Why Mismatches Between Coronary Angiography and FFR

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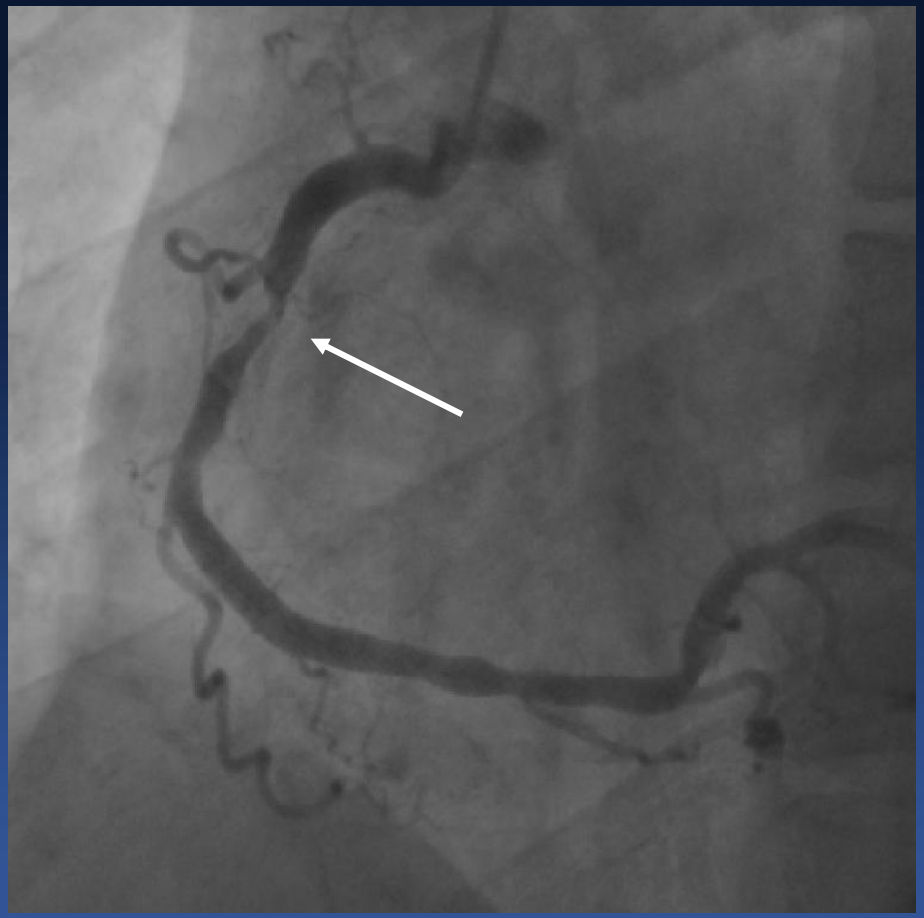
M/72,

