Paradigm Shift to Functional Angioplasty

Save Stents, Save Money and Save Lives !

Seung-Jung Park, MD, PhD

Professor of Medicine, University of Ulsan College of Medicine,
Heart Institute, Asan Medical Center, Seoul, Korea

What we have done,
Since 1979,

Balloon Angioplasty
DCA, Rotablation Atherectomy,
Laser, PMR, Brachytherapy,
Bare Metal Stent
Drug Eluting Stent
PCI
Coronary Intervention
PCI

PCI is a
Revolution of Evolution
in Therapeutic Cardiovascular Medicine !

Treat or Not treat

Evidence Based Medicine

Treatment(PCI) relies primarily on noninvasive stress test (objective ischemia).

In Reality,

Frequency of Stress Testing to Document Ischemia Prior to Elective PCI

Lin GA, JAMA 2008;300:1765-1773

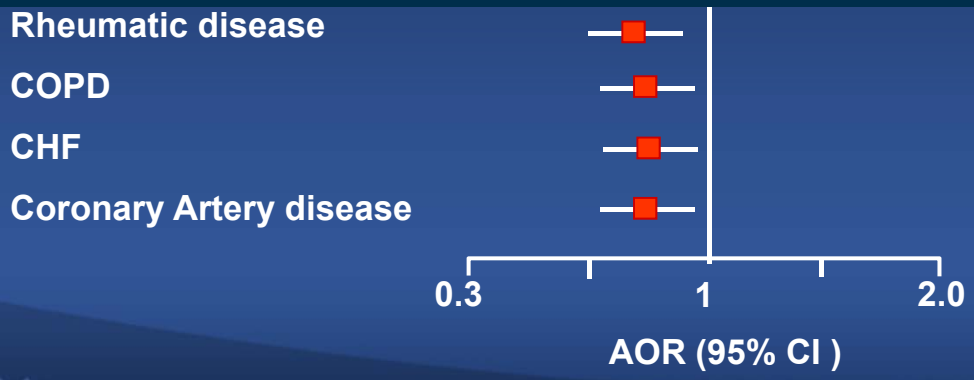
In the US, 44.5% of patients underwent stress testing within the 90 days prior to elective PCI.

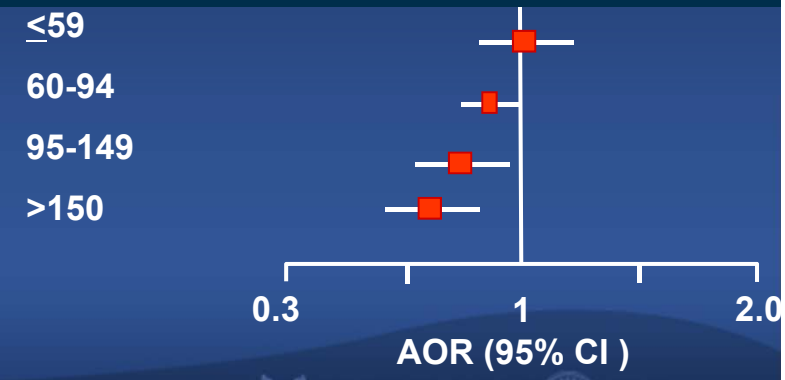
Why
Less likely
to undergo stress test ?

Frequency of Stress Testing

Less likely to undergo stress test	More	Less likely to undergo stress test	More

Who take a CAG first, Experienced Physician in High Volume Center





CardioVascular Research Foundation

UNIVERSITY OF ULSAN COLLEGE MEDICINE

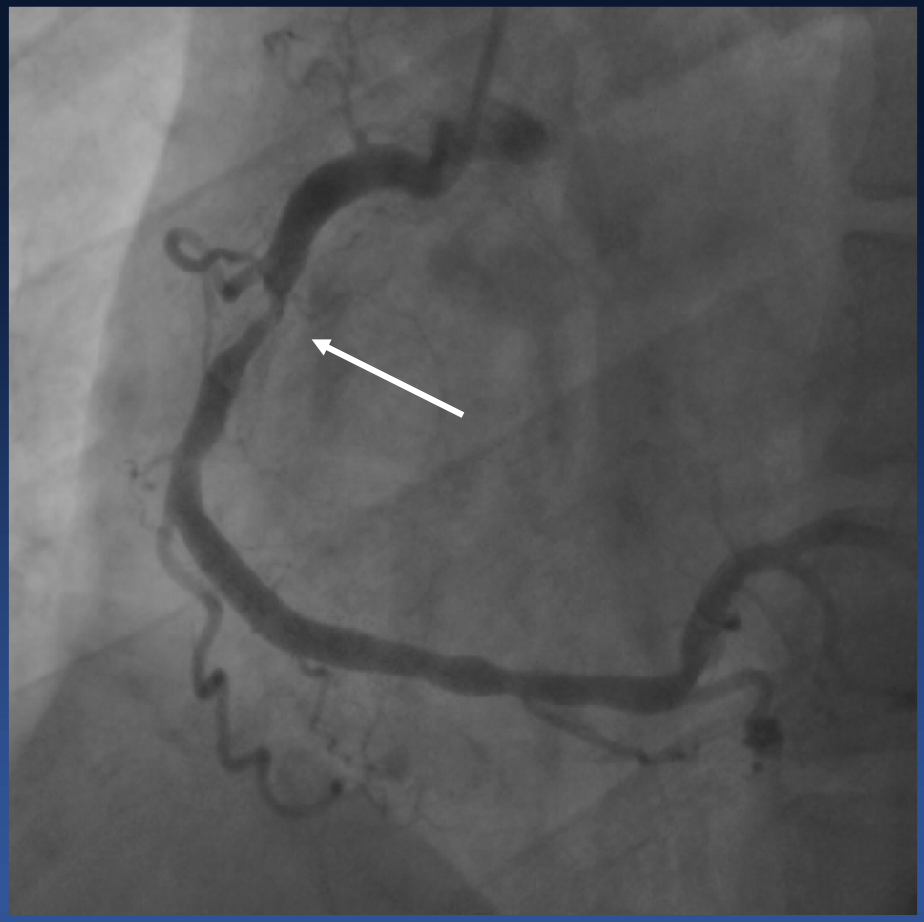
ASAN Medical Center

Issue is,

Do you want to treat the **Lesion** ?
based on angiography

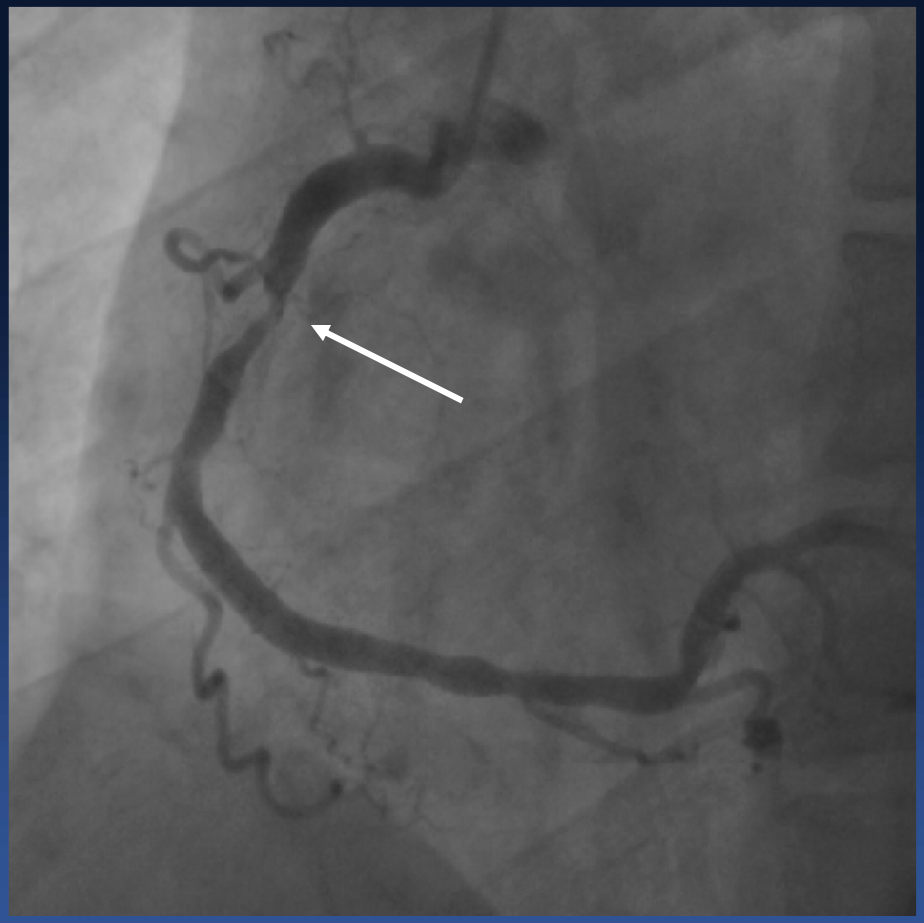
Do you want to treat the **Patient** ?
based on non-invasive stress test
and/or FFR

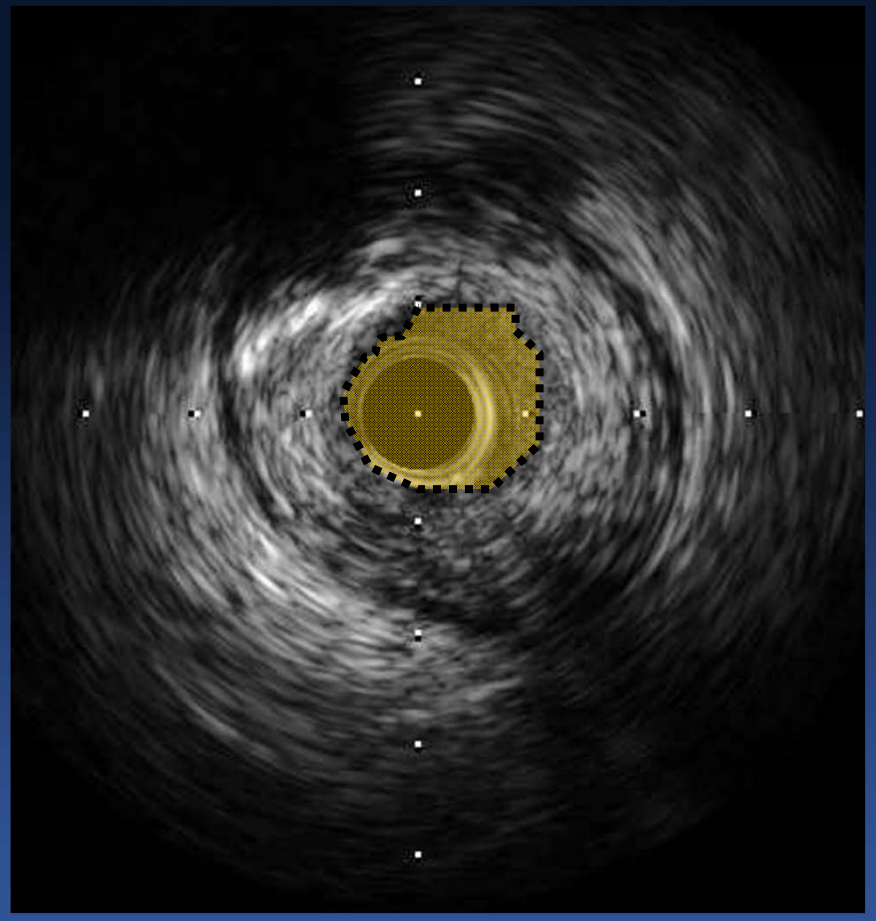
M/52,
Recent developed Effort chest pain, Hyperlipidemia, Smoker
We took a coronary angiogram first,



Visual Estimation 85%

IVUS





MLA 2.8 mm²

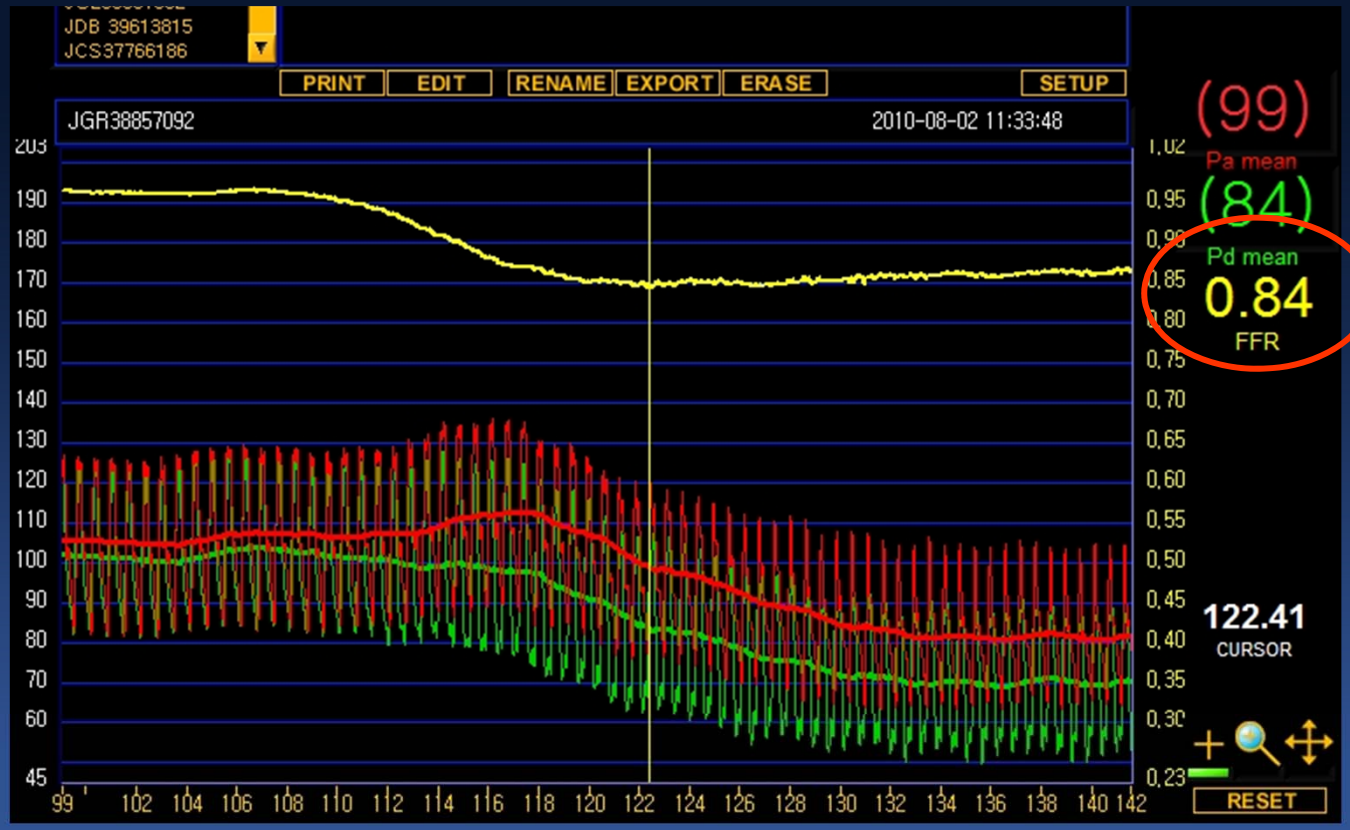
What would you do ?

No Doubt about Stenting !

IVUS MLA:
2.8 mm^2

FFR

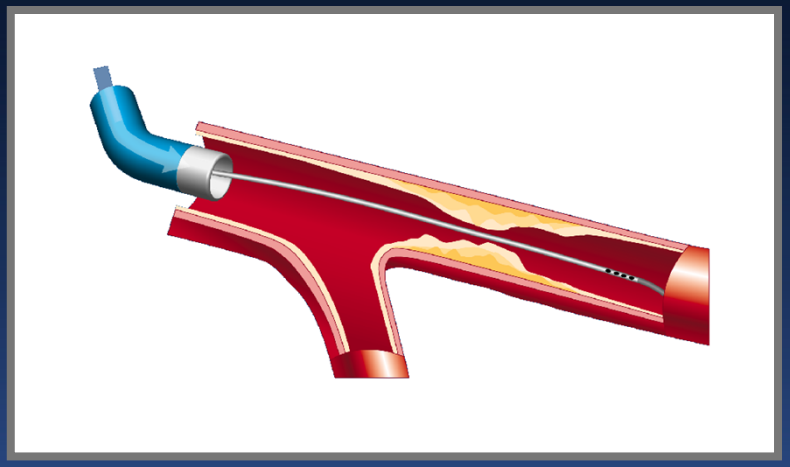
Intravenous adenosine, 160 μg/kg/min



What is the Fractional Flow Reserve (FFR) ?

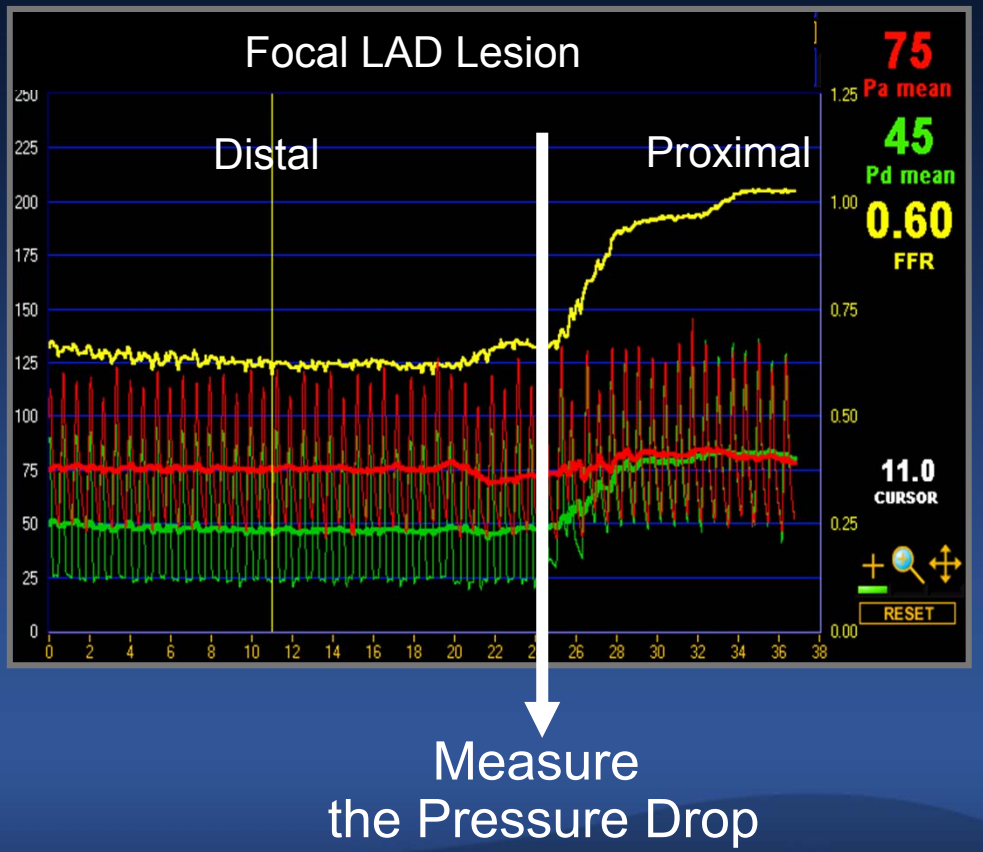
Pressure Measurement
Cross the Stenotic Lesion

Wiring the Lesion



- 100-200 ug IC NTG
- Adenosine infusion
- intracoronary bolus 60-70 ug
- intravenous continuous infusion
  140-200ug/kg/min

Pressure Pullback



Why
Pressure Measurement ?

FFR
(Fractional Flow Reserve)

$$FFR = \frac{Q_S^{max}}{Q_N^{max}}$$

Q_S^{max}: Hyperemic myocardial flow in the stenotic territory

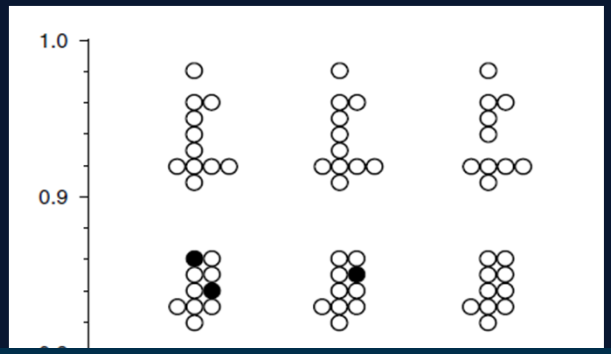
Q_N^{max}: Normal hyperemic myocardial flow

$$\text{Coronary Flow} = \frac{\text{Pressure}}{\text{Resistance}}$$

At Maximal Hyperemia

Coronary Flow ≈ Pressure

$$FFR = \frac{\textbf{Pressure}\ (\text{Distal})}{\textbf{Pressure}\ (\text{Aorta})}$$

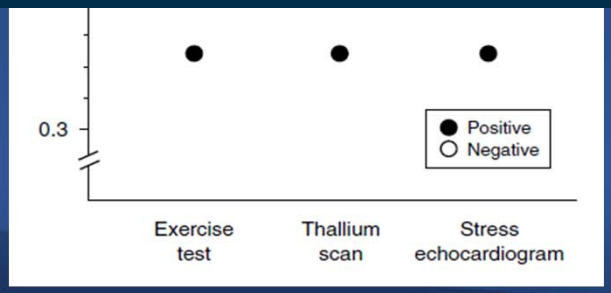


First Validation

with Non-invasive Stress Test Results

(n=45 patients, intravenous adenosine infusion)

FFR <0.75 is well matched with positive stress test (TMT and Thallium SPECT).

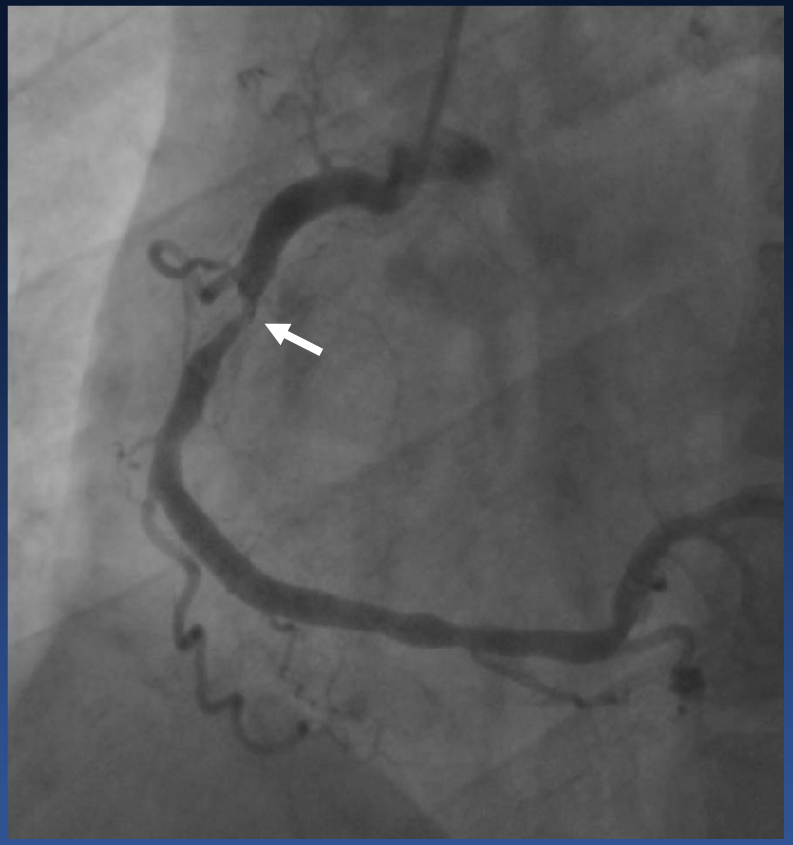


Pijls NHJ, NEJM 1996;334:1703-8

Physiologic Meaning of FFR < 0.75

Decreased 25% of maximal coronary flow, which can induce clinical ischemia.

What would you do ?

