Contemporary Thinking of Optimal Bifurcation PCI: Current State-of-the-Art

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RAMSAY GÉNÉRALE DE SANTÉ

Bifurcation is life

(and vice versa)

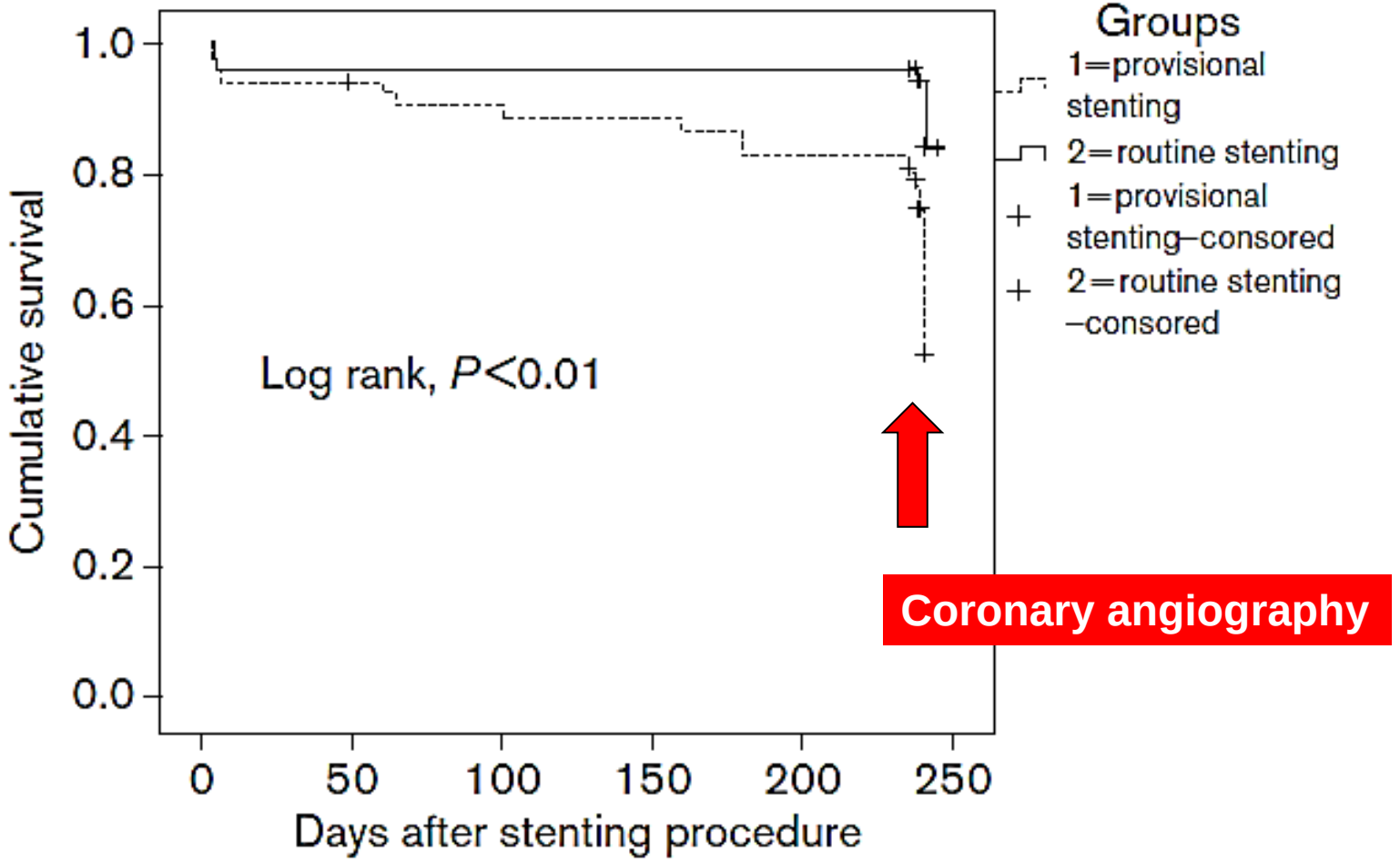
SB are over treated

All comers Provisional versus 2 stents randomized trials (n= 5)

	1 ary Endpoint	Syst. angio	Endpoint %	(Cardiac) death %	MI %	TVR %	TLR %	Rest.	ST
Nordic 2006 Circ.	C. death MI ST TVR 6 m	6 m	2.9 3.4	1 1	0 0.5	1.9 1.9			0.5 0
CACTUS 2009 Circ.	C. death MI ST TVR 6 m	8 m	15 15.8	0.5 0	8.6 10.7	6.2 6.8			Def 1.1 1.7
BBC 1 2010 Circ.	Death MI TVF 9 m	No	8 15.1	2 1	3.6 11.2	5.5 7.2			1 5
Lin 2010 Coron Art Dis	C. death MI ST TVR 8 m	8 m	38.9 11	0 0	1.9 1.9		26.9 6.4		1.9 0
PERFECT 2015 JACCi	% restenosis 2 branch	8 m	SB 8.3/3.9 MB 4.8/5.2	0.5 0.9	14.1 14.1	3.4 2.9	3.4 1.9	11 8.4	0 0.5

Choice of stenting strategy in true coronary artery bifurcation lesions

Survival rate-free from MACE



Lin, Coron Artery Dis 21:345–351

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Assessment of Clinical, Electrocardiographic, and Physiological Relevance of Diagonal Branch in Left Anterior Descending Coronary Artery Bifurcation Lesions

