

Late breaking clinical trial session 4

Drug Eluting Balloons in Coronary Bifurcations ;

The Drug Eluting Balloon In BifUrcation Trial

On behalf of all co-investigators

By: Pieter R. Stella, MD, PhD

University Medical Center of Utrecht

The Netherlands



Internationales Herz- und
Gefäßzentrum Rhein-Ruhr



University Medical Center
Utrecht



Potential conflicts of interest

Speaker's name: P.R.Stella

I have the following potential conflicts of interest to report:

X Member Advisory Board Eurocor GmbH

Study Aim :

To assess the safety and efficacy of the DIOR™ Drug Eluting Balloon in coronary bifurcations in combination with a BMS, with a specific focus on the side branch (SB) using the provisional T-stenting technique with final kissing balloons.



Hypothesis :

I Optimizing current standard 1 stent strategy with;
better long-term SB patency
reducing the need for SB stenting

II Optimizing patient safety by;
achieving “DES-like” results with BMS+DEB
avoiding prolonged DAPT



Methods 1:

Prospective randomised multi-center study comparing 3 study arms :

BMS + poba vs. BMS + DEB vs. DES + poba

Using the provisional T-stenting technique

Using the same stent platform in all three study arms (Liberte™)

Comparing the same drug (Paclitaxel) with Taxus Liberte™ & Dior™

Sequential predilatation with DEB in MB and SB in arm II

With just 3 month of DAPT in arms I & II

Angiographic follow-up at 6 months and clinical up to 5 years

The study was approved by all Ethical committees and an independent safety committee and an independent core-lab (Genae) were installed



Methods 2:

Primary endpoints:

angiographic late lumen loss MB 0.8 mm(BMS)→0.4(DEB)
and 50% reduction of LL in SB (BMS vs. DEB)
safety as assessed by occurrence of stent thrombosis

Secondary endpoints:

binary restenosis , MACCE and clinical FU up to 5 years
DES added as a ‘control –arm’

Based on the assumption of a reduction in late loss from 0.8 (BMS) to 0.4 (DEB)

A total of 120 patients were enrolled in Utrecht (60), Leuven (37), Genk (21) and Essen (2)



DIOR 1st generation

- Paclitaxel balloon surface: 3 $\mu\text{g}/\text{mm}^2$
- Crystallin coating method with Paclitaxel (Ph.Eur. 5.0) and DMSO (Dimethylsulfoxid)
- 3-folded to protect the drug from early wash-off

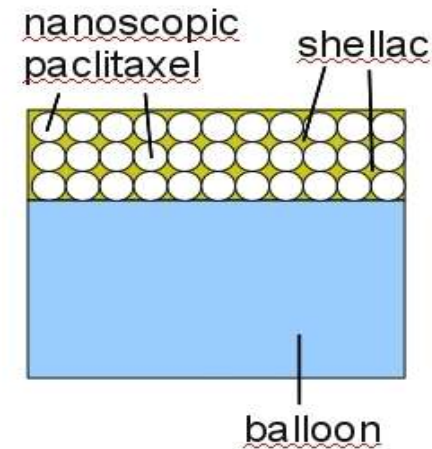
DIOR 2nd generation

- Paclitaxel balloon surface: 3 $\mu\text{g}/\text{mm}^2$
- Coating method is a 1:1 mixture of Paclitaxel (Ph.Eur. 5.0) and Shellac (Ph.Eur. 4.8)
- Shellac is FDA approved and well established in cosmetics, as food coating and tablet coating
- 3-folded to protect the drug from early wash-off

DIOR 2nd generation



DIOR 2nd – Shellac gives the balloon a shiny experience.



DIOR 2nd – 1:1 mixture of Paclitaxel and Shellac

Procedure`s Flowchart

Randomization



Dilatation of main and side branch with DEB (arm A) or non DEB (arm B and C)
(balloon / vessel ration 1:1)



Stent deployment in the main vessel
BMS (arm A and B) or DES (arm C)



