One Stent, Two Stents, or Special Stents in Coronary Bifurcations: Evidence-Based Medicine Review

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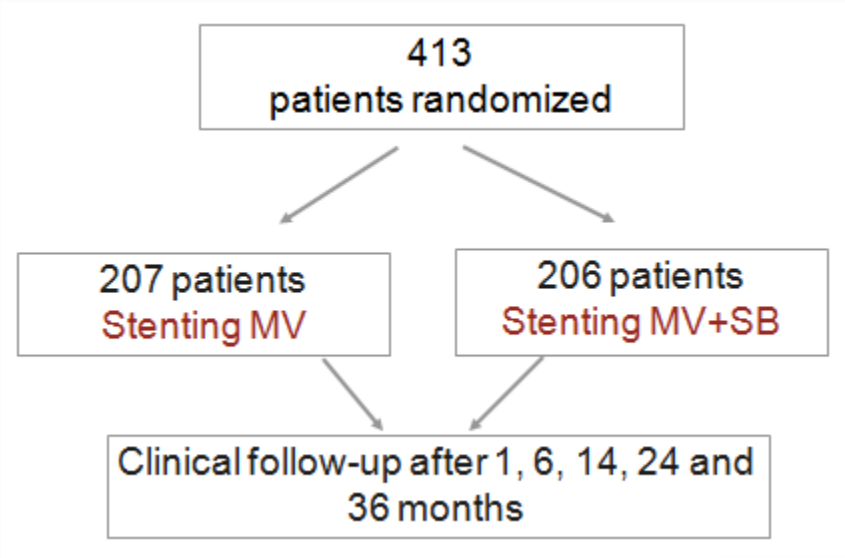
Disclosure Statement of Financial Interest

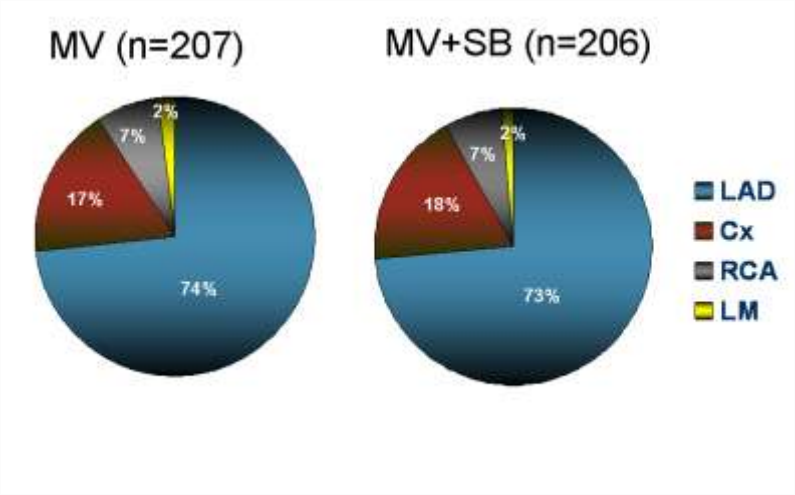
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott Vascular
• Consulting Fees/Honoraria	• Boston Scientific, Cordis J&J
• Major Stock Shareholder/Equity	
• Royalty Income	
• Ownership/Founder	
• Intellectual Property Rights	
• Other Financial Benefit	

Nordic Bifurcation Study

Nordic Bifurcation Study (NORDIC I): the randomized study on simple versus complex stenting of coronary artery bifurcation lesions /completed/

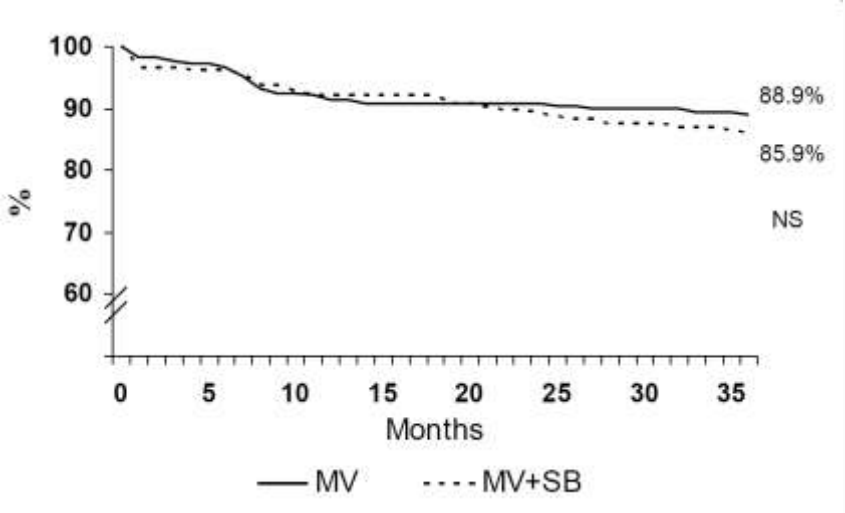




True bifurcations 71%
(DS>50% in MV and SB)

Nordic Bifurcation Study (Nordic I)

MACE: cardiac death, index lesion MI, TVR, stent thrombosis



Individual Endpoints

	MV n=207	MV + SB n=206	P value
6 months			
Cardiac death, n(%)	2 (1.0)	2 (1.0)	1.00
Total death, n(%)	2 (1.0)	3 (1.5)	0.61
MI, n(%)	0 (0.0)	1 (0.5)	0.31
TVR, n(%)	4 (1.9)	4 (1.9)	0.99
Stent thrombosis, n(%)	1 (0.5)	0 (0.0)	0.31
TLR, n(%)	4 (1.9)	2 (1.0)	0.36
36 months			
Total death (%)	2.9	5.8	0.15
Cardiac death (%)	1.4	1.5	1.00
MI (%)	3.0	3.6	0.78
TLR (%)	8.0	9.7	0.60
TVR (%)	9.5	11.7	0.52
Stent thrombosis (%)	2.5	1.0	0.45

Bifurcations Bad Krozingen (BBK)

