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Physiology and Fluid Dynamics of Bifurcation Lesions

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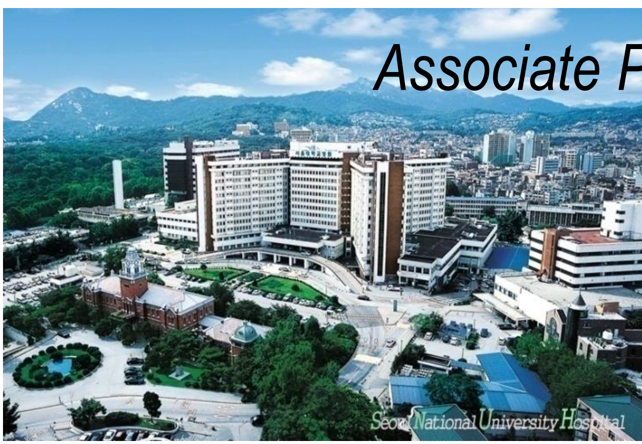


Evaluation of Bifurcation lesions

Is there a room for more?

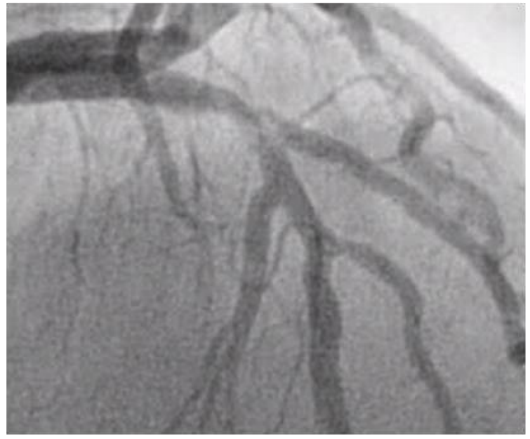
- Clinical information: Symptom, risk factors, …..
- Functional study: SPECT, TMT, …..
- Angiographic findings
- Quantitative coronary angiography
- Intravascular ultrasound
- OCT, …..

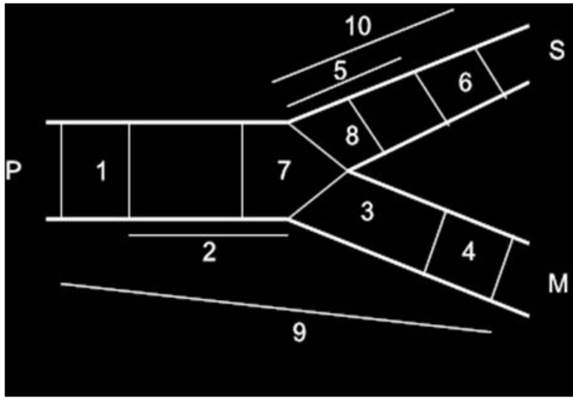
Pitfalls of anatomical evaluation

- Angiography
  - Single directional assessment
  - Variability in stenosis assessment
  - No validated criteria for side branch intervention

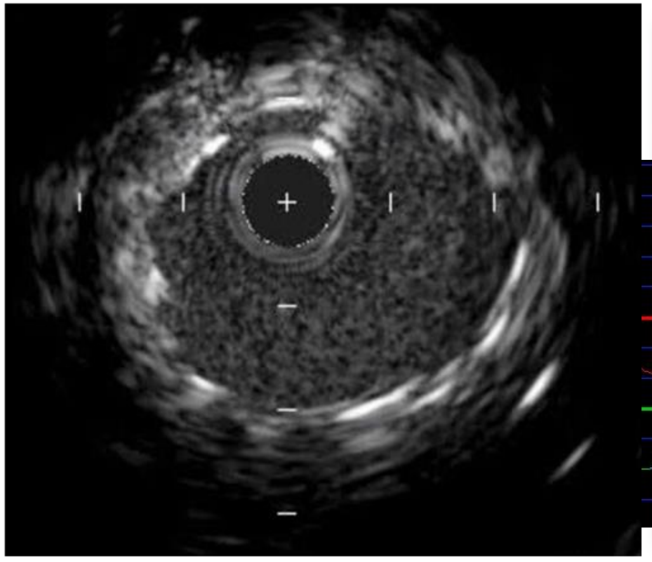
- IVUS/OCT
  - Can not be performed in tight stenosis
  - Does not reflect the amount of supplying myocardium
  - No validated criteria for side branch intervention

PCI for bifurcation lesions should be successful in terms of ….



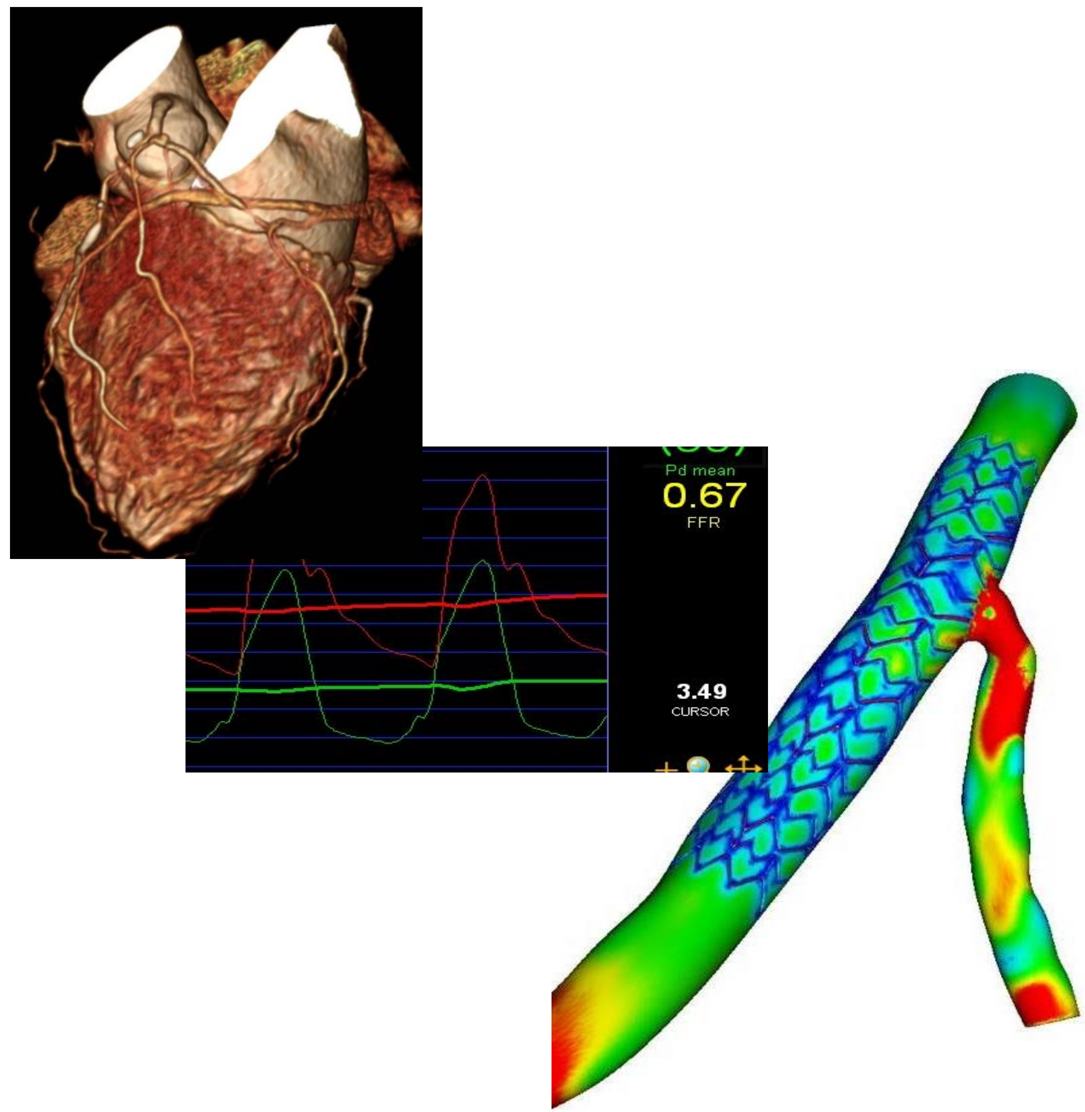


	Prox pos (mm)	Length (mm)	%D (%)	Min D (mm)	Max D (mm)	Mean D (mm)	Ref D (mm)
1	4.01	4.97	4.84	2.76	3.02	2.87	2.90
2	8.97	5.28	12.05	2.29	3.73	3.16	2.60
3	14.25	8.61	6.08	2.25	2.66	2.51	2.40
4	22.86	5.04	22.04	1.77	2.25	1.89	2.28
5	14.17	13.82	14.95	2.08	2.54	2.35	2.45
6	28.00	4.11	33.39	1.54	2.37	1.94	2.32
7 Main	10.27	3.98	12.05	2.29	-	-	2.60
7 Side	10.27	3.90	12.05	2.29	-	-	2.60
8	14.17	1.99	9.64	2.24	2.54	2.38	2.48
9	4.01	23.89	22.04	1.77	3.73	2.57	2.28
10	14.17	17.93	33.39	1.54	2.54	2.26	2.32



PCI for bifurcation lesions should be successful in terms of ….

- Natural Anatomy
- Physiology
- Fluid dynamics



Physiology and Fluid Dynamics of Bifurcation Lesions

Cardiology Is Flow

Yoram Richter, PhD; Elazer R. Edelman, MD, PhD

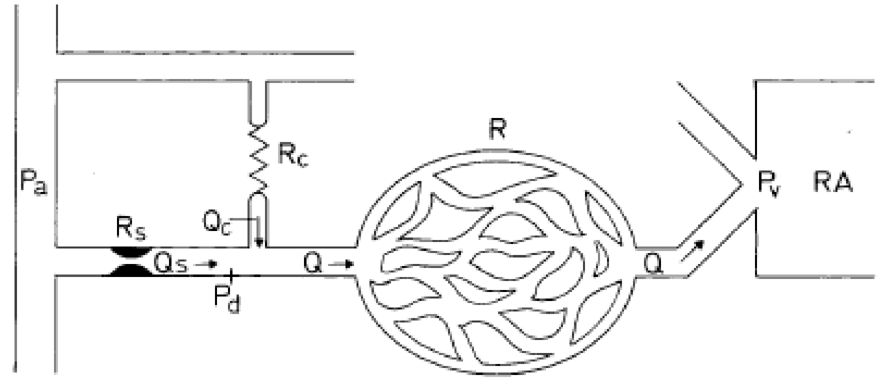
Panta rhei. *(Everything flows).*[1]

Cardiology is about flow. The primary purpose of the

rosis. Flow disturbances are therefore ubiquitous; they are a fundamental feature of the vascular system. An entire field of study arose correlating disease with its overlying flow pat-

- Physiologic evaluation assess the quantity of FLOW.
- Fluid dynamics assess the quality of FLOW.

I love "Images", But, I hate "Physiology" !



$$= \left(1 - \frac{\Delta^{(2)}P}{P_a^{(2)} - P_w^{(2)}}\right) : \left(1 - \frac{\Delta^{(1)}P}{P_a^{(1)} - P_w^{(1)}}\right) \quad (5b)$$

The expression $FFR_{cor}^{(2)}/FFR_{cor}^{(1)}$ represents the improvement of FFR_{cor} of the dilated artery and is identical to what we called pressure-corrected maximum flow ratio (MFR_c) in a previous study[9].

Equation 5a can also be derived directly from figure 4.7 by the following:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{Q^{(2)} - Q_c^{(2)}}{Q^{(1)} - Q_c^{(1)}} = \frac{(P_d^{(2)} - P_v^{(2)})/R - (P_a^{(2)} - P_d^{(2)})/R_c}{(P_d^{(1)} - P_v^{(1)})/R - (P_a^{(1)} - P_d^{(1)})/R_c}$$

and by substituting Equation 1b.

