



Drug-Eluting Balloon in OOI Bifurcated Lesions: *Acute and 6 mo Clinical and Angiographic Results*

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Potential conflicts of interest

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I do not have any potential conflict of interest

001 Bifurcated lesions

- **Ostial lesions placed in secondary branches (001) are also lesions placed in “small vessels”**

- **Independently of the type of PCI (BMS/DES): coronary vessel size (small) is a strong predictor of restenosis following angioplasty¹⁻³**

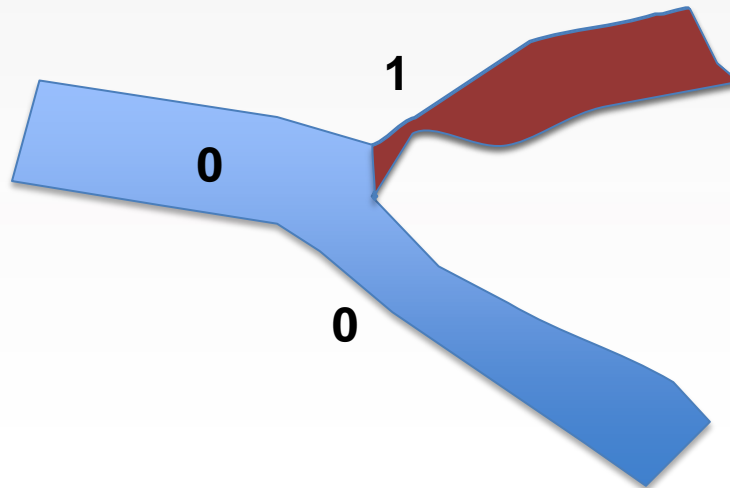
1. Elezi S, et al. *Circulation* 1999

2. Moses JW et al. *N Engl J Med* 2003

3. Elezi S et al. *JACC* 2006

001 Bifurcated lesions

- How to deal with ostial bifurcated lesions in which the lesion is just in the ostium of the SB (001 Medina Classification⁴)
 - All suggested methodologies have specific limitations
 - The best strategy remains debatable⁵



4.- Medina A, et al. Rev Esp Cardiol. 2006; 59:183

5.- Louvard Y, et al. Eurointervention 2010



001 Bifurcated lesions

Consensus from the 5th European Bifurcation Club meeting

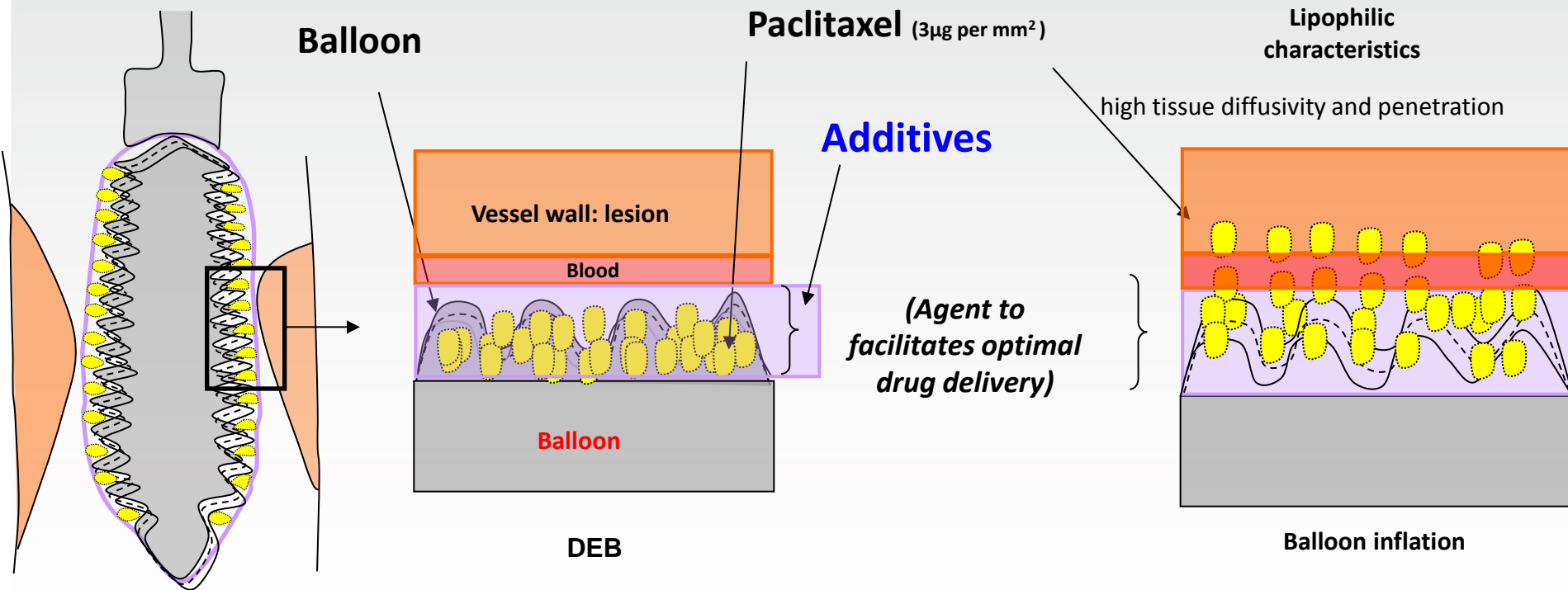
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The EBC consensus was that further studies were required. The first area concerns large calibre true bifurcations with significant ostial side branch length disease. These lesions are currently considered by most experts to require a systematic two-stent strategy, but evidence to support this approach is lacking. The second area is the perennial thorny issue of the 0,0,1 lesion. An EBC Registry has been set up for the interventional management of such cases.

Louvard Y, et al. Eurointervention 2010

DEB Technology (2⁰n Generation)

- To enhance the solubility of the lipophilic paclitaxel, DEB needs of the use of a smaller amount of **additives**



- In the 2ⁿ generation of DEB (*SeQuent please, Dior II, In-Pact Falcon and Pantera Lux*) different types of **water-soluble matrix** (*iopromide, shellac, BTHC, and urea*) have been introduced by the manufacturer



Antiproliferative Agent: Paclitaxel

- **Lipophilic** characteristics (efficacy of local drug delivery is 10-20 x higher than hydrophilic drugs)
- **High adsorption rates**
- Rapid uptake by intima in order to compensate for short contact time
- **High retention rate (remain in the vessel wall during one week)⁶**
- Dose dependant effect associated with a large therapeutic window
- **The structural intracellular** (irreversible binding to microtubules, inhibiting cell division and migration) **changes caused by paclitaxel explain its long-lasting effects⁷**

Cell-culture experiments:

- the brief contact between vascular and smooth-muscle cells and lipophilic taxane compounds (paclitaxel) **inhibits the proliferation of such cells for at least 15 days**

