DCB in the treatment of bifurcations

Scenarios for future studies

Juan Luis Gutiérrez-Chico

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Considerations for DCB studies

- No class effect
- Adequate use of DCB
  - Aggressive plaque preparation
  - Short transit time < 3'
  - Enough transfer time >60''
    - Unsuitable for LM
- DCB must be the last device in the intervention
  - No OCT, no IVUS post procedure

Paclitaxel-coated balloon in combination with bare metal stent for treatment of *de novo* coronary lesions: an optical coherence tomography first-in-human randomised trial, balloon first vs. stent first

Juan Luis Gutiérrez-Chico[1], MD, PhD, FESC; Robert Jan van Geuns [1], MD, PhD, FESC; Karel T. Koch[2], MD, PhD; Jacques J. Koolen[3], MD, PhD, FSCAI; Henricus Duckers[1], MD, PhD, FESC; Evelyn Regar[1], MD, PhD, FESC; Patrick W. Serruys[1]*, MD, PhD, FESC, FACC

	DCB first	BMS first	*p*-value	All
Lesion length (mm)	10.7±4.9	11.2±5.1	0.960	10.9±4.9
RVD (mm)	2.81±0.45	2.41±0.37	0.026	2.61±0.45
MLD (mm)	1.07±0.28	0.91±0.23	0.204	0.99±0.26
% diameter stenosis	61.8±9.4	61.9±8.1	0.920	61.8±8.6
In-DCB				
Acute gain (mm)	1.42±0.45	1.09±0.42	0.087	1.26±0.46
Late loss (mm)	0.53±0.52	0.45±0.57	0.833	0.49±0.54
Binary restenosis	1 (9.1%)	2 (16.7%)	1.000*	3 (13.0%)
In-segment				
Acute gain (mm)	1.20±0.40	0.90±0.41	0.098	1.06±0.43
Late loss (mm)	0.52±0.65	0.31±0.41	0.651	0.41±0.54
Binary restenosis	3 (27.3%)	2 (16.7%)	0.640*	5 (21.7%)

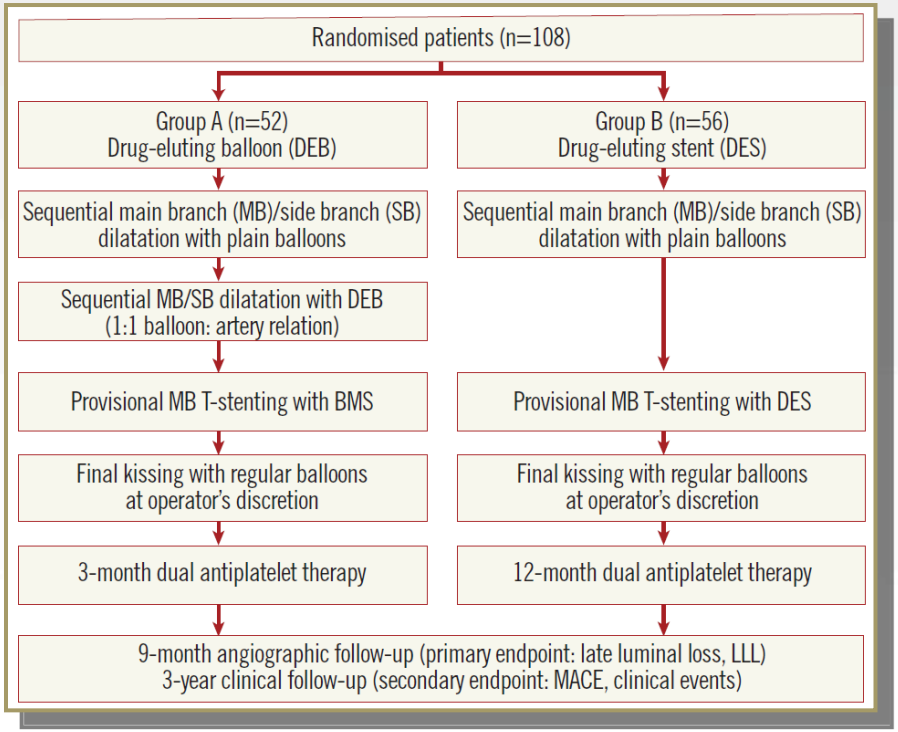
Considerations for DCB studies

- **DCB must be the last device in the intervention**
  - **No OCT, no IVUS post procedure**
  - **No stent**

A prospective randomised study of the paclitaxel-coated balloon catheter in bifurcated coronary lesions (BABILON trial): 24-month clinical and angiographic results

José Ramón López Mínguez[1]*, MD, PhD; Juan Manuel Nogales Asensio[1], MD, PhD; Luis Javier Doncel Vecino[1], MD; Jorge Sandoval[2], MD; Sebastián Romany[3], MD; Pedro Martínez Romero[4], MD, José Antonio Fernández Díaz[5], MD; Javier Fernández Portales[3], MD, PhD; Reyes González Fernández[1], MD, PhD; Ginés Martínez Cáceres[1], MD; Antonio Merchán Herrera[1], MD, PhD; Fernando Alfonso Manterola[2], MD, PhD; on behalf of the BABILON Investigators