Theoretically, maximum blood flow through the myocardium can be compared before and after the intervention by:

$$\frac{Q^{(2)}}{Q^{(1)}} = \frac{(P_d^{(2)} - P_v^{(2)})/R}{(P_d^{(1)} - P_v^{(1)})/R} = \frac{P_d^{(2)} - P_v^{(2)}}{P_d^{(1)} - P_v^{(1)}} \quad (6a)$$

or, if correction for pressure changes is made, by:

$$\frac{FFR_{myo}^{(2)}}{FFR_{myo}^{(1)}} = \frac{P_d^{(2)} - P_v^{(2)}}{P_a^{(2)} - P_v^{(2)}} : \frac{P_d^{(1)} - P_v^{(1)}}{P_a^{(1)} - P_v^{(1)}}$$

$$= \left(1 - \frac{\Delta^{(2)}P}{P_a^{(2)} - P_v^{(2)}}\right) : \left(1 - \frac{\Delta^{(1)}P}{P_a^{(1)} - P_v^{(1)}}\right) \quad (6b)$$

In the case of coronary interventions, it should be realized that flow at maximum vasodilation is directly proportional to the driving pressure (P_a - P_v). Therefore, the ratio between maximum flow through the coronary artery before (situation 1) and after the intervention (situation 2) can be written as follows:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{Q_s^{(2)}}{Q_s^{(2)N}} \cdot \frac{Q_s^{(2)N}}{Q_s^{(1)N}} \cdot \frac{Q_s^{(1)N}}{Q_s^{(1)}}$$

$$= FFR_{cor}^{(2)} \cdot \frac{P_a^{(2)} - P_v^{(2)}}{P_a^{(1)} - P_v^{(1)}} \cdot \frac{1}{FFR_{cor}^{(1)}}$$

$$= \frac{FFR_{cor}^{(2)}}{FFR_{cor}^{(1)}} \cdot \frac{P_a^{(2)} - P_v^{(2)}}{P_a^{(1)} - P_v^{(1)}}$$

By substitution of Equations 1b and 2:

$$\frac{Q_s^{(2)}}{Q_s^{(1)}} = \frac{P_d^{(2)} - P_w^{(2)}}{P_d^{(1)} - P_w^{(1)}} \quad (5a)$$

Note that for evaluation of the functional improvement of a stenotic artery after PTCA, $FFR_{cor}^{(2)}/FFR_{cor}^{(1)}$ theoretically is a better measure than $Q_s^{(2)}/Q_s^{(1)}$ because the first expression is independent of arterial pressure. From Equation 2 it is clear that

$$\frac{FFR_{cor}^{(2)}}{FFR_{cor}^{(1)}} = \frac{P_d^{(2)} - P_w^{(2)}}{P_a^{(2)} - P_w^{(2)}} : \frac{P_d^{(1)} - P_w^{(1)}}{P_a^{(1)} - P_w^{(1)}}$$

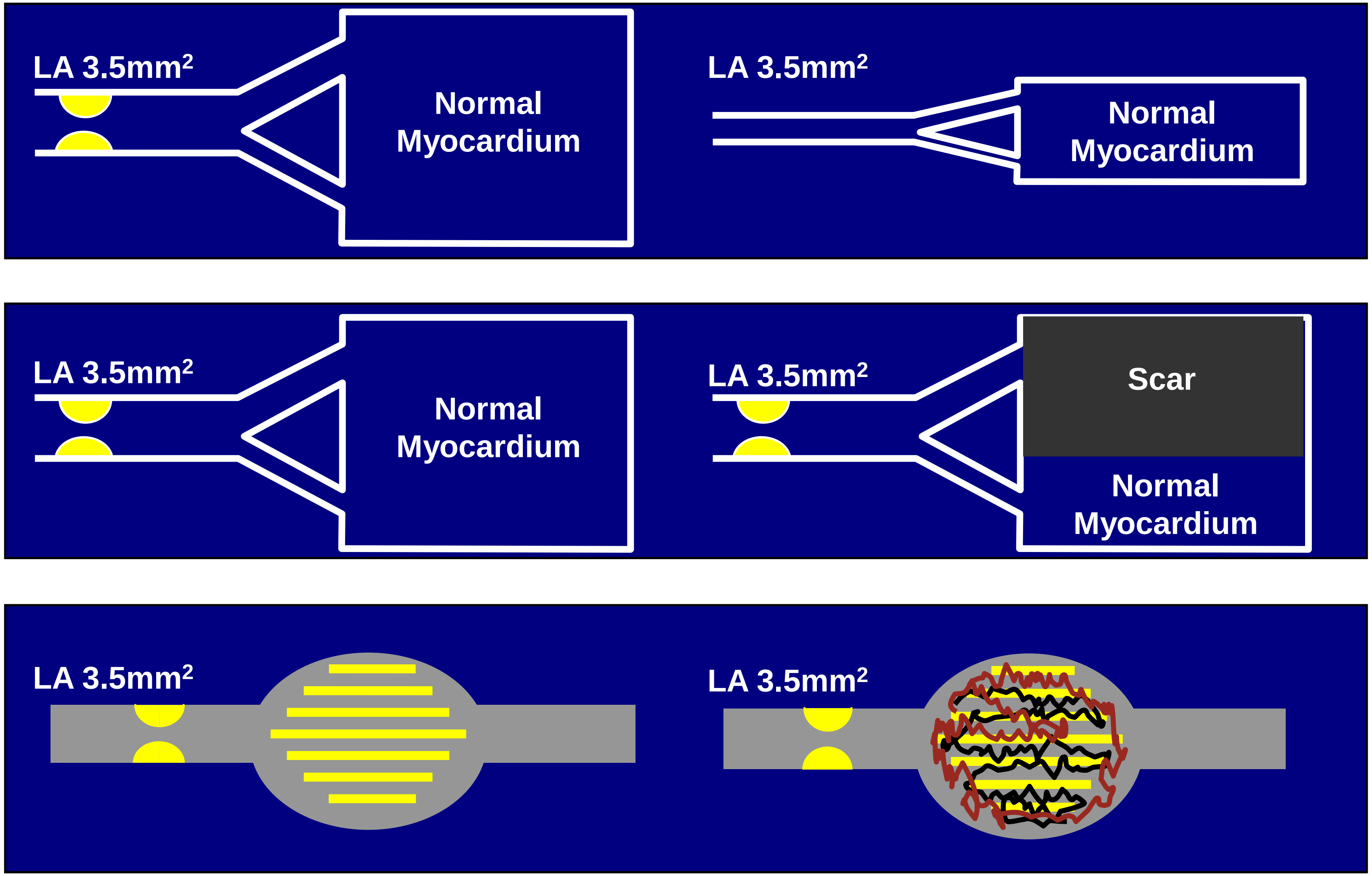
Evaluation of Coronary Stenosis

A reliable parameter should account for the interaction between

- *epicardial stenosis severity*,
- *extent of the perfusion territory*,
- *myocardial blood flow including collaterals*
- *microvascular function*

→ **Physiologic evaluation**

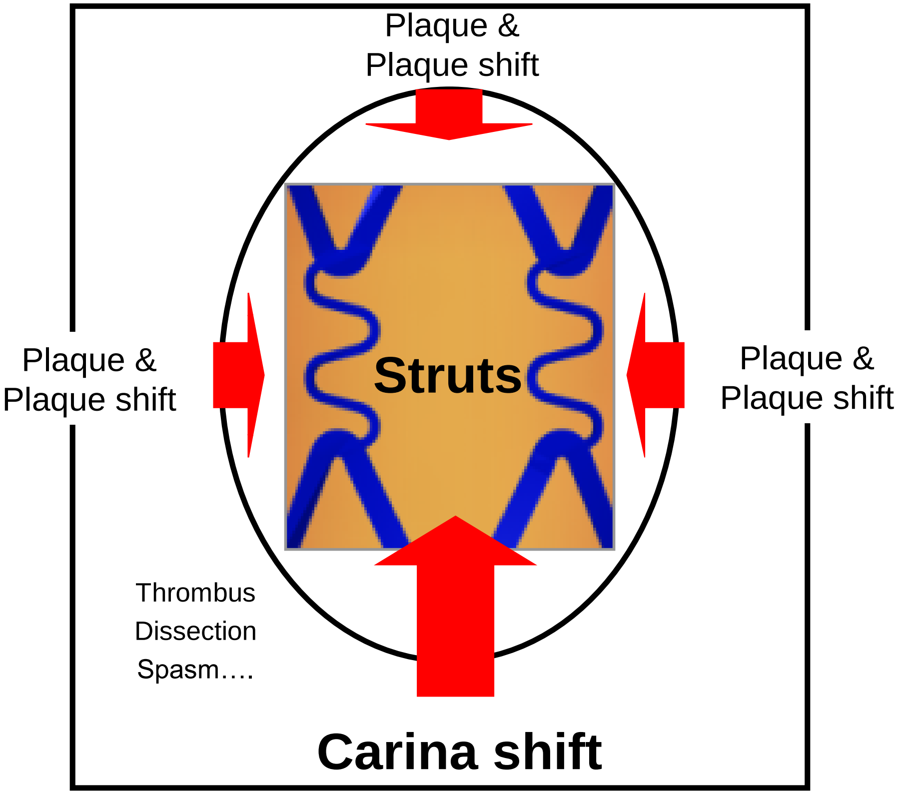
Same stenosis, same functional significance ?



LA: Lumen cross sectional area

Why "Physiologic evaluation" for bifurcation?

- Various amount of supplying myocardium
- Combination of 3 ostial lesions
- Jailed SB ostial lesion is unique
  - Underlying plaque → Eccentric plaque
  - Remodeling → Negative remodeling
  - Mechanisms of luminal narrowing
    - Shifted plaque
    - Shifted carina
    - Stent struts, thrombus, dissection flap,……



What kind of physiologic parameter does really reflect the physiologic significance of a stenosis ??

- *Blood flow ?*

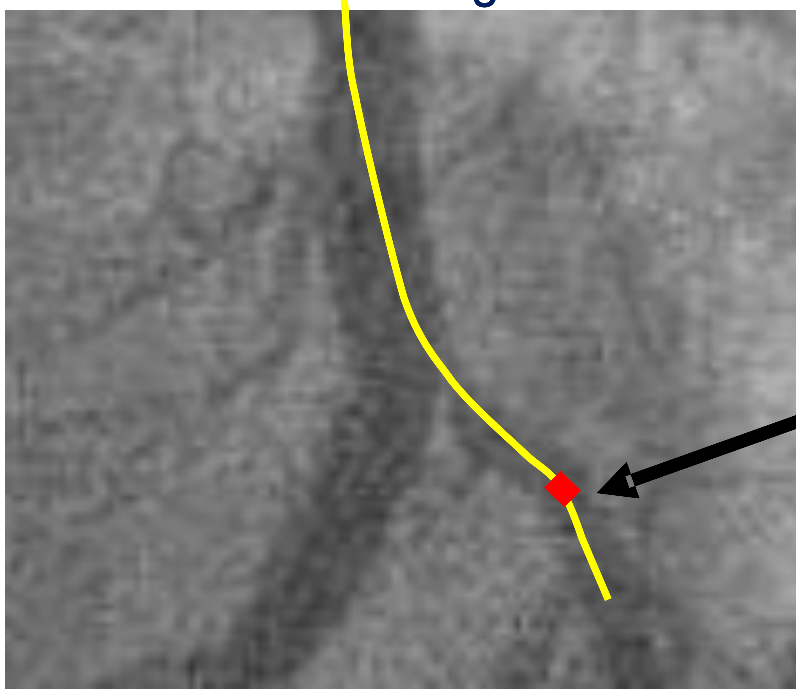
- *Flow-derived parameters (such as CFR) ?*

- *Transstenotic gradient itself or indexes of stenosis resistance ?*

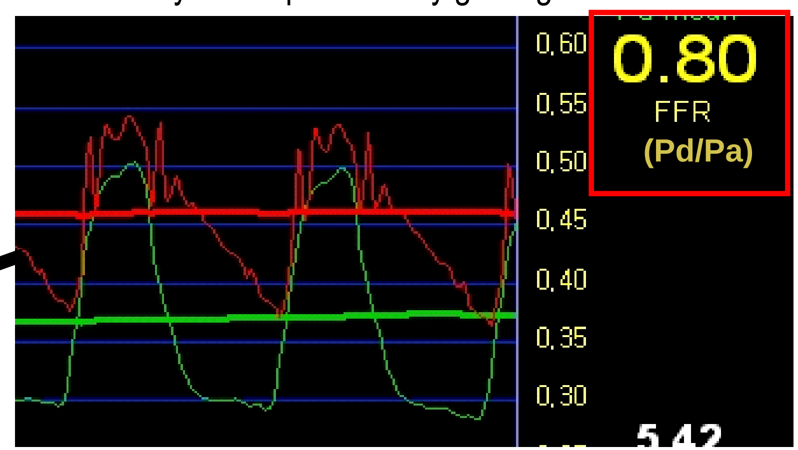
Fractional Flow Reserve (FFR)

$$\text{FFR} = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{(Pd-Pv)/R}{(Pa-Pv)/R} = \frac{P_d}{P_a}$$

- Easily obtained, stenosis specific, simple (<0.75 or 0.8 → ischemia)
- Reflects both degree of stenosis and myocardial territory



Pa: systemic pressure by guiding catheter



Pd: distal pressure by pressure wire

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Physiologic Assessment of Jailed Side Branch Lesions Using Fractional Flow Reserve

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Seoul, Seongnam, Gyeonggi-do, and Suwon, Republic of Korea

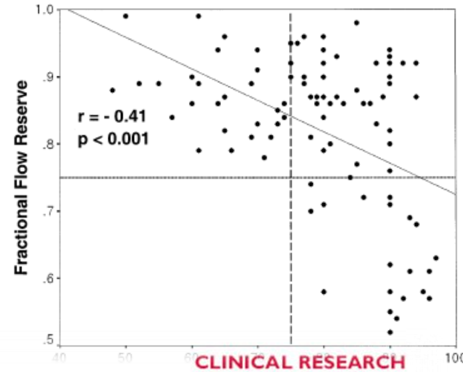
OBJECTIVES This study was performed to evaluate the feasibility of the physiologic assessment of jailed side branches using fractional flow reserve (FFR) and to compare the measured FFR with the stenosis severity assessed by quantitative coronary angiography (QCA).

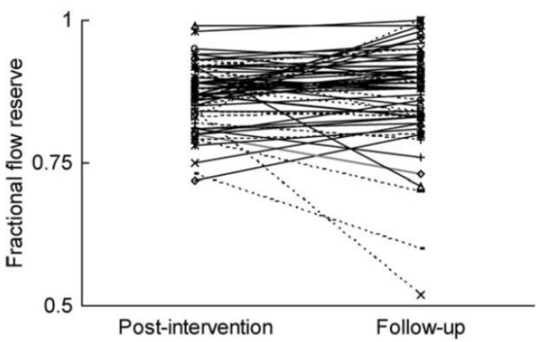
BACKGROUND It is not well-known which side branches should be treated after stent imp... branches and how to assess the functional significance of these lesions.

METHODS Ninety-seven jailed side branch lesions (vessel size >2.0 mm, percent stenos... estimation) after stent implantation at main branches were consecutively en... was measured using a pressure wire at 5 mm distal and proximal to the o... jailed side branch.

RESULTS The FFR measurement was successful in 94 lesions. Mean FFRs were 0.94 ... 0.11 at the main branches and jailed side branches, respectively. There was a n... between the percent stenosis and FFR (r = −0.41, p < 0.001). However, no... stenosis had FFR <0.75. Among 73 lesions with ≥75% stenosis, only 20 lesion... significant.