Recent developed Effort chest pain, Hyperlipidemia, Smoker

We took a coronary angiogram first,

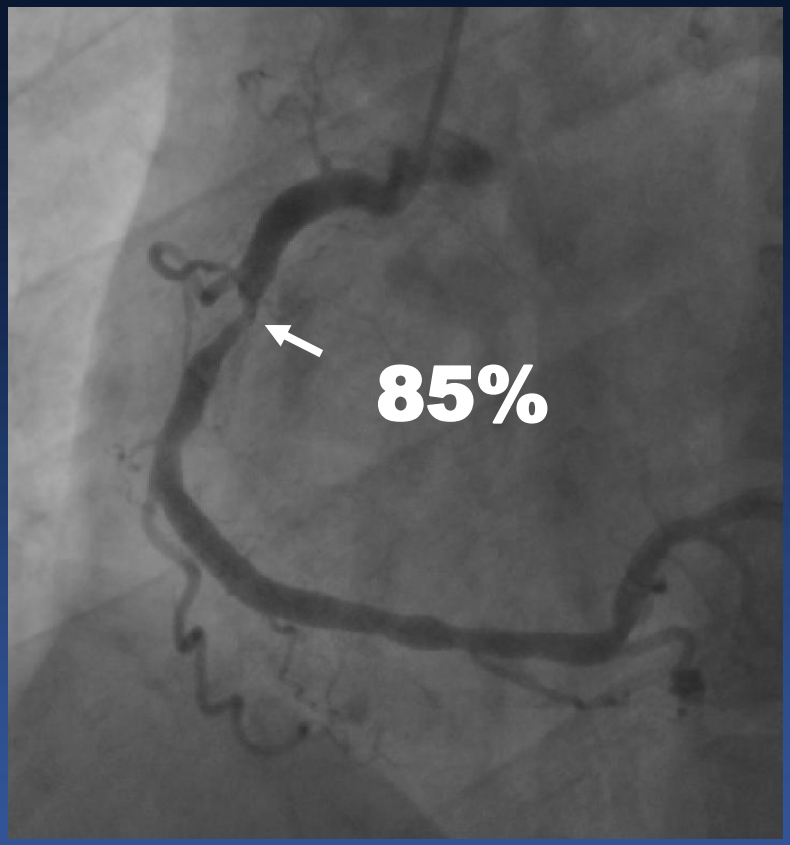


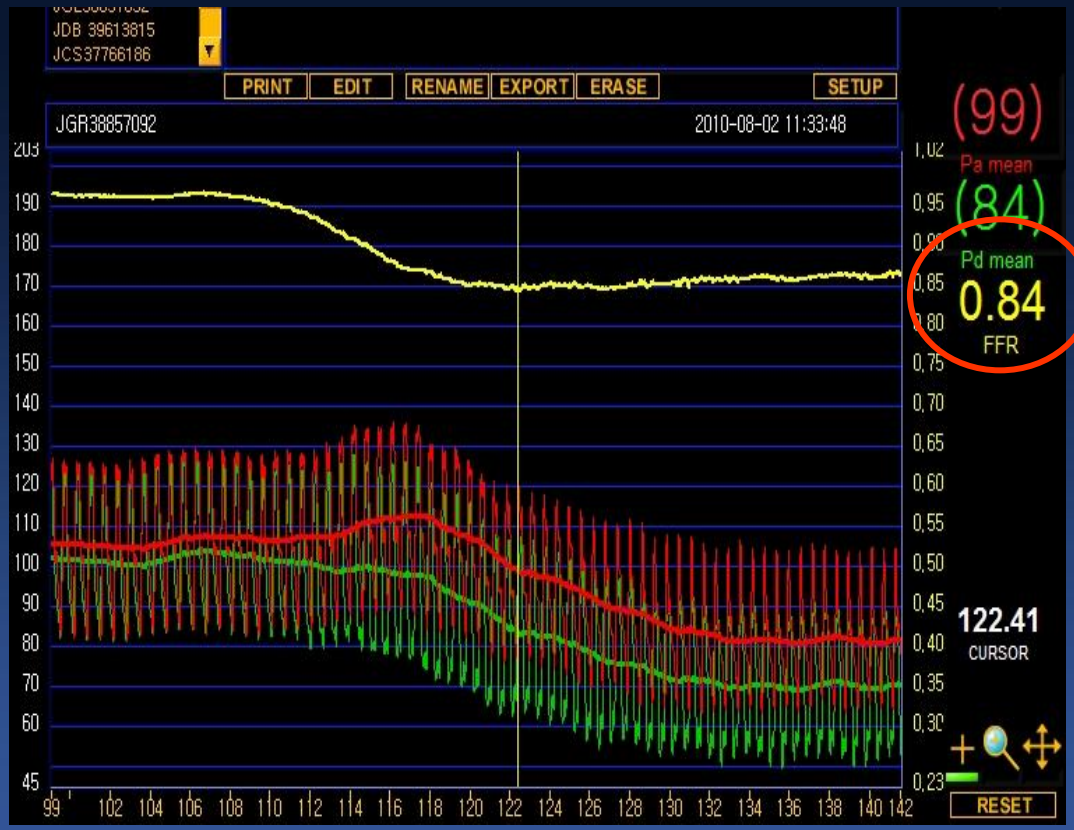
Visual Estimation 85%

FFR

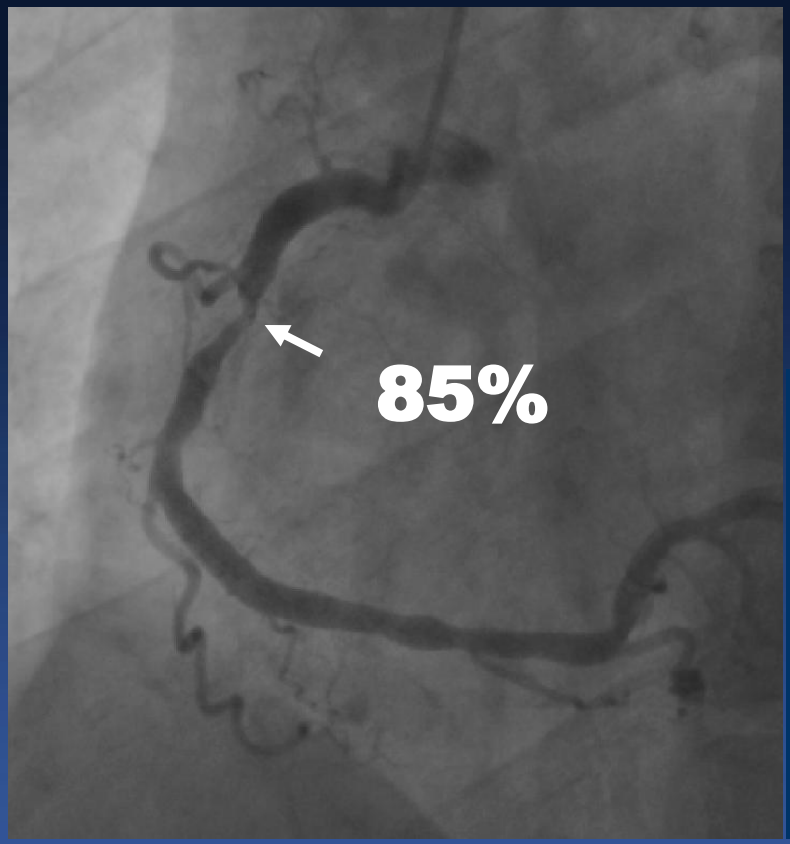
Intravenous adenosine, 160 μg/kg/min

Angiography - FFR Mismatch





Visual - Functional Mismatch



Angiographic DS : 85%

IVUS MLA : 2.8 mm^2

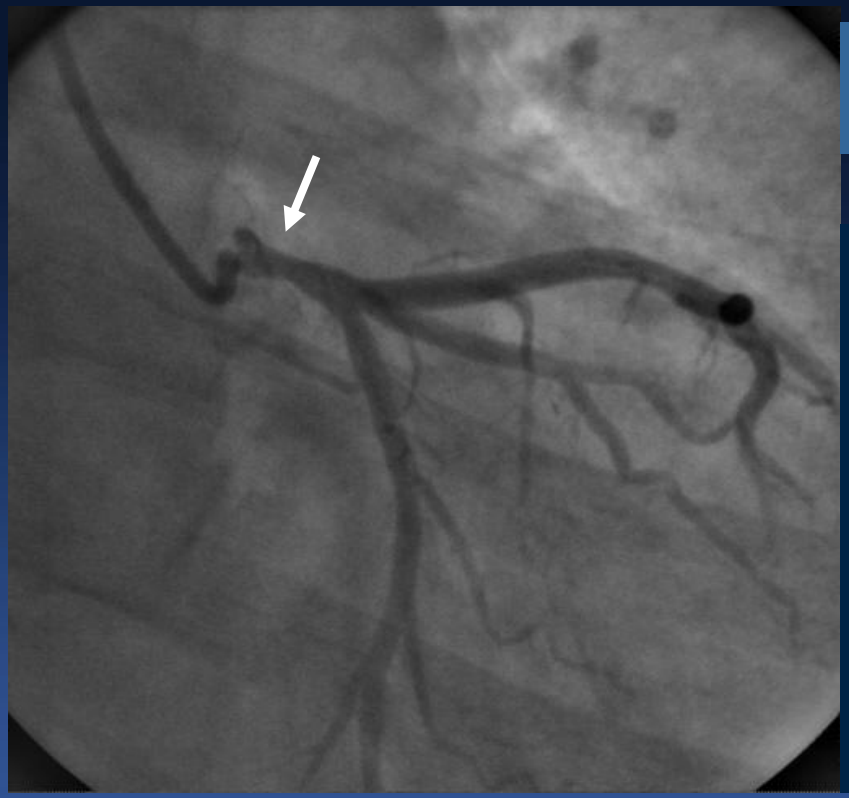
FFR : 0.84

Treadmill test : Negative

Thallium spect : Normal

Stress Echo : Normal

Reverse Mismatch



Visual Estimation : 30%

FFR : 0.70

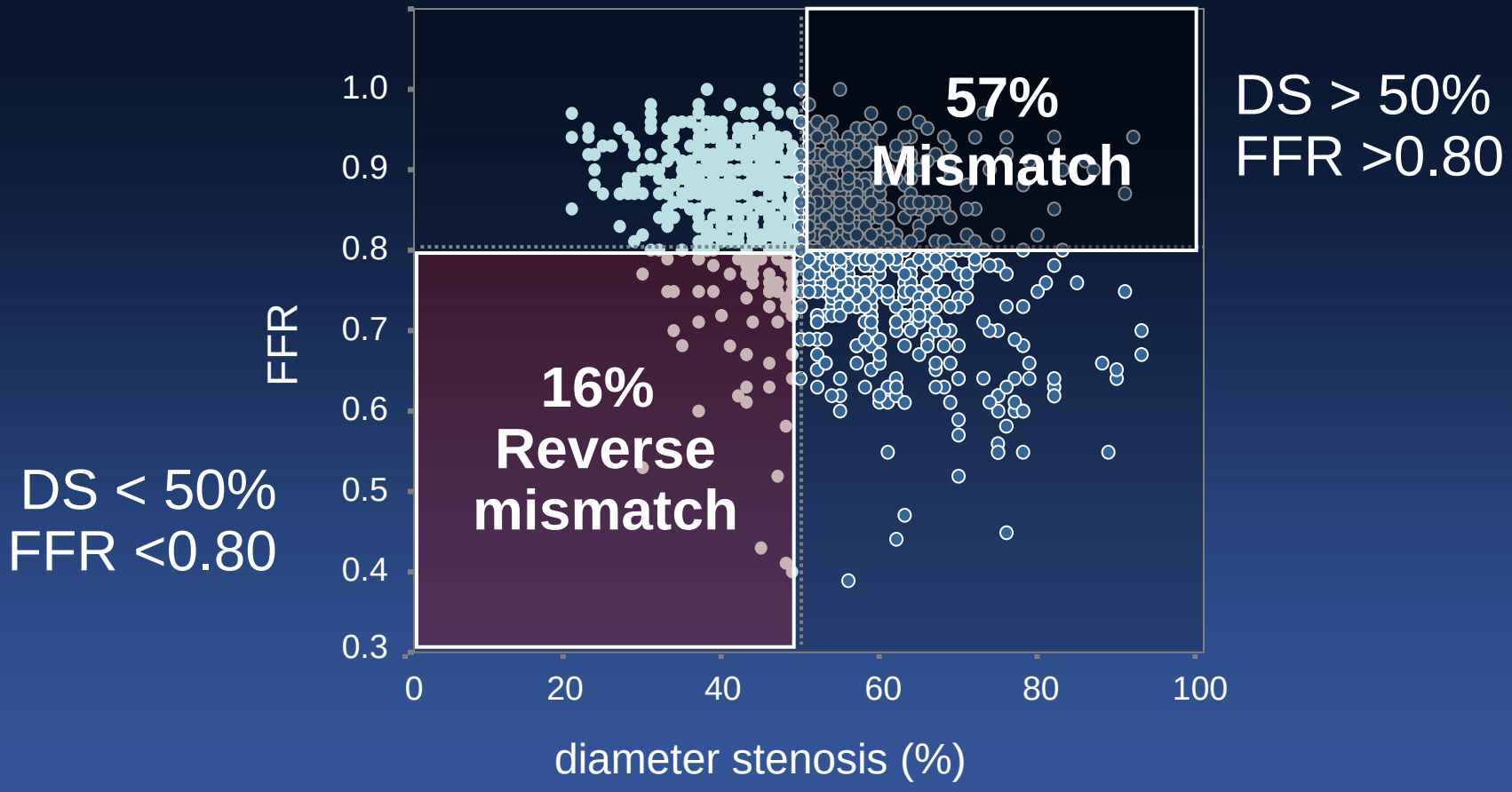
IVUS MLA: 4.5 mm2

Treadmill test: + stage 2

Thallium spect : + large LAD

Many Mismatches

1066 Non-LM lesions, AMC data



Park SJ et al, JACC Intv 2012;5:1029 –36

Why Mismatches ?
Background

- Lesion severity determined by coronary angiography has not been well-correlated with the physiologic significance of the stenosis

- However, the reasons why mismatches are still poorly understood.

Methods 1
Computational Simulation

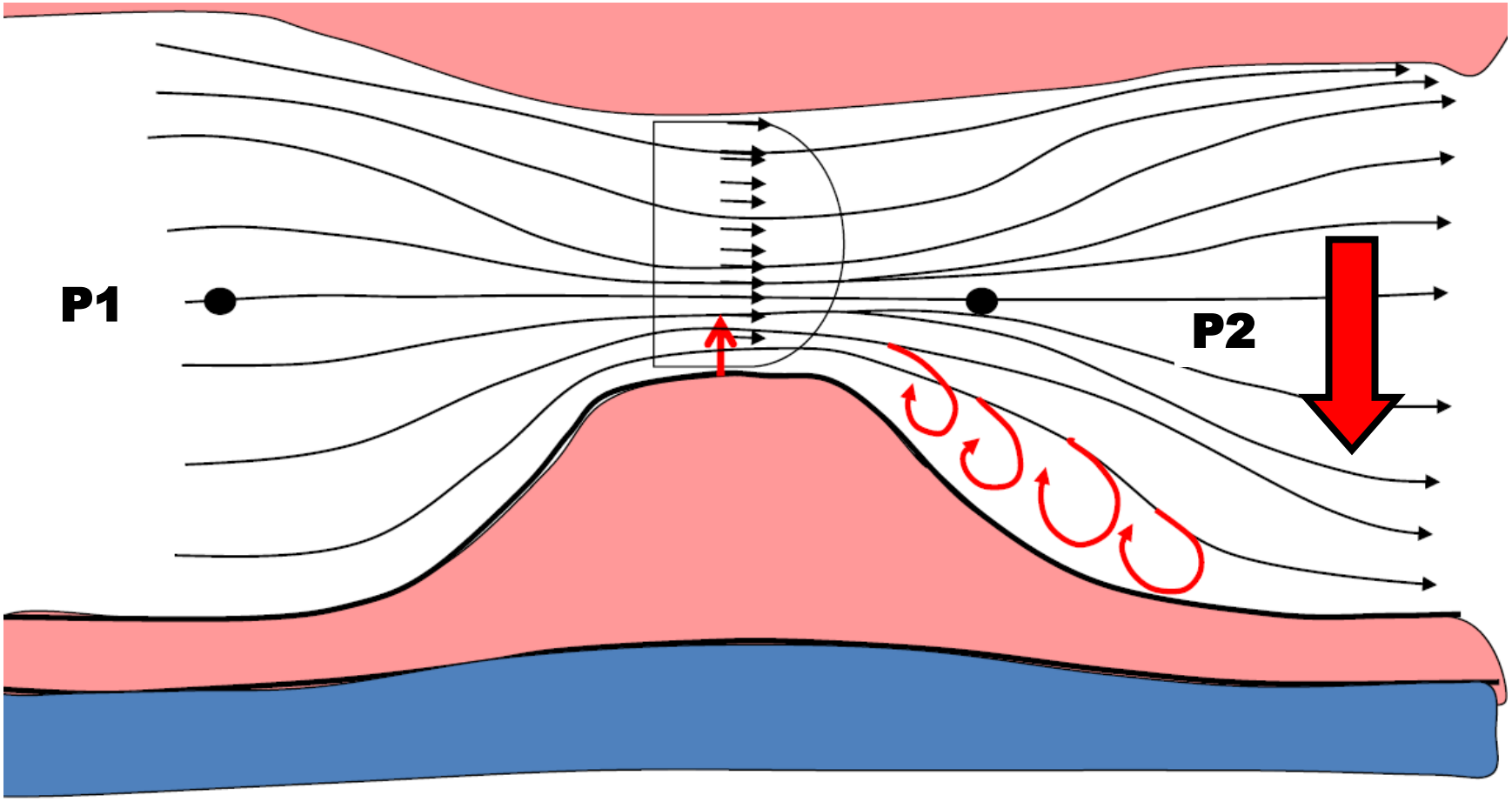
- Numerical simulation was performed using a commercial computational fluid dynamics simulation code, ANSYS FLUENT® release 13.0

