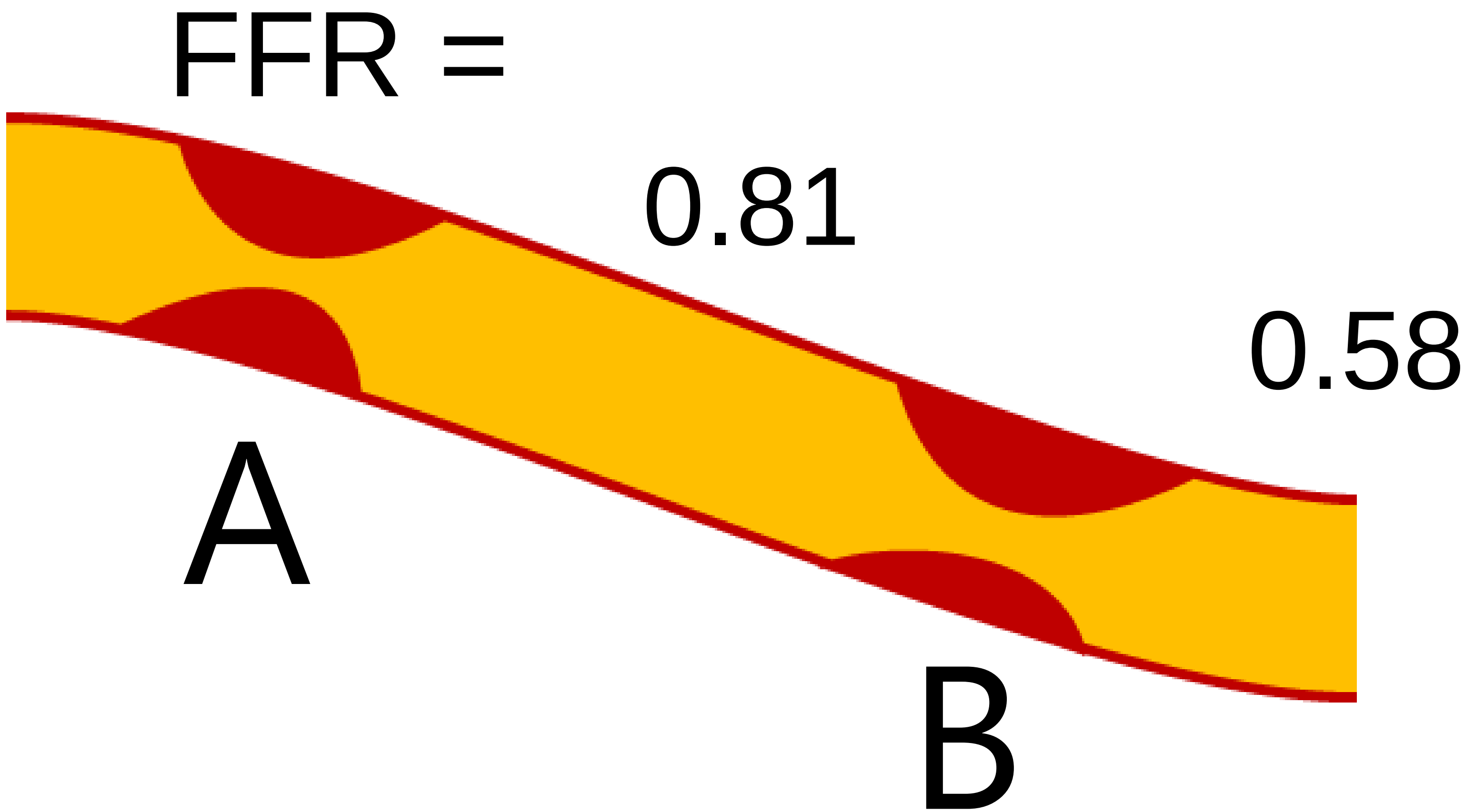
True Functional Severity of An Individual Coronary Stenosis With Accounting for Hemodynamic Interaction Between Stenoses

