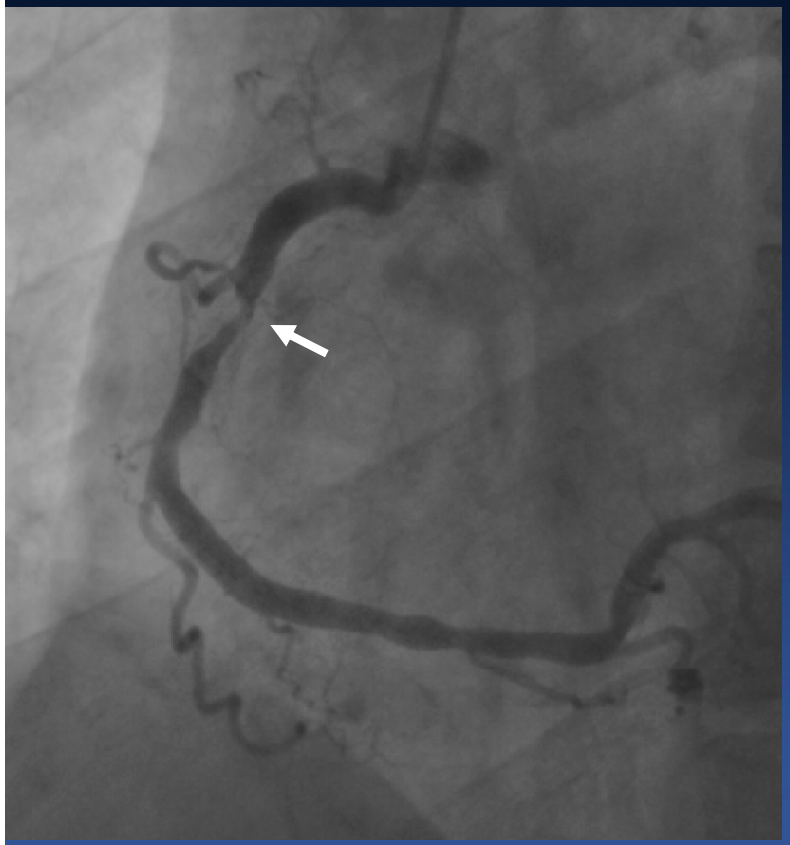
Visual-Functional Mismatch Between Coronary Angiography and Fractional Flow Reserve

Seung-Jung Park, MD., PhD.

University of Ulsan, College of Medicine
Asan Medical Center, Seoul, Korea

Visual - Functional Mismatch



Angiographic DS(%) : 85%

IVUS MLA : 2.8 mm^2

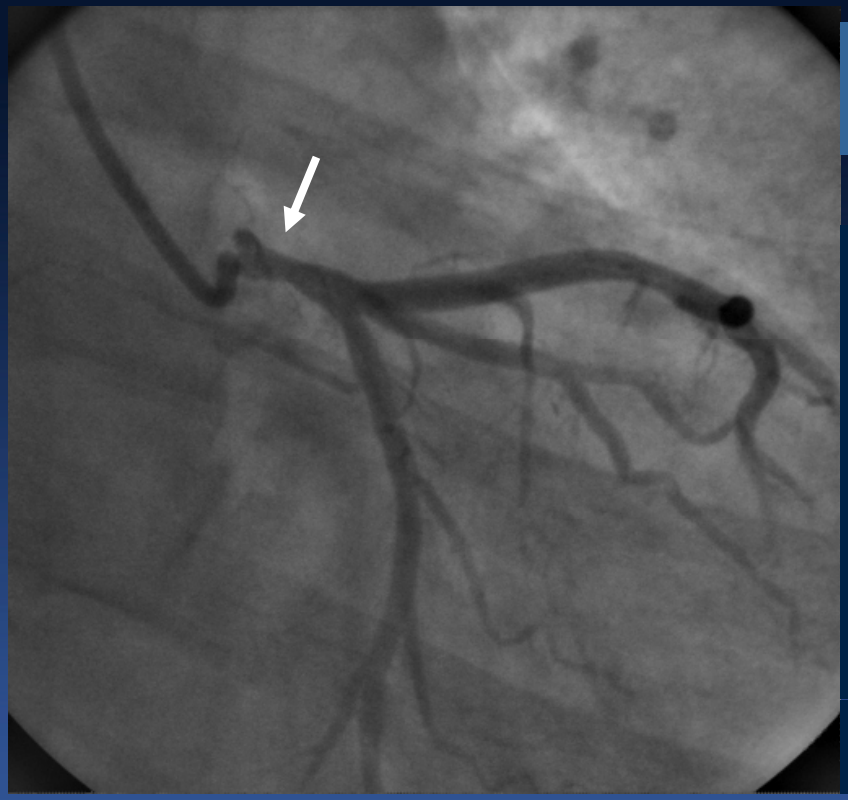
FFR : 0.84

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

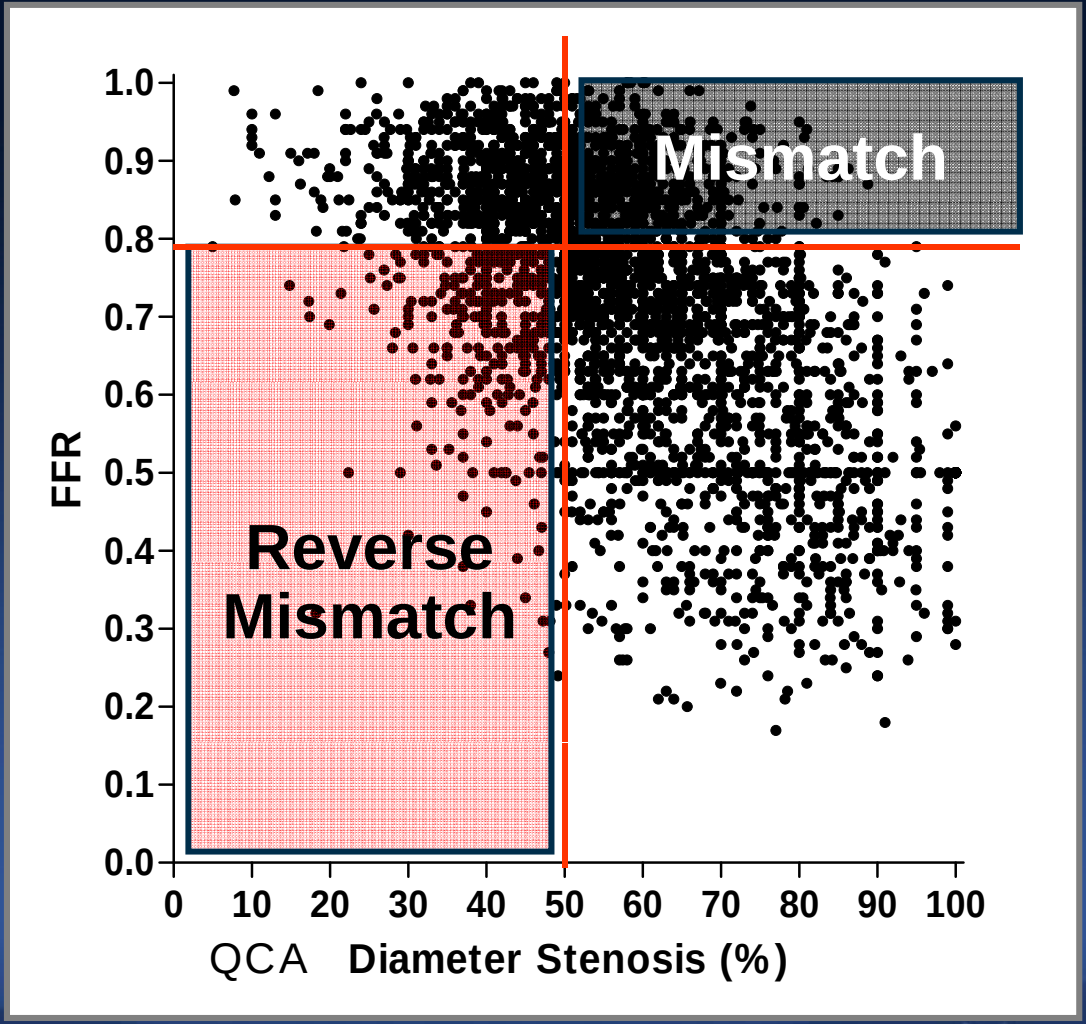
Thallium spect : + large LAD

How many Mismatches ?

