

Key Messages of CROSS and PERFECT Trials: Prognostic Factors and Mechanisms

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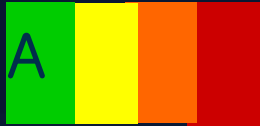
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RCTs for Bifurcation Lesions

Trials	Comparison
NORDIC 1	Provisional T vs. Systemic T stenting
NORDIC 2	Crush vs. Culotte
NORDIC 3	Kissing balloon vs. leave alone
BBC	Simple vs. Complex
CACTUS	Provisional T vs. Crush
CROSS	FKB vs. no FKB for non-diseased SB
PERPECT	Crush vs. Provisional T for diseased SB

Guideline Consensus

I IIa IIb III



Provisional side-branch stenting should be the initial approach in patients with bifurcation lesions when the side branch is not large and has only mild or moderate focal disease at the ostium

I IIa IIb III



It is reasonable to use elective double stenting in patients with complex bifurcation morphology involving a large side branch where the risk of side-branch occlusion is high and the likelihood of successful side branch re access is low

However, bifurcation stenting still accompanies controversies on ...

- IVUS benefit
- Non-compliant balloon
- Pre-dilation
- Final kissing balloon (FKB) inflation
- Optimal pressure at FKB
-

Patients with non-LM bifurcation lesions

SB < 50%

No

Side branch stenosis *

Yes

SB ≥ 50%

No

SB TIMI grade 3 & stenosis ≥ 50% after MB stenting

Yes

Registry
(N=195)

CROSS
(N=306)

PERFECT
(N=419)

Randomization

Randomization

Routine FKB
(N=151)

Leave-alone
(N=155)

Crush
(N=213)

Single-stent
(N=206)

Angiography
at 8 months
(N=106, 70.2%)

Angiography
at 8 months
(N=108, 69.7%)

Angiography
at 8 months
(N=155, 72.8%)

Angiography
at 8 months
(N=145, 70.4%)

Clinical follow-up
at 12 months
(N=150, 99.3%)

Clinical follow-up
at 12 months
(N=155, 100%)

Clinical follow-up
at 12 months
(N=213, 100%)

Clinical follow-up
at 12 months
(N=205, 99.5%)

