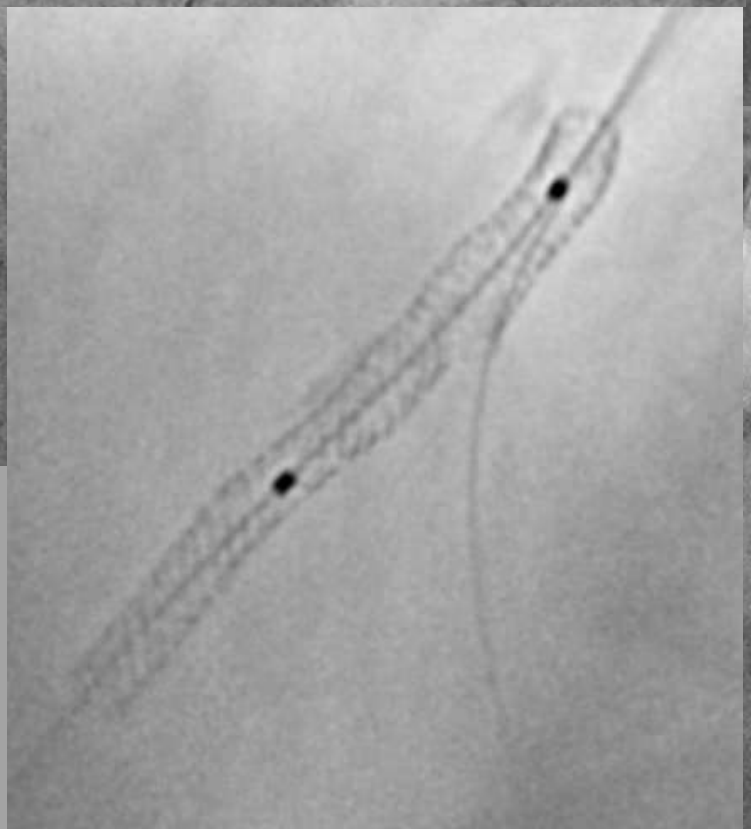
Conformabilidad







Access to side branches



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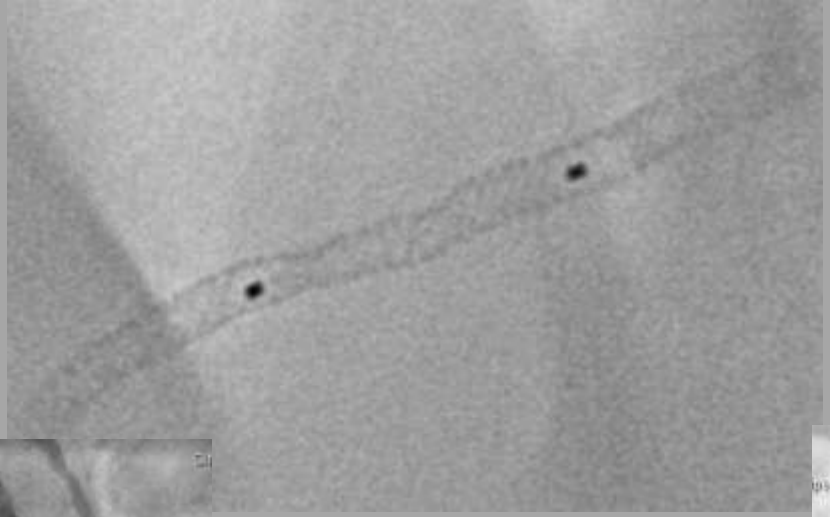
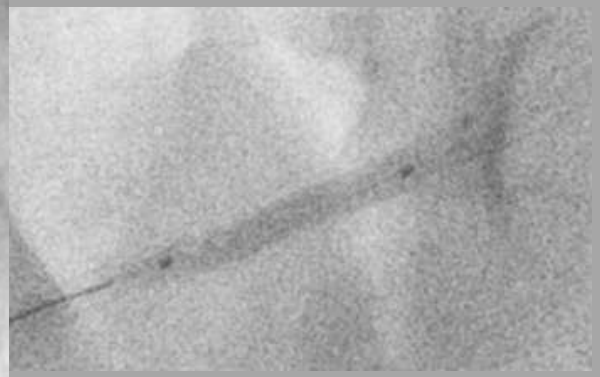
Fuerza Radial





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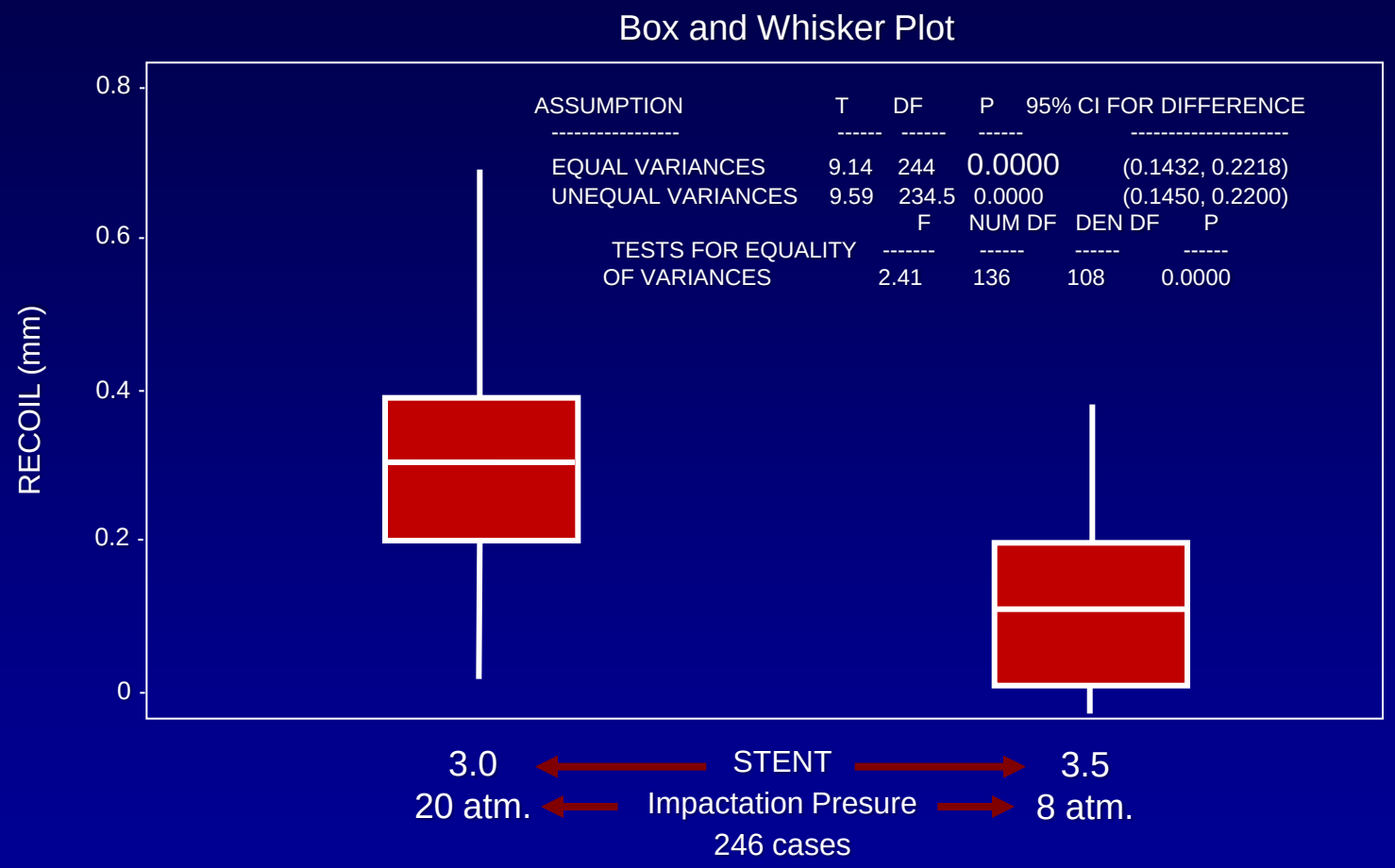
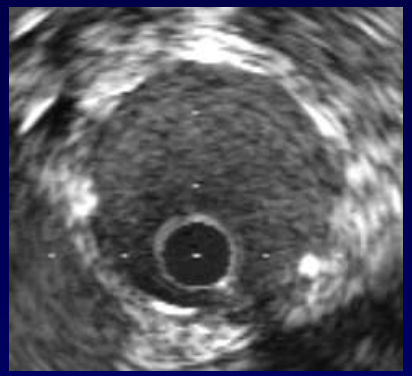
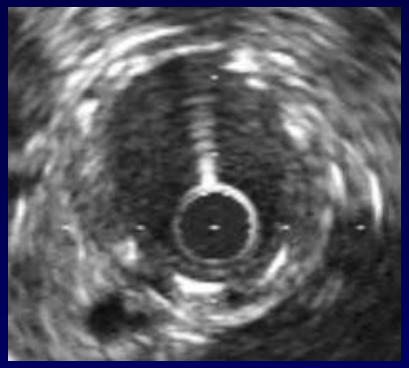
Overexpansion and acute loss