„Kissing balloon“ post-dilatation with
uncoated ballons

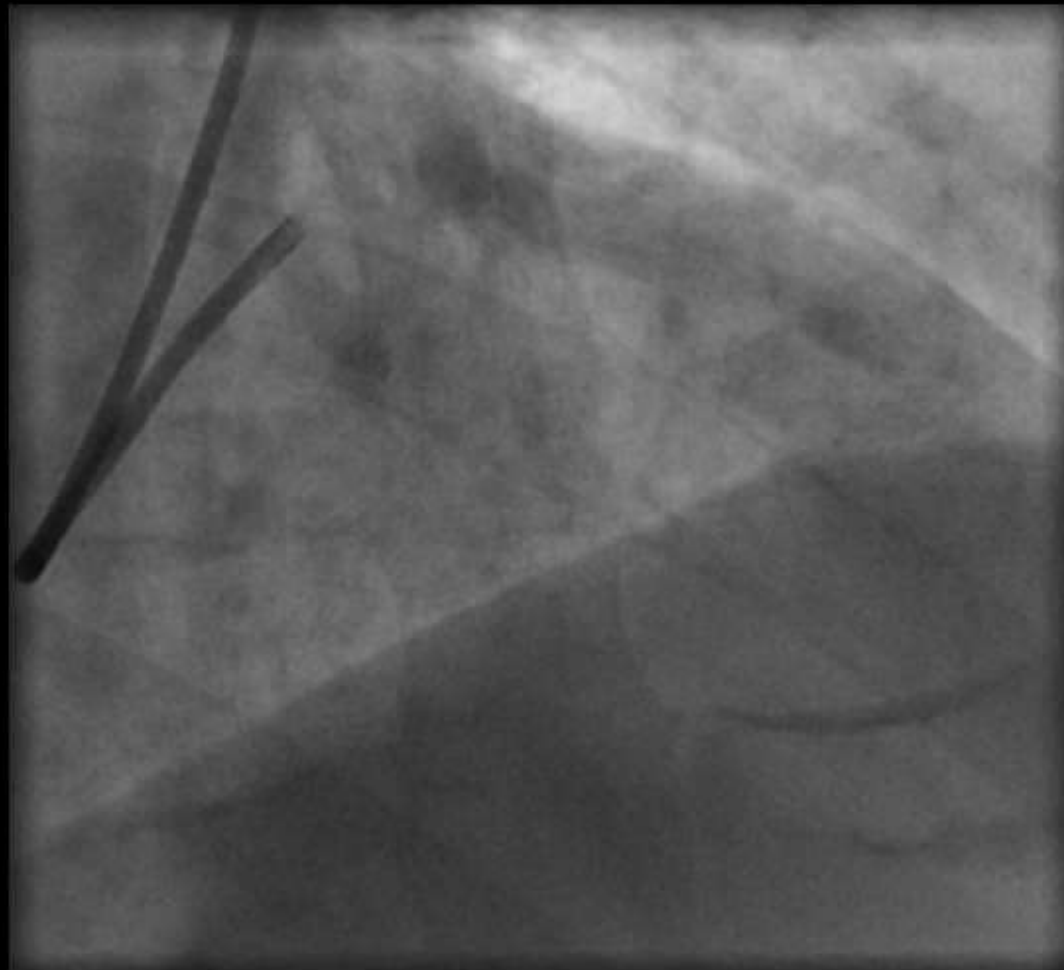


Drug Eluting Balloon in bifurcation Trial Methods-1

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 3 - Frame 1 / 41

UMC
79kV, 879mA, 7s

Baseline
Medina 1,1,1



LAO -29,9°
Caudal 24,1°

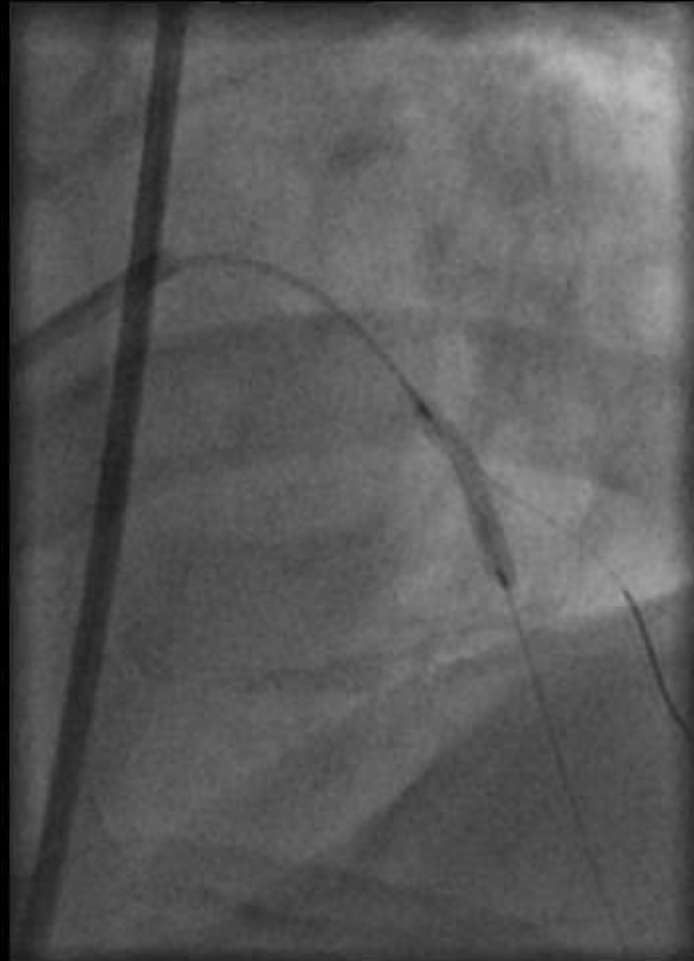
L 128
W 256

Drug Eluting Balloon in bIfUrcation Trial Methods-2

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 5 - Frame 1 / 15

UMC
79kV, 848mA, 6s

**Pre-dil MB
(poba)**

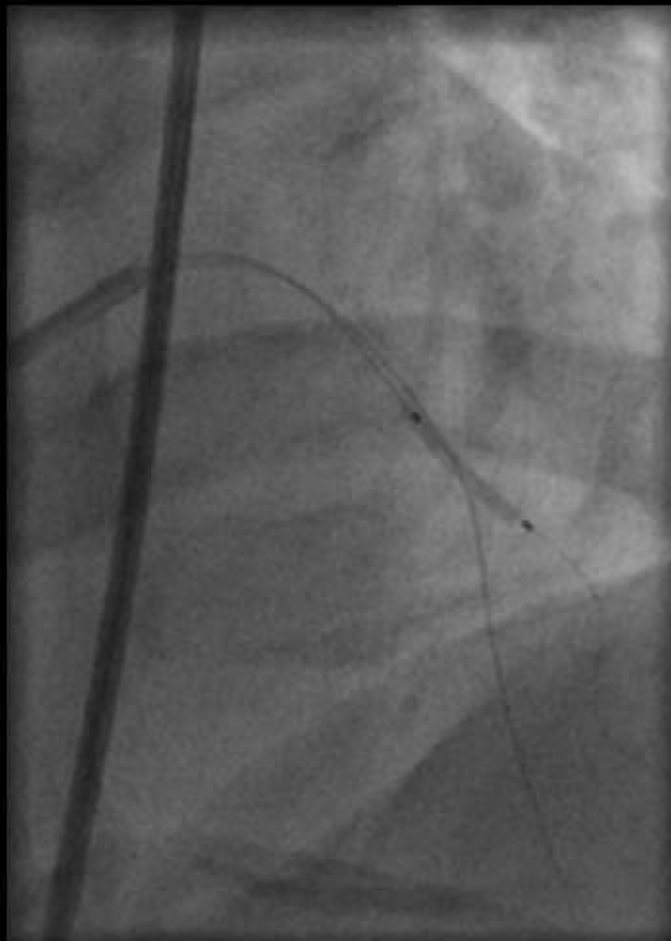


Drug Eluting Balloon in bifurcation Trial Methods-3

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 8 - Frame 1 / 9

UMC
80kV, 909mA, 7s

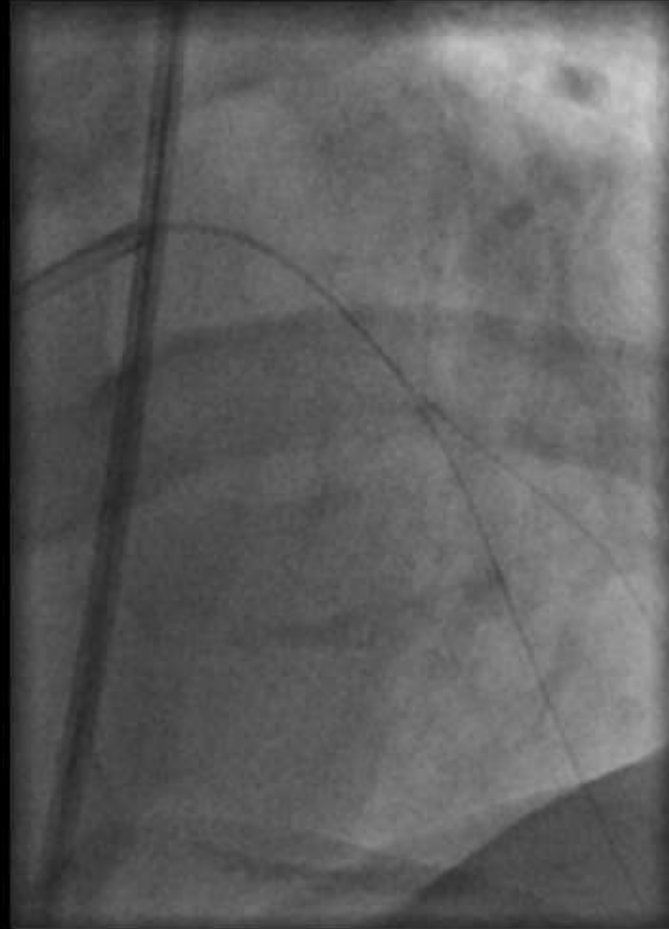
***Pre-dil SB
(poba)***



Drug Eluting Balloon in bifurcation Trial Methods-4

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 11 - Frame 1 / 25

UMC
79kV, 879mA, 7s



After POBA

LAD -1,9°
Caudal 31,1°

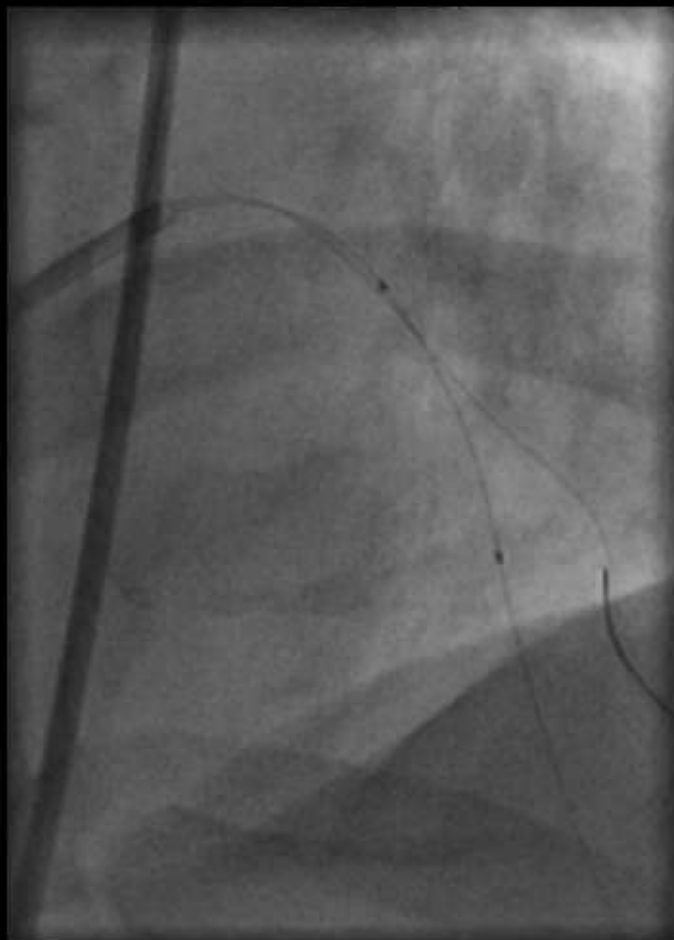
L 128
W 256

Drug Eluting Balloon in bifurcation Trial Methods-5