CONCLUSIONS The FFR measurement in jailed side branch lesions is both safe and feasi... coronary angiography is unreliable in the assessment of the functional sev... branch lesions, and measurement of FFR suggests that most of these les... functional significance. (J Am Coll Cardiol 2005;46:633–7) © 2005 ... College of Cardiology Foundation





European Heart Journal (2008) 29, 726–732
doi:10.1093/eurheartj/ehn045

CLINICAL RESEARCH
Interventional cardiology

Physiological evaluation of the provisional side-branch intervention strategy for bifurcation lesions using fractional flow reserve

Bon-Kwon Koo[1], Kyung-Woo Park[1], Hyun-Jae Kang[1], Young-Seok Cho[2], Woo-Young Chung[2], Tae-Jin Youn[2], In-Ho Chae[2], Dong-Ju Choi[2], Seung-Jae Tahk[3], Byung-Hee Oh[1], Young-Bae Park[1] and Hyo-Soo Kim[1]*

[1]Division of Cardiology, Department of Internal Medicine, Seoul National University College of Medicine, Cardiovascular Center and Cardiovascular Research Institute, Seoul National University Hospital, Yongon-dong 28, Jongno-gu, Seoul 110-744, Republic of Korea; [2]Heart Center, Bundang Seoul National University Hospital, Gyeonggi-do, Republic of Korea; and [3]Ajou University School of Medicine, Gyeonggi-do, Republic of Korea

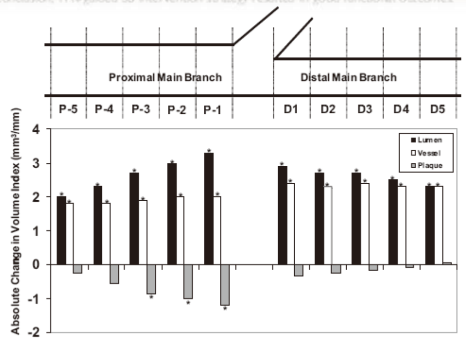
Received 26 March 2007; revised 8 January 2008; accepted 17 January 2008; online publish-ahead-of-print 28 February 2008

See page 704 for the editorial comment on this article (doi:10.1093/eurheartj/ehn054)

Aims This study was performed to evaluate the functional outcomes of fractional flow reserve (FFR)-guided jailed side-branch (SB) intervention strategy.

Methods and results One hundred and ten patients treated by provisional strategy were consecutively enrolled and SB F... in 91 patients. SB intervention was allowed when FFR was <0.75. FFR measurement was repeated ... tion and at 6-month follow-up angiography. In 26 of 28 SB lesions with FFR <0.75, balloon angiop... artery ratio = 0.84 ± 0.14) was performed and FFR ≥0.75 was achieved in 92% of the lesions a... residual stenosis was 69 ± 10%. During follow-up, there were no changes in SB FFR in lesions ... to 0.84 ± 0.01, $P = 0.4$) and without SB angioplasty (0.87 ± 0.06 to 0.89 ± 0.07, $P = 0.1$). Fun... (FFR <0.75) rate was only 8% (5/65). When clinical outcomes of these patients were compared ... with similar bifurcation lesions treated without FFR-guidance, there was no difference in 9-month c... (4.6 vs. 3.7%, $P = 0.7$) between the two groups.

Conclusion In conclusion, FFR-guided SB intervention strategy resulted in good functional outcomes.



Anatomic and Functional Evaluation of Bifurcation Lesions Undergoing Percutaneous Coronary Intervention

Bon-Kwon Koo, MD, PhD; Katsuhisa Waseda, MD, PhD; Hyun-Jae Kang, MD, PhD; Hyo-Soo Kim, MD, PhD; Chang-Wook Nam, MD, PhD; Seung-Ho Hur, MD, PhD; Jung-Sun Kim, MD, PhD; Donghoon Choi, MD, PhD; Yangsoo Jang, MD, PhD; Joo-Yong Hahn, MD, PhD; Hyeon-Cheol Gwon, MD, PhD; Myeong-Ho Yoon, MD, PhD; Seung-Jea Tahk, MD, PhD; Woo-Young Chung, MD, PhD; Young-Seok Cho, MD, PhD; Dong-Ju Choi, MD, PhD; Takao Hasegawa, MD; Toru Kataoka, MD; Sung Jin Oh, MD; Yasuhiro Honda, MD; Peter J. Fitzgerald, MD, PhD; William F. Fearon, MD

Background—We sought to investigate the mechanism of geometric changes after main branch (MB) stent implantation and to identify the predictors of functionally significant "jailed" side branch (SB) lesions.

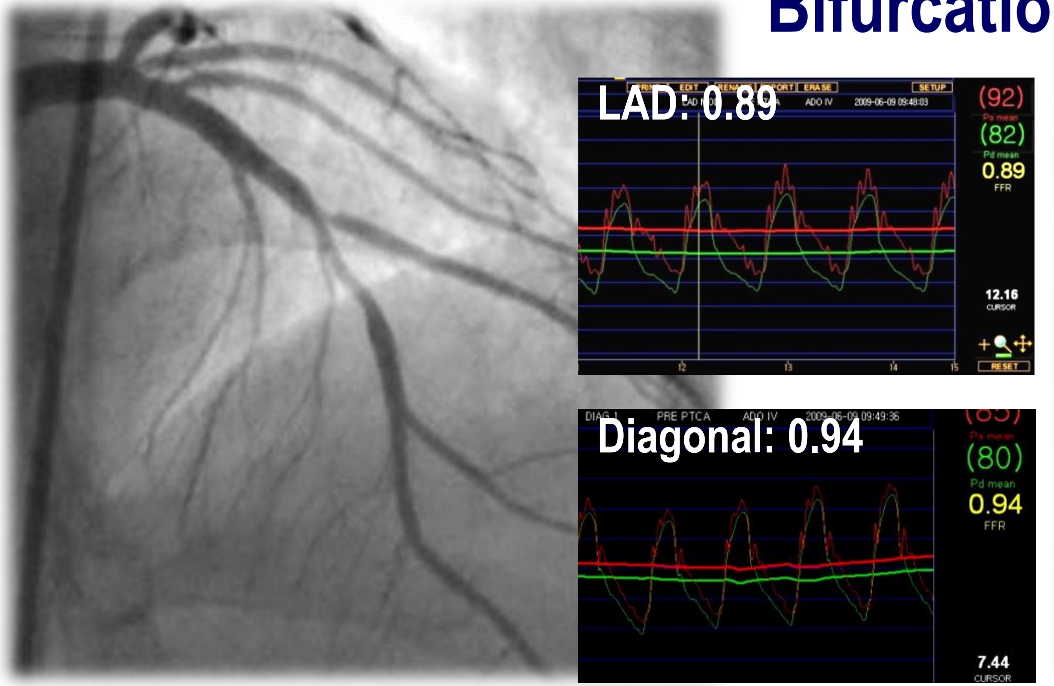
Methods and Results—Seventy-seven patients with bifurcation lesions were prospectively enrolled from 8 centers. MB intravascular ultrasound was performed before and after MB stent implantation, and fractional flow reserve was measured in the jailed SB. The vessel volume index of both the proximal and distal MB was increased after stent implantation. The plaque volume index decreased in the proximal MB (9.1±3.0 to 8.4±2.4 mm³/mm, P=0.001), implicating plaque shift, but not in the distal MB (5.4±1.8 to 5.3±1.7 mm³/mm, P=0.227), implicating carina shifting to account for the change in vessel size (N=56). The mean SB fractional flow reserve was 0.71±0.20 (N=68) and 43% of the lesions were functionally significant. Binary logistic-regression analysis revealed that preintervention % diameter stenosis of the SB (odds ratio=1.05; 95% CI, 1.01 to 1.09) and the MB minimum lumen diameter located distal to the SB ostium (odds ratio=3.86; 95% CI, 1.03 to 14.43) were independent predictors of functionally significant SB jailing. In patients with ≥75% stenosis and Thrombolysis In Myocardial Infarction grade 3 flow in the SB, no difference in poststent angiographic and intravascular ultrasound parameters was found between SB lesions with and without functional significance.

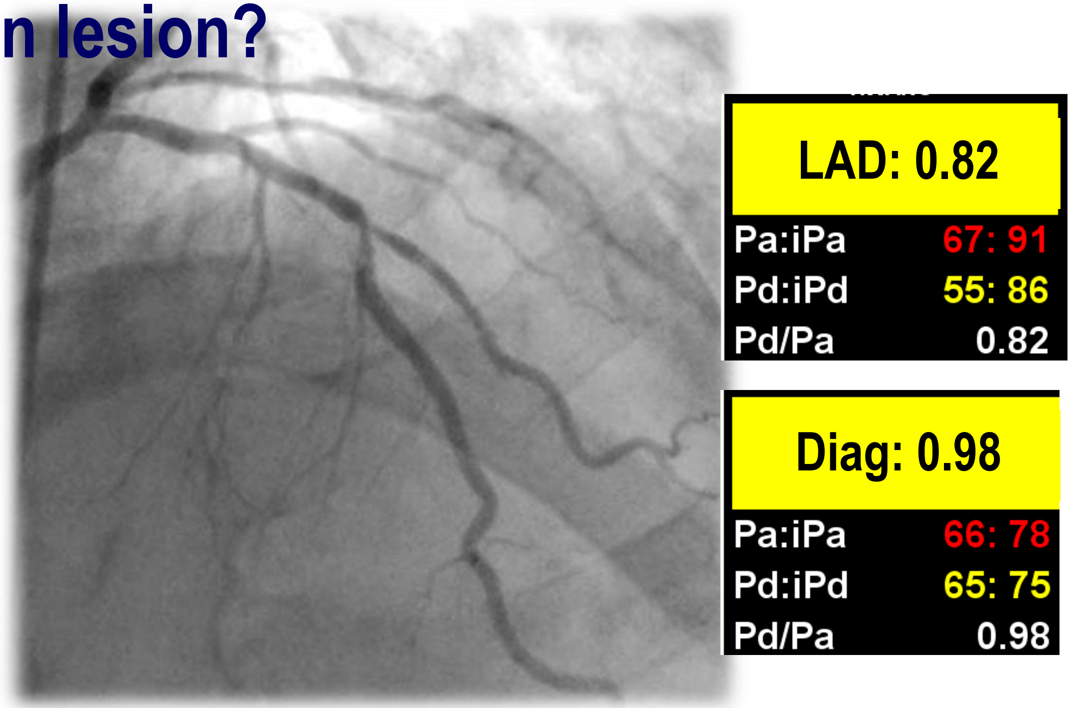
Conclusions—Both plaque shift from the MB and carina shift contribute to the creation/aggravation of an SB ostial lesion after MB stent implantation. Anatomic evaluation does not reliably predict the functional significance of a jailed SB stenosis.

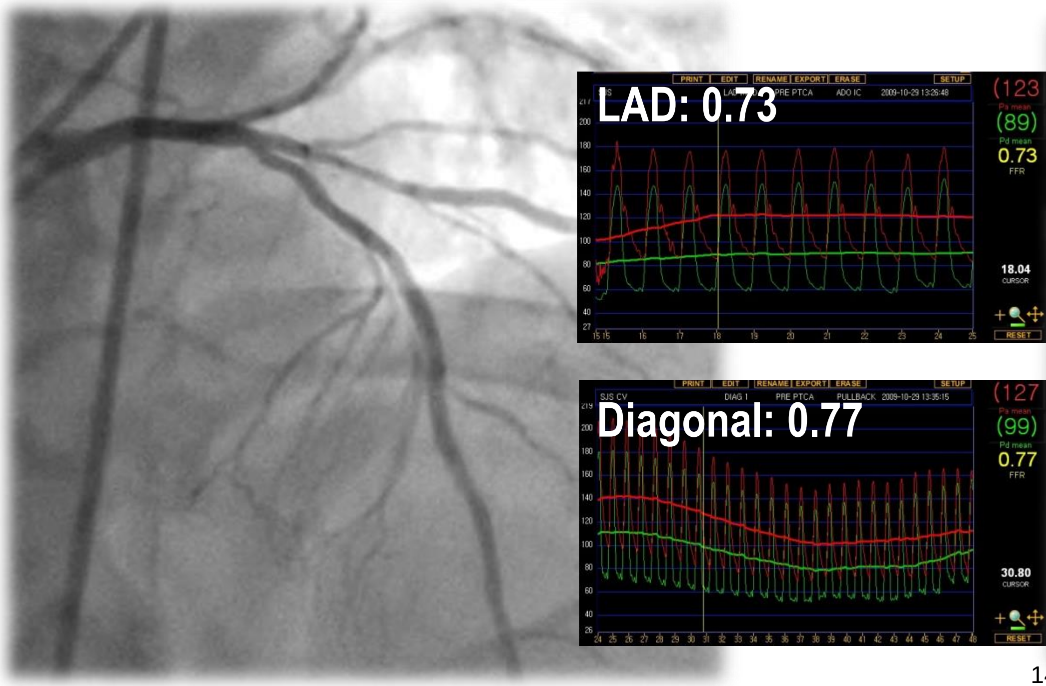
Clinical Trial Registration: http://www.clinicaltrials.gov. Unique Identifier: NCT00553670.