N=202
Routine T-stenting in both branches vs. provisional T-stenting in MB followed by kissing-balloon angioplasty and provisional SES placement in SB only for inadequate
Results
68% true bifurcations

1 year outcome

	Provisional T-stenting ($n = 101$)	Routine T-stenting ($n = 101$)	*P*-value
Death (%)	2 (2.0)	1 (1.0)	1.0
Non-fatal myocardial infarction (%)	1 (1.0)	2 (2.0)	1.0
Death or non-fatal myocardial infarction (%)	3 (3.0)	3 (3.0)	1.0
Target lesion revascularization (%)	11 (10.9)	9 (8.9)	0.64
Main branch	7 (6.9)	3 (3.0)	0.19
Side branch	5 (5.0)	8 (7.9)	0.39
Any MACE (%)	13 (12.9)	12 (11.9)	0.83
Stent thrombosis by ARC definition (%)			
Definite	1 (1.0)	2 (2.0)	1.0
Probable	1 (1.0)	0 (0)	1.0
Possible	1 (1.0)	1 (1.0)	1.0

Ferenc M et al. Eur Heart J 2008; 29: 2859–2867

CACTUS study

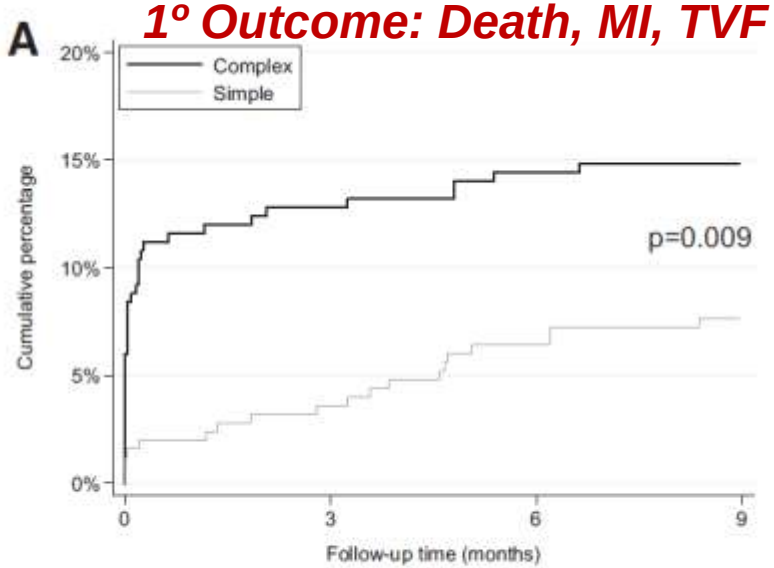
N=350,
Elective "crush" vs only MB stenting, with provisional side-branch T-stenting.
Mandatory final kissing-balloon inflation
100% true bifurcations (50% in both the MB and the ostium of the SB)

	Crush Group (n=177)	Provisional-Stenting Group (n=173)	*P*
30-day MACE (days 0–30)			
Q-wave MI	3 (1.7)	2 (1.1)	1.00
Non–Q-wave MI	15 (8.5)	12 (6.9)	0.69
TLR	3 (1.7)	1 (0.5)	0.63
TVR (including TLR)	3 (1.7)	1 (0.5)	0.63
Death	0	0	...
6-month MACE (days 31–180)			
MI	1 (0.5)	1 (0.5)	1.00
TLR	10 (5.6)	10 (5.8)	1.00
TVR (including TLR)	11 (6.2)	12 (6.8)	0.83
Death	0	1* (0.5)	0.49
Cumulative MACE (days 0–180)			
MI	19 (10.7)	15 (8.6)	0.59
TLR	13 (7.3)	11 (6.3)	0.83
TVR (including TLR)	14 (7.9)	13 (7.5)	1.00
Death	0	1* (0.5)	0.49

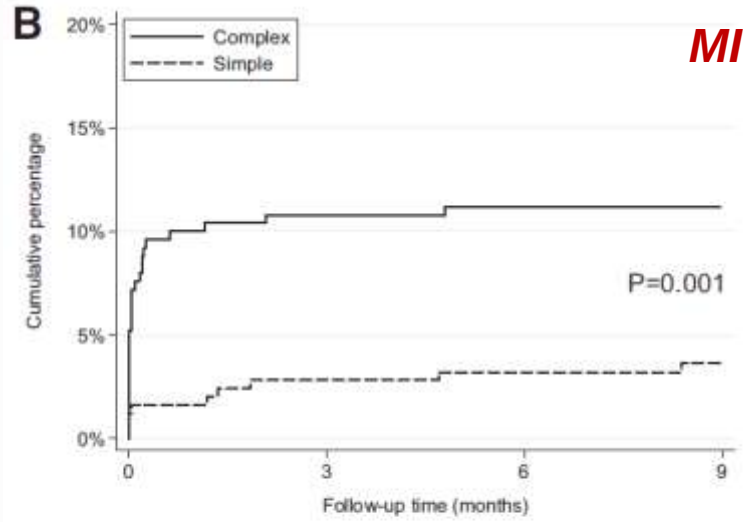
British Bifurcation Study (BBC ONE)

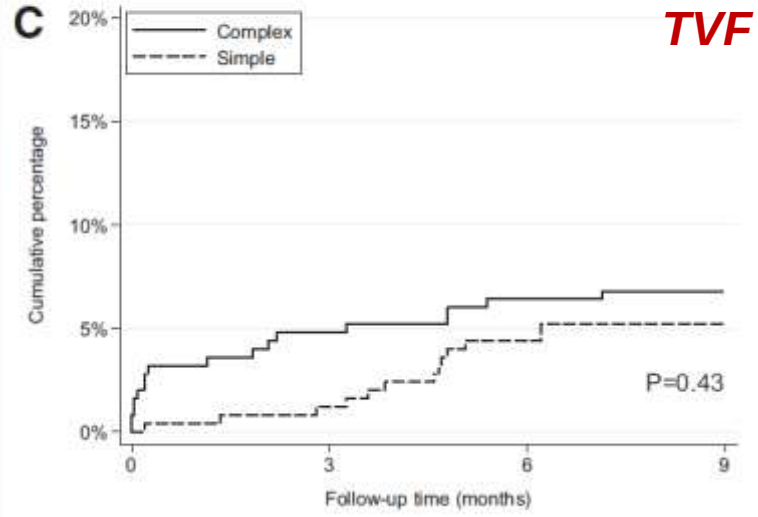
N=500, Simple vs. Complex strategy
Simple: MV stented, optional kissing balloon dilatation/T-stent.
Complex: Culotte or crush with mandatory kissing balloon dilatation
82% true bifurcations (50% narrowing in both vessels).

