Gap Between Randomization Trial and Real Practice

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Disclosures of Conflict of Interest

Speaker's name: Andrejs Erglis

☑ **I have the following** potential conflicts of interest to report:

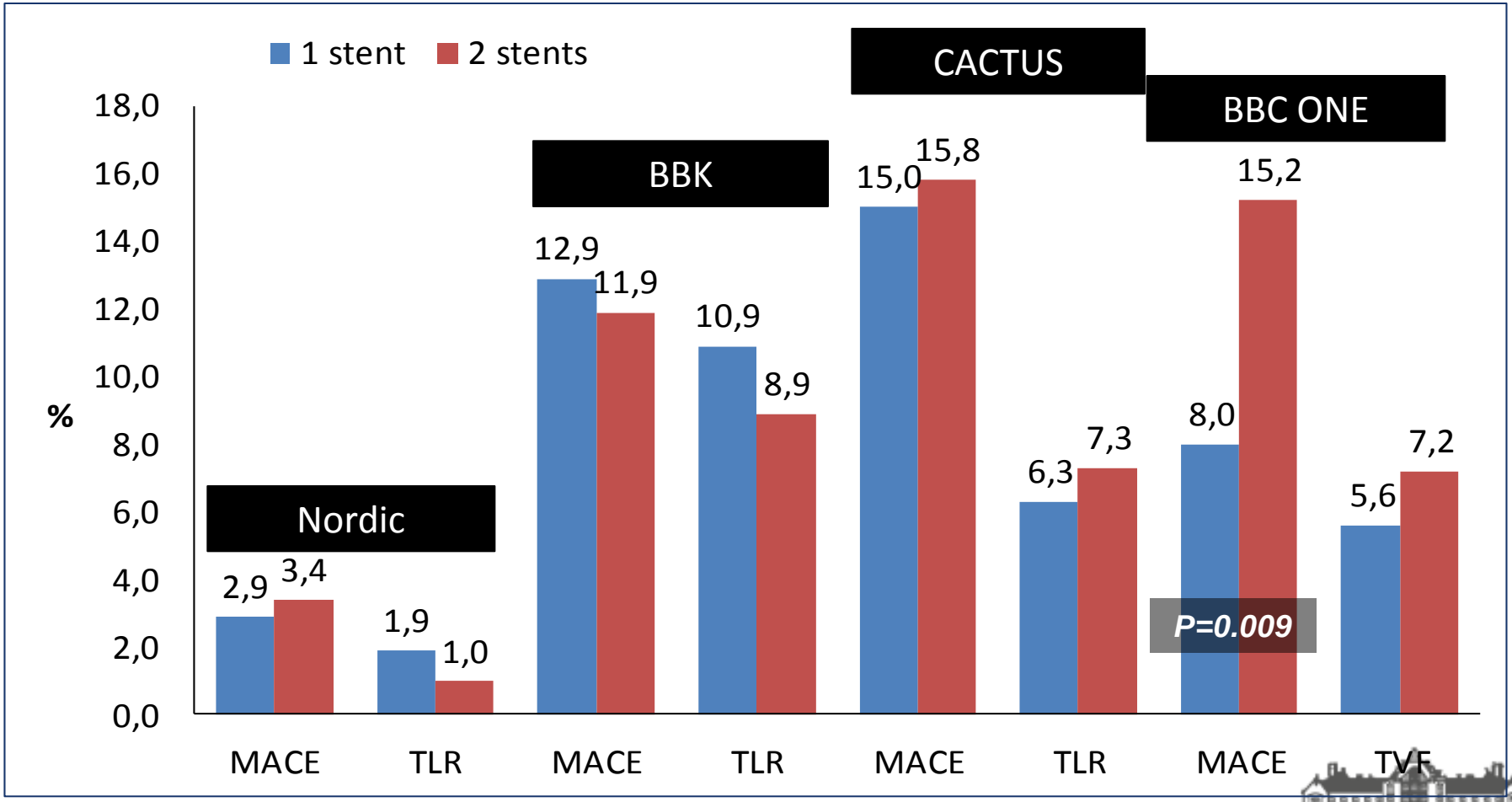
☑ Research contracts (Abbott Vascular, Boston Scientific)
☑ Consulting, Speakers Bureau (Abbott Vascular, Boston Scientific, Medtronic, Cordis J&J, Biosensors)
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☐ **I do not have any potential conflict of interest**

Introduction

- There is marked variability in the morphology of coronary bifurcation lesions.
- The variability includes vessel size (MB and SB), lesion location, eccentricity, length, morphology, and SB takeoff angle.
- The research methodology used in the randomized clinical trials does not simulate all the questions asked in real clinical practice

MACE and TLR in randomized clinical trials (RCT)



Steigen TK et al. Circulation. 2006;114:1955-1961 Ferenc M et al. Eur Heart J 2008; 29: 2859–2867
Colombo A et al. Circulation. 2009;119:71–78 Hildick-Smith D et al. Circulation. 2010;121:1235-1243

RCT: Keep it simple!

- There is no statistical difference in main vessel (MV) or side branch (SB) restenosis or target vessel revascualrization (TVR) between provisional stenting and elective double stenting.
- There is no statistical difference in stent thrombosis between provisional stenting and elective double stenting
- The NORDIC and BBC ONE trials showed increased procedure time and contrast use with elective double stenting compared to provisional stenting while the CACTUS and BBK trials did not.
- The NORDIC and BBC ONE trials showed higher rate of post-procedure cardiac biomarker elevation in the elective double stenting arm but no difference in MI at follow-up.

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Lesions treated in RCT

Study	NORDIC[7]		BBK[8]		CACTUS[9]		BBC-ONE[10]	
	Elective ($N = 206$)	Provisional ($N = 207$)	Elective ($N = 101$)	Provisional ($N = 101$)	Elective ($N = 177$)	Provisional ($N = 173$)	Elective ($N = 250$)	Provisional ($N = 250$)
Bifurcation morphology								
Medina 1,1,1	NA		30.7%	35.6%	75%		60%	60%
No SB involvement	NA		26%	27%	6%		15%	18%
Bifurcation angle (degrees)	<70		47.6 + 17.6	49.9 + 59.9	NA		<60 (87%)	<60 (85%)
Main vessel								
Reference (mm)	3.3 ± 0.41	3.3 ± 0.41	3.08 ± 0.40	3.08 ± 38	2.80 ± 0.3	2.74 ± 0.35	NA	NA
Lesion length (mm)	7.5 ± 7.5	8 ± 8.3	21.7±7.5	20.9 ± 8.2	15.8 ± 8.7	14.7 ± 8.2	NA	NA
Diameter stenosis (%)	50 ± 25	52 ± 24	54.9 ± 24.3	54.9 ± 24.3	68 ± 12	69 ± 12	NA[a]	NA*a*
Side branch								
Reference (mm)	2.6 ± 0.3	2.6 ± 0.4	2.39 ±0.31	2.38 ± 0.37	2.3 ± 0.31	2.16 ± 0.33	NA	NA
Lesion length (mm)	6.4 ± 4.7	6.0 ± 4.8	10.4 ± 4.1	9.9 ± 4.2	5.9 ± 4.7	5.7 ± 4.2	NA	NA
Diameter stenosis (%)	47 ± 26	46 ± 2	53.1 ± 23.5	54.4 ± 22.3	63 ± 12	61 ± 13	NA[a]	NA[a]

