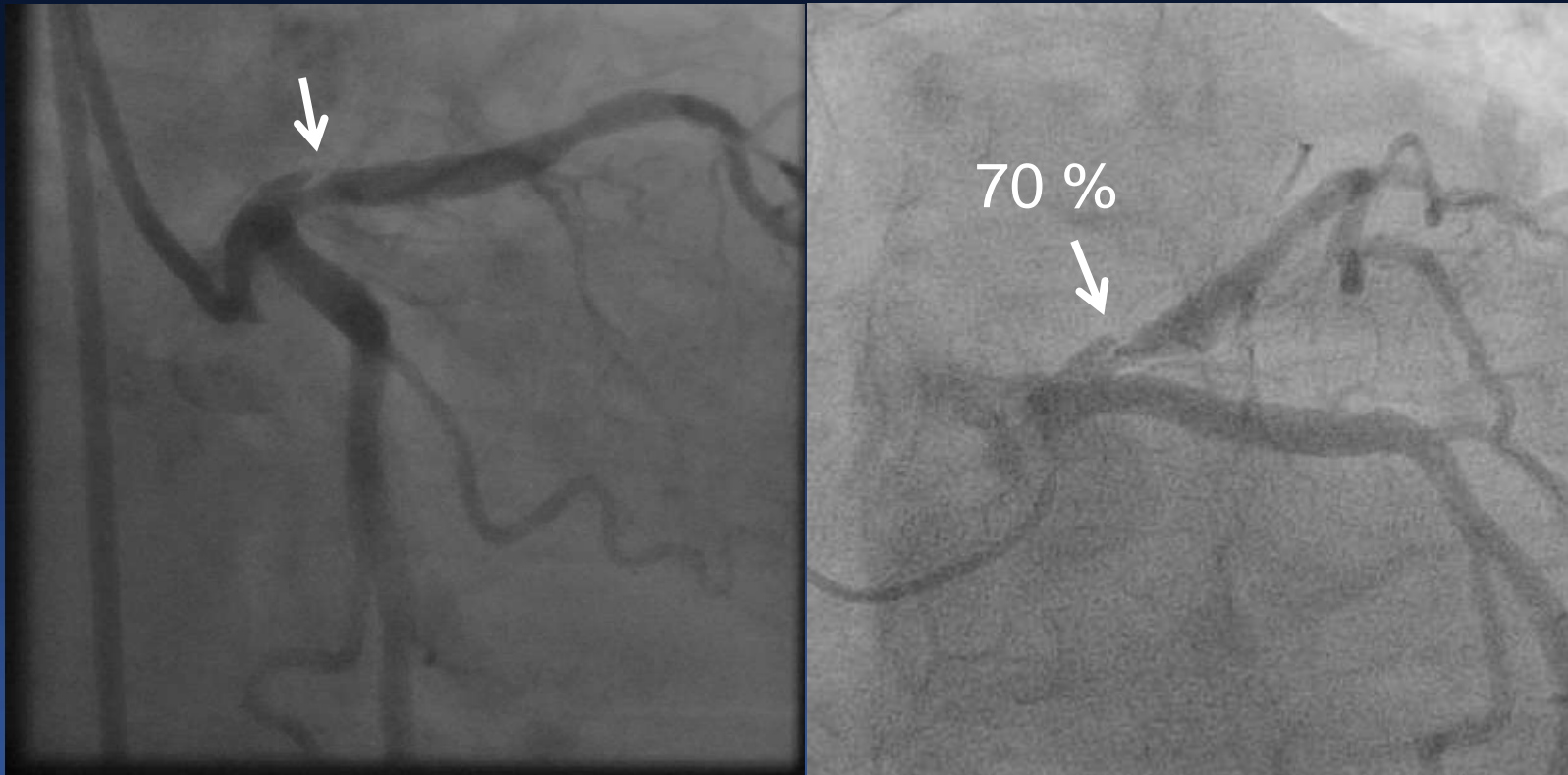


Can We Prevent Events of Vulnerable Plaque ? From Stable to PREVENT

Seung-Jung Park, MD, PhD

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

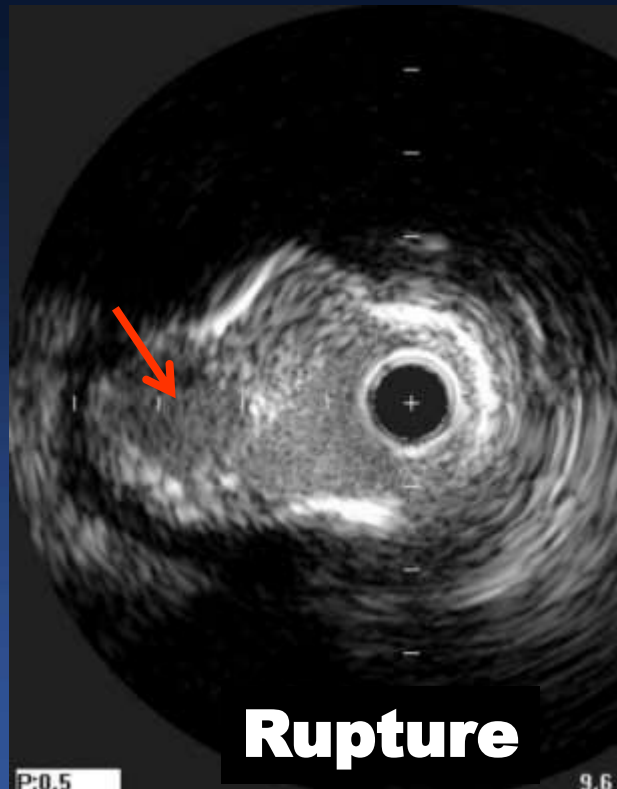
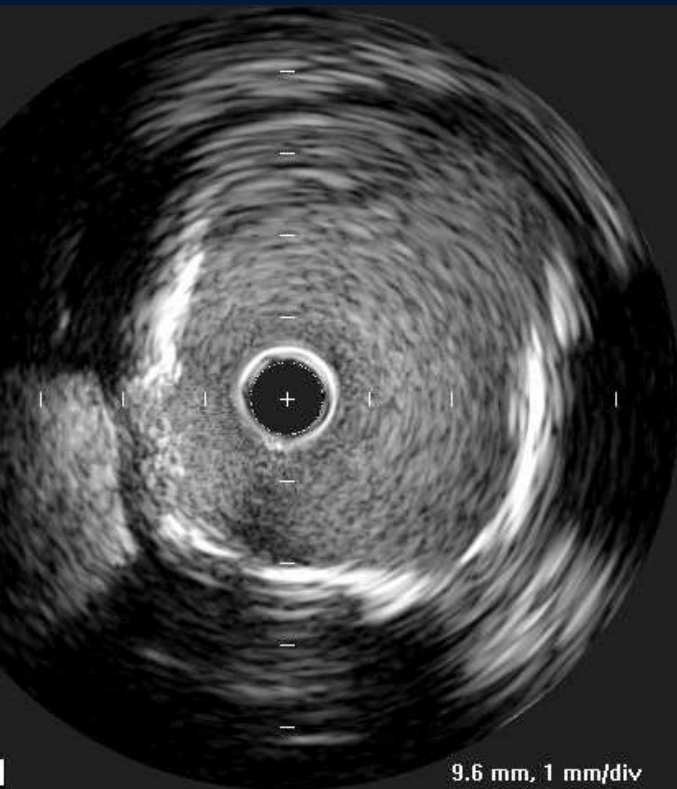
M/74, Asymptomatic Plaque Rupture