1º Outcome: Death, MI, TVF



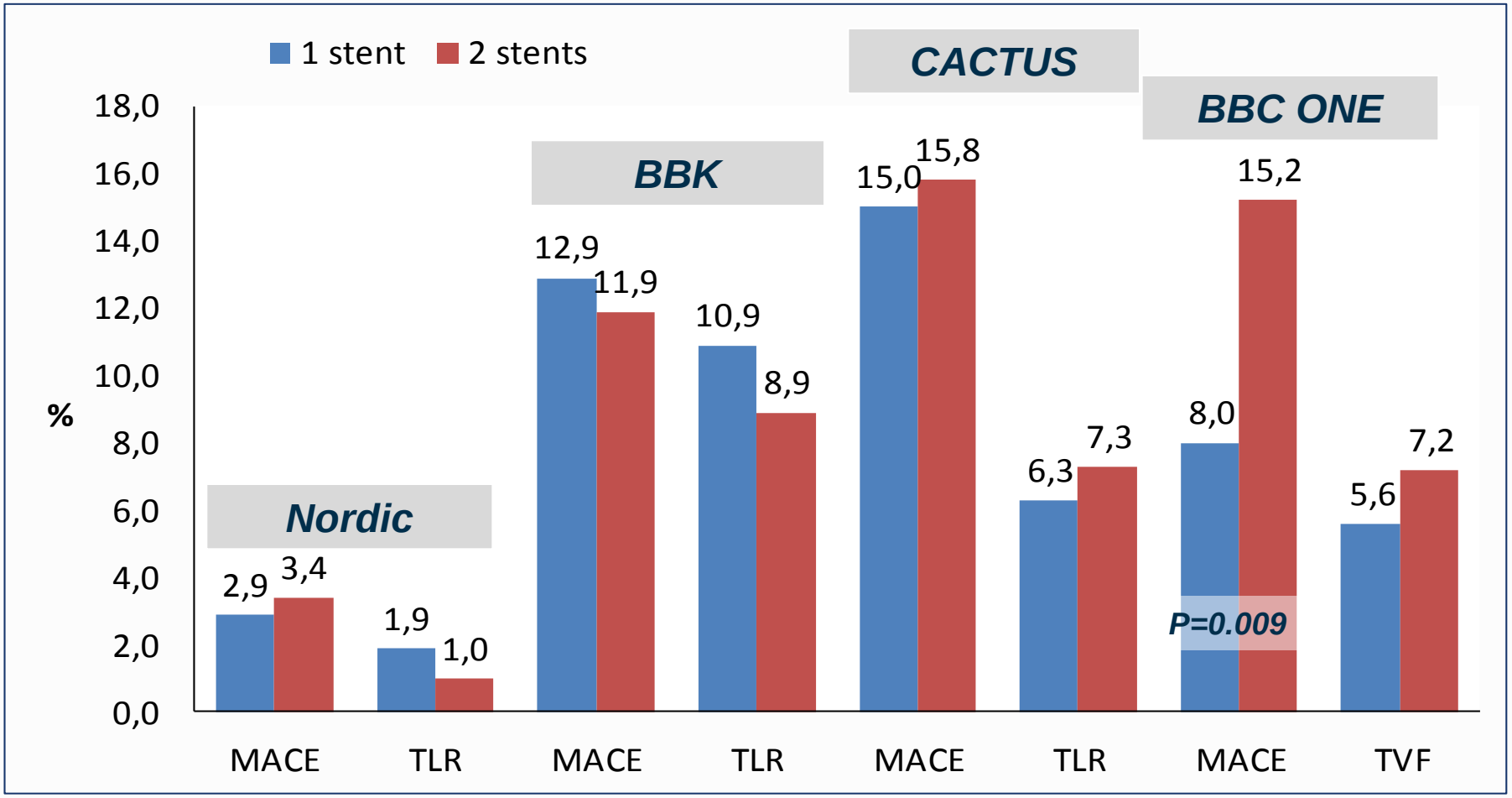
Complex	250	218	214	208
Simple	250	241	234	227





