Challenge of Treating Small Vessel Disease

Partnership Session:
MyLive at TCTAP 2014

Gim-Hooi Choo MD

22nd. April, 2014

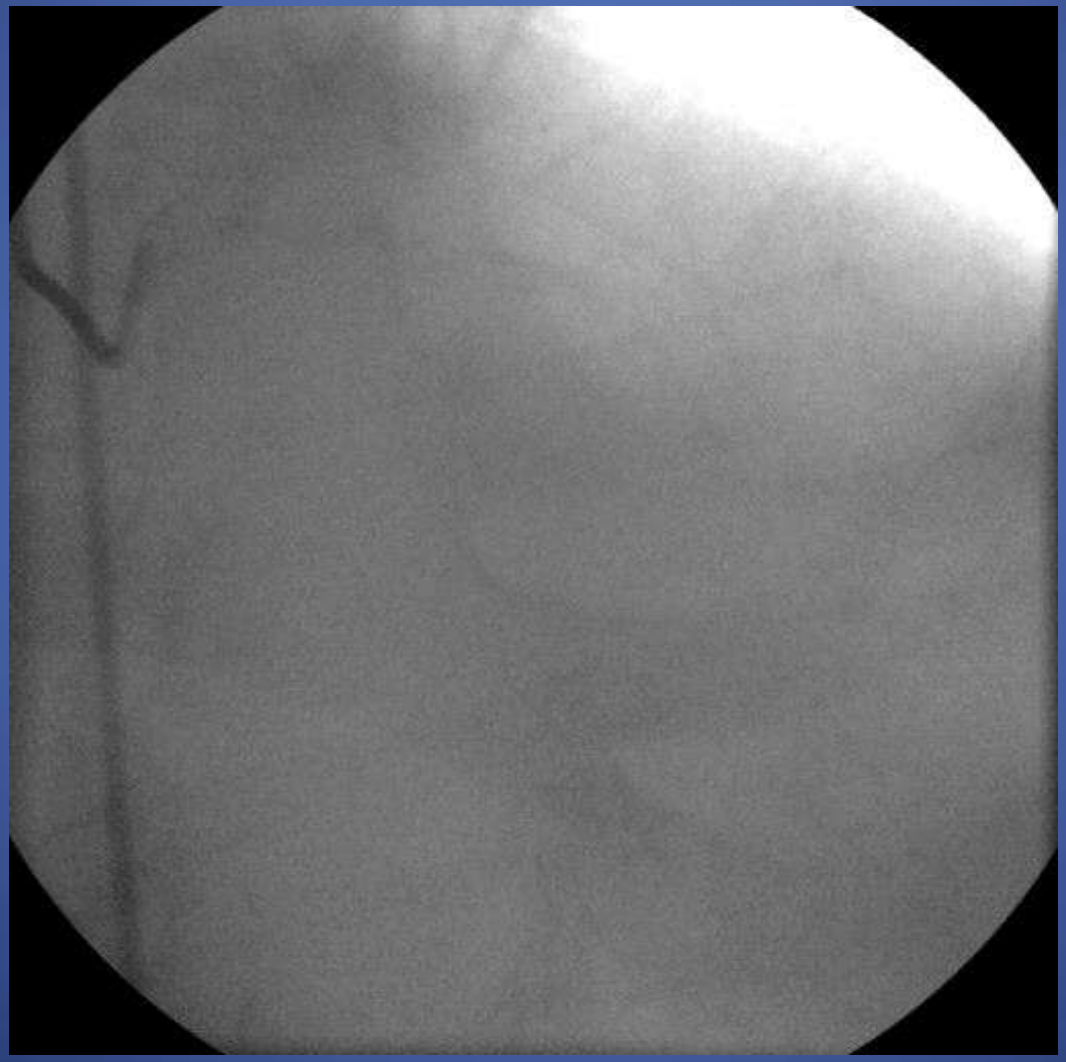
Disclosure

- Speaking, Faculty and Advisory Board honorariums from Novartis, MSD, Roche, Solvay Pharma, Xepa-Soul Pattinson, Servier, Sanofi, Cordis J&J, Astra Zeneca, Lilly, Medtronic, Biosensor, Terumo
- No conflict of interest with reference to this lecture or meeting

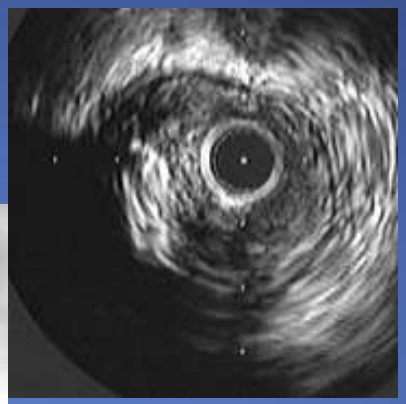
Sypnosis

- What's a small vessel?
- Implications of Small Vessel Intervention
- Therapeutic strategies & Technical issues
- Summary

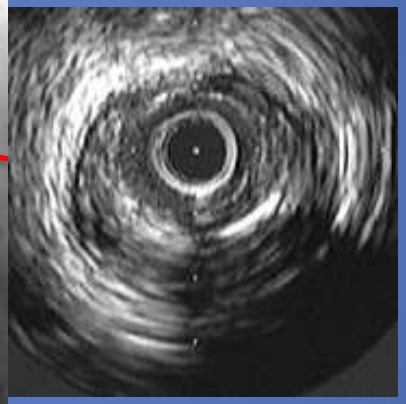
Angiographic Small Vessel



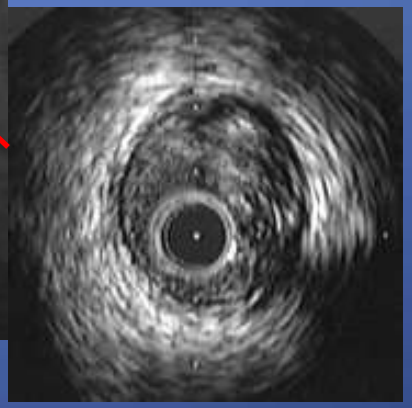
≤ 2.5mm or
≤ 2.75mm
in diameter



MLD: 1.7 mm
Vessel diameter: 3.0-3.5mm
LCSA: 3.3 mm^2
% area stenosis: 71%



MLD: 2.0mm
Vessel diameter : 3.0mm
LCSA: 3.5 mm^2
% area stenosis: 70%

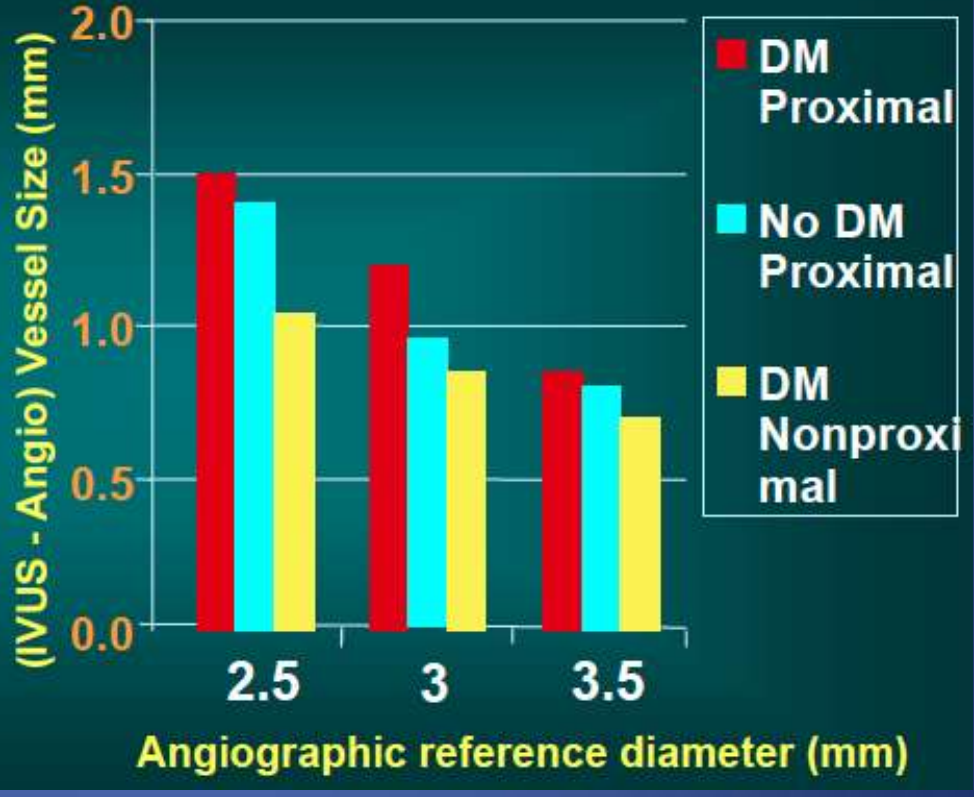


MLD: 1.5mm
Vessel diameter : 2.75-3.0mm
LCSA: 2.1mm^2
% area stenosis: 71%

Discrepancy in vessel size : IVUS vs. Angiography

The maximum Discrepancy between IVUS and angiography is found in:

1. Diabetics
2. Angiographically Small vessels
3. Proximal segments



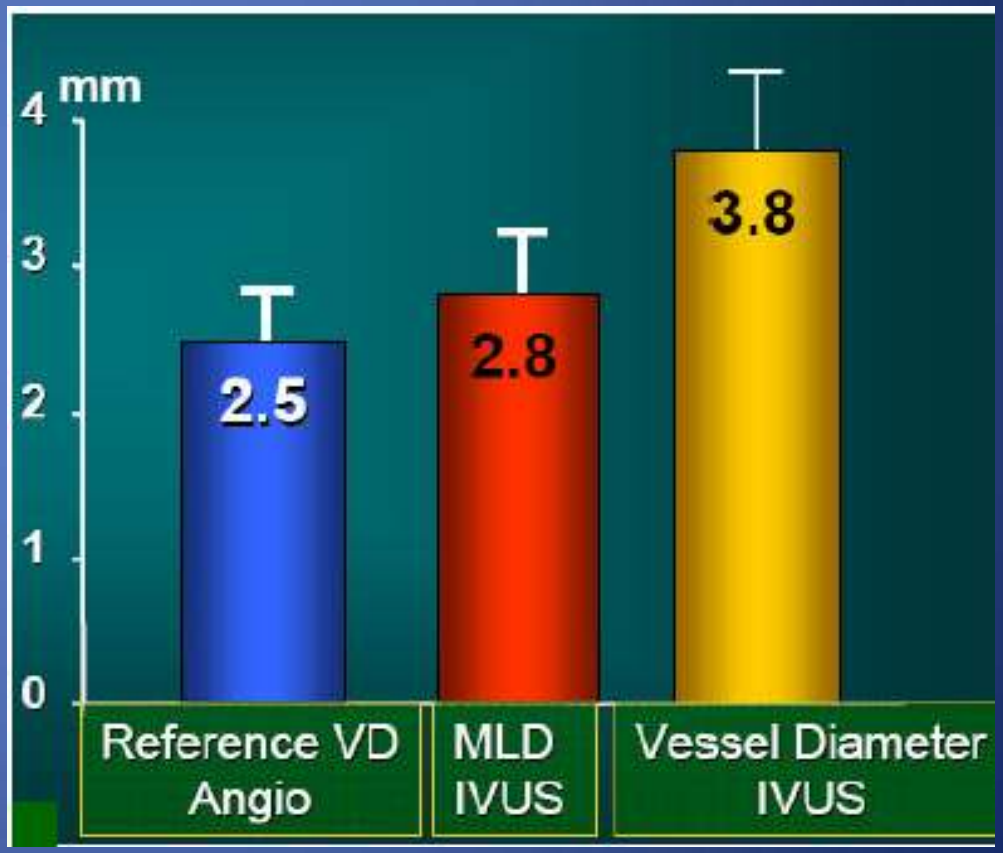
Moussa I et al. AJC 2001; 1,88:294

Angiography vs IVUS discrepancy:

Predictors of IVUS – Angiography discrepancy of > 0.5mm:

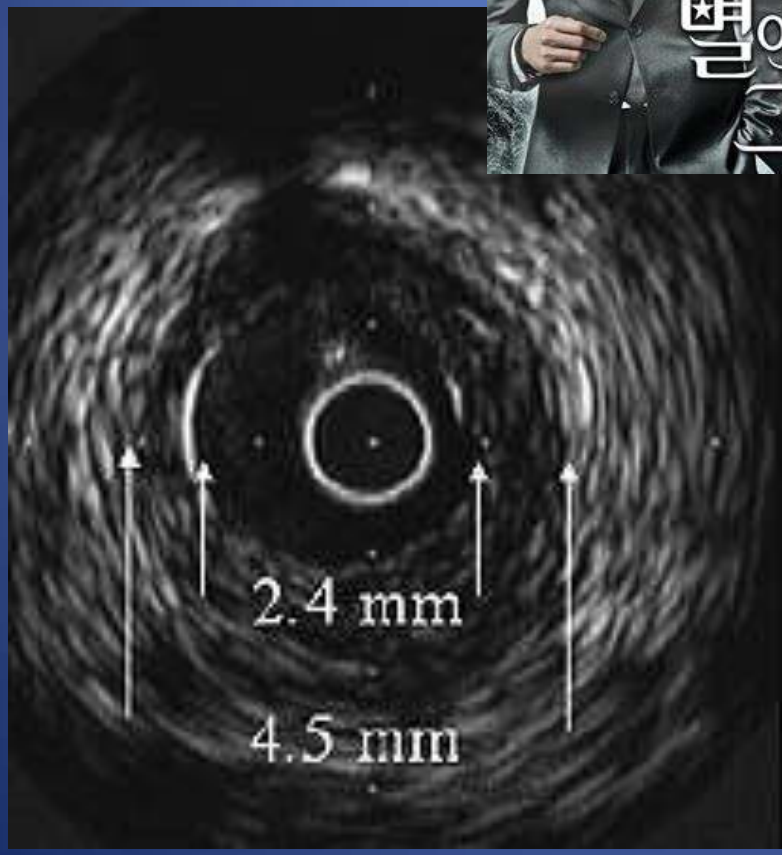
1. Proximal or middle location
2. Vessel type: LAD, Diagonal, Marginal
3. Female sex

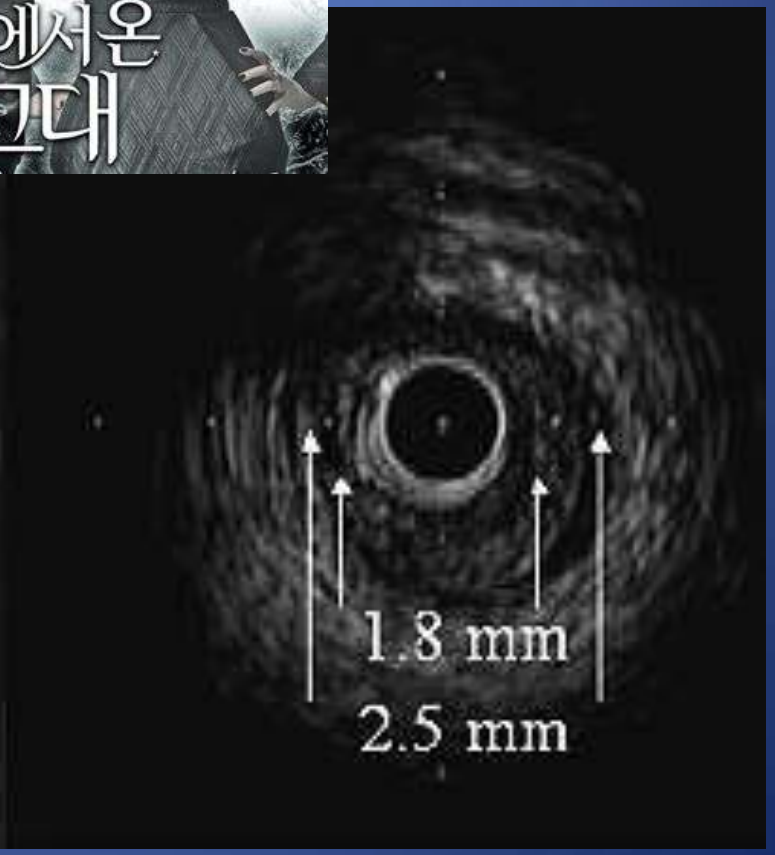
N=419 : Angiographically ≤2.75mm



Briguori et al. EHJ 2002; 23: 247-54

“Do not judge a book by its cover”





Lesson No.1: Consider IVUS/OCT in angiographically small vessel disease

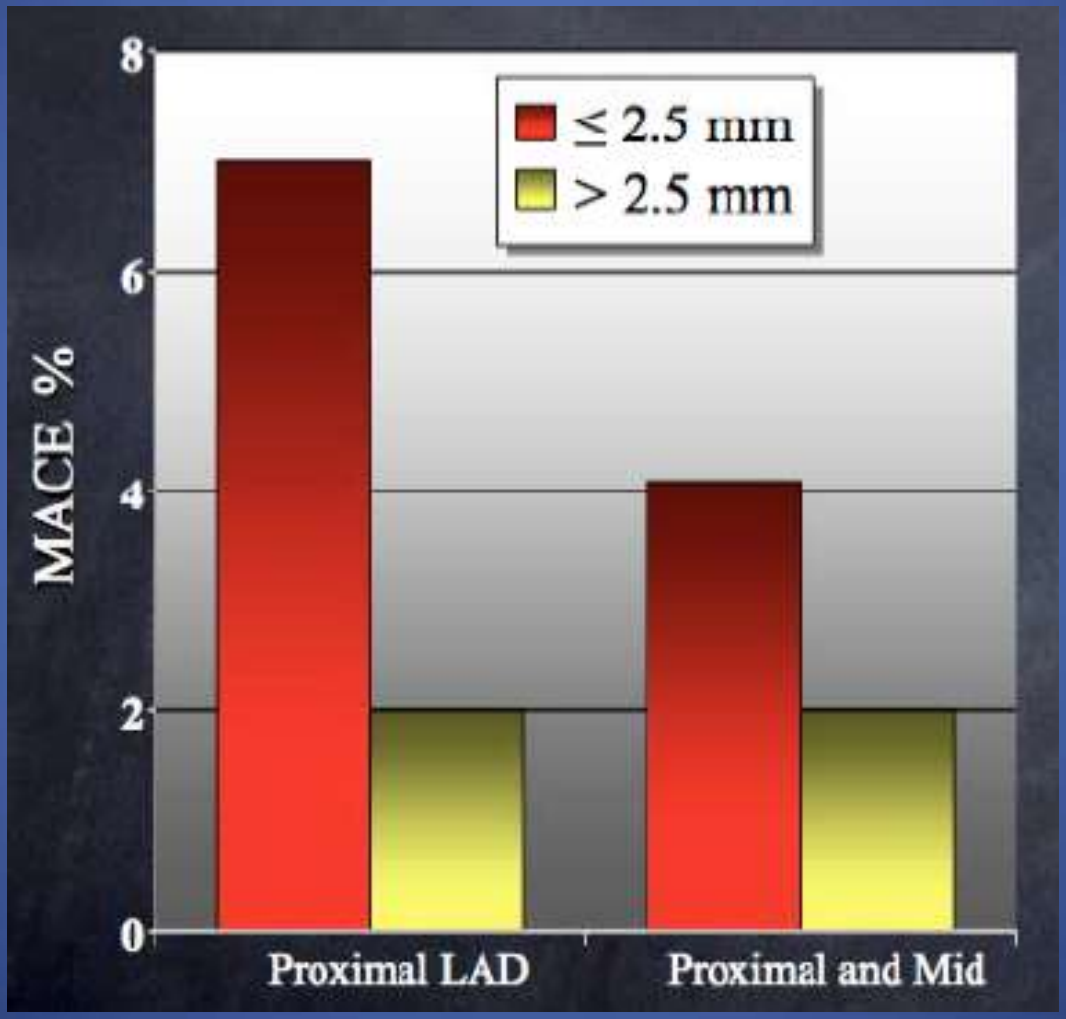
- Angiographically small vessel may be related to large plaque burden and diffuse disease
- Especially in proximal/mid coronary artery segments, diabetics, female
- Consider IVUS/OCT :
  - For balloon & stent sizing
  - For stent landing zone & optimisation

Why the fuss with small vessel disease?

Small vessel = Small problem?