* ≥ 2mm diameter and ≥ 50% stenosis

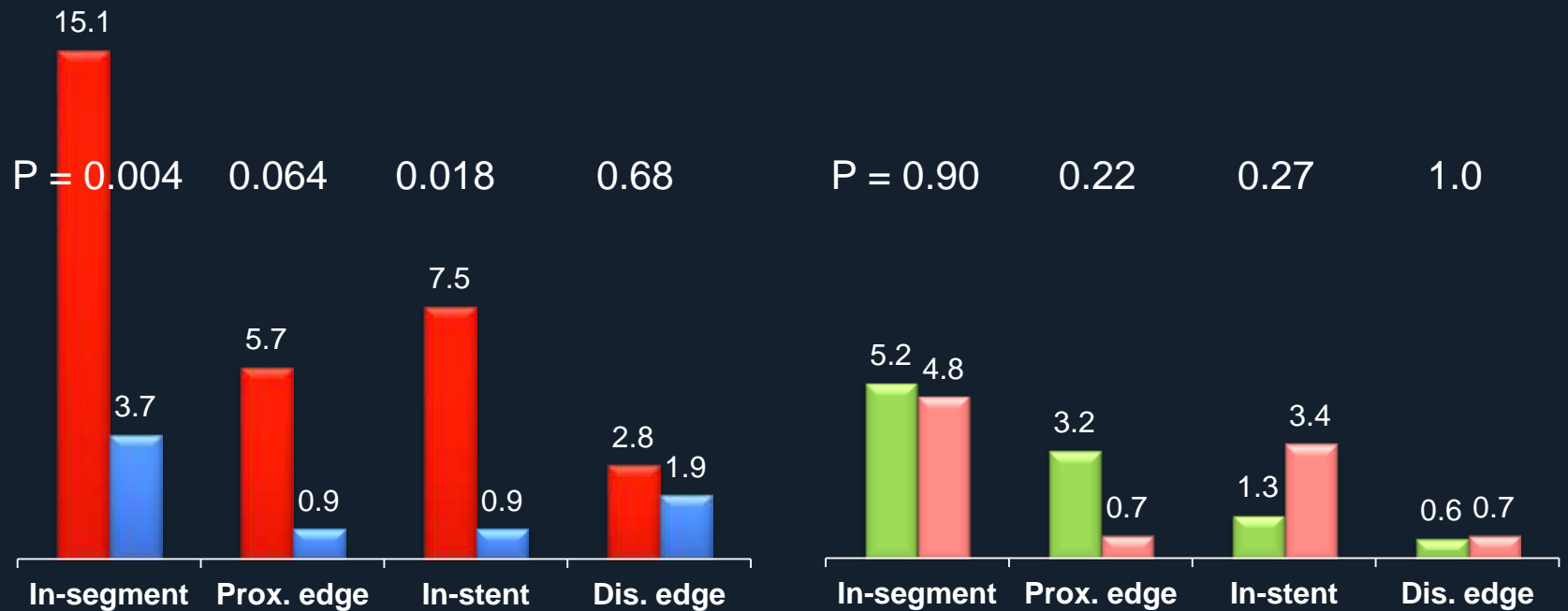
MB Restenosis

CROSS

PERFECT

■ FKB ■ Leave-alone

■ Crush ■ 1-stent

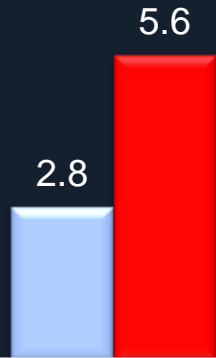


SB Restenosis

CROSS

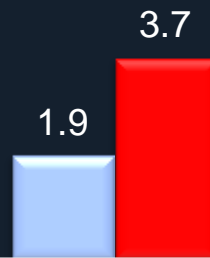
■ FKB ■ Leave-alone

P = 0.50



In-segment

0.68

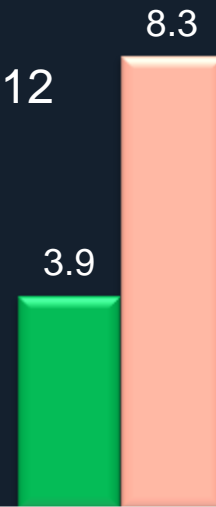


Ostium

PERFECT

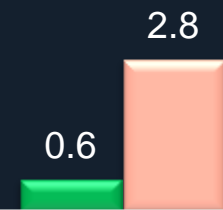
■ Crush ■ 1-stent

P = 0.12



In-segment

0.20



Ostium

Overall Restenosis Rate

CROSS

PERFECT



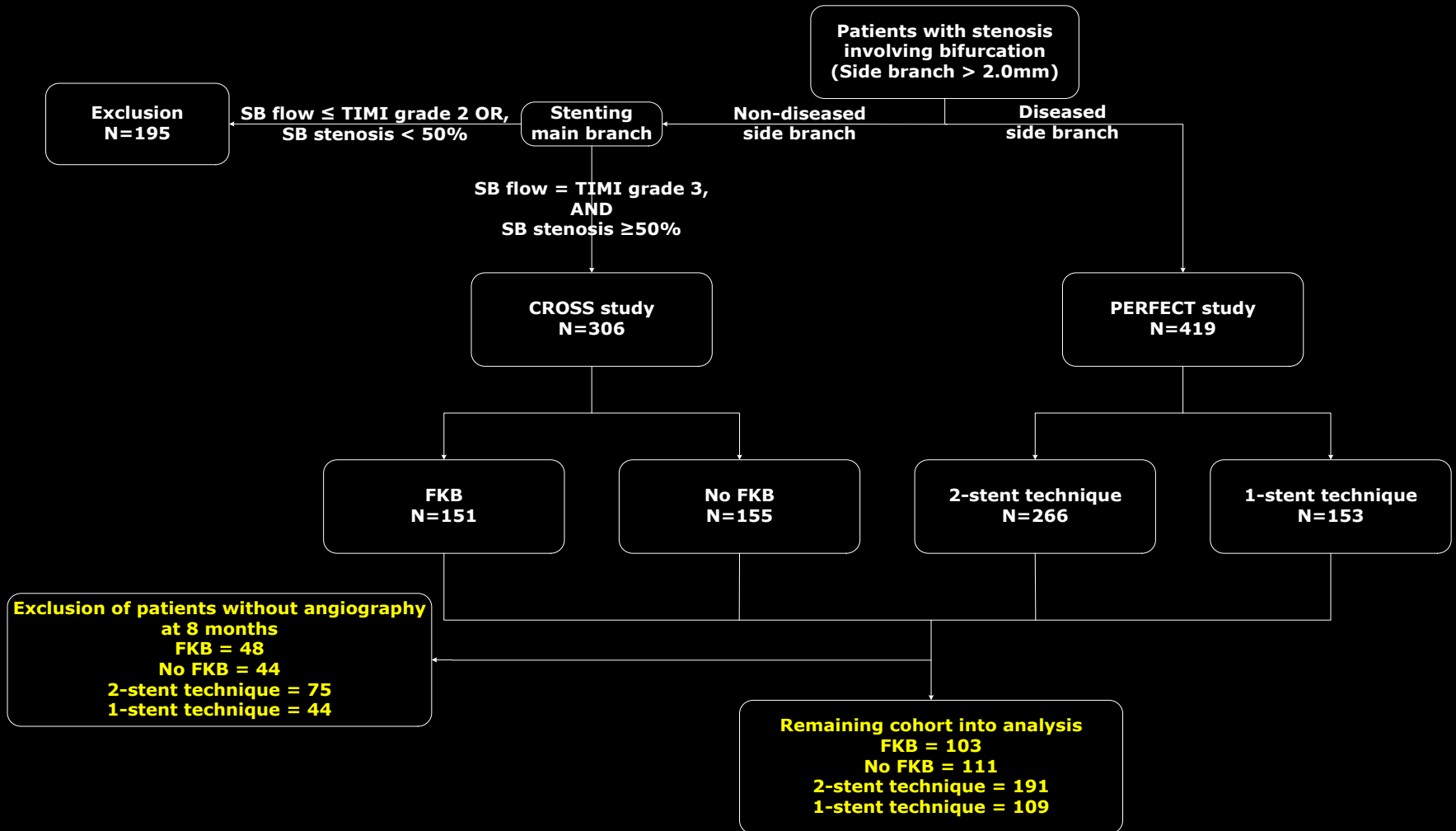
1-Year Clinical Outcomes

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
Death	2 (1.3)	0	0.15	3 (1.4)	2 (1.0)	0.68
Cardiac	2 (1.3)	0	0.15	2 (0.9)	1 (0.5)	0.58
Non-cardiac	0	0		1 (0.5)	1 (0.5)	0.98
MI	9 (6.0)	13 (8.4)	0.42	30 (14.1)	29 (14.1)	0.98
Q-wave	0	1 (0.6)	0.32	0	0	
Non-Q wave	9 (6.0)	12 (7.7)	0.55	30 (14.1)	29 (14.1)	0.98
TVR	11 (7.4)	5 (3.2)	0.11	6 (2.9)	7 (3.4)	0.73
Clinically-driven	4 (2.7)	1 (0.6)	0.16	1 (0.5)	3 (1.5)	0.30
TLR	10 (6.7)	4 (2.6)	0.088	4 (1.9)	7 (3.4)	0.33
PCI	10 (6.7)	4 (2.6)	0.088	4 (1.9)	6 (2.9)	0.48
CABG	0	0		0	1 (0.5)	0.31
Stent thrombosis	0	1 (0.6)	0.33	1 (0.5)	0	0.32
MACE	21 (14.0)	18 (11.6)	0.57	38 (17.8)	38 (18.5)	0.85