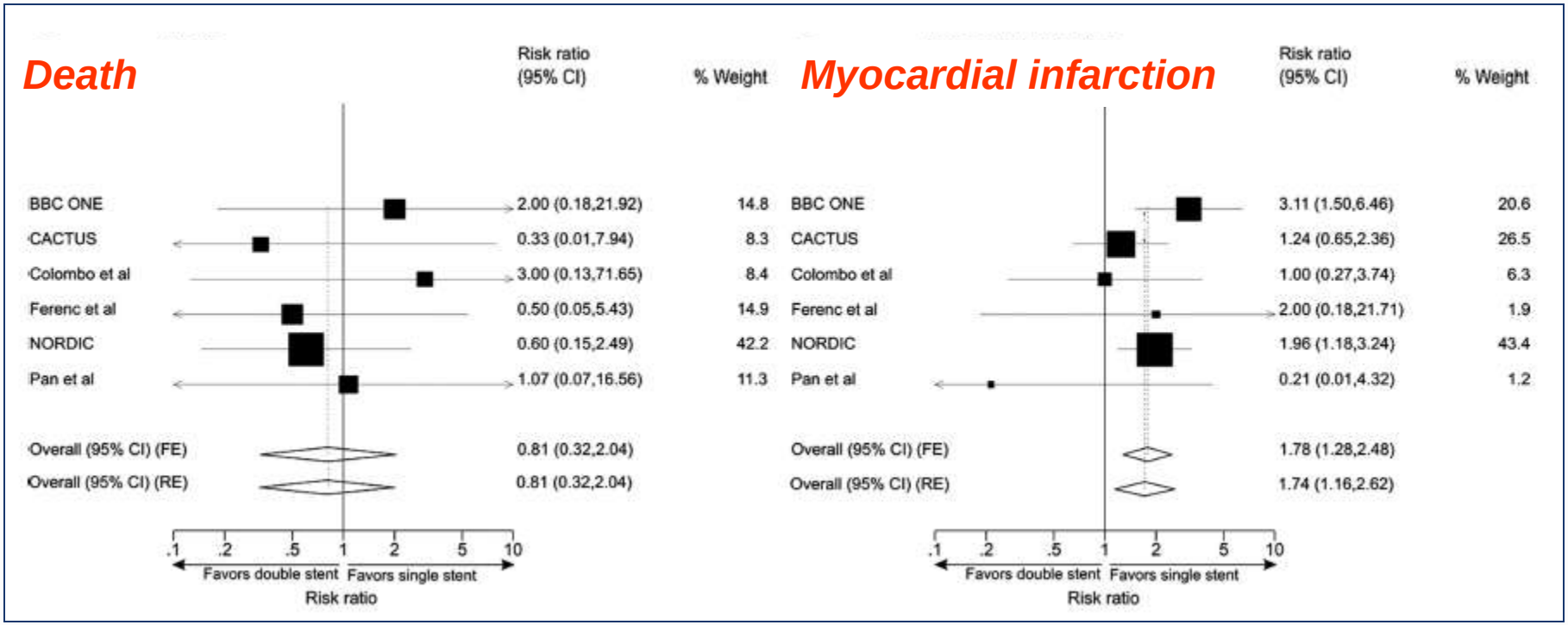
Hildick-Smith D, et al. *Circulation. 2010;121:1235-1243*

