

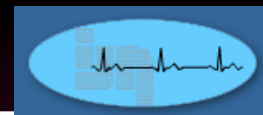
INSTITUT JANTUNG NEGARA
National Heart Institute



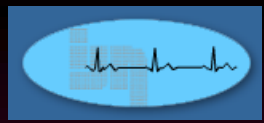
DEB in CAD: Past, Present & Future

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Head
Department of Cardiology
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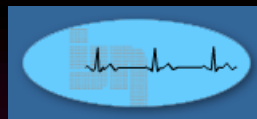
Summary Clinical Evidence SeQuent Please



Study	Study aim	Patients	State	Follow Up	Publication
PACCOATH® ISR I / II	DEB vs. POBA BMS-ISR	108	completed	6, 24, 72 Months	2006 in N Engl J Med 2006;355:2113e24 2008 in Clin Res Cardiol 97:773–781 (2008)
PEPCAD I	SQP De novo - Small Vessel	118	completed	6, 12, 36 Months	2010 in Clin Res Cardiol 2010;99:165e74.
PEPCAD II	SQP vs. DES BMS-ISR	131	completed	6, 12, 36 Months	2009 in Circulation 2009;119;2986-2994
PEPCAD IV	SQP + BMS vs. DES De novo - Diabetics	84	completed	9 Months	2011 in EuroIntervention 2011; 7: K83 – K92
PEPCAD V	SQP + BMS Bifurcations	28	completed	9 Months	2011 in EuroIntervention 2011; 7: K61 – K65
PEPCAD CTO	SQP + BMS vs. DES CTO	48	completed	6 Months	TCT 2010
DEBAMI	SQP + BMS AMI-STEMI	30	completed	9, 12 Months	EuroPCR 2011
PERFECT	SQP + EPC vs. EPC De-novo	120	completed	6 Months	2011 in Heart (2011). doi:10.1136/hrt.2011.226563
Kurashiki	SQP vs. POBA DES-ISR (Sirolimus)	50	completed	6 Months	2011 in JACC: VOL. 4, NO.2, 2011
DEB DE NOVO ISR	DEB De novo + ISR	100	completed	6, 12 Months	2011 in JPMA 61:157; 2011
PEPCAD DES	SQP vs. POBA DES-ISR	110	completed	6 Months	TCT 2011
INDICOR	SQP + BMS vs. CFB + SQP	97	completed	9 Months	AsiaPCR 2012
SQP-Registry	SQP all comer	2095	completed	9 Months	TCT 2011/ACC 2012
OCTOPUS	BMS+SQP vs. Xience V	95	completed	6 Months	ACC 2012



DEB in BMS ISR



ORIGINAL ARTICLE

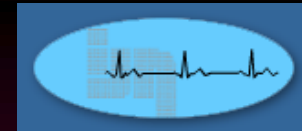
Treatment of Coronary In-Stent Restenosis with a Paclitaxel-Coated Balloon Catheter

Bruno Scheller, M.D., Christoph Hehrlein, M.D., Wolfgang Bocksch, M.D.,
Wolfgang Rutsch, M.D., Dariush Haghi, M.D., Ulrich Dietz, M.D.,
Michael Böhm, M.D., and Ulrich Speck, Ph.D.

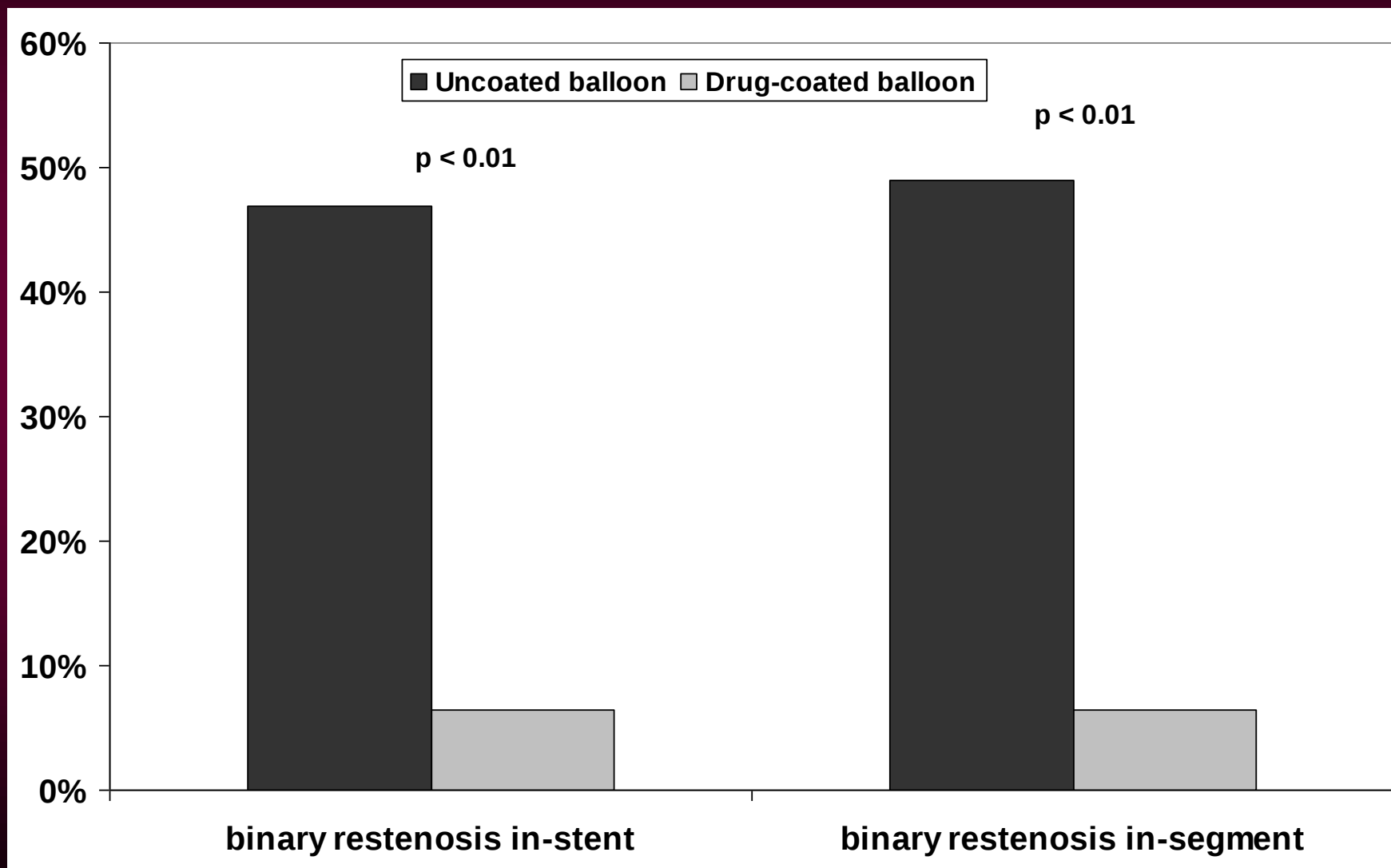
**Primary endpoint: late lumen
loss in-segment – ISR 1**

Uncoated balloon	PACCOCATH
0.74 ± 0.86 mm	0.03 ± 0.48 mm

p = 0.002



Secondary Endpoint: Binary Restenosis Rate

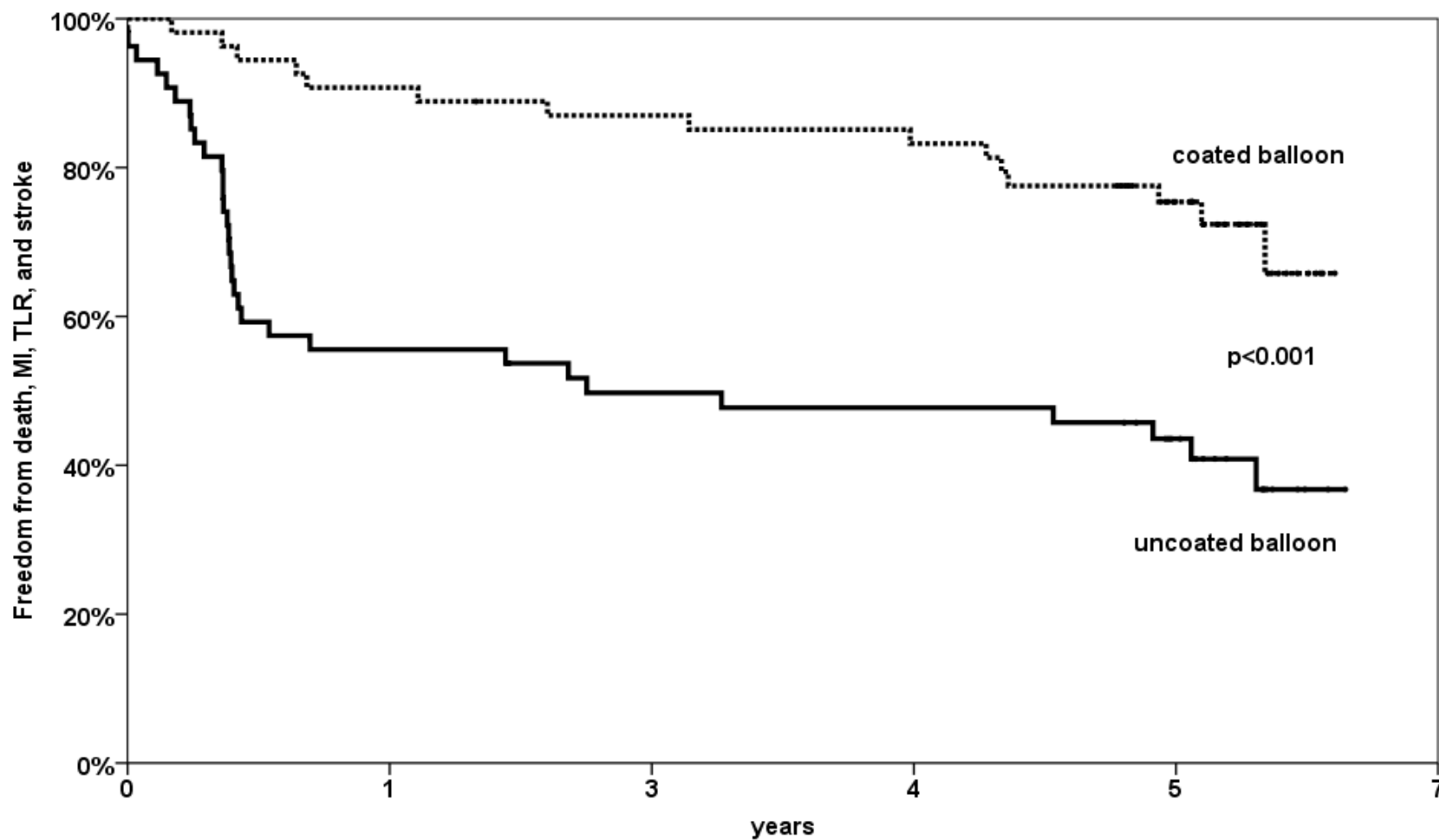
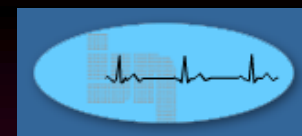


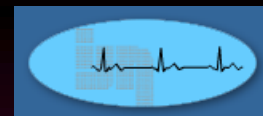


24 mo. Clinical FU (ITT Analysis)

	Uncoated	DEB	p
TLR	20 (37%)	3 (6%)	0.001
MI	5 (9%)	1 (2%)	0.577
Death	3 (6%)	2 (4%)	0.912
Stroke	3 (6%)	2 (4%)	0.840
MACE	25 (49%)	6 (11%)	0.001

Update Paccocath ISR I/II

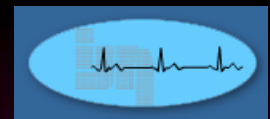




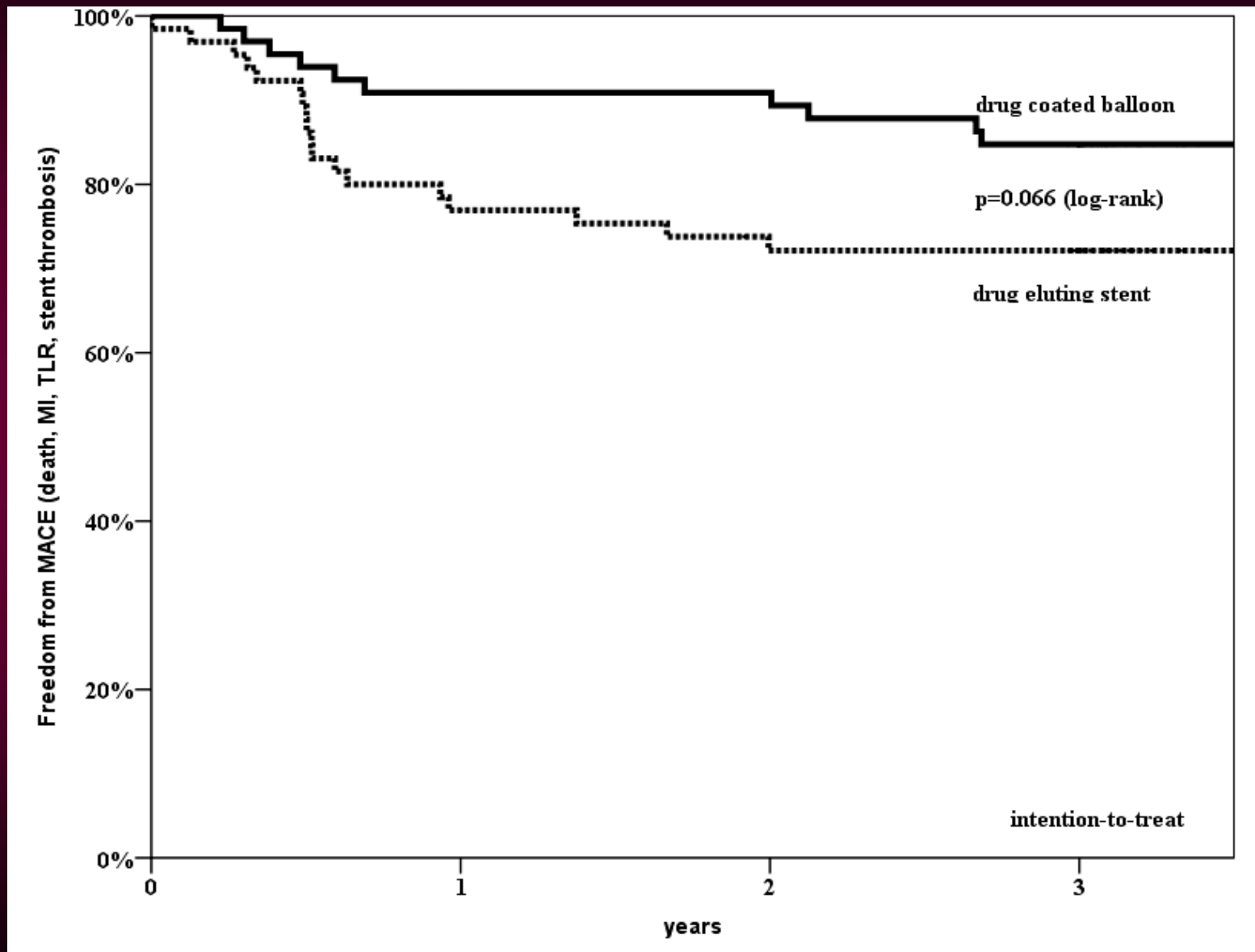
PEPCAD II

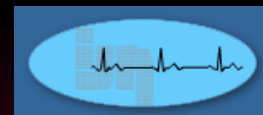
Results: 6 Months FU (As Treated)