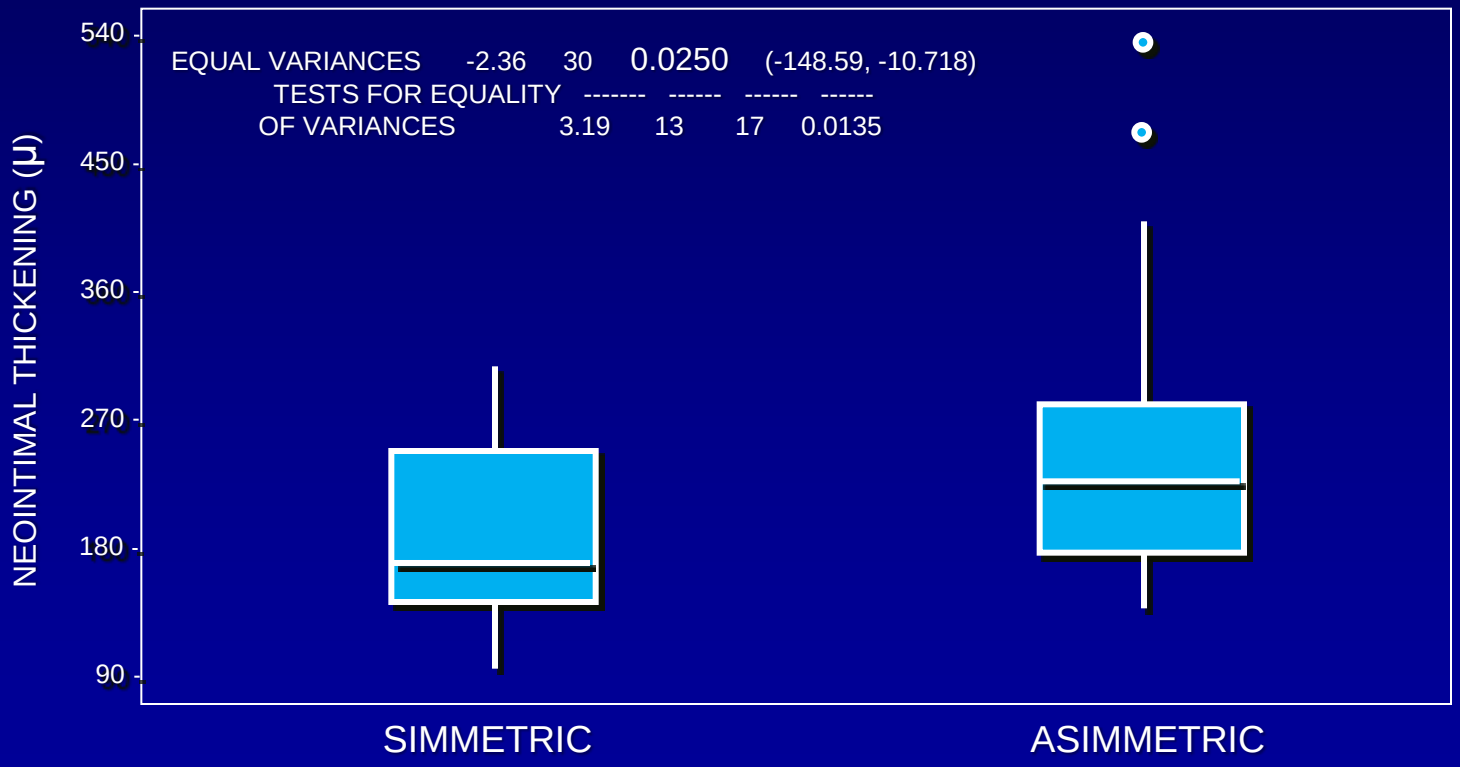
Berrocal D et al. Cardiovasc Pathol. 2008 Sep-Oct;17(5):289-96. Epub 2008 Feb 19.

Symmetry and restenosis



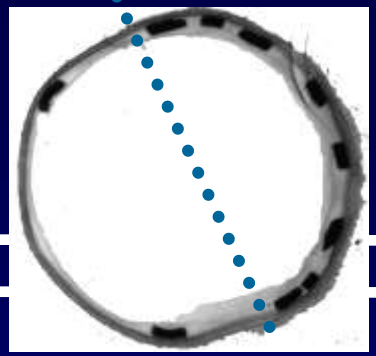


Box and Whisker Plot

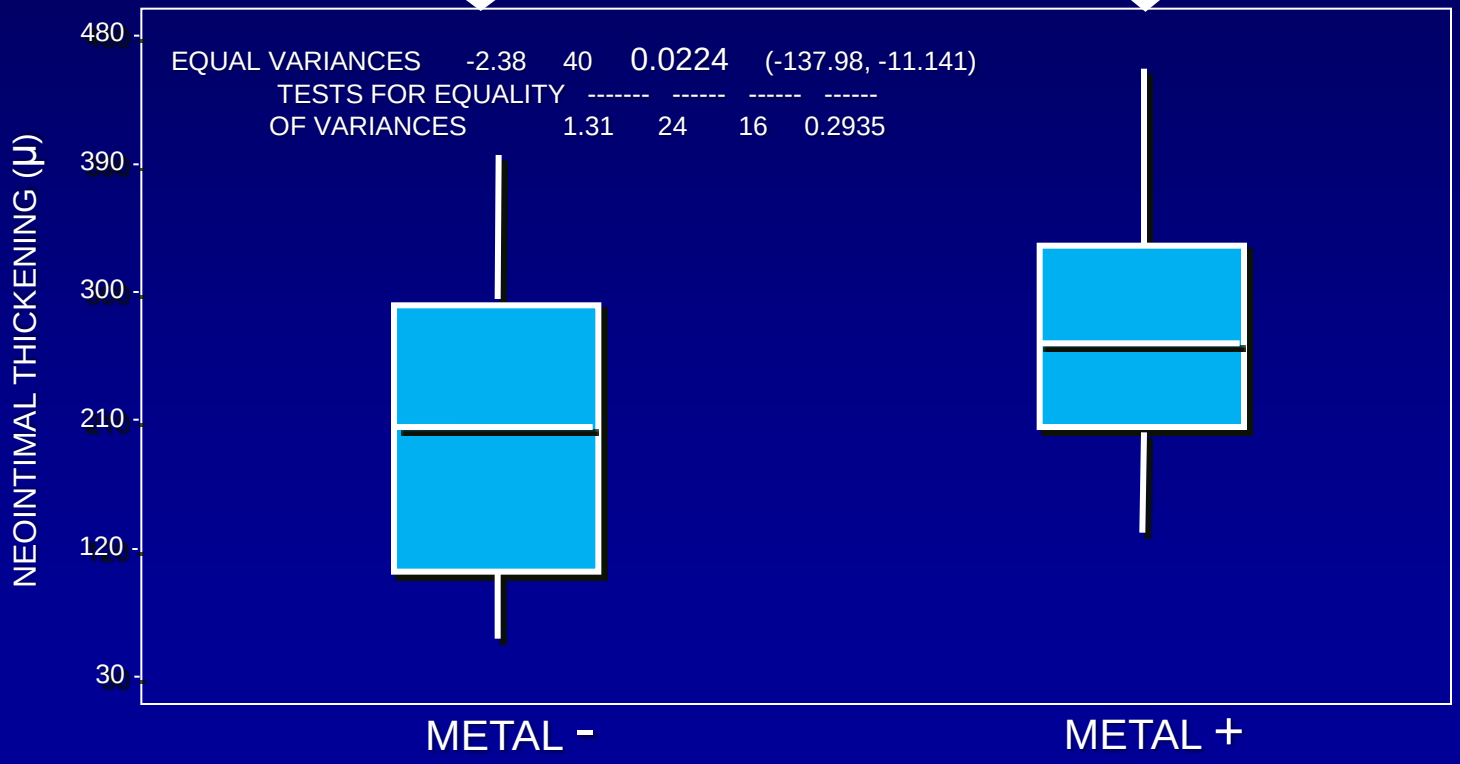


Berrocal D et al. Cardiovasc Pathol. 2008 Sep-Oct;17(5):289-96. Epub 2008 Feb 19.

Metal amount and restenosis

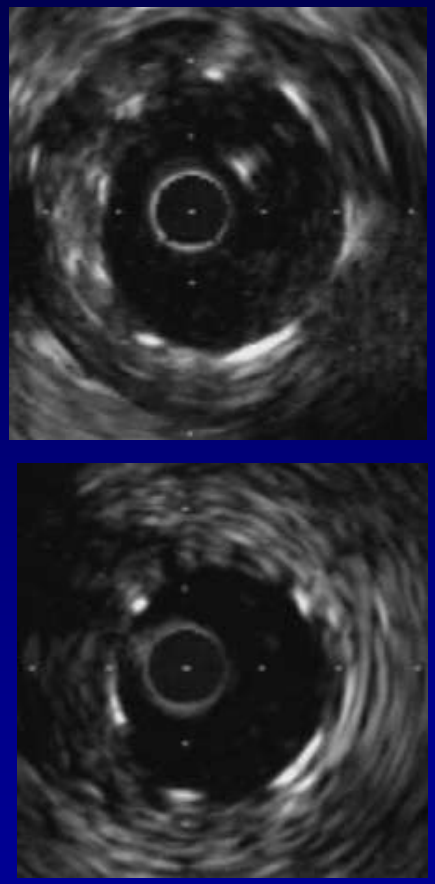


Box and Whisker Plot

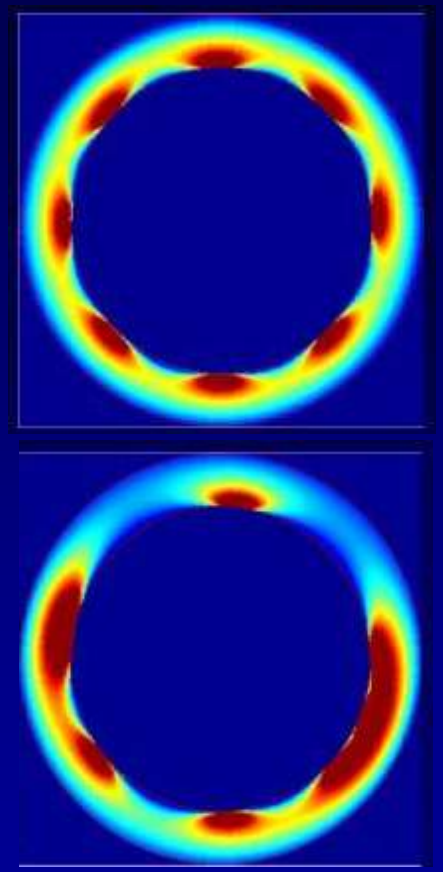


Berrocal D et al. Cardiovasc Pathol. 2008 Sep-Oct;17(5):289-96. Epub 2008 Feb 19.