MACE and TLR in Bifurcation Studies



Double vs. Single Stenting Meta-Analysis

N=1642 patients

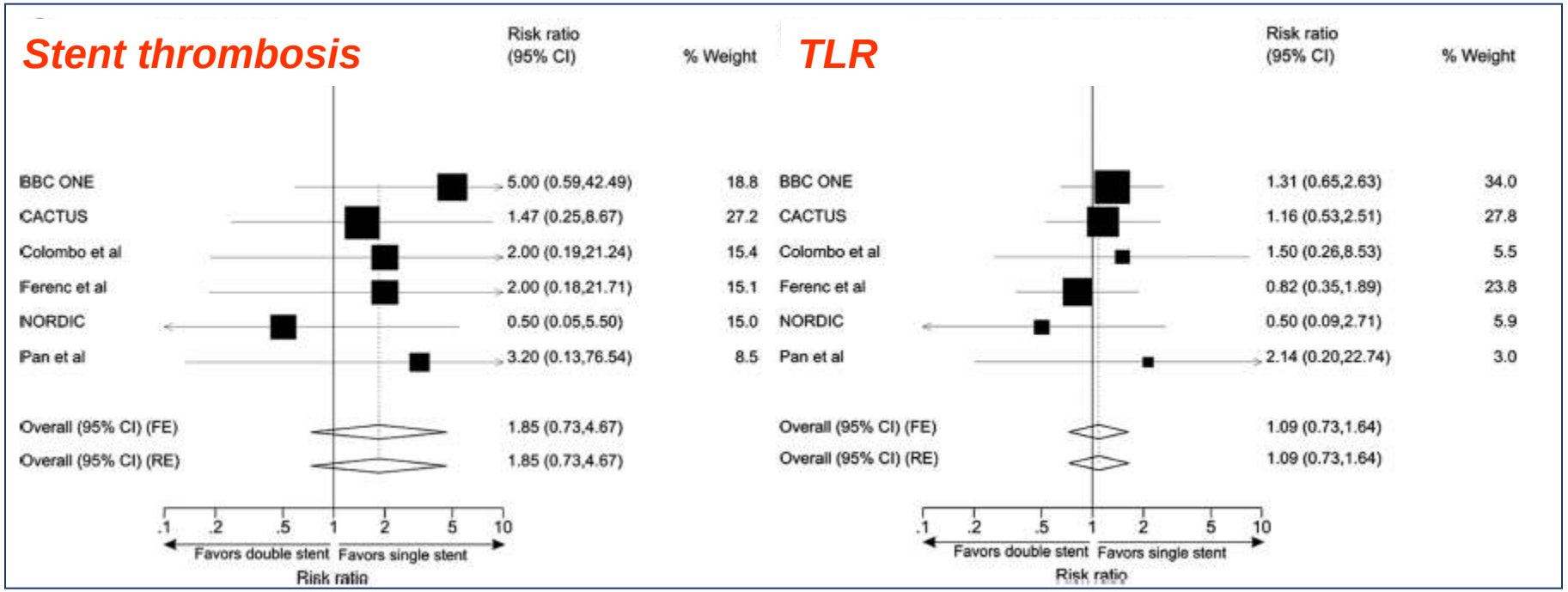


2 stents 1 stent ***2 stents 1 stent***

Katritsis DG et al. *Circ Cardiovasc Intervent*. 2009;2:409-415

Double vs. Single Stenting Meta-Analysis

N=1642 patients

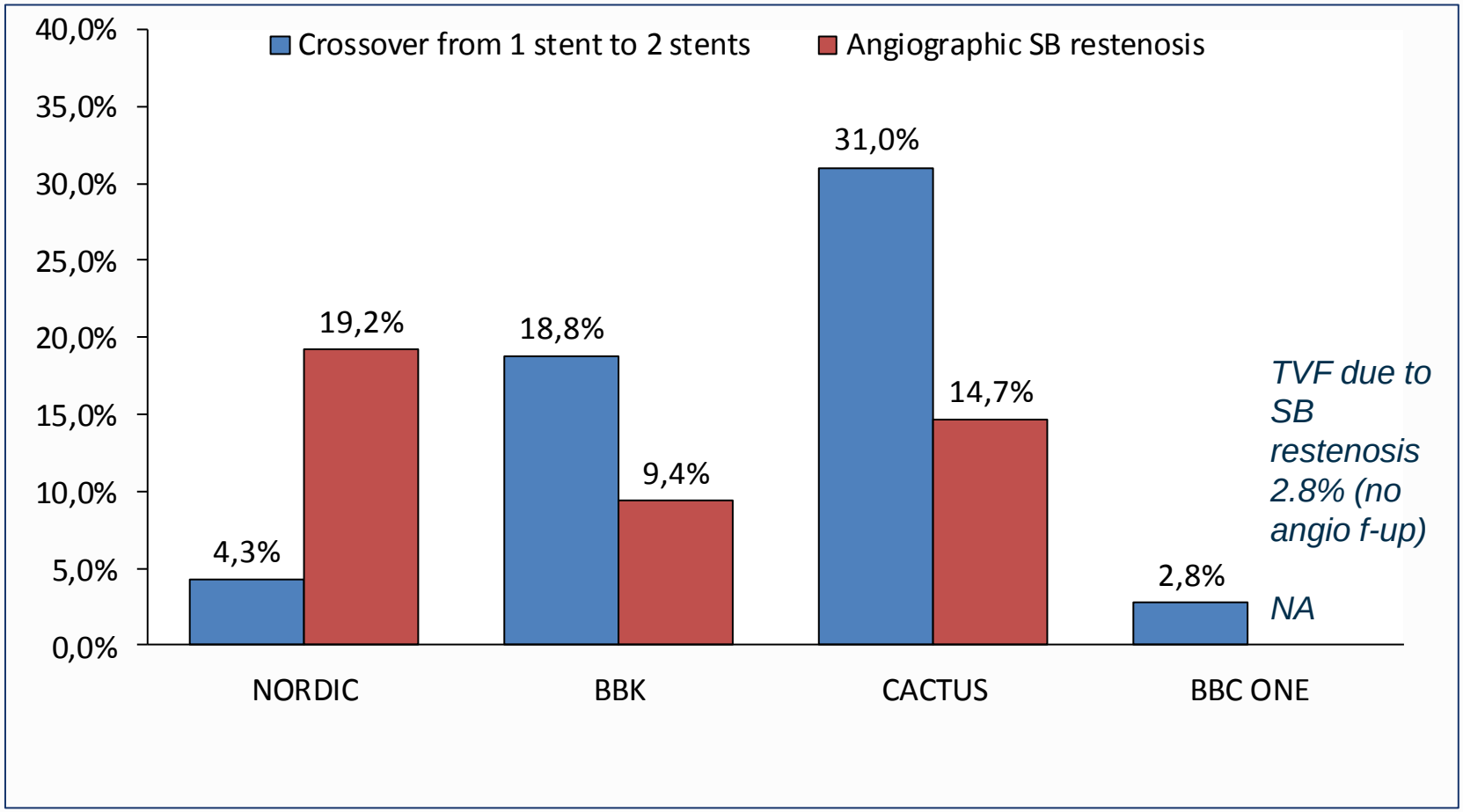


2 stents *1 stent* *2 stents* *1 stent*

Katritsis DG et al. *Circ Cardiovasc Intervent*. 2009;2:409-415

How Often We Need 2nd Stent after MV Stent?

Crossover from 1 Stent to 2 Stents



When We Need 2nd Stent after MV Stenting?

Suboptimal Result in SB after MV Stenting

Nordic Bifurcation Study:
If TIMI<3 → SB dilation; SB stenting if TIMI flow = 0 after dilation

Steigen TK et al. Circulation. 2006;114:1955-1961

Bifurcations Bad Krozingen:
Flow limiting dissection or residual stenosis of ≥ 75%

Ferenc M et al. Eur Heart J 2008; 29: 2859–2867

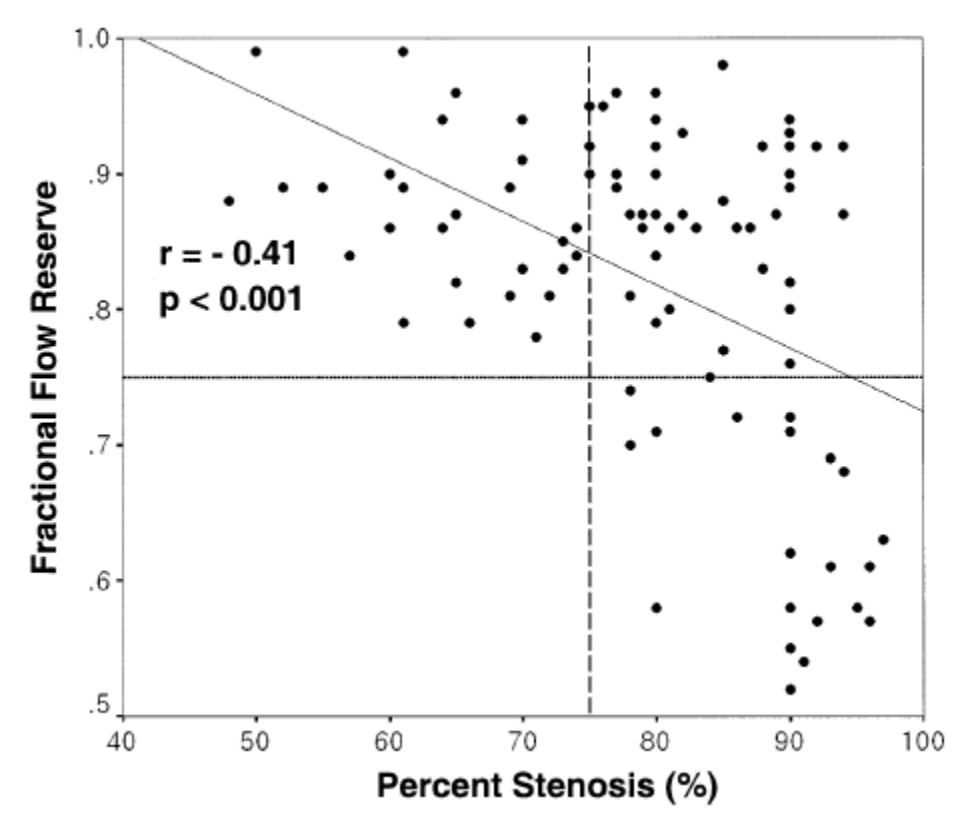
CACTUS:
Residual stenosis ≥50%; dissection of type B or worse; TIMI flow ≤2

Colombo A et al. Circulation. 2009;119:71–78

BBC ONE:
TIMI flow <3, persistent ostial pinching of SB (<70%), threatened SB closure, or SB dissection > type A

Hildick-Smith D et al. Circulation. 2010;121:1235-1243

Correlation Between FFR and % Stenosis (QCA) in Jailed Side Branches



There was a negative correlation between the percent stenosis and FFR (r=0.41, p<0.001).