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 12 - Frame 1 / 35

UMC
80kV, 907 mA, 7s

DEB – @6atm, margins !



Arnold, D. J.W., 7950753, 6-9-1952, M
Run 12 - Frame 1 / 35

UMC
80kV, 907 mA, 7s



LAD -1.9°
Caudal 31.1°

L 129
W 256

LAD -1.9°
Caudal 31.1°

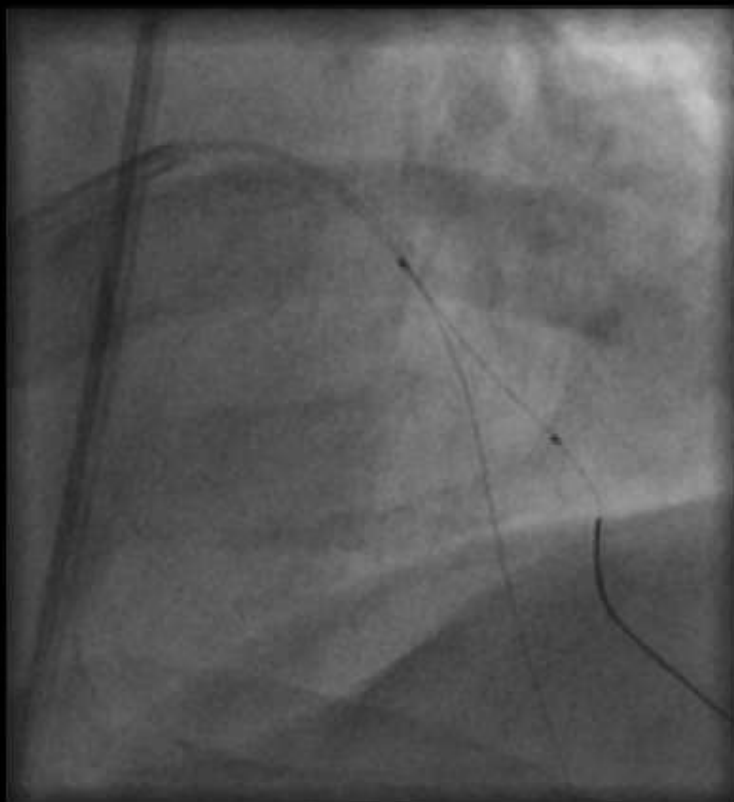
L 128
W 256

Drug Eluting Balloon in bifurcation Trial Methods-6

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 15 - Frame 1 / 27

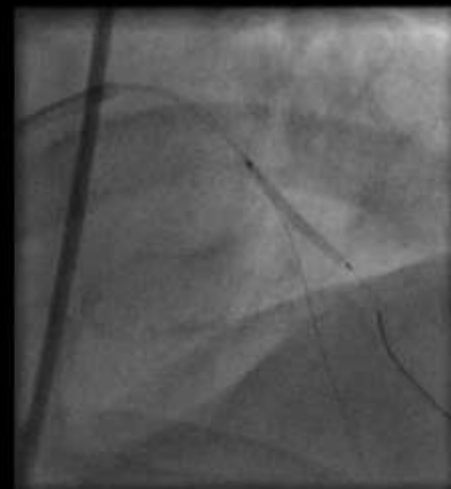
UMC
79kV, 866mA, 7s

DEB – @6atm, margins !



Arnold, D. J.W., 7950753, 6-9-1952, M
Run 16 - Frame 1 / 9

UMC
81kV, 901mA, 7s



LAO -1,9°
Caudal 31,1°

L 129
W 256

LAO -1,9°
Caudal 31,1°

L 128
W 256

Drug Eluting Balloon in bifurcation Trial Methods-7

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 19 - Frame 1 / 9

UMC
79kV, 878mA, 7s

BMS impl.



LAD -1,9°
Caudal 31,1°

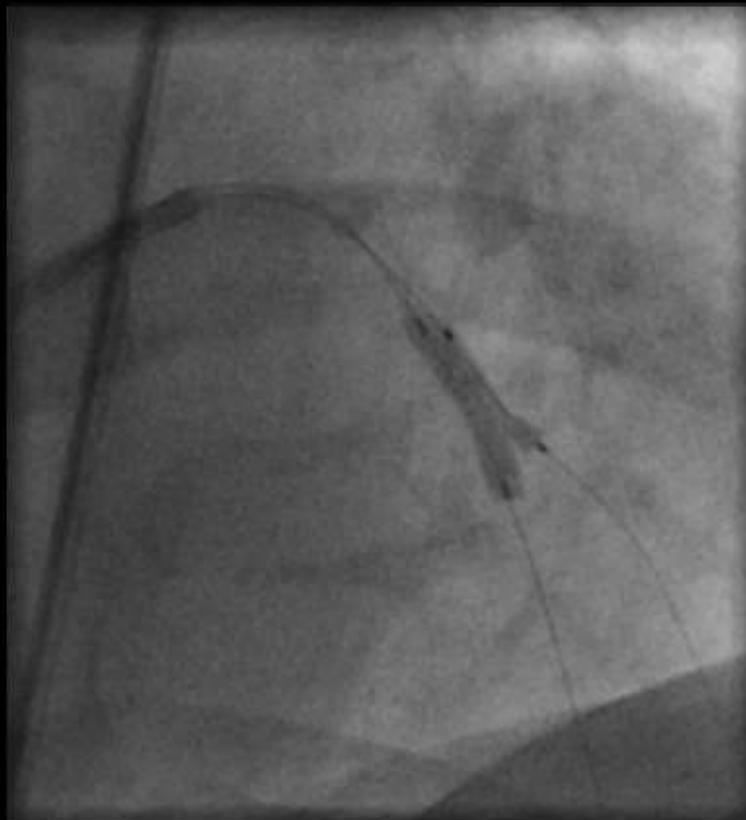
L 128
W 256

Drug Eluting Balloon in bifurcation Trial Methods

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 24- Frame 1 / 5

UMC
79kV, 887mA, 7s

Recrossing + final
kissing (POBA)