Post-hoc Analysis of CROSS and PERFECT

- To discover technical predictors of 8-month angiographic restenosis after bifurcation stenting
- To address interactions, if any, between the proven predictors and bifurcation type, or between them and bifurcation stenting technique

Angiographic FU Cohort



Univariate OR for MB Restenosis

MB Factors

Variables	CROSS Study			PERFECT Study		
	+	-	OR (CI)	+	-	OR (CI)
MB restenosis	(N=20)	(N=194)		(N=15)	(N=285)	
NC balloon, %	45.0	58.8	0.57 (0.23-1.45)	40.0	55.4	0.54 (0.19-1.55)
IVUS, %	95.0	94.3	1.14 (0.14-9.33)	93.3	95.8	0.62 (0.07-5.07)
Predilation, %	100	96.4	-	100	97.9	-
Max. pr atm	18.6	19.0	0.98 (0.89-1.09)	15.0	17.3	0.88 (0.78-1.00)
Number of stents	1.3	1.3	1.15 (0.44-3.00)	1.4	1.4	0.99 (0.37-2.61)
Stent diameter, mm	3.3	3.4	0.87 (0.31-2.43)	3.3	3.3	0.90 (0.12-6.99)
Stent length, mm	34.1	32.8	1.01 (0.97-1.04)	35.9	37.6	0.99 (0.96-1.03)
Post MLD	2.2	2.4	0.43 (0.15-1.24)	2.2	2.5	0.41 (0.15-1.09)

Univariate OR for MB Restenosis SB Factors

Variables	CROSS Study			PERFECT Study		
	+	-	OR (CI)	+	-	OR (CI)
MB restenosis	(N=20)	(N=194)		(N=15)	(N=285)	
NC balloon, %	5.0	6.7	0.73 (0.09-5.91)	6.7	36.8	0.12 (0.02-0.94)
IVUS, %	35.0	42.8	0.72 (0.28-1.88)	80.0	86.7	0.62 (0.17-2.28)
Predilation, %	5.0	4.6	1.08 (0.13-9.01)	86.7	80.7	1.55 (0.34-7.09)
Max pr, atm	9.7	10.3	0.94 (0.79-1.13)	13.0	15.2	0.92 (0.82-1.04)
Stent implantation	0	1.0	NA	46.7	64.6	0.48 (0.17-1.36)
Post MLD	1.5	1.6	0.54 (0.17-1.69)	1.5	1.8	0.25 (0.07-0.85)
FKB, %	80.0	44.8	4.92 (1.59-15.25)	66.7	88.8	0.25 (0.08-0.79)

Univariate OR for SB Restenosis

MB Factors

Variables	CROSS Study			PERFECT Study		
	+	-	OR (CI)	+	-	OR (CI)
SB restenosis	(N=9)	(N=205)		(N=18)	(N=282)	
NC balloon, %	55.6	57.6	0.92 (0.24-3.53)	33.3	56.0	0.39 (0.14-1.08)
IVUS, %	100	94.1	NA	83.3	96.5	0.18 (0.05-0.74)
Predilation, %	88.9	97.1	0.24 (0.03-2.25)	100	97.9	NA
Max. pr atm	18.7	18.9	0.99 (0.85-1.14)	15.9	17.3	0.93 (0.83-1.04)
Number of stents	1.2	1.3	0.78 (0.17-3.65)	1.6	1.4	1.68 (0.74-3.81)
Stent diameter, mm	3.4	3.4	0.97 (0.59-1.60)	3.3	3.3	1.54 (0.23-10.35)
Stent length, mm	32.3	33.0	1.00 (0.95-1.05)	44.7	37.1	1.03 (1.00-1.06)
Post MLD	2.5	2.4	1.27 (0.34-4.74)	2.5	2.4	1.09 (0.47-2.54)

Univariate OR for SB Restenosis

SB Factors

Variables	CROSS Study			PERFECT Study		
	+	-	OR (CI)	+	-	OR (CI)
MB restenosis	(N=9)	(N=205)		(N=18)	(N=282)	
NC balloon, %	0	6.8	NA	22.2	36.2	0.50 (0.16-1.57)
IVUS, %	22.2	42.9	0.38 (0.08-1.87)	66.7	87.6	0.28 (0.10-0.80)
Predilation, %	0	4.9	NA	66.7	81.9	0.44 (0.16-1.23)
Max pr, atm	12.0	10.2	1.15 (0.80-1.65)	14.3	15.2	0.97 (0.87-1.08)
Stent implantation	0	1.0	NA	44.4	64.9	0.43 (0.17-1.13)
Post MLD	1.6	1.6	1.20 (0.23-6.21)	1.4	1.8	0.11 (0.03-0.37)
FKB, %	22.2	49.3	0.29 (0.06-1.45)	66.7	89.0	0.25 (0.09-0.70)