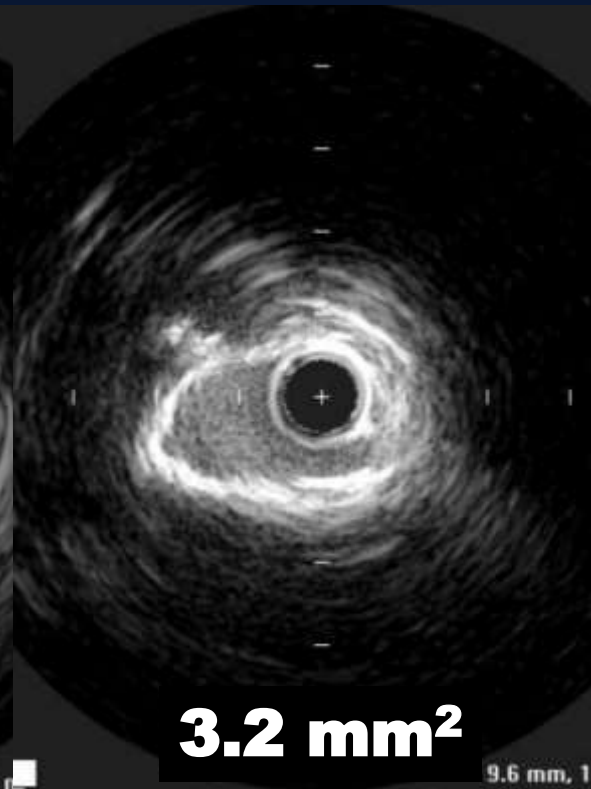
IVUS

LM

LAD, Culprit



Rupture

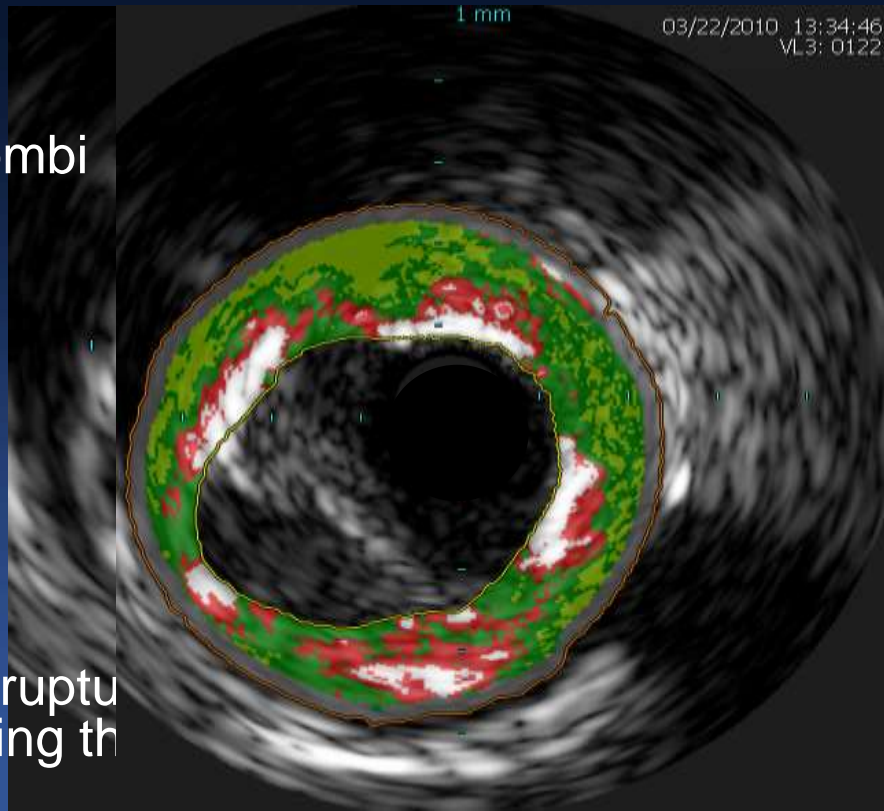


3.2 mm²

VH-IVUS

LAD, Culprit

Thrombi



Plaque rupture
organizing the

PB: 71.3%

FI : 41.4%

FF: 20.0%

NC: 23.0%

DC: 15.6%

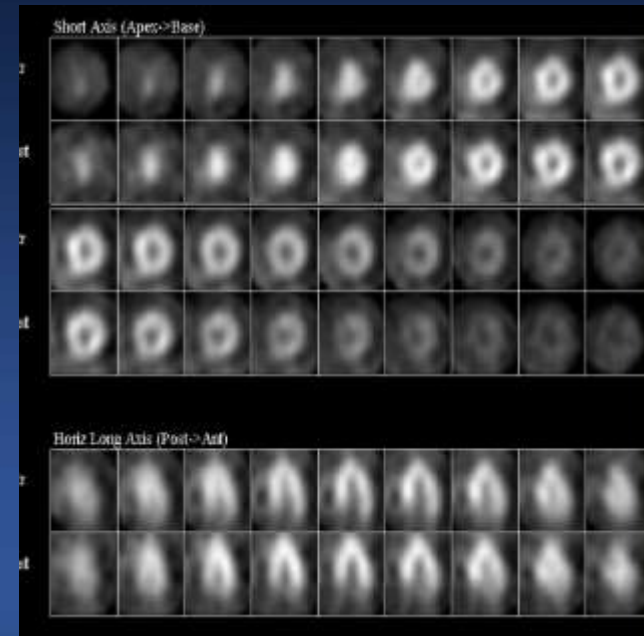
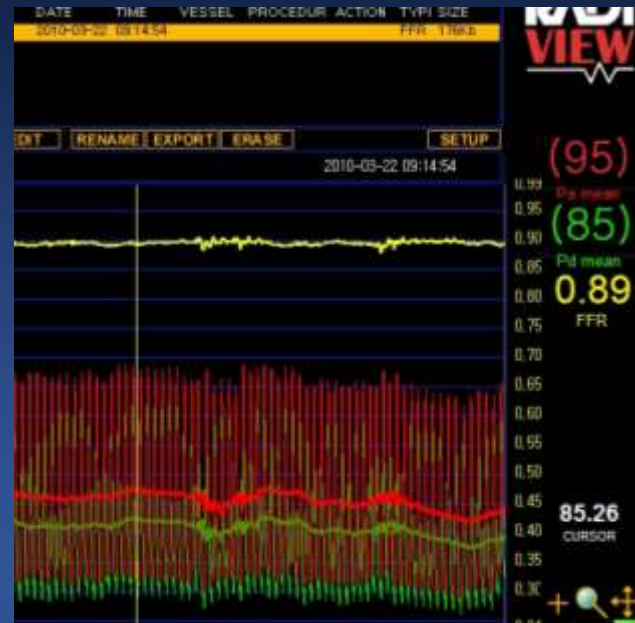
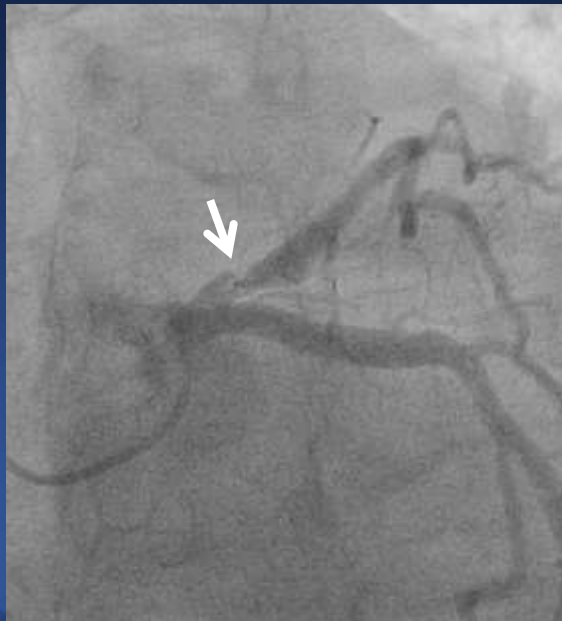
Vulnerable Plaque !

Functionally Insignificant To Treat or Not To Treat? Vulnerable Plaque

**Vulnerable
Plaque**

**Negative FFR
0.89**

**Normal
Thallium Spect**



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.