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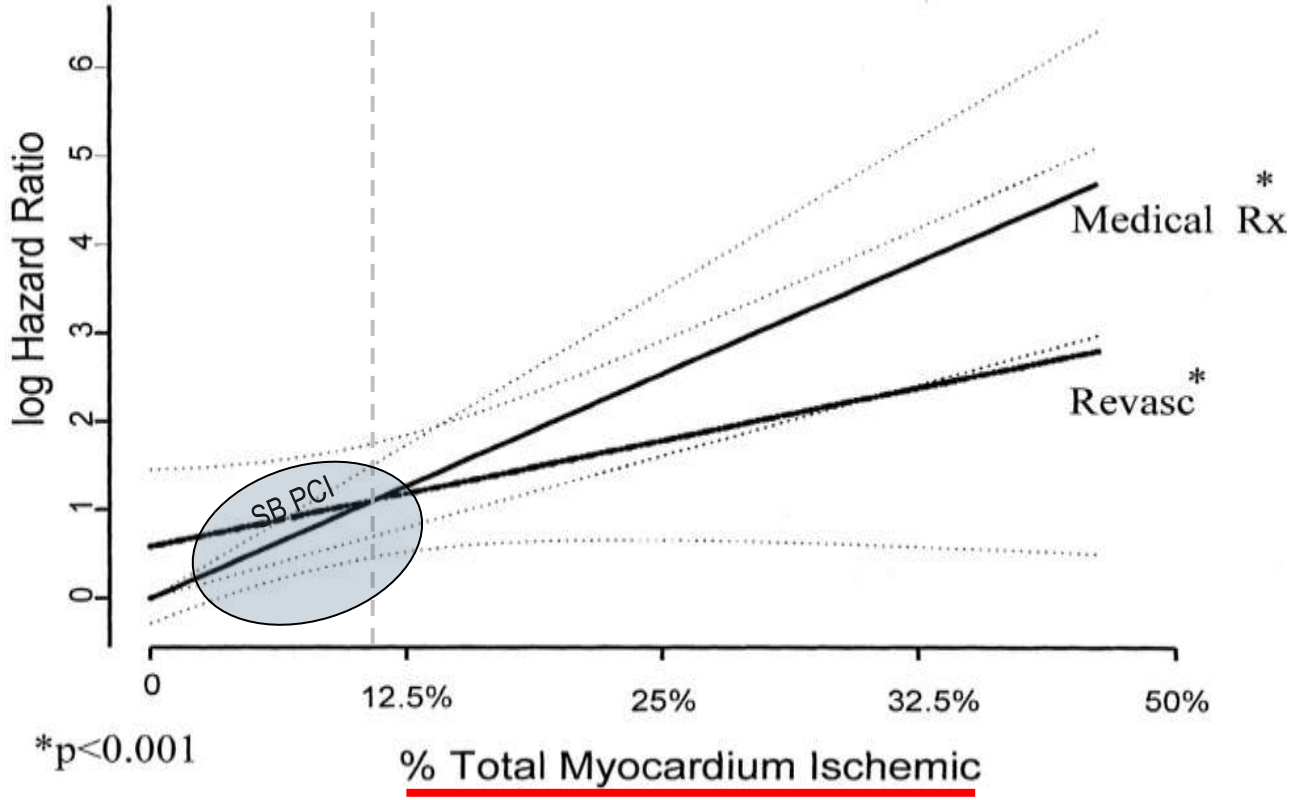
Revascularization for clinically insignificant side branches cannot be translated into clinical benefit and may even be harmful

What is a significant or (chronically) relevant SB ?

Which side branch deserves stent implantation?

- In terms of ischemia at risk, revascularization is better than medical treatment when moderate to severe ischemia exists. Therefore, it is important **to define the side branches that can cause ≥10% ischemia**



Hachamovitch, Circulation 2003

How to recognized a relevant SB ?

Identification of Coronary Artery Side Branch Supplying Myocardial Mass That May Benefit From Revascularization

Multivariate Generalized Estimating Equations Modeling for Prediction of %FMM >10%

	Odds Ratio ± SE	p Value
Side branch length ≥73 mm	41.9 ± 2.1	<0.001
Left main bifurcation	345.2 ± 2.9	<0.001
Reference vessel diameter ≥2.68 mm	1.5 ± 1.9	0.73
Left ventricular mass >104.8 g	1.4 ± 1.8	0.61
Fractional flow reserve <0.80	2.3 ± 2.2	0.24

Multivariate generalized estimating equations modeling was performed using optimal cutoffs of each parameters predicting FMM >10%. The respective c-statistics of left main bifurcation, reference vessel diameter >2.68 mm, left ventricular mass >104.8 g, and FFR <0.80 were 0.820, 0.734, 0.609, and 0.526 ($p < 0.05$, all)

HY Kim, J Am Coll Cardiol Intv 2017;10:571–81

SNuH score

Variables	Description	Score
Size (**S**)	Vessel diameter ≥ 2.5mm	1
Number (**Nu**)	Number of diagonal branches ≤ 2	1
Highest (**H**)	No branch below the target branch	1

Koo BK, et al., JACC Intv, 2012

Modified SNUH (mSNUH) score

Variables	Description	Score
Size	Vessel diameter ≥ 2.5mm	1
Number	Number of diagonal branches = 1	2
	Number of diagonal branches = 2	1
	Number of diagonal branches ≥ 3	0
Ubiety	Left dominant or Apical area reaching OM branch	-1*
Highest	No branch below the target branch in proximal to mid LAD	1

*If total score is 0, then -1 is not added (The lowest total score is 0

Courtesy of BK Koo

Non relevant SB = SB wire protection

Single stenting better in majority of cases

Randomized trials in true non LM bifurcation lesions w large SB (n=3)

	Centers	Stent	1 / 2	True bif. %	SB	2 stents technique	Crossover 1:2 / 2:1
DKCRUSH-II 2011 JACC	7	Excel	185 / 185	100 / 100	>2.5, long L.	DK crush	28.6% / -
Nordic-Baltic IV 2013	16	Cypher Xience	221 / 229	100 / 100	>2.75	Culotte, …	**3.7% / 4%**
EBC 2 2015	20	Nobori	103 / 97	100 / 100	> 2.5, long L.	Culotte	16% / 3%

Randomized trials in true non LM bifurcation lesions w large SB (n=3)

	Centers	Stent	1 / 2	SB stenosis	SB	2 stents technique	Crossover 1:2 / 2:1
DKCRUSH-II 2011 JACC	7	Excel	185 / 185	**63% / 63%**	>2.5, long L.	DK crush	28.6% / -
Nordic-Baltic IV 2013	16	Cypher Xience	221 / 229	**44% / 47%**	>2.75	Culotte, …	3.7% / 4%
EBC 2 2015	20	Nobori	103 / 97	**? / ?**	> 2.5	Culotte	16% / 3%

Randomized trials in true non LM bifurcation lesions w large SB (n=3)