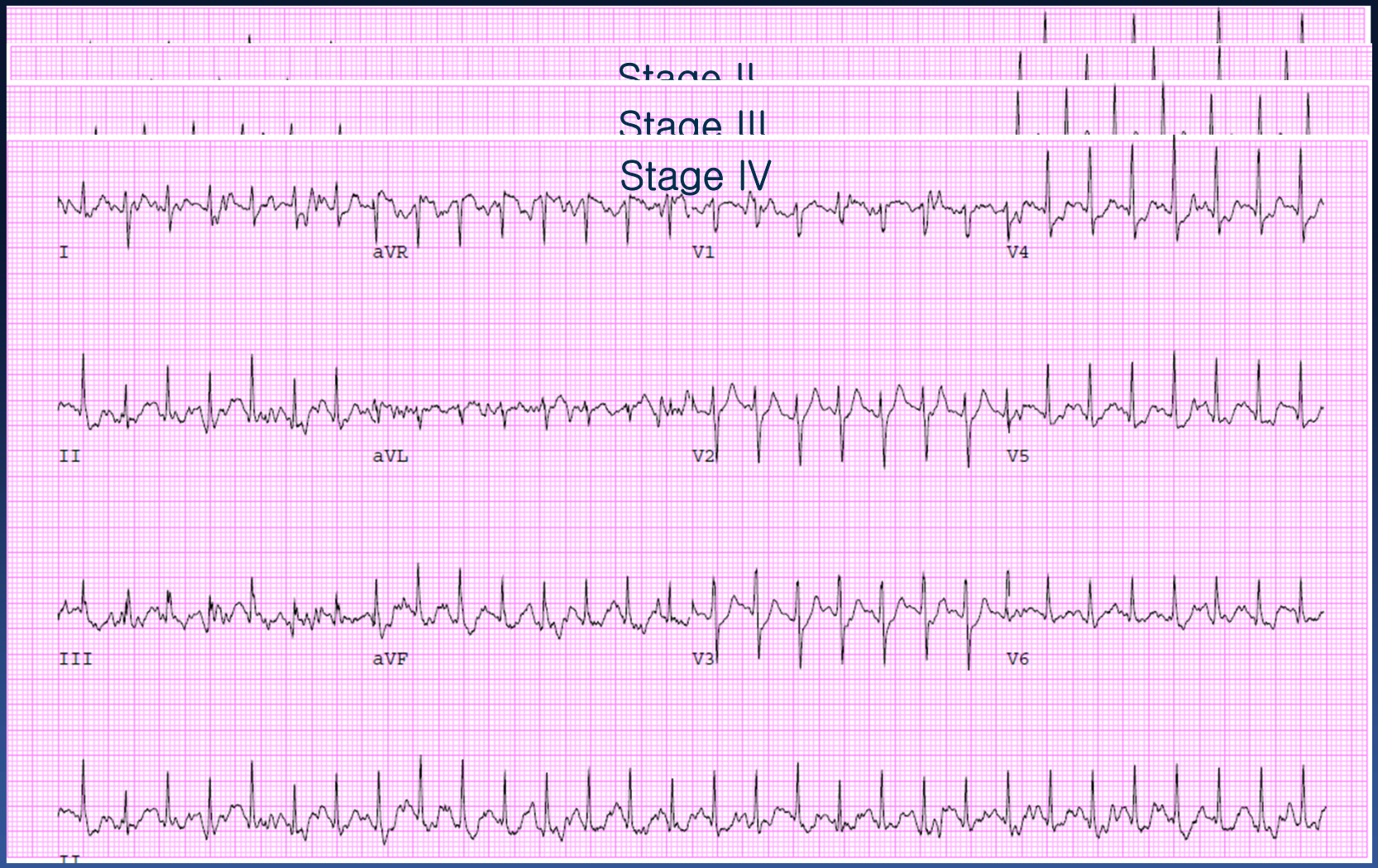


Angiographic DS : 85%
IVUS MLA : 2.8 mm^2

FFR : 0.84
Negative FFR

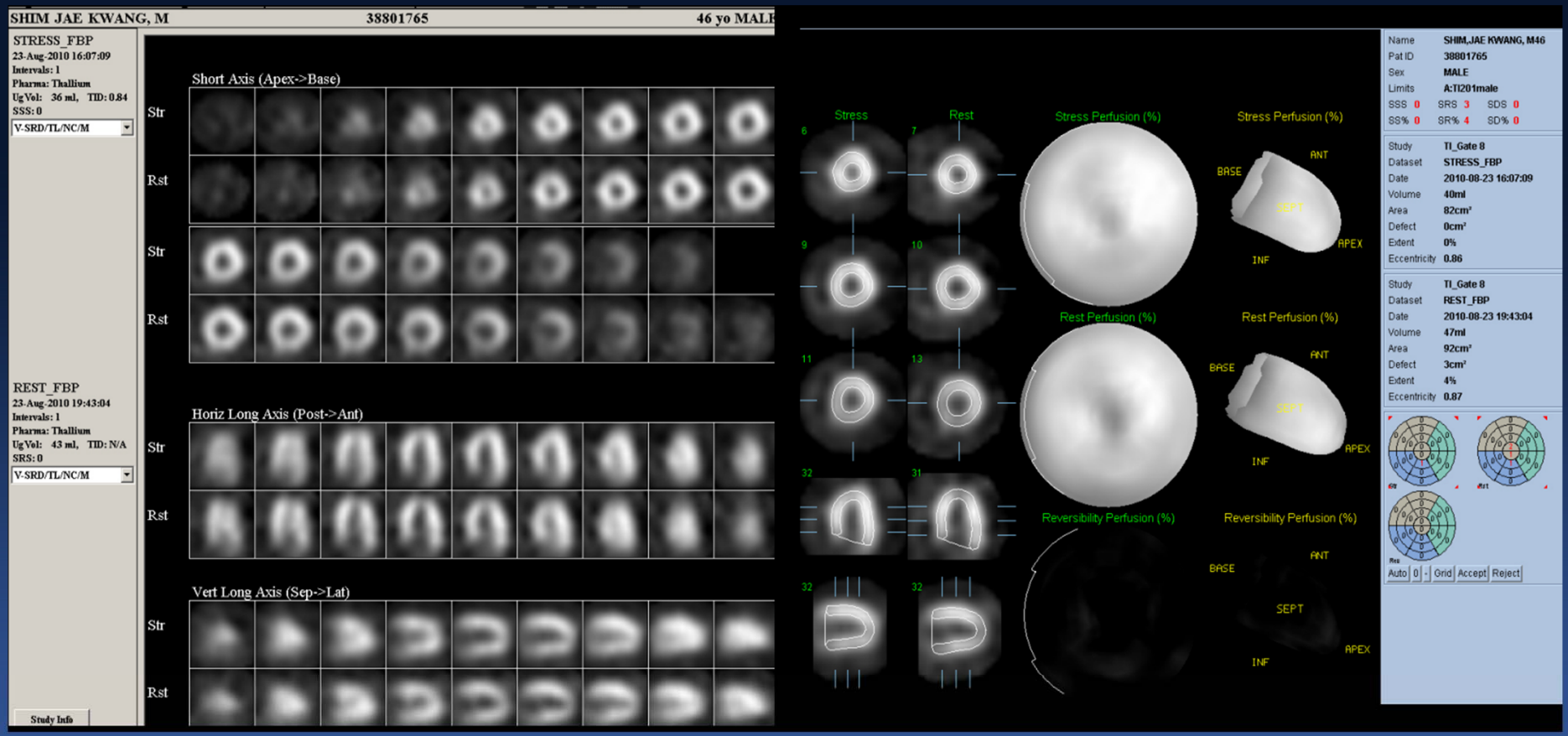
Finding
Objective ischemia,

Treadmill test



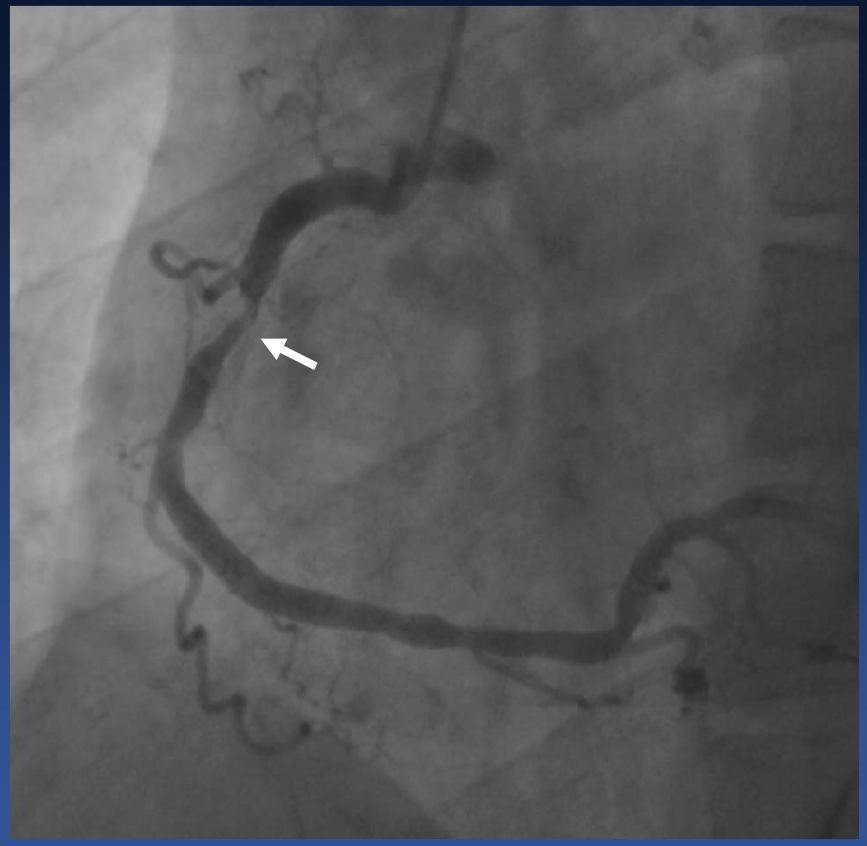
Stage 4 Negative

Thallium SPECT



Normal

Visual estimation: 85%
IVUS MLA: 2.8 mm^2

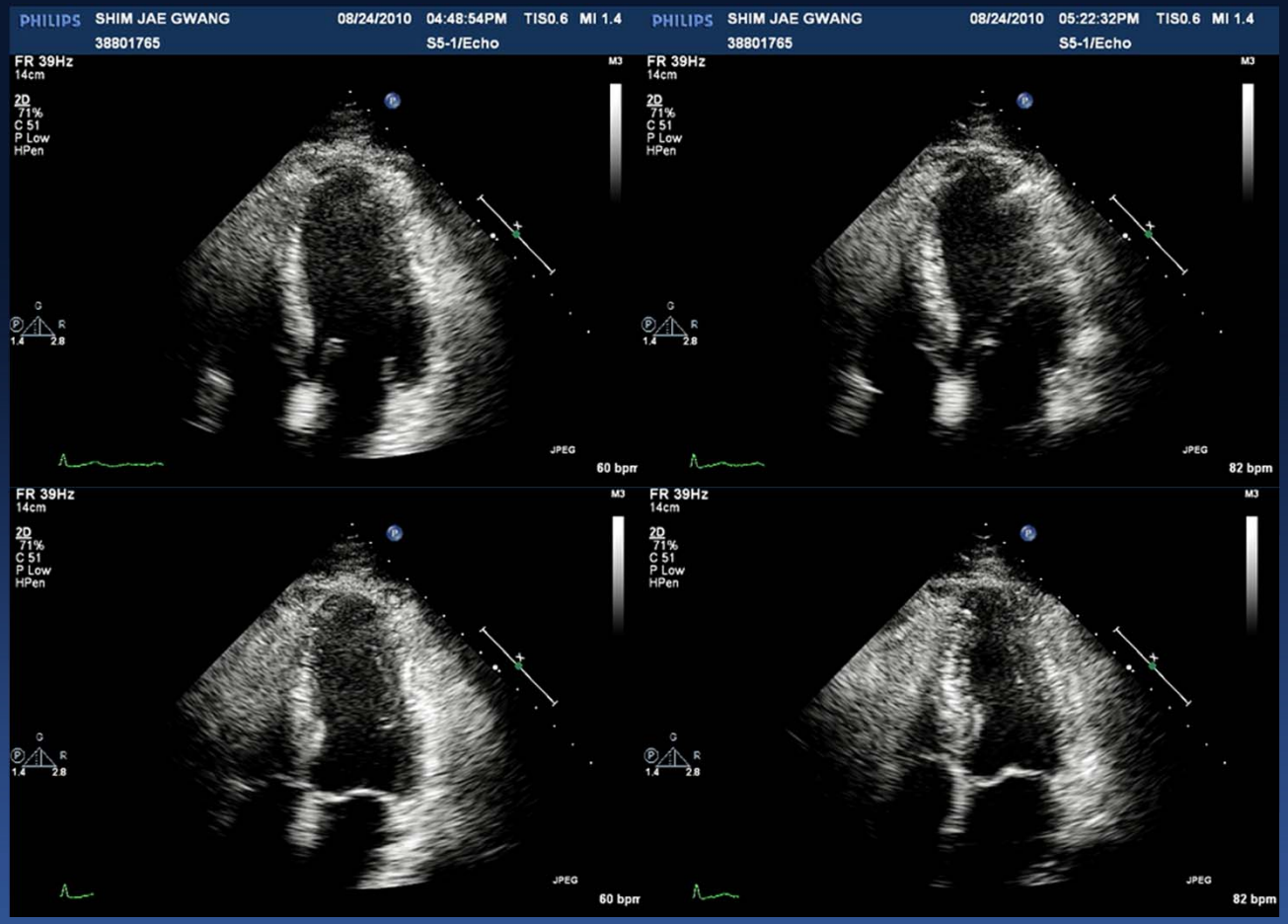


Negative stress test ?

Dobutamine Stress EchoCG

Diastole

Systole

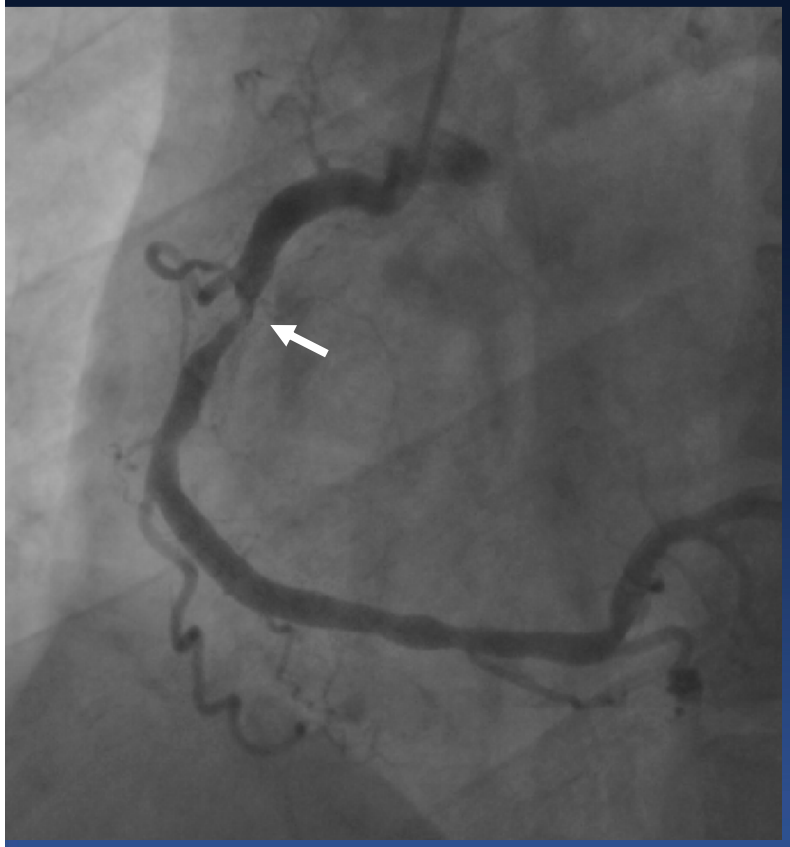


Baseline

Stimulation

Negative

Visual - Functional Mismatch



Angiographic DS(%) : 85%

IVUS MLA : 2.8 mm^2

FFR : 0.84

Treadmill test : Negative

Thallium spect : Normal

Stress Echo : Normal

What would you do ?

Treat or Not treat

Evidence Based Medicine

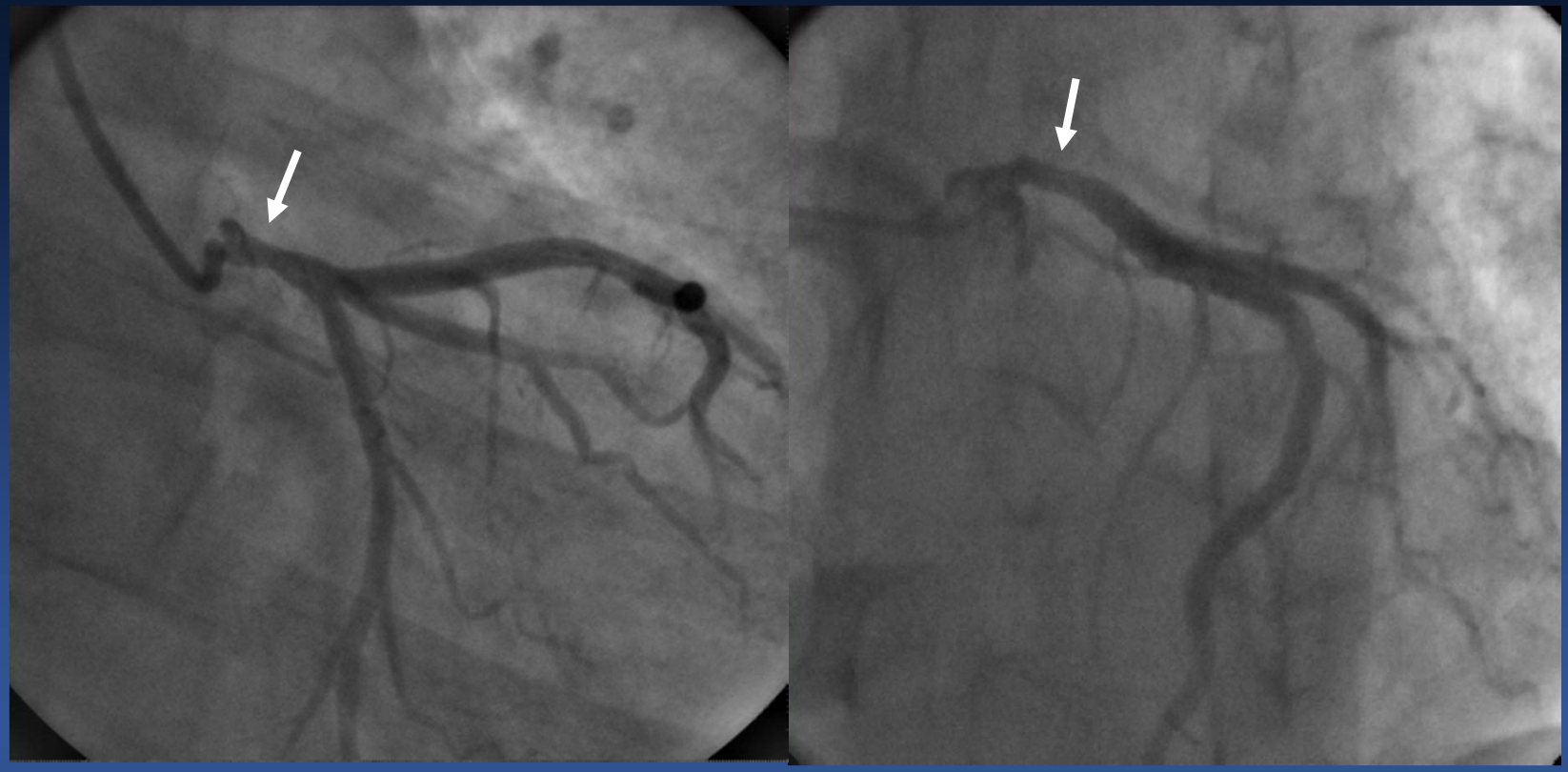
Please Don't touch !

Negative non-invasive stress tests means excellent prognosis. (0.6%/year, Cardiac Death and MI, In patients with normal myocardial perfusion scan, even in the presence of angiographically proven CAD).

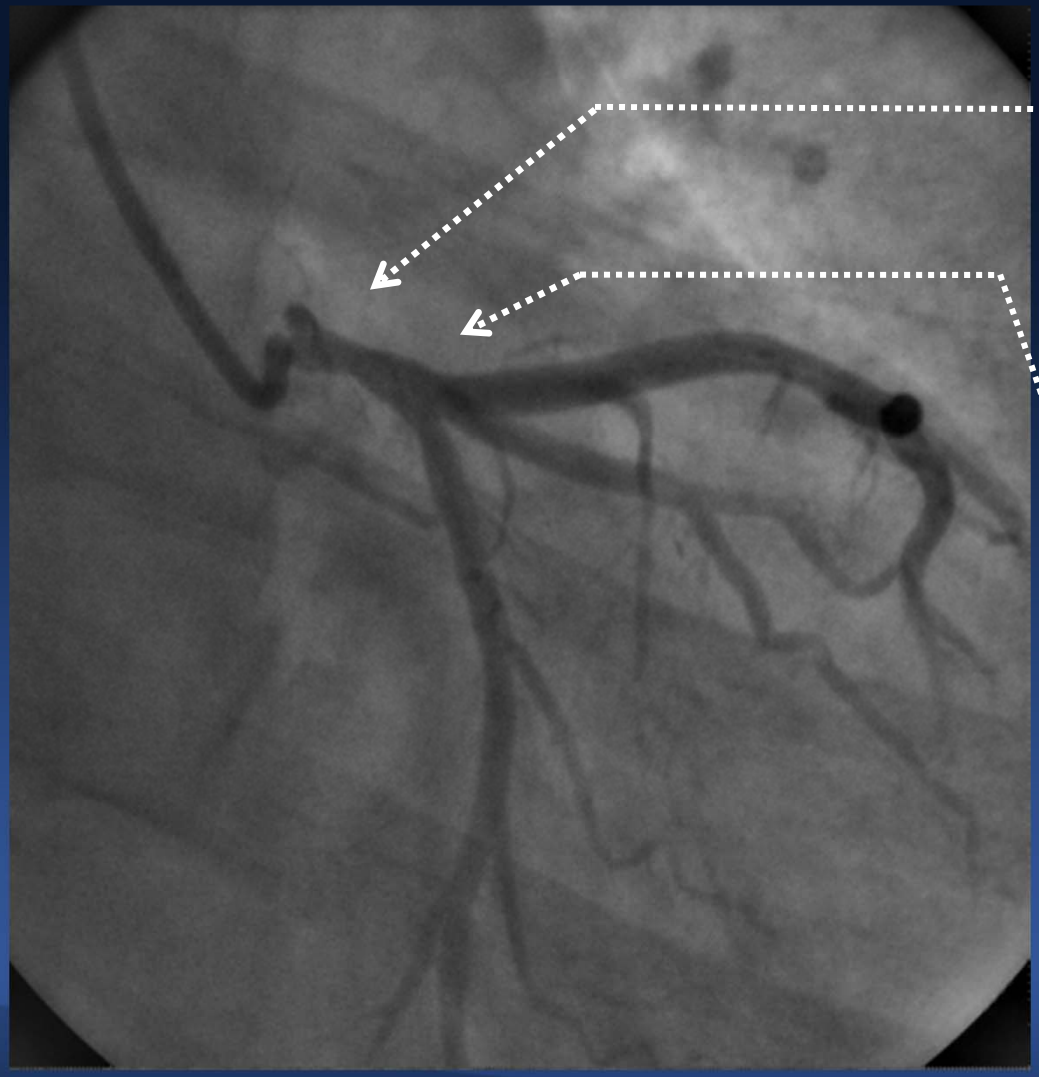
Shaw LJ, J Nucl Cardiol 2004;11:171-85 ,
Prognostic value of gated myocardial perfusion SPECT.
Very large meta-analysis. (n=39,173 patients)

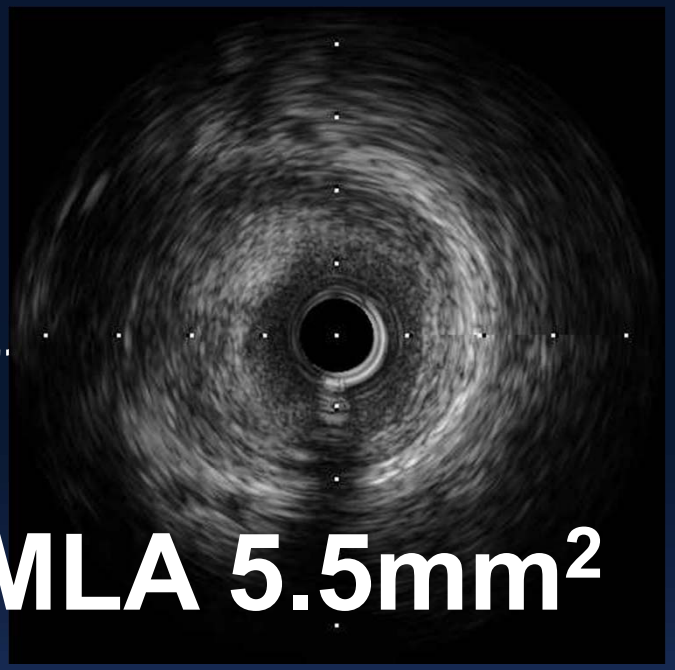
Visual Estimation
30% ?