PEPCAD II	SeQuent Please N=66	Taxus N=60	p-value
Follow-up [mo]	6.2±0.8	6.2±0.8	0.70
Follow-up: clinical	62 (93.9%)	59 (98.3%)	0.40
Late loss [mm]	0.19±0.39	0.45±0.69	0.01
Restenosis (segment)	2/54 (3.7%)	11/53 (20.8%)	0.02
TLR	2/62 (3.2%)	11/59 (18.6%)	>0.01
Myocardial infarction	0/62 (0.0%)	1/59 (1.7%)	1.00
Death	1/62 (1.6%)	1/59 (1.6%)	1.00
Total MACE	3/62 (4.8%)	13/59 (22.0%)	>0.01



Update PEPCAD II at 3 Years





ESC Guidelines 2010 for ISR

Table 33 Recommendations for specific percutaneous coronary intervention devices and pharmacotherapy

	Class ^a	Level ^b	Ref. ^c
FFR-guided PCI is recommended for detection of ischaemia-related lesion(s) when objective evidence of vessel-related ischaemia is not available.	I	A	15, 28
DES ^d are recommended for reduction of restenosis/re-occlusion, if no contraindication to extended DAPT.	I	A	45, 46,

Drug-eluting balloons^d should be considered for the treatment of in-stent restenosis after prior BMS.

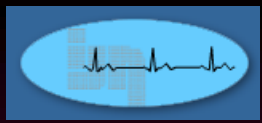
For PCI of unstable lesions, i.v. abciximab should be considered for pharmacological treatment of no-reflow.	IIa	B	55, 209, 212
Drug-eluting balloons ^d should be considered for the treatment of in-stent restenosis after prior BMS.	IIa	B	174, 175
Proximal embolic protection may be considered for preparation before PCI of SVG disease.	IIb	B	214
For PCI of unstable lesions, intracoronary or i.v. adenosine may be considered for pharmacological treatment of no-reflow.	IIb	B	209
Tornus catheter may be used for preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilated before planned stenting.	IIb	C	—
Cutting or scoring balloons may be considered for dilatation of in-stent restenosis, to avoid slipping-induced vessel trauma of adjacent segments.	IIb	C	—
IVUS-guided stent implantation may be considered for unprotected left main PCI.	IIb	C	—
Mesh-based protection may be considered for PCI of highly thrombotic or SVG lesions.	IIb	C	—
For PCI of unstable lesions, intracoronary nitroprusside or other vasodilators may be considered for pharmacological treatment of no-reflow.	IIb	C	—

^aClass of recommendation.

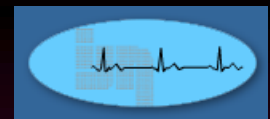
^bLevel of evidence.

^cReferences.

^dRecommendation is only valid for specific devices with proven efficacy/safety profile, according to the respective lesion characteristics of the studies.



DEB in DES ISR



69 yr F

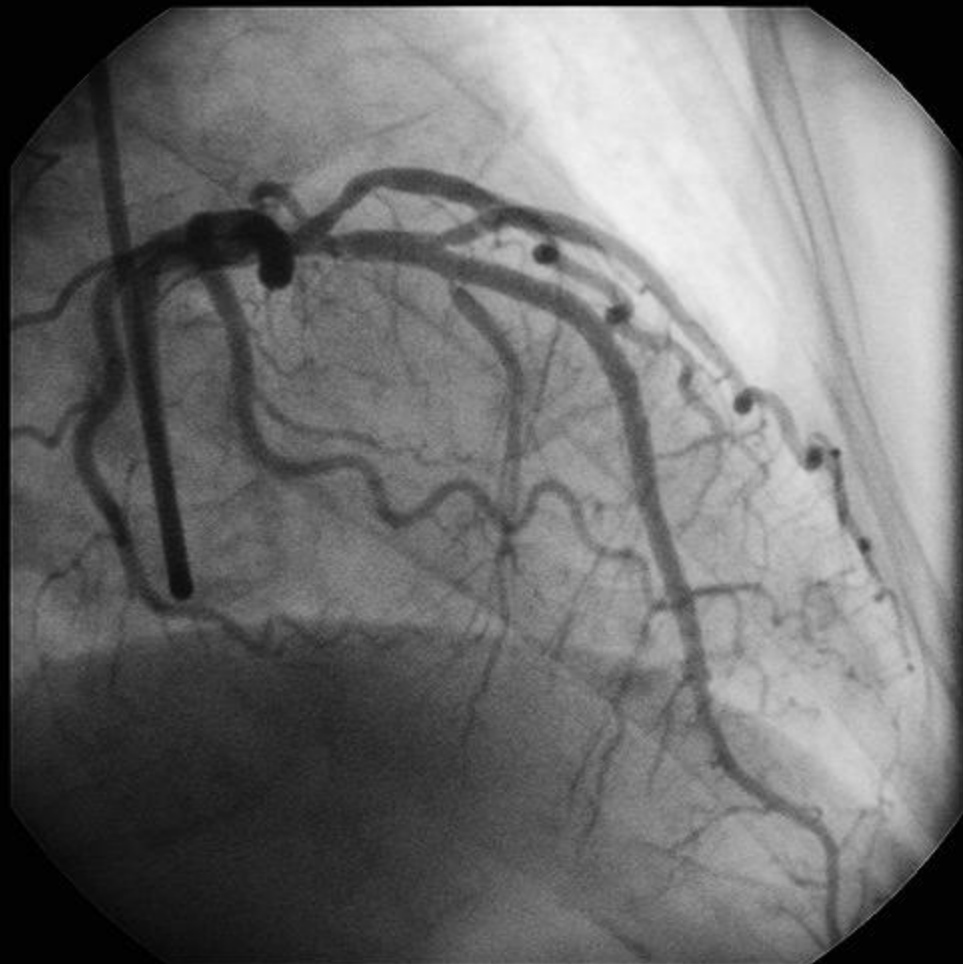
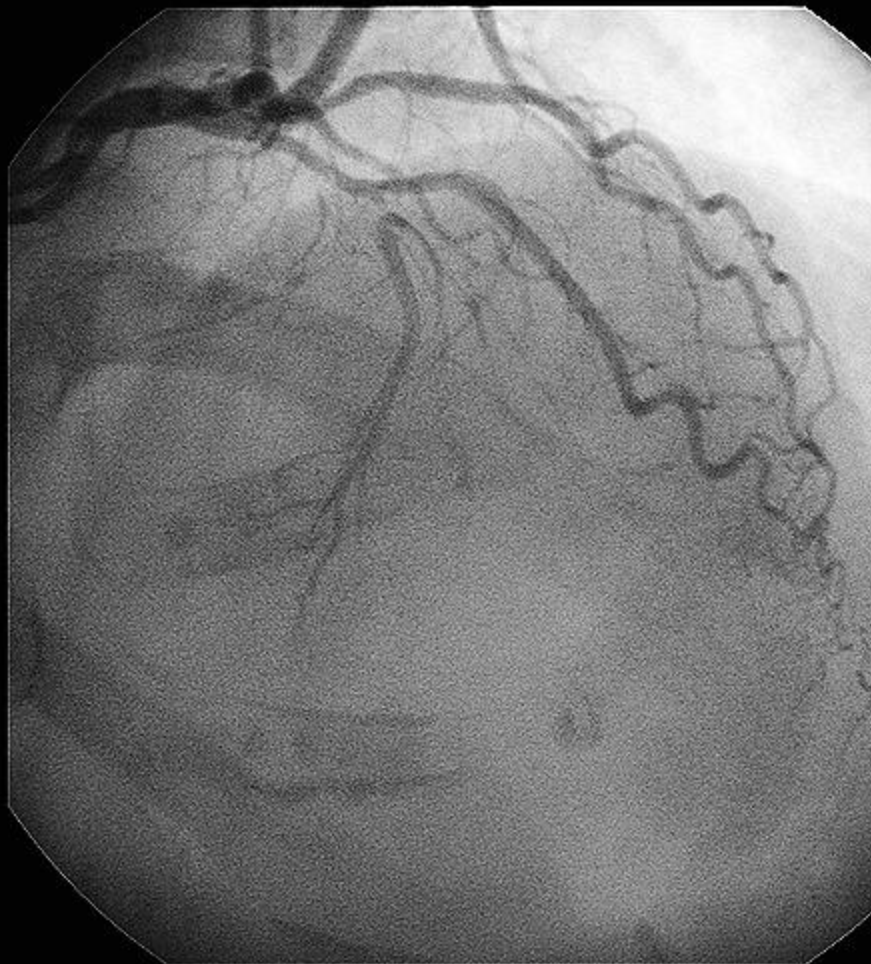
DM on Insulin Therapy

Hypertension, Dyslipidaemia

Obesity

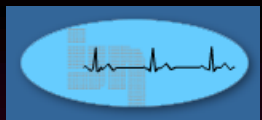
Good LV function

Cypher 2.25 x 33 mm (upsized to 2.5 mm)
2.5 x 33 (upsized to 2.75 mm)

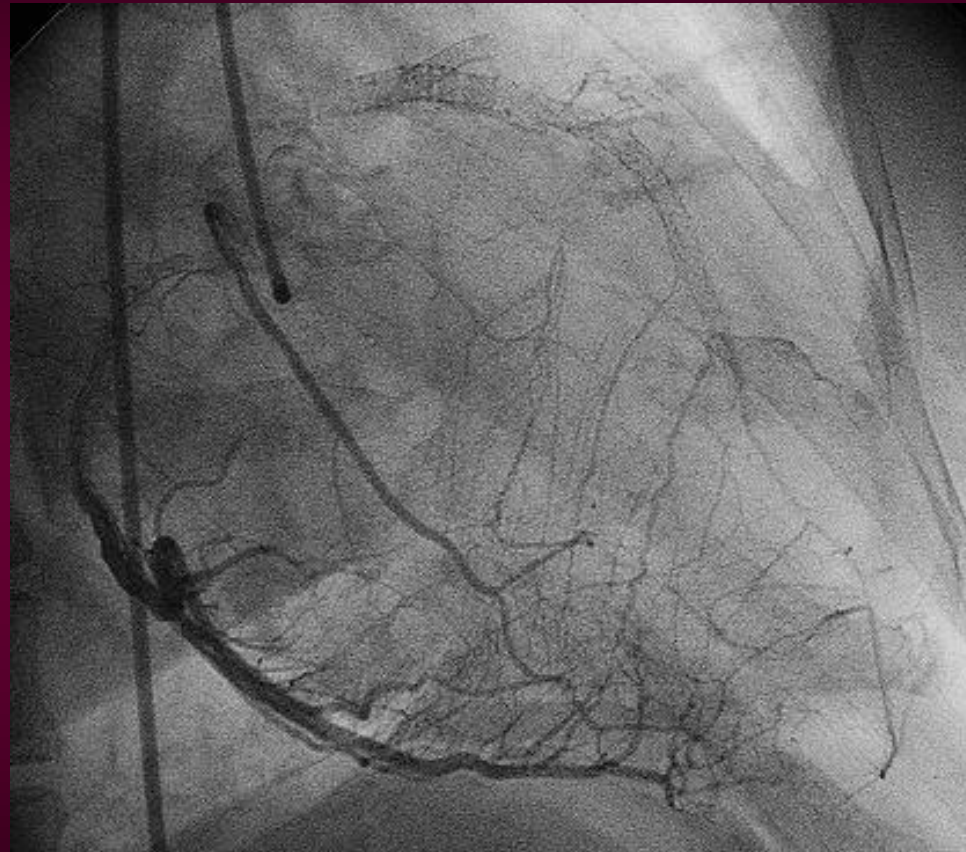
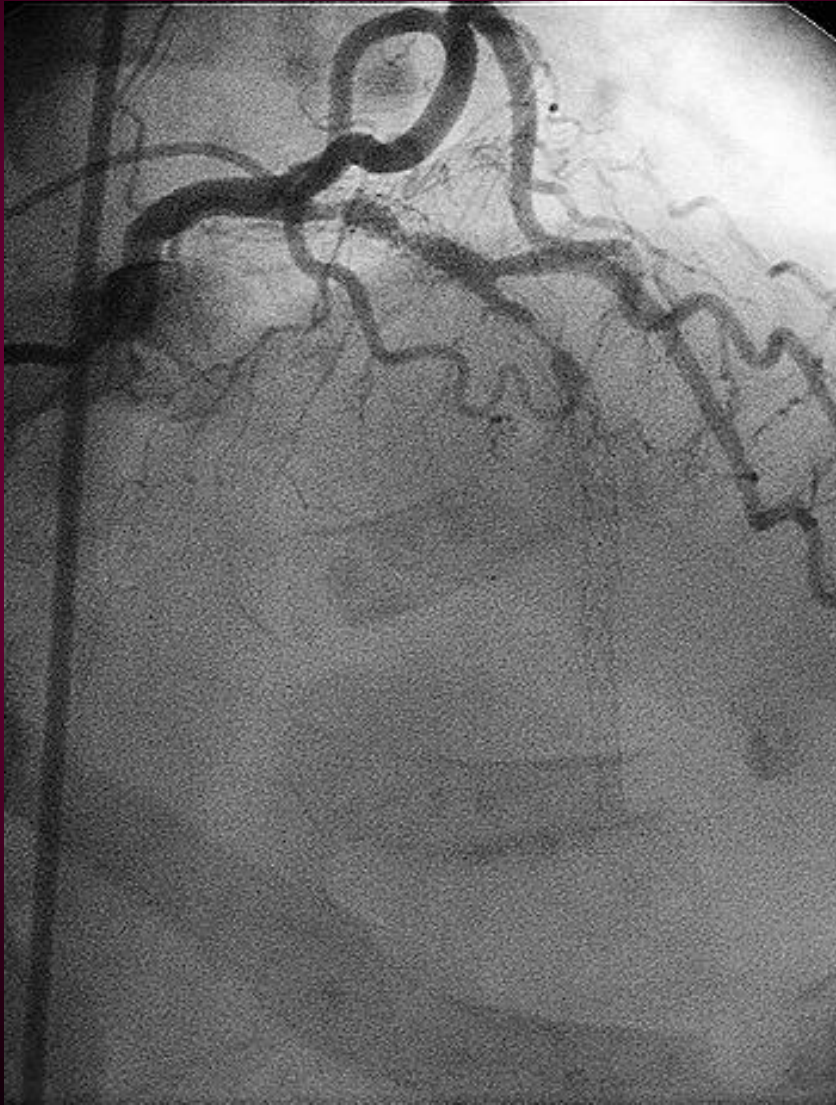


