Functionally Insignificant, Vulnerable Plaque: Do You Want to Treat?

No, I Don't

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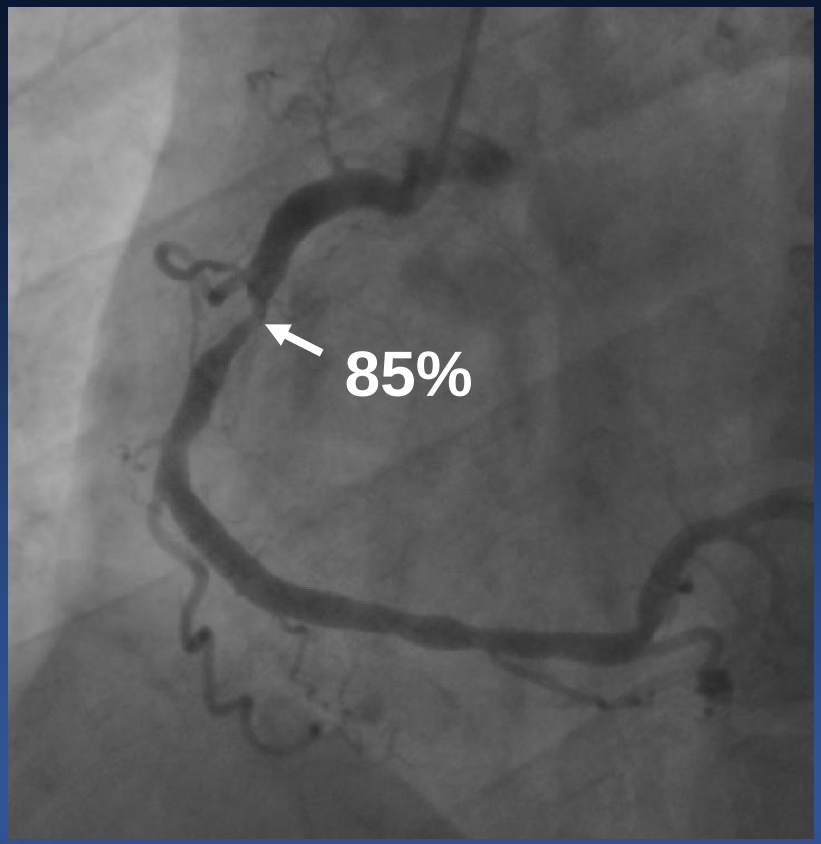
Q1,

Is Angiography Enough for Diagnosis of Clinical Ischemia ?

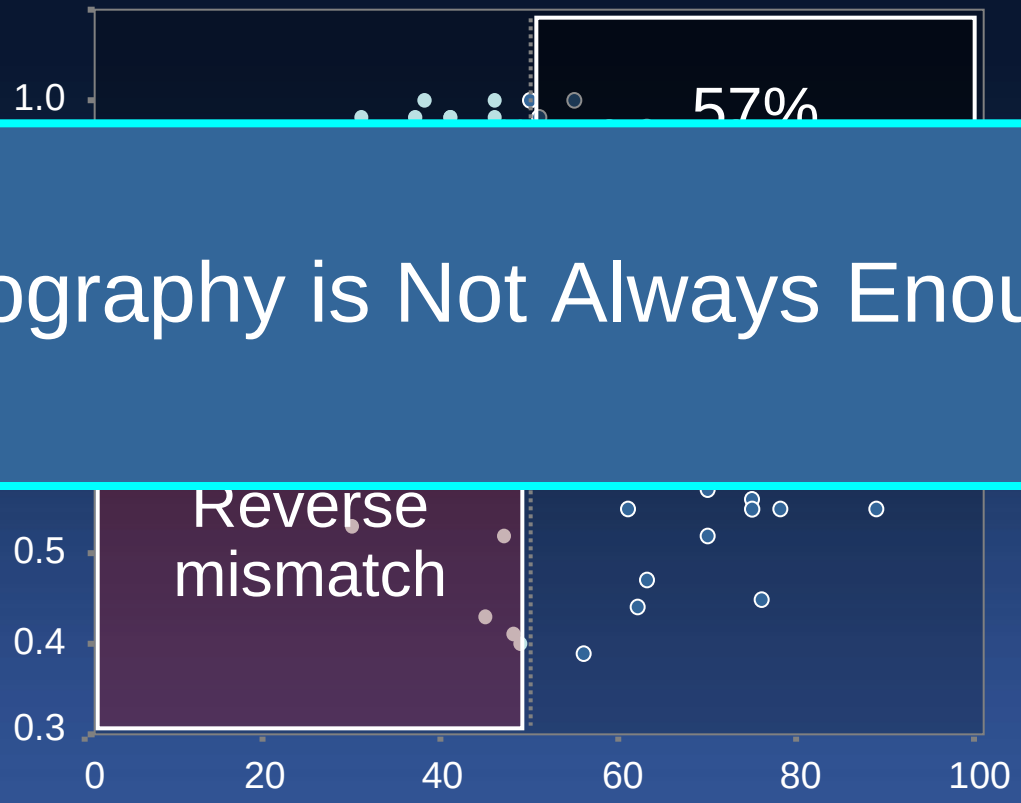
Visual Estimation, Mismatches

73/M, Atypical Chest Pain,



Many Mismatches

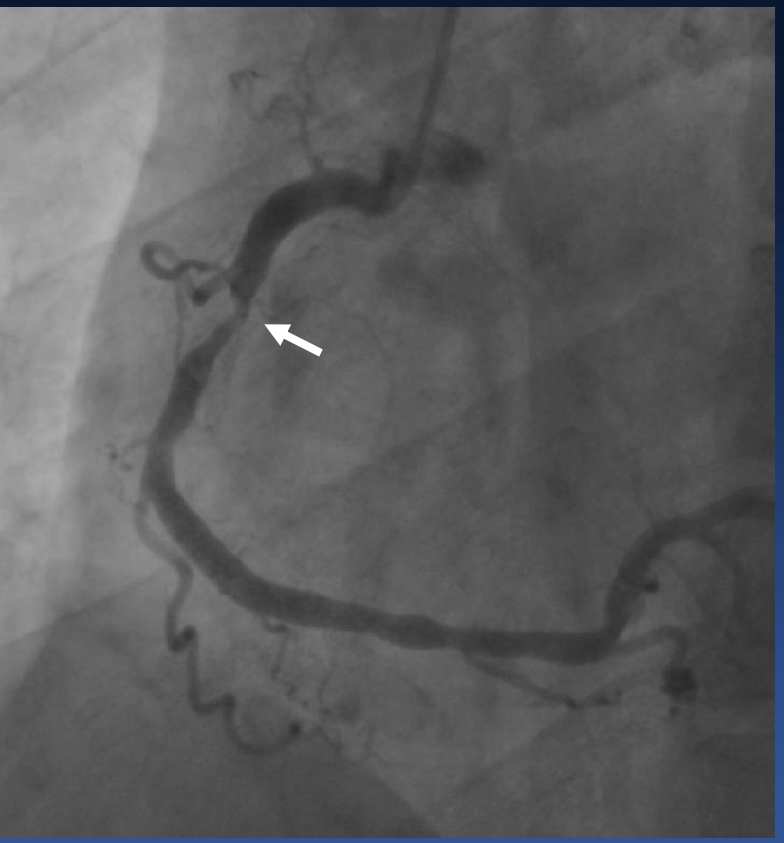
1066 Non-LM lesions



Angiography is Not Always Enough !

Park SJ, JACC. Cardiovascular Interventions. 2012 ; 5(10):1029-36

To Treat or Not to Treat ?



Angiographic DS(%) : 85%

IVUS MLA : 2.8 mm^2

FFR : 0.84

Treadmill test : Negative

Thallium spect : Normal

Stress Echo : Normal

Why

1. I am a FFR believer.
2. FFR is well matched with non-invasive stress tests.
3. In patients with normal myocardial perfusion scan (negative non-invasive stress tests) means just excellent prognosis. (0.6%/year, Cardiac Death and MI), 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)

Q2,

Do You Want to Treat ?
Functionally Insignificant Vulnerable Plaque.

No, I Don't !

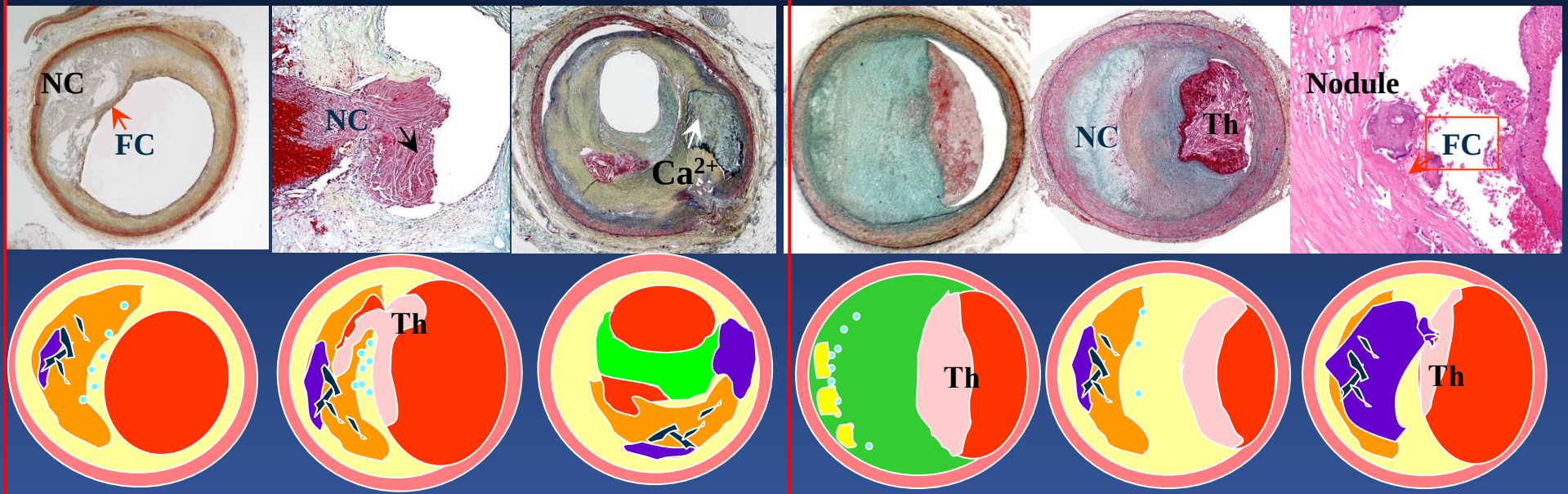
Vulnerable Plaque, Pathology

Thin-cap Fibroatheroma

Rupture/ Healed Rupture

Erosion

Calcified Nodule



70% of ACS

Naghavi et al. Circulation 2003;108:1664-72
Virmani R, et al. ATVB2000;20:1262

Vulnerable Plaque,
Imaging

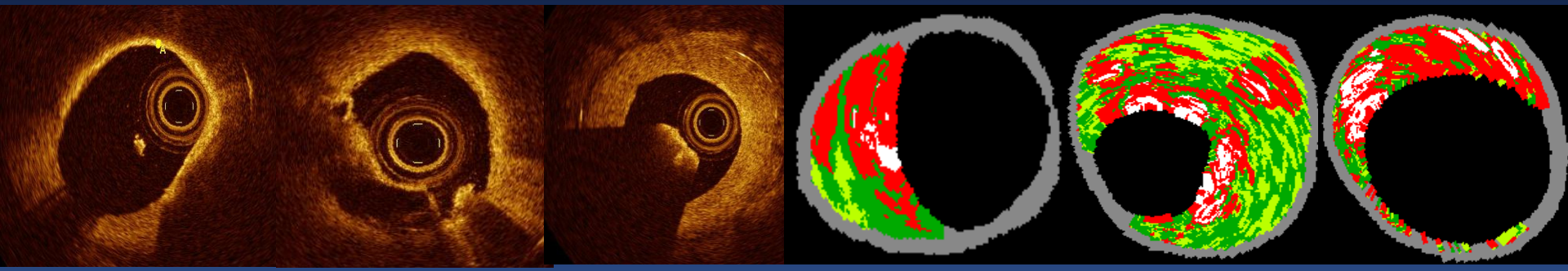
Thin-cap Fibroatheroma (TCFA)

Rupture/ Healed Rupture

Confluent Necrotic Core

>50% Area Narrowing

Calcium >5%



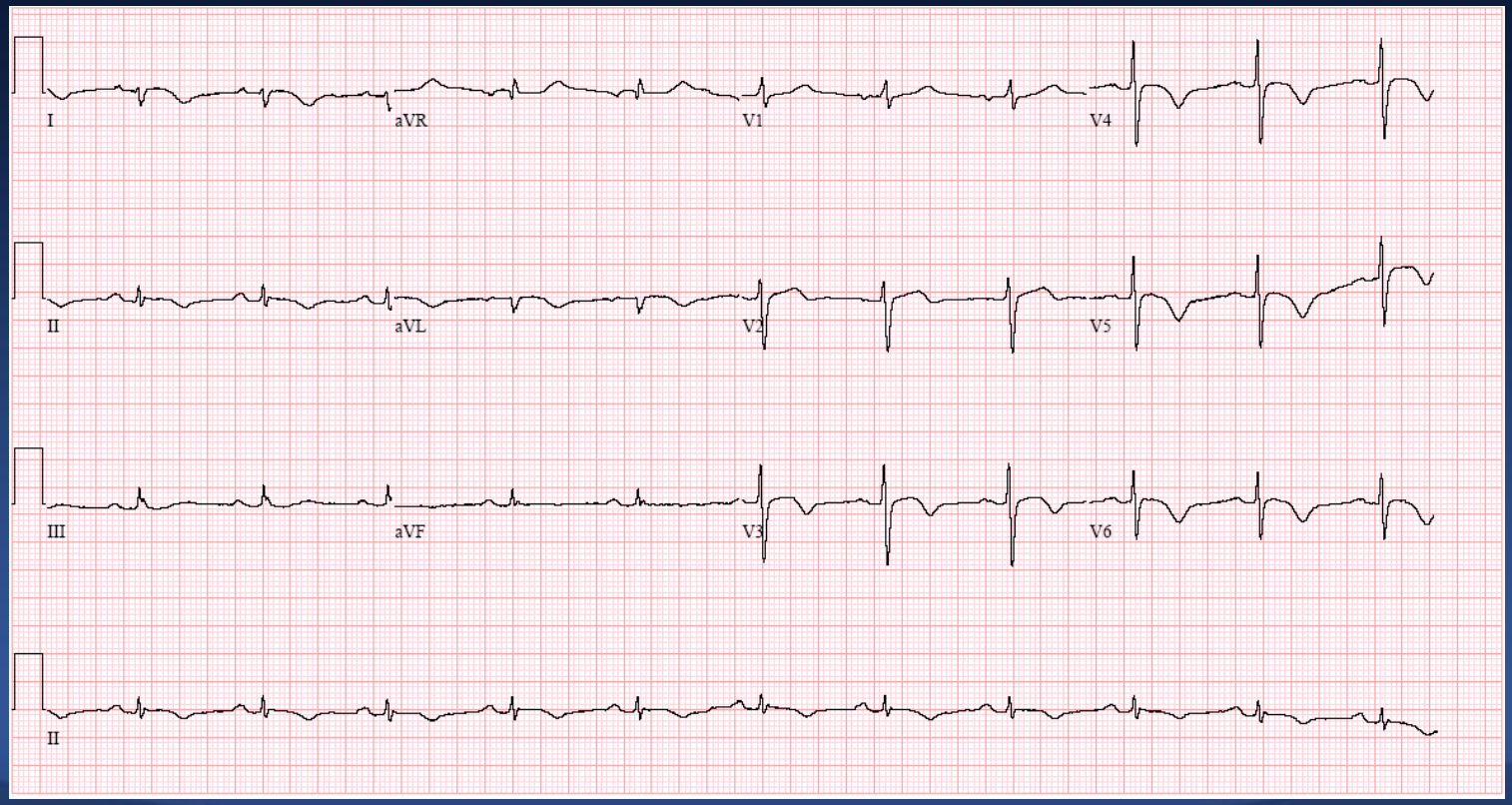
Case1,

NSTMI,
Vulnerable Plaque
Angiographically Significant,
Functionally Insignificant

72/F, NSTMI

Resting chest pain, stabilized symptom, Hyperlipidemia

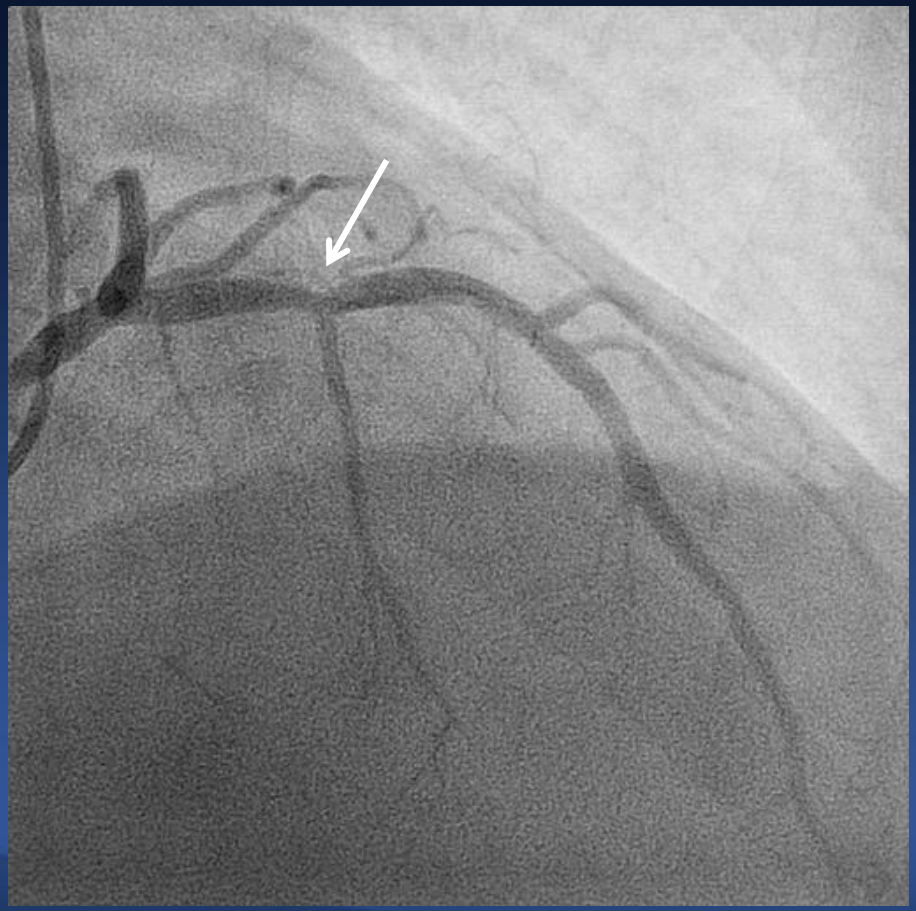
CKMB 29.9 ng/mL (~ 5ng/mL), Tn-I 6.9 ng/mL (~1.5ng/mL)