Asymmetry and heterogeneous drug distribution

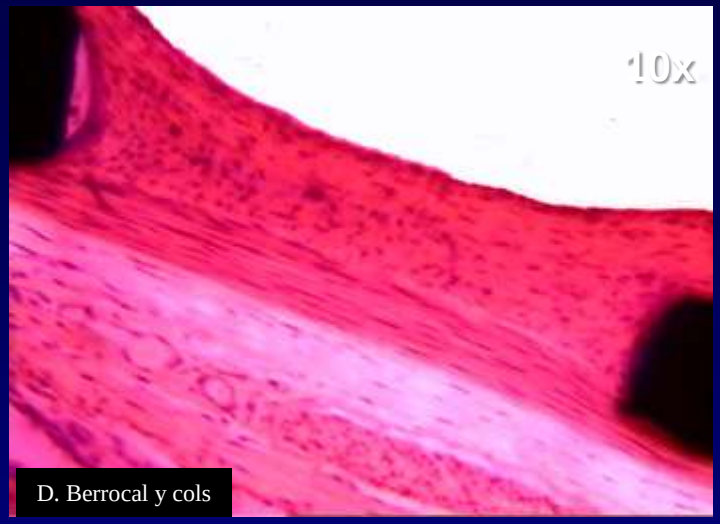


Berrocal et al,
Catheter Cardiovasc Interv. 2006

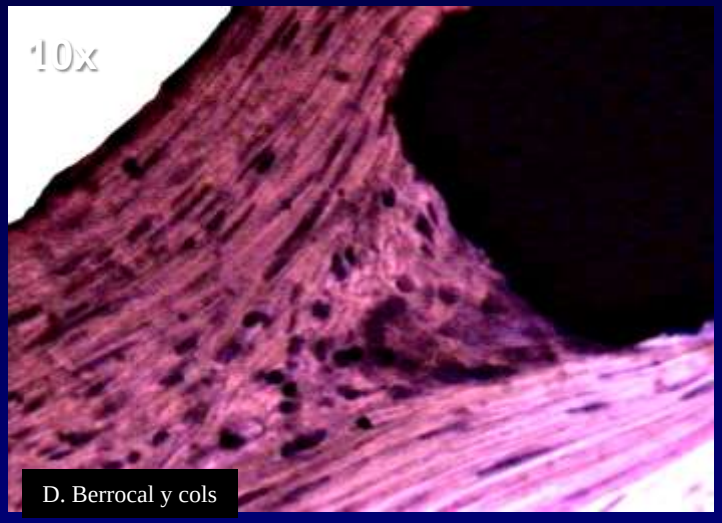


Hwang et al,
Circulation 2001

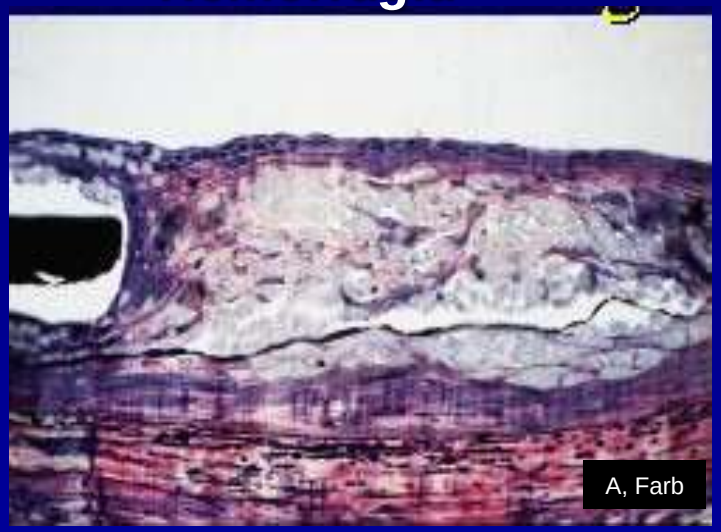
Reparación



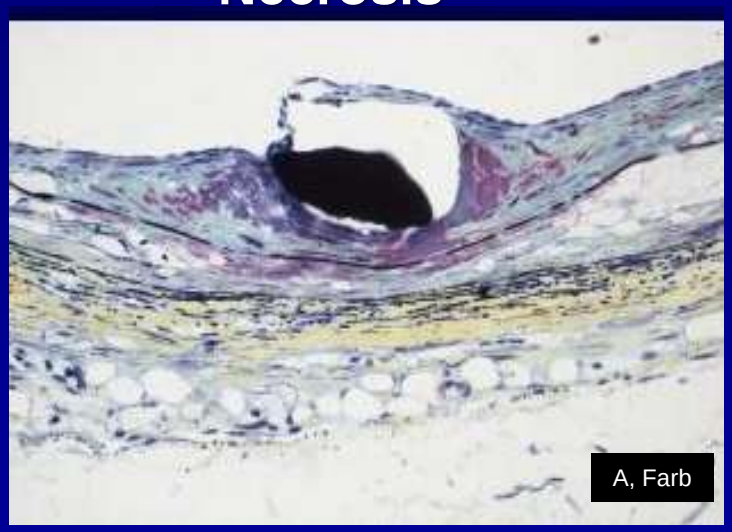
Inflamación

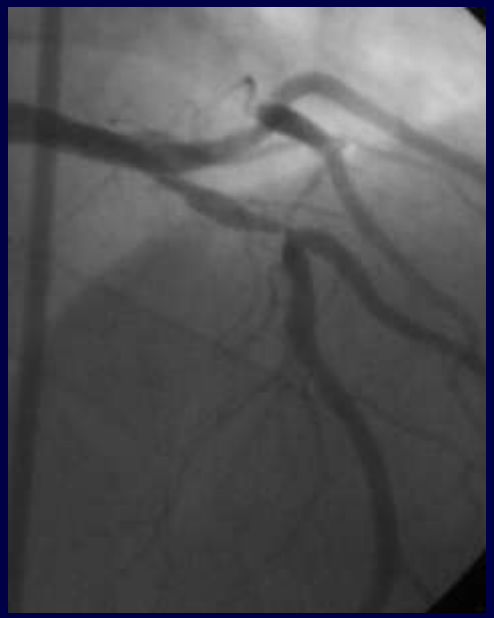


Hemorragia



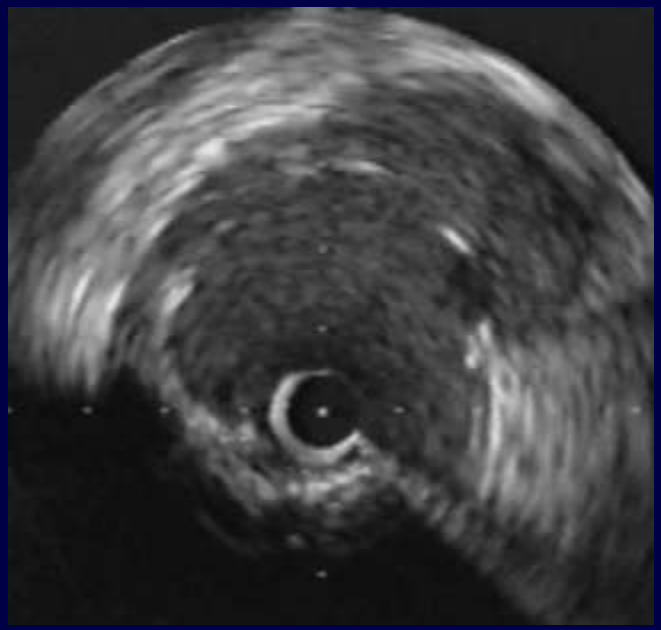
Necrosis





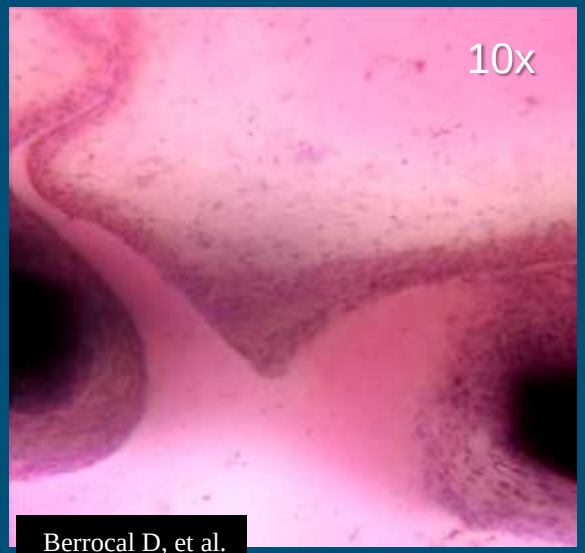
Berrocal D, et al.