- A built-in porous media model in ANSYS FLUENT® release 13.0 was used to simulate microvascular bed resistance change of myocardium due to change of coronary severity under hyperemic flow condition

Recirculation (Vortex)

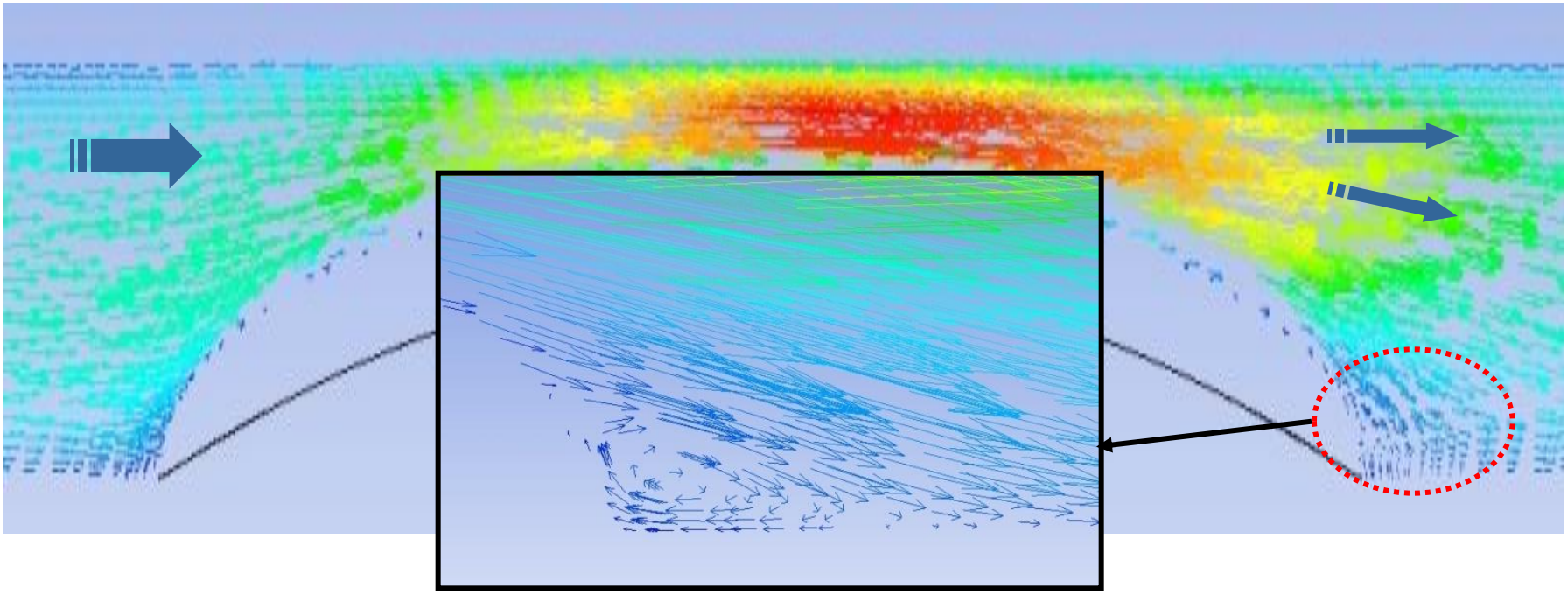
Can make a Energy Loss of Fluid

⟶ Pressure Drop



Recirculation
(Vortex Flow)

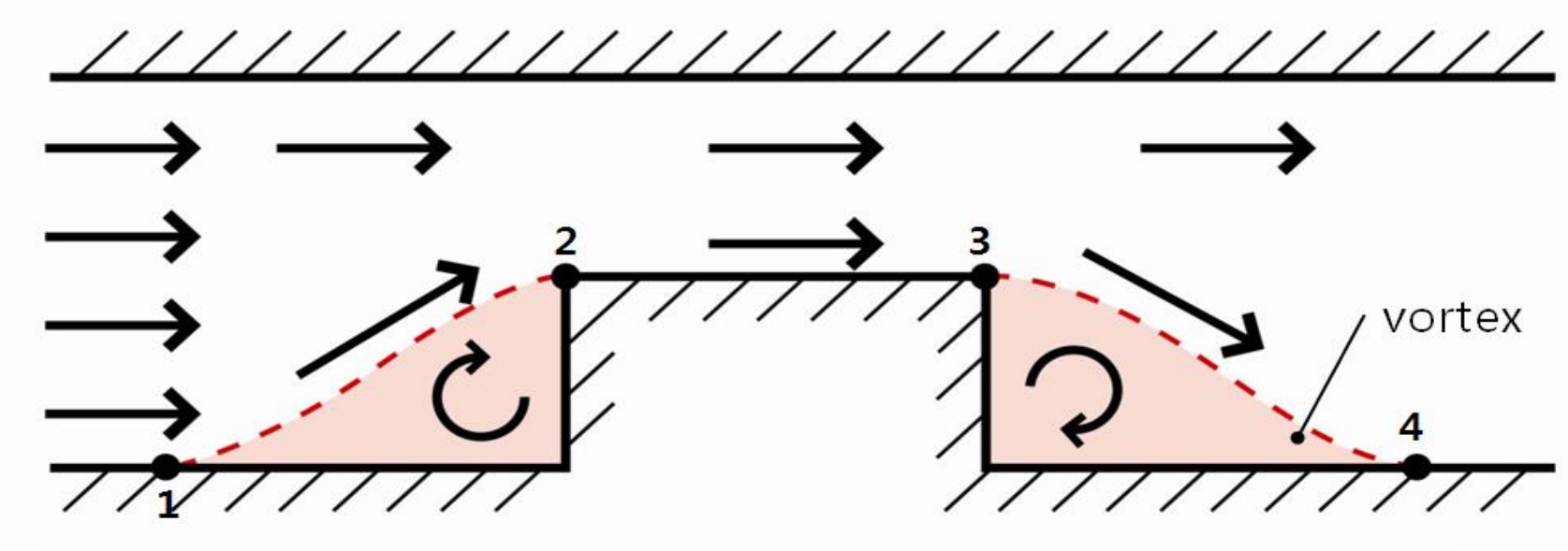
FFR 0.62



Recirculation

Energy Loss of Fluid by Vortex Flow

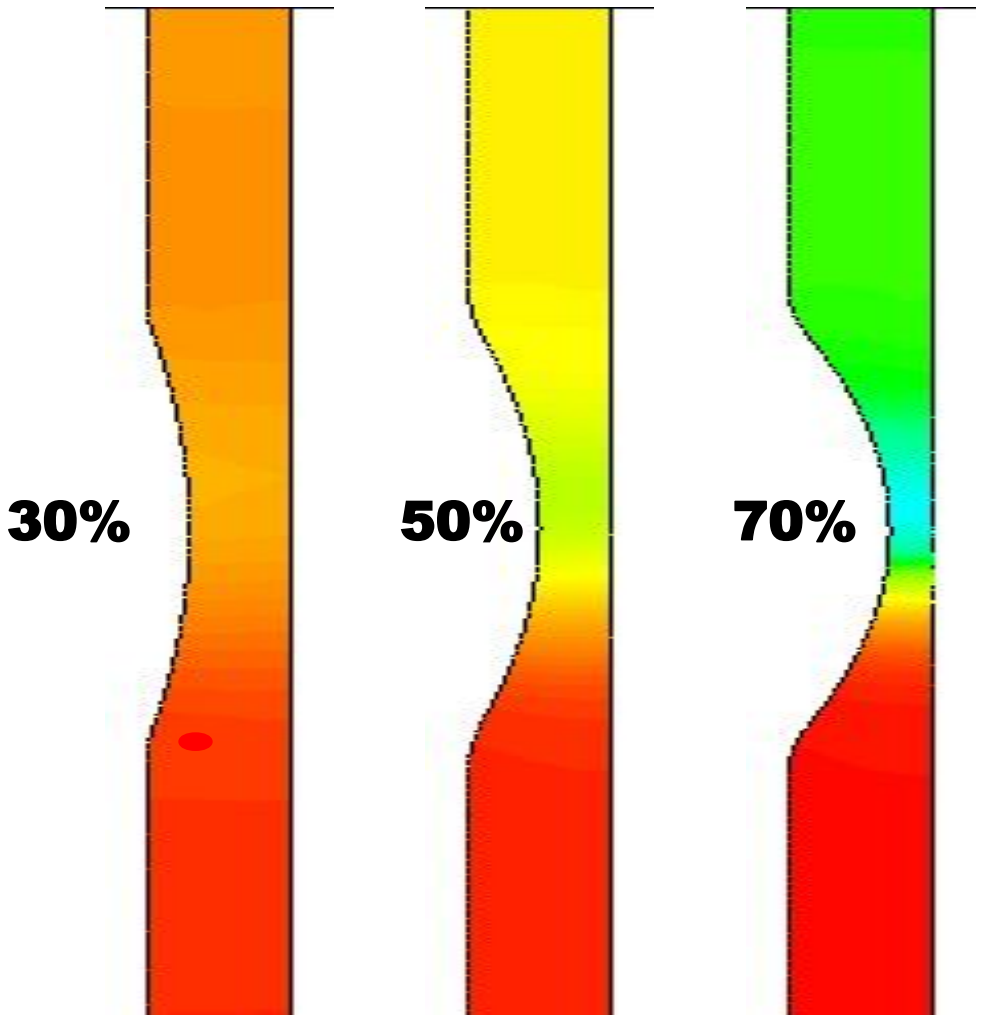
$1 : P1 + 1/2pv1^2 = Pt_1 \quad 2 : P2 + 1/2pv2^2 = Pt_2 \quad 3 : P3 + 1/2pv3^2 = Pt_3$