	Centers	Stent	1 / 2	True bif. %	SB QCA diameter	2 stents technique	Crossover 1:2 / 2:1
DKCRUSH-II 2011 JACC	7	Excel	185 / 185	100 / 100	**2.3 / 2.4**	DK crush	28.6% / -
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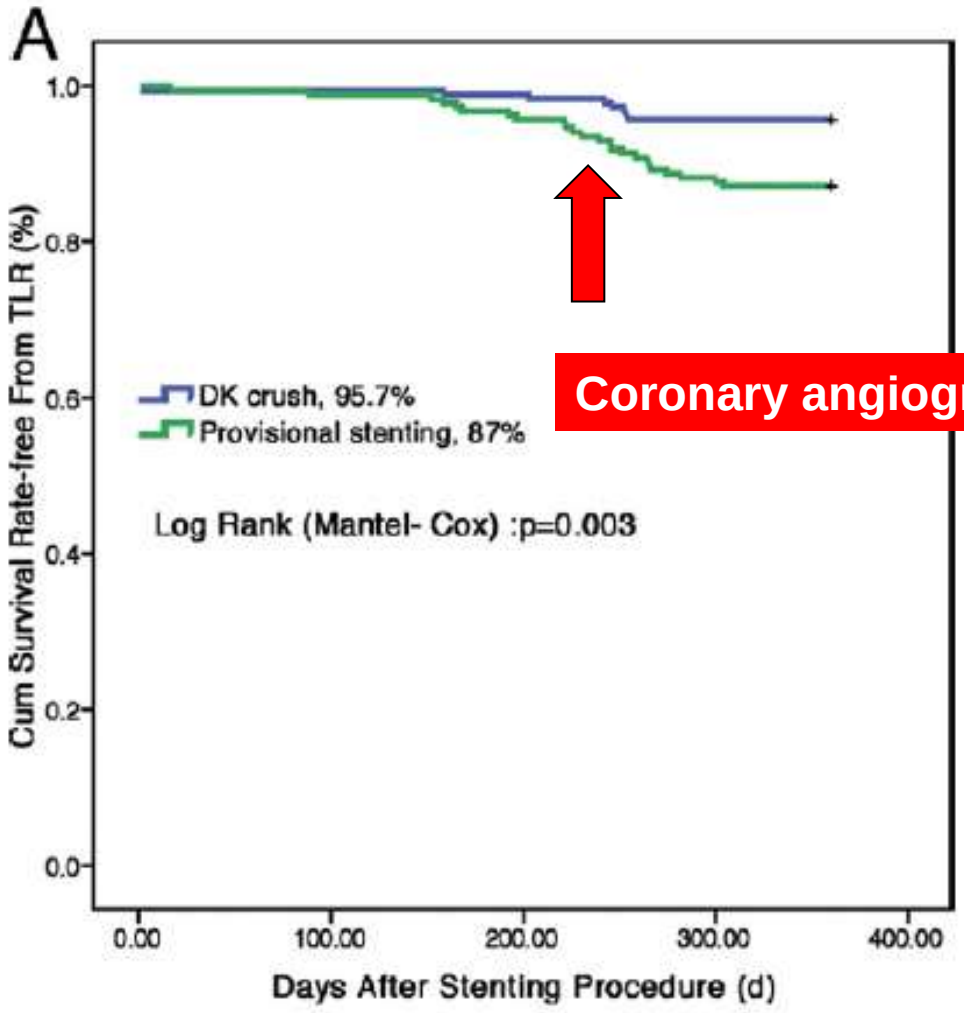
EBC 2 2015	20	Nobori	103 / 97	100 / 100	**? / ?**	Culotte	16% / 3%

Randomized study comparing Double Kissing Crush with Provisional Stenting for treatment of coronary bifurcation lesions: DK-CRUSH-II