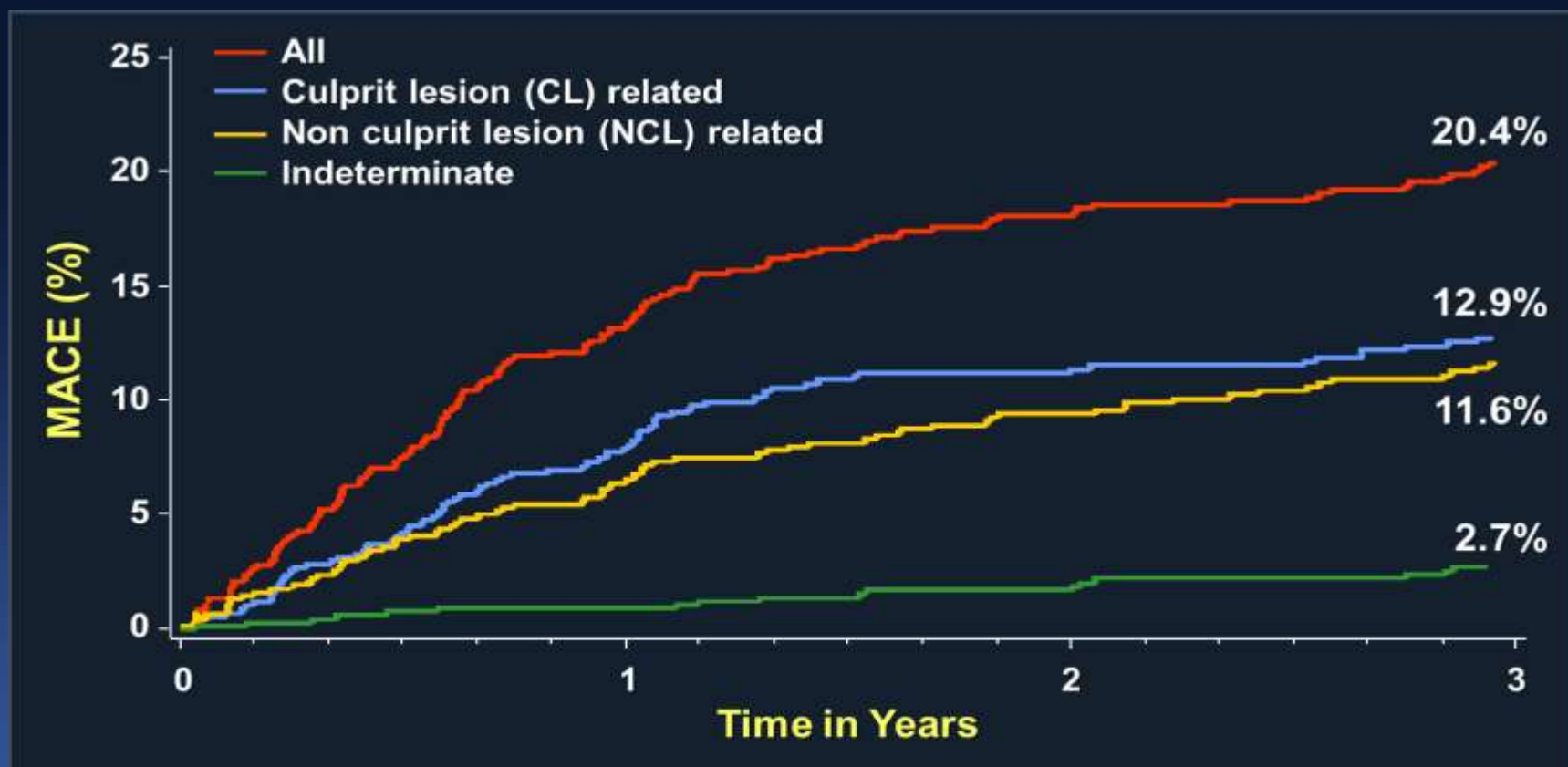
Shaw LJ, J Nucl Cardiol 2004;11:171-85 ,Prognostic value of gated myocardial perfusion SPECT. Very large meta-analysis (n=39,173 patients)

To Treat ?

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

PROSPECT: MACE

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

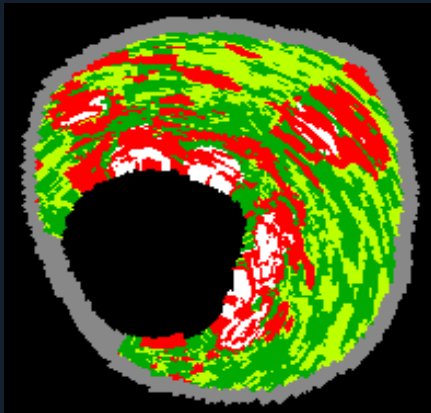


Number at risk

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

Vulnerable Plaque Defined by VH-IVUS

Independent Predictors of Non-Culprit Lesion Events



$PB_{MLA} \geq 70\%$

VH-TCFA

$MLA \leq 4.0 \text{ mm}^2$

HR [95% CI]

P value

5.03 [2.51, 10.11]

<0.0001

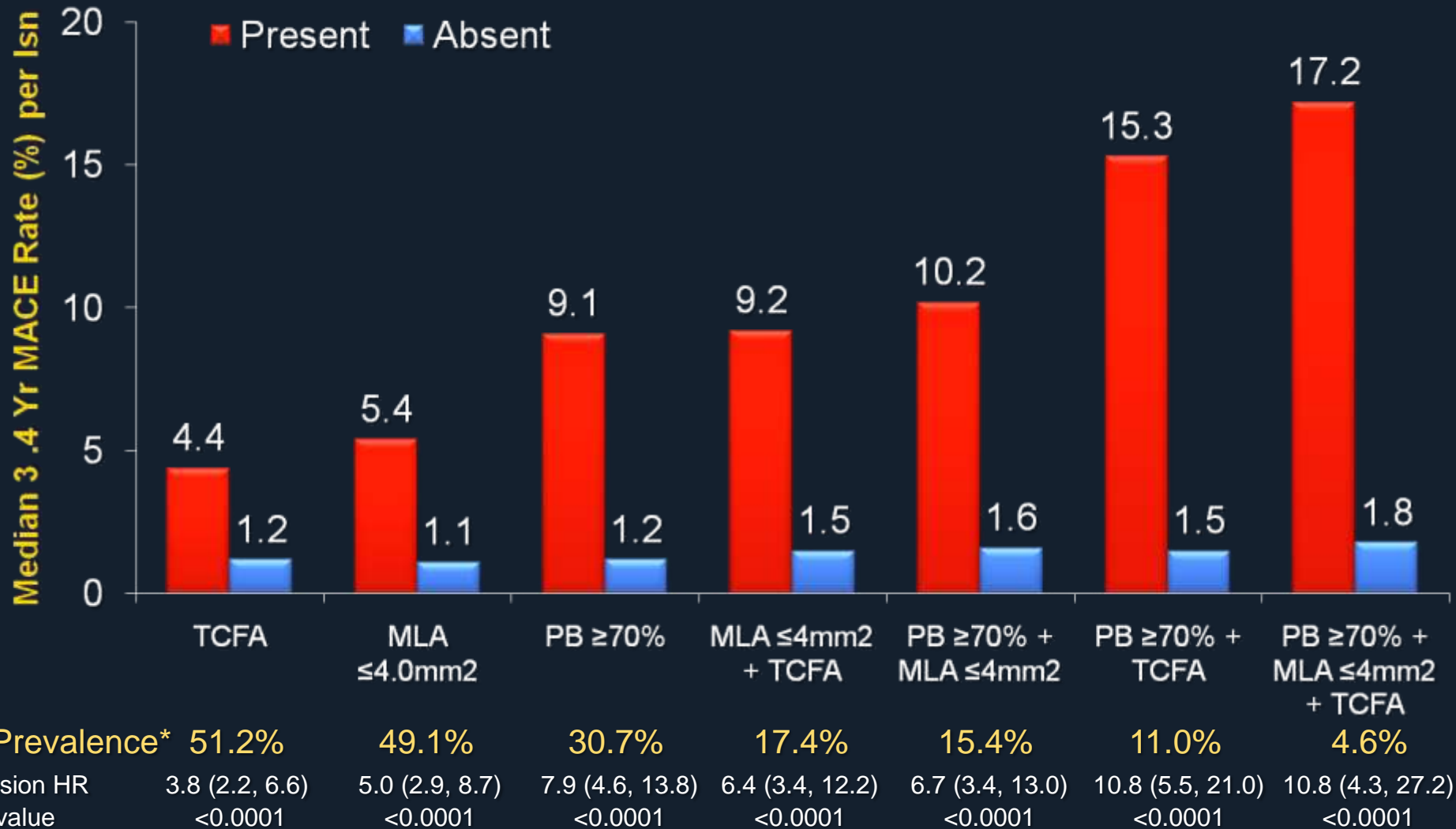
3.35 [1.77, 6.36]

