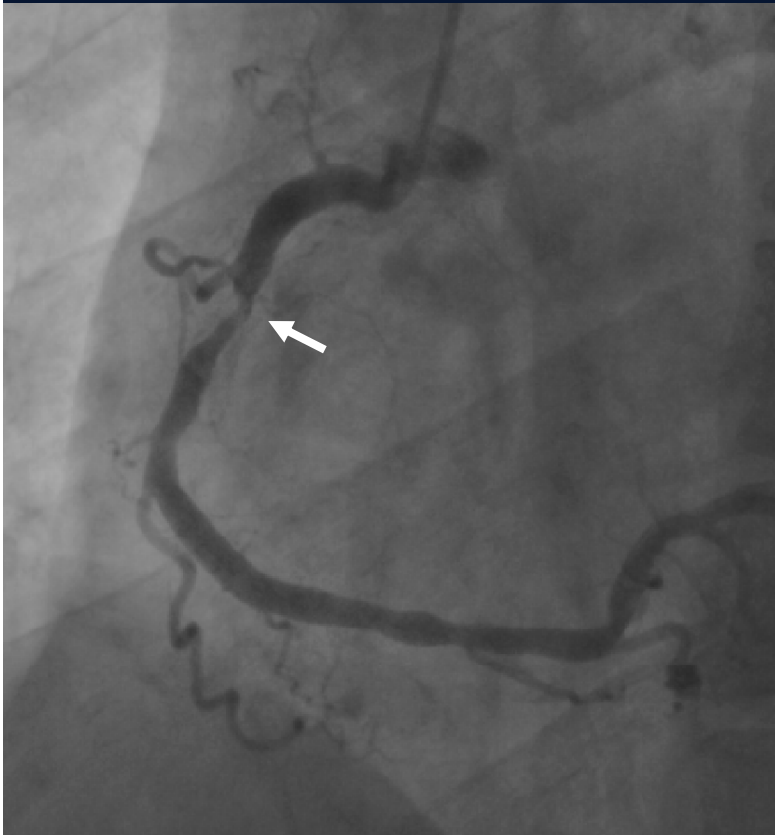


# Visual-Functional Mismatch Between Coronary Angiography and Fractional Flow Reserve

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# Visual - Functional Mismatch