DEB technology

- According to initial investigation in porcine model of coronary restenosis^{8,9} and in humans¹⁰: **The efficacy of DEB** (*in terms of antiproliferative effect*), could be related with the final tissue dosage
 - **The final tissue dosage**, may depend on
 - the formulation used to coat the balloon &
 - on the type of the coronary lesion treated
 - Thus it seems that the highest drug retention in the vessel wall, the most effective DEB
-

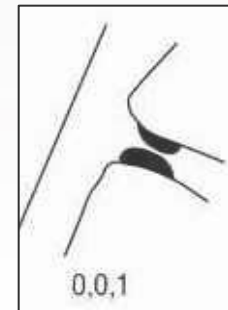
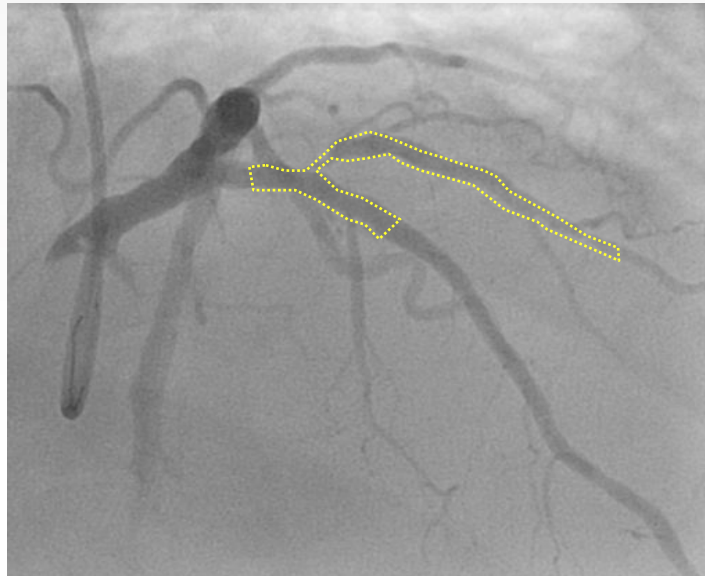
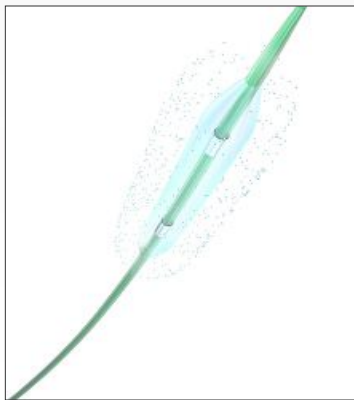


DEB Technology (2⁰n Generation)

PEB	Type of Coating	Formulation	Release from balloon surface 30/60(s)	Vessel wall paclitaxel concentration & time of inflation	Company
SeQuent™ Please	Iopromide	3 µg paclitaxel/mm ² balloon surface, modified Paccocath™	NA/93%	45-95µg- 60s	B. Braun, Melsungen, Germany
DIOR I	No carrier	Paclitaxel micro-crystals coated onto a 3 fold-microporous balloon surface structure	20/25%	1.5-6µg - 60s	Eurocor, GmbH, Germany
DIOR II	Shellac	3 µg paclitaxel/mm ² balloon surface, 1:1 mixture of paclitaxel and shellac	75/85%	167µg - 30s	Eurocor, GmbH, Germany
IN-PACT (FALCON)	Urea	FreePac™ paclitaxel-coated balloon catheters (Invatec, S.P.A., Italy)	NA	NA	Medtronic, Inc., Santa Rosa, California
Pantera Lux	Butyryl-tri-hexyl citrat (BTHC)	3 µg paclitaxel/mm ² balloon surface, matrix: BTHC	NA	165µg - 30s	Biotronik, Berlin, Germany

Study Objectives_(S)

- **Prospective, multicenter registry of PCI to assess efficacy and safety of the PEB, second generation DIOR™ (EuroCor, Germany), for the treatment of *de novo ostial* bifurcated lesions (001 of Medina classif)**





The 001-DIOR Multicenter Registry

This study is ongoing, but not recruiting participants.

Sponsor: Eurocor GmbH

Information provided by (Responsible Party): Eurocor GmbH

ClinicalTrials.gov Identifier:

NCT01375465

7 centers: Inclusion Period (02/2011-9/2013): 2 years & 7 months

- **Inclusión criteria:**

- 001 *de novo* Bifurcated lesion (ostium SB \geq 2.0mm)
 - **Clinical evidence of myocardial ischemia related to the TL**
 - Target lesion \geq 50%
-

- **Exclusion criteria:**

- Cardiogenic shock
- Patients survival to less than one year
- ✓ **Angiographic:**
 - LM bifurcation lesion: Ostial LAD and LCx lesions
 - Lesion length > 25 mm
 - Target vessel reference diameter < 2mm
 - Severe angiographic calcification

- **Primary end-points:**
 - **MACE (cardiac death and/or MI and/or TLR)**

- **Secondary end-points:**
 - **Overall death**
 - **TVR symptom or ischemia driven**
 - **Segment treated thrombosis/occlusion**
 - **6-7 months angiographic late luminal loss**
 - **6-7 months target segment binary restenosis**



Study's Flowchart

Ostial Bifurcated lesion



Clinical and Angiographic eligible patients (SB diameter \geq 2.0 mm)



TL SB Pre-dilatation (Recommended: cutting balloon)



Dior dilatation: longer than regular balloon, above nominal pressure + **at least during 45sec**



TL SB Post-dilatation (if needed, shorter than Dior)

Angiographic success: a residual lesion stenosis $<$ 50% in the TL and absence of $>$ type B coronary dissection

└───→ No angio success: **BMS**

Clinical Characteristics (n=50)

Age (years) (mean±SD)	62.1 ± 11.2
Male gender	78.0 (39)
Risk Factors	
• Diabetes	42.0 (21)
• Hypertension	54.0 (27)
• Dyslipidemia	60.0 (30)
• Current Smoker	44.0 (22)
Previous of PCI	32.0 (16)
ACS as clinical presentation	56.0 (28)
STEMI	10.0 (5)
LVEF (≤ 50%)	21.6 (8/37)
No or 1- other vessel disease >50%	60% (24 & 36) (12 & 18)

Unless specified otherwise, values are % and (n) of patients

Lesion Characteristics (n=50)

Target Vessel

- First Diagonal 40.8 (20)
- First Marginal 22.4 (11)
- Second diagonal 12.2 (6)
- Second Marginal 8.3 (4)

Angio Lesion calcification (*moderate*) 22.5 (11)

Vessel tortuosity (≥ 2 bends 90°) 8.5 (4)

Lesion Angulation ($>45^\circ$) 21.3 (10)

Presence of thrombus 0 (0)

Pre-TIMI flow grade (0-I) 10.2 (5)

Unless specified otherwise, values are % and (n) of patients



Procedural Characteristics (n=50)