72/F, NSTMI

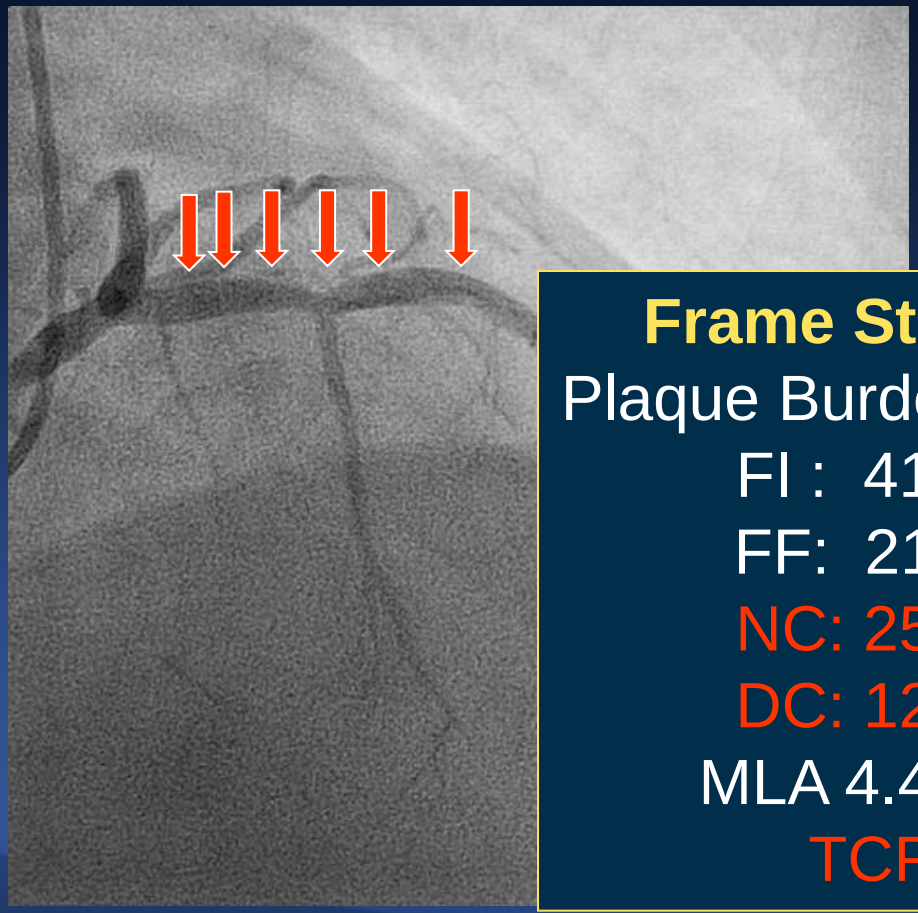
60% stenosis in proximal LAD

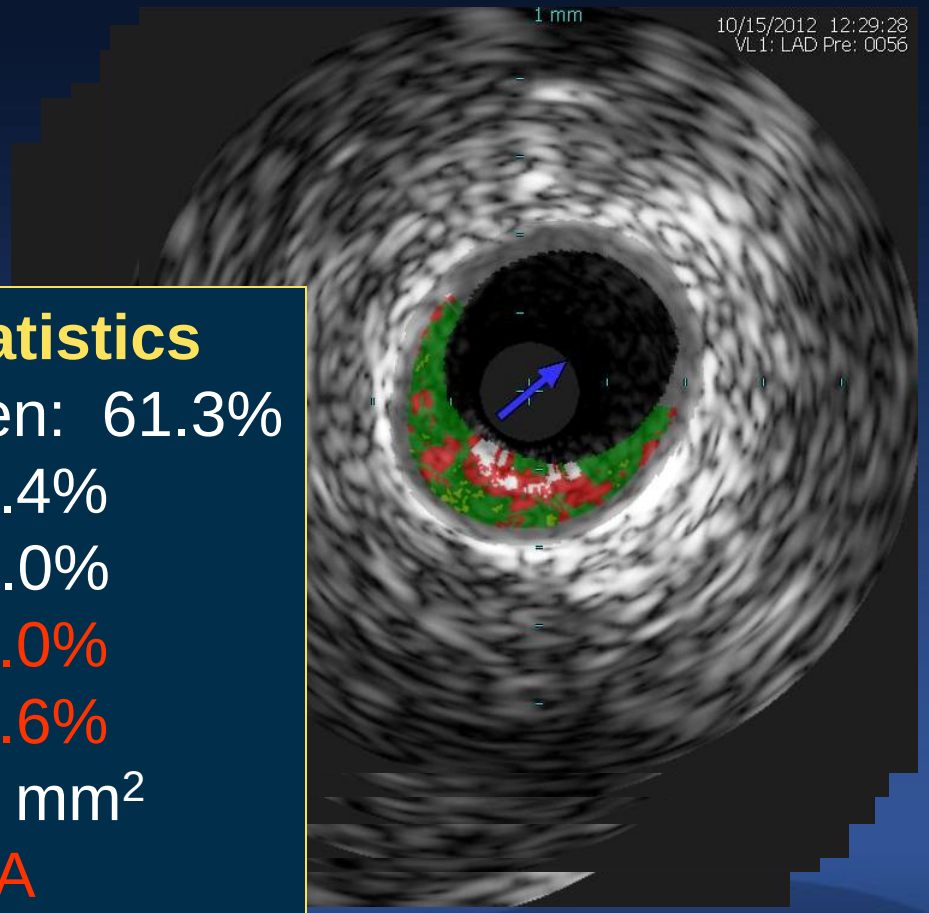
Do You Want to Treat at 1st HD?



72/F, NSTMI

IVUS





Frame Statistics

Plaque Burden: 61.3%

FI : 41.4%

FF: 21.0%

NC: 25.0%

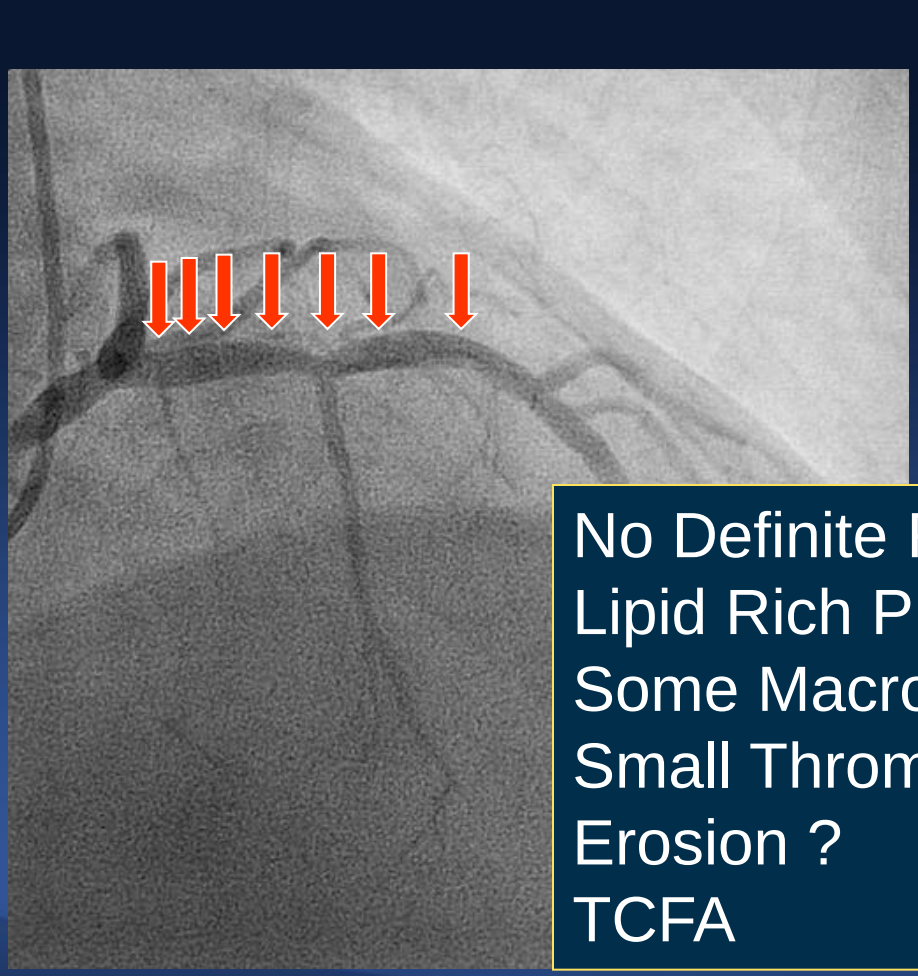
DC: 12.6%

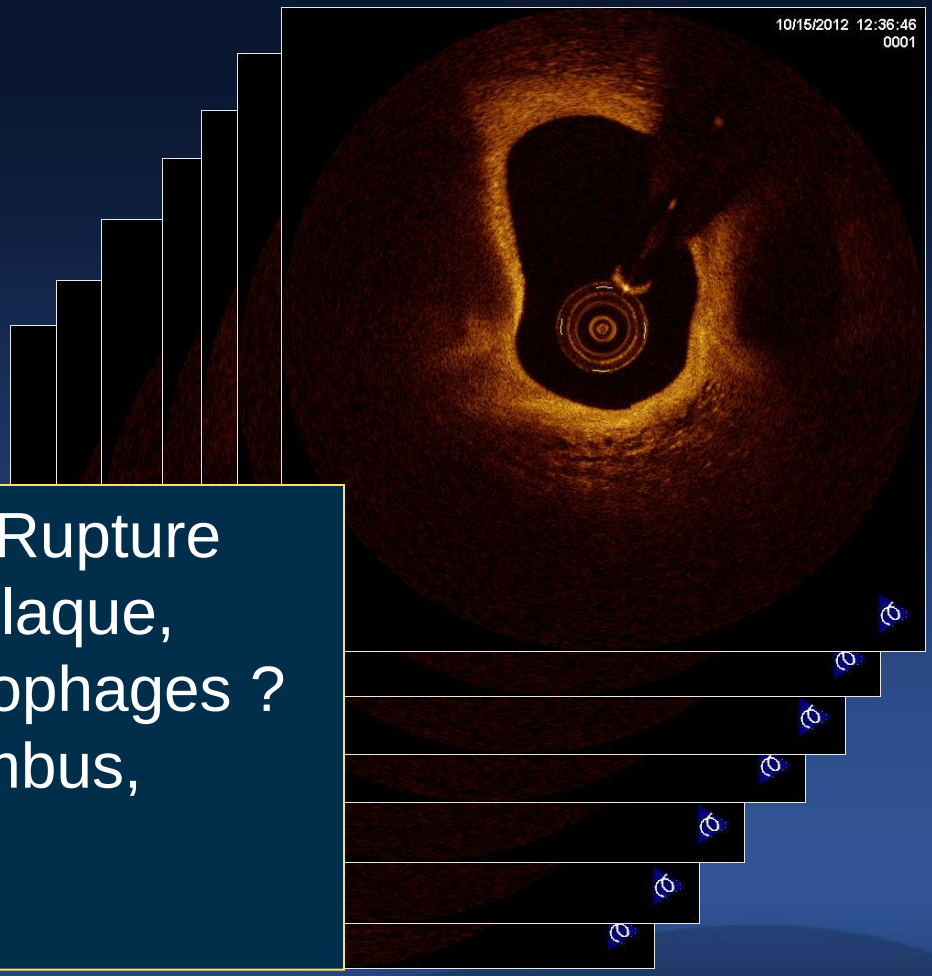
MLA 4.4 mm^2

TCFA

72/F, NSTMI

OCT

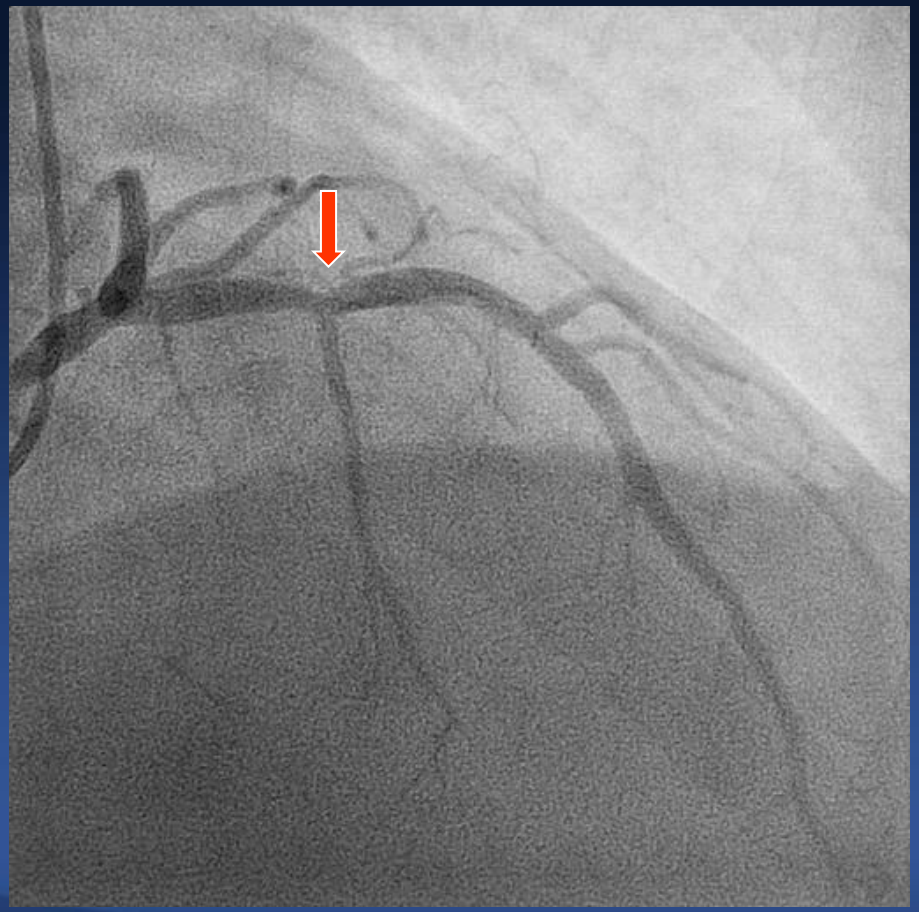


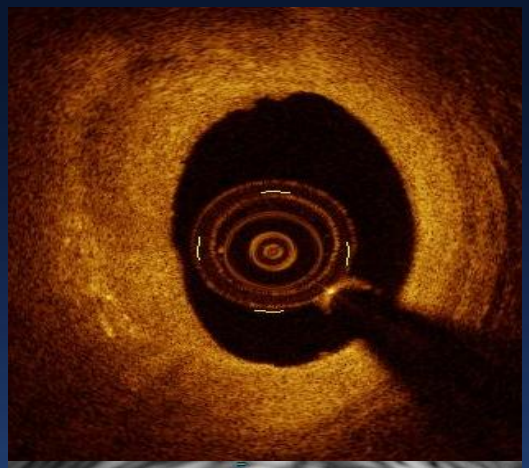


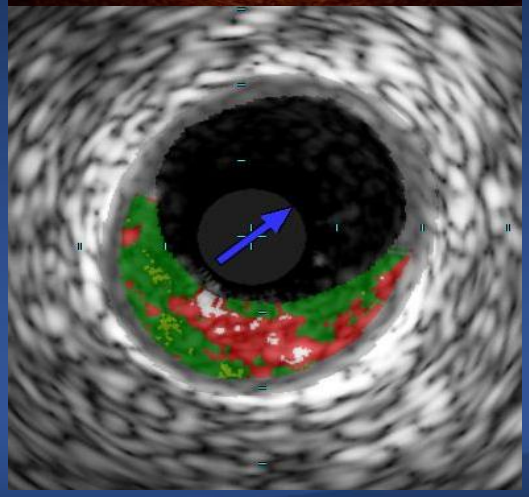
No Definite Rupture
Lipid Rich Plaque,
Some Macrophages ?
Small Thrombus,
Erosion ?
TCFA

72/F, NSTMI

Do You Want to Treat ?

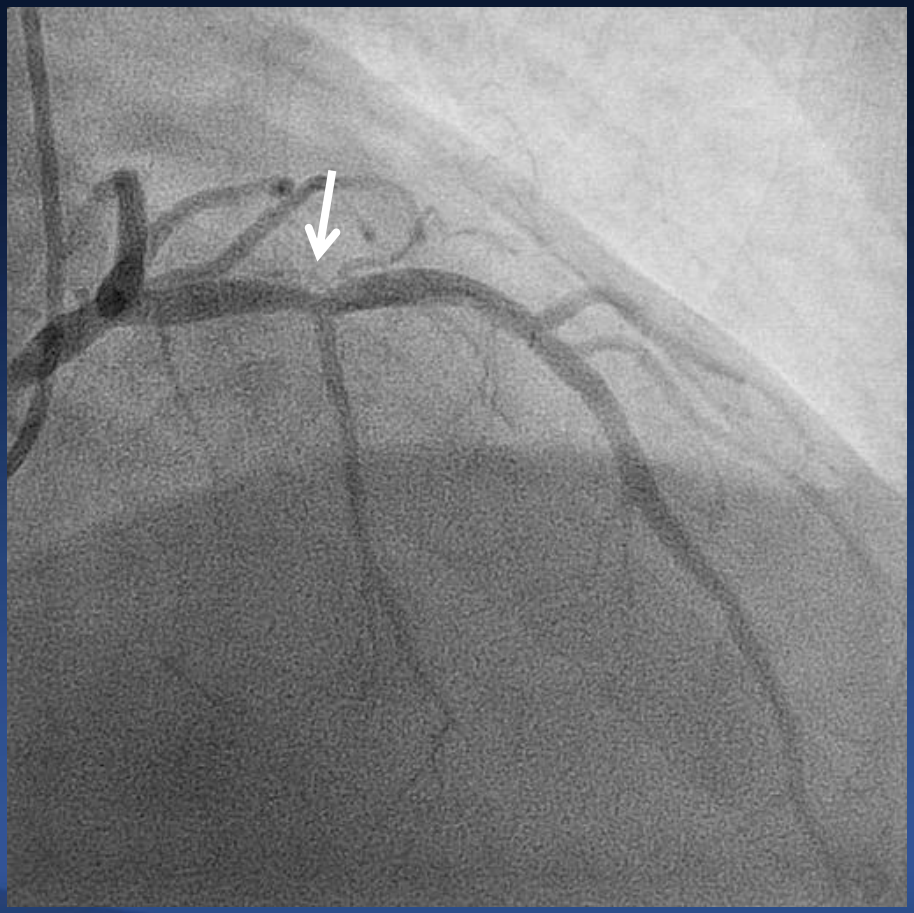




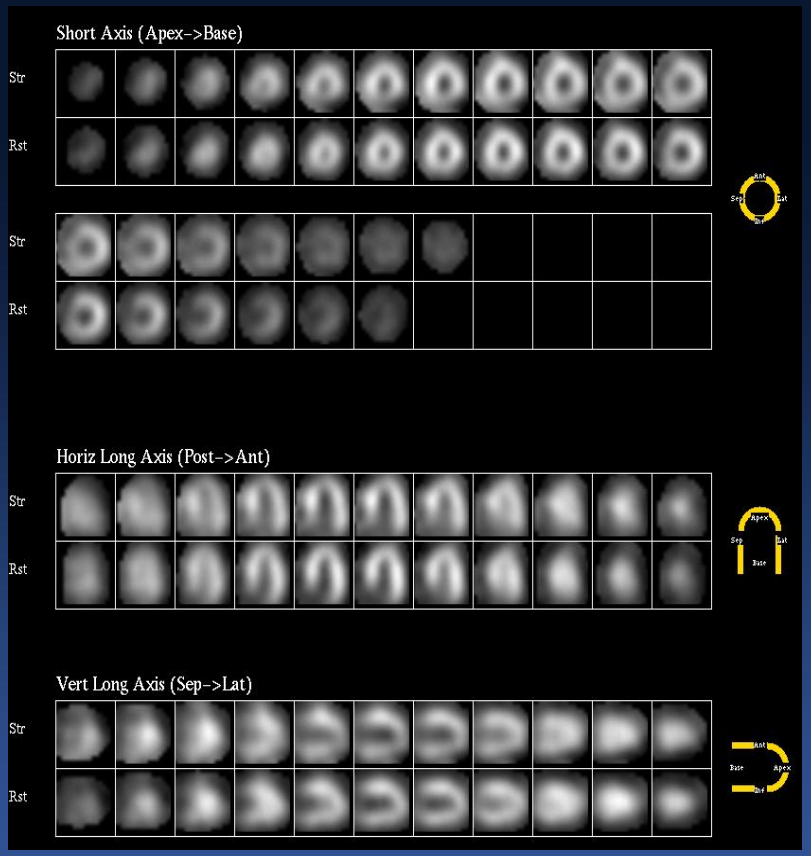


FFR is 0.87

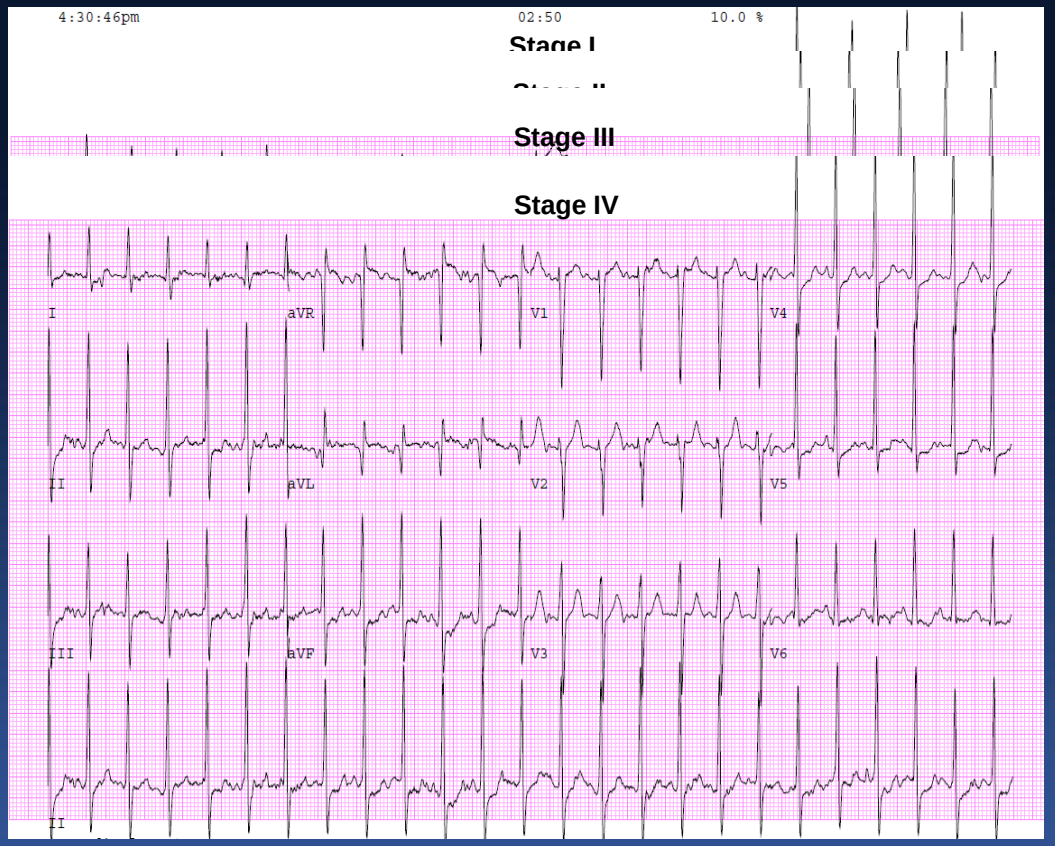
Do You Want to Treat ?