Mismatch Disease
in the Cath Lab

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

FFR



QCA

Courtesy of Bernard De Bruyne, MD, PhD,

Mismatches ;

Significant Stenosis (>50%) with Negative FFR

Reverse Mismatches ;

Insignificant Stenosis (<50%) with Positive FFR

Background

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

- However, the reasons why mismatches between the two, 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

Methods 2
Clinical Data in 1000 Patients

- Between November 2009 and June 2011, in a prospective cohort, 1000 consecutive patients with 1129 coronary lesions, underwent angiographic, IVUS, and FFR assessment prior to intervention
  (ClinicalTrials.gov numbers NCT01366404)

- All patients were aged 35-85 years and had one target vessel with >30% of QCA-DS on visual estimation

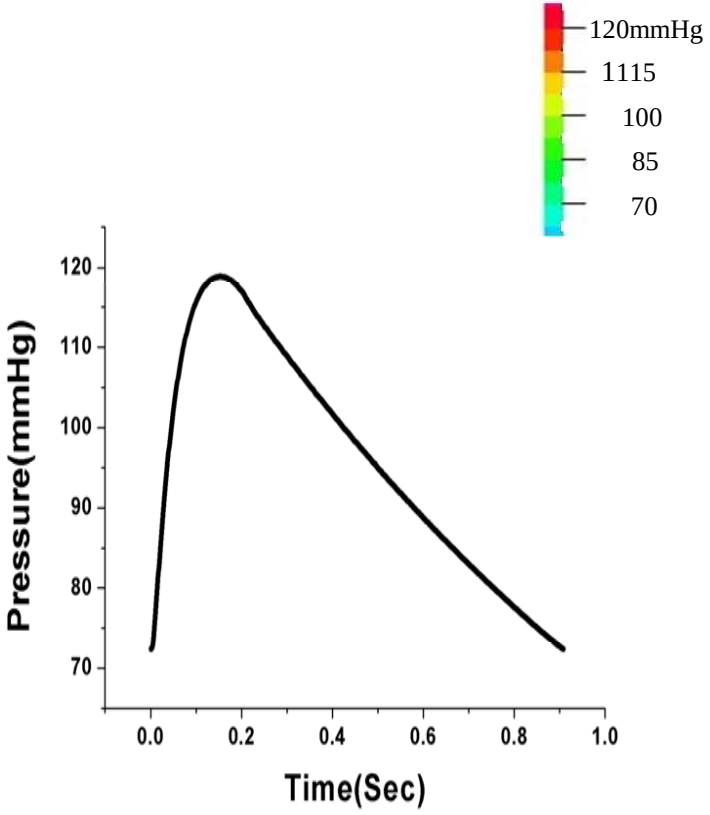
FFR **is determined by**

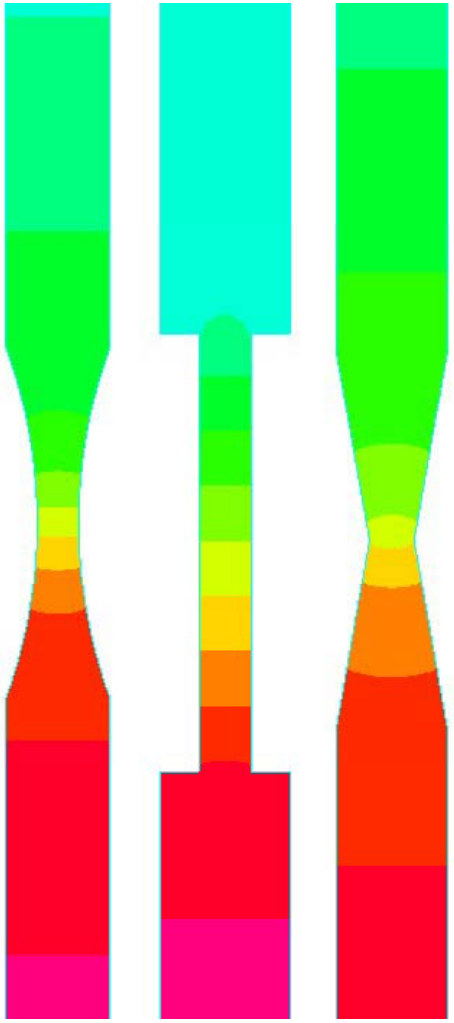
1. **Size of myocardium**
2. **Many lesion specific local factors at maximal hyperemia.**