• Radial approach	84.0 (39)
• Pts with stent implanted out the TL	38.7 (19)
• <u>Cutting Balloon (CB) Predilatation</u>	59.2 (29)
• <u>Pre-dilatation (NC plain balloon)</u>	42.8 (21)
✓ Diameter, mm (mean±SD)	2.24 ± 0.31
✓ Length, mm (mean±SD)	10.6 ± 2.4
✓ Main balloon pressure, mmHg (mean±SD)	11.2 ± 4.5
• <u>Dior Balloon</u>	
✓ Diameter, mm (mean±SD)	2.4 ± 0.3
✓ Length, mm (mean±SD)	18.8 ± 5.3
✓ Main balloon pressure, mmHg, (mean±SD)	11.5 ± 3.4
✓ Inflation time (sec). (mean ± SD)	70.0 ± 24.6
• <u>Post-dilatation with NC balloon</u>	2.04 (1)



Results (n=50)

Immediate Results

Angiographic Success **86.0% (43)**

Bail-out BMS implantation **14.0% (7)**

Reason:

- **Acute recoil (residual stenosis $\geq 50\%$) or ($> 40 - < 50\%$ & FFR positive)** **5***
 - **Coronary Dissection > type B (Ellis Classif.)** **2**
-

**Post-dilatation with NC Balloon in only 1 patient.*

Unless specified otherwise, values are % and (n) of patients



Results (n=50)

***Mean follow-up of 10.3 ± 3.2 months**

	1_months FU	10_months FU*
Cardiac Death	0	0
MI	0	0
TLR	0	12.0 (6)
MACE	0	12.0 (6)
Treated segment occlusion/Thrombosis*	0	1.0 (1)*

STEMI patient. Effort angina in the FU. Angio control occlusion. Remained in medical treatment

Non-hierarchical adverse events

Unless specified otherwise, values are % and (n) of patients



Results (n=50)

All the adverse events occurred between 1 and 6 months FU

	1_months FU (n=50/50) 98%	6_months FU (n=44/50) 88%	12-14 months FU (n=30/50) 60%
Cardiac Death	0	0	0
MI	0	0	0
TLR	0	13.6 (6)	0
MACE	0	13.6 (6)	0
Treated segment occlusion/Thrombosis*	0	2.27 (1)*	0

STEMI patient. Effort angina in the FU. Angio control occlusion. Remained in medical treatment

Non-hierarchical adverse events

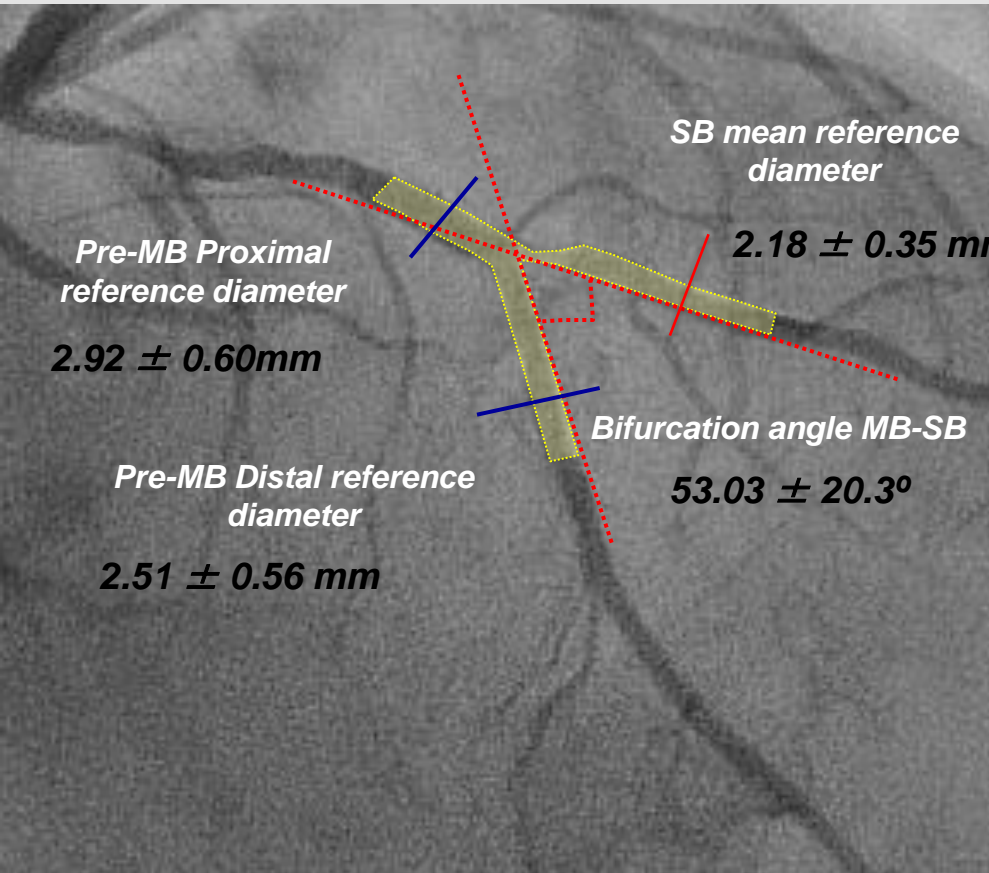
Unless specified otherwise, values are % and (n) of patients