0.0002

3.21 [1.61, 6.42]

0.001

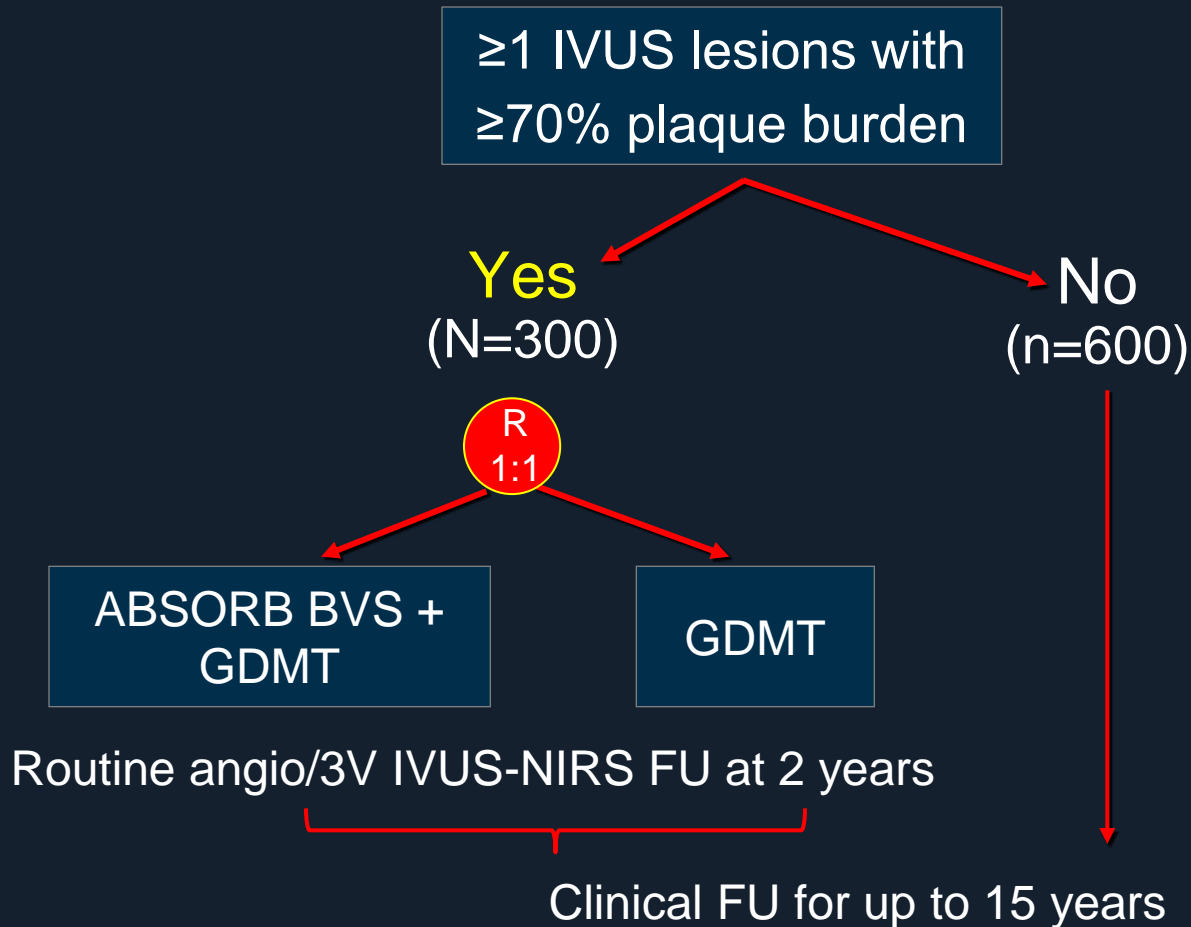
PROSPECT: Correlates of Non Culprit Lesion Related Events



*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

(Statin and Atheroma VulneraBility Evaluation)

