Can We Prevent Events of Vulnerable Plaque ? From Stable to PREVENT

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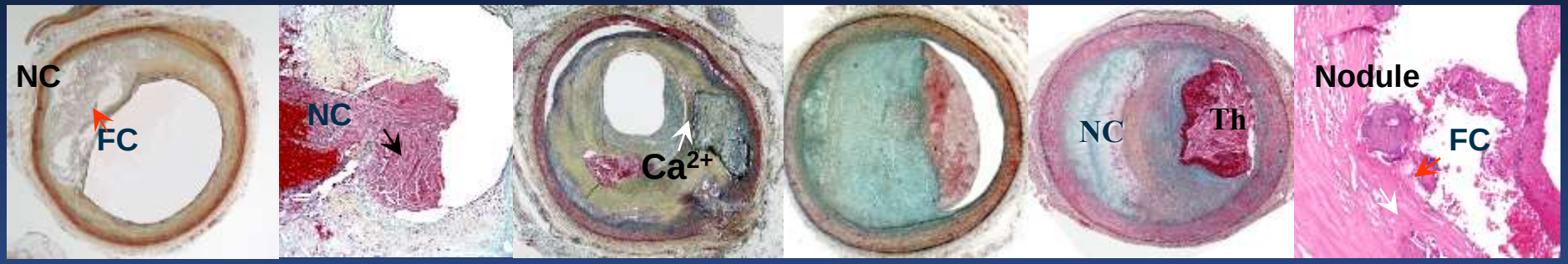
Vulnerable Plaque,
Pathology Definition

Thin-cap Fibroatheroma (TCFA) | Rupture/ Healed Rupture | Erosion | Erosion/ Thrombus | Calcific Nodule



Virmani R, et al. ATVB 2000;20:1262
Naghavi et al. Circulation 2003;108:1664-72

Vulnerable Plaque,
Imaging Definition

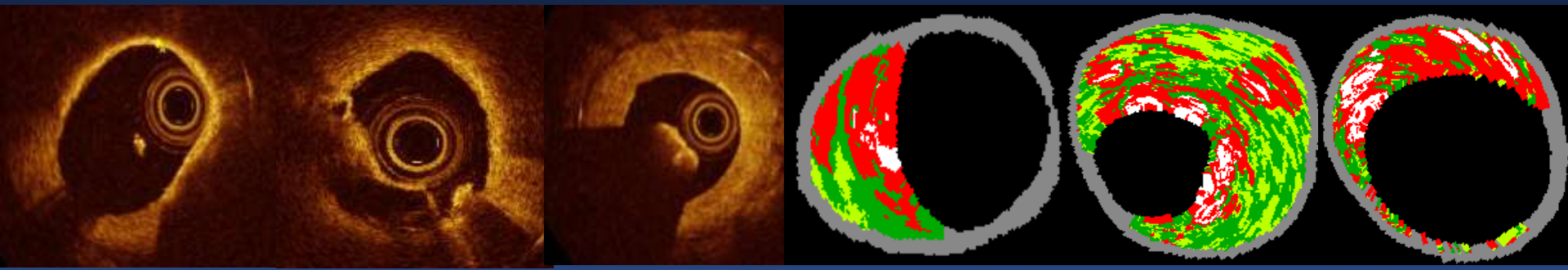
Thin-cap Fibroatheroma (TCFA)

Rupture/ Healed Rupture

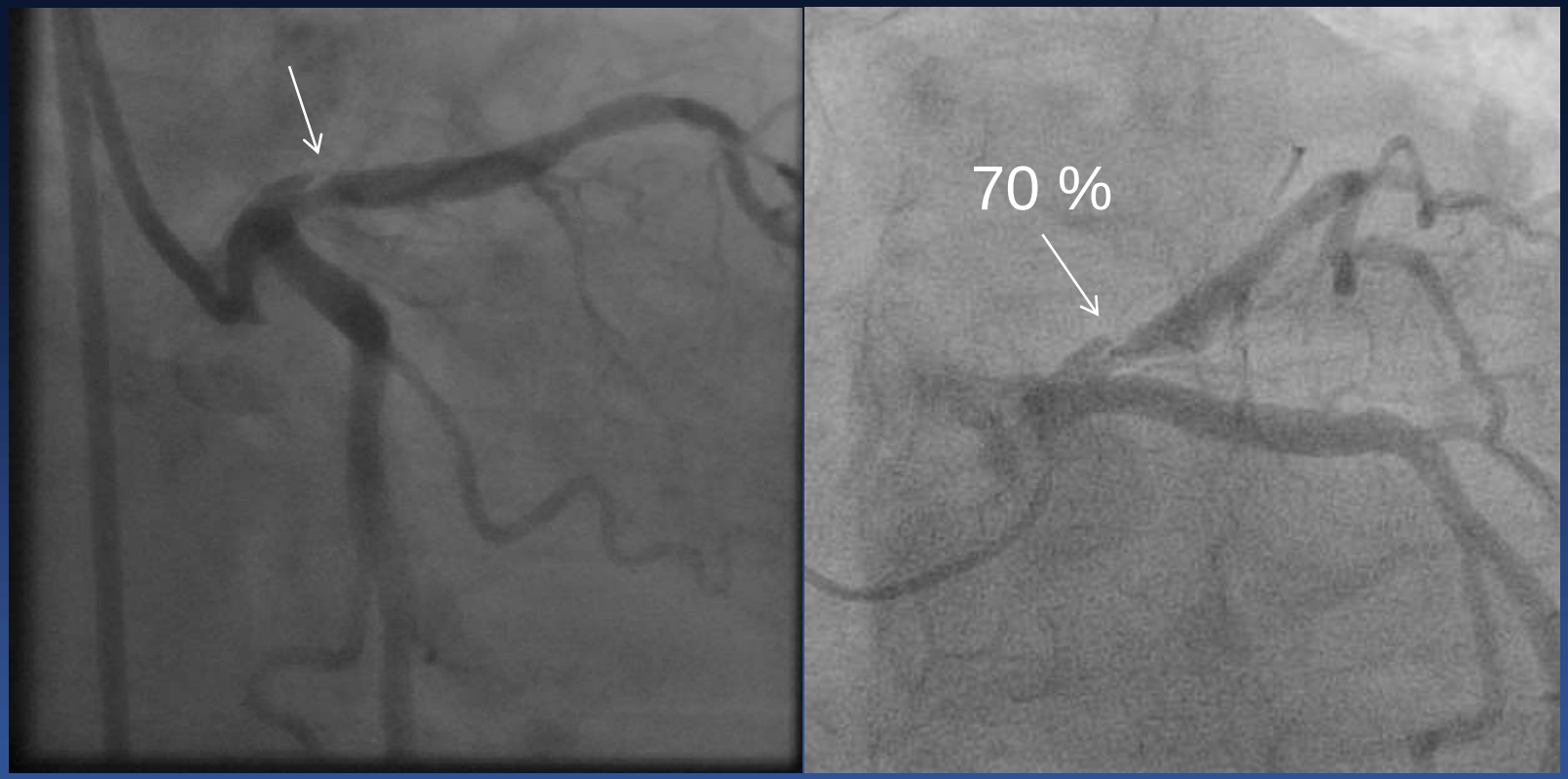
Confluent Necrotic Core

>50% Area Narrowing

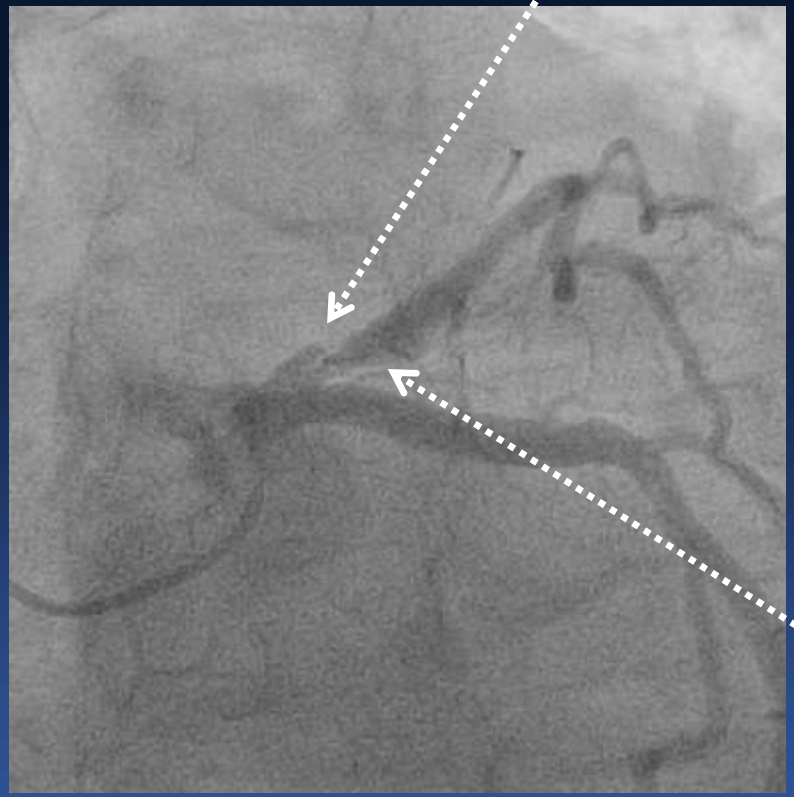
Calcium >5%

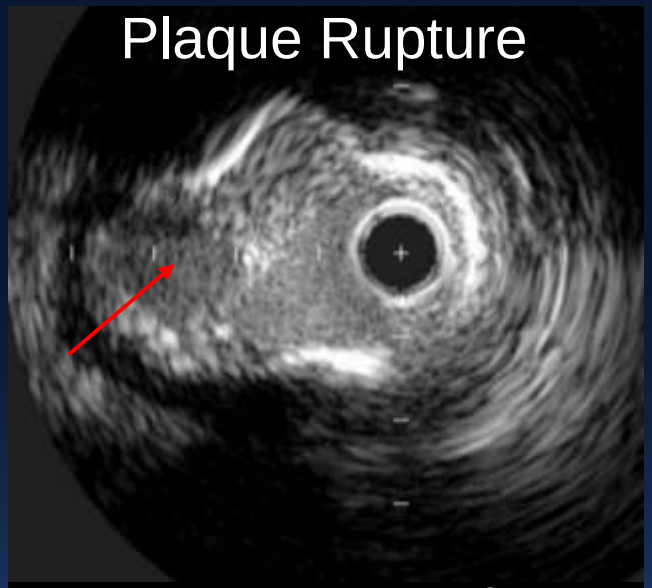


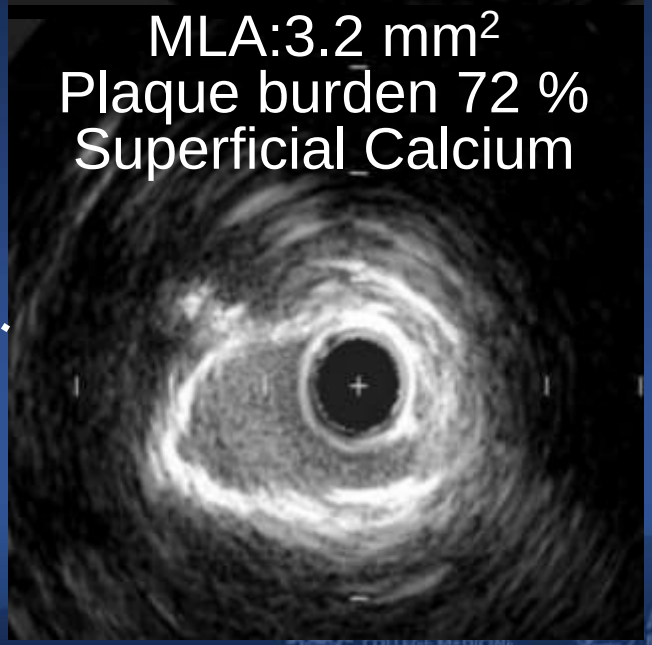
M/74,
Asymptomatic Plaque Rupture



IVUS



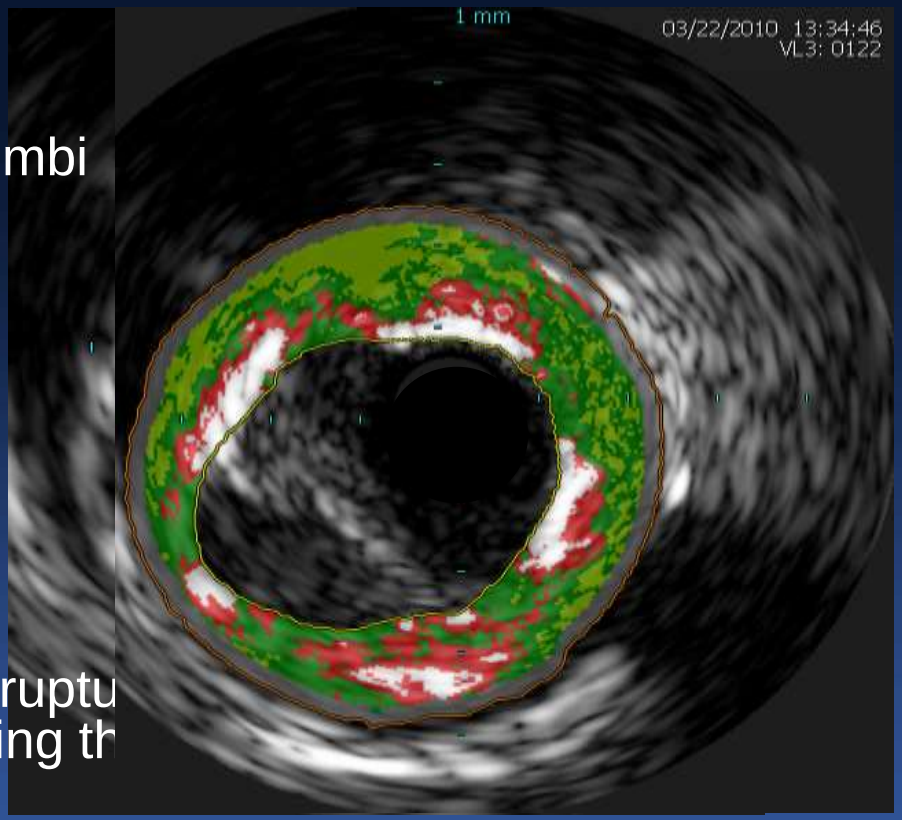

Plaque Rupture


MLA:3.2 mm2
Plaque burden 72 %
Superficial Calcium

VH-IVUS

Thrombi

Plaque ruptu
organizing th



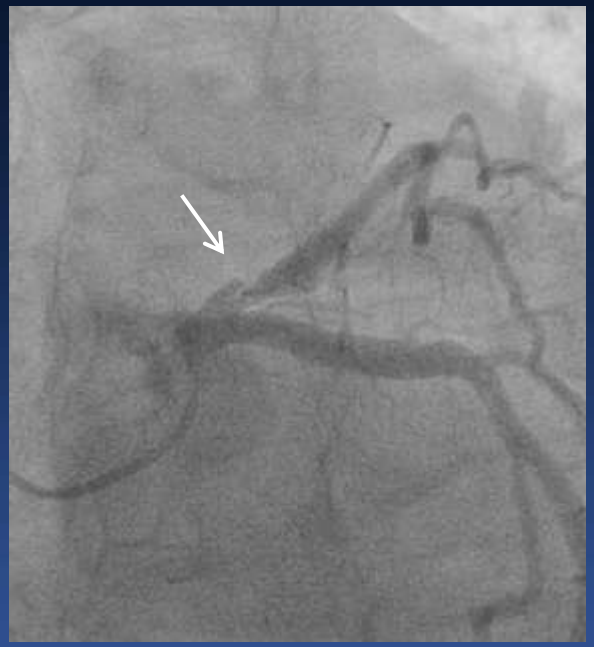
PB: 71.3%
FI : 41.4%
FF: 20.0%
NC: 23.0%
DC: 15.6%