Berrocal D, et al.

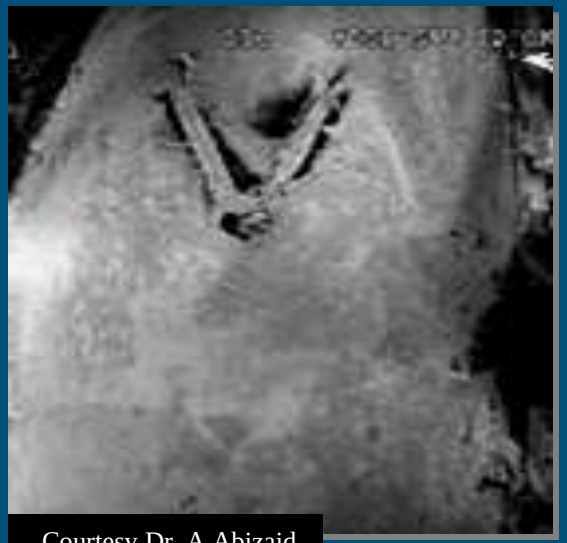


Berrocal D, et al.

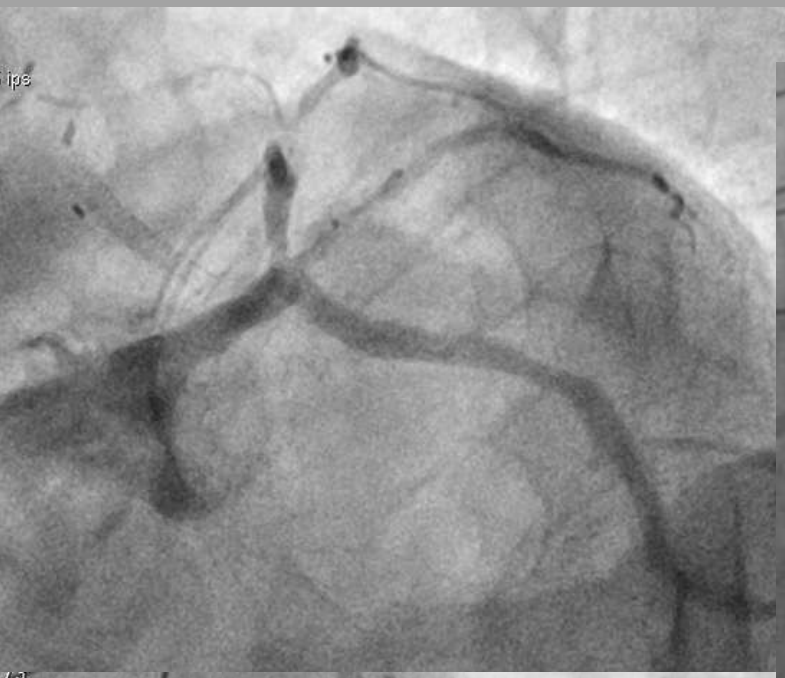
Berrocal D, et al.

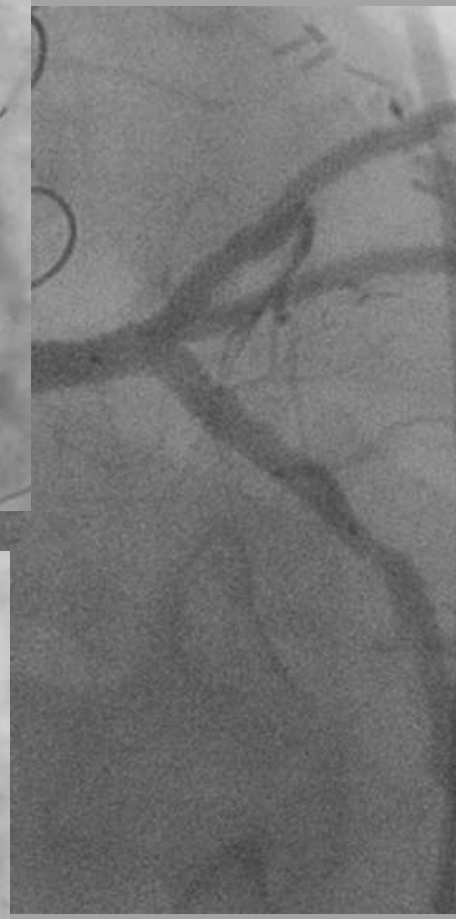


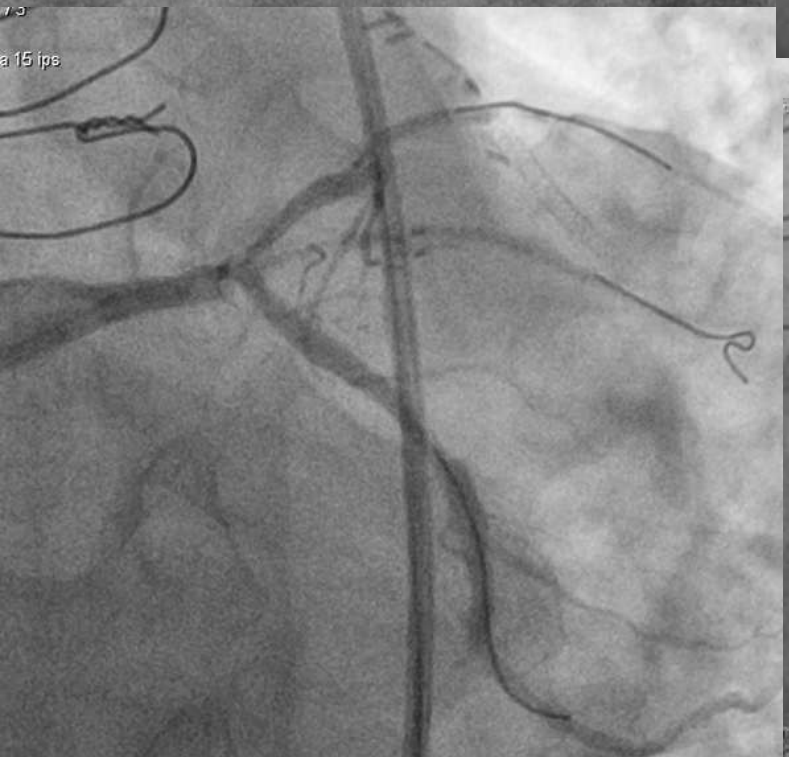
Berrocal D, et al.



Courtesy Dr. A Abizaid







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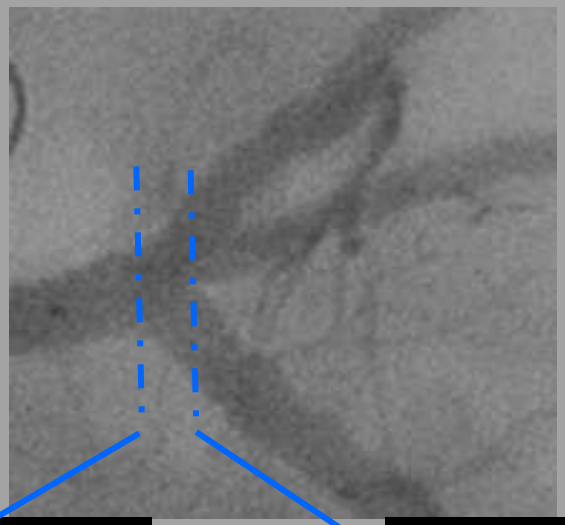