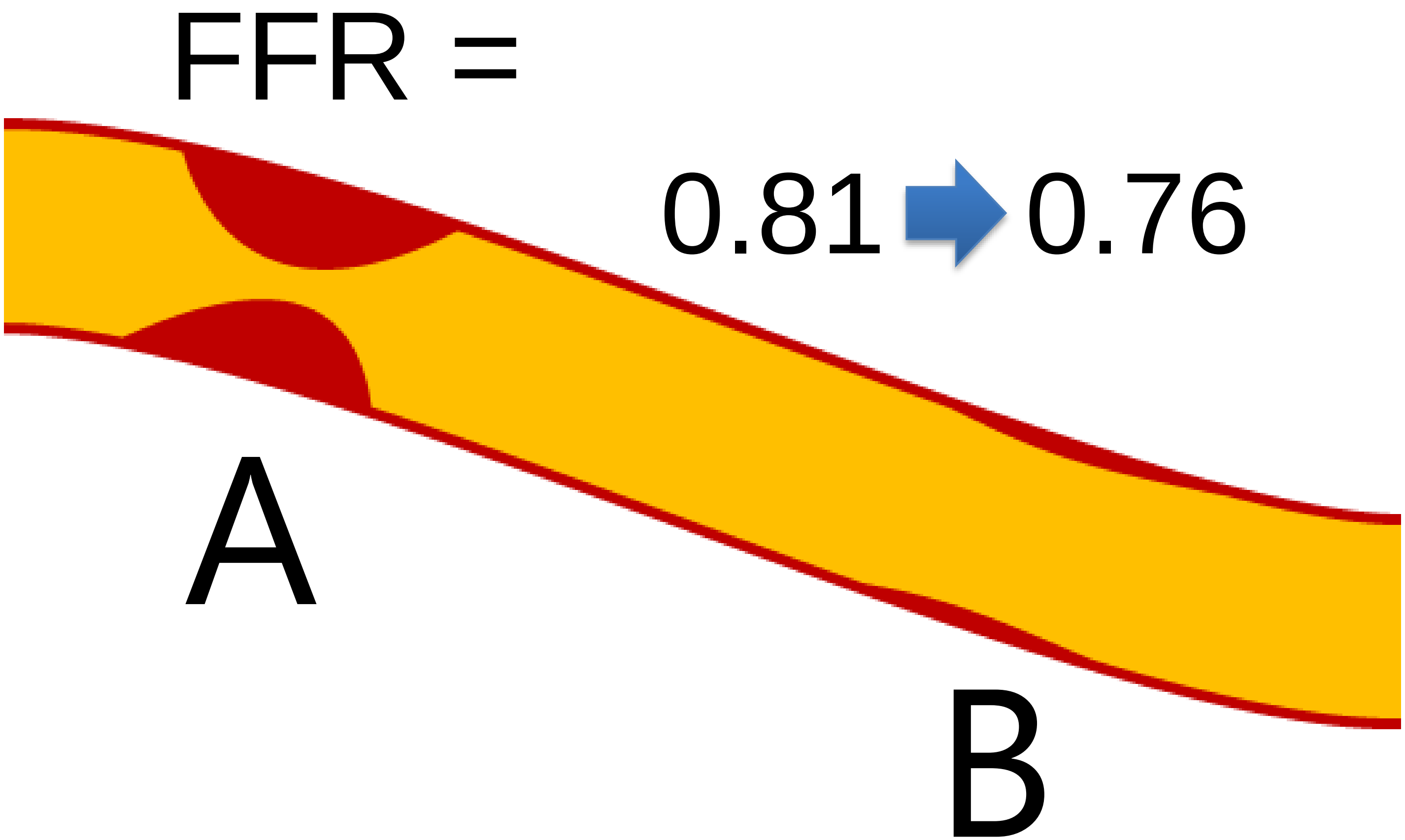
Naritatsu Saito

Department of Cardiology, Kyoto University Hospital

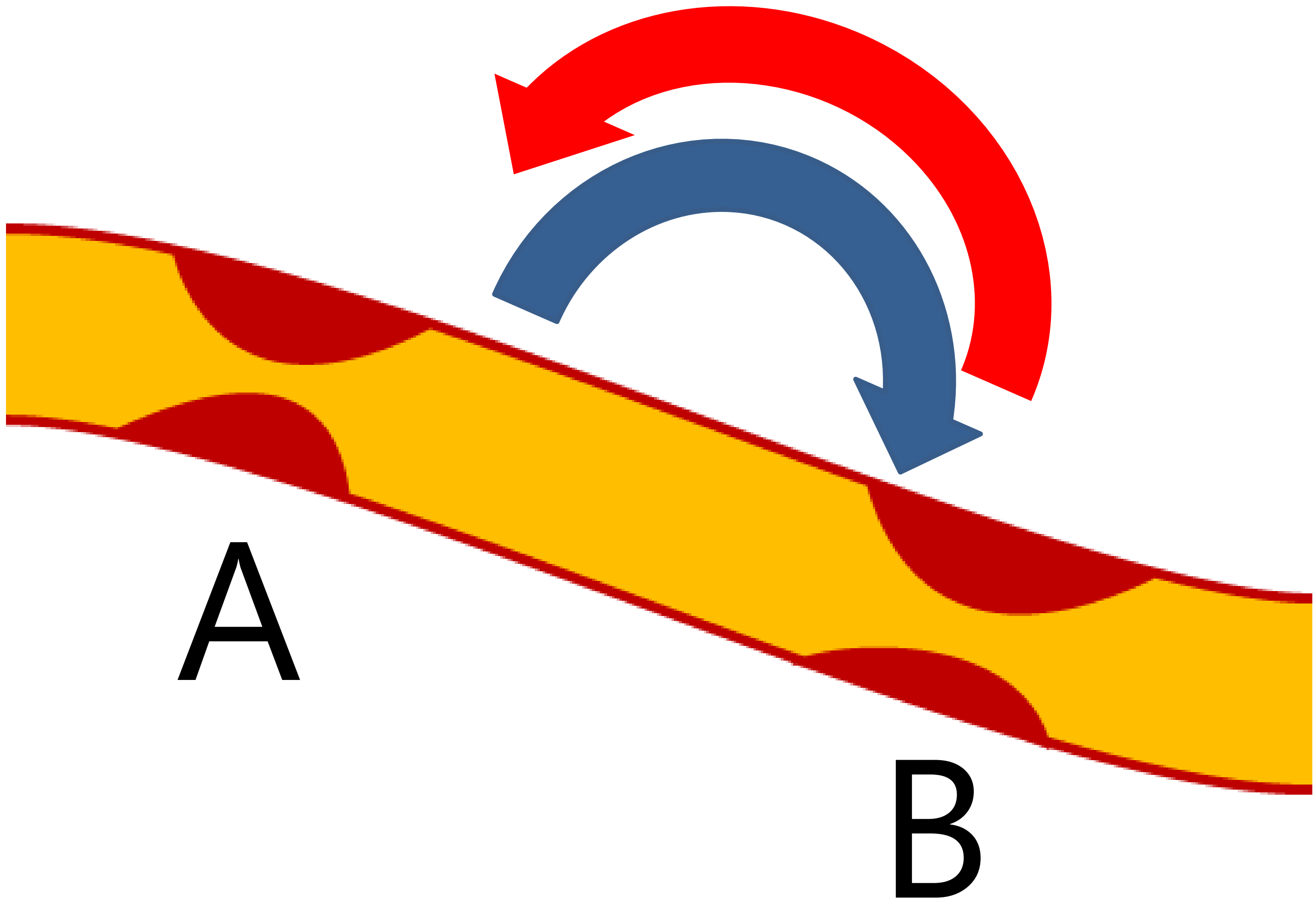
Tandem Lesion



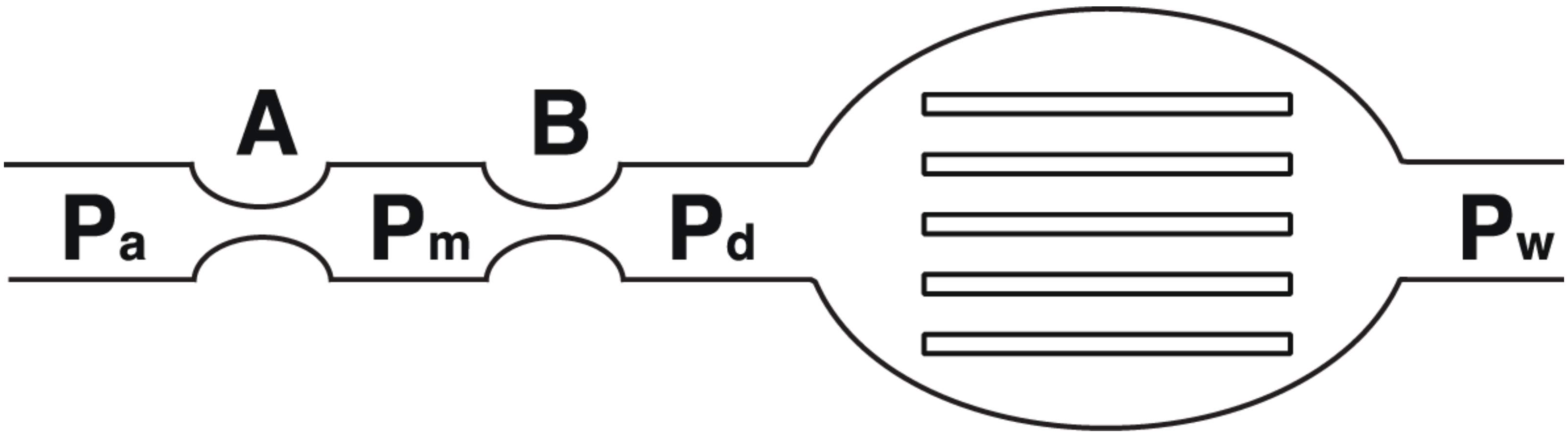
Tandem Lesion



Hemodynamic Interaction



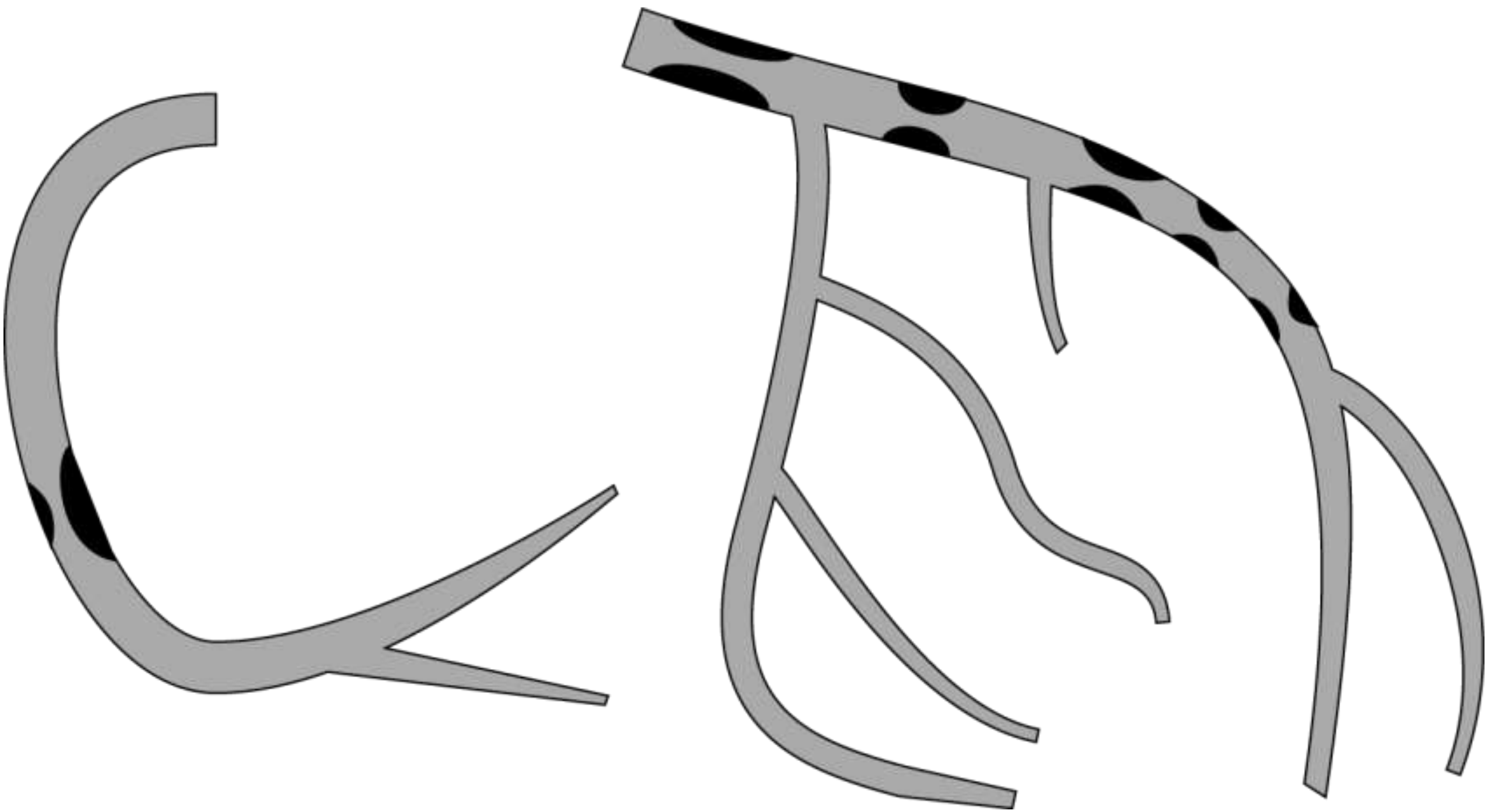
Tandem lesion



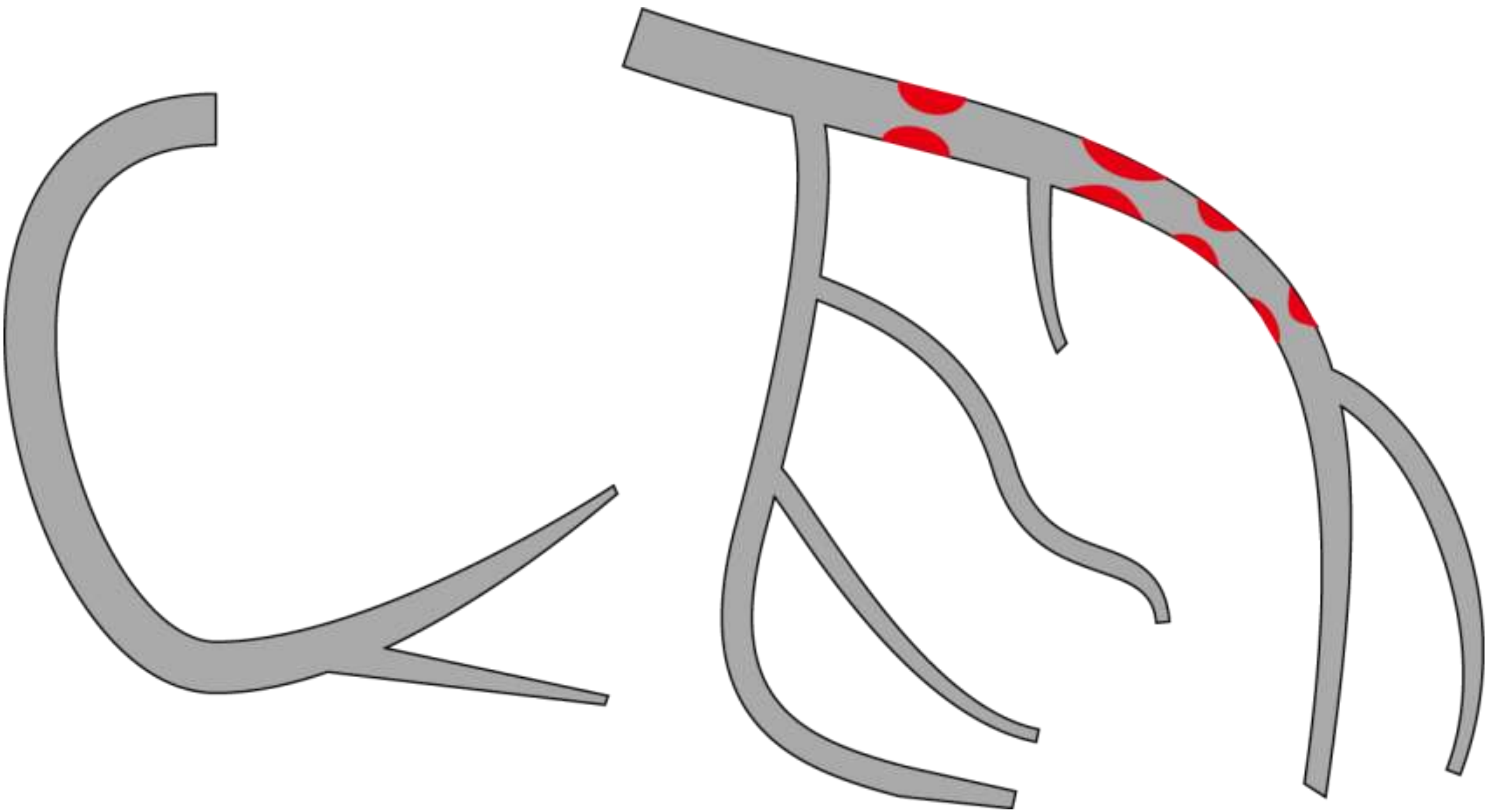
$$FFR(A)_{pred} = \frac{P_d - \left(\frac{P_m}{P_a}\right)P_w}{P_a - P_m + P_d - P_w}$$

$$FFR(B)_{pred} = 1 - \frac{(P_a - P_w)(P_m - P_d)}{P_a(P_m - P_w)}$$

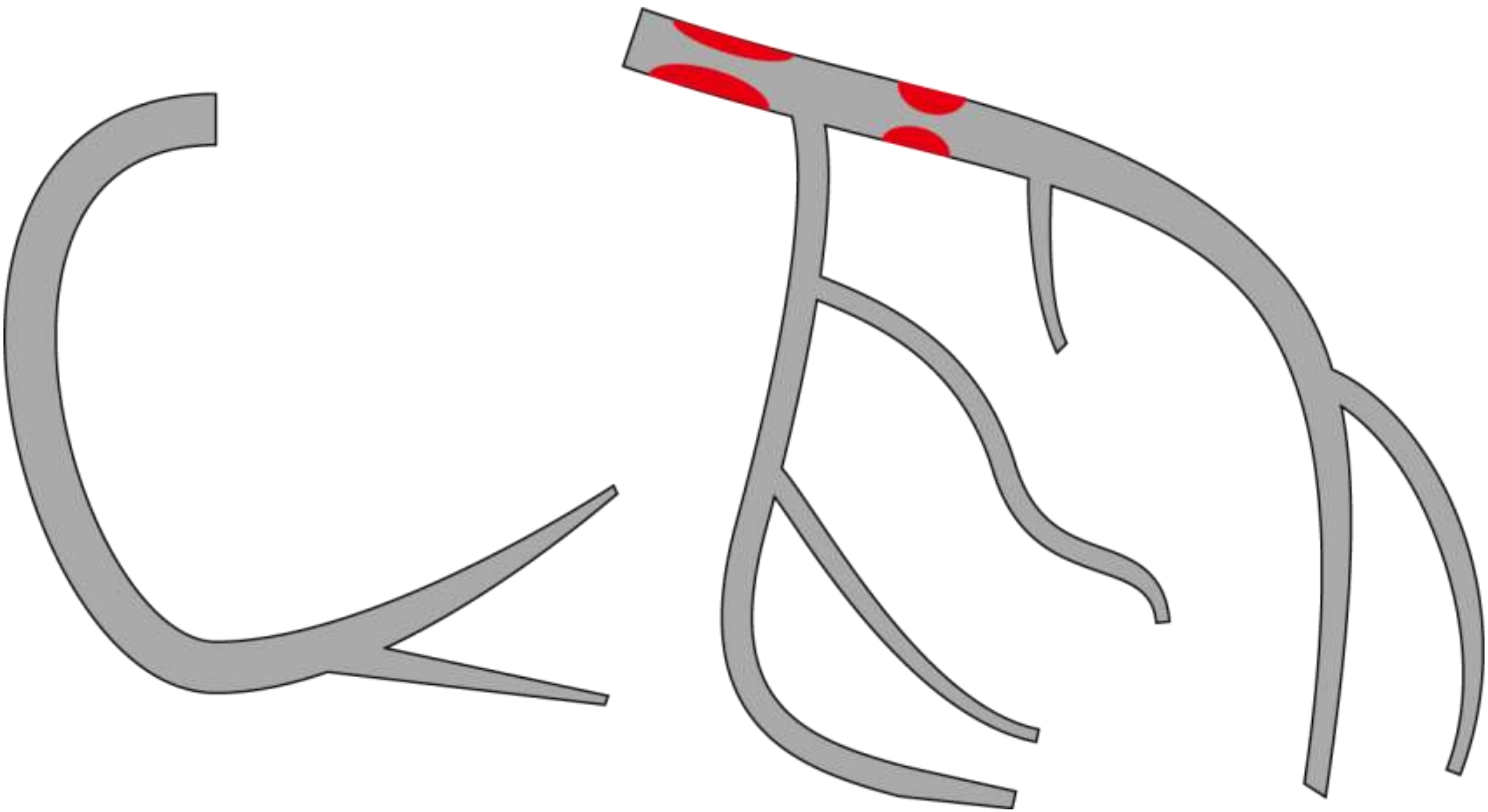
De Bruyne B, et al. Circulation 2000 18;101(15):1840–1847.