Comparison of Survival Rate Free From TLR Between DK Crush and PS Groups

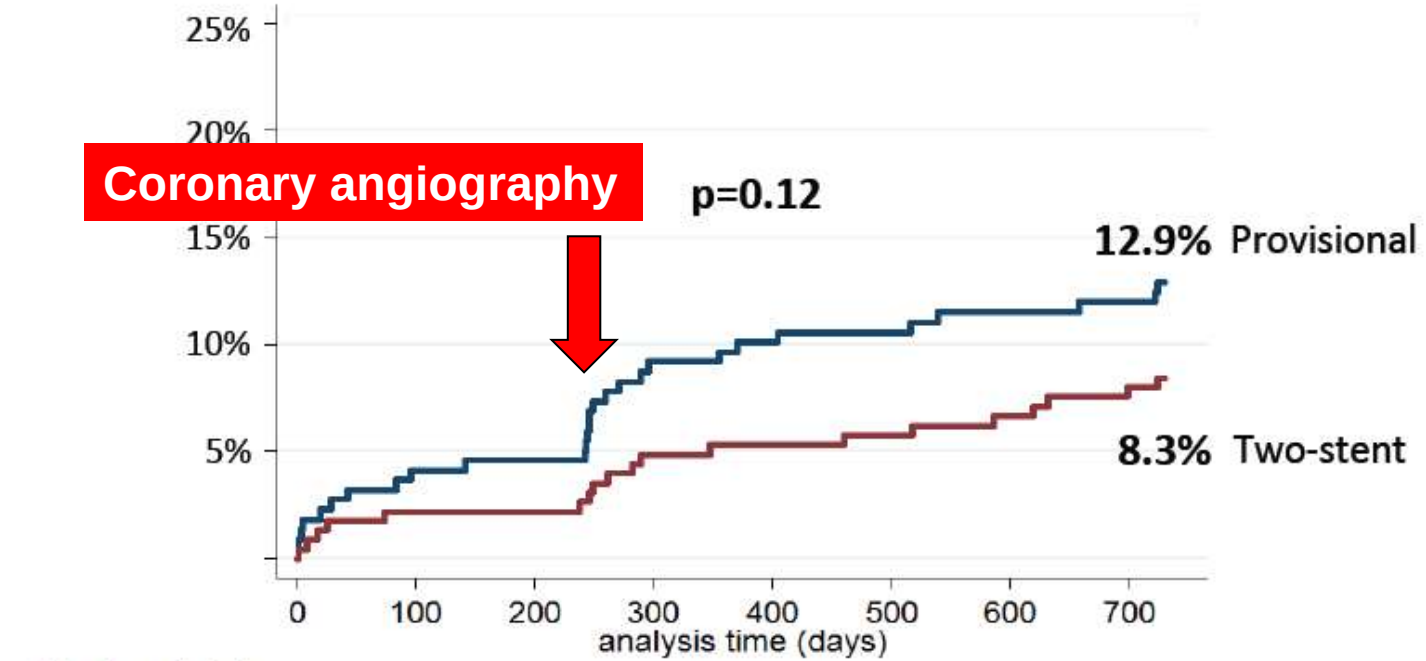


Coronary angiography

SL Chen J. Am. Coll. Cardiol. 2011;57;914-920

Nordic-Baltic Bifurcation Study IV

Two-year MACE



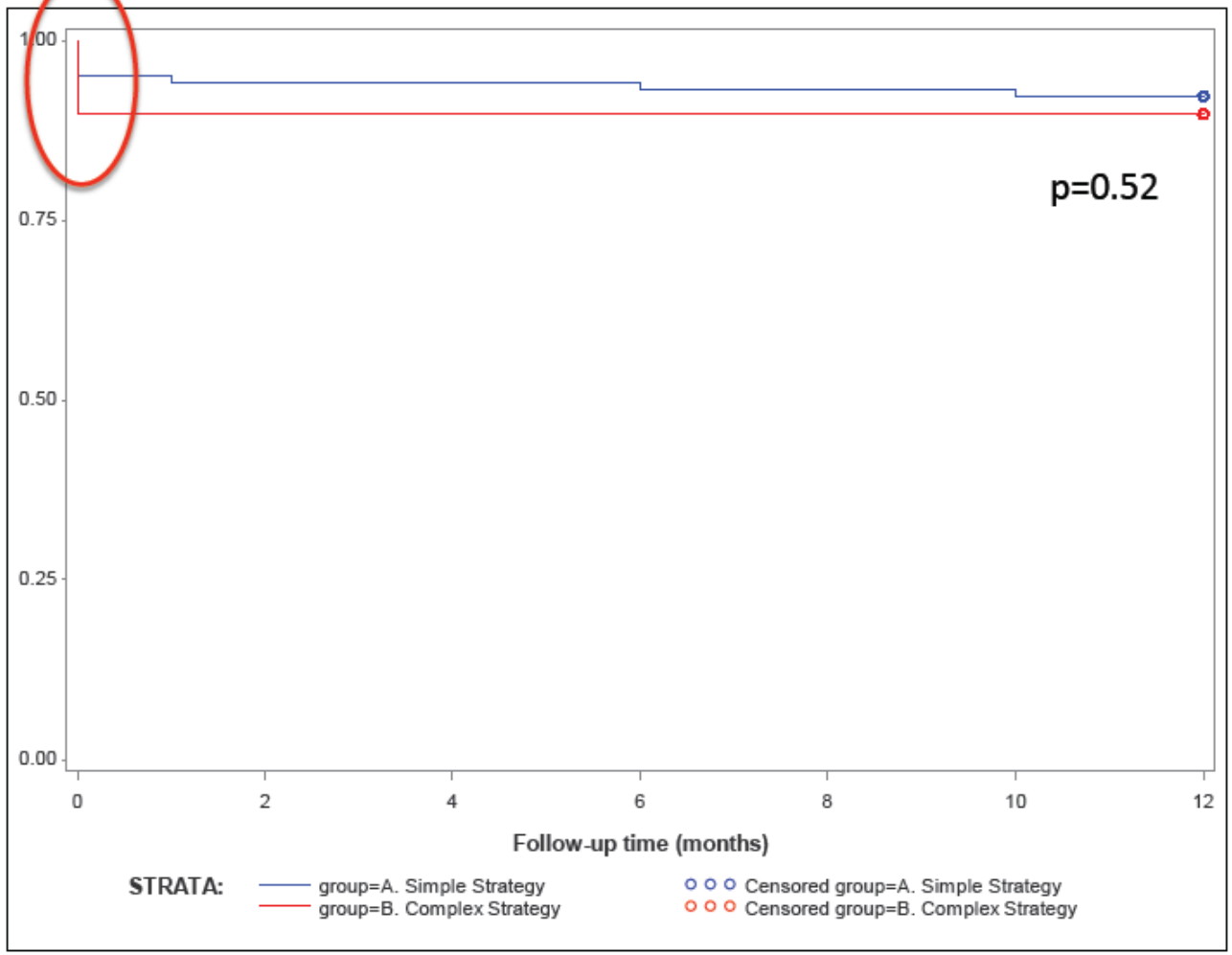
MACE: cardiac death, non-procedural myocardial infarction, target lesion revascularization and definite stent thrombosis

niels.holm@clin.au.dk

euro PCR 2015

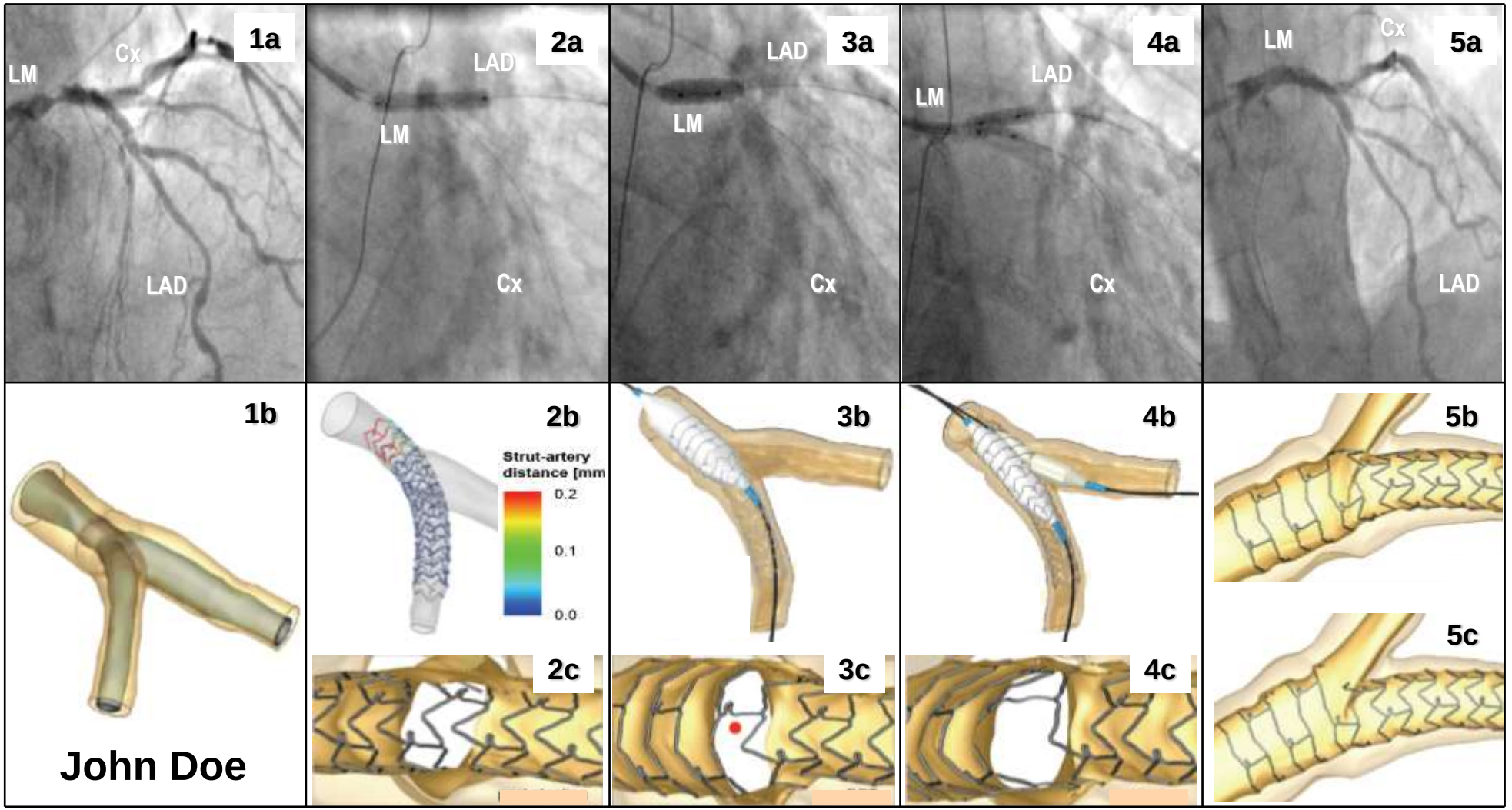
The EBC TWO Trial

12 M Outcome : Death, MI and TVR at 12



EBC 2012: stimulation era

Provisional stenting strategy



Peter mortier, Jolanda Wentzel, Gabriele Dubini, Yves Louvard

COBIS II POT Study: Clinical outcomes

- Patients with **SB diameter ≥ 2.5 mm in core-lab QCA (N=1,191)**
- Propensity score-matching population