Negative Stress Tests



Normal Thallium

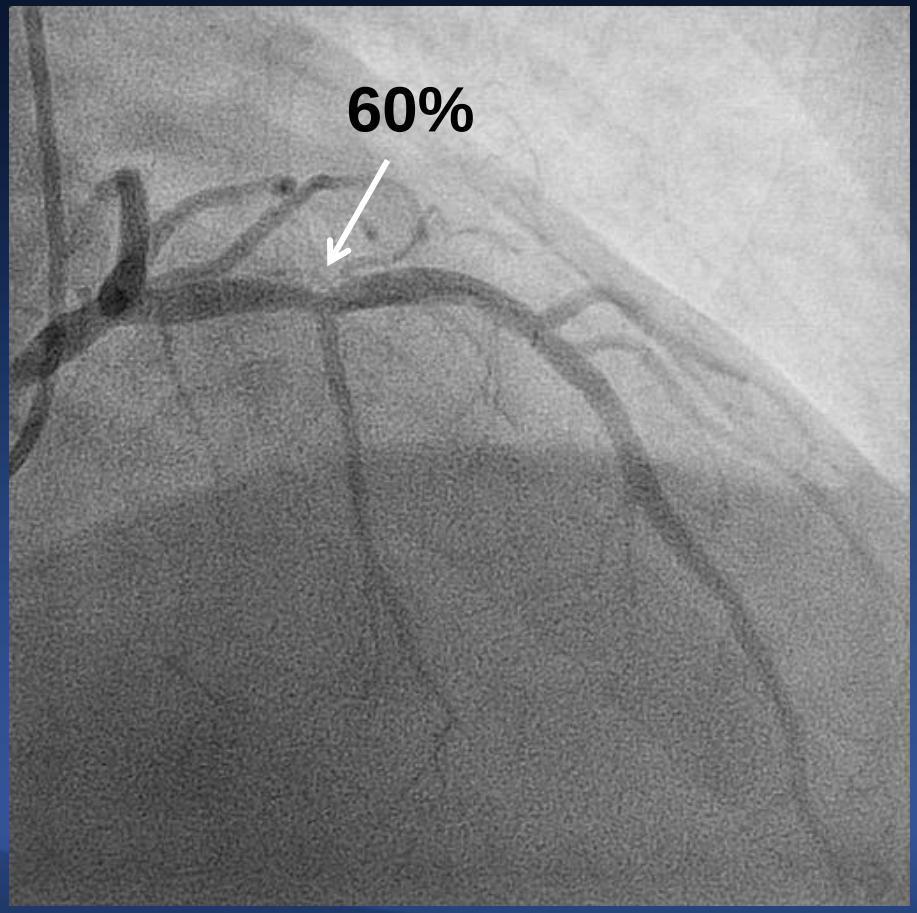


Treadmill Test: Negative

72/F, NSTMI

Do You Still Want to Treat ?

Functionally Insignificant
Vulnerable Plaque

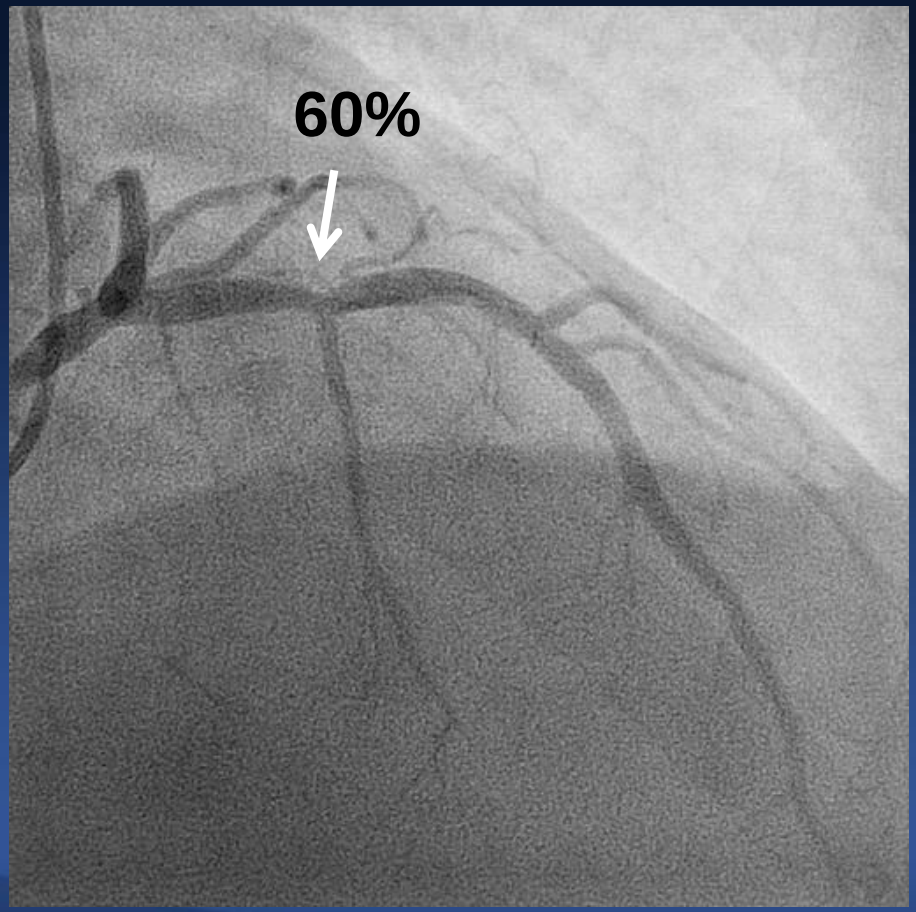


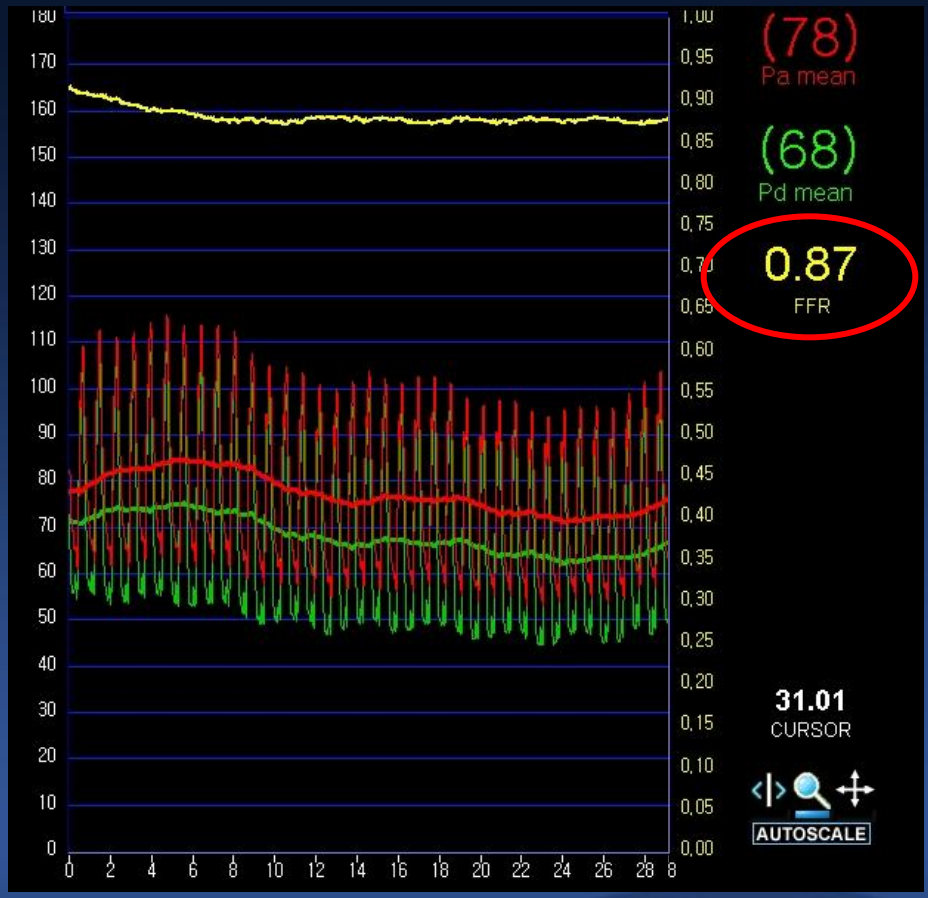
Vulnerable Plaque (TCFA, 61% plaque burden, 25% necrotic core, MLA 4.4 mm^2)

FFR 0.87,
Negative Treadmill test,
Normal Thallium scan.

I Deferred !

Based on FFR



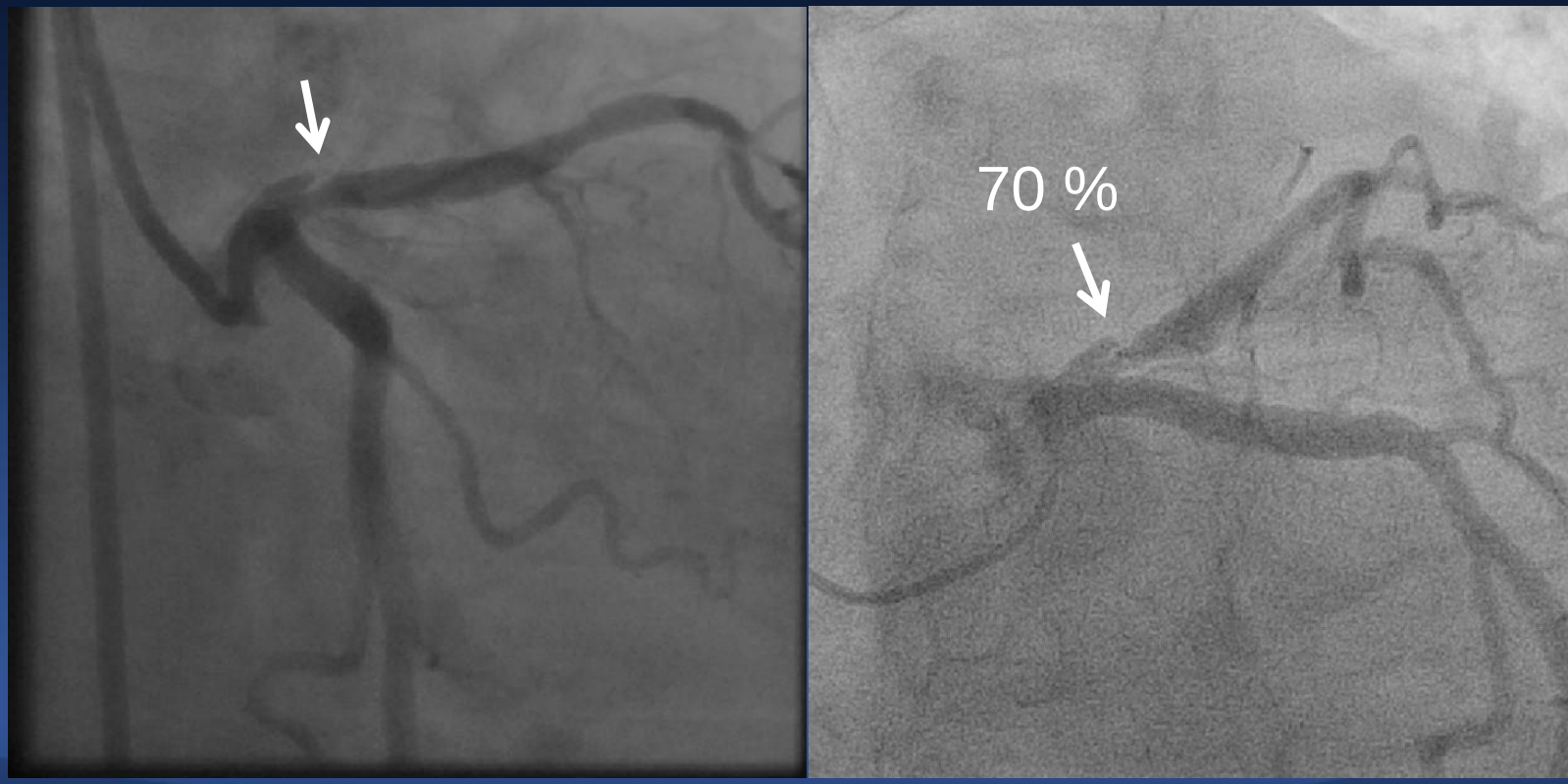


Case2,

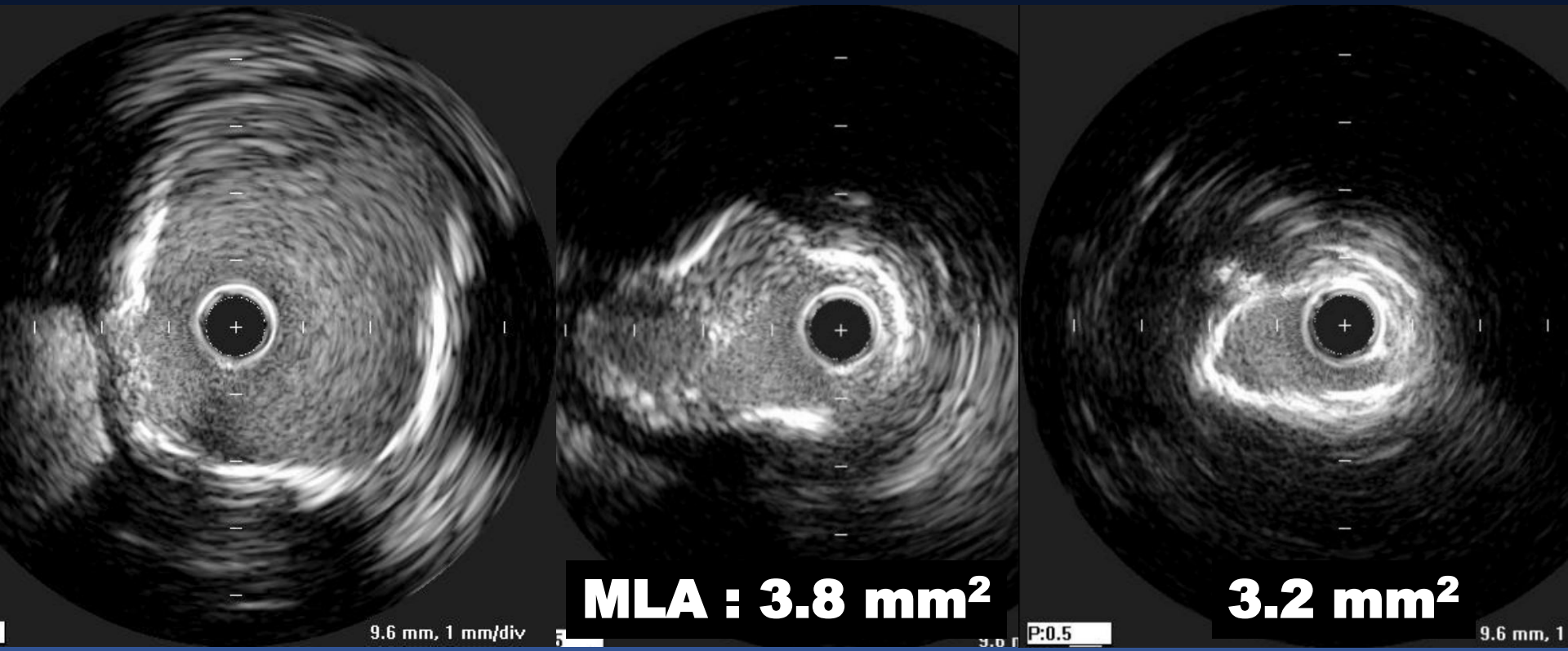
Asymptomatic,
Ruptured Plaque,
Angiographically Significant,
Functionally Insignificant

M/74, Asymptomatic

Multiple stenosis on Coronary CT,
Hypertension, DM, Hyperlipidemia, Ex-smoker

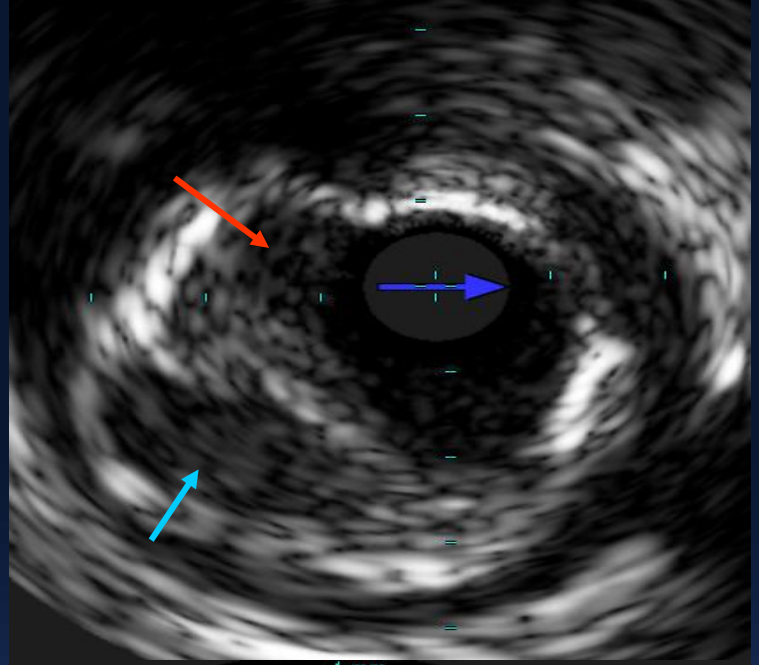


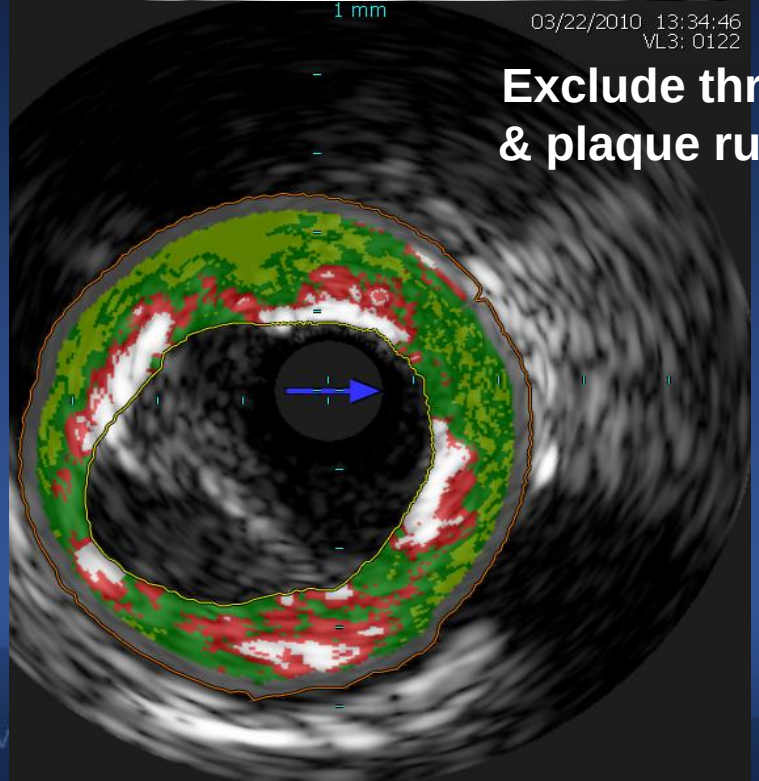
IVUS
(LAD pullback)



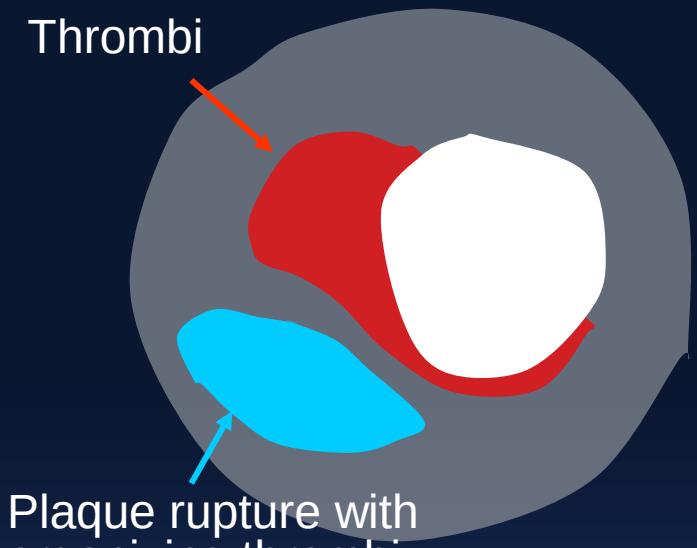
LM

LAD





Exclude thrombi & plaque rupture



Frame Statistics

Plaque Burden: 71.3%

FI : 41.4%

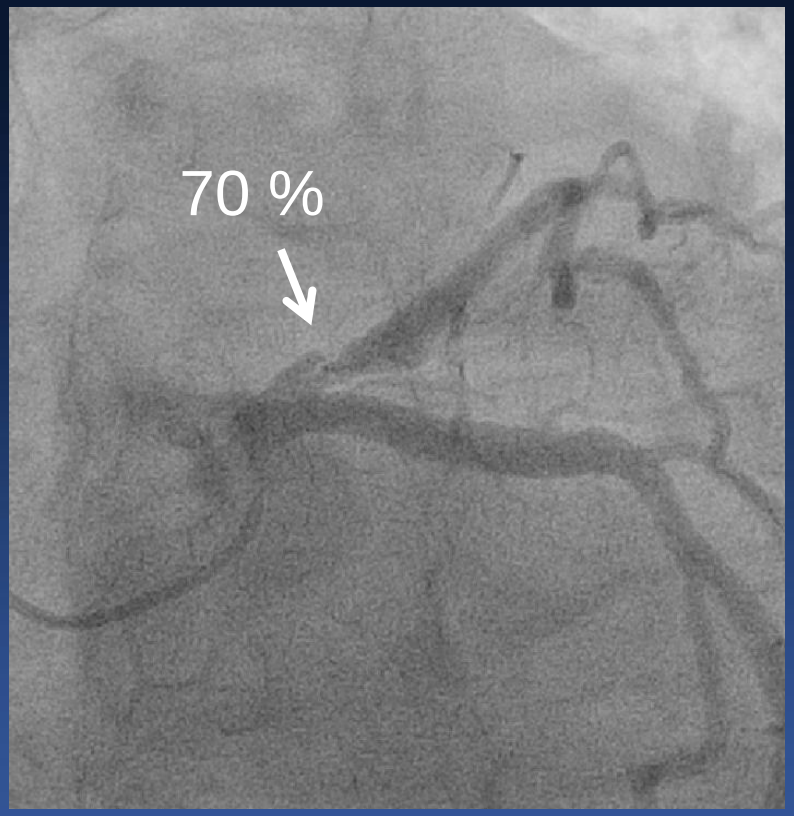
FF: 20.0%

NC: 23.0%

DC: 15.6%

M/74, Asymptomatic

Do You Want to Treat ?