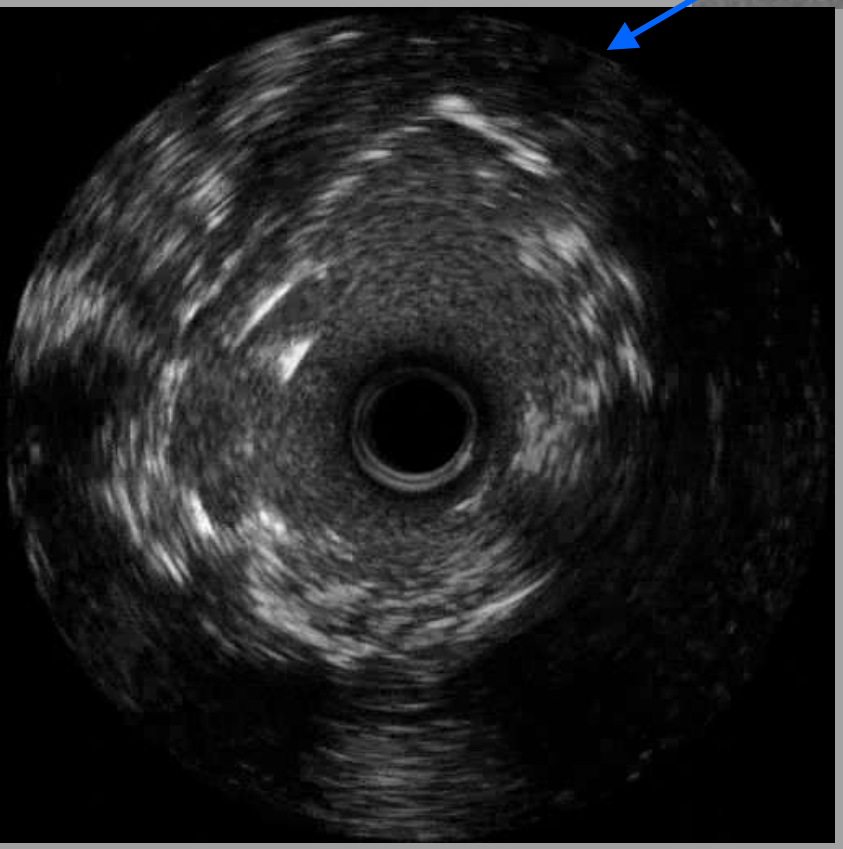

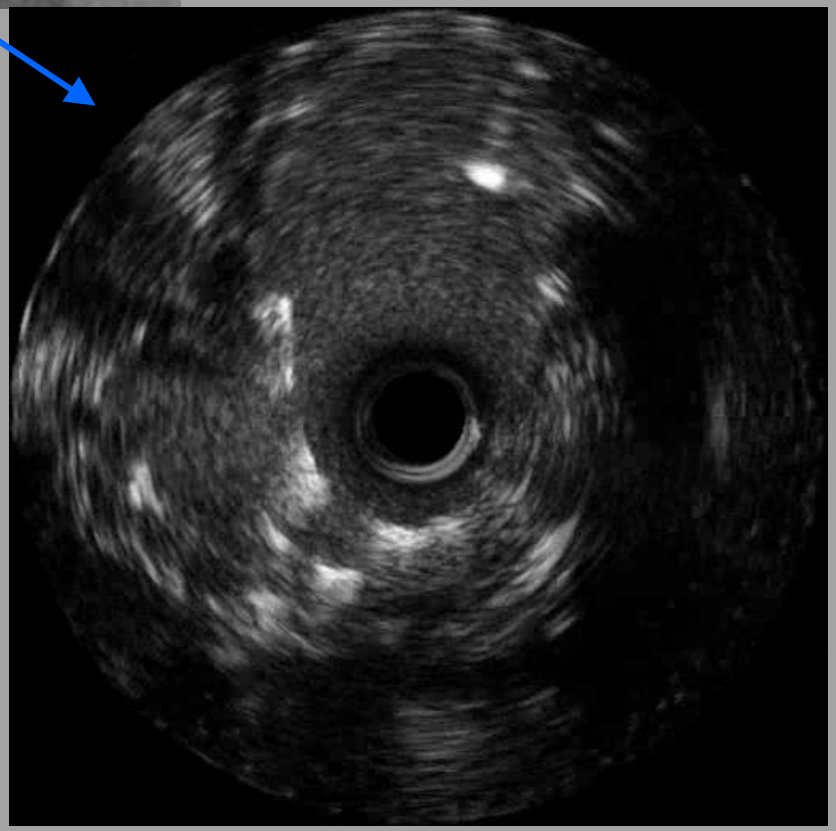

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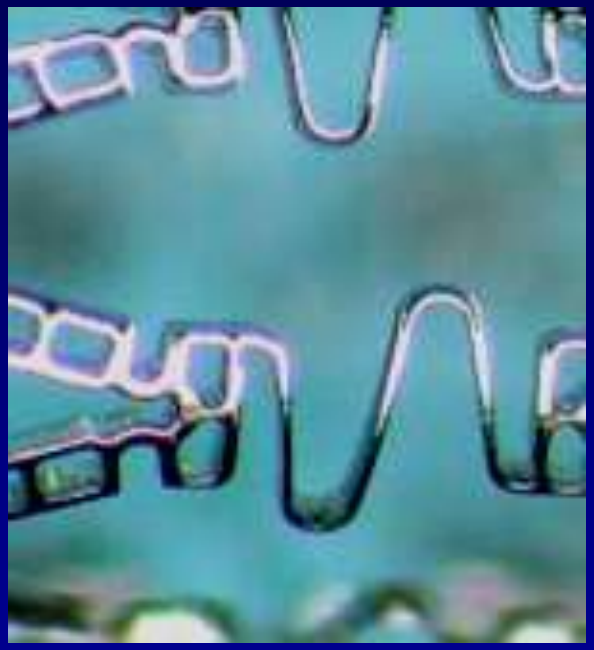
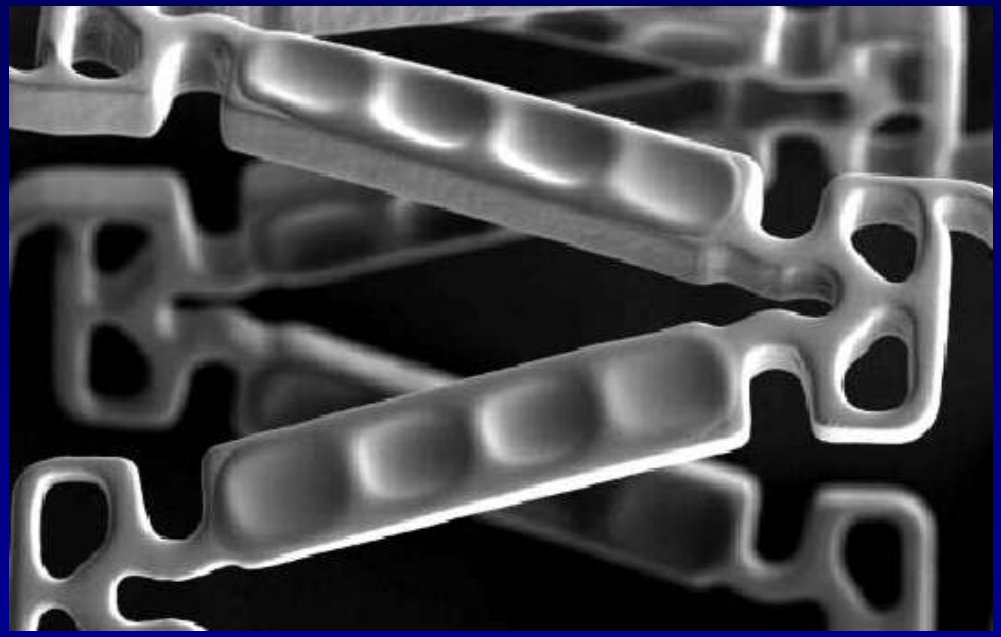
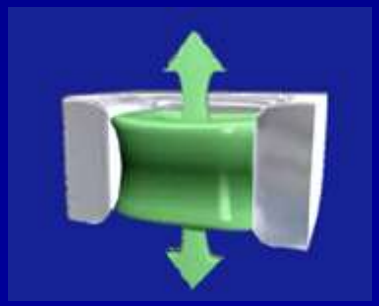
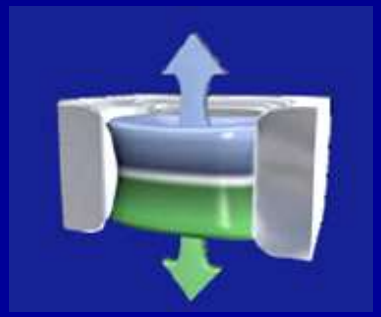
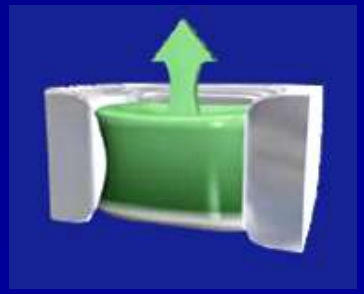
Drugs deposited in multi-layered degradable polymer inlays