	POT (n=204)	No POT (n=665)	HR (95% CI)	p value
MACE	**6 (2.9)**	**78 (11.7)**	**0.25 (0.11-0.60)**	**0.002**
All-cause death	7 (3.4)	25 (3.8)	0.97 (0.41-2.33)	0.95
Cardiac death	1 (0.5)	9 (1.4)	0.37 (0.05-2.97)	0.35
Myocardial infarction	0	12 (1.8)	-	-
Stent thrombosis	2 (1.0)	8 (1.2)	0.98 (0.20-4.77)	0.98
TLR	5 (2.5)	61 (9.2)	0.27 (0.10-0.69)	**0.006**
MV, proximal	**3 (1.5)**	**40 (6.0)**	**0.25 (0.07-0.82)**	**0.02**
MV, distal	**4 (2.0)**	**47 (7.1)**	**0.28 (0.10-0.80)**	**0.02**
SB	4 (2.0)	35 (5.3)	0.37 (0.13-1.09)	0.07
Both vessels	5 (2.5)	48 (7.2)	0.34 (0.13-0.88)	**0.03**

Preliminary analysis:, HC. Gwon at EBC 2016

Long-term Clinical outcomes of final KB in coronary bifurcation lesions treated with the 1-stent technique: results from the COBIS II registry

Clinical Outcomes in FKB Group Compared With Non-FKB Group in Propensity-Matched Population During FU Period

	FKB (n = 545)	Non-FKB (n = 545)	Unadjusted HR (95% CI)	p Value	Adjusted HR* (95% CI)	p Value
All-cause death	17 (3.1)	20 (3.7)	0.67 (0.30-1.48)	0.32	0.68 (0.28-1.63)	0.39
Cardiac death	3 (0.6)	8 (1.5)	0.43 (0.11-1.66)	0.22	0.50 (0.11-2.29)	0.37
MI	4 (0.7)	5 (0.9)	0.50 (0.09-2.73)	0.42	0.18 (0.01-20.36)	0.48
Stent thrombosis†	3 (0.6)	4 (0.7)	0.72 (0.16-3.23)	0.67	0.77 (0.17-3.45)	0.73
Target lesion revascularization	32 (5.9)	43 (7.9)	0.53 (0.30-0.94)	0.03	0.51 (0.28-0.91)	0.02
Main vessel	31 (5.7)	40 (7.3)	0.53 (0.30-0.96)	0.04	0.51 (0.28-0.93)	0.03
Side branch	12 (2.2)	18 (3.3)	0.57 (0.24-1.36)	0.21	0.57 (0.24-1.37)	0.21
Both vessels	23 (4.2)	38 (7.0)	0.47 (0.25-0.88)	0.02	0.47 (0.25-0.90)	0.02
MACE‡	37 (6.8)	53 (9.7)	0.54 (0.32-0.89)	0.02	0.50 (0.30-0.85)	0.01

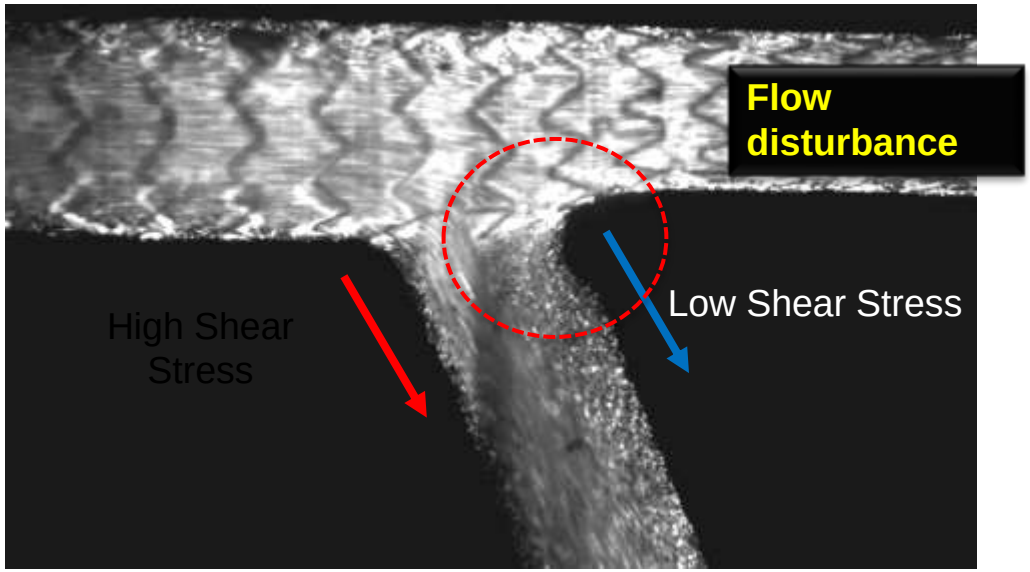
*Adjusted covariates include hypertension, history of coronary artery bypass graft, and distal RD of SB

CW Yu, J Am Coll Cardiol Intv 2015;8:1297–307

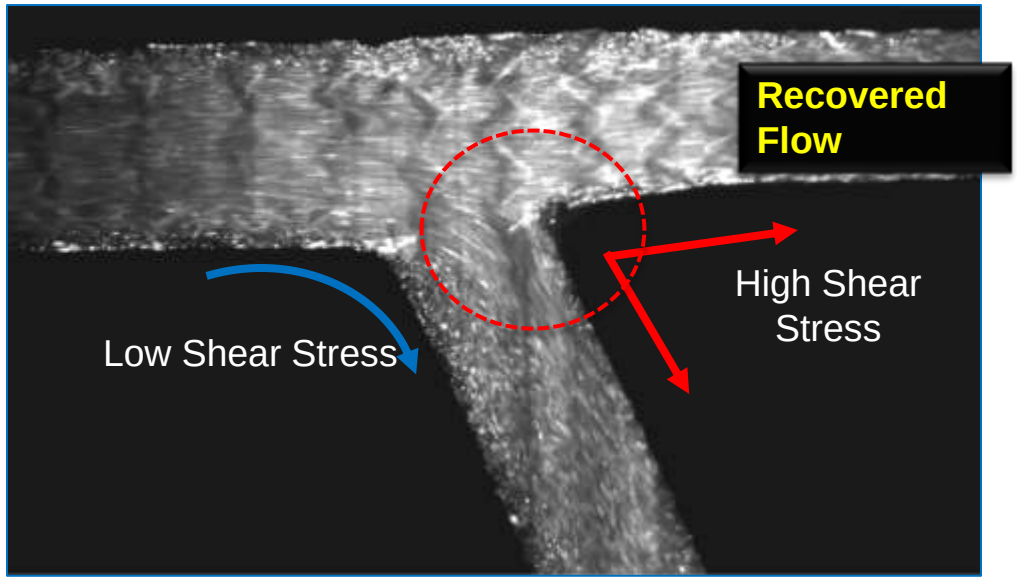
How to perform optimal Final Kissing?