169 cm (5’ 7”)

Procedural risks with small vessel intervention

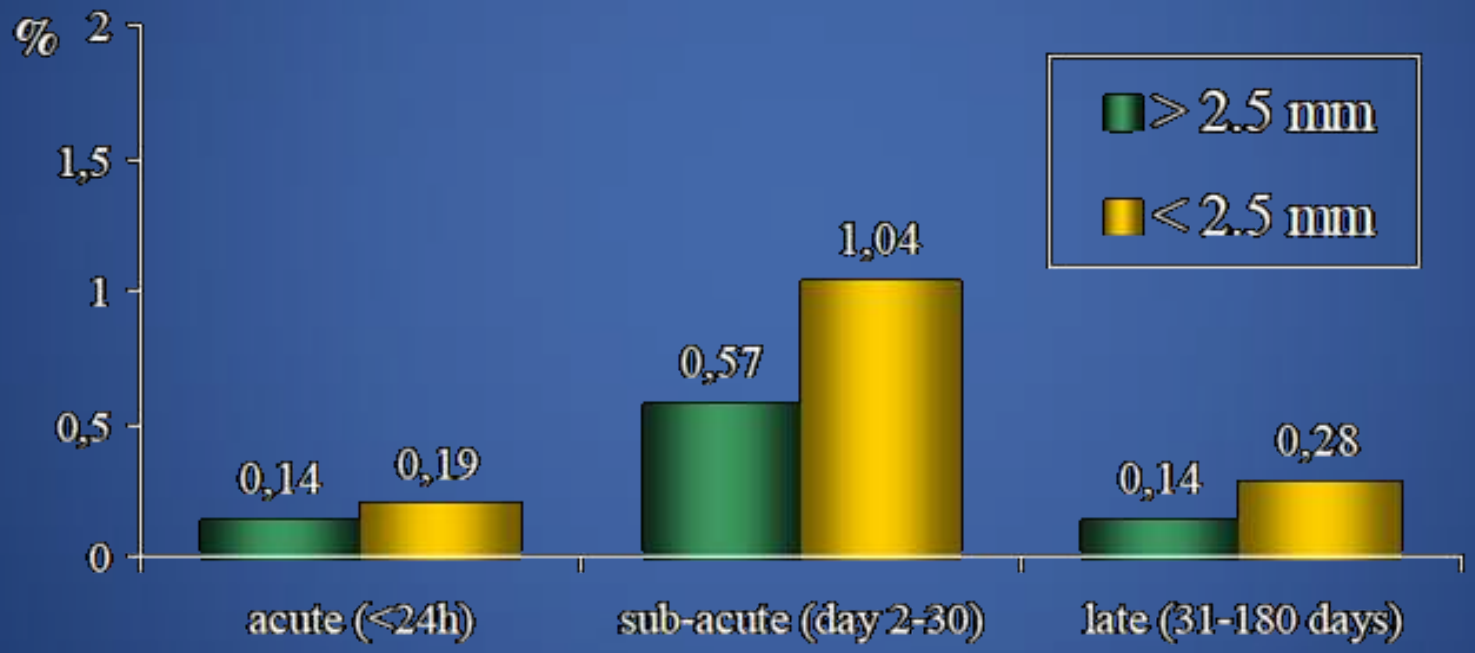


MACE = Death/MI/Emergency CABG

Schunkert et al. JACC 1999; 34:40-8

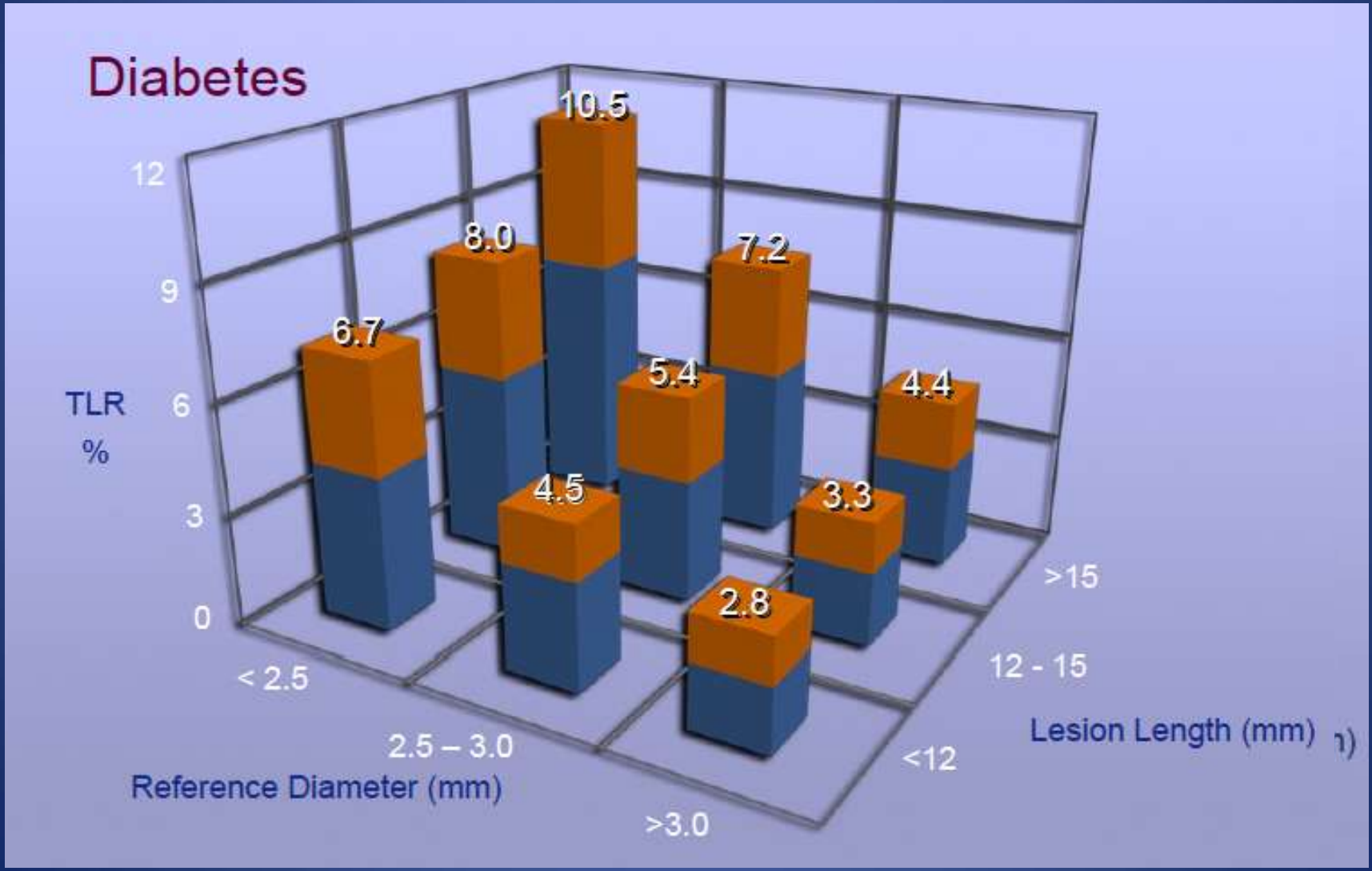
Stent Thrombosis & Vessel size

E-Cypher Registry :
Overall ST at 6 months:
"Small" 1.51% vs. "large" 0.85% (p=0.08)

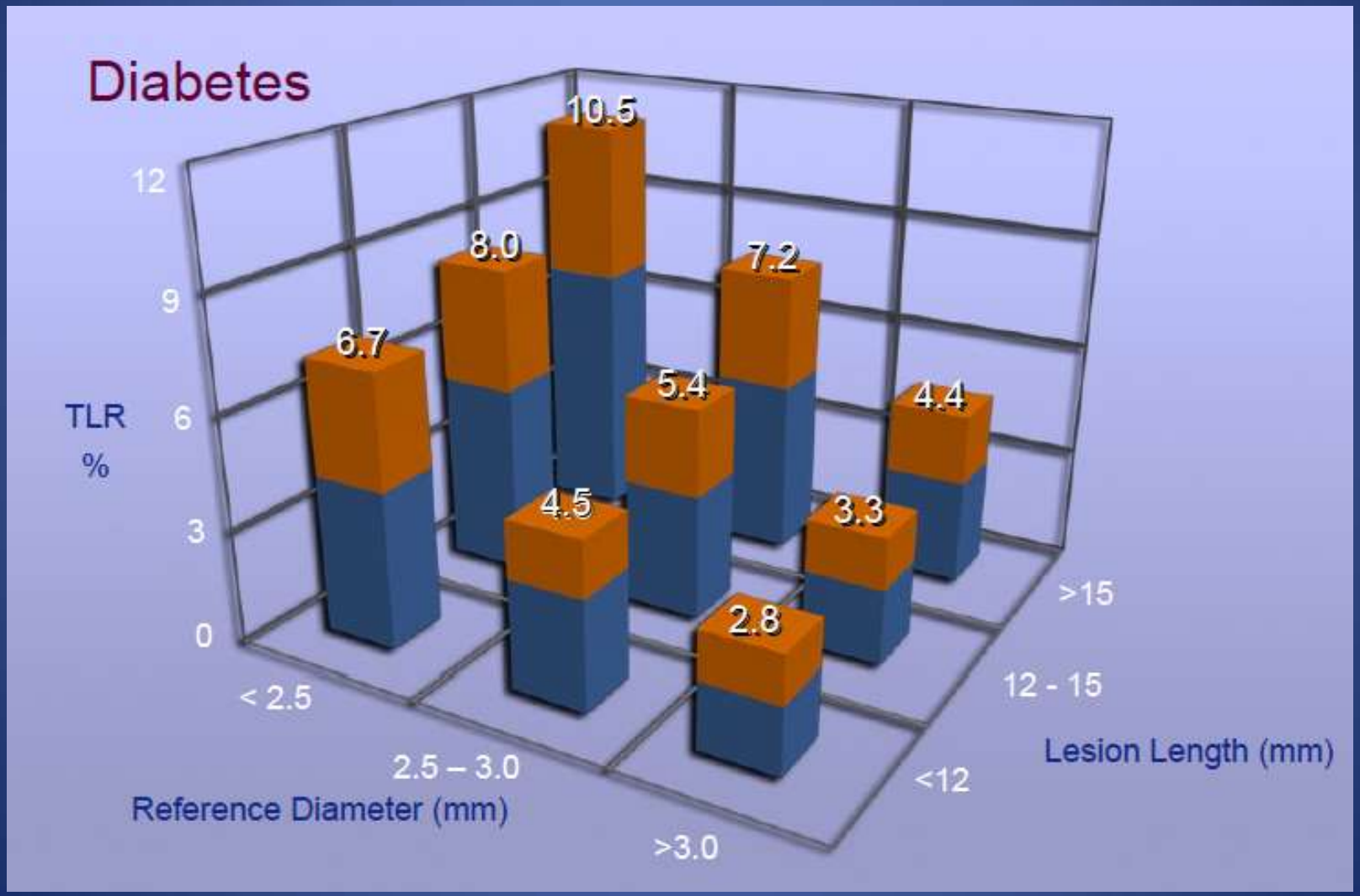


All cases with reported death, AMI, TLR or stent thrombosis were reviewed and adjudicated by CEC: ST was considered "definite" if supporting documentation was available and "likely" if limited or unclear documentation was available

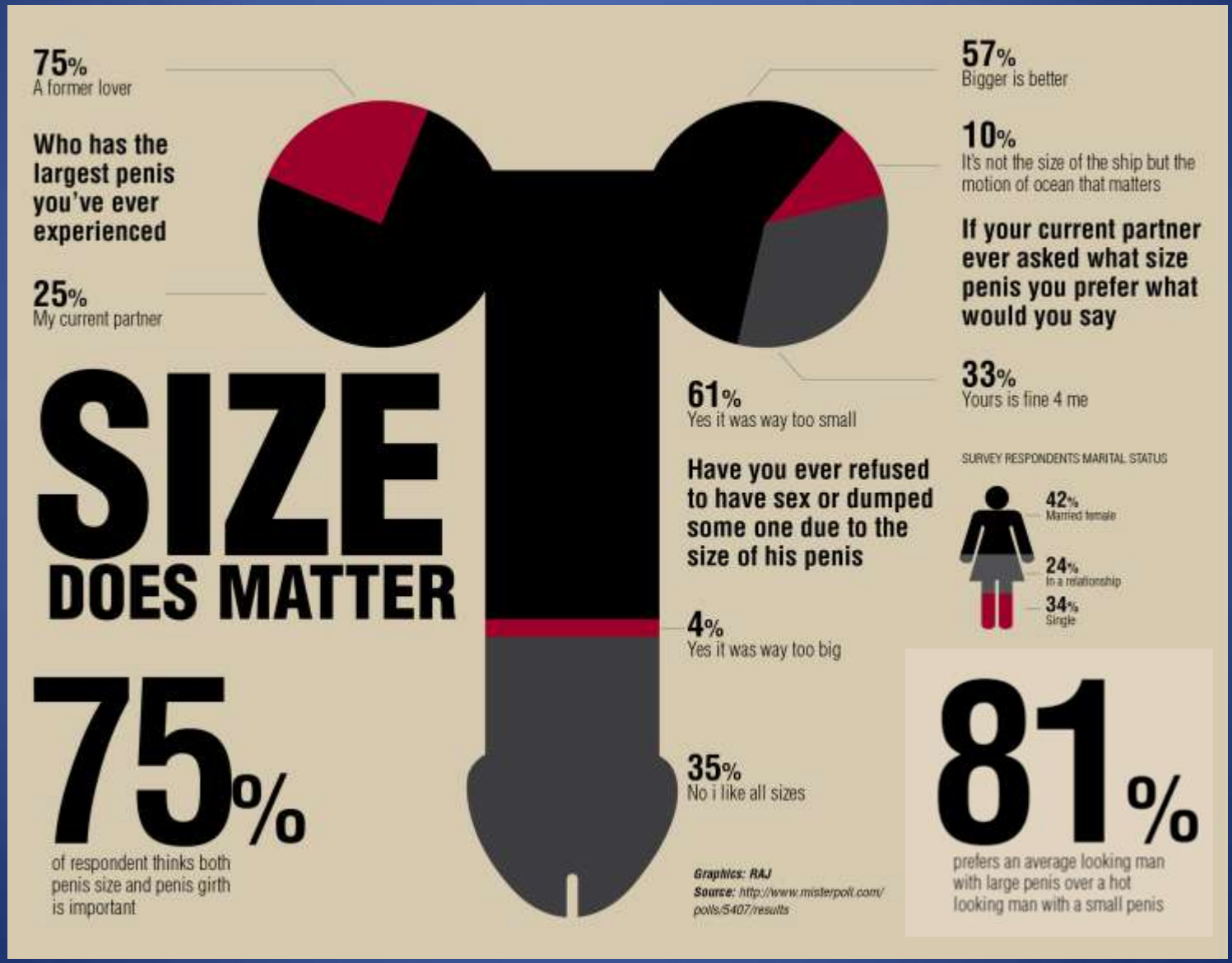
DES : Multi-variate Predictors of TLR



TLR and Diabetes



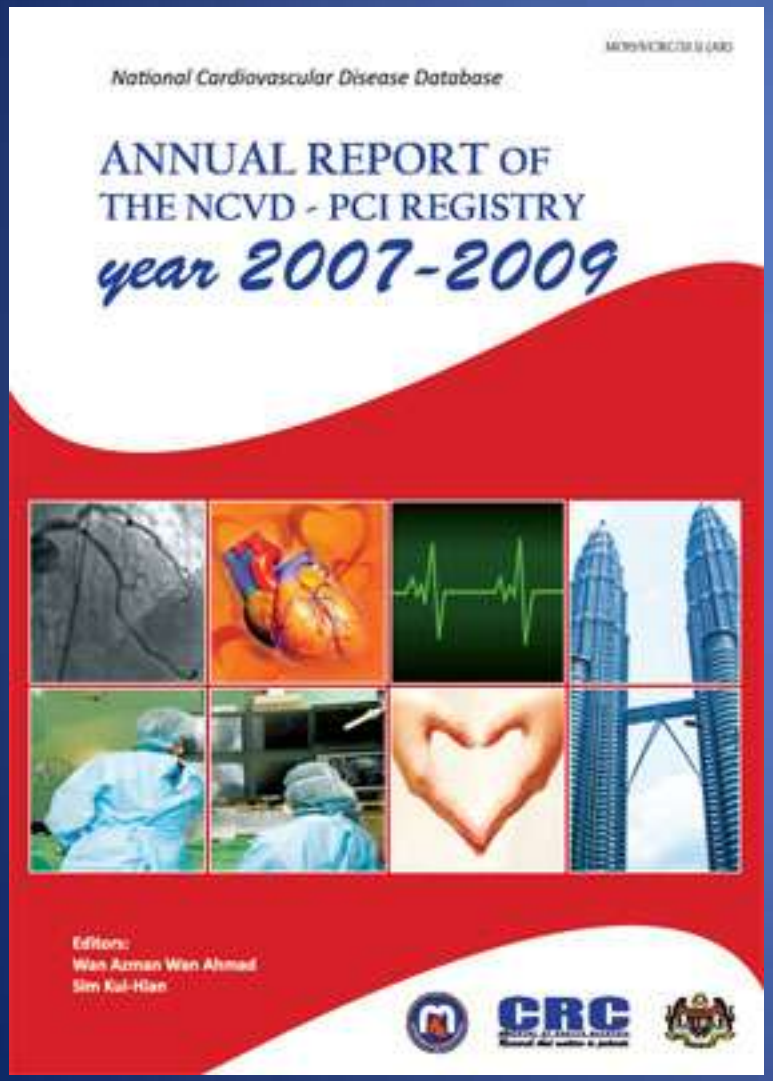
So, Size does matter



Why it matters?
Small Vessel Intervention Issues:

- Decreased procedural success
- Increased complication rates
- Increased restenosis and TLR rates
- Increased MACE rates

Malaysia National Cardiovascular Database – PCI Registry (2007-2009)



Small Vessel – vessel stented with one or more stents - ≤2.75mm in diameter

W A Wan Ahmad, K H Sim. Annual Report of the NCVD-PCI Registry, Year 2007-2009.

‘Small vessel’ location:

	Small vessel	Large vessel
Lesion, N	**8188**	**9668**
Lesion location, %		
RCA	19.9	35.5
PDA	1.2	0.2
PLV	1.2	0.4
LM	1.4	2.9
LCx	17.8	12.1
OM	5.5	1.5
LAD	50.0	45.0
D	2.1	0.4
LIMA	0.2	0.1
RIMA	0	0
SVG	0.8	1.7
RAD	0	0

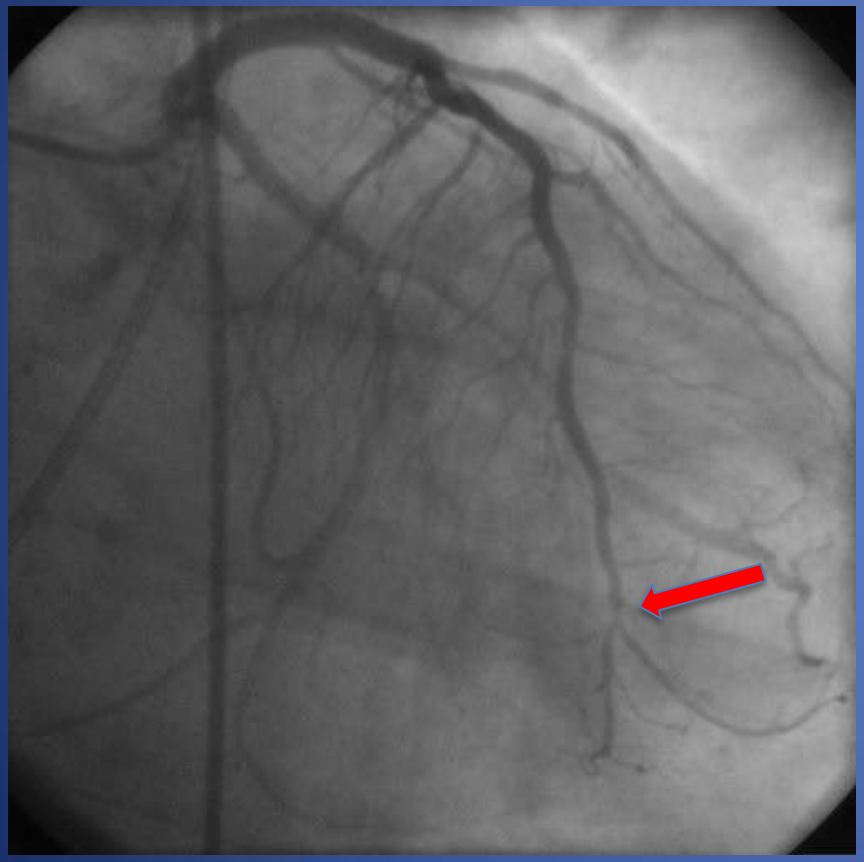
Lesion & Procedural characteristics

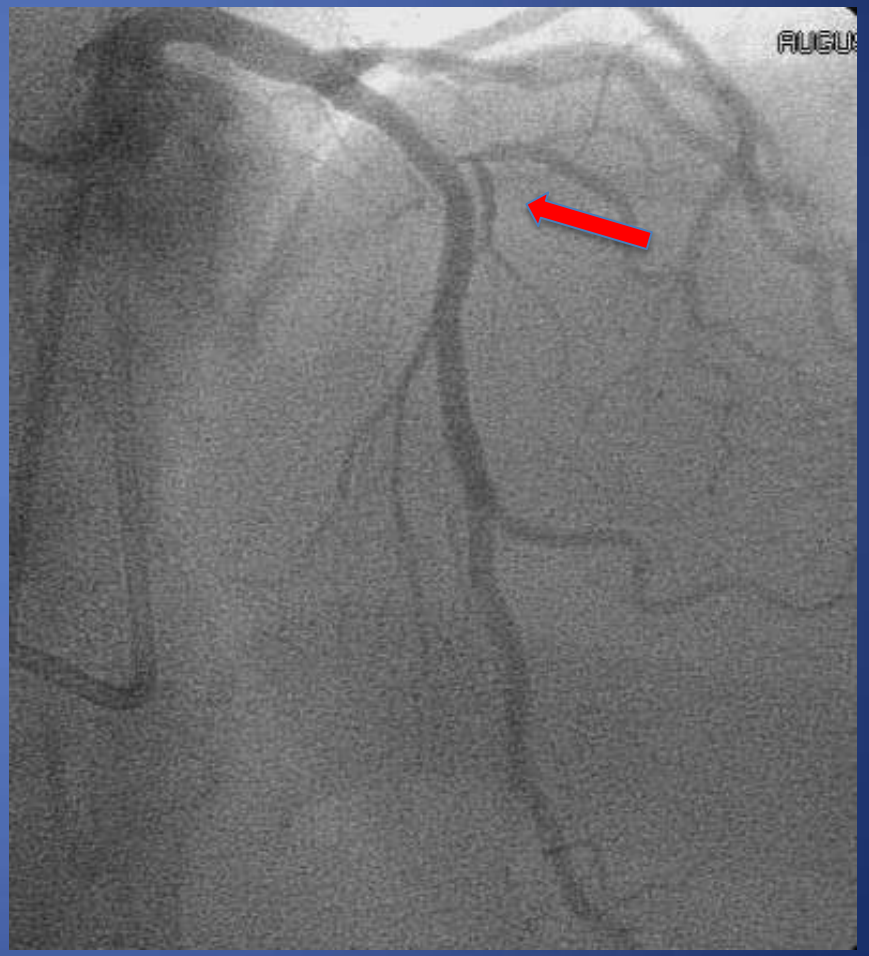
	Small vessel	Large vessel
Lesion, N	**8188**	**9668**
Lesion type, %		
A	9.6	13.7
B1	23.3	30.6
B2	24.8	23.0
C	41.6	32.0
Missing	0.7	0.7
	Small vessel	Large vessel
Lesion, N	**8188**	**9668**
Acute closure, %	0.4	0.3
Dissection, %	5.4	3.2
Perforation, %	0.1	0.3
	Small vessel	Large vessel
Lesion results, %		
Successful	99.3	99.4

Therapeutic approaches to small vessel disease

- Leave it alone!
- POBA
- Stent : BMS vs DES
- DES : 1st. Vs. 2nd. Generation
- DEB
- ?BVS
- Adjunctive use of FFR?, Debulking?