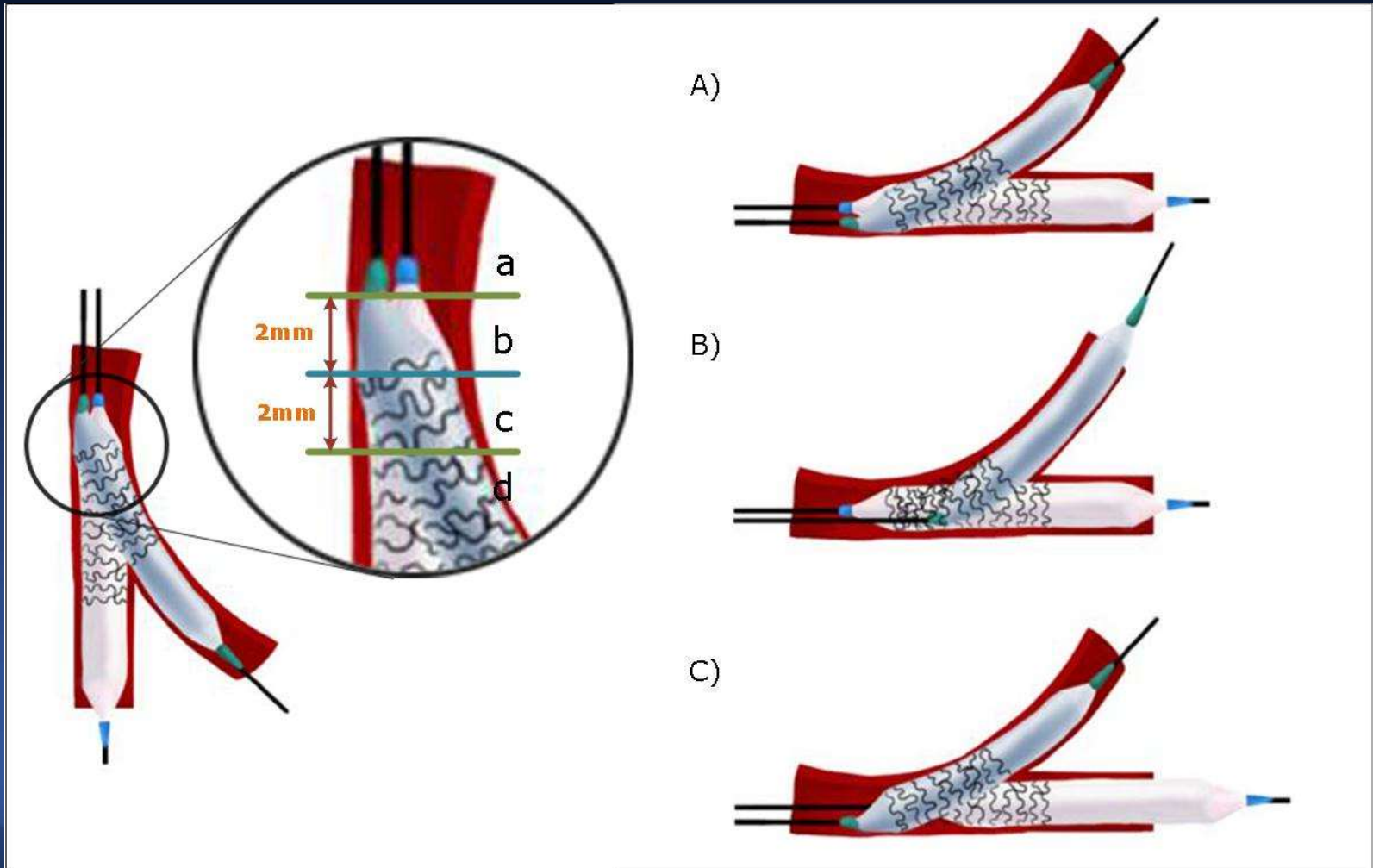
Multivariate OR for Restenosis

Variables	CROSS Study			PERFECT Study		
	OR	95% CI	P	OR	95% CI	P
Predictors, MB restenosis						
SB NC balloon				0.17	0.02 – 1.36	0.09
Post-SB MLD				0.56	0.14 – 2.17	0.40
FKB inflation	4.61	1.46 – 14.58	0.009	0.48	0.13 – 1.77	0.27
Predictors, SB restenosis						
IVUS for MB				0.16	0.03 – 1.00	0.050
Total stent length in MB				1.02	0.99 – 1.06	0.25
IVUS for SB				0.77	0.21 – 2.75	0.68
Post-SB MLD				0.14	0.03 – 0.62	0.010
FKB inflation				1.01	0.25 – 4.14	0.99

Technical Features of FKB

Impact of Barotrauma

Impact of Kissing Arrangement



FKB used in 1-stent Technique

Variables	MB restenosis			SB restenosis		
	+	-	P	+	-	P
MB restenosis	(N=18)	(N=156)		(N=6)	(N=168)	
Position of overlapping segment			0.83			0.81
a	10 (55.6)	92 (59.0)		3 (50.0)	99 (58.9)	
b	6 (33.3)	51 (32.7)		3 (50.0)	54 (32.1)	
c	2 (11.1)	11 (7.1)		0	13 (7.7)	
d	0	2 (1.3)		0	2 (1.2)	
Arrangement of balloons			0.44			1.00
a	2 (11.1)	8 (5.1)		0	10 (6.0)	
b	2 (11.1)	25 (16.0)		1 (16.7)	26 (15.5)	
c	14 (77.8)	123 (78.8)		5 (83.3)	132 (78.6)	