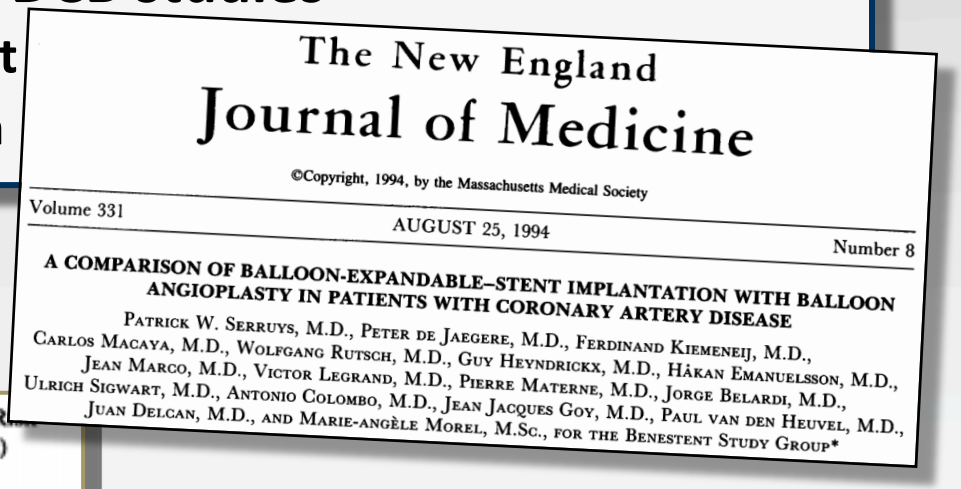
EuroIntervention 2014;10:50-57



	All patients n=108	pDEB group n=52	DES group n=56	*p*-value
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
Non-fatal MI	4 (3.7%)	2 (3.8%)	2 (3.6%)	1
Stroke	1 (0.9%)	1 (1.9%)	0 (0.0%)	0.477
CABG	2 (1.9%)	1 (1.9%)	1 (1.8%)	1
New PCI	17 (15.7%)	11 (21.2%)	6 (10.7%)	0.125
TVR	11 (10.2%)	9 (17.3%)	2 (3.6%)	0.018
TLR	10 (9.3%)	8 (15.4%)	2 (3.6%)	0.045
Other vessel PCI	9 (8.3%)	5 (9.6%)	4 (7.1%)	0.734
Follow-up MACE	13 (12%)	9 (17.3%)	4 (7.1%)	0.105
In-hospital or follow-up MACE	16 (14.8%)	9 (17.3%)	7 (12.5%)	0.456
Restenosis (global)	12 (11.1%)	9 (17.3%)	3 (5.4%)	0.048
MB restenosis	8 (7.4%)	7 (13.5%)	1 (1.8%)	0.027
SB restenosis	5 (4.6%)	3 (5.8%)	2 (3.6%)	0.670
MB stent occlusion	2 (1.9%)	1 (1.9%)	1 (1.8%)	0.958

Considerations for DCB studies

- **LLL is not a good endpoint for DCB studies**
  - **Good to compare stent vs. stent**
  - **Misleading for stent vs. balloon**



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A COMPARISON OF BALLOON-EXPANDABLE–STENT IMPLANTATION WITH BALLOON ANGIOPLASTY IN PATIENTS WITH CORONARY ARTERY DISEASE