Baseline QCA: Mean reference diameters and &

Small SB: 2.2mm

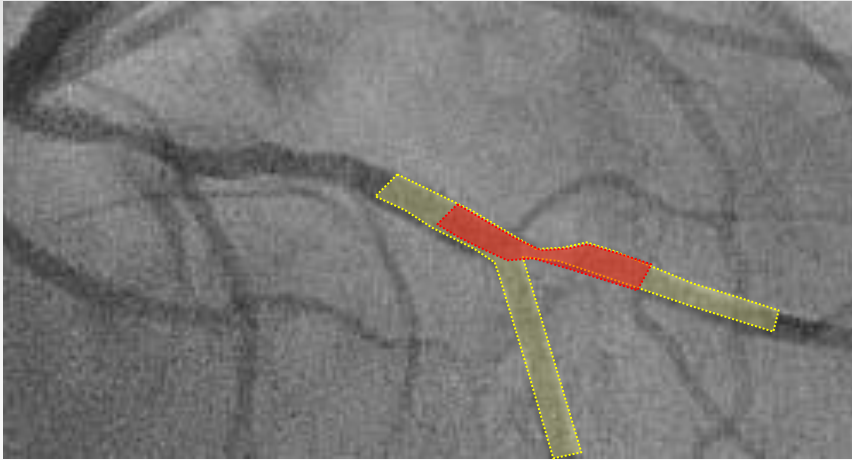
Mean Miss-Match=0.75mm

Y angle < 70°

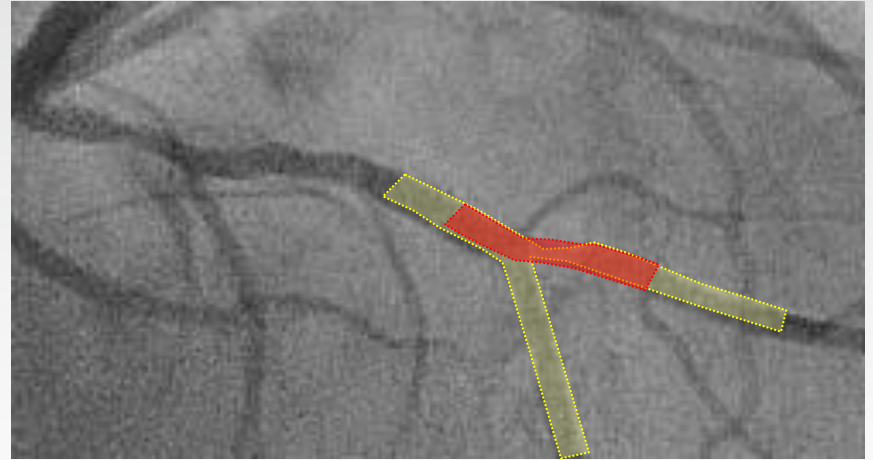


QCA: post-Angioplasty

Pre-PCI



Post-PCI

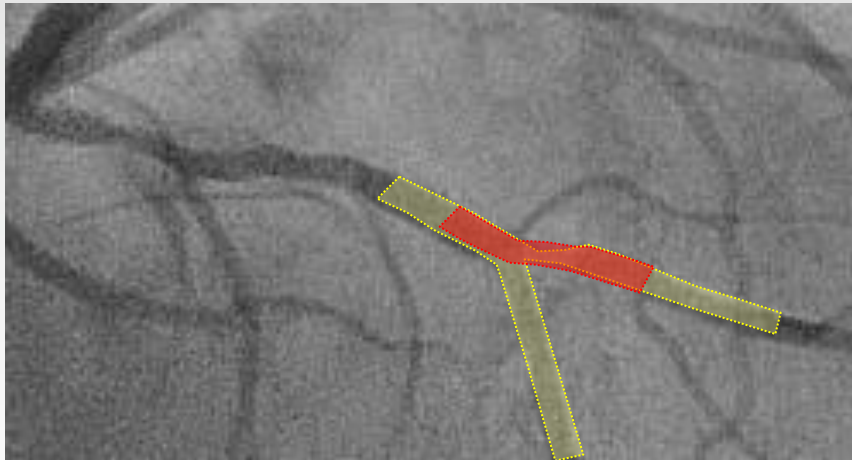


- *Pre-SB reference vessel diameter: $2.18 \pm 0.35\text{mm}$*
- *Pre-minimum Luminal diameter: $0.56 \pm 0.34\text{mm}$*
- *Pre-lesion Length: $9.18 \pm 5.84\text{mm}$*
- *Pre-stenosis (%): $78.1 \pm 10.9\%$*
- *Post-SB reference vessel diameter: $2.18 \pm 0.32\text{mm}$*
- *Post-minimum Luminal diameter: $1.51 \pm 0.39\text{mm}$*
- *Post-lesion Length: $9.29 \pm 4.31\text{mm}$*
- *Post-stenosis (%): $29.9 \pm 12.5\%$*

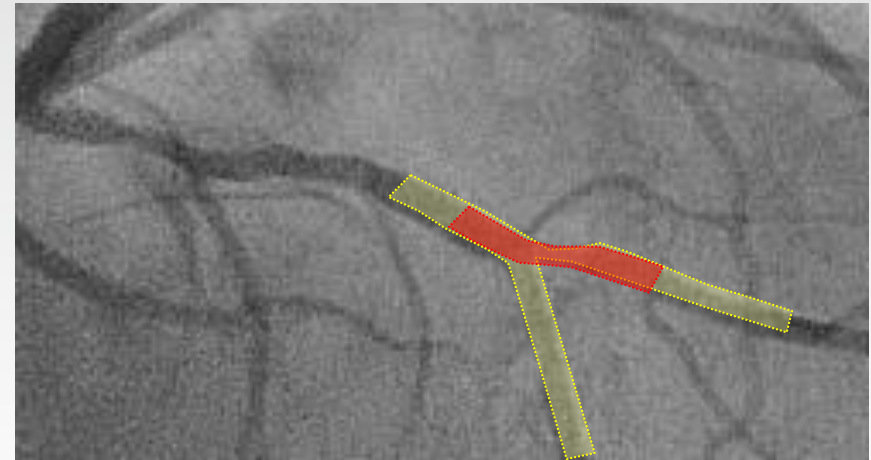
Acute Gain: $0.95 \pm 0.15\text{mm}$

7.2 ± 1.1 months Angio FU (70.5% completed 31/44)

Post-PCI



7 mo Angio FU



- *Pre-SB reference vessel diameter: 2.18 ± 0.32mm*
 - **Post-minimum Luminal diameter: 1.51 ± 0.39mm**
 - *Pre-lesion Length: 9.29 ± 4.31mm*
 - **Post-stenosis (%): 29.9 ± 12.5mm**
- *Pre-SB reference vessel diameter: 2.18 ± 0.32mm*
 - **6mo-minimum Luminal diameter: 1.20 ± 0.56mm**
 - *Pre-lesion Length: 9.29 ± 4.31mm*
 - **6mo-stenosis (%): 46.3 ± 25.9mm**

Late Luminal Loss: 0.31 ± 0.15 mm

Binary restenosis 20.0% (6/31)

All were symptomatic Restenosis

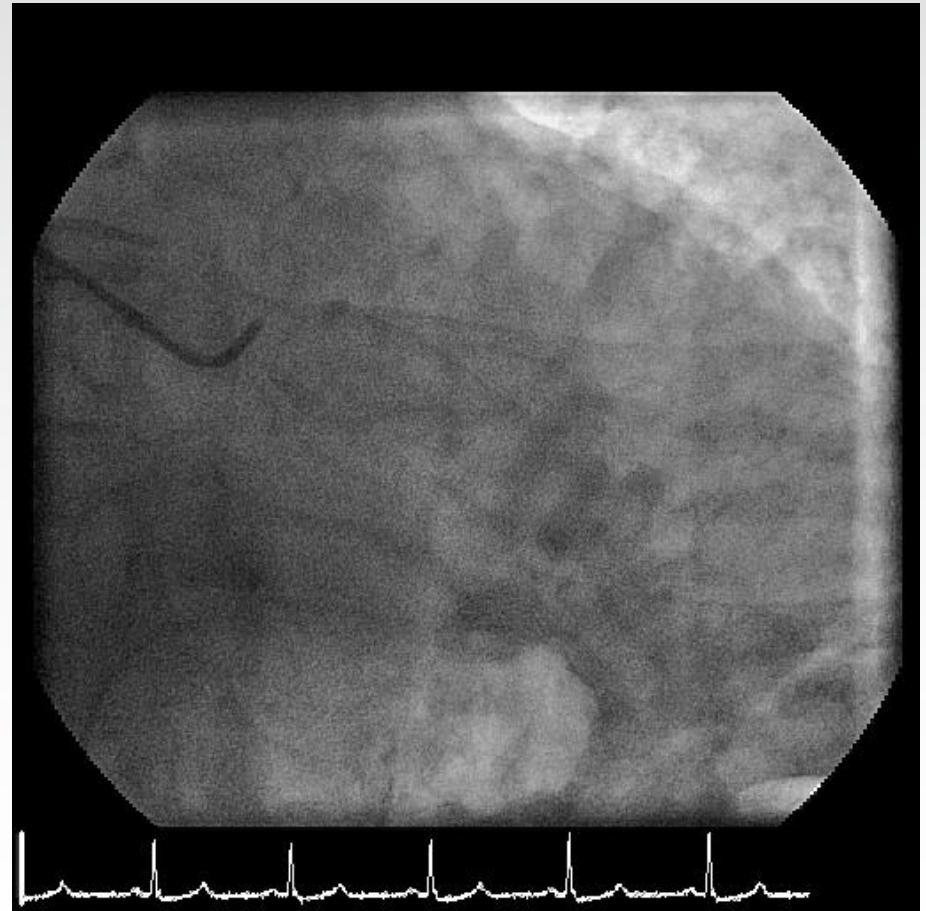
Impact of Cutting Balloon pre-dilatation