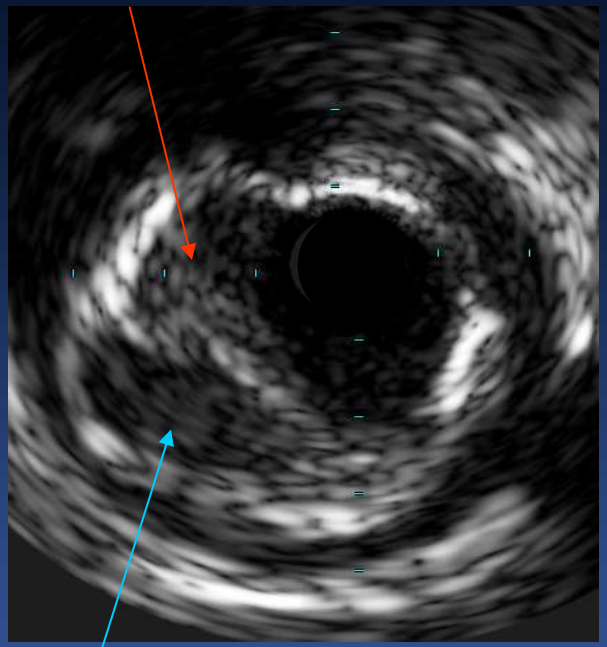
LAD, FFR

Intravenous adenosine, 200 μg/kg/min

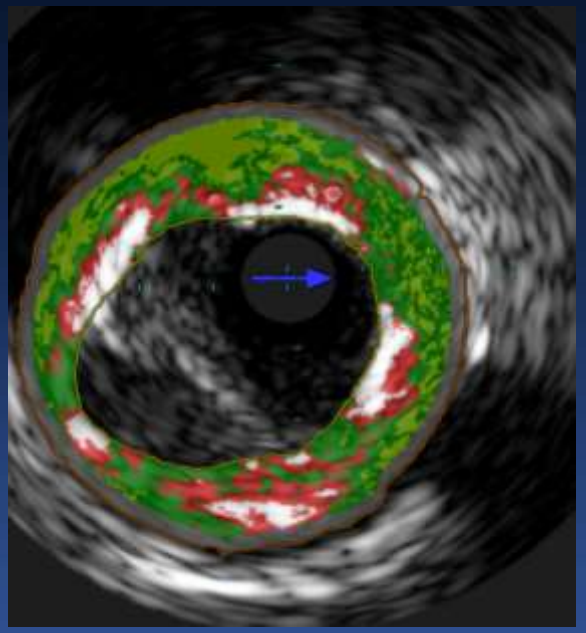
Functionally Insignificant
Vulnerable Plaque

Organized Thrombus



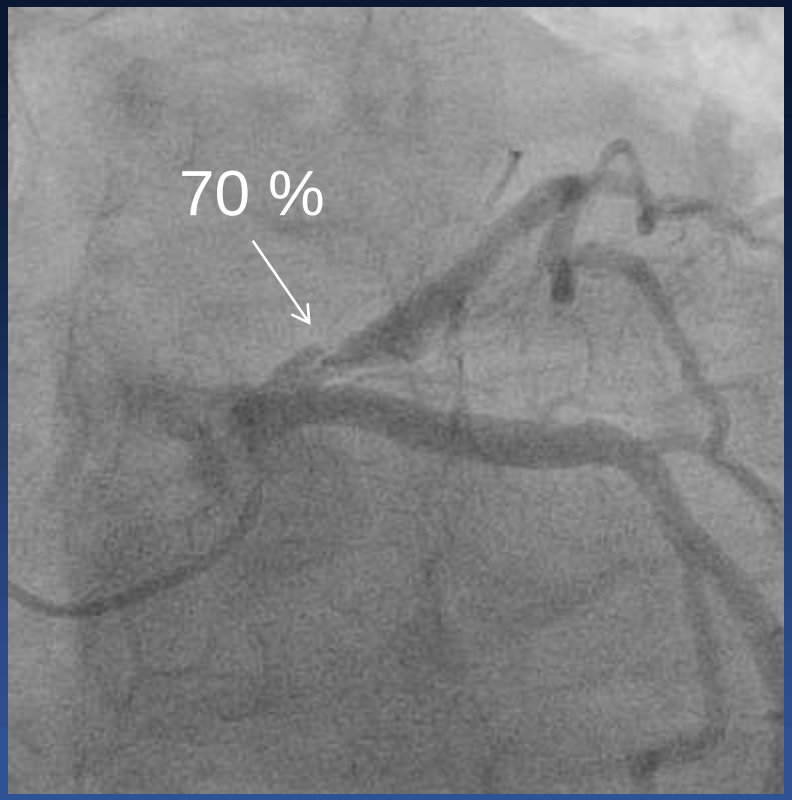


Rupture
Plaque Burden 72%
MLA:3.2 mm^2



Necrotic Core 25%
Dense Calcium 16%

~~Functionally Insignificant~~ To Treat or Not To Treat ? *Vulnerable Plaque*



FFR : 0.89

Angiographic DS : 70%

IVUS MLA : 3.2 mm^2

Plaque burden : 72%

Necrotic Core : 25%

Dense Calcium ; 16%

Plaque Rupture with Thrombus Containing

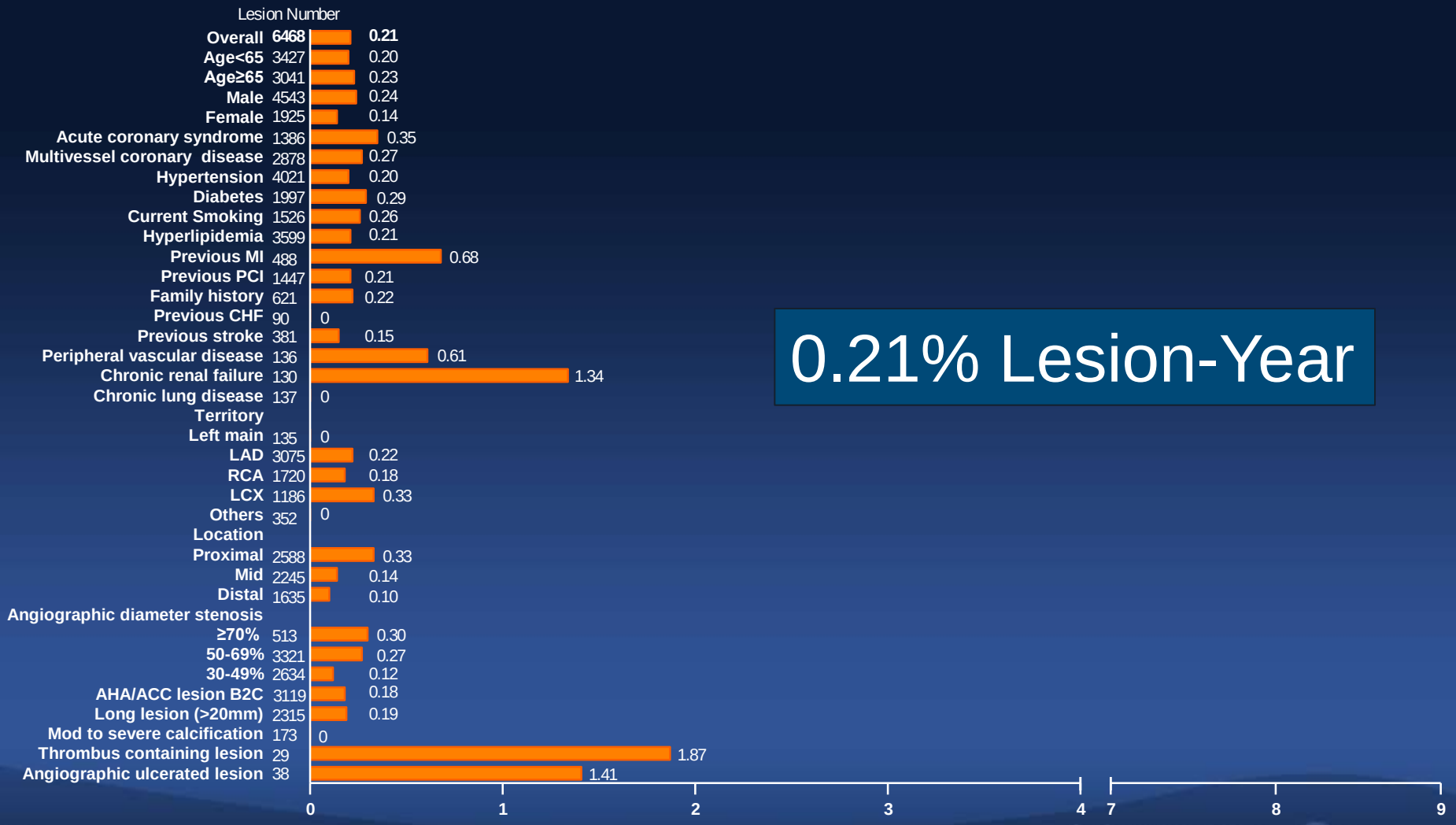
Not to Treat ?

Negative FFR (non-invasive stress tests) means *just excellent prognosis (0.6%/year, Cardiac Death and MI),* even in the presence of angiographically proven coronary artery disease.

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

Cardiac Death/MI

(IRIS-FFR Registry, 8633 Deferred Lesions Analysis, AMC data)



0.21% Lesion-Year

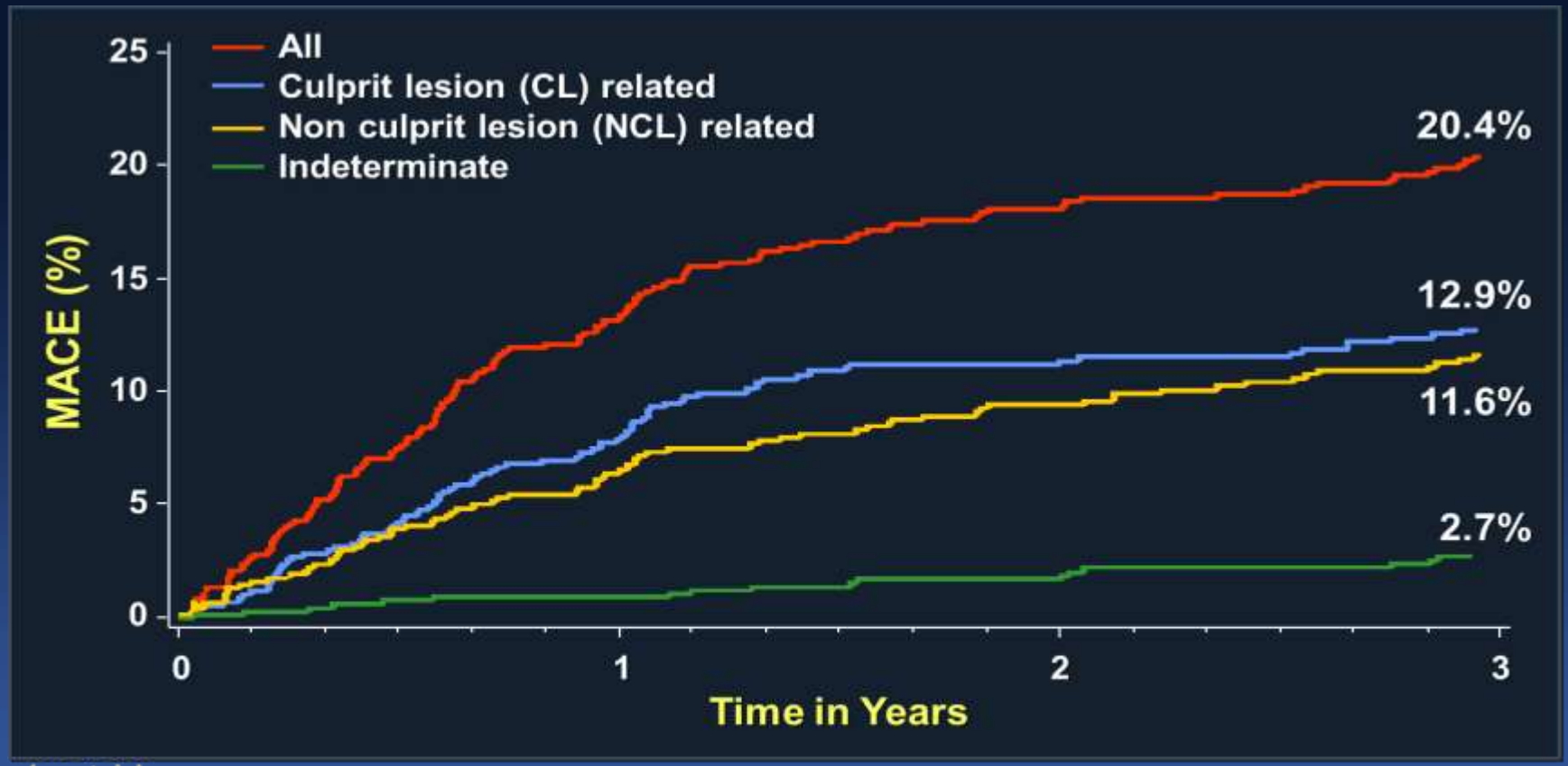
To Treat ?