- Optional for provisional, mandatory for complex techniques;
- Short & NC balloons, size according to distal reference;
- *Side* branch first (equal *or* alternate 12 atm vs. 4 atm);
- Simultaneous deflation;
- Longer inflation (at least 20-30 seconds);

Single stent: pre FKBI



Single stent: post FKBI



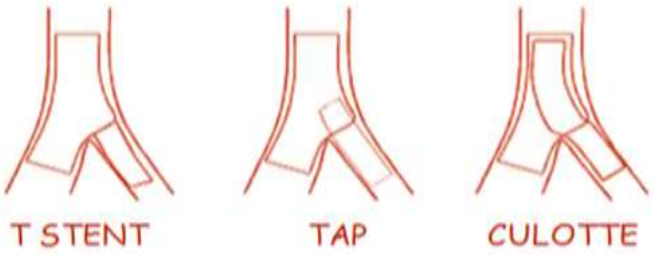
Courtesy of Y. Fujino

Main technical options for elective double stent implantation

"True" bifurcation lesion with an important SB > 5-10 mm lesion length

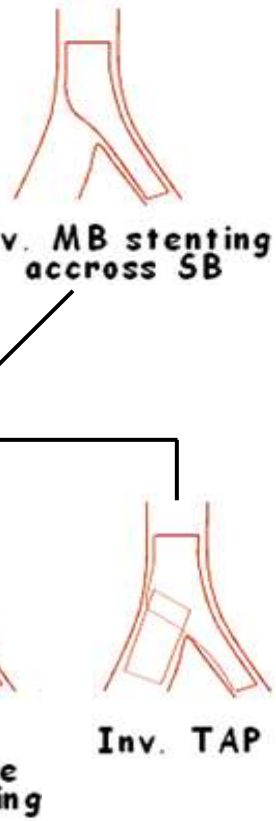
Low risk of loosing the SB after MB stenting

MB stenting followed by planned SB implantation



Major concerns regarding the SB after MB stenting

Mini DK-CRUSH



Always end with a Final Kiss !

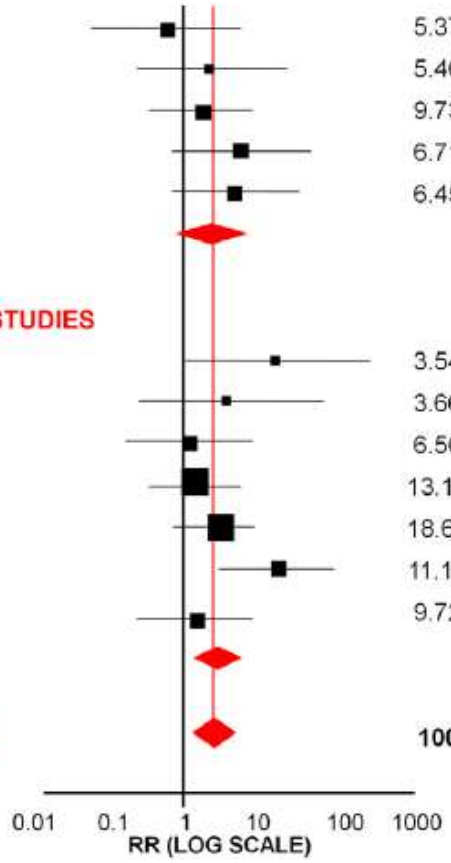
Courtesy of T. Lefevre

Mechanisms of stent thrombosis: strut / flow interactions

Late Thrombosis After 2 Versus 1 DES in the Treatment of Coronary Bifurcations. Meta-analysis of Randomized and Observational Studies