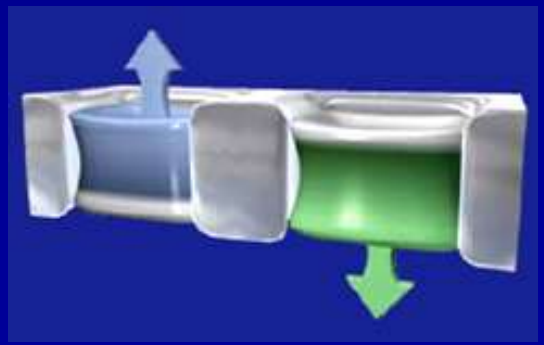




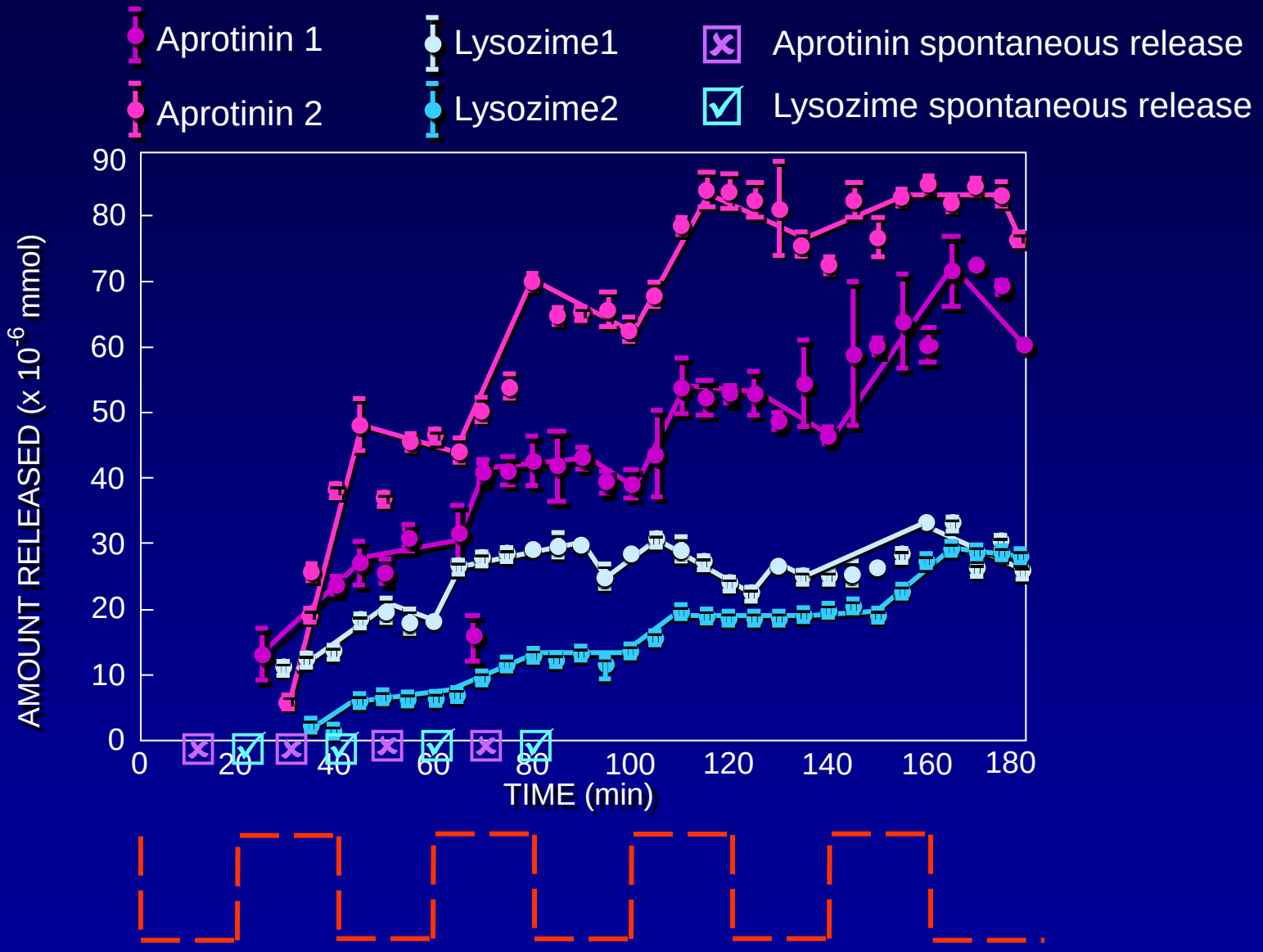






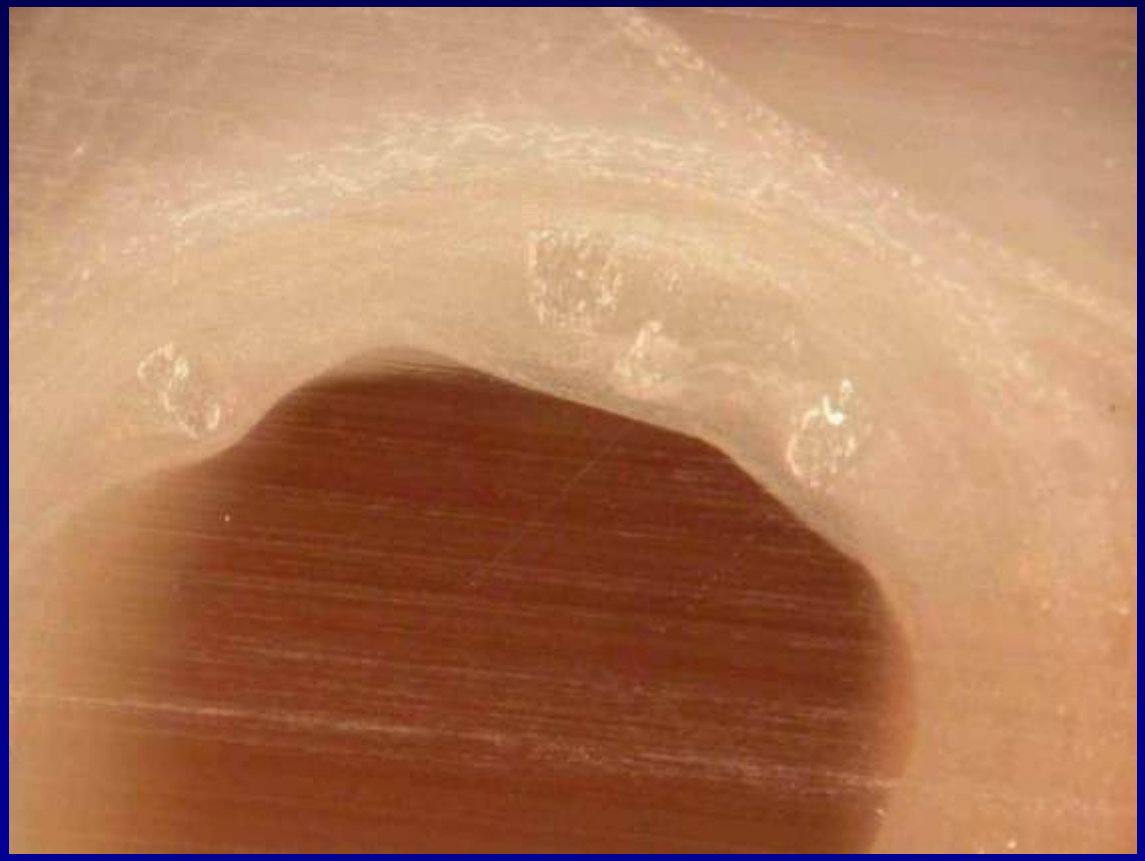


Chondrityn 4-sulphate hydrogel



Jensen et al. European Journal of Pharmacological Sciences. 15(2002) 139-148

Absorbable metallic Mg+ stent



Porcine Coronary Artery: Representative Photomicrographs (2x)

BVS Cohort A

CYPHER

Photos taken by and on file at Abbott Vascular.

Tests performed by and data on file at Abbott Vascular.

BVS

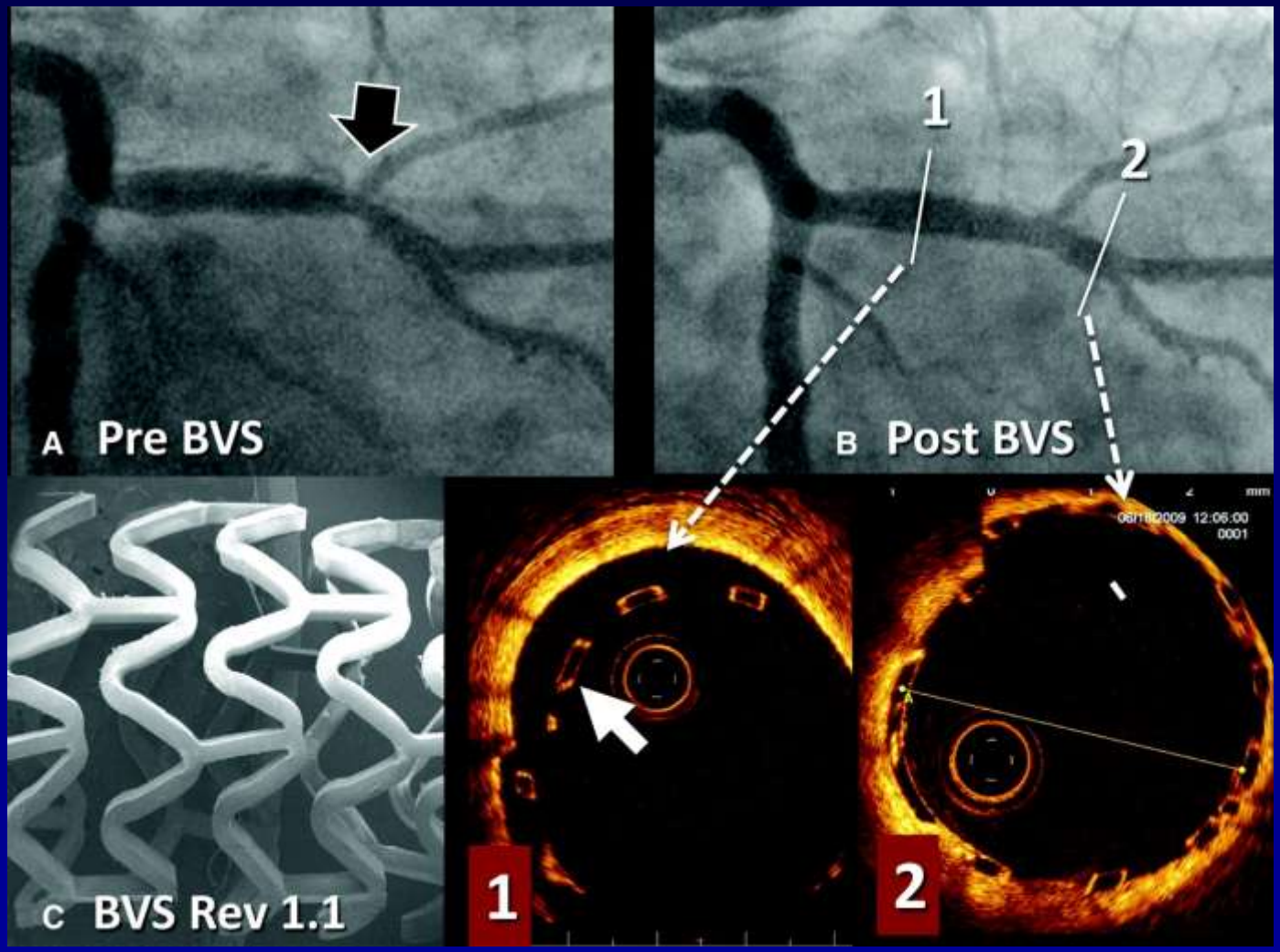
Bioabsorbable e**V**erolimus-eluting **S**tent; Abbott Vascular