Vulnerable Plaque (defined by PROSPECT study) *has more tendency to increase MACE.*

PROSPECT Study
Stone GW et al. NEJM 2011;364:226-35

PROSPECT: MACE

(N=700, ACS, 3-Vessel Imaging after PCI)

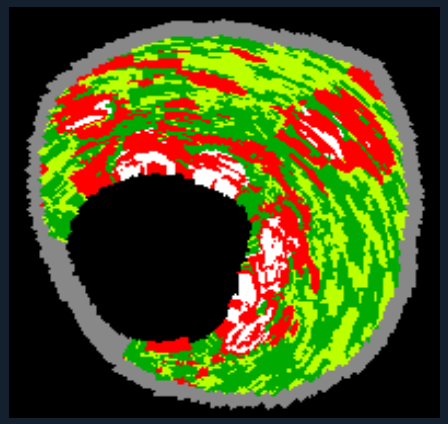


Number at risk				
ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

Stone GW et al. NEJM 2011;364:226-35

Vulnerable Plaque
Defined by VH-IVUS

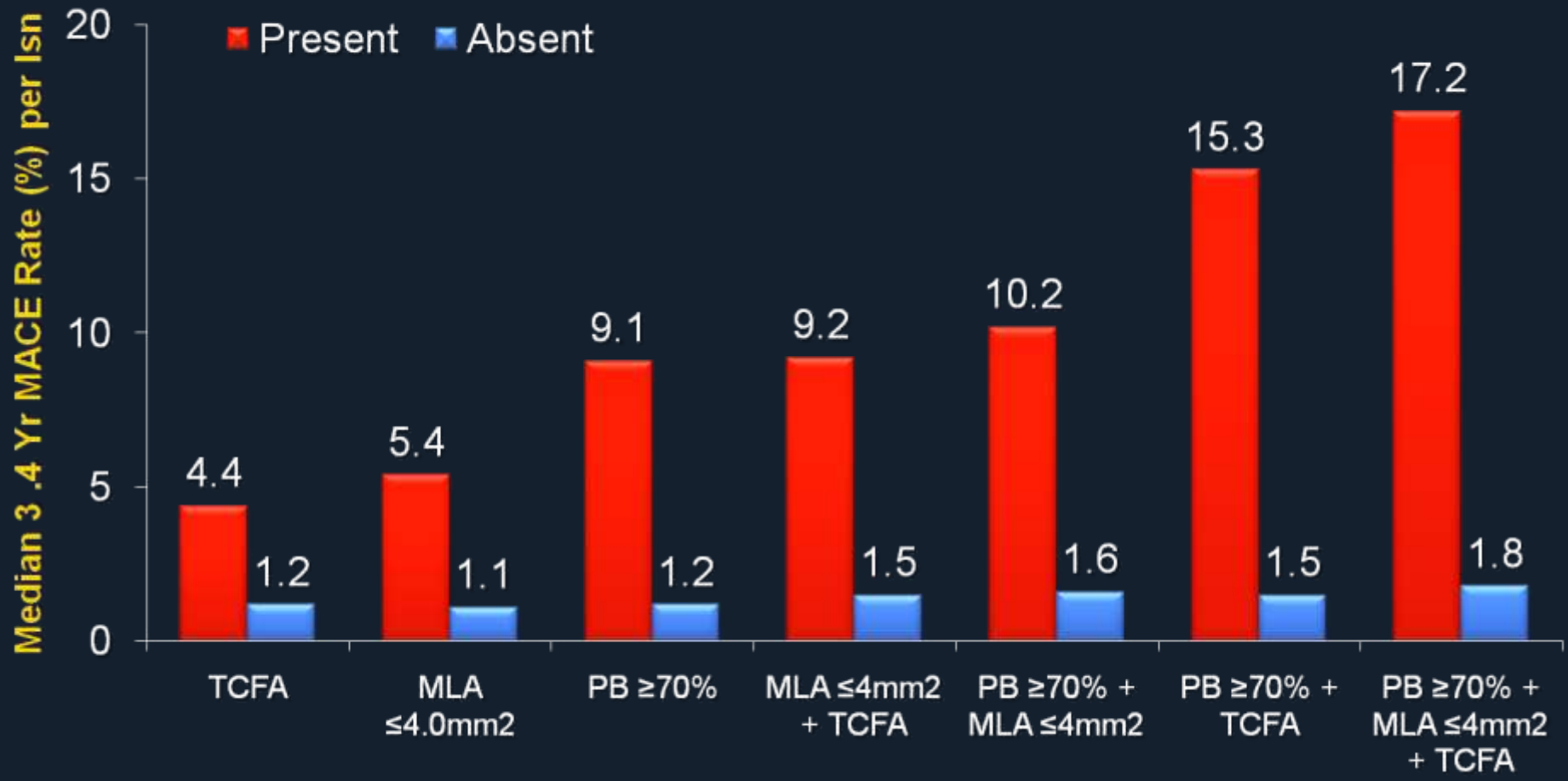
Independent Predictors of Non-Culprit Lesion Events



	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Stone GW et al. NEJM 2011;364:226-35

PROSPECT: Correlates of Non Culprit Lesion Related Events

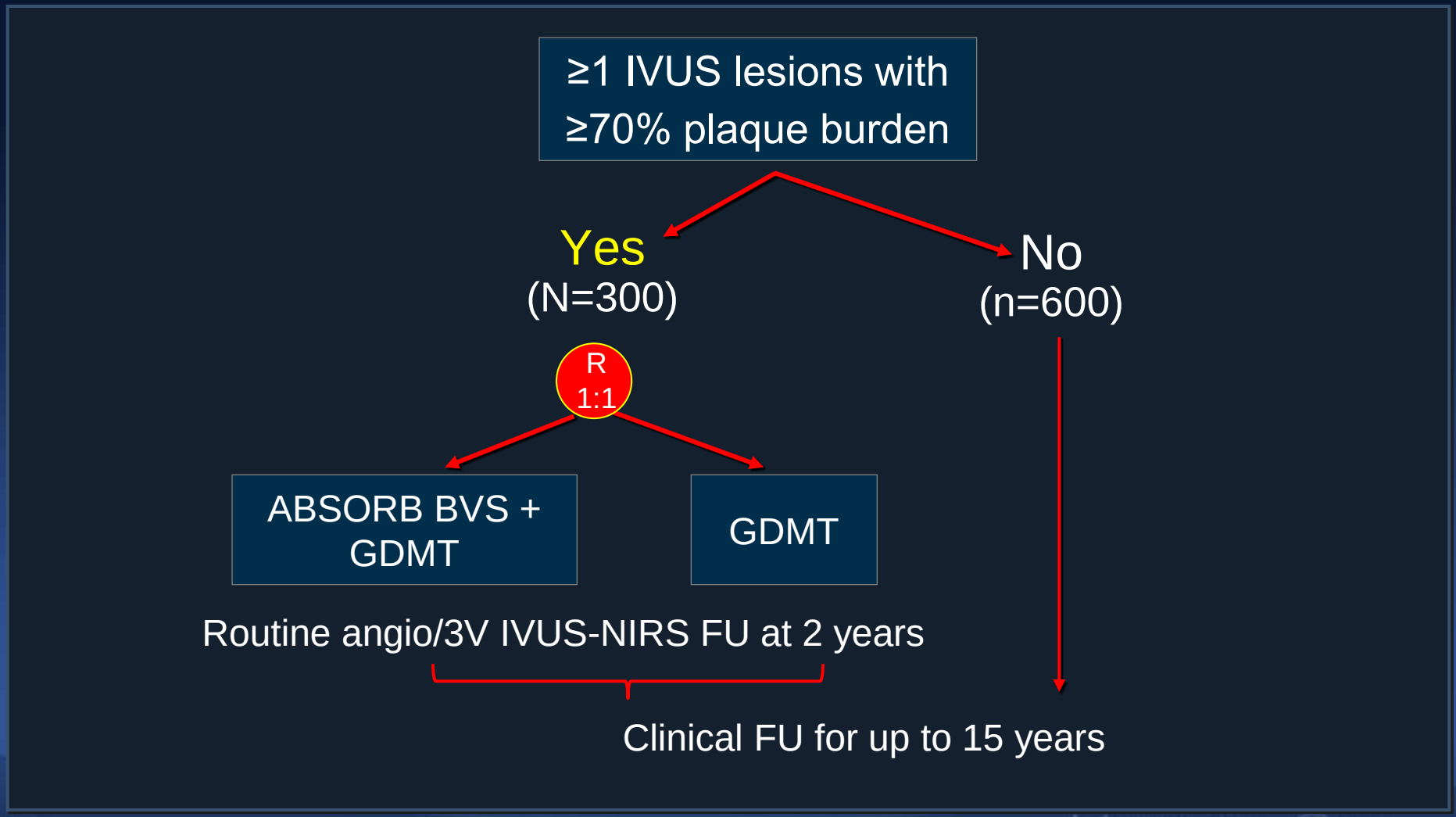


	TCFA	MLA ≤4.0mm2	PB ≥70%	MLA ≤4mm2 + TCFA	PB ≥70% + MLA ≤4mm2	PB ≥70% + TCFA	PB ≥70% + MLA ≤4mm2 + TCFA
Prevalence*	51.2%	49.1%	30.7%	17.4%	15.4%	11.0%	4.6%
Lesion HR	3.8 (2.2, 6.6)	5.0 (2.9, 8.7)	7.9 (4.6, 13.8)	6.4 (3.4, 12.2)	6.7 (3.4, 13.0)	10.8 (5.5, 21.0)	10.8 (4.3, 27.2)
P value	<0.0001	<0.0001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

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

PROSPECT ABSORB

900 pts with ACS after successful PCI
3 vessel IVUS + NIRS (blinded)



Q1,

Can Optimal Medical Treatment Stabilize Plaque Vulnerability ?

STABLE Trial

(*ST*atin and *A*theroma Vulnera*B*i*L*ity *E*valuation)
Double-blinded, Prospective, Randomized, Controlled Trial

290 patients with
Deferred native coronary artery lesion

2:1 randomization, double-blinded

Rosuvastatin 40mg

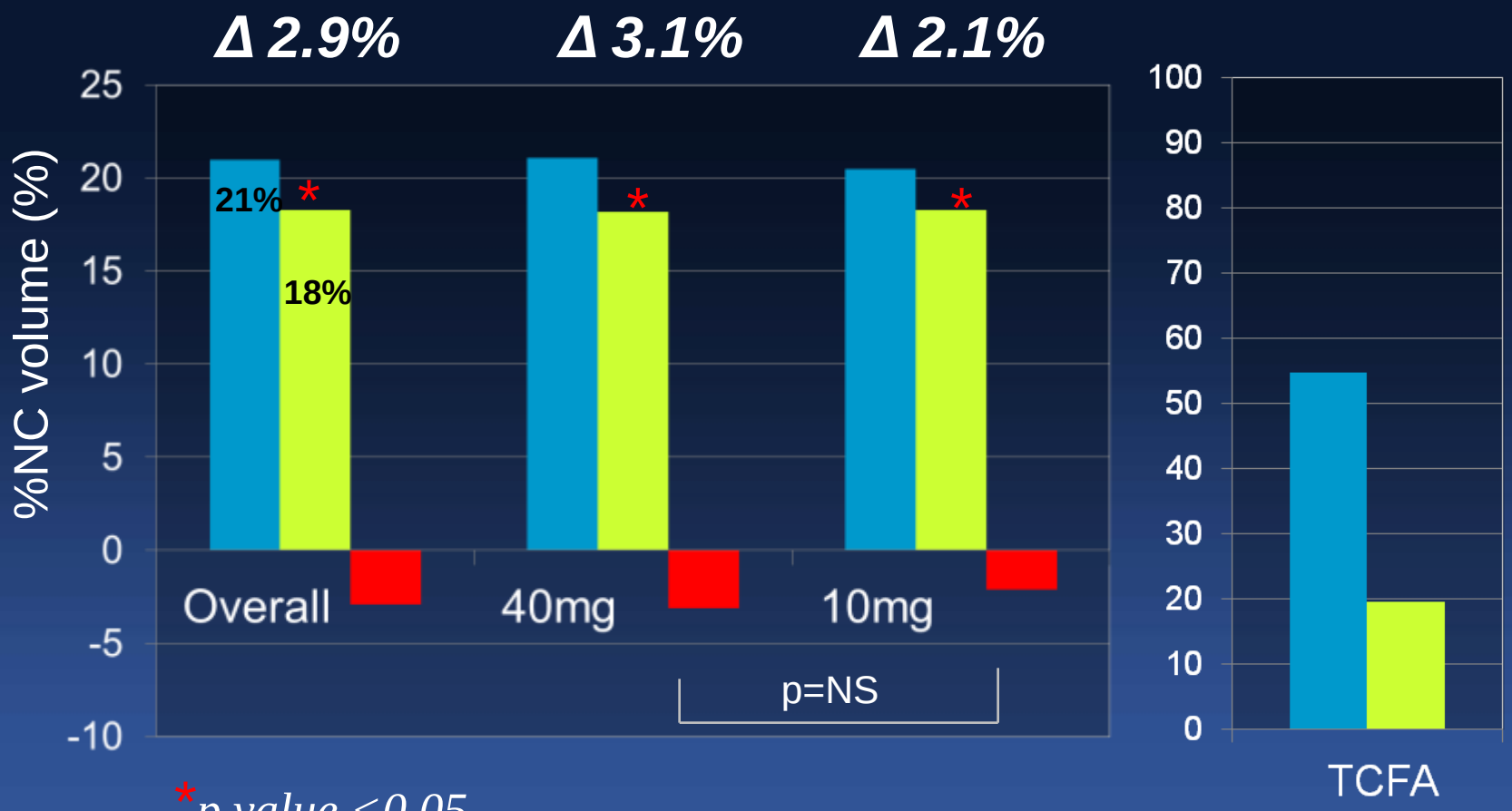
Rosuvastatin 10mg

Primary efficacy endpoint; Change in %NC volume within target segment by VH-IVUS at 1 year

Secondary endpoint: change in %NC volume comparing rosuvastatin 40mg vs. 10mg.

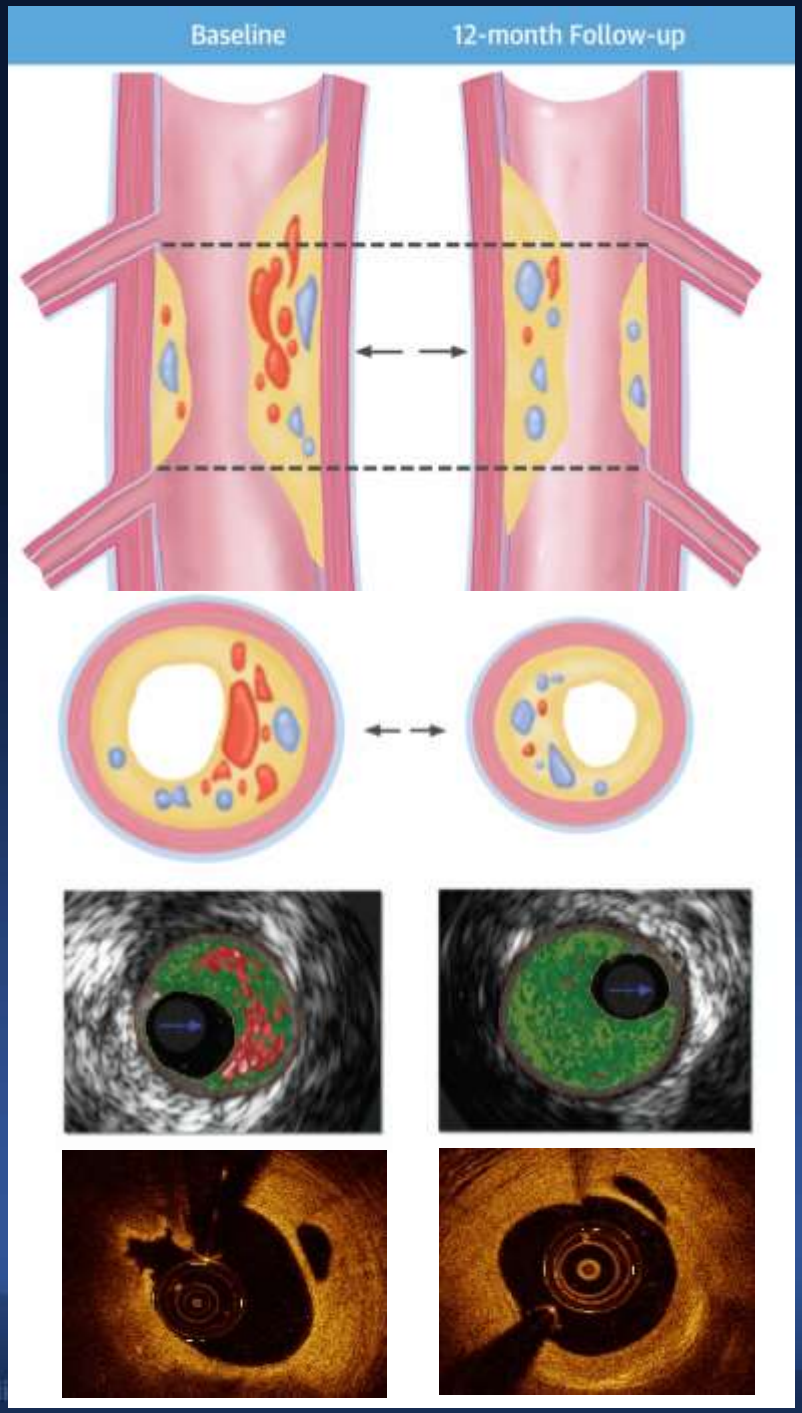
Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783