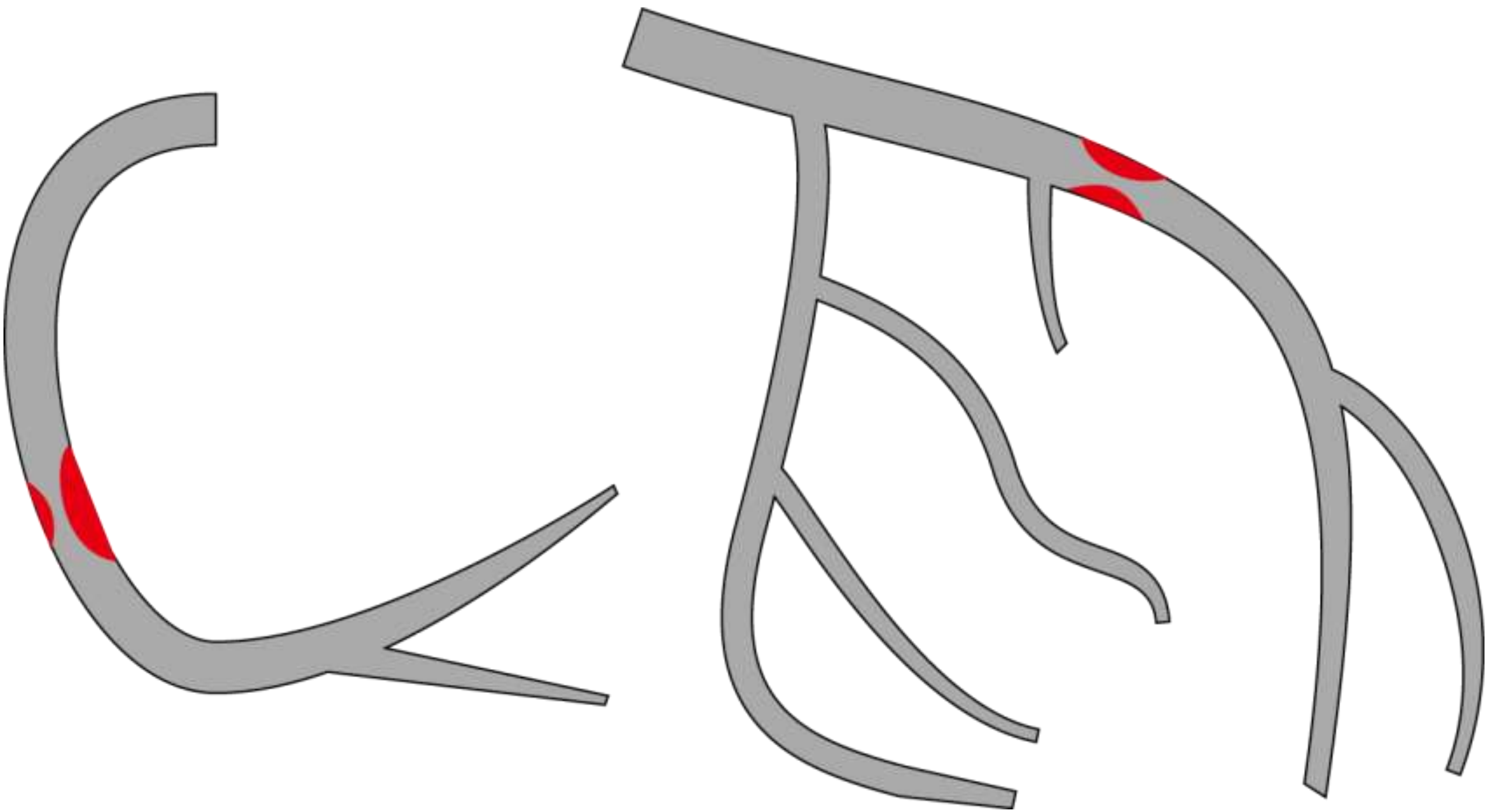
Sequential / Diffuse



Bifurcation



Remote



Hemodynamic Interaction

1. Sequential

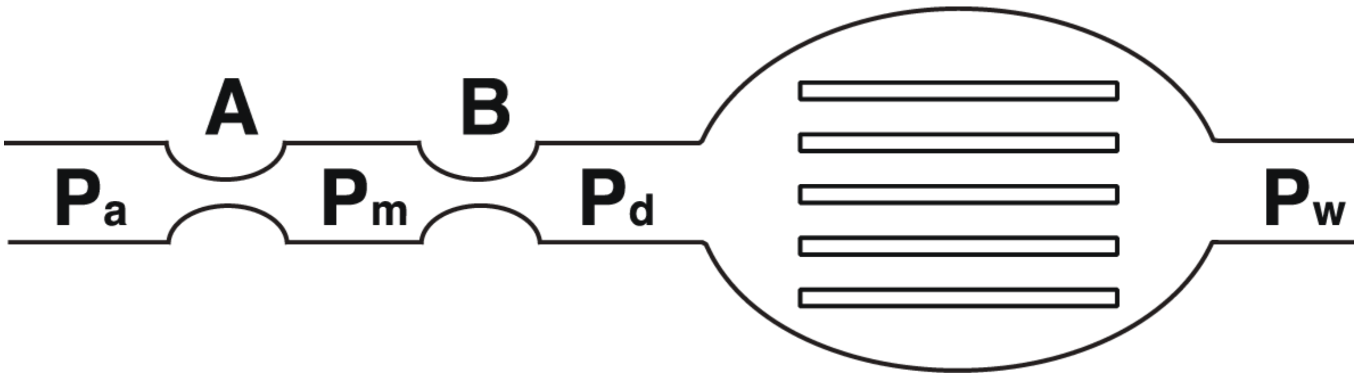
2. Bifurcation

3. Remote

Hemodynamic Interaction

1. Sequential
2. Bifurcation
3. Remote

Tandem lesion

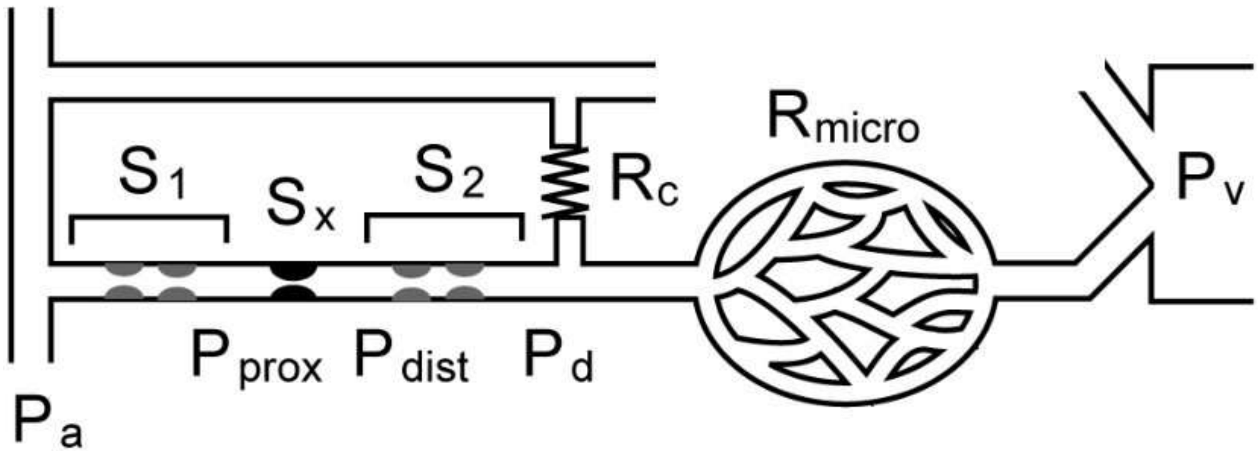


$$FFR(A)_{pred} = \frac{P_d - (\frac{P_m}{P_a})P_w}{P_a - P_m + P_d - P_w}$$

$$FFR(B)_{pred} = 1 - \frac{(P_a - P_w)(P_m - P_d)}{P_a(P_m - P_w)}$$

De Bruyne B, et al. Circulation 2000 18;101(15):1840–1847.

Generalization: n sequential lesions



True FFR after releasing Sx:

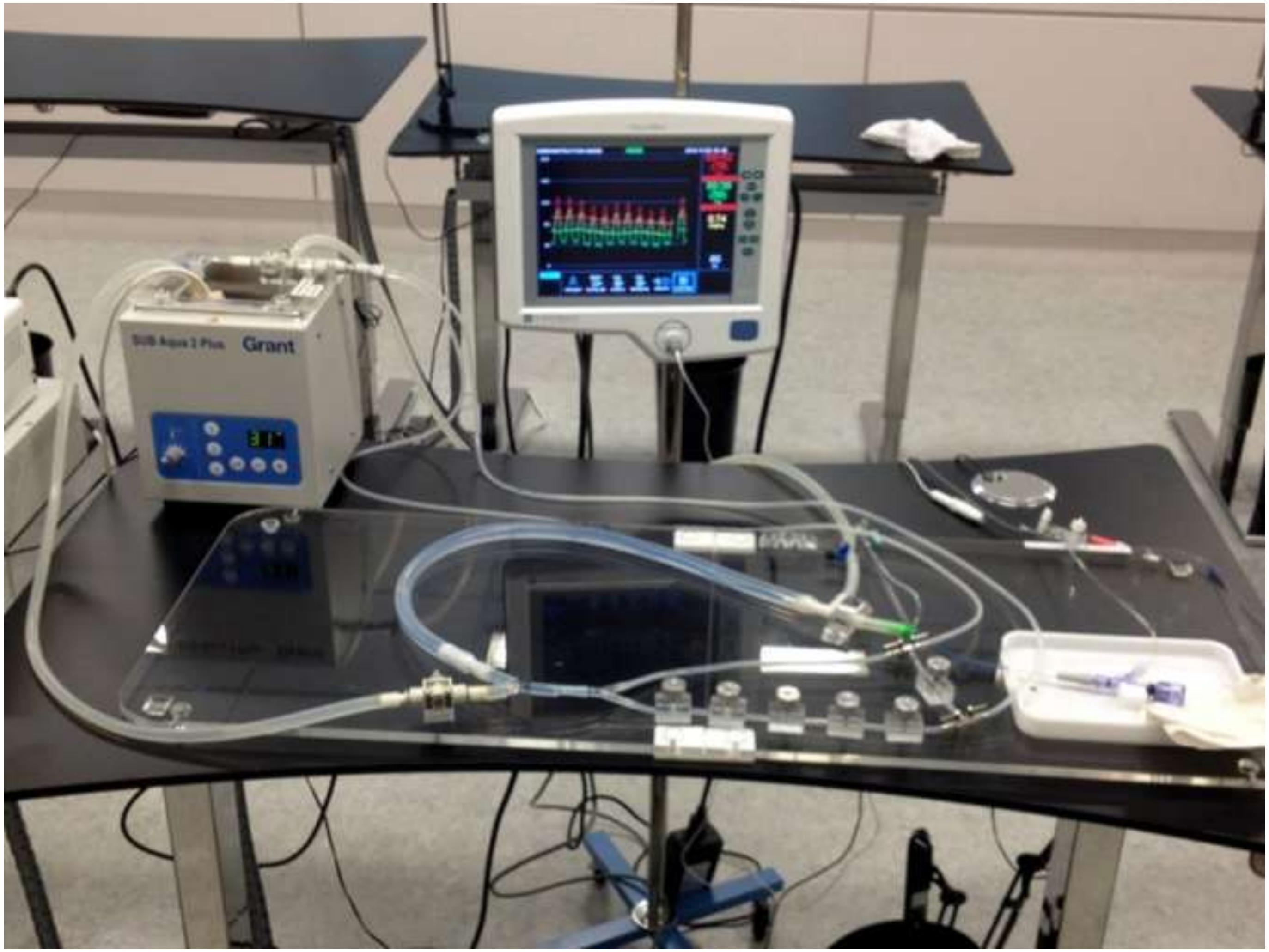
$$FFR(X-)_{pred} = \frac{P_d - P_w}{P_a - P_{prox} + P_{dist} - P_w} + \frac{P_w(P_a - P_{prox} + P_{dist} - P_d)}{P_a(P_a - P_{prox} + P_{dist} - P_w)}$$

True FFR of Sx:

$$FFR(X)_{pred} = \frac{(P_d - P_w) + \frac{P_w}{P_a}(P_{prox} - P_{dist})}{P_{prox} - P_{dist} + P_d - P_w}$$

Saito N, et al. J. Invasive Cardiol. 2013;25:642–9.

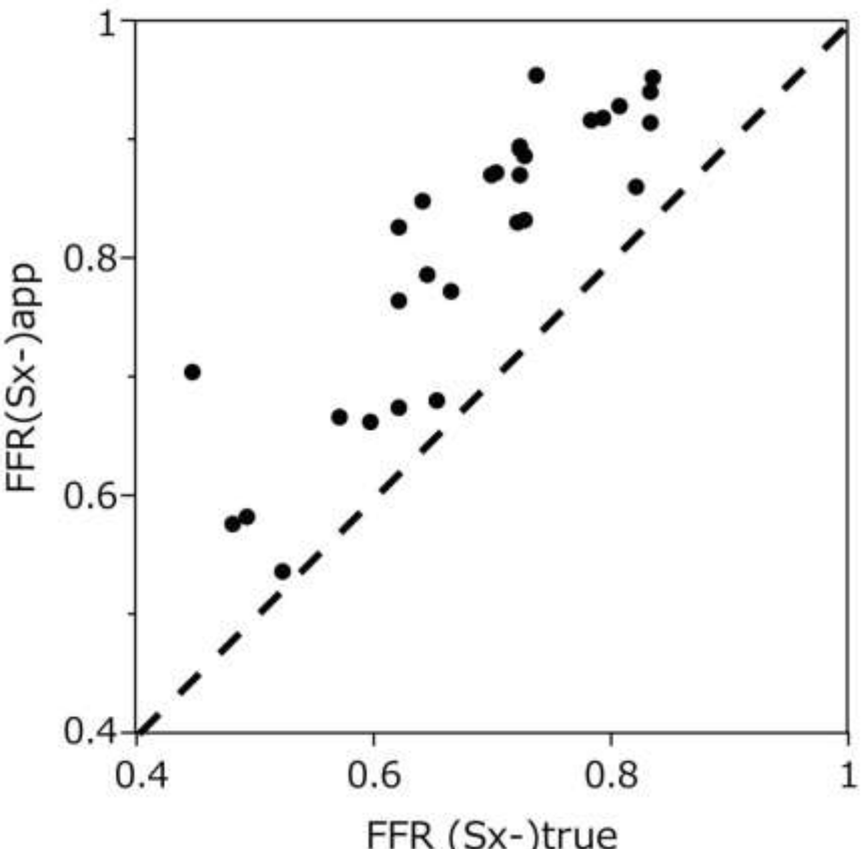
In Vitro Experiment



Saito N, et al. J. Invasive Cardiol. 2013;25:642–9.