Issam D. Moussa. Catheterization and Cardiovascular Interventions 77:537–545 (2011)

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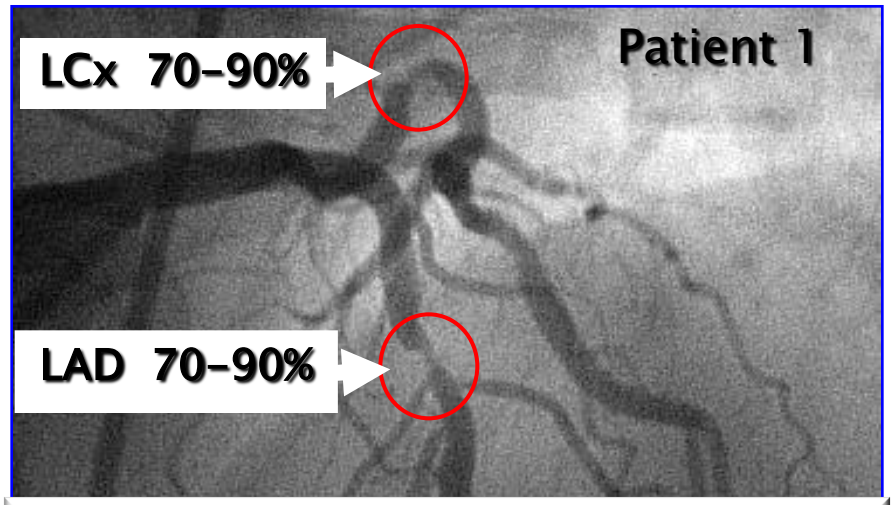
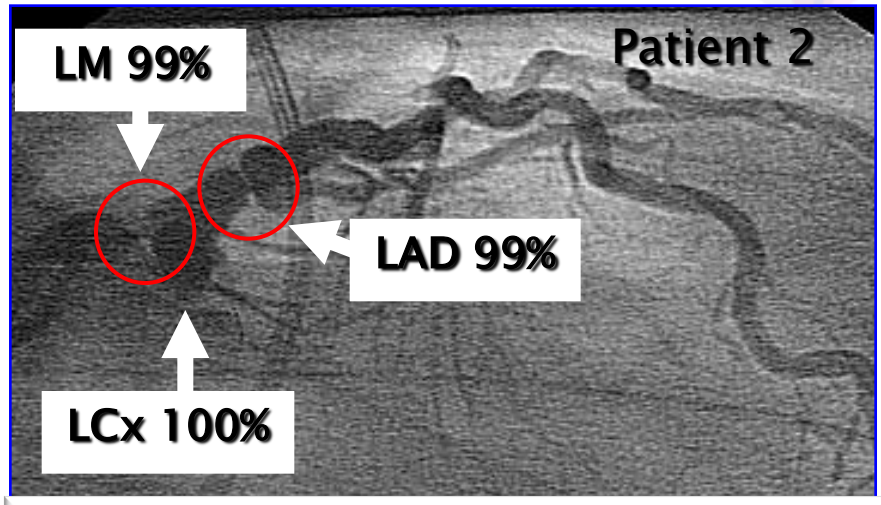
Questions before making a decision how to treat?

- How large is the SB (diameter, vessel length, and myocardial territory supplied)
- Is the SB ostium diseased? If yes, what is the severity and length of the lesion?
- Is there severe disease in the SB beyond the ostium?
- What is the angle of the SB takeoff? Is it difficult to wire/rewire?
- What is the severity and distribution of the MV lesion?
- What will happen to the SB after MV stenting (mild or significant compromise or occlusion)?
- What are the clinical consequences of SB occlusion (depends on the territory supplied)?

Issam D. Moussa. Catheterization and Cardiovascular Interventions 77:537–545 (2011)

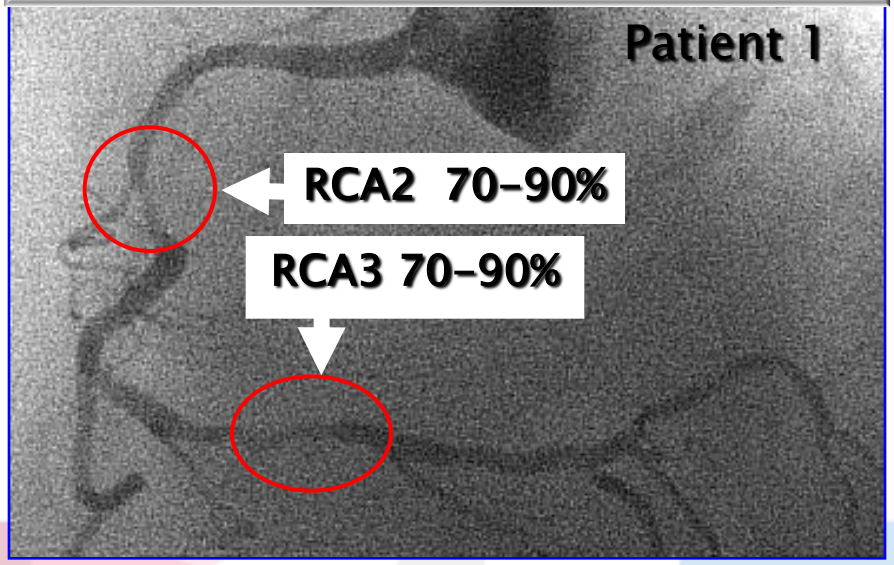
SYNTAX score: 3 vessel disease and 3 vessel disease