Primary Endpoint
%NC Volume Changes at 1 Year



*p value <0.05

Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783



	Baseline	1 year
EEM, mm^2	19.0	14.0
Plaque, mm^2	14.6	10.3
Lumen, mm^2	4.4	3.7
VH-%NC	30%	15%
VH-TCFA	+	–
OCT-TCFA	+	–

Rousvastatin Treatment Can Make A Plaque Regression and Stabilization

Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783

Clinical Outcomes at 1 Year

- No cardiac death
- Culprit-related MACE: 4 pts (2.3%).
- Non Culprit-related MACEs: 8 pts (3.6%).
- No Difference in Non Culprit-MACE between rosuvastatin 40 vs.10mg (3.9 vs. 2.7%, p=NS)

Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783

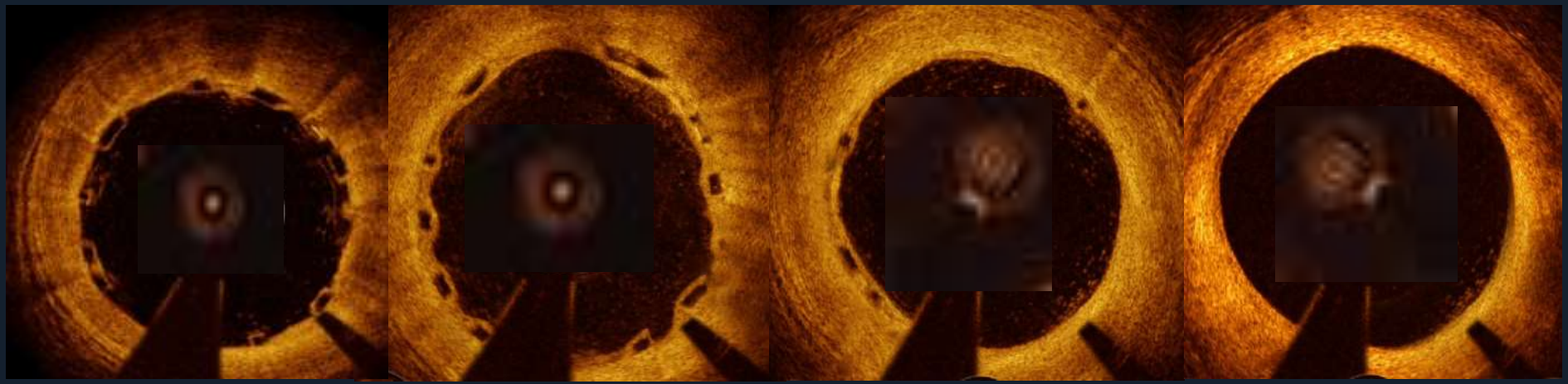
Can Optimal Medical Treatment Stabilize Plaque Vulnerability ?

Yes, Rosuvastatin Therapy Can Make A Plaque Regression and Stabilization.

Q2,

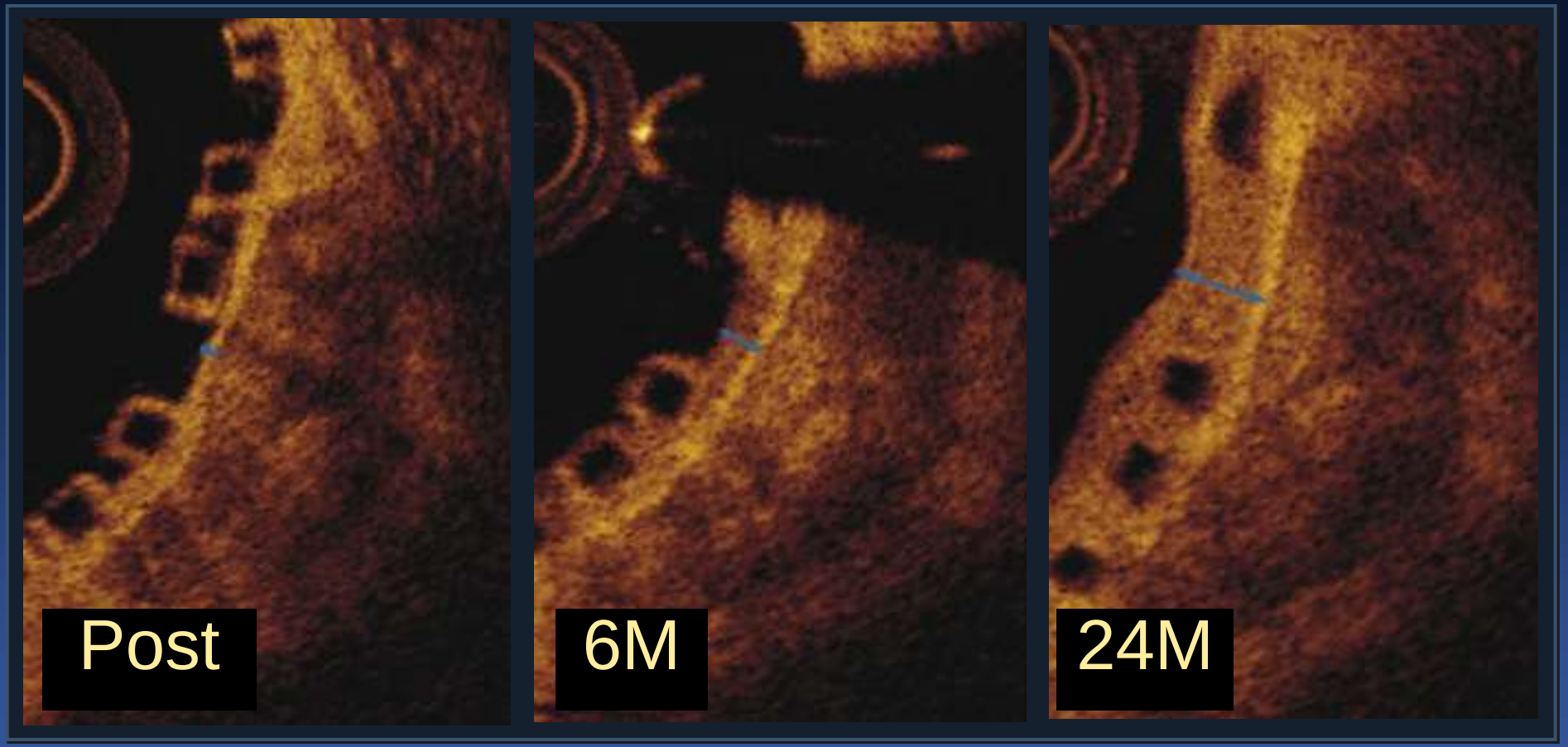
Can BVS Stabilize Plaque Vulnerability and Make an Any Difference ?

Different Concept ;
Do their Job and Disappear !



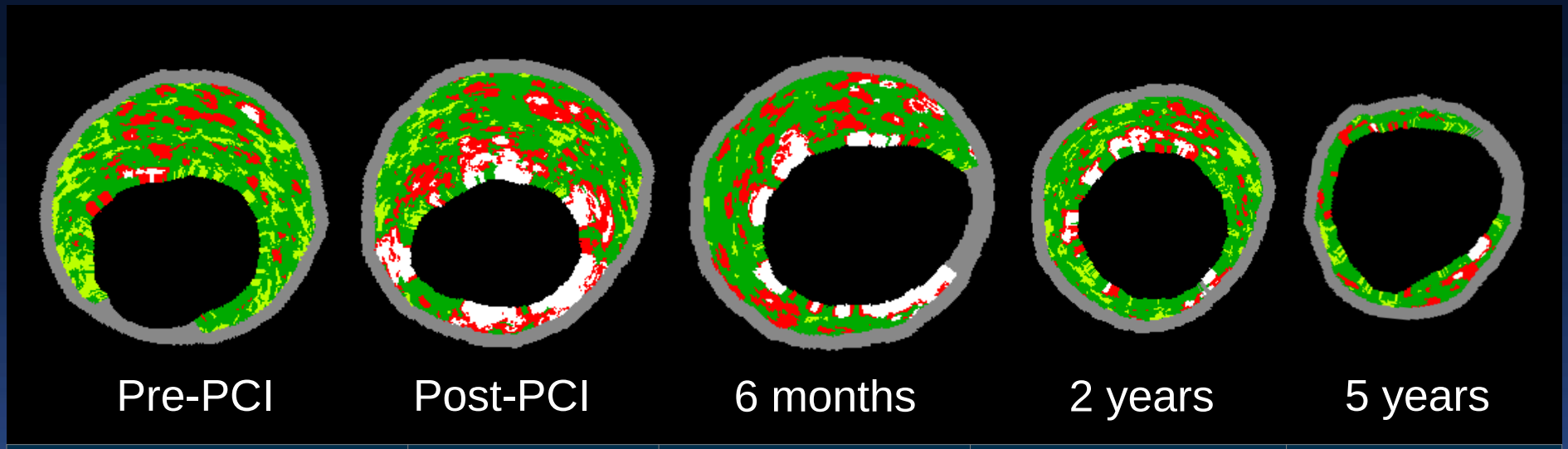
1 month | 6 month | 2 year | 5 year

BVS Over A Calcified Plaque, Sealing and Shielding of Plaques



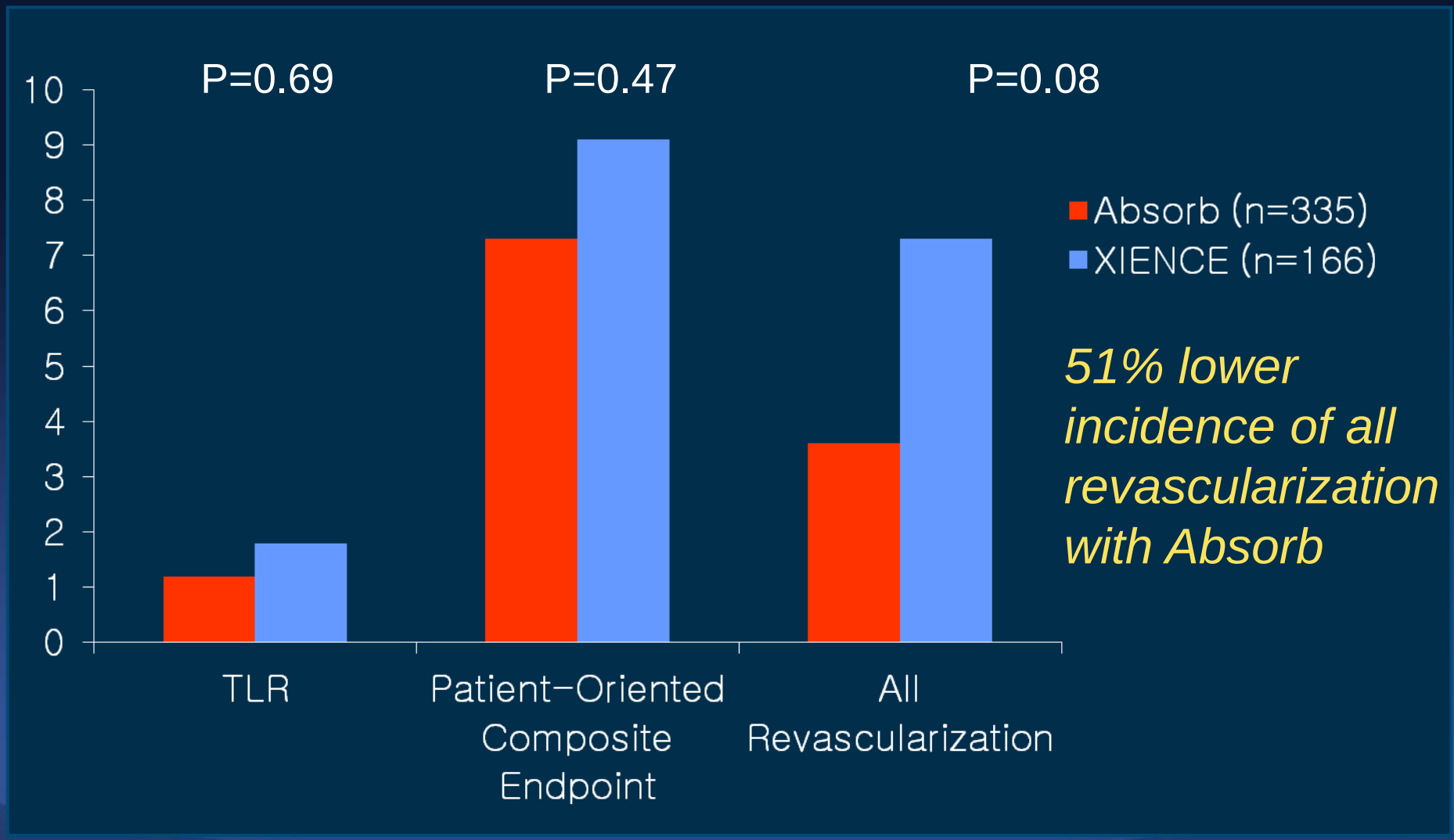
Brugaletta S et al. Atherosclerosis 2012