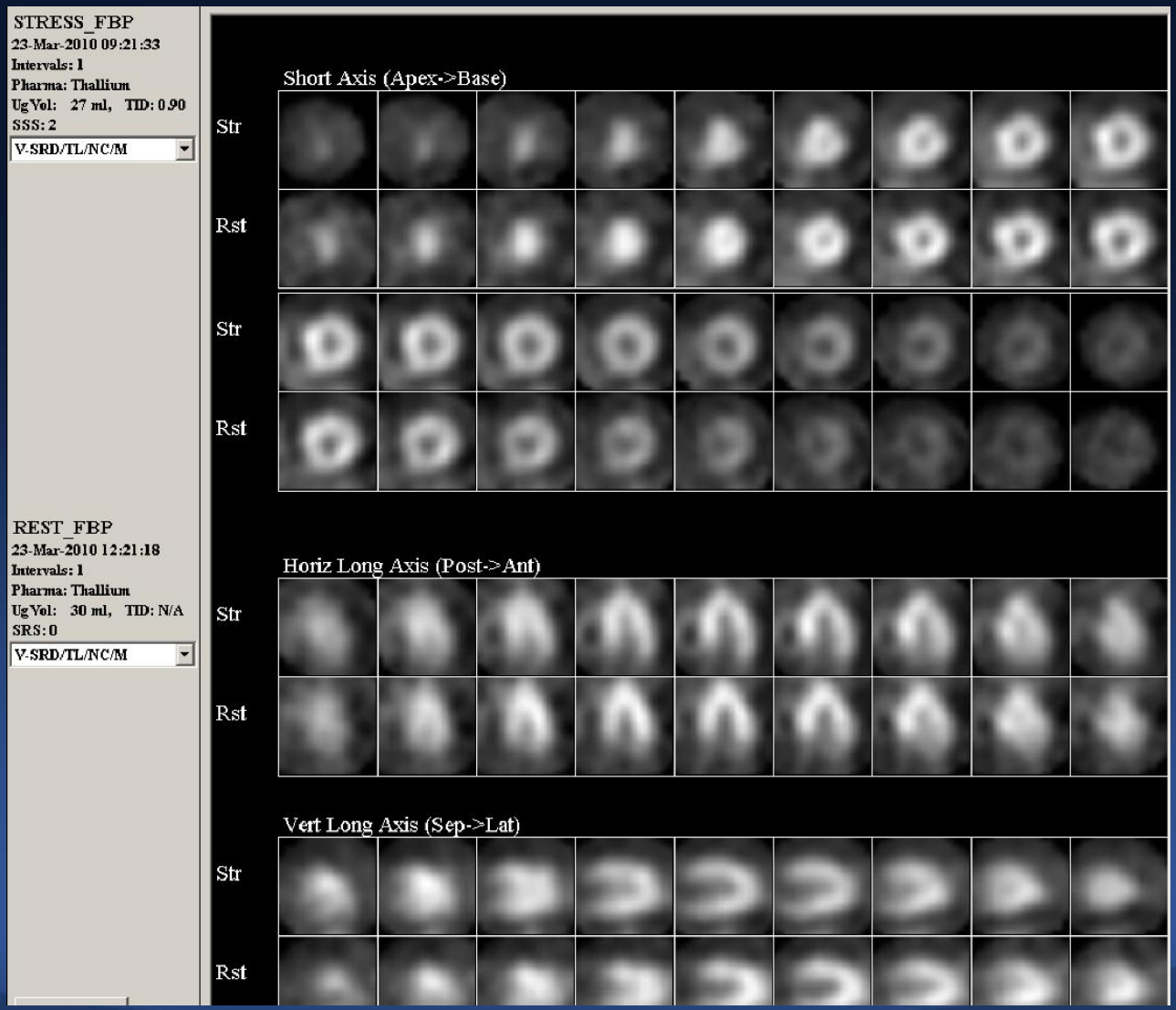


Visual Estimation: 70%
Large Plaque Rupture
Vulnerable Features
IVUS MLA : 3.2mm^2

FFR

(intravenous adenosine, 240 μg/kg/min)

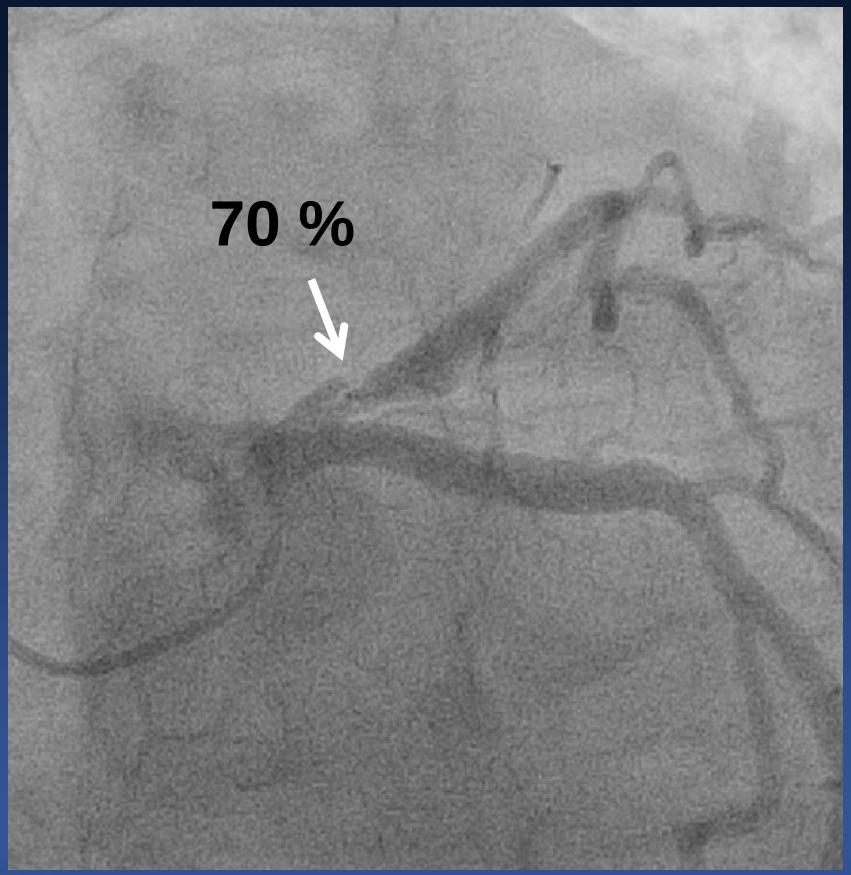
Thallium Spect ; Normal Perfusion



74/M, Asymptomatic

Functionally Insignificant
Vulnerable Plaque

Do You Still Want to Treat ?

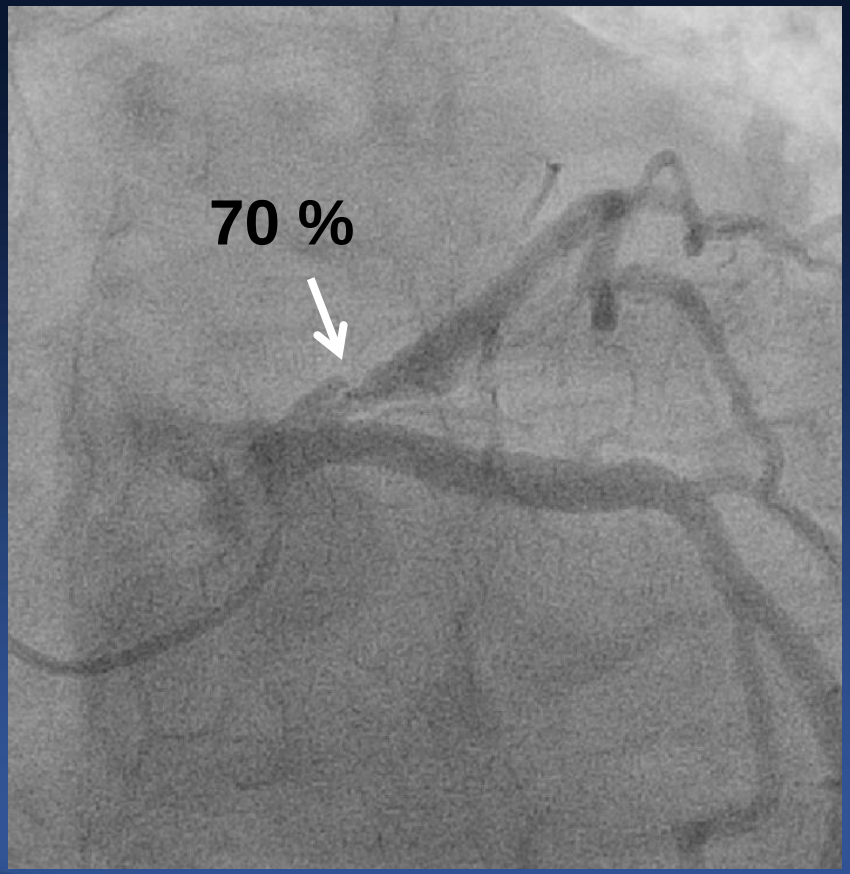


Ruptured,
Vulnerable Plaque (TCFA, 71% plaque burden, 23% necrotic core, MLA 3.2 mm^2)

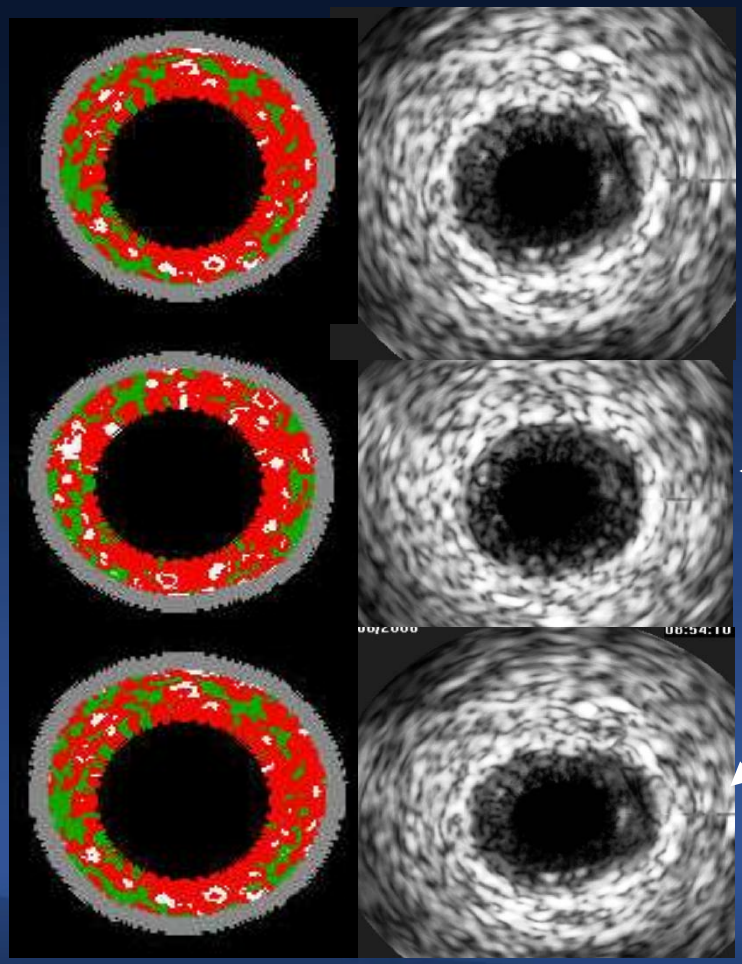
FFR 0.89,
Normal Thallium scan.

I Deferred !

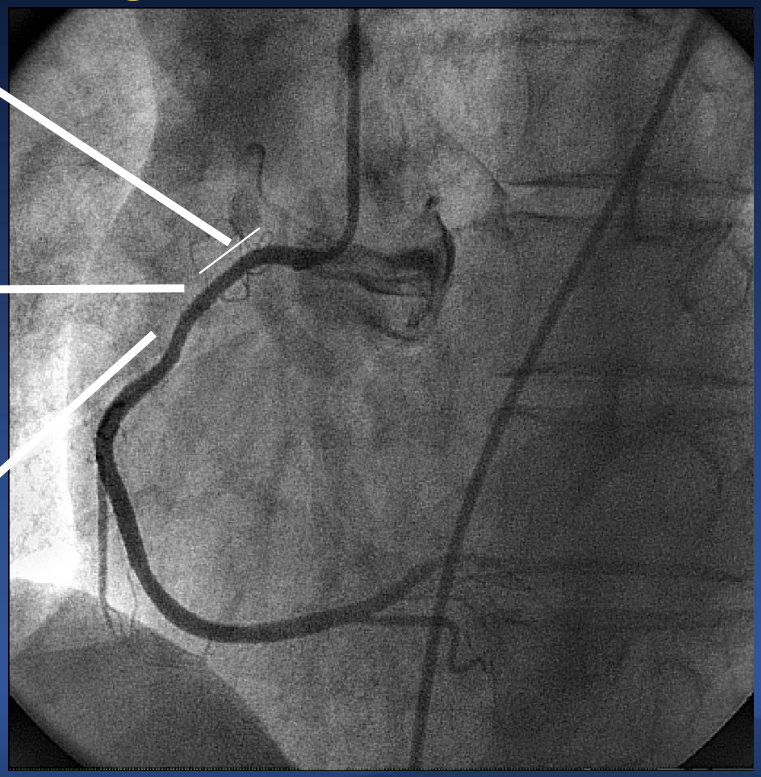
Based on FFR



Functionally Insignificant
Akiko, Do You Want to Treat ?
Vulnerable Plaque



FFR 0.92
Negative Treadmill Test

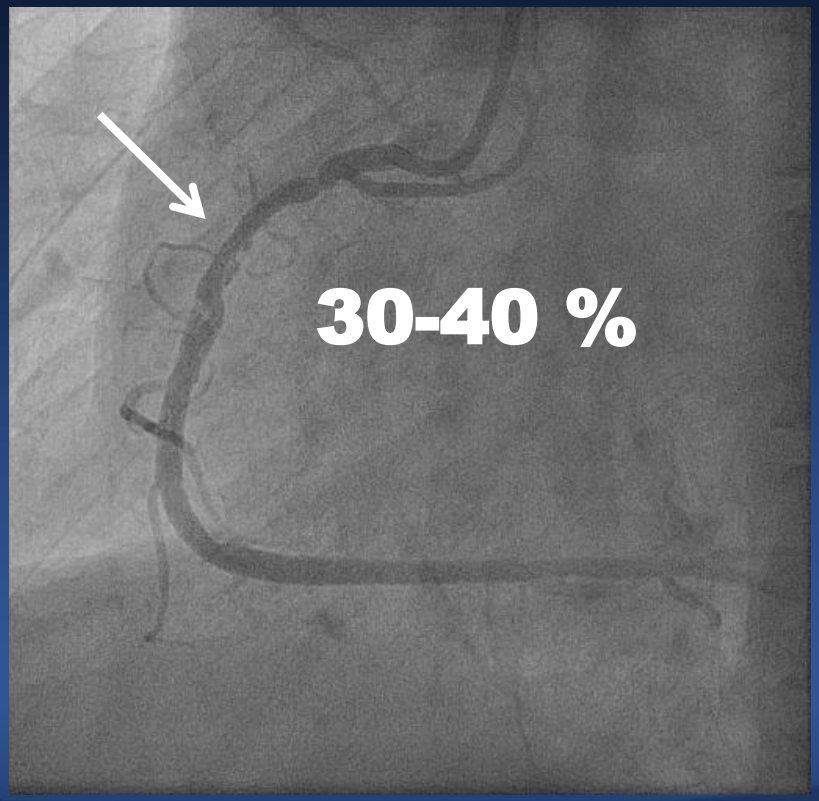


Case3,

NSTMI,
Ruptured Plaque,
Angiographically Insignificant,
Functionally Significant

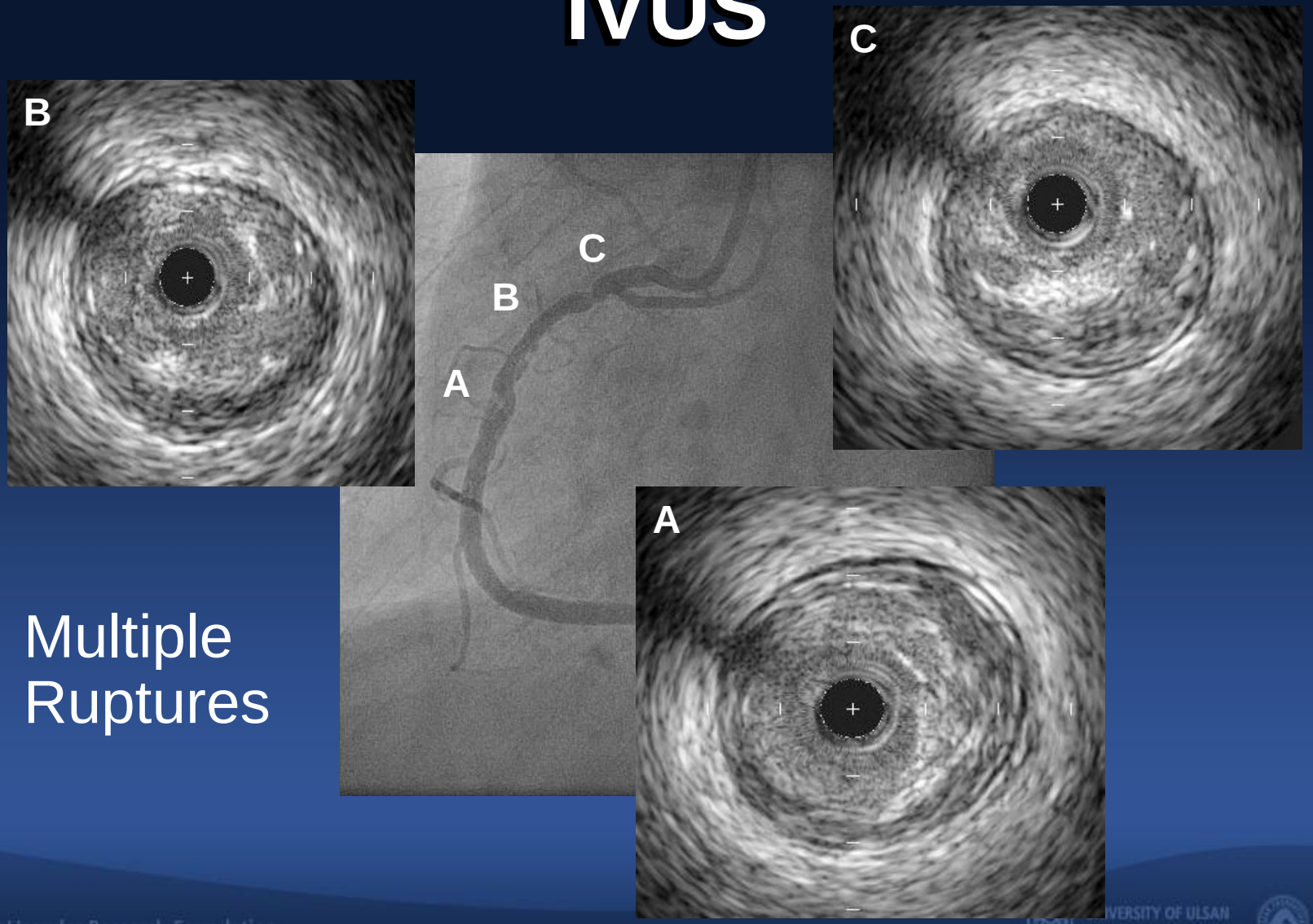
M/62, NSTMI

Severe esting chest pain 4 days ago, and stabilized symptom, Hypertension. Mild Elevated Tn-I 3.4 ng/mL (~1.5ng/mL)