67 yr F
DM on Insulin

138220 – 10th Apr '08



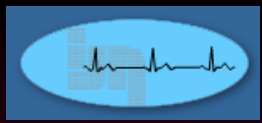
LAD ISR – 6 mo. Post Cypher (Mehran's 4)



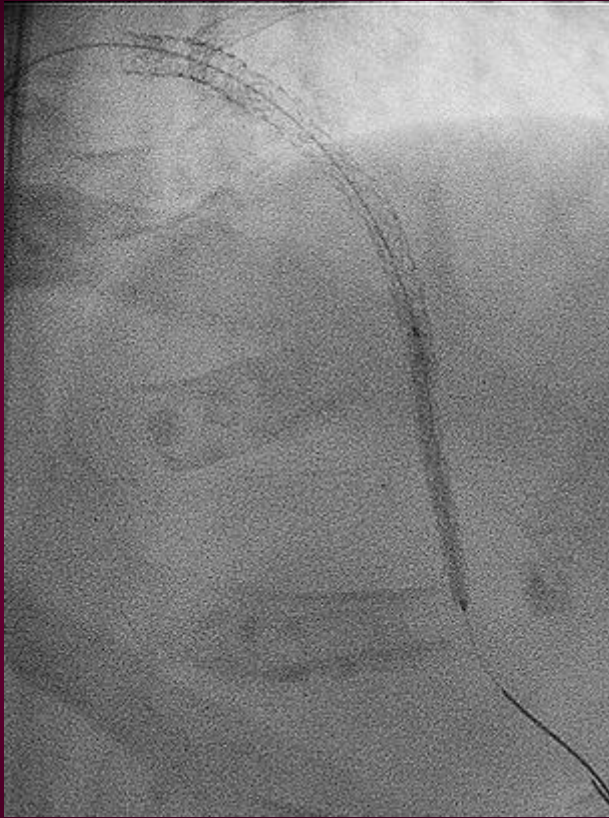
Retrograde filling
From RCA

Sequent Please

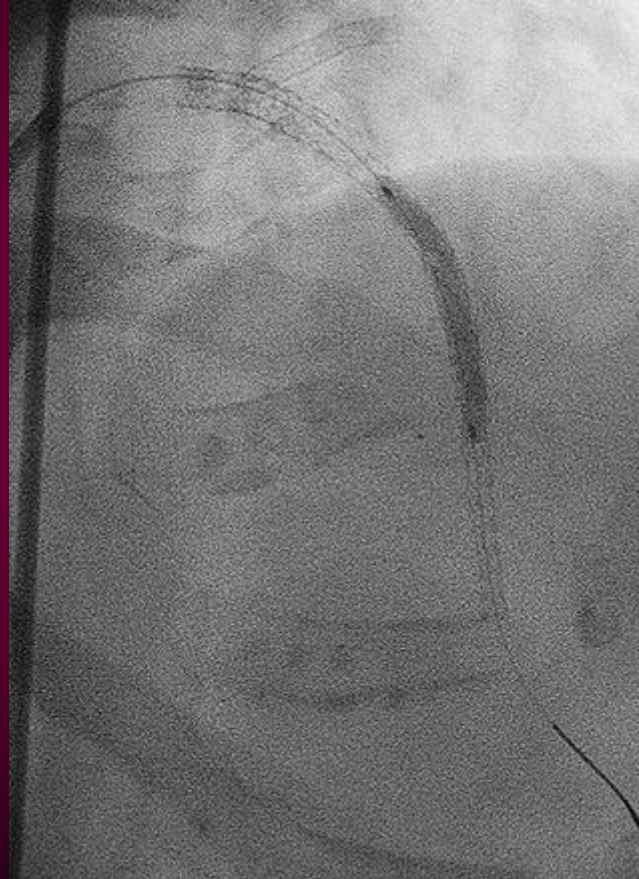
Predilatation followed by Sequential Balloon Dilatation 30 sec