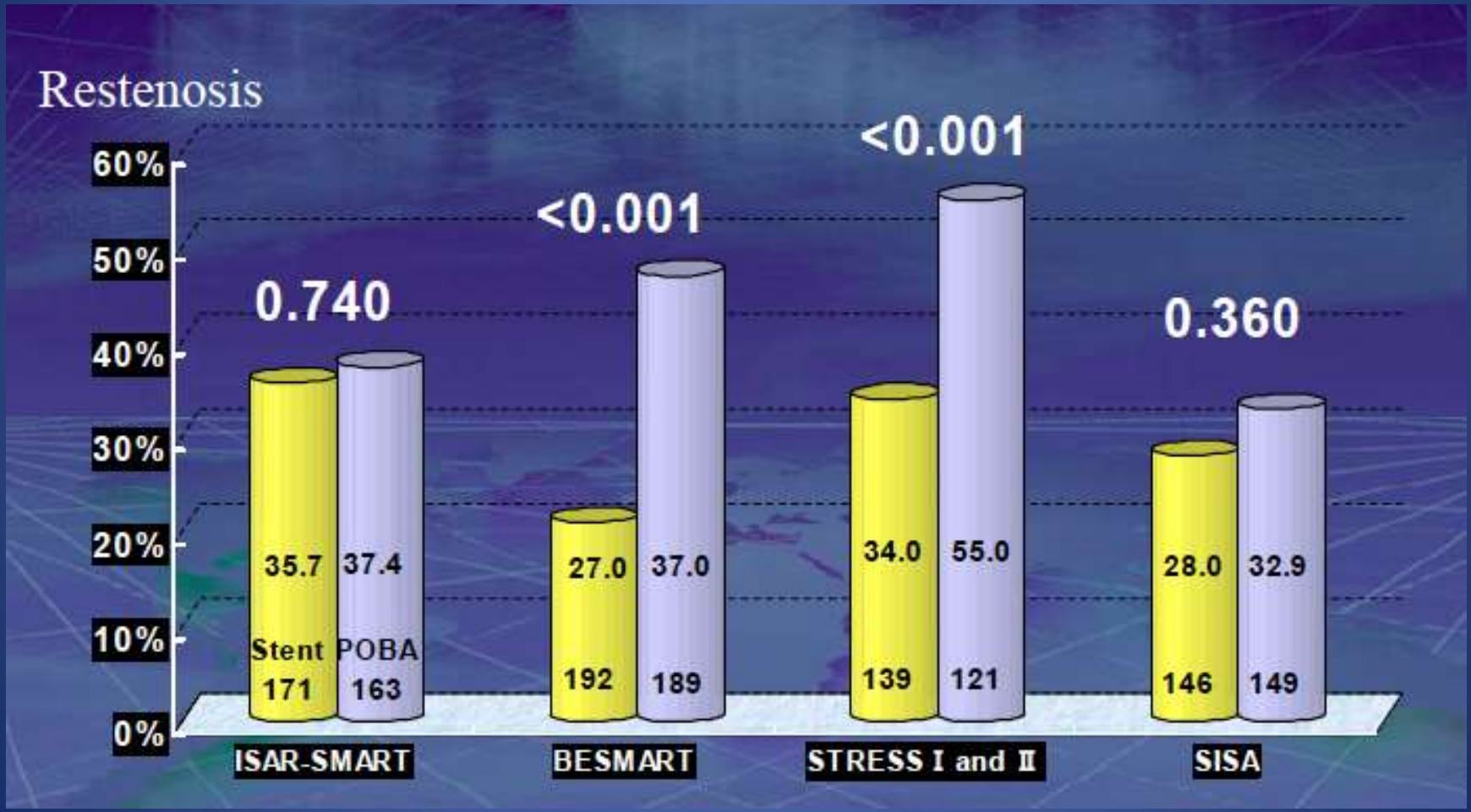
Leave it Alone Strategy – True Small Vessel : Relevance?



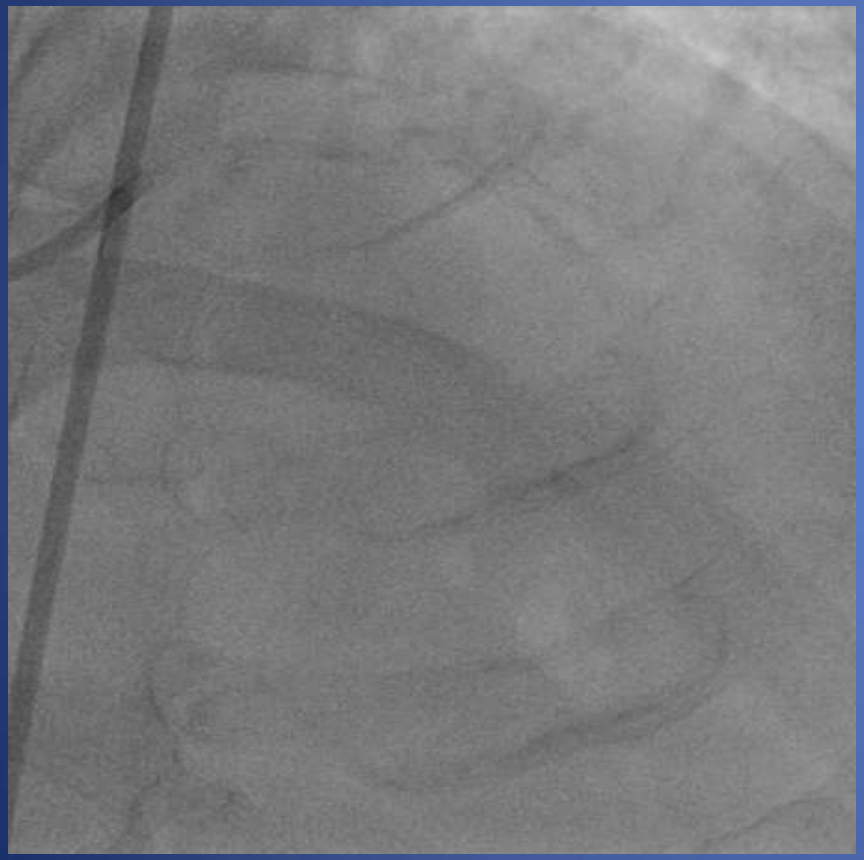


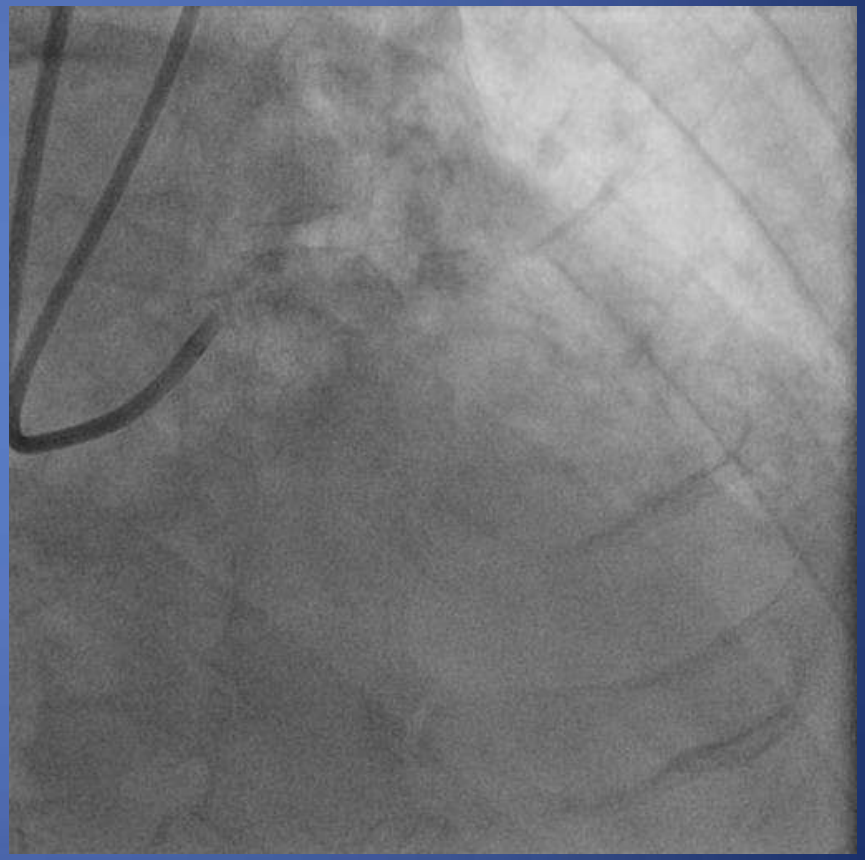
Only a small area of perfusion

POBA vs BMS PCI

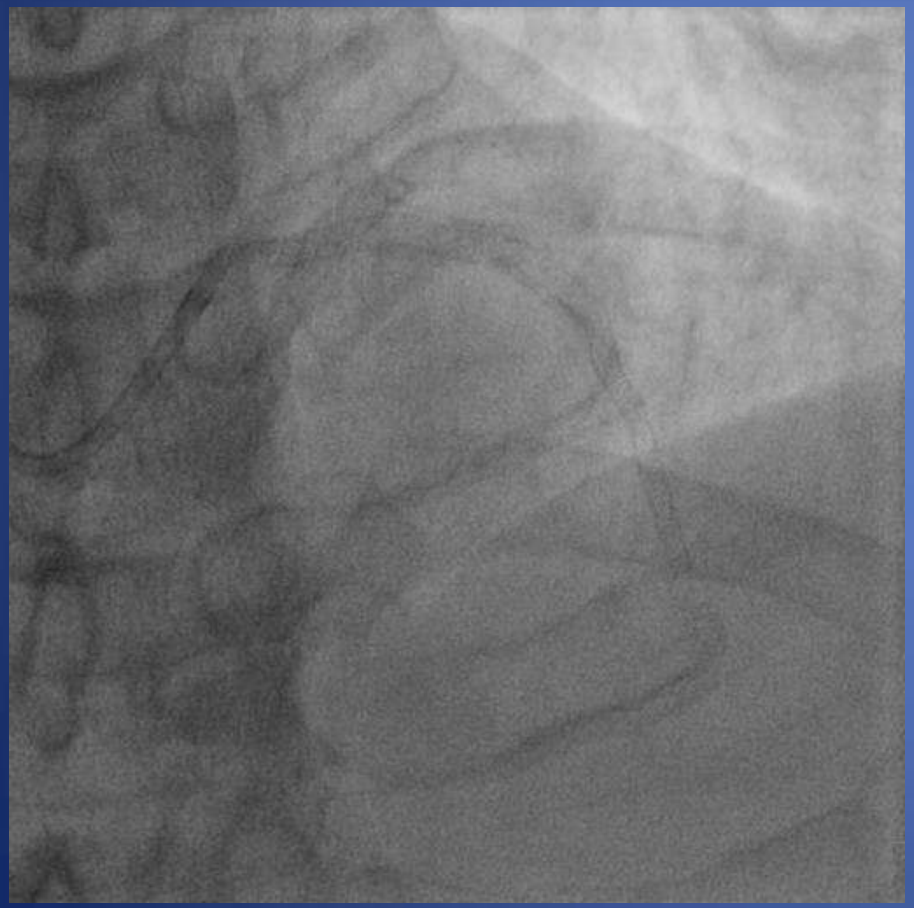


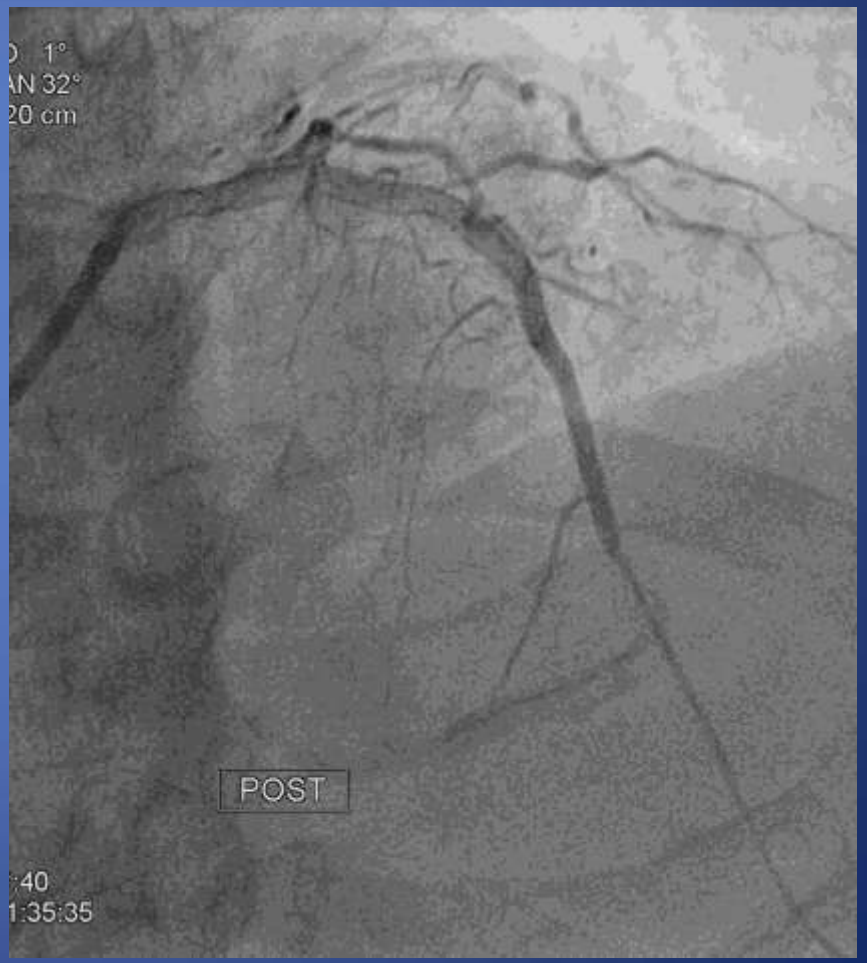
But sometimes we have no choice: Distal LAD too small & diffusely diseased



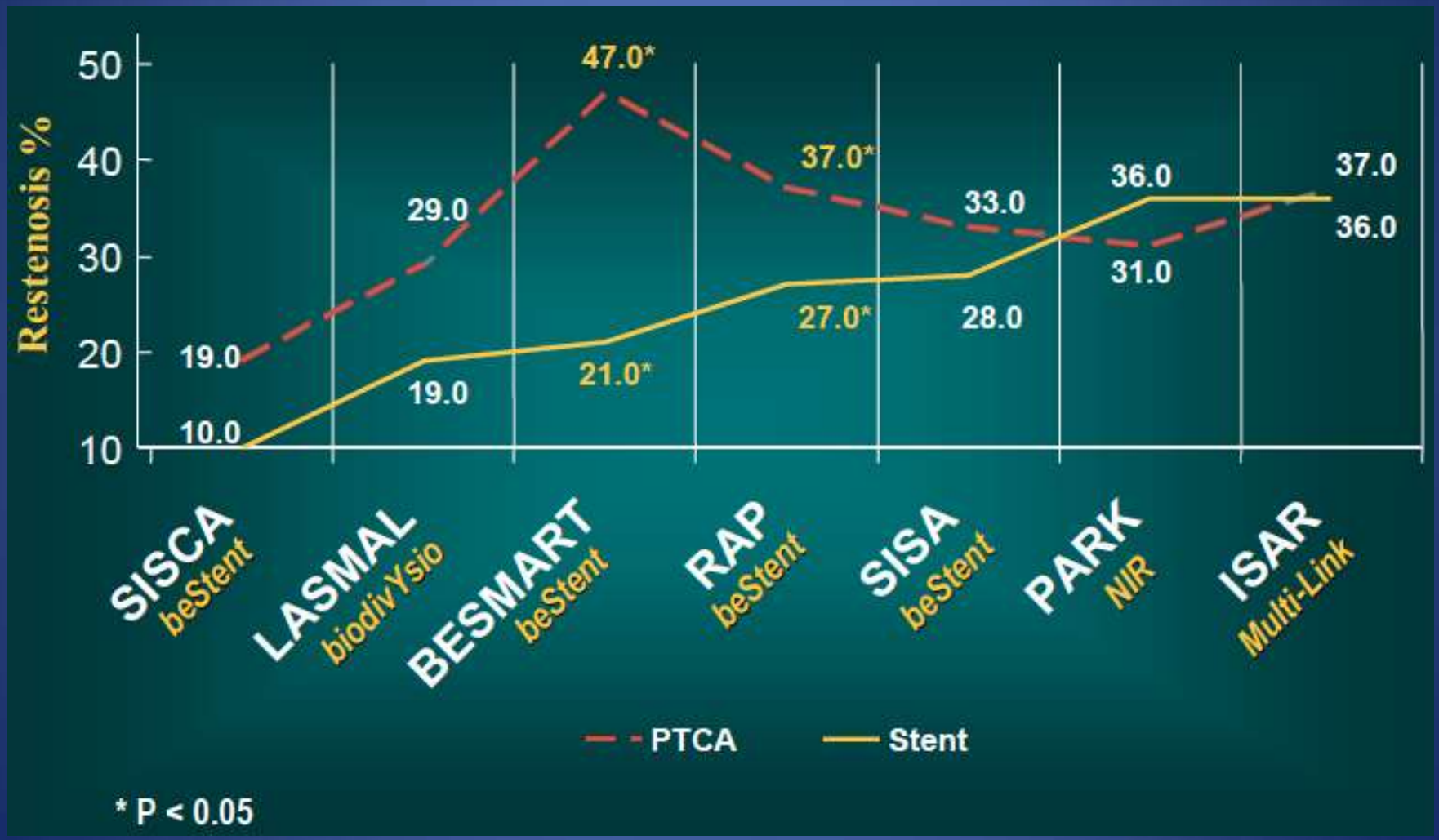


After rotational atherectomy, PCI/stenting LMCA bifurcation & mid-LAD & POBA 2.0mm distal LAD



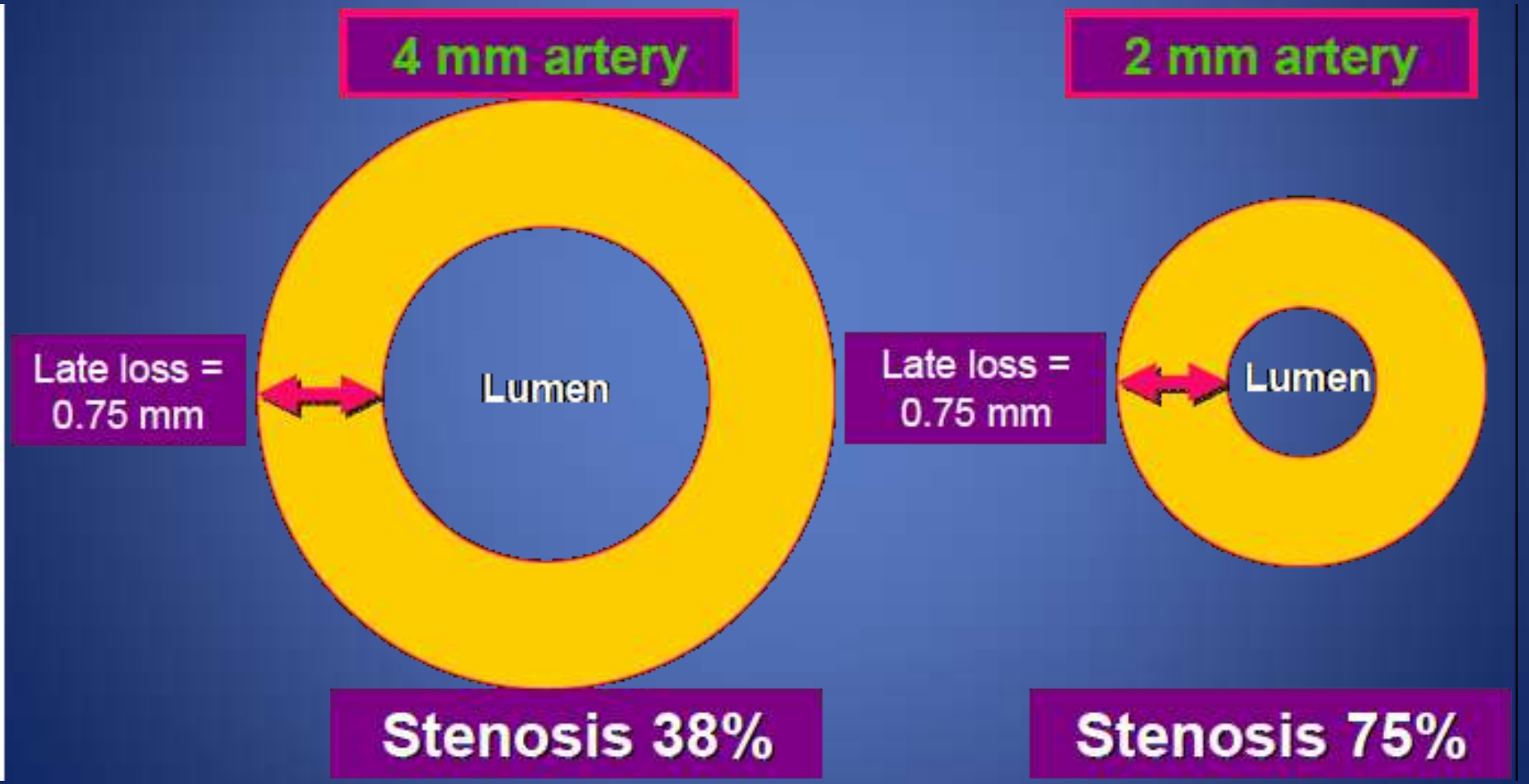


BMS vs POBA in small vessels



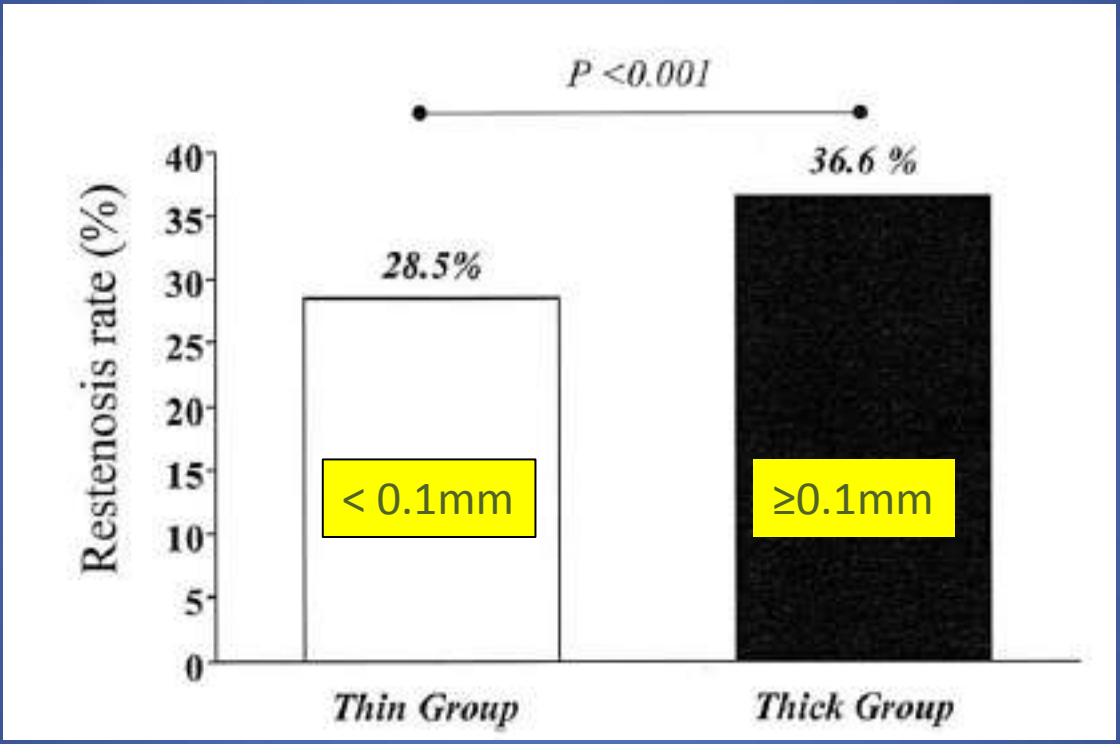
Courtesy of Issam Mousa, Columbia Univ Med, CRF