No lesion with <75% stenosis had FFR<0.75.

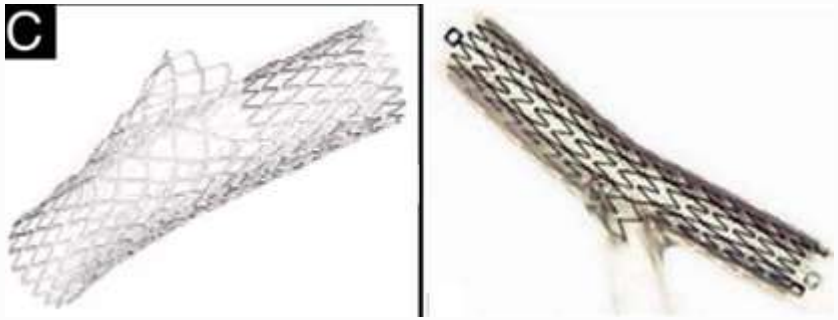
Among 73 lesions with ≥75% stenosis, only 20 lesions were functionally significant.

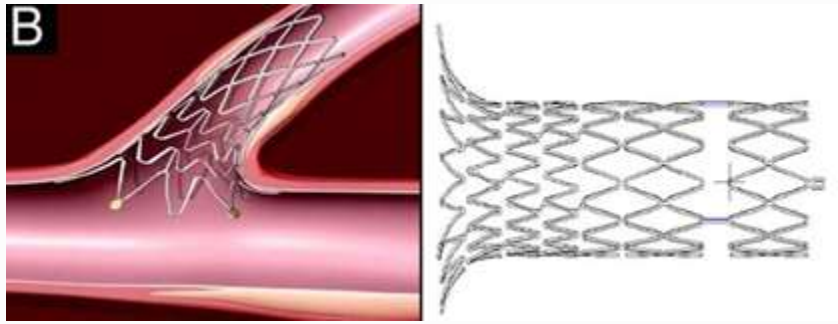
FFR measurements demonstrate that most of stenotic SB do not have functional significance

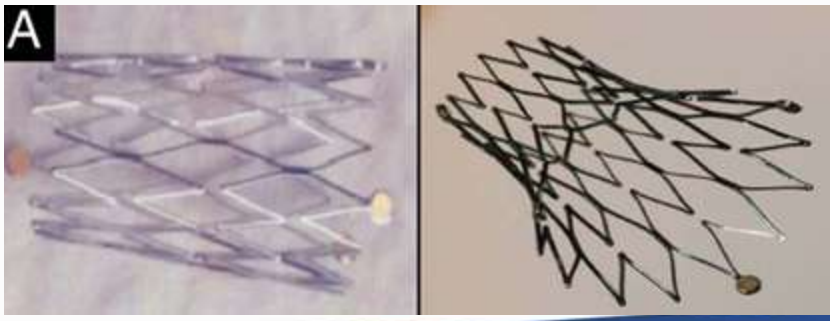
Koo BK et al J Am Coll Cardiol 2005;46:633–7)

Dedicated Bifurcation Stents

- **Stents that facilitate provisional SB stenting and maintain direct access to the SB after MV stenting; Pre-formed MV stent with side ports to facilitate access to the SB (Antares, Invatec Twin-rail, Multi-Link Frontier, Nile Croco, Petal, SLK-view, StenTys, Y-Med Side-Kick)**
- **Stents designed to treat the SB first; Second stent is required for the main branch (Sideguard, Tryton)**
- **Conical stents for the geometry of the ostium; These may require additional stents to be implanted in the main branch or side branch (Axxess)**







Currently Available Dedicated Stents

Stent Type (Company) (Ref. #)	Device Profile	Stent Material	Drug Coating	SB Protection	Ostial SB Coverage
Balloon-expandable stents					
Antares† (TriReme Medical) (148)	6-F	SS	—	+	+
Invatec Twin-Rail (Invatec) (149)	6-F	SS	—	+	+/−
Multi-Link Frontier† (Abbott Vascular) (150)	7-F	SS	—	+	+/−
Nile Croco† (Minvasys) (151)	6-F	CoCr	—	+	+/−
Nile Pax† (Minvasys) (152)	6-F	CoCr	Abluminal Paclitaxel	+	+/−
Petal (Boston Scientific) (153,154)	7-F	PtCr	Paclitaxel	+	+
SideKick (Y-Med) (155)	5-F	CoCr	—	+	+/−
SLK-View† (Advanced Stent Tech) (156)	8-F	SS	—	+	−
Tryton† (Tryton Medical) (157)	6-F	CoCr	—	NA	++
Self-expanding stents					
Axxess (Devax) (32,55)	7-F	Nitinol	Abluminal Biolimus A9	+	−
Sideguard† (Cappella) (158,159)	6-F	Nitinol	—	NA	++
Stentys† (Stentys) (160,161)	7-F	Nitinol	Paclitaxel	−	+/−