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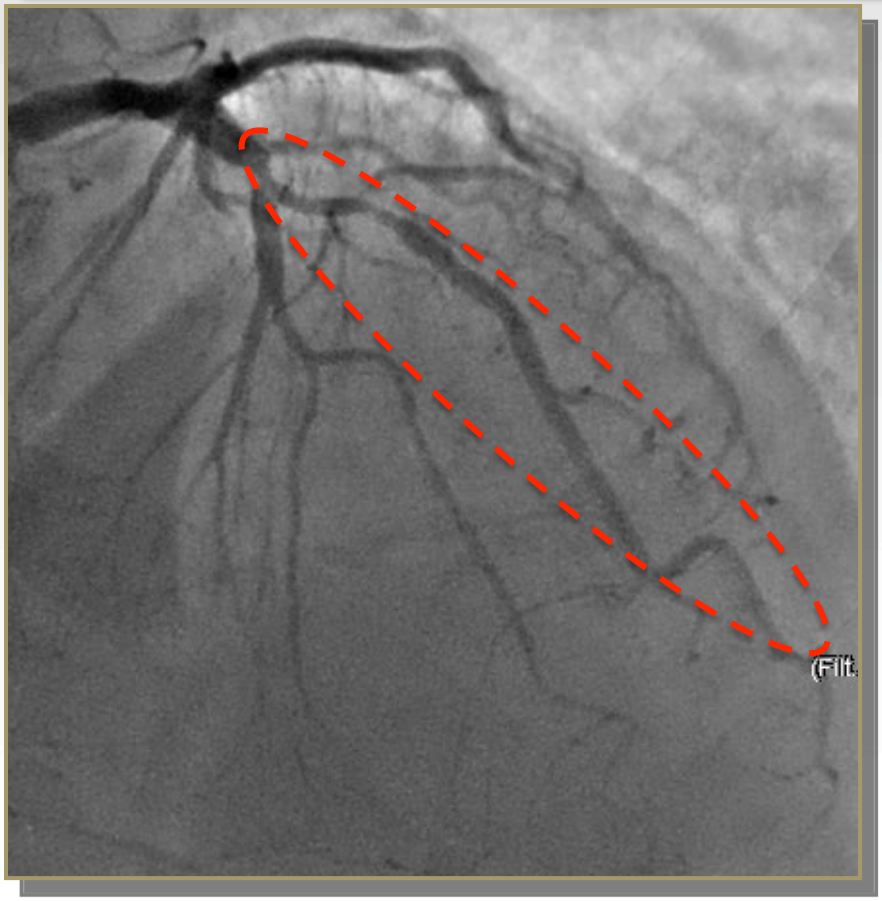
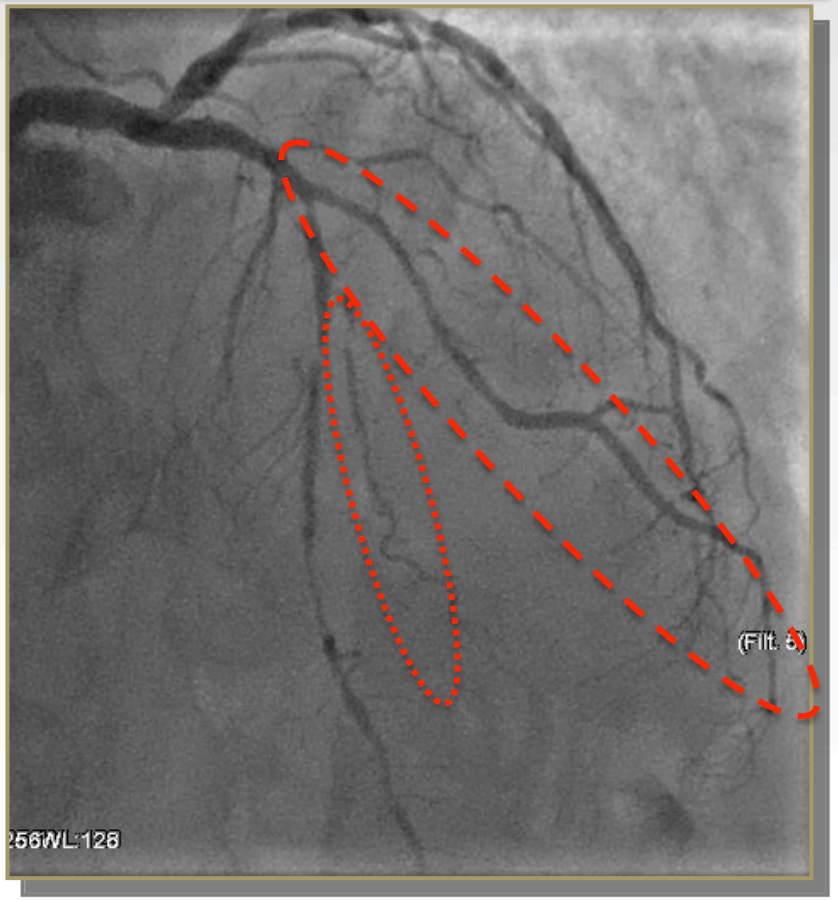
EVENT	ANGIOPLASTY (N = 257)	STENT (N = 259)	RELATIVE R… (95% CI)
Reference diameter (mm)			
Before	3.01±0.46	2.99±0.45	NS
After	3.09±0.44	3.16±0.43	0.045
Follow-up	3.05±0.49	2.96±0.48	0.04
Minimal luminal diameter (mm)			
Before	1.08±0.31	1.07±0.33	NS
After	2.05±0.33	2.48±0.39	<0.001
Follow-up	1.73±0.55	1.82±0.64	0.09‡
Stenosis (%)			
Before	64±10	64±10	NS
After	33±8	22±8	<0.001
Follow-up	43±16	38±18	0.003
Restenosis rate (%)	32	22	0.02
Gain (mm)	0.97±0.39	1.40±0.44	<0.001
Loss (mm)	0.32±0.47	0.65±0.57	<0.001
Net gain (mm)	0.65±0.59	0.75±0.66	0.09

Considerations for DCB studies

- **For bifurcation studies:**
  - **Choose a relevant SB**





Scenarios for future DCB studies

4 possible scenarios
4 possible designs

1st scenario: NORDIC-III-like

Indulis Kumsars

Jens Flensted Lassen

Randomized Comparison of Final Kissing Balloon Dilatation Versus No Final Kissing Balloon Dilatation in Patients With Coronary Bifurcation Lesions Treated With Main Vessel Stenting

The Nordic-Baltic Bifurcation Study III

Matti Niemelä, MD; Kari Kervinen, MD; Andrejs Erglis, MD; Niels R. Holm, MD; Michael Maeng, MD; Evald H. Christiansen, MD; Indulis Kumsars, MD; Sanda Jegere, MD; Andis Dombrovskis, MD; Pål Gunnes, MD; Sindre Stavnes, MD; Terje K. Steigen, MD; Thor Trovik, MD; [illegible] ID; Hannu Romppanen, MD; [illegible] sen, MD; Lars Åberge, MD; [illegible] inen, MD; Mikko Pietilä, MD; [illegible] s Aarøe, MD; Jan S. Jensen, MD; [illegible] MD; Heikki Miettinen, MD; [illegible]-Baltic PCI Study Group