Angiographic DS(%) : **85%**  
IVUS MLA : **2.8 mm<sup>2</sup>**

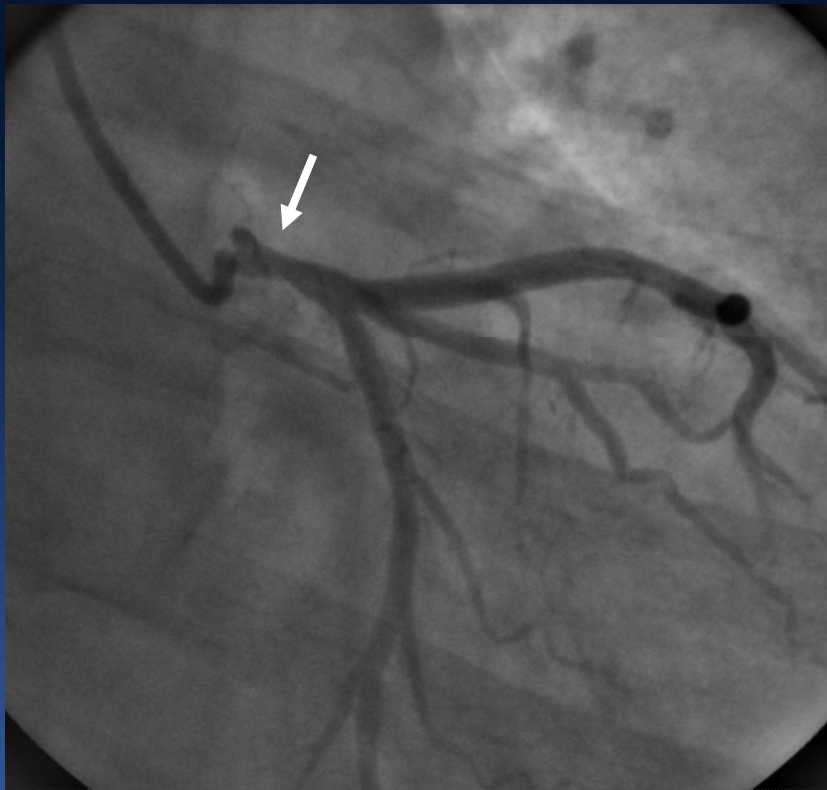
FFR : 0.84

Treadmill test : Negative

Thallium spect : Normal

Stress Echo : Normal

# Reverse **Mismatch**



Visual Estimation : 30%

FFR : **0.70**

IVUS MLA: **4.5 mm<sup>2</sup>**

Treadmill test: **+ stage 2**

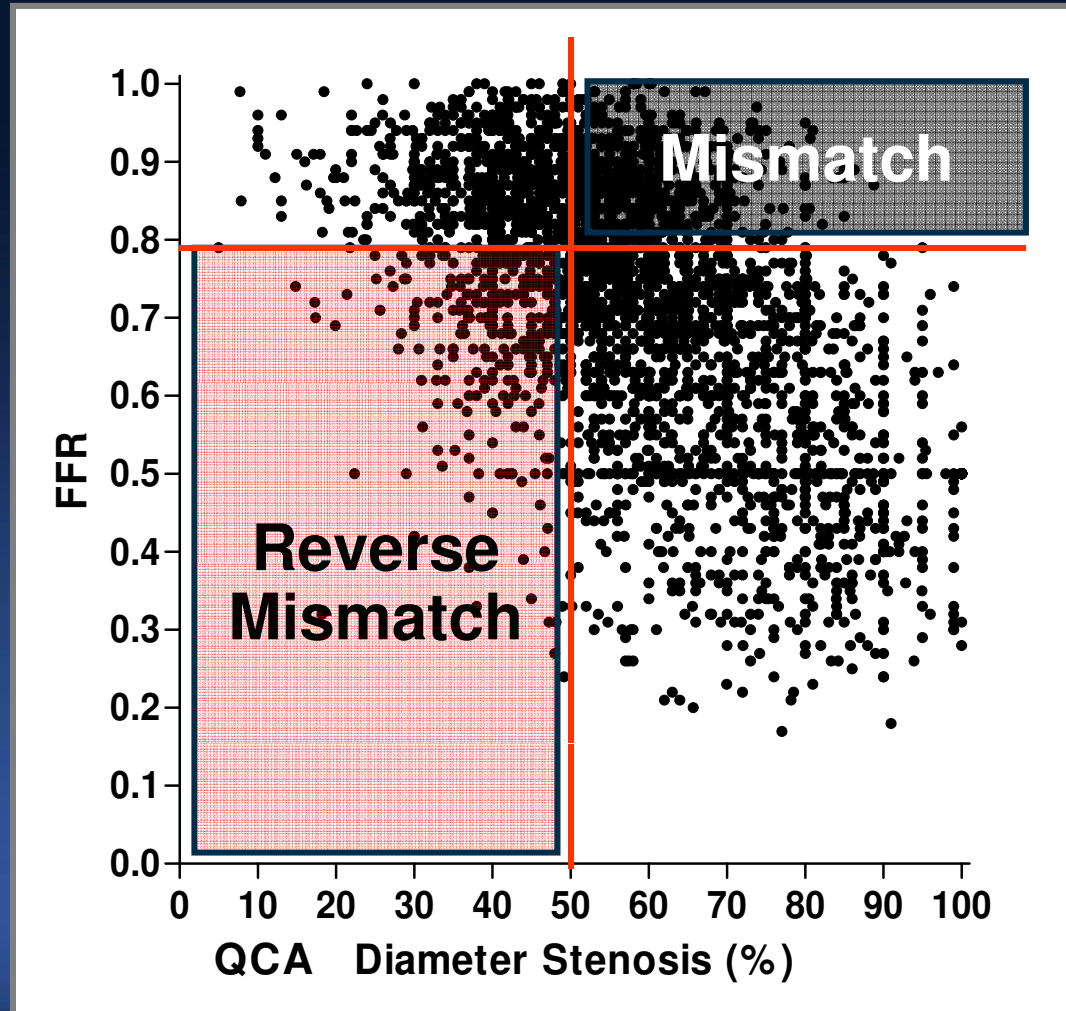
Thallium spect : **+ large  
LAD**

# How many **Mismatches** ?

# Mismatch Disease in the Cath Lab

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

FFR



QCA

**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

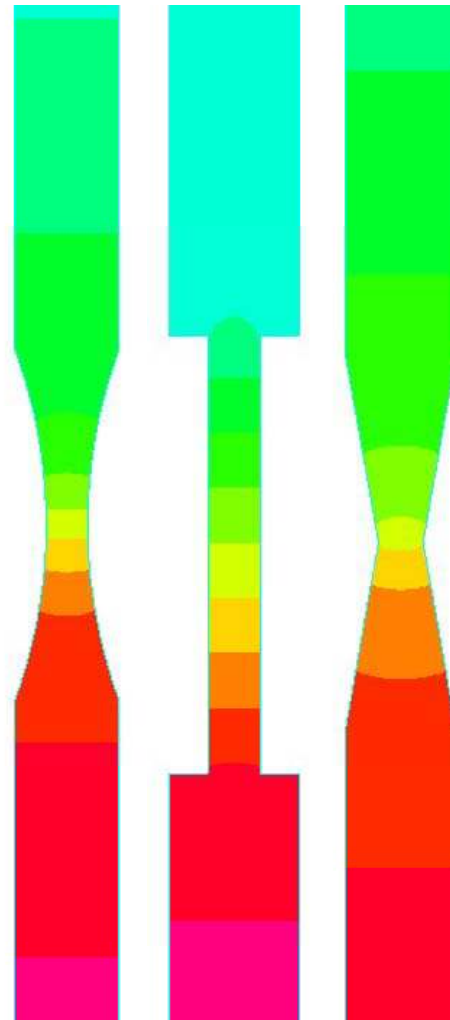
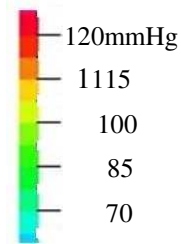
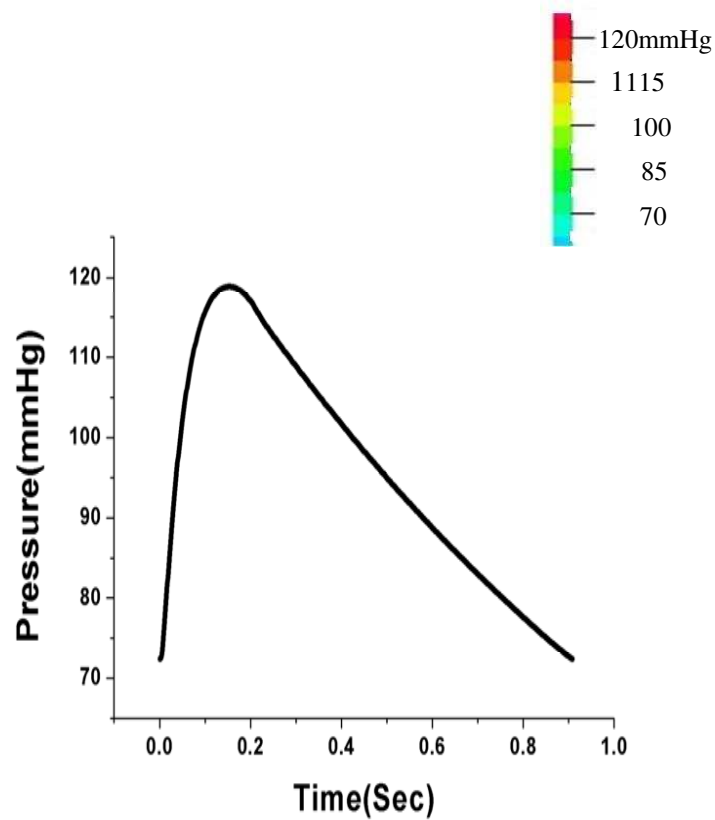
**FFR is determined by**