	6 Months (n = 26)	2 Years (n = 19)	*P* Value
In-Stent RVD, mm	2.64	2.43	0.0058
In-Stent MLD, mm	1.89	1.76	0.23
In-Stent DS	27.0%	27.0%	0.81
In-Stent Late Loss, mm	0.43	0.48	0.233
Proximal Late Loss, mm	0.23	0.34	0.0553
Distal Late Loss, mm	0.23	0.36	0.0091
In-Stent Binary Restenosis	7.7%	0%	1.00
In-Segment Binary Restenosis	7.7%	0%	1.00

34.5% struts reduction over 2 years

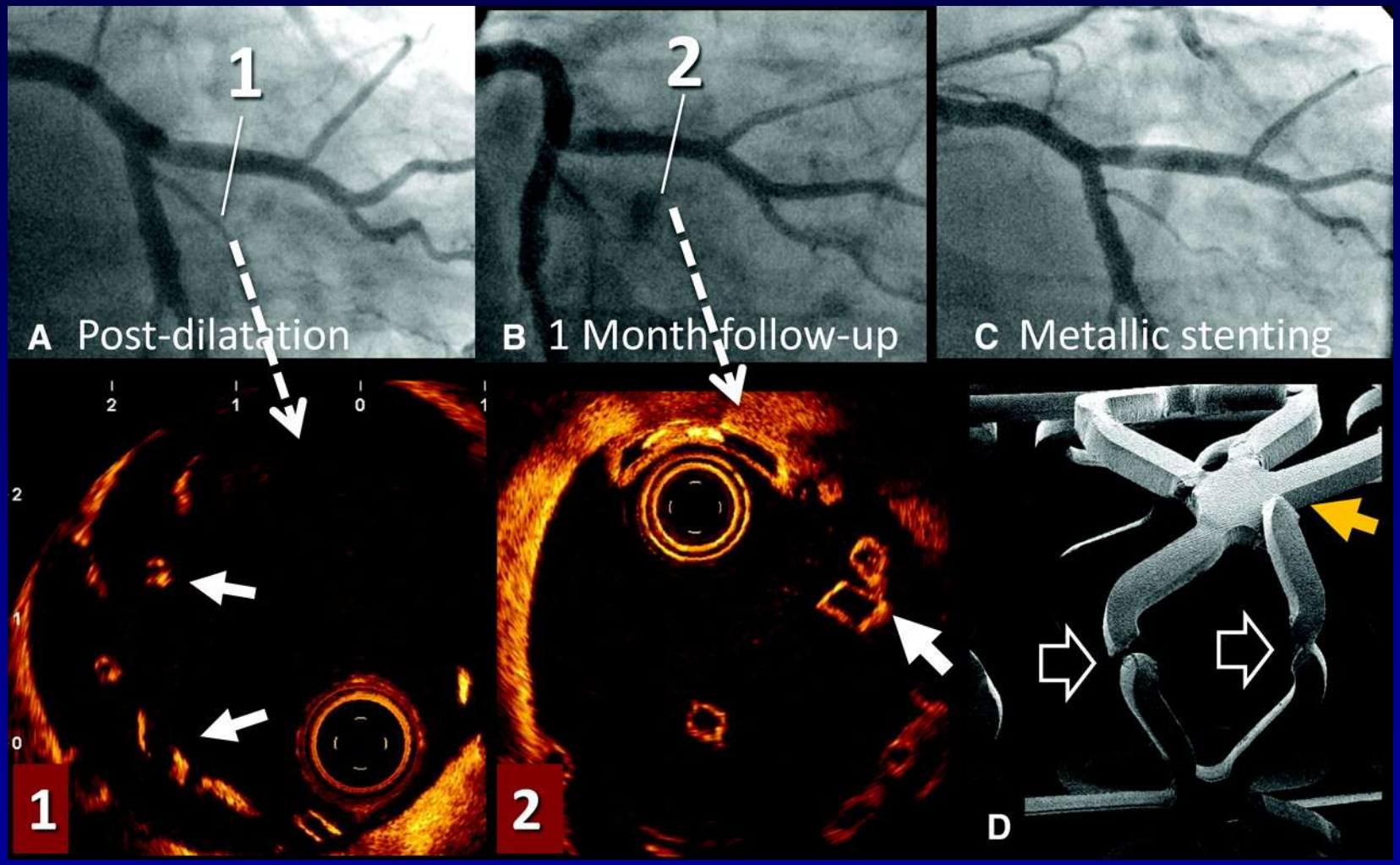
JA Ormiston, PW **Serruys** et al
Lancet, 373, 9667: 887,.**March 2009**

A, Stenosis in the obtuse marginal branch of the left circumflex coronary artery before ABSORB bioresorbable vascular scaffold (BVS) implantation; B, artery after deployment of a 3.0×18 mm ABSORB BVS scaffold and after dilatation with a 3.25-mm noncompliant...



Ormiston J A et al. Circ Cardiovasc Interv 2011;4:535-538

A, Apparently good angiographic result after postdilatation with a compliant 3.5-mm balloon at 16 atm.



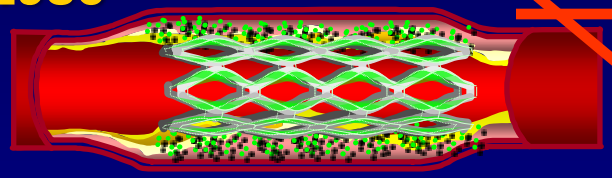
Ormiston J A et al. Circ Cardiovasc Interv 2011;4:535-538