LAO -1,9°
Caudal 31,1°

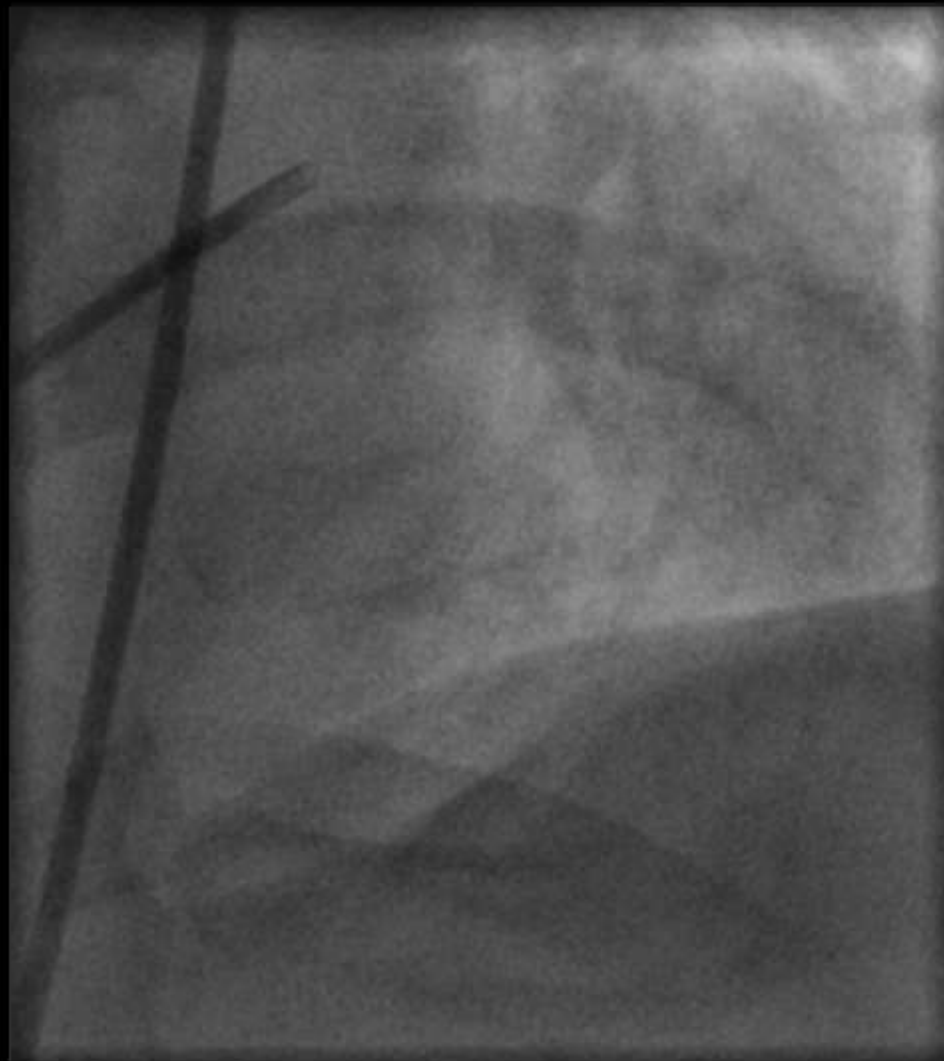
L 128
W 266

Drug Eluting Balloon in bifurcation Trial Methods

Arnold, D. J.W., 7950753, 6-9-1952, M
Run 28 - Frame 1 / 30

UMC
81kV, 896mA, 7s

Final



LAO -1,9°
Caudal 31,1°

L 128
W 258

Baseline Characteristics 1:

	BMS	DEB	DES
Age (years)	70.3y	68y	68.7y
Male sex (%)	78.4%	62.5%	77.5%
Hypertension	56.8%	55.0%	60.0%
Current or ex-smoker (%)	64.8%	60%	52.5%
Hypercholesterolemia (%)	59.5%	52.5%	55.0%
Diabetes mellitus (%)	13.5%	7.5%	15.0%
Previous myocardial infarction (%)	21.6%	17.5%	25.0%
Previous PCI (%)	32.4%	32.5%	32.5%
Previous CABG (%)	5.4%	2.5%	2.5%

P-value in all *n.s.*



Baseline Characteristics 2:

	BMS		DEB		DES
Target Lesion LAD	83.8%		77.5%		89.0%
Medina (x,x,1)	70%		60%		60%
> 2-VD	37.8%		37.5%		35.0%
Angle > 70° (%)	18.9%		45%		40.0%
>> Mild calcium	37.8%		28.0%		39.0%
Total fluoroscopy time (min)	14.6		14.7		13.0
Total procedure time (min)	51.9		56.5		53.5
Contrast used (cc)	230		225		203

P-value in all *n.s.*



Angiographic Characteristics * 1:

	BMS	BMS SB	DEB	DEB SB	DES	DES SB
Lesion Length (mm)	9.08	4.60	10.06	4.29	8.79	4.11
Balloon length	13.53	12.53	27.38	17.63	12.28	12.09
Balloon diam	2.58	2.51	2.60	2.39	2.48	2.37
Balloon atm	8.89	7.72	8.59	7.28	9.20	8.06
Stent Length (mm)	21.0	-	21.5	-	20.63	-
Stent diameter	3.15	-	3.08	-	3.10	-
Stent pressure	15.0	-	13.15	-	13.29	-
Number of stents used	1.07	5%	1.02	7.5%	1.08	2.5%
Final Kissing	97.3%		97.5%		100%	
Success of Procedure	100%	100%	100%	100%	100%	100%



QCA analysis according to MEDIS analysis– like Nordic studies P-value in all *n.s.*

Results: Angiographic outcomes Prox.MB at 6 months (FU in 91.5%)

	BMS prox.		DEB prox.		DES prox.
Ref. Diam (mm)	2.87		2.78		2.81
MLD (mm)	0.89		0.93		1.08
Post PCI MLD	2.61		2.61		2.42
Res. Stenosis %	15.6%		16.7%		18.4%
F.U. MLD (mm)	1.97		2.19		2.24
Diam stenosis %	22.5%		21.4%		22.6%
Binary restenosis	3.0%		0%		5.4%
Late loss (mm)	0.64		0.42		0.18

P-value in all *n.s.*



Results: Angiographic outcomes Dist.MB at 6 months (FU in 91.5%)