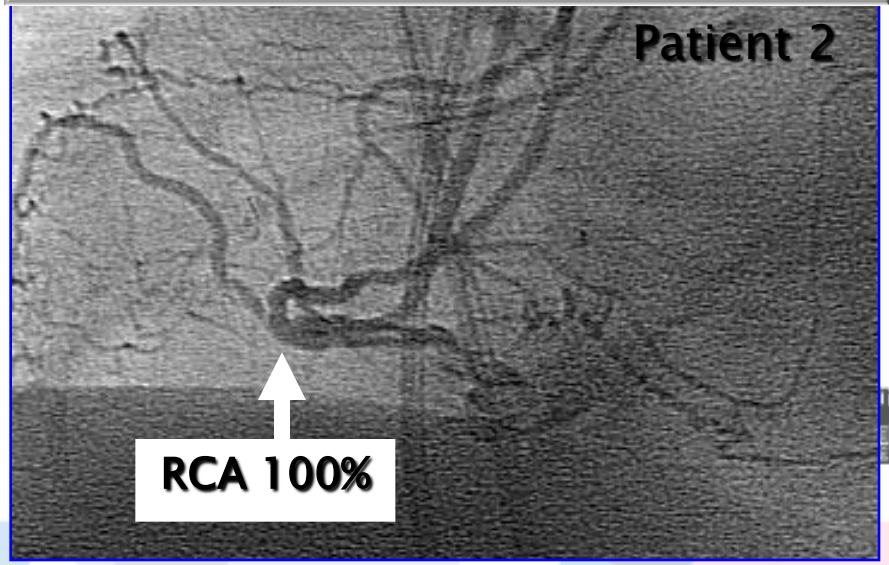




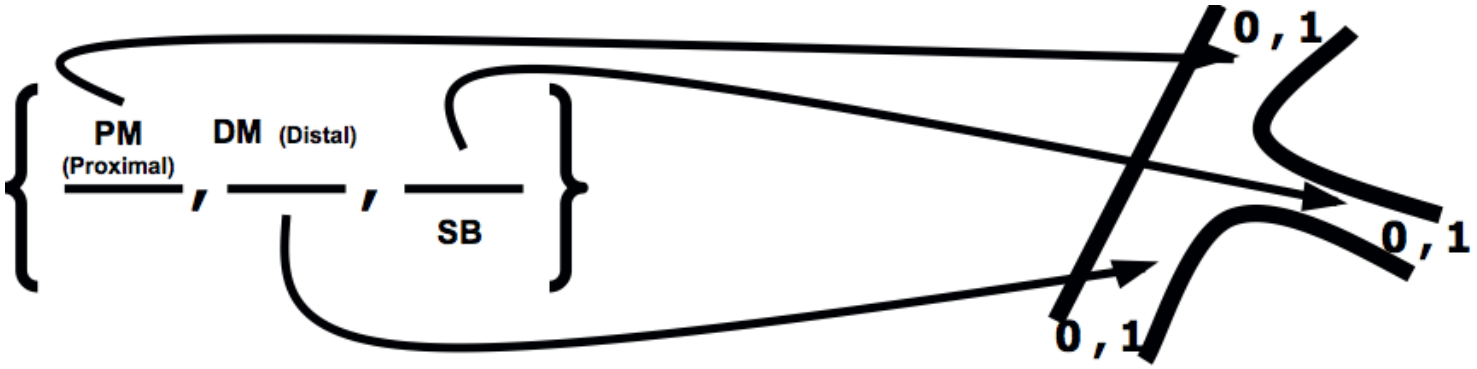
SYNTAX SCORE 21

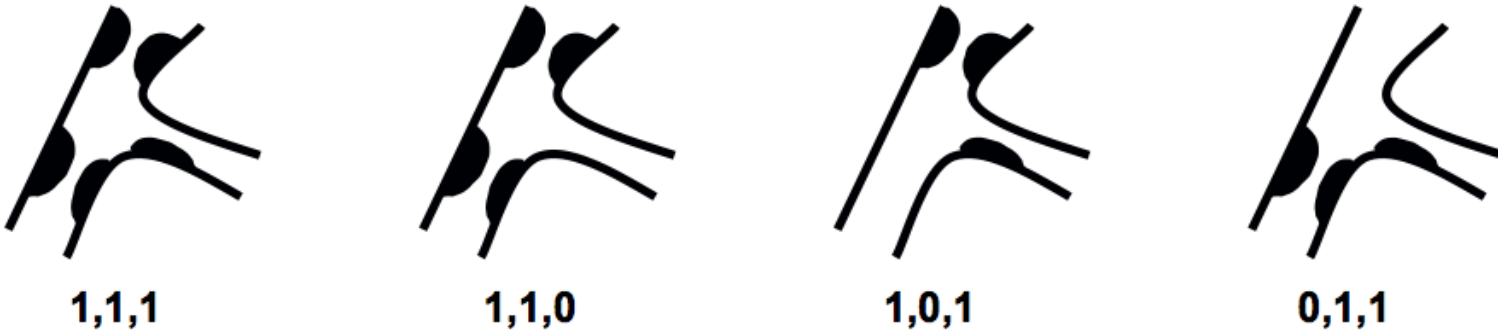
SYNTAX SCORE 52





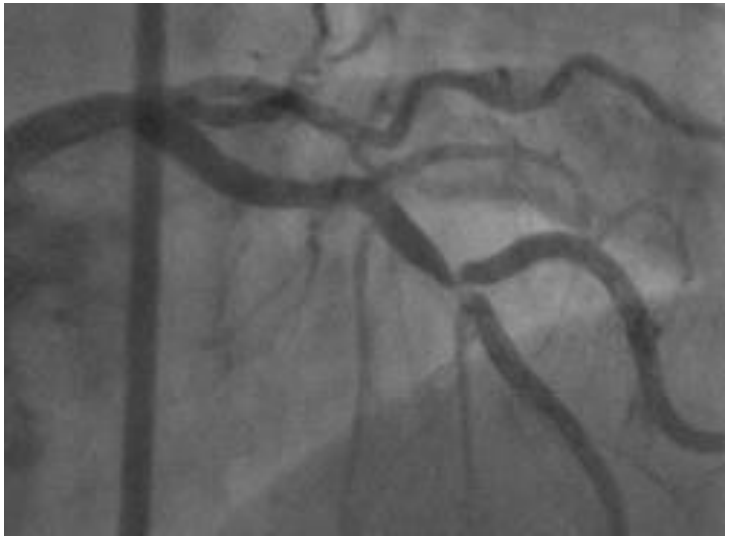
Medina classification

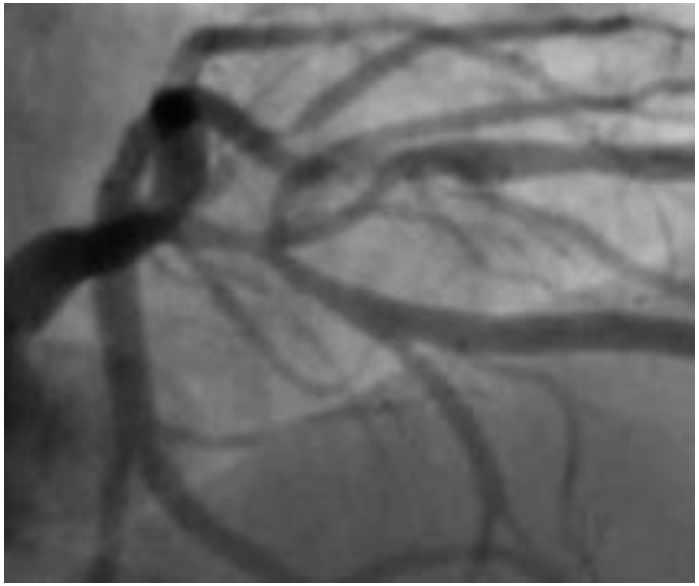


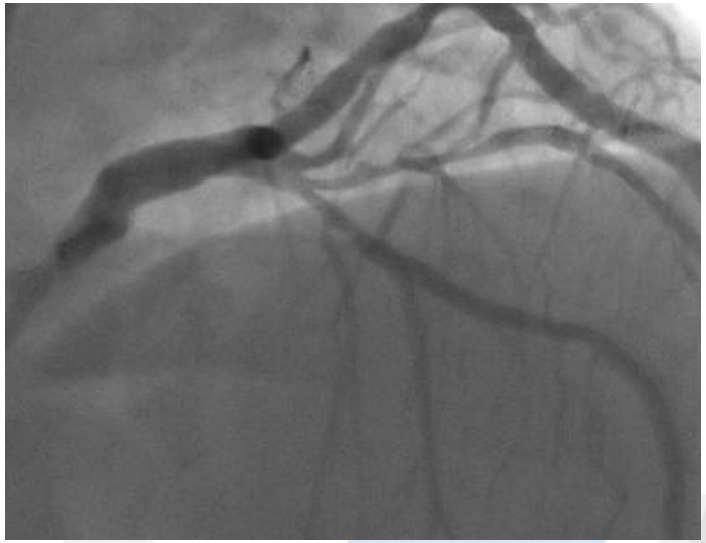


Louvard Y et al. *EuroIntervention.* 2010;6 Suppl J: J31-J35

Medina 1,1,1 and Medina 1,1,1







Disadvantages of Medina's classification

- Medina's classification does not provide a complete description of lesions that may influence the choice of the treatment strategy and the outcome:
  - Presence of calcification
  - Angles between the vessel segments
  - Lesion length, especially in the SB
  - SB diameter
  - Flow conditions