$Pt_1 > Pt_2$ $\quad Pt_1 >> Pt_4$

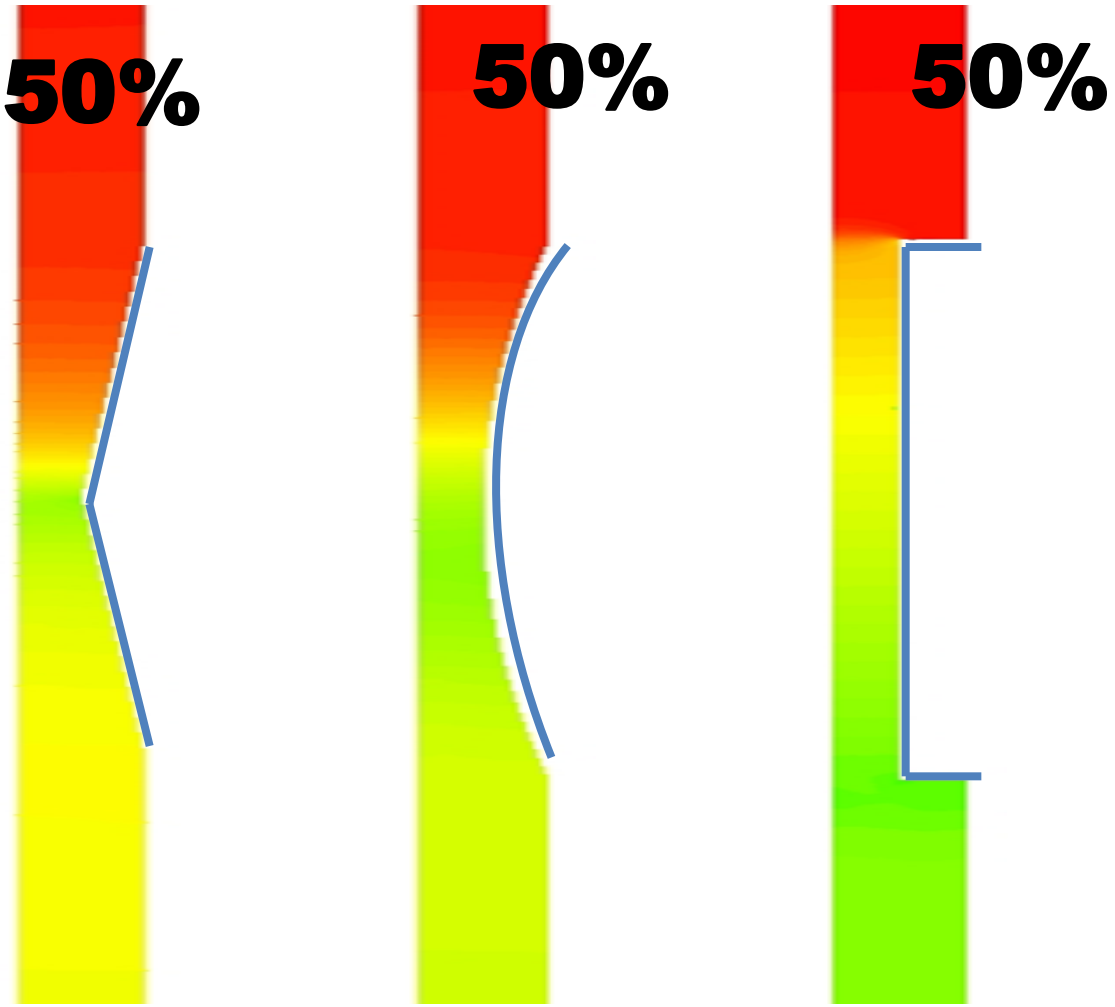
Courtesy of Prof. Shim

Degree of Stenosis



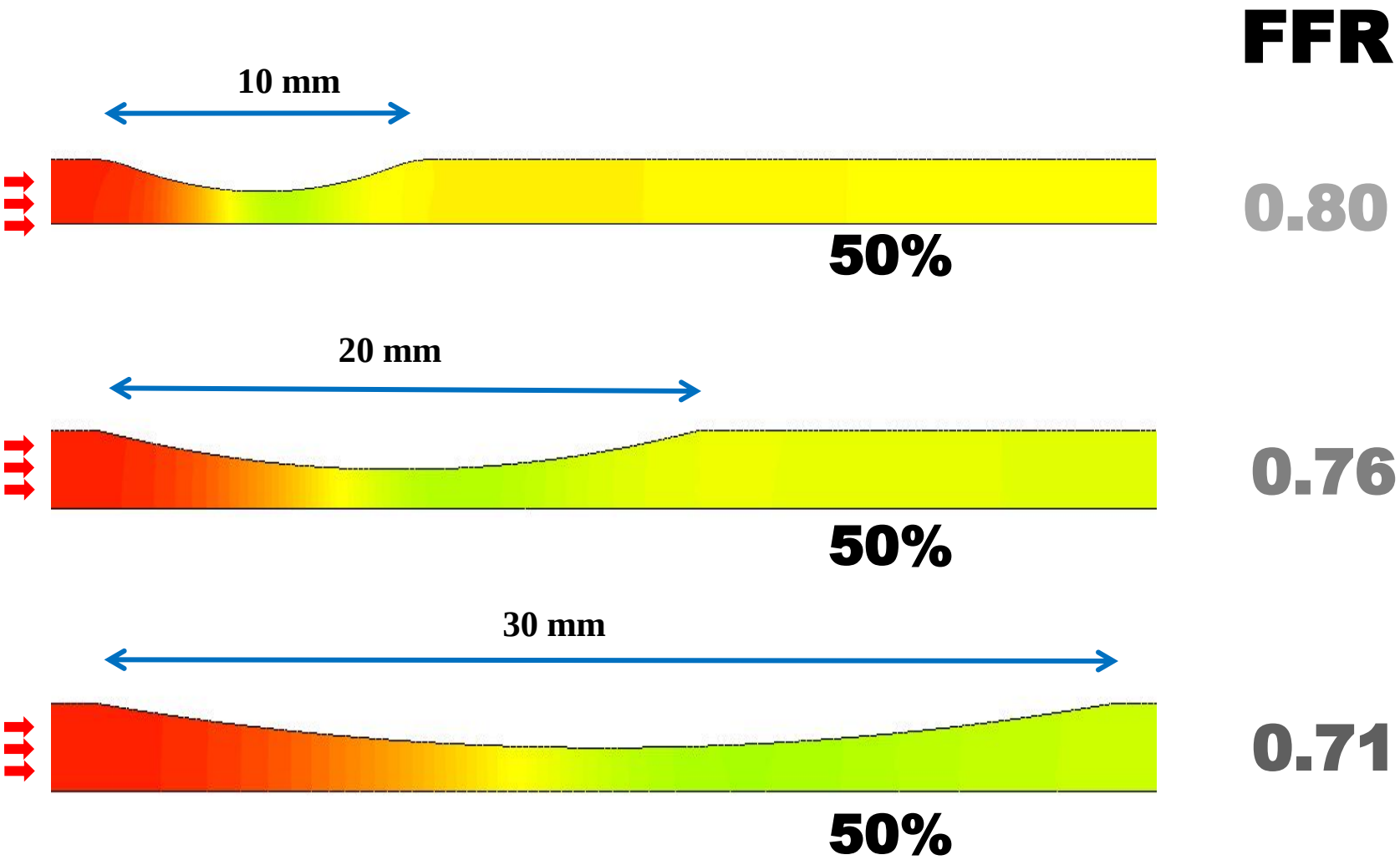
FFR	0.91	0.80	0.58

Different Lesion Morphology



FFR 0.76 0.71 0.61

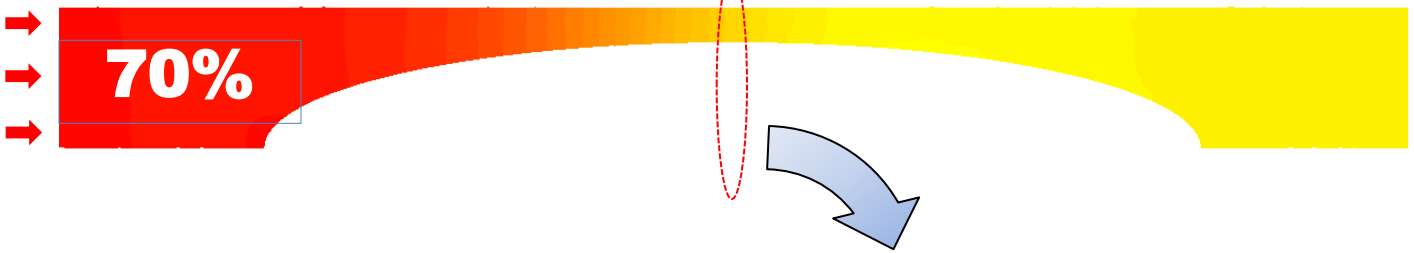
Different Lesion Length



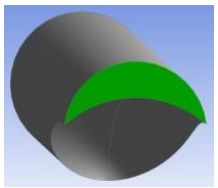
Lesion Eccentricity
(cross-sectional)