2.5 x 30 mm

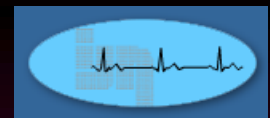


3.0 x 30 mm

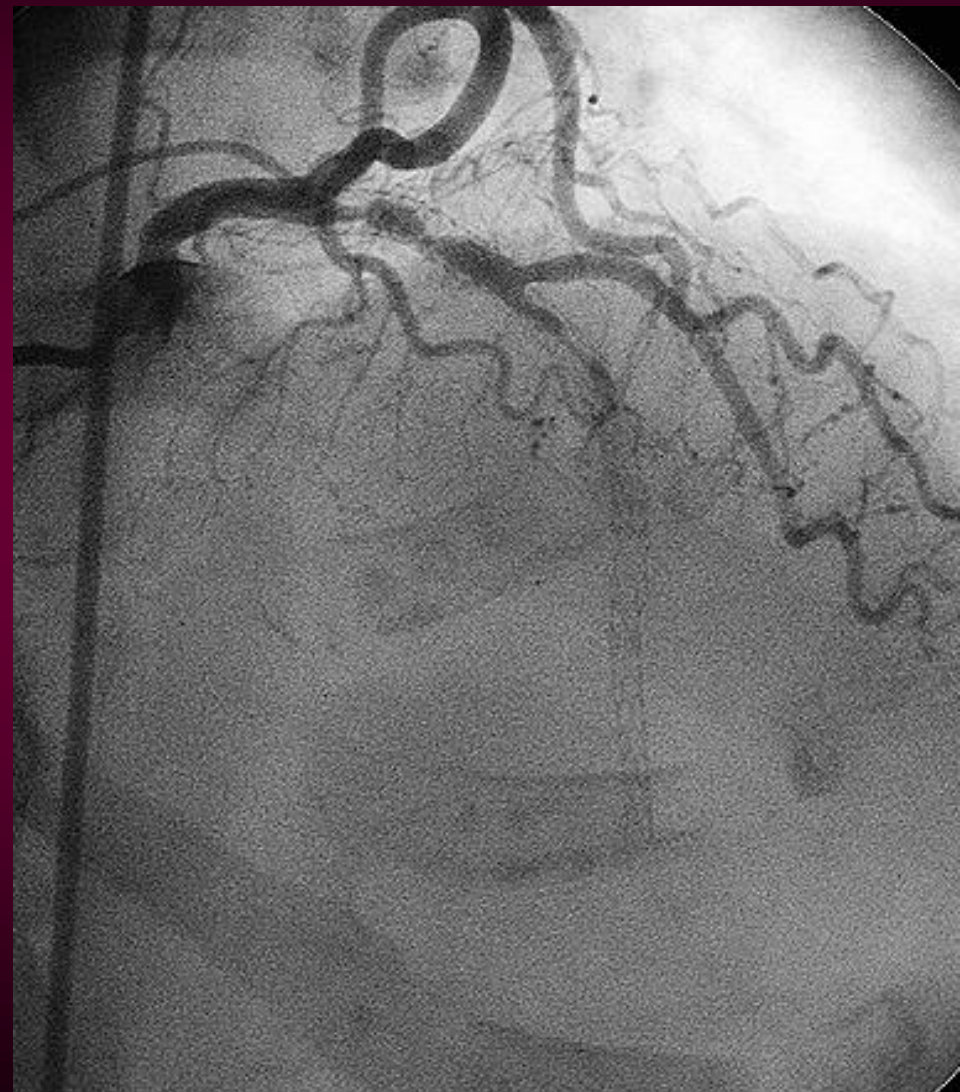


3.5 x 26 mm

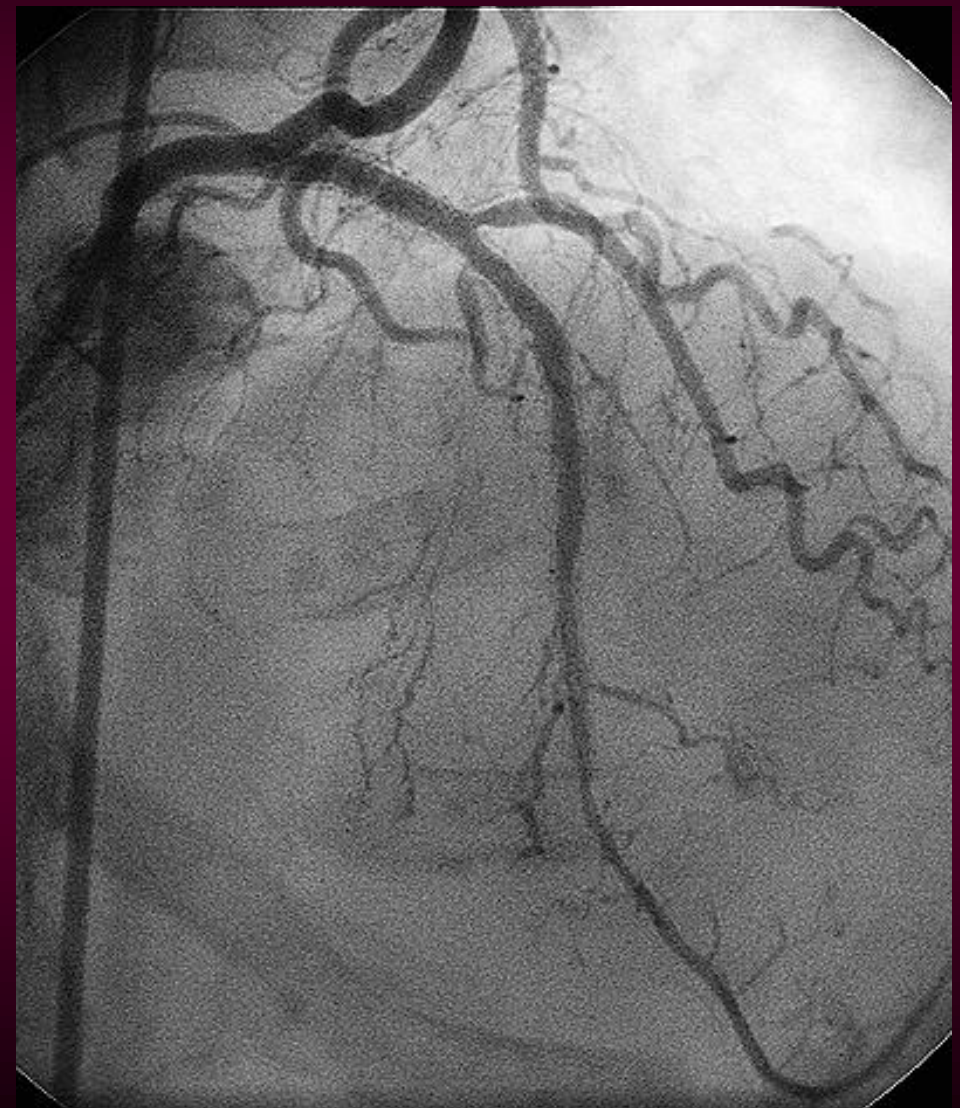


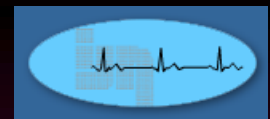


Pre



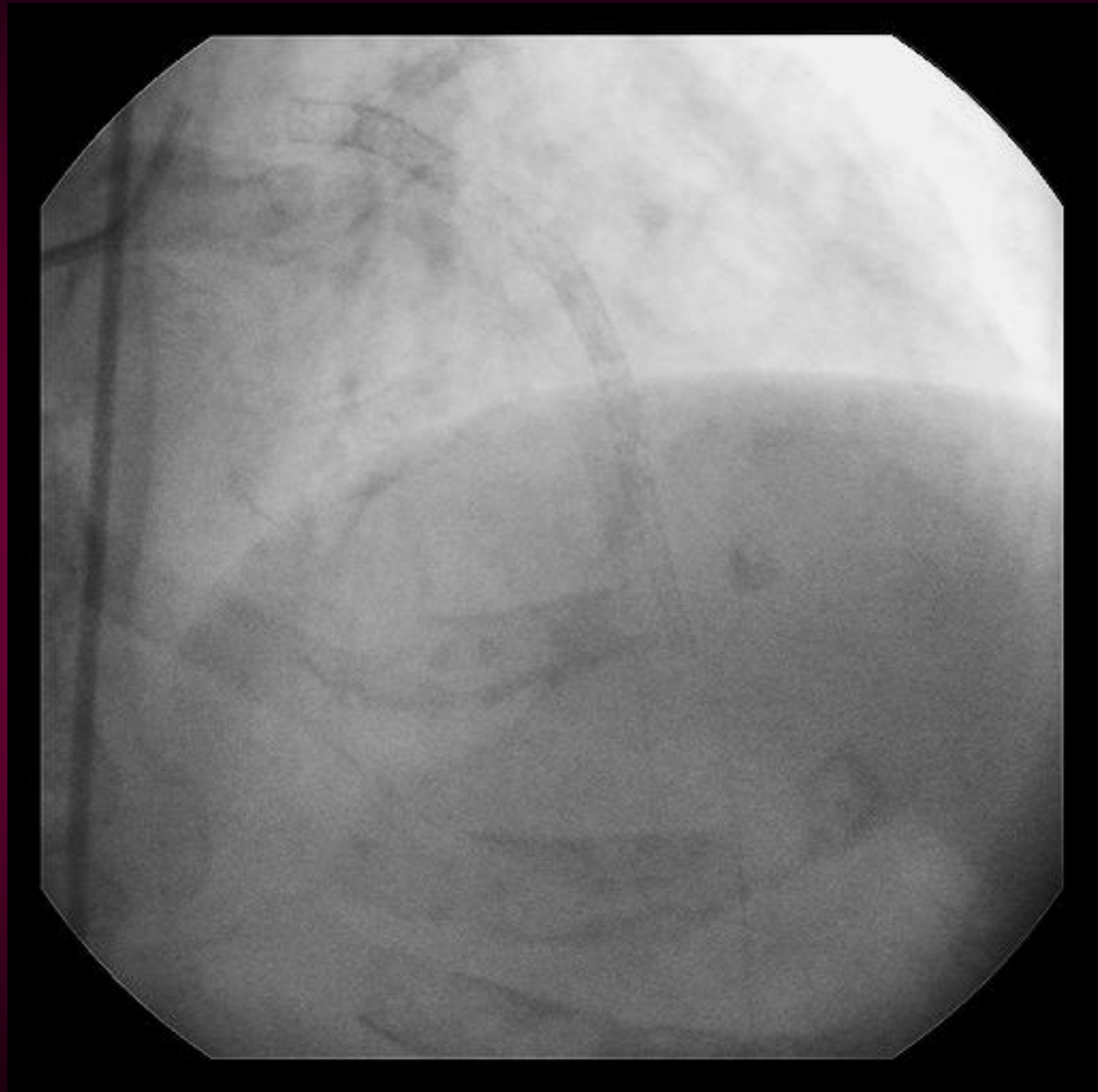
Post



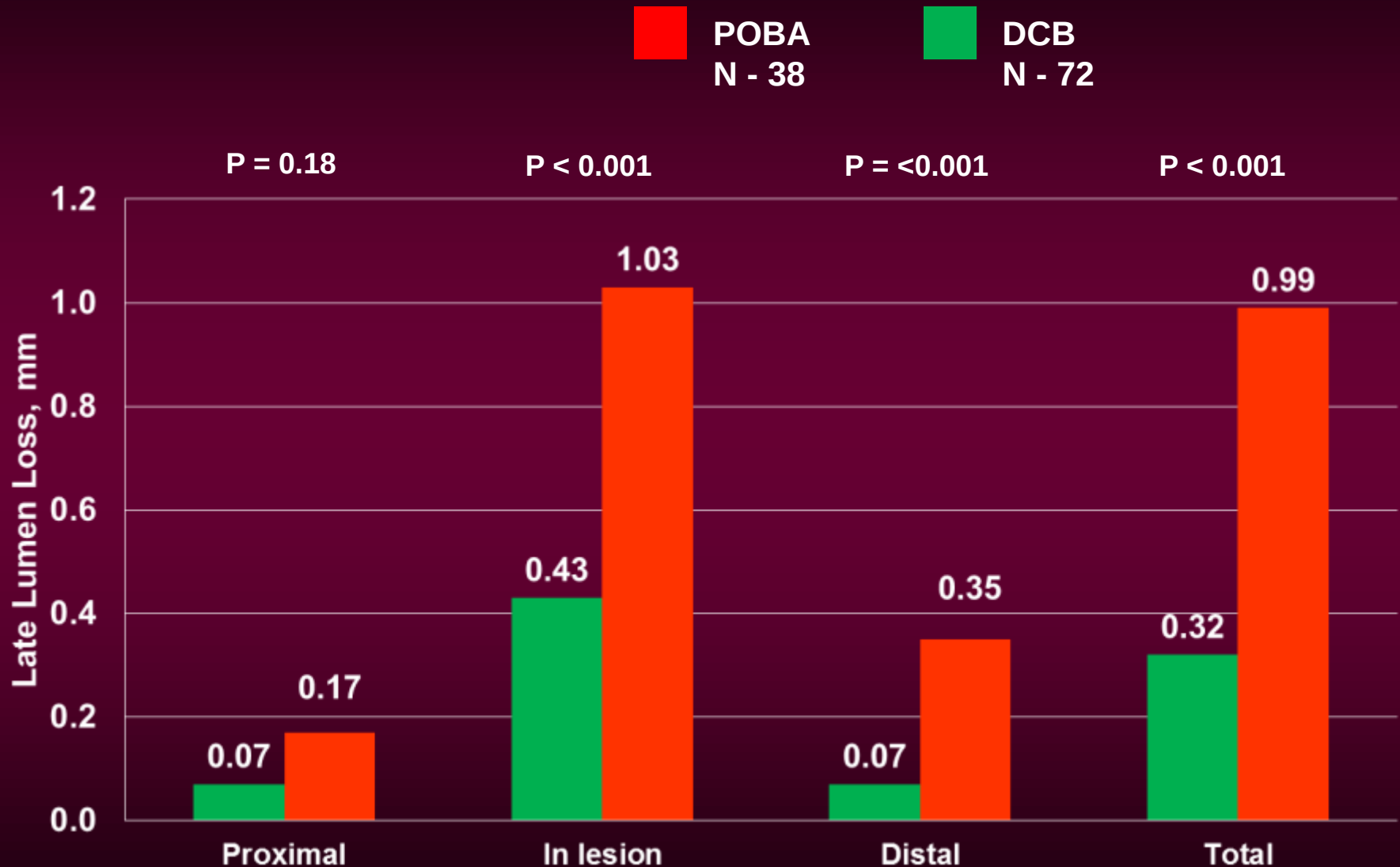
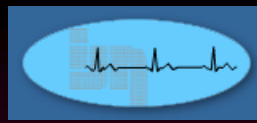


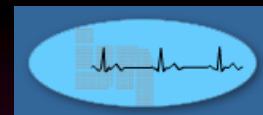
9 Month FU Angiogram (15 Jan '09)

Last clinic FU
On June '12
47 mo. Post DEB



PEPCAD- DES Late Loss at 6 Months





ISAR-DESIRE 3 – Treatment of ISR of Limus-eluting stents

Design

PRIMARY ENDPOINT:

Percent diameter stenosis at follow-up angiography

TEST HYPOTHESES:

PEB non-inferior to **PES**

%DS 35%; Delta = 7%

alpha = 0.05; Power = 80%

102 Patients/group

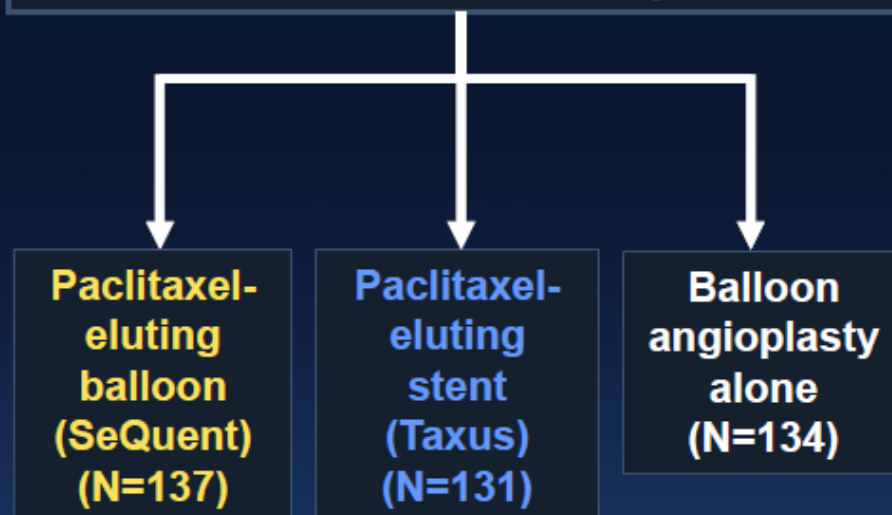
PEB and **PES** superior to balloon angioplasty

%DS 35% vs. 45%

alpha = 0.025; Power 90%

101 Patients/group

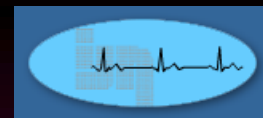
402 patients with DES-restenosis enrolled between August 2009 and October 2011 in 3 centers in Germany



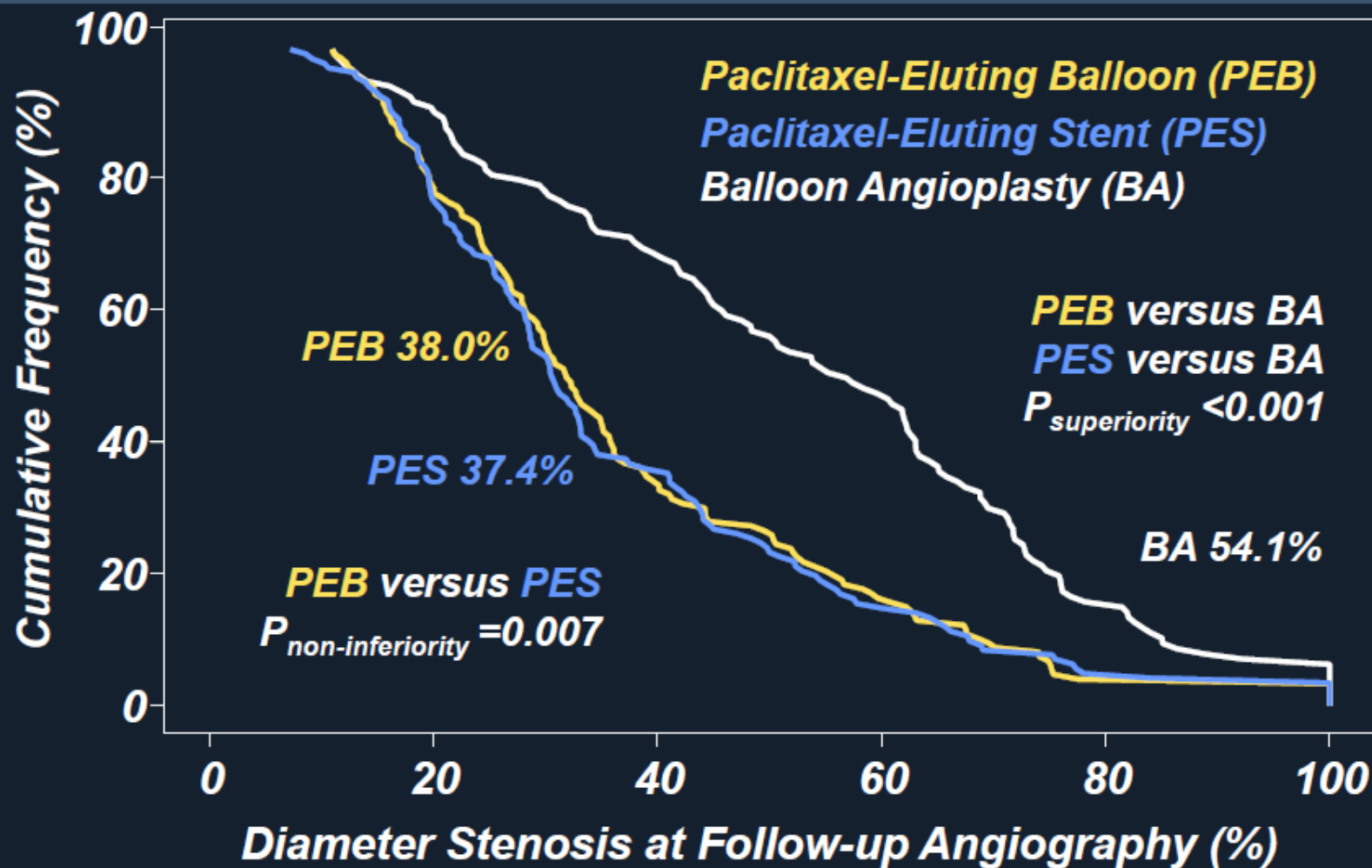
Angiographic follow-up at 6-8 months in 84.1% (N=338)