M/62, NSTMI

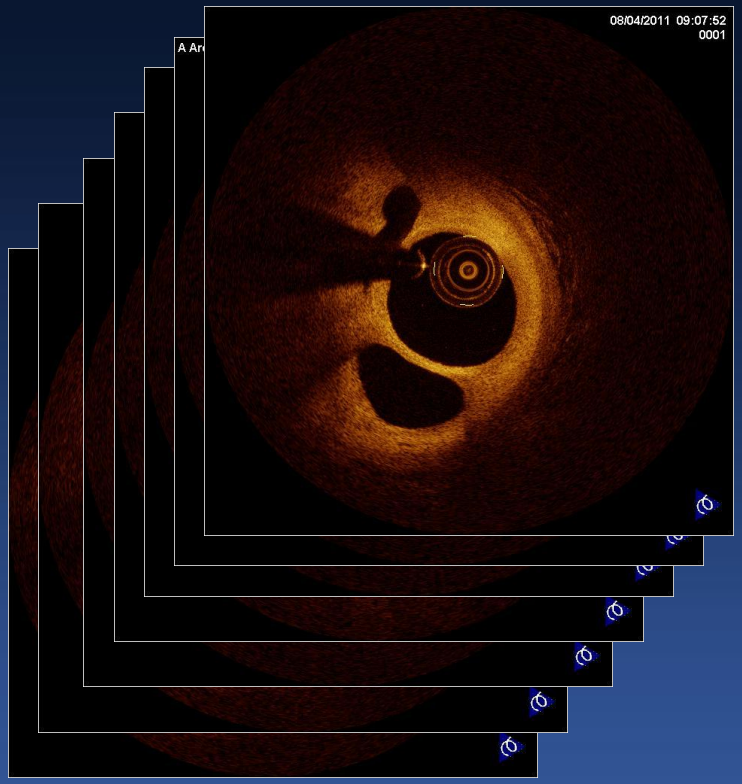
IVUS

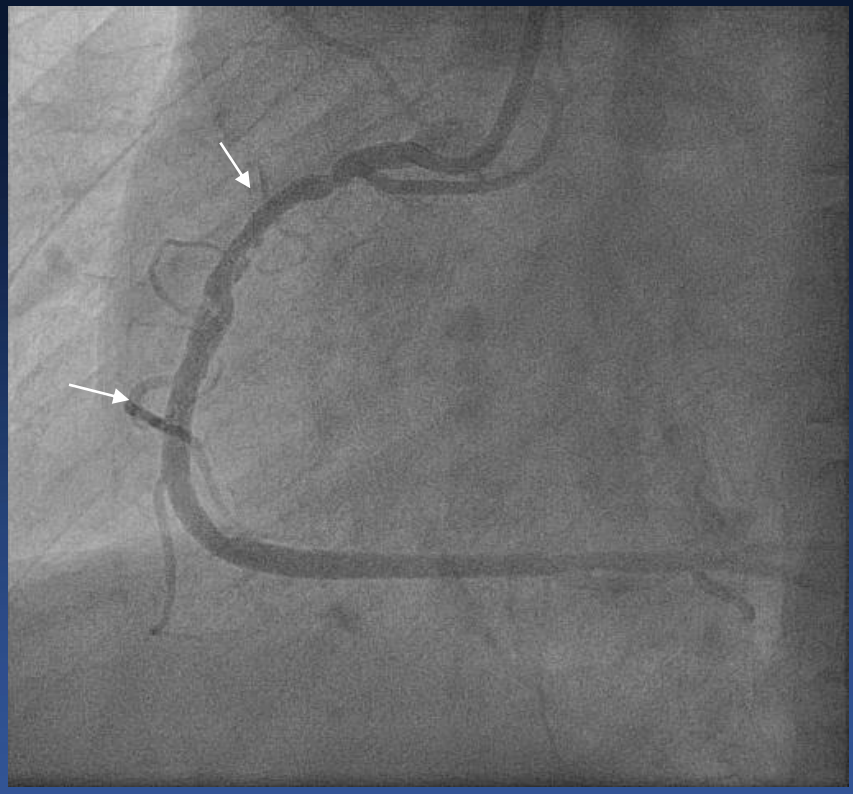


Multiple Ruptures

M/62, NSTMI

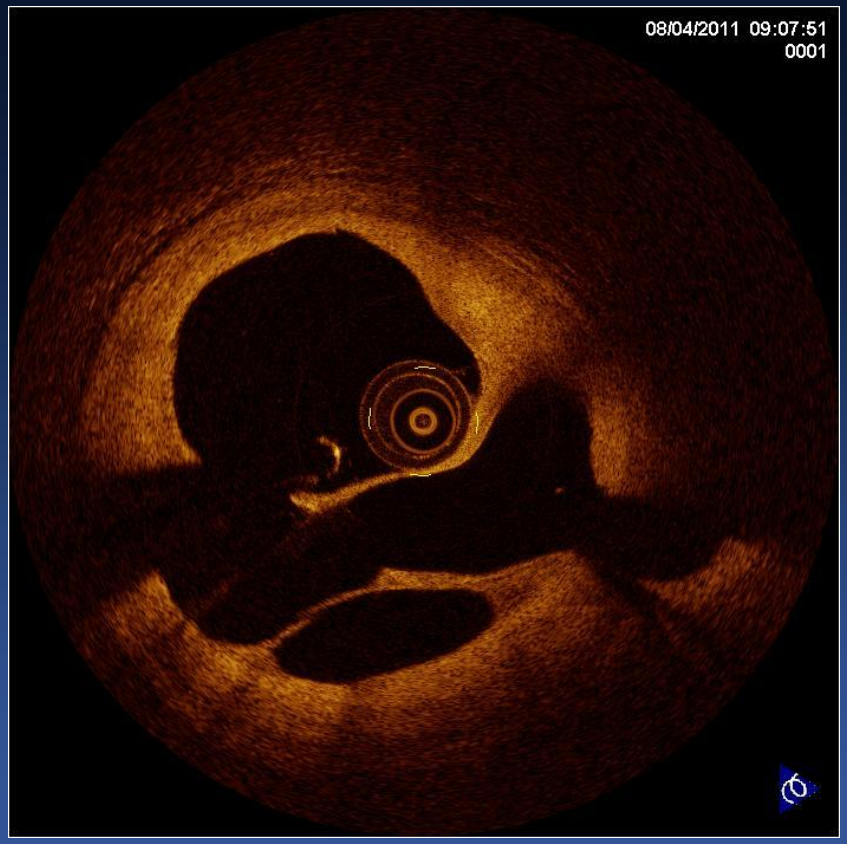
OCT

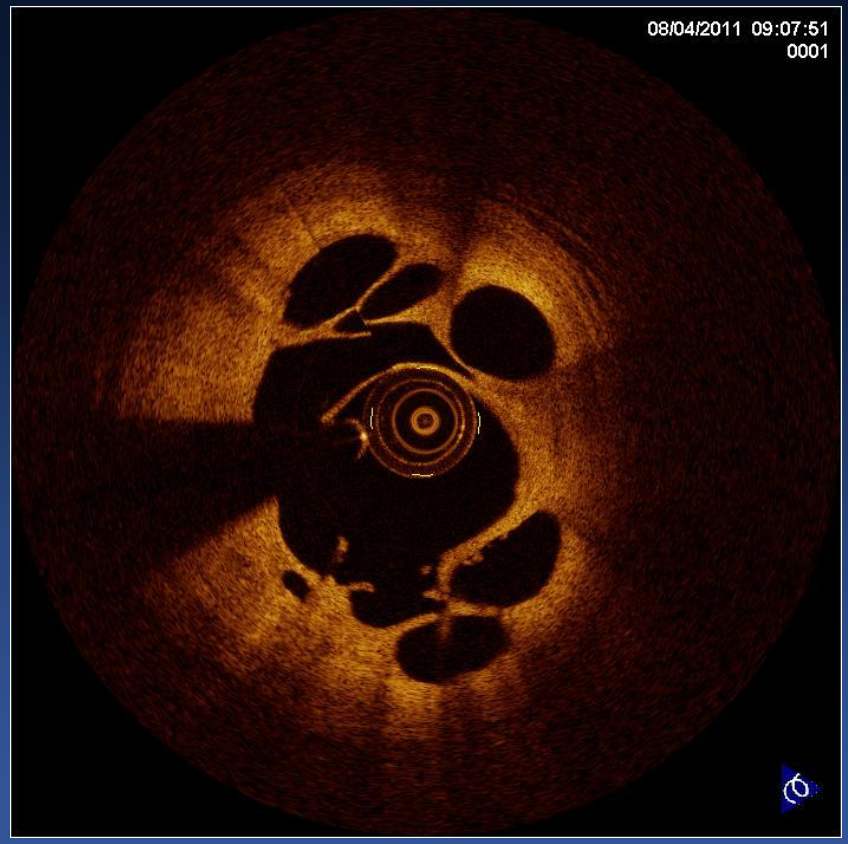




Signal-rich, high backscattered septum, dividing the lumen into multiple small channels

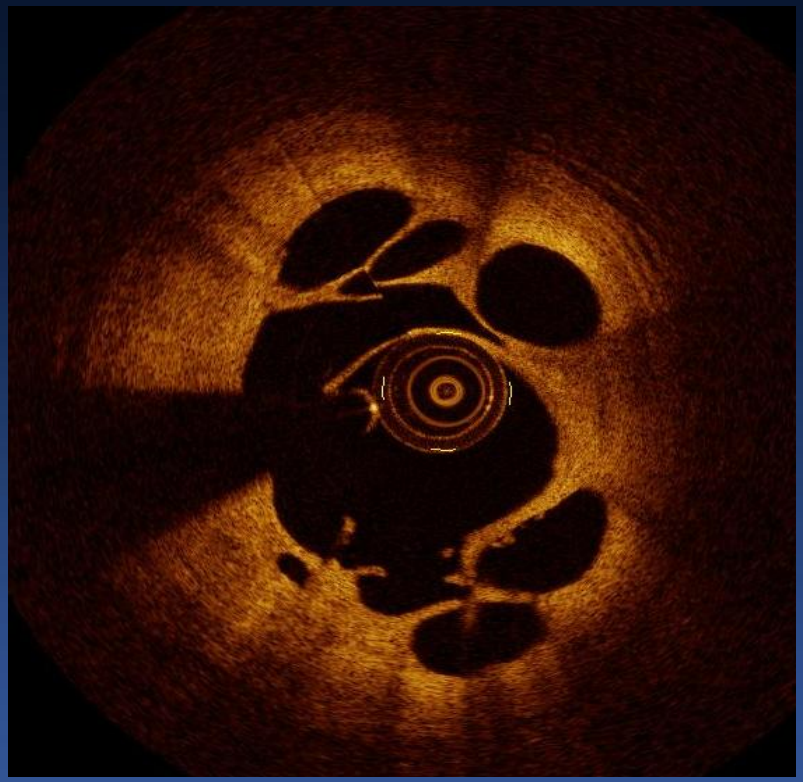
M/62, NSTMI
Recanalized Thrombus

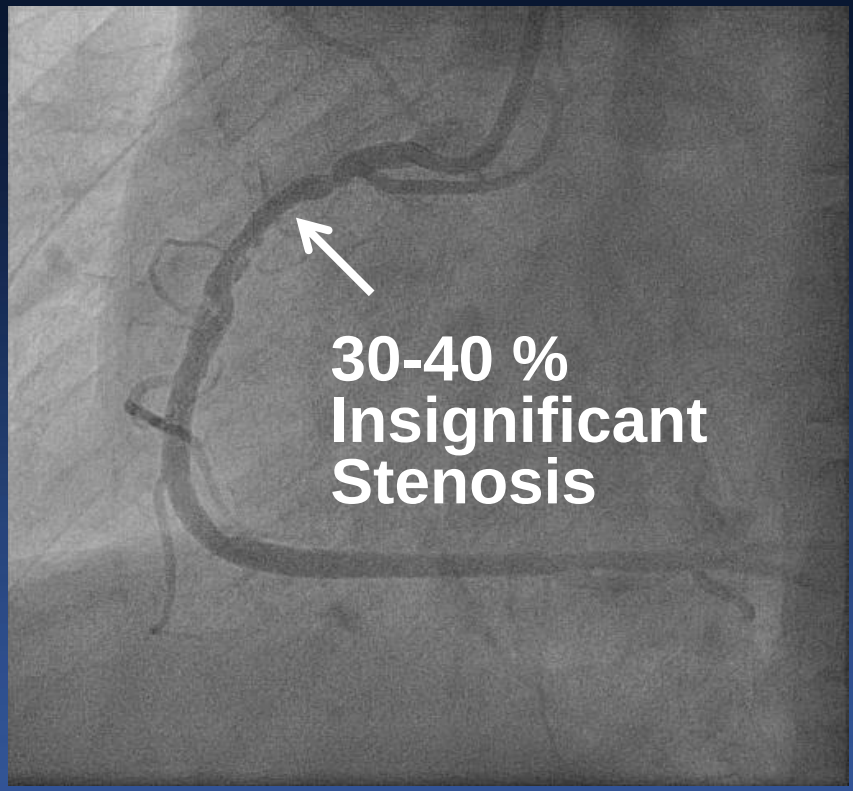




M/62, NSTMI

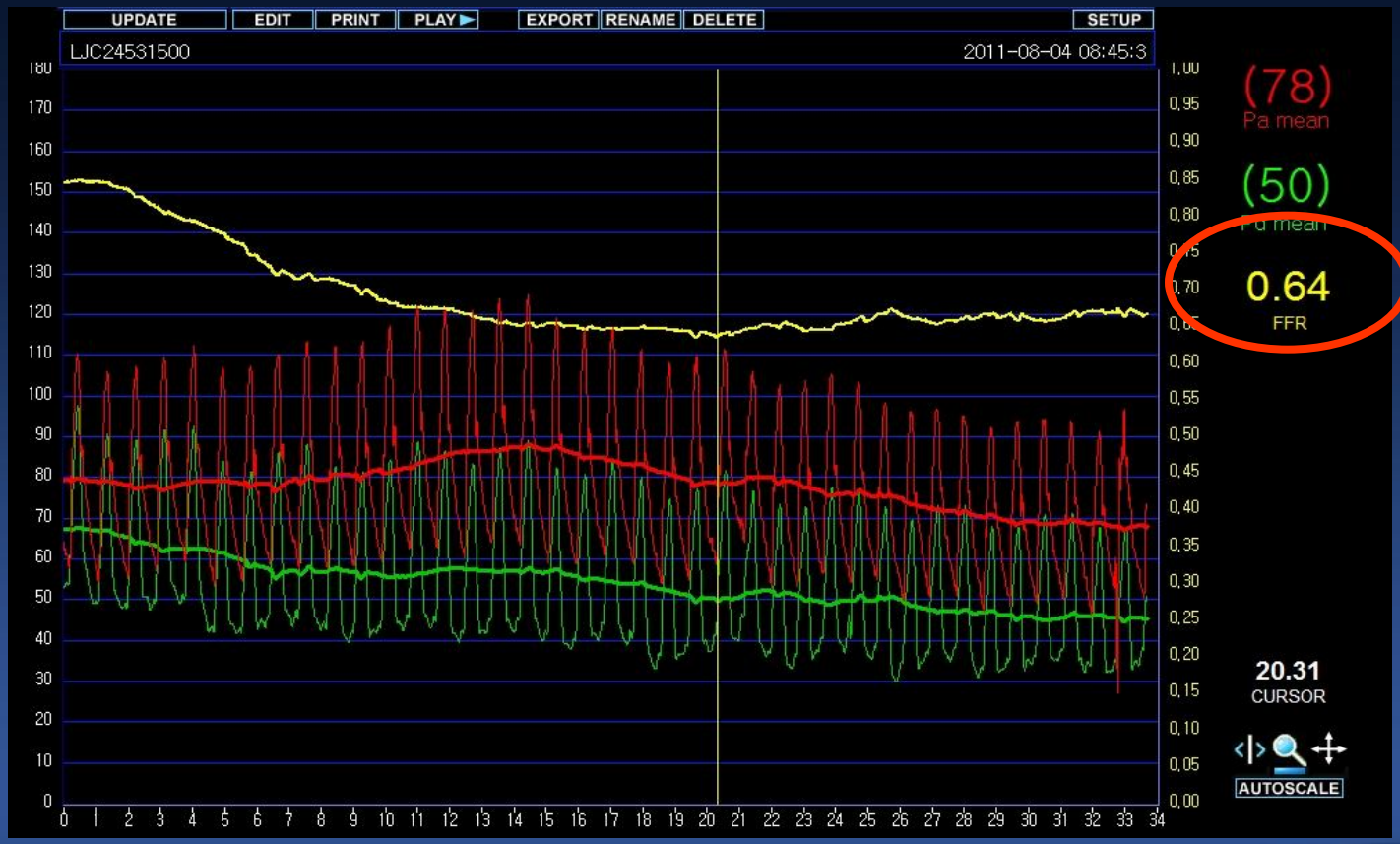
Do You Want to Treat ?



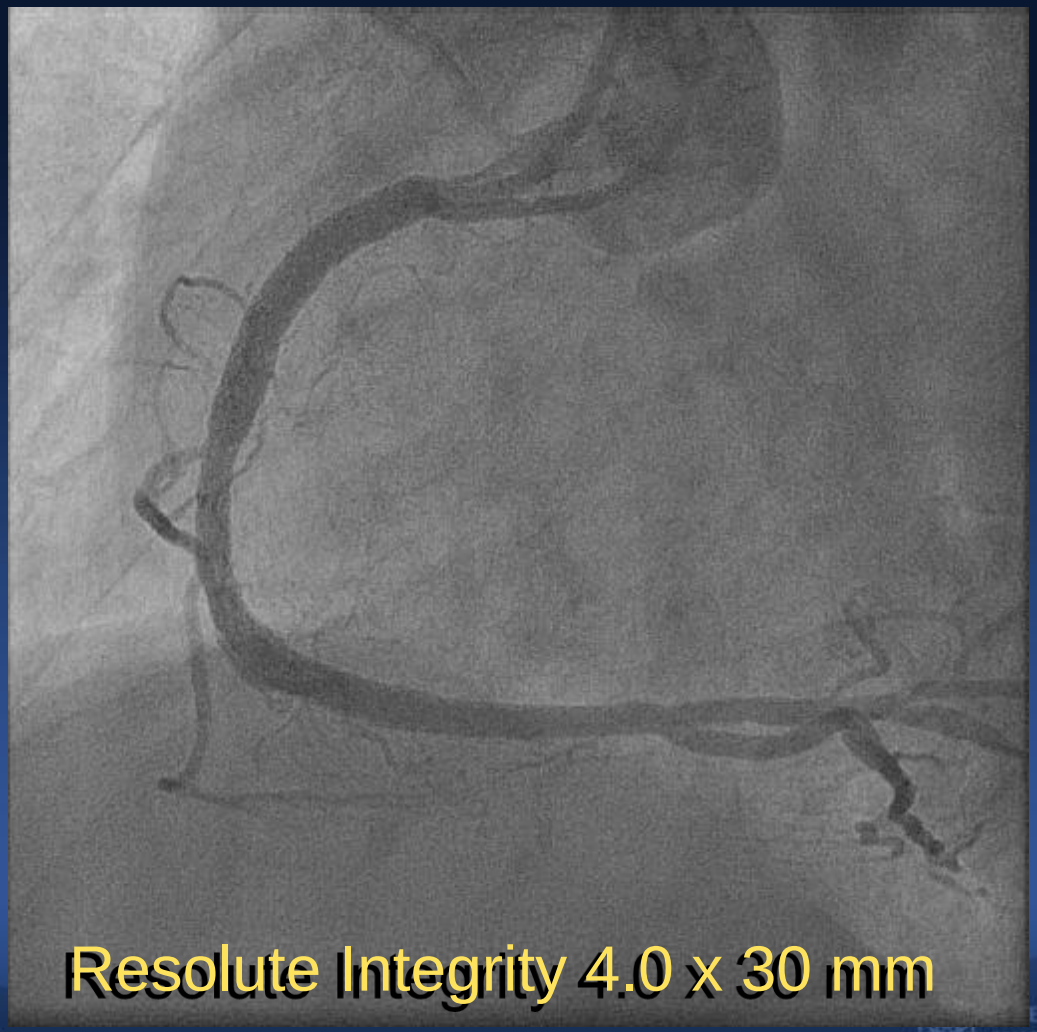


FFR 0.64

Do You Want to Treat ?