FFR

Eccentric Model

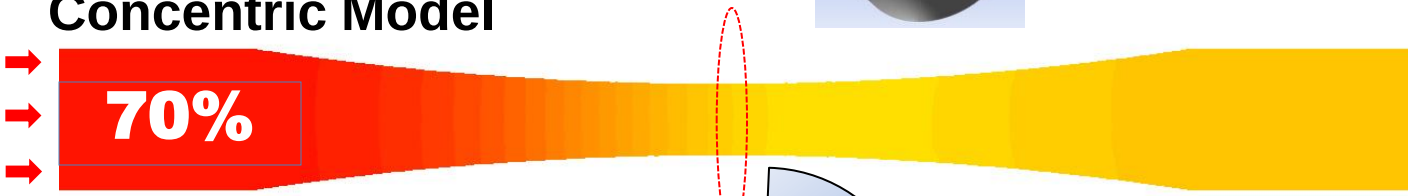


0.71

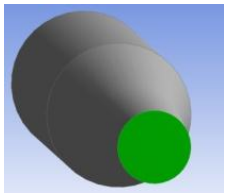


CSA
: 1.83 mm²

Concentric Model

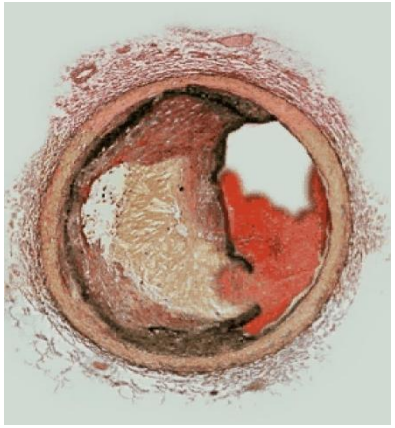


0.77



CSA
: 1.83 mm²

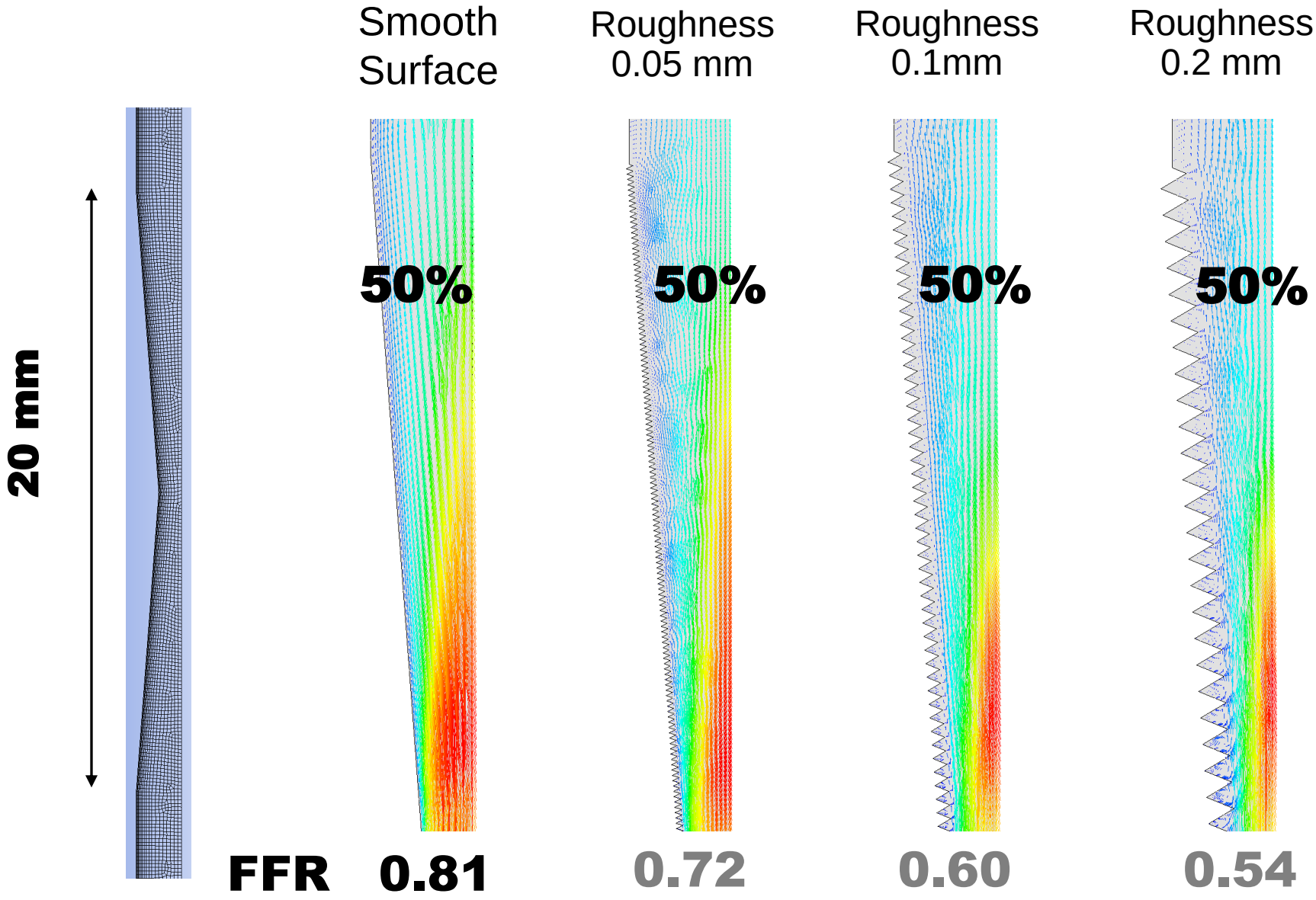
Vulnerable Plaque Simulation



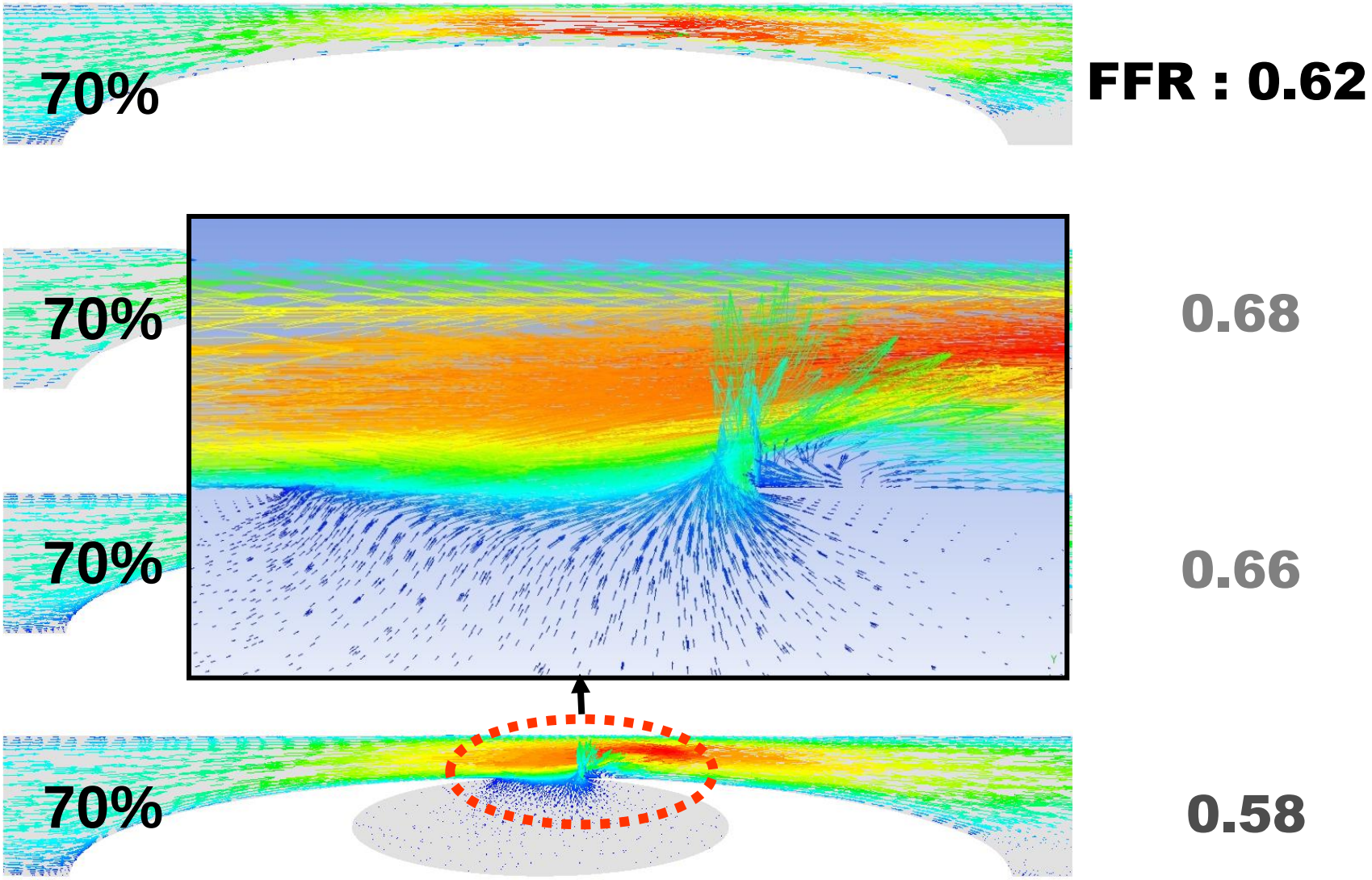
Plaque rupture

Thrombus, surface roughness

Different Surface Roughness

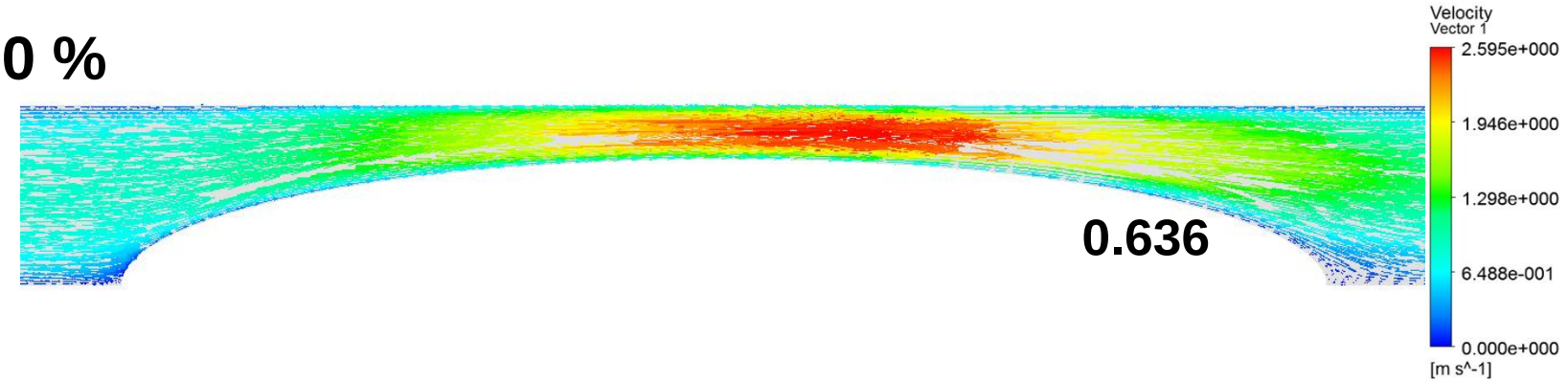