Garg S, Serruys PW. *J. Am. Coll. Cardiol.* 2010;56;S43-S78

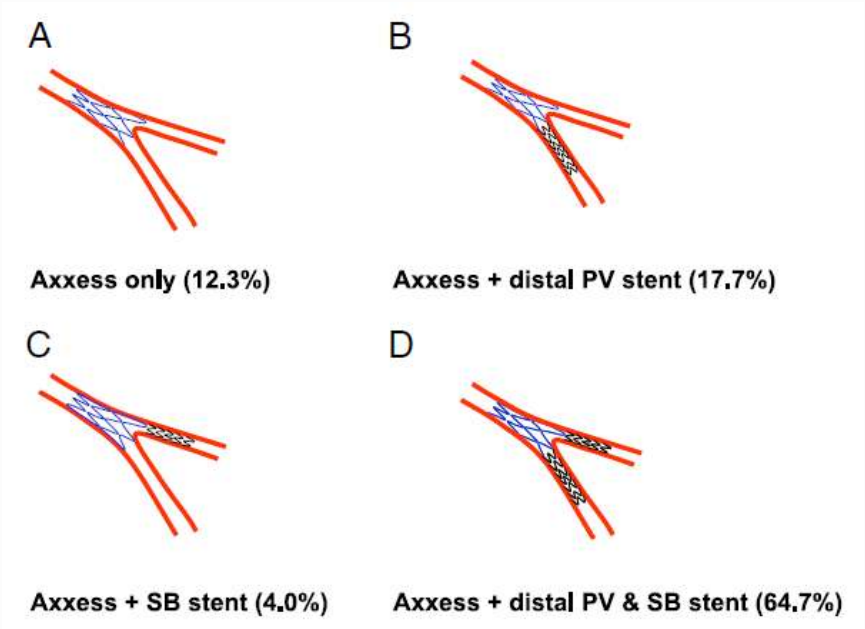
Currently Available Dedicated Stents

Stent Type (Company) (Ref. #)	Study Name*	No. of Patients (Follow-Up, Months)	Additional Stenting, % MB/SB	Binary In-Stent Restenosis % MB/SB	LLL, mm MB/SB	MACE, %	Death, %	MI, %	TLR, %
Balloon-expandable stents									
Antares† (TriReme Medical) (148)	FIM (TOP study)	39 (1)	NA	NA	NA	5.9	0.0	5.1	2.9
Invatec Twin-Rail (Invatec) (149)	FIM (DESIRE)	15 (7)	17/23	NA	NA	14.3	0.0	0.0	14.3
Multi-Link Frontier† (Abbott Vascular) (150)	Registry	105 (6)	40/43	25.3/—	0.84/0.34	17.1	0.0	3.8	13.3
Nile Croco† (Minvasys) (151)	Registry	93 (6)	NA	NA	NA	12.0	2.0	0.0	9.4
Nile Pax† (Minvasys) (152)	FIM	102 (30)	—/27	NA	NA	1.0	1.0	1.0	0.0
Petal (Boston Scientific) (153,154)	FIM (Petal Trial)	28 (12)	28/25	10/10	0.41/0.18	14.8	0.0	3.7	7.4
SideKick (Y-Med) (155)	FIM	17 (2–3)	40‡	NA	NA	5.8	0.0	5.8	0.0
SLK-View† (Advanced Stent Tech) (156)	Registry	81 (4)	14/25	28.7/37.7	1.1/0.81	31.0	1.3	2.5	21.3
Tryton† (Tryton Medical) (157)	FIM (Tryton I)	30 (6)	39/—	0/0	0.25§/0.17	9.9	3.3‖	6.6	6.6
Self-expanding stents									
Axxess (Devax) (32,55)	Registry (DIVERGE)	302 (9)	64.7‡	2.3/4.8	0.29/0.29	7.7	0.7	4.3	4.3
Sideguard† (Cappella) (158,159)	FIM (Sideguard I & II)	93 (12)	NA	12/25	0.21/0.58	12.0	1.2‖	3.6	7.2
Stentys† (Stentys) (160,161)	FIM (OPEN I)	40 (3¶, 6#)	9/13	25/14	0.83§	5.1	0.0	2.5	2.5

Garg S, Serruys PW. *J. Am. Coll. Cardiol.* 2010;56;S43-S78

DIVERGE study

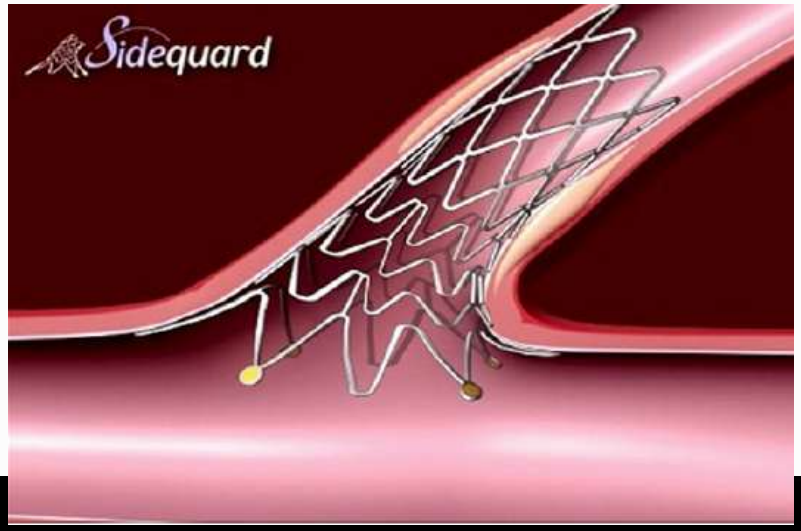
N=302
AXXESS stent: sef expanding nitinol alloy, drug biolimus A9, carier: bioabsorbable PLA polymer