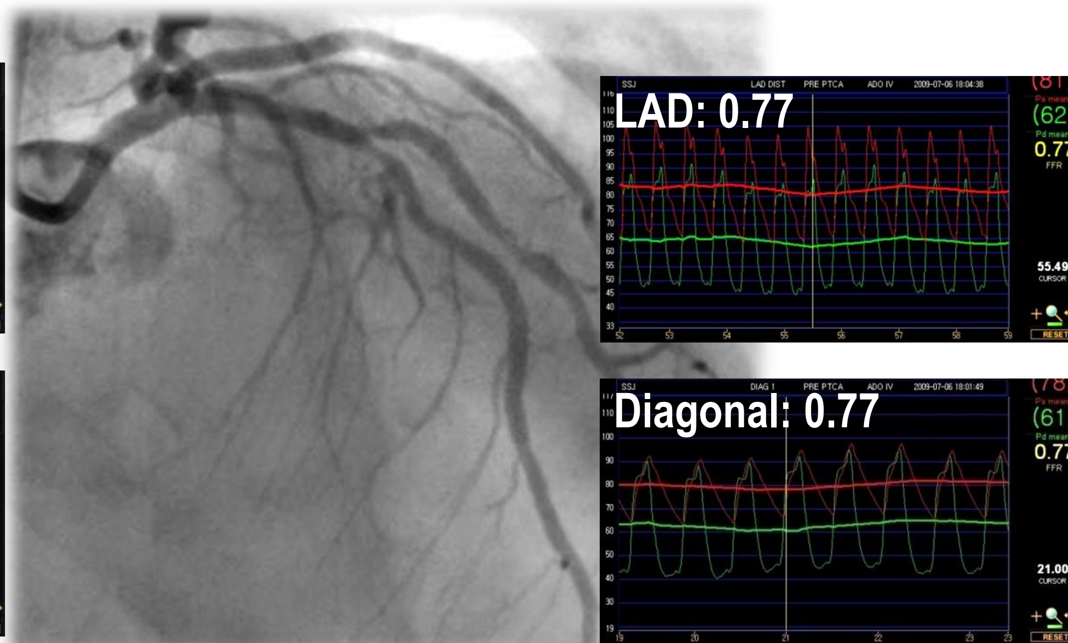
(*Circ Cardiovasc Interv*. 2010;3:113-119.)

Bifurcation lesion?

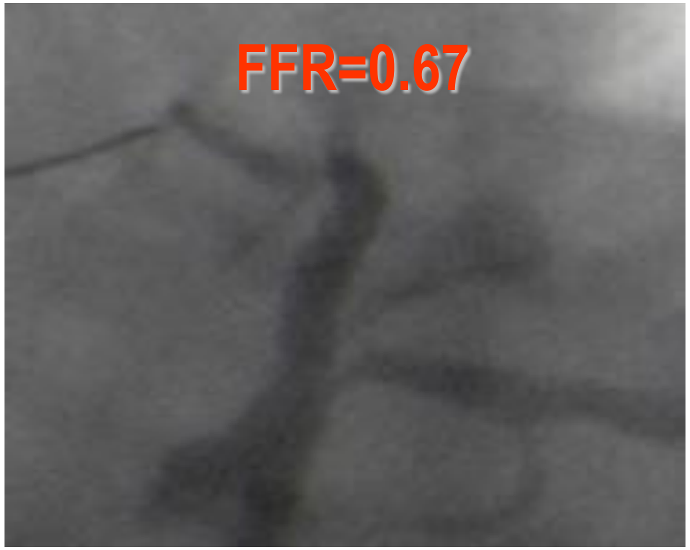


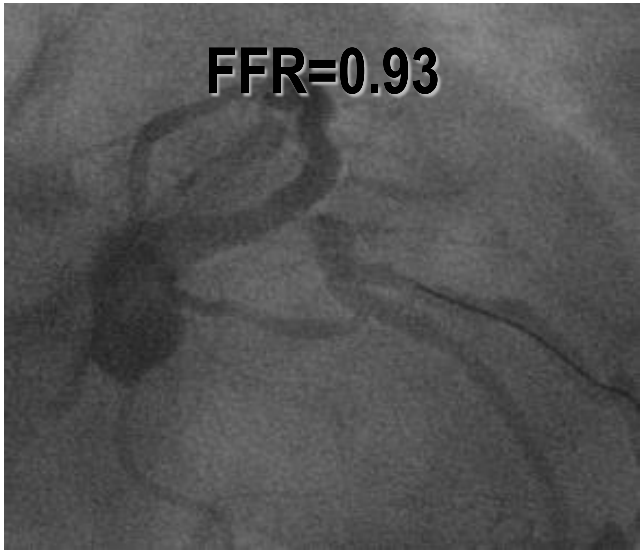


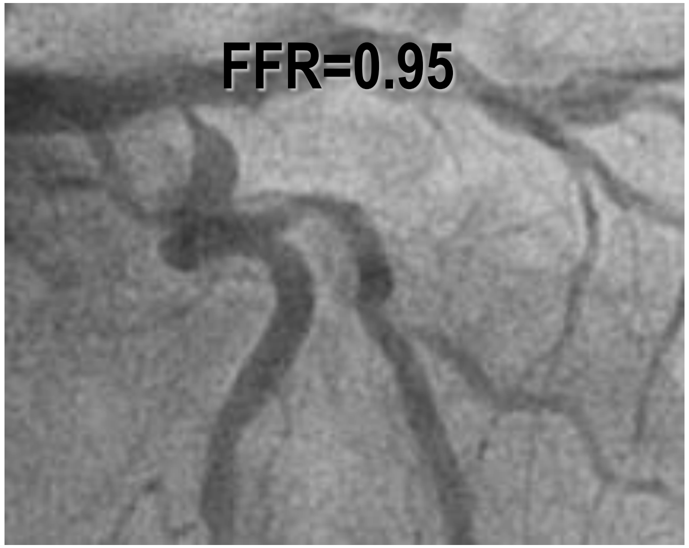


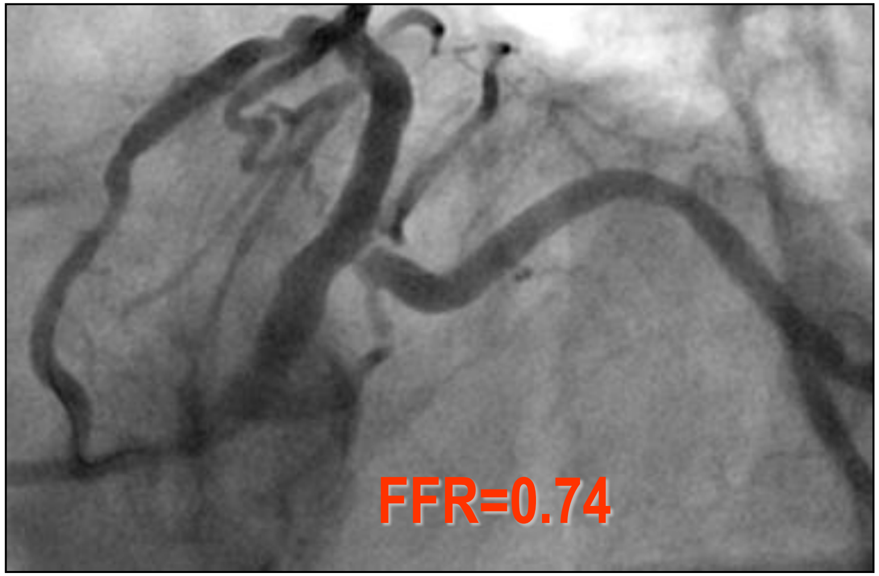


Should we measure FFR in these lesions?

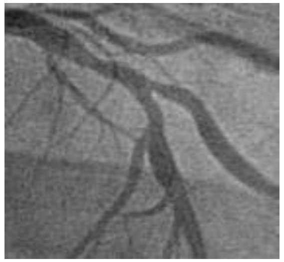


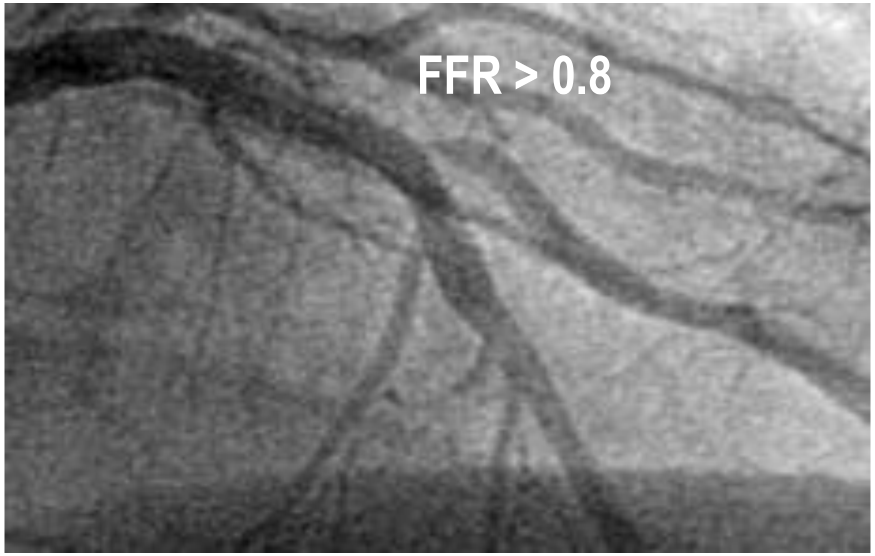


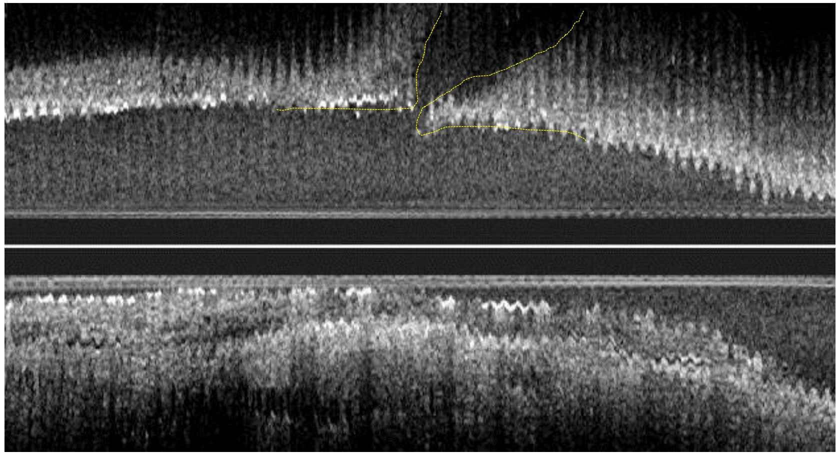




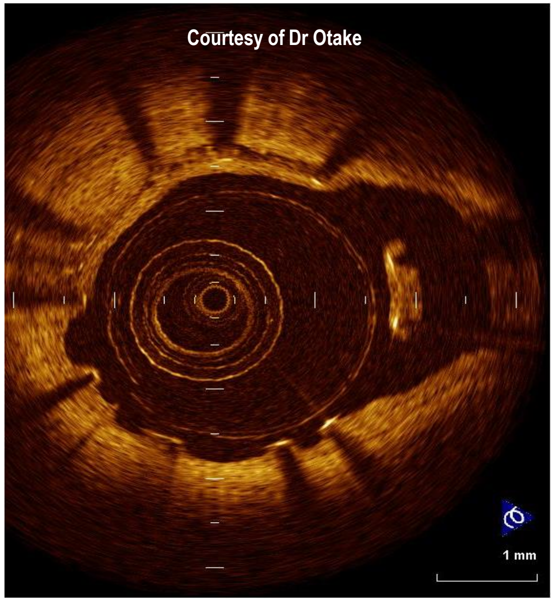
Is this the best we can achieve?