I Treated !
Based on FFR

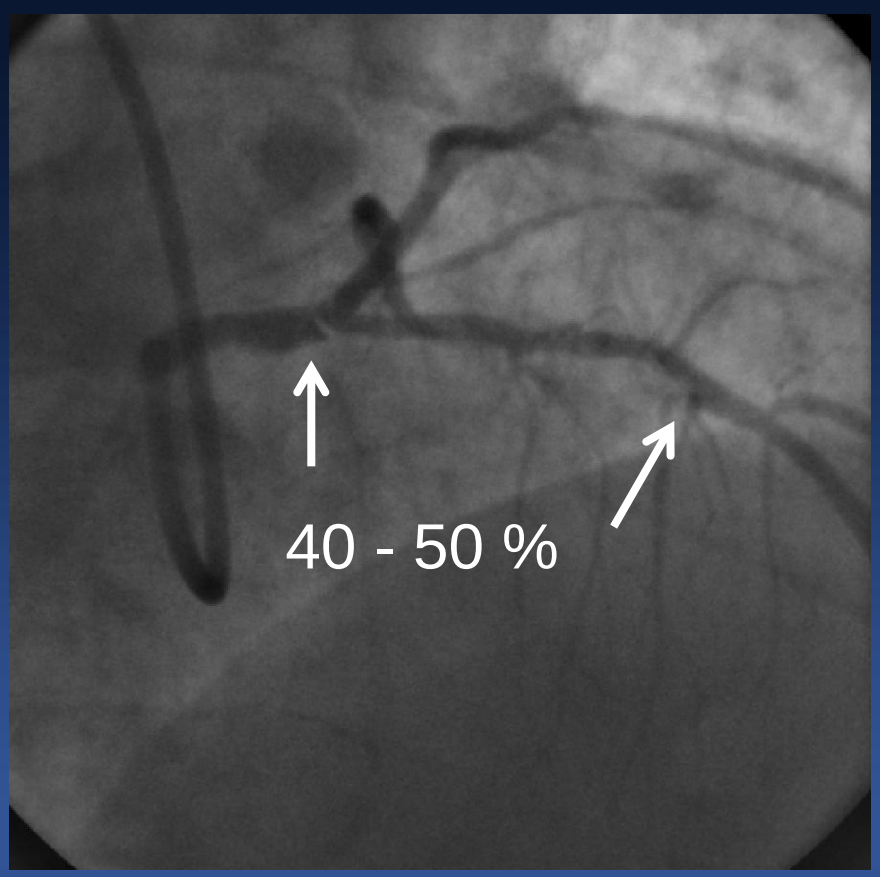


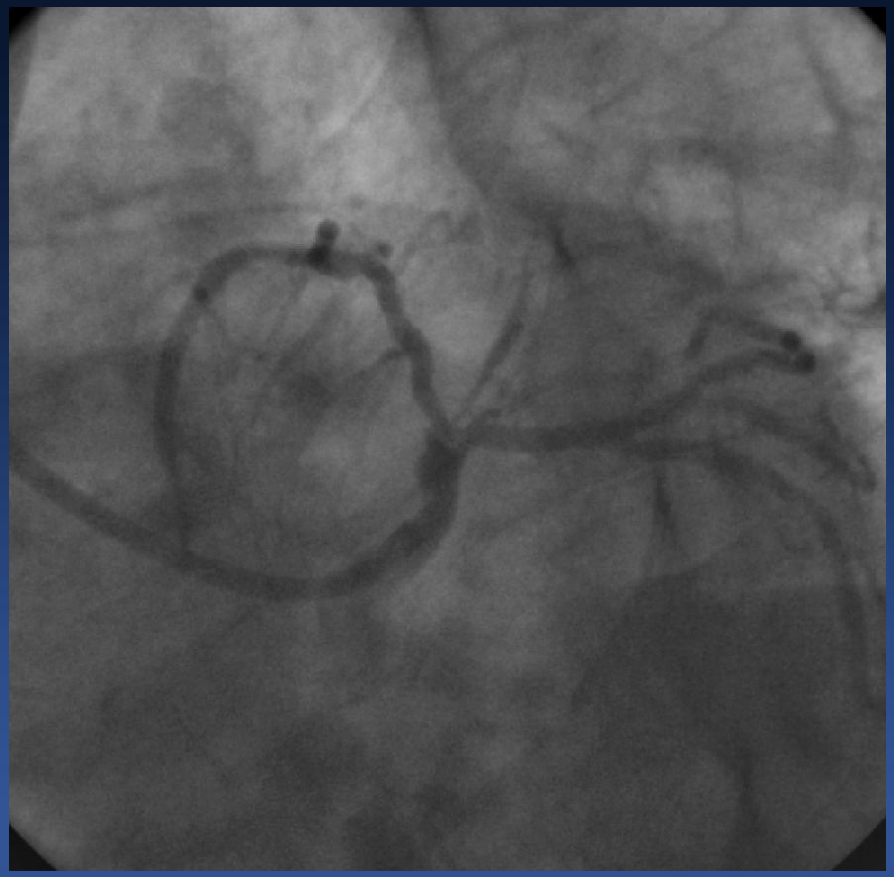
Case4,

Unstable Angina,
Ruptured Plaque,
Angiographically Insignificant,
Functionally Significant

M/80, Unstable Angina

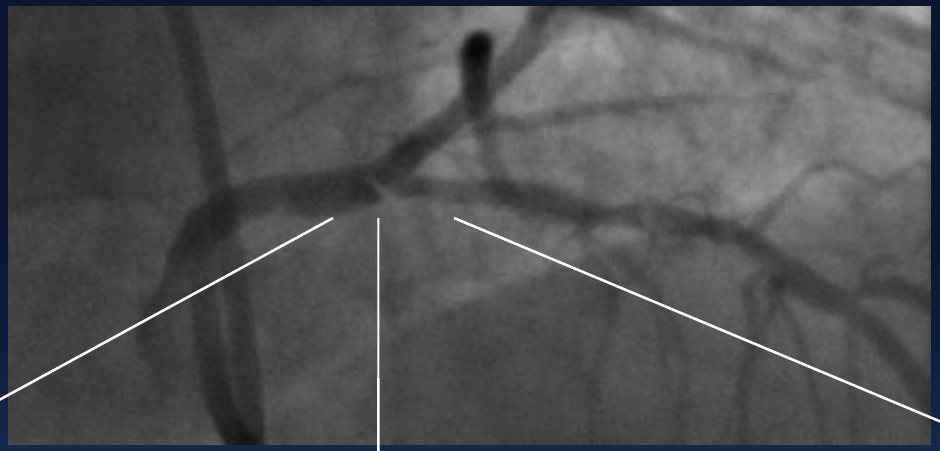
Resting chest pain, Hypertension

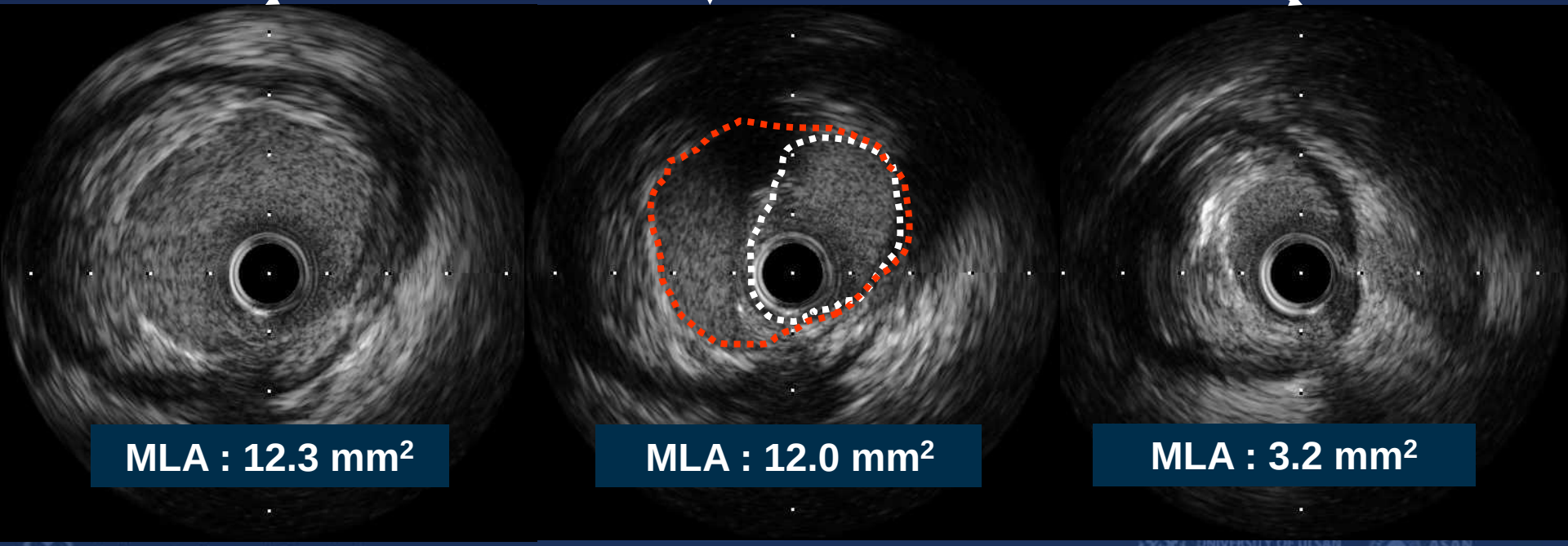




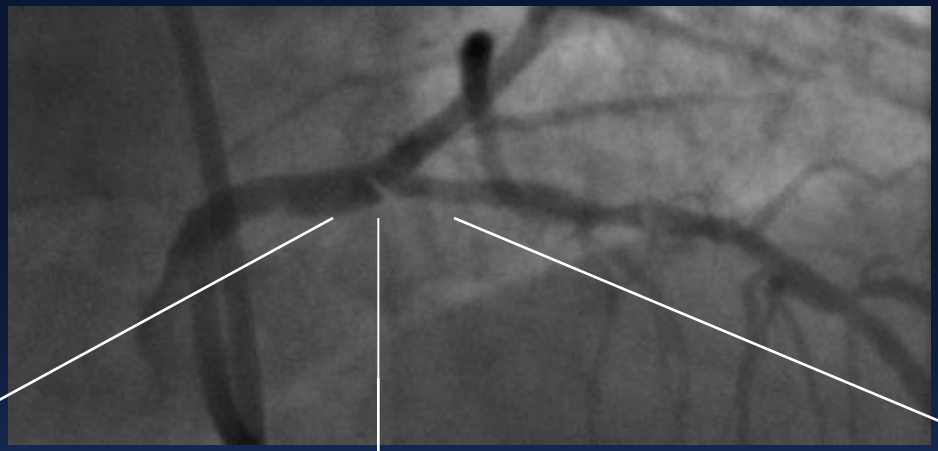
Intermediate diffuse long lesion, plaque rupture

IVUS

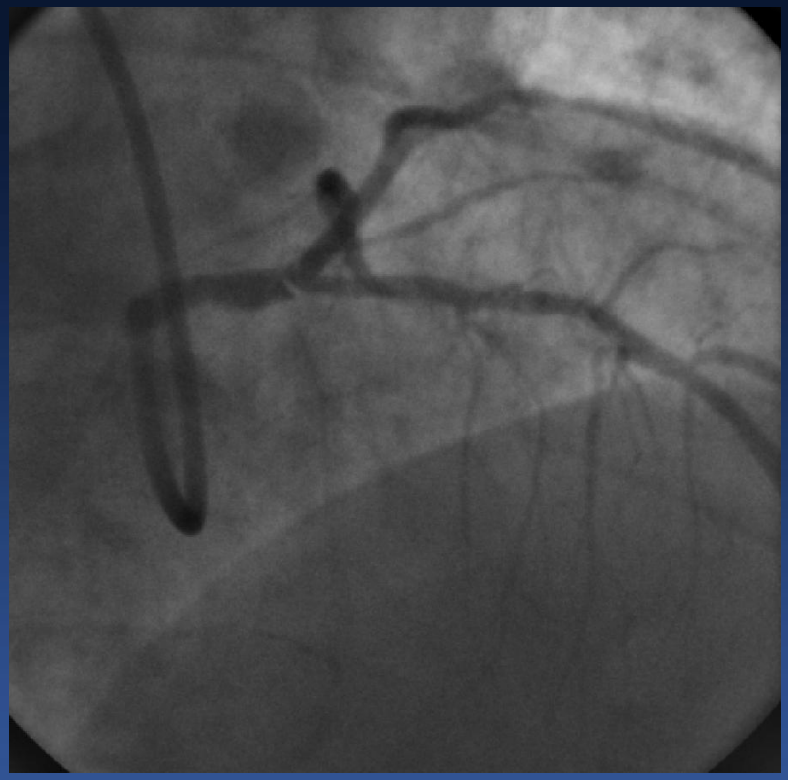




OCT



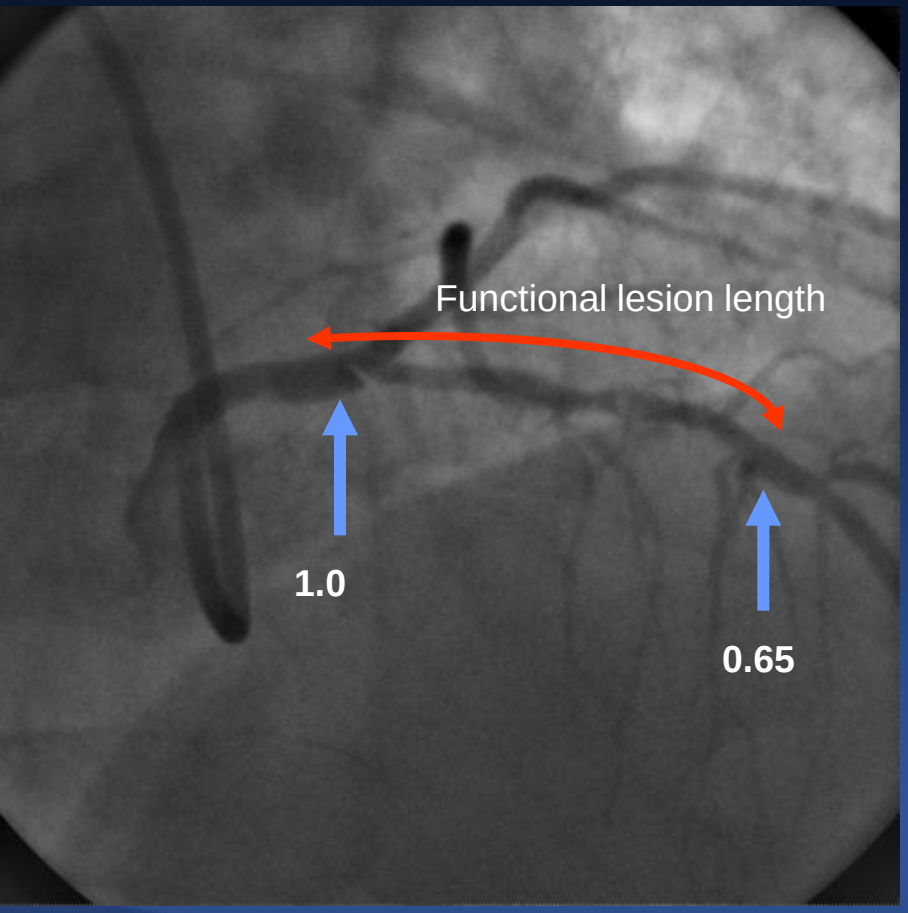
Do You Want to Treat ?



80/M, Unstable angina,
Ruptured Plaque

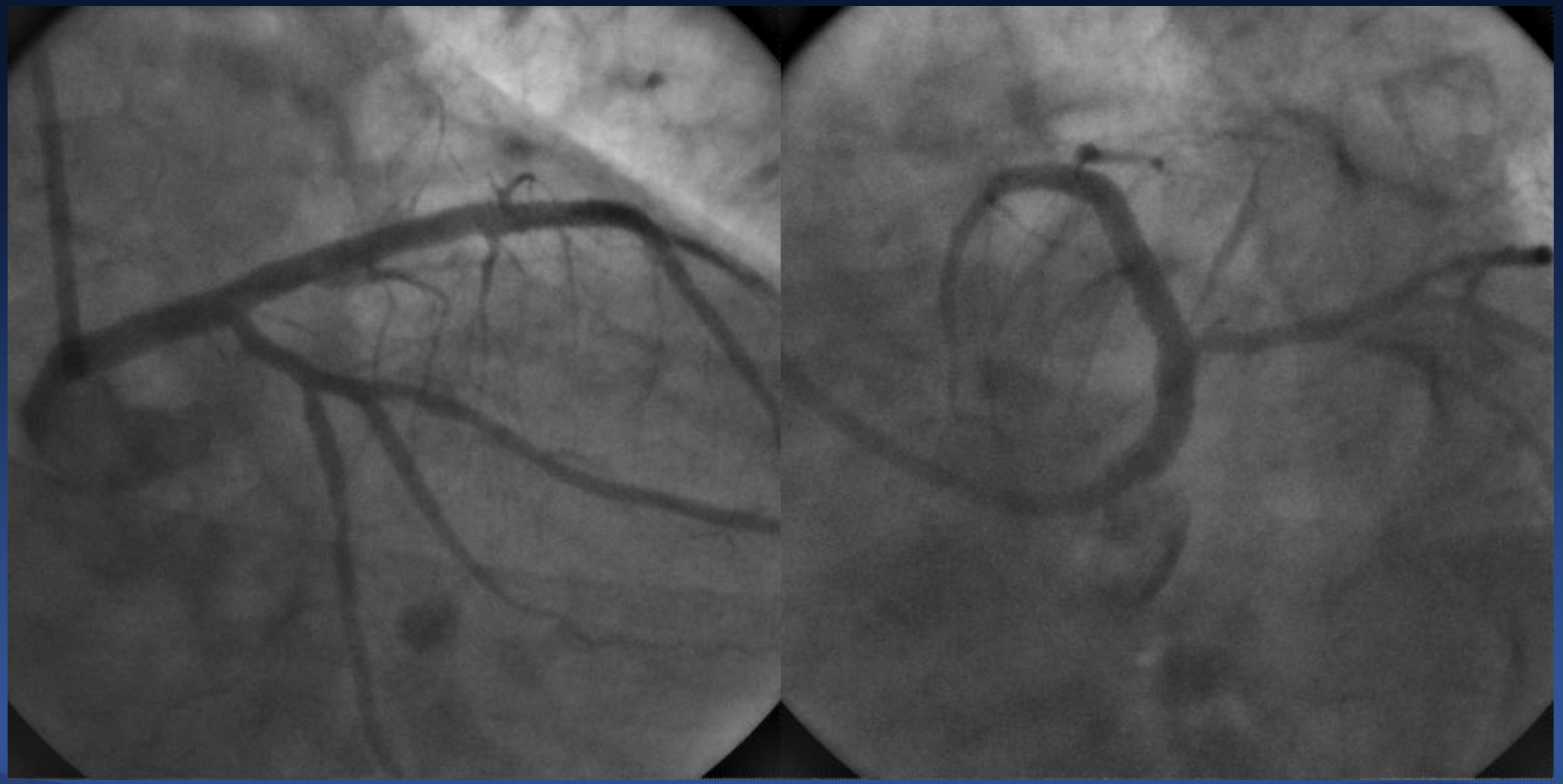
Visual Estimation: 50%
Diffuse long lesion
IVUS MLA : 3.2mm^2

FFR 0.65



during continuous hyperemia

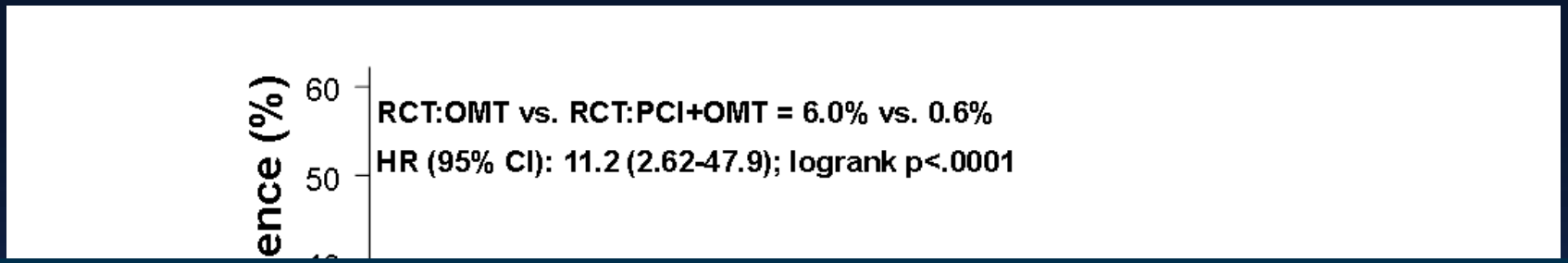
I Treated !
Based on FFR



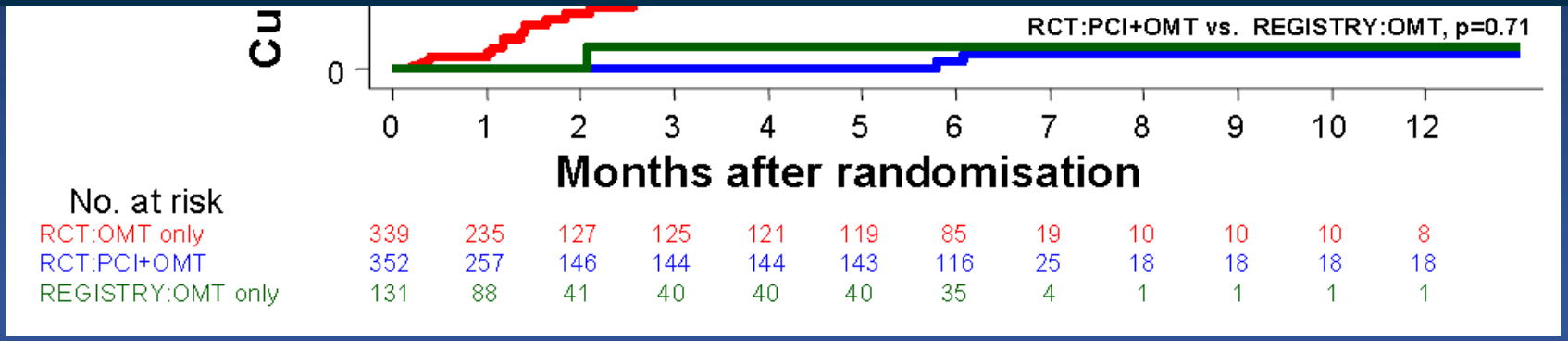
Total stented length 79mm (3 Xience V : 3.0x28, 3.5x23, 4.0x28 mm)

FAME II : 1-Year

Urgent Revascularization



FFR <0.80, Should Be Treated



De Bruyne B, et al. NEJM 2012;367:991-1001

To Treat or Not To Treat ?