Methods 1

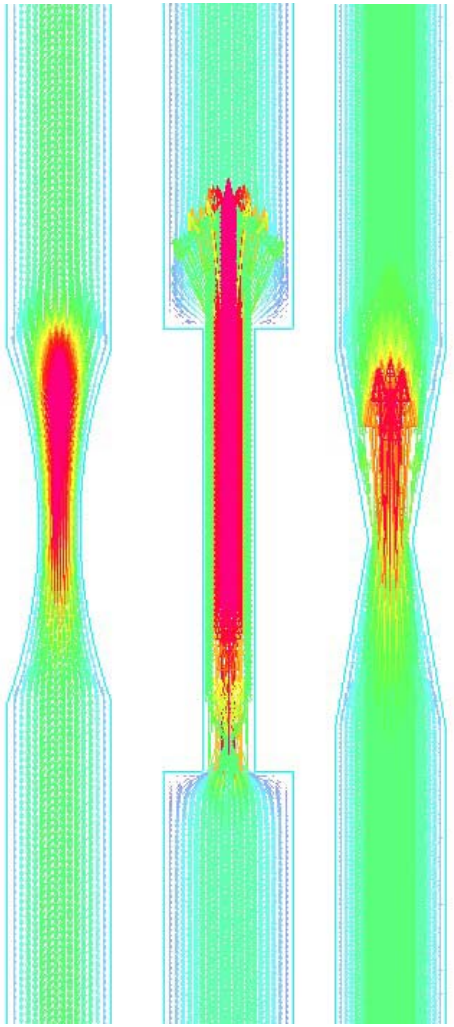
Computational Simulation Study

Steady-state 3D Simulation under Hyperemic Condition





Pressure contours



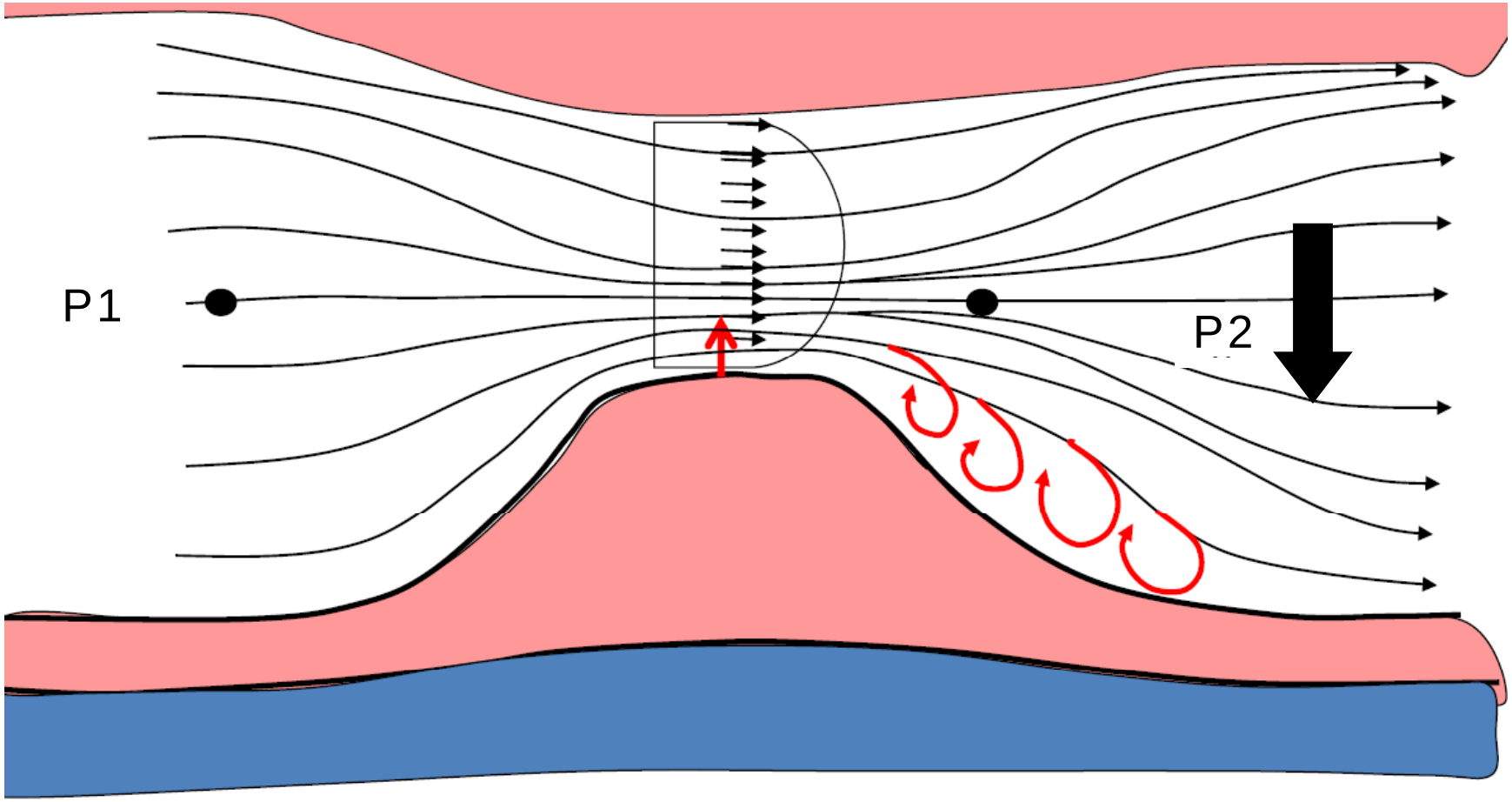
Velocity vectors

Recirculation (Vortex)

Can make a Energy Loss of Fluid

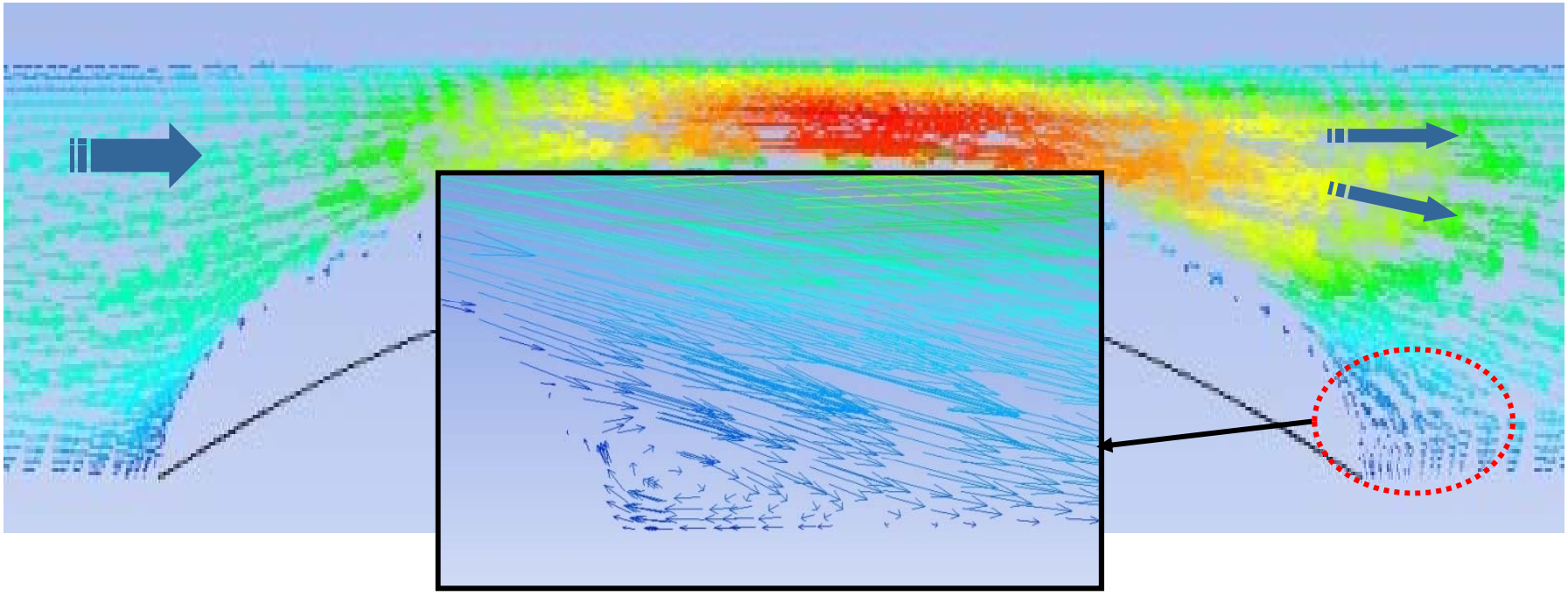
Why
Pressure Drop ?