M/49, Recent Onset effort chest pain for 2 months, Hypertension, DM

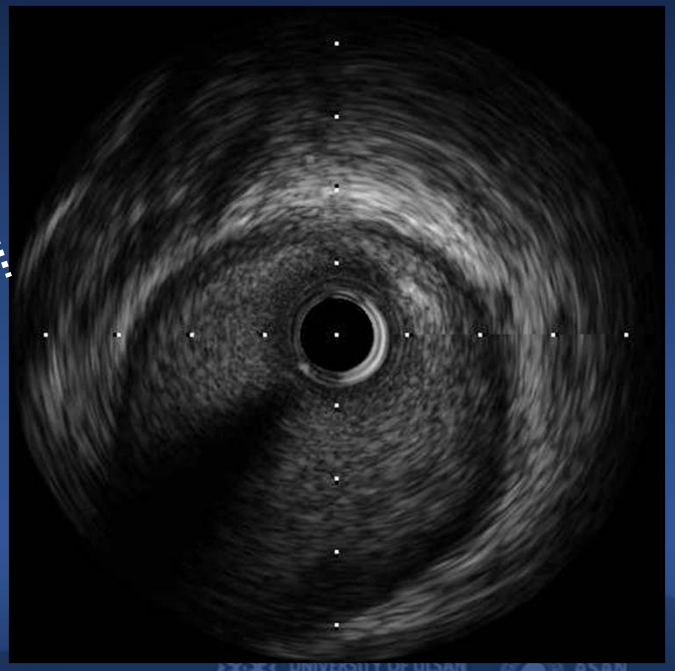


IVUS



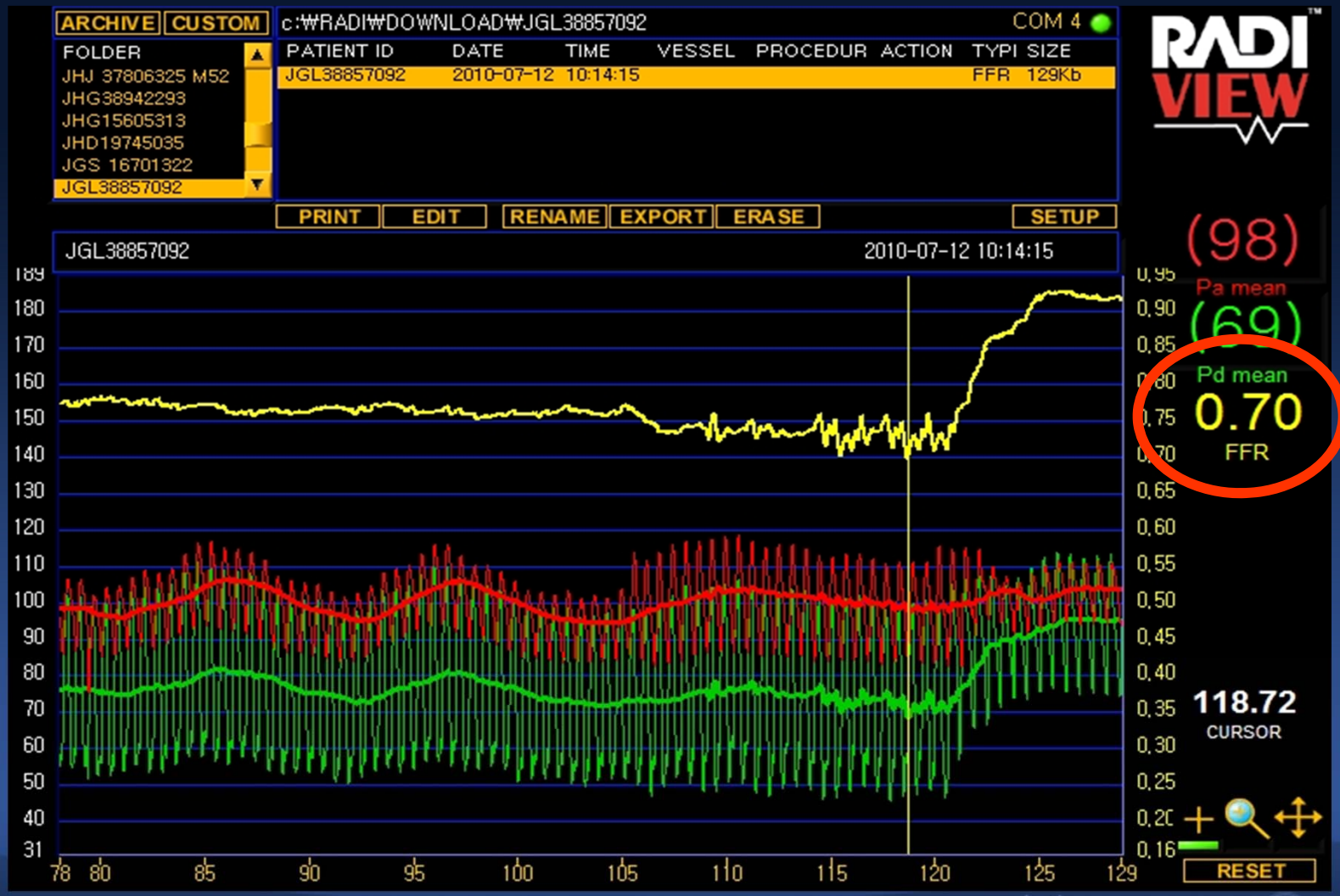


MLA 5.5mm^2

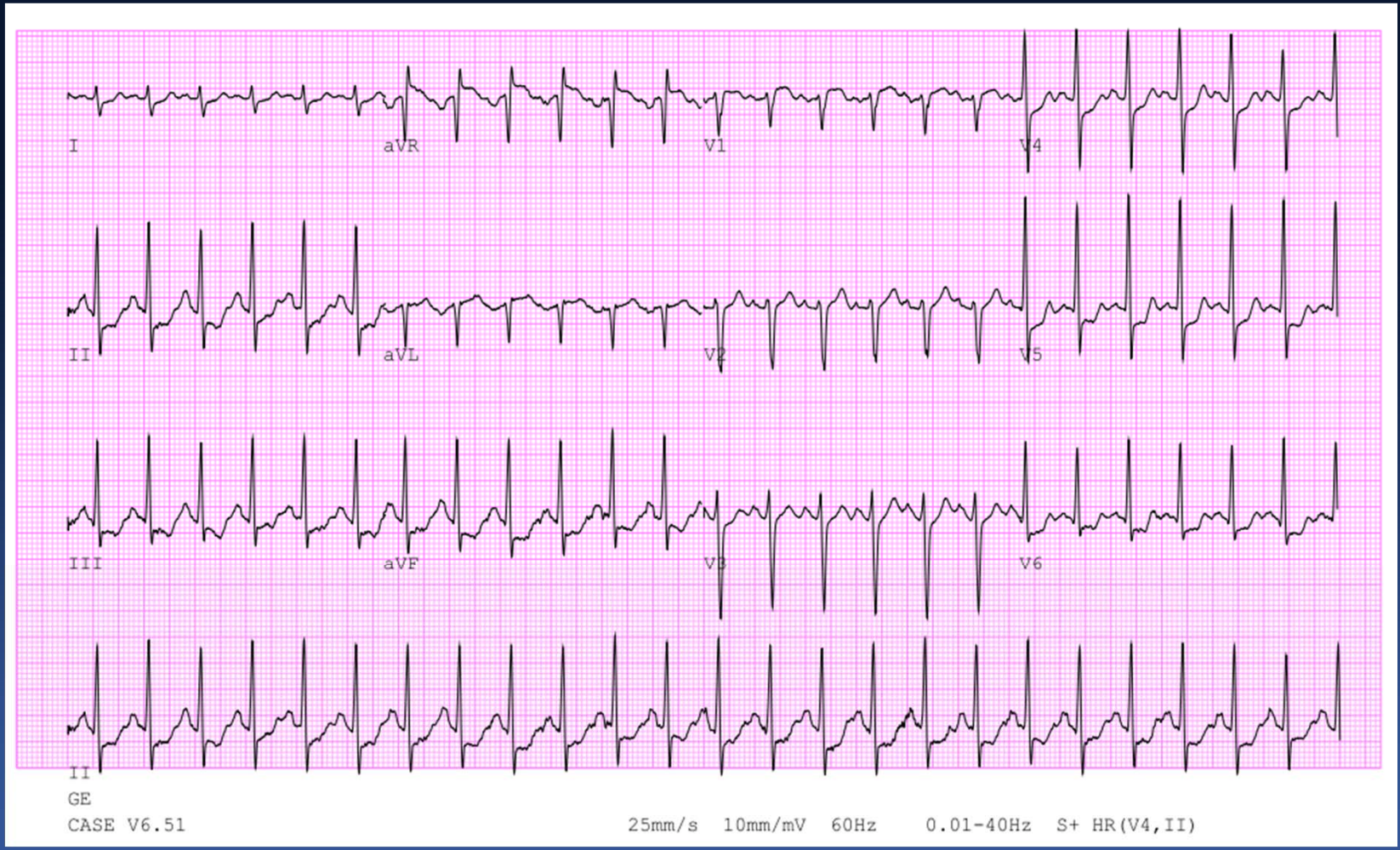


FFR

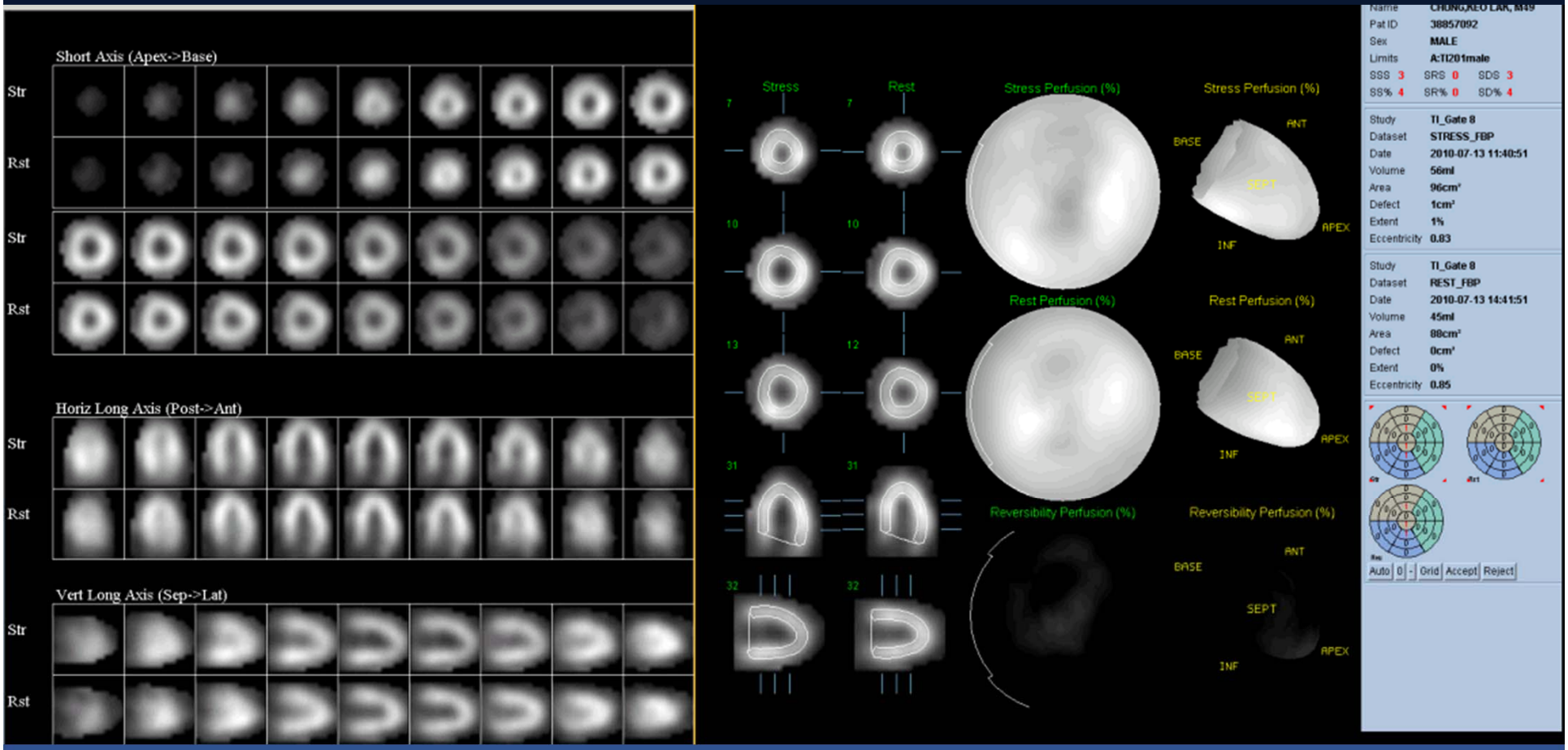
Continuous Intravenous Infusion 140 μg/kg/min



Treadmill test + , stage 2

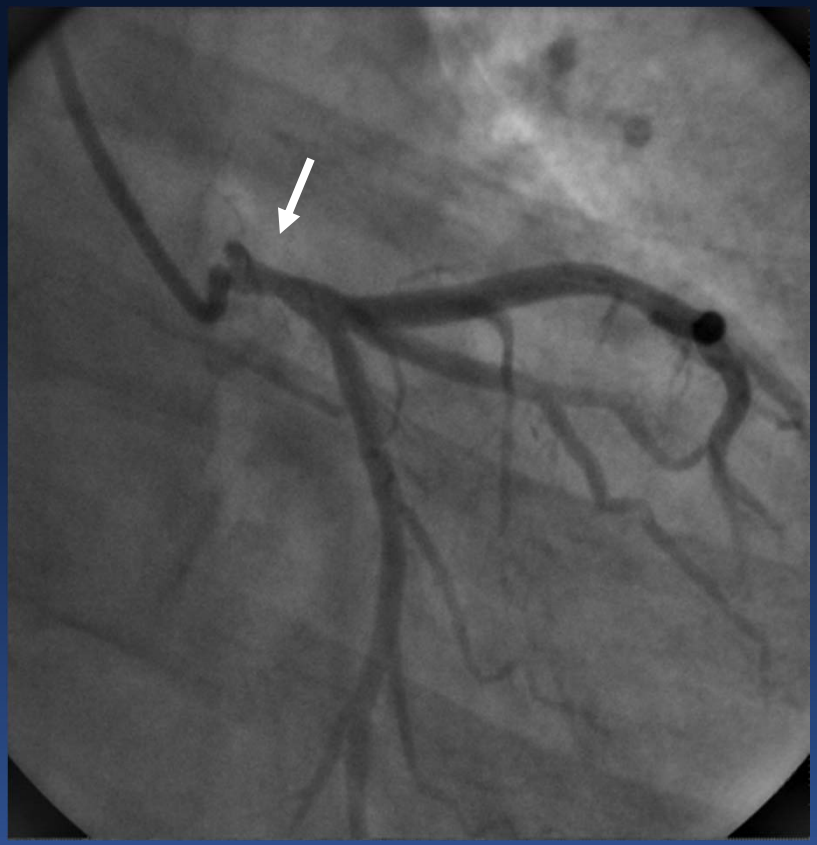


Thallium SPECT + ,



Large Perfusion Defect in LAD territory

Reverse Mismatch



Visual Estimation
30%

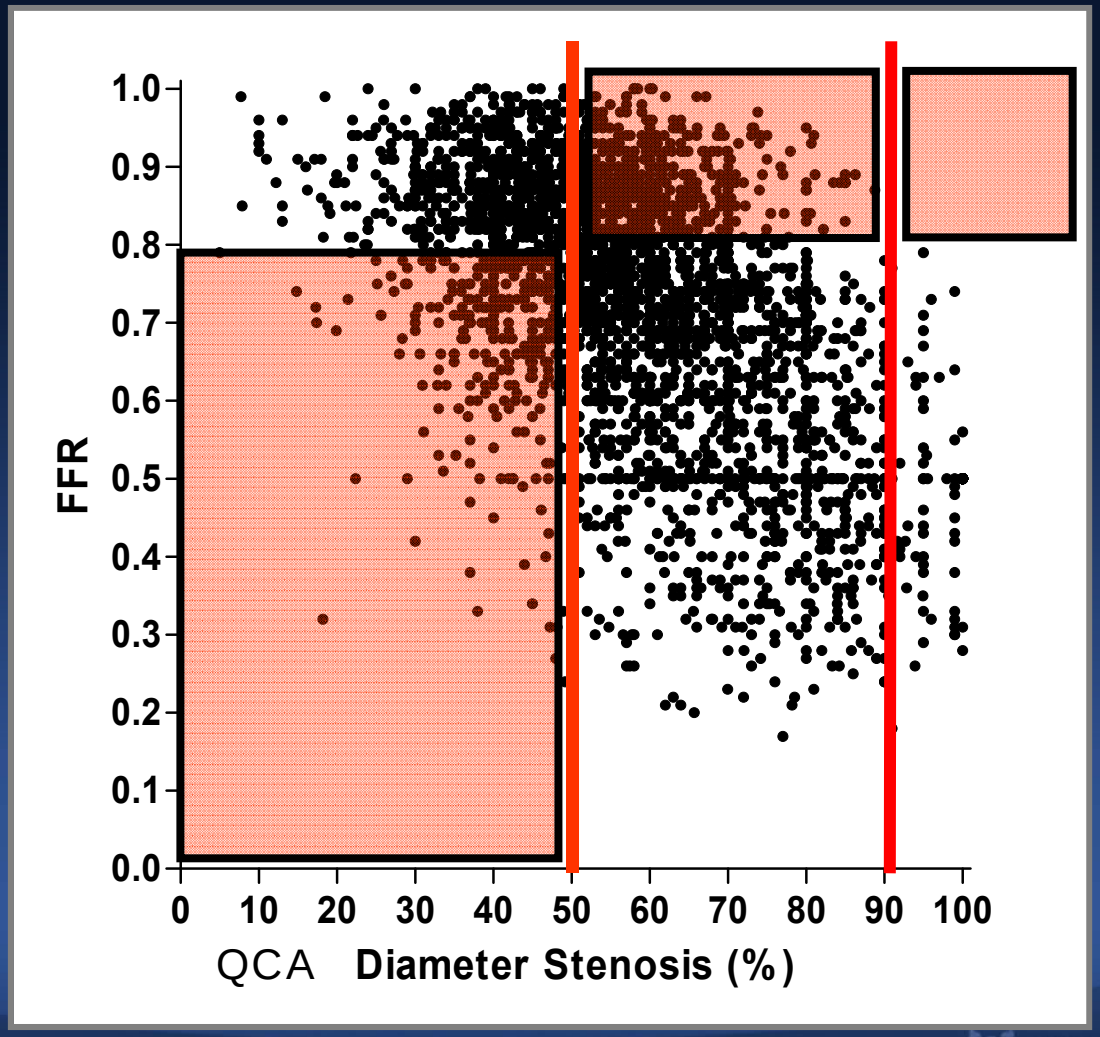
IVUS MLA: 5.5 mm^2
FFR : 0.70
Treadmill test: + stage 3
Thallium spect : + large LAD

FFR is constantly matched with non-invasive stress test !

How many % of Mismatches are in daily practice ?

Mismatch Disease
in the Cath Lab

Comparison analysis; Angiography vs. FFR (n=3000)



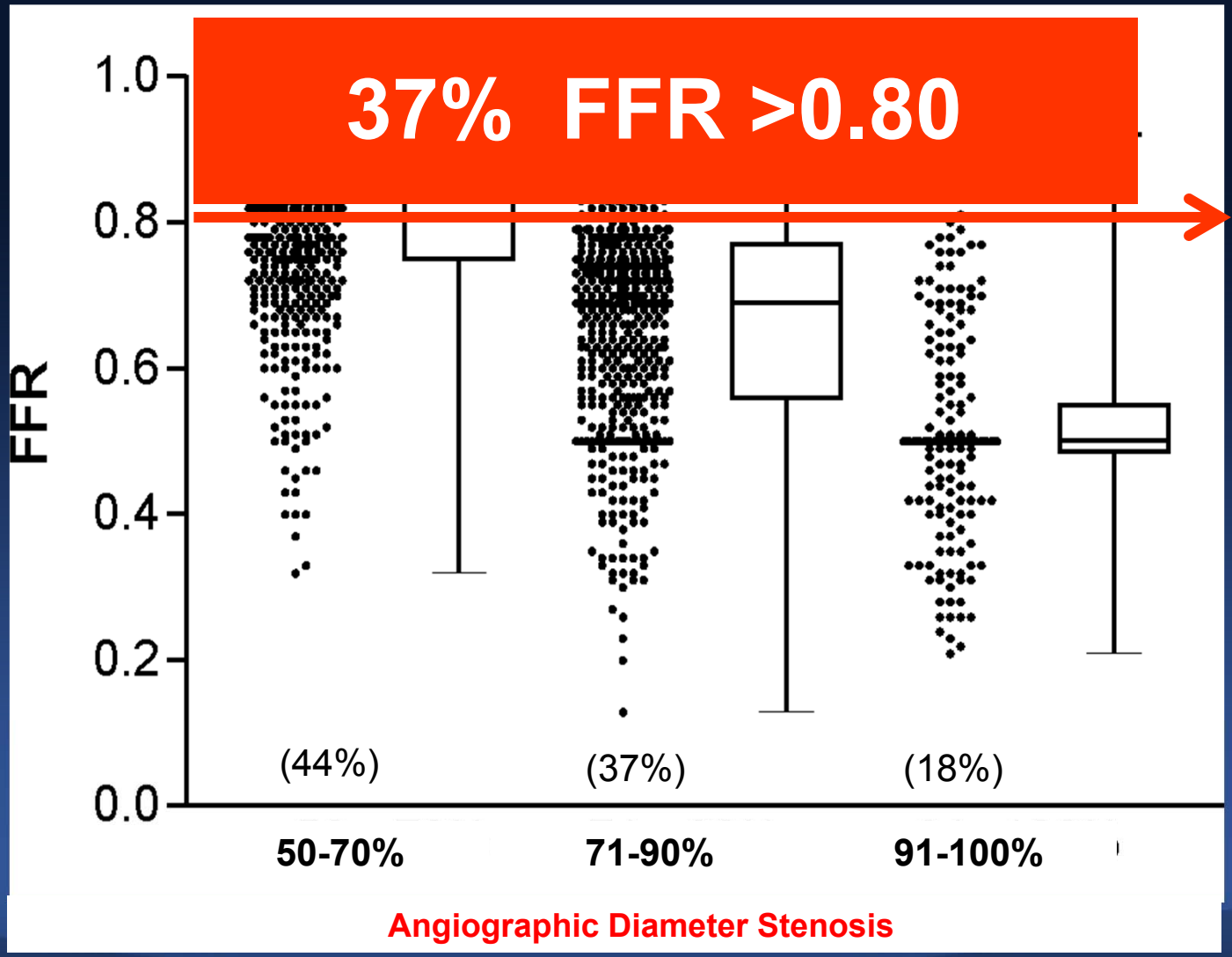
FFR

QCA

Courtesy of Bernard De Bruyne, MD, PhD,

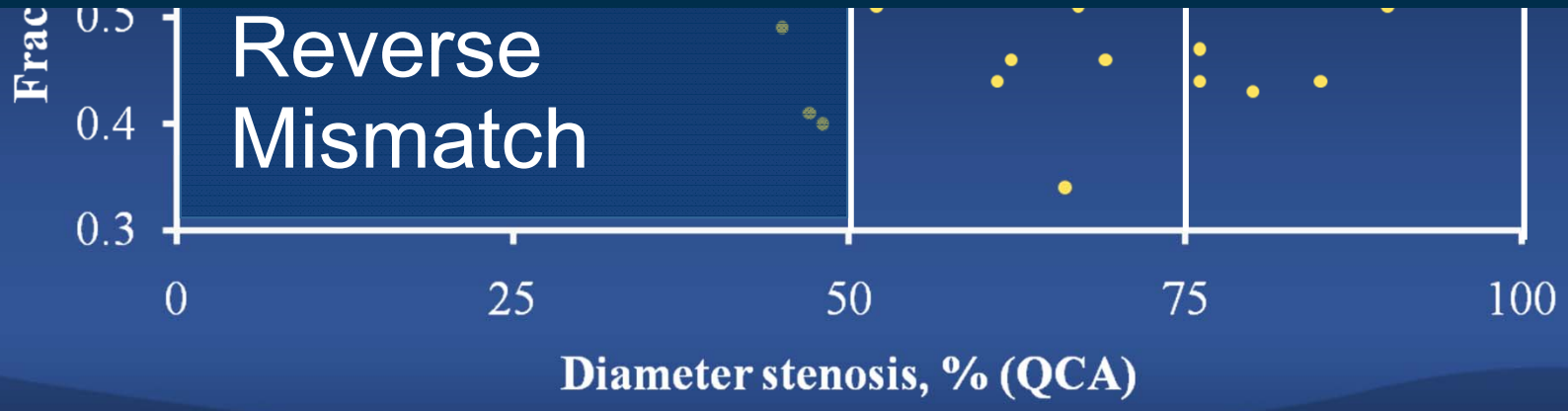
FAME Study

1329 lesions in the FFR-guided arm



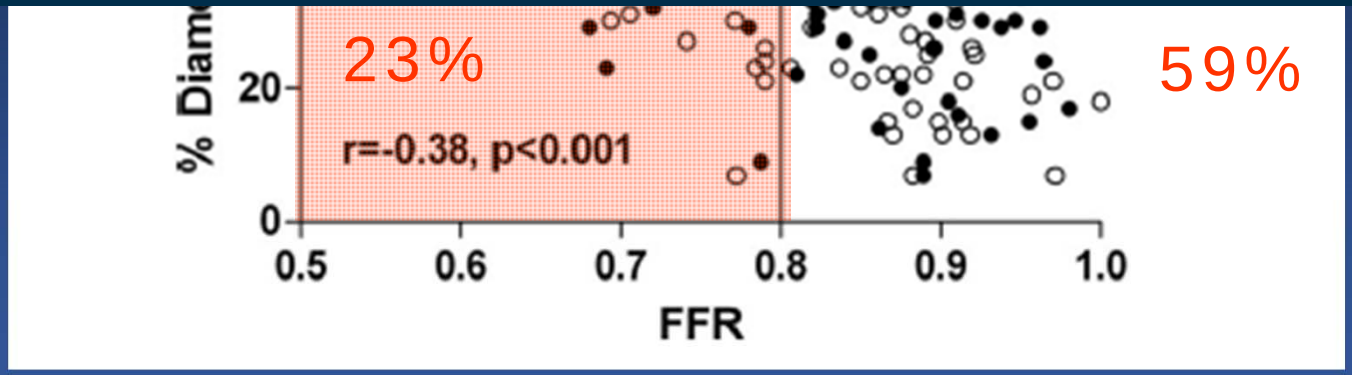
In Real Practice at AMC
708 lesions (QCA Analysis)

Overall 31% of cases are mismatch !



Mismatch
in intermediate LM Disease

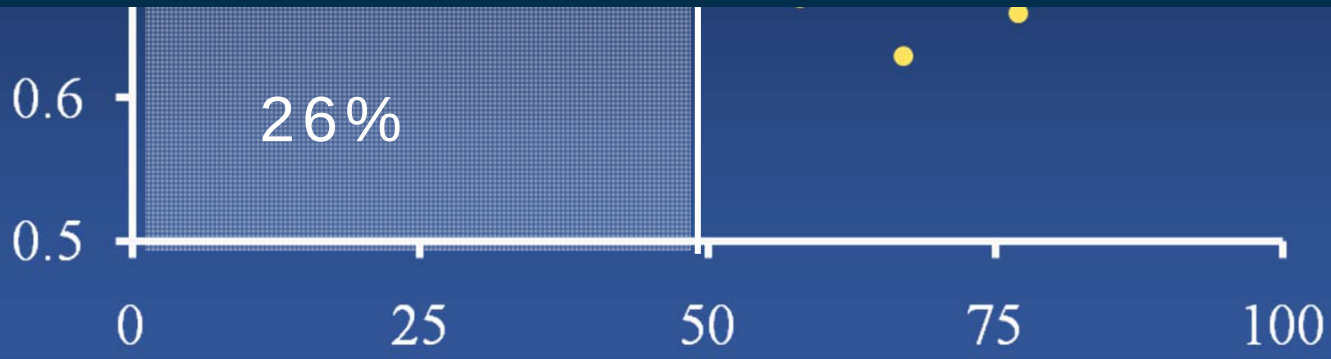
29% of cases are mismatch !



Hamilos M, Circulation 2009; 120: 1505-1512

Mismatch
in Isolated intermediate LM Disease (n=47)

35%, Mismatch is not unommon !



Although we recognize the Visual-Functional Mismatches,

Still Unresolved Question !

1. Mismatches problems between the angiographic DS(%) and FFR in real practice. Why, How many, and How to treat them ?
   High degree of stenosis (>80%) with negative FFR (>0.80) and/or negative non-invasive stress tests.
   Is it really Safe for defer ?
   Any difference compared to intermediate stenosis with negative FFR (>0.80) ?

Multicenter, Prospective Registry to Evaluate The Natural History of FFR-Guided Deferred Coronary Lesions

IRIS FFR DEFER Registry

About 3,000 patients with ≥1 Deferred Target Lesions
(DS>30% by visual estimation and FFR>0.80)

Clinical Study
(N=2,000)

1,200 patients in Clinical Study

Imaging Study

Clinical follow-up
At 1,2,3 and 5 year

Imaging follow-up
(IVUS,VH-IVUS,OCT)
At 2 year

Primary Endpoint : 2 year TVF
Target vessel related Cardiac Death, MI, and Clinical driven TVR

* 2-year CAG & Imaging FU will be conducted after Completion of 2-year Clinical FU

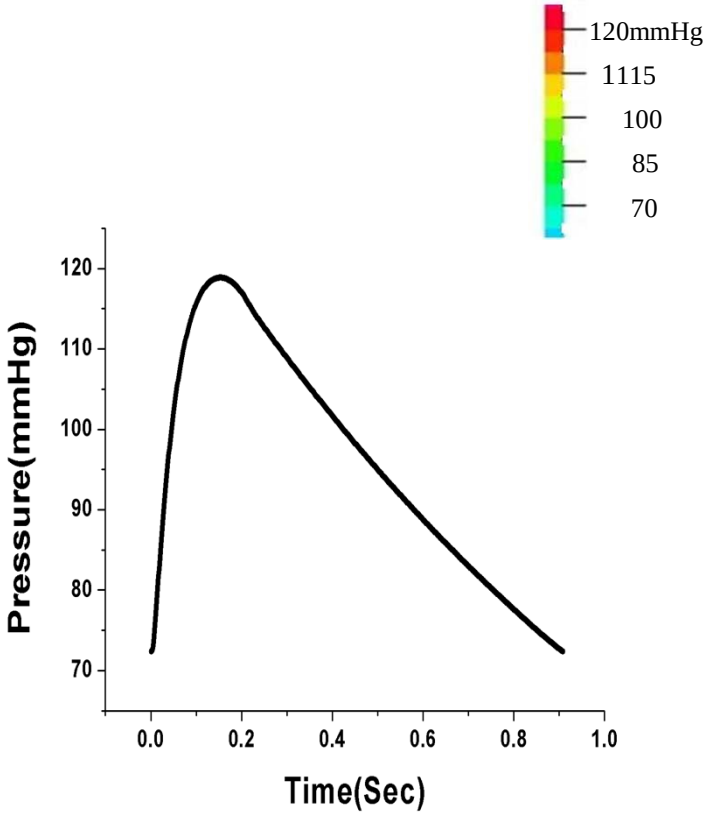
Still Unresolved Question !

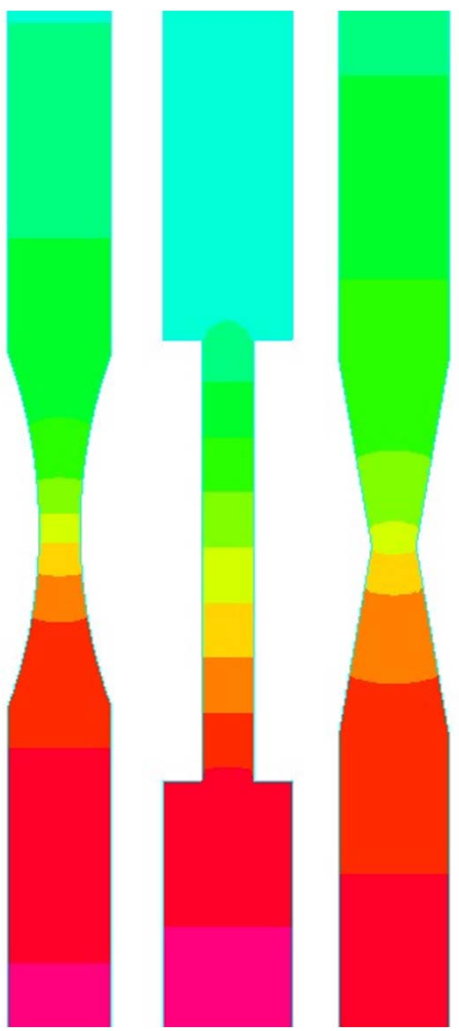
2. Especially, Reverse Mismatches - Insignificant stenosis (<50%) with positive FFR (<0.80): Stent or Medical treatment ?
3. What about the role of FFR in the clinical setting of ACS ?
4. Current IVUS MLA of 4 mm^2 would be OK for your practice ? The IVUS MLA can predict functional significance of stenosis ?

Why Mismatches Occur ?

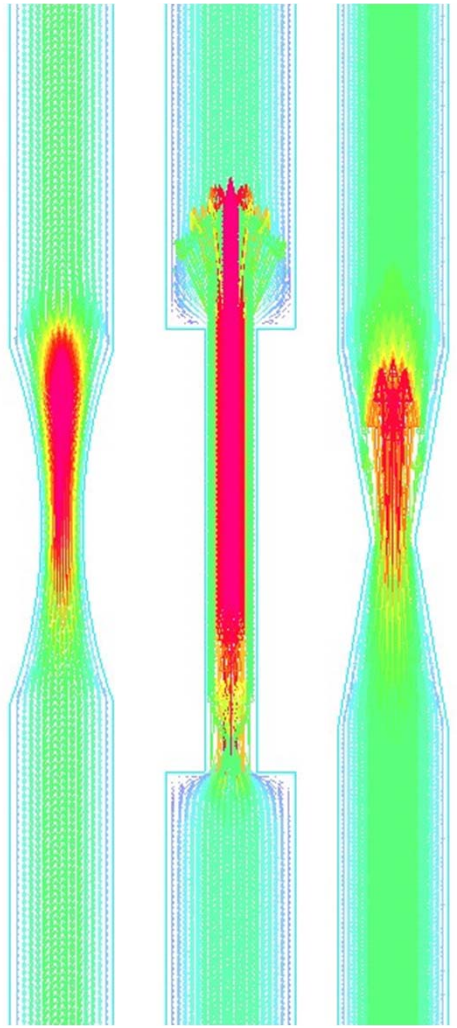
Just due to Under-estimation and Over-estimation of angiographic DS% ?

Mathematically Computed Simulation for FFR





Pressure contours

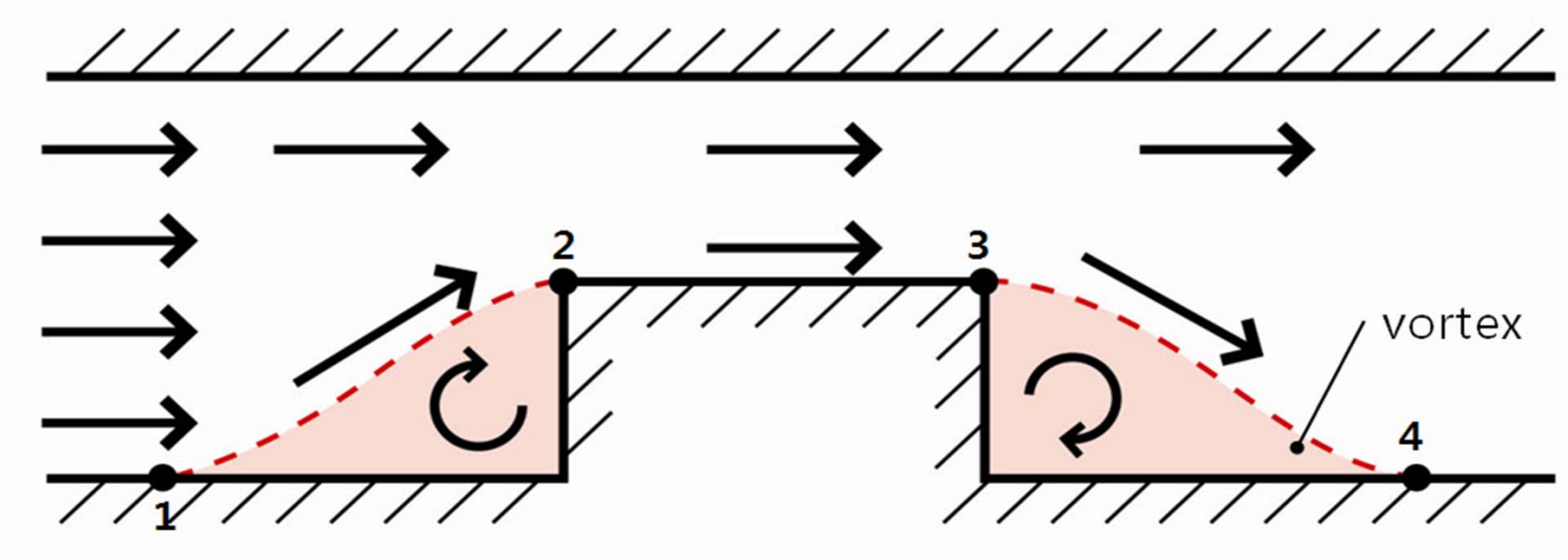


Velocity vectors

Why pressure drop ?