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

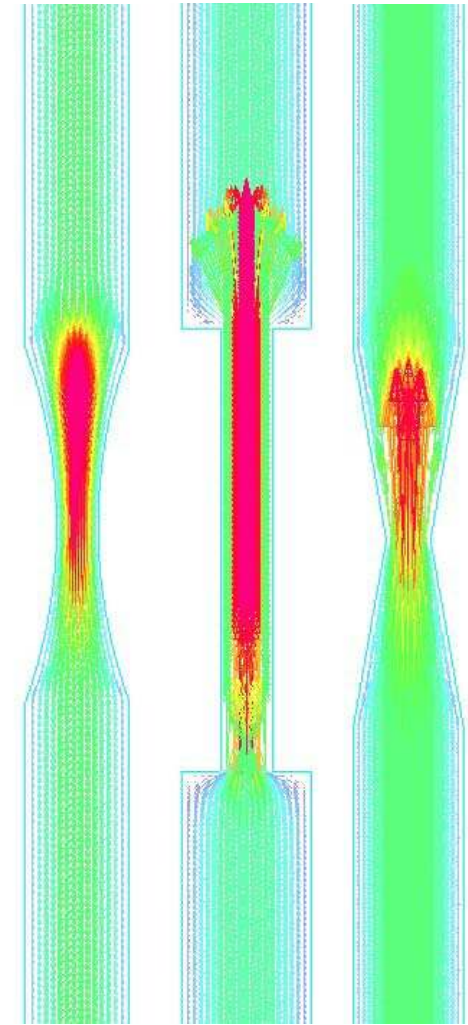
# Methods 1

## Computational Simulation Study

# Steady-state 3D Simulation under Hyperemic Condition



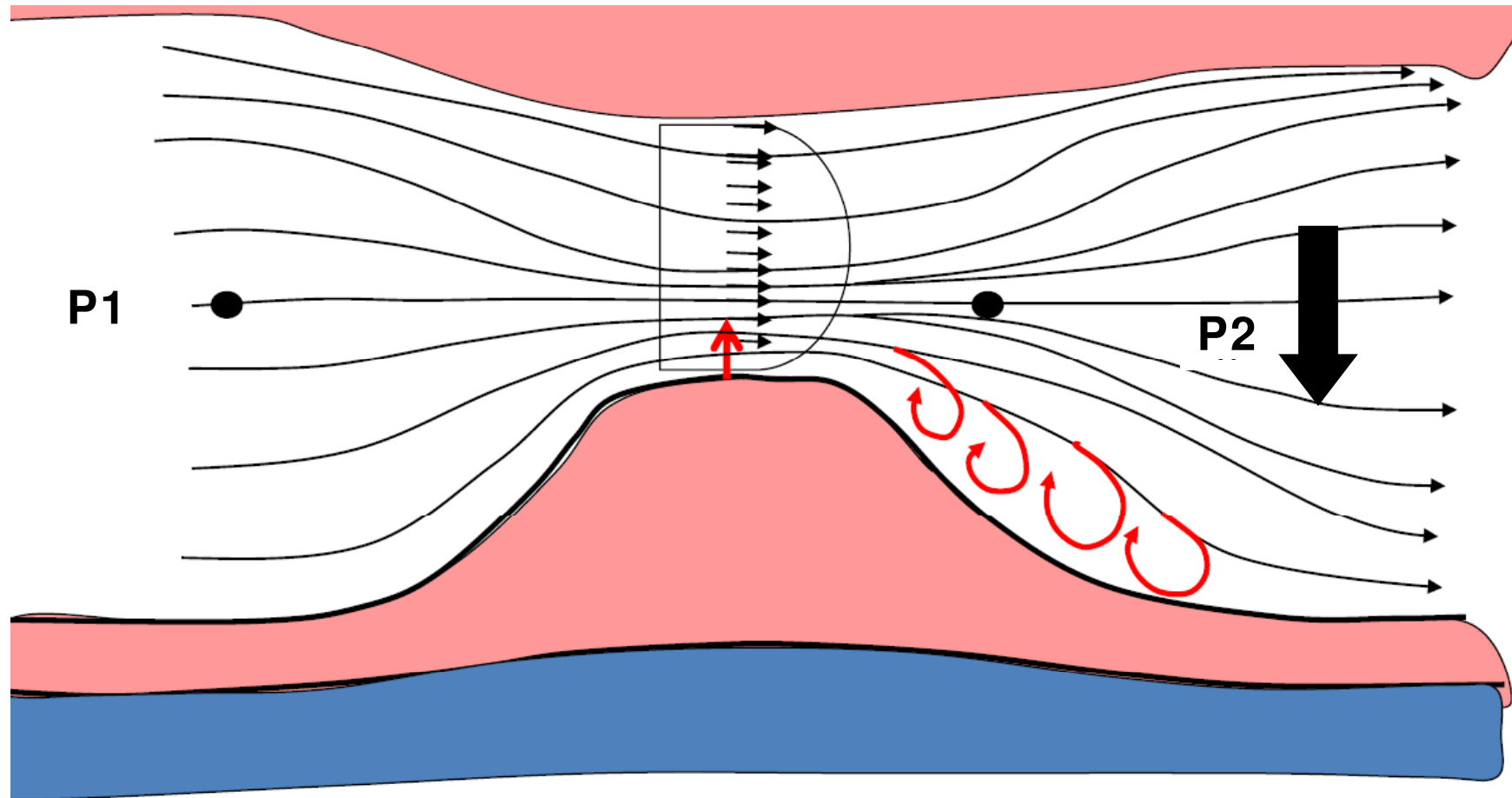
Pressure contours



Velocity vectors

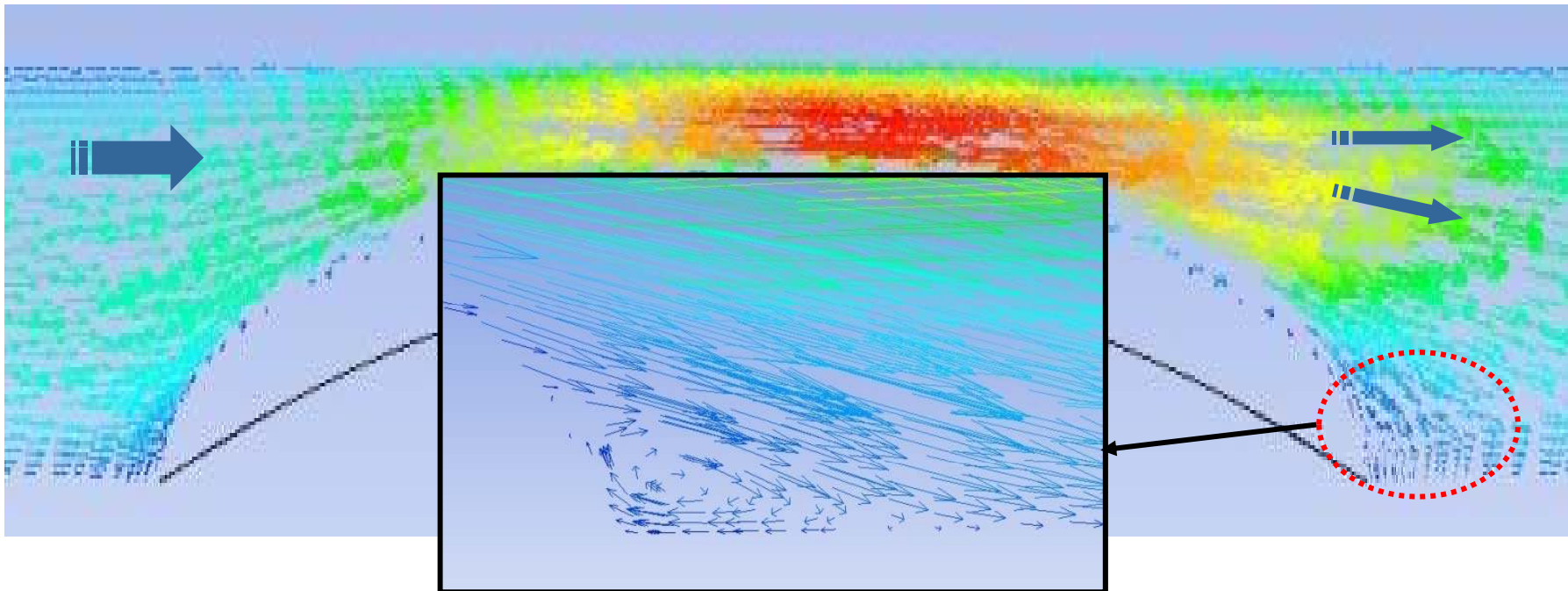
# Recirculation (Vortex)

Why  
Can make a Energy Loss of Fluid  
Pressure Drop?