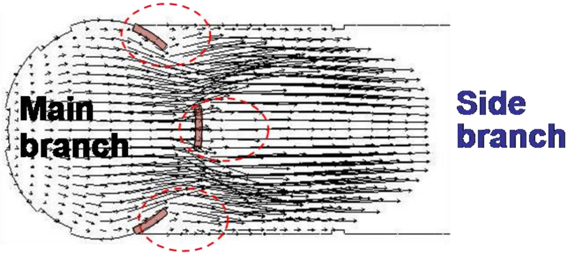


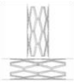


Human cast model



OCT: 18 mo after Cypher

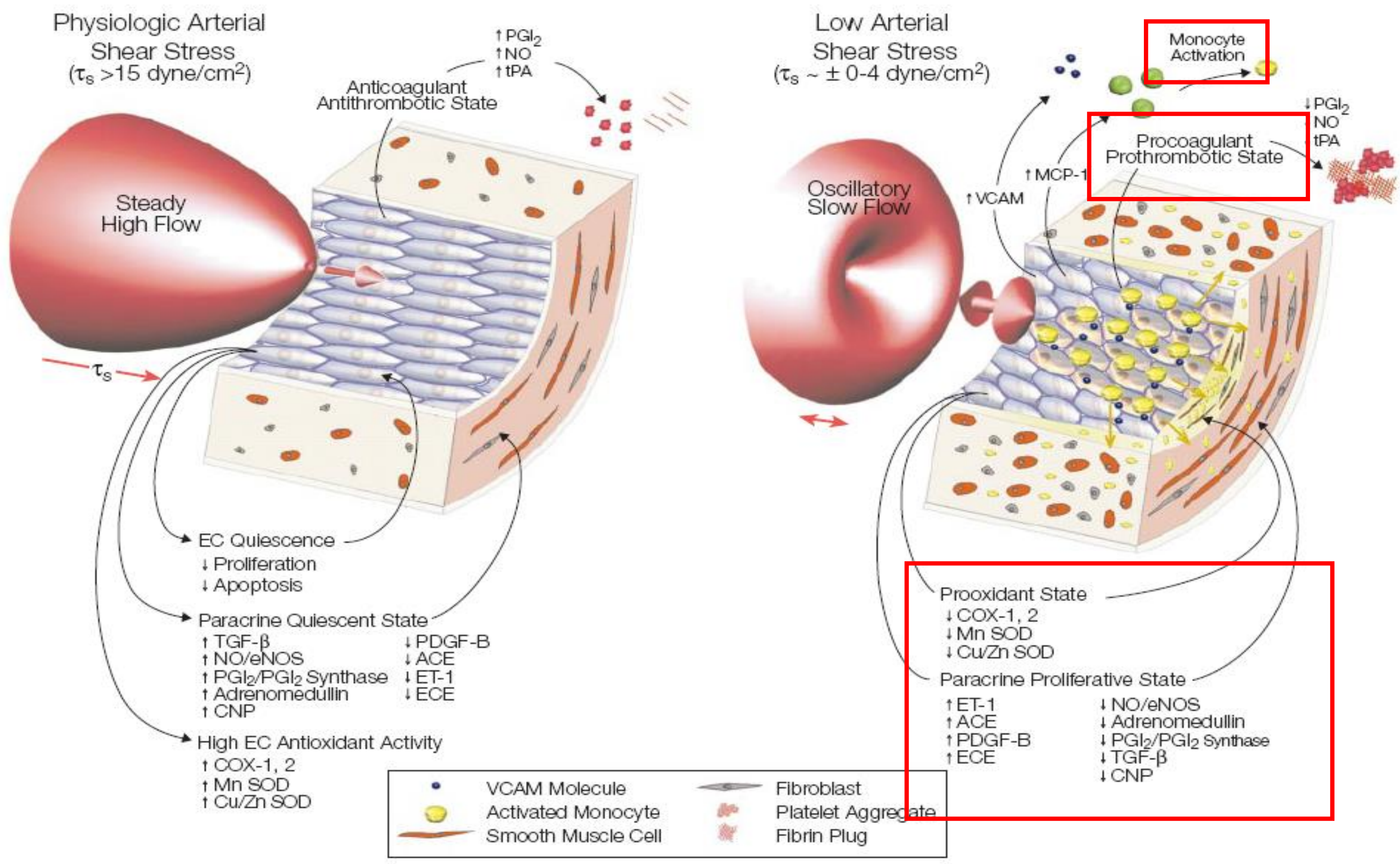




Deplano et al, Med Biol Eng Comput 2004

Low or abnormal wall shear stress

→ Proliferative, pro-inflammatory, pro-thrombotic stimulus



Malek AM, JAMA 1999

How can we assess local "flow conditions"?

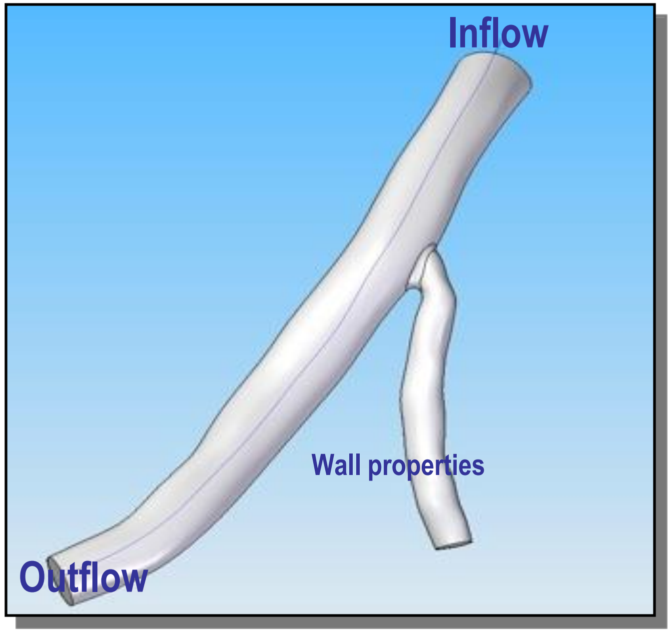
- Computational Fluid Dynamics -

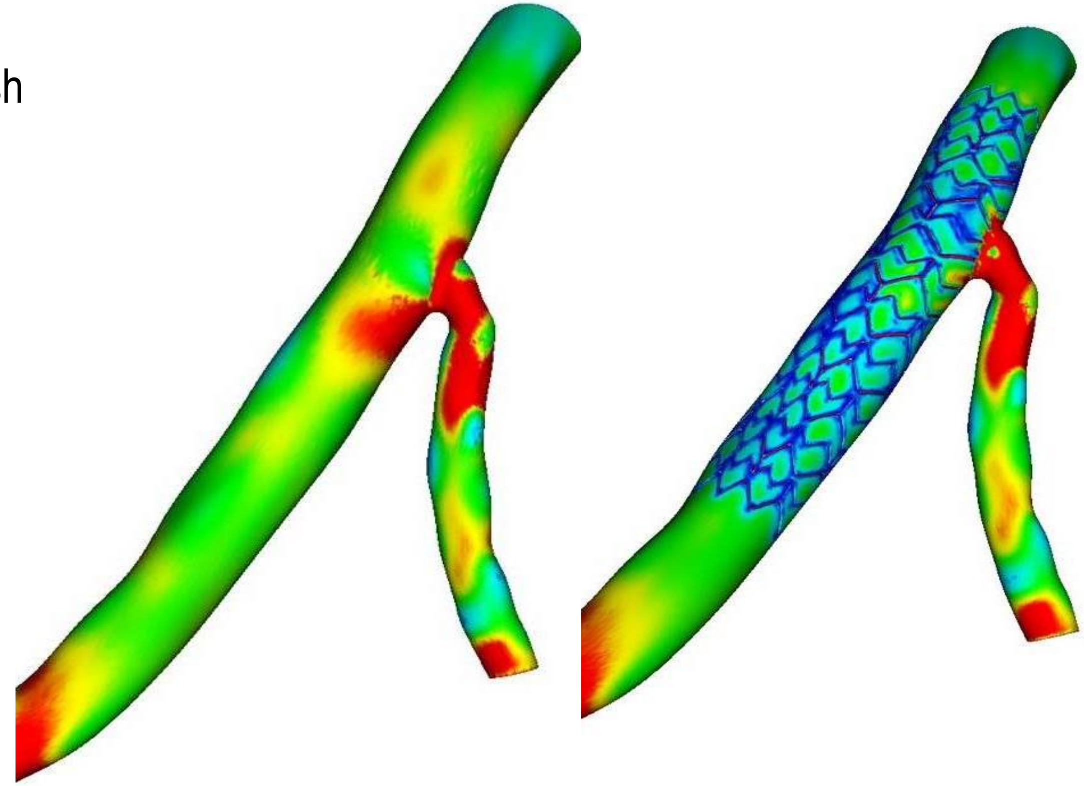
- CFD quantifies fluid pressure and velocity, based on physical laws of mass conservation and momentum balance
- An ideal simulation tool for studying the local effects of blood flow
    - Requirements

      Model geometry and Computational mesh

      Inflow/Out flow boundary conditions

      Wall properties

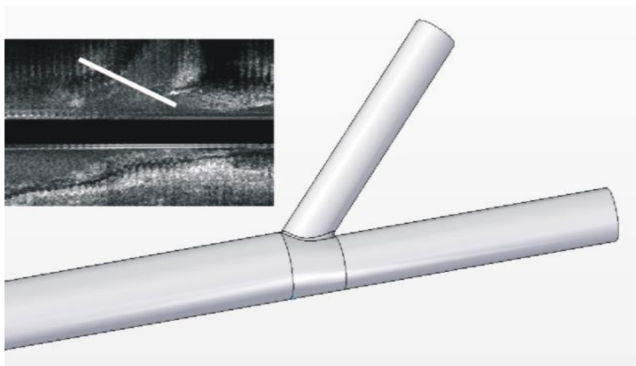


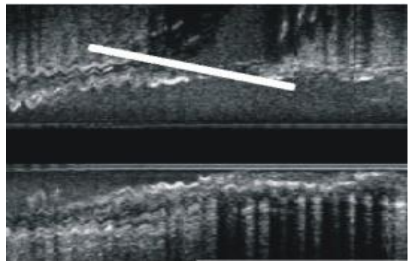


Stent cross over & Distal MB over-expansion

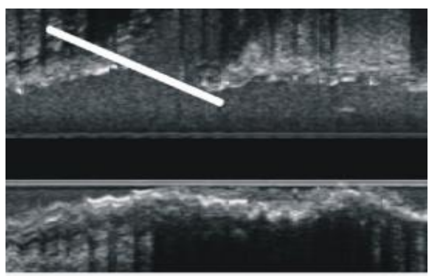
MB Stent Implantation: Carina shift and distal MB over-expansion

Idealized Bifurcation Model





Side Branch Angioplasty



Finet's law

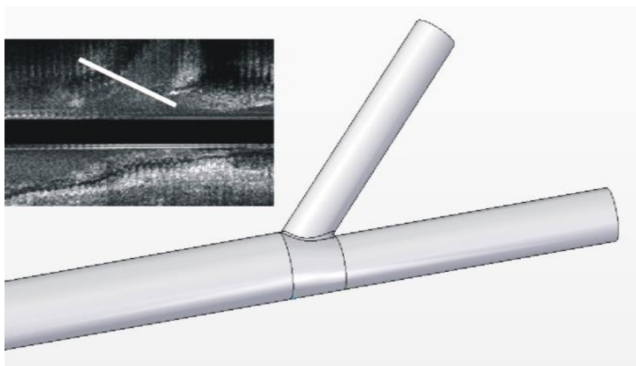
Fractal ratio [prx MB /(SB + dist MB)] = 0.678

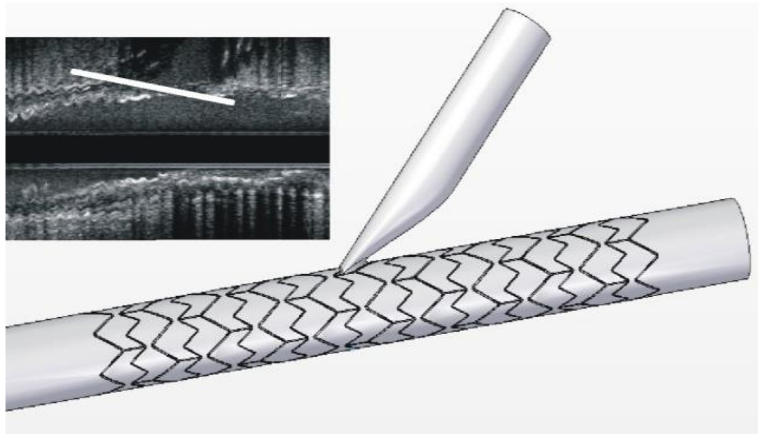
Williams & Koo, J Appl Physiol 2010

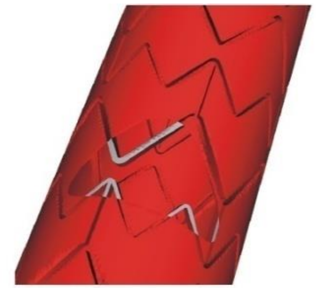
Stent cross over & Distal MB over-expansion