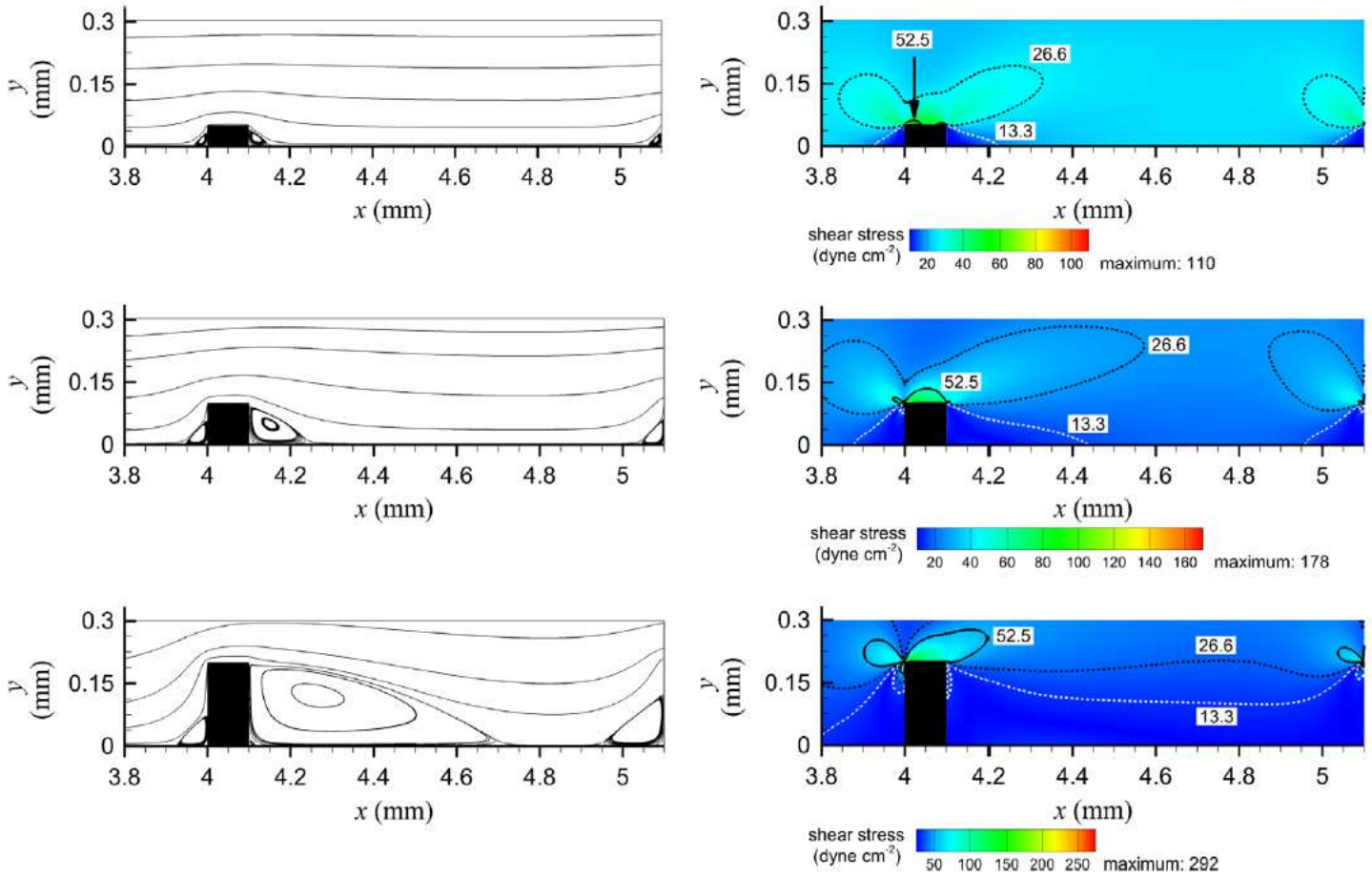
A DES Thrombosis

Study	Year	DDS	SDS	Weight*	RR (random) 95% CI
RANDOMIZED, CONTROLLED TRIALS					
NORDIC	2008	1/196	2/199	5.37%	0.50 (0.04–5.55)
Ferenc et al.	2008	2/101	1/101	5.40%	2.00 (0.18–21.71)
CACTUS	2009	3/177	2/173	9.73%	1.46 (0.24–8.66)
BBC-ONE	2010	5/249	1/248	6.71%	4.97 (0.58–42.31)
DK-CRUSH-II	2011	4/185	1/185	6.45%	4.00 (0.45–35.44)
META-ANALYSIS		**15/908**	**7/906**		**2.01 (0.77–5.23)**
Cochrane Q: 2.46 (p: 0.651) I^2: 0%					
NONRANDOMIZED, OBSERVATIONAL STUDIES					
Ge et al.	2007	3/57	0/117	3.54%	14.24 (0.74–271.13)
Di Mario et al.	2007	4/109	0/38	3.66%	3.19 (0.17–57.92)
ARTS II	2007	1/61	4/263	6.50%	1.07 (0.12–9.47)
COBIS	2010	2/292	9/1376	13.17%	1.04 (0.22–4.82)
J-CYPHER	2011	3/263	10/1870	18.64%	2.13 (0.59–7.70)
J-PMS	2011	4/37	2/263	11.12%	14.21 (2.69–74.92)
Assali et al.	2011	2/141	3/260	9.72%	1.23 (0.21–7.27)
META-ANALYSIS		**19/960**	**27/4187**		**2.55 (1.13–5.78)**
Cochrane Q: 8.06 (p: 0.234) I^2: 25.57%					
META-ANALYSIS		**34/1868**	**35/5093**	**100%**	**2.31 (1.33–4.03)**
Cochrane Q: 10.65 (p: 0.473) I^2: 0%					



Zimarino J Am Coll Cardiol Intv 2013

Simulation of the microscopic process during initiation of stent thrombosis



Streamlines (left panels) and shear stress contours (right panels) for different strut heights,including 50 (top panels), 100 (middle panels), and 200 mm (bottom panels)

J. Chesnutt, Computers in Biology and Medicine 56 (2015) 182–191

Pathological Findings at Bifurcation Lesions: Impact of Flow Distribution on Atherosclerosis and Arterial Healing After Stent Implantation

	DES (12 Lesions, 17 Stents)		
	Flow Divider	Lateral	p Value
Neointimal thickness (mm)	0.07 (0.03-0.15)	0.17 (0.09-0.23)	0.001
Fibrin deposition (% struts)	60 (21-67)	17 (0-55)	0.01
Uncovered struts (% struts)	40 (16-76)	0 (0-15)	0.001

Nakazawa, Virmani, J Am Coll Cardiol 2010;55:1679–87

Correlates and outcomes of late and very late DES thrombosis: results from DESERT

Clinical and Angiographic Correlates of Late/Very Late Stent Thrombosis

Variable	Clinical, OR (95% CI)	Angiographic	Combined, OR (95% CI)
Age	**0.964 (0.95-0.98)**	*	**0.793 (0.96-0.99)**
Hypertension	0.757 (0.51-1.12)	*	0.863 (0.56-1.34)
Body mass index	0.979 (0.95-1.01)	*	0.981 (0.95-1.01)
ACS/NSTEMI	1.084 (0.70-1.67)	*	0.831 (0.54-1.28)
Left anterior descending lesion	1.107 (0.77-1.59)	**1.671 (1.21-2.32)**	1.302 (0.87-1.96)
Current smoker	**1.890 (1.26-2.85)**	*	**1.633 (1.05-2.53)**
STEMI or thrombus (QCA)	1.059 (0.62-1.80)	**1.486 (1.03, 2.14)**	1.062 (0.66-1.71)
African American	**2.346 (1.21-4.54)**	*	1.612 (0.65-3.99)
Diabetes	0.915 (0.60-1.40)	*	1.021 (0.65-1.60)
Renal insufficiency	1.019 (0.50-2.09)	*	*
No. of diseased vessels	**1.313 (1.05-1.65)**	*	**1.712 (1.32-2.22)**
Type C lesion (QCA)	*	0.939 (0.54-1.63)	**2.188 (1.38-3.47)**
Final reference vessel diameter, mm	*	1.190 (0.77-1.85)	1.436 (0.84-2.44)
Acute gain, mm	*	0.982 (0.64-1.51)	1.013 (0.64-1.61)
Final in-stent diameter stenosis	*	**1.021 (1.00-1.04)**	1.014 (0.99-1.04)
Total stented length	**1.015 (1.00-1.03)**	1.022 (1.00-1.05)	**0.977 (0.97-0.99)**
Bypass graft lesion	**3.306 (1.18-9.27)**	**3.900 (1.55-9.84)**	1.997 (0.60-6.70)
Lesion length (QCA)	*	0.999 (0.97-1.03)	*
Overlapping stents	**1.757 (1.18-2.61)**	*	**2.220 (1.34-3.69)**

Waksman, J Am Coll Cardiol Intv 2014;7:1093–102

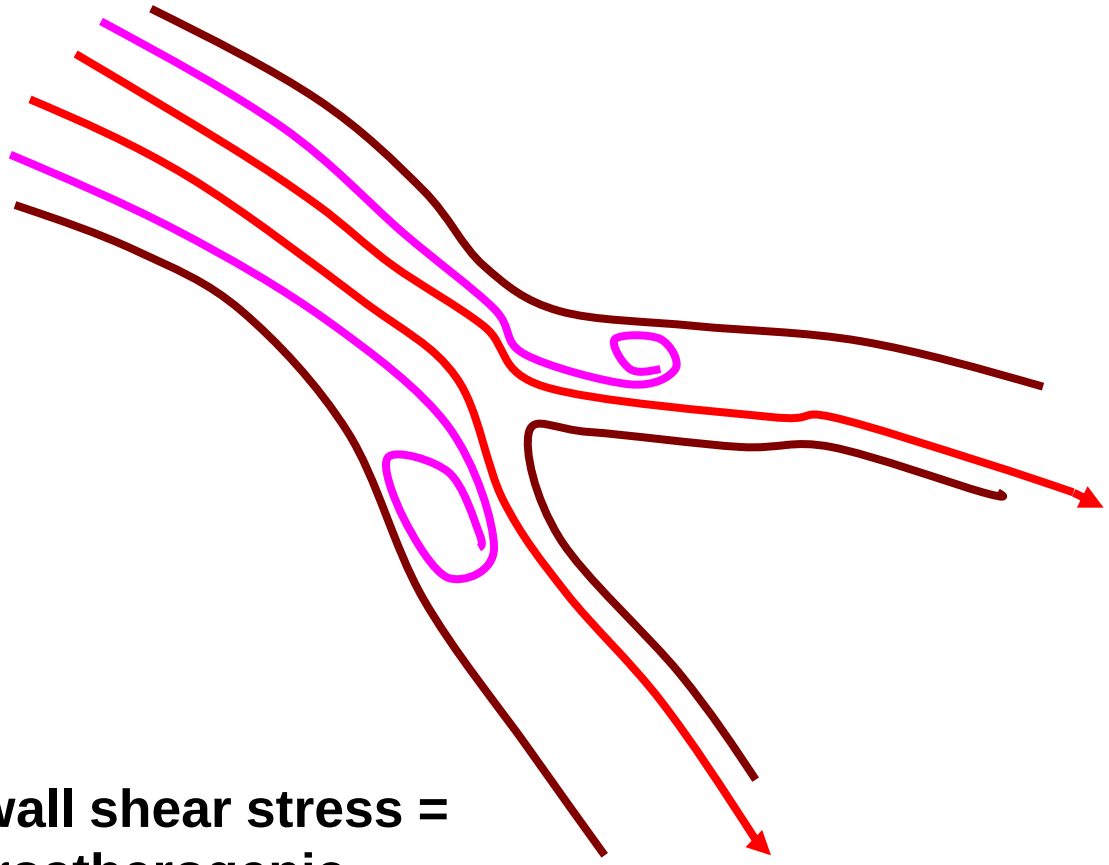
- Minimize overlapping (carena…)
- Stent deployment
- Wall apposition
- Imaging