# Steady-state 3D Simulation under Hyperemic Condition

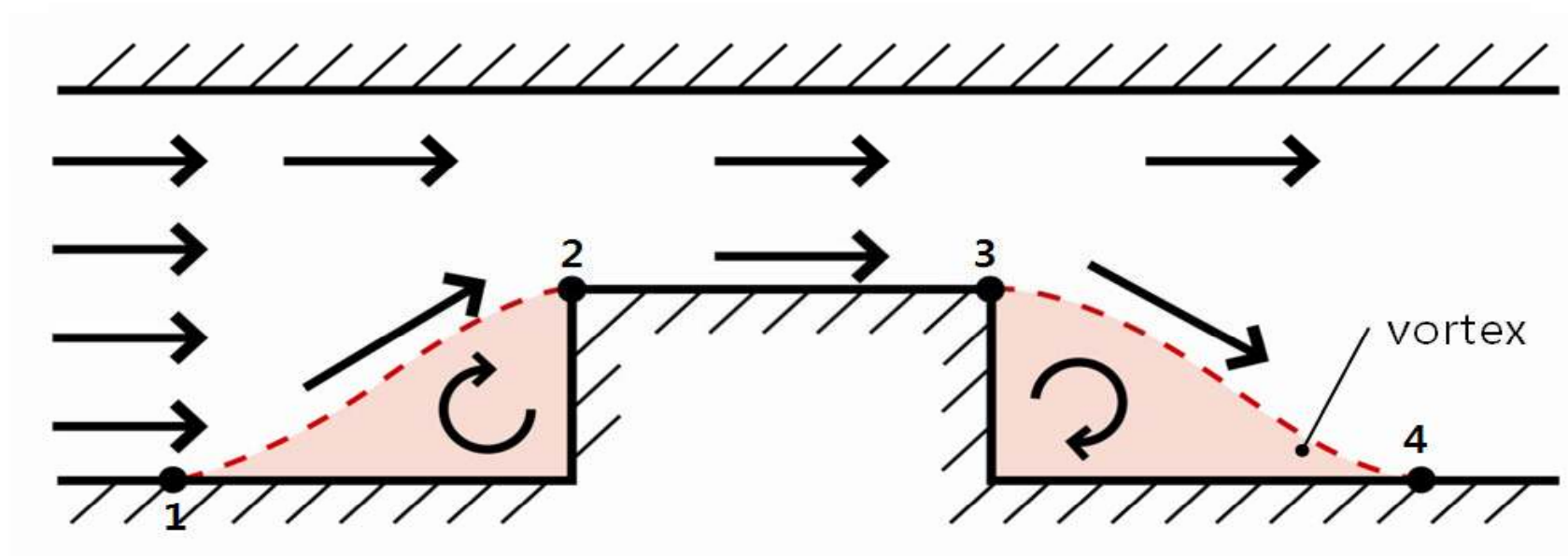
**FFR 0.62**



**Recirculation**

# Pressure Drop due to **Energy Loss of Fluid** by **Vortex Flow**

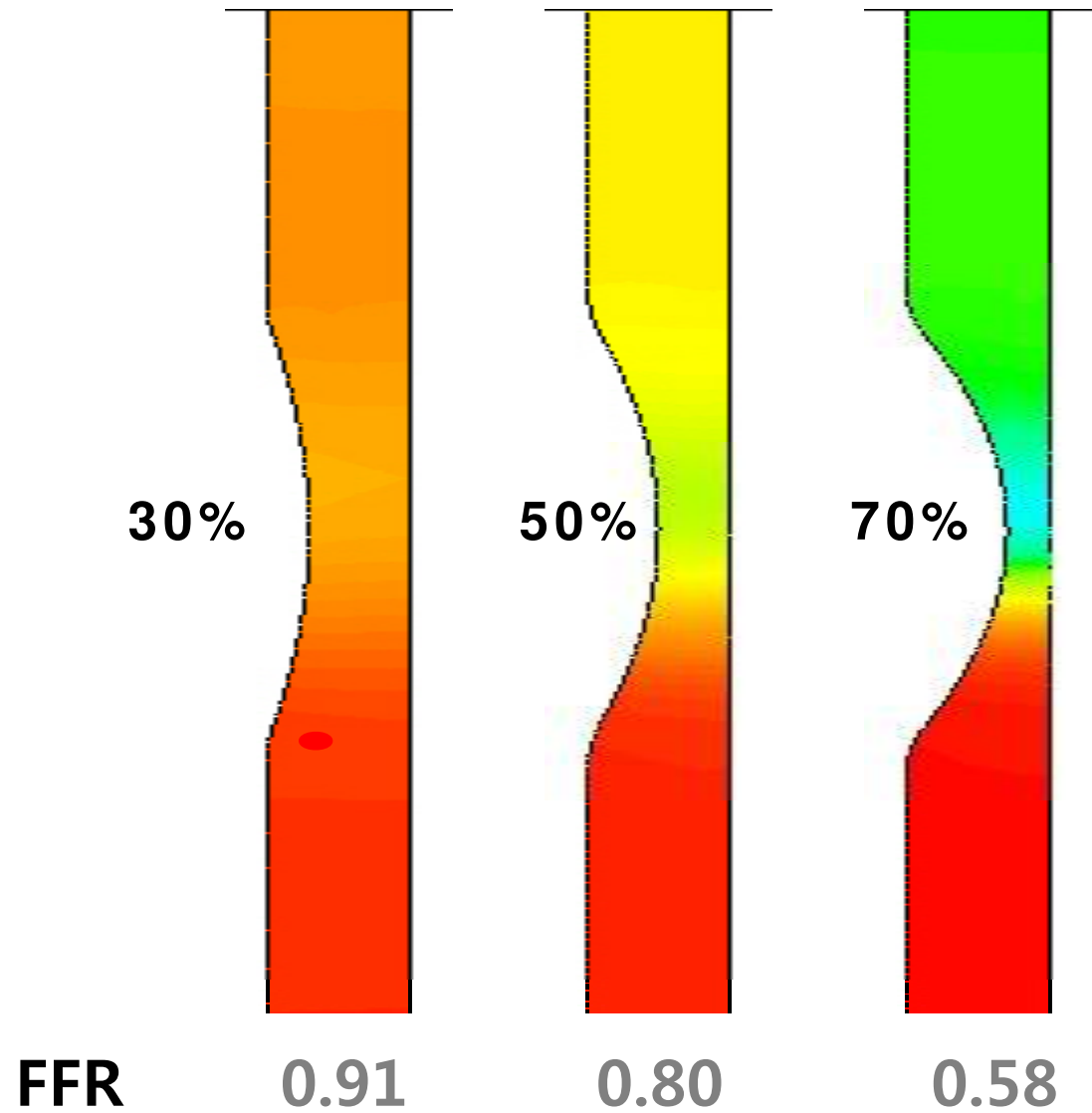
$$1 : P_1 + \frac{1}{2}\rho v_1^2 = P_{t_1} \quad 2 : P_2 + \frac{1}{2}\rho v_2^2 = P_{t_2} \quad 3 : P_3 + \frac{1}{2}\rho v_3^2 = P_{t_3}$$