	BMS distal	DEB distal		DES distal	
Ref. Diam (mm)	2.50	2.70		2.32	
MLD (mm)	0.95	0.99		1.01	
Post PCI MLD	1.55	1.46		1.34	
Res. Stenosis %	29.3%	33.5%		29.7%	
F.U. MLD (mm)	1.45	1.50		1.43	
Diam stenosis %	35.9%	35.9%		30.6%	
Binary restenosis	18.2%	9.4%		13.5%	
Late loss (mm)	0.1	- 0.04		- 0.11	

P-value in all *n.s.*



Results: Angiographic outcomes SB at 6 months (91.5%)

	BMS SB	DEB SB		DES SB
Ref. Diam (mm)	2.59	2.63		2.32
MLD (mm)	1.07	1.18		1.04
Post PCI MLD	1.85	1.76		1.72
Res. Stenosis %	22%	26%		24.8%
F.U. MLD (mm)	1.62	1.65		1.77
Diam stenosis %	30.5%	31.6%		25.8%
Binary Rest. %	12.1%	6.3%		2.7%
Late loss (mm)	0.23	0.11		-0.08

P-value in all *n.s.*



Results: Clinical outcomes at 6 months (100%)

	BMS	DEB	DES
MI (periprocedural) (3x 'N')	5.4%	7.7%	6.9%
MI (postprocedural) (3x 'N')	0%	0%	2.5%
SAT	0%	0%	2.5%
TVR (non TLR)	5.4%	4.5%	7.5%
TLR	27.0%	12.5%	10.0%
Death	0%	0%	0%
MACE	27.0%	15.0%	17.5%

P=0.09

P-value in all *n.s.*



Conclusions:

1. Due to un-anticipated good results in de POBA arm, the primary endpoint was not reached (Late loss prox.MB (0.64 vs 0.42)). And, because of this lack of power also the 50 % reduction in SB-late loss was not statistically significant (0.23 vs. 0.11).
2. However there are strong trends which show a favorable outcome combining DEB with a BMS in MB and using a DEB in SB with regards to late loss and especially binary restenosis rates.
3. Also in secondary endpoints there is a strong trend towards favoring DEB + BMS in terms of TVR, TLR and total MACE rates compared to BMS/POBA.
4. No cases of Geographical Miss were observed in DEB arm
5. The use of BMS + DEB in bifurcations with only 3 months of DAPT seems very safe with 0% occurrence of SAT.
6. The non-powered randomised comparison between all three arms shows a clear unfavorable outcome for the use of BMS/ POBA in bifurcations.

DEBIUT trial



Based on these numbers a larger randomised study is warranted between DEB+ CoCr vs. DES + POBA



University Medical Center
Utrecht

PF.Agostoni, E.v Belle



C.Dubois, T.Adriaenssens



J.Dens

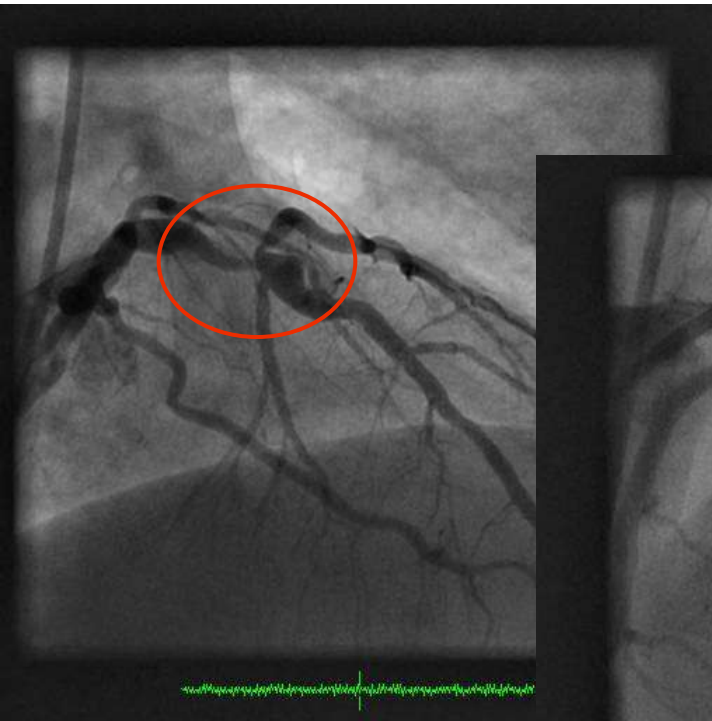
Internationales Herz- und
Gefäßzentrum Rhein-Ruhr