True bifurcations (Medina 111,101, 011): 50.1%

- n=477
- FKB vs. no FKB
- Cypher SES
- Clinical FU 6m
  - No difference
- SB binary restenosis
  - In true bifurcations, better FKB
    - FKB 7.6%
    - No FKB 20.0%

Table 5. True Versus Nontrue Bifurcation Subgroup Comparison: 8-Month Angiographic Follow-Up

	True Bifurcation Subgroup			Nontrue Bifurcation Subgroup		
Variable	FKBD (n=92)	No FKBD (n=80)	*P*	FKBD (n=72)	No FKBD (n=82)	*P*
In-segment MV						
DS, %	22±15	22±15	0.85	22±14	21±12	0.90
≥50% DS, n (%)	3 (3.8)	2 (2.2)	0.67	3 (4.2)	1 (1.2)	0.34
Ostial 5 mm of the SB						
MLD, mm	1.71±0.42	1.50±0.53	0.005	1.79±0.54	1.77±0.61	0.79
DS, %	25±14	32±21	0.009	23±15	27±19	0.21
≥50% DS, n (%)	7 (7.6)	16 (20)	0.024	6 (8.3)	9 (11)	0.79

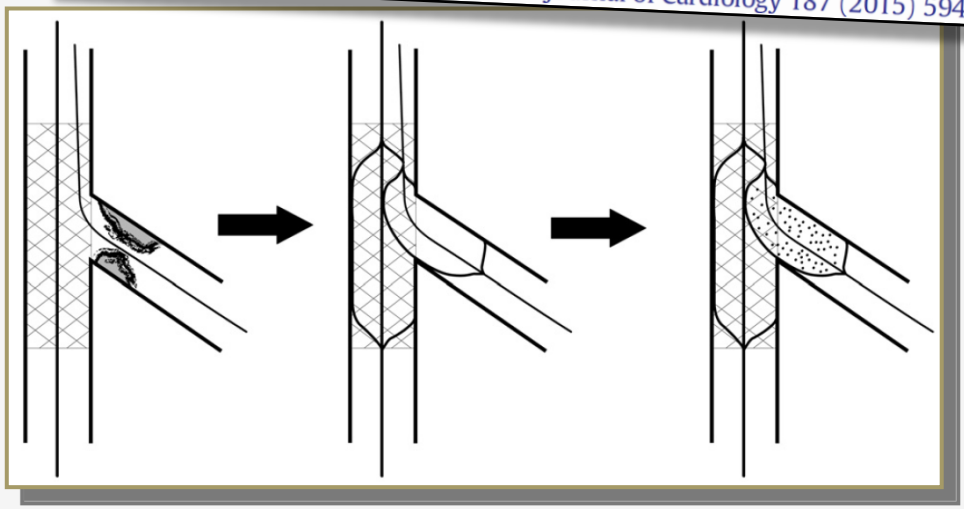
Circulation. 2011;123:79-86

1st scenario: NORDIC-III-like

- **Why this angio-clinical discrepancy?**
  - **Irrelevant SB?**
- **What about FKB with DCB?**
  - **Already done**
    - **N=58**
    - **Pantera Lux (Biotronik)**
    - **Restenosis 10%**
      - **MV 4%**
      - **SB 6%**
    - **LLL**
      - **MV 0.21 mm**
      - **SB 0.09 mm**

Six month angiographic result of supplementary paclitaxel-eluting balloon deployment to treat side branch ostium narrowing (SARPEDON)

Man-Hong Jim [a,*], Michael Kang-yin Lee [b], Raymond Chi-yan Fung [a], Alan Ka-Chun Chan [b], Kam-Tim Chan [b], Kai-Hang Yiu [c] International Journal of Cardiology 187 (2015) 594–597

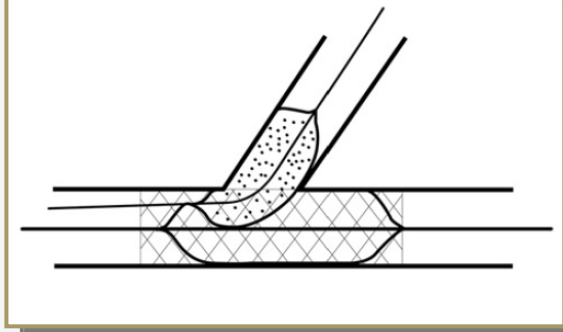


	In-hospital (n = 58)	One-year (n = 58)
Any death (%)	0	2 (3.4)
Nonfatal myocardial infarction (%)	6 (10.3)	6 (10.3)
Target vessel revascularization (%)	0	3 (5.2)
Major adverse cardiac event (%)	6 (10.3)	11 (19.0)