MB Stent Implantation: Carina shift and distal MB over-expansion

Idealized Bifurcation Model

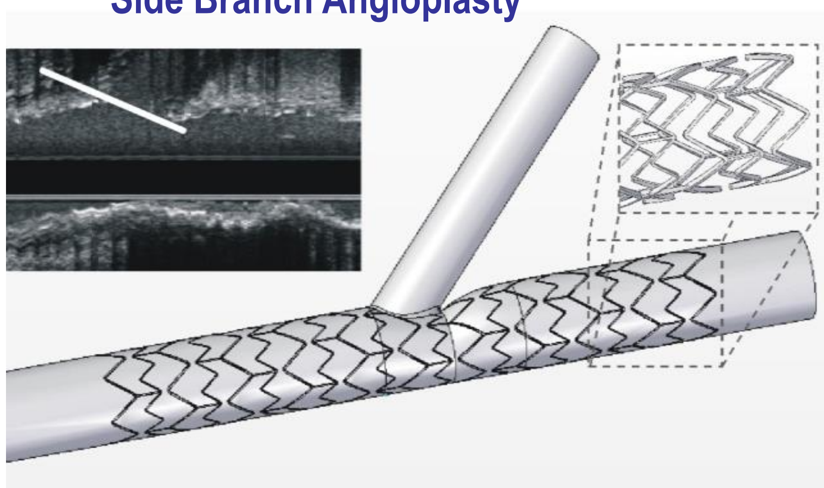


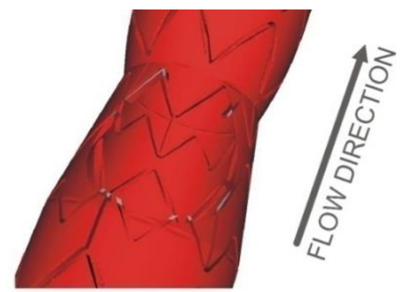




Ostium Area = 1.94 mm^2
Diameter stenosis = 54%
Area stenosis = 51%

Side Branch Angioplasty





Ostium Area = 3.89 mm^2
Diameter stenosis = 0%
Area stenosis = 0%

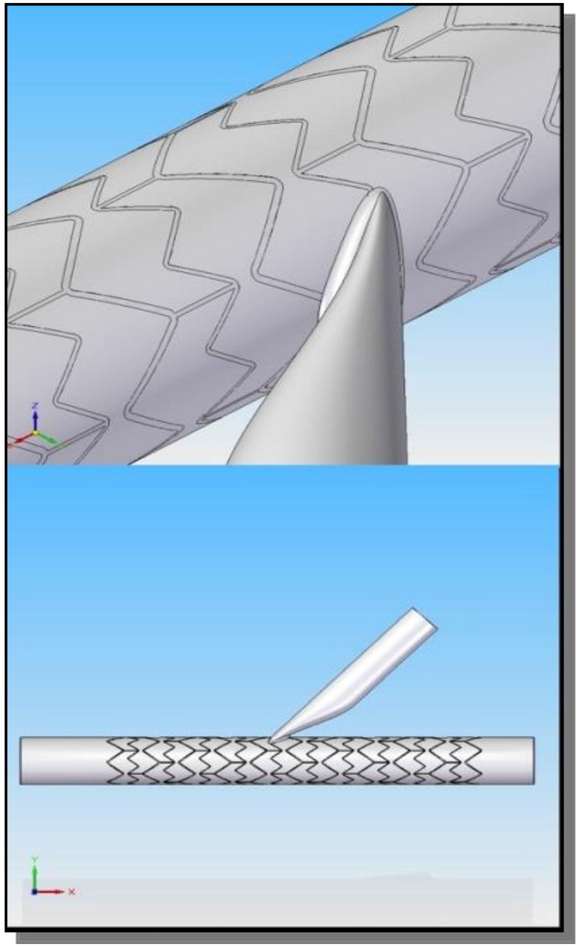
Finet's law

Fractal ratio [prx MB /(SB + dist MB)] = 0.678

Williams & Koo, J Appl Physiol 2010

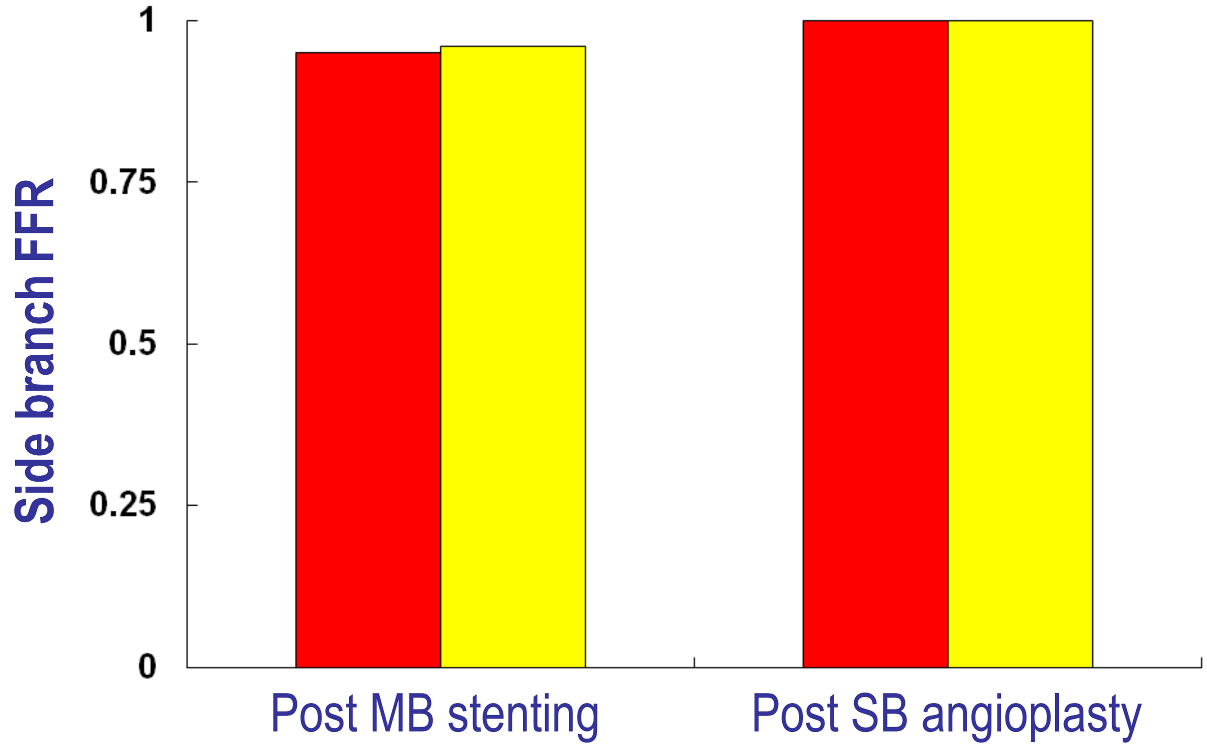
Stent cross over & Distal MB over-expansion

Fractional flow reserve of Side branch



Post MB stenting

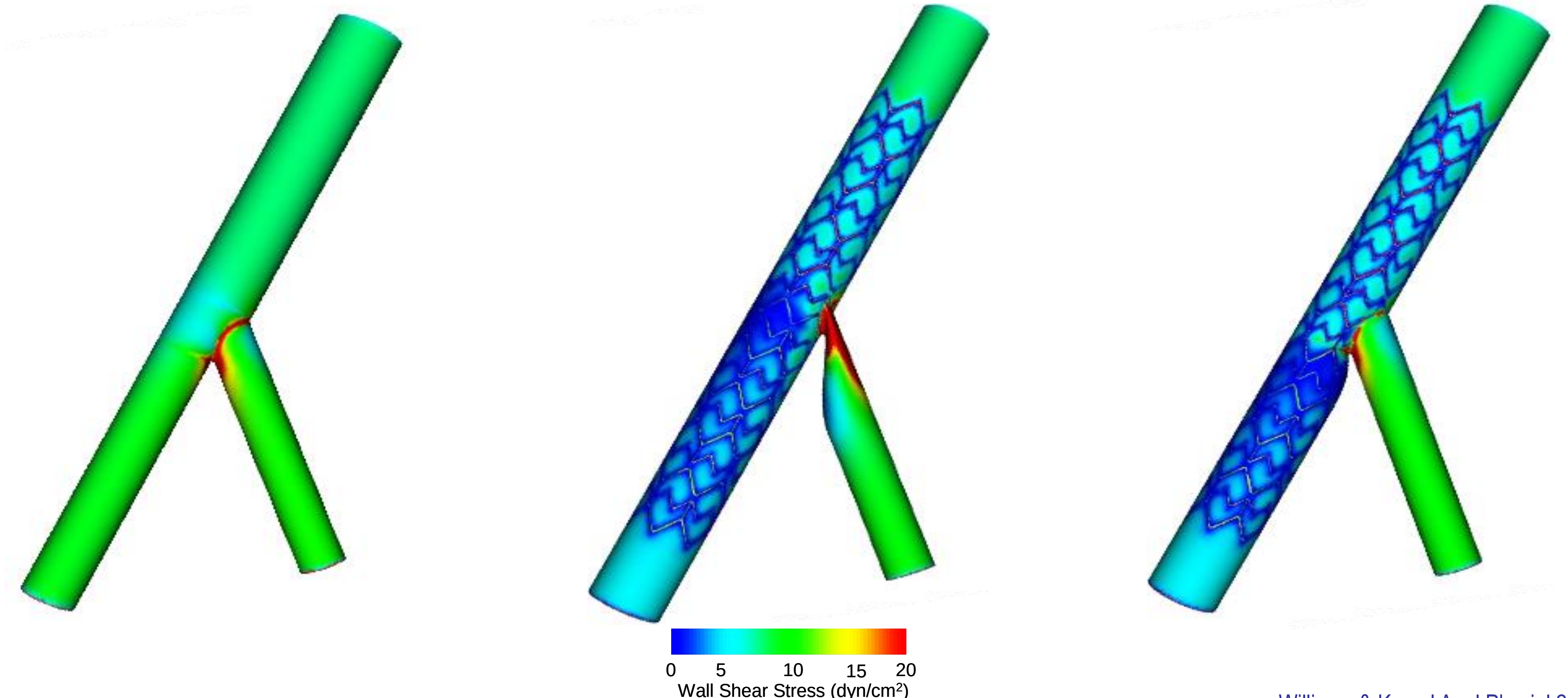
$$FFR = \frac{Q^S_{max}}{Q^N_{max}} = \frac{P_d}{P_a}$$



Stent cross over & Distal MB over-expansion

Time Averaged Wall Shear Stress

Normal bifurcation model | **MB stenting** | **MB stenting + SB angioplasty**

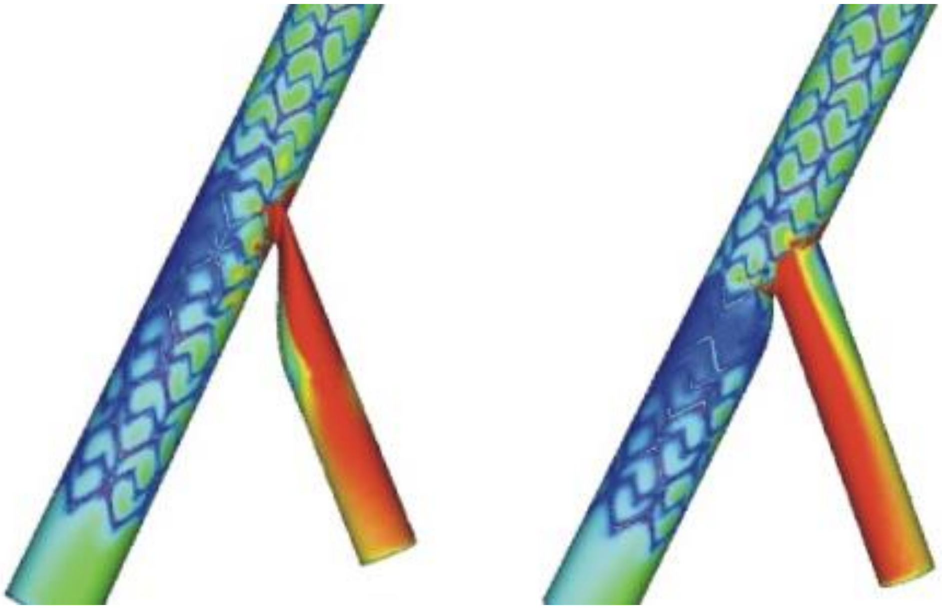


Williams & Koo, J Appl Physiol 2010

Stent cross over & Distal MB over-expansion

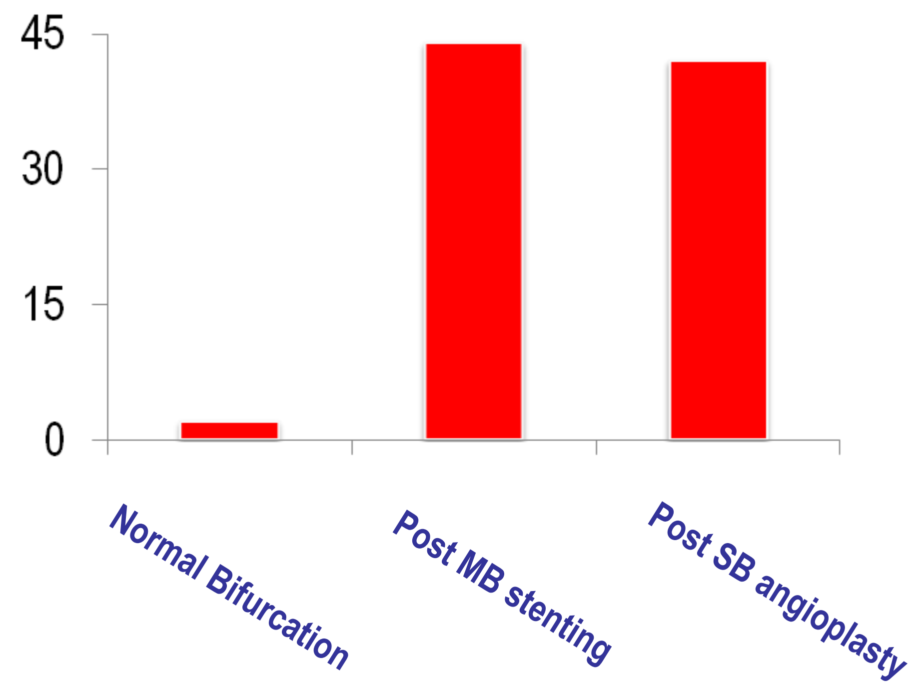
Time Averaged Wall Shear Stress

Shear stress distribution



Post MB stenting Post SB angioplasty

% area of low WSS (< 4dyne/cm^2)



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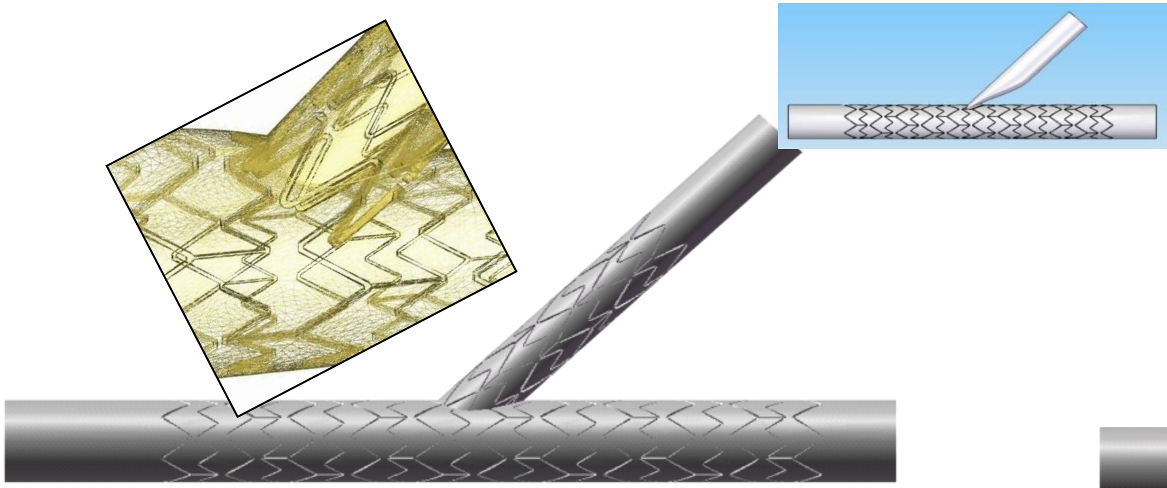
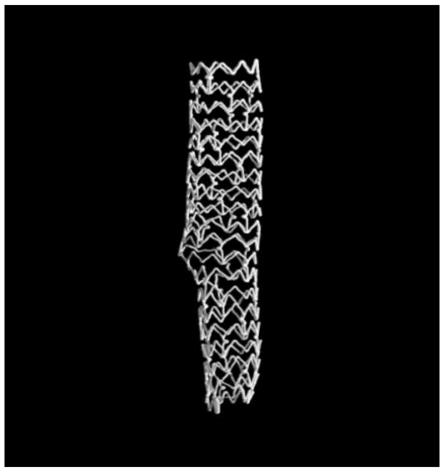
Additional side branch intervention?