BVS Can Make Plaque Stabilization and Lumen Enlargement

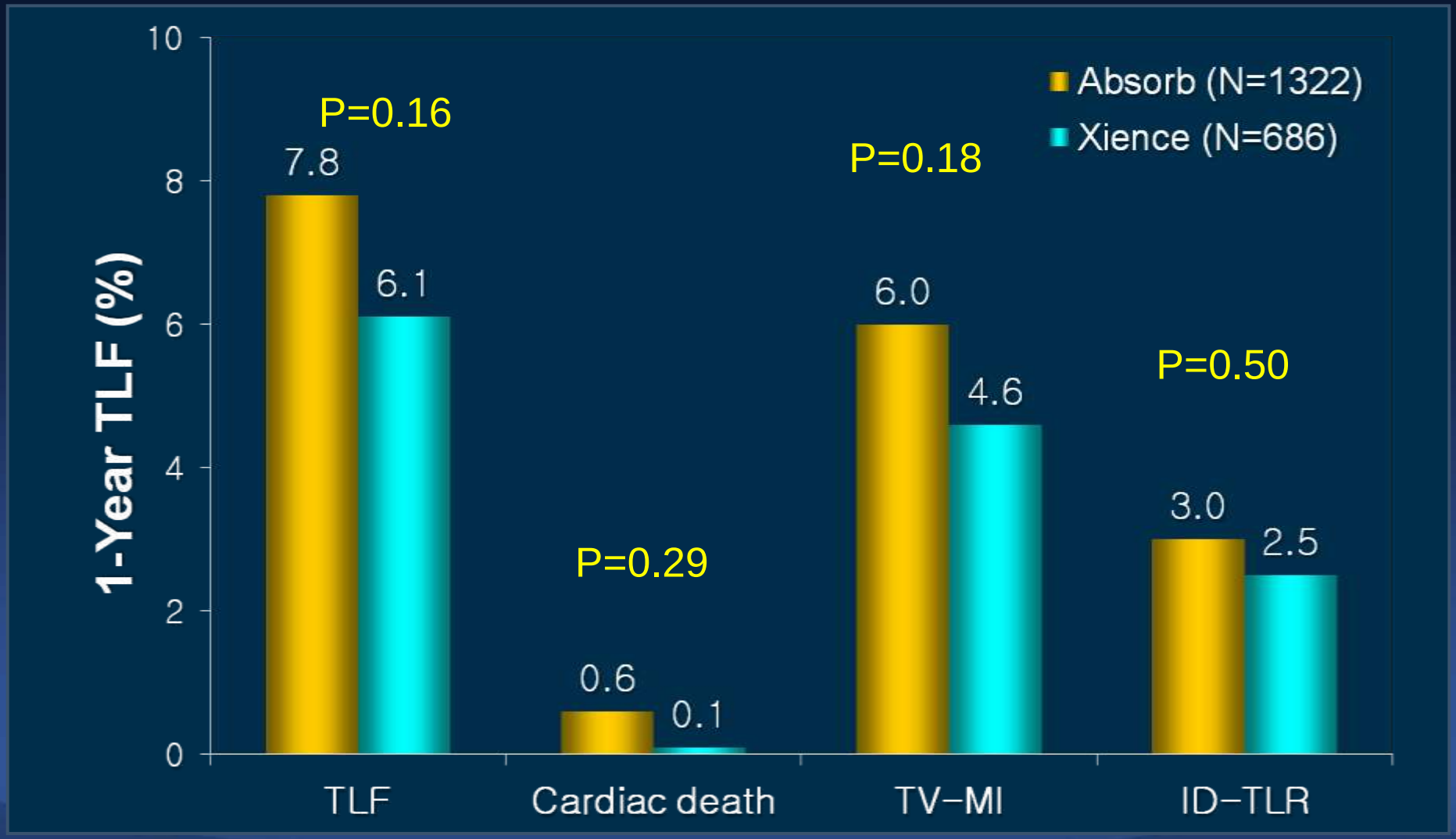


Vessel area (mm^2)	15.72	15.34 (3%)	14.09 (10%)	13.76 (12%)
Plaque area (mm^2)	8.78	9.17 (4%)	7.54 (14%)	7.07 (19%)
Mean LA (mm^2)	6.95	6.17 (11%)	6.56 (5.6%)	8.09 (16%)

ABSORB II, 1-year Results

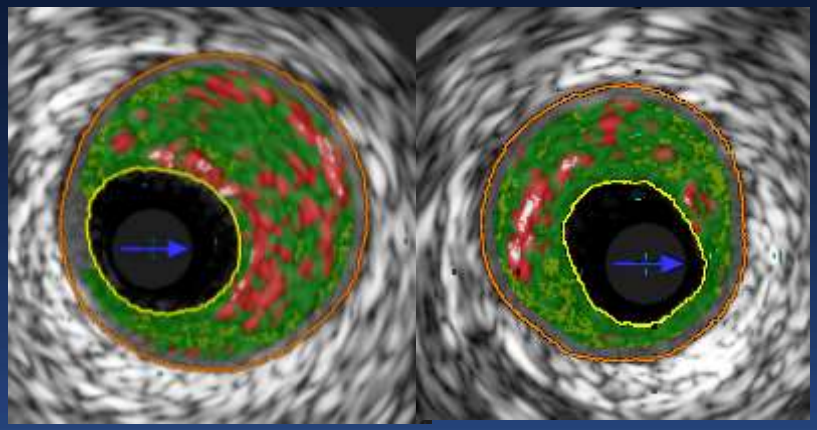
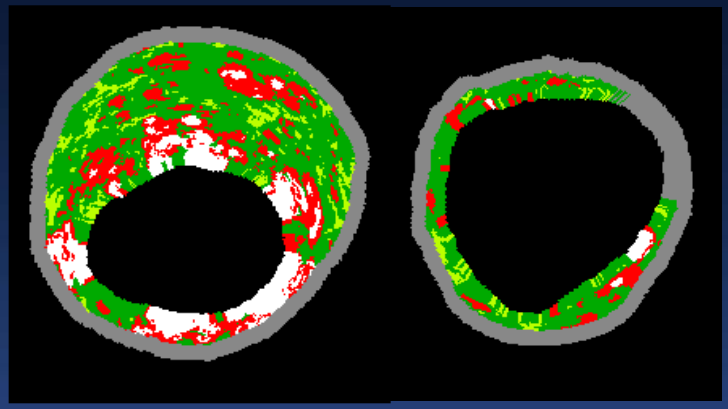


ABSORB III, 1-year Results



Stephan G Ellis, et al. NEJM 2015

What's the Difference ?

Optimal Medical Treatment	BVS
	
Stabilized Plaque Decreased Plaque Decrease Vessel Size Decreased Lumen	Stabilized Plaque Decreased Plaque Decrease Vessel Size Increased Lumen

PREVENT Study,

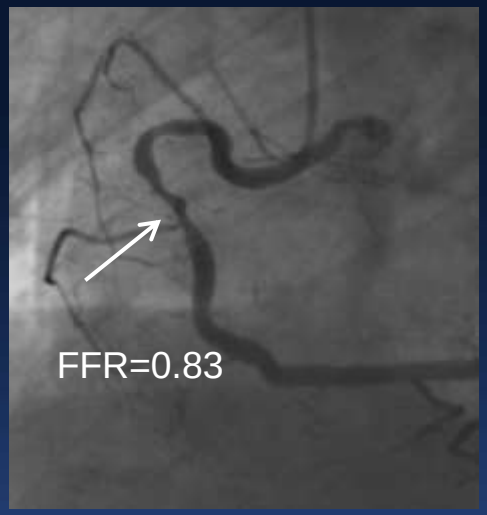
The ***PREVENT***ive Implantation of BVS on Stenosis With Functionally Insignificant Vulnerable Plaque Compared to Optimal Medical treatment.

Objective,

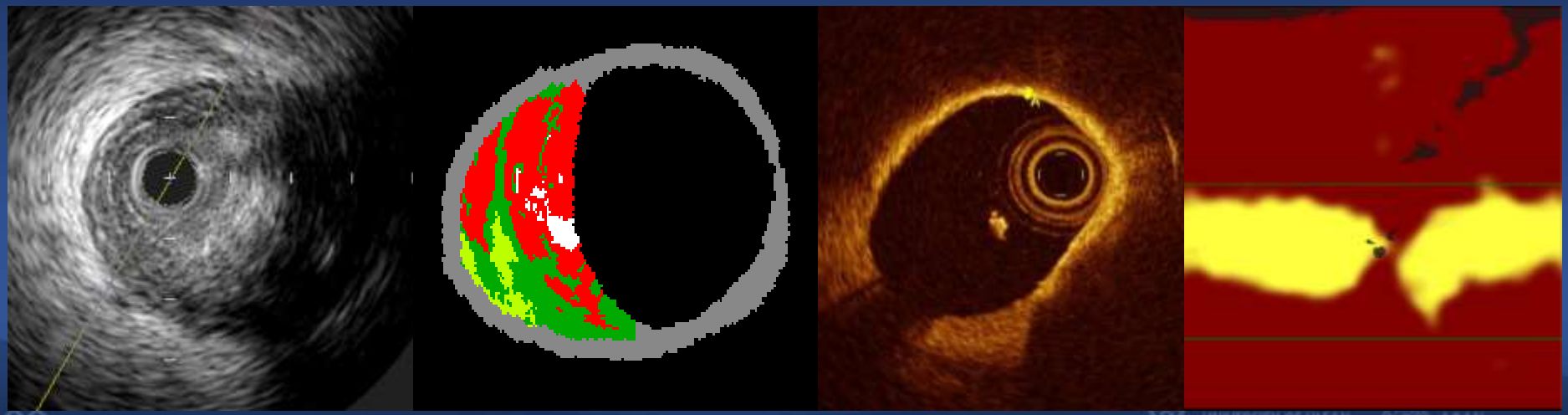
To determine whether BVS implantation on functionally insignificant vulnerable plaque, reduce the incidence of the composite of MACEs compared with optimal medical therapy alone.

A prospective, randomized, multicenter, clinical trial with ‘all comers’ design. Approximately 2,000 patients will be enrolled from international heart centers.

Defining, *Functionally Insignificant Vulnerable Plaque*



1. PB_{MLA} ≥70%
2. MLA ≤4.0 mm^2
3. TCFA by OCT or VH-IVUS
4. LRP on NIRS ($_{max}LCBI_{4mm}$>315)



PREVENT Trial

Any Epicardial Coronary Stenosis (≤ 40 mm) **with** ***FFR ≥0.80*** **and with** ***Two*** **of the following**

1. Plaque Burden >70%
2. MLA ≤4.0mm^2
3. TCFA by OCT or VH-IVUS
4. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>315)

R

BVS+OMT
N=800

OMT
N=800

Primary endpoint *at 2 years*:
CV death, MI, Hospitalization d/t unstable angina

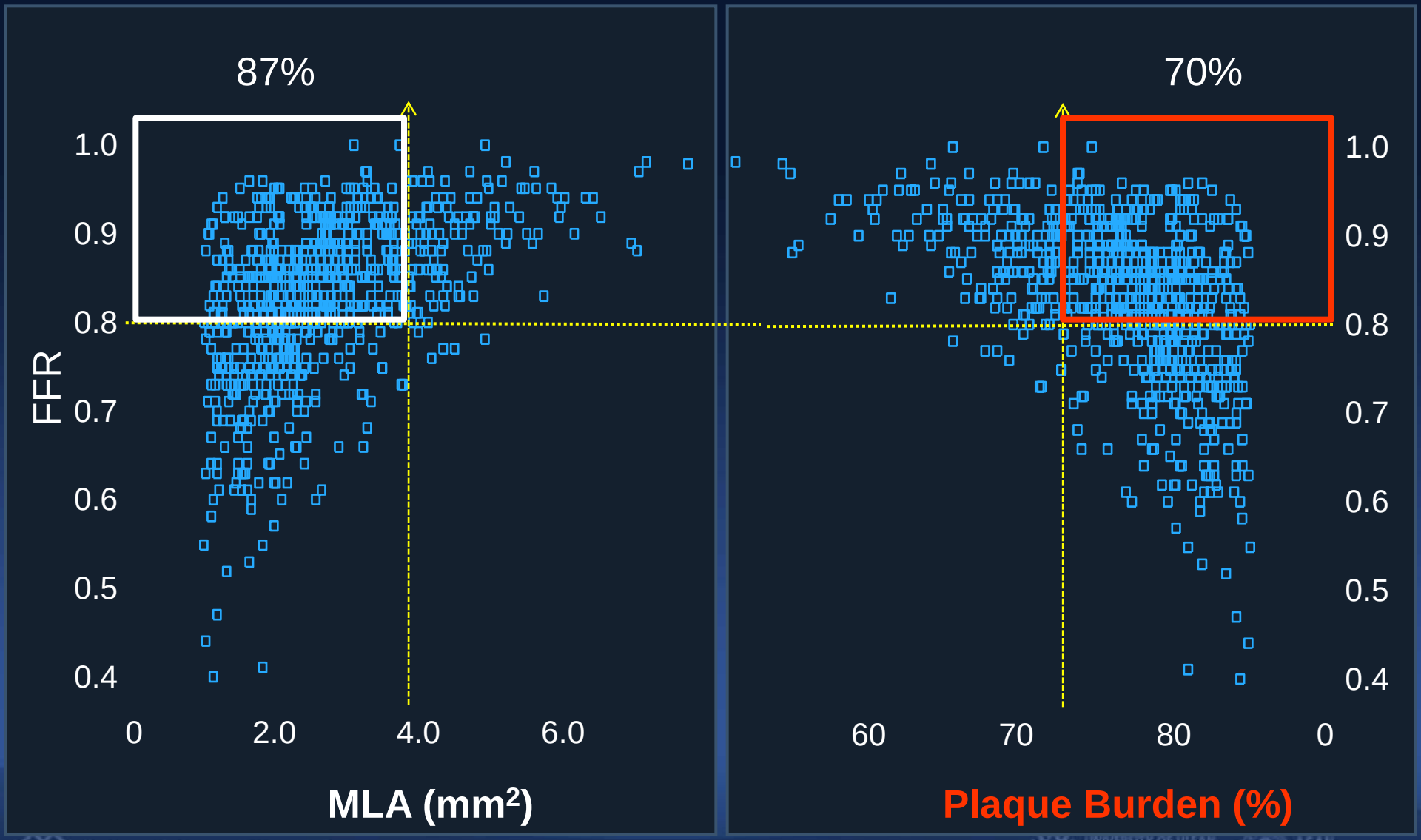
OCT sub-study/ NIRS sub-study, (300 patients in each arm at 2 years)

Inclusion Criteria

Age 18 years or older,
Symptomatic or asymptomatic coronary stenosis,
Eligible lesions for PCI (≤ 40 mm), with
FFR >0.80 and met the two of the following