Double-blinded, Prospective, Randomized, Controlled Trial

290 patients with
Deferred native coronary artery lesion

2:1 randomization, double-blinded

Rosuvastatin 40mg

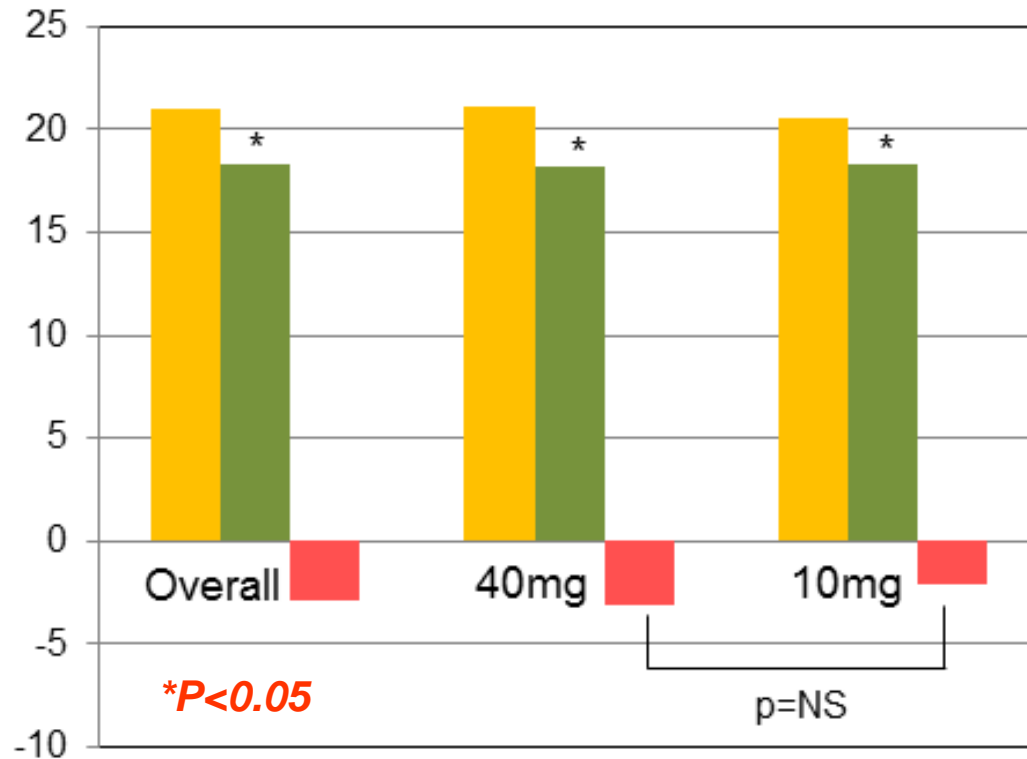
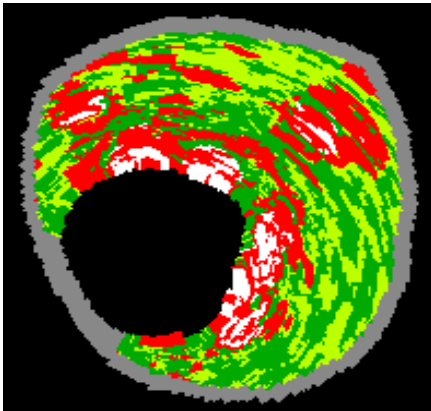
Rosuvastatin 10mg

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.