→ Pressure Drop



Steady-state 3D Simulation under Hyperemic Condition

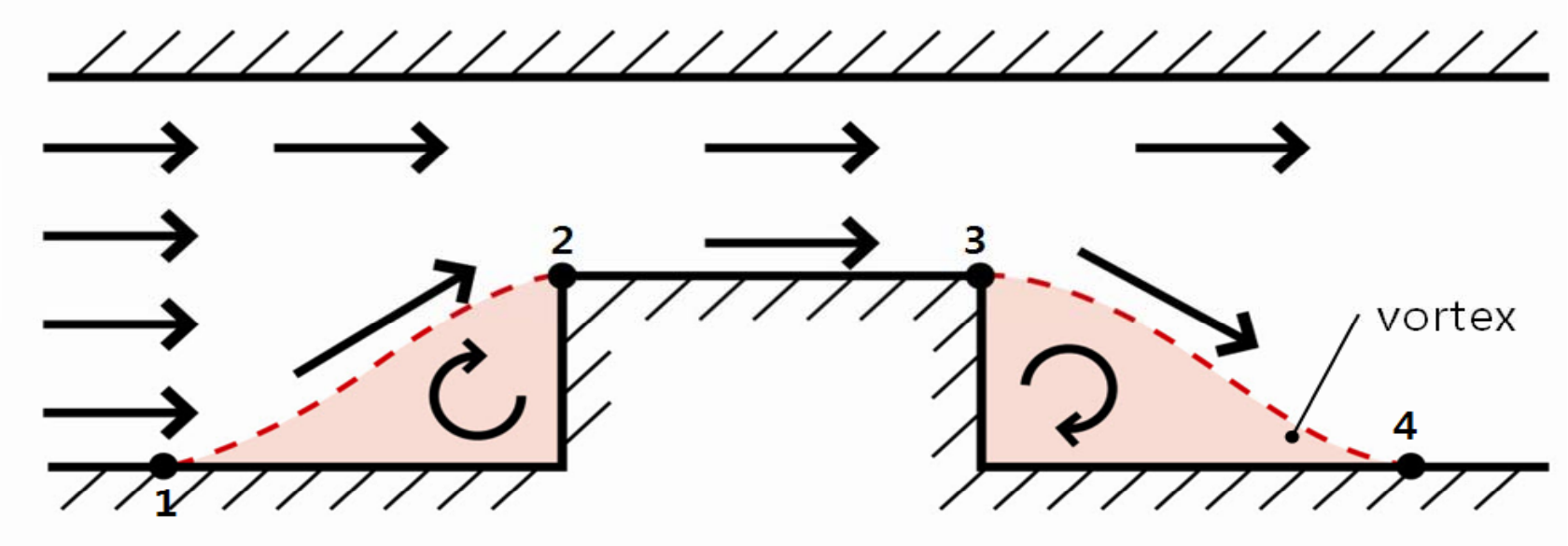
FFR 0.62



Recirculation

Pressure Drop due to Energy Loss of Fluid by Vortex Flow

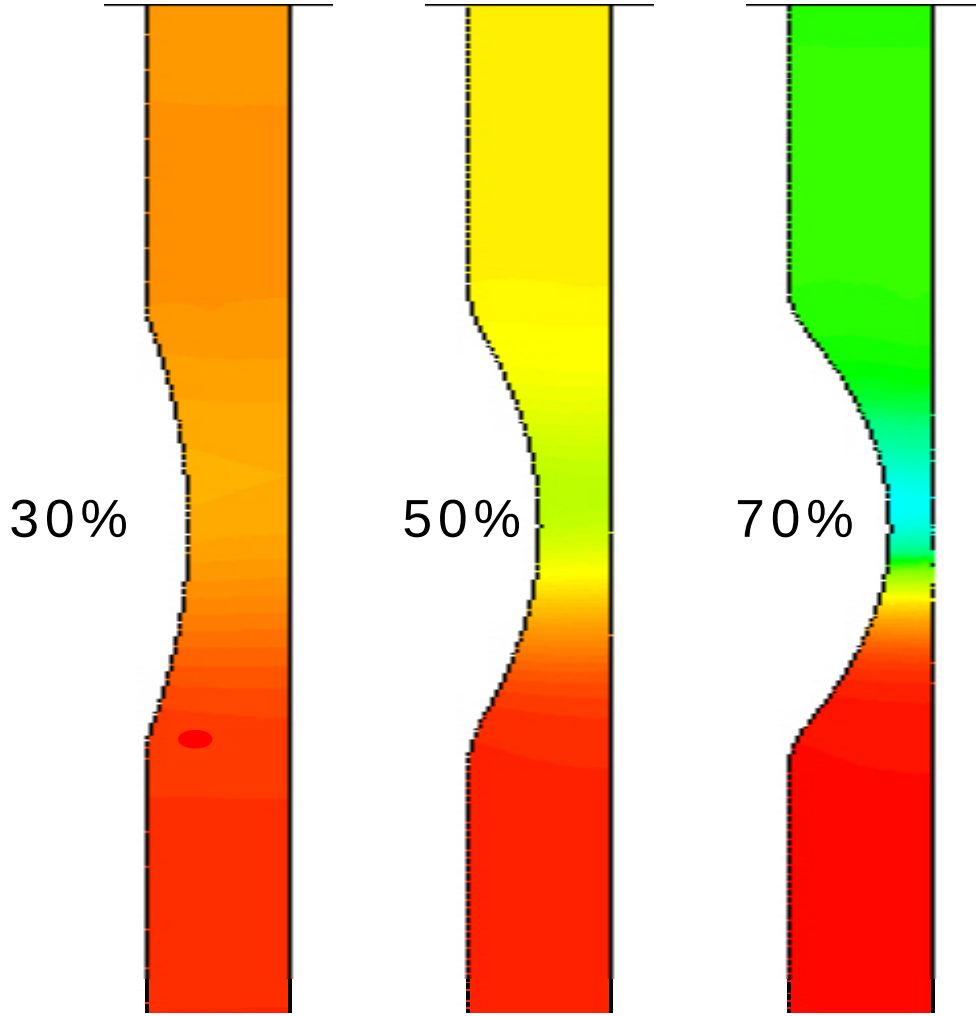
$1 : P1 + 1/2\rho v1^2 = Pt_1 \quad 2 : P2 + 1/2\rho v2^2 = Pt_2 \quad 3 : P3 + 1/2\rho v3^2 = Pt_3$