Pressure Drop due to Energy Loss of fluid by Vortex flow

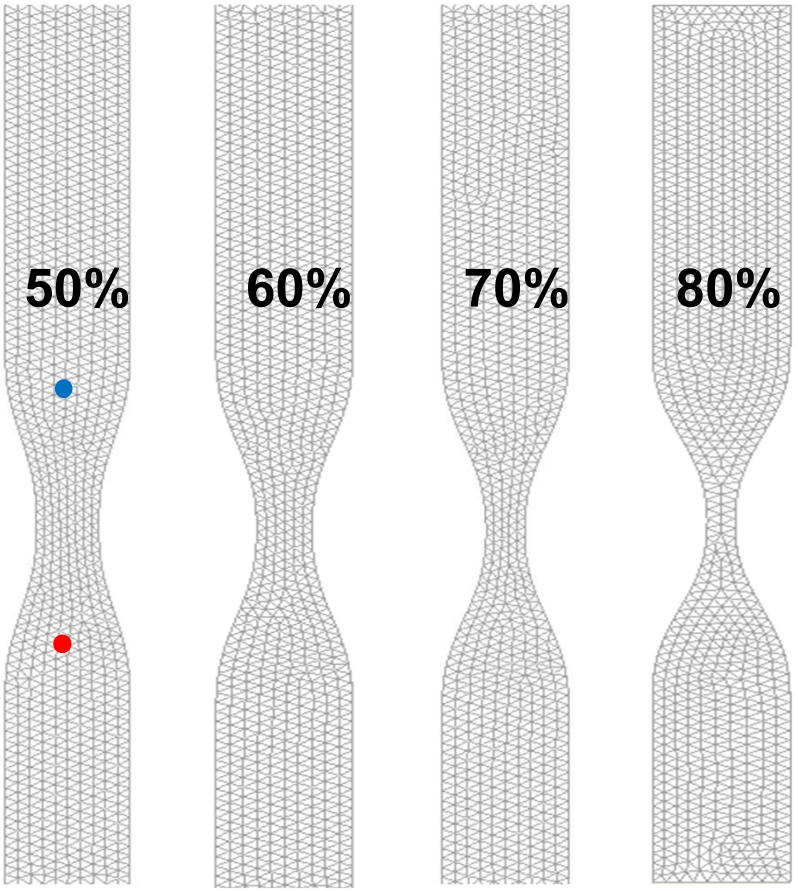
$1 : P1 + 1/2pv1^2 = Pt_1 \quad 2 : P2 + 1/2pv2^2 = Pt_2 \quad 3 : P3 + 1/2pv3^2 = Pt_3$



$Pt_1 > Pt_2$ $Pt_1 >> Pt_4$

Courtesy of Prof. Shim

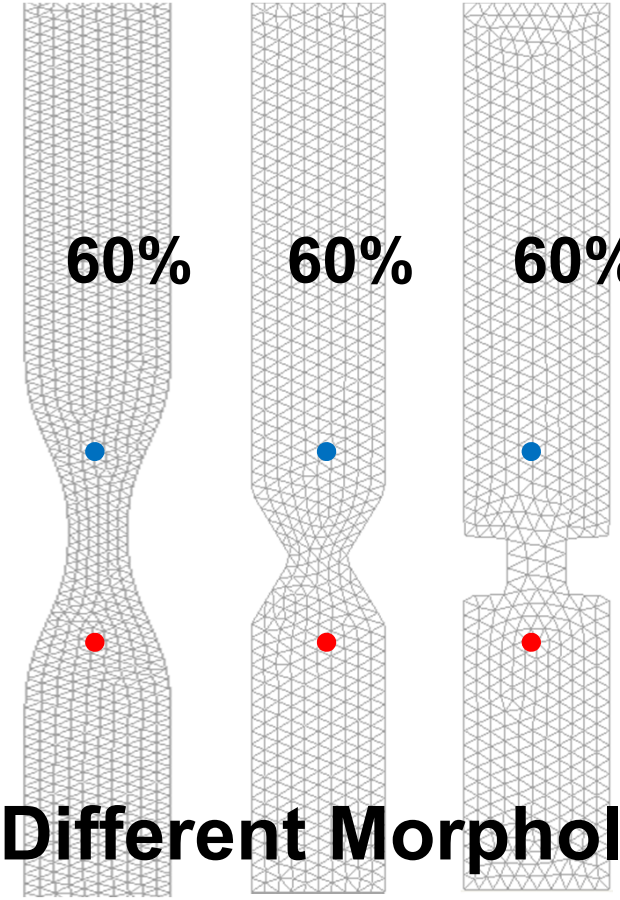
Degree of Stenosis



FFR

0.89 0.81 0.76 0.70

Same degree of stenosis

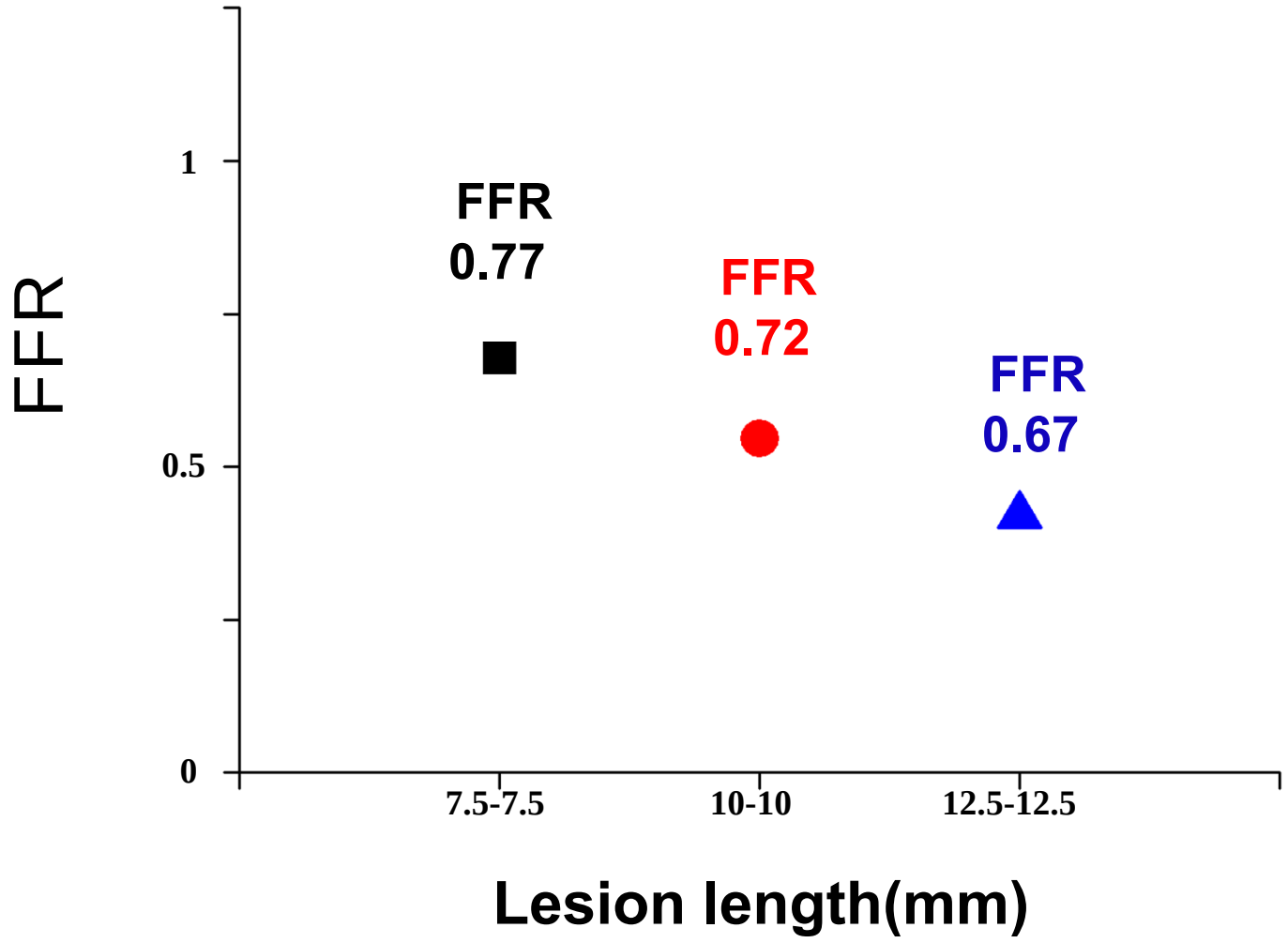


Different Morphology

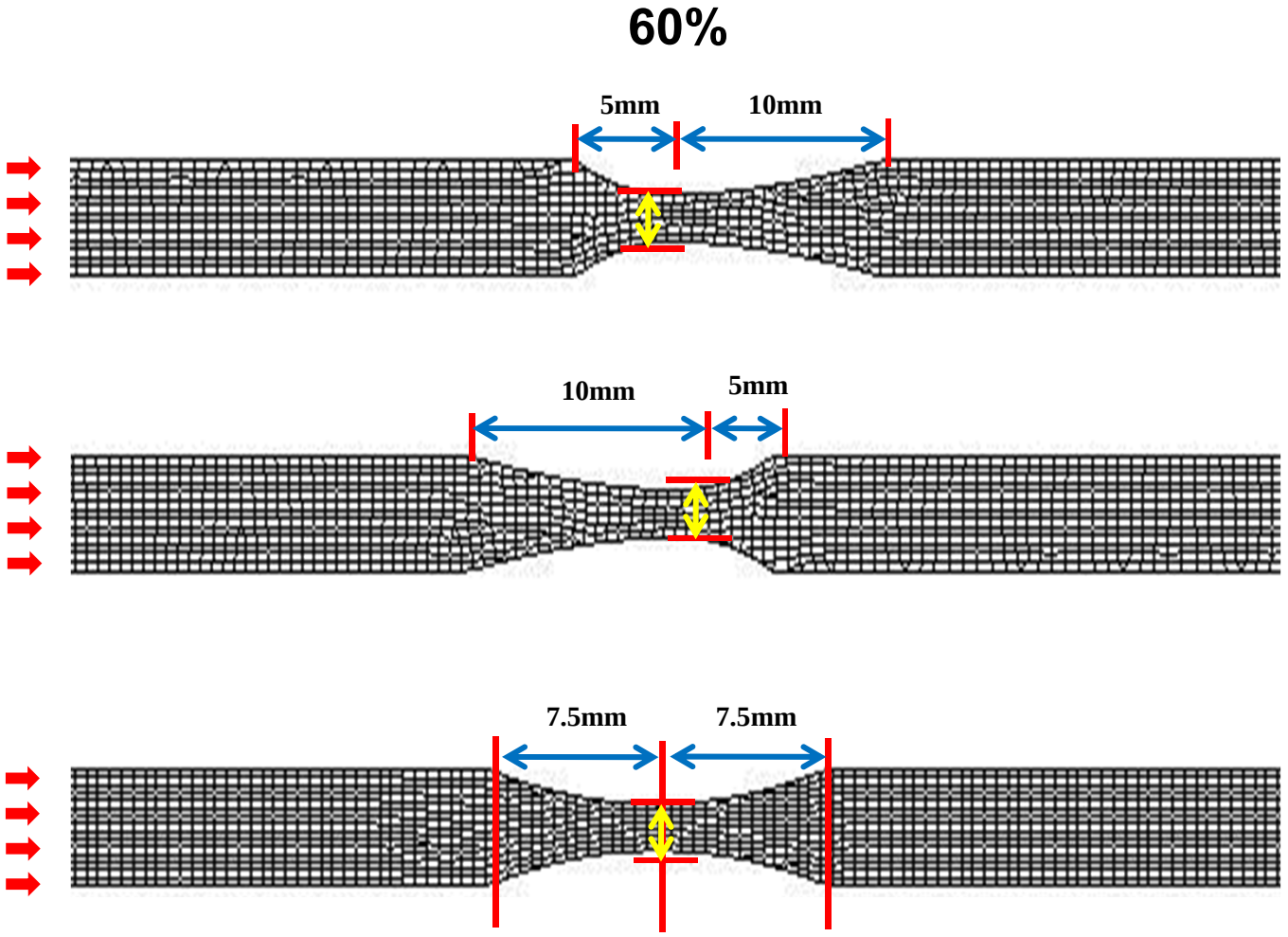
0.81 0.77 0.63

Different FFR

Different Lesion Length



Lesion Eccentricity
(longitudinal, cross-sectional)



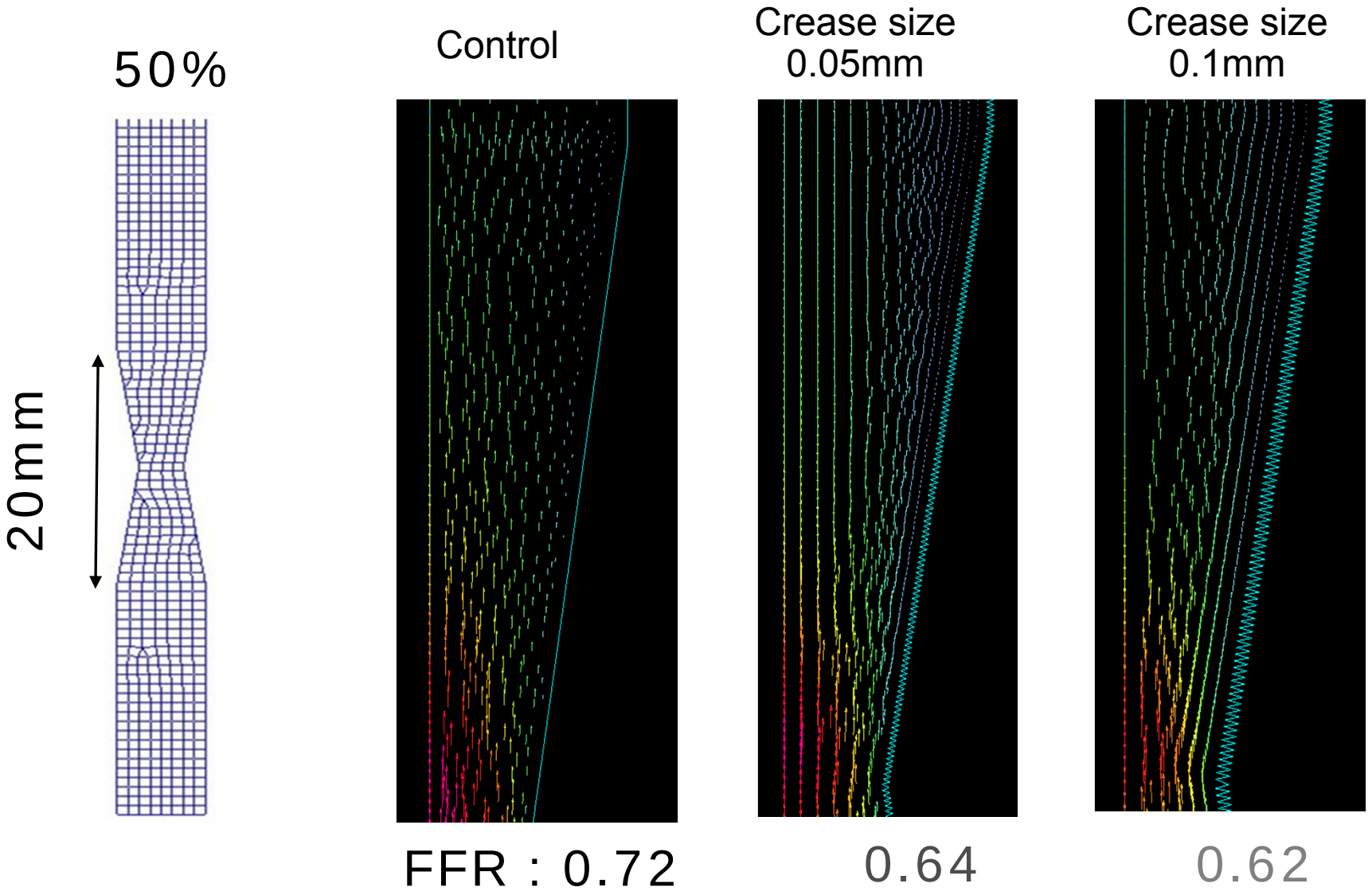
FFR

0.70

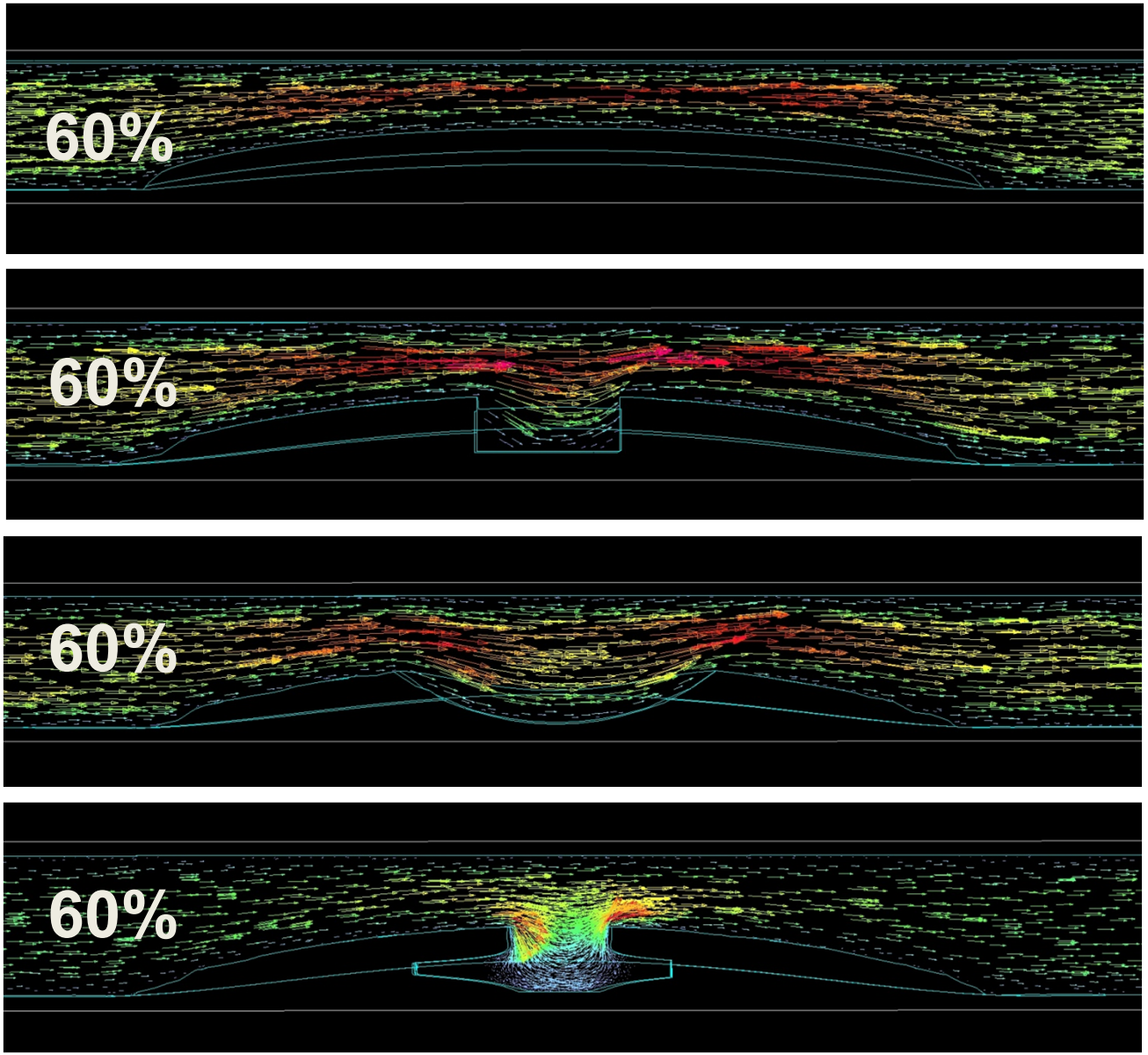
0.67

0.73

Different Surface Roughness



Presence of Plaque Rupture



FFR : 0.81

0.79

0.74

0.70

FFR is influenced by Many Lesion Specific Factors

- Degree of diameter stenosis
- Reference vessel diameter
- Lesion morphology
- Eccentricity
- Lesion length
- Plaque burden, Plaque rupture
- Surface roughness
- Viscous friction, flow separation, turbulence, and eddies

We can not compare side by side directly, between the 2-dimensional imaging of angiographic DS% and more integrated representative, 3-dimensional FFR.
You can make sense Mismatches !

How did I Implement FFR in my daily practice ?

Validation and Threshold of Ischemia

FFR < 0.80
is a good surrogate
for clinical ischemia.

Treat or Not Treat
Operator's discretion

Validation and Threshold of Ischemia

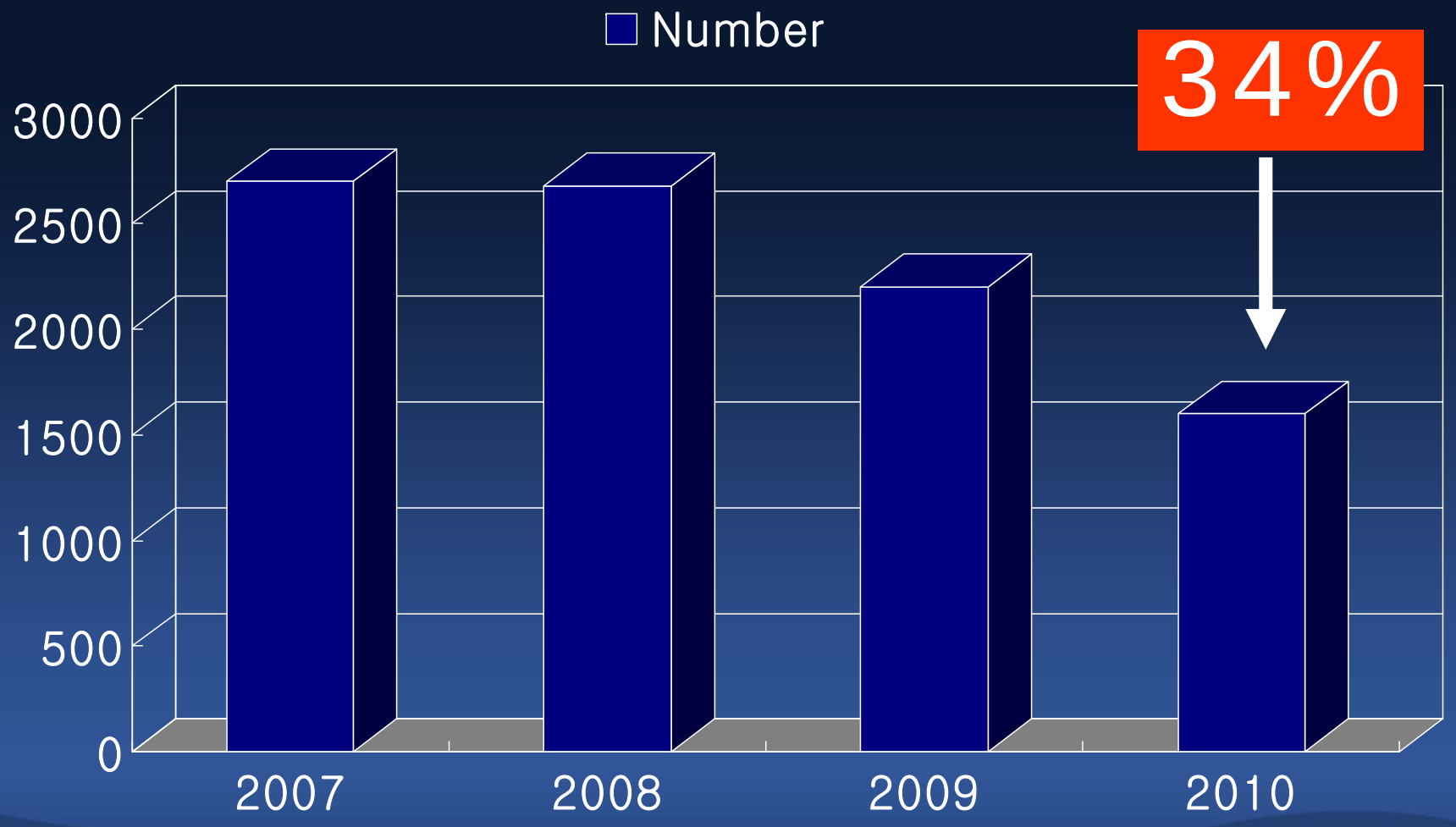
FFR > 0.80
is a perfect surrogate
for absence of ischemia.