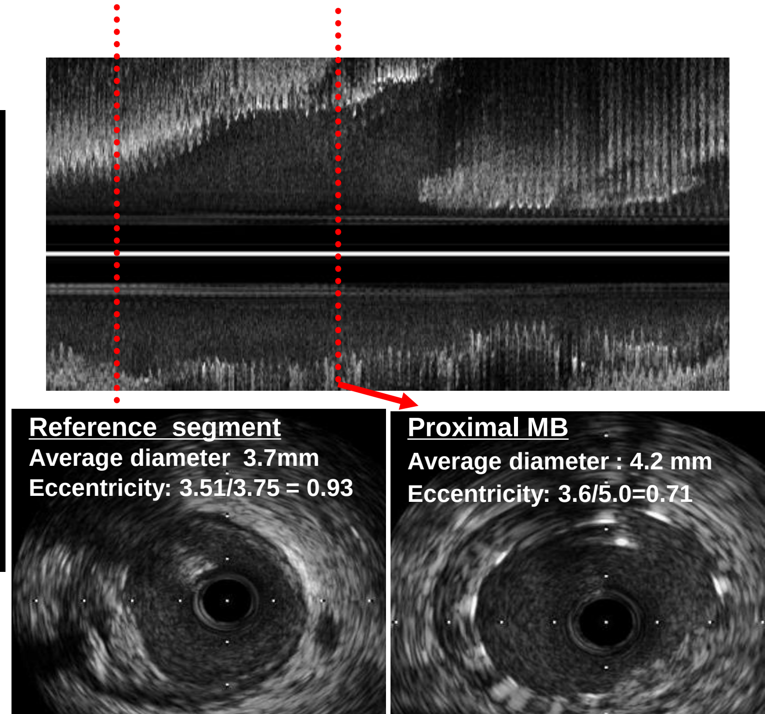


SB stenting without kissing

MB stenting → Aggressive kissing



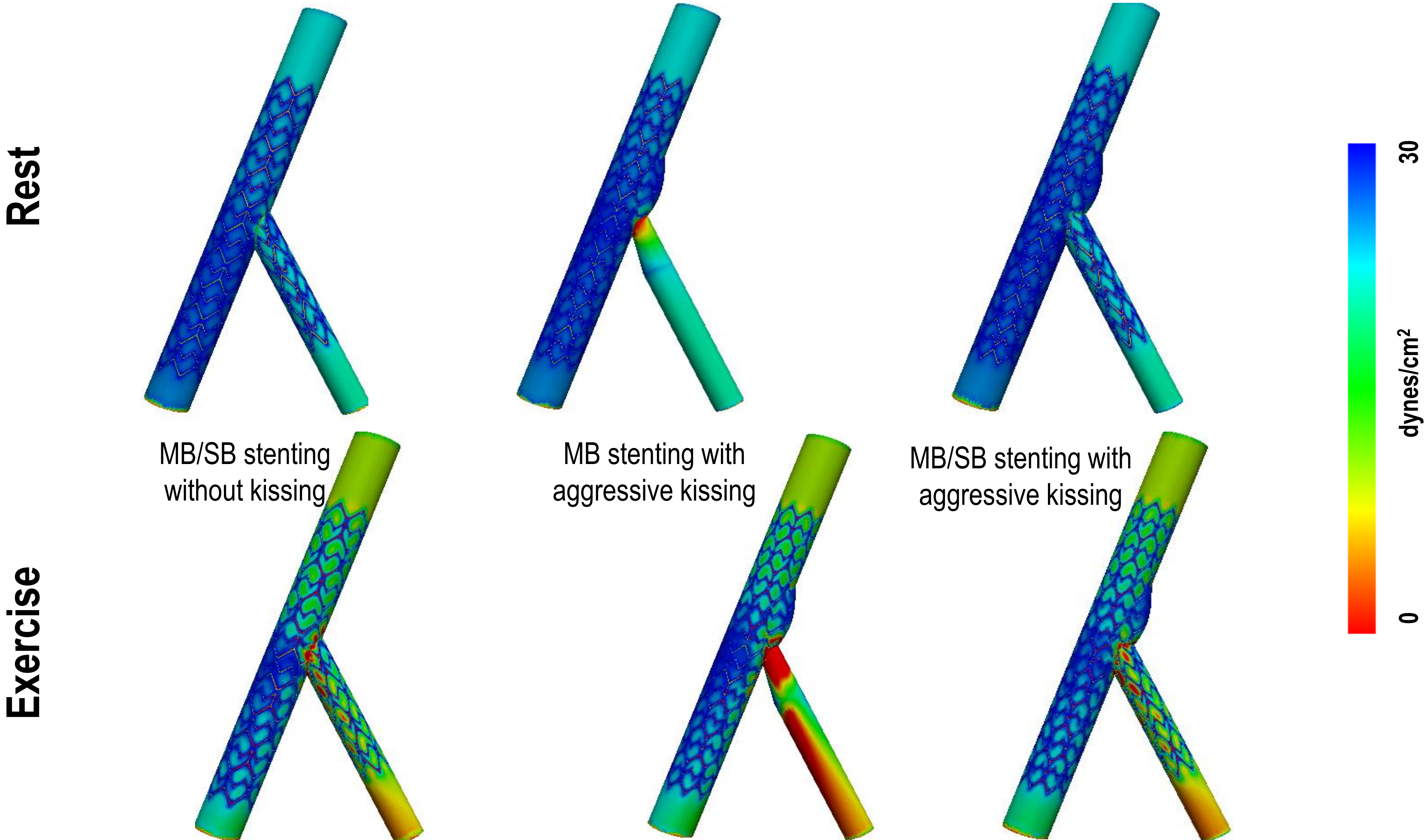
Courtesy of Dr. Murasato



MB and SB stenting → Aggressive kissing

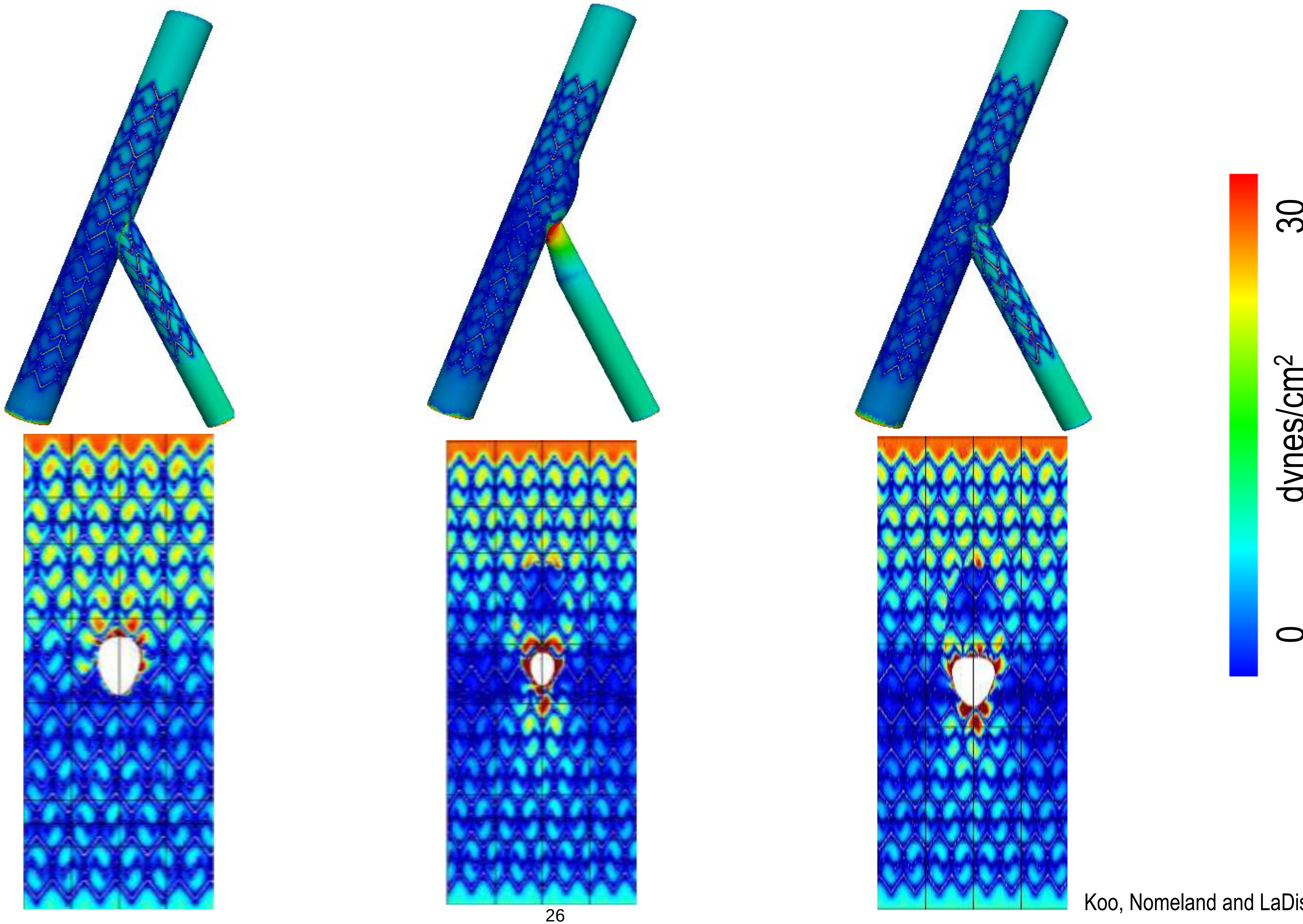
Koo, Nomeland and LaDisa

Distribution of Wall Shear Stress



Koo, Nomeland and LaDisa

Distribution of wall shear stress



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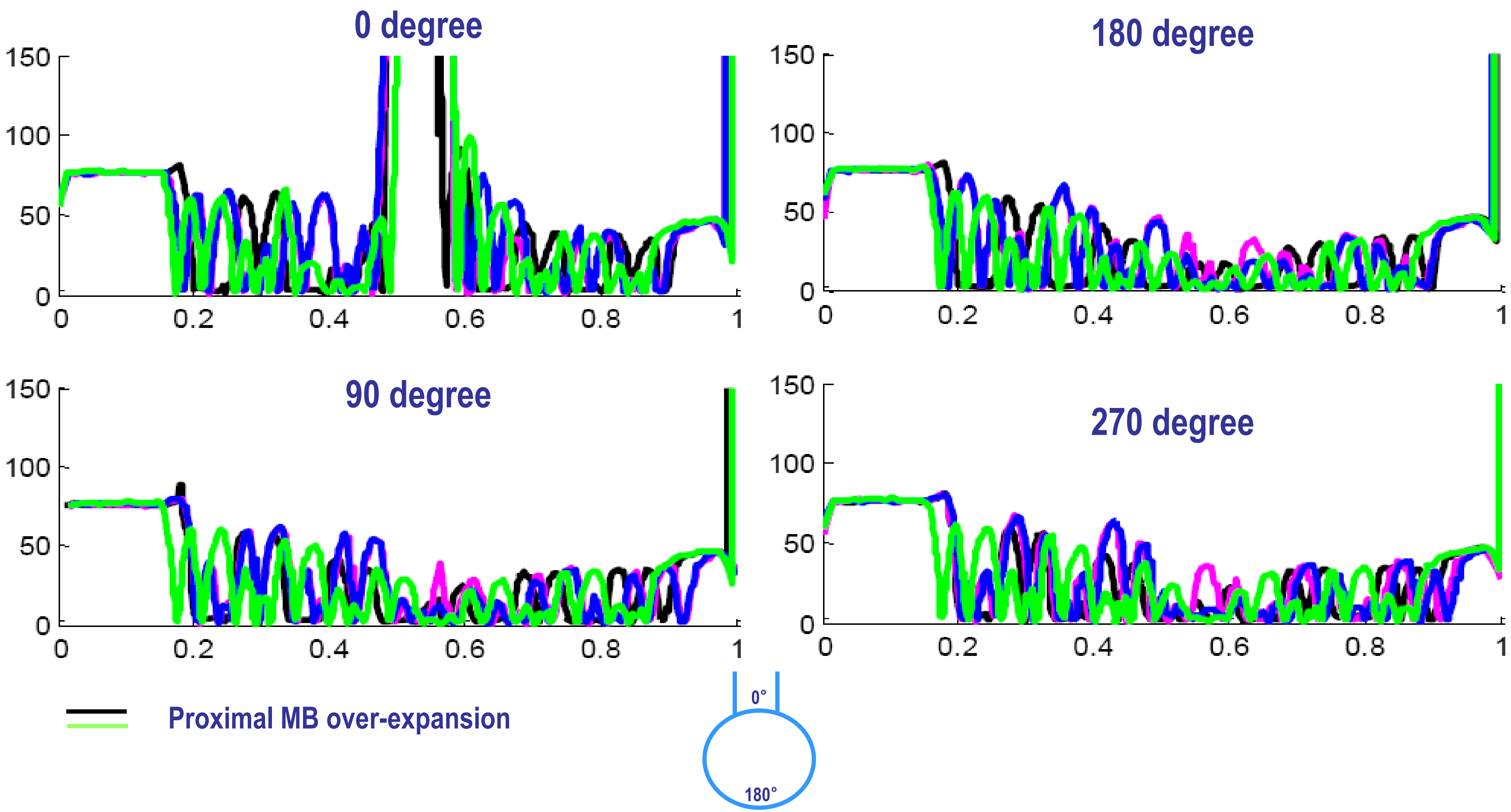
Wall Shear Stress Distribution along Axis



Clinical relevance of "abnormal flow"?