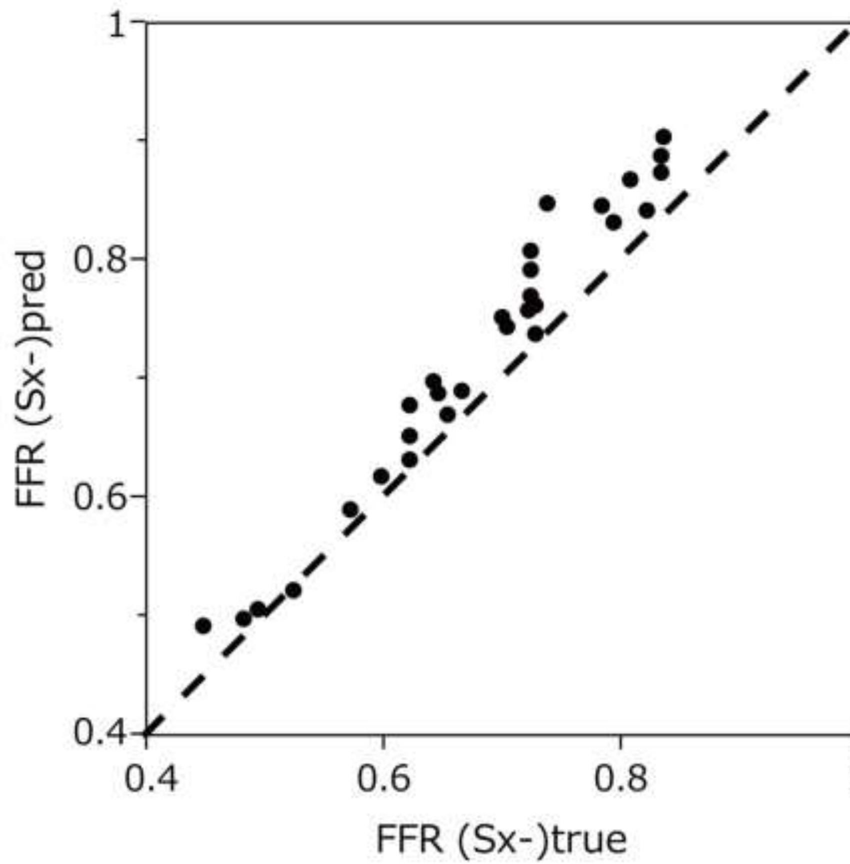
$$FFR(X-)_{pred} = \frac{P_d - P_w}{P_a - P_{prox} + P_{dist} - P_w} + \frac{P_w(P_a - P_{prox} + P_{dist} - P_d)}{P_a(P_a - P_{prox} + P_{dist} - P_w)}$$

Apparent FFR



r^2=0.60

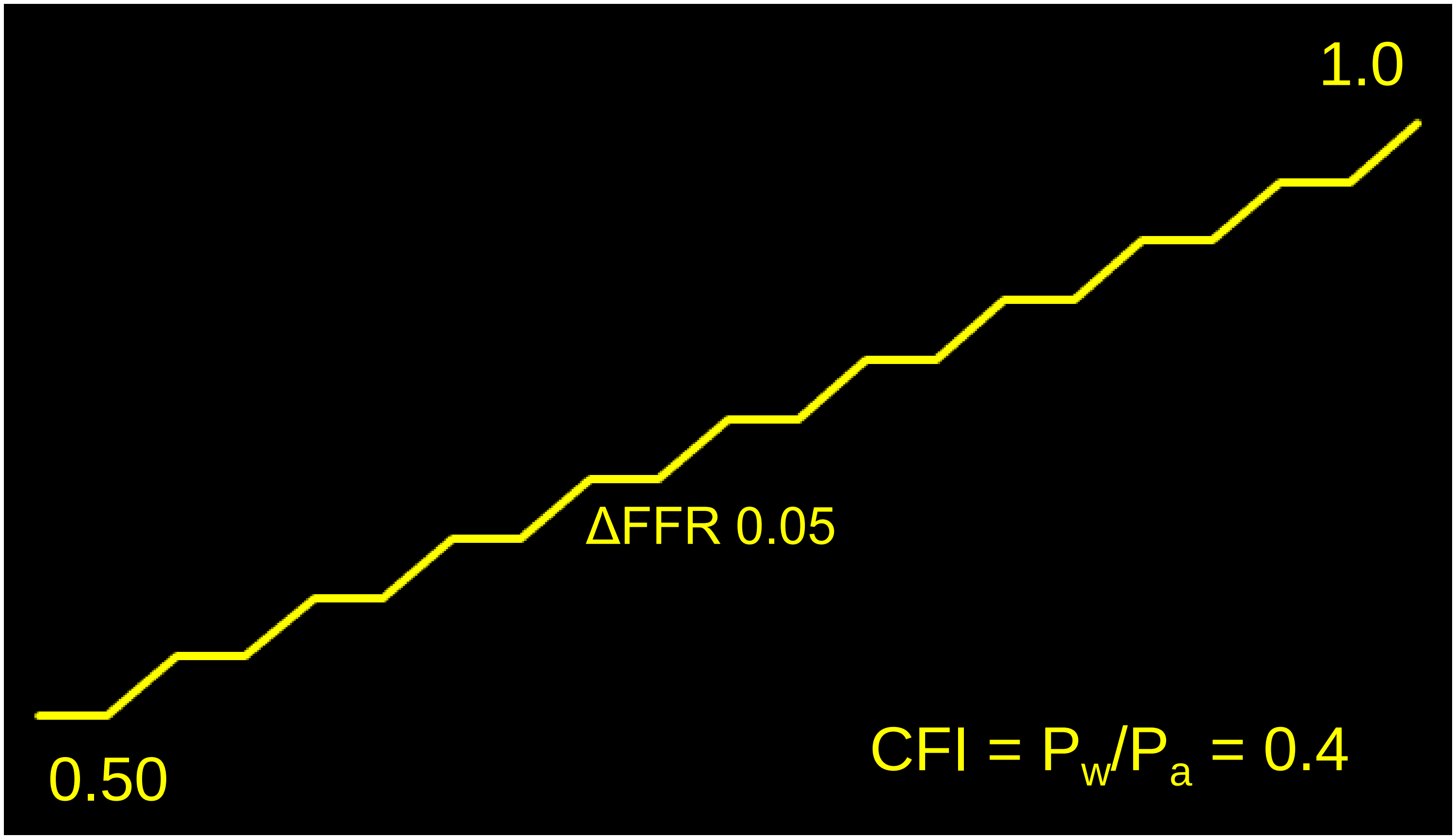
Predictive FFR



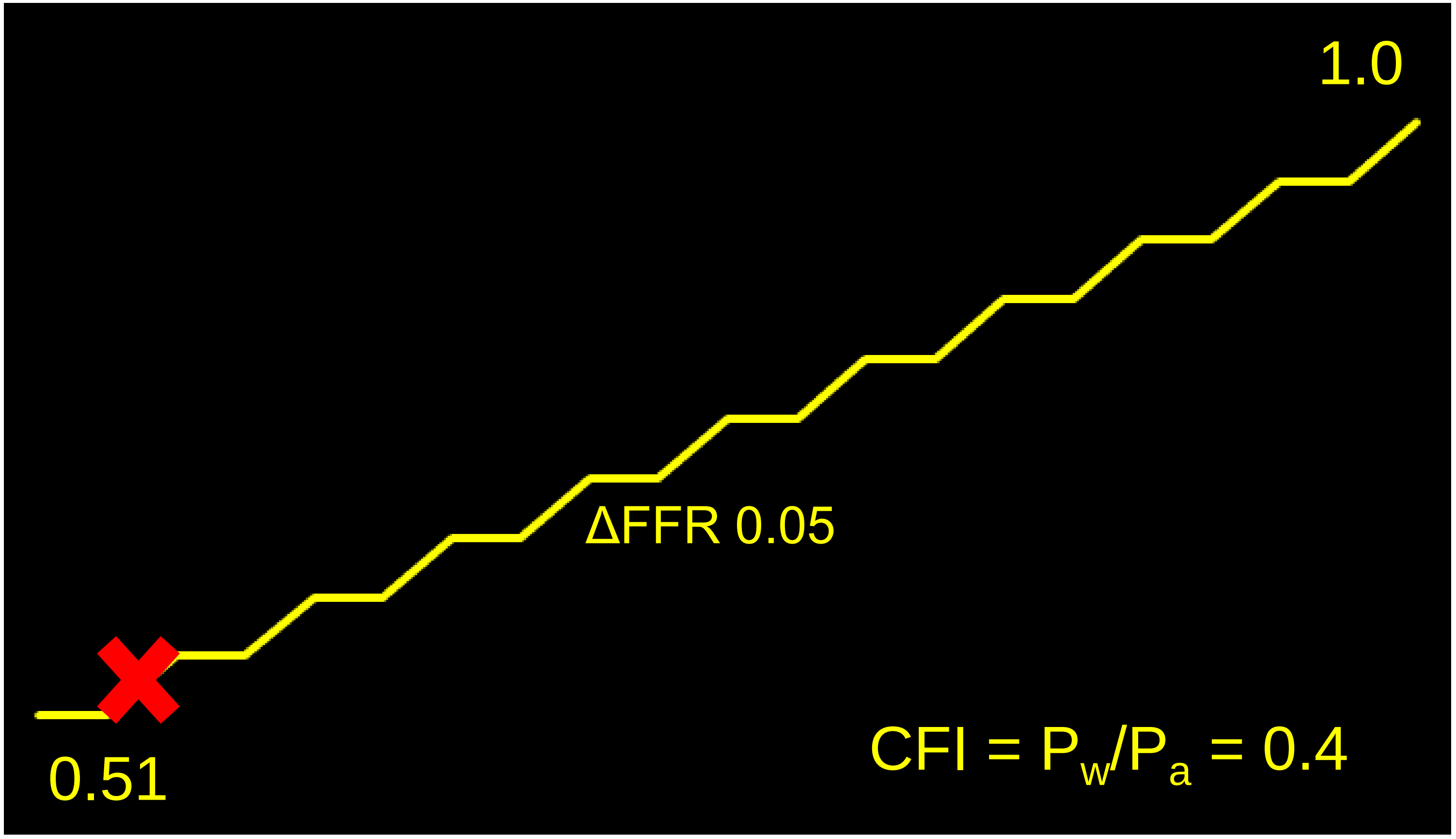
r^2=0.92

Saito N, et al. J. Invasive Cardiol. 2013;25:642–9.