$$P_{t_1} > P_{t_2}$$

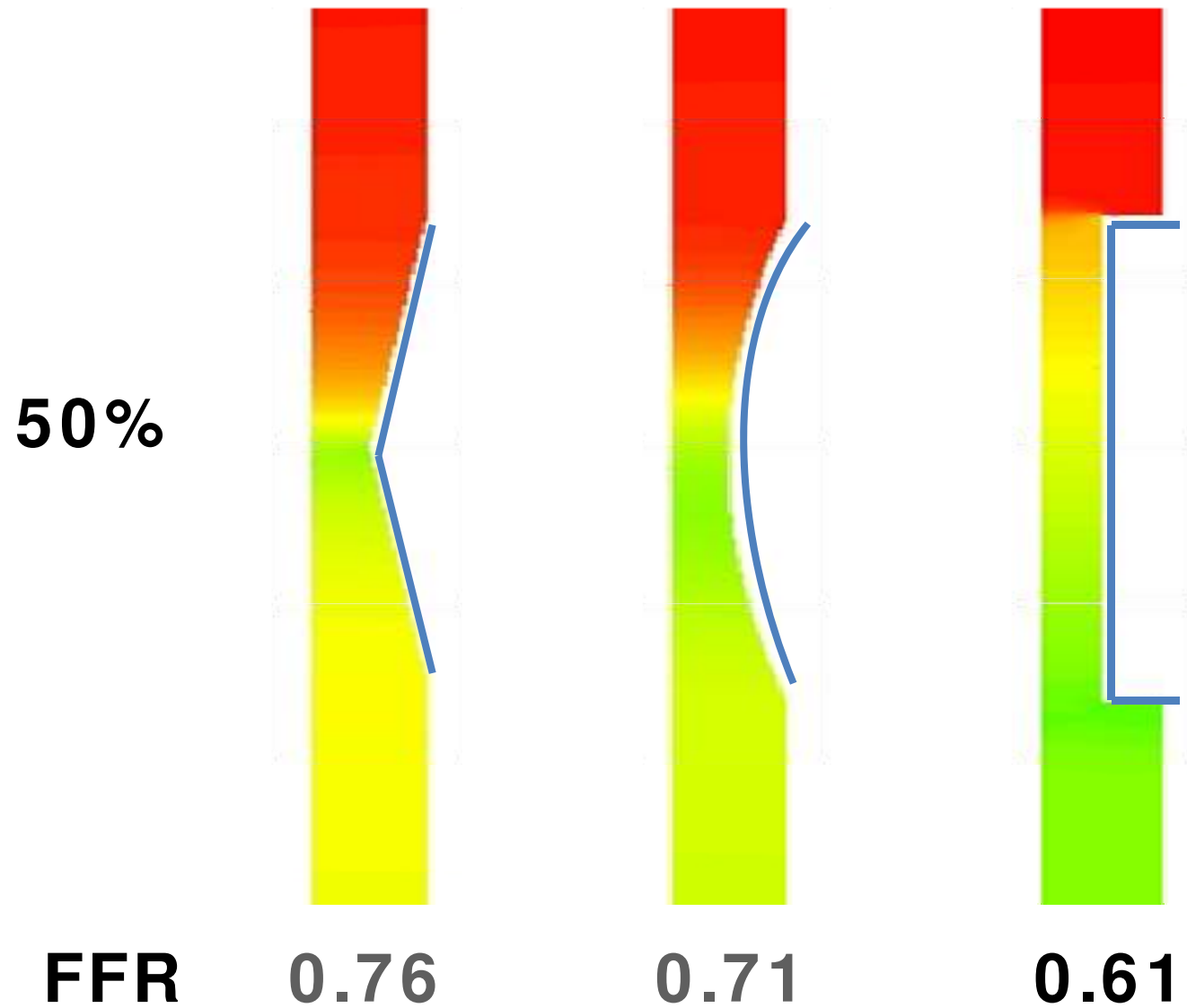
$$P_{t_1} \gg P_{t_4}$$

# Degree of Stenosis





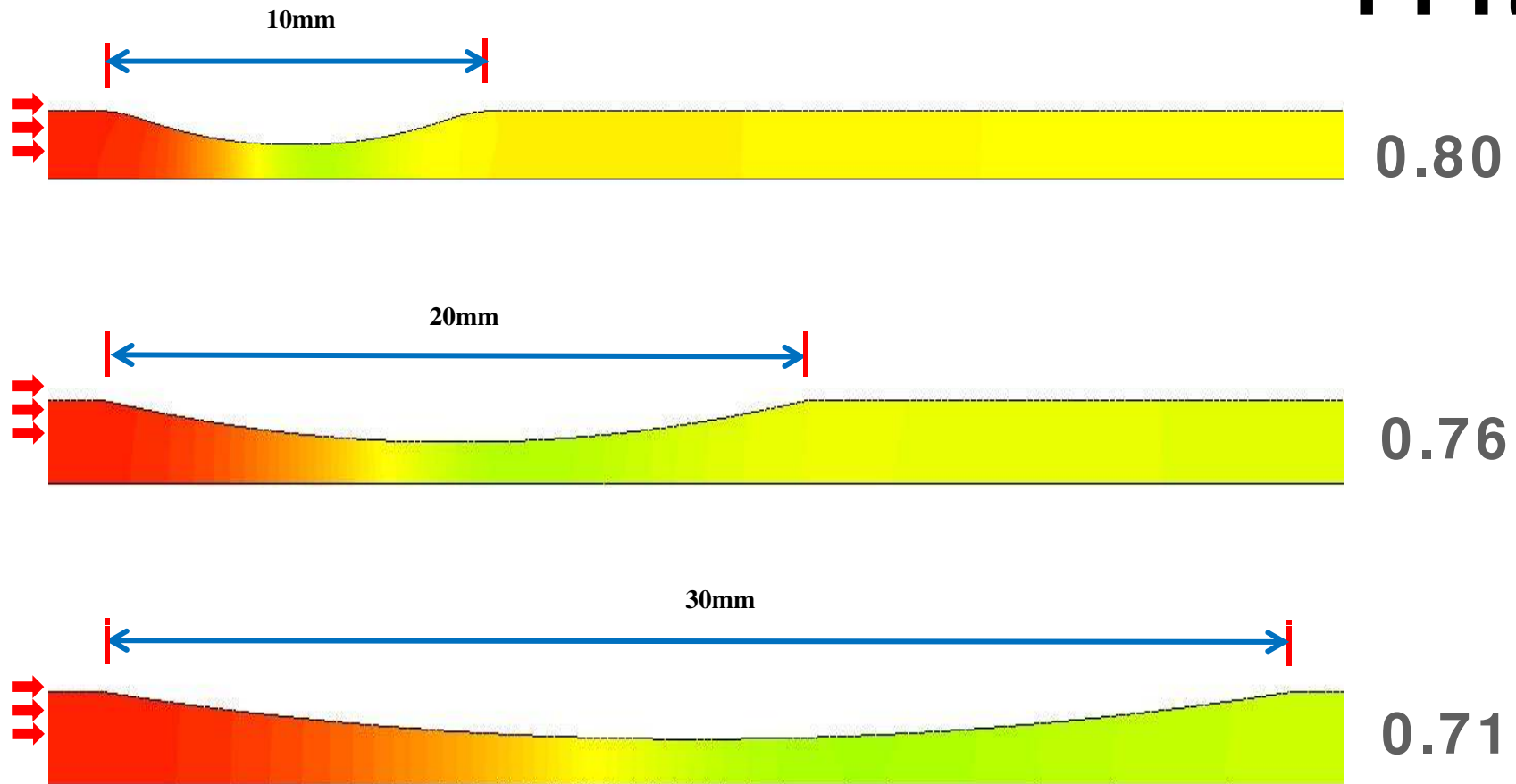
# Different Morphology



# Different Lesion Length

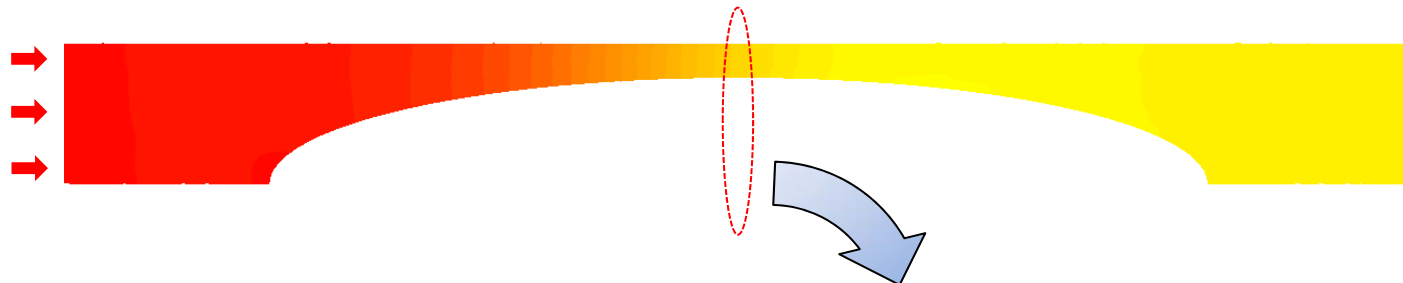
Degree of stenosis : 50%

**FFR**



# Lesion Eccentricity (cross-sectional)

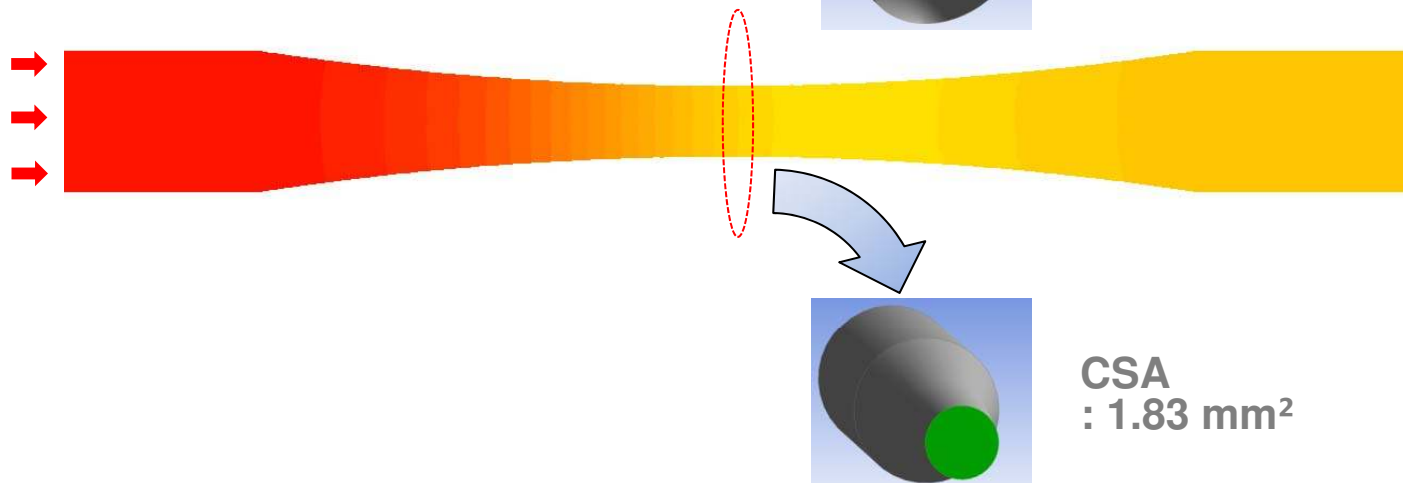
Eccentric Model



**FFR**

0.71

Concentric Model

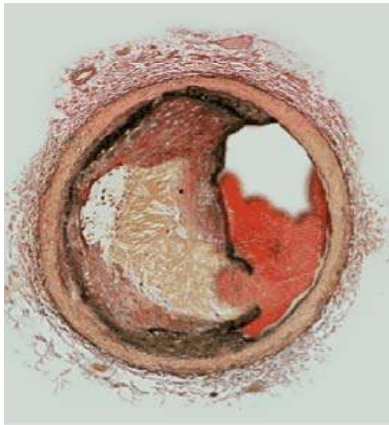


CSA  
: 1.83 mm<sup>2</sup>

0.77

CSA  
: 1.83 mm<sup>2</sup>

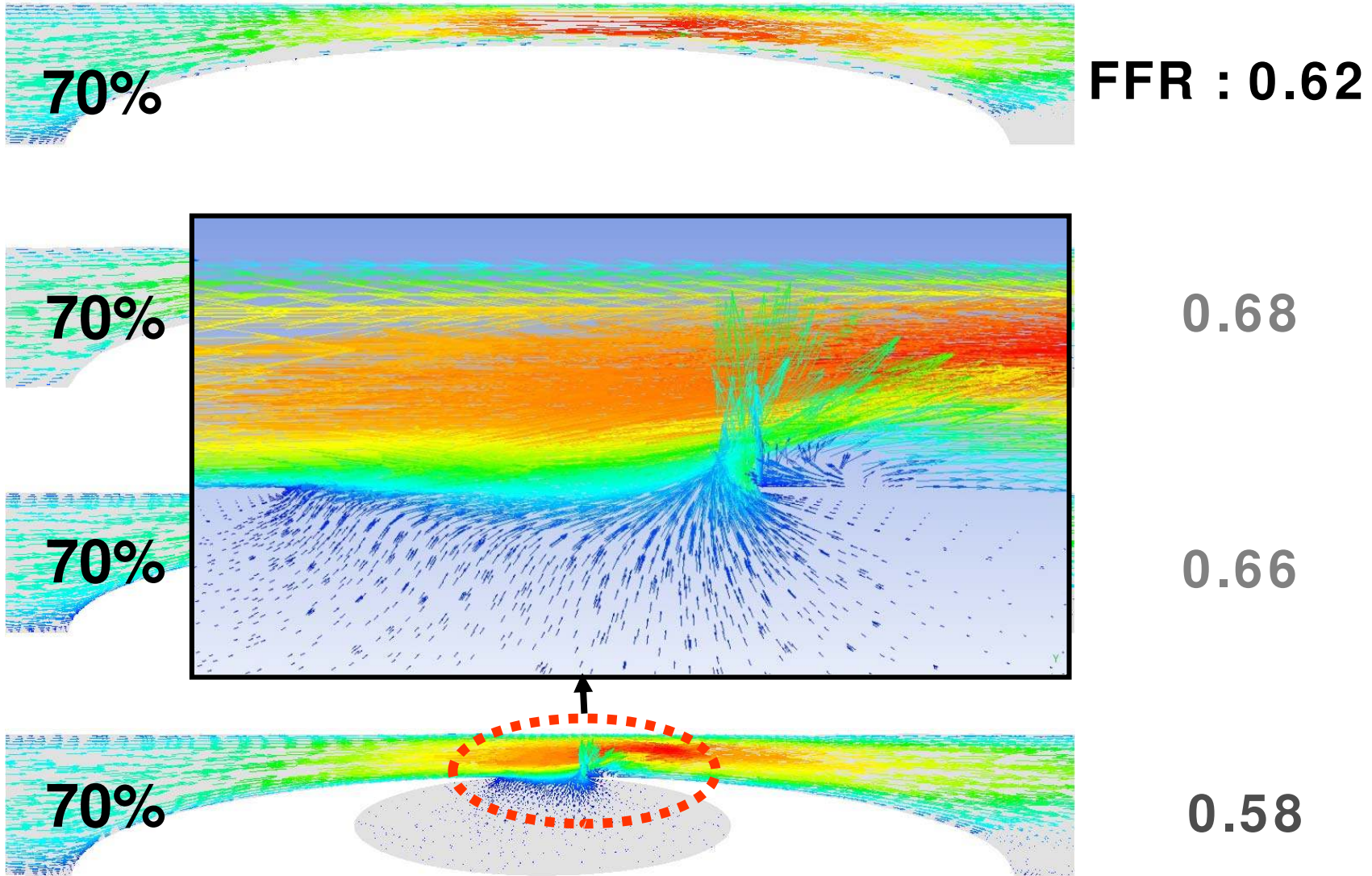
# **Vulnerable Plaque** **Simulation**



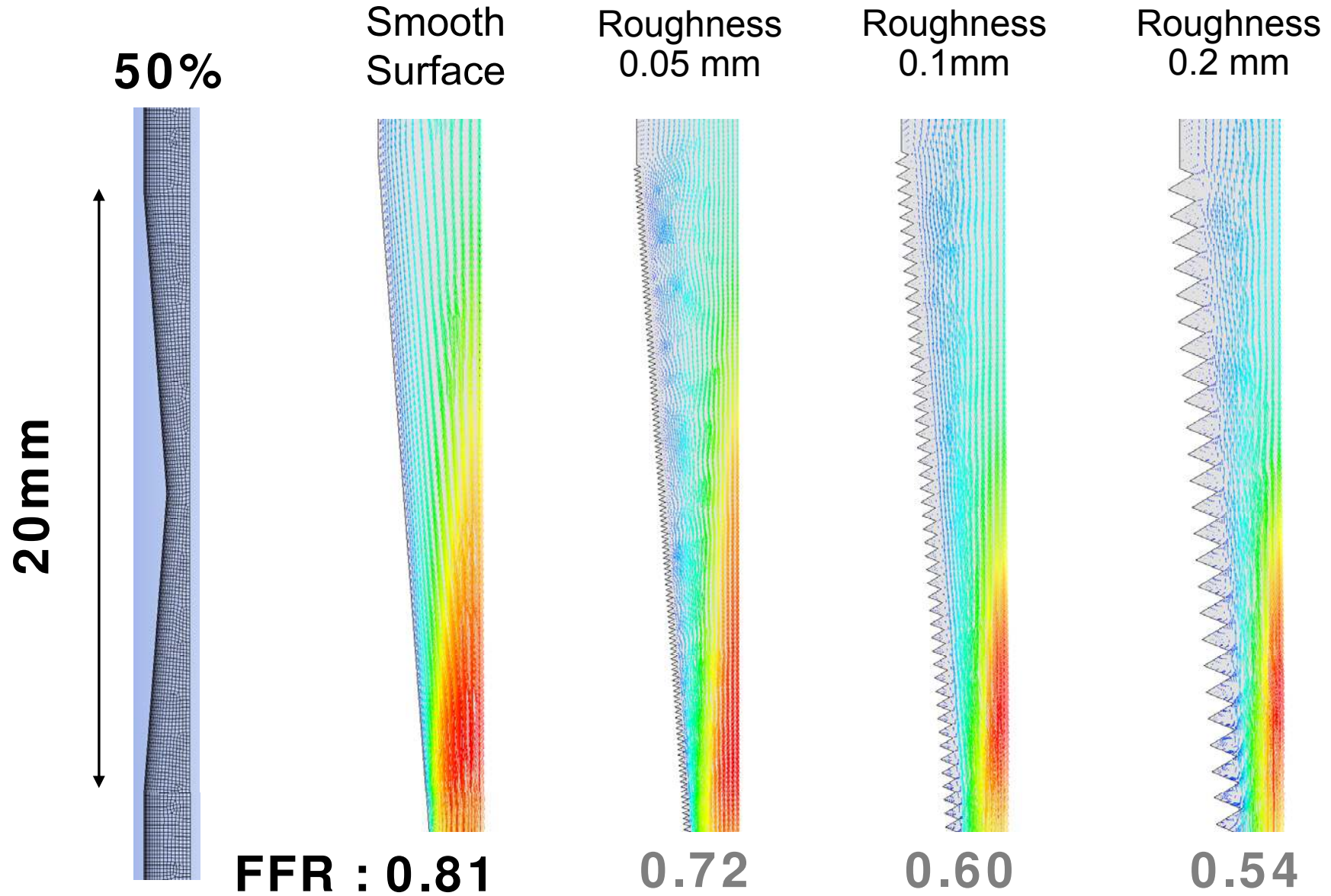