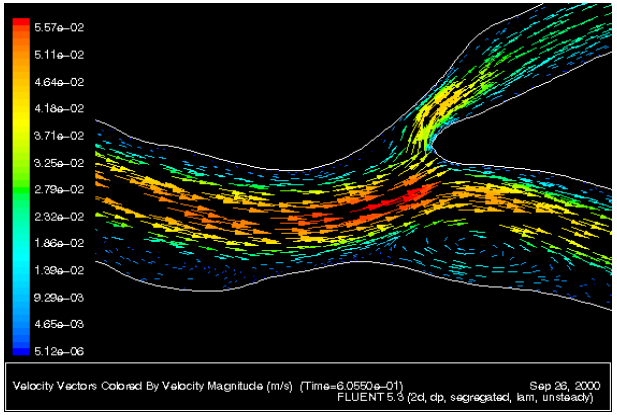
What are the objectives of bifurcation stenting ?

Objectives of bifurcation lesion treatment ?

- Suppress ischemia
- Suppress stenosis
- Obtain « protective » diameters
- On the long term: prevent neo atheroma?

Flow Patterns and Spatial Distribution of Atherosclerotic Lesions in Human Coronary Arteries





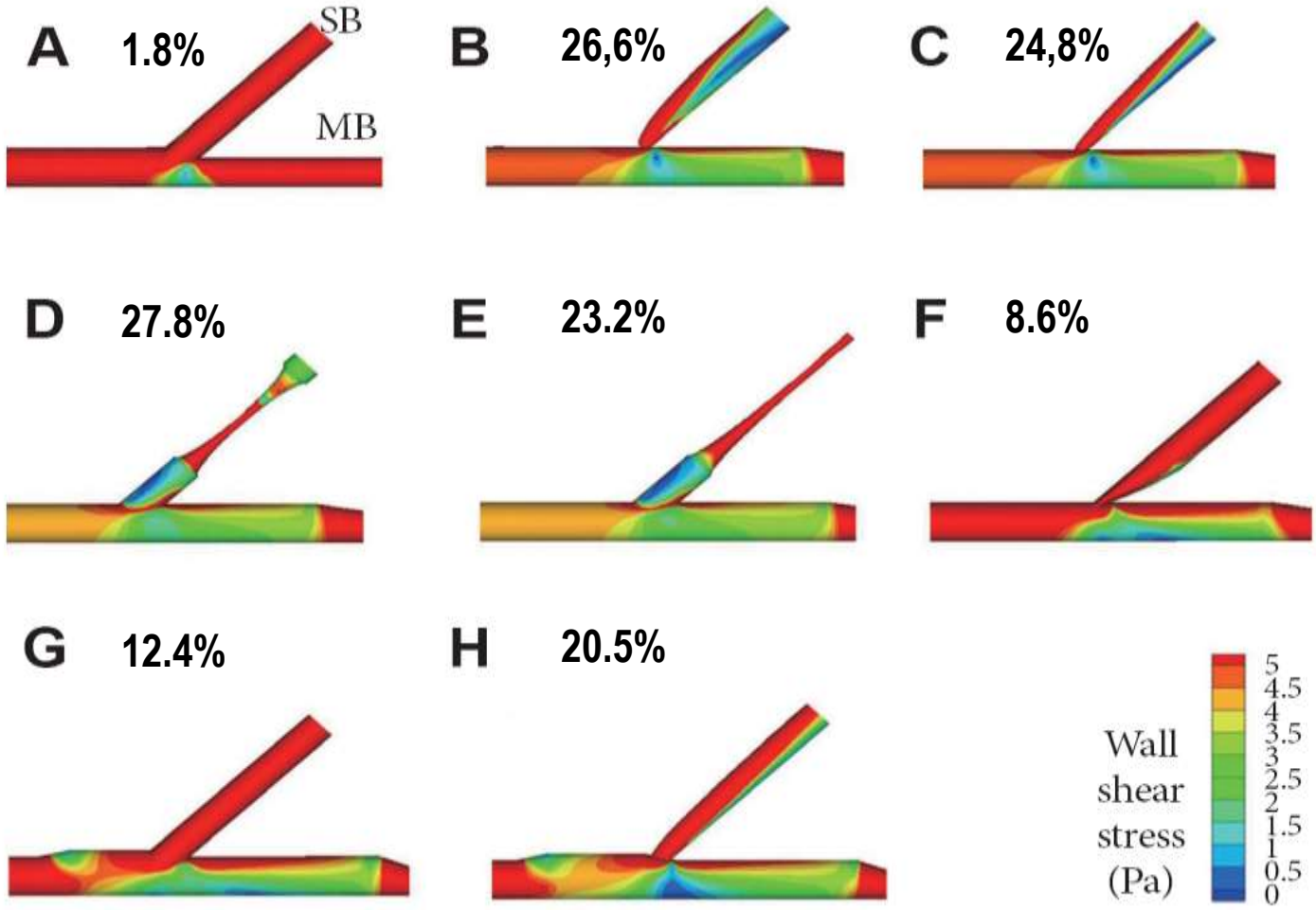
Low wall shear stress = proatherogenic

Asakura, Circulation Research 1990; 66:1045-1066

From Virmani, Chatzizisis

Evaluation of Local Flow Conditions in Jailed Side Branch Lesions Using Computational Fluid Dynamics

Area of low WSS (<4 Pa) in 8-computational bifurcation models



SH. Na, BK. Koo, Korean Circ J 2011;41:91-96

Bifurcation lesion treatment principles

1. **Protection only for non clinically relevant SB (non left main, length, diameter …)**
2. **Limit the number of stents (provisional, FFR)**
3. **Single stent layer, well apposed**
4. **Respect the original anatomy**