Clinical follow-up at 12 months in 97.5% (N=392)

No significant differences across groups



Primary Endpoint: Diameter Stenosis at Follow-up Angiography

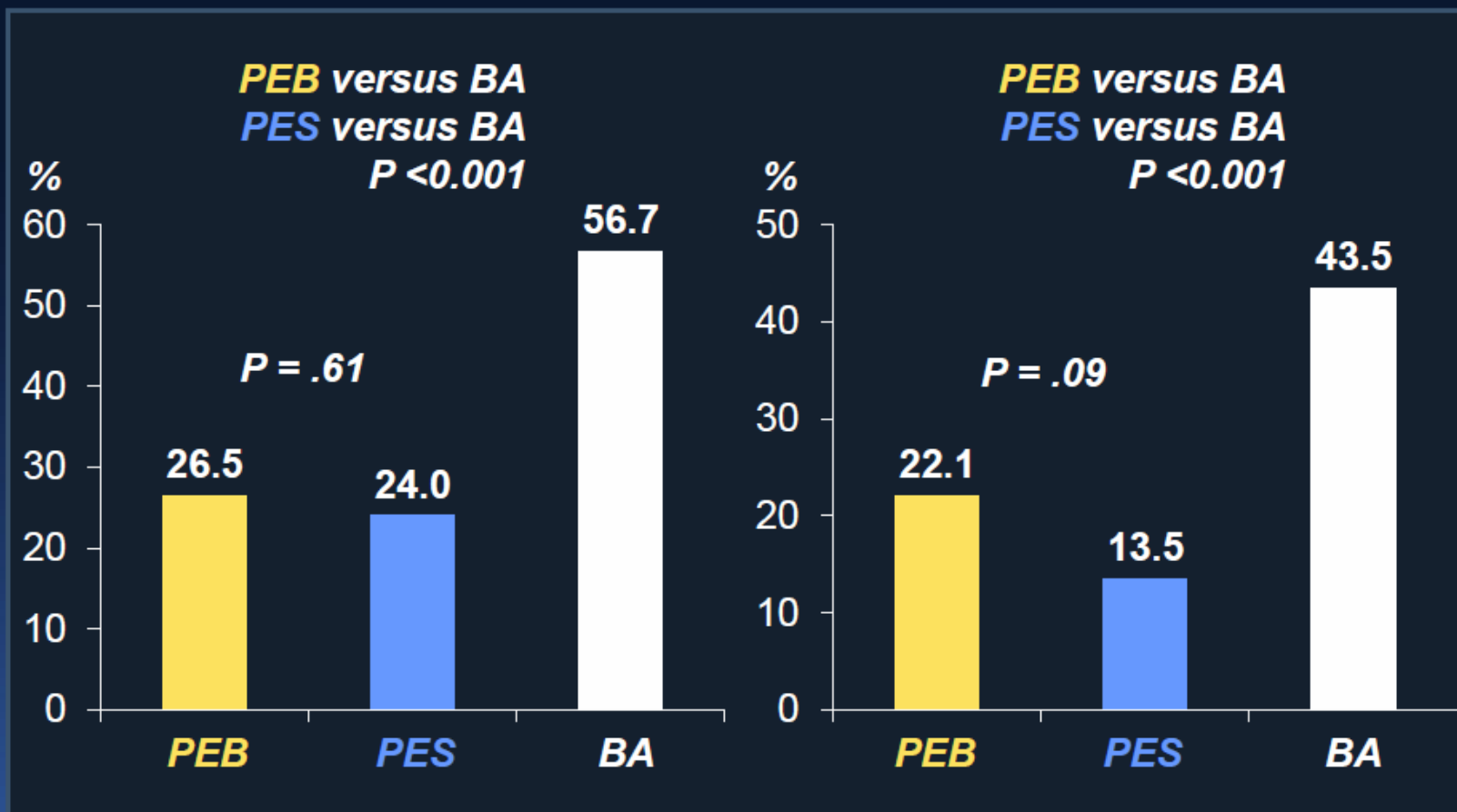




ISAR Desire 3: Secondary Endpoint

Binary Restenosis

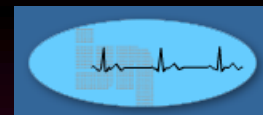
Target Lesion Revascularization



Death/MI
At 12 mo.

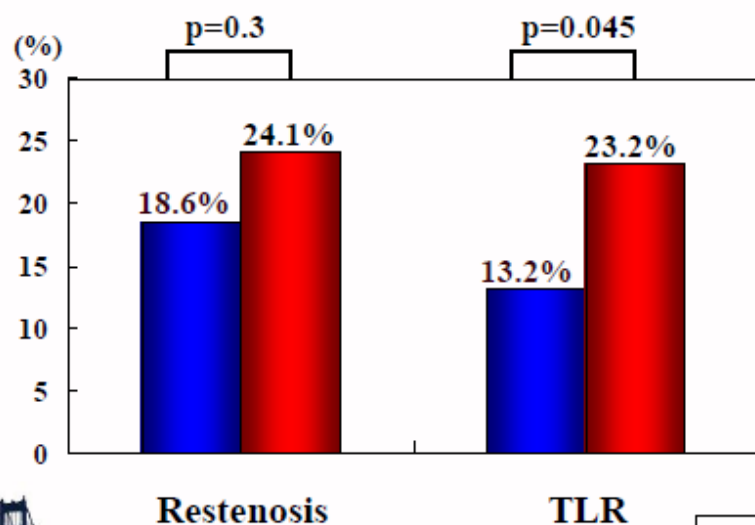
PEB 4.4%, PES 6.9%, POBA 6.8%

DEB vs Cypher in the Treatment of Cypher ISR: 6 – 8 mo angiographic follow-up (n – 218 pt)

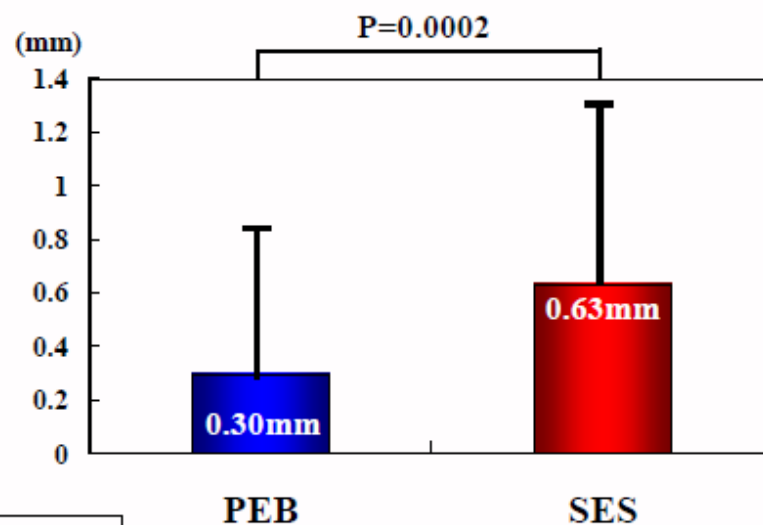


Follow-up rate : 93.3 % (237/254 Lesions)
(at 6-8 months) PEB:129 SES:108

Binary restenosis, TLR



Late loss



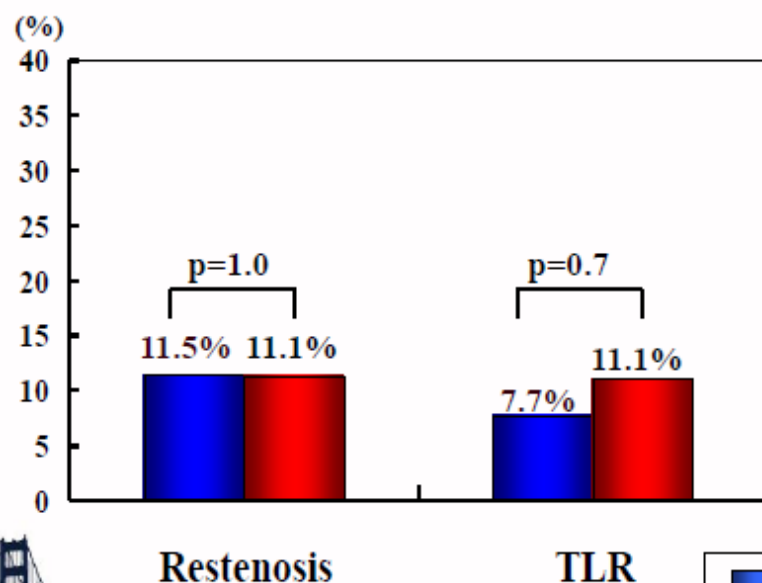


Six (8)-months angiographic follow-up

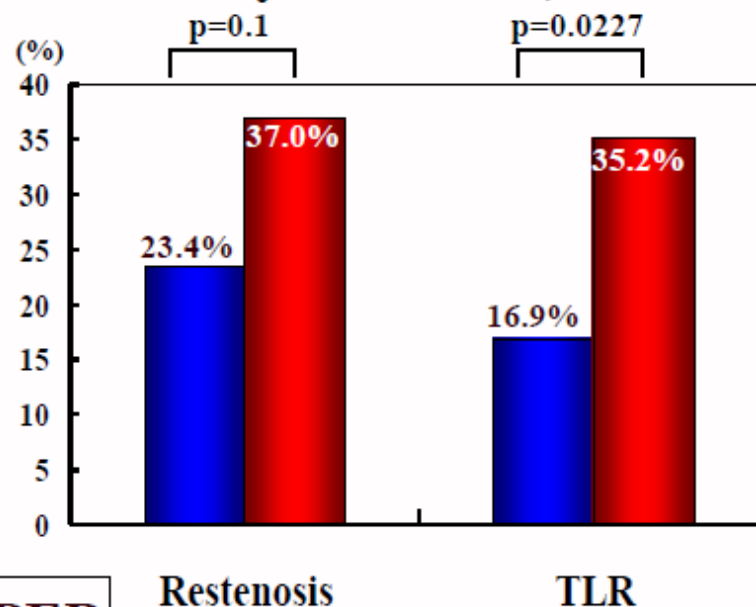
Focal lesion: n=115
(I b, I c)

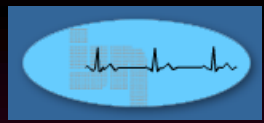
Non-focal lesion: n=139
(I d, II, III, IV)

Binary restenosis, TLR



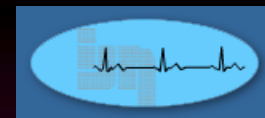
Binary restenosis, TLR





DEB in Small Vessels

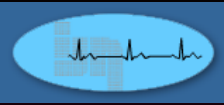
PEPCAD I : 6-Month FU



Treatment of Small Vessel Coronary Artery Disease by the
Sequent® Please Paclitaxel coated balloon

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

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%	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%