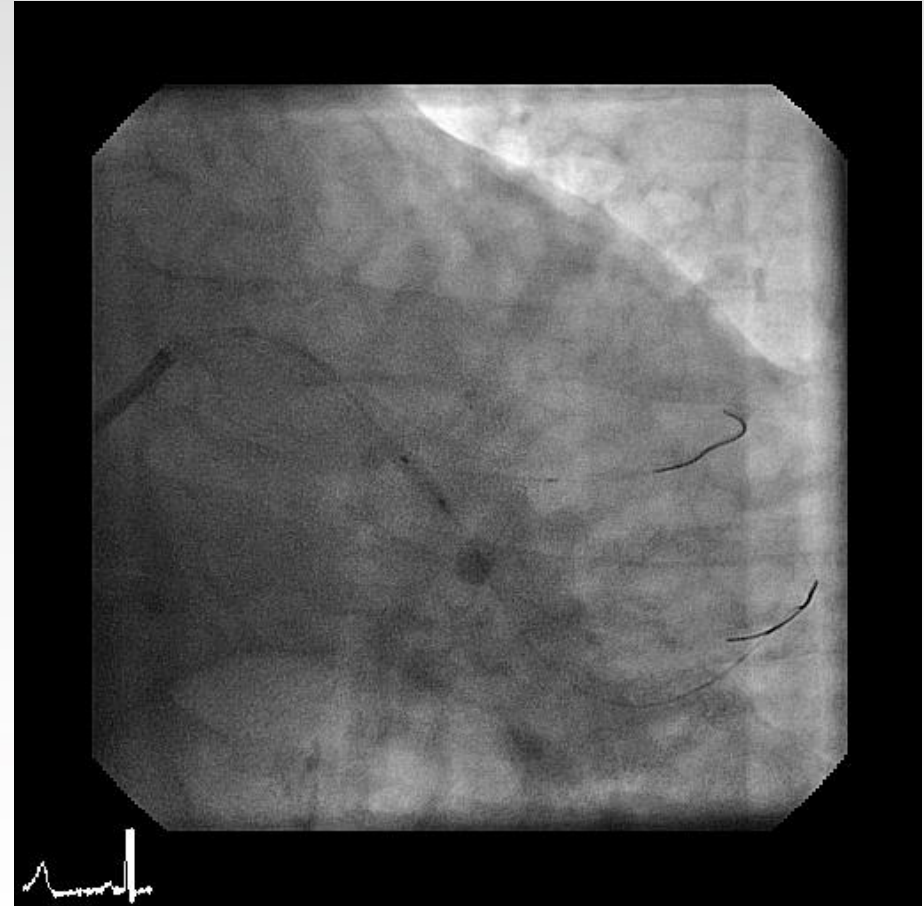
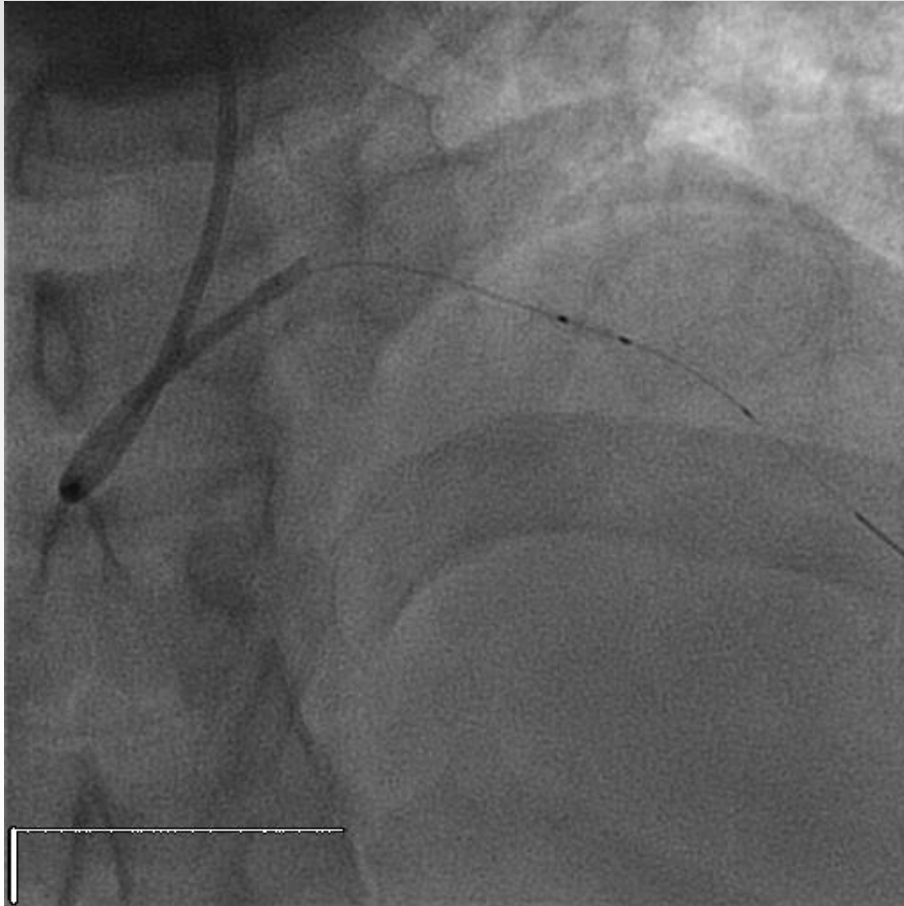
- **Flextome pre-dilatation: 59.2%**

Pre-dilatation with	CB	NC or C Balloon
Binary Restenosis (6)	2	4
Occlusion (1)	0	1