Potentially better than FKB

1st scenario: NORDIC-III-like

- **Hypothesis:**
  - In true bifurcations with meaningful SB
  - DCB-FKB will be better than PS without FKB
- **Assumption**
  - At least as good as FKB in NORDIC
- **Primary endpoint: SB restenosis / FFR≤0.80 in SB at 8m?**
  - No FKB: 20%
  - DCB-FKB: 8%
  - Sample size
    - α = 0.05
    - β = 0.20
    - Fleiss´ correction
    - n= 147
    - Allocation 1:1 = 294
    - +10% loss at FU = 324



n = 324

Proportion (%) of events in: Group 0 = 20,00%
Group 1 = 8,00%
Minimum expected effect size: Difference= -12,0%
Alpha Risk = 5%; Beta Risk = 20% (Power= 80,00%)

	SAMPLE SIZE by group	
	Two-Sided Test	One-Sided Test
Normal*	131	103
Normal corrected	147	120
ArcoSinus	126	99

2nd scenario: BBC-ONE-like

David Hildick-Smith

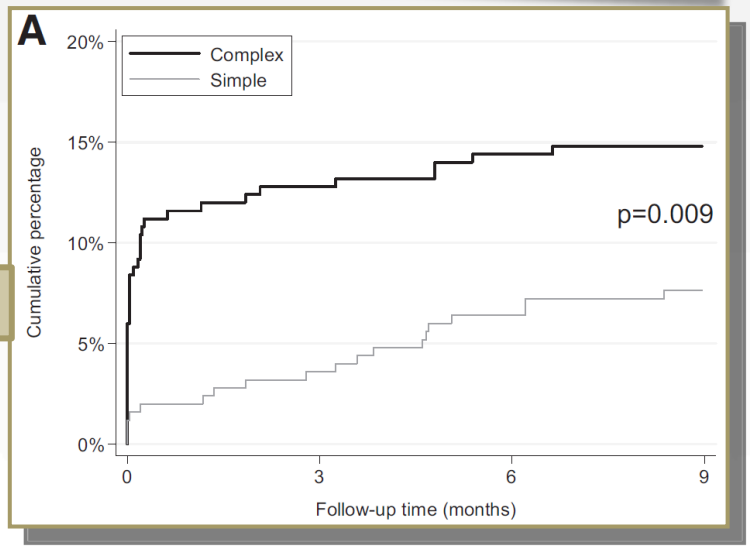
Randomized Trial of Simple Versus Complex Drug-Eluting Stenting for Bifurcation Lesions

The British Bifurcation Coronary Study: Old, New, and Evolving Strategies

David Hildick-Smith, MD, FRCP; Adam J. de Belder, MD, FRCP; Nina Cooter, MSc; Nicholas P. Curzen, PhD, FRCP; Tim C. Clayton, MSc; Keith G. Oldroyd, MD, FRCP; Lorraine Bennett, MSc; Steve Holmberg, MD, FRCP; James M. Cotton, MD, FRCP; Peter E. Glennon, PhD, FRCP; Martyn R. Thomas, MD, FRCP; Philip A. MacCarthy, PhD, FRCP; Andreas Baumbach, MD, FRCP; Niall T. Mulvihill, MD; Robert A. Henderson, DM, FRCP; Simon R. Redwood, MD; Ian R. Starkey, BSc, FRCP; Rodney H. Stables, DM, FRCP

- N =500
- Provisional vs. 2-stents
  - Provisional: FKB optional (31%)
  - Crush or culotte
- Taxus PES
- Primary endpoint: POCE
  - Death, MI, TVF at 9m
- Provisional better: 8.0% vs. 15.2%

True bifurcations: 82%



Circulation. 2010;121:1235-1243

2nd scenario: BBC-ONE-like

Impact of the Complexity of Bifurcation Lesions Treated With Drug-Eluting Stents

The DEFINITION Study (Definitions and impact of complEx biFurcation leslons on clinical outcomes after percutaNeous coronary IntervenTIOn using drug-eluting steNts)

Shao-Liang Chen, MD,* Imad Sheiban, MD,† Bo Xu, MBBS,‡ Nigel Jepson, MD,§ Chitprapai Paiboon, MD,‖ Jun-Jie Zhang, PhD,¶ Fei Ye, MD,¶ Teugh Sansoto, MD,# Tak W. Kwan, MD,** Michael Lee, MD,†† Ya-Ling Han, MD,‡‡ Shu-Zheng Lv, MD,§§ Shang-Yu Wen, MD,‖‖ Qi Zhang, MD,¶¶ Hai-Chang Wang, MD,## Tie-Ming Jiang, MD,*** Yan Wang, MD,††† Liang-Long Chen, MD,‡‡‡ Nai-Liang Tian, MD,* Feng Cao, MD,## Chun-Guang Qiu, MD,§§§ Yao-Jun Zhang, PhD,¶ Martin B. Leon, MD‖‖‖

- **Complex bifurcations**
  - **DK-crush better**
    - **In-hospital, less MACE**
    - **At 1y, less cardiac death**

MACE = Cardiac death, MI and TVR

Major 1: Distal LM bifurcation: SB-DS ≥70% and SB lesion length ≥10 mm
Major 2: Non-LM bifurcation: SB-DS ≥90% and SB lesion length ≥10 mm
Minor 1: Moderate to severe calcification
Minor 2: Multiple lesions
Minor 3: Bifurcation angle <45°
Minor 4: Main vessel RVD <2.5 mm
Minor 5: Thrombus-containing lesions
Minor 6: MV lesion length ≥25 mm
Major 1 + any 2 minor 1-6 = complex
Major 2 + any 2 minor 1-6 = complex