FKB used in 1-stent Technique

Variables	MB restenosis			SB restenosis		
	+	-	P	+	-	P
MB restenosis	(N=18)	(N=156)		(N=6)	(N=168)	
Sequential balloon dilation	14 (77.8)	122 (78.2)	1.00	5 (83.3)	131 (78.0)	1.00
SB-first dilation	3 (21.4)	50 (41.0)	0.16	2 (40.0)	51 (38.9)	1.00
Prox. RD of MB – Estimated dia. of 2 balloons, mm	-0.5 ± 0.5	-0.4 ± 0.8	0.62	-0.6 ± 0.4	-0.4 ± 0.8	0.70
Dist. RD of MB – dia. of MB balloon, mm	-0.7 ± 0.5	-0.7 ± 0.4	0.60	-1.0 ± 0.5	-0.7 ± 0.4	0.071
Dist. RD of SB – Dia. of SB balloon, mm	-0.3 ± 0.4	-0.2 ± 0.4	0.096	-0.2 ± 0.4	-0.2 ± 0.4	0.84
NC balloon for MB	9 (50.0)	89 (57.1)	0.57	2 (33.3)	96 (57.1)	0.41
NC balloon for SB	0	20 (12.8)	0.23	0	20 (11.9)	1.00
Pressure applied toward MB, atm	8.9 ± 3.0	9.8 ± 2.9	0.25	9.3 ± 1.0	9.7 ± 2.9	0.76
Pressure applied toward SB, atm	8.2 ± 2.3	9.2 ± 2.9	0.13	8.5 ± 1.8	9.2 ± 2.9	0.58
Total pressure applied, atm	17.1 ± 4.7	19.0 ± 4.9	0.12	17.8 ± 1.3	18.9 ± 5.0	0.15

FKB used in 2-stent Technique

Variables	MB restenosis			SB restenosis		
	+	-	P	+	-	P
MB restenosis	(N=6)	(N=181)		(N=8)	(N=179)	
Position of overlapping segment			0.12			1.00
a	2 (33.3)	129 (71.3)		6 (75.0)	125 (69.8)	
b	3 (50.0)	38 (21.0)		2 (25.0)	39 (21.8)	
c	1 (16.7)	9 (5.0)		0	10 (5.6)	
d	0	5 (2.8)		0	5 (2.8)	
Arrangement of balloons			0.72			1.00
a	0	12 (6.6)		0	12 (6.7)	
b	1 (16.7)	22 (12.2)		1 (12.5)	22 (12.3)	
c	5 (83.3)	147 (81.2)		7 (87.5)	145 (81.0)	

FKB used in 2-stent Technique

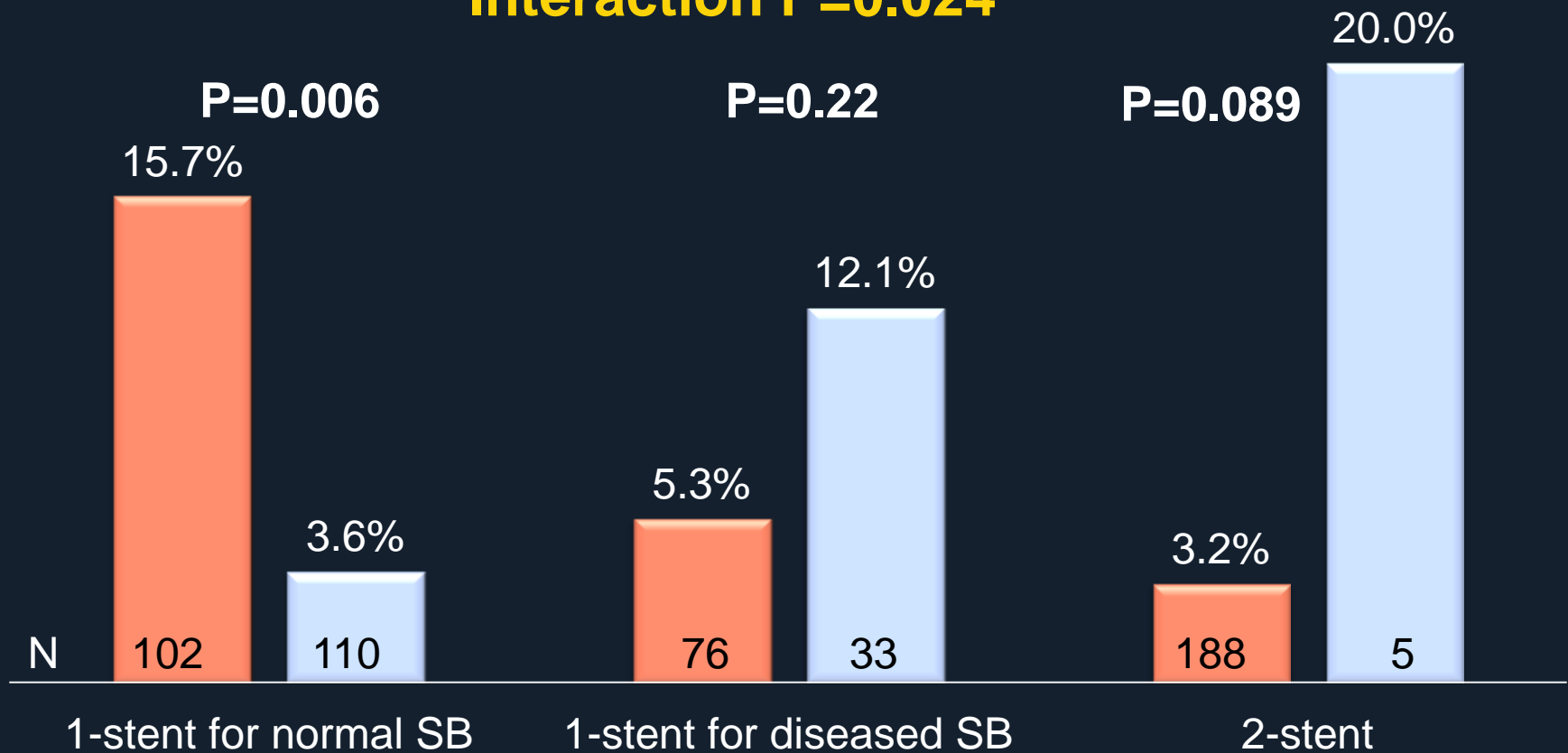
Variables	MB restenosis			SB restenosis		
	+	-	P	+	-	P
MB restenosis	(N=6)	(N=181)		(N=8)	(N=179)	
Sequential balloon dilation	5 (83.3)	158 (87.3)	0.57	6 (75.0)	157 (87.7)	0.27
SB-first dilation	3 (60.0)	101 (63.9)	1.00	4 (66.7)	100 (63.7)	1.00
Prox. RD of MB – Estimated dia. of 2 balloons	-0.8 ± 0.4	-0.7 ± 0.8	0.73	-0.6 ± 0.5	-0.7 ± 0.8	0.70
Dist. RD of MB – dia. of MB balloon	-1.0 ± 0.4	-0.7 ± 0.4	0.086	-0.8 ± 0.2	-0.7 ± 0.4	0.33
Dist. RD of SB – Dia. of SB balloon	-0.6 ± 0.3	-0.5 ± 0.3	0.43	-0.4 ± 0.3	-0.5 ± 0.3	0.92
NC balloon for MB	2 (33.3)	114 (63.0)	0.20	4 (50.0)	112 (62.6)	0.48
NC balloon for SB	1 (16.7)	92 (50.8)	0.21	4 (50.0)	89 (49.7)	1.00
Pressure applied toward MB, atm	9.8 ± 4.5	10.6 ± 3.4	0.57	9.9 ± 2.5	10.6 ± 3.4	0.54
Pressure applied toward SB, atm	8.8 ± 3.4	10.8 ± 3.2	0.13	10.6 ± 4.1	10.8 ± 3.2	0.89
Total pressure applied, atm	18.7 ± 7.6	21.5 ± 6.0	0.26	20.5 ± 6.1	21.4 ± 6.1	0.67