Prognostic value of lesion characteristics
NORDIC I + BBC I

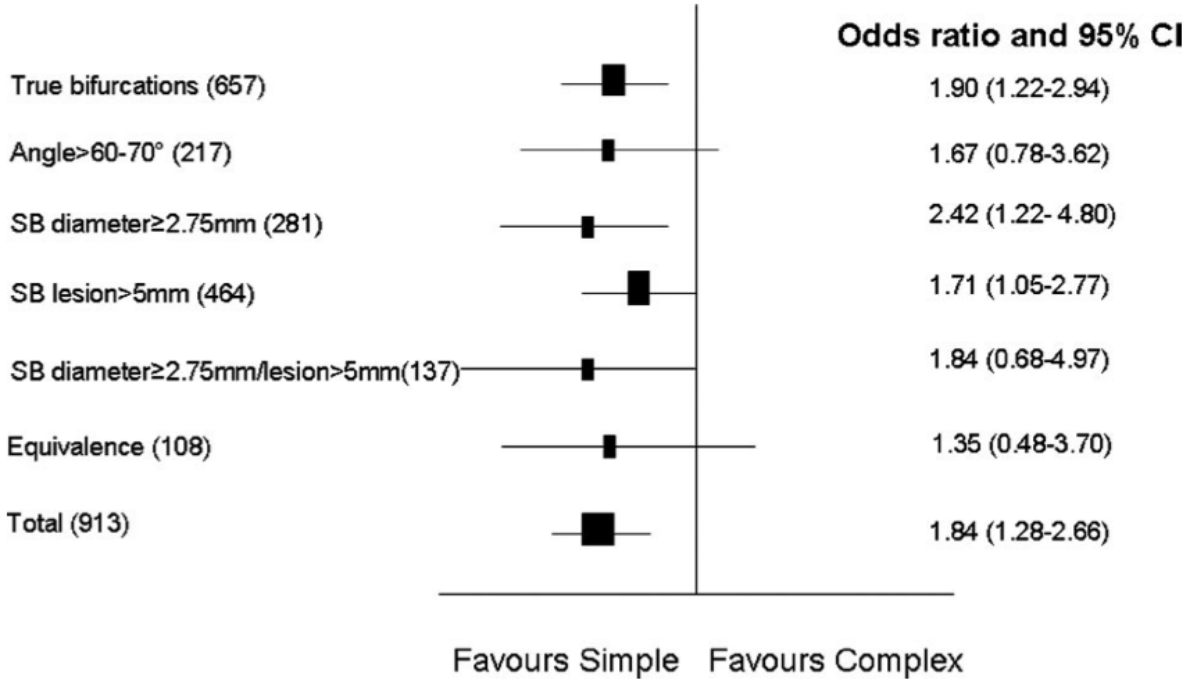


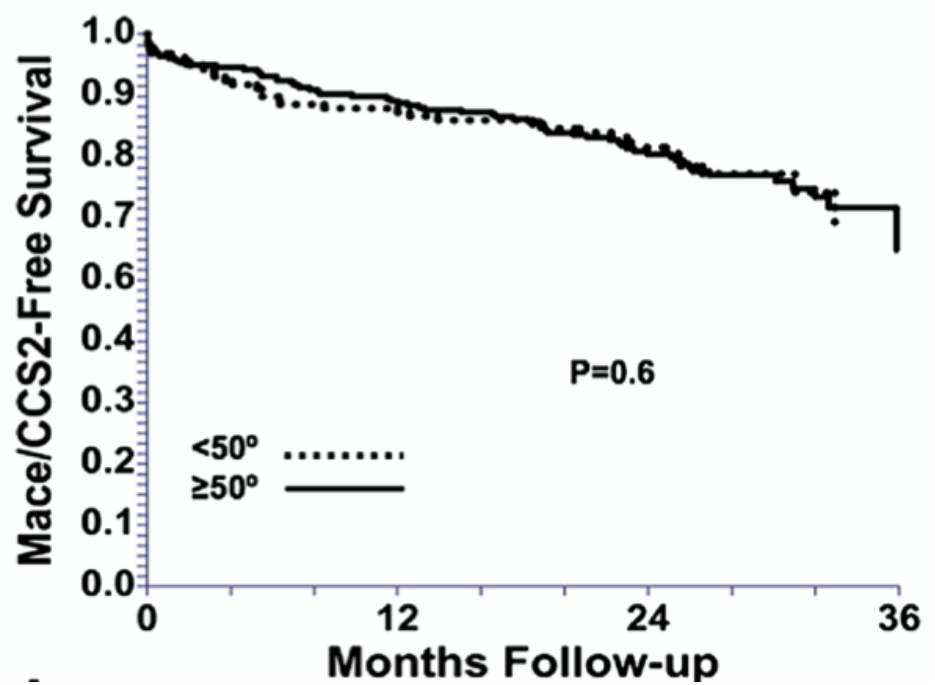
Figure 2. Odds ratio plot of the primary outcome for individual subgroups. Equivalence indicates that the SB is <0.25 mm smaller than the MV. Size of data markers indicates the number of patients in that subgroup. SB indicates side branch; MV, main vessle; CI, confidence interval.