**Plaque rupture**

**Thrombus, surface roughness**

# Presence of Plaque Rupture

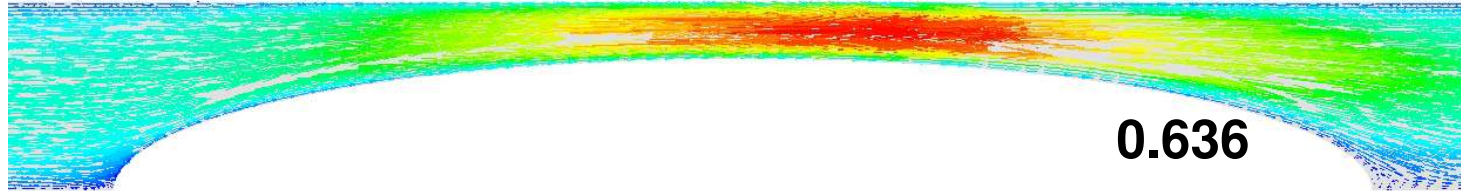


# Different Surface Roughness

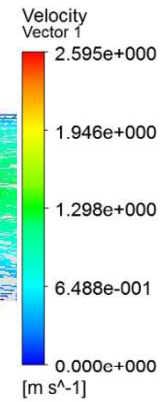


# Rupture and Roughness

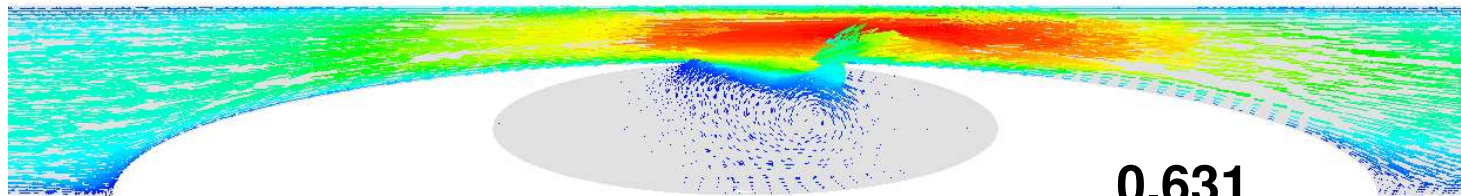
70 %



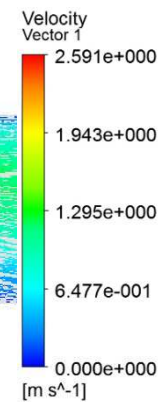
0.636



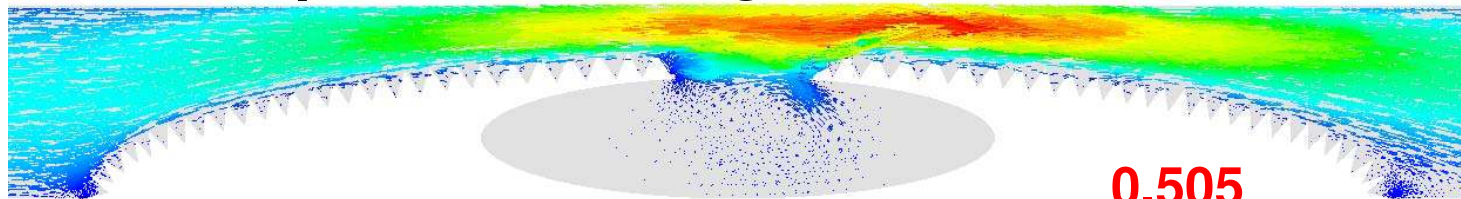
70 %, Rupture



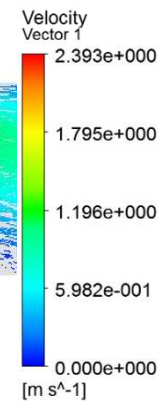
0.631



70 %, Rupture and Roughness



0.505



# **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

<b>Angiographic findings</b>	
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
<b>IVUS findings</b>	
Proximal reference mean lumen area, mm <sup>2</sup>	9.10±3.3
Proximal reference mean EEM area, mm <sup>2</sup>	15.6±4.9