Shao-Liang Chen

	Complex Group (n = 1,108)			
	2-Stent (n = 537)	PS (n = 571)	Adjusted HR (95% CI)	p Value
Final kissing inflation	473 (88.1)	165 (28.9)	–	<0.001
Side branch stenting	537 (100.0)	103 (18.1)	–	<0.001
In-hospital				
Myocardial infarction	27 (5.0)	48 (8.4)	0.58 (0.35-0.94)	0.026
Cardiac death	3 (0.6)	6 (1.1)	0.53 (0.13-2.12)	0.368
Target lesion revascularization	0	0	–	NS
Target vessel revascularization	0	0	–	NS
Coronary artery bypass graft	0	0	–	NS
Major adverse cardiac events	27 (5.0)	48 (8.4)	0.58 (0.35-0.94)	0.026
Stent thrombosis	0	0	–	NS
At 1 year				
Myocardial infarction	30 (5.6)	48 (8.4)	0.64 (0.40-1.03)	0.067
Cardiac death	15 (2.8)	30 (5.3)	0.52 (0.28-0.97)	0.041
Target lesion revascularization	33 (6.1)	33 (5.8)	1.07 (0.65-1.75)	0.803
Target vessel revascularization	45 (8.4)	42 (7.4)	1.12 (0.74-1.18)	0.532
Coronary artery bypass graft	6 (1.1)	3 (0.5)	2.14 (0.52-8.58)	0.285
Major adverse cardiac events	81 (15.1)	105 (18.4)	0.79 (0.57-1.08)	0.138
Stent thrombosis	9 (1.7)	9 (1.6)	1.06 (0.42-1.69)	0.899
Definite and probable	6 (1.1)	6 (1.1)	1.06 (0.34-3.13)	0.917
Possible	3 (0.6)	3 (0.5)	1.06 (0.21-5.28)	0.942

2nd scenario: BBC-ONE-like

- **Hypothesis:**
  - In complex lesions (DEFINITION)
  - PS+DCB-FKB might be superior to 2-stents techniques
- **Assumptions**
  - PS+DCB-FKB: same POCE as in BBC ONE (8.0%)
    - In DEFINITION DOCE = 18.4% in complex lesions
  - 2-stents: same DOCE as in DEFINITION (15.1%)
- **Primary endpoint: DOCE at 12m**
  - Sample size
    - $\alpha = 0.05$
    - $\beta = 0.20$
    - Fleiss´ correction
    - n= 346
    - Allocation 1:1 = 692
    - +10% loss at FU = 761

n = 761

Proportion (%) of events in: Group 0 = 15,10%
Group 1 = 8,00%
Minimum expected effect size: Difference= -7,10%
Alpha Risk = 5%; Beta Risk = 20% (Power= 80,00%)

	SAMPLE SIZE by group	
	Two-Sided Test	One-Sided Test
Normal*	317	250
Normal corrected	346	278
ArcoSinus	311	245

3rd scenario: rePOT

Gérard Finet

- Pilot study
- Provisional vs. DCB-rePOT ?

Influence of platform design of six different drug-eluting stents in provisional coronary bifurcation stenting by rePOT sequence: a comparative bench analysis