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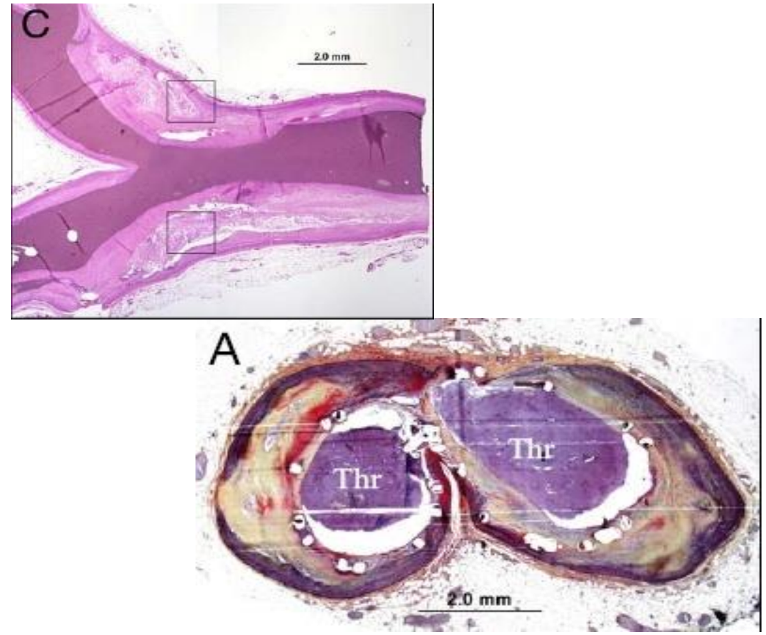
Pathological Findings at Bifurcation Lesions

The Impact of Flow Distribution on Atherosclerosis and Arterial Healing After Stent Implantation

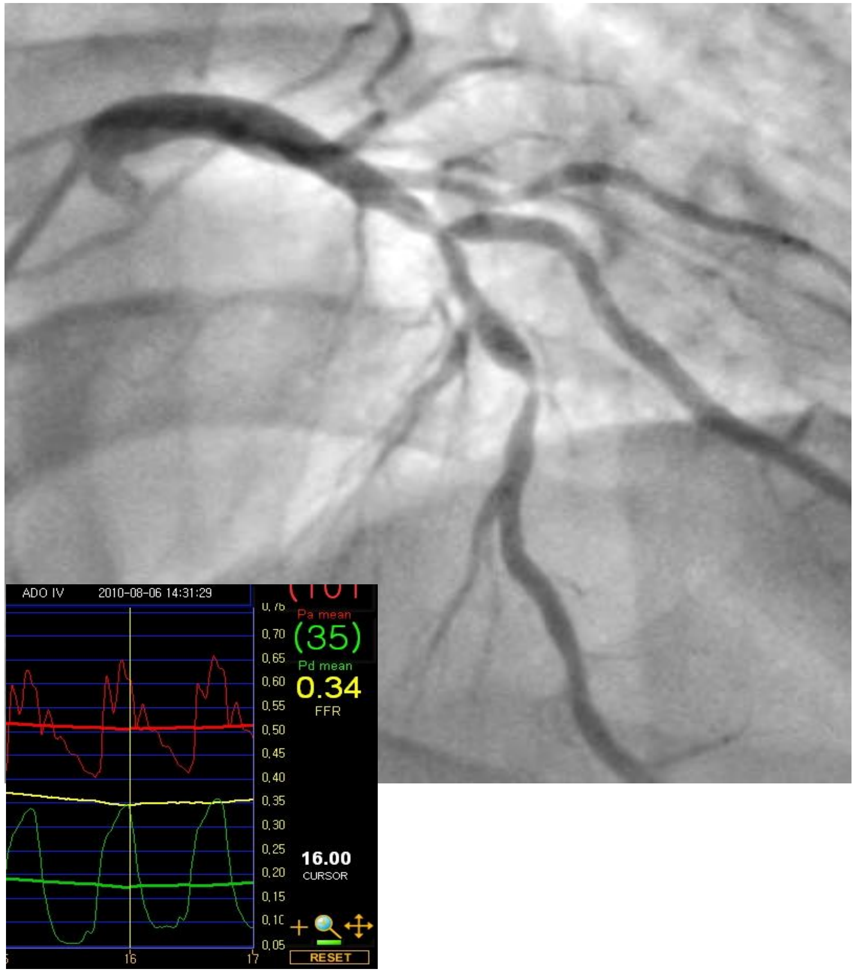
Gaku Nakazawa, MD,* Saami K. Yazdani, PHD,* Aloke V. Finn, MD,† Marc Vorpahl, MD,* Frank D. Kolodgie, PHD,* Renu Virmani, MD*
Gaithersburg, Maryland; and Atlanta, Georgia

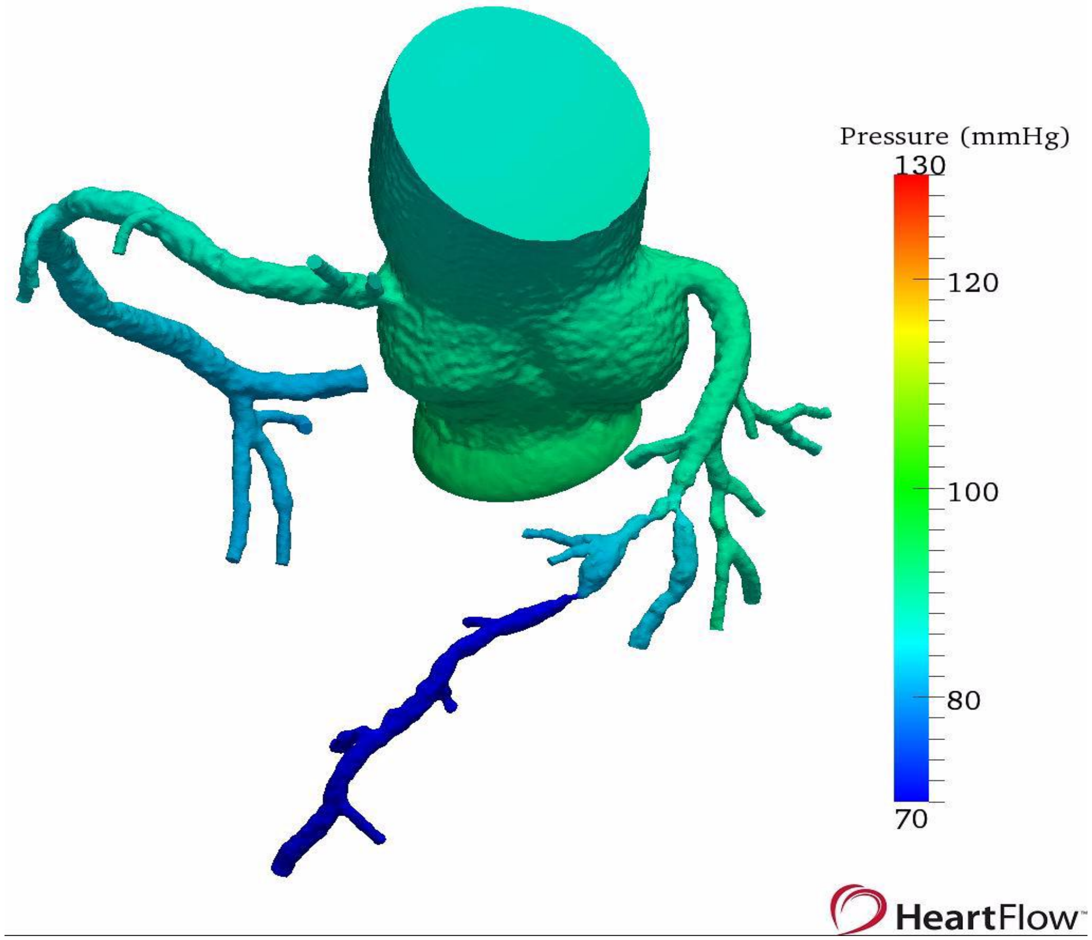


Limitations of current CFD analyses

- Simple models, not patient-specific
- Not completely reflects human coronary circulation
- No established clinical relevance

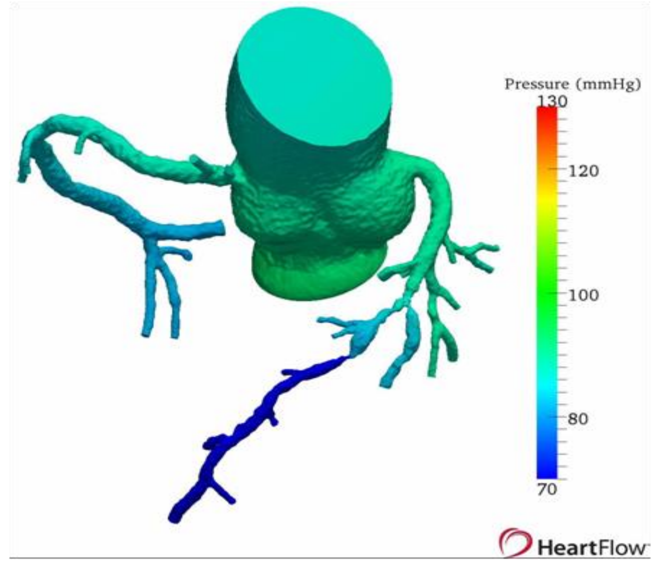
Patient-specific CFD analysis

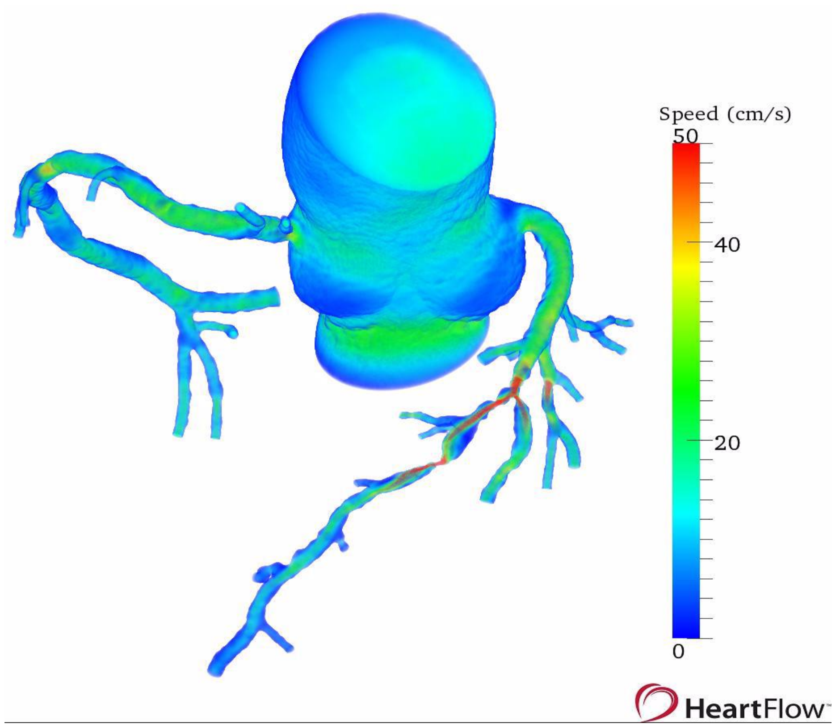


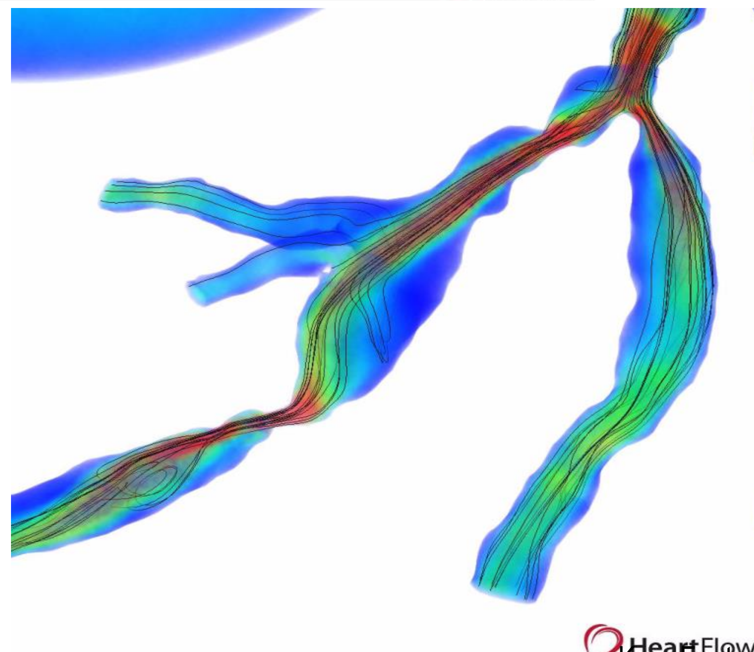


Koo, Fonte and Taylor

Patient-specific CFD analysis







Koo, Fonte and Taylor

Summary

- Coronary bifurcation is complex.
- Physiologic evaluation is helpful to overcome the limitation of anatomical tools in bifurcation lesions.
- Evaluation of local flow dynamics using CFD can provide the local flow conditions in bifurcation lesions.
- Successful PCI for bifurcation lesions in terms of anatomy, physiology and flow dynamics may further improve the patients' outcome.