$Pt_1 > Pt_2$ $Pt_1 >> Pt_4$

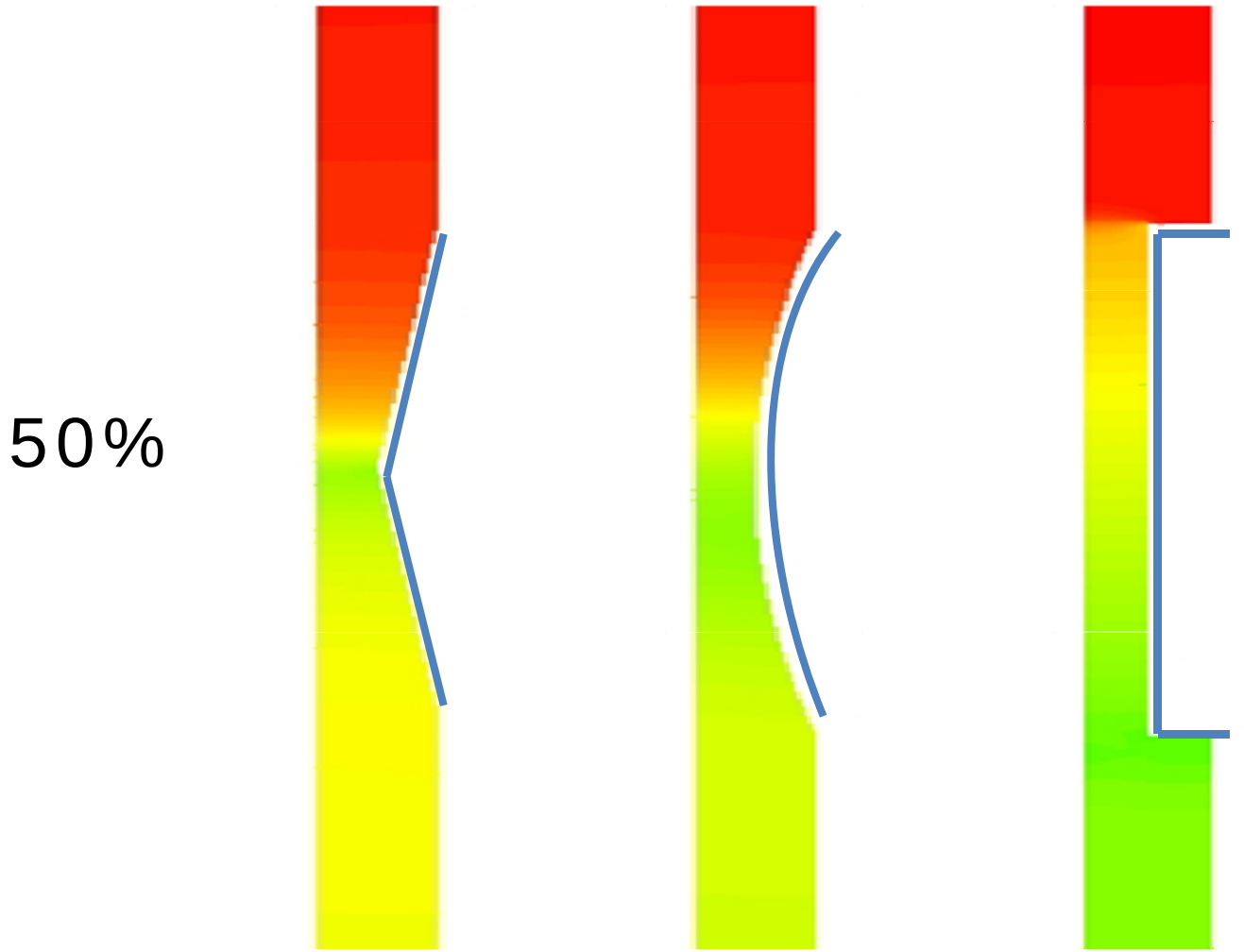
Courtesy of Prof. Shim

Degree of Stenosis



FFR	0.91	0.80	0.58

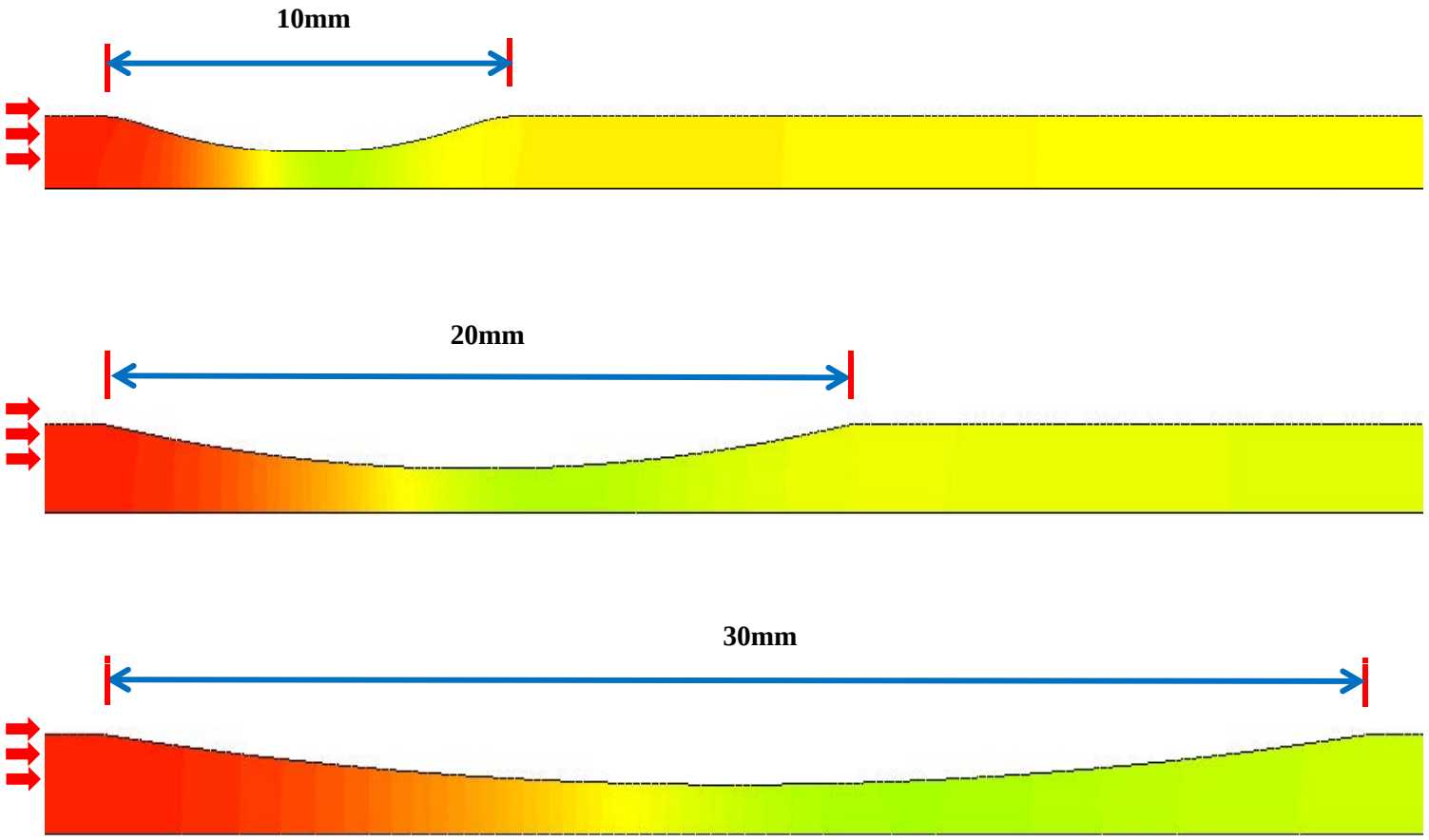
Different Morphology



Different Lesion Length

Degree of stenosis : 50%

FFR



0.80

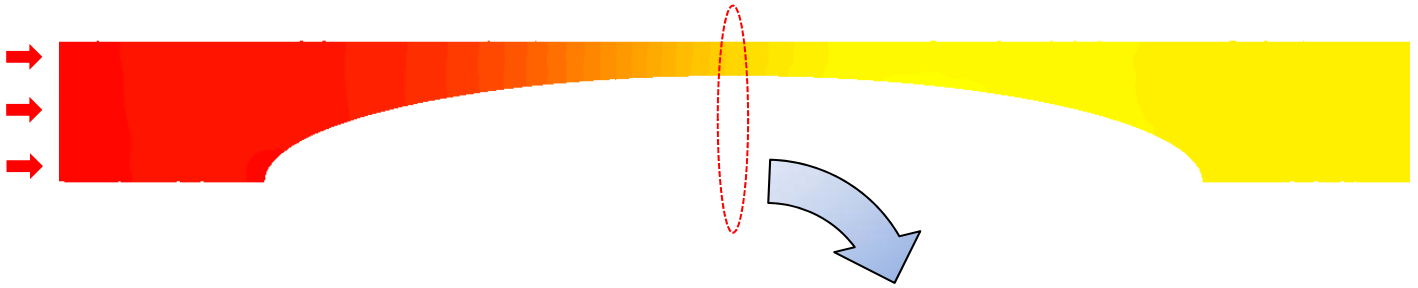
0.76

0.71

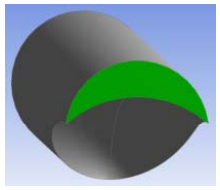
Lesion Eccentricity
(cross-sectional)