Primary Endpoint

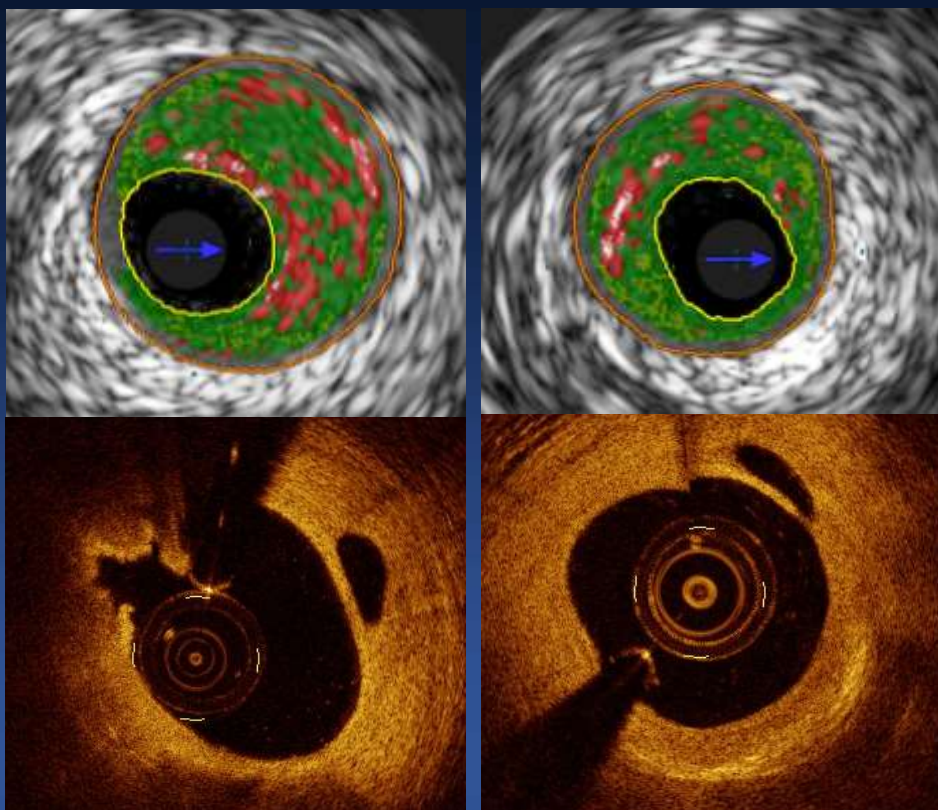
%NC Volume Changes at 1 Year



Rosuvastatin Therapy Can Make A Plaque Regression and Stabilization

Baseline

1 year



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	+	—

Clinical Outcomes at 1 Year

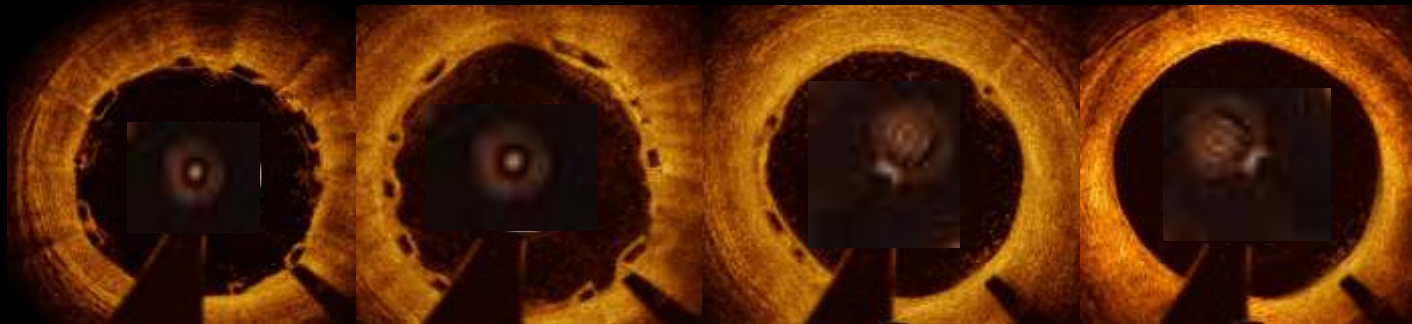
- No cardiac death
- Culprit-related MACE: 4 pts (2.3%).
- Non Culprit-related MACEs: 8 pts (3.6%).
- No Difference in Non Culprit-MACE between rosuvastatin 40 vs.10mg (3.9 vs. 2.7%, $p=NS$)

Q2,
Can **BVS** Make An Any Difference ?



Abbott Absorb, Everolimus Eluting BVS
PLLA ; Poly (L-lactide), Multi-link pattern, 150 um

Different Concept ; Do their Job and Disappear !