100% Specificity
Negative FFR Never Lies

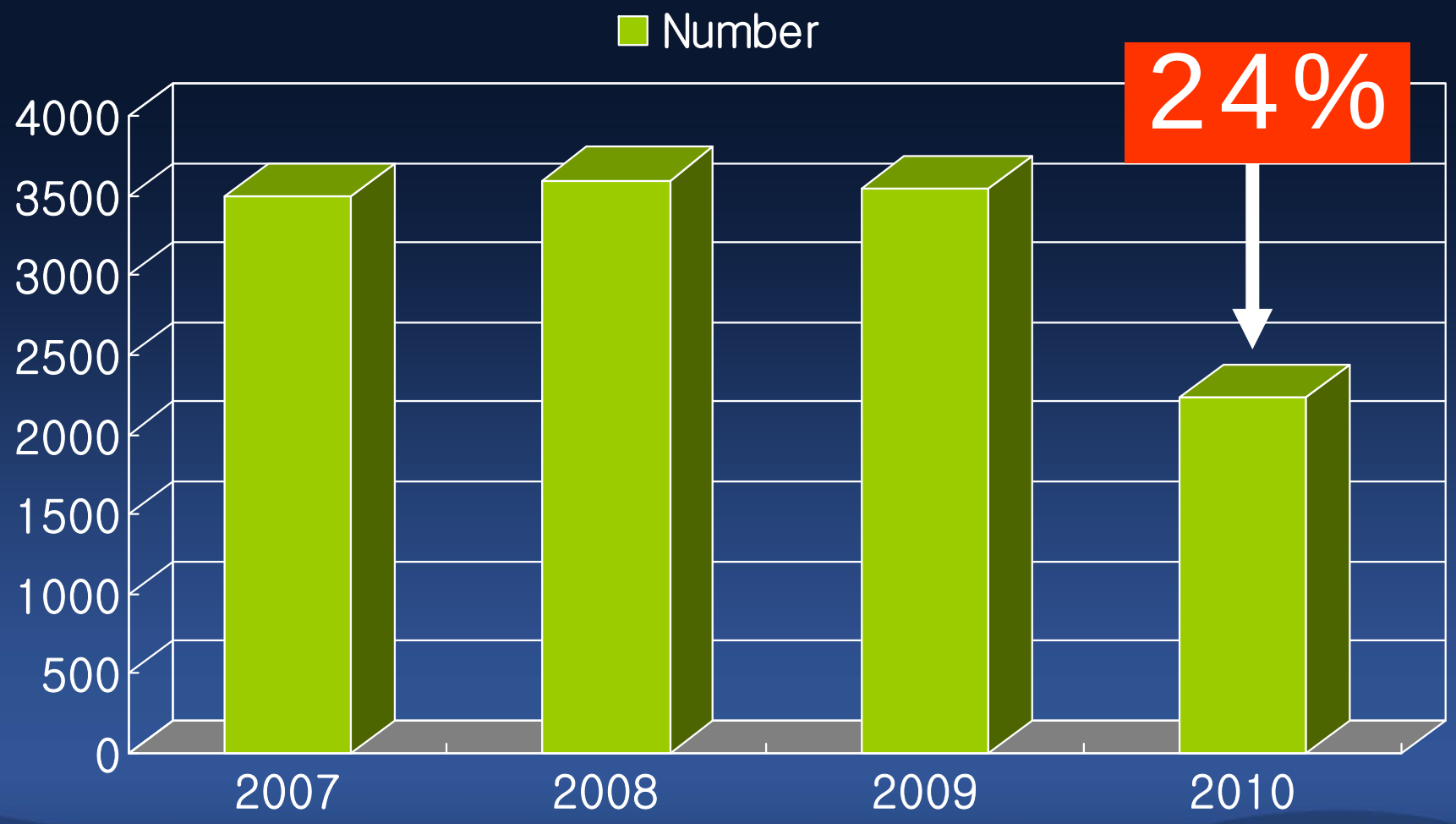
After I Became a Believer,

FFR >0.80 ⟶ Defer
FFR <0.75 ⟶ PCI or Surgery
Cosmetic angioplasty were also excluded.
(small myocardium, good response to medical treatment, etc)

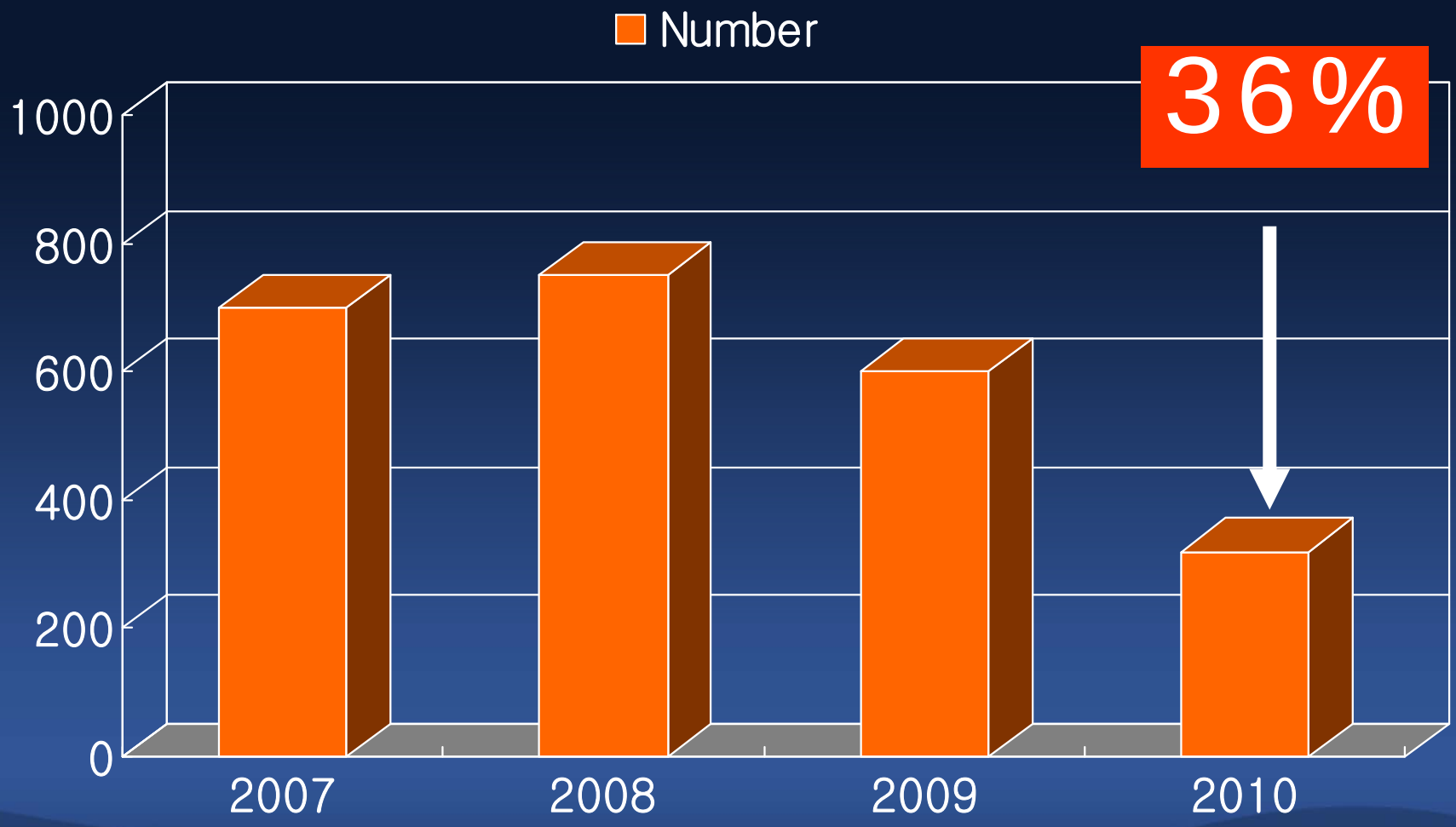
Number of PCI in AMC



Stents


Number
24%
4000
3500
3000
2500
2000
1500
1000
500
0
2007
2008
2009
2010

CABG



After I Became a Believer,

I have to renounce the incentive from the hospital,
I have to take the blame from many of my busy friends and cardiac surgeons too,
and I have to face the territorial of FFR Insiders today…

Be careful !

Being a Believer was not as good as I expected.

New Insight
for FFR vs. IVUS MLA

In Epicardial Artery

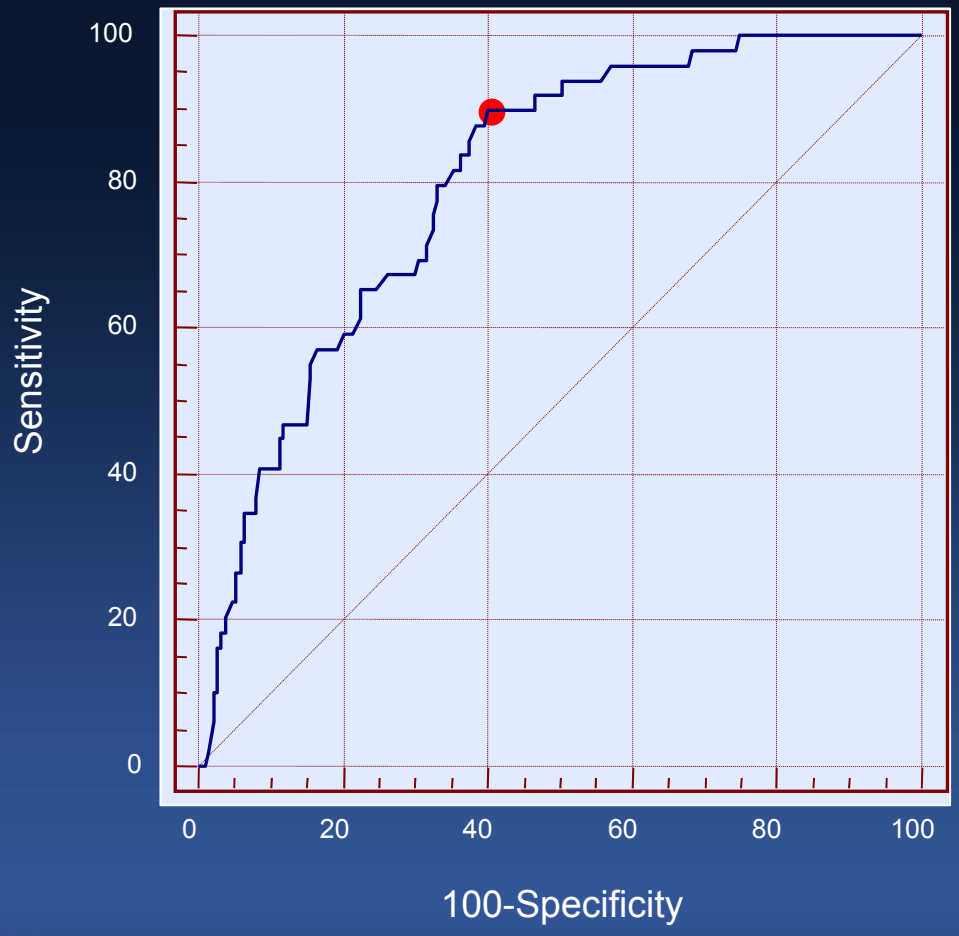
Published IVUS MLA Cut-off Value

	Nishioka T, JACC 1999	Briguori et al AJC 2001	Takaki et al Cir. 1999	Abizaid et al AJC 1998
	70 lesions	53 lesions	42 pts	86 pts
Cut-off of MLA (mm^2)	<4.0 (Thallium +)	< 4.0 (FFR<0.75)	<3.0 (FFR<0.75)	> 4.0 (CFR >2.0)
Sensitivity Specificity	80% 90%	92% 54%	83 % 92.3 %	Accuracy 92%
QCA VD (mm) DS (%)		3.08±0.3 52±11		
MLA (mm^2)	3.3±2.3	3.9±2.5	3.9±2.0	4.4±2.0
MVA (mm^2)		12.0±4.6		13.2±4.4
Area stenosis%		65±18	55±24	43±24

Published Data Review

In Epicardial Artery

IVUS MLA matched with FFR <0.80 (n=236)



New Cut-off = 2.42mm^2,
AUC=0.800,
95% CI=0.742-0.848

Sensitivity=90%
Specificity=60%
PPV=37%
NPV=96%
Accuracy=68%

Kang SJ, et al, Circ Cardiovasc Interv. 2011;4: 65-71

New IVUS MLA
matched with FFR <0.80

2.4 mm^2

Kang SJ, Park SJ, Circ Cardiovasc Interv. 2011;4: 65-71

In My Practice

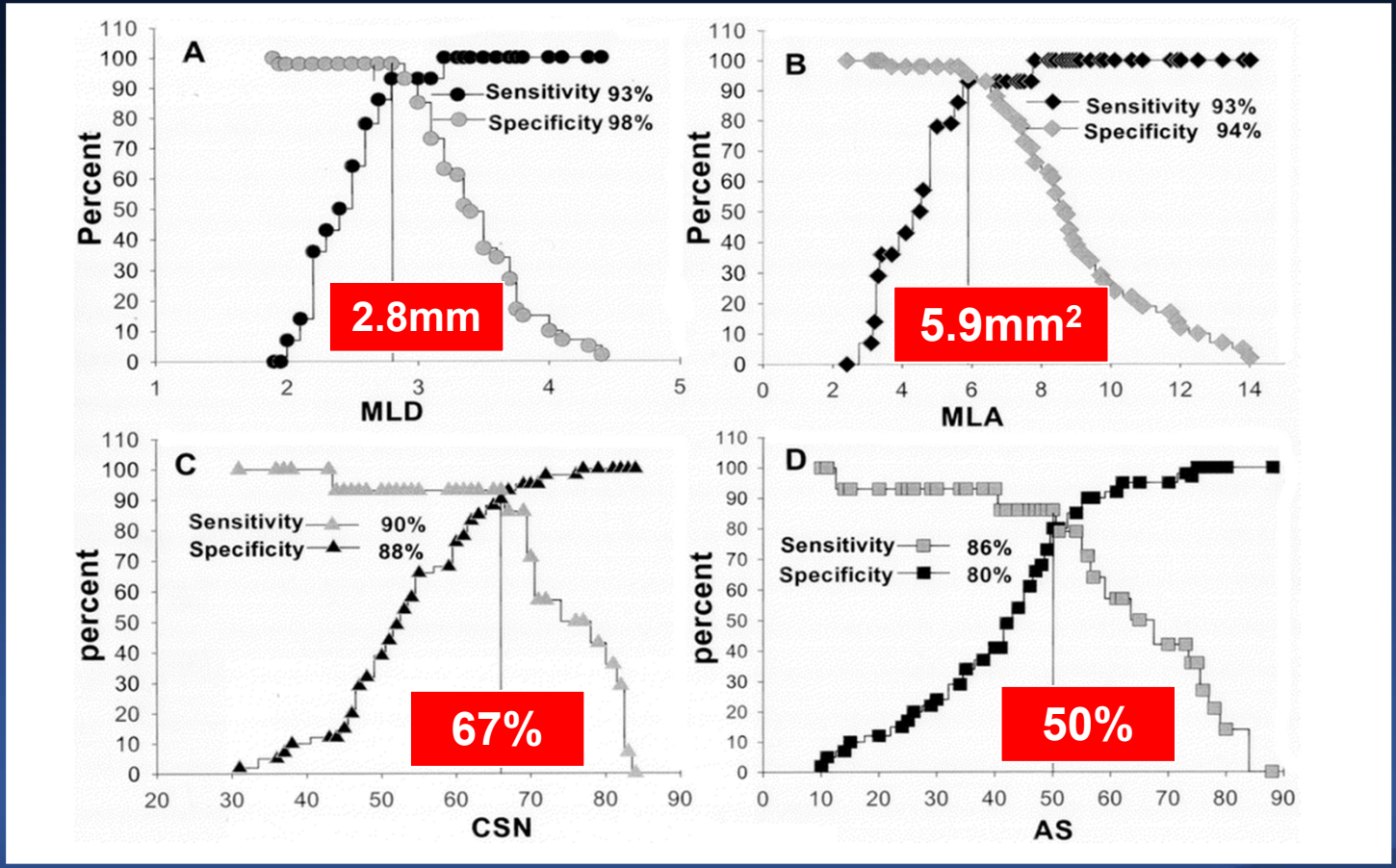
32%

Treat or not treat decision making should be done by FFR not by IVUS MLA.

Left Main Disease

In Left Main Disease

IVUS MLA < 6.0 mm^2 is matched with FFR <0.75



Jasti V et al. Circulation 2004;110:2831-6

New Comparison

AMC prospective cohort registry
(n=47 lesions), 2011

FFR vs.
IVUS MLA

Preliminary Data, 2011

Univariable Analysis to Predict FFR <0.8

Variables	C-OR	95%CI	p-value
MLA within LM	0.312	0.164-0.593	<0.001
Plaque burden	1.095	1.031-1.164	0.003
Lesion length	1.192	1.038-1.368	0.013
Rupture	3.273	0.953-11.243	0.060
Angiographic DS	1.049	0.993 – 1.108	0.088
Lesion location	2.081	1.070 – 4.046	0.031
Male	0.511	0.127-2.057	0.345
Age	0.965	0.917-1.016	0.172
Diabetes melitus	1.062	0.304-3.710	0.924
Hypertension	1.3	0.412-4.101	0.654
Smoker	2.701	0.816-0.8945	0.104
Hyperlipidemia	1.167	0.324-4.200	0.814
Stable presentation	0.476	0.078-2.894	0.42

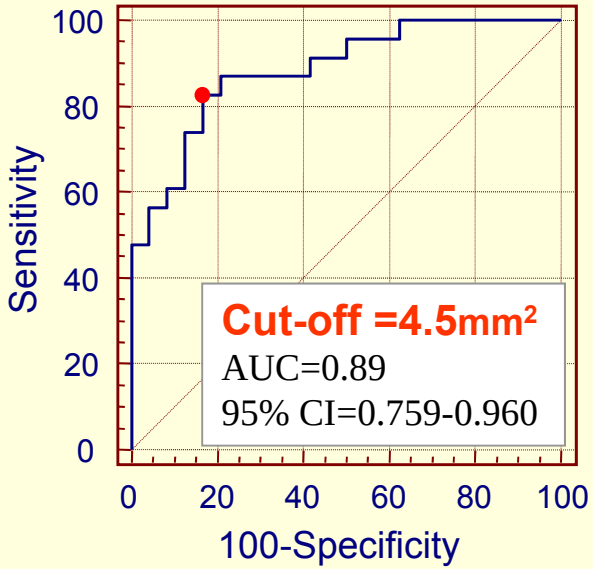
Multivariable Analysis to Predict FFR

Independent predictors for FFR as continuous variable

MLA (β=0.58, 95% CI=0.02 - 0.04, p<0.001)

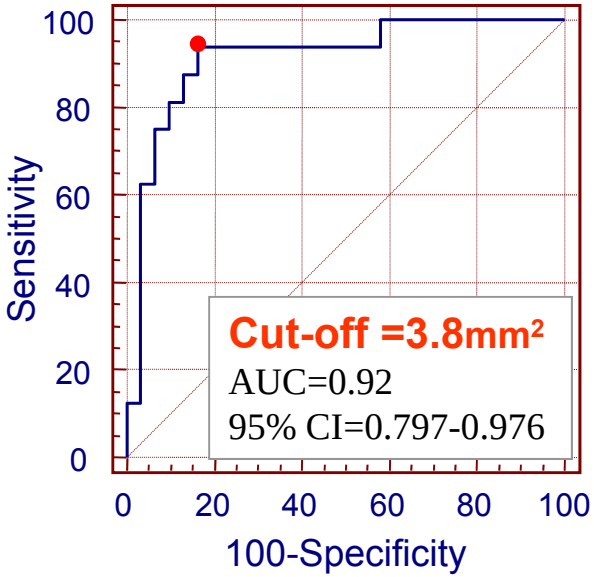
Plaque rupture (β=-0.24, 95% CI= -0.09-0.01, p=0.036)

A. MLA predicting FFR<0.80



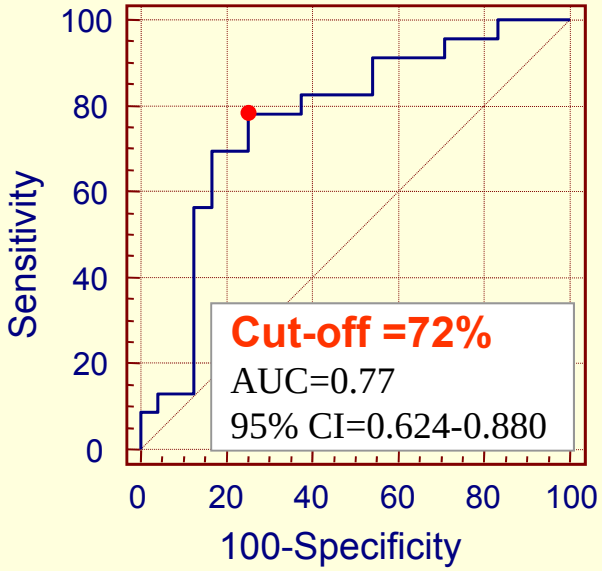
Sensitivity 83%
Specificity 83%
PPV 83%
NPV 83%
Accuracy 83%

B. MLA predicting FFR<0.75



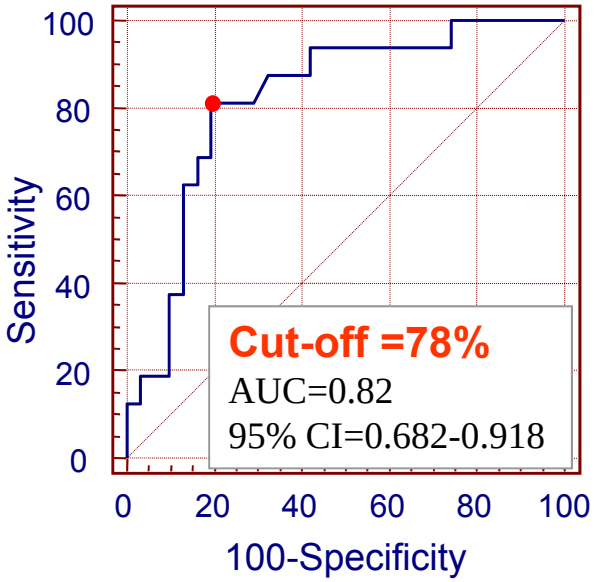
Sensitivity 94%
Specificity 84%
PPV 75%
NPV 96%
Accuracy 87%

C. PB predicting FFR<0.80



Sensitivity 78%
Specificity 75%
PPV 75%
NPV 78%
Accuracy 77%

D. PB predicting FFR<0.75



Sensitivity 81%
Specificity 81%
PPV 68%
NPV 89%
Accuracy 81%

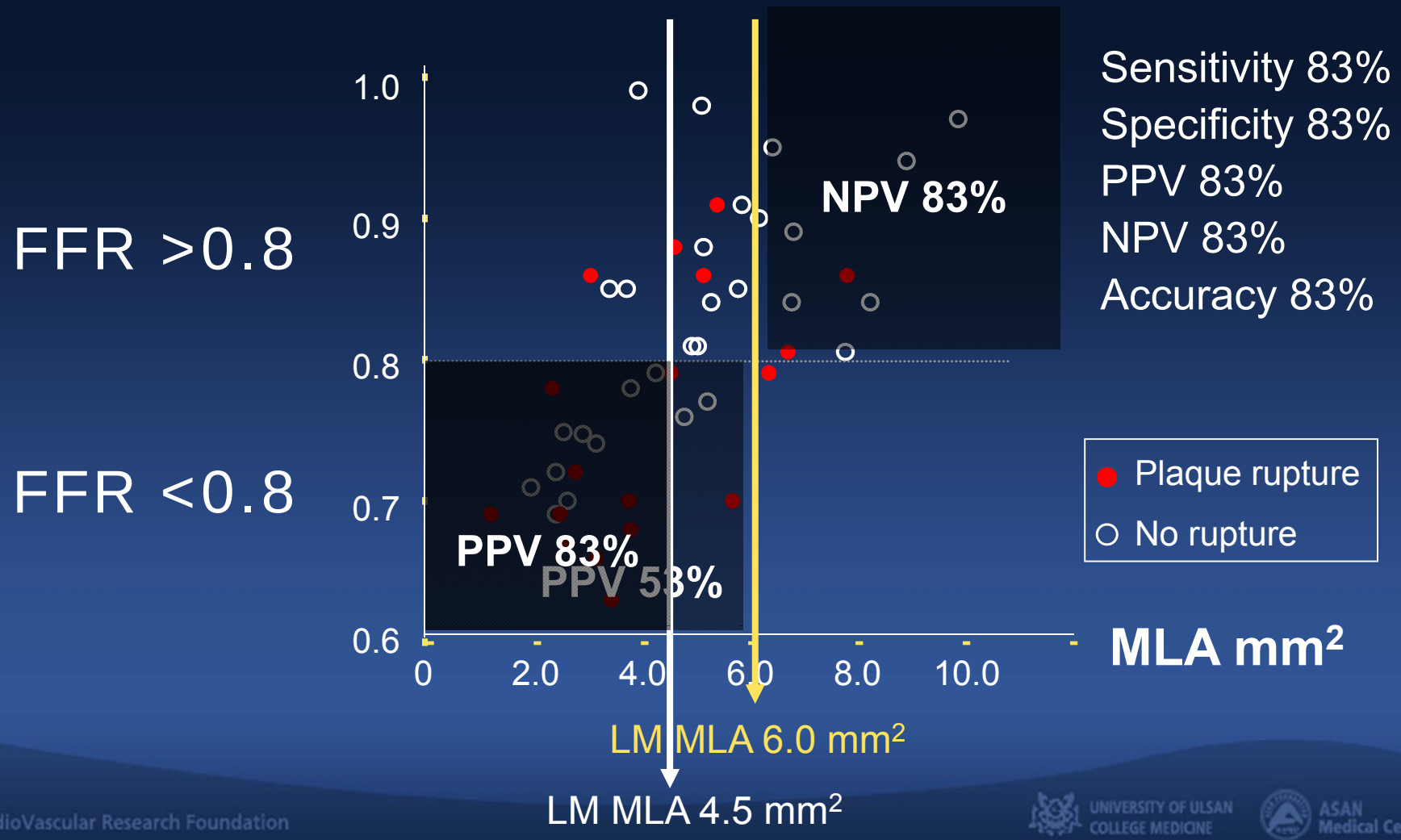
New IVUS MLA

Matched with FFR <0.80 in LM Disease

4.5 mm^2

AMC data, Preliminary

The IVUS MLA (4.5mm^2) can predict FFR <0.8 in left main disease.



FFR vs IVUS
in LM disease

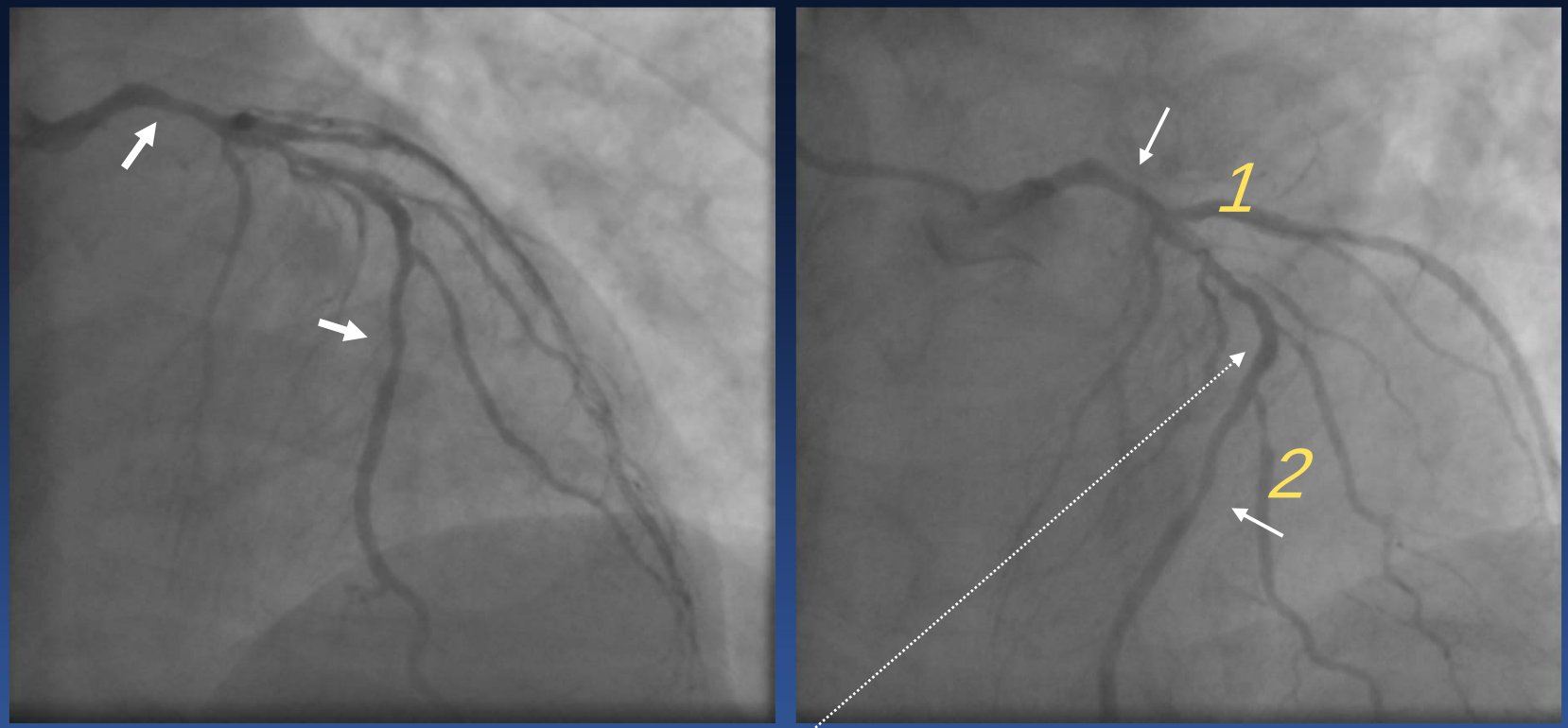
- **FFR is the only matched index with objective ischemia even in the LM disease.**
- **Unlikely in epicardial artery, new IVUS MLA of 4.5 mm^2 can predict FFR <0.8 (PPV : 83%).**

Tandem Lesions

Tandem lesion

Defined by
lesions requiring > 2 DES, which
can be divided by
normal looking area.