Presence of Plaque Rupture

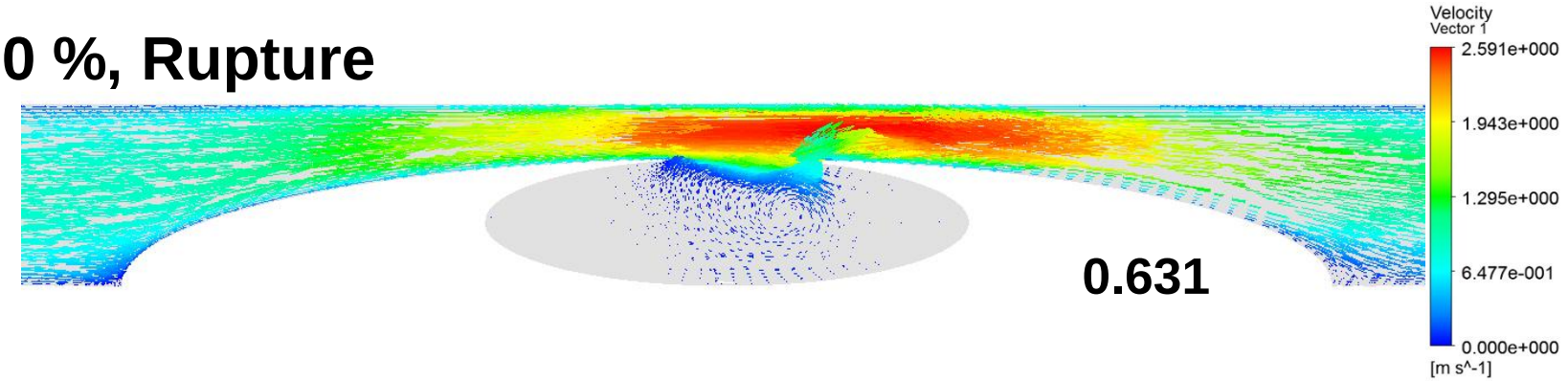


Rupture and Roughness

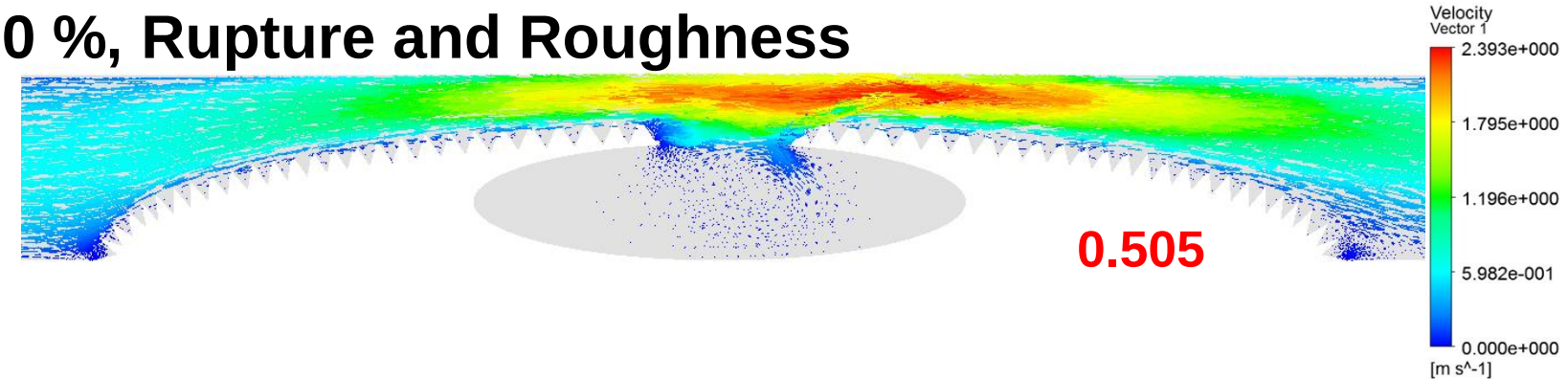
70 %



70 %, Rupture



70 %, Rupture and Roughness

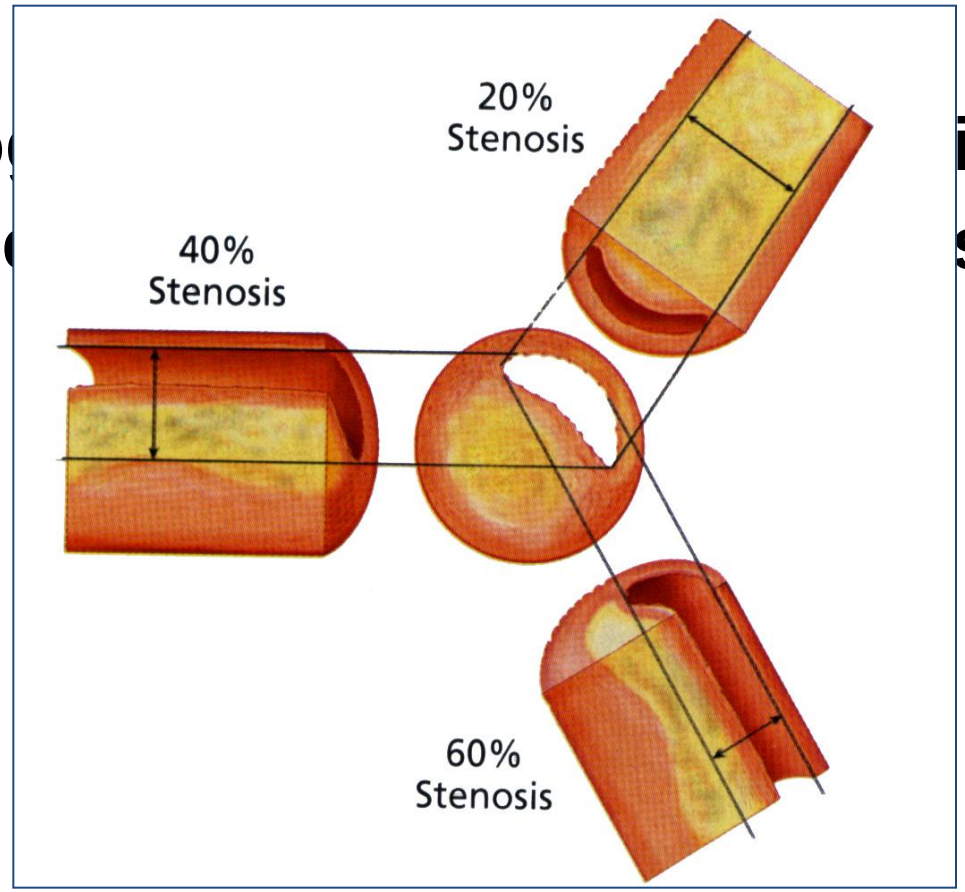


Lesion Specific, Local Factors influenced the FFR

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

Why Mismatches ?

1. Angio is simply,
   2-Dim s.



Why Mismatches ?