Interventional Procedure

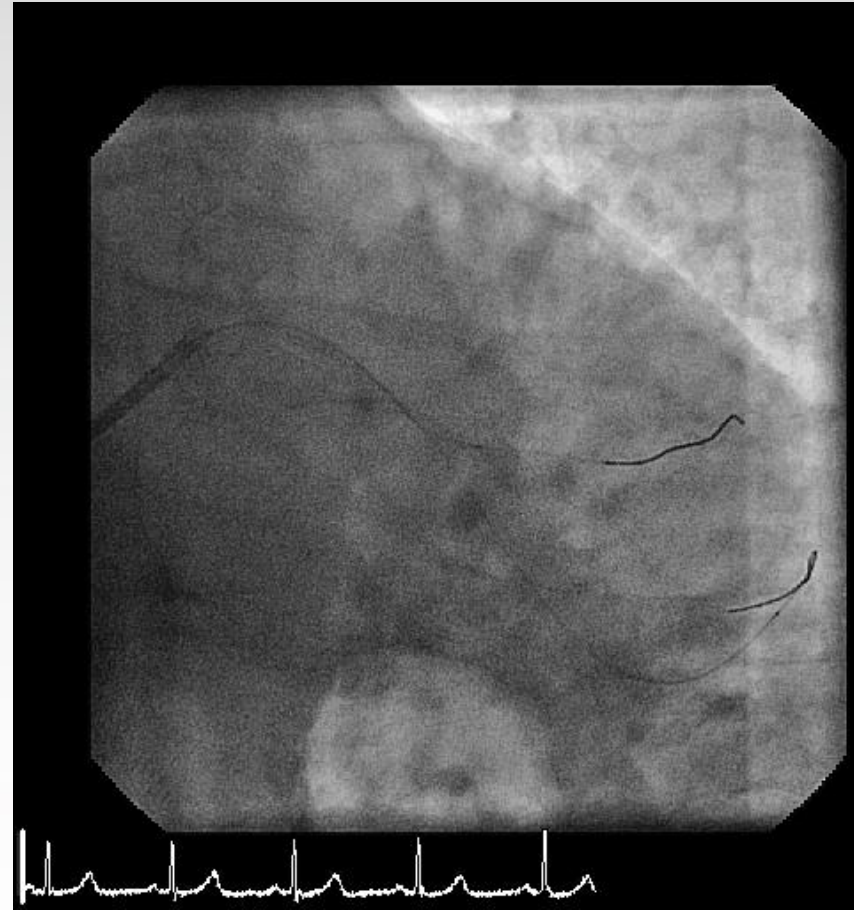
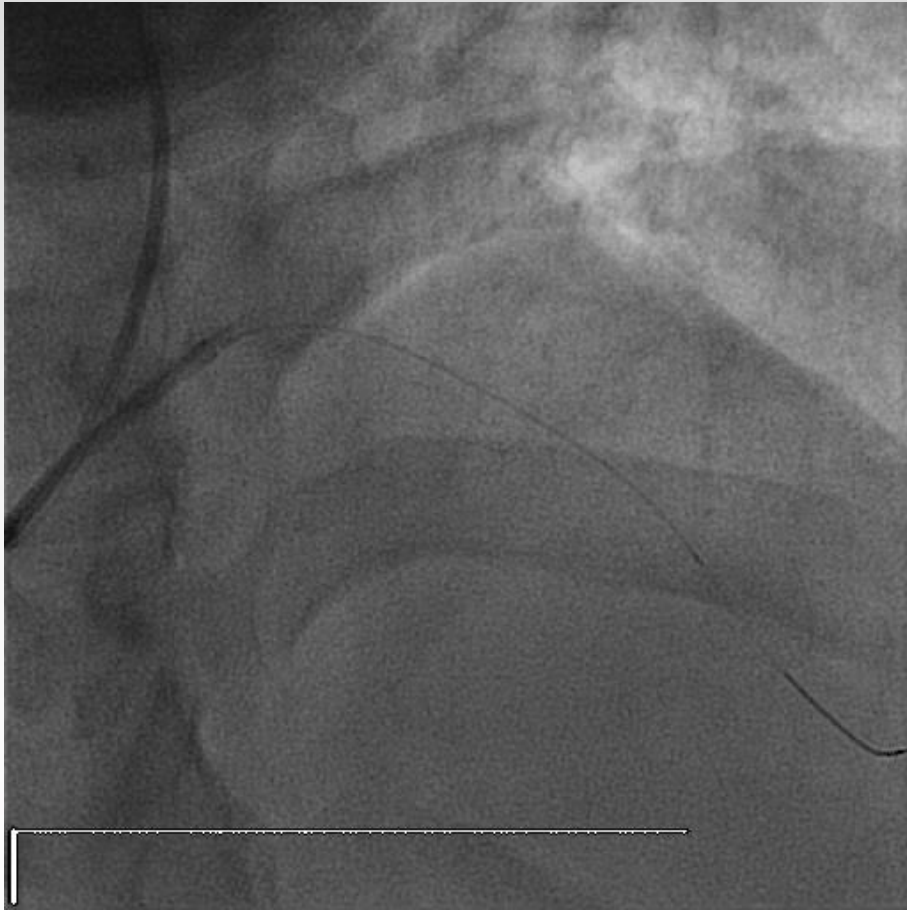