Distal reference mean lumen area, mm <sup>2</sup>	7.3±2.9
Distal reference mean EEM area, mm <sup>2</sup>	11.4±4.9
Minimal lumen area, mm <sup>2</sup>	2.7±1.2
Plaque burden at the minimal lumen area site, %	73.6±12.1
Plaque rupture	123 (11.5%)

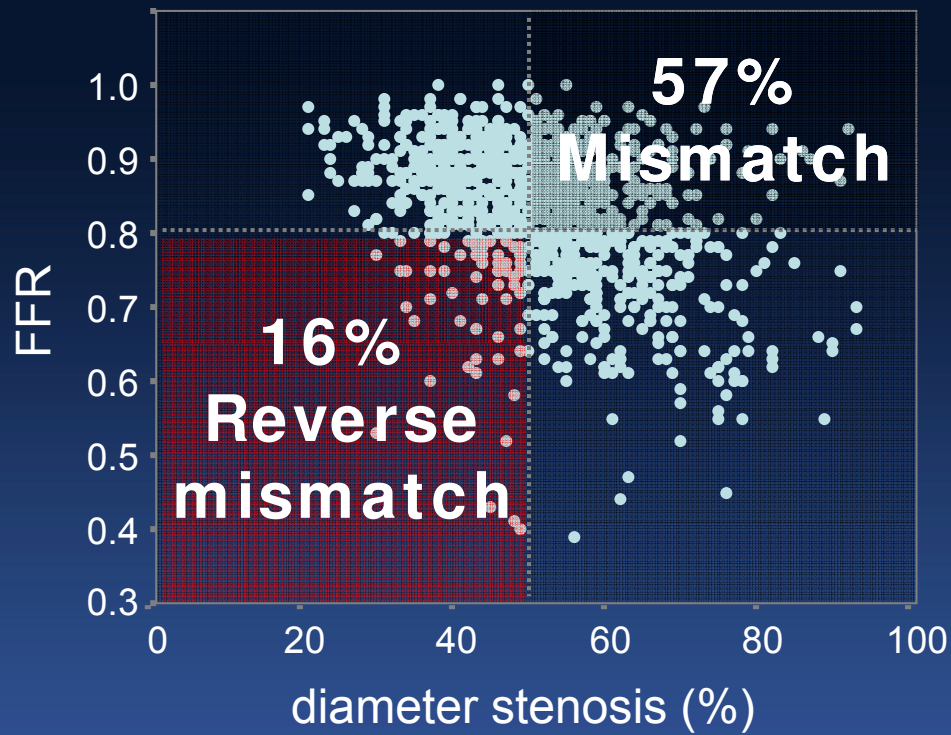


# QCA and IVUS Data in 63 LM Lesions

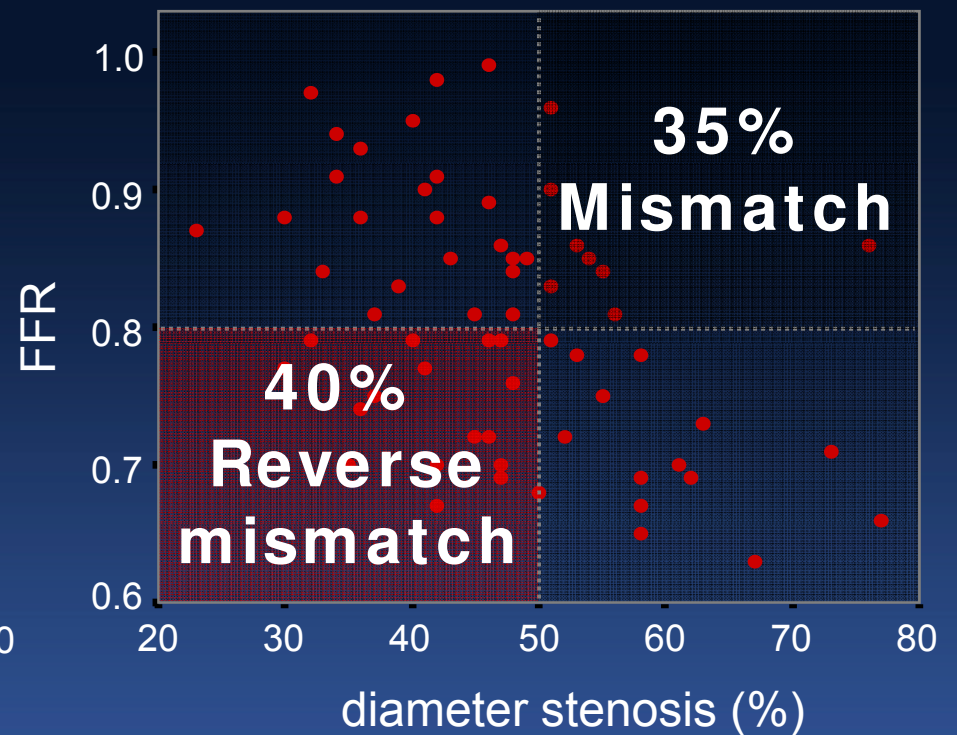
<b>Angiographic findings</b>	
Proximal reference lumen diameter, mm	3.8±0.6
Distal reference lumen diameter, mm	3.4±0.5
Minimal lumen diameter, mm	1.9±0.5
Diameter stenosis, %	47.0±11.1
Lesion length (mm)	11.1±8.3
<b>IVUS findings</b>	
EEM at the minimal lumen area site, mm <sup>2</sup>	18.0±5.4
Minimal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