FFR

Eccentric Model

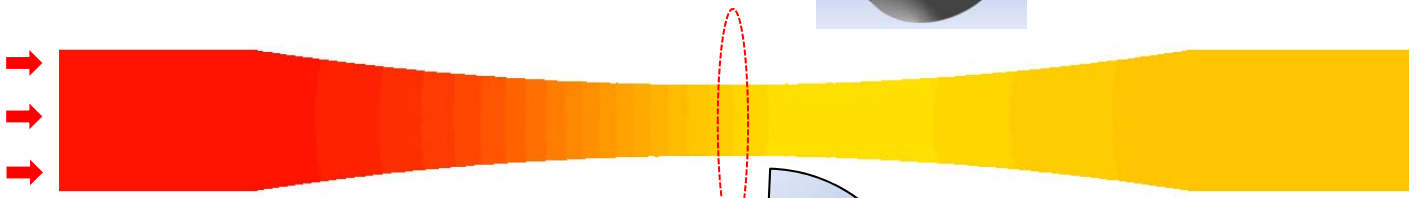


0.71

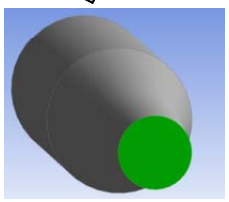


CSA : 1.83 mm²

Concentric Model

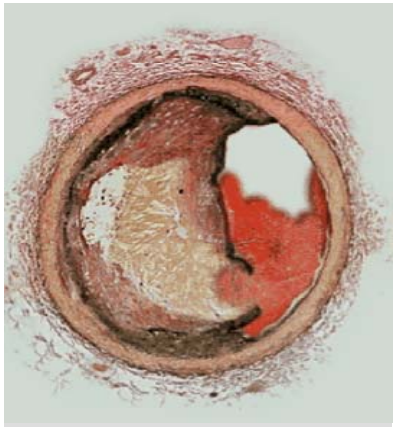


0.77



CSA : 1.83 mm²

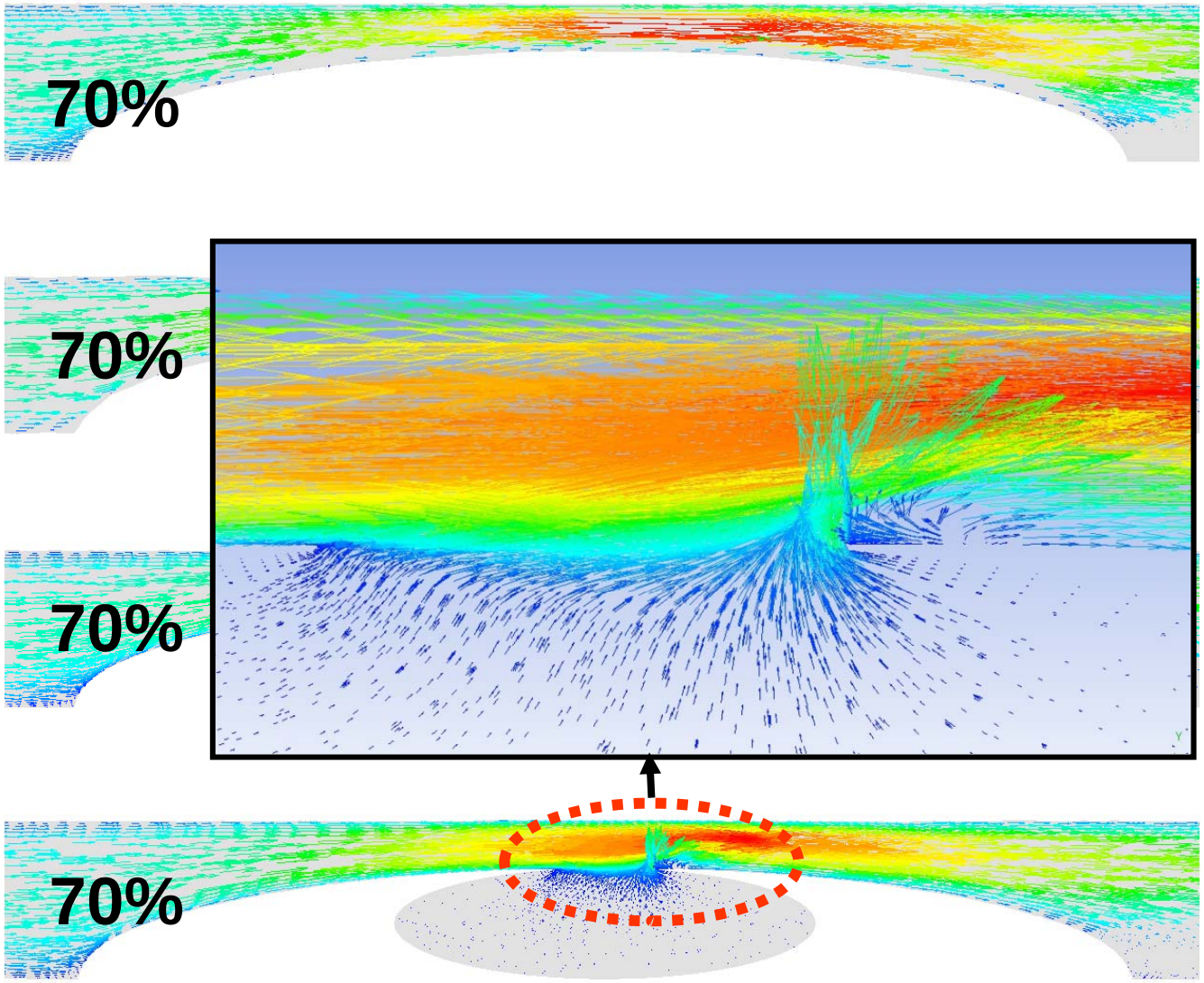
Vulnerable Plaque Simulation



Plaque rupture

Thrombus, surface roughness

Presence of Plaque Rupture



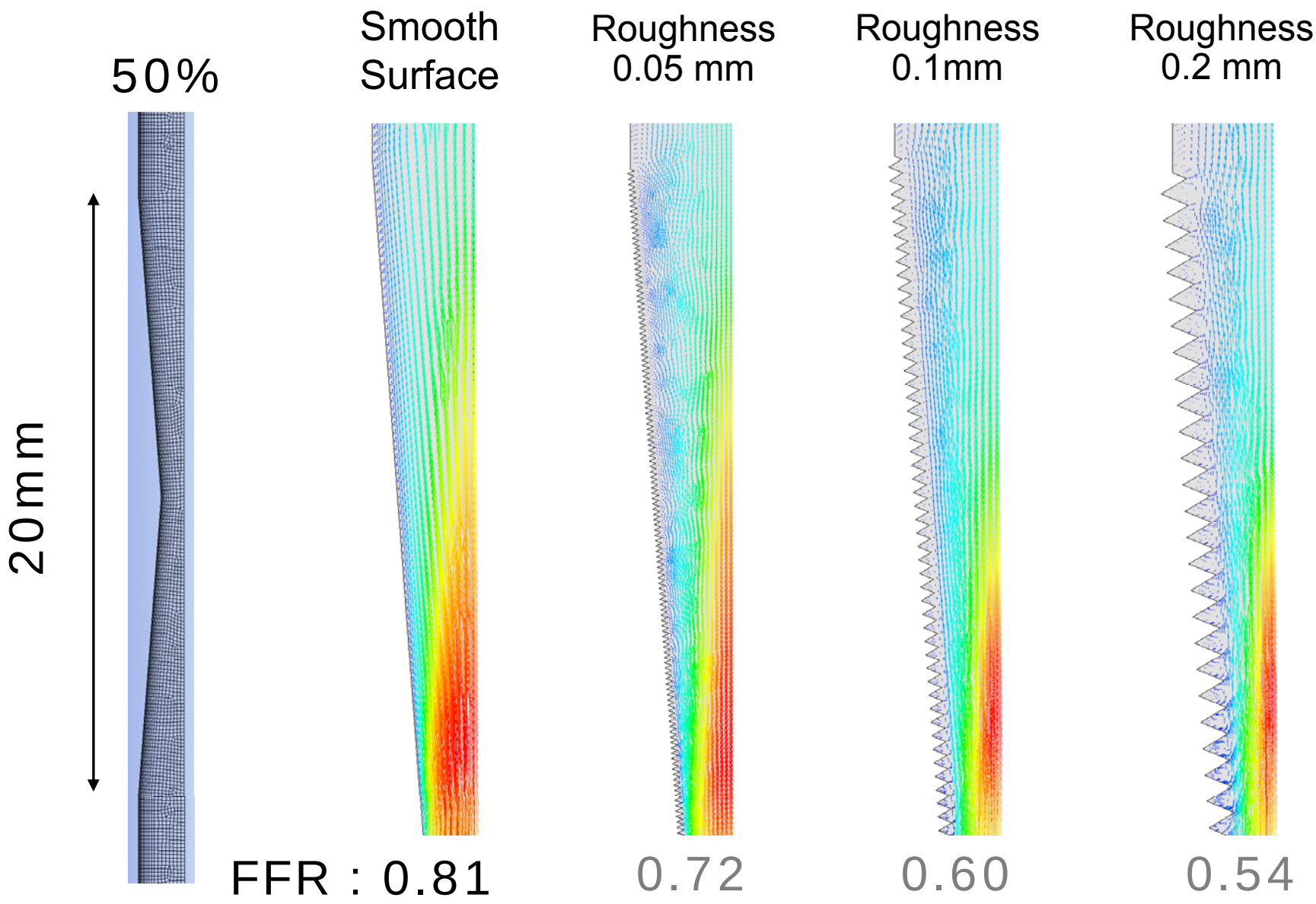
FFR : 0.62

0.68

0.66

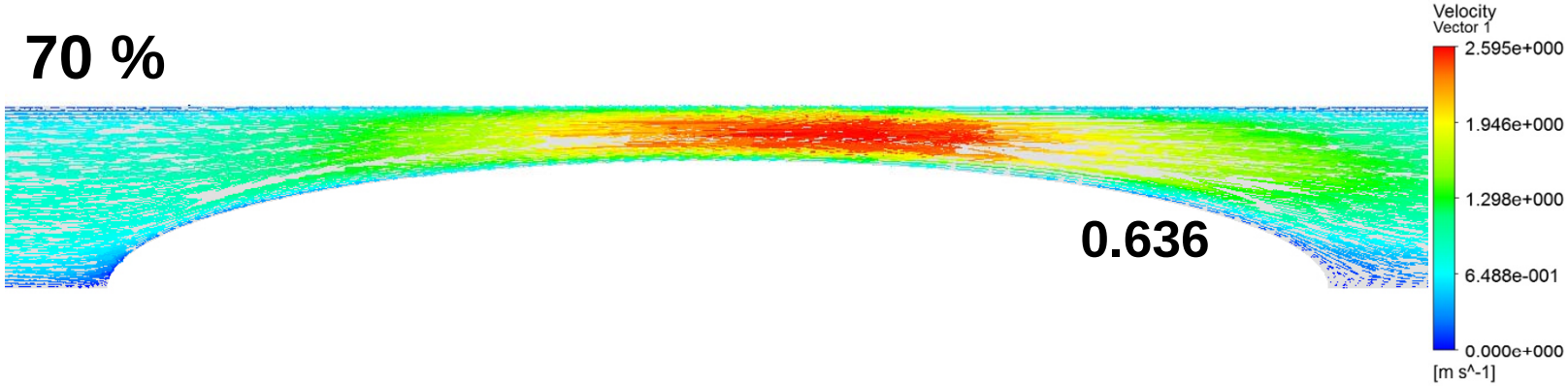
0.58

Different Surface Roughness

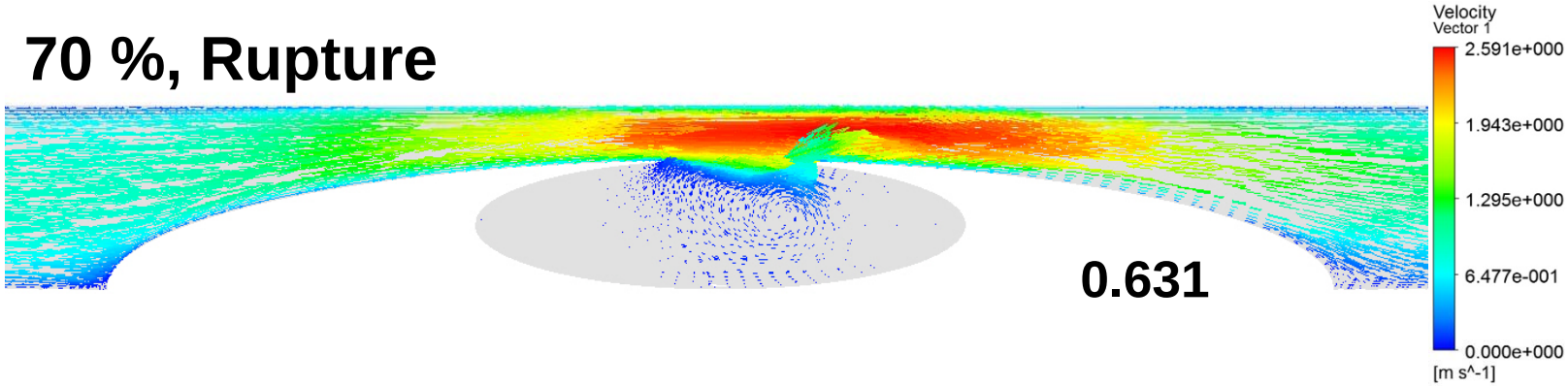


Rupture and Roughness

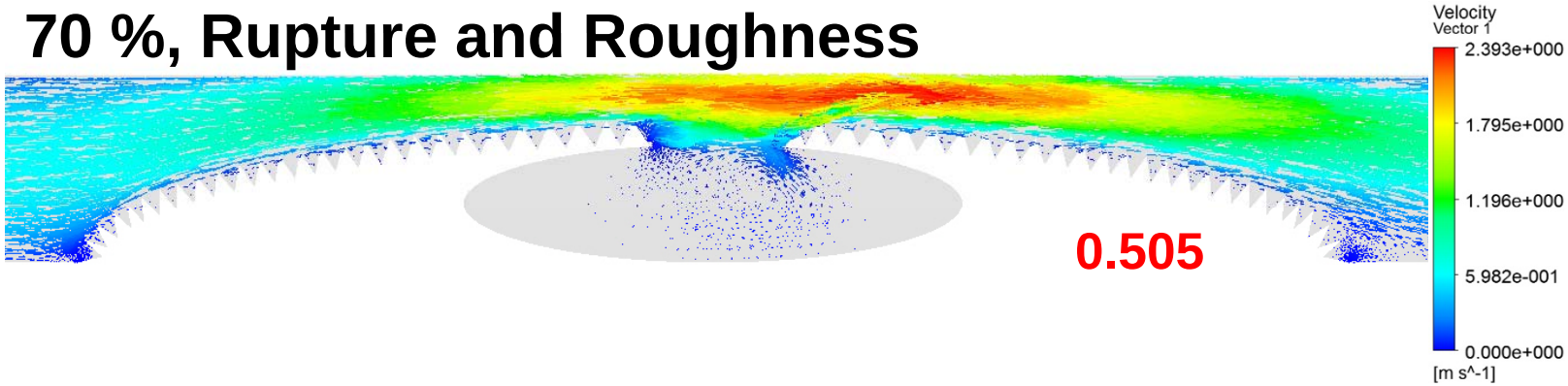
70 %



70 %, Rupture



70 %, Rupture and Roughness



FFR is influenced by Many Lesion Specific Factors

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

Conclusion 1

1. Although the same degree of stenosis can make a different FFR value according to the different lesion morphologic factors.

2. FFR, a very sensitive index integrating various local factors, is more reliable than angiographically determined stenosis severity.

Methods 2

Clinical Data
in 1000 Patients

Prospective Cohort,
1000 patients (1129 lesions)

100% QCA analysis
100% FFR
100% IVUS assessment and
core lab analysis

(ClinicalTrials.gov numbers NCT01366404)

Inclusion Criteria,

All patients were aged 35-85 years and had one target vessel with >30% diameter stenosis on visual estimation.

Exclusion Criteria,