Interventional Procedure



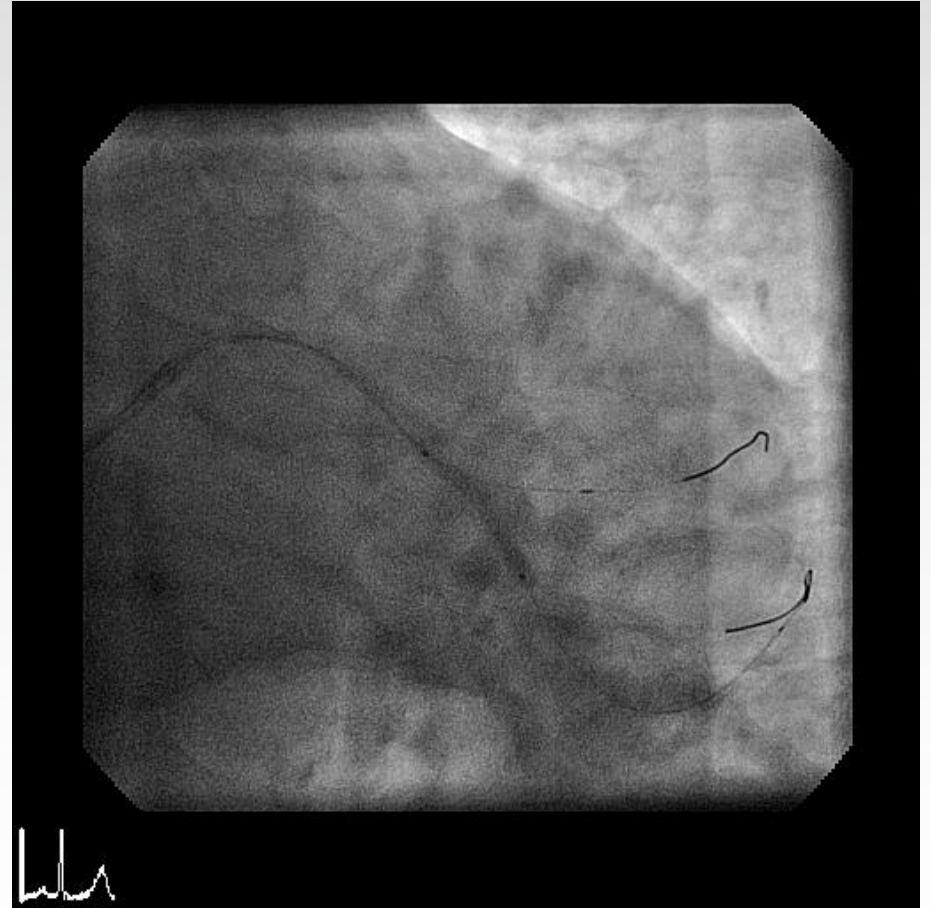
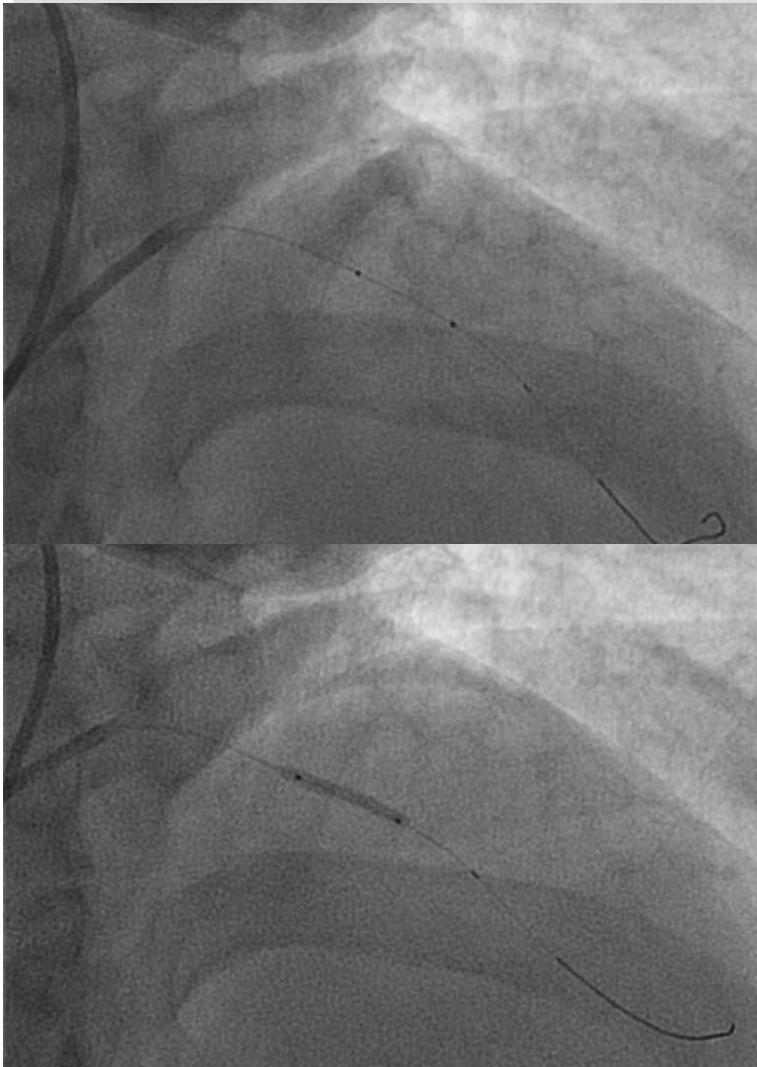
Cutting Balloon Pre-dilatation