Tandem lesion

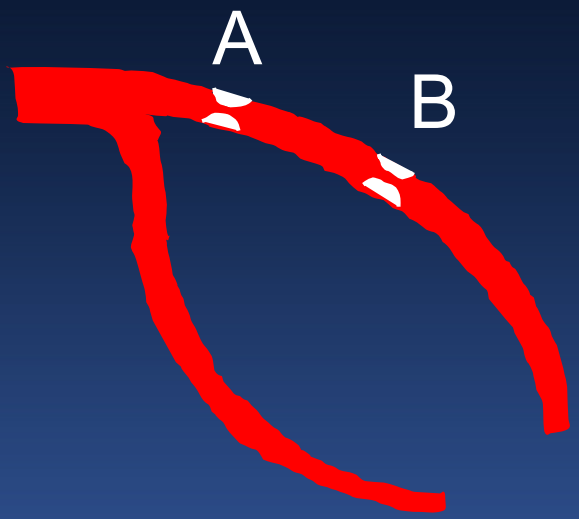


normal looking area

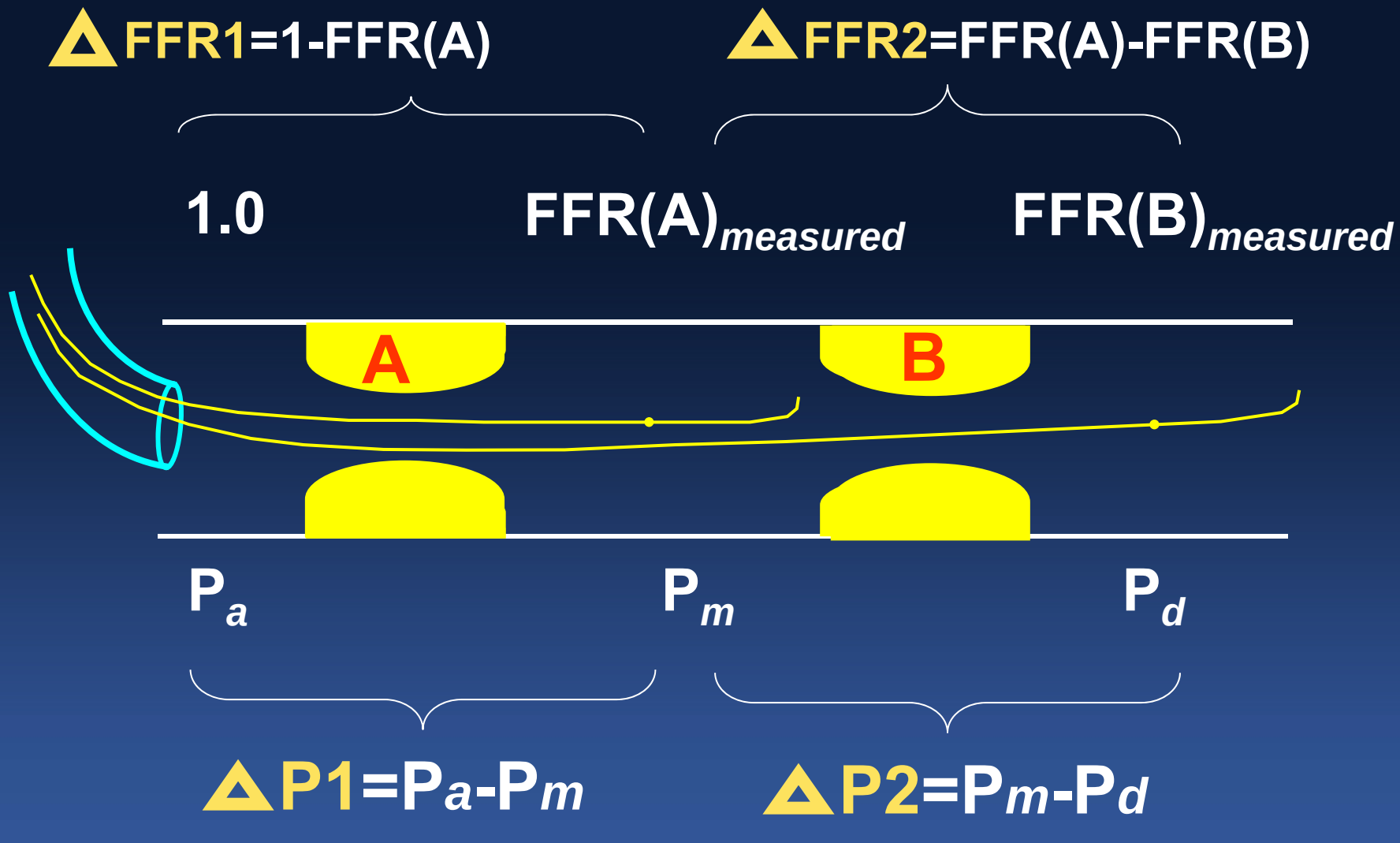
Tandem lesion

FFR guided
Spot Stenting

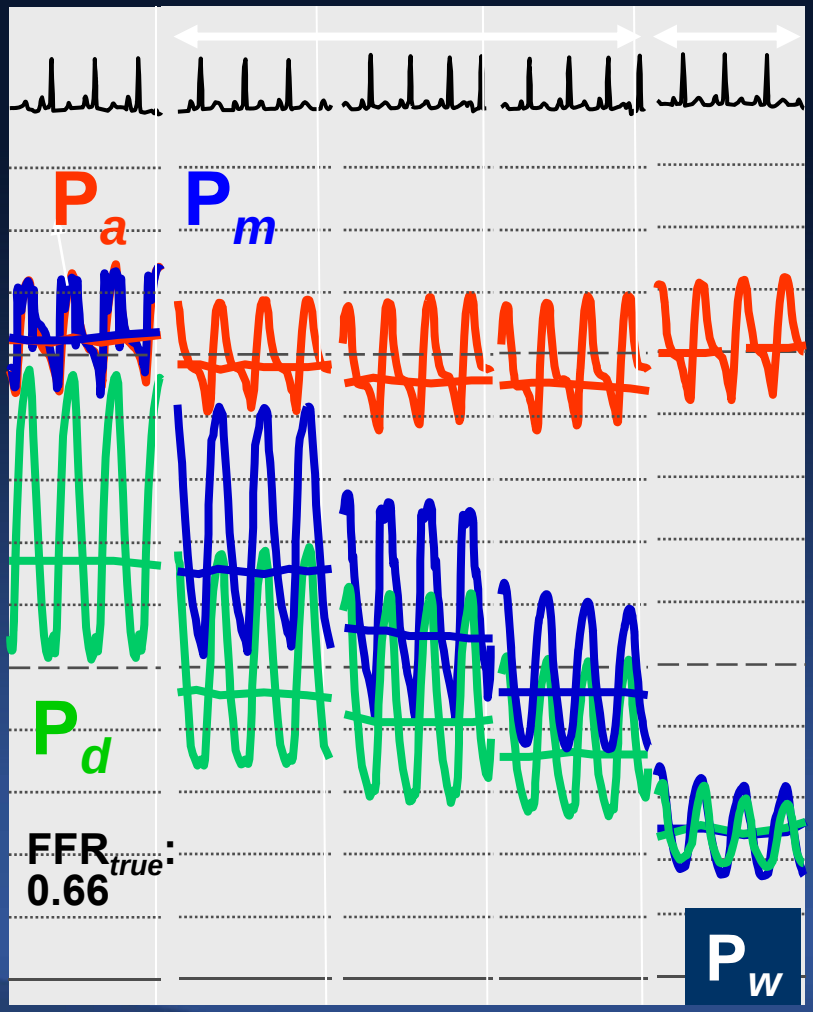
FFR guided Spot Stenting

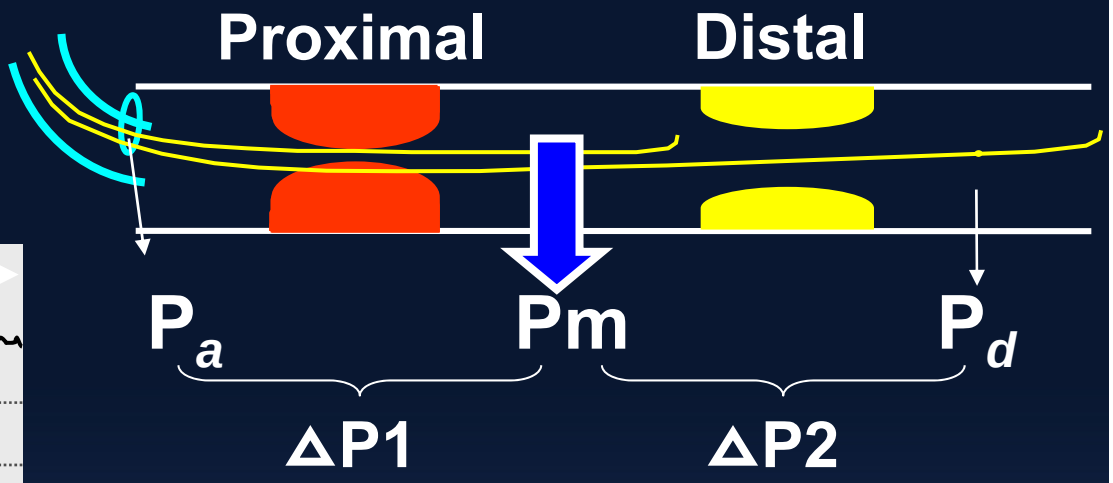


How can we select the first target lesion ?


ΔFFR1=1-FFR(A)
ΔFFR2=FFR(A)-FFR(B)
1.0
FFR(A)measured
FFR(B)measured
A
B
Pa
Pm
Pd
ΔP1=Pa-Pm
ΔP2=Pm-Pd

Tighter Proximal





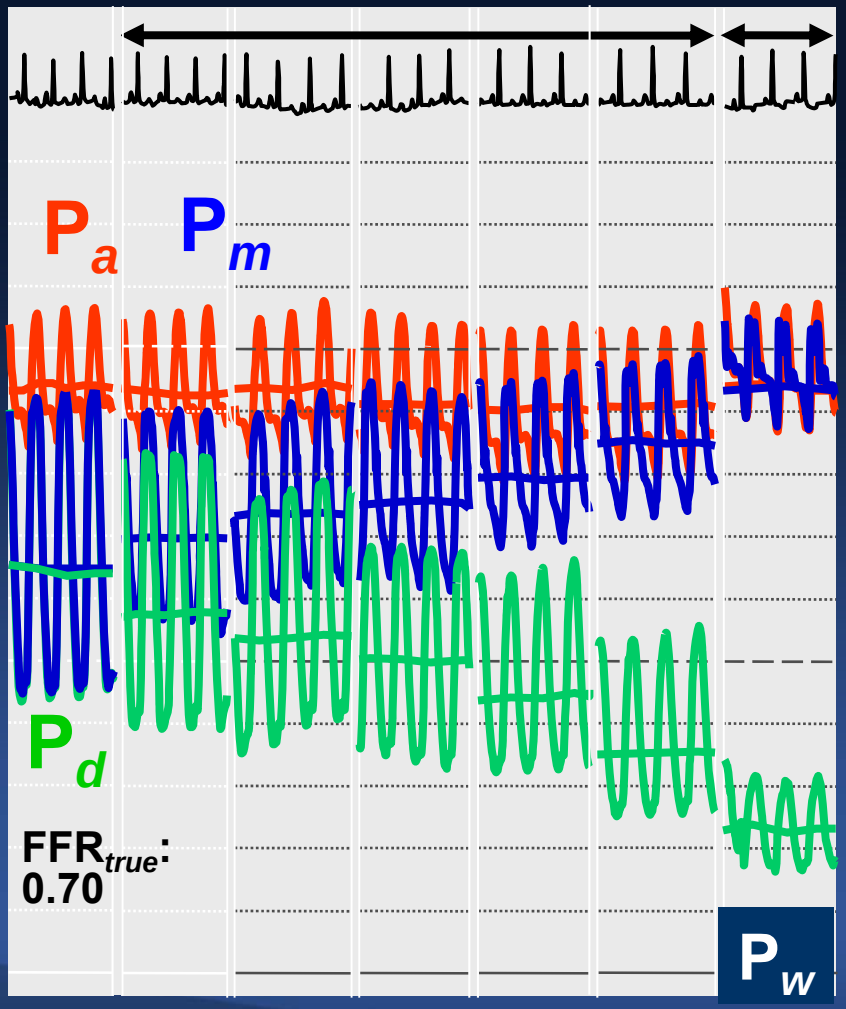
ΔP1 increased

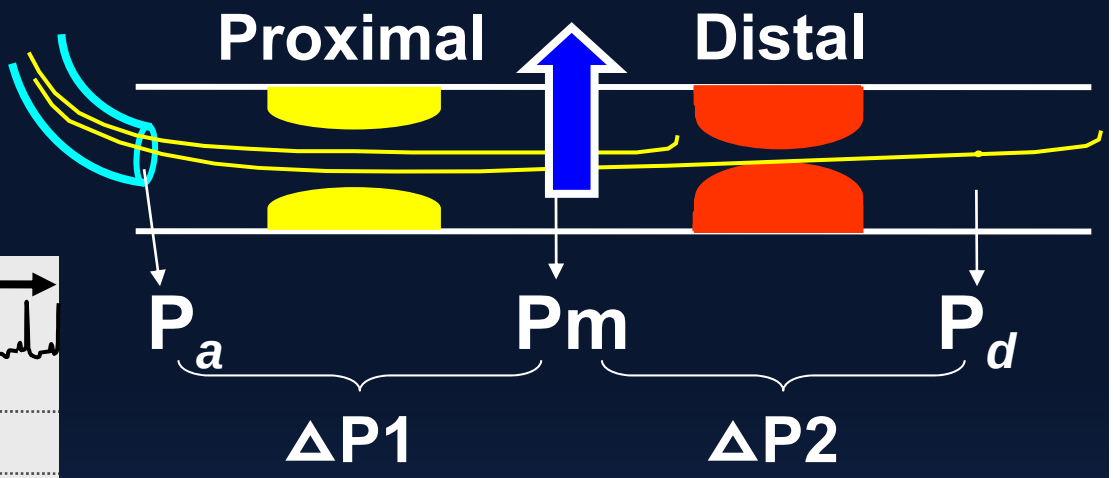
decreased P_m

decreased P_d

Courtesy of Bernard De Bruyne, MD, PhD, *Circulation* 2000;101;1840-1847

Tighter Distal





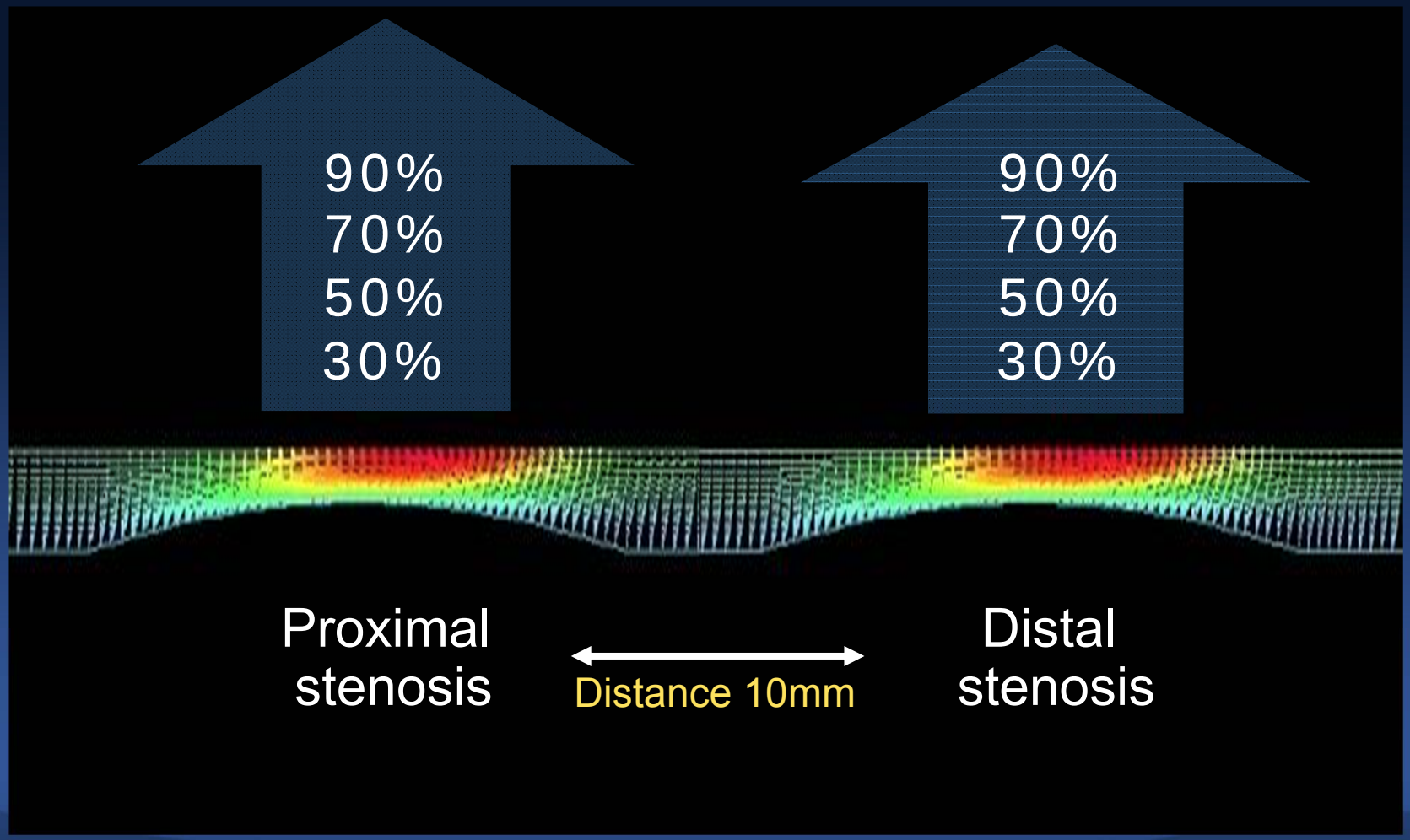
increased P_m

ΔP2 increased

decreased P_d

Courtesy of Bernard De Bruyne, MD, PhD,

Mathematically
Computed Simulation for Tandem Stenosis

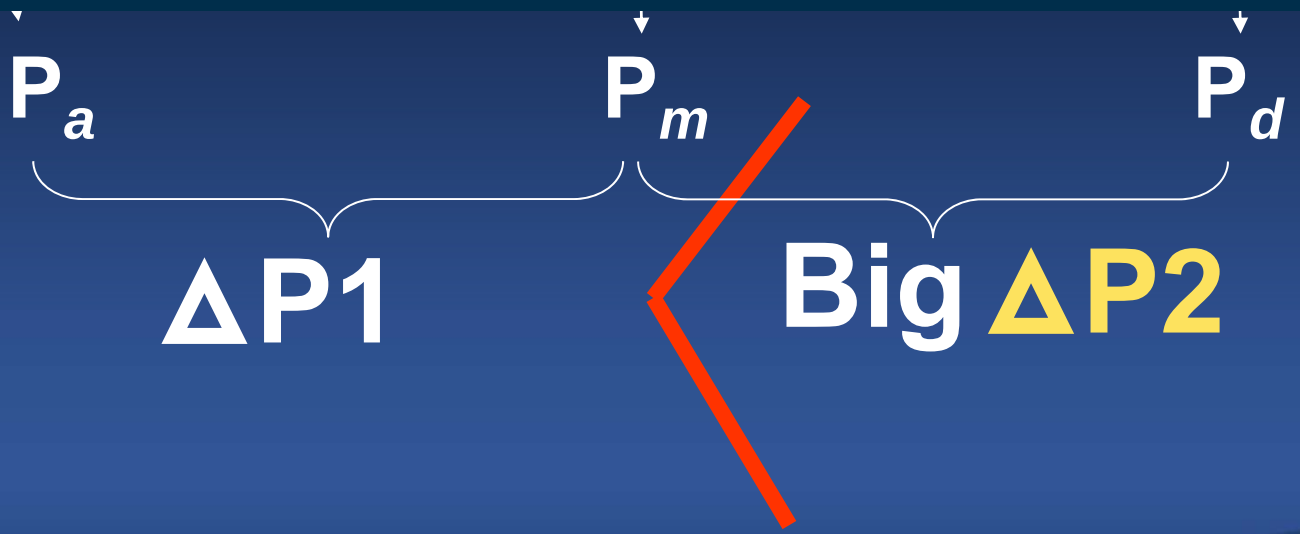


Results of 32 Cases of Simulation

Diameter Stenosis (%)		Pressure (mmHg)			ΔPressure		FFR		ΔFFR	
Proximal Stenosis (A)	Distal Stenosis (B)	Pa	Pm	Pd	ΔP1	ΔP2	FFR(A)	FFR(B)	ΔFFR(1)	ΔFFR(2)
30	30	93.2	80.8	69.9	12.4	10.9	0.87	0.75	0.13	0.12
	50	95.8	89.7	71.9	6.1	17.8	0.94	0.75	0.06	0.19
	70	97.1	94.7	64.1	2.4	30.6	0.98	0.66	0.02	0.32
	90	98.5	98.5	62.1	0	36.4	1.00	0.63	0.00	0.37
50	30	95.8	77.4	71.9	18.4	5.5	0.81	0.75	0.19	0.06
	50	96.3	82.4	69.4	13.9	13	0.86	0.72	0.14	0.13
	70	97.6	92.9	64.5	4.7	28.4	0.95	0.66	0.05	0.29
	90	98.5	98.4	62.1	0.1	36.3	1.00	0.63	0.00	0.37
70	30	97.1	66.4	64.1	30.7	2.3	0.68	0.66	0.32	0.02
	50	97.6	69.2	64.5	28.4	4.7	0.71	0.66	0.29	0.05
	70	97.7	80.6	63.5	17.1	17.1	0.82	0.65	0.18	0.18
	90	98.5	97.7	62.1	0.8	35.6	0.99	0.63	0.01	0.36
90	30	98.5	63.1	62.1	36.7	1.0	0.63	0.63	0.37	0.00
	50	98.5	63.1	62.1	36.6	1.0	0.63	0.63	0.37	0.00
	70	98.5	62.6	62.1	35.9	0.5	0.64	0.63	0.36	0.01
	90	98.5	80.7	62.1	17.8	18.6	0.82	0.63	0.18	0.19

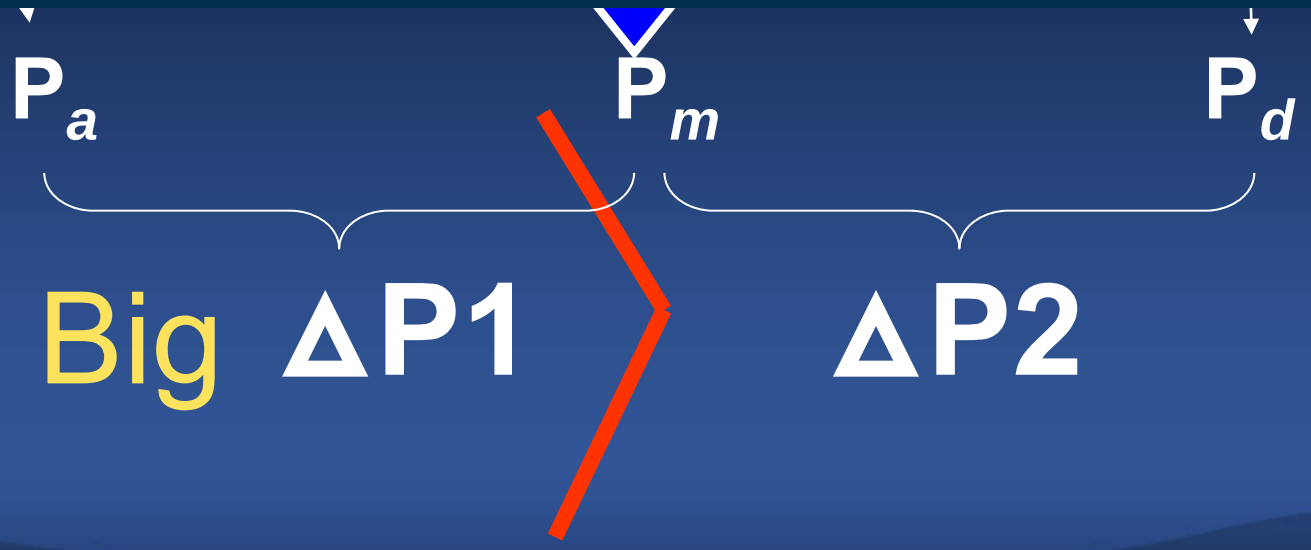
Rule of Big Delta

Treat
Distal lesion First !



Rule of Big Delta

Treat
Proximal lesion First !