1. Plaque burden>70%
2. MLA<4mm2
3. TCFA by OCT or VH-IVUS
4. Lipid-rich plaque on NIRS ($_{max}LCBI_{4mm}$>315)

Study Candidate in Real Practice



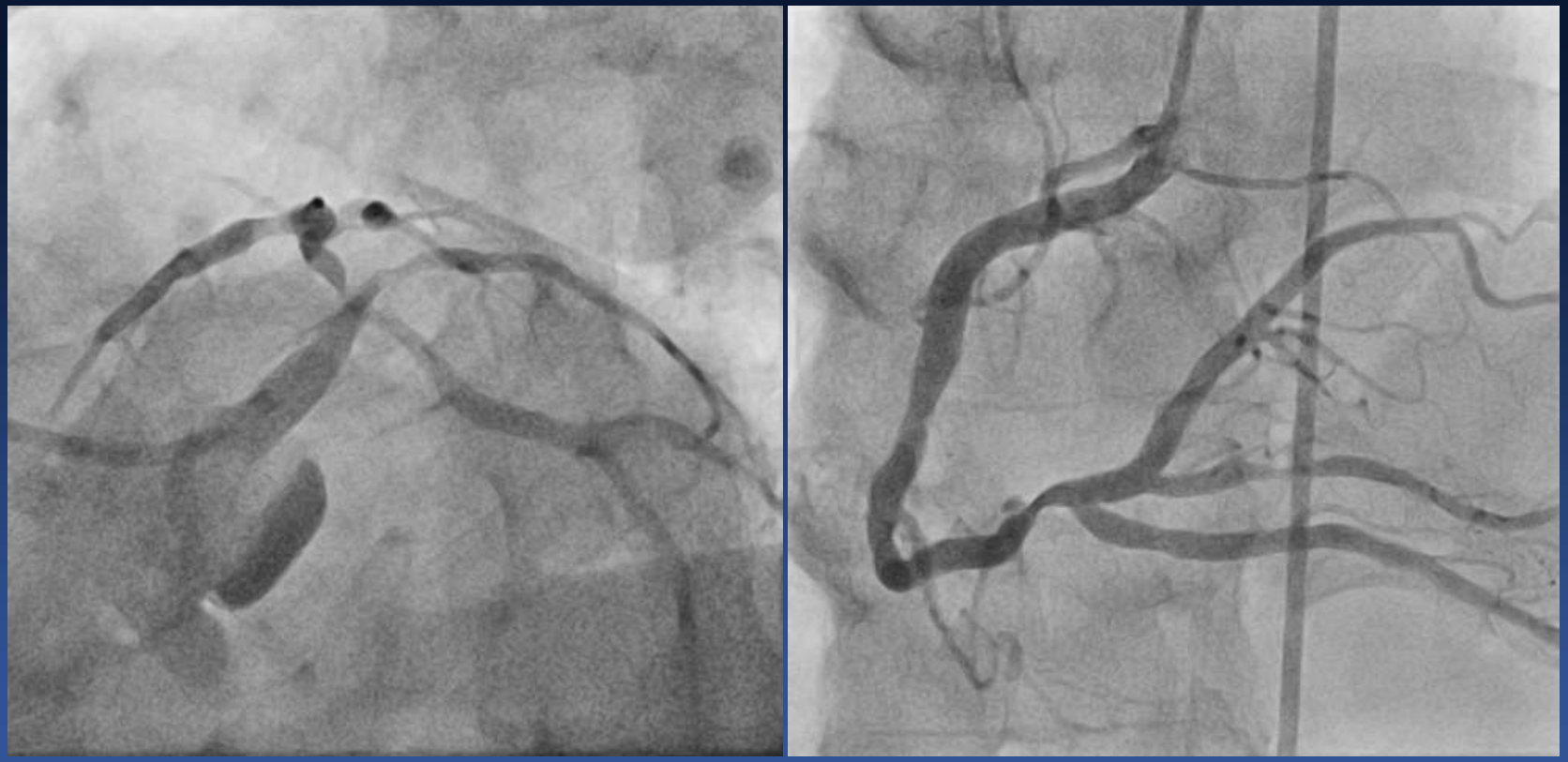
Primary and Major Secondary End Point,

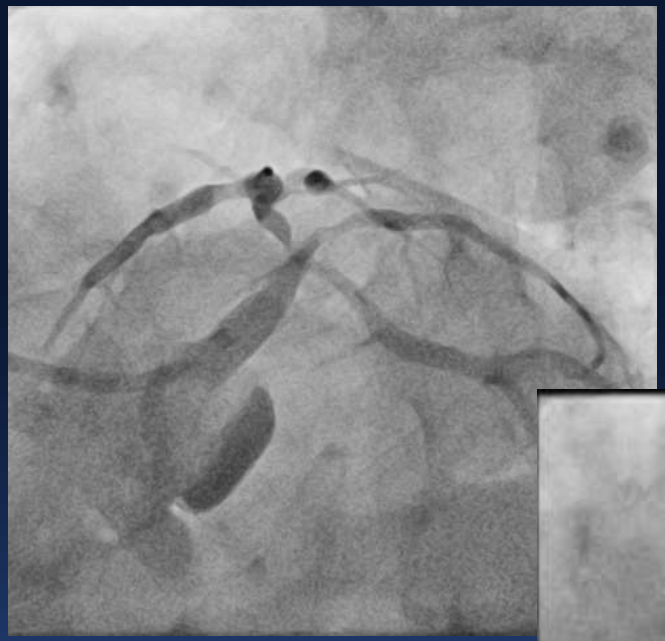
The primary endpoint is the 2-year MACE (cardiovascular death, nonfatal MI, unplanned rehospitalization due to unstable angina).

The secondary endpoints include overall MACE, non-urgent revascularization, and rate of cerebrovascular event.

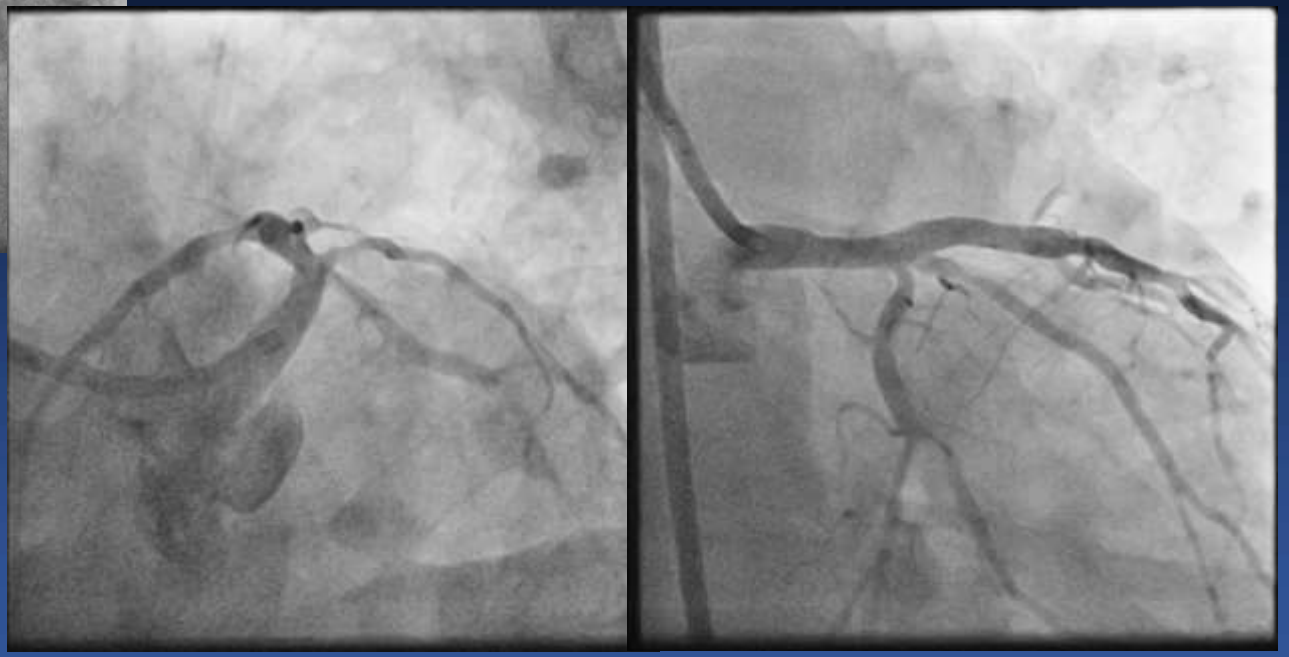
A Case

55 y/o male, Effort Chest Pain, *Stable Angina*

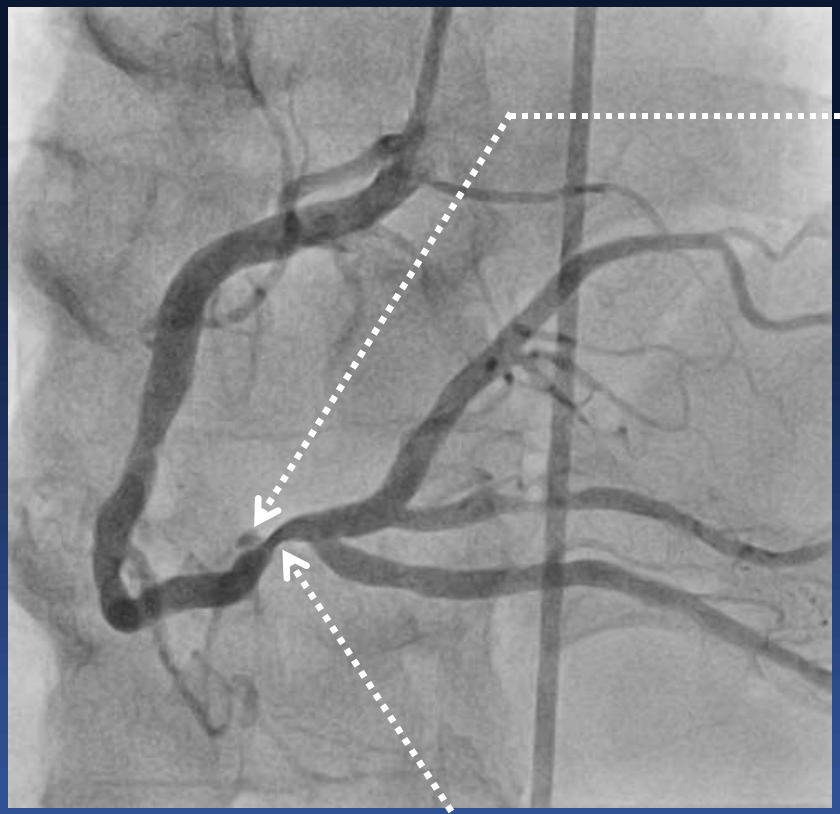


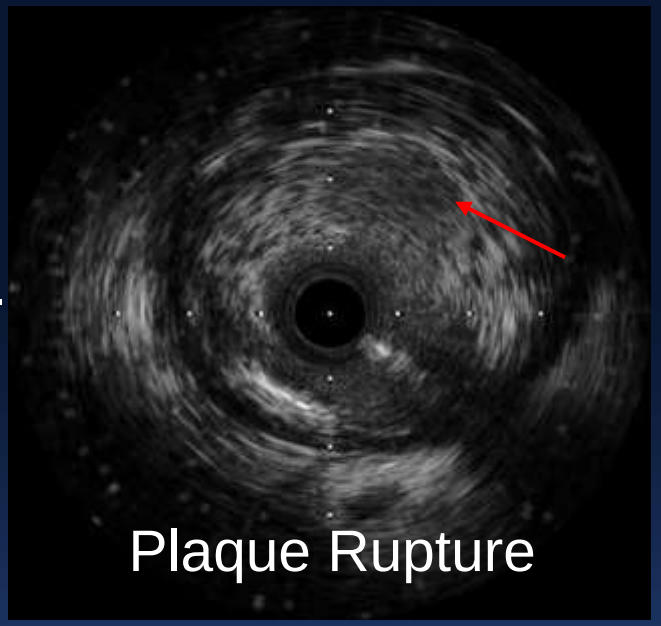


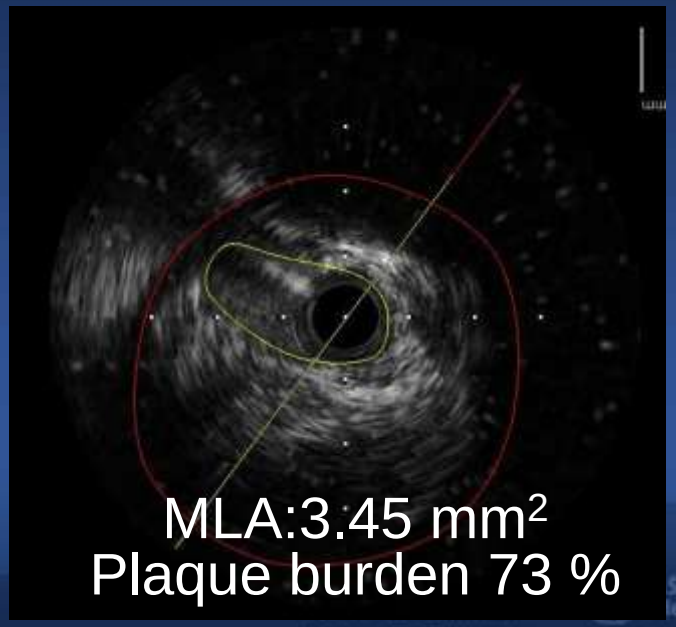
LM disease, Treated with
Single Stent Cross-Over