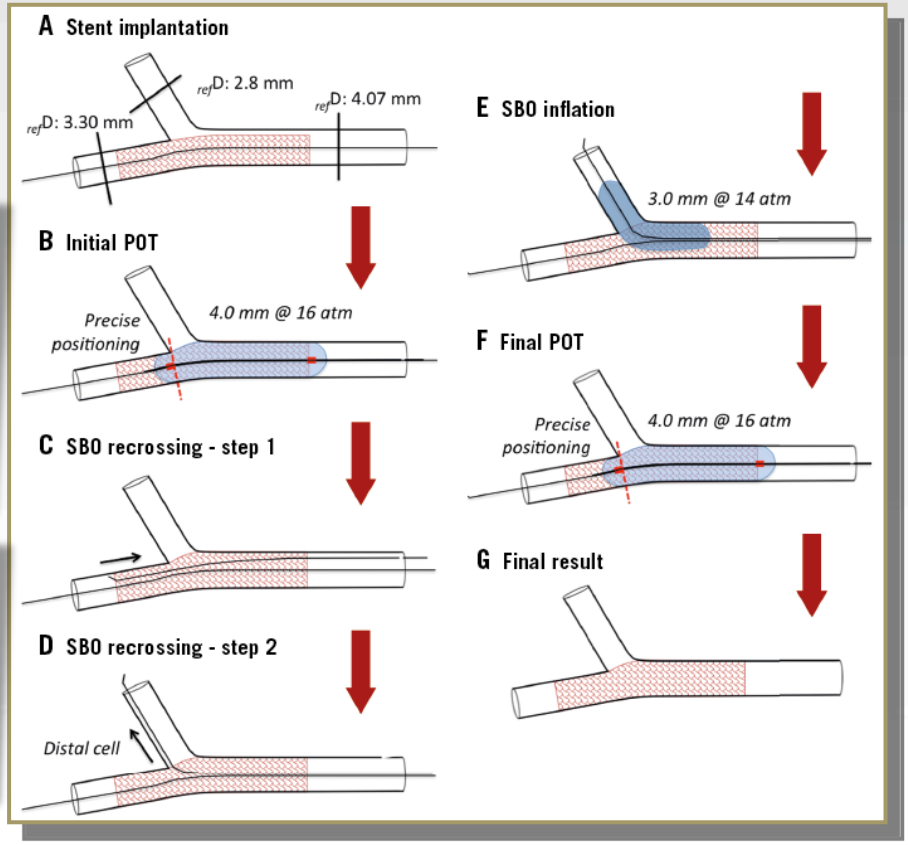
EuroIntervention 2017;13:e1092-e1095

François Derimay[1]*, MD; Geraud Souteyrand[2], MD; Pascal Motreff[2], MD, PhD; Gilles Rioufol[1], MD, PhD; Gerard Finet[1], MD, PhD

Benefit of a new provisional stenting strategy, the re-proximal optimisation technique: the rePOT clinical study

EuroIntervention 2018;14:e325-e332

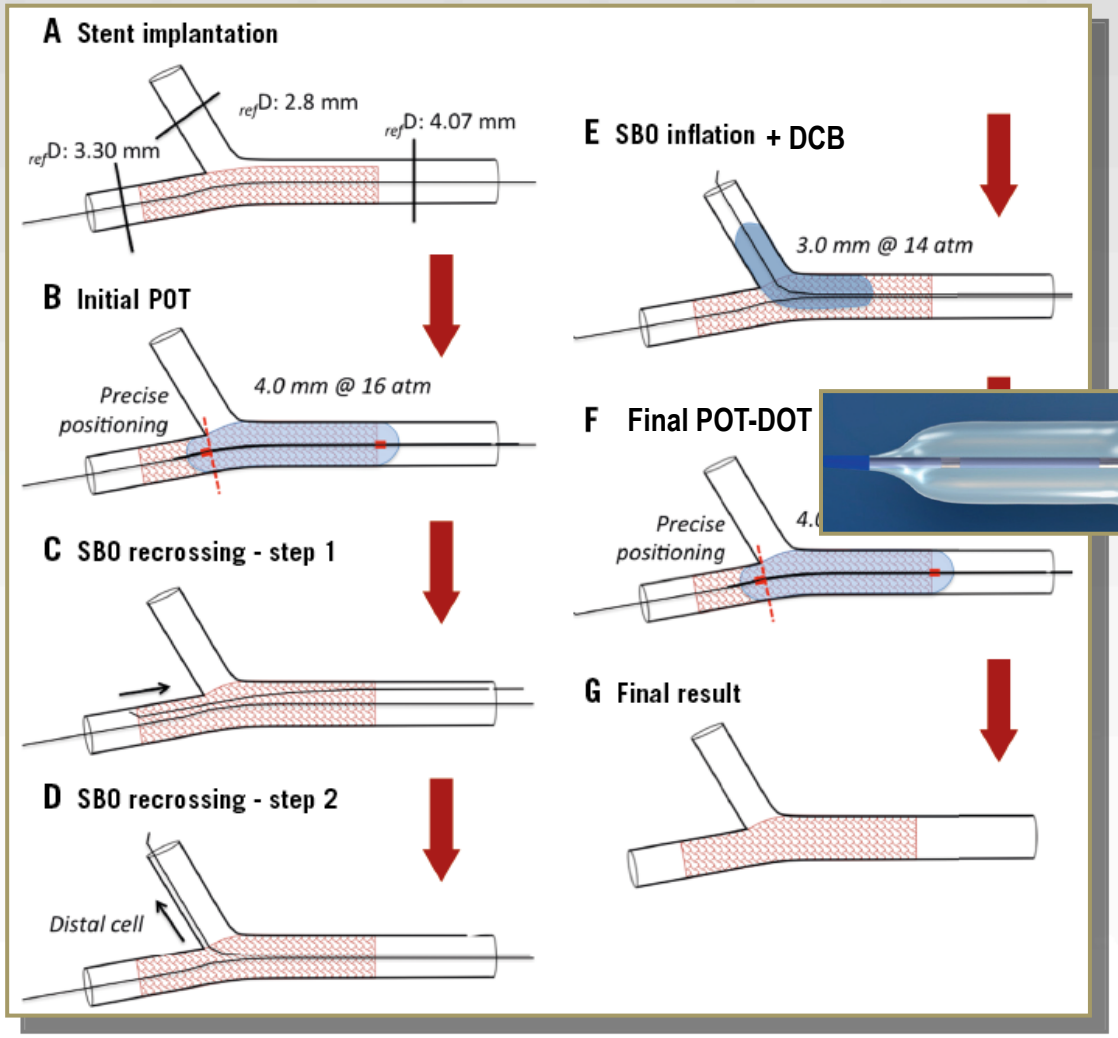
François Dérimay[1]*, MD; Gérard Finet[1], MD, PhD; Géraud Souteyrand[2], MD, PhD; Luc Maillard[3], MD, PhD; Adel Aminian[4], MD; Benoit Lattuca[5], MD; Guillaume Cayla[5], MD, PhD; Guillaume Cellier[1], MD; Pascal Motreff[2], MD, PhD; Gilles Rioufol[1], MD, PhD