PCI CON BALON

1978

STENTS

1986

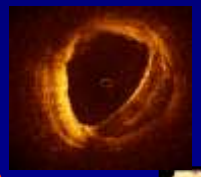


DES

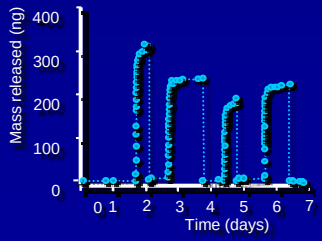
2000

SCAFFOLDS

2012

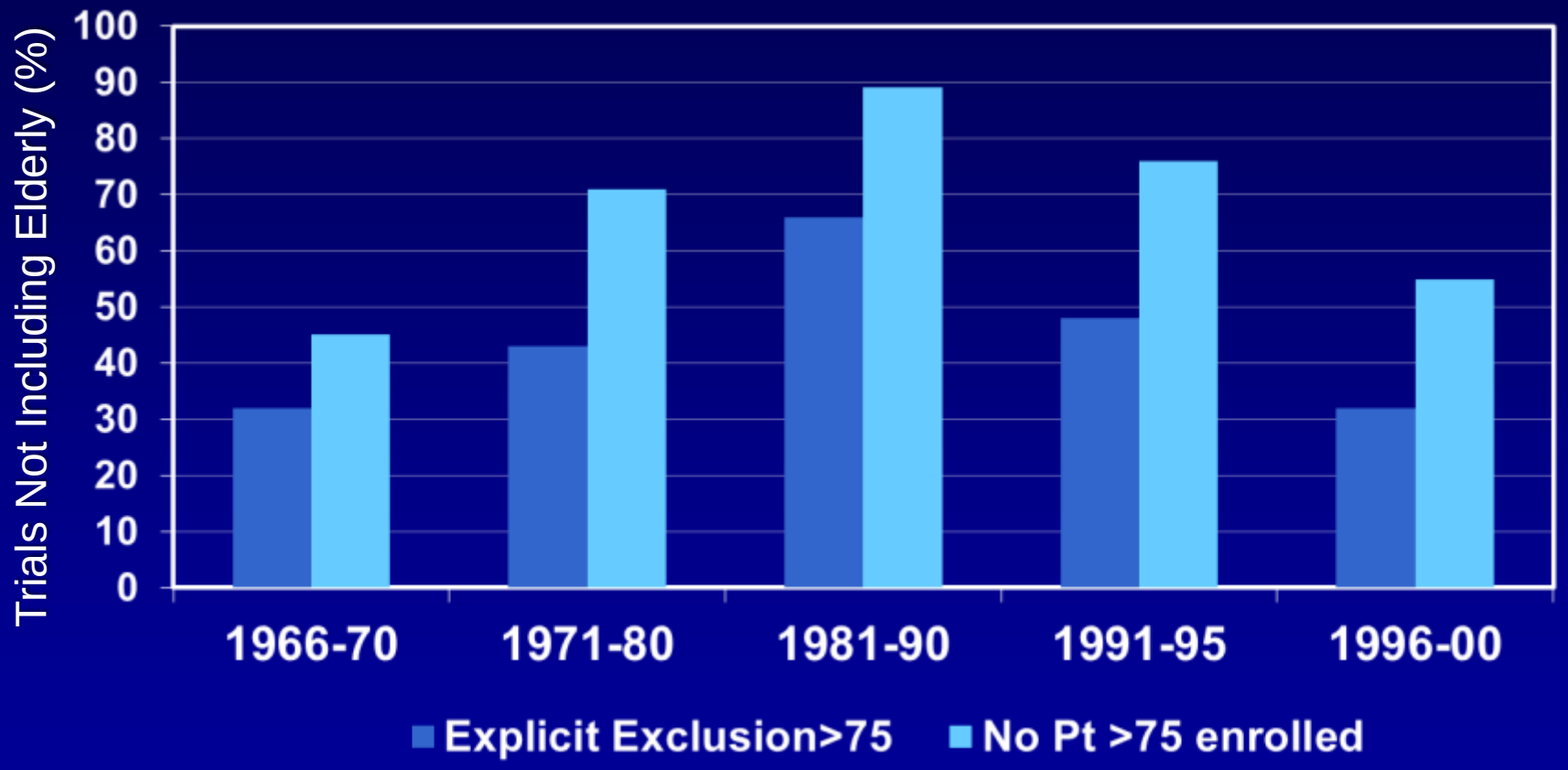


FUTURO



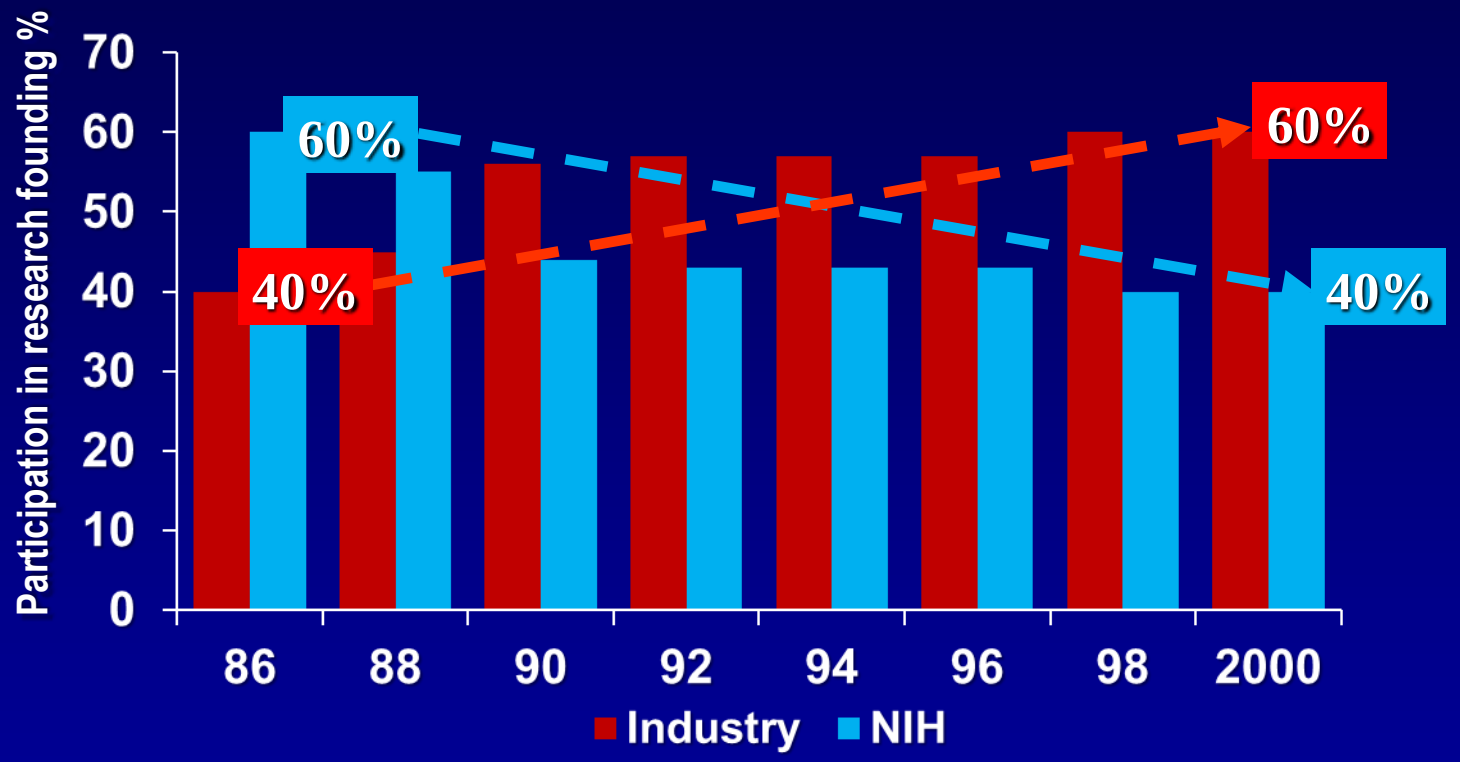
Exclusion de los >75 años de los RCTs

Review of 593 UA/MI Trials

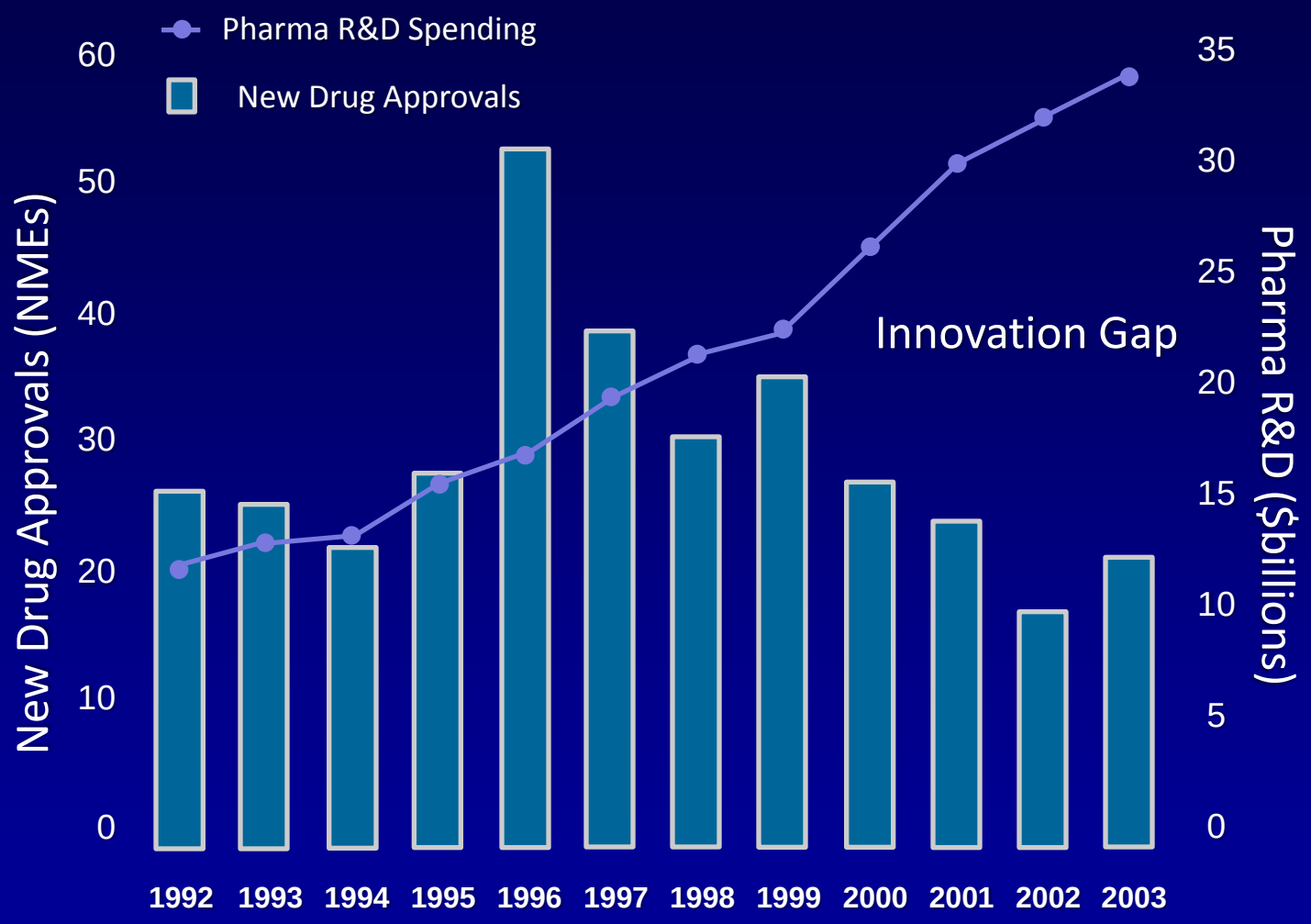


Lee, JAMA 2001

"Market share" of GRANTS



Modified from Holmes D et al.
Am Heart J. 2004; 147: 228-237



Carol B. VanBuren. Removing Roadblocks Along the Medical Pipeline
The FDA's Critical Path Initiative: Update on Progress & Outlook for 2007
http://www.dawnbreaker.com/about/phase3_sum07/medical.php

XXII Jornadas SOLACI

7° Región Cono Sur

21 / 22 de Noviembre 2013

SOLACI
SOCIEDAD LATINOAMERICANA DE CARDIOLOGIA INTERVENCIONISTA

- ✓ **Los stents han representado el máximo avance desde que nació la angioplastia**
- ✓ **La capacidad de liberar substancias localmente, los convirtió en un nuevo concepto terapéutico**
- ✓ **El futuro nos traerá nuevos desarrollos en drogas y polímeros, stents dedicados (DAPT mas corta)**
- ✓ **Deberán seguir mejorando desde el punto de vista mecánico**
- ✓ **Lo "scaffolds" bioabsorvibles NO son simplemente otro stent**
- ✓ **Stents inteligentes?**

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