RCA, IVUS

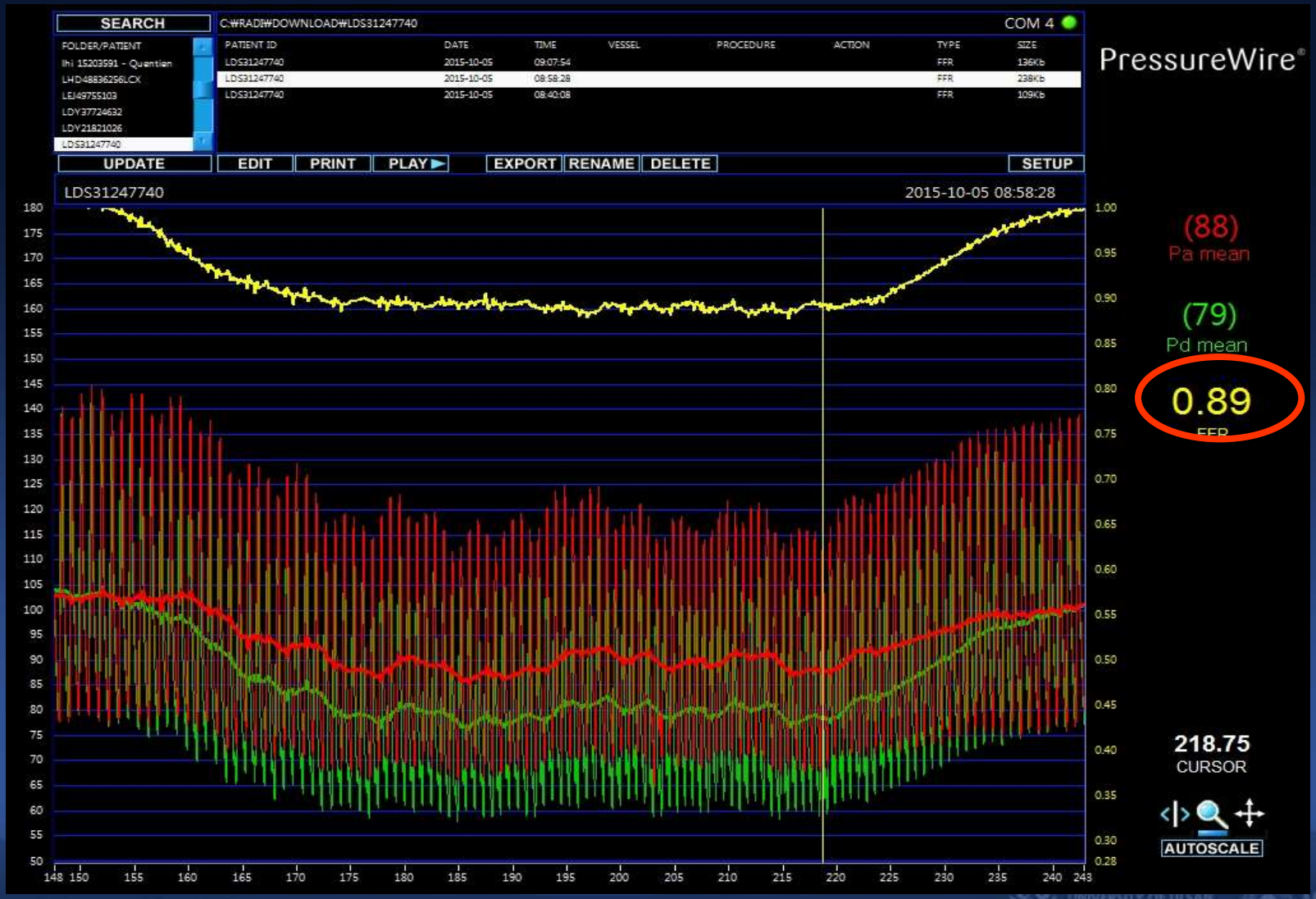






RCA, FFR

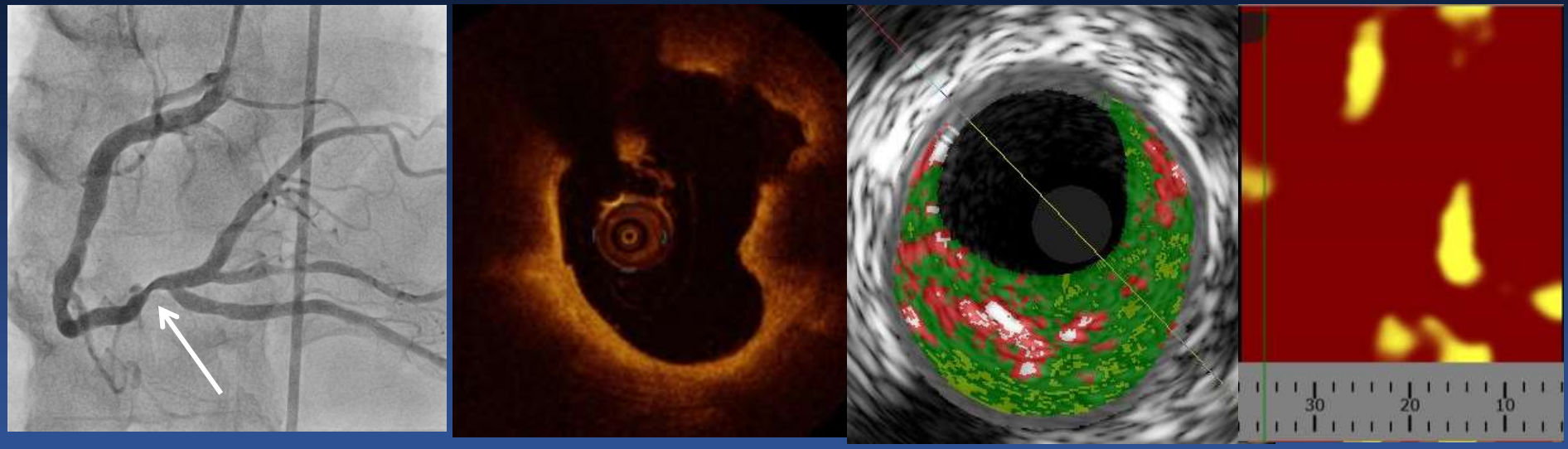
Intravenous adenosine, 200 μg/kg/min



Clinically Stable, with Vulnerable Plaque

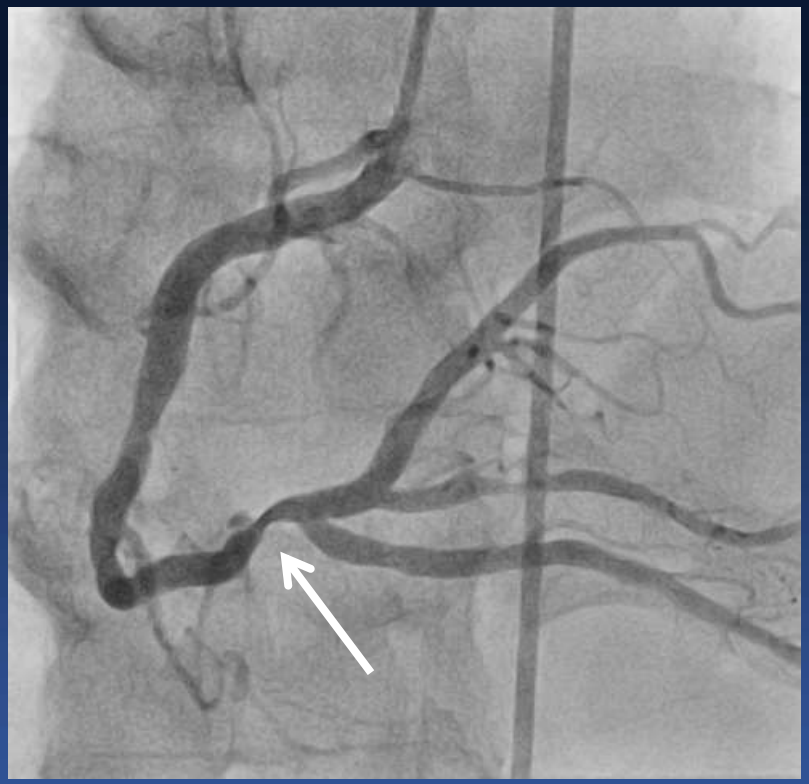
Rupture,
TCFA (+)

$_{max}LCBI_{4mm}$= 404



Necrotic Core 25%

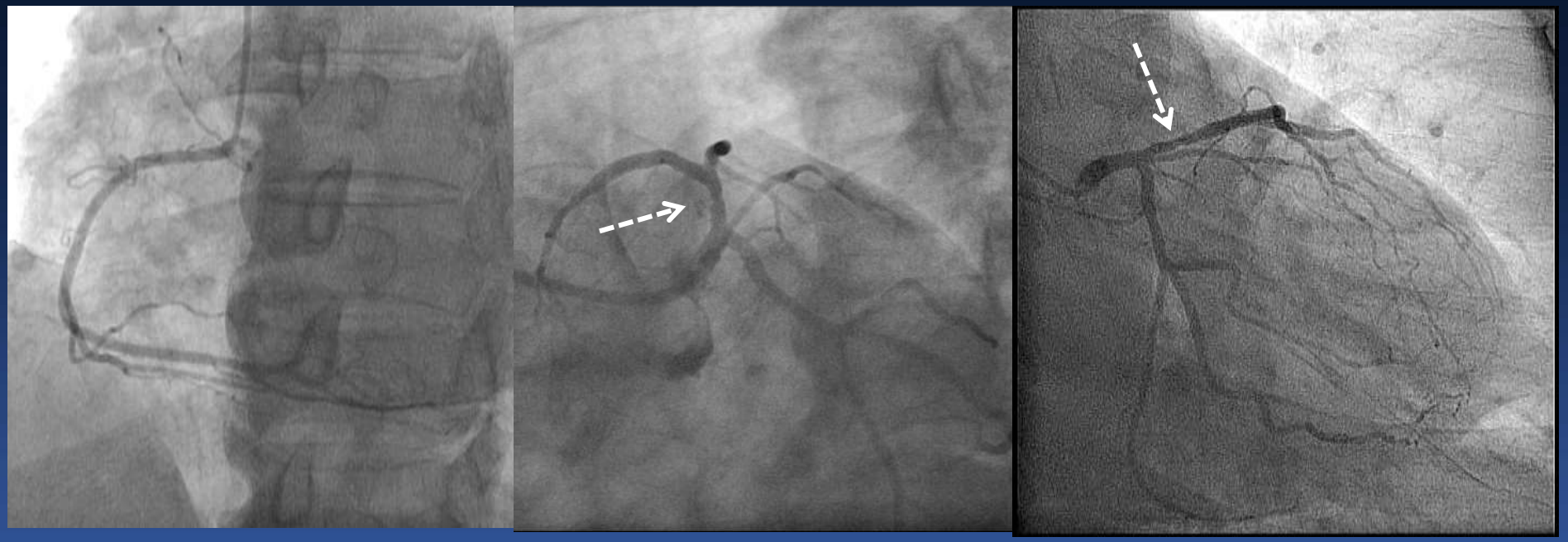
Randomized with OMT



FFR : 0.89
Angiographic DS : 70%
IVUS MLA : 3.45 mm^2
Plaque burden : 73%
$_{max}LCBI_{4mm}$: 404
TCFA (+)