As-treated Groups

MB Restenosis Rate

■ FKB ■ no FKB

Interaction P=0.024

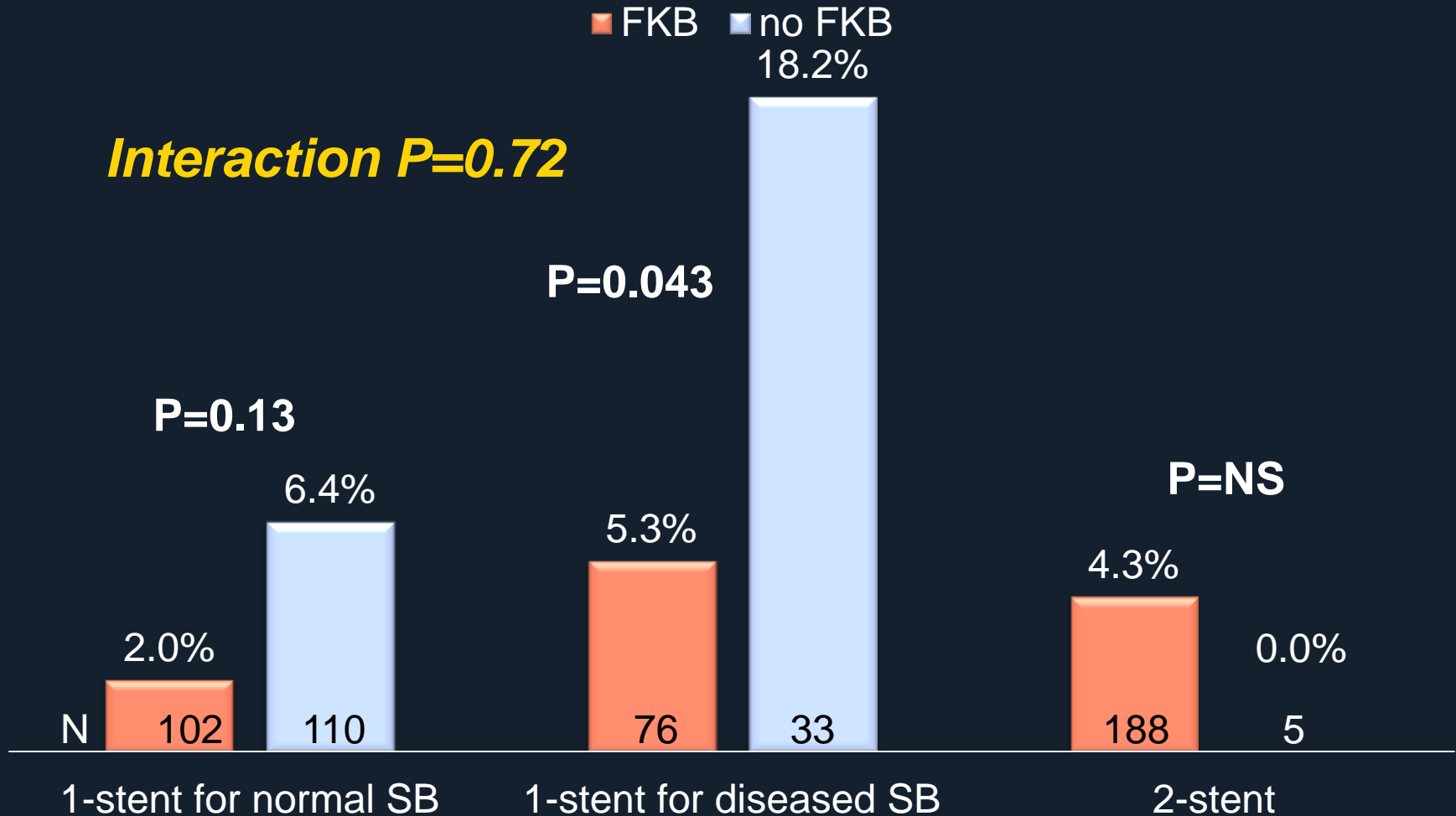


As-treated Groups

SB Restenosis Rate

■ FKB ■ no FKB
18.2%

Interaction P=0.72



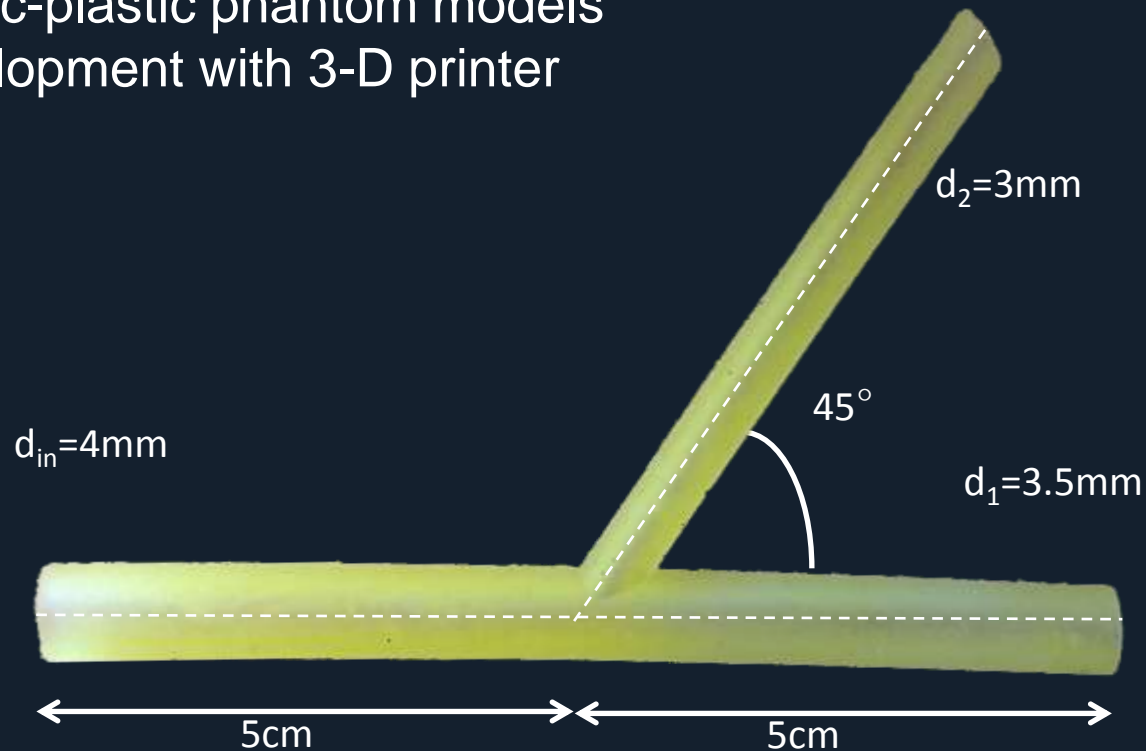
Predictor Analysis

- Final kissing balloon inflation (FKB)
 - Was an independent predictor of MB restenosis for bifurcations WITHOUT SB stenosis
 - Was likely to be a protective factor of SB restenosis for bifurcations WITH SB stenosis
 - But, balloon types or techniques used during FKB did not influence MB or SB restenosis
- IVUS-guidance was a protective factor of restenosis particularly for bifurcations with diseased SB

**Why FKB is not good, but potentially bad,
for main branch in bifurcation lesions with
normal SB?**

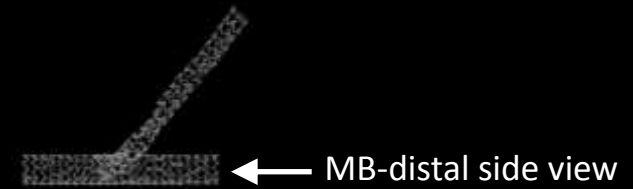
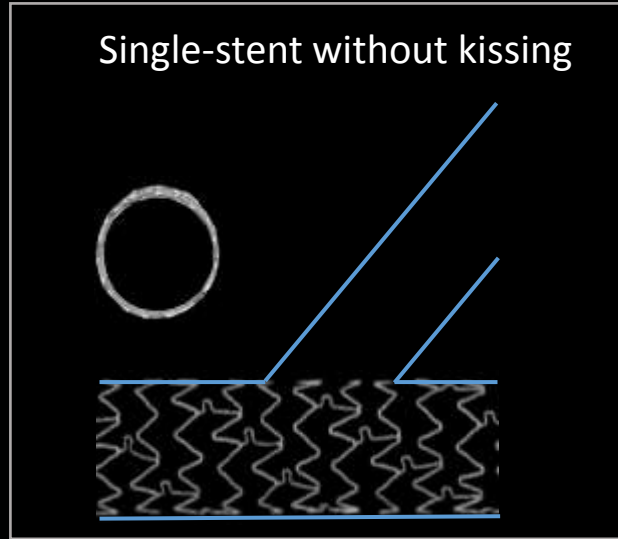
Bifurcation Phantom