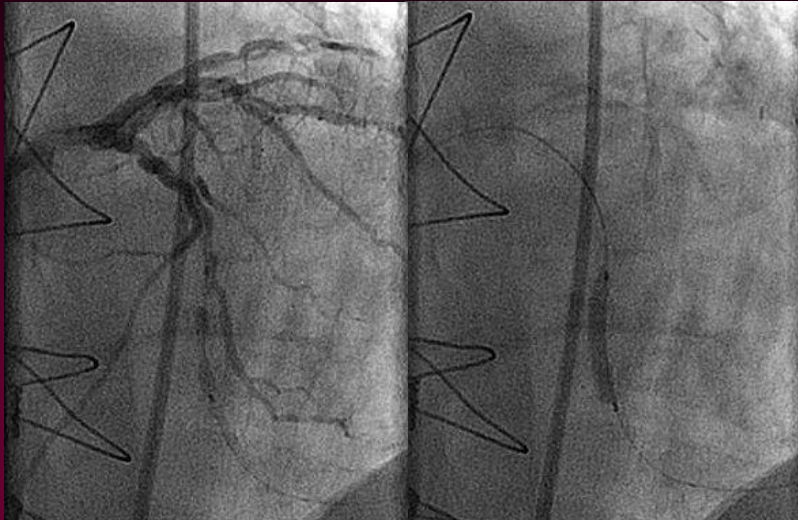


PEPCAD I – Outcome

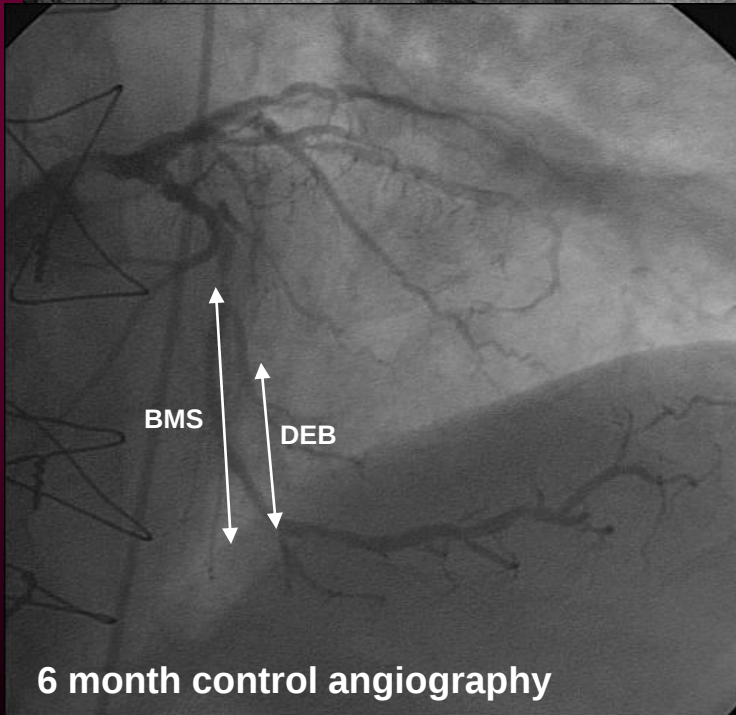
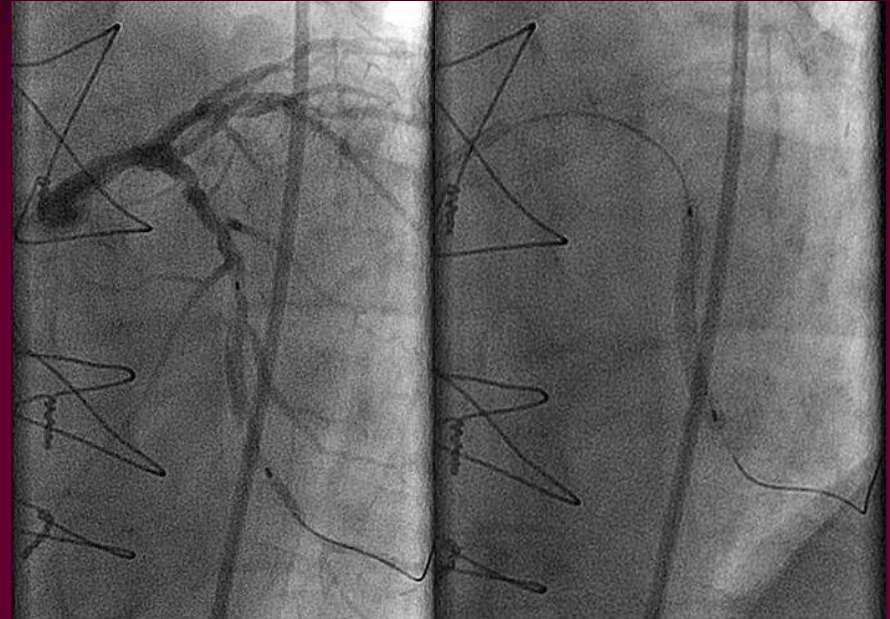
	DEB only	DEB & BMS	p
n	82	32	
Follow-up	6.4 ± 1.2 months	6.5 ± 1.5 months	0.9
Control angiography	73 (89 %)	29 (91 %)	1
<i>Late lumen loss</i>	<i>0.18 ± 0.38 mm</i>	<i>0.73 ± 0.74 mm</i>	<i>0.0006</i>
Binary restenosis in-segment	4 / 73 (5.5 %)	13 / 29 (44.8 %)	<0.0001
Binary restenosis in-lesion	4 / 73 (5.5 %)	12 / 29 (41.3 %)	<0.0001
TLR	4 (4.9 %)	9 (28.1 %)	0.001
Stent thromboses and TLR	N/A	2 (6.3%)	
Myocardial infarction	1 (1.2 %)	1 (3.3 %)	1
Death	0 (0 %)	0 (0 %)	1
Total MACE	5 (6.1 %)	12 (37.5 %)	<0.0001

Geographic Mismatch

DEB 2.5 17 mm

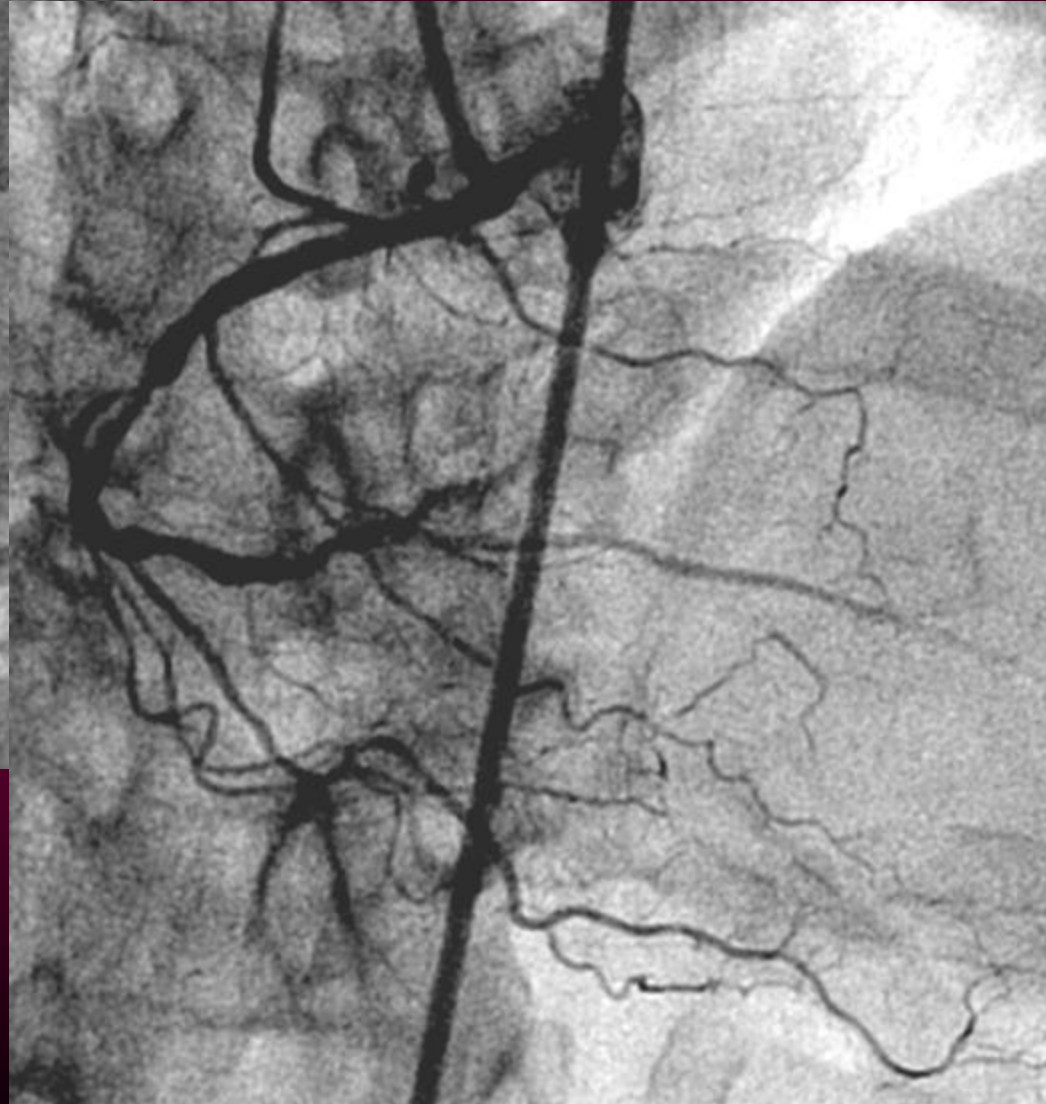
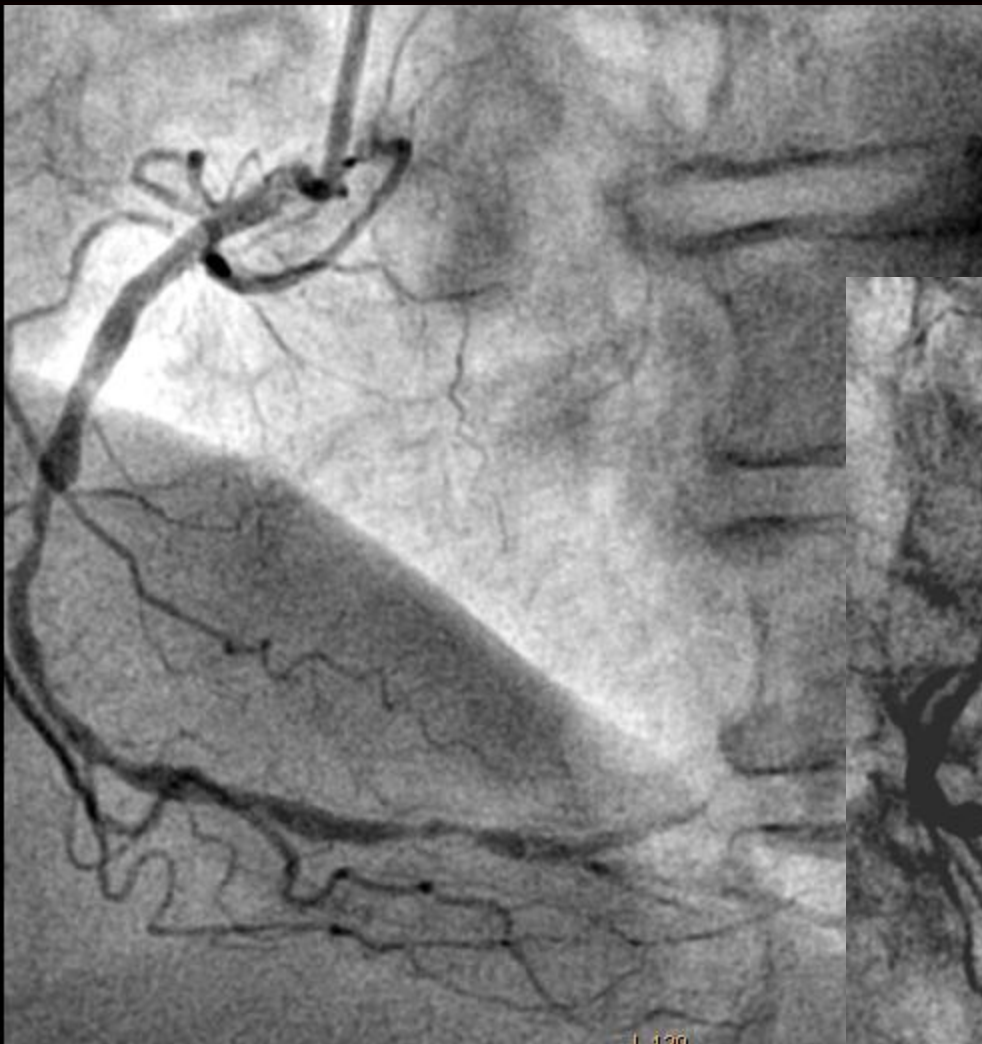
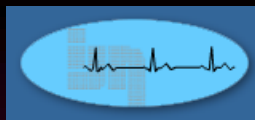


BMS 2.5 25 mm

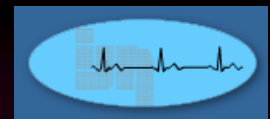


	Restenosis (N=13)	No restenosis (N=16)	p
Geographic mismatch	10 / 13 (77 %)	3 / 16 (19 %)	0.029
Total stent length	19.4 ± 8.4 mm	14.4 ± 10.2 mm	0.035
Balloon length – stent length	-2.31 ± 10.72 mm	2.75 ± 7.71 mm	0.096