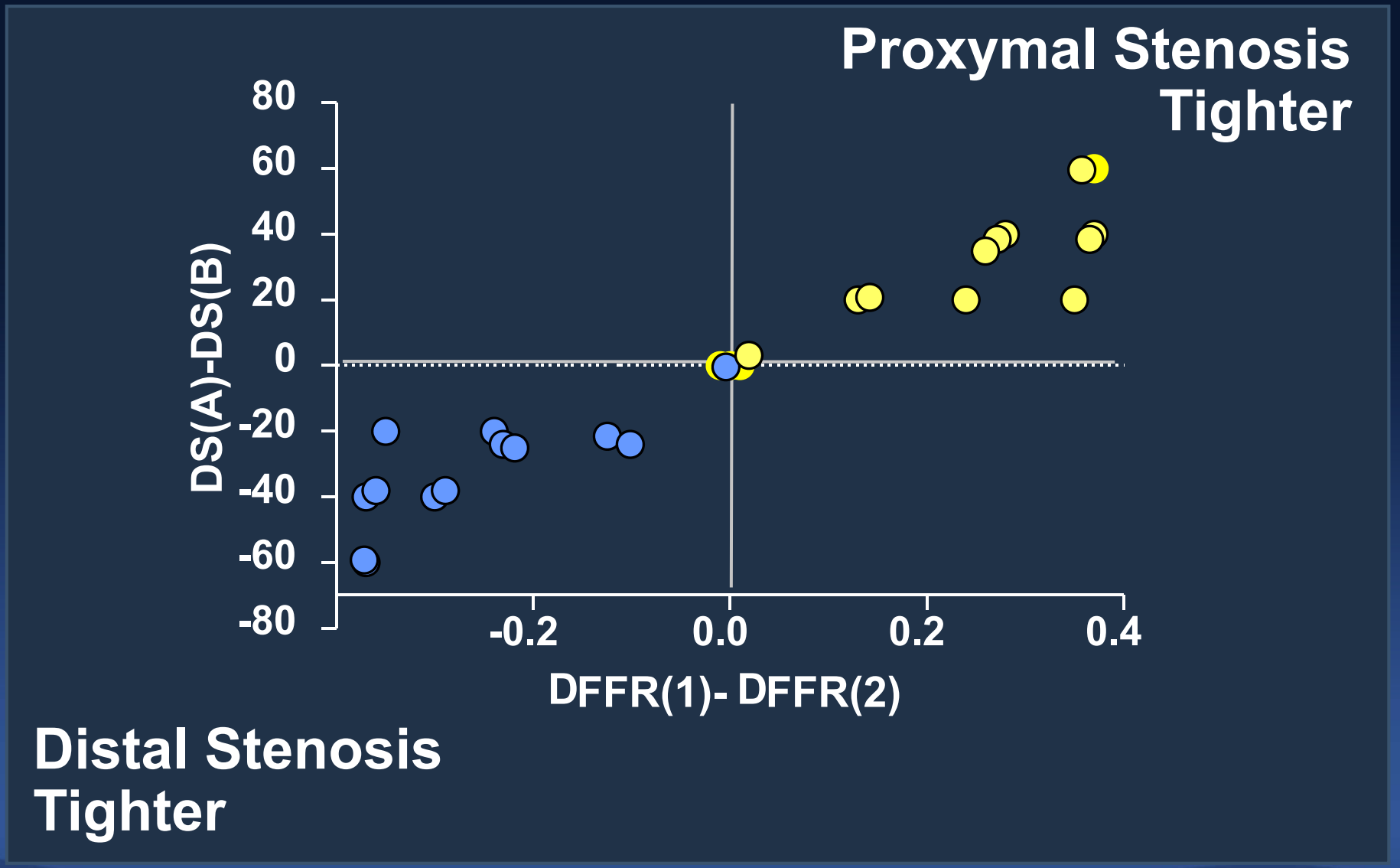


ΔP vs. ΔFFR

$$\Delta P(1) \propto \Delta FFR(1) = \frac{Pa-Pm}{Pa}$$

$$\Delta P(2) \propto \Delta FFR(2) = \frac{Pm-Pd}{Pa}$$

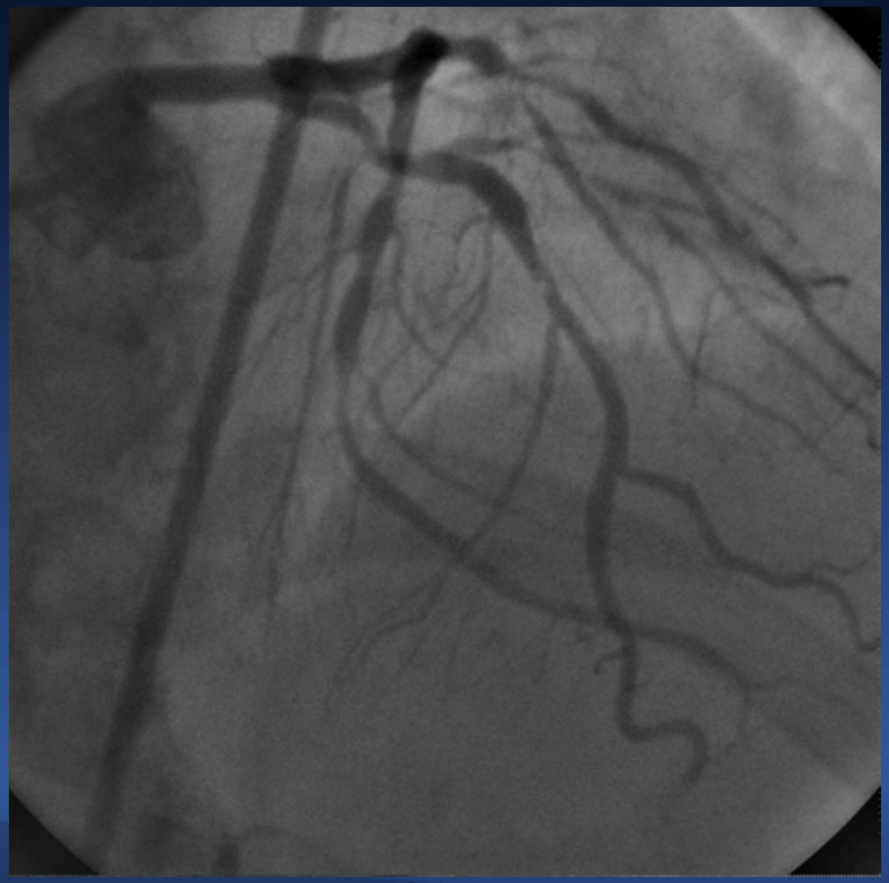
Δ FFR vs. Δ DS

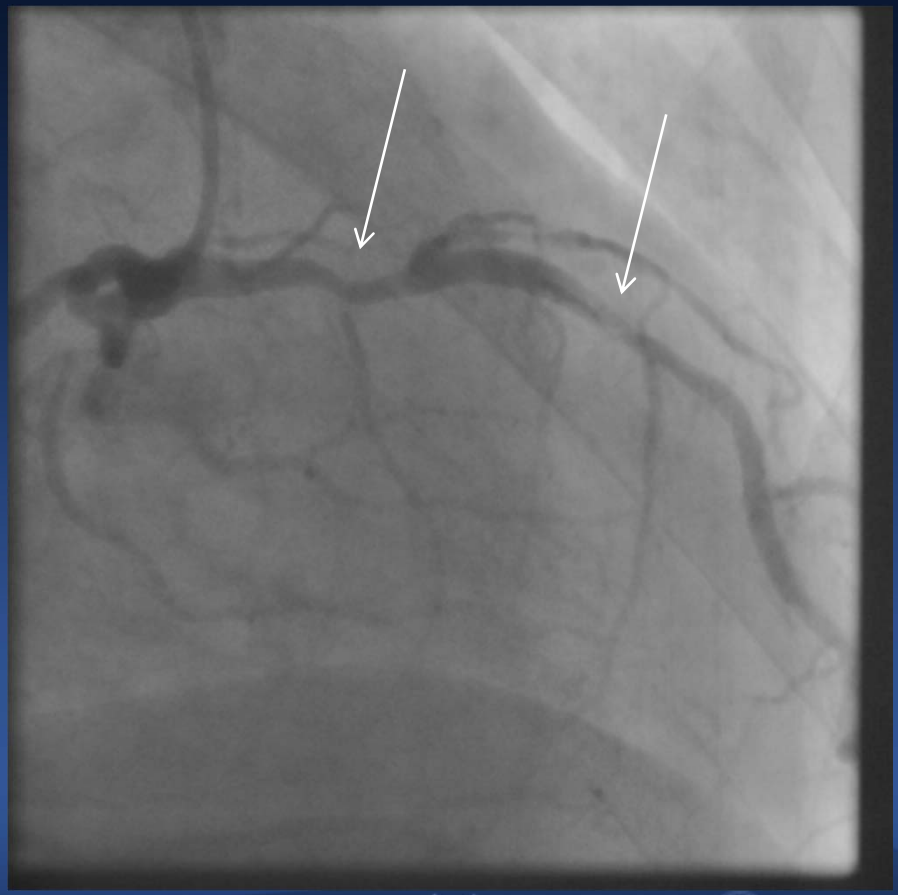


Δ DS means difference of true functional significance

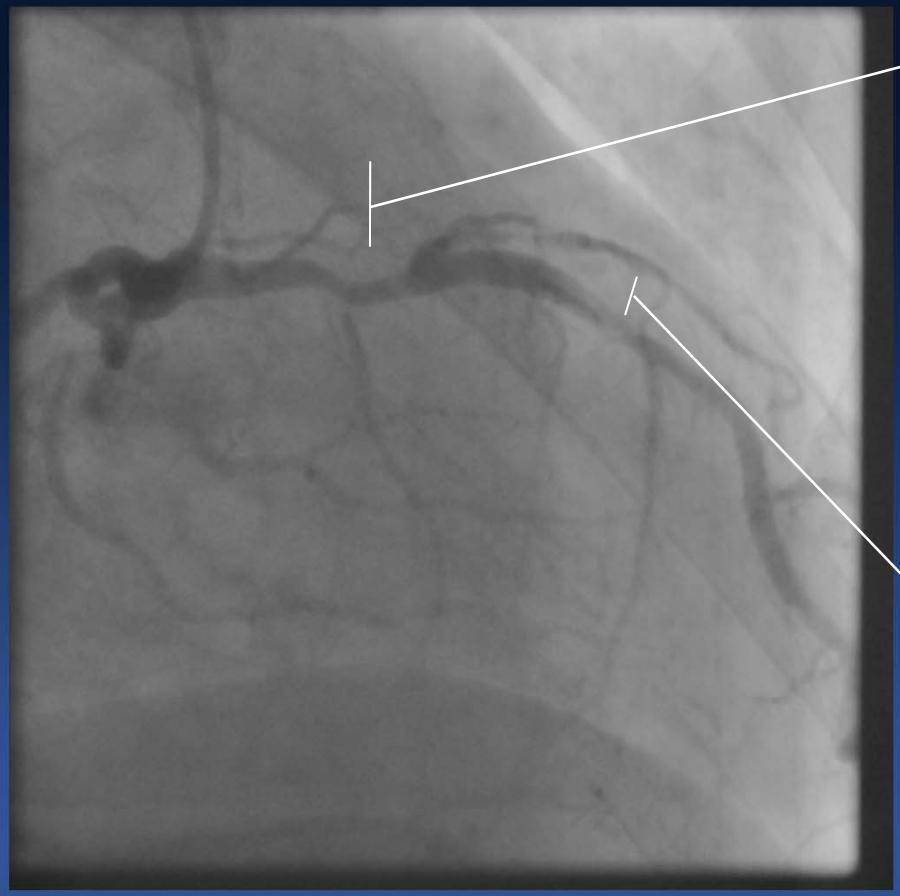
Tandem Lesions

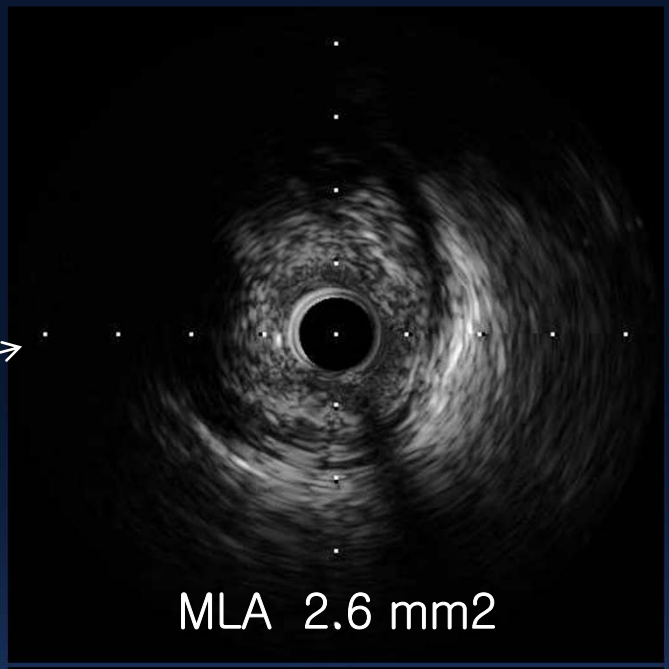
67/F, Effort Chest pain for 2 months
DM, Hypertension, Hyperlipidemia, Smoking

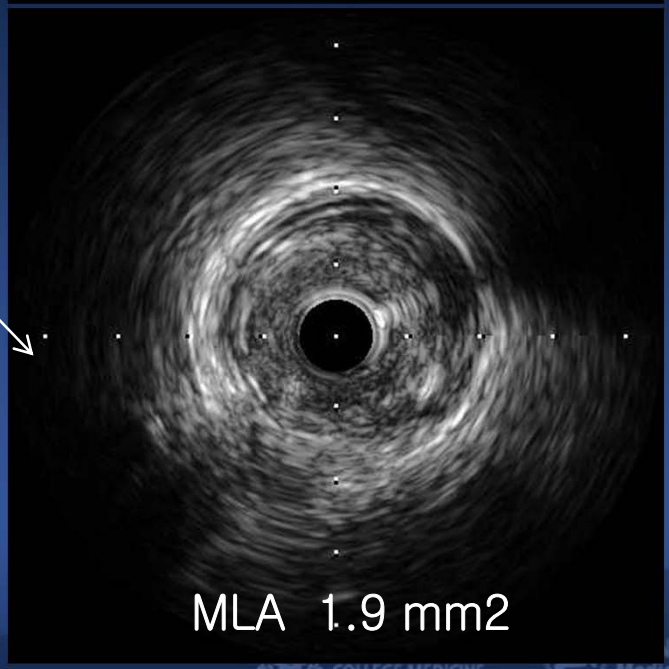




IVUS

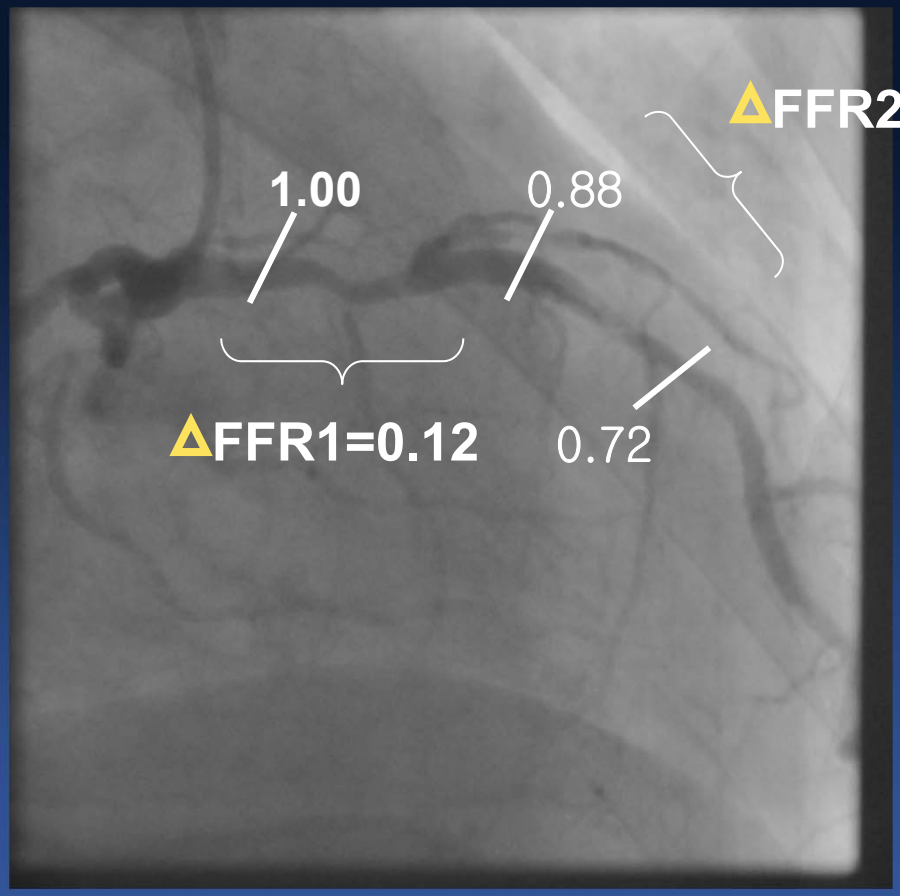






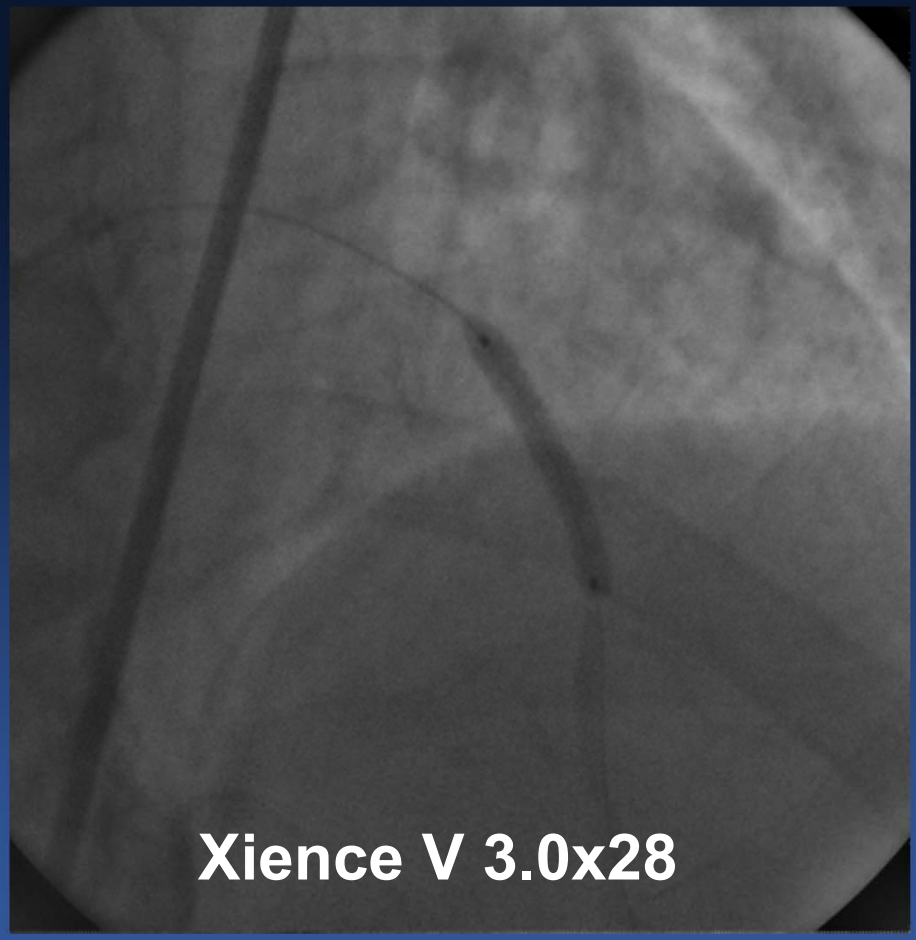
FFR

Intravenous adenosine (140ug/kg/min)

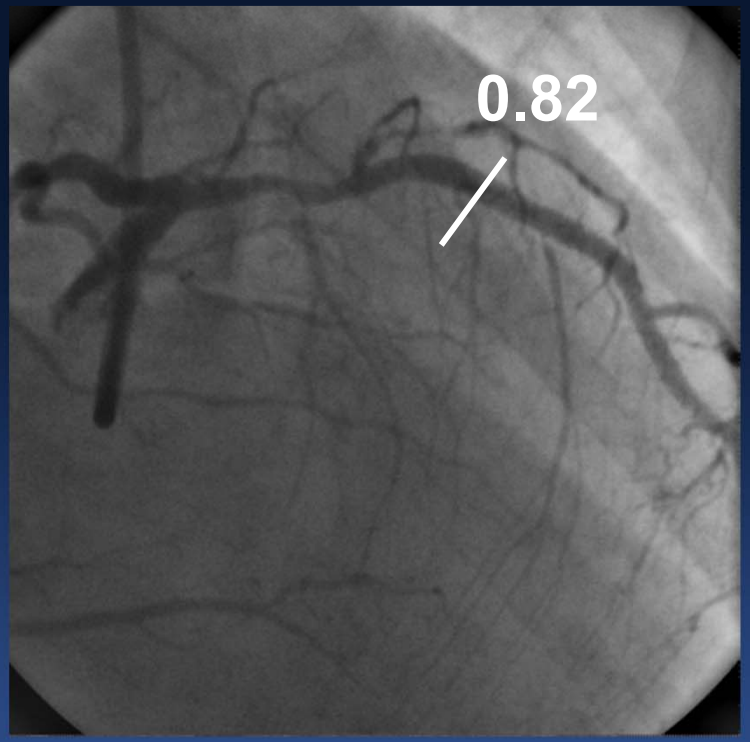


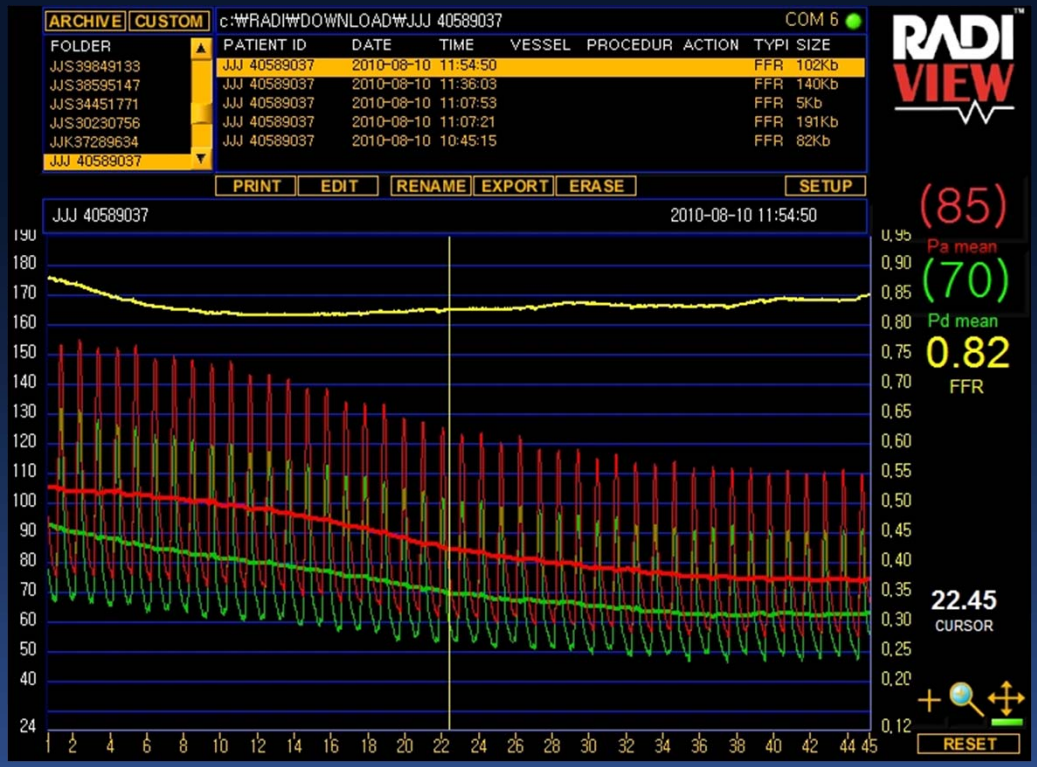
ΔFFR1 < ΔFFR2

Dilate Distal First !



FFR again : 0.82

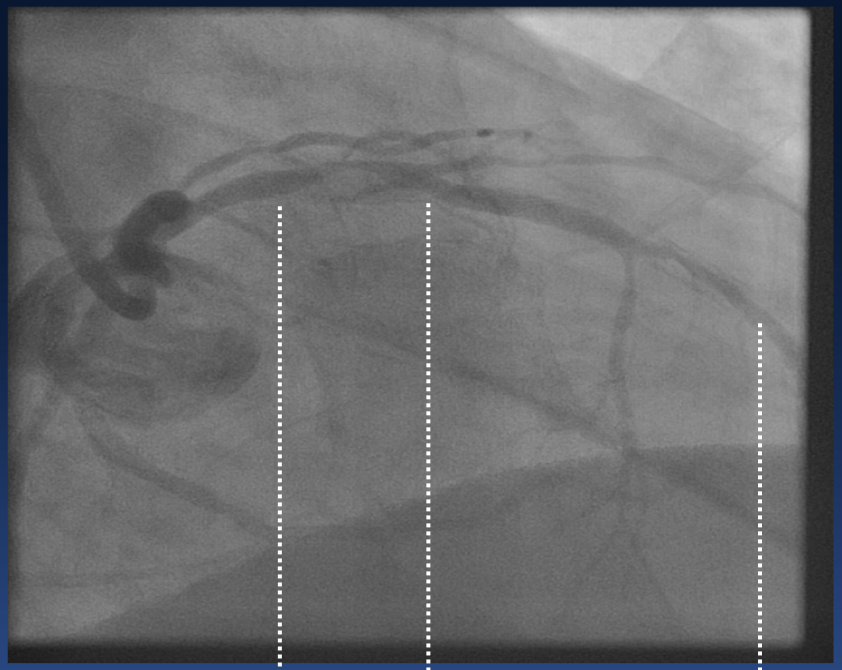


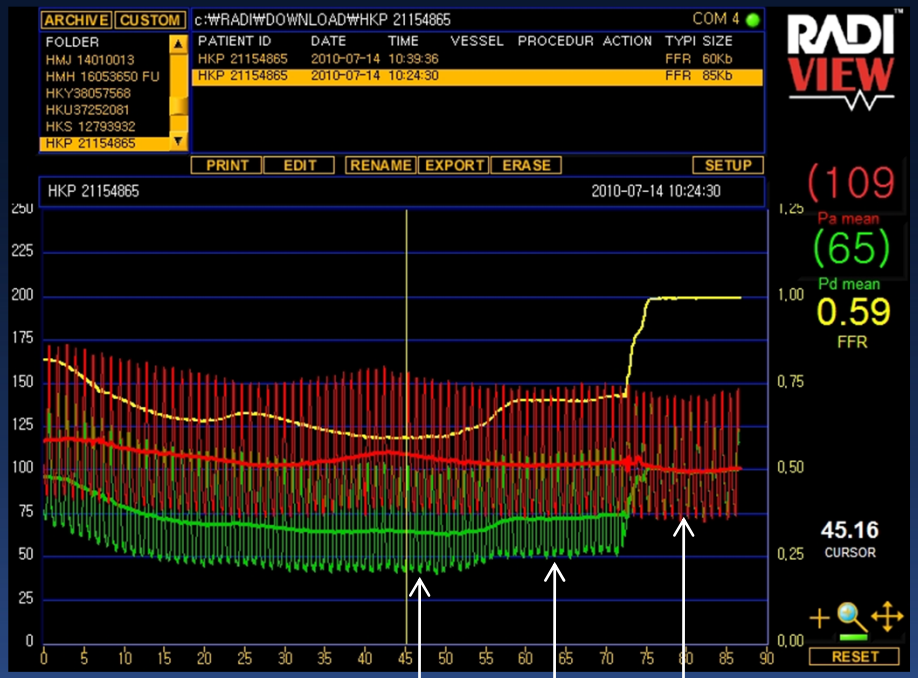


avoid unnecessary stent !

FFR

Continuous Intravenous Infusion 140 μg/kg/min





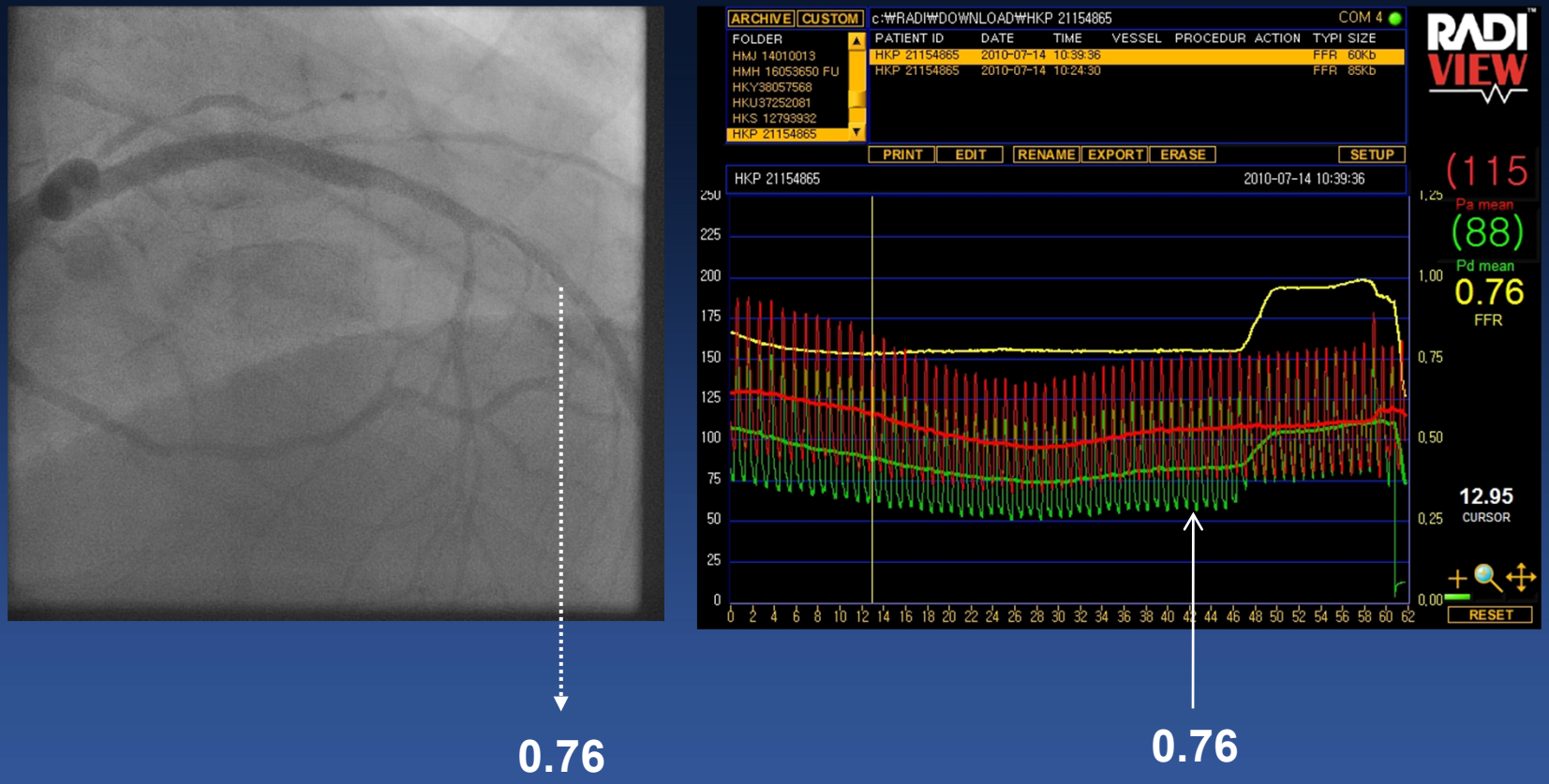
1.0 0.70 0.59

ΔFFR1=0.30 ΔFFR2=0.11

0.59 0.70 1.0

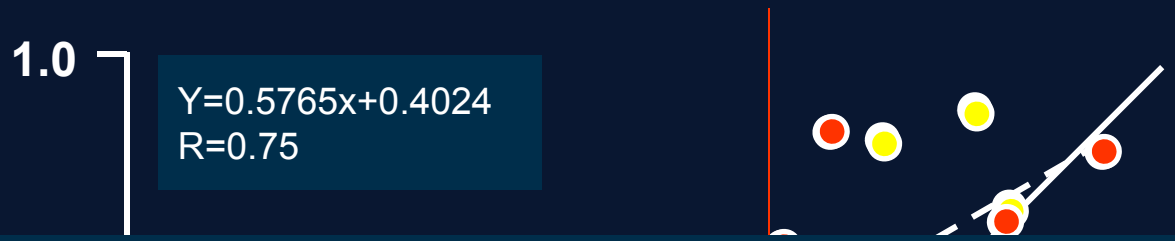
ΔFFR1 > ΔFFR2

FFR again
after proximal stent placement : 0.76

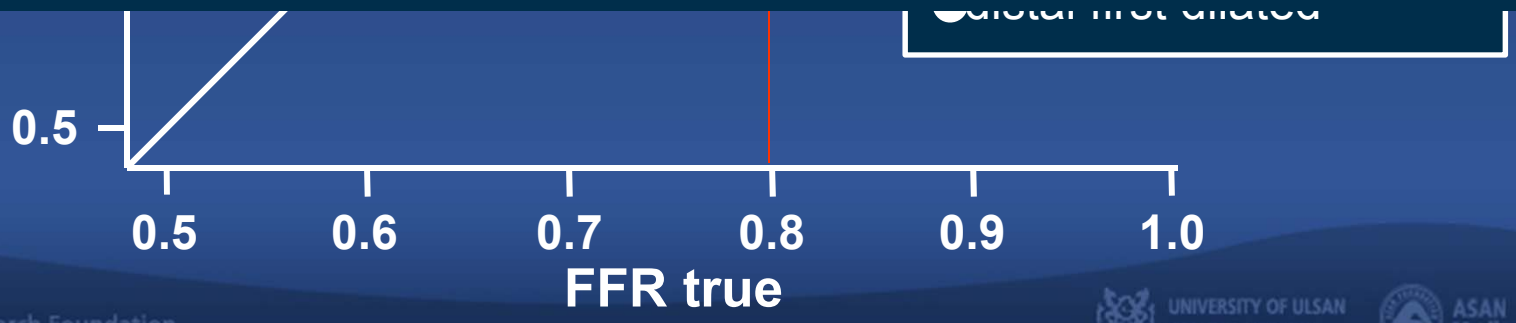


How many Stent can be saved ?