- Acrylic-plastic phantom models
- Development with 3-D printer

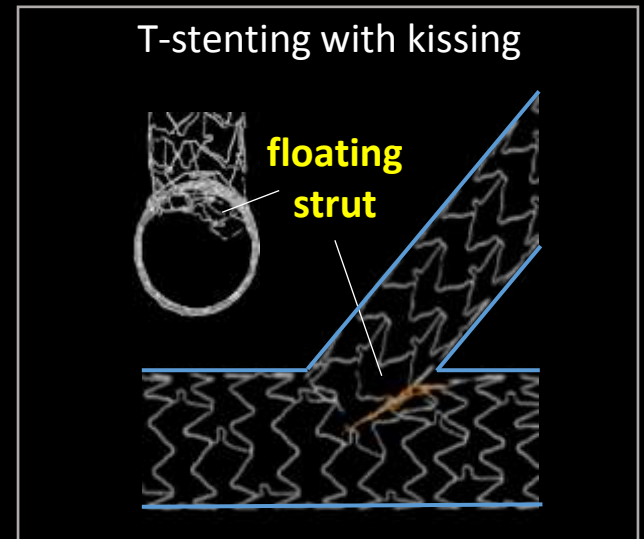
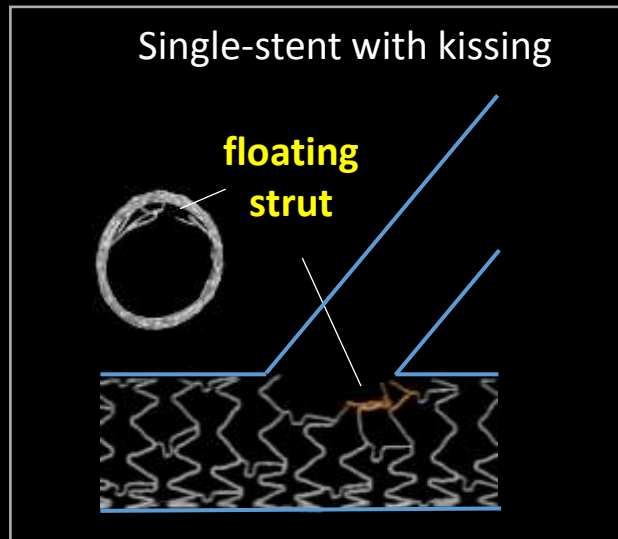


Floating Stent Strut after Final Kissing on Micro-CT

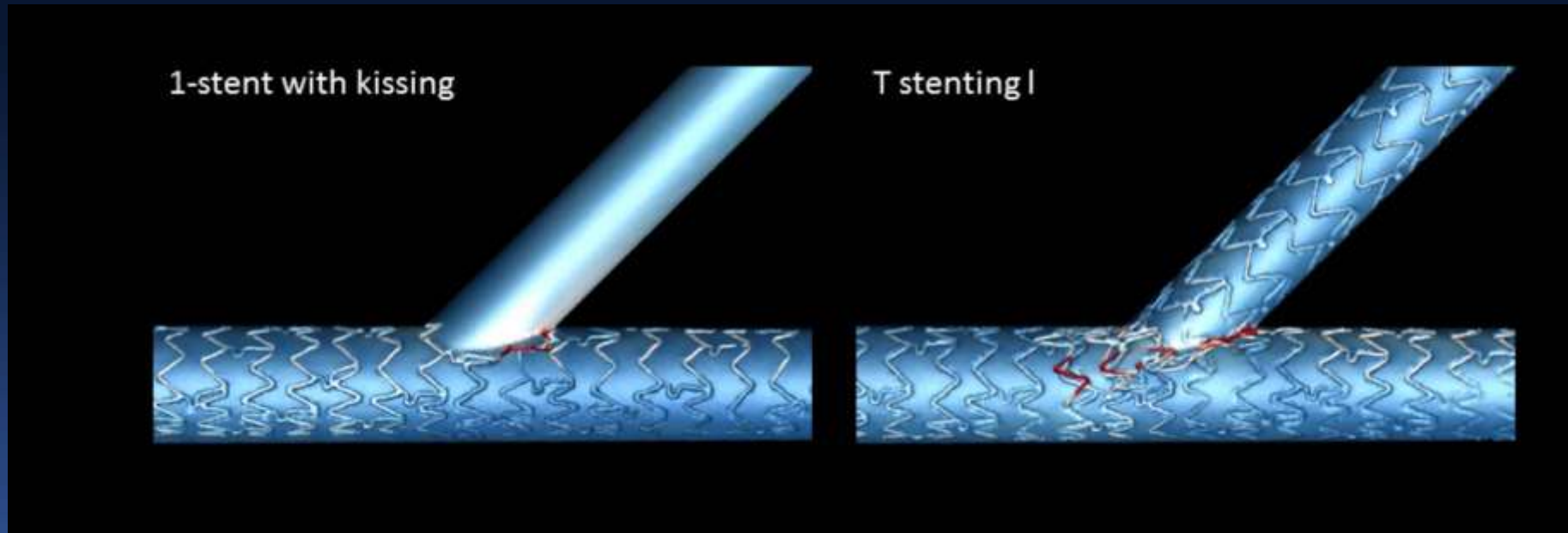
No kissing



Kissing



Time-averaged Wall Shear Stress



Impairment of flow pattern, indicated by shift of **low WSS to distal MB** due to **floating stent strut** made by FKB, may be one of mechanisms of higher rate of MB restenosis.

Floating stent	Total	Prox. MB	Dist. MB	SB	POC	Dist. MB (prox. half)
Yes	3.13	3.50	1.87	3.65	4.42	2.83
No	3.49	3.18	2.78	3.91	5.08	4.68
p value	0.093	0.285	0.001	0.493	0.358	0.001