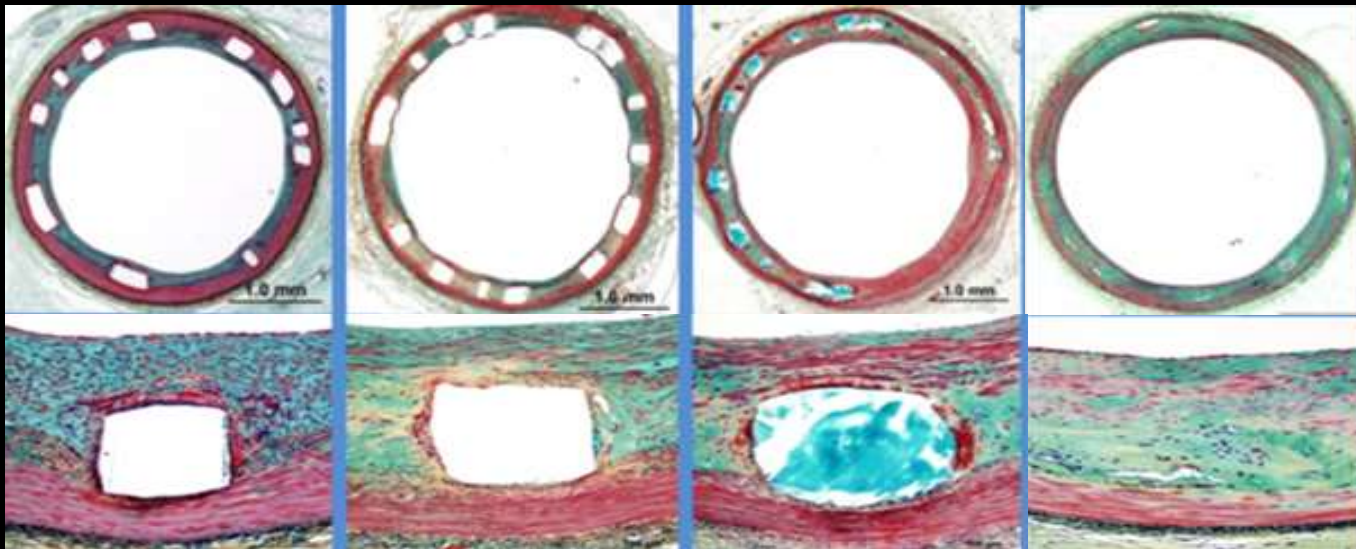


1 month

6 month

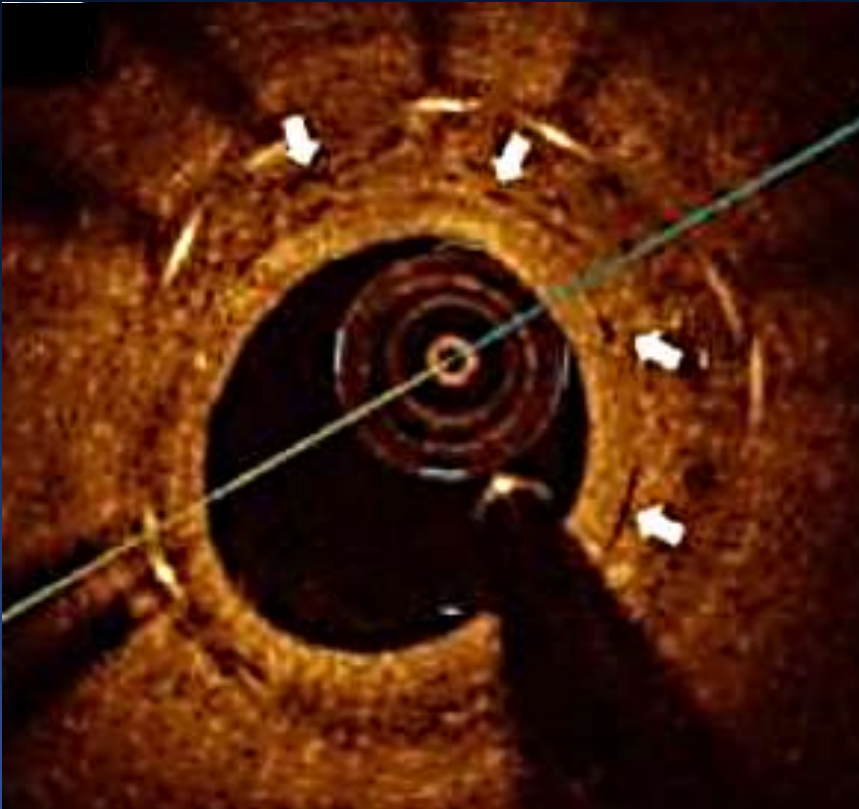
2 year

5 year

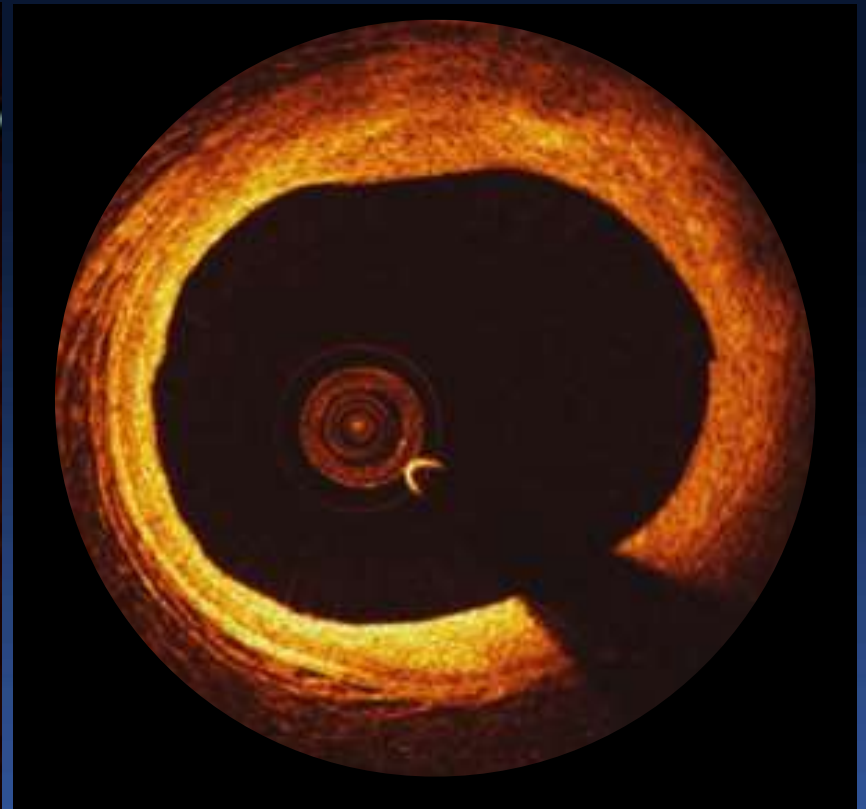


*Replaced With SMCs
and Myofibroblasts*