Behan MW et al. *Circ Cardiovasc Interv*. 2011;4:57-64

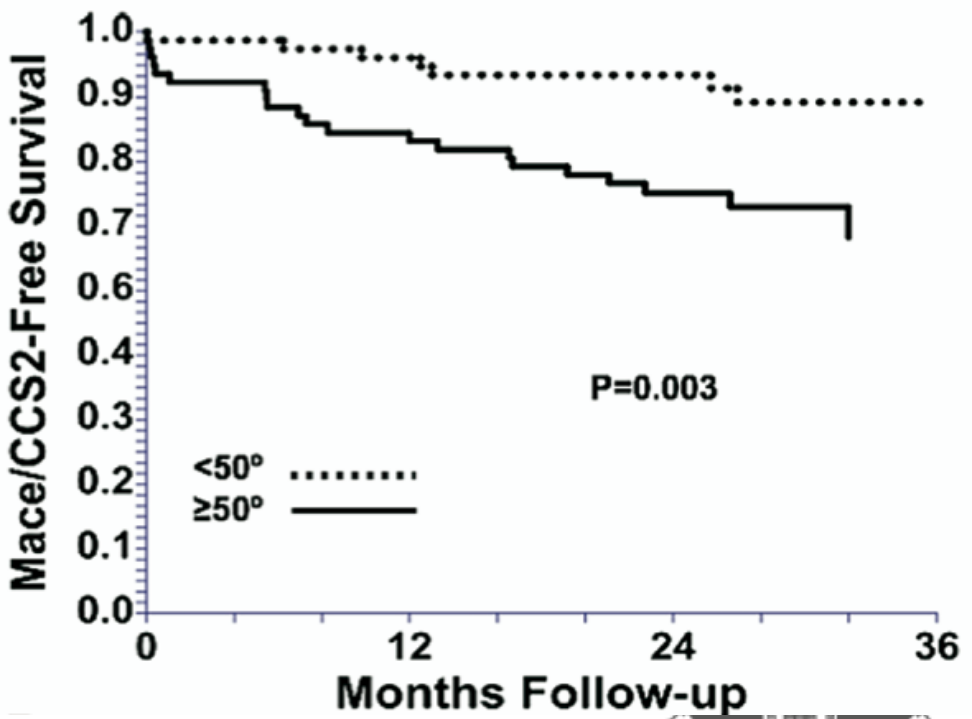
The role of bifurcation angle

Kaplan-Meier curves for MACEs or CCS class ≥2 angina-free survival

MV stenting only

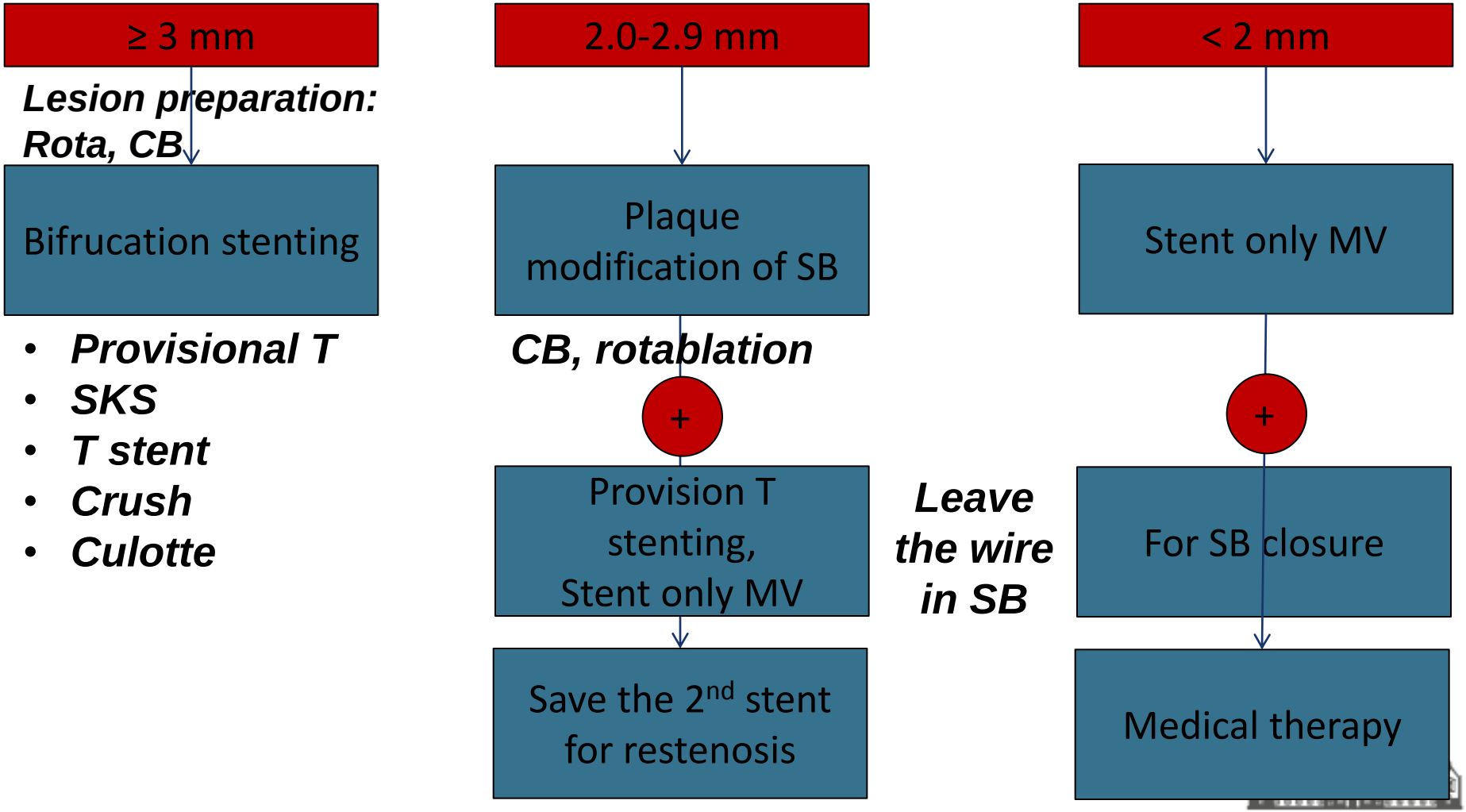


Crush/Culotte stenting



Collins N et al. *Am J Cardiol* 2008;102:404–410

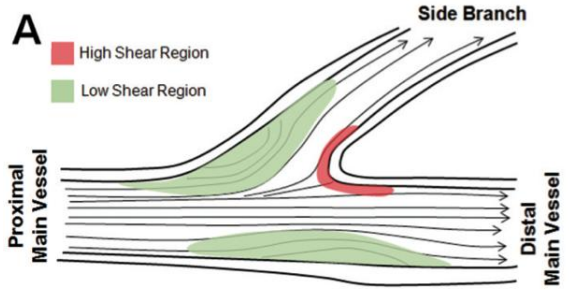
Side Branch Size and Strategy

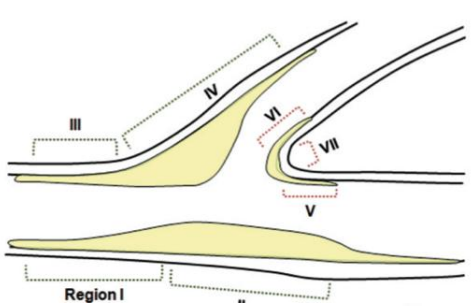


Sharma SK et al. *Cardiol Clin* 2010;28:55–70

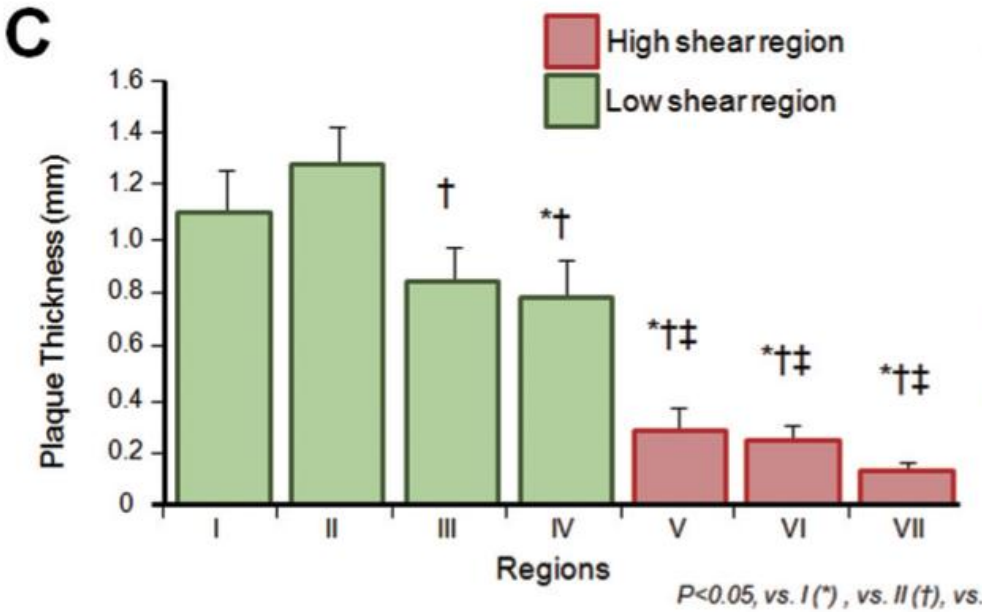