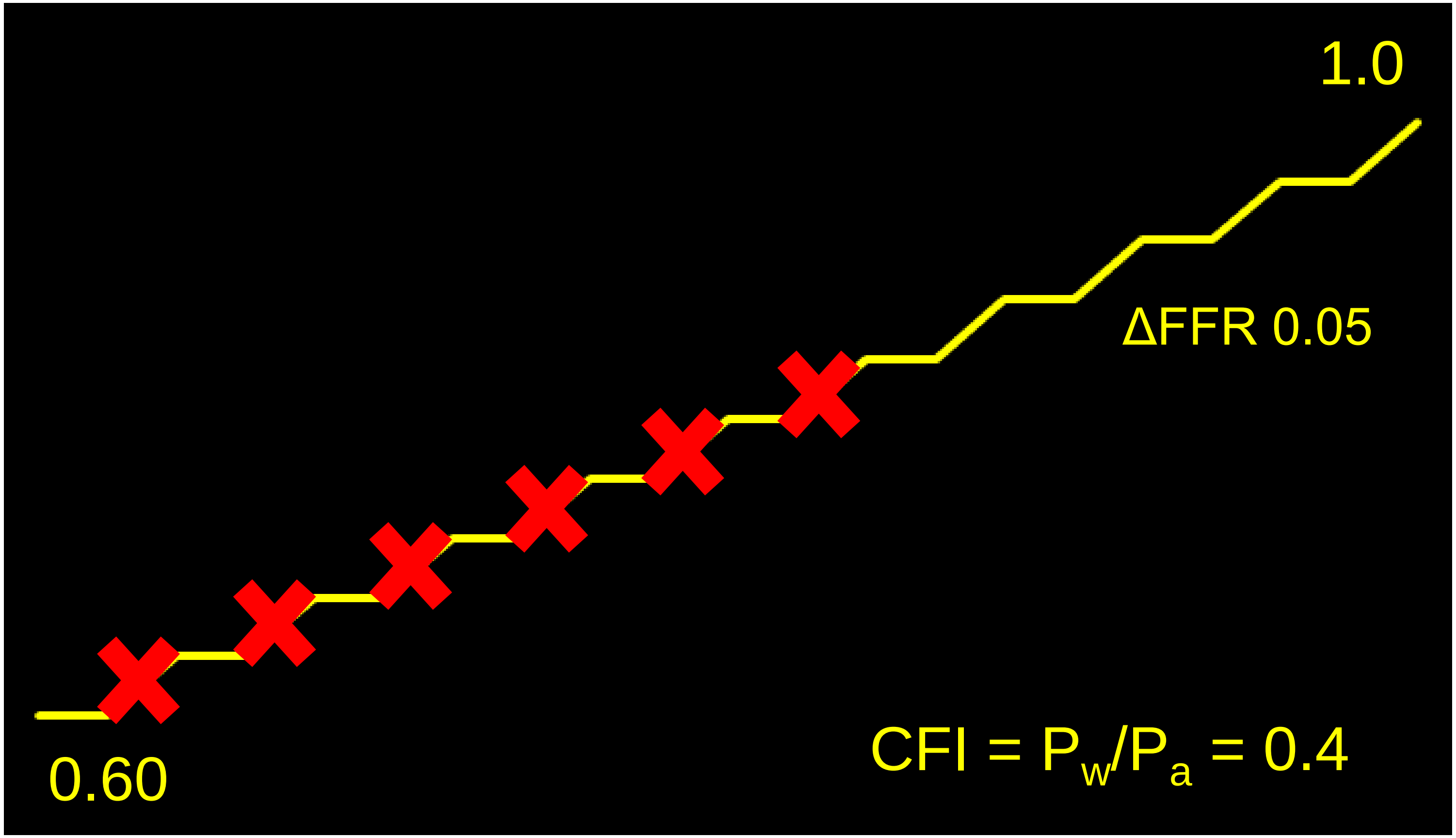
Diffuse Lesion



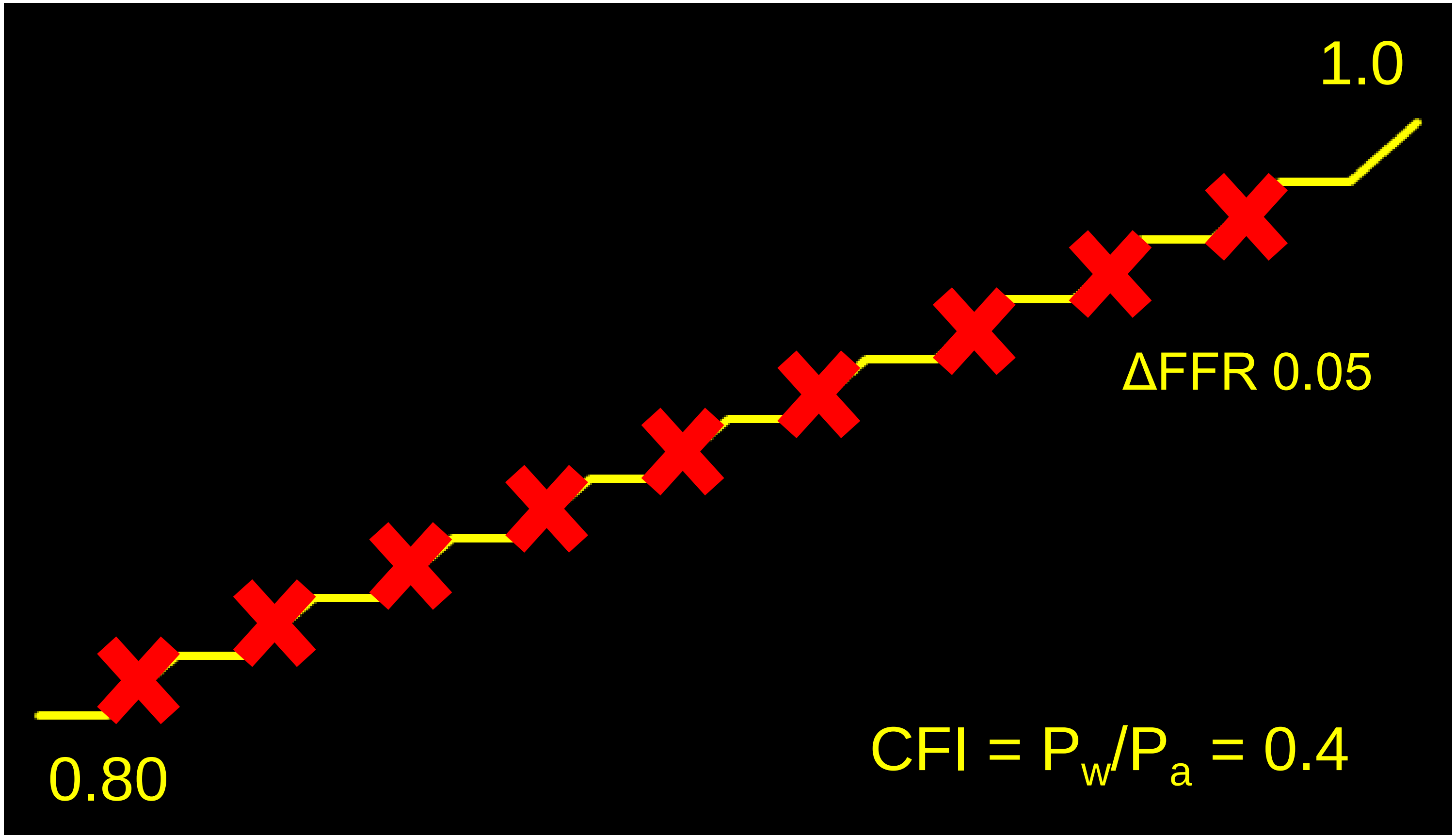
Diffuse Lesion



Diffuse Lesion



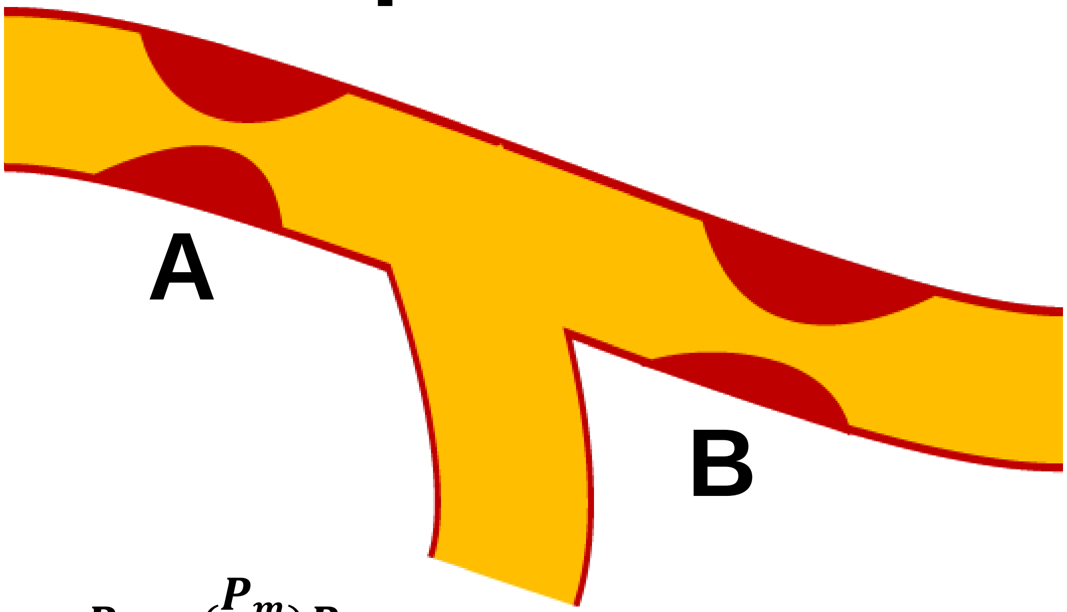
Diffuse Lesion



Hemodynamic Interaction

1. Sequential
2. Bifurcation
3. Remote

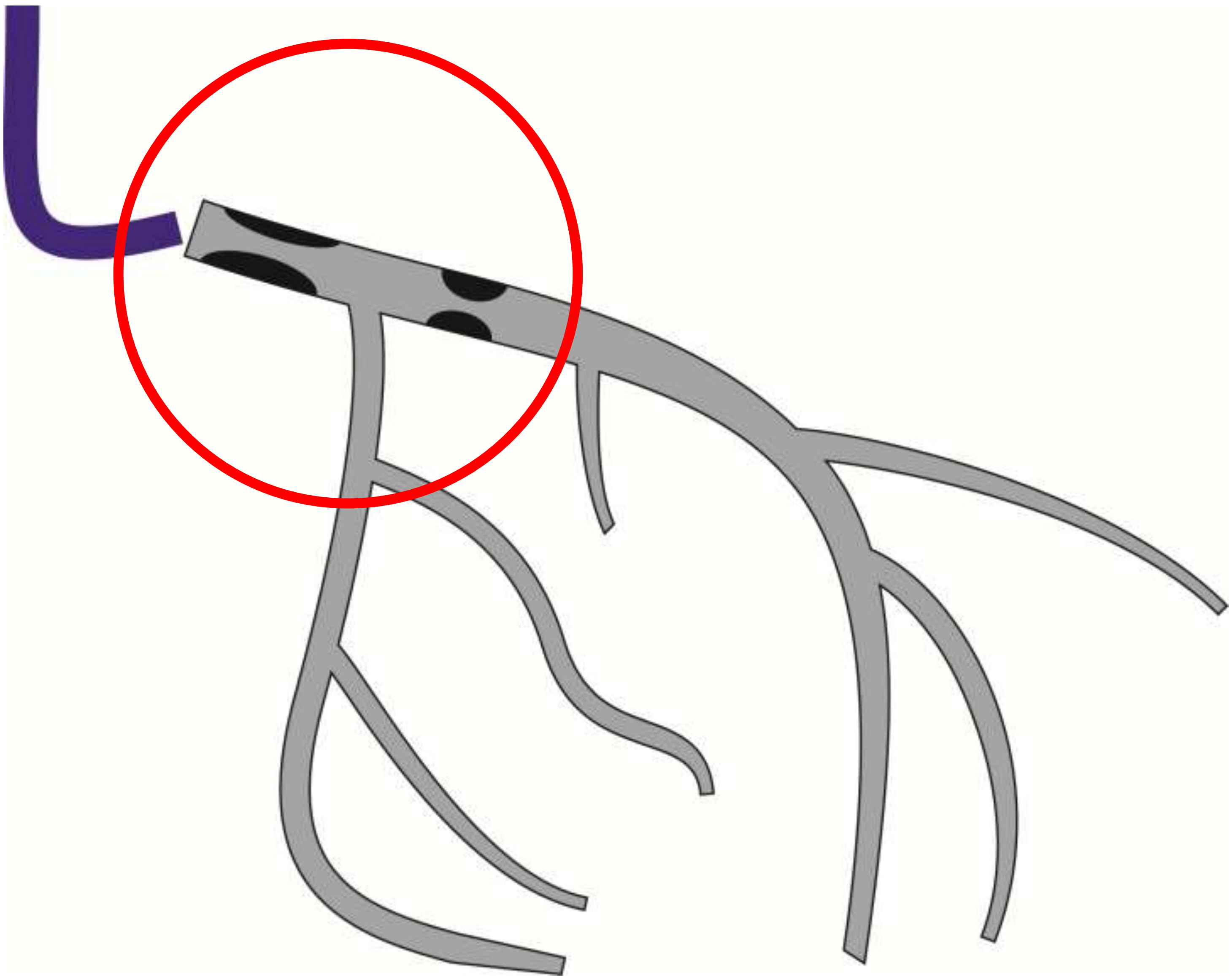
Limitation: Tandem lesion Equations



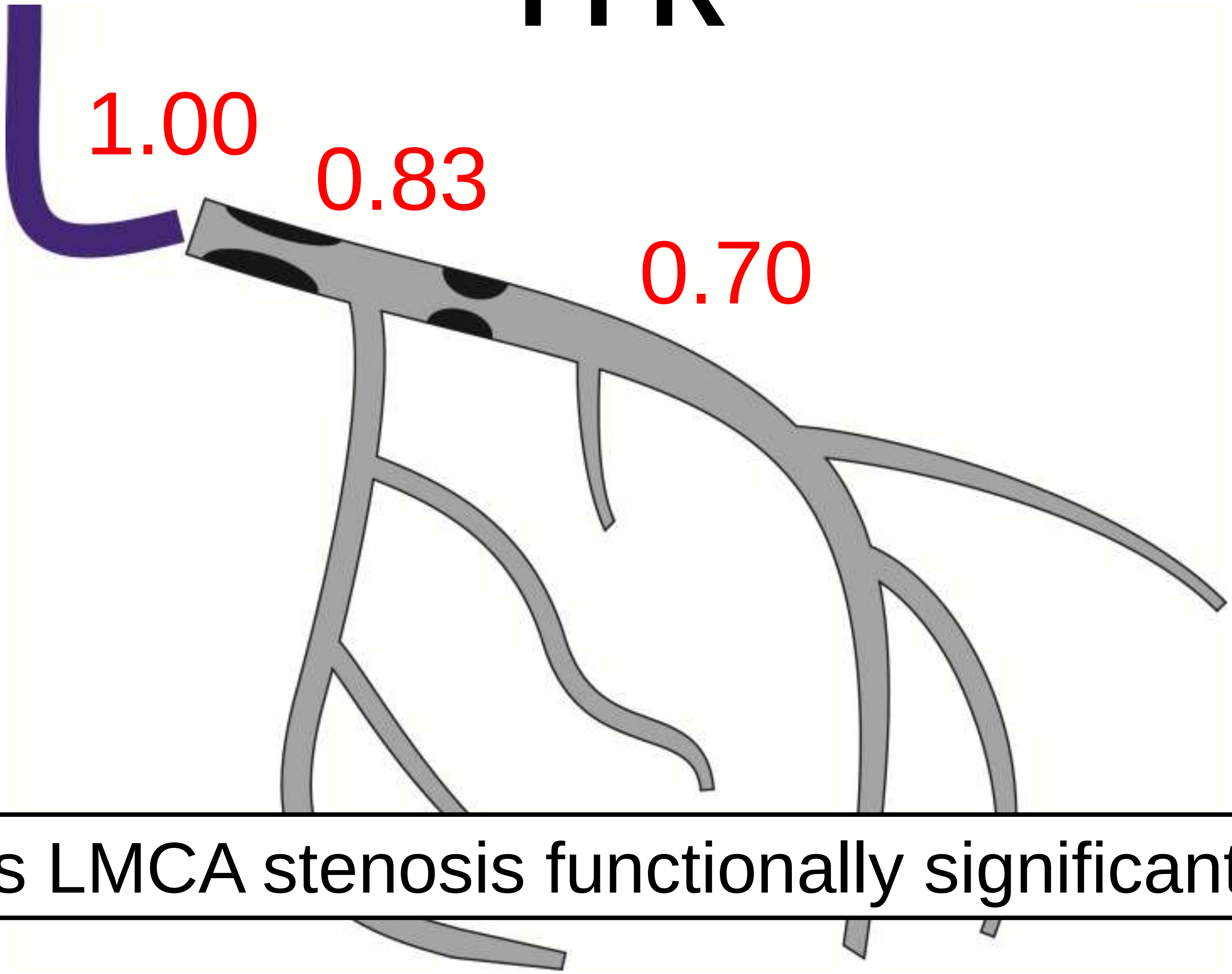
$$FFR(A)_{pred} = \frac{P_d - (\frac{P_m}{P_a})P_w}{P_a - P_m + P_d - P_w} \qquad FFR(B)_{pred} = 1 - \frac{(P_a - P_w)(P_m - P_d)}{P_a(P_m - P_w)}$$

For the 2 stenosis equations to be applicable, there should be no major arterial branch between the 2 stenoses.

De Bruyne B, et al. Circulation 2000 18;101(15):1840–1847.



FFR



Is LMCA stenosis functionally significant?

In vitro study

In vivo study

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The Impact of Downstream Coronary Stenoses on Fractional Flow Reserve Assessment of Intermediate Left Main Disease

David V. Daniels, MD,* Marcel van't Veer, MSc, PhD,†‡ Nico H. J. Pijls, MD, PhD,†‡ Arjen van der Horst, MSc,‡ Andy S. Yong, MBBS, PhD,* Bernard De Bruyne, MD, PhD,§ William F. Fearon, MD*

Stanford, California; Eindhoven, the Netherlands; and Aalst, Belgium

Objectives The aim of this study was to assess the validity of measuring fractional flow reserve (FFR) of the left main (LM) coronary artery in the setting of concomitant left anterior descending (LAD) or left circumflex (LCX) stenoses.

Background The theoretical impact of a stenosis in the LAD on the FFR assessment of intermediate LM disease with the pressure wire in an unobstructed LCX is currently unknown.

Methods A previously validated in vitro model of the coronary circulation was used to create a fixed intermediate stenosis of the LM and a variable downstream LAD or LCX stenosis. The true LM FFR ($FFR_{LM\ true}$), with no concomitant downstream disease, was compared to the apparent LM FFR ($FFR_{LM\ apparent}$), with concomitant downstream disease measured with different degrees of LAD or LCX disease. Additionally, an equation based on a resistors model was derived to predict the effect of downstream stenosis on LM FFR ($FFR_{LM\ predicted}$).