Late loss and impact depending on vessel size



Courtesy of J Orniston

In-stent restenosis in small coronary arteries- impact of strut thickness



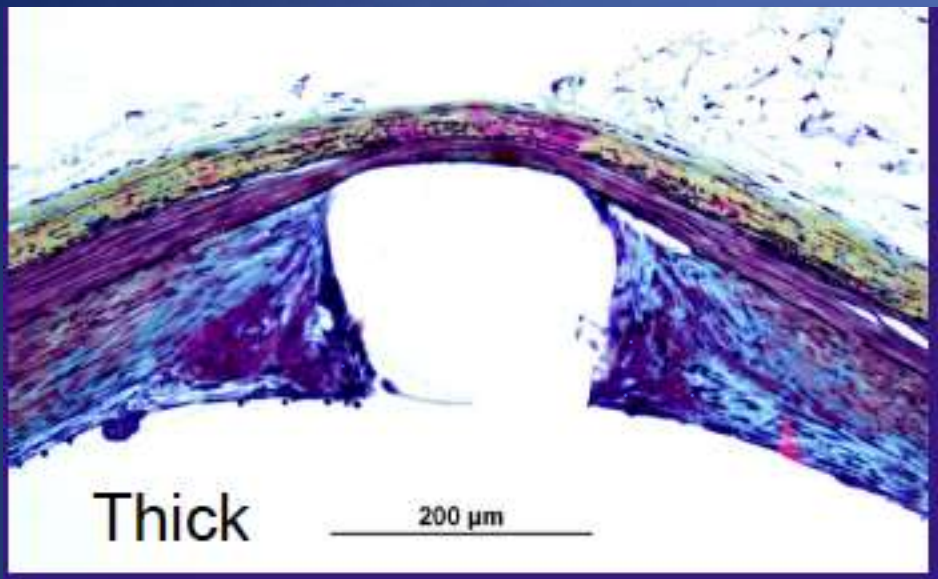
Bare metal stents

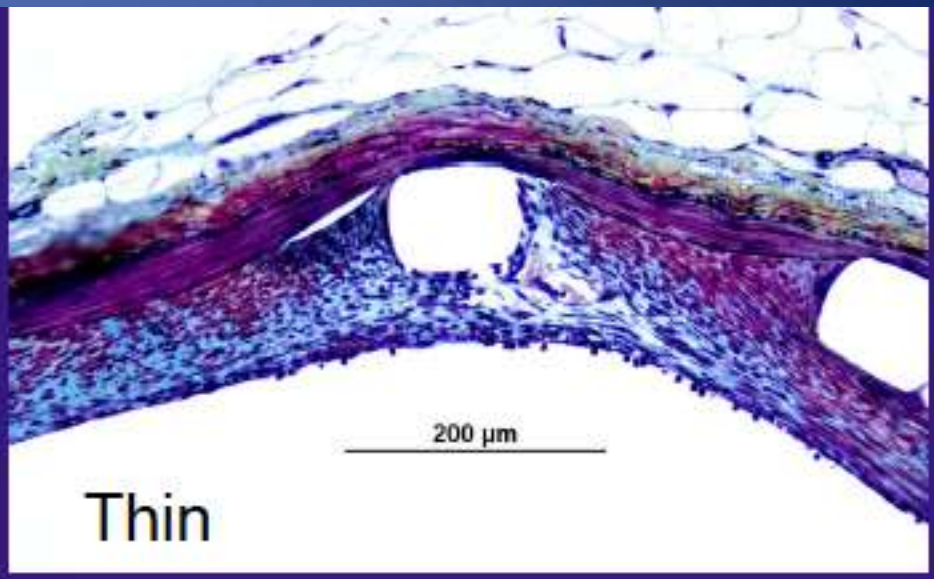
Figure 1. Restenosis rates in lesions treated with a stent with a strut thickness of 0.10 mm (thin group; open bar) and a stent with a strut thickness of 0.10 mm (thick group; solid bar).

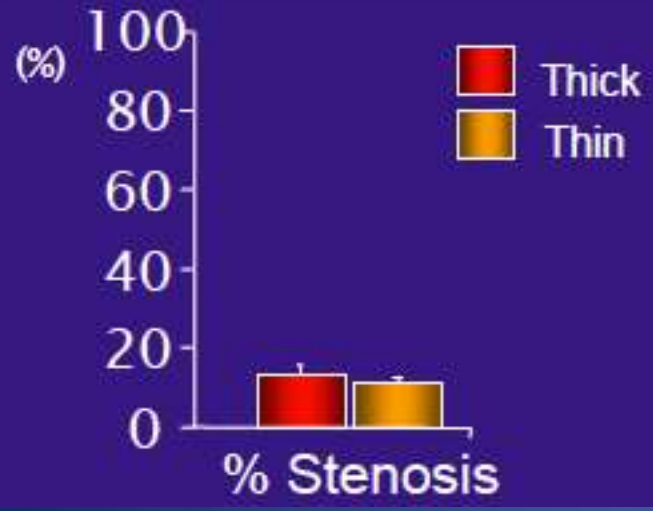
C. Briguori et al. J Am Coll Cardiol 2002;40:403–9

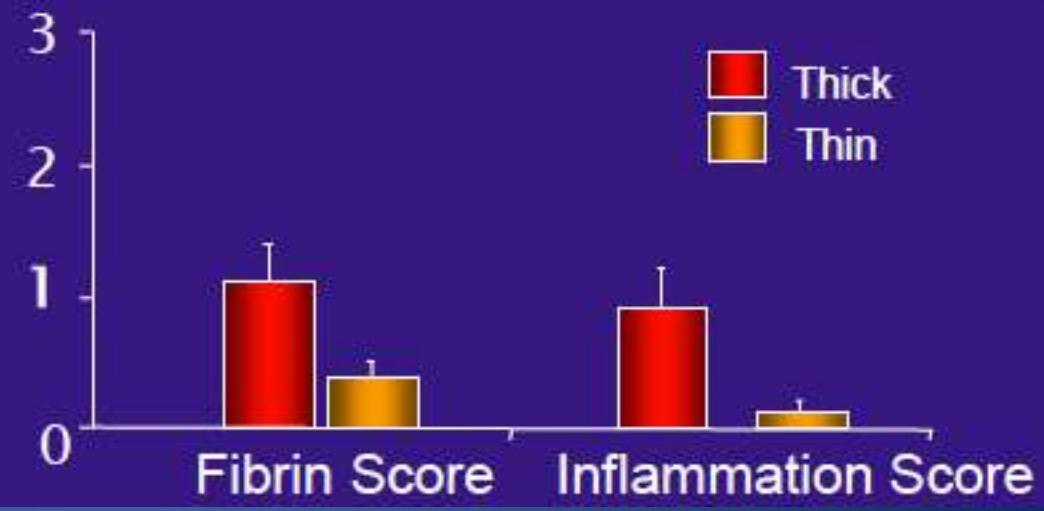
Strut Thickness & Inflammation

14 day Rabbit Iliac Artery



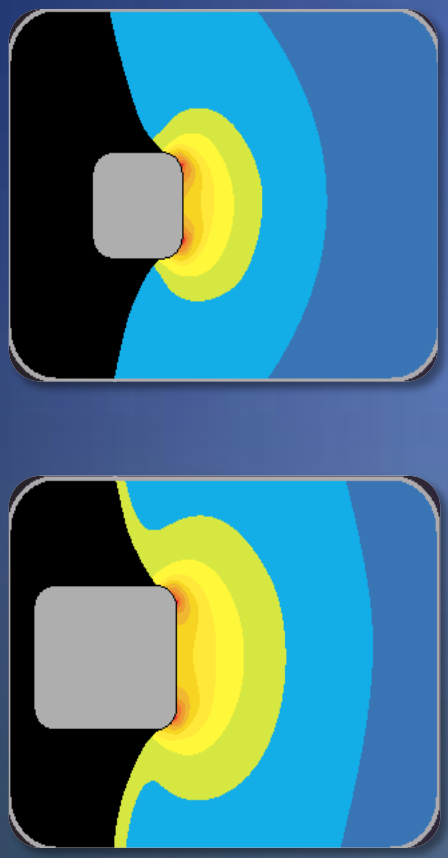






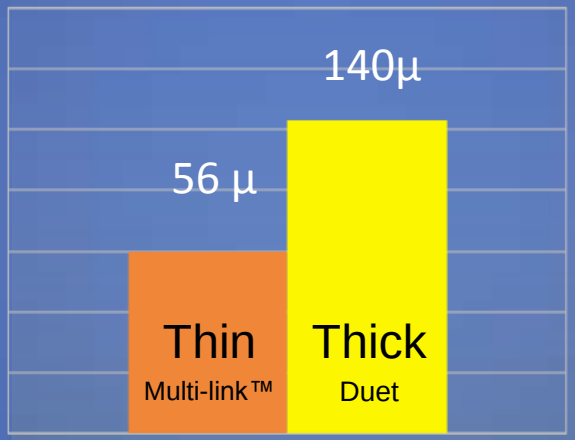
Virmani. TCT 2008: A New Standard in DES Symposium

Thicker Struts and Restenosis



ISAR STEREO[1]

6 month binary restenosis



Thin, Binary Restenosis (6 months), 15%

Thick, Binary Restenosis (6 months), 26%

ISAR STEREO[2]

6 month binary restenosis

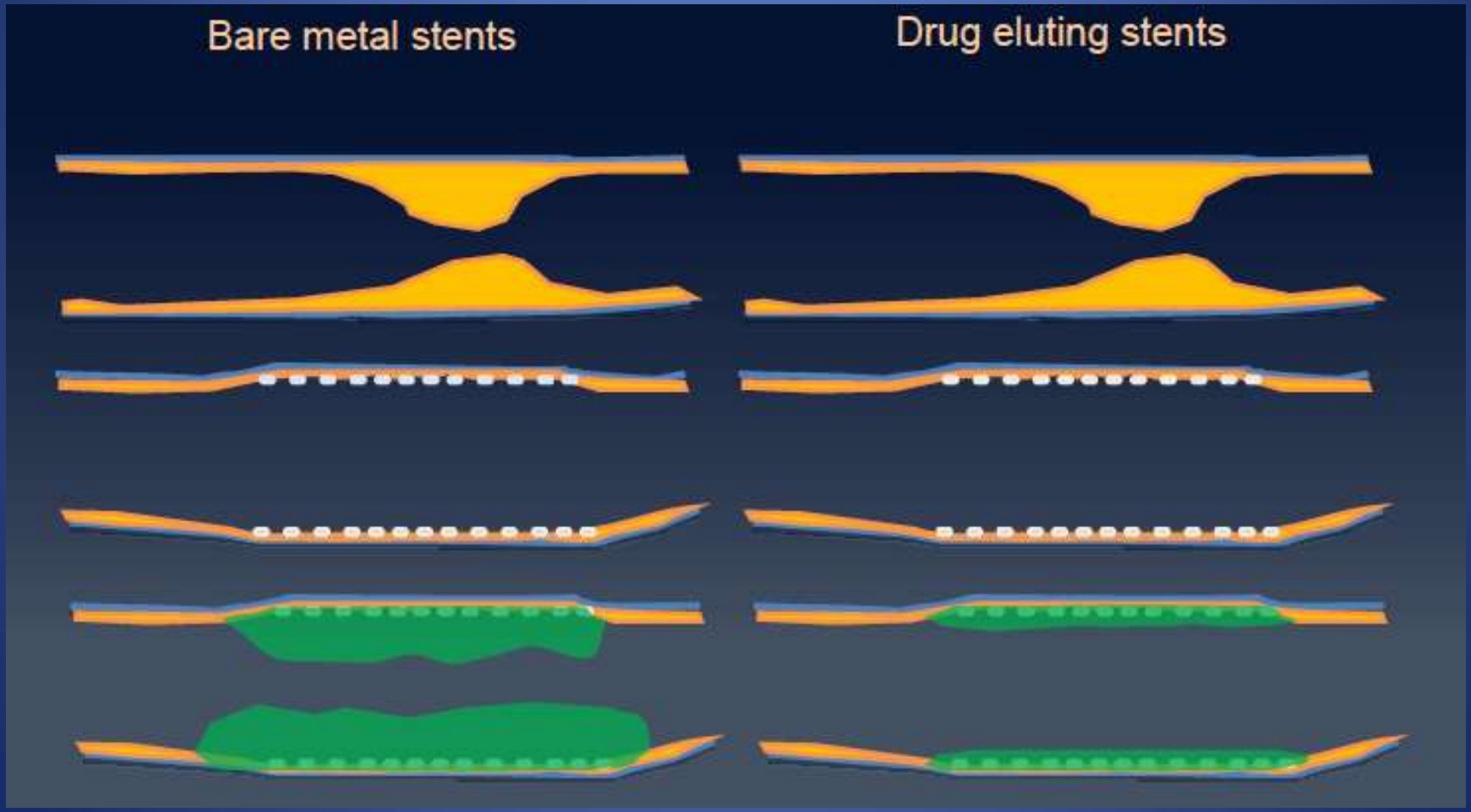
Thin, Binary Restenosis (6 months), 18%

Thick, Binary Restenosis (6 months), 31%

[1]ISAR STEREO II JACC Vol. 41, No. 8, 2003 April 16, 2003:1283-8.

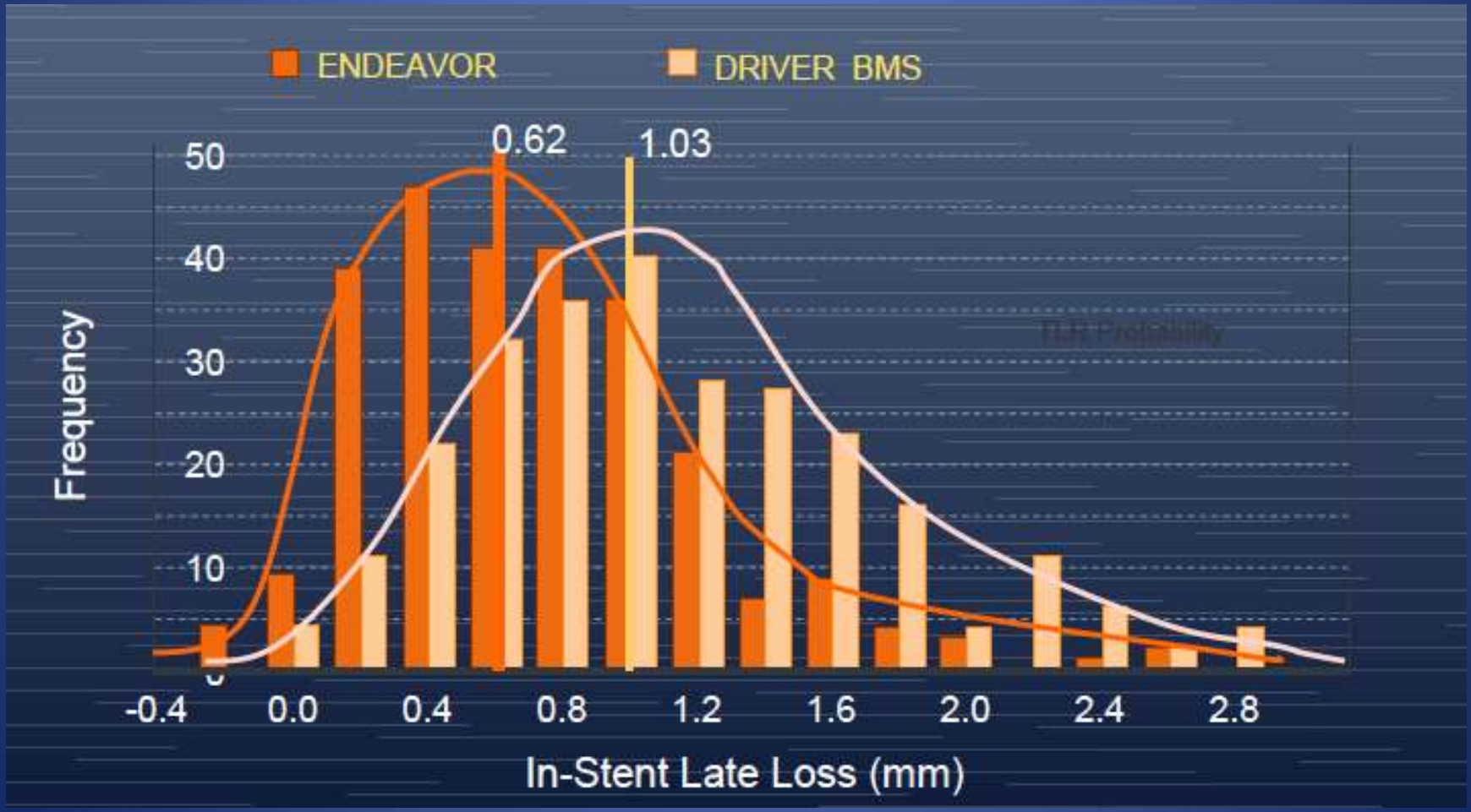
[2]ISAR STEREO I Kastrati et al. Circulation; 103:2816. June 12, 2001

Small Vessels: Impact on late loss with DES



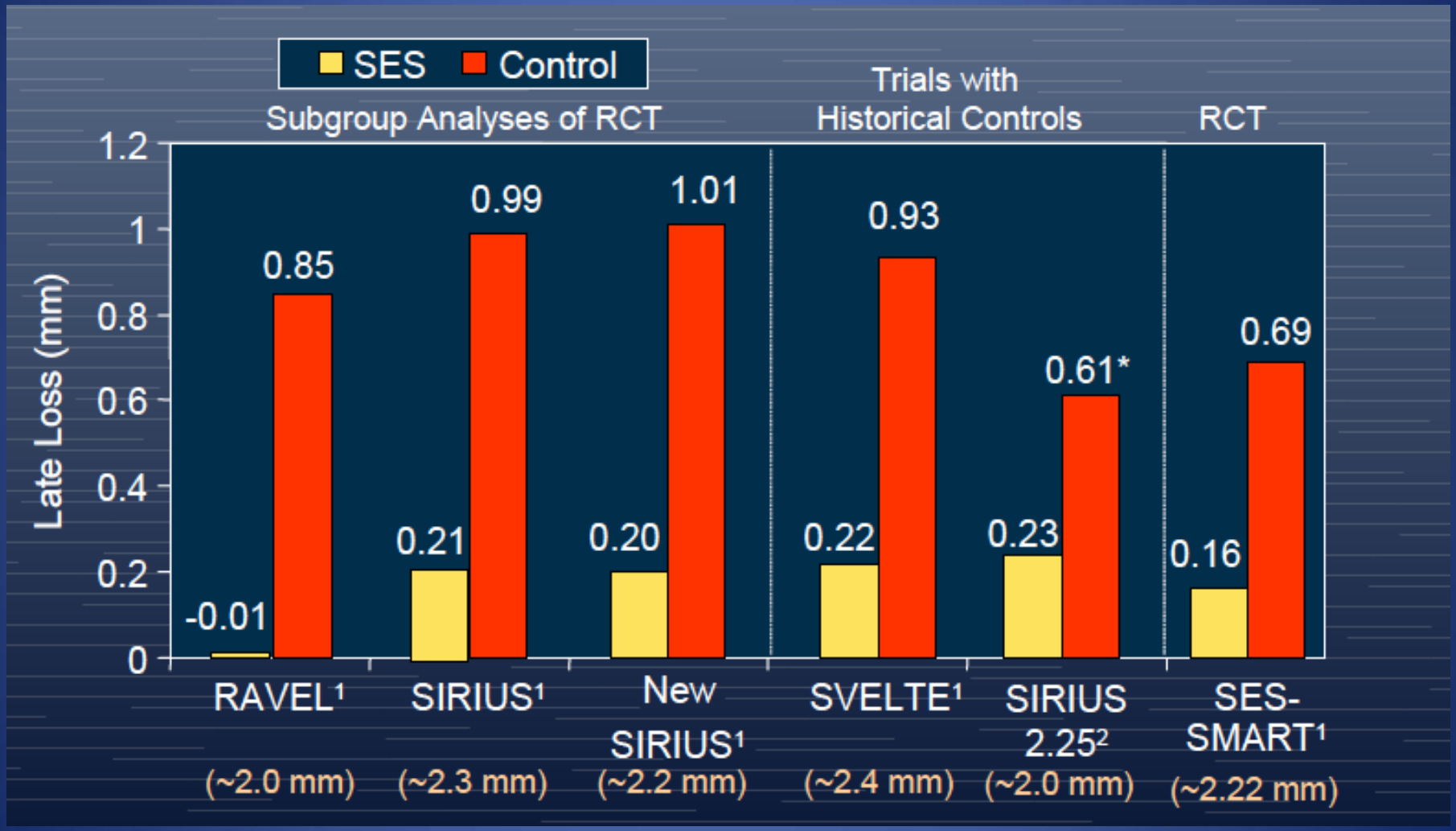
Distribution of late loss with DES vs BMS

Vessel size = 2.75 mm; Lesion Length 13.8 mm



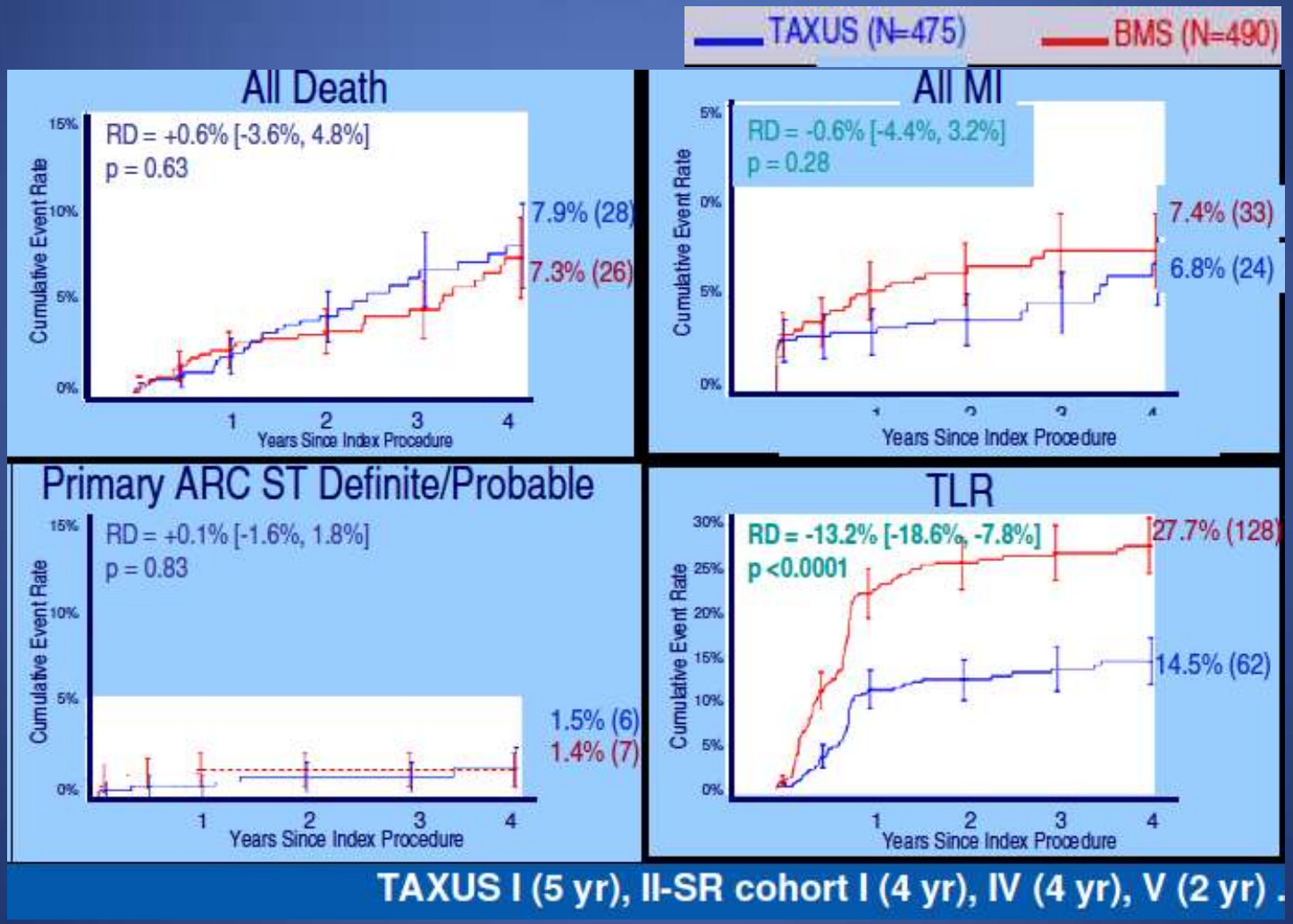
ENDEAVOR II

Late Loss in Small vessels



Perin E. Rev Cardiovasc Med. 2005; 6 (suppl 1):S13-S21.