1. **Angiographic diameter stenosis is simply, 2-Dimensional, Single Cut Images.**
2. **FFR is 3-D, functional integration of stenosis. "Total Morphology Perception"**
3. **They are Totally Different !**

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Methods 2
Clinical Data in 1000 Patients

Prospective cohort, 1000 consecutive patients with 1129 coronary lesions, underwent QCA, IVUS, and FFR assessment prior to intervention

(ClinicalTrials.gov numbers NCT01366404)

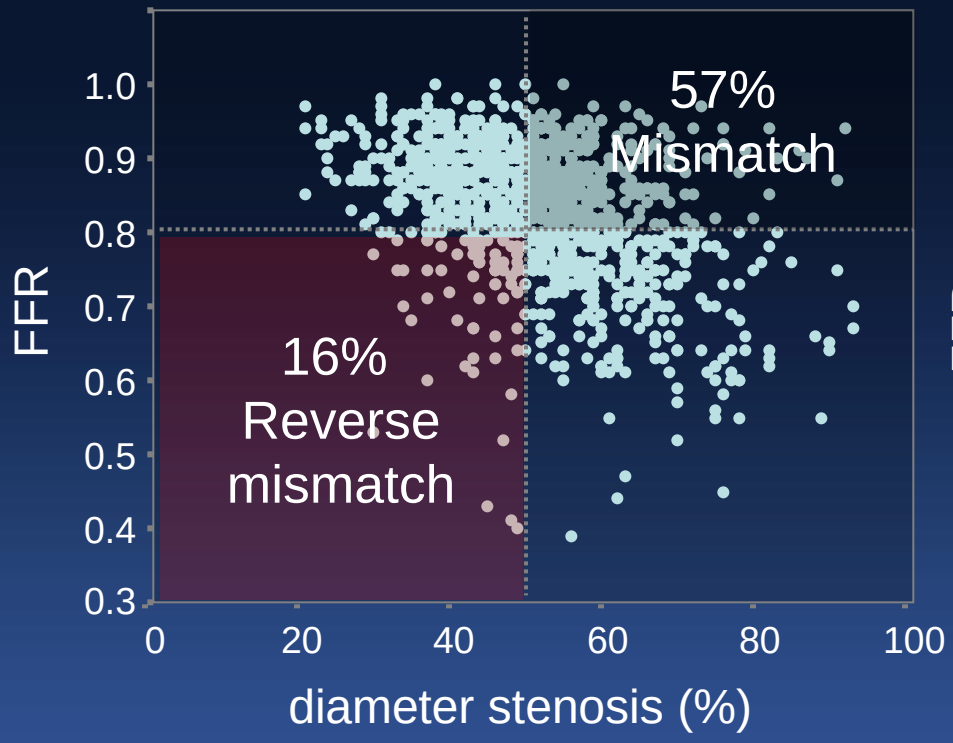
Clinical Characteristics (overall pt.)

Age (years)	61±9
Male	731 (73%)
Diabetes, N (%)	322 (32%)
Hypertension, N (%)	589 (59%)
Smoking, N (%)	493 (49%)
Hyperlipidemia, N (%)	670 (67%)
Previous PCI, N (%)	122 (12%)
Left main coronary artery disease	63 (6%)
Clinical manifestation	
Stable angina, N (%)	742 (74%)
Unstable angina, N (%)	219 (22%)
Non-ST elevation MI, N (%)	39 (4%)

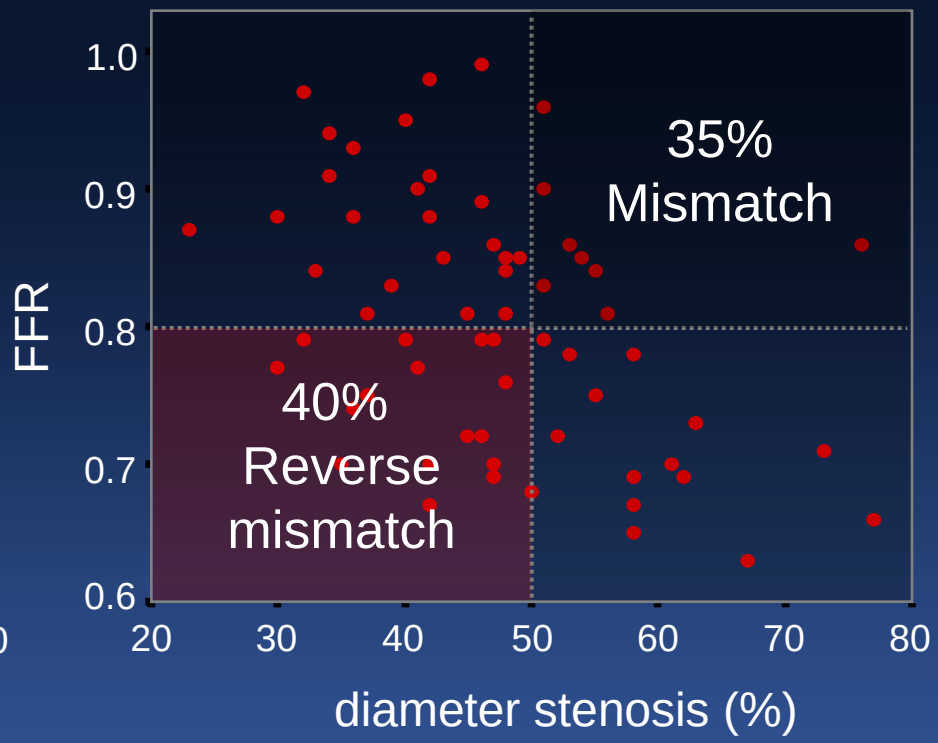
Lesion Characteristics (overall lesions)

Lesion location	N=1129
Syntax No 5 (LMCA)	63 (6%)
Syntax No 6 (proximal LAD)	236 (21%)
Syntax No 7 (mid LAD)	432 (38%)
Syntax No 8 (distal LAD)	36 (3%)
Syntax No 11 (proximal LCX)	39 (3%)
Syntax No 13 (distal LCX)	60 (5%)
Syntax No 1 (proximal RCA)	111 (10%)
Syntax No 2 (mid RCA)	114 (10%)
Syntax No 3 (distal RCA)	38 (3%)
FFR in non-left main lesions	0.82±0.09
FFR in left main lesions	0.80±0.09
FFR <0.80	368 (32.6%)