Impact of flow on atheroma in bifurcation

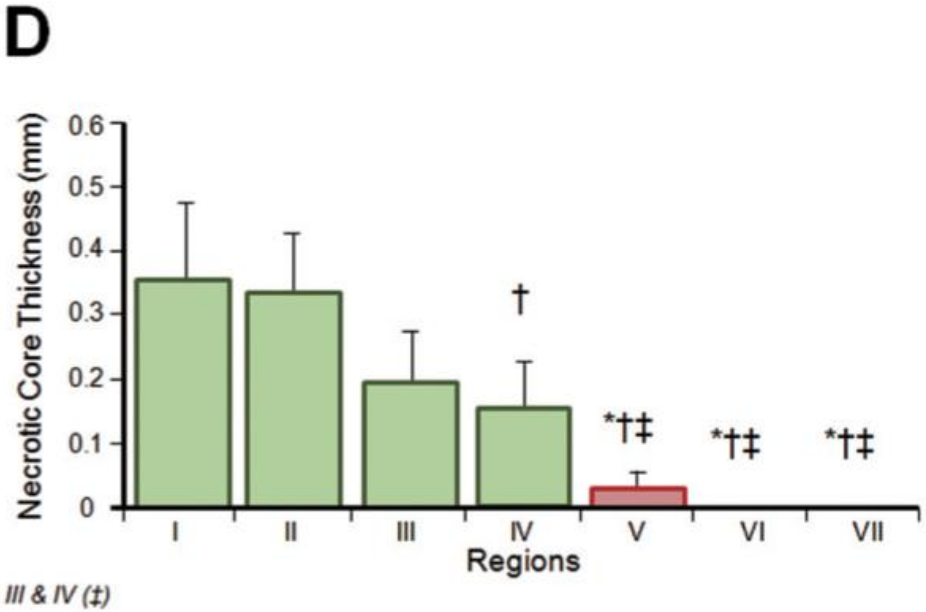
Flow behavior with low shear regions in the lateral walls and high shear regions at the carina.





Regions: I - Proximal MV, II - Distal MV on the lateral wall, III - Proximal MV on the SB, IV - Distal SB on the lateral wall, V - Distal MV on the flow divider side, VI - Distal SB on the flow divider side, VII – Carina.





P<0.05, vs. I (*) , vs. II (†), vs. III & IV (‡)

C: Plaque thickness was greater in regions of low shear as compared to high shear.