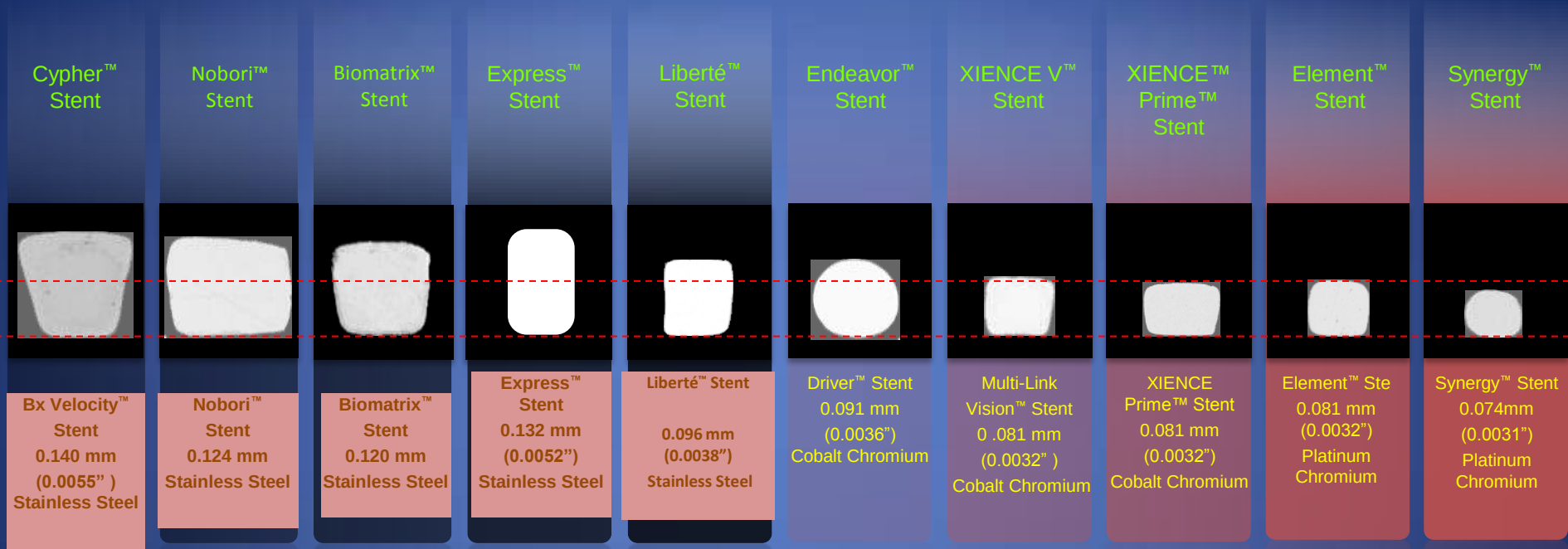
TAXUS Subgroup : RVD <2.5mm n=965



Late Loss in different DES & BMS

Metal Drug Eluting Stent Evolution

Improved healing? Safer, less complex delivery?



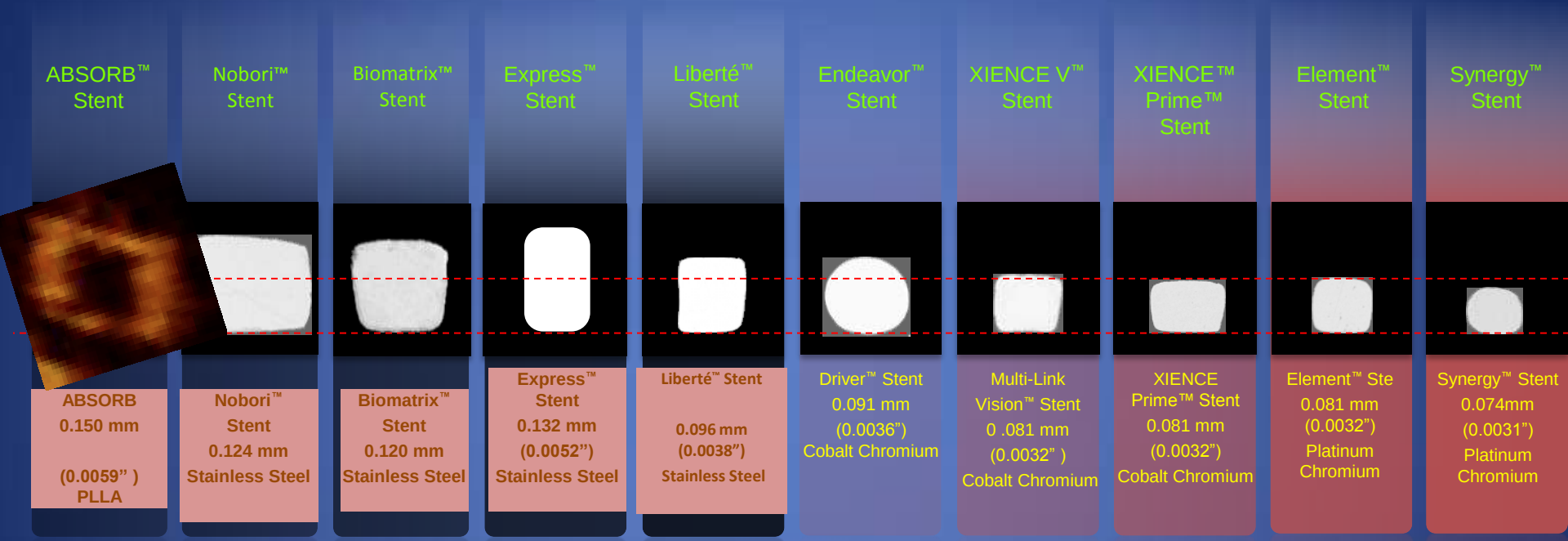
NB: Orsiro 0.060mm

Excellent platforms with good deliverability, good radial strength – minimal recoil, good wall coverage – to reduce plaque prolapse and minimise longitudinal shortening.

Material change : to Co Cr or Pt Cr alloys – allow thinner struts with enhance flexibility and visibility.

Metal Drug Eluting Stent Evolution

Improved healing? Safer, less complex delivery?



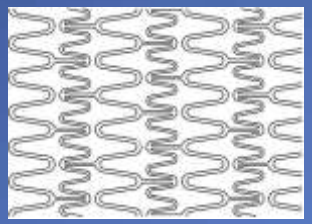
NB: Orsiro 0.060mm

Excellent platforms with good deliverability, good radial strength – minimal recoil, good wall coverage – to reduce plaque prolapse and minimise longitudinal shortening.

Material change : to Co Cr or Pt Cr alloys – allow thinner struts with enhance flexibility and visibility.

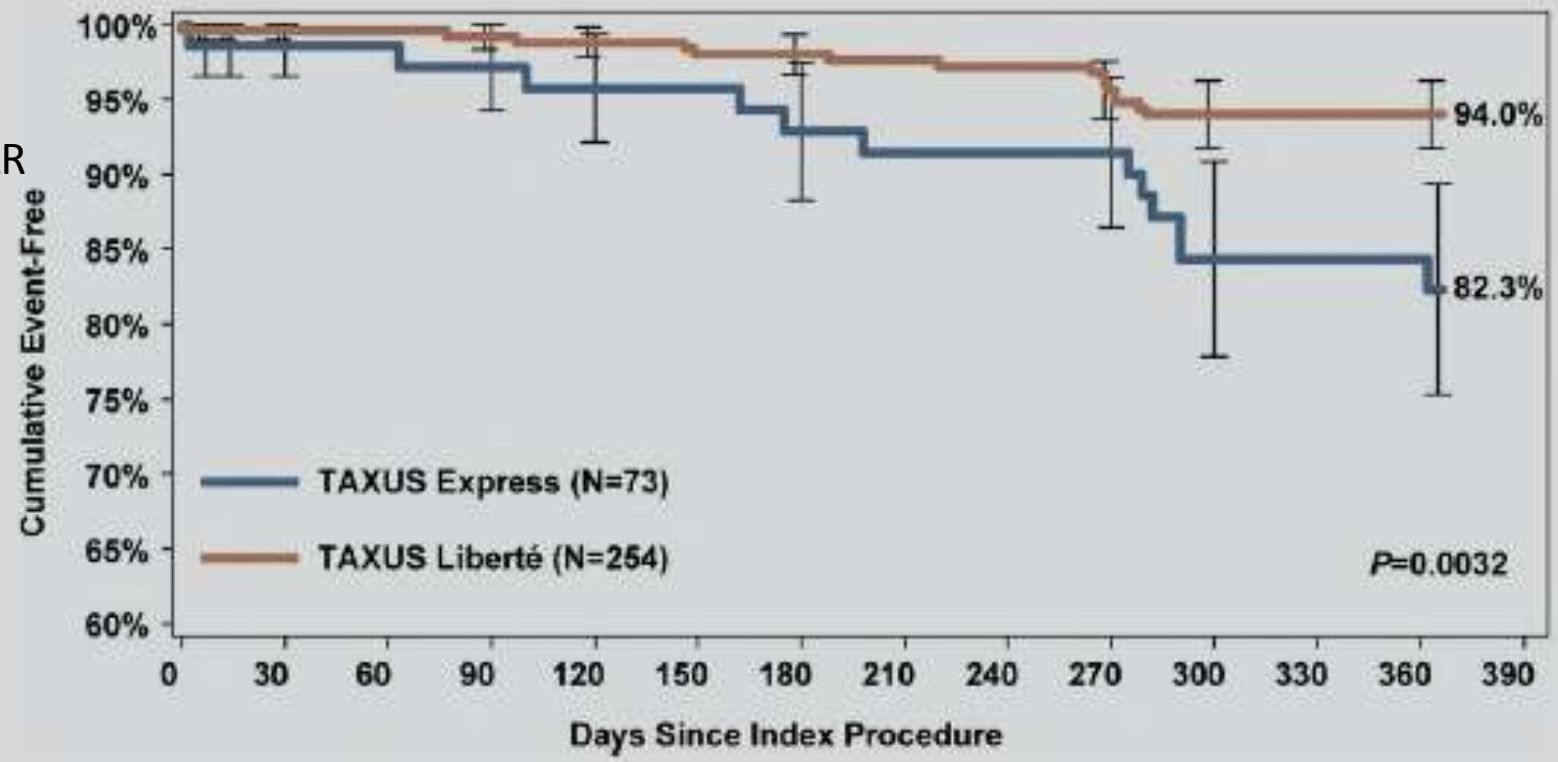
TAXUS ATLAS Small Vessel (2.25mm stents)

TAXUS Express :
0.0052” strut thickness



TAXUS Liberte :
0.0038” strut thickness

TLR

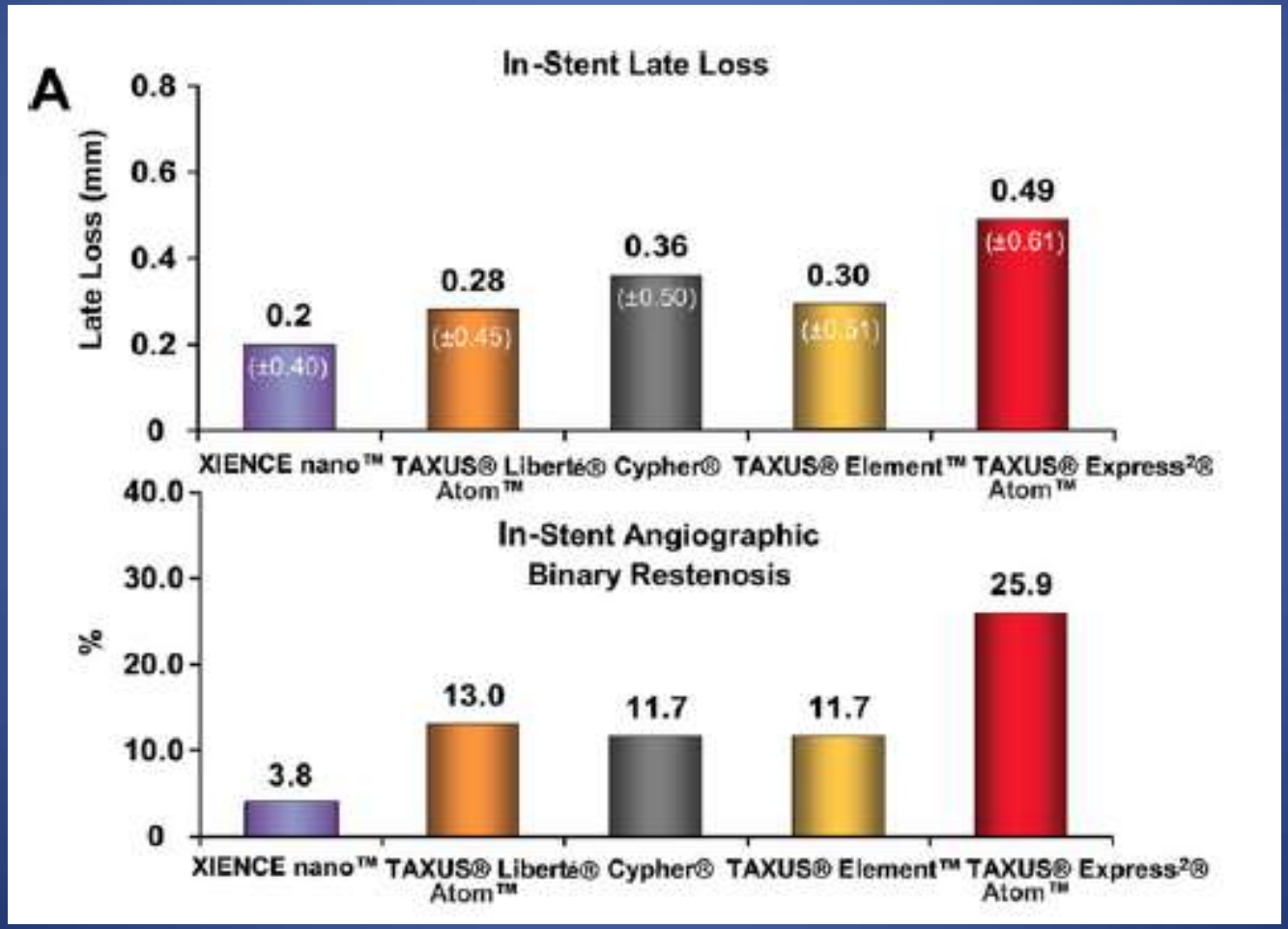


(J Am Coll Cardiol Intv 2008;1:699 –709)

Xience nano Everolimus Eluting Coronary System (EECSS) vs other DES platforms – 2.25mm

SPIRIT Small Vessel Trial

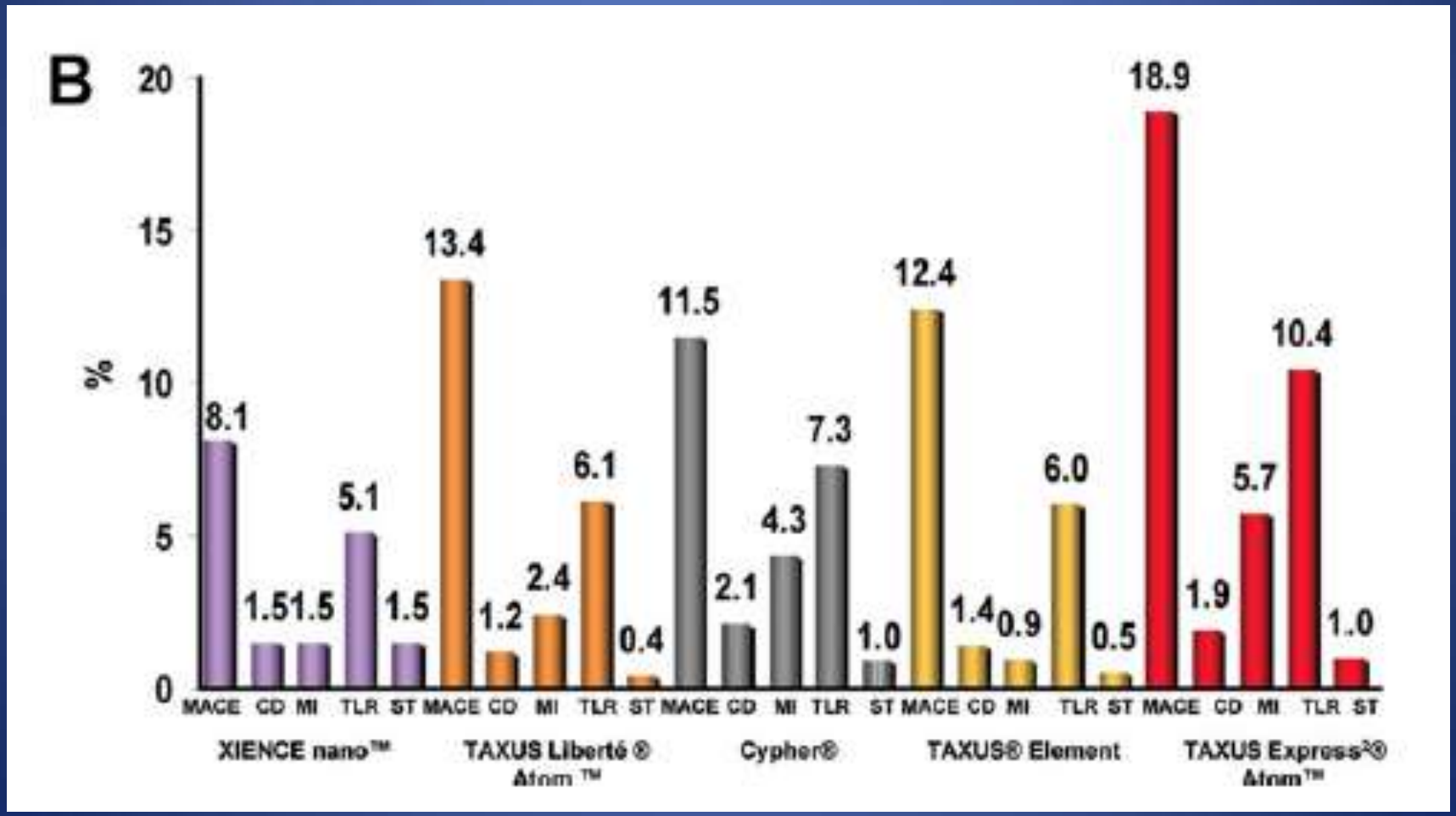
8 mth Angiographic data



LA Cannon et al. Cath and CV Interventions 80; 546-553(2012)

Xience nano Everolimus Eluting Coronary System (EECSS) vs other DES platforms – 2.25mm

SPIRIT Small Vessel Trial



LA Cannon et al. Cath and CV Interventions 80; 546-553(2012)

Impact of Lesion Length and Vessel Size on Clinical Outcomes After Percutaneous Coronary Intervention With Everolimus- Versus Paclitaxel-Eluting Stents

Pooled Analysis From the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials

Bimmer E. Claessen, MD, PhD,* Pieter C. Smits, MD,† Dean J. Kereiakes, MD,‡
Helen Parise, ScD,* Martin Fahy, MSc,* Elvin Kedhi, MD,† Patrick W. Serruys, MD, PhD,§‖
Alexandra J. Lansky, MD,¶ Ecaterina Cristea, MD,* Krishnankutty Sudhir, MD, PhD,‖
Poornima Sood, MD,‖ Charles A. Simonton, MD,‖ Gregg. W. Stone, MD*

N= 6,183 pts
EES : n=3,944 & PES : n=2,239
Long lesions – median LL 13.4mm
Small vessel – RV diameter median 2.65mm

Group A	Group B	Group C
LL ≤ 13.4mm & RVD >2.65mm N=1,297	RVD ≤ 2.65mm & LL ≤ 13.4mm or RVD >2.65mm & LL > 13.4mm N=2,981	RVD ≤2.65mm & LL > 13.4mm N=1,905

J Am Coll Cardiol Intv. 2011;4(11):1209-1215. doi:10.1016/j.jcin.2011.07.016

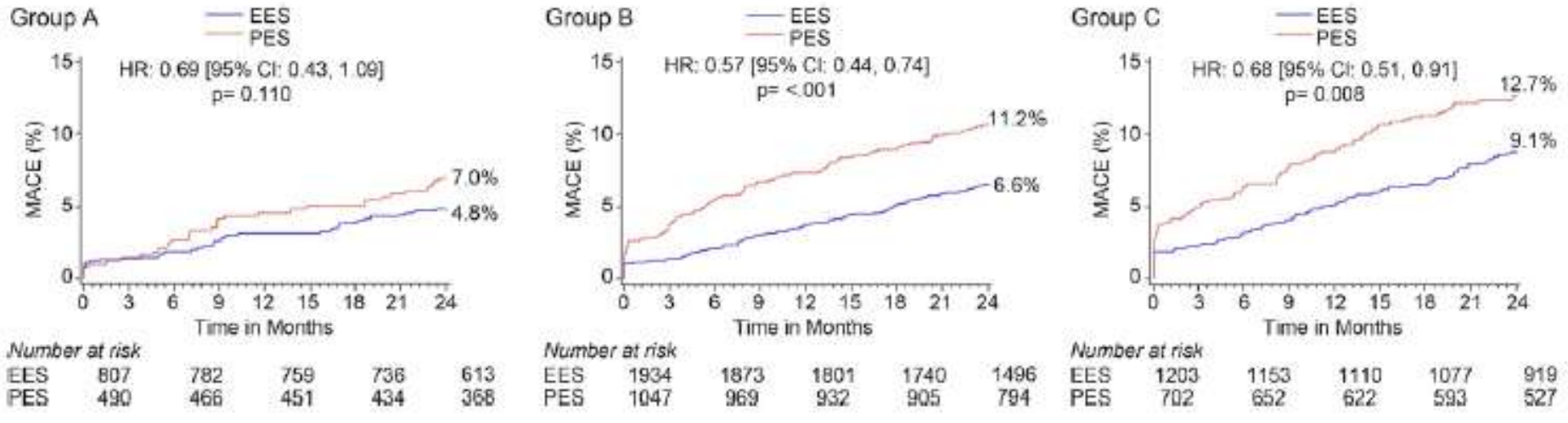
2-Year Outcomes According to Vessel Diameter and Lesion Length

	Group A LL ≤13.4 mm and RVD >2.65 mm (n = 1,297)	Group B RVD ≤2.65 mm and LL ≤13.4 mm or RVD >2.65 mm and LL >13.4 mm (n = 2,981)	Group C RVD ≤2.65 mm and LL >13.4 mm (n = 1,905)	p Value
Major adverse cardiac events	5.6%	8.2%	10.4%	<0.0001
Death	2.7%	2.6%	2.1%	0.50
Cardiac death	0.6%	1.4%	1.1%	0.13
Myocardial infarction	3.3%	3.0%	4.5%	0.02
ID target lesion revascularization	2.9%	5.0%	6.3%	0.0002
Definite or probable stent thrombosis	0.8%	1.1%	1.4%	0.25
Definite stent thrombosis	0.5%	0.8%	0.9%	0.37

ID = ischemia-driven; other abbreviations

Bimmer E. Claessen, et al. *J Am Coll Cardiol Intv*. 2011;4(11):1209-1215

MACE (D, MI & ID-TLR) : EES vs PES – interaction with Lesion Length & Vessel Size.