Results In the setting of isolated moderate LM disease (FFR 0.72 ± 0.08), mild to moderate proximal LAD or LCX lesions did not significantly affect LM FFR. Lesions with a composite FFR (LM + downstream disease) ≥0.65 resulted in an $FFR_{LM\ apparent}$ that was not significantly different from $FFR_{LM\ true}$ (0.76 ± 0.06 vs. 0.76 ± 0.05, p = 0.124). Our equation for $FFR_{LM\ predicted}$ accurately modeled the effects of concomitant disease (r = 0.95, p < 0.001).

Conclusions These data suggest that in the presence of proximal mild to moderate LAD or LCX disease, LM FFR can be reliably measured with the pressure wire placed in the uninvolved epicardial artery. (J Am Coll Cardiol Intv 2012;5:1021–5) © 2012 by the American College of Cardiology Foundation

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...ay 25, 2012, accepted July 4, 2012.

In vitro study

Coronary Artery Disease

Fractional Flow Reserve Assessment of Left Main Stenosis in the Presence of Downstream Coronary Stenoses

Andy S.C. Yong, MBBS, PhD*; David Daniels, MD*; Bernard De Bruyne, MD, PhD; Hyun-Sook Kim, MD; Fumiaki Ikeno, MD; Jennifer Lyons, RVT; Nico H.J. Pijls, MD, PhD; William F. Fearon, MD

Background—Several studies have shown that fractional flow reserve (FFR) measurement can aid in the assessment of left main coronary stenosis. However, the impact of downstream epicardial stenosis on left main FFR assessment with the pressure wire in the nonstenosed downstream vessel remains unknown.

Methods and Results—Variable stenoses were created in the left main coronary arteries and downstream epicardial vessels in 6 anaesthetized male sheep using balloon catheters. A total of 220 pairs of FFR assessments of the left main stenosis were obtained, before and after creation of a stenosis in a downstream epicardial vessel, by having a pressure-sensor wire in the other nonstenosed downstream vessel. The apparent left main FFR in the presence of downstream stenosis (FFR_{app}) was significantly higher compared with the true FFR in the absence of downstream stenosis (FFR_{true}; 0.80±0.05 versus 0.76±0.05; estimate of the mean difference, 0.035; P<0.001). The difference between FFR_{true} and FFR_{app} correlated with composite FFR of the left main plus stenosed artery (r=−0.31; P<0.001) indicating that this difference was greater with increasing epicardial stenosis severity. Among measurements with FFR_{app} >0.80, 9% were associated with an FFR_{true} of <0.75. In all instances, the epicardial lesion was in the proximal portion of the stenosed vessel, and the epicardial FFR (combined FFR of the left main and downstream stenosed vessel) was ≤0.50.

Conclusions—A clinically relevant effect on the FFR assessment of left main disease with the pressure wire in a nonstenosed downstream vessel occurs only when the stenosis in the other vessel is proximal and very severe. (*Circ Cardiovasc Interv*. **2013;6:161-165.**)

Key Words: fractional flow reserve ■ left main coronary artery ■ stenosis

Left main coronary artery (LMCA) disease is prevalent, occurring in 4% to 7% of patients undergoing coronary angiography.[1,2] Several studies have highlighted the inadequacies of coronary angiography in the assessment of intermediate LMCA stenosis,[3-5] leading to the use of other modalities to determine LMCA stenosis severity.

Fractional flow reserve (FFR) is now considered the gold standard technique to determine the functional significance of epicardial coronary stenoses in the cardiac catheterization laboratory,[6,7] and the use of FFR to guide revascularization of multivessel epicardial disease results in improved outcomes.[8] Several studies have demonstrated the usefulness of measuring FFR to guide the decision for revascularization of intermediate LMCA disease.[9,10] However, LMCA stenosis is usually associated with downstream disease in the epicardial vessels.[11,12] The effect of downstream epicardial disease in the left anterior descending (LAD) or left circumflex (LCX) arteries on the FFR assessment of LMCA stenosis remains unclear.

Disease in the LAD will certainly affect FFR assessment of the LMCA when the pressure-sensor wire is in the LAD.[13,14] For this reason, it is recommended to position the pressure sensor in an artery that is free of significant stenosis. However, in theory, LAD disease might also affect FFR assessment of the LMCA when the pressure sensor is positioned in a nondiseased LCX. Blood flow across the LMCA is dependent on the outflow to the LAD and LCX. Therefore, significant LAD stenosis may decrease flow across the LMCA and could falsely elevate the FFR.

Editorial see p 128

The goal of this study is to explore the effect of downstream disease in either the LAD or the LCX on FFR assessment of intermediate LMCA disease with the pressure wire positioned in the nondiseased downstream vessel using an in vitro sheep model.

Methods

Animal Instrumentation

The study was approved by our Institutional Animal Care and Use Committee. Male sheep were premedicated with intramuscular tiletamine (8 mg/kg) and buprenorphine (0.005 mg/kg). Anesthesia was maintained with 1% to 5% isoflurane, and supplemental oxygen

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*Drs Yong and Daniels contributed equally to this work.

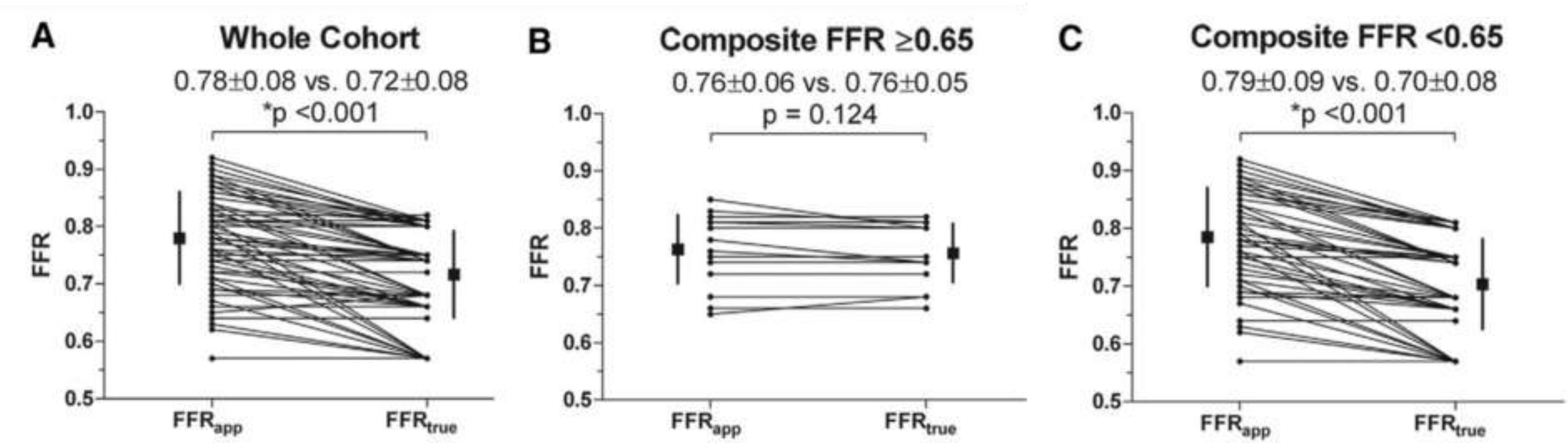
Correspondence to William F. Fearon, MD, Division of Cardiovascular Medicine, Stanford University Medical Center, 300 Pasteur Dr, H2103, Stanford, CA 94305. E-mail wfearon@stanford.edu

Circ Cardiovasc Interv is available at http://circinterventions.ahajournals.org DOI: 10.1161/CIRCINTERVENTIONS.112.000104

JACC Cardiovasc Interv 2012 5:1021–5

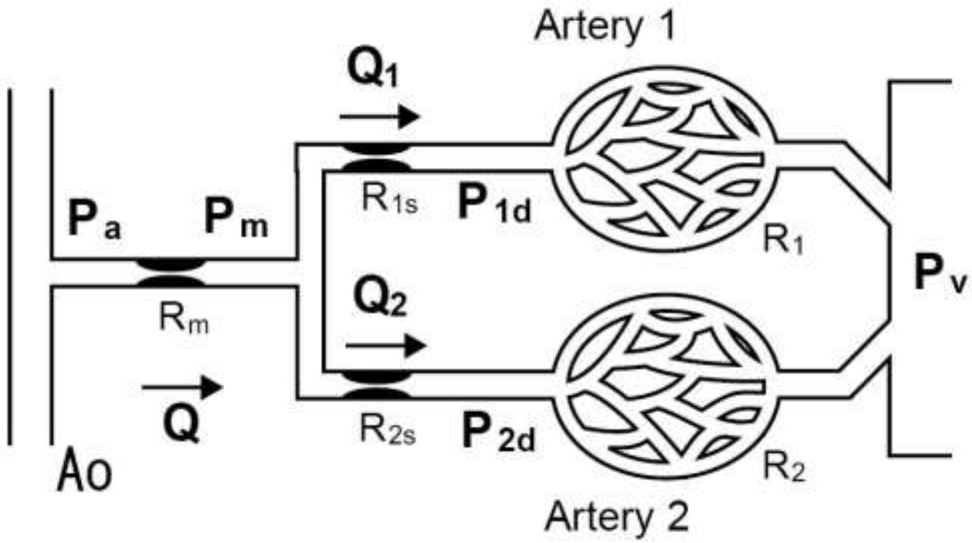
Circulation. Cardiovasc Interv 2013 6(2), 161–5.

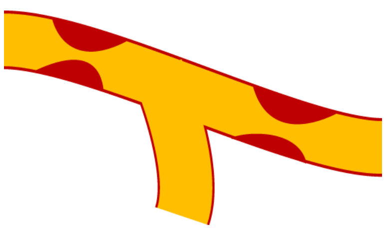
Study Results: Key Figure



The effect of downstream stenosis become larger when the downstream stenosis become severer.

Daniels DV et al, JACC Cardiovasc Interv 2012 5:1021–5





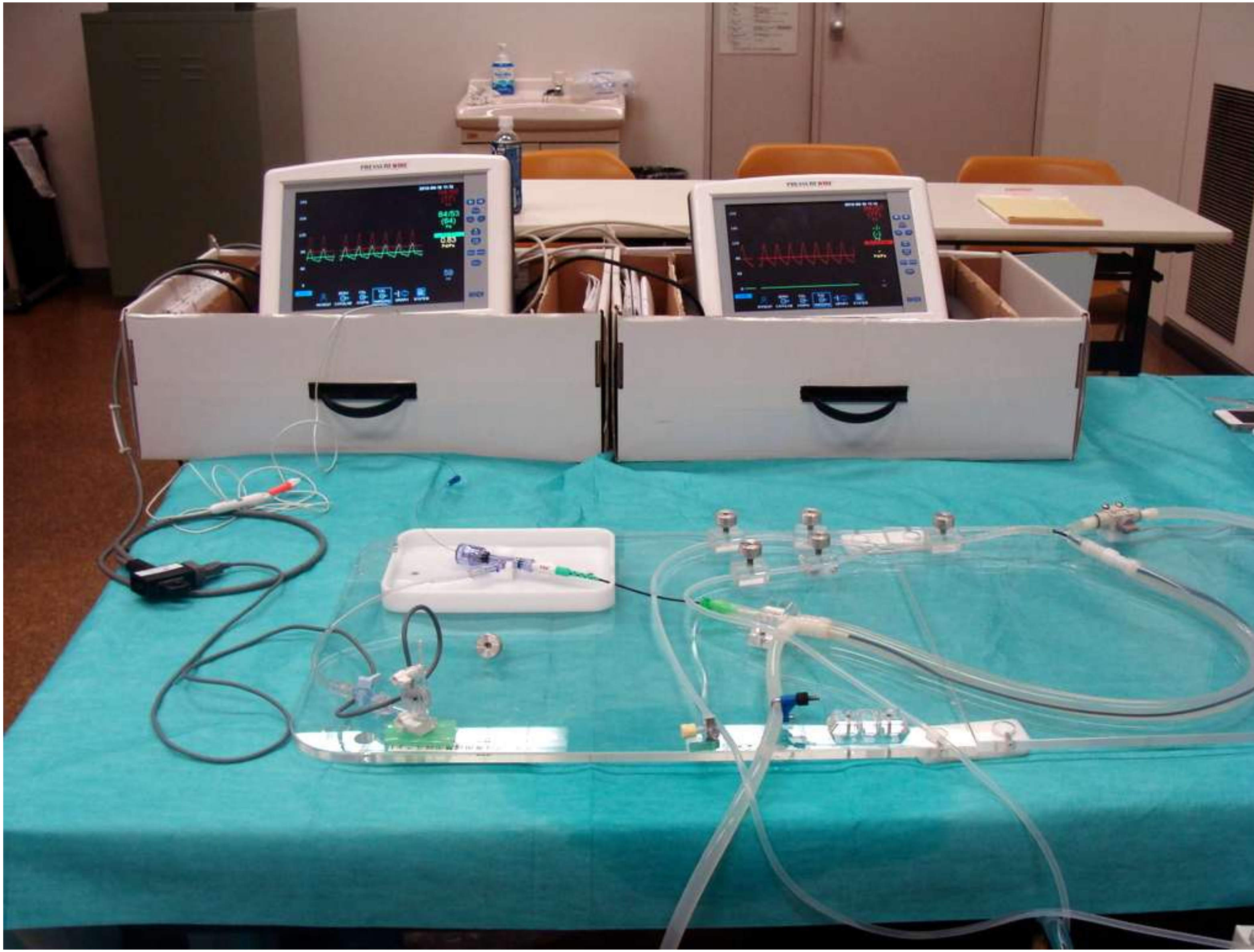
LMCA + One Vessel Disease

$$FFR_{pred-m} = \frac{P_{1d}P_{1w}}{P_a(P_{1w} - P_m + P_{1d})} = \frac{nFFR_1 + FFR_m}{1 + n(1 - (FFR_m - FFR_1))}$$

LMCA + Two Vessel Disease

$$FFR_{pred-m} = \frac{P_{1d}P_{2d}P_{1w}}{P_{1d}P_{2d}P_{1w} + P_aP_{2d}(P_{1w} - P_m) + P_mP_{1d}(P_a - P_{1w})} = \frac{nFFR_1 + FFR_2}{1 - (FFR_m - FFR_2) + n(1 - (FFR_m - FFR_1))}$$

Yamamoto E, Saito N, et al. Eurointervention, Accepted for Publication.