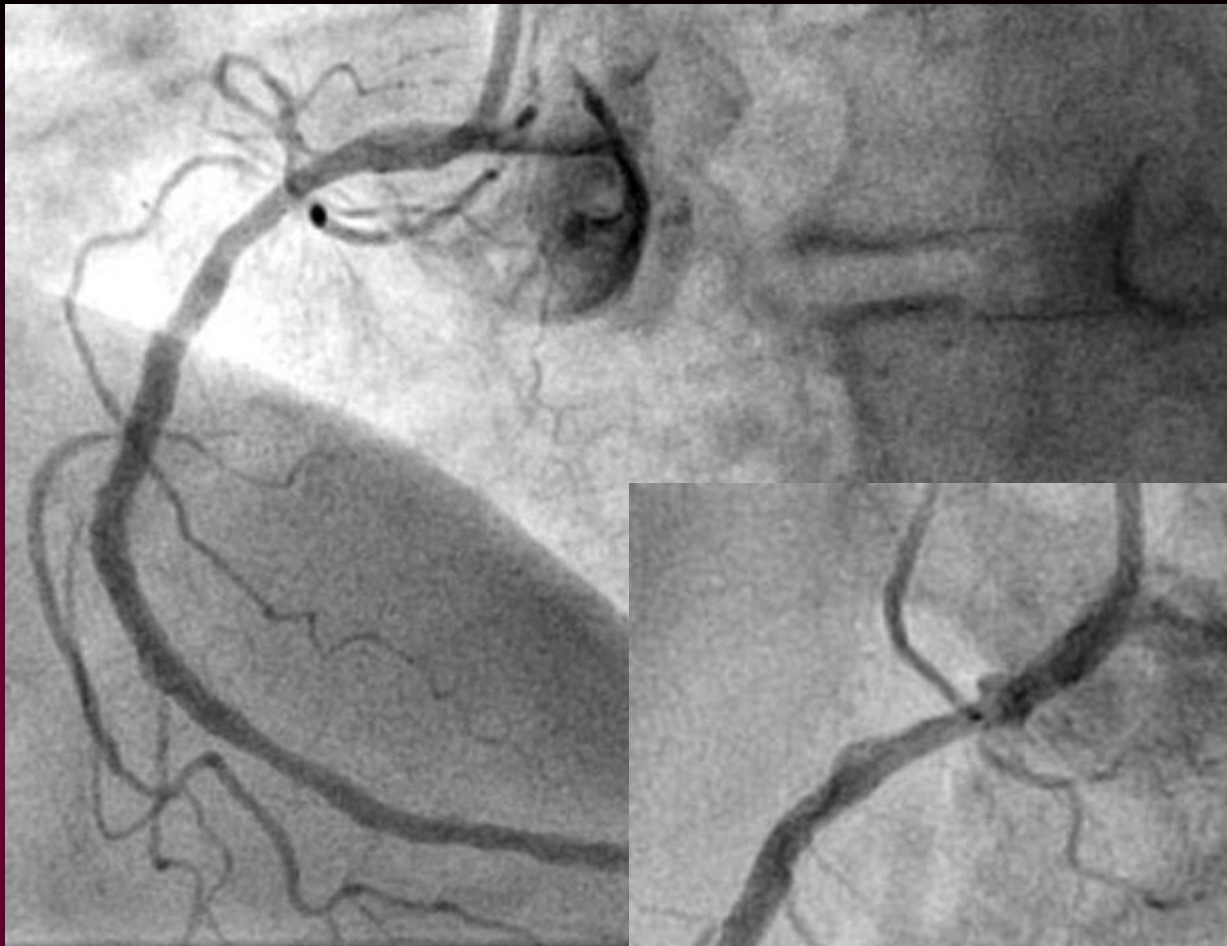
17 Feb. 11 - 263214



60 yr old F
DM, Dyslipidaemia, HT



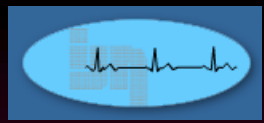
Post PCI



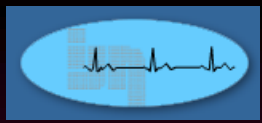
2 Dior DEB 2.5 x 30
PL & PD br

Biomatrix 3.0 x 36 mm
Mid RCA



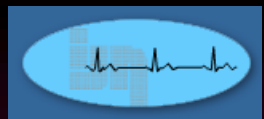


DEB in Bifurcation Lesions



RCA / PD Br. Medina 1,0,1

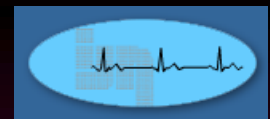




Distal RCA to PD
Biomatrix 2.75 x 15

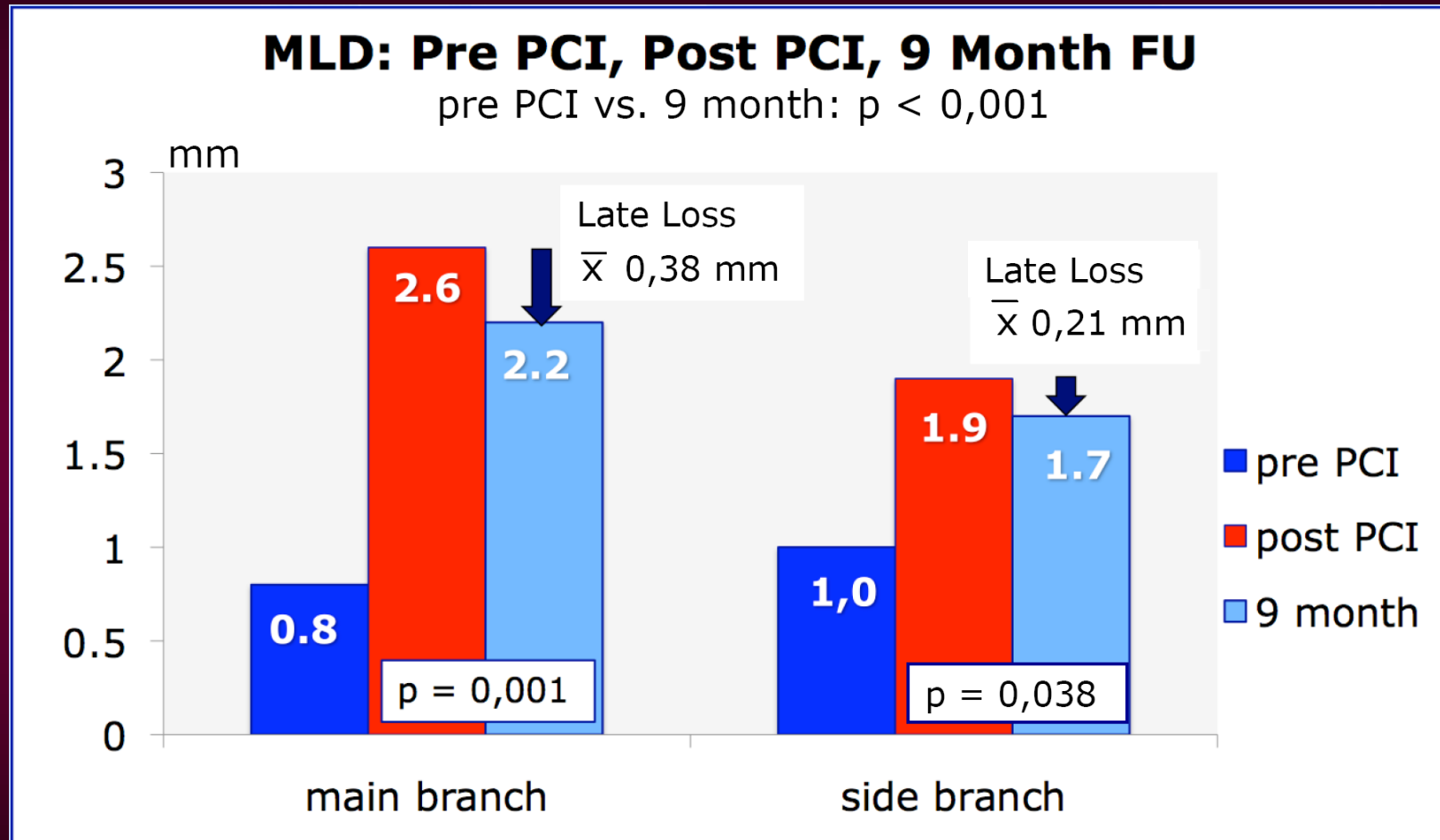
DEB RCA to PL



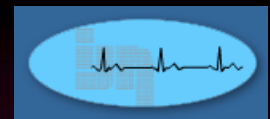


PEPCAD V Bifurcation Study

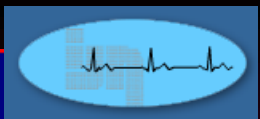
MV – DEB & BMS, SB - DEB



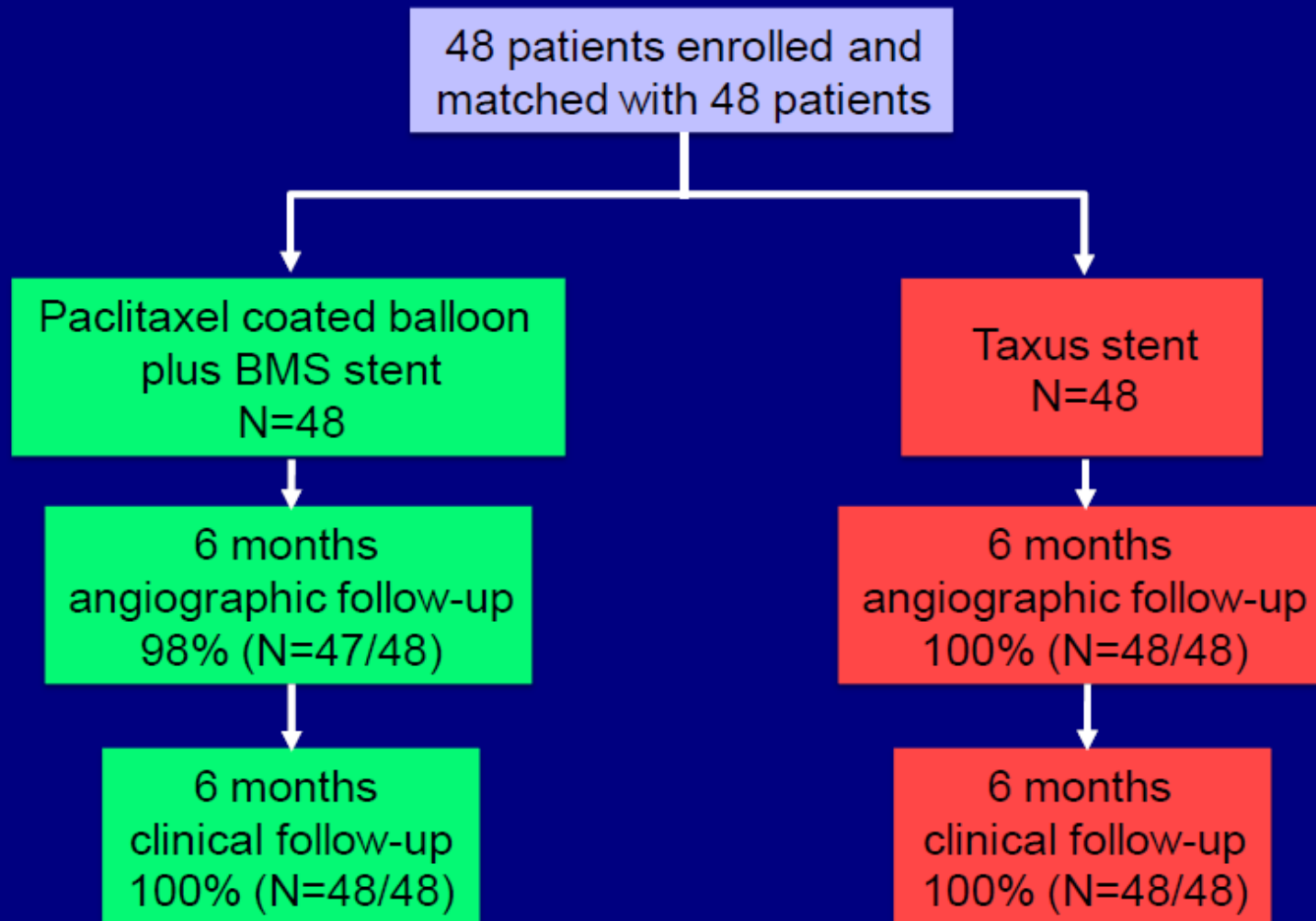
Restenosis with TLR – 3.6% (1/28 pt)



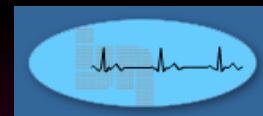
DEB in CTO



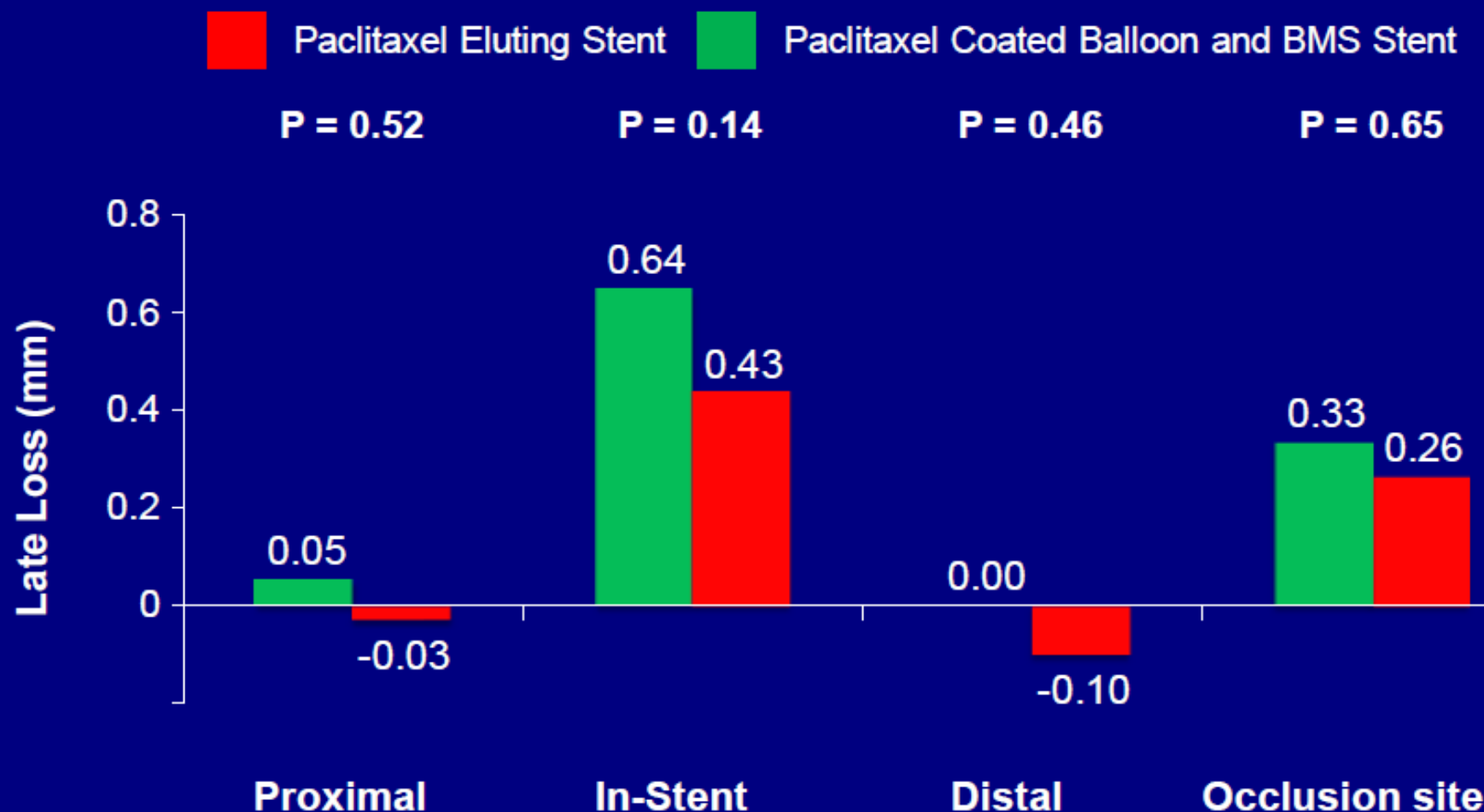
Study flow chart

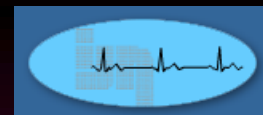


Taxus historical - control for DM, length of stented segment & reference vessel diameter



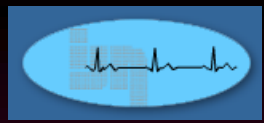
Primary Endpoint: Angiographic Late Loss at 6 mo.