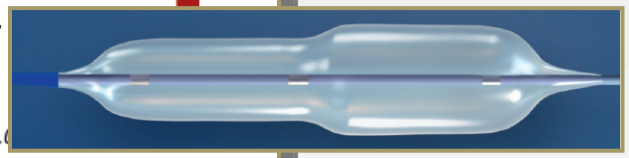


4th scenario: rePOT-DOT

Evald H Christiansen

Niels R Holm



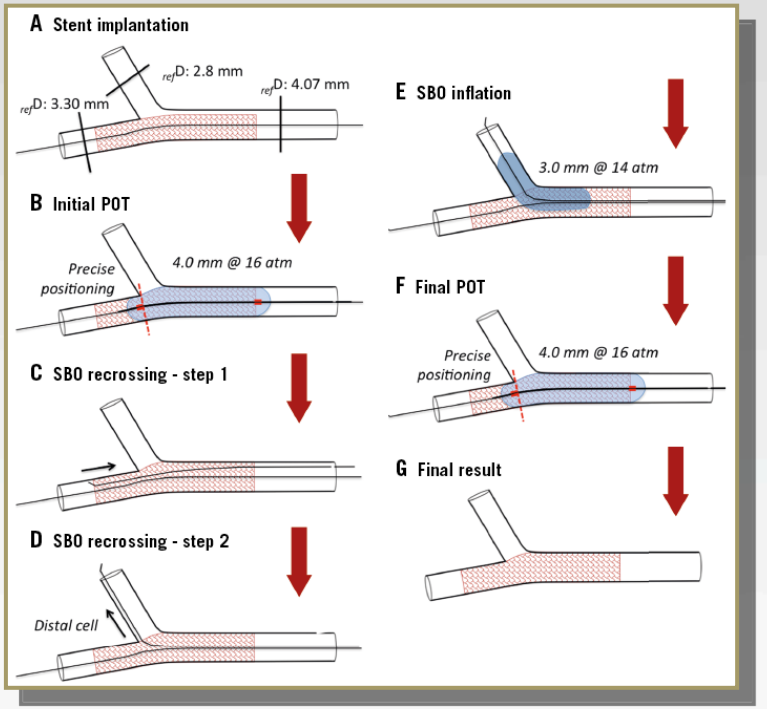


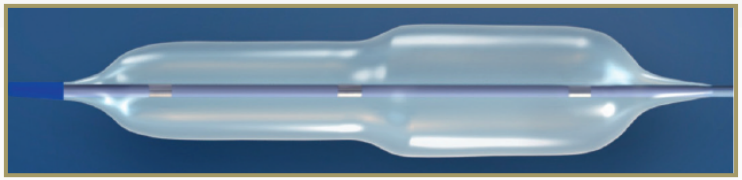
Bottle-balloon, BALTON

Study for rePOT & rePOT-DOT

- PS vs. rePOT / rePOT-DOT
  - Pilot study
  - Endpoint
    - SB restenosis
    - FFR≤0.80 in SB?
  - Same assumptions as in NORDIC-III
    - PS 20%
    - RePOT / RePOT-DOT 8%
  - Superiority
    - α = 0.05
    - β = 0.20
    - Fleiss´ correction
    - n= 147
    - Allocation 1:1 = 294
    - +10% loss at FU = 324

n = 324





Study for rePOT & rePOT-DOT

- 2-stents vs.rePOT / rePOT-DOT
  - Complex lesions
  - Non-inferiority
    - 2-stents 15.1
    - RePOT / RePOT-DOT 15.1
    - Δ = 3%
    - n= 3500
  - Non-inferiority
    - 2-stents 15.1
    - RePOT / RePOT-DOT 15.1
    - Δ = 5%
    - n= 1260
  - Non-inferiority
    - 2-stents 15.1
    - RePOT / RePOT-DOT 8.0
    - Δ = 3%
    - n= 250

- 2-stents vs. rePOT / rePOT-DOT
  - Pilot study
  - Endpoint
    - SB restenosis
    - FFR≤0.80 in SB?
  - Same assumptions as in BBC
    - PS 15.1%
    - RePOT / RePOT-DOT 8.0%
  - Superiority
    - α = 0.05
    - β = 0.20
    - Fleiss´ correction
    - n= 346
    - Allocation 1:1 = 692
    - +10% loss at FU = 761

n = 761

Conclusions

- General considerations for DCB studies in bifurcations
  - No class effect
  - Adequate technique
  - DCB: last device
  - LLL misleading endpoint
  - Choose a relevant SB
- Possible scenarios
  - DCB-FKB vs. PS w/o FKB vs. : n = 324
  - DCB-FKB vs. 2 stents: n = 761
  - DCB-rePOT vs. PS: n =324

    DCB-rePOT-DOT vs. PS
  - DCB-rePOT vs. 2 stents:

    DCB-rePOT-DOT vs. PS
    - Superiority n=761
    - Non-inferiority n=3500 1260 250

Thank you very much for your attention

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