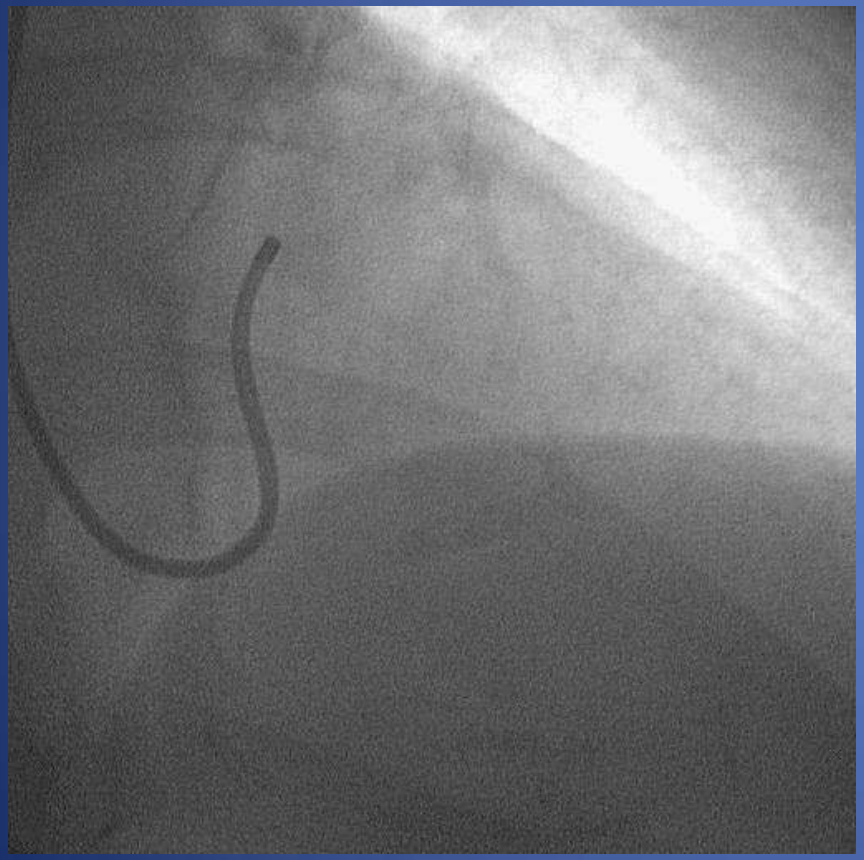


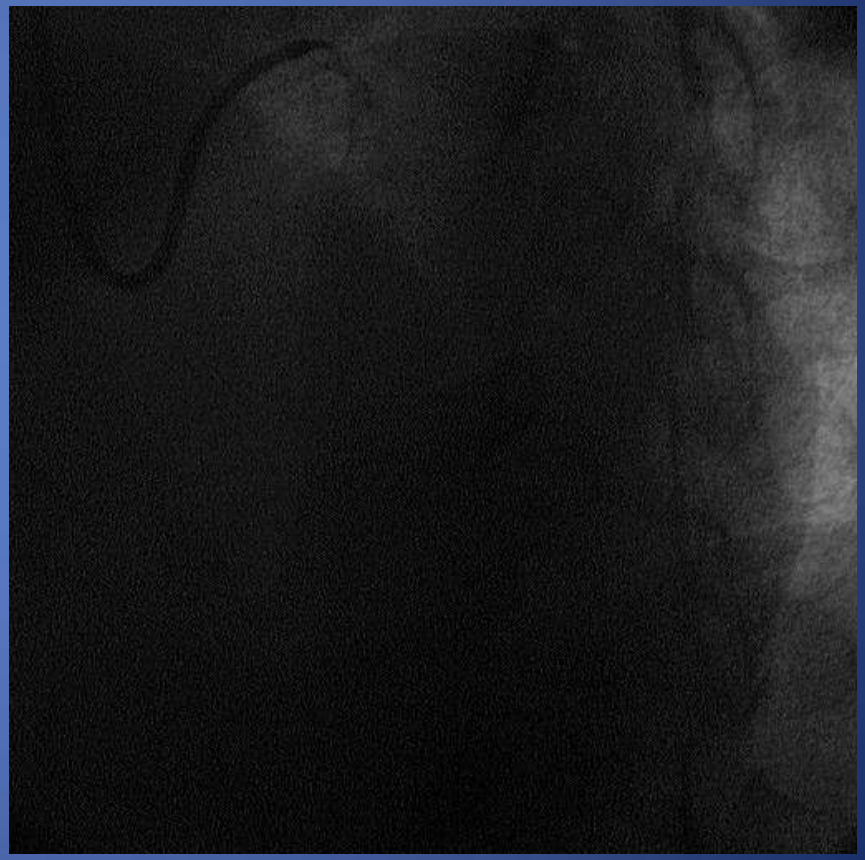
Time-to-Event Curves of MACE

Time-to-event curves of major adverse cardiac events (MACE) in patients randomized to everolimus-eluting stents (EES) versus paclitaxel-eluting stents (PES) according to lesion length and reference vessel diameter. CI = confidence interval; HR = hazard ratio.

J Am Coll Cardiol Intv. 2011;4(11):1209-1215. doi:10.1016/j.jcin.2011.07.016

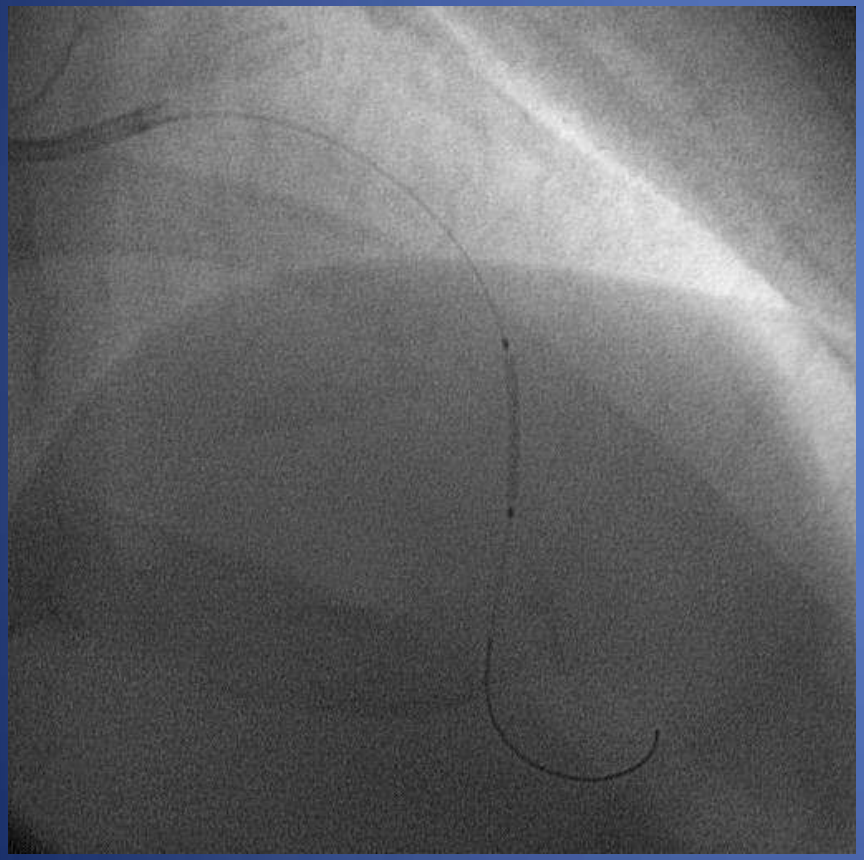
2nd. Generation DES for small vessel disease

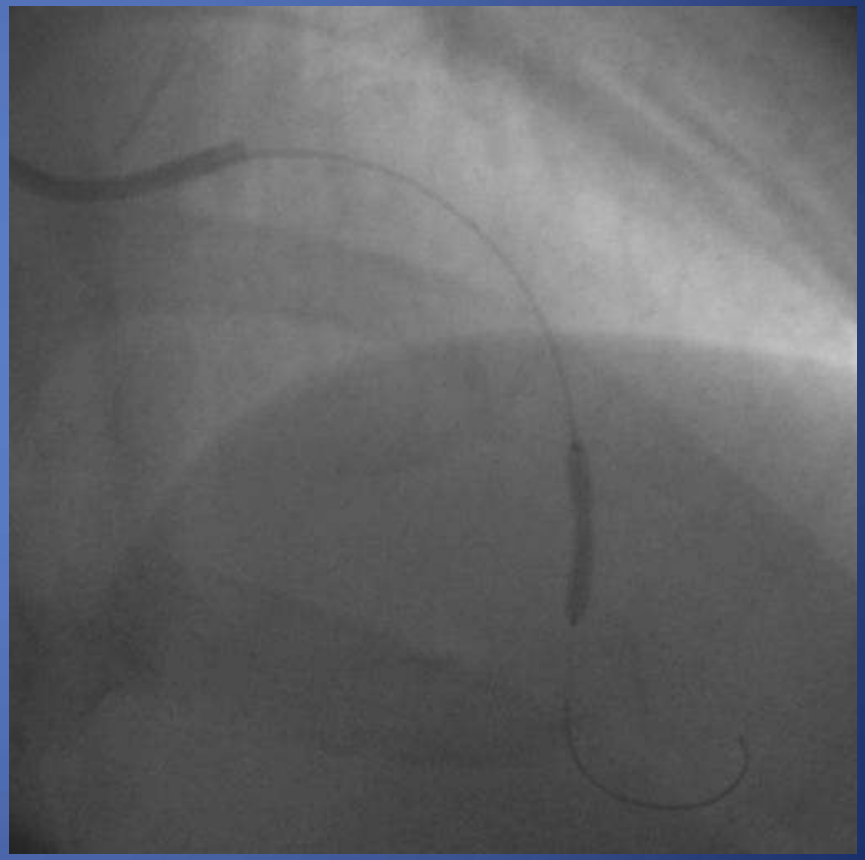




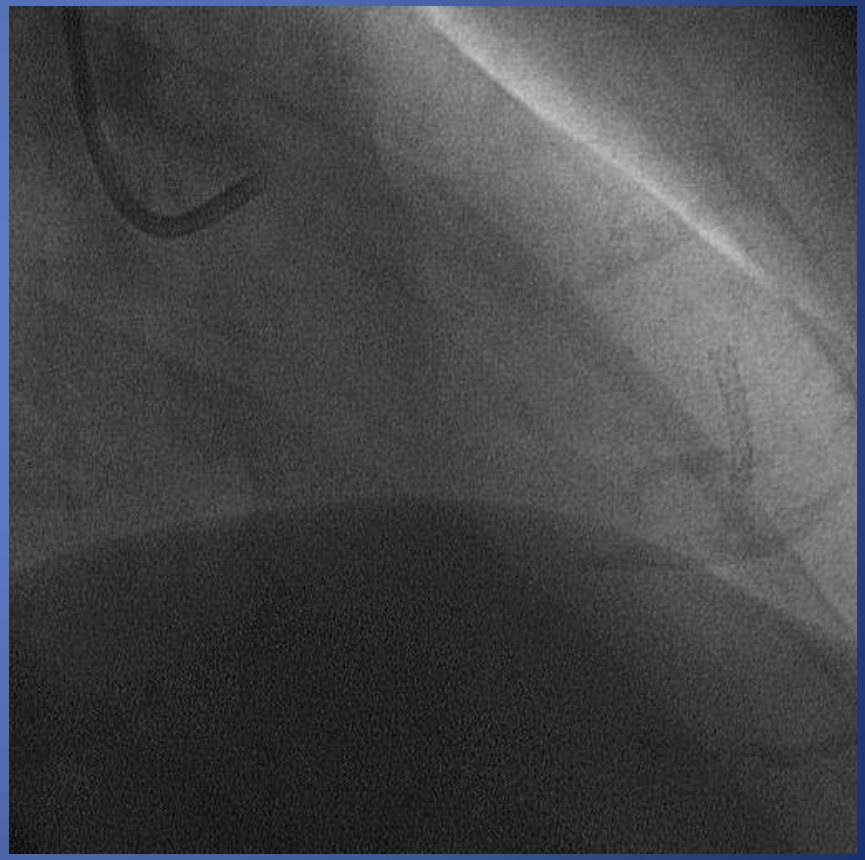
29th. July, 2011

Biomatrix 2.25 x 14mm

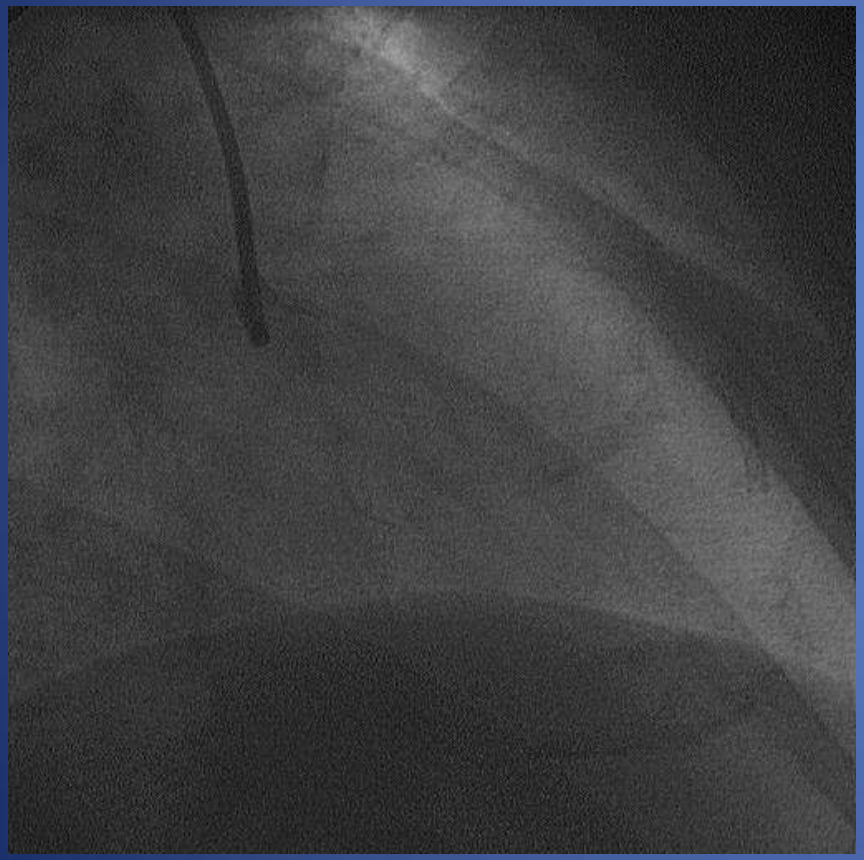


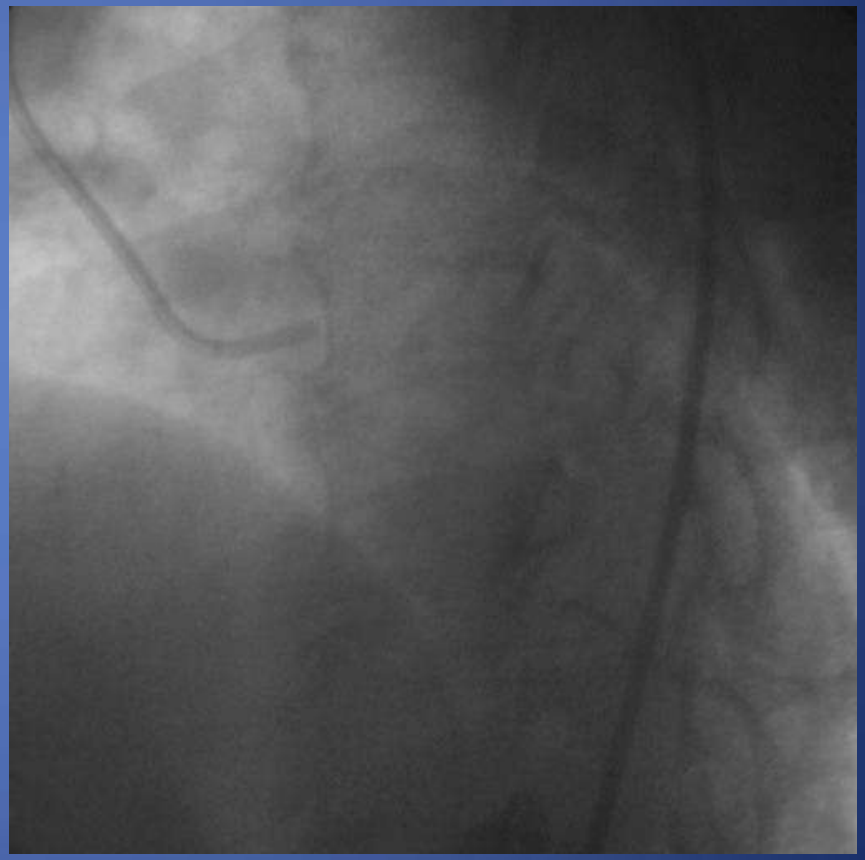


Final Results



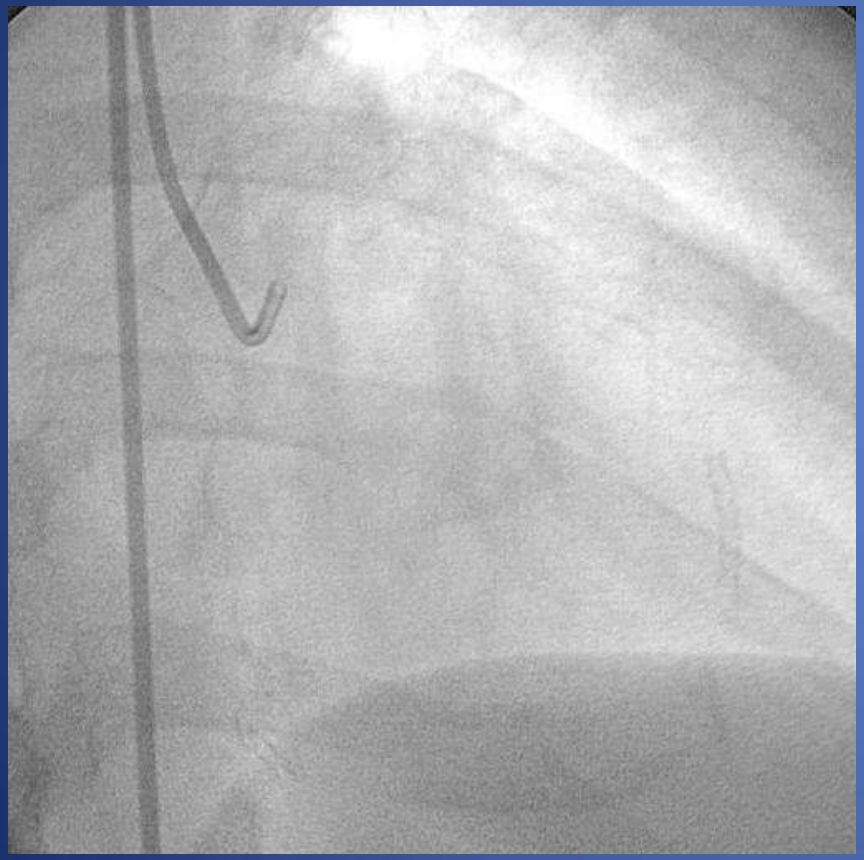
Follow-up Angio: 25.1.2013 (18 mths)



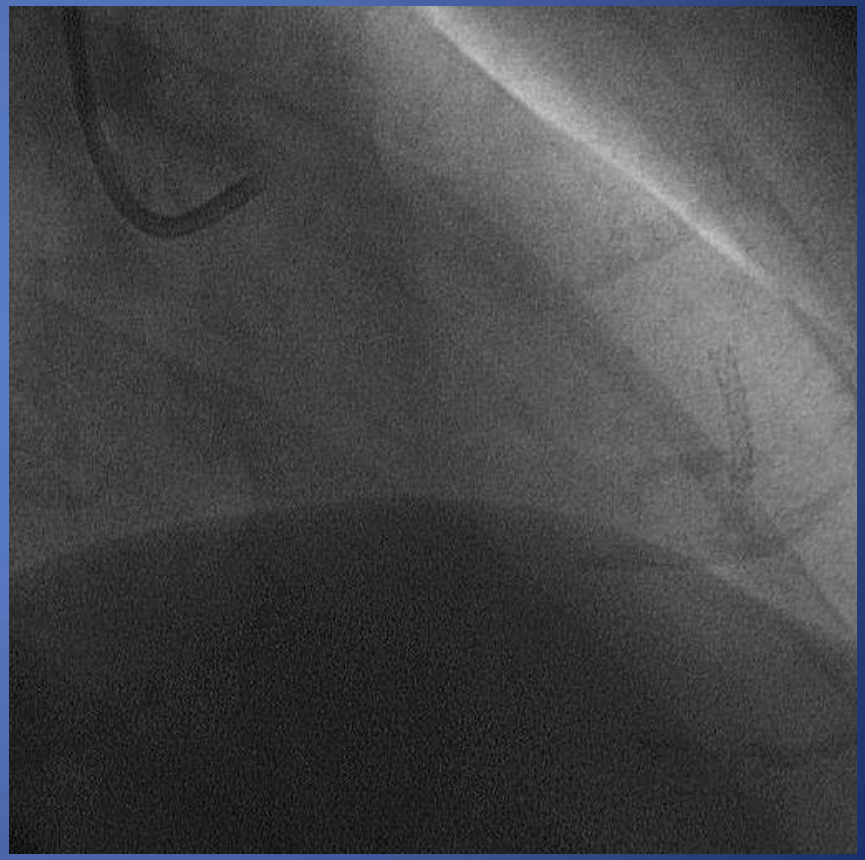


Distal LAD: 18 mth f/up angio

25.1.2013



29.7. 2011



Lessons no.2:

- POBA may be reserved for very small vessels – to achieve flow
- Stenting may give better angiographic results & less TLR & improved clinical outcomes
- DES preferred especially newer generation DES – Limus eluting, thinner struts, ?bio-absorbable polymer, ?non-polymer

Drug-eluting Balloons

No stents – no related issues

DIOR-eluting Balloon: The Spanish Registry Focus on Small Vessels

A. Serra[1], B. Vaquerizo[1], F. Miranda[1], V. Martínez[2], JA. Gómez-Hospital[2], A. Cequier[2], A. Iñiguez[3], JA. Baz[3], G. Bastos[3], E. Fernández[4], O. Rodríguez[4], J. Mauri[4], M. Sádaba[5], JA. Rumoroso[5], A. Subinas[5], R. García-Borbolla[6], A. Gomez[6], J. Oneto Otero[6], A. Martínez[7], F. Bossa[8], S. Rodríguez[8], R. Moreno[9], A. Saez[9], E. Pinar[10], M. Valdés[10].