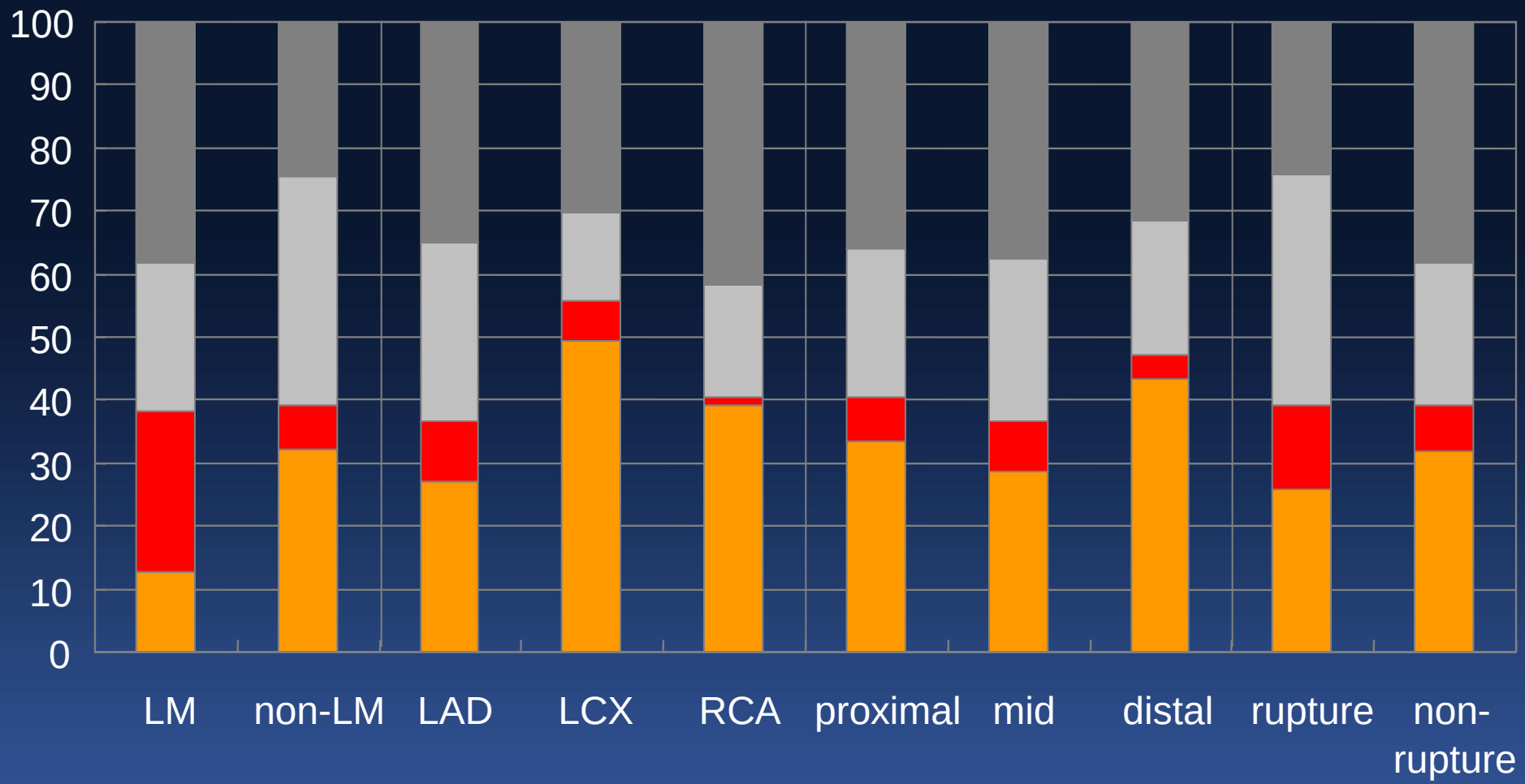
1066 Non-LM lesions



63 LM lesions

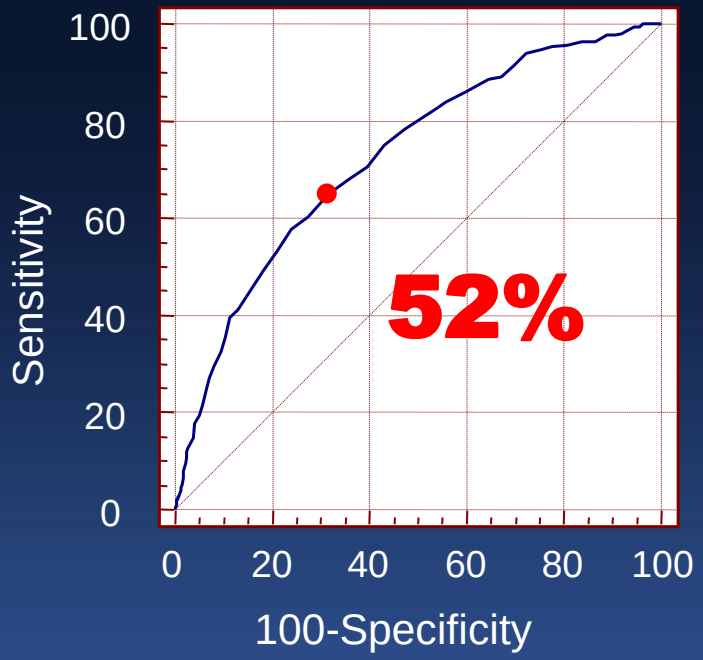


Frequencies of Mismatch



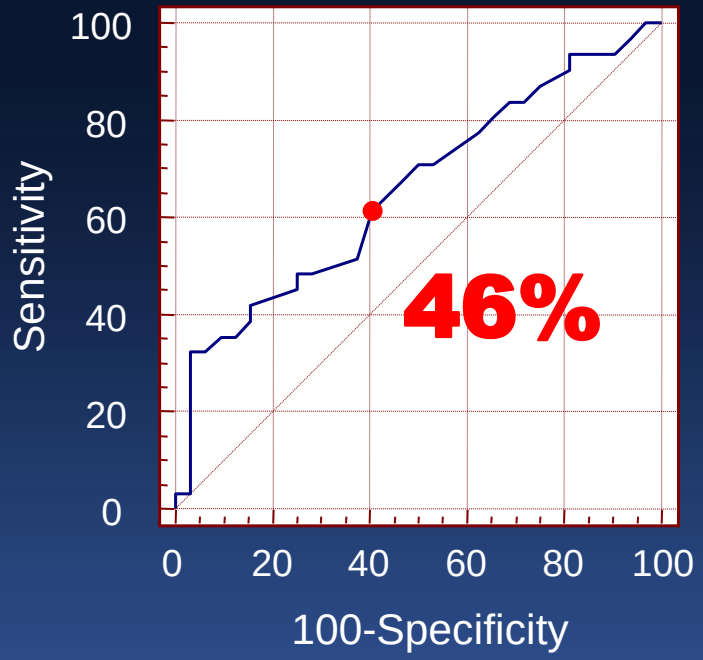
Cut-off of QCA-DS
to Predict FFR <0.80

Non-LMCA



Sensitivity 66%
Specificity 67%
PPV 48%
NPV 81%
Accuracy 66%

LMCA



Sensitivity 61%
Specificity 59%
Accuracy 60%

Correlations of Variables with FFR

	Non-LM lesions		LM lesions	
	r	p	r	p
Angiographic DS	-0.395	p<0.001	-0.428	p<0.001
Angiographic MLD	0.414	p<0.001	0.436	p<0.001
Lesion length	-0.235	p<0.001	-0.216	0.089
Minimal lumen area	0.467	p<0.001	0.560	p<0.001
Plaque burden	-0.350	p<0.001	-0.473	p<0.001

- Univariate Analysis -

Why Mismatches

Comparison of Clinical Data

	QCA-DS>50%		QCA-DS≤50%	
	FFR<0.80	FFR≥0.80 *Mismatch*	FFR≥0.80	FFR<0.80 *Rev-mismatch*
N	262	343	386	75
Age (years)	59.7±10.0	62.1±10.0#	62.9±9.2	59.7±10.0*
Female, N (%)	55 (21%)	107 (31%)#	103 (27%)	13 (17%)
Diabetes, N (%)	82 (31%)	111 (32%)	121 (31%)	17 (23%)
Hypertension, N (%)	157 (60%)	201 (59%)	227 (59%)	43 (57%)
Smoking, N (%)	142 (54%)	160 (47%)	195 (51%)	45 (60%)
ACS, N (%)	72 (28%)	101 (29%)	115 (30%)	20 (27%)
LAD, N (%)	201 (77%)	191 (56%)#	246 (64%)	66 (88%)*
LCX, N (%)	14 (5%)	49 (14%)#	30 (8%)	6 (8%)
RCA, N (%)	47 (18%)	103 (30%)#	110 (29%)	3 (4%)*

 # p value <0.05, vs. 262 lesions with QCA-DS>50 and FFR<0.80
** p value <0.05, vs. 386 lesions with QCA-DS≤50% and FFR≥0.80*

Comparison of QCA and IVUS Findings

	QCA-DS>50%		QCA-DS≤50%	
	FFR<0.80	FFR≥0.80 *Mismatch*	FFR≥0.80	FFR<0.80 *Rev-mismatch*
N	262	343	386	75
Proximal segment	91 (35%)	129 (38%)	139 (36%)	27 (36%)
Distal segment	29 (11%)	58 (17%)#	42 (11%)	5 (7%)
Lesions length, mm	24.1±13.4	18.8±10.6#	16.7±11.2	19.3±12.3
QCA-DS, %	62.3±9.2	57.6±7.4#	40.1±6.6	43.2±5.2*
QCA-MLD, mm	1.2±0.3	1.4±0.3#	1.9±0.3	1.7±0.3*
Averaged RLD, mm	3.1±0.5	3.2±0.5#	3.1±0.5	3.0±0.5*
MLA, mm^2	1.9±0.7	2.6±0.9#	3.4±1.3	2.4±0.8*
Plaque burden, %	80.8±8.7	74.7±9.9#	67.8±13.0	73.1±12.1*
Plaque rupture	44 (17%)	35 (10%)#	32 (8%)	12 (16%)*

 # p value <0.05, vs. 262 lesions with QCA-DS>50 and FFR<0.80

** p value <0.05, vs. 386 lesions with QCA-DS≤50% and FFR≥0.80*

Comparison of Clinical Data in LM

	QCA-DS>50%		QCA-DS≤50%	
	FFR<0.80	FFR≥0.80 *Mismatch*	FFR≥0.80	FFR<0.80 *Rev-mismatch*
N	15	8	24	16
Age (years)	61.8±11.5	63.8±10.3	60.8±12.4	56.1±9.8
Age (years)	4 (27%)	2 (25%)	9 (38%)	2 (13%)
Female, N (%)	5 (33%)	2 (25%)	98 (33%)	6 (38%)
Diabetes, N (%)	11 (73%)	3 (38%)	12 (50%)	8 (50%)
Hypertension, N (%)	8 (53%)	5 (62%)	9 (38%)	12 (75%)*
ACS, N	8 (53%)	2 (25%)	13 (54%)	7 (44%)

 # p value <0.05, vs. 15 lesions with QCA-DS>50 and FFR<0.80
** p value <0.05, vs. 24 lesions with QCA-DS≤50% and FFR≥0.80*

Comparison of QCA and IVUS in LM

	QCA-DS>50%		QCA-DS≤50%	
	FFR<0.80	FFR≥0.80 *Mismatch*	FFR≥0.80	FFR<0.80 *Rev-mismatch*
N	15	8	24	16
Lesions length, mm	14.7±13.4	6.5±1.9	9.4±5.1	12.8±6.4
QCA-DS, %	60.0±7.8	55.9±8.4	40.0±6.8	41.3±5.7
QCA-MLD, mm	1.4±0.3	1.6±0.4	2.3±0.4	2.1±0.4
Averaged RLD, mm	3.5±0.5	3.7±0.6	3.6±0.5	3.5±0.5
MLA, mm^2	3.4±1.6	4.8±1.6#	6.6±2.0	4.2±1.4*
Plaque burden, %	81.0±8.4	69.5±18.3	61.2±14.3	73.1±9.6*
EEM area, mm^2	18.3±3.8	19.4±8.7	18.8±5.8	16.1±3.5
Plaque rupture	10 (67%)	3 (38%)	4 (17%)	8 (50%)*

 # p value <0.05, vs. 15 lesions with QCA-DS>50 and FFR<0.80
** p value <0.05, vs. 24 lesions with QCA-DS≤50% and FFR≥0.80*

- Multivariable Analysis -

Why Mismatches

Independent Factors for "Mismatch"

	Beta	SE	p-value	Adjusted OR	95% CI
Age	0.040	0.012	<0.001	1.040	1.017 – 1.064
Female	0.430	0.250	0.085	1.537	0.942 – 2.508
LAD location	-1.094	0.227	<0.001	0.335	0.214 – 0.522
Plaque rupture	-0.956	0.334	0.004	0.385	0.200 – 0.740
Lesion length	-0.033	0.008	<0.001	0.966	0.950 – 0.982
IVUS-MLA	0.687	0.189	0.001	1.989	1.371 – 2.886
Plaque burden	-0.050	0.014	<0.001	0.951	0.926 – 0.977
QCA-MLD	0.086	0.040	0.034	1.089	1.007 – 1.179

** assessed by GEE in 937 patients with 1066. non-LMCA lesions included age, female gender, lesions length, LAD location, proximal segment, plaque rupture, RLD, MLA, plaque burden, and averaged RLD*

Independent Factors for "Reverse-Mismatch"

	Beta	SE	p-value	Adjusted OR	95% CI
Age	-0.044	0.015	0.003	0.957	0.929 – 0.985
LAD location	1.691	0.457	<0.001	5.427	2.216 – 13.29
Plaque rupture	1.150	0.452	0.011	3.159	1.301 – 7.667
IVUS-MLA	-1.064	0.203	<0.001	0.345	0.232 – 0.514
Plaque burden	0.032	0.014	0.027	1.032	1.003 – 1.061

- ** assessed by GEE in 937 patients with 1066. non-LMCA lesions*
- *included age, female gender, lesions length, LAD location, proximal segment, plaque rupture, RLD, MLA, plaque burden, and averaged RLD*

Independent Predictors
-Multivariable Analysis-

Mismatch

- Older age
- Non-LAD location
- Shorter lesion length
- Larger MLA by IVUS
- Larger MLD by QCA
- Smaller PB

Reverse-Mismatch

- Younger age
- LAD location
- Plaque Rupture
- Smaller MLA by IVUS
- Larger PB

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Conclusions

- The mismatches between coronary angiography and FFR, was attributable to various clinical and lesion-specific factors frequently unrecognizable in coronary angiography.

- Thus, FFR, a clinical ischemia index integrating various local factors, is more reliable than angiographically determined stenosis severity.