- multiple stenoses within a single target vessel,
- bypass graft lesions,
- side branch lesions,
- in-stent restenosis,
- previous PCI in the target vessel,
- STEMI,
- TIMI flow <3,
- angiographic thrombi-containing lesions,
- IVUS-imaging catheter or FFR wire failed to cross the lesion

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%)

QCA and IVUS Data in 1066 Non-LM Lesions

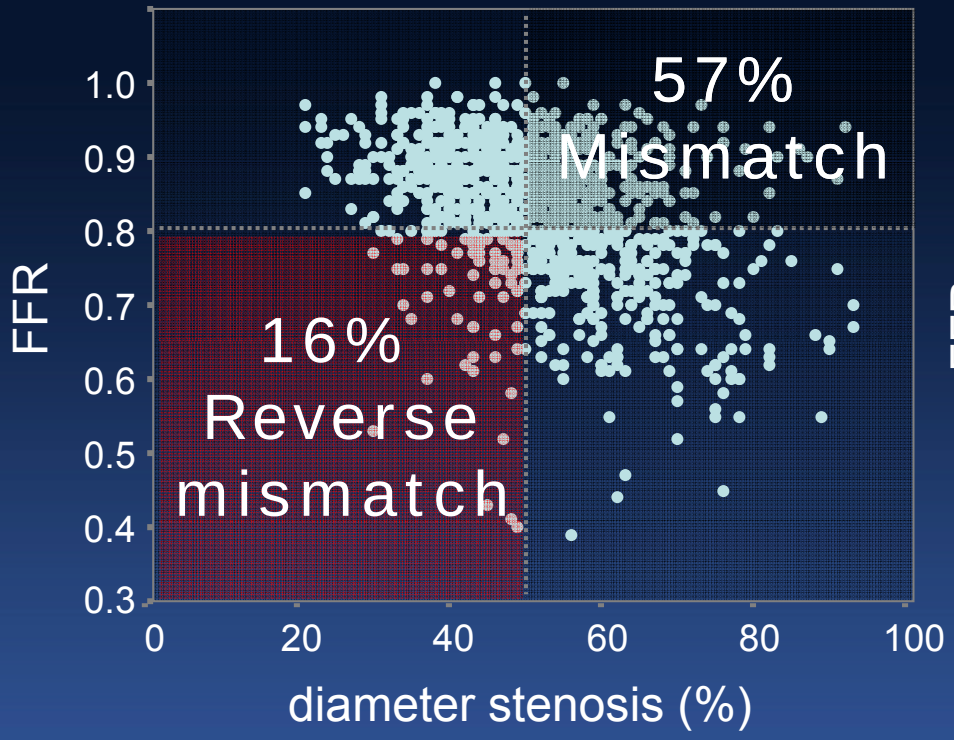
Angiographic findings	
Proximal reference lumen diameter, mm	3.4±0.5
Distal reference lumen diameter, mm	2.8±0.5
Minimal lumen diameter, mm	1.5±0.4
Diameter stenosis, %	51.4±12.2
Lesion length (mm)	19.4±12.2
IVUS findings	
Proximal reference mean lumen area, mm^2	9.10±3.3
Proximal reference mean EEM area, mm^2	15.6±4.9
Distal reference mean lumen area, mm^2	7.3±2.9
Distal reference mean EEM area, mm^2	11.4±4.9
Minimal lumen area, mm^2	2.7±1.2
Plaque burden at the minimal lumen area site, %	73.6±12.1
Plaque rupture	123 (11.5%)

QCA and IVUS Data in 63 LM Lesions

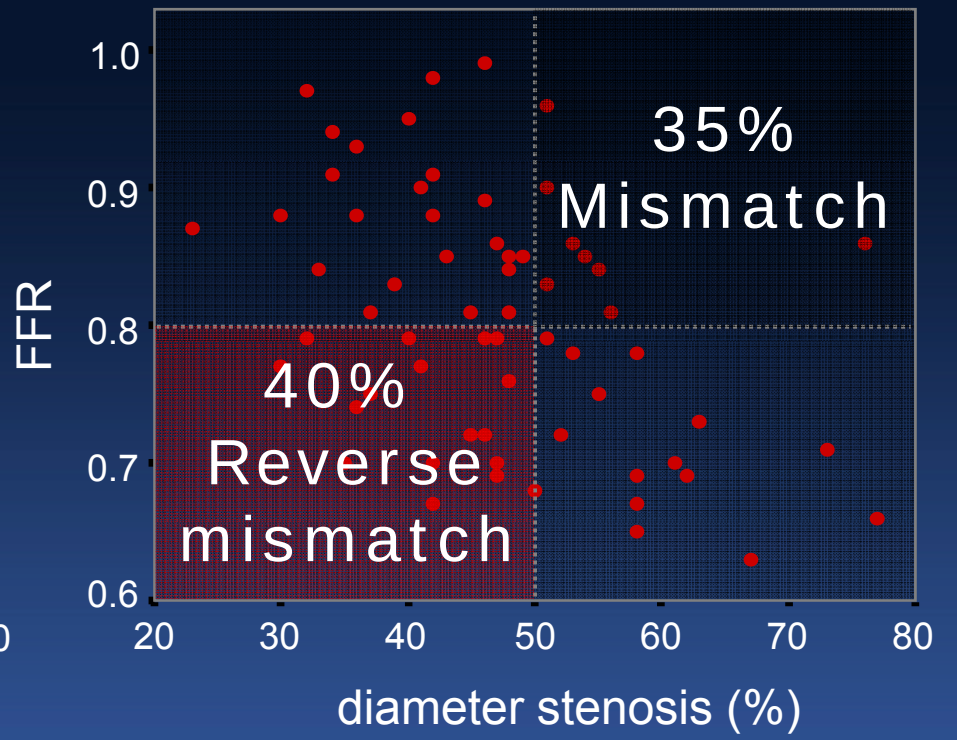
Angiographic findings	
Proximal reference lumen diameter, mm	3.8±0.6
Distal reference lumen diameter, mm	3.4±0.5
Minimal lumen diameter, mm	1.9±0.5
Diameter stenosis, %	47.0±11.1
Lesion length (mm)	11.1±8.3
IVUS findings	
EEM at the minimal lumen area site, mm^2	18.0±5.4
Minimal lumen area, mm^2	5.0±2.1
Plaque burden at the minimal lumen area site, %	70.3±14.4
Plaque rupture	22 (34.9%)

How many Mismatches ?