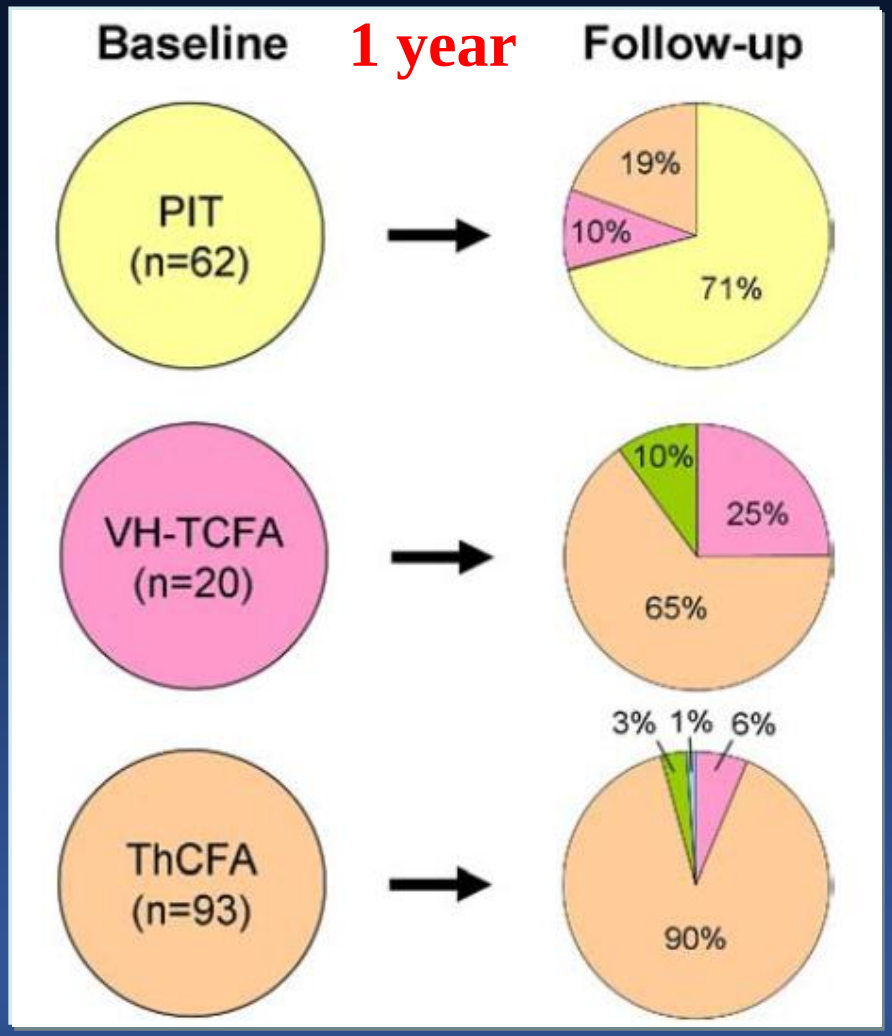
Why I Rely on FFR,
Not on Vulnerability of Plaque ?

Natural History of Vulnerability,

Symptomatic or Asymptomatic,
Stable or Unstable,

How many vulnerable plaque in An artery ?
How many vulnerable plaque in A person ?
Can we predict the fate of vulnerable plaque ?

Natural History of Plaque Vulnerability
(Global VH-IVUS Registry of CRF, NY)

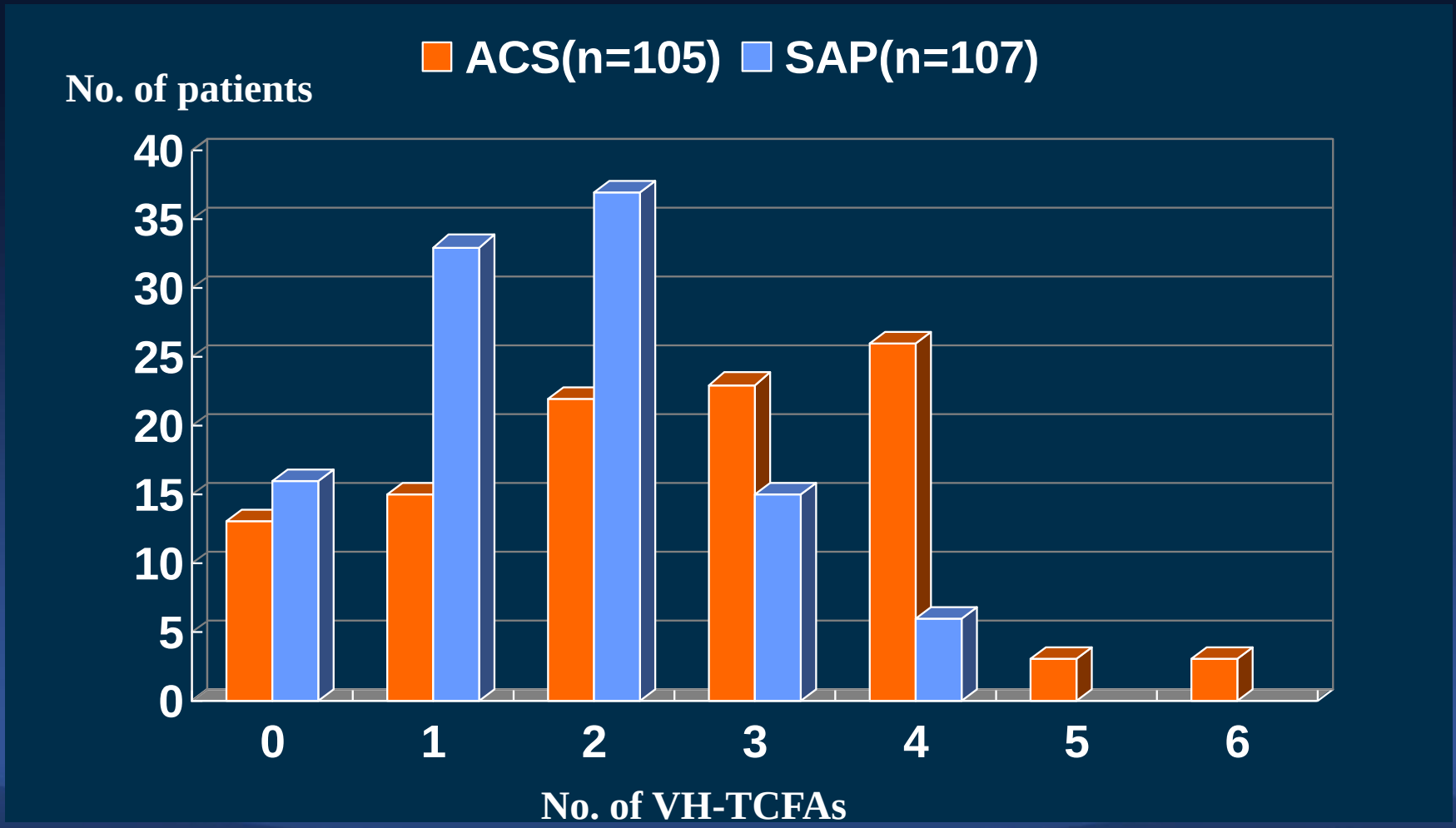


Kubo et al. J Am Coll Cardiol 2010;55:1590-7

VH-TCFA in ACS and Stable Angina

Before Rupture

3-Vessel VH-IVUS Study (n=213 pts)

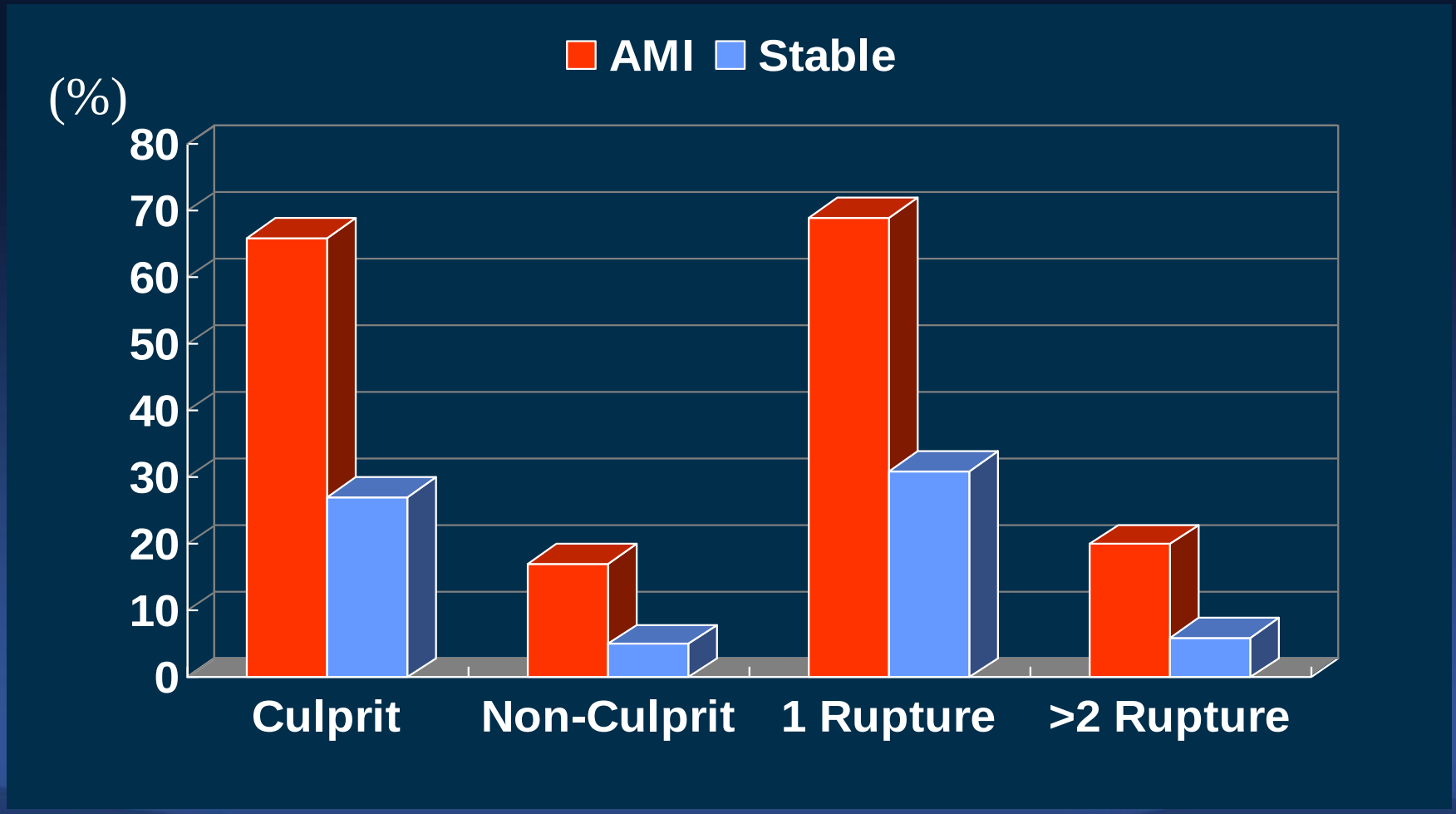


Hong MK et al, AJC. 2008;101:568-572

Plaque Rupture in AMI and Stable Angina

After Rupture

3-Vessel IVUS Study (n=235 pts)



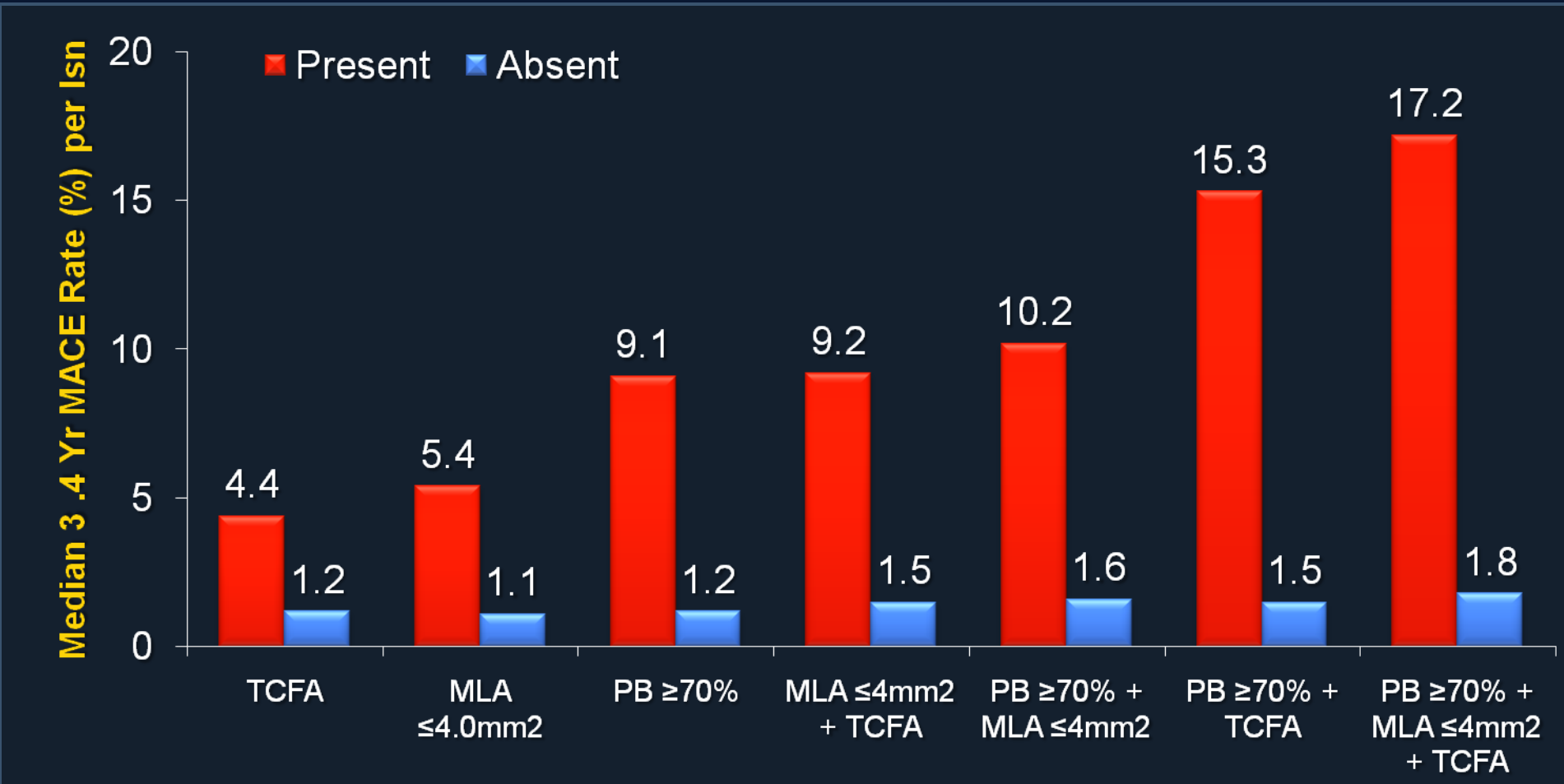
Hong MK et al, Circulation. 2004;110:928-933

Why I Rely on FFR, Not on Vulnerability of Plaque

1. The presence of vulnerable features (TCFAs) at a given time can not predict any future events.

2. Vulnerability is usually widespread, not focal. It is the patient that is vulnerable, not the plaque. No studies demonstrated improved outcomes following focal intervention of “vulnerable plaque”.

PROSPECT: Correlates of Non Culprit Lesion Related Events



	TCFA	MLA ≤4.0mm2	PB ≥70%	MLA ≤4mm2 + TCFA	PB ≥70% + MLA ≤4mm2	PB ≥70% + TCFA	PB ≥70% + MLA ≤4mm2 + TCFA
Lesion HR	3.8 (2.2, 6.6)	5.0 (2.9, 8.7)	7.9 (4.6, 13.8)	6.4 (3.4, 12.2)	6.7 (3.4, 13.0)	10.8 (5.5, 21.0)	10.8 (4.3, 27.2)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Prevalence*	51.2%	49.1%	30.7%	17.4%	15.4%	11.0%	4.6%

*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA

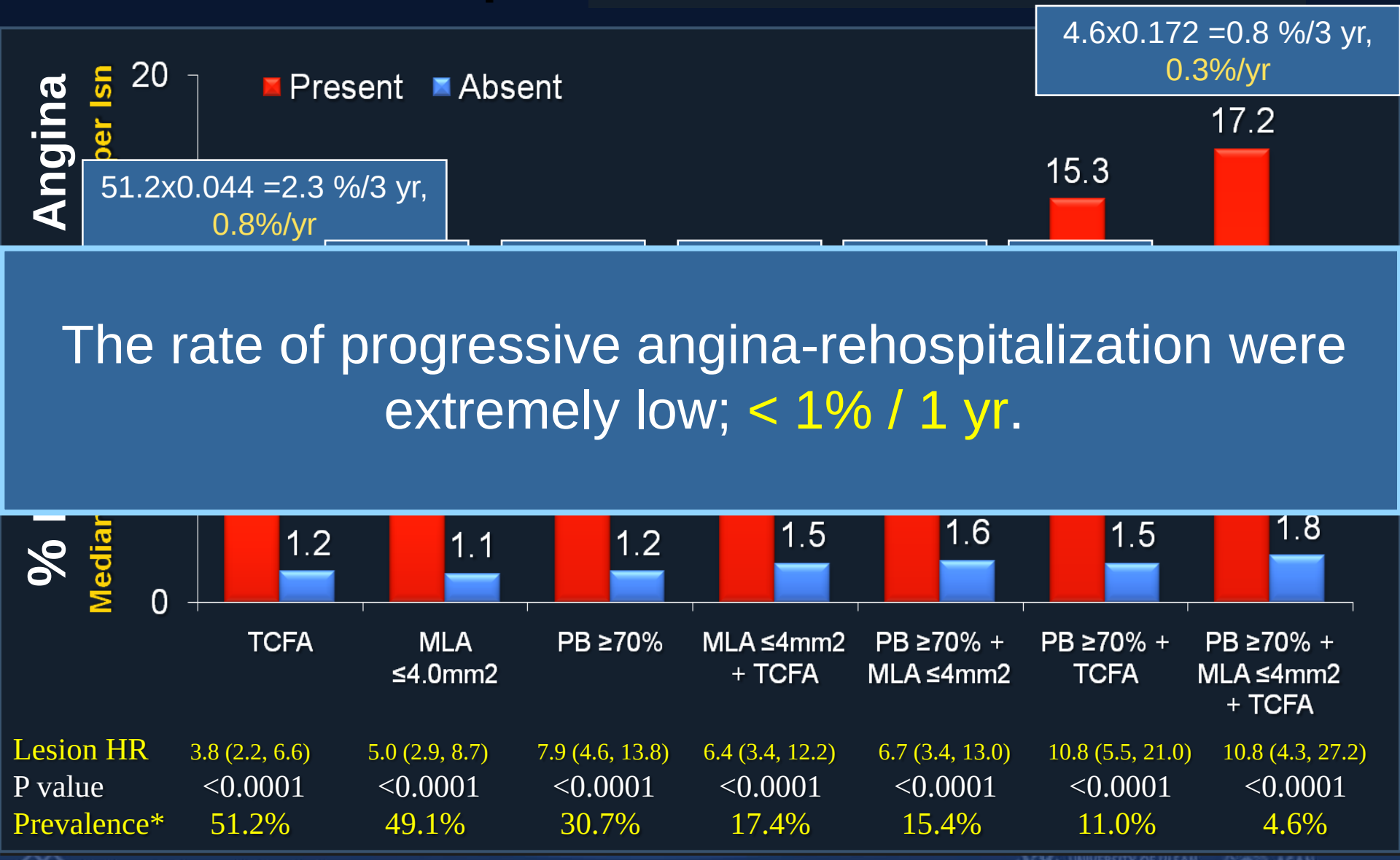
Cumulative Rates of 3-year MACE

	Culprit -related	Nonculprit -related	Indeterminate events	All events
Myocardial infarction	2.0% (13)	1.0% (6)	0.3% (2)	3.3% (21)
Rehospitalization for unstable/progressive angina	11.5% (74)	10.8% (69)	0.8% (5)	17.5% (113)
Revascularization	10.9% (70)	10.5% (67)	0	17.1% (110)

Rates of death and MI are extremely low; 1% / 3 yr.