D: Necrotic core thickness was significantly greater in low shear regions as compared to high shear with absent of necrotic core at the carinal region (VII)

Yazdani SK, Virmani R et al. *EuroIntervention.* 2010;6 Suppl J: J24-J30

Impact of flow on arterial healing after stenting

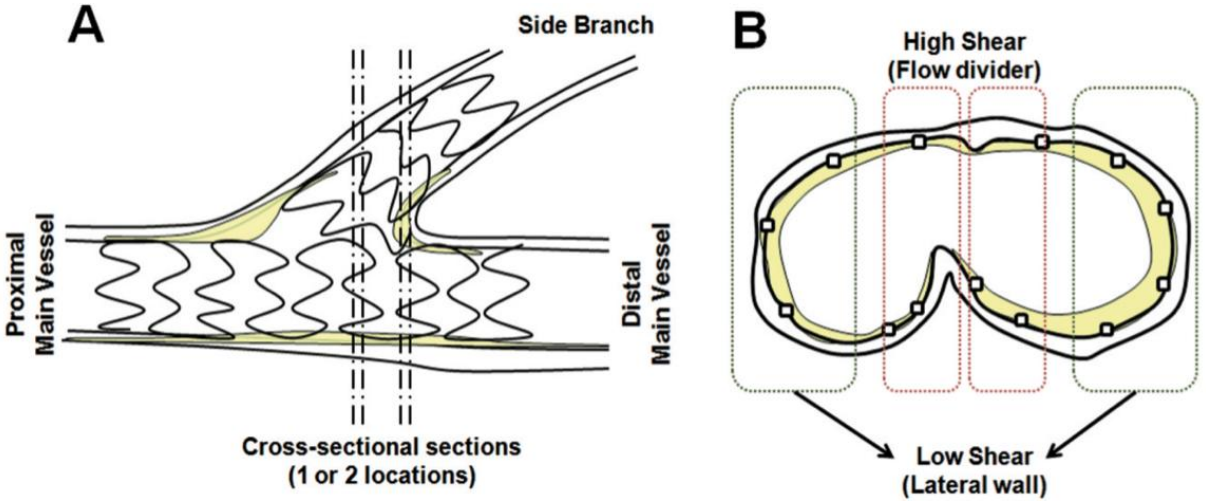
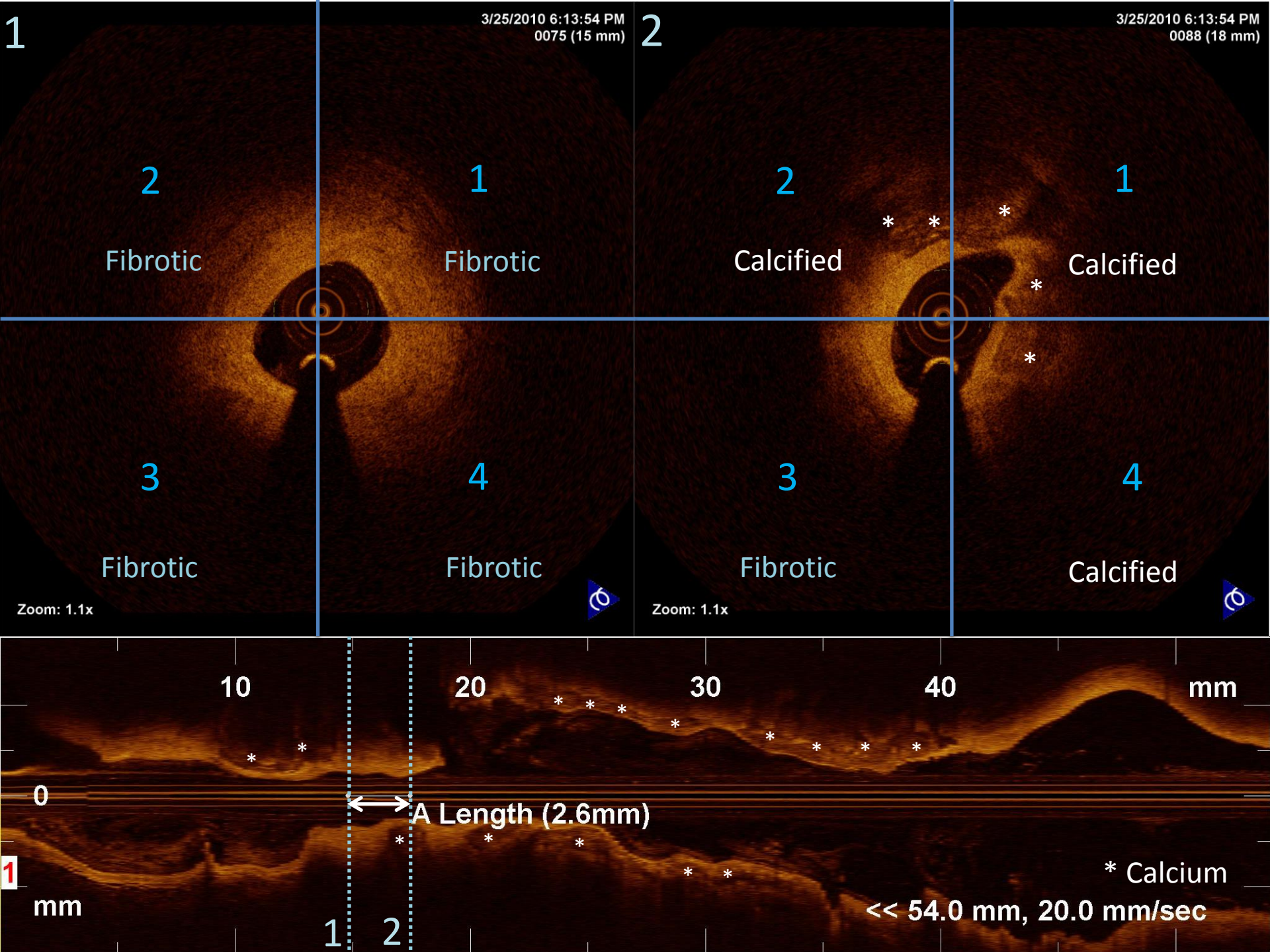