Interventional Procedure



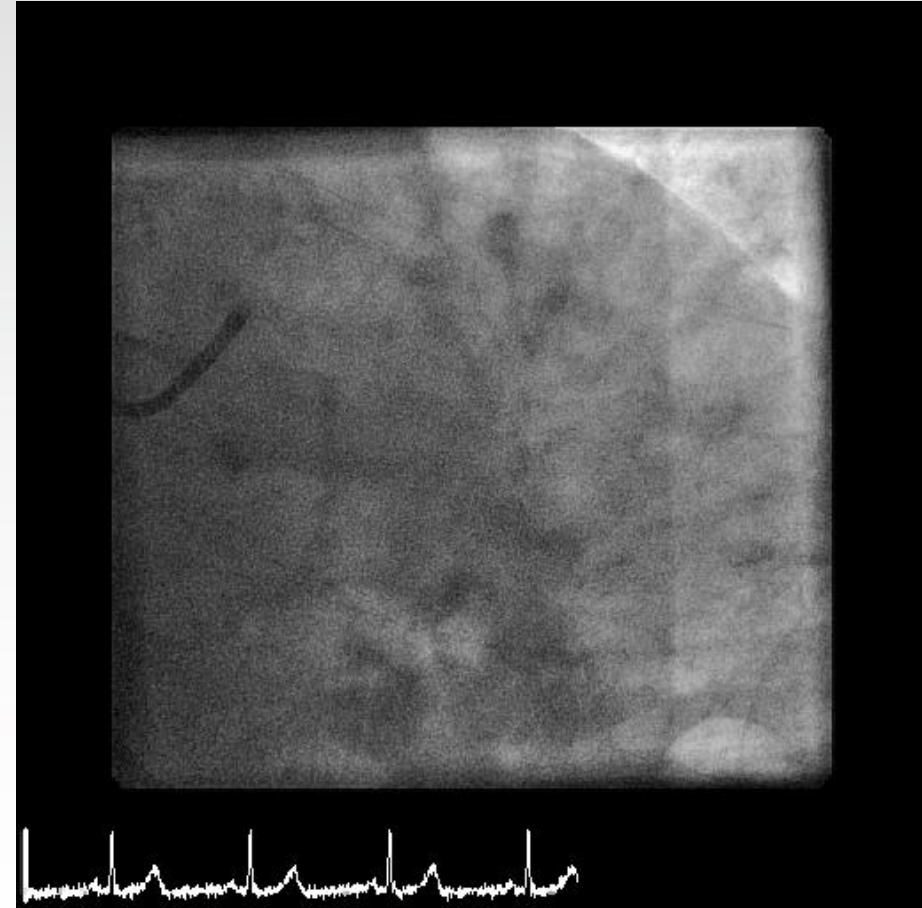
Results

Interventional Procedure



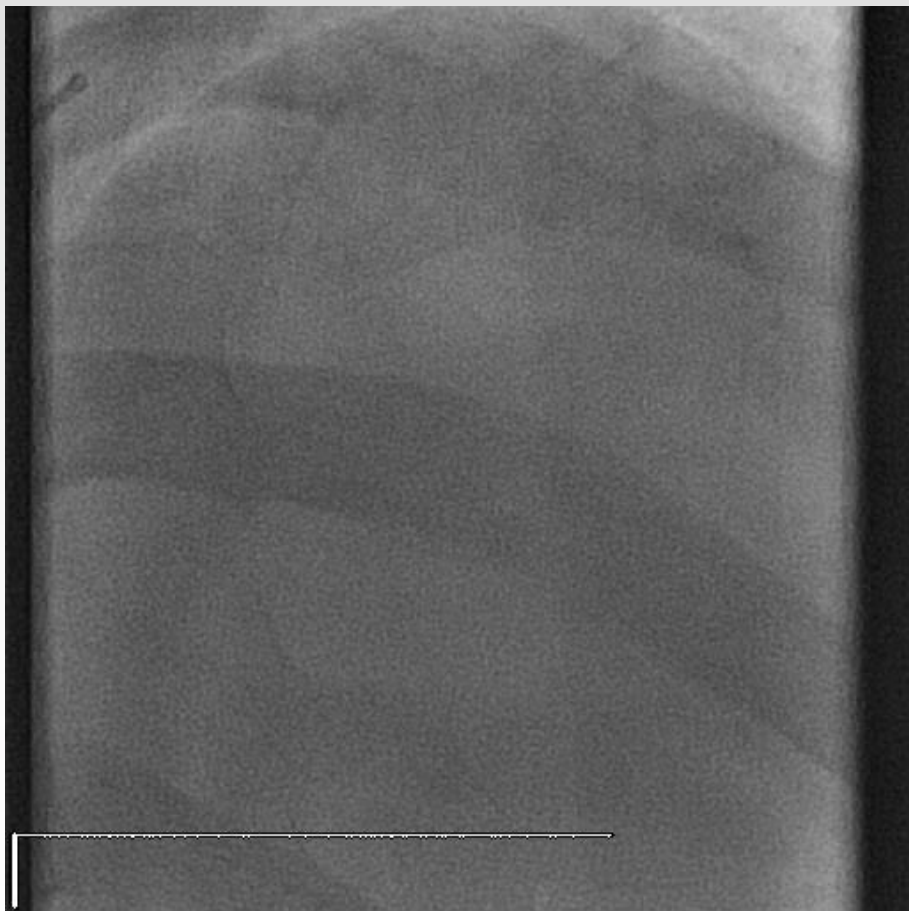
Dior II

Interventional Procedure



Immediate results

Interventional Procedure



12 months angio FU



8 monthsAngio FU

Conclusions

- **Fisrt prospective registry assessing 001 bifurcated lesions placed in small vessels (2.23mm)**
- **By protocol pre-procedural symptoms were attributed to the target SB lesion**
- **This is a rare type of coronary lesion (2.8 years) that was observed in a relative young population (62 yo) with a high rate of DMII (42%)**

Conclusions

- **Y-angle (53°) was the most frequent and lesions were placed in “diferent” small vessel in which acute recoil seems to be the most important limiting factor for DEB angioplasty**
- **Importance of plaque preparation with cutting balloon pre-dilatation needs to be determined**

Conclusions

- **Treatment of 001 bifurcated lesions with second generation of DEB-DIOR**
 - **Is safe (no cardiac death, no MI, no *classical* ST)**
 - **May facilitate PCI of ostial bifurcation lesions and may help to avoid complex stenting procedures**
 - **It is associated with a relatively low rate of TLR at 10 mo**
- **It seems that the adverse events occurred between 1 and 6 months from the index procedure**



BACK UP SLIDES



PCI of Small vessels

	Device	Ref Diam	TLR	Restenosis	Late loss
ISAR SMART (Castrati A, et al, Circulation 2000)	POBA (200)	2.37±0.27	16.5*	35.7	0.72±0.71
	BMS (204)	2.41±0.25	20.1*	31.4	1.04±0.73
ISAR-SMART 3 (Mehilli J, Eur Heart J 2006)	PES (180)	2.40±0.38	14.7**	19.0	0.56±0.59
	SES (180)	2.44±0.34	6.6**	11.4	0.25±0.55
PEDCAD I (Unverdorben M, et al Clin Res Cardiol 2010)	DEB (SeQuent Please) (118)	2.35±0.19	4.9**	NA	0.28±0.53
Bello Trial (Latib et al, JACC 2012)	DEB (In-Pact Falcon) (94)	2.15±0.27	4.4*	10.0	0.08±0.38
	PES (97)	2.26±0.24	7.6*	12.6	0.29±0.44

001 Bifurcated lesion

- **Prevalence:**
 - No specific data assessing this kind of coronary lesion
 - Publications regarding analysis of stenting bifurcation coronary lesions (SB >2.25mm): 1-5% of bifurcated lesions^{1,2}.

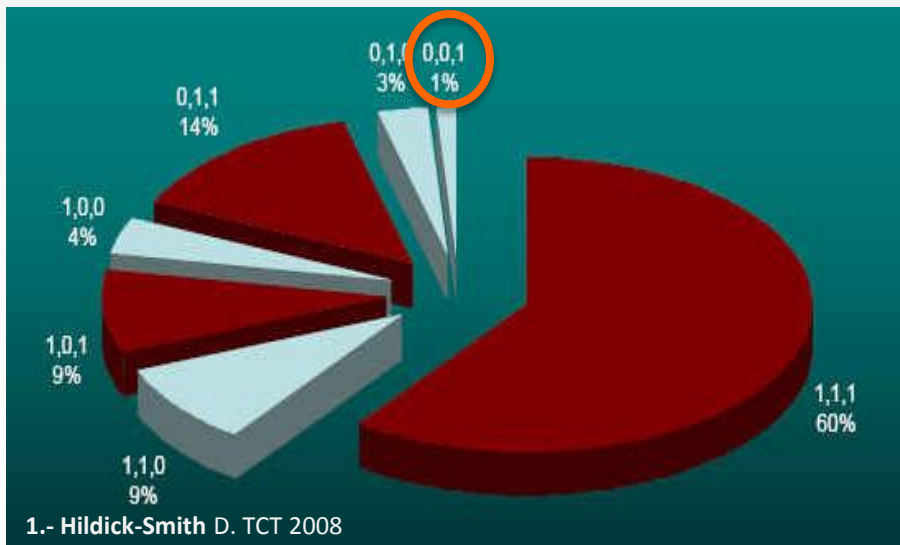


Table 2. Lesion Characteristics (n = 477)

Lesion Location	n (%)
LAD/diagonal	315 (66)
Circumflex/obtuse marginal	100 (21)
PDA/PLA	38 (8)
Other	24 (5)
Restenosis	25 (5.2)
Lesion type	
Type 1	348 (73)
Type 2	23 (4.8)
Type 3	17 (3.6)
Type 4	41 (8.6)
Type 4a	24 (5.1)
Type 4b	24 (5.1)

2.- Routledge H, et al. J Am Coll Cardiol Intv 2008;1:358-65