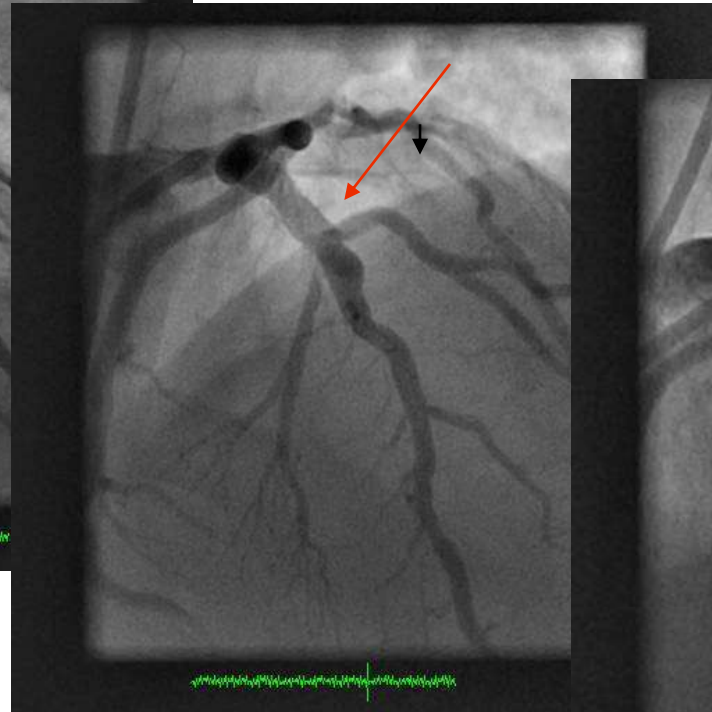
C.Naber



Bifurcation intervention with DIOR balloon: DEBIUT study

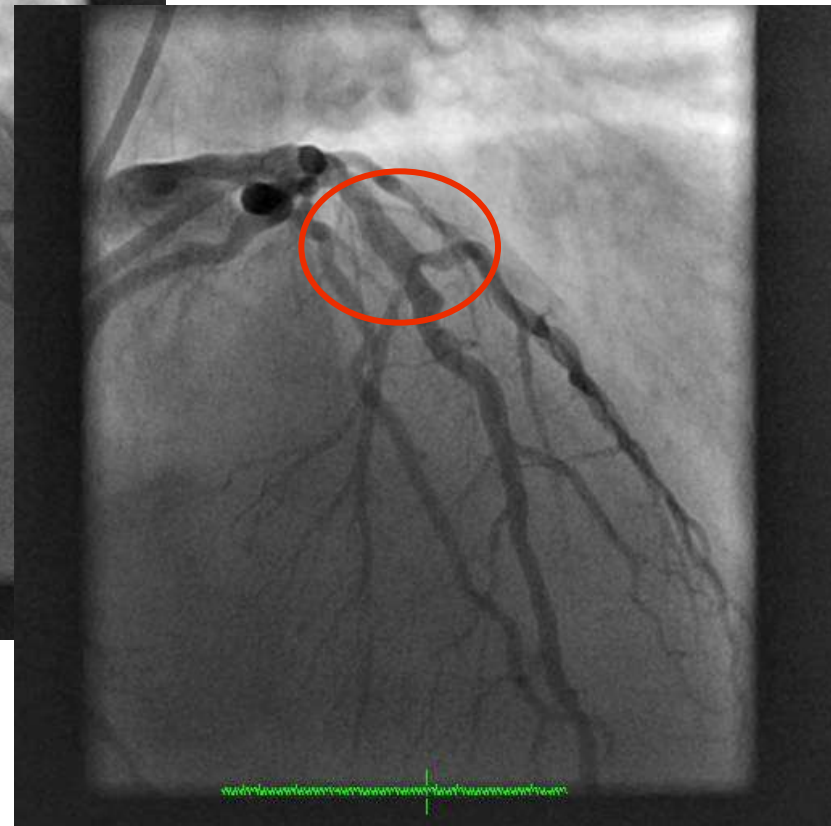


Initial



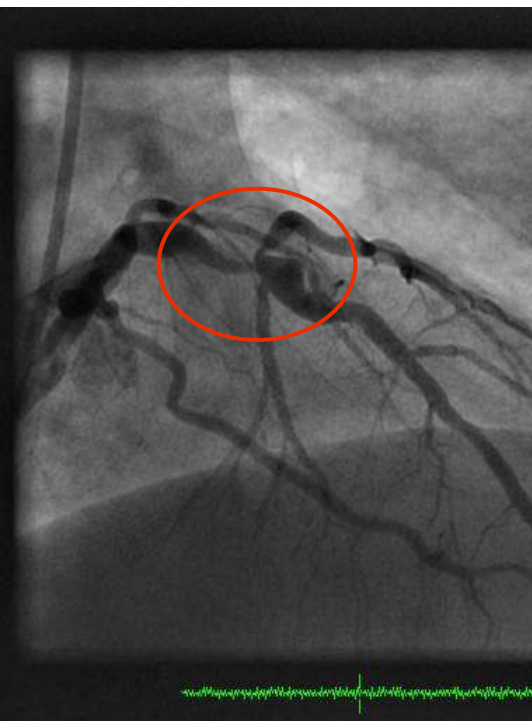
Baseline

Medina: 1,1,1

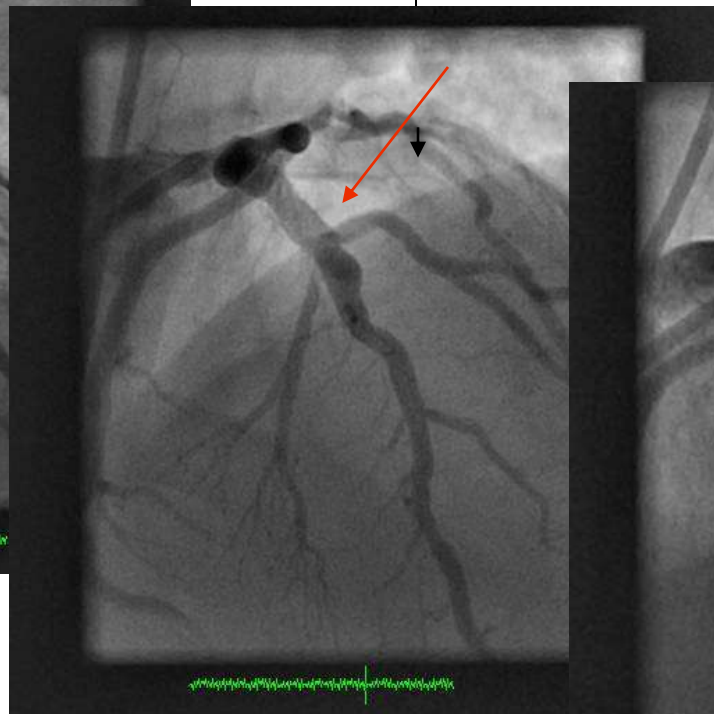


Follow-up

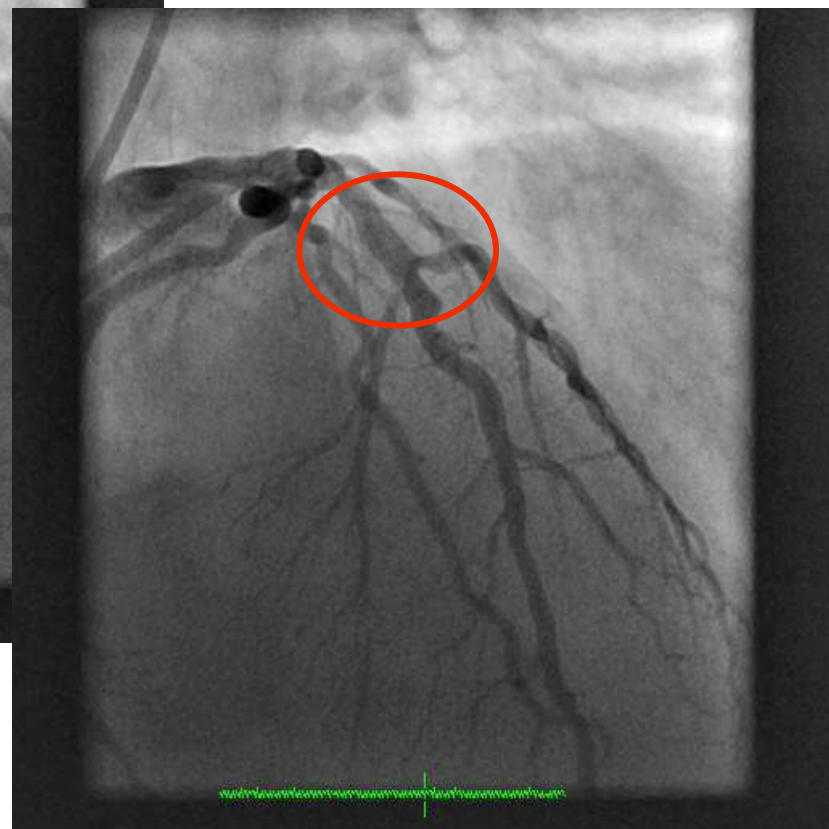
Bifurcation intervention with DIOR balloon: DEBIUT study