Different Concept ; **Metallic DES vs. Absorb BVS**

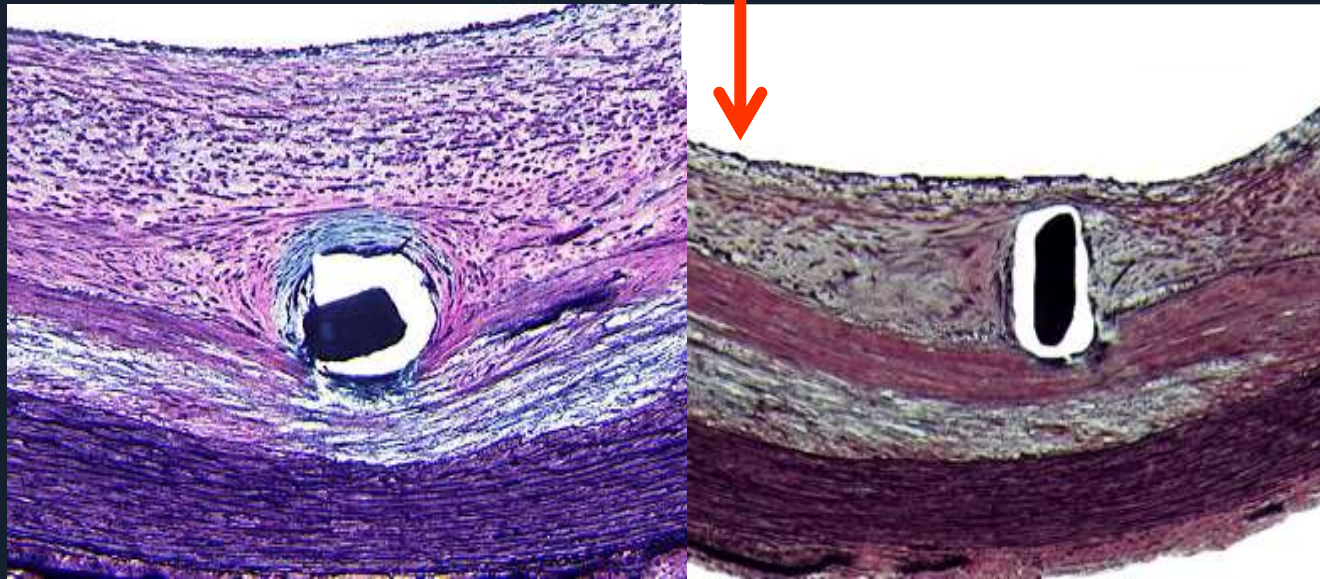


Metallic DES¹



Absorb-Treated Artery²

Everolimus Induced, Less Neointimal Hyperplasia