	All Patients	Angiographic Subgroup
In-hospital	(n = 302)	(n = 150)
MACE	9 (3%)	5 (3.3%)
MI (all non–Q-wave periprocedural)	9 (3%)	5 (3.3%)
30-day	(n = 302)	(n = 150)
MACE	12 (4%)	7 (4.7%)
Death (cardiac)	1 (0.3%)	1 (0.7%)
MI	11 (3.6%)	6 (4%)
Q-wave	2 (0.7%)	1 (0.7%)
Non–Q-wave	9 (3%)	5 (3.3%)
TLR (percutaneous)	3 (1%)	2 (1.3%)
Early stent thrombosis	2 (0.7%)	1 (0.7%)
9-month	(n = 300)	(n = 149)
MACE	23 (7.7%)	14 (9.4%)
Death	2 (0.7%)	1 (0.7%)
Cardiac death	2 (0.7%)	1 (0.7%)
MI	13 (4.3%)	8 (5.4%)
Q-wave	3 (1%)	2 (1.3%)
Non–Q-wave	10 (3.3%)	6 (4%)
TLR	13 (4.3%)	8 (5.4%)
Percutaneous	12 (4%)	8 (5.4%)
Bypass surgery	1 (0.3%)	0
Stent thrombosis by Academic Research Consortium criteria	3 (1%)	2 (1.3%)
Early (probable/possible)	0	0
Early (definite)	2 (0.7%)	1 (0.7%)
Late (probable/possible)	0	0
Late (definite)	1 (0.3%)	1 (0.7%)
Remote target vessel revascularization	19 (6.3%)	11 (7.4%)
Target vessel failure	29 (9.7%)	17 (11.4%)

Verheye S et al. J Am CollCardiol 2009;53:1031–

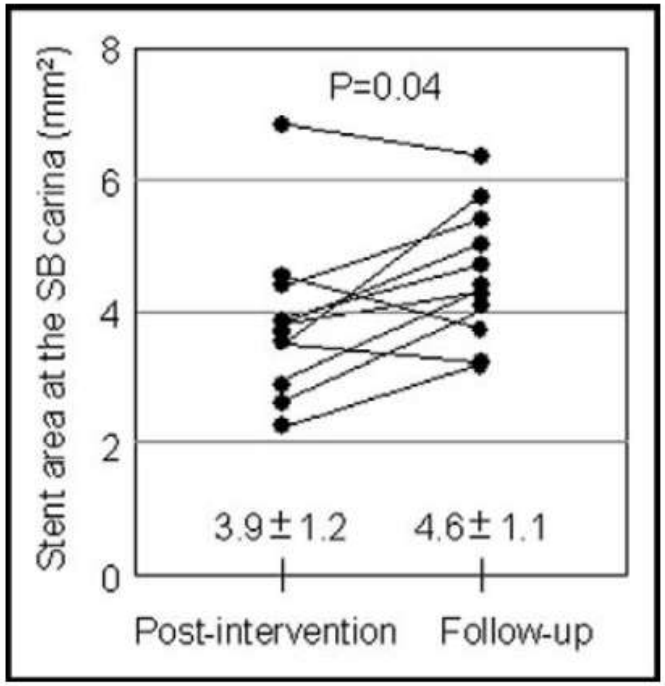
SIDEGUARD I & II



MACE (all)	All Patients (90 pts)	Sideguard (80 pts)
Up to 30 Days	4.4% (4/90)	3.8% (3/80)
Up to 6 Mos	11.1% (7/63)	10.2% (6/59)
MACE Events @ 6 mos		
Cardiac Death	1.6% (1/63)	1.7% (1/59)
Myocardial Infarction	4.8% (3/63)	3.4% (2/59)
Target Lesion Revascularization	4.8% (3/63)	5.1% (3/59)
Other Revascularizations @ 6 mos		
Ischemia Driven TVR	6.3% (4/63)	6.8% (4/59)
Stent Thrombosis*		
Up to 30 Days	3.3% (3/90)	2.5% (2/80)
Up to 6 Mos	4.8% (3/63)	3.3% (2/59)

*One ST @ 10 days in MV

IVUS analysis of Sideguard I (N=11)



Cappella Sideguard stent area at the carina of the SB increased from 3.9±1.2 to 4.6 ± 1.1 mm2 (p= 0.04).

Tryton I, FIM study

N=30
Tryton in SB + DES in MV
6M clinical + angio f-up

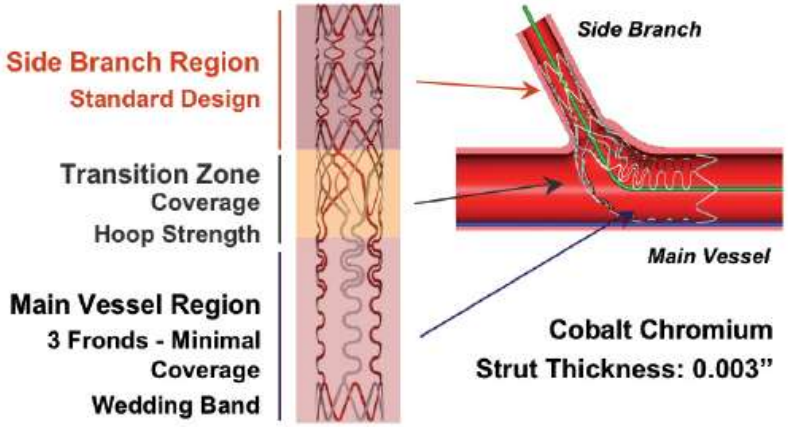


Figure 1. Schematic representing the Tryton™ Side-Branch Stent showing three zones: distal (side-branch) zone, central (transition) zone and proximal (main vessel) zone.

In-stent binary restenosis*	0 (0)
In-segment binary restenosis**	1 (4.3)

In-hospital outcome	
Angiographic success	29(96.7)
Cardiac death	1(3.3)
MI	2(6.6)
CABG	0
TLR	1(3.3)
Cardiac Dearth or MI	2(6.6)
MACE (Cardiac death, MI, CABG or TLR)	2(6.6)
Procedural Success	28(93.3)
6 month outcome	
Cardiac death	1(3.3)
MI	2(6.6)
CABG	0
TLR	2(6.6)
TVR	1(3.3)
Stent thrombosis	0
Cardiac Dearth or MI	2(6.6)
MACE (Cardiac Death, MI, CABG or TLR)	3(9.9)

Onuma Y et al. EuroInterv 2008;3:546-552

Conclusions

- The technique of stenting of main vessel and optional stenting of side branch can be recommended as the routine bifurcation stenting technique
- Stenting of both the main vessel and side branch in bifurcation lesions may increase myocardial infarction risk compared with stenting of the main vessel only
- The second generation dedicated bifurcation stents seem to be promising, however randomized trials against conventional DES are still lacking.