Initial



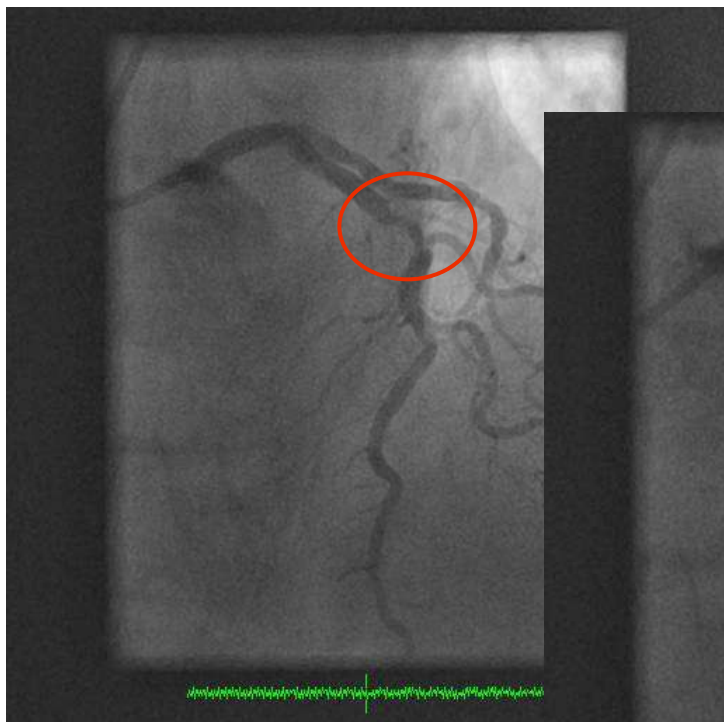
Baseline



Follow-up

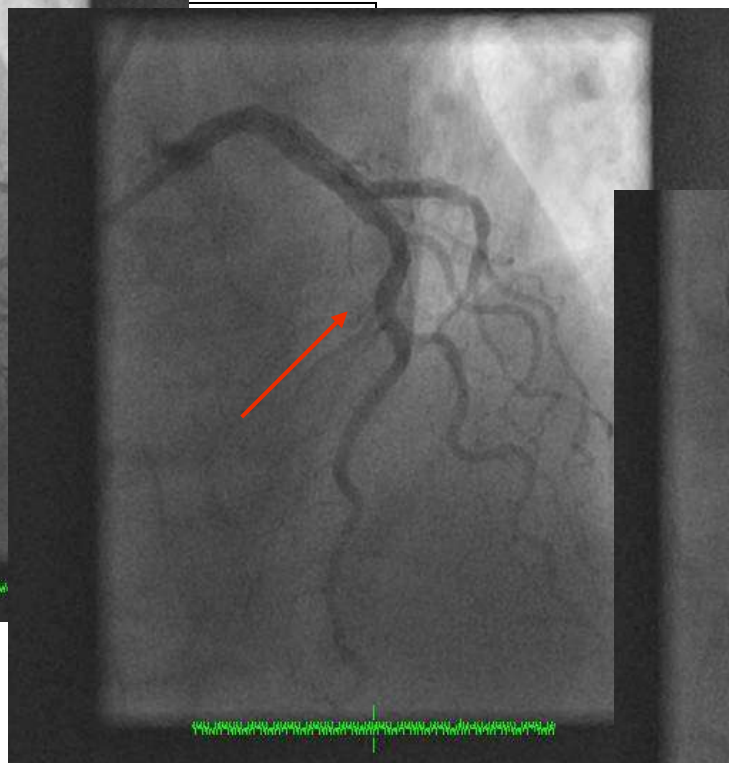
Medina: 1,1,1

Bifurcation intervention with DIOR balloon: DEBIUT study

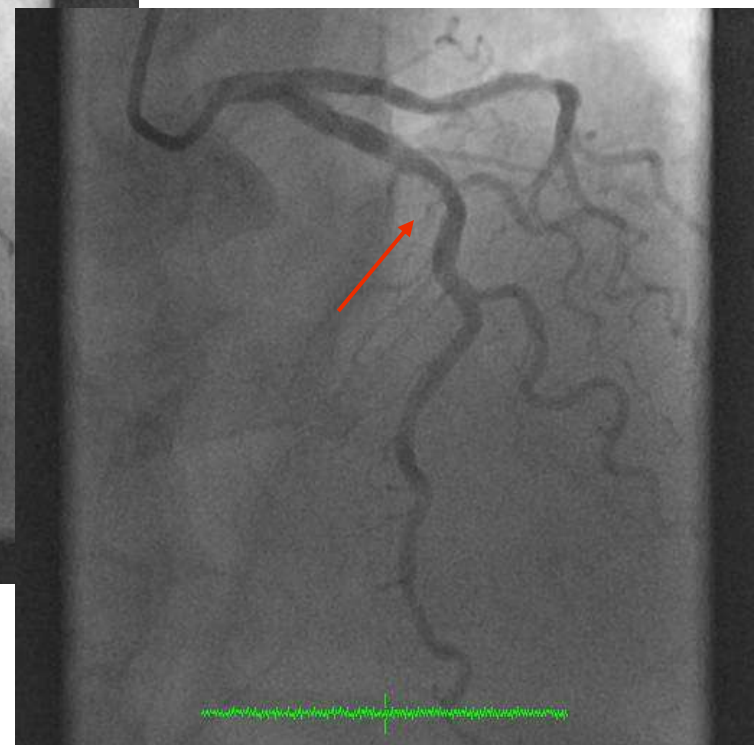


Initial

Medina: 1,1,0



Baseline



Follow-up

BBC 1 Study

	SIMPLE (N = 249)	COMPLEX (N = 248)	P- Value
PROCEDURE TIME, MIN	57	78	< 0.001
FLUOROSCOPY TIME, MIN	15	22	<0.001
DIAMENTOR, CGY·CM²	6,140	7,900	< 0.001
NO. OF GUIDEWIRES USED	2.2	3.1	<0.001
NO. OF BALLOONS USED	2.3	4.0	<0.001
NO. OF STENTS USED	1.2	2.2	<0.001

So . . . Leave it alone ??

BBC 1 Study
Clinical outcomes @ 9 months

	SIMPLE (N = 250)	COMPLEX (N = 250)	HR (95% CI)	P-VALUE
PRIMARY ENDPOINT*	88.0%	115.2%	2.02 (1.17- 3.47)	0.009
DEATH	0.4%	0.8%	—	—
MI	3.6%	11.2%	3.24 (1.53- 6.86)	0.001
TVF	5.6%	7.2%	1.32 (0.66- 2.66)	0.43