H. Del Mar[1] (Barcelona), H. de Bellvitge[2] (Barcelona), H. Meixoeiro[3] (Vigo), H. Trías i Pujol[4] (Barcelona), H. de Galdakao[5] (Galdakao), H. de Jerez[6] (Jerez), H. Gral. de Castellón[7] (Castellón), H. Univ. Canarias[8] (Tenerife), H. La Paz[9] (Madrid), H. V. Arrixaca/La Vega[10] (Murcia)

Spanish DIOR Registry: Small vessel - Angiographic f/up

N=190; Lesions = 199

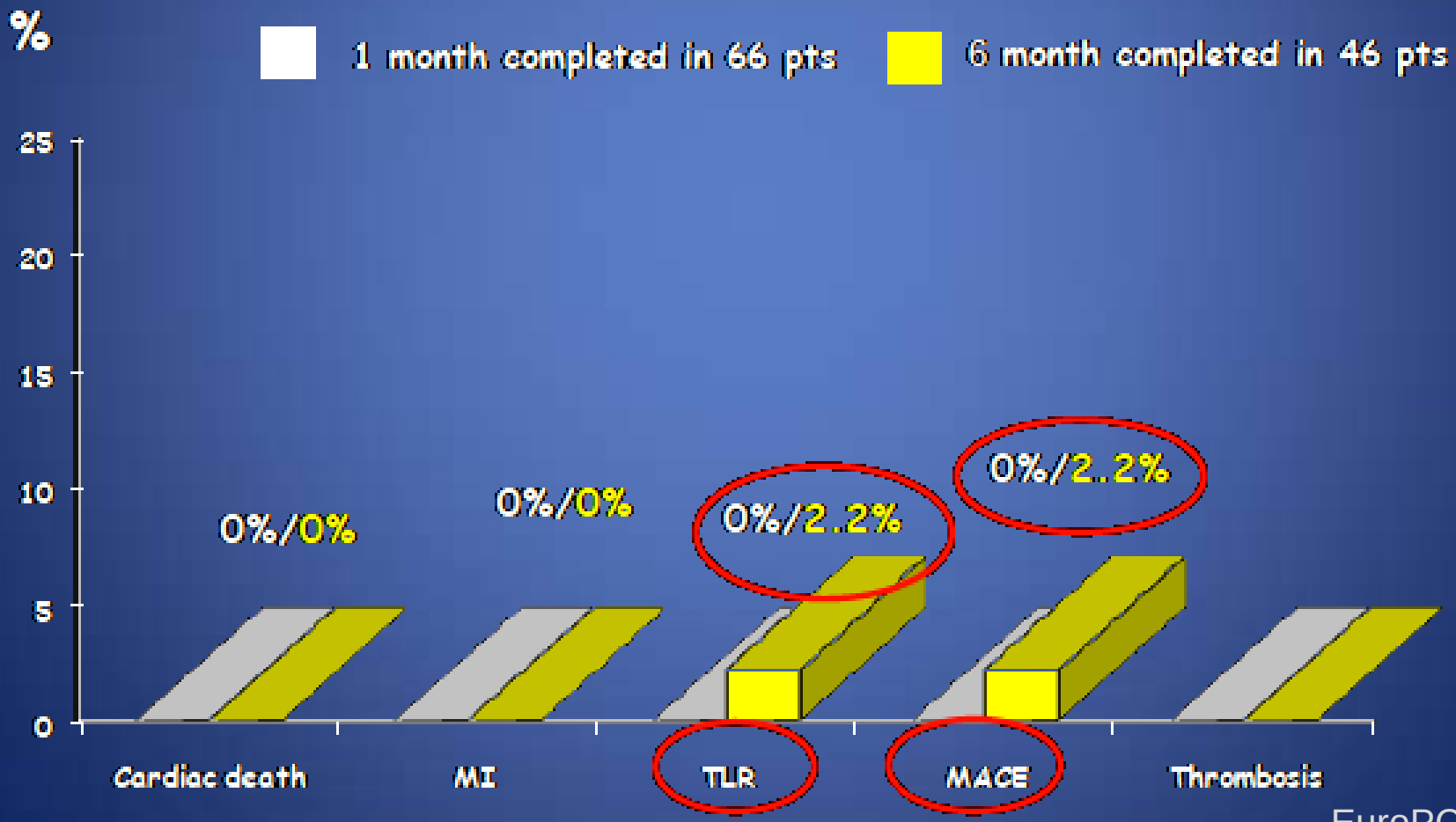
38.2% treated for small vessels (<2.5mm diameter)

Variable	Pre-PCI	Post-PCI	6mo FU
Reference diameter	1.9±0.3		
Lesion length	15.3±6.6		
MLD	0.41±0.31	1.55±0.40	1.28±0.47
Diameter stenosis %	81.2±13.4	24.8±14.9	36.6±23.1
Acute Gain		1.14 ±0.12	
In-segment late loss			0.27±0.07
Binary Restenosis, (n) %			4/30 (13.3%)

DIOR – Spanish Registry : Clinical follow-up 6 mths.

92.1% of Angiographic success

(BMS after Dior 7.9% (7): coronary dissection)



Treatment of Small Vessel Coronary Artery Disease by the Sequent® Please Paclitaxel coated balloon: PEPCAD I SVD-Study

- prospective, non-randomized, multi-center, one-arm phase-II study
- De-novo lesions, reference diameter 2.25 - 2.8 mm

Primary endpoint

o Late lumen loss in segment (6 months)

Secondary endpoints

o Procedural success
o Binary restenosis rate
o MACE (6 months)
o MACE (1 and 3 years)

Inclusion criteria

- Stable or unstable angina
- De-novo lesions in native coronary arteries

Medication

o ASS > 100 mg daily
o Clopidogrel 75 mg daily
o 1 month DEB only
o 3 months DEB + BMS

PEPCAD I

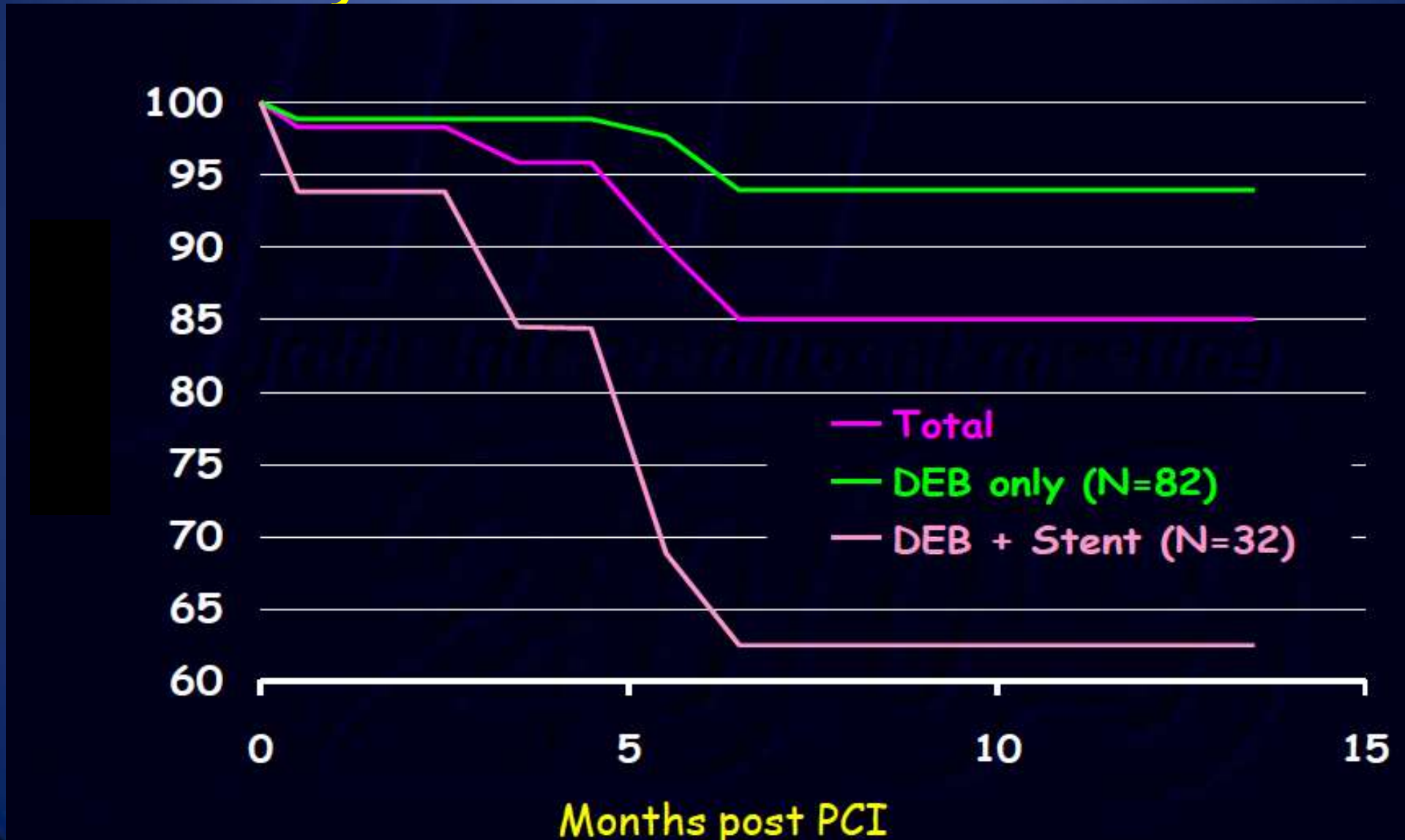
Vessel ≤ 2.8mm diameter

PEPCAD I	DEB ITT N=120	DEB Only N=82	Taxus*	BMS*
Follow-up [mo]	6.7±2.1	6.7±1.9	9	9
Late loss [mm]	0.3±0.55	0.18±0.38	0.49±0.61	0.90±0.63
Restenosis (segment)	15.5% (~30% in DEB + BMS)	5.5%	31.2%	49.4%
TLR	12%	4.9%	10.4%	21.5%
Myocardial infarction	0.8%	1.2%	5.7%	2.2%
Cardiac death	0%	0%	1.9%	1.1%
Total MACE	13.7%	6.1%	18.9%	26.9%

EuroPCR 2010

Circulation 2010; 99:165-174

PEPCAD I :
1 year event-free survival

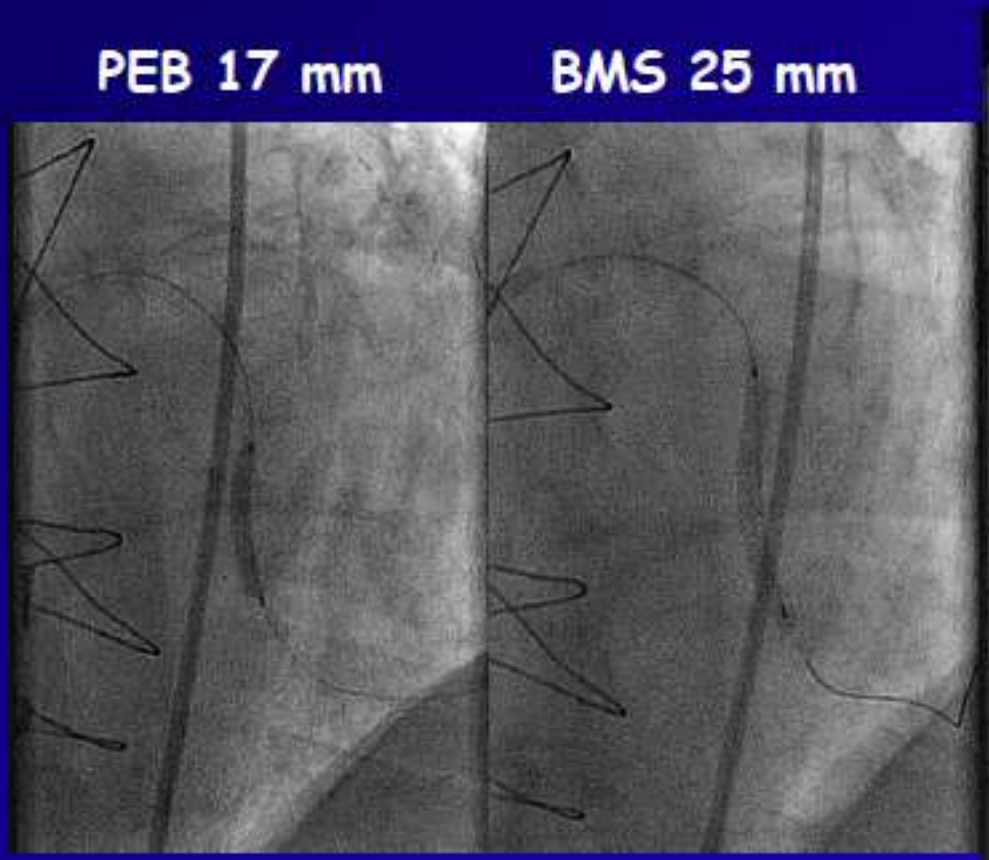


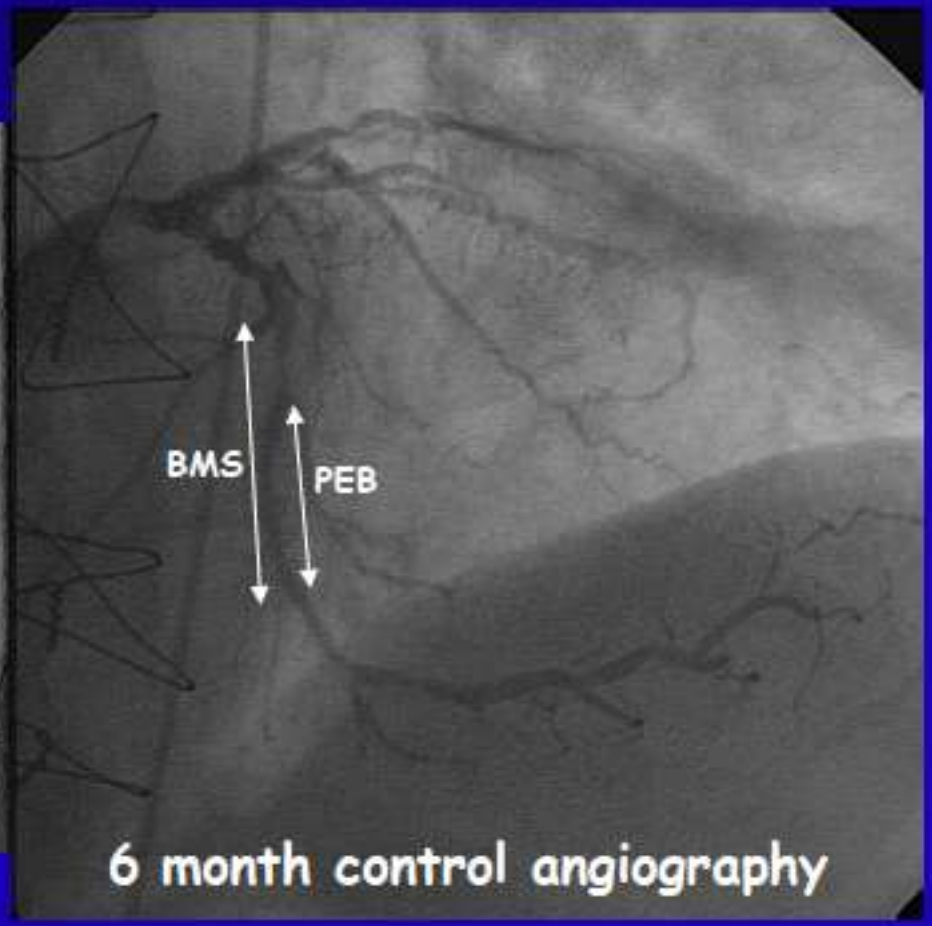
PEPCAD I, 6 month F/up

	DEB & BMS N=32	DEB Only N=82
Follow-up [mo]	**6.5** ±1.5	**6.4** ±1.2
Late loss [mm]	**0.73** ±0.74	**0.18** ±0.38
Restenosis (segment)	**44.8%**	**5.5%**
TLR	**27.1%**	**4.9%**
Myocardial infarction	**3.3%**	**1.2%**
Cardiac death	**0%**	**0%**
Total MACE	**37.5%**	**6.1%**

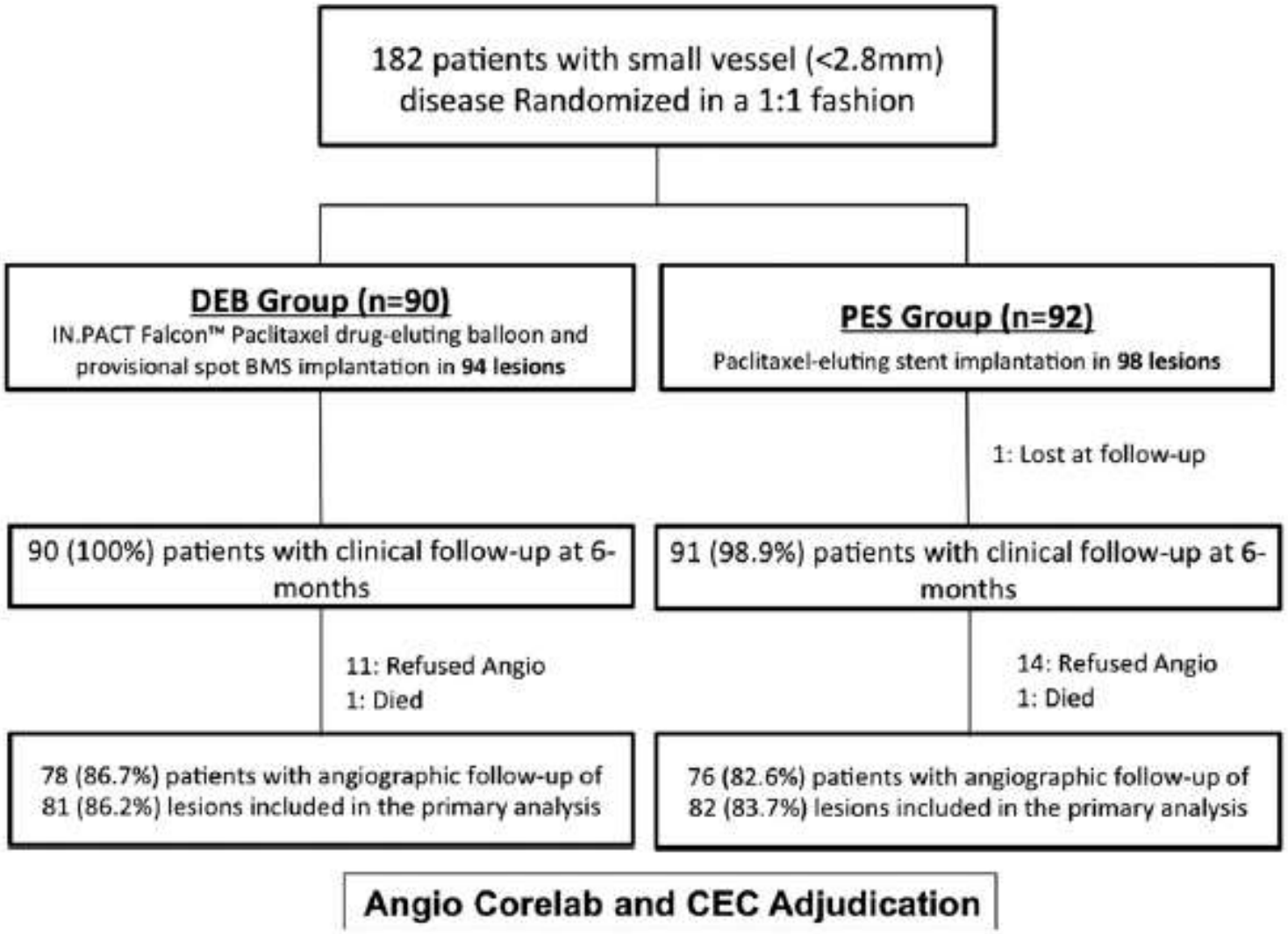
Circulation 2010; 99:165-174

Explanation for higher restenosis & late loss when combining BMS + DEB: Geographic mis-match