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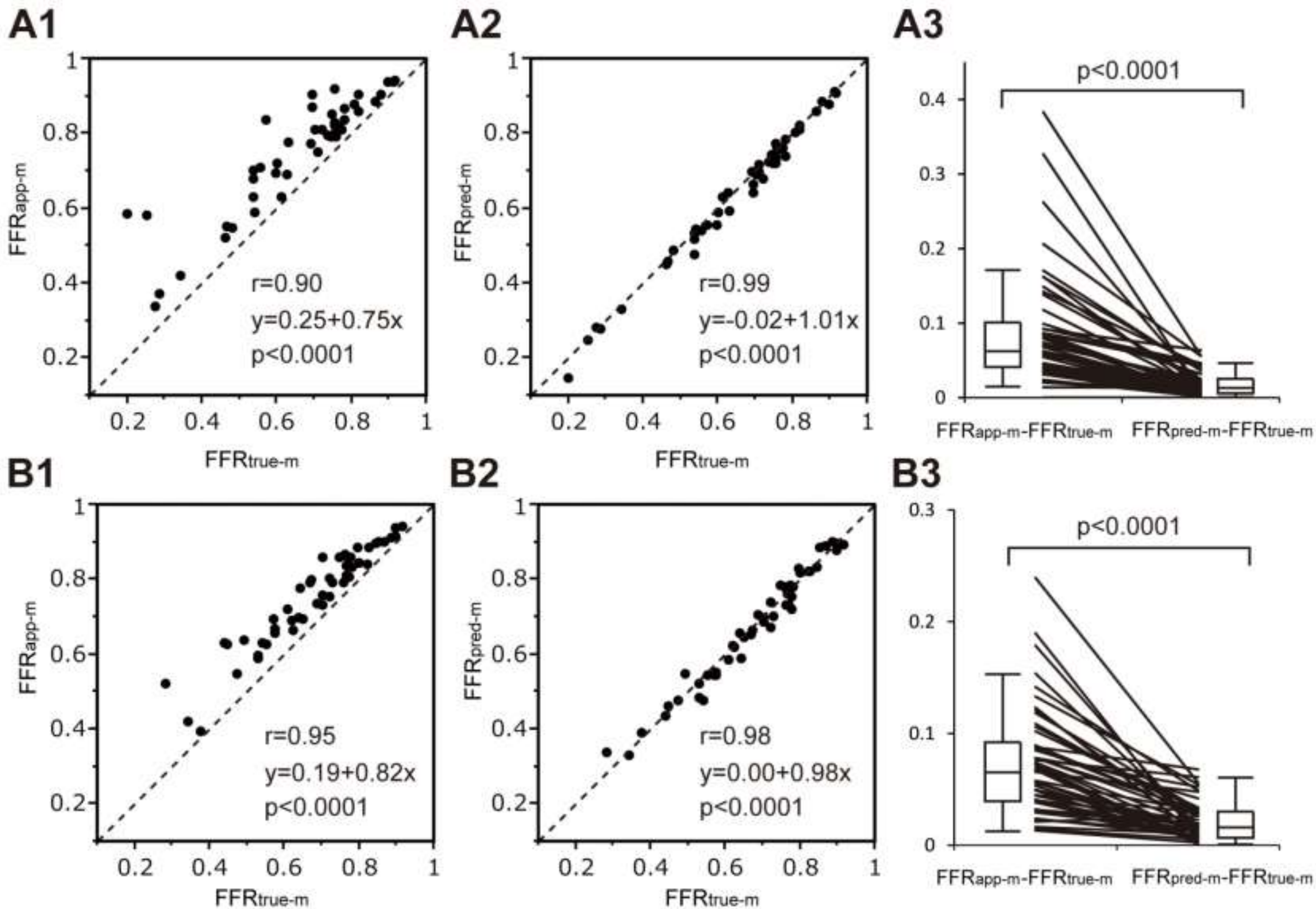
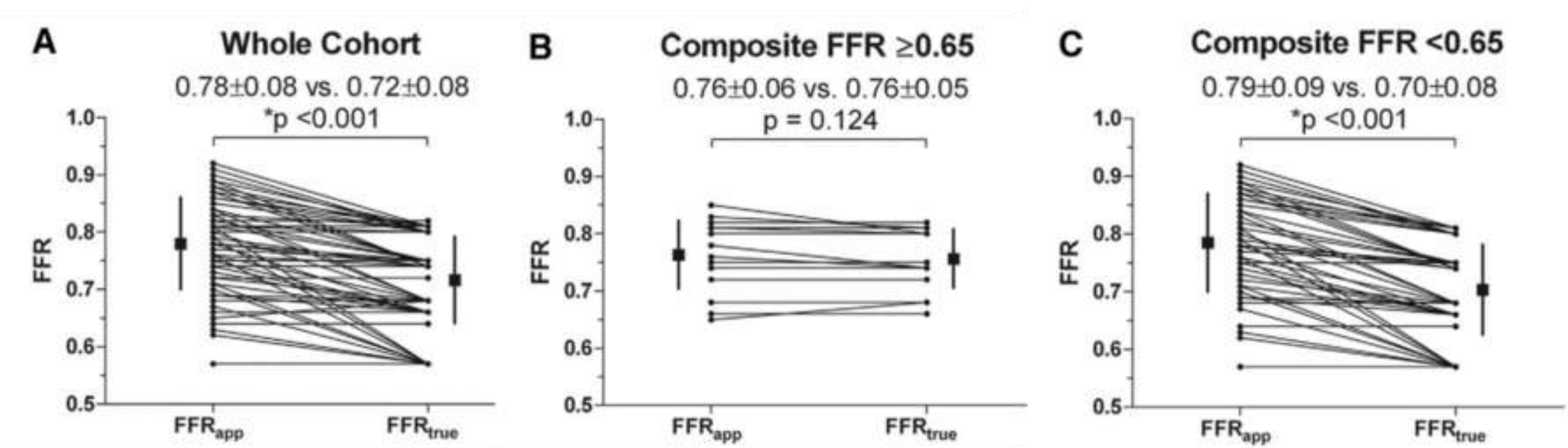


Yamamoto E, Saito N, et al. Eurointervention, Accepted for Publication.

LAD/LCX Flow = 2, FFR_1 > 0.65, FFR_m > 0.80

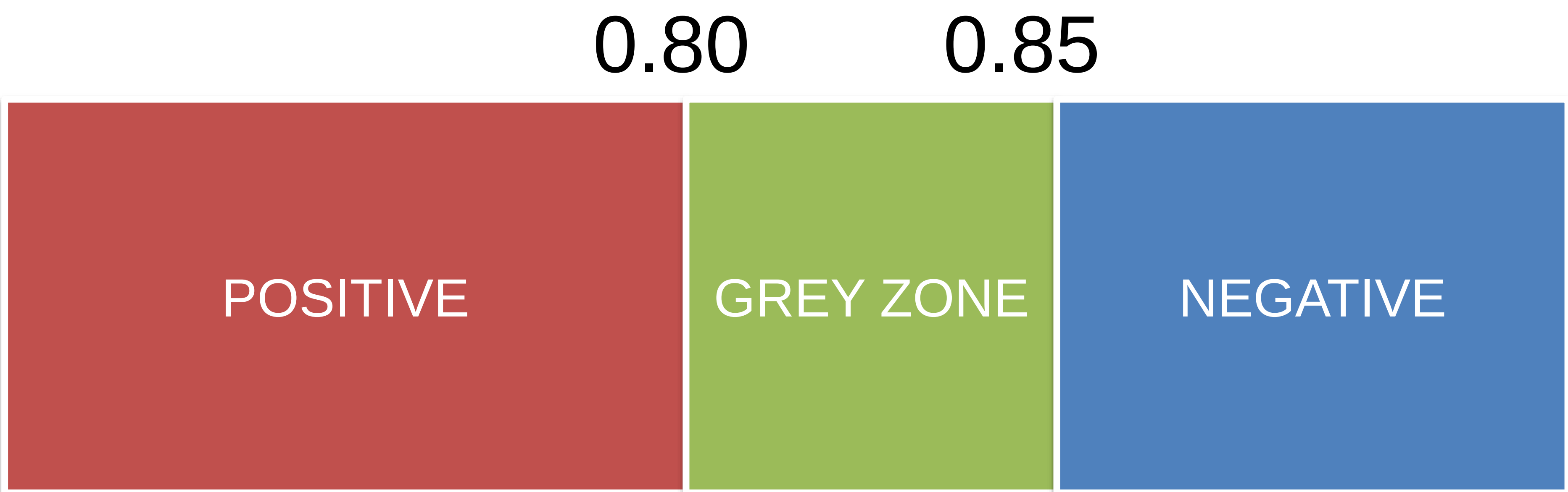
$FFR_{pred\text{-}m}$ > 0.78
FFR_m-$FFR_{pred\text{-}m}$ < 0.03



Daniels DV et al, JACC Cardiovasc Interv 2012 5:1021–5

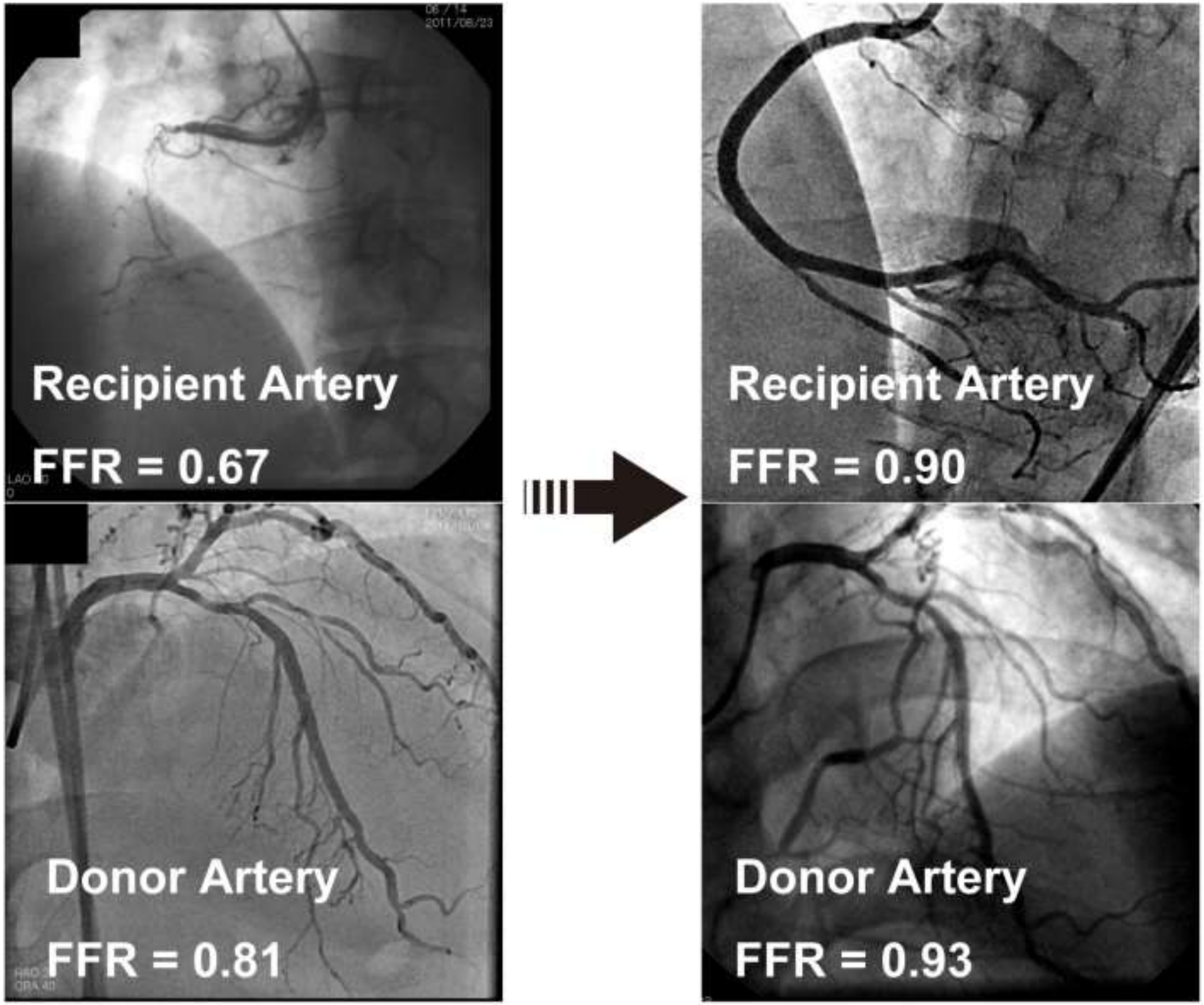
LMCA + Downstream LAD/LCX Stenoses Recommendation

An apparent LMCA FFR between 0.80 and 0.85 is in a gray zone when downstream LAD/LCX stenoses existed and are severe.