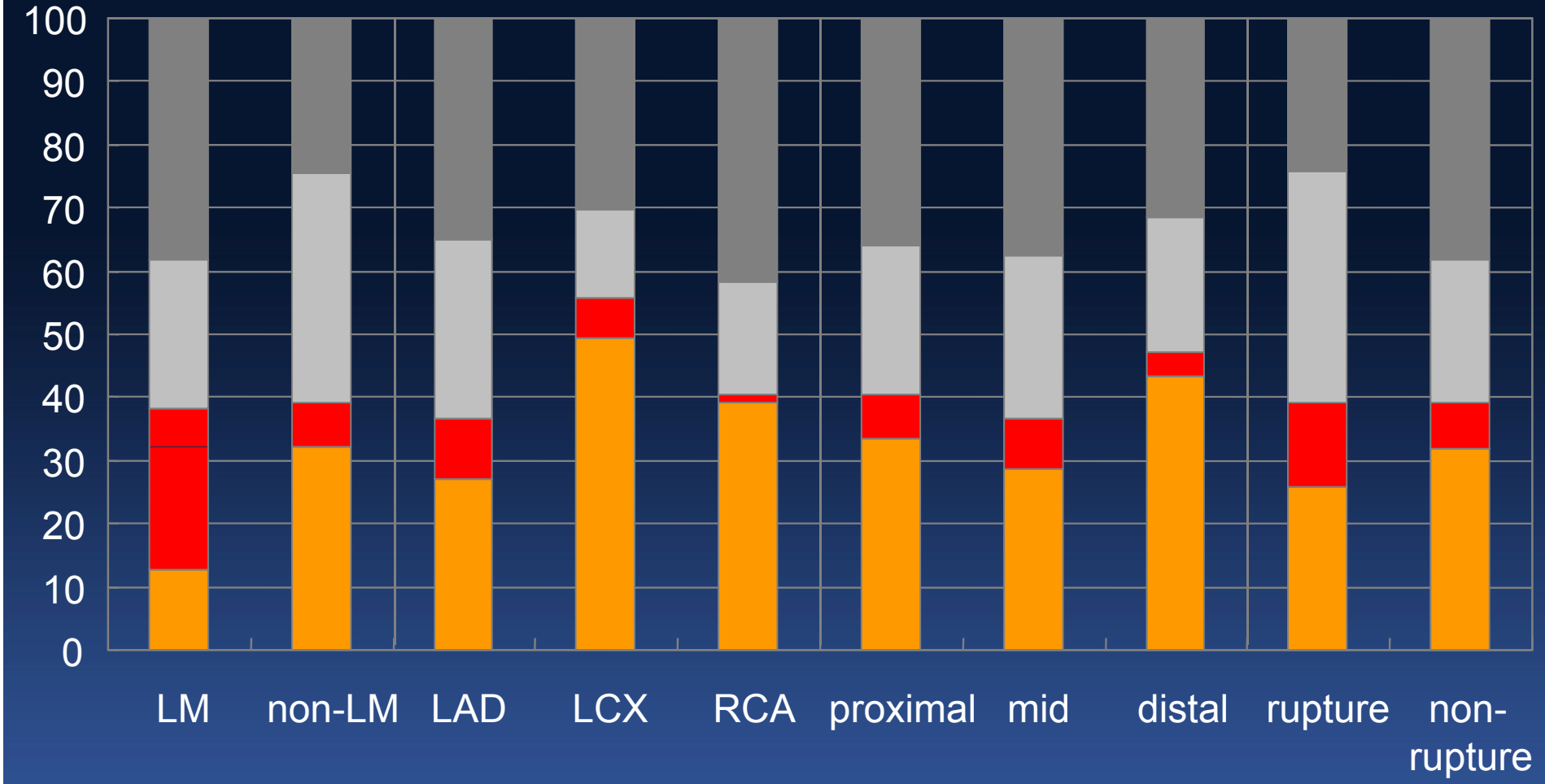
1066 Non-LM lesions



63 LM lesions

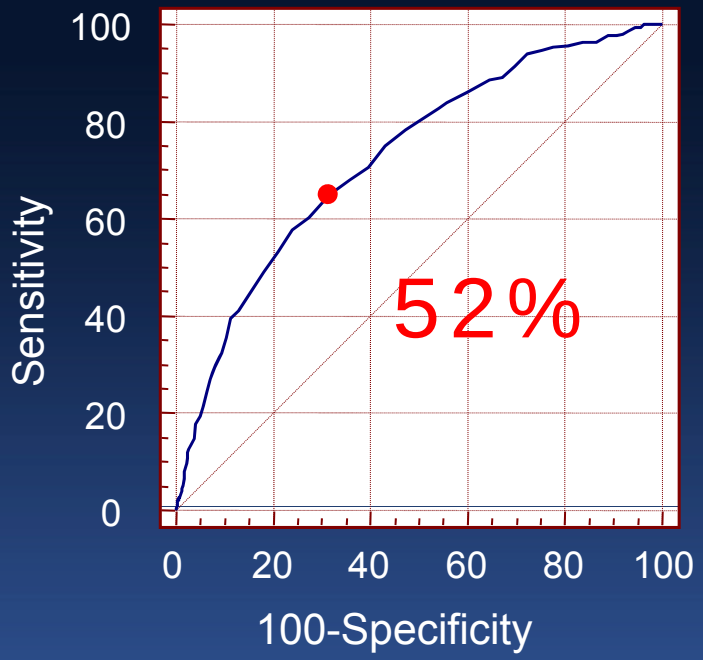


Frequencies of Mismatch



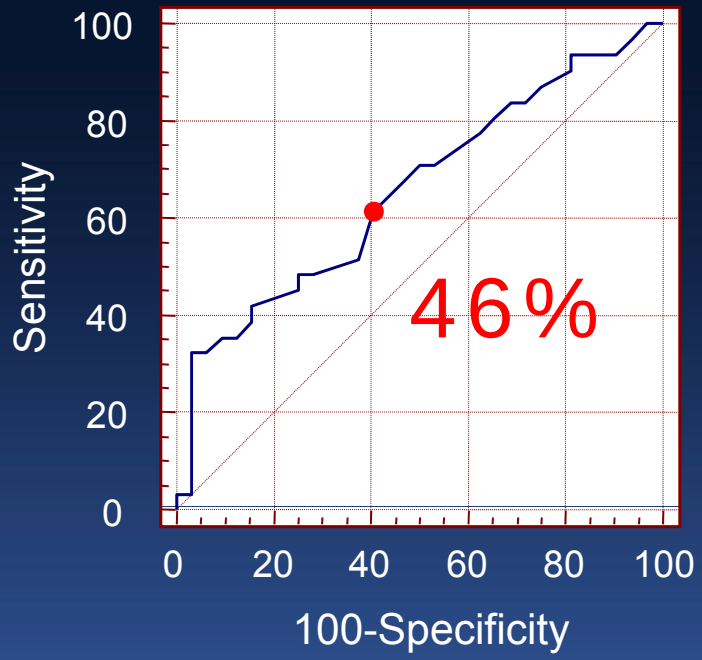
Cut-off of QCA-DS
to Predict FFR <0.80

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 Predicting "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

Conclusions

- The discrepancy between coronary angiography and FFR, was attributable to various clinical and lesion-specific factors frequently unrecognizable in diagnostic coronary angiography.
- Thus, FFR, a clinical ischemia index integrating various local factors, is more reliable than angiographically determined stenosis severity.