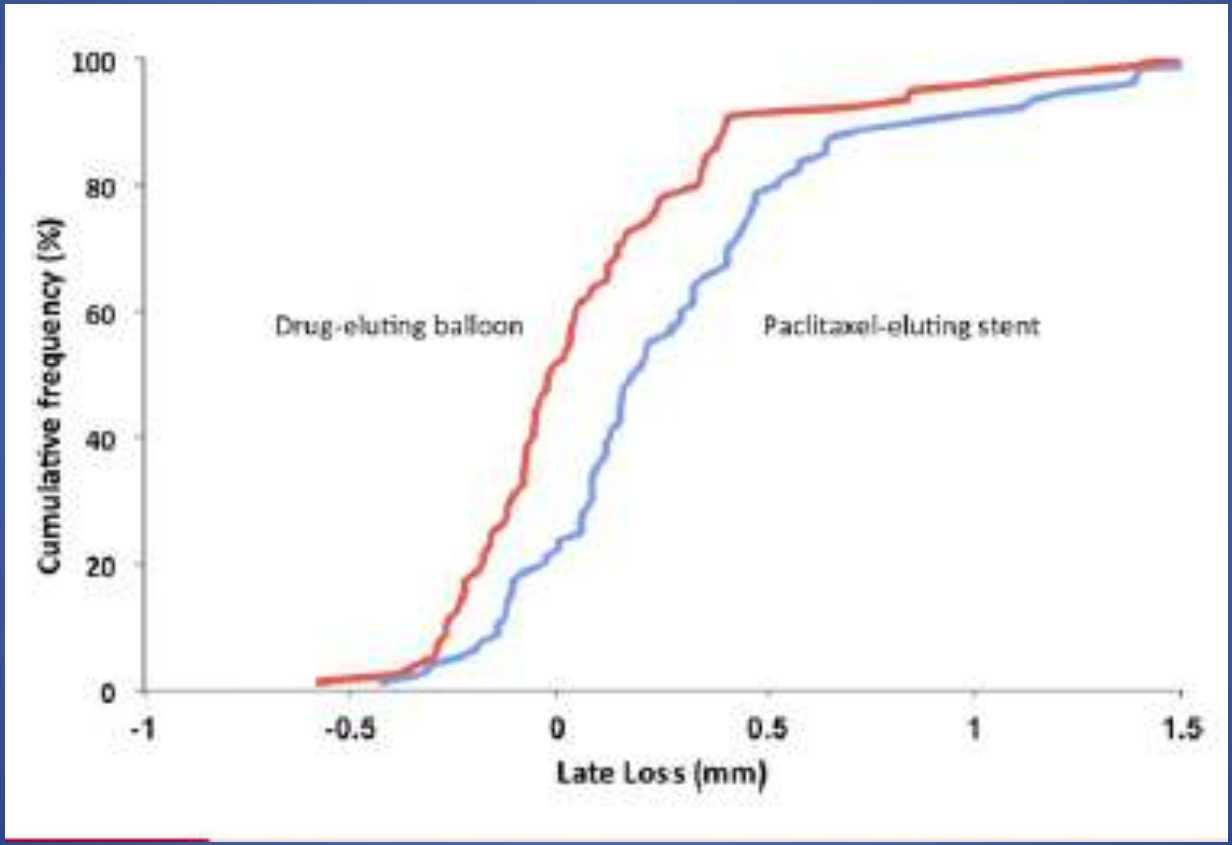


The BELLO (Balloon Elution and Late Loss Optimization) Study



A Latib et al. J Am Coll Cardiol 2012;60:2473–80

The BELLO
(Balloon Elution and Late Loss Optimization) Study



A Latib et al. J Am Coll Cardiol 2012;60:2473–80

Piccoleto Trial

Paclitaxel-eluting balloon vs Paclitaxel-eluting stent in small coronary vessel disease

Bernado Cortese, A.Michell, A.Picchi,
A.Coppolaro, S.Severi, U.Limbruno
U.O. Emodinamica, Cardiologic Dpt.
Ospedale Misericordia Grosseto

EuroPCR 2009

Study Design

Pts. undergoing PCI of small coronary arteries

(≤ 2.75mm)

randomized
1:1

Paclitaxel-eluting balloon
Dior® (Eurocor)
DIOR I DEB
45" X 2

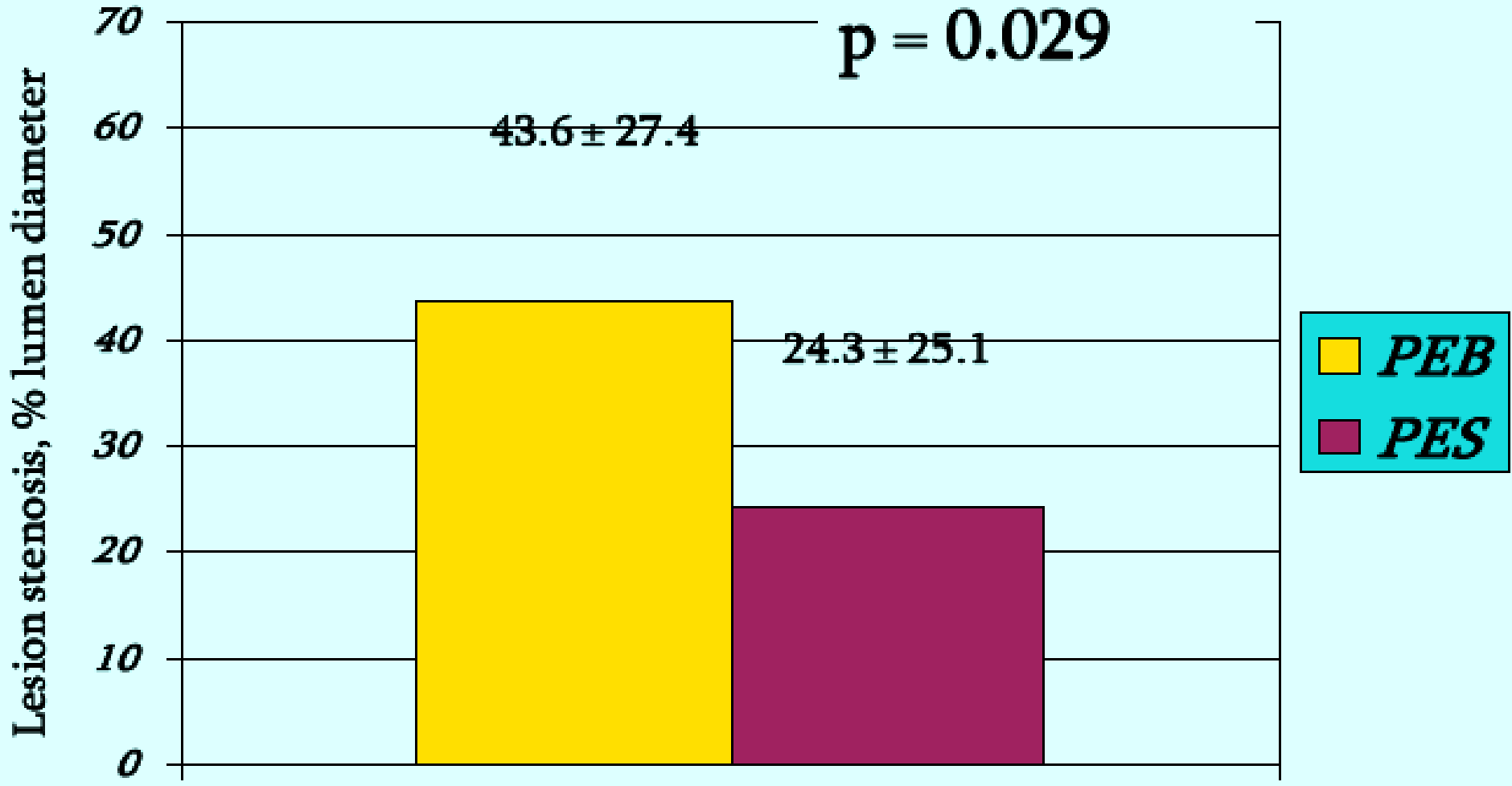
Paclitaxel-eluting stent
Taxus Libertè® (Boston Scientific)

Provisional BMS implantation (Vision®, Abbott V.): stenosis >50%, dissection, TIMI flow <3

ASA indef. + Clopidogrel (PEB 1 mo., PEB+BMS 3 mo.)

ASA indef. + Clopidogrel 12 mo.

Primary Endpoint: % Diameter stenosis at 6 months (by QCA)



DEB in Small Vessels-Summary :

- Small coronary vessels may be treated with DEB as a stand-alone strategy
- However, if there is a need for bail-out stenting eg. For dissection, the LLL and TLR rates may be higher with DEB+BMS strategy
- This may be improved with attention to technical details eg. Avoiding geographic miss, adequate predilatation, balloon pressure & ?selection of specific DEB platforms

Bioresorbably Vascular Scaffold ?

Long Diffuse Disease BUT Current platform only ≥ 2.5mm
& Big strut thickness & Deliverability issues

Watch this space!

Other adjunctive techniques & technical issues

Long-term Clinical Outcome After FFR-Guided PCI in Patients with Small-Vessel Disease

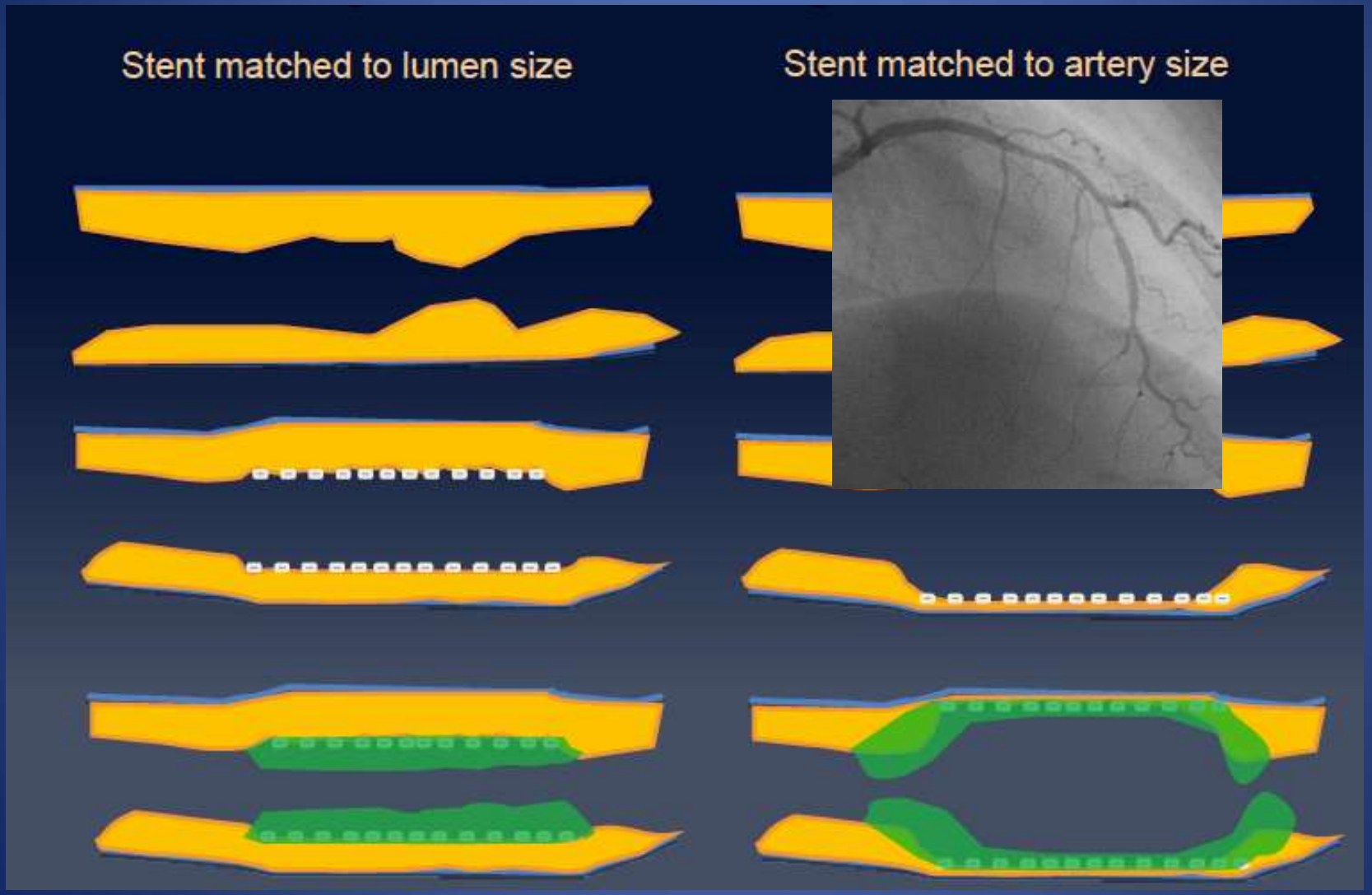
Retrospective registry study with aged-matched controls who underwent angiography-guided PCI.

3-Year Follow Up	FFR (n = 222)	Angiography (n = 495)	*P* Value
Death or Nonfatal MI	6%	14%	0.004
Nonfatal MI	1%	7%	0.007
MACE (Cardiac Death, Nonfatal MI, and TVR)	14%	28%	< 0.001

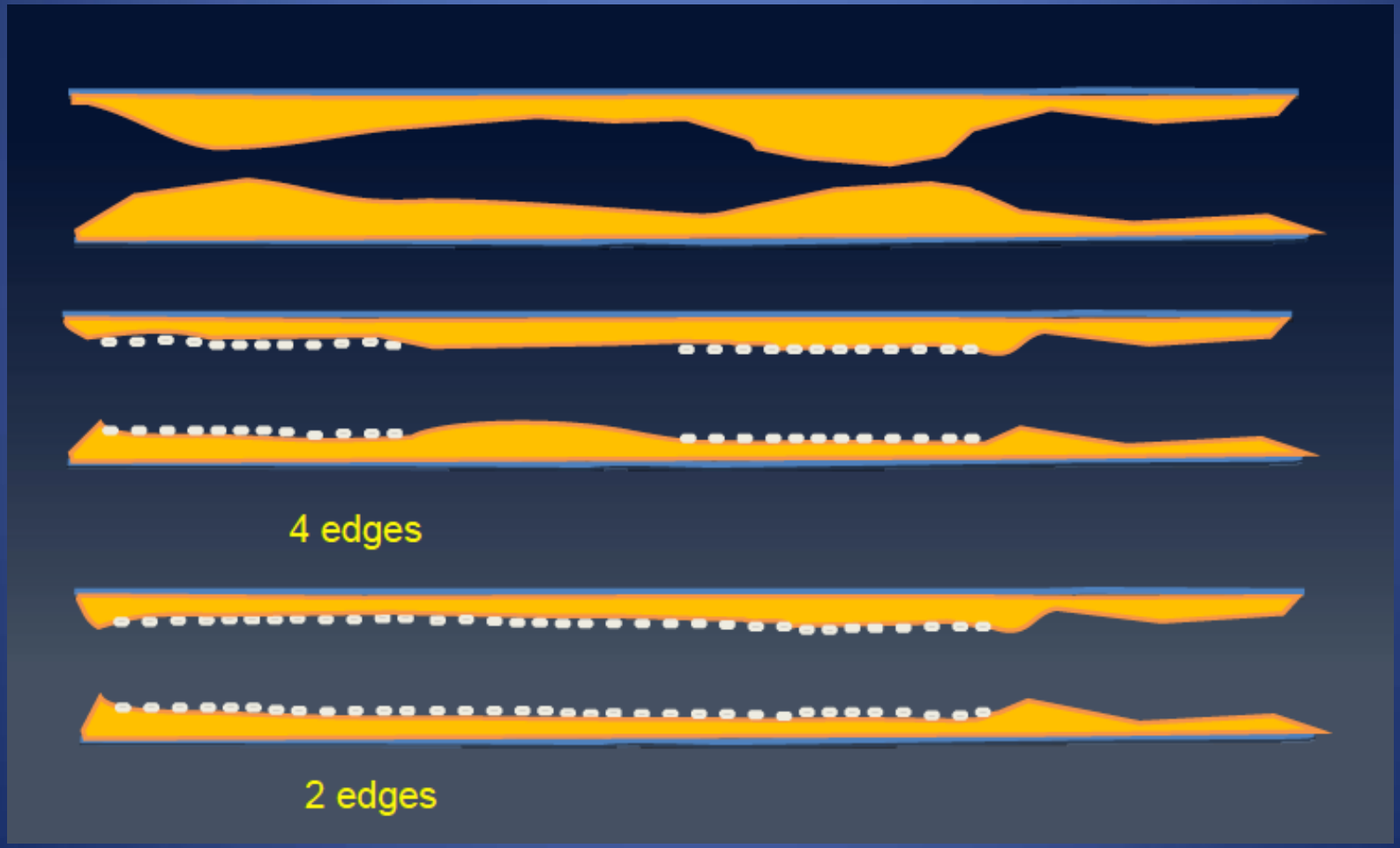
Conclusion: FFR-guided PCI of small coronary arteries is safe and results in better clinical outcomes compared with angiography-guided PCI.

Puymirat E, et al. *Circ Cardiovasc Interv* . 2012;Epub ahead of print.

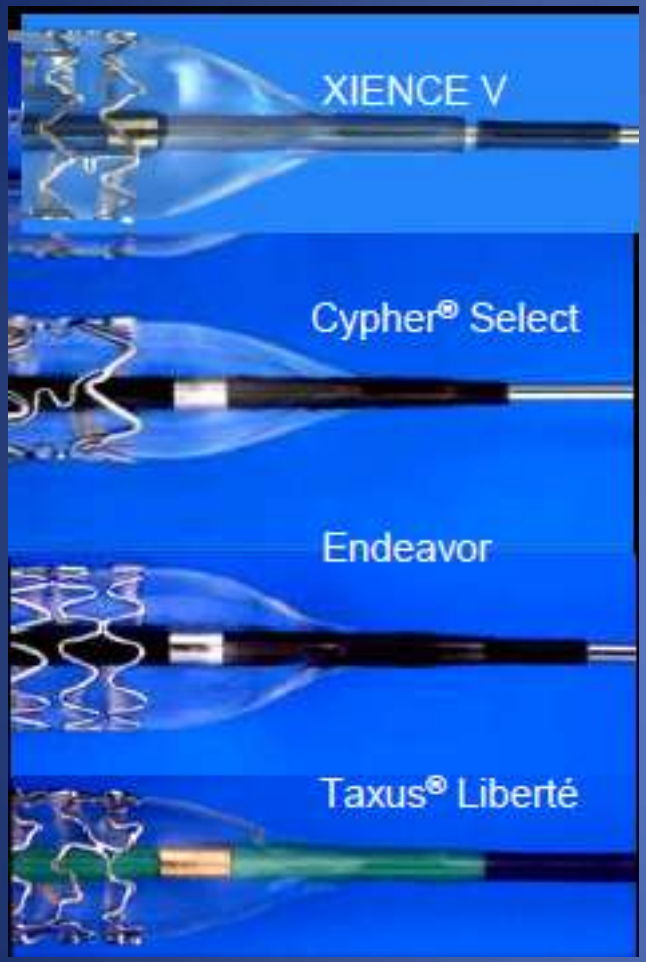
Technical issues: Stent sizing

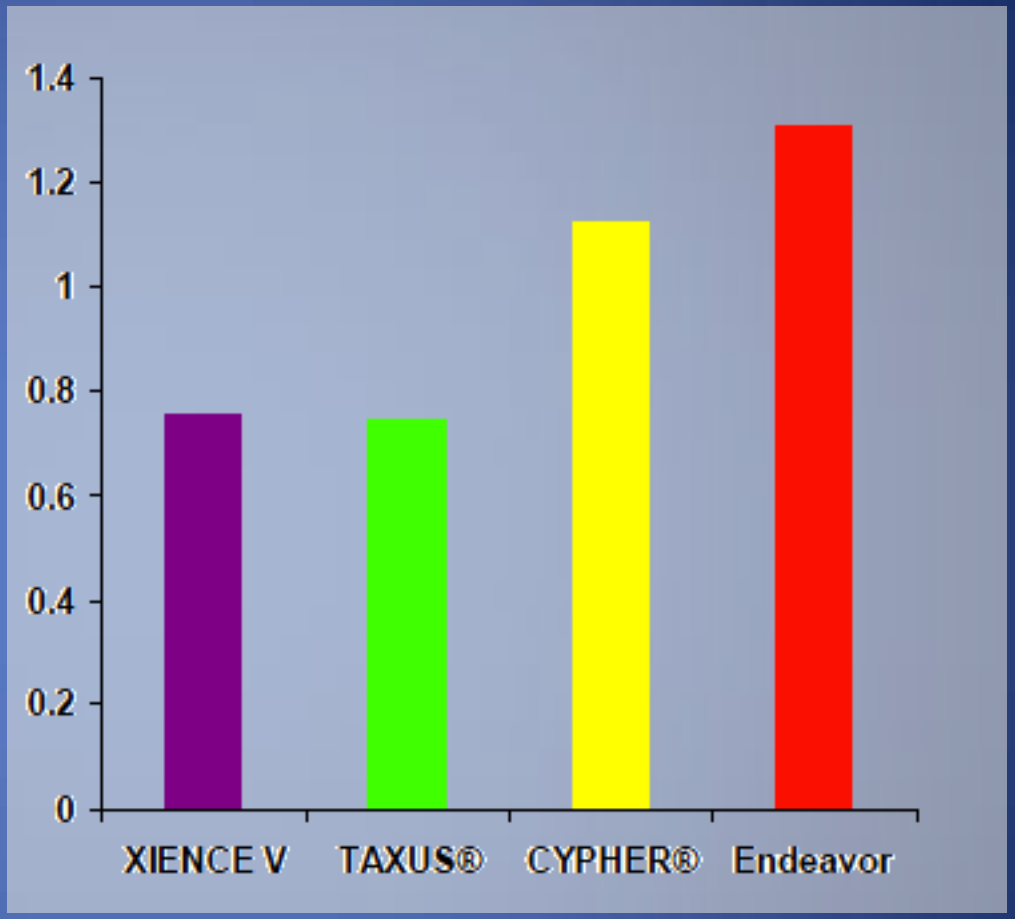


Small vessel and long segment disease : potential for edge dissection and restenosis



Technical tips:





Stent choice - minimal balloon overhang

Post-dilate with non-compliant balloon within stent margins

Conclusion (1):

- Achieving optimal results in Small vessel disease PCI – continues to be a challenge
- Higher procedural risks, poorer outcomes
- Appropriate use of invasive imaging – IVUS/OCT to confirm angiographically small vessel – assist in procedure planning and results

Conclusion (2):

- Optimal treatment options include DEB, newer generation DES.
- BVS : exciting and viable concept but needs technological refinement and outcome data
- Selective use of adjunctive devices eg. FFR, debulking strategies may be appropriate
- Optimal medical therapy and risk factors intervention backbone of all strategies

감사합니다