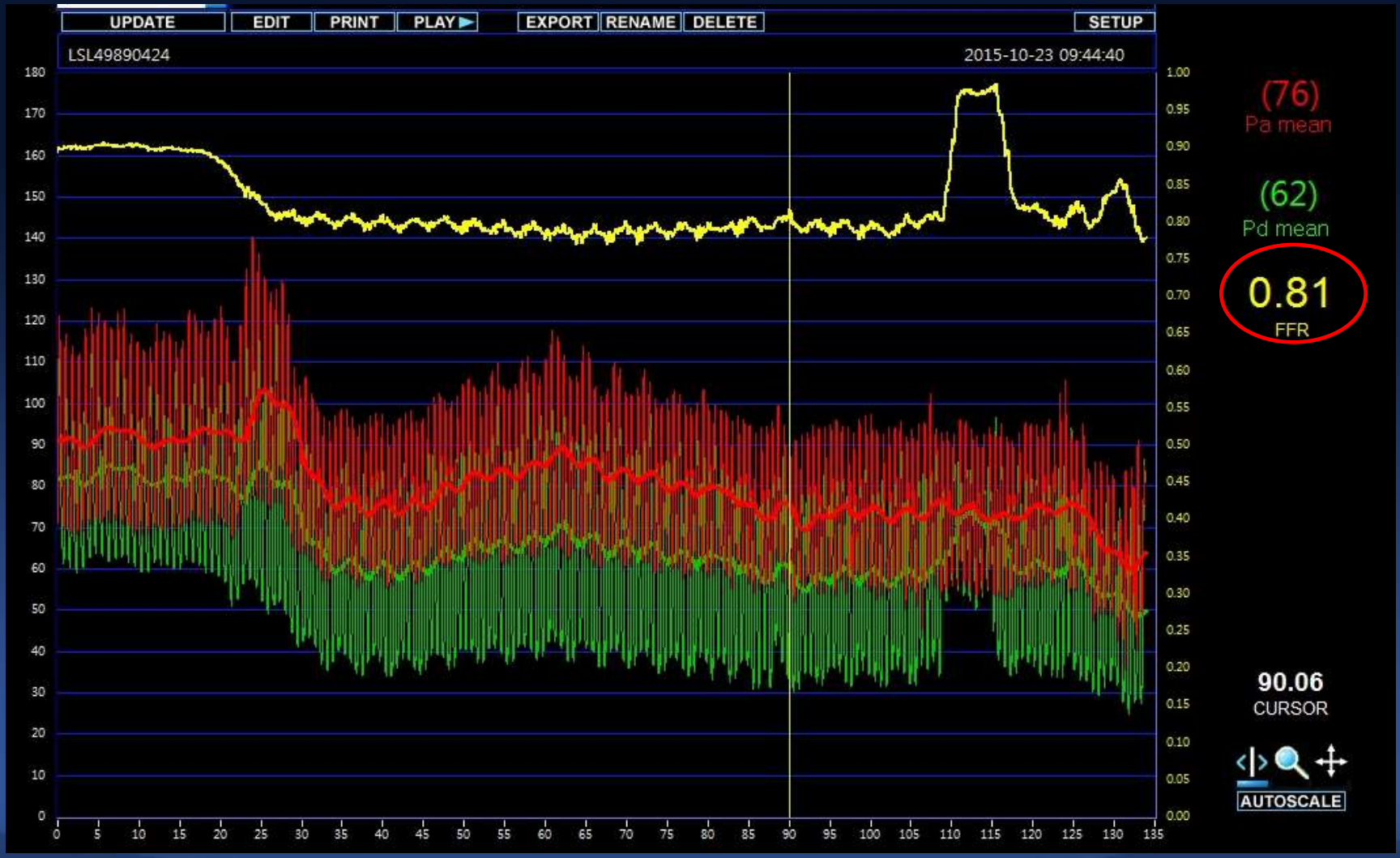
A Case

58 y/o male, *Unstable Angina*

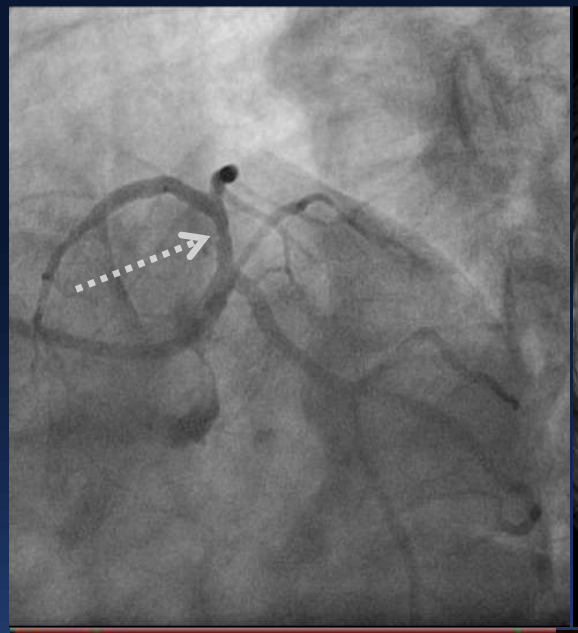


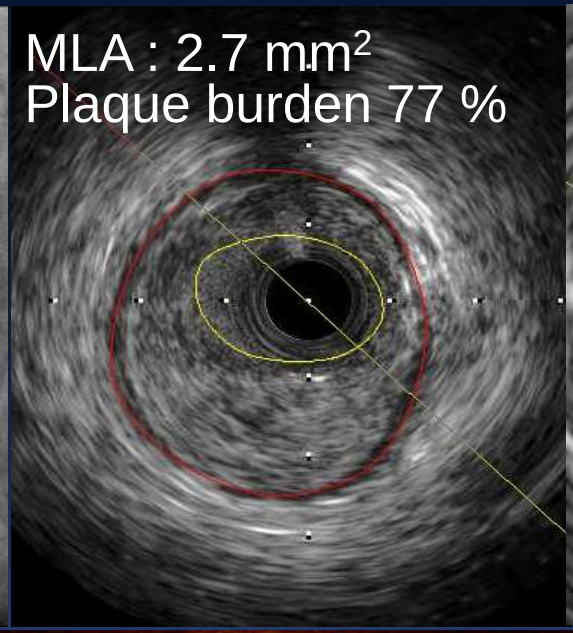
FFR

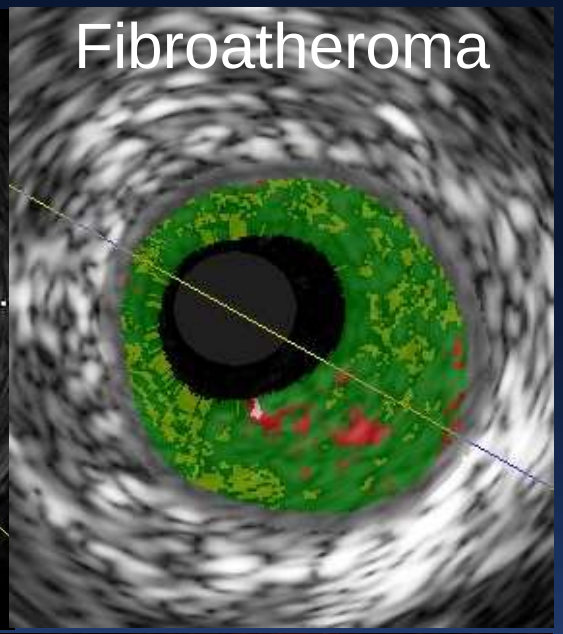
Intravenous adenosine, 140 μg/kg/min

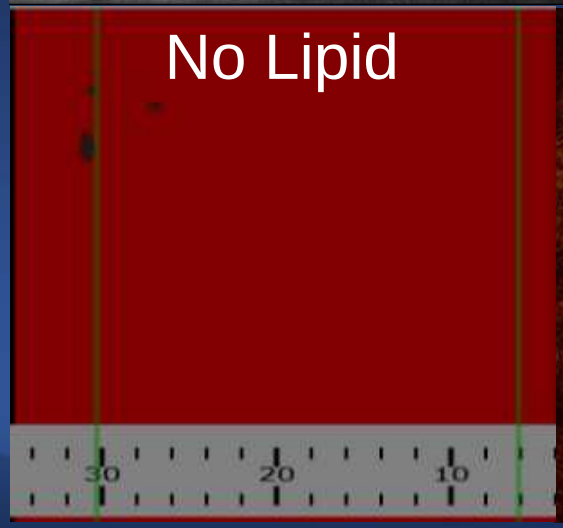


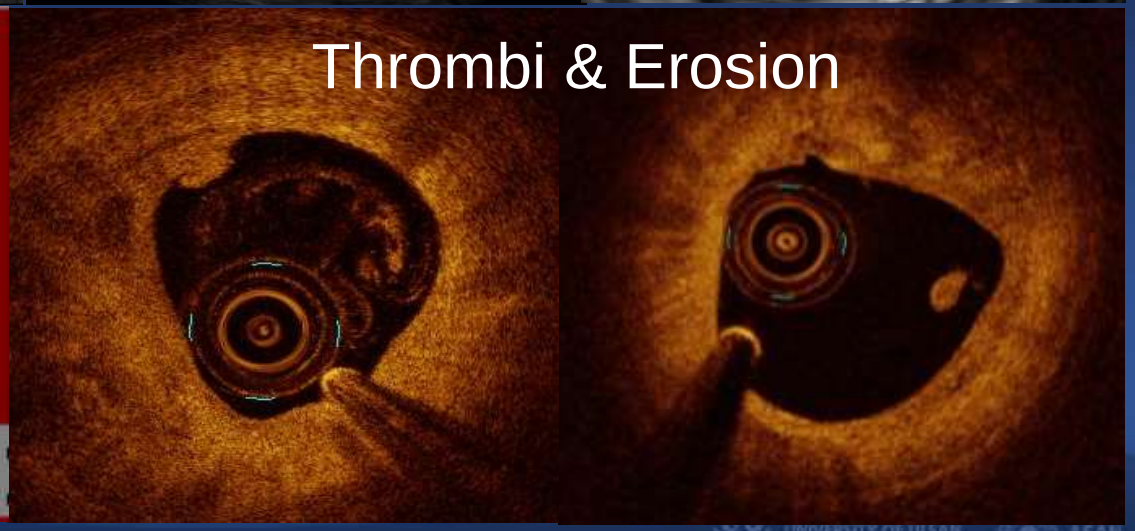
Unstable Angina, with Plaque Erosion







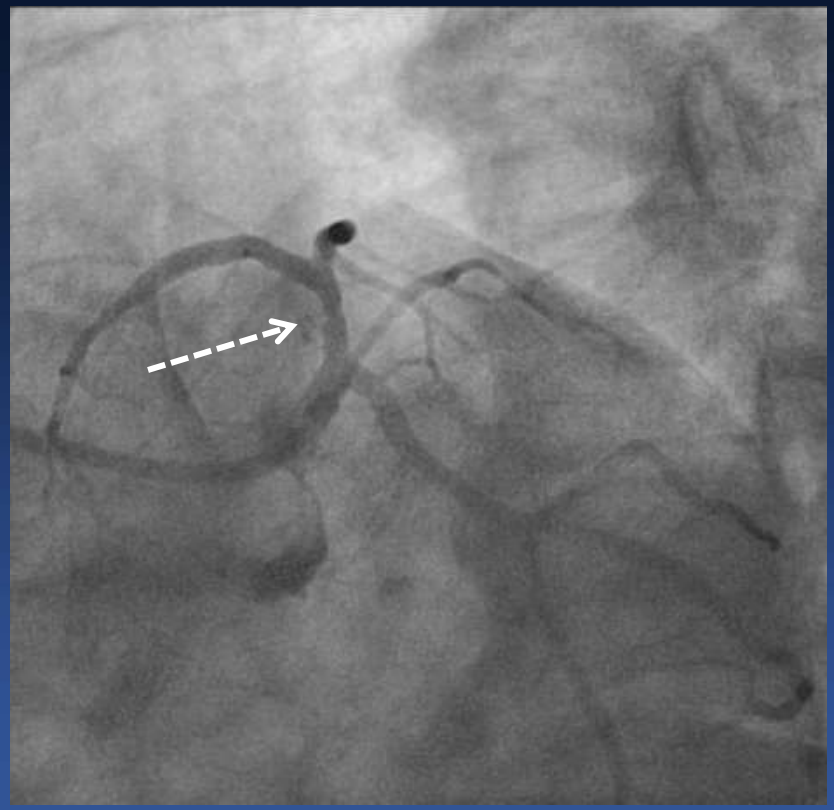




$_{max}LCBI_{4mm} = 0$

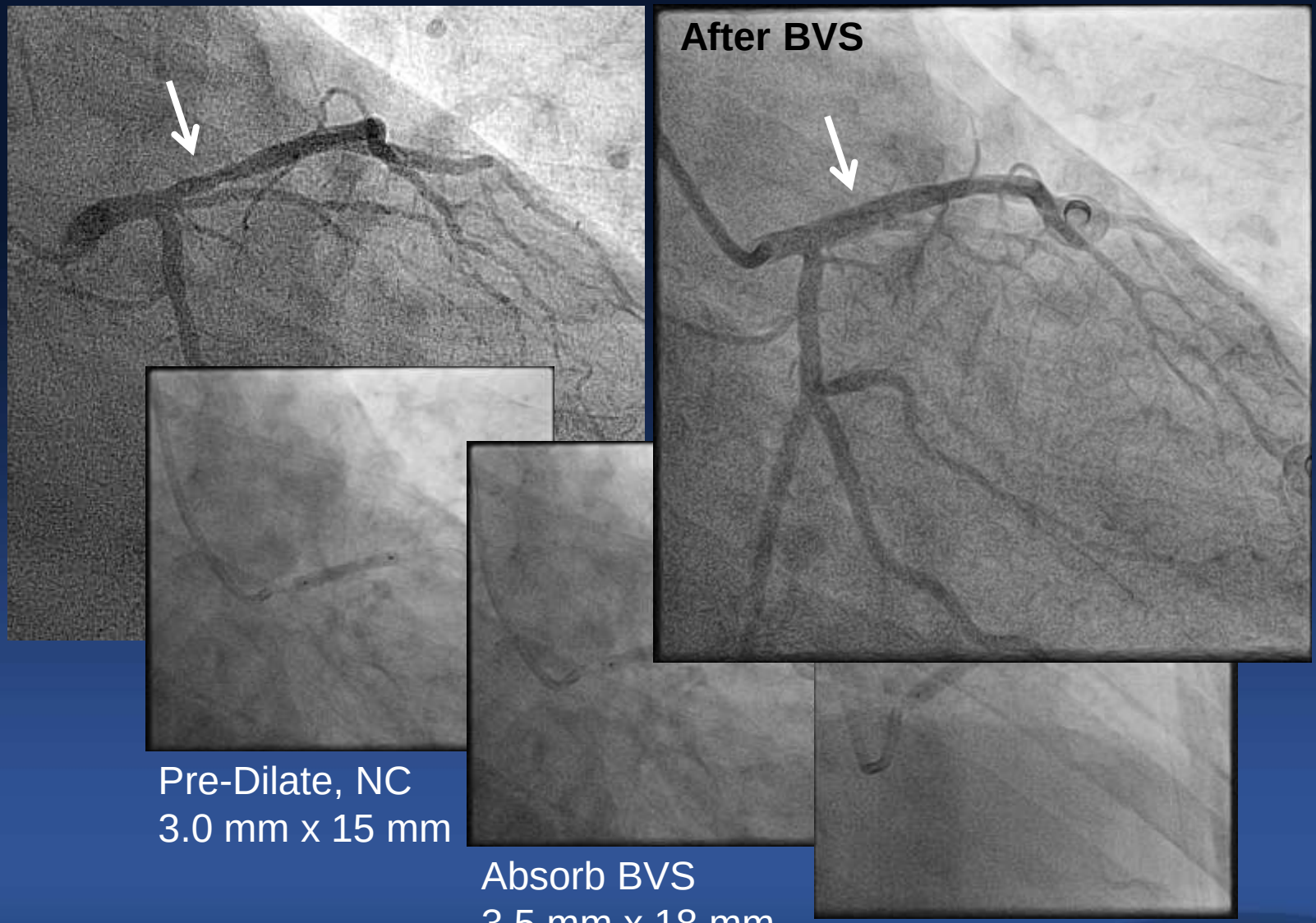
Randomized with BVS

Unstable Angina

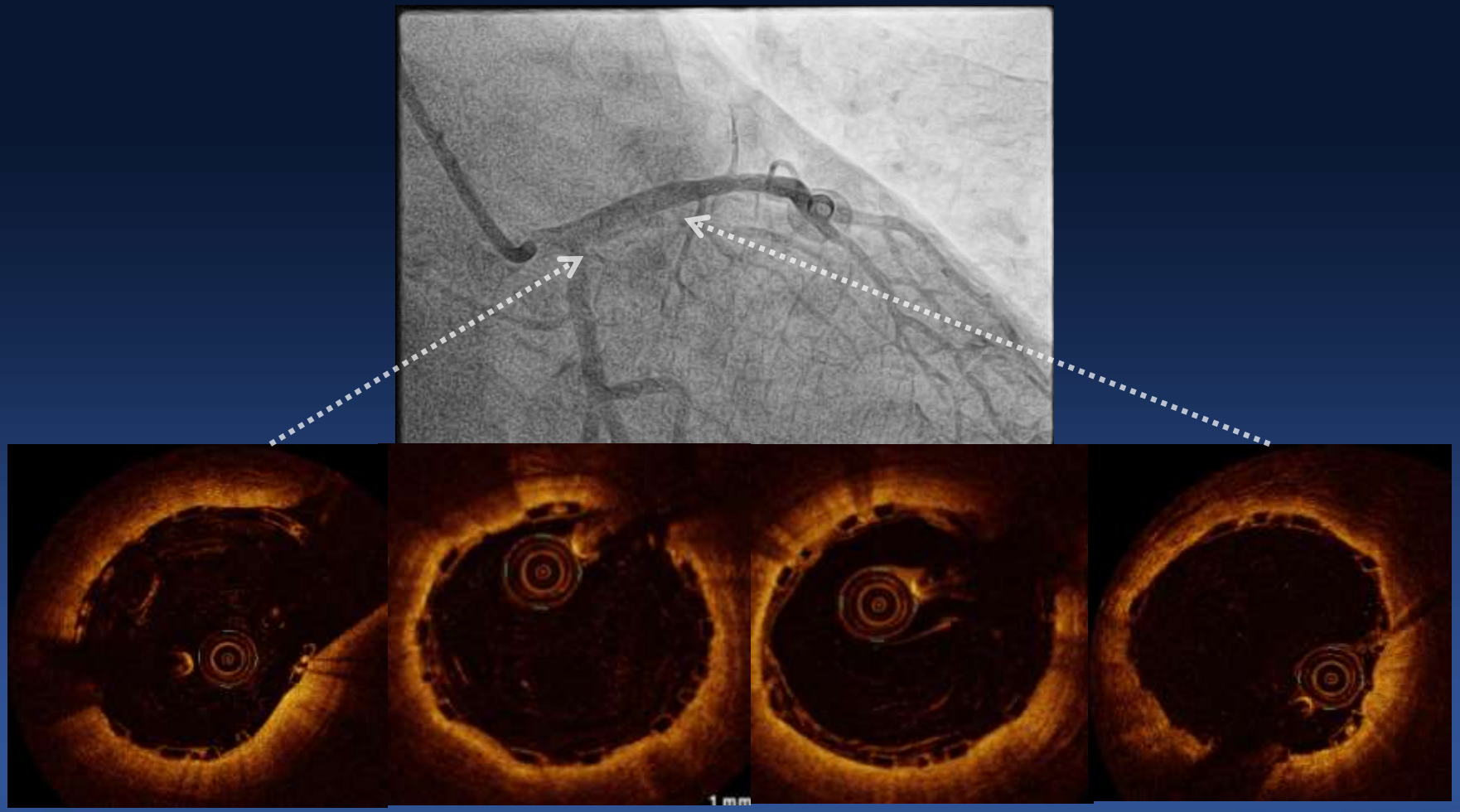


Angiographic DS : 50%
FFR : 0.81
IVUS MLA : 2.7 mm^2
Plaque burden : 77 %
with Plaque Erosion
$_{max}LCBI_{4mm}$: 0

BVS, Absorb


After BVS
Pre-Dilate, NC
3.0 mm x 15 mm
Absorb BVS
3.5 mm x 18 mm
NC Balloon,
4.0 mm x 13 mm

1st BVS Randomized Case



PREVENT Trial,

8 Countries, 33 Centers

Principal Investigators
Seung-Jung Park, MD, PhD. Korea

Co-Principal Investigator
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The Catholic University of Korea Seoul St. Mary's Hospital	Ki-Yuk Chang
Kangwon National University Hospital	Bong-Ki Lee
Keimyung University Dongsan Medical Center	Chang Wook Nam
Korea University Guro Hospital	Seung Un Na
Daegu Catholic University Medical Center	Kee-Sik Kim
Seoul National University Bundang hospital	In-Ho Chae
Seoul National University hospital	Bon-Kwon Koo
Ulsan University Hospital	Eun-Seok Shin
Chonnam National University Hospital	Young-Keun Ahn

ChonBuk National University Hospital	Jei Keon Chae
Chungnam National University Hospital	Si Wan Choi
Hallym University Sacred Heart Hospital	Hyun Sook Kim
Bundang Cha Medical Center	Won-Jang Kim
Inje University Busan Paik Hospital	Tae Hyun Yang
Samsung Medical Center	Joo-Yong Hahn
Prince of Wales Hospital	Nigel Jepson
Queen Elizabeth Hospital	Michael Kang-Yin Lee
San Raffaele Hospital, Italy	Antonio Colombo
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Thank You !!

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