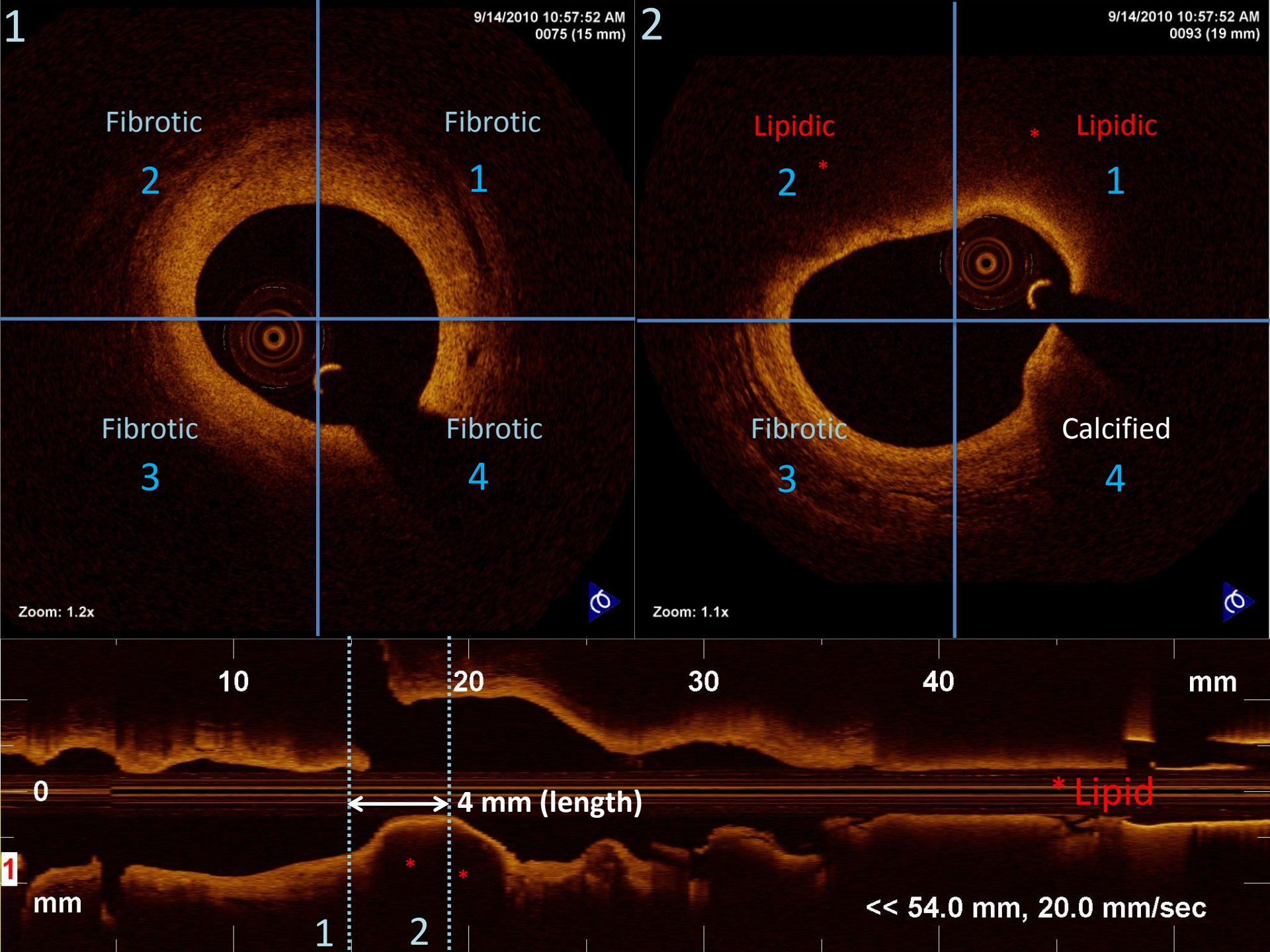
Table 2. Morphometric comparison between high shear vs. low shear regions in DES and BMS.

	DES (12 lesion, 17 stents)		p value	BMS (14 lesion, 18 stents)		p value	P value for DES vs. BMS	
	High shear (flow divider)	Low shear (lateral walls)		High shear (flow divider)	Low shear (lateral walls)		High shear	Low shear
Neointimal thickness (mm)	0.07 [0.03, 0.15]	0.17 [0.09, 0.23]	0.001	0.26 [0.16, 0.73]	0.44 [0.17, 0.67]	0.25	0.0002	0.004
Fibrin deposition (%Struts)	60 [21, 67]	17 [0, 55]	0.01	8 [0, 33]	3 [0, 21]	0.21	0.008	0.19
Uncovered struts (%Struts)	40 [16, 76]	0 [0, 15]	0.001	0 [0, 21]	0 [0, 0]	0.10	0.004	0.38

DES: drug-eluting stent; BMS: bare metal stent; Values are expressed as median and interquartile range

Yazdani SK, Virmani R et al. *EuroIntervention.* 2010;6 Suppl J: J24-J30


1
3/25/2010 6:13:54 PM
0075 (15 mm)
2
Fibrotic
1
Fibrotic
3
Fibrotic
4
Fibrotic
Zoom: 1.1x
2
3/25/2010 6:13:54 PM
0088 (18 mm)
2
Calcified
1
Calcified
3
Fibrotic
4
Calcified
Zoom: 1.1x
10
20
30
40
mm
0
A Length (2.6mm)
1
mm
1
2
* Calcium
<< 54.0 mm, 20.0 mm/sec


1
9/14/2010 10:57:52 AM
0075 (15 mm)
Fibrotic
2
Fibrotic
1
Fibrotic
3
Fibrotic
4
Zoom: 1.2x
2
9/14/2010 10:57:52 AM
0093 (19 mm)
Lipidic
2
*
Lipidic
*
1
Fibrotic
3
Calcified
4
Zoom: 1.1x
10
20
30
40
mm
0
4 mm (length)
* Lipid
1
mm
*
*
1
2
<< 54.0 mm, 20.0 mm/sec

Consensus from European Bifurcation Club, 2010

- Provisional T stenting remains the gold standard technique for most bifurcations
- Large side branched with ostial disease extending >5 mm from the carina are likely to require a two-stent strategy
- Side branches whose access is particularly challenging should be secured by stenting once accessed
- Bifurcations with angulation > 60 degree between the daughter vessels should be approached with single stent strategies where possible

***Eurointervention* 2010;6:34-38**

Conclusions

- The current evidence-base pertaining to PCI in coronary bifurcation lesions is not adequate to inform decision making in all patients, hence a gap still exists between the evidence-base and patient-centered decision-making.
- Bifurcations is the art of geometry, fluid dynamics and rheology. Atherosclerosis, plaque vulnerability and thrombosis are closely associated with the geometric and fluid dynamics factors at the bifurcation.
- Bifurcation stenting should respect geometric rules
- Advances in the current imaging modalities will enable the development of more accurate models for the study of geometry and flow conditions in coronary bifurcations.

Appropriate tools should reach apropriate hands