Stone G et al. N Engl J Med 2011;364:226-35

PROSPECT: Correlates of Non Culprit Revascularization Rate(%)



The rate of progressive angina-rehospitalization were extremely low; < 1% / 1 yr.

Lesion HR	3.8 (2.2, 6.6)	5.0 (2.9, 8.7)	7.9 (4.6, 13.8)	6.4 (3.4, 12.2)	6.7 (3.4, 13.0)	10.8 (5.5, 21.0)	10.8 (4.3, 27.2)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Prevalence*	51.2%	49.1%	30.7%	17.4%	15.4%	11.0%	4.6%

Message from PROSPECT study

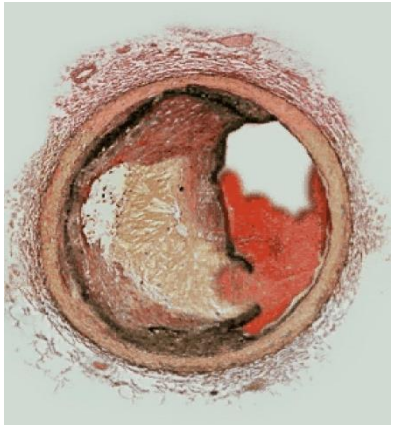
1. Non-culprit vulnerable plaque - large plaque burden, TCFA, and smaller MLA are prone to rapid lesion progression. Most of those events were angina and revascularization, not hard events of death and MI.

2. The prevalence of defined vulnerable plaque is very low and overall event rate is extremely low, and so we can not translate the risk of these vulnerable plaque into the any concerns about death and MI.

Q3,

Can FFR Represent the Plaque Vulnerability ?

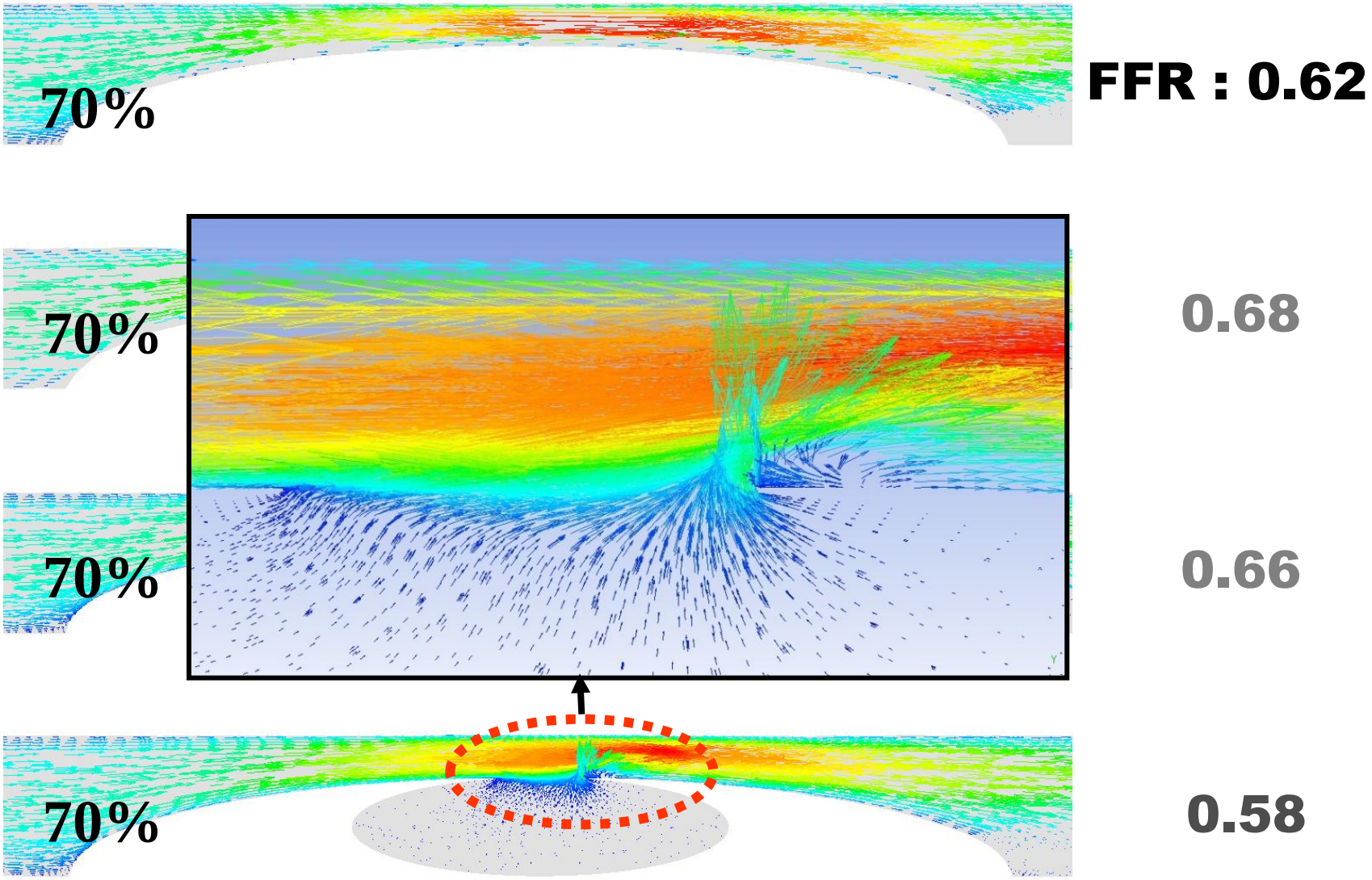
Vulnerable Plaque Simulation



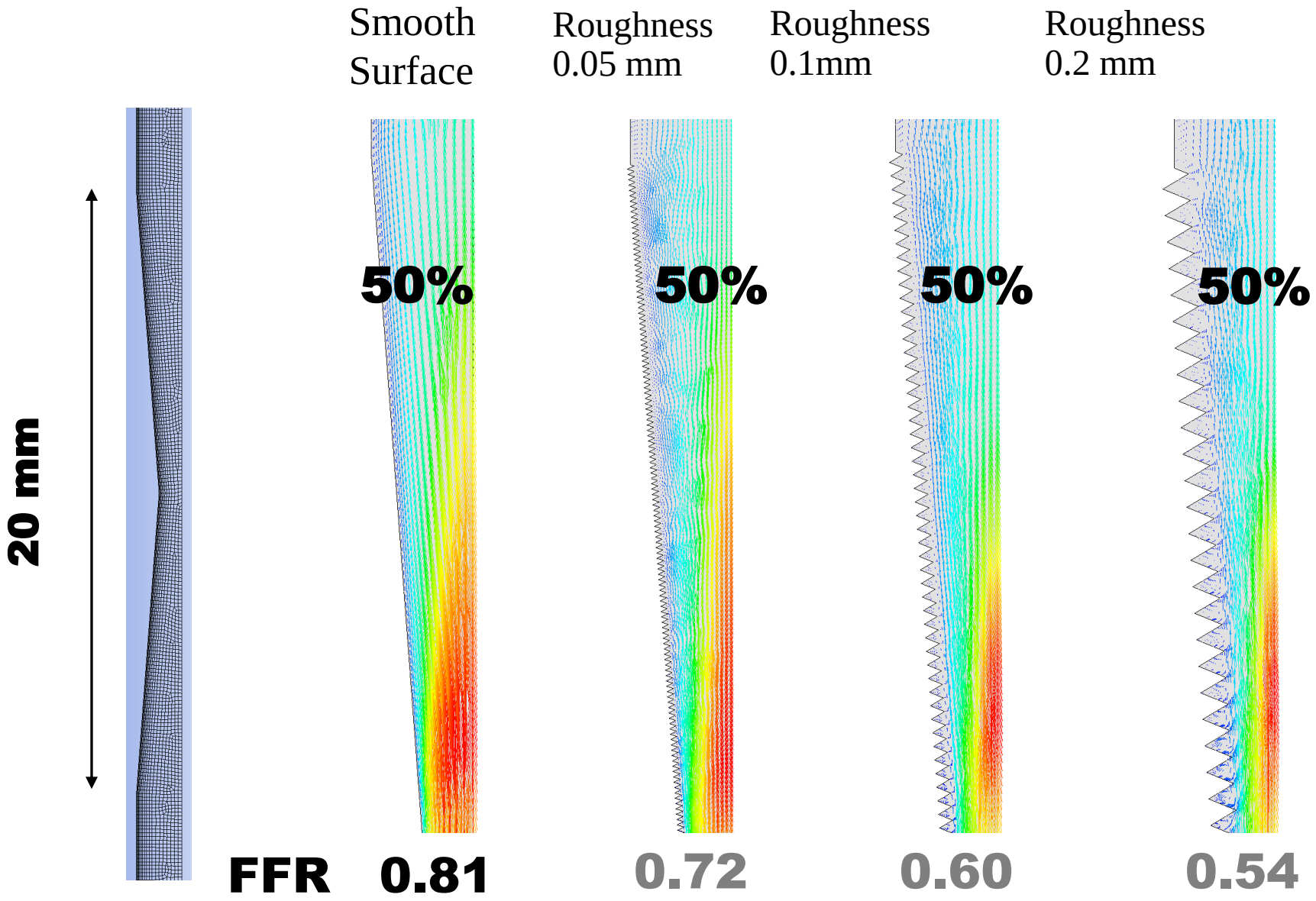
Plaque rupture

Thrombus, surface roughness

Presence of Plaque Rupture

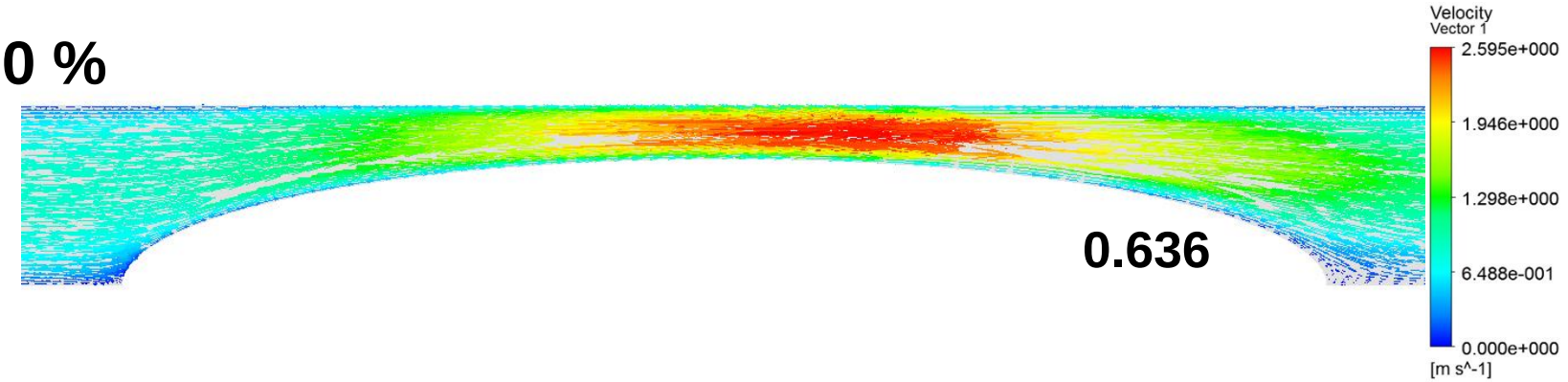


Different Surface Roughness

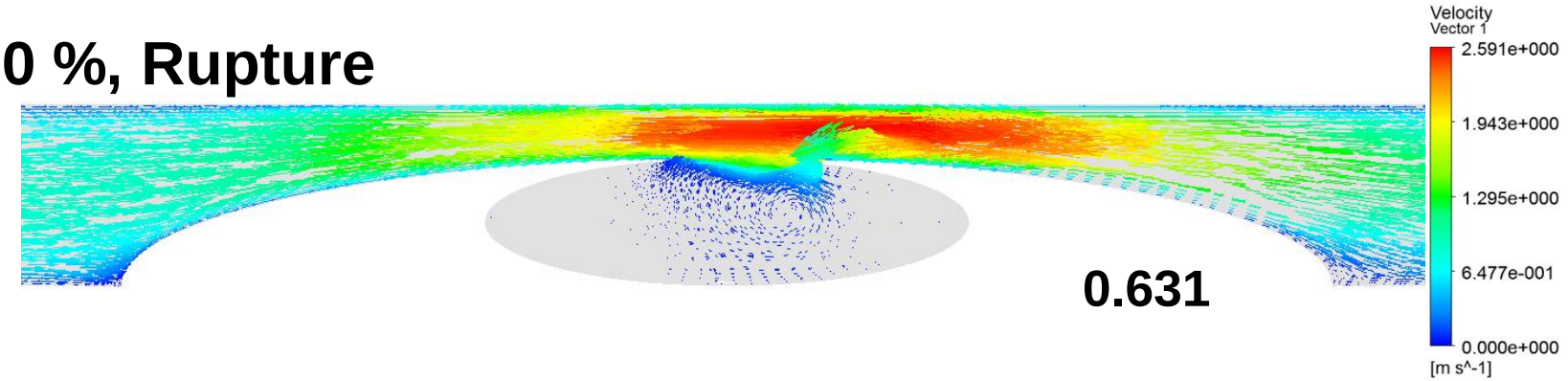


Rupture and Roughness

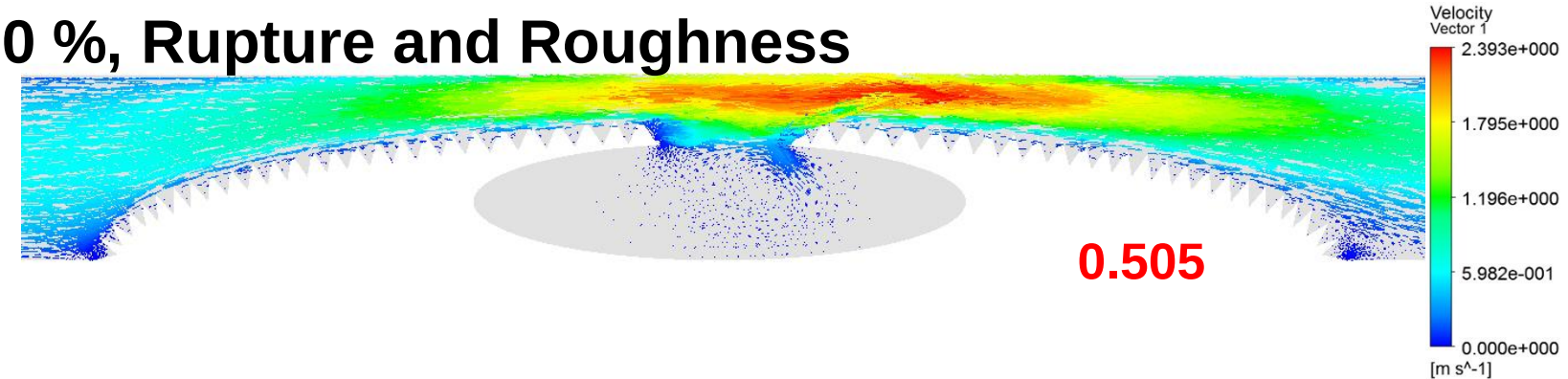
70 %



70 %, Rupture



70 %, Rupture and Roughness



Why I Rely on FFR, Not on Vulnerability of Plaque

1. The presence of vulnerable features (TCFAs) at a given time can not predict any future events.

2. FFR have already reflected the plaque vulnerability such as rupture and thrombus. Rupture and thrombus would be one of the local characteristics to determine the FFR. If there was not serious myocardial damage, FFR still works even in the setting of ACS except STEMI.

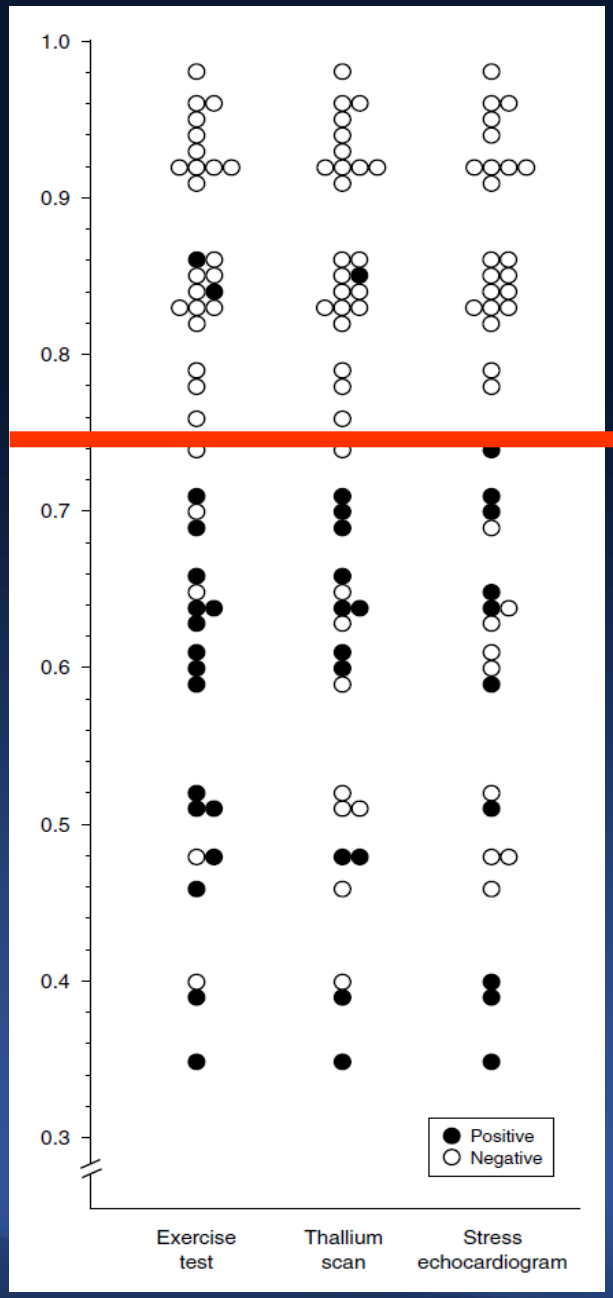
Q4,

What Does it Mean, FFR Guided ?

First Validation

with Non-invasive Stress Test Results

(n=45 patients, intravenous adenosine infusion)



FFR <0.75

Sensitivity	**88%**
Specificity	**100%**
Positive PV	**100%**
Negative PV	**88%**
Accuracy	**93%**

Pijls NHJ, NEJM 1996;334:1703-8

Best Cut-off Value of FFR

Author	Number	Stress Test	BCV	Accuracy
Pijls et al.	60	X-ECG	0.74	97
DeBruyne et al.	60	X-ECG/SPECT	0.72	85

Cut-off value of 0.72 - 0.78 is extremely reproducible and very solid.

Usui et al.	167	SPECT	0.75	79
Yanagisawa et al.	167	SPECT	0.75	76
Meuwissen et al.	151	SPECT	0.74	85
DeBruyne et al.	57	MIBI-SPECT post-MI	0.78	85
Samady et al.	48	MIBI-SPECT post-MI	0.78	85
Ahn JM et al.(2011)	151	SPECT	0.77	89

Validation and Threshold of Ischemia

FFR < 0.80
is a good surrogate
for clinical ischemia.

To Treat or Not To Treat
Operator's discretion

Validation and Threshold of Ischemia

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

Negative FFR Never Lies
100% Specificity

Why I Rely on FFR, Not Vulnerability of Plaque

1. The presence of vulnerable features (TCFAs) at a given time can not predict any future events.

2. FFR have already reflected the plaque vulnerability such as rupture and thrombus.

3. FFR guided means, ischemia guided decision making based on non-invasive stress tests.

My Thought,

In Any Lesions with Negative FFR (>0.80),

Just Defer !