Pijls NHJ,Circulation. 2000;102:2371-2377.)



FFR guided Spot stenting can save at least 4 stent out of 10.



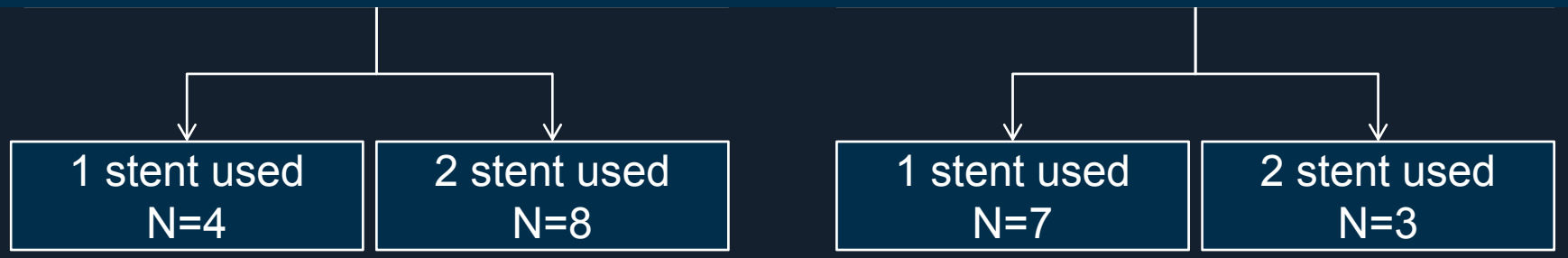
CardioVascular Research Foundation

UNIVERSITY OF ULSAN COLLEGE MEDICINE

ASAN Medical Center

Result of Pilot Trial

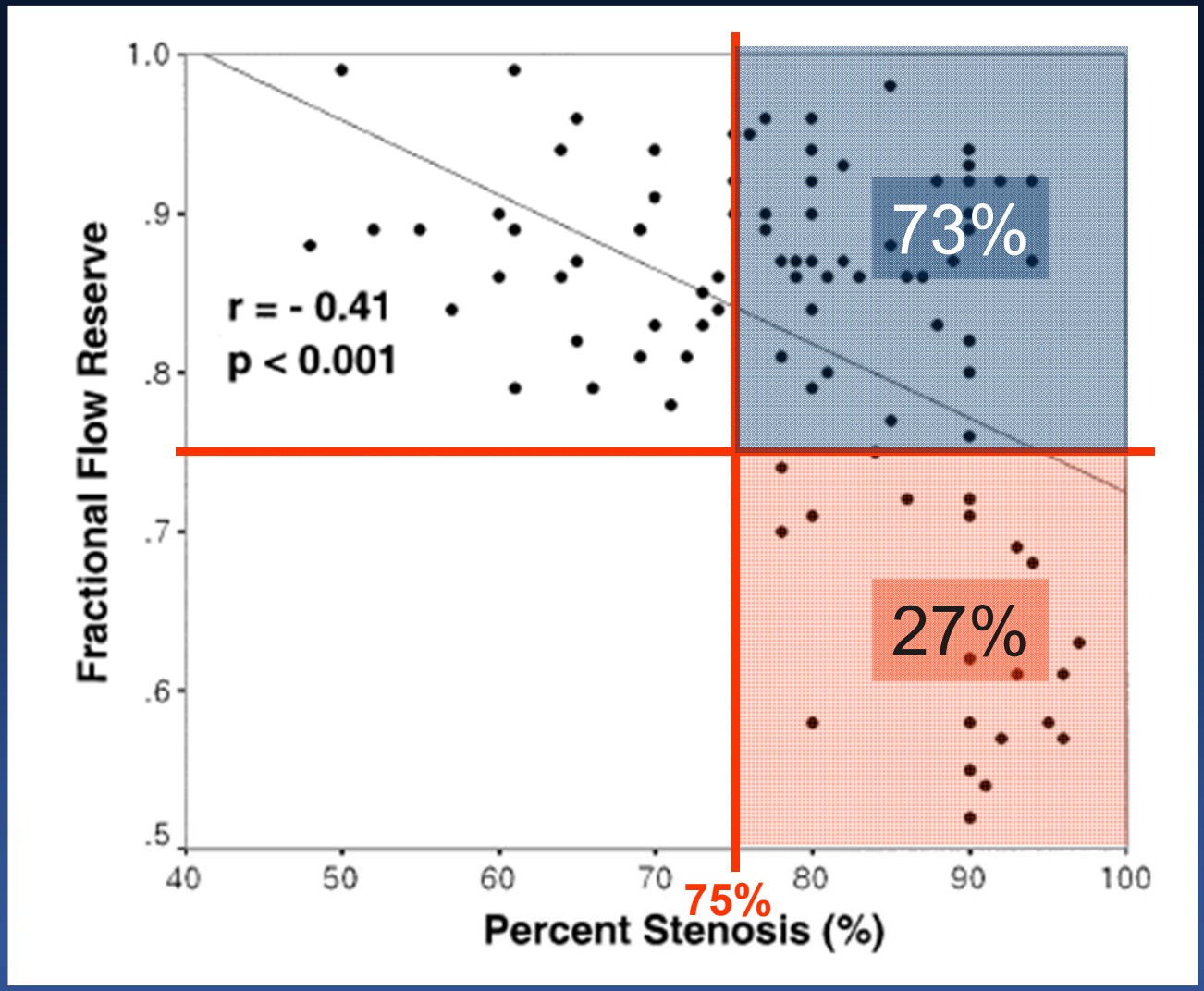
FFR guided Spot stenting can save 5 stents out of 10.



Bifurcation PCI

Side Branch FFR vs IVUS Predictors

FFR of the Jailed side branch

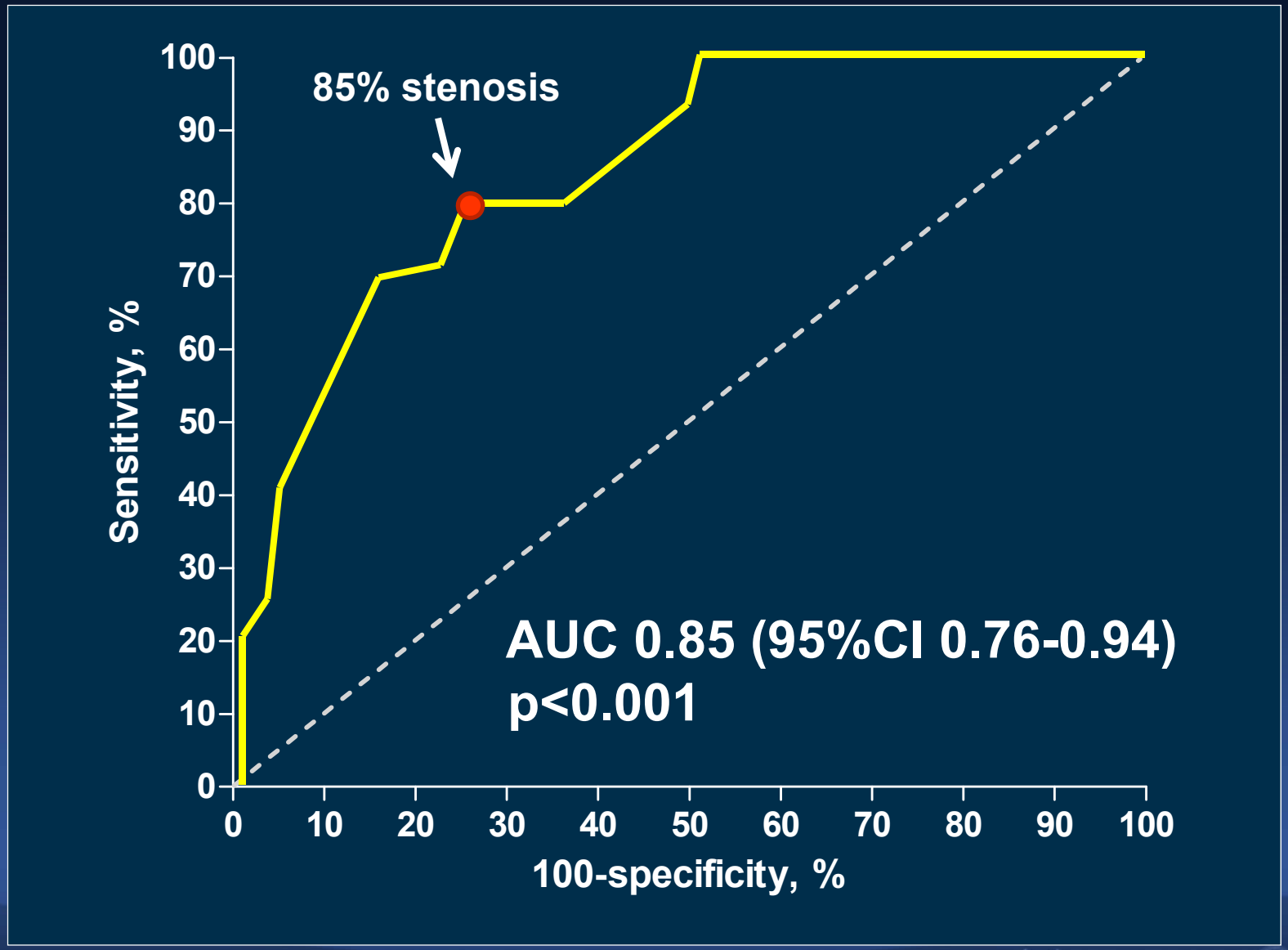


FFR >0.75

FFR <0.75

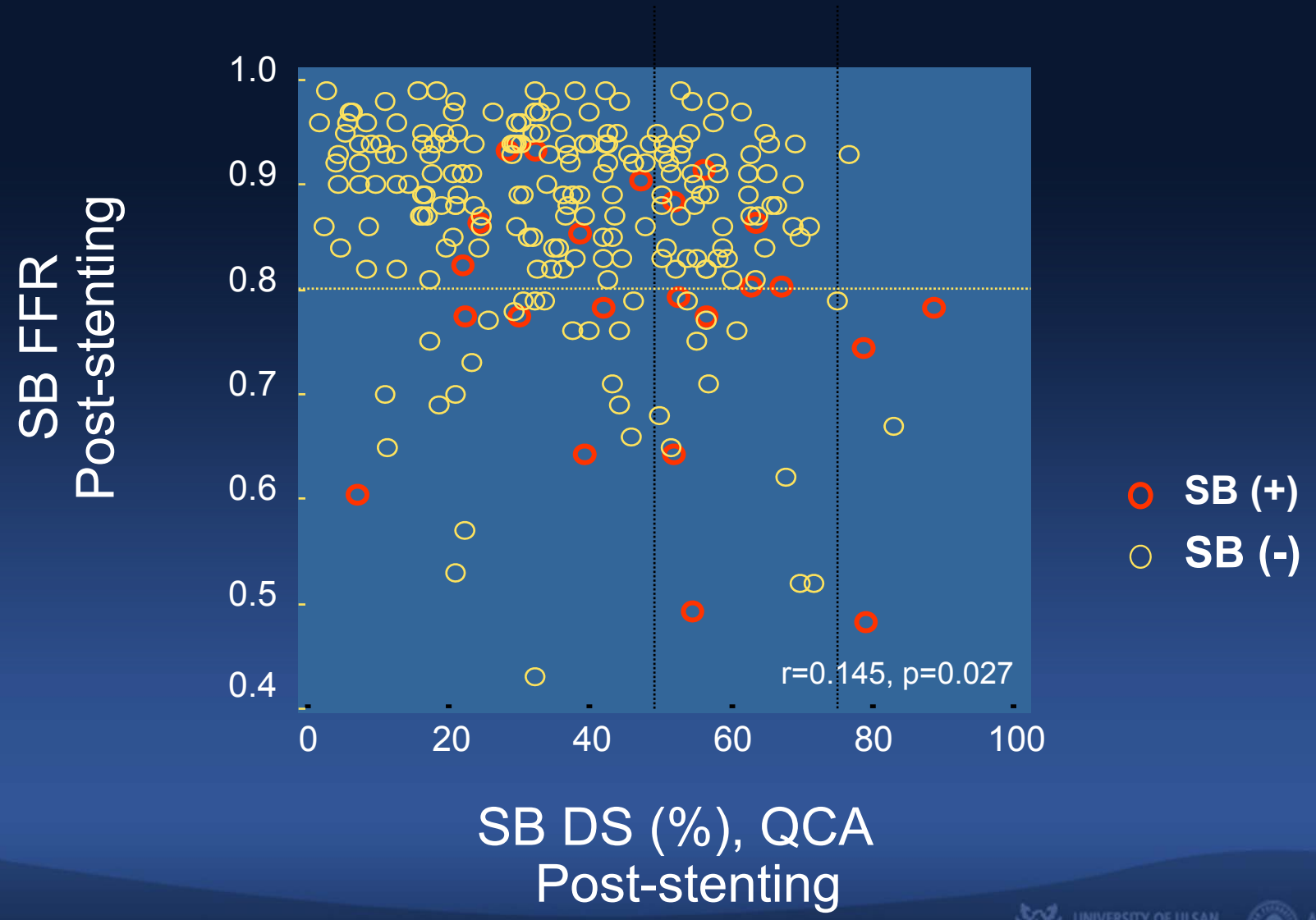
Koo BK, JACC 2005; 46: 633-7

ROC curve of SB DS(%) for FFR≤0.75

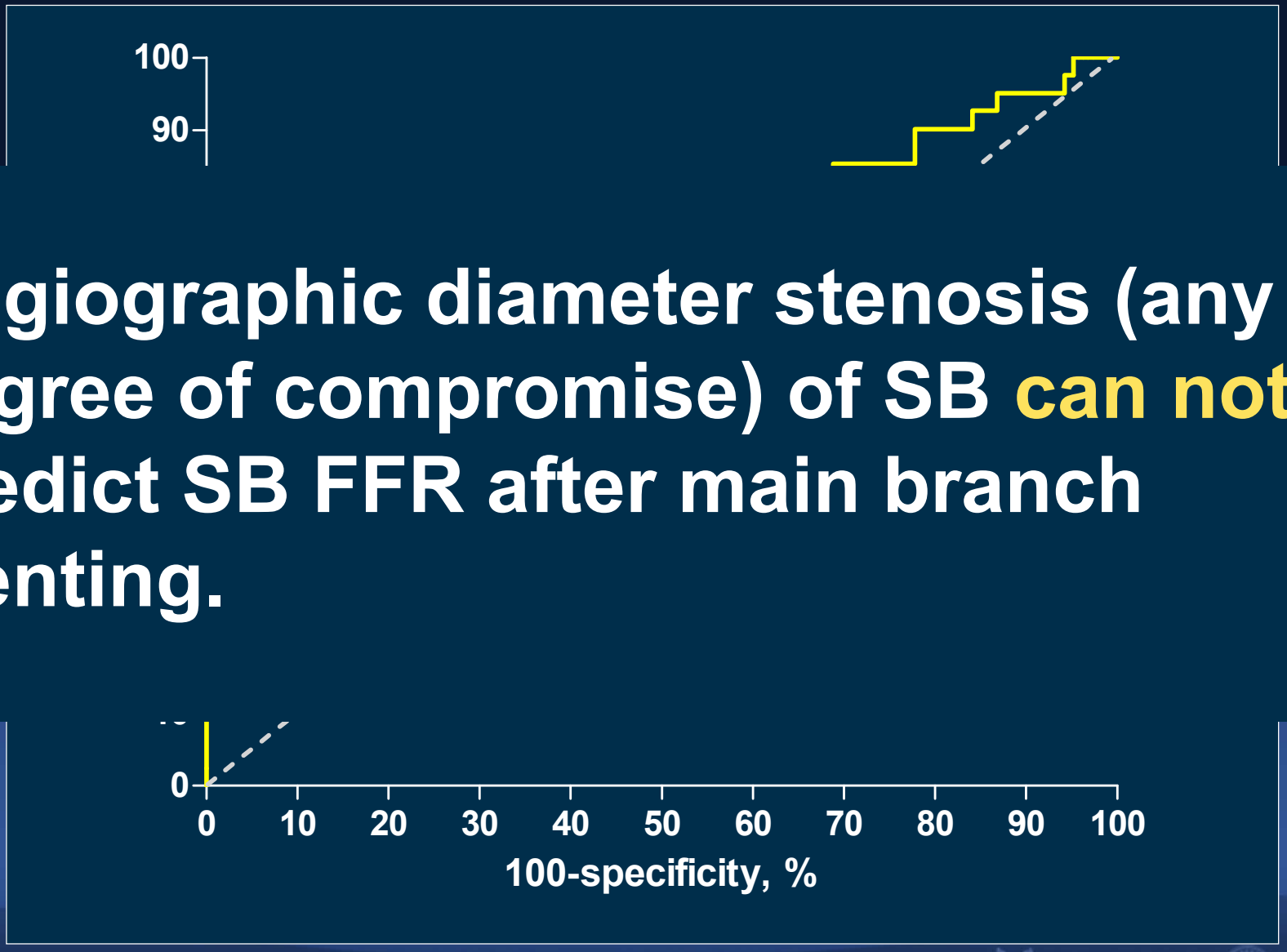


Koo et al JACC 2005;46:633-7

Post-stent SB FFR
232 Bifurcation lesions = 0.86±0.10



ROC curve of SB DS(%) for FFR≤0.80



Angiographic diameter stenosis (any degree of compromise) of SB can not predict SB FFR after main branch stenting.

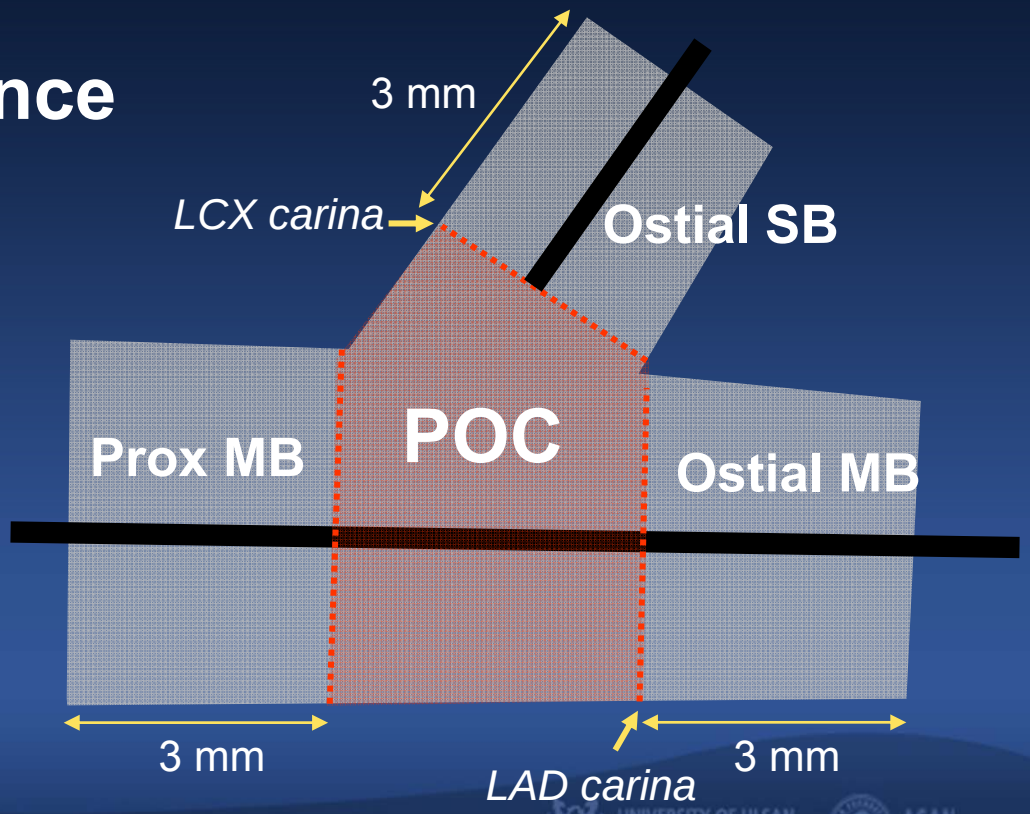
FFR vs. IVUS parameters (n=90)

RVD > 2 mm and Lesion length <10 mm
40% of Medina 1,1,1 included

Kang SJ et al, Am J Cardiol, 2011(in print)

Four Segments of IVUS Measurement

- MB Ostium
- SB Ostium
- Polygon of Confluence
- Proximal MB

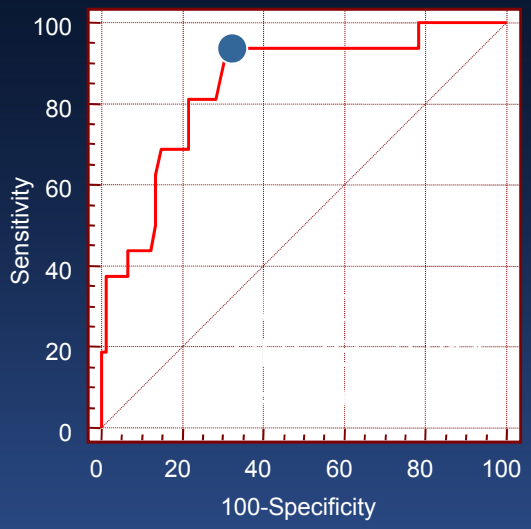


Independent IVUS Predictors
for SB FFR (<0.80) Post-Stenting as a continuous variable

	β	95% CI	p
Maximal Balloon Pressure	-0.265	-0.010 – -0.002	0.003
MLA of SB ostium	0.216	0.001 – 0.035	0.040
Plaque Burden at SB ostium	-0.296	-0.003 – -0.001	0.005
MLA of MB distal	0.250	0.005 – 0.027	0.025

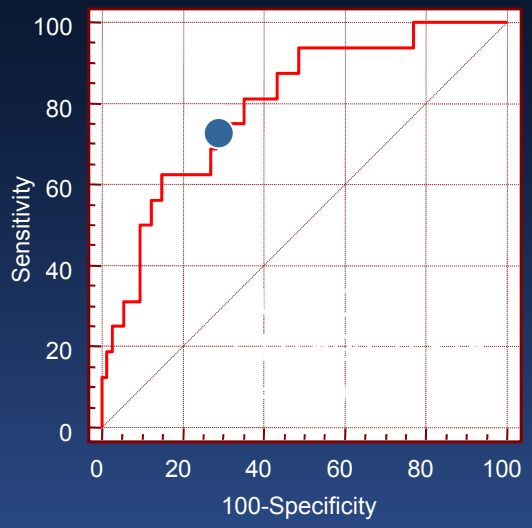
IVUS MLA Cut-Off matched with SB FFR (<0.80)

MLA of SB ostium



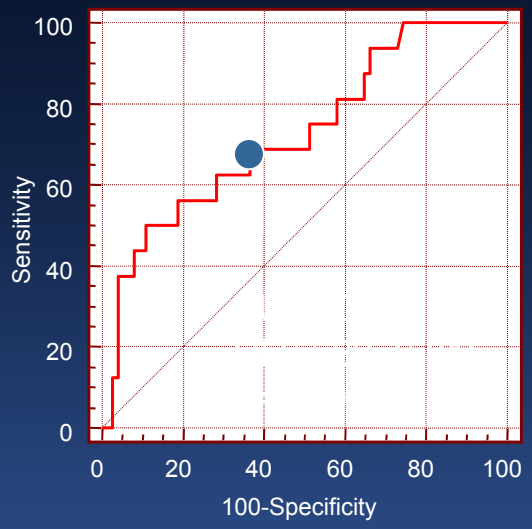
Cut-off value;
2.4mm^2
Sensitivity=94%
Specificity=68%
PPV=40%
NPV=98%

Plaque burden within SB ostium



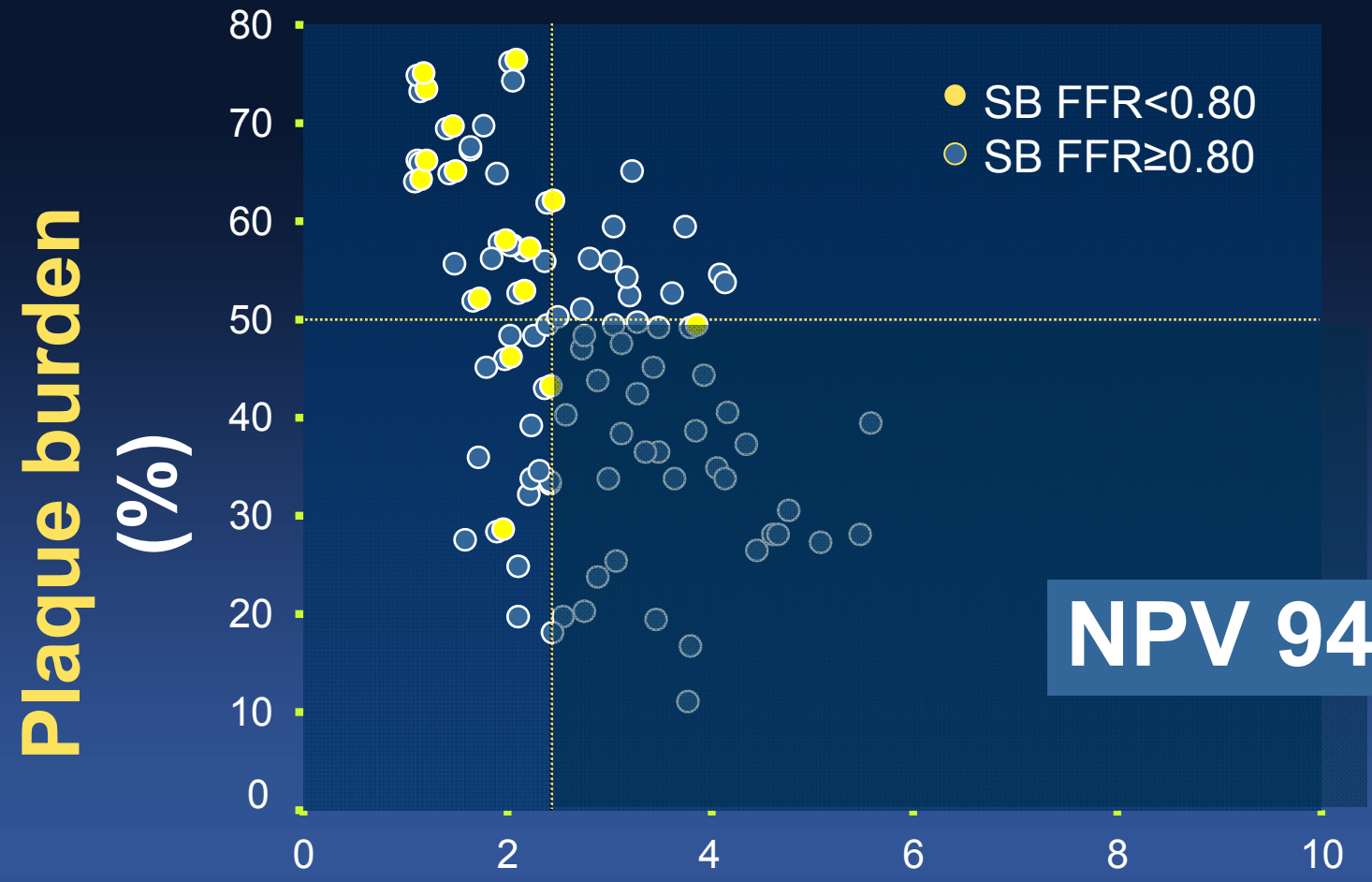
Cut-off value;
51%
Sensitivity=75%
Specificity=71%
PPV=36%
NPV=93%

MLA within POC



Cut-off Value;
3.7mm^2
Sensitivity=70%
Specificity=64
PPV=50%
NPV=89%

Combining IVUS criteria
(MLA >2.4 mm^2 and PB <50% at SB ostium)



From Data, to Practice.

Normal Side Branch

- If the side branch ostium is angiographically normal (whatever size is), just main branch stenting would be always good.

Diseased Side Branch

- If the side branch ostium has significant disease (angiographic DS >50%), IVUS study may be helpful to predict the fate of side branch.
- Combined IVUS criteria of MLA >2.4 mm2 and PB <50% in SB may be able to predict functionally good patency after main branch stenting.

Bifurcation Lesion PCI

- Treat or not treat concerns is mainly rely on the size of jeopardy myocardium of SB.
- If operator get decide to treat them (operator's discretion), FFR is the only guiding tool for decision making.

Summary

Back to the Principle-
Objective ischemia guided PCI,

FFR guided decision making and
IVUS guided stent optimization can
make a good clinical outcomes.


Thank You !!
summitMD.com