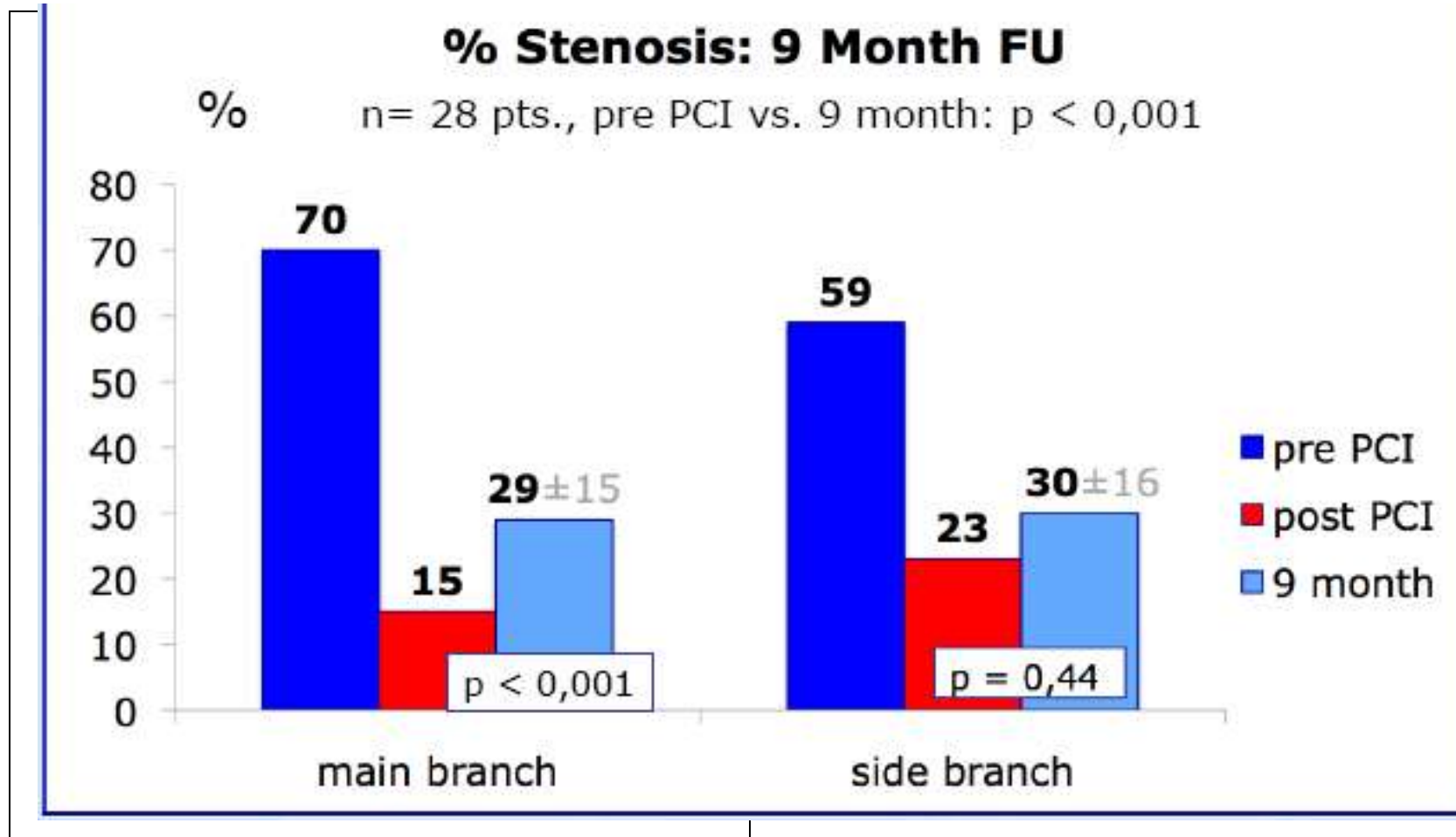
***Death, MI, and TVF**

By: Hildick Smith TCT 09

The PEPCAD V Bifurcation Study; Results from a Paclitaxel-Eluting Balloon for Bifurcation Coronary Lesions



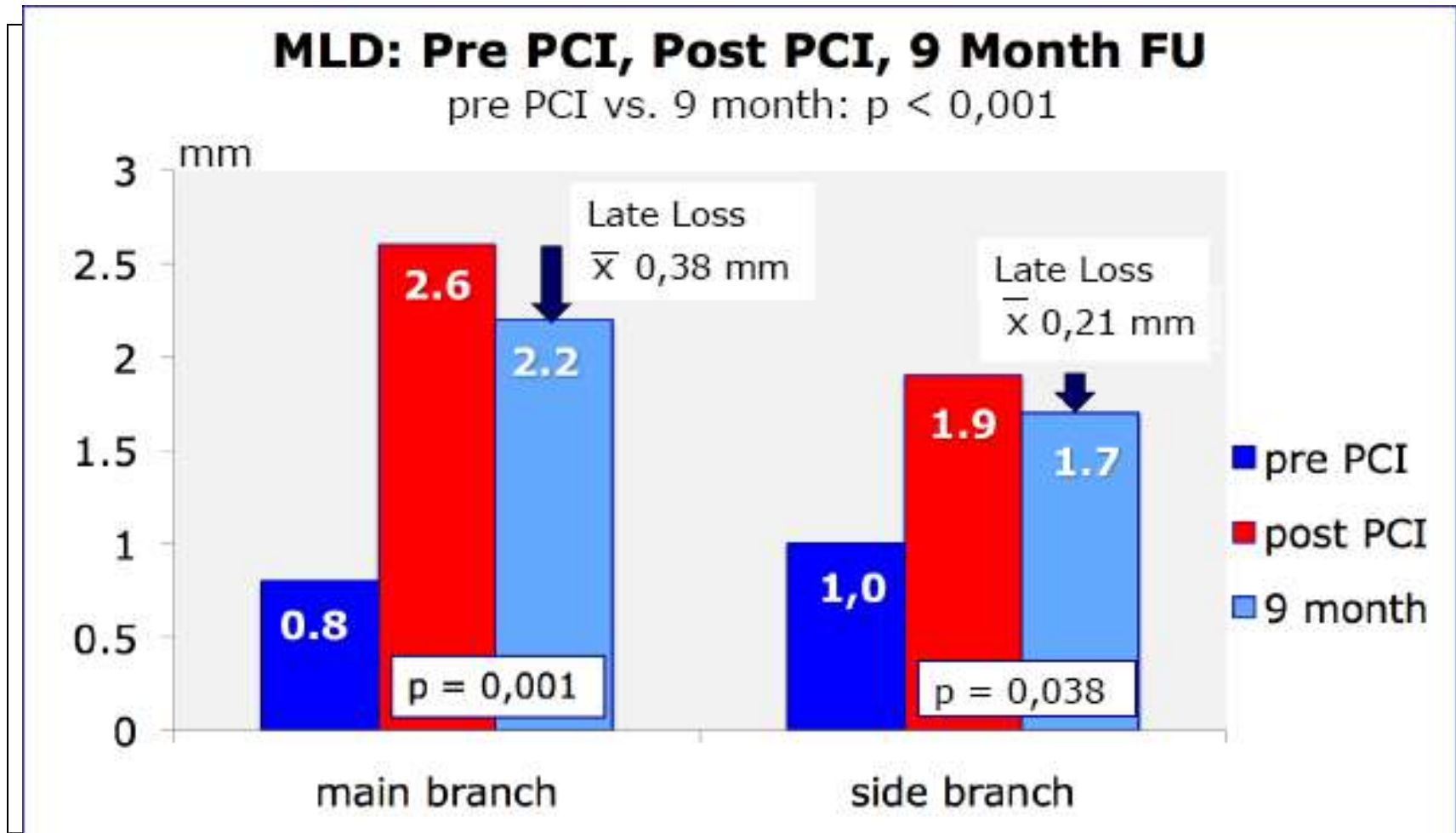
By: Detlef G. Mathey @ TCT2009



The PEPCAD V Bifurcation Study; Results from a Paclitaxel-Eluting Balloon for Bifurcation Coronary Lesions



By: Detlef G. Mathey @ TCT2009



The PEPCAD V Bifurcation Study; Results from a Paclitaxel-Eluting Balloon for Bifurcation Coronary Lesions

PCR

Adverse Events By: Detlef G. Mathey @ TCT2009

30 day follow up

Final Kissing in only 8 %

MACE	0/28 (0%)
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9 month follow up

Death	0/28 (0%)
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Late Stent Thrombosis (1x definite, 1x probable)	2/28 (7,1%)
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Restenosis with TLR	1/28 (3,6%)
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Restenosis (SB) without TLR	2/28 (7,1%)
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