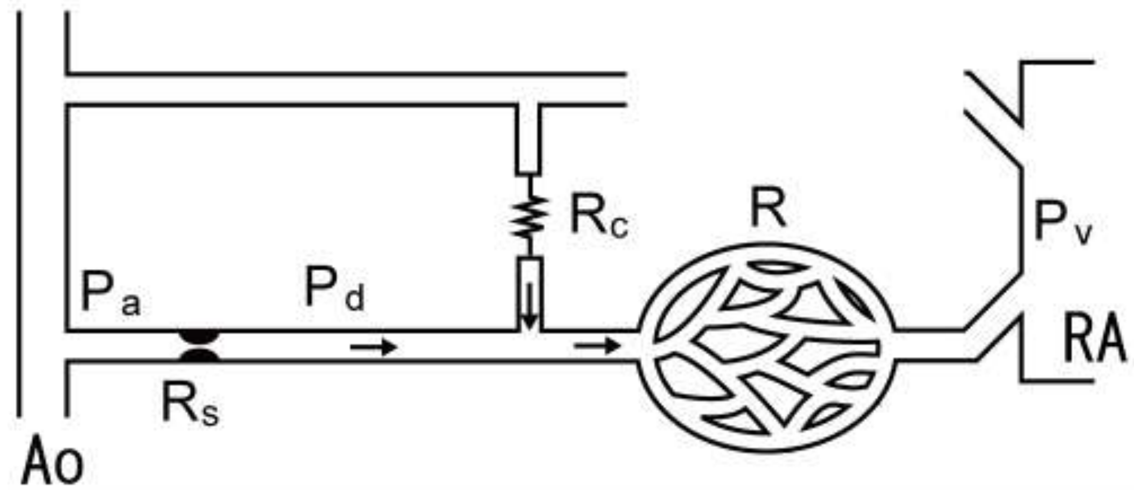


Hemodynamic Interaction

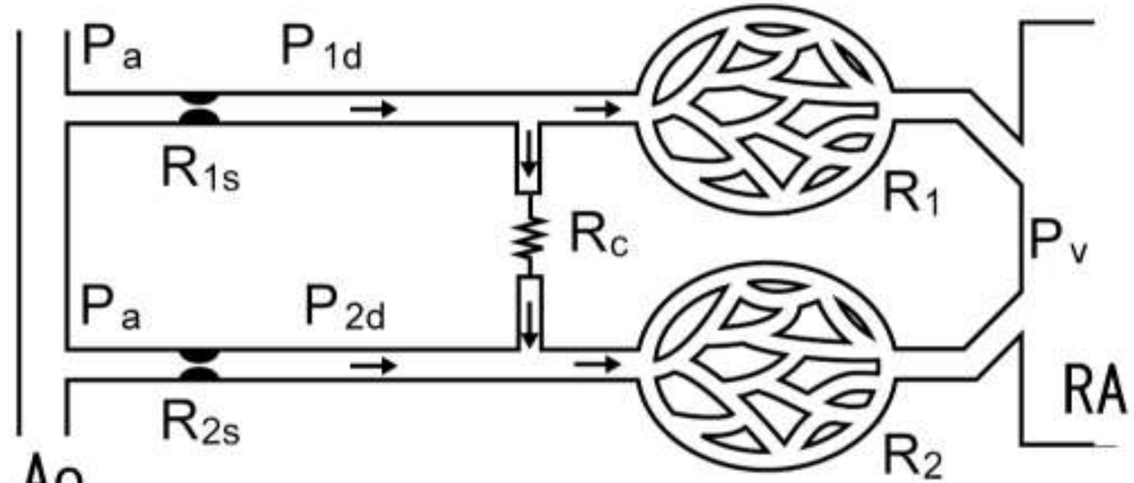
1. Sequential
2. Bifurcation
3. Remote



Matsuo H, Kawase Y, et al. Catheter Cardiovasc Interv 2013 82:E459–64.



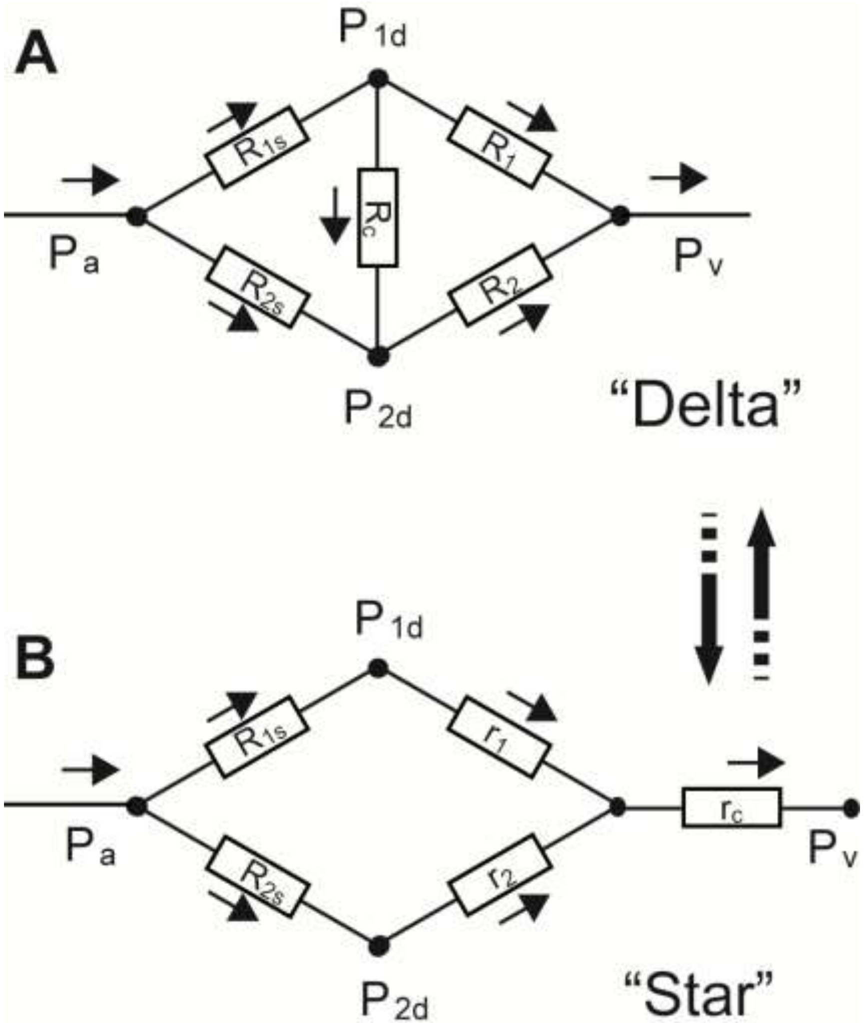
Artery 1 - Donor Artery



Artery 2 - Recipient Artery

Watanabe H, Saito N, et al. J Cardiovasc Revascularization Med 2015;16:90–100.

Delta-Star Transformation



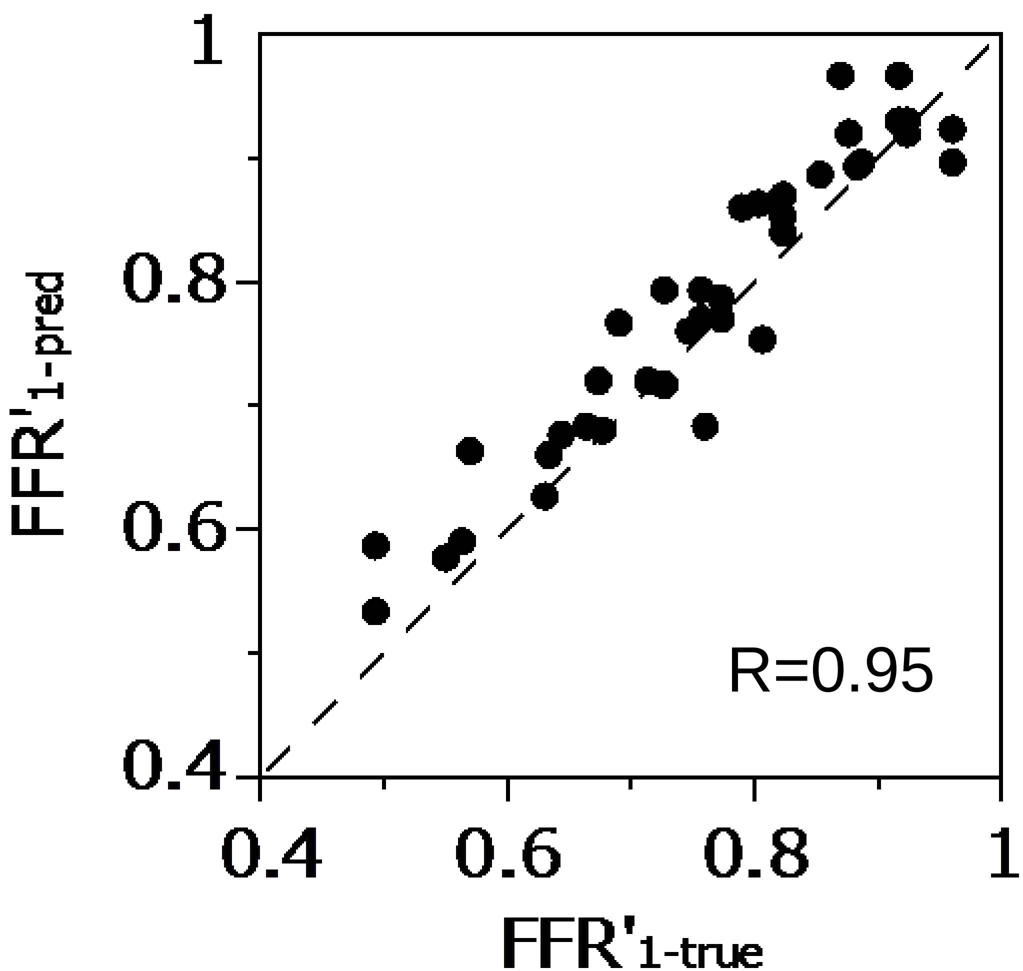
$$r_c = \frac{R_1 R_2}{R_1 + R_2 + R_c}$$

$$r_1 = \frac{R_1 R_c}{R_1 + R_2 + R_c}$$

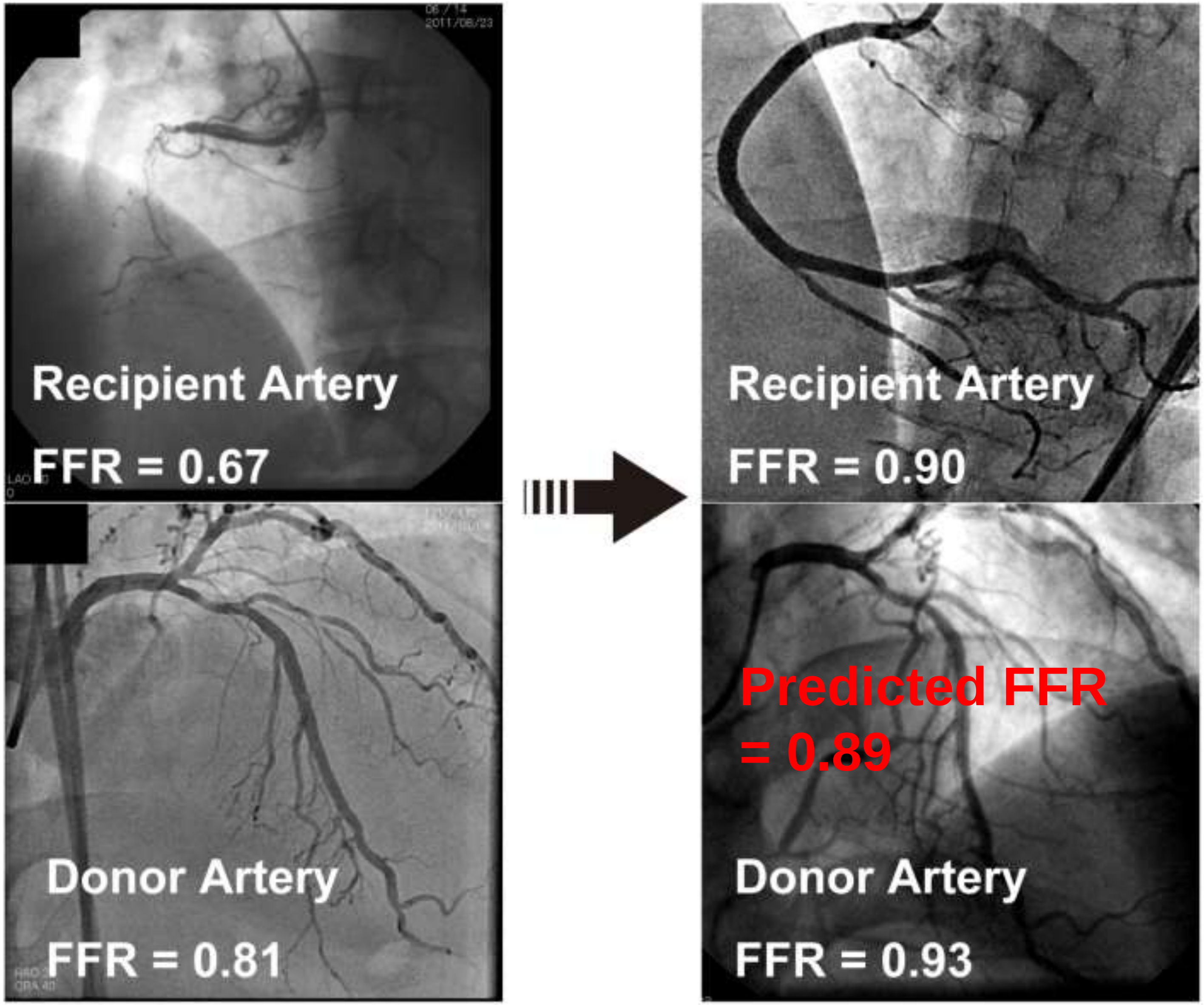
$$r_2 = \frac{R_2 R_c}{R_1 + R_2 + R_c}$$

Watanabe H, Saito N, et al. J Cardiovasc Revascularization Med 2015;16:90–100.

$$FFR'_{1-pred} = \frac{(FFR_1 - CFI_1)(FFR_2 - CFI_2) - CFI_1 CFI_2 (1 - FFR_1)(1 - FFR_2) + CFI_1 (1 - FFR_1)(1 - CFI_2)}{(1 - CFI_1)(FFR_2 - CFI_2)}$$



Watanabe H, Saito N, et al. J Cardiovasc Revascularization Med 2015;16:90–100.


Recipient Artery
FFR = 0.67
Donor Artery
FFR = 0.81
Recipient Artery
FFR = 0.90
Predicted FFR = 0.89
Donor Artery
FFR = 0.93

3 Patterns of Hemodynamic Interaction

1. Sequential

J. Invasive Cardiol. 2013;25:642–9.

2. Bifurcation

Eurointervention, Accepted for Publication.

3. Remote

J Cardiovasc Revascularization Med 2015;16:90–100.

Summary

- Functional interaction between stenoses do exist, even when the stenoses are located in different coronary arteries.
- Understanding the background mechanism will improve the performance of daily clinical practice.