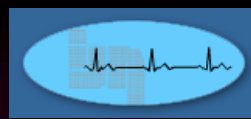
Clinical Outcomes at 6 Months

	Paclitaxel Coated Balloon plus BMS Stent	Paclitaxel Eluting Stent	P Value
Target lesion revascularization	6 (12.5 %)	6 (12.5 %)	1.0
Target vessel revascularization	7 (14.6 %)	6 (12.5 %)	0.78
Myocardial infarction			
Non-target vessel	0 (0 %)	0 (0 %)	-
Target vessel	0 (0 %)	1 (2.1 %)	0.31
Death	0 (0 %)	0 (0 %)	-
TLR, myocardial infarction attributable to target vessel, or cardiac death	6 (12.5 %)	7 (14.6 %)	0.78
Stent thrombosis	0	0	-



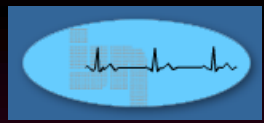
DEB in de-novo Diabetic Lesions

PEPCAD IV: 9 Mo. FU Data Based on 90% FU



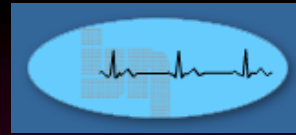
	PEB + BMS (39Px)	PES (36Px)	p
MLD FU [mm]	2.01 ± 0.66	2.09± 0.69	0.62
Stenosis FU [%]	29.0 ± 20.8	26.0 ±22.7	0.54
Late Loss In-stent [mm]	0.51 ± 0.61	0.53 ± 0.67	0.87
Late Loss In-segment [mm]	0.37 ± 0.59	0.35 ± 0.63	0.90
TLR Segment	3 (7.7%)	3 (8.3%)	1.00
TVR (incl TLR)	3 (7.7%)	4 (11.1%)	0.70
Myocardial Infarction	1 (2.6%)	2 (5.5%)	1.00
PCI other vessel	3 (7.7%)	8 (22.2%)	0.11
All Deaths	3 (7.7%)	0	0.24
Cardiac Death	2 (5.1%)	0	0.49
MACE (TLR, MI, Cardiac Death)	6 (15.3%)	5 (16.1%)	1.00

Rosli MA et al, Eurointerven 2011; 7: K83 - 92



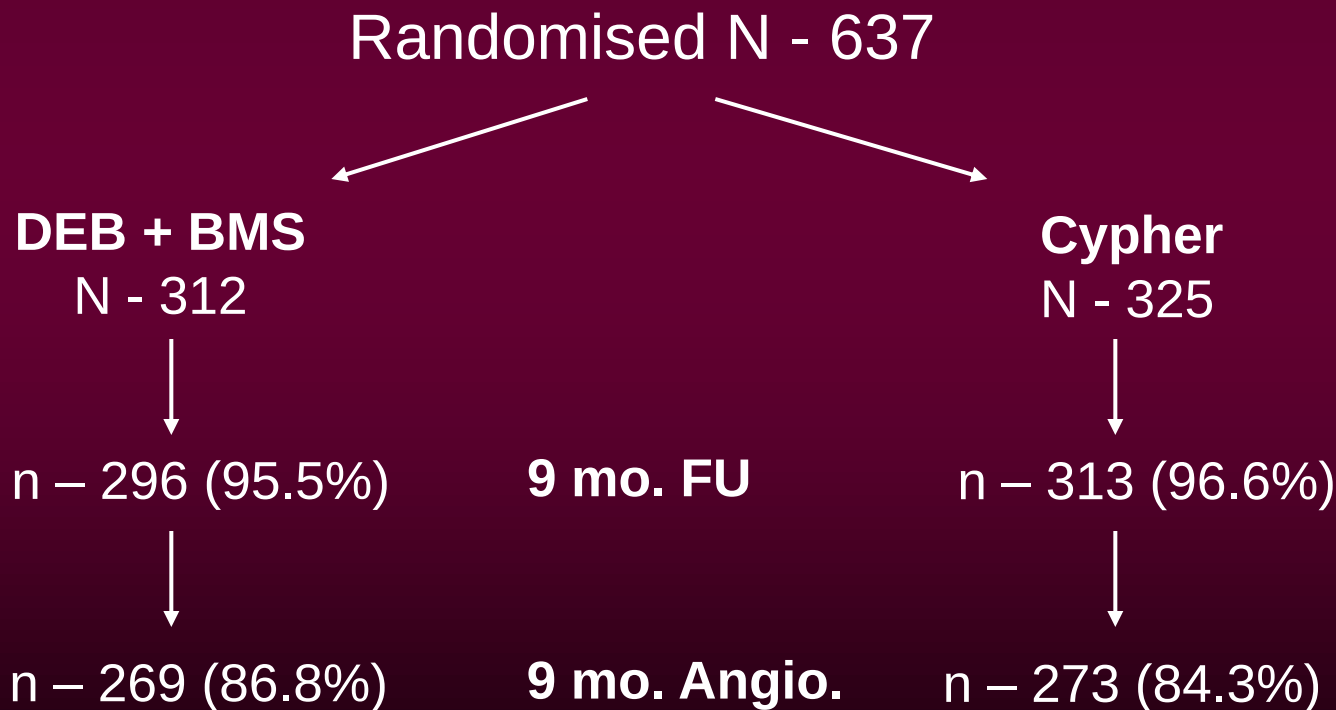
DEB vs DES in de-novo lesions

DEB + BMS Compared to DES

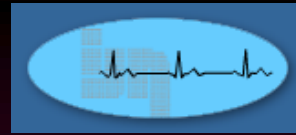


PEPCAD III

*Paclitaxel-eluting PTCA Balloon in Combination with
Coroflex Blue Stent vs the Sirolimus Coated Cypher Stent
In the Treatment of Advanced Coronary Artery Disease*



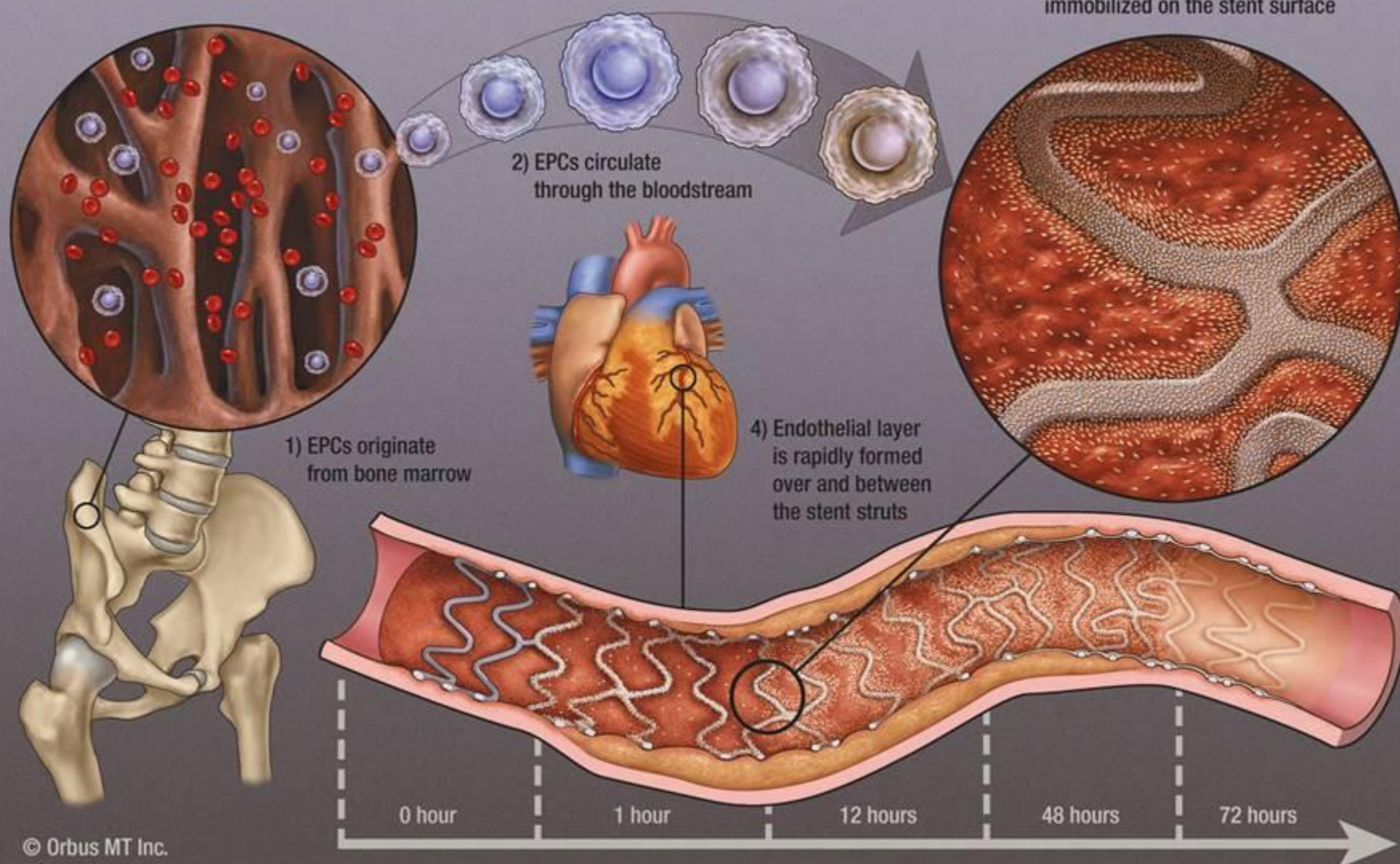
PEPCAD III Results at 9 mo.

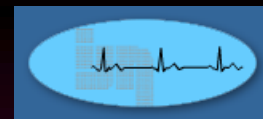


	DEB + BMS	Cypher	p
Late Lumen Loss			
In-stent	0.41 +/- 0.51	0.16 +/- 0.39	< 0.001
In-segment	0.20 +/- 0.52	0.11 +/- 0.40	0.06
Binary restenosis	10.0 %	2.9 %	< 0.01
TVR	13.8 %	6.9 %	< 0.01
TLR	10.5 %	4.7 %	< 0.01
MI	4.5 %	0.3 %	< 0.01
Stent Thrombosis (ARC)	2.0 %	0.3 %	< 0.05



GENOUS: the Role of Endothelial Progenitor Cells (EPCs)





PERFECT Study: 6 mo FU

Outcome	EPC stent only N - 62	EPC stent + DEB N - 58	P value
Proximal late loss(mm)	0.21	0.04	0.01
In-stent late loss(mm)	0.88	0.34	<0.001
Distal late loss (mm)	0.09	0.02	0.20
Total late loss (mm)	0.61	0.16	<0.001
Total segment Binary restenosis(%)	23.2	5.1	0.005
TLR (%)	15.5	4.8	0.05
MACE (%)	17.2	4.8	

Late Lumen Loss DEB Only vs DEB + BMS



DEB Only

ISR

ISR I + II	0.18 mm (6 mo.)
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PEPCAD II	0.20 mm (6 mo.)
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Sm. Vessel

PEPCAD I	0.18 mm (6 mo.)
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Side-branch

PEPCAD V	0.21 mm (6 mo.)
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DEBIUT (Dior)	0.11 mm (9 mo.)
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DEB + BMS

Diabetics

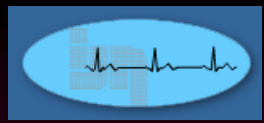
PEPCAD IV	0.51 mm (9 mo.)
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Bifurcation – Main vessel

DEBIUT (Dior)	0.42 mm (6 mo.)
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PEPCAD V	0.38 mm (9 mo.)
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Best results obtained only when DEB is used without stenting



Challenges of Using DEB

- Formidable data on DES
 - A lot of different devices
- Expectation of stent-like results
- Preparation of vessel is vital

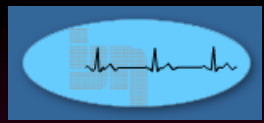
Predilatation

Goes against the expectation of regular balloons

DEB inflation times

Longer

Avoid geographical mismatch



Current Indications of DEB

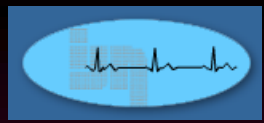
1. ISR
strongest indication
2. Small vessels
3. Bifurcation lesions for side-branch
(Medina 1,1,1 or 1,0,1 or 0,1,1)
only if there is no flow-limiting dissection
4. Other lesions
diabetics, other de-novo lesions

Malaysia National Cardiovascular Registry - PCI

Intracoronary devices used



Device (%)	2007 (n=5455)	2008 (n=4948)	2009 (n=5139)	2010 (n=6043)	2011 (n=5901)	2012 (n=6043)
Balloon only	8.0	8.0	8.0	8.0	6.0	5.0
Drug Eluting Balloon	0.05	1.0	2.0	6.0	6.0	7.0
Cutting Balloon	2.0	2.0	2.0	2.0	1.7	1.2
IVUS	2.0	5.0	4.0	4.0	3.3	2.5
Rotablator	1.0	1.0	1.0	1.1	0.9	0.7
Drug Eluting Stent (DES)	43.0	49.0	53.0	65.0	64.0	70.0
Bare Metal Stent (BMS)	43.0	35.0	33.0	21.0	21.0	17.0
Distal Embolic Protection	0.05	0.7	0.3	0.2	0.4	0.6



Drug Eluting Balloon

At Present

This technology is here to stay !

The Future:

It's role needs to be further defined!