# How many **Mismatches** ?

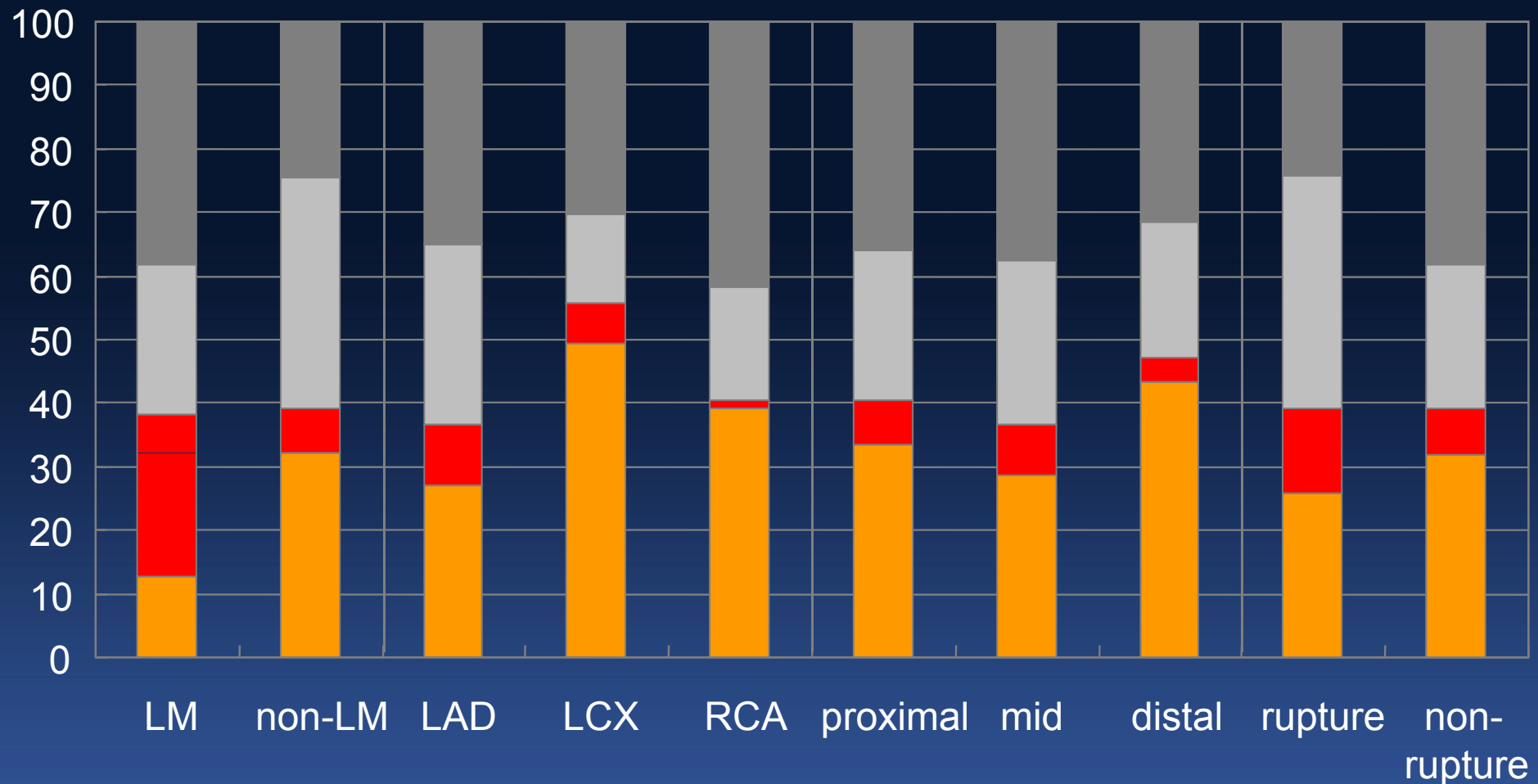
## 1066 Non-LM lesions



## 63 LM lesions



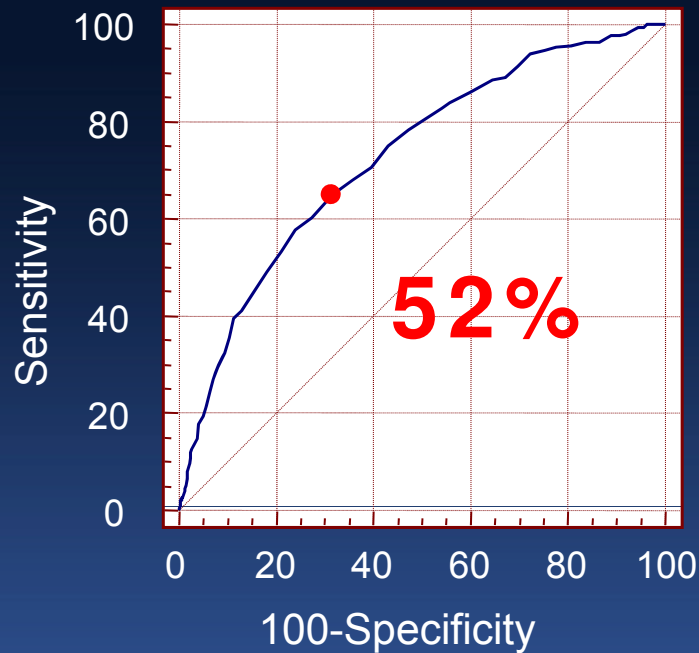
# Frequencies of Mismatch



- DS ≤ 50% and FFR ≥ 0.80
- DS > 50% and FFR < 0.80
- Reverse-mismatch
- Mismatch

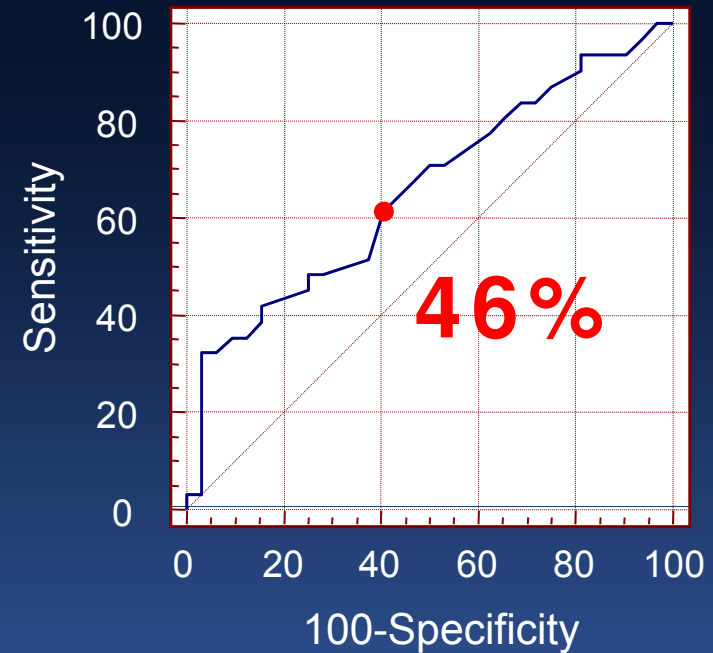
# Cut-off of QCA-DS to Predict FFR <0.80

## 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 <i>Mismatch</i>	FFR≥0.80	FFR<0.80 <i>Rev-mismatch</i>
N	262	343	386	75
Age (years)	59.7±10.0	62.1±10.0 <sup>#</sup>	62.9±9.2	59.7±10.0 <sup>*</sup>
Female, N (%)	55 (21%)	107 (31%) <sup>#</sup>	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%) <sup>#</sup>	246 (64%)	66 (88%) <sup>*</sup>
LCX, N (%)	14 (5%)	49 (14%) <sup>#</sup>	30 (8%)	6 (8%)
RCA, N (%)	47 (18%)	103 (30%) <sup>#</sup>	110 (29%)	3 (4%) <sup>*</sup>

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

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

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

<sup>\*</sup> *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 <i>Mismatch</i>	FFR≥0.80	FFR<0.80 <i>Rev-mismatch</i>
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%)	9 (38%)	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 <i>Mismatch</i>	FFR≥0.80	FFR<0.80 <i>Rev-mismatch</i>
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 <sup>2</sup>	3.4±1.6	4.8±1.6 <sup>#</sup>	6.6±2.0	4.2±1.4 <sup>*</sup>
Plaque burden, %	81.0±8.4	69.5±18.3	61.2±14.3	73.1±9.6 <sup>*</sup>
EEM area, mm <sup>2</sup>	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%) <sup>*</sup>

<sup>#</sup> *p* value <0.05, vs. 15 lesions with QCA-DS>50 and FFR<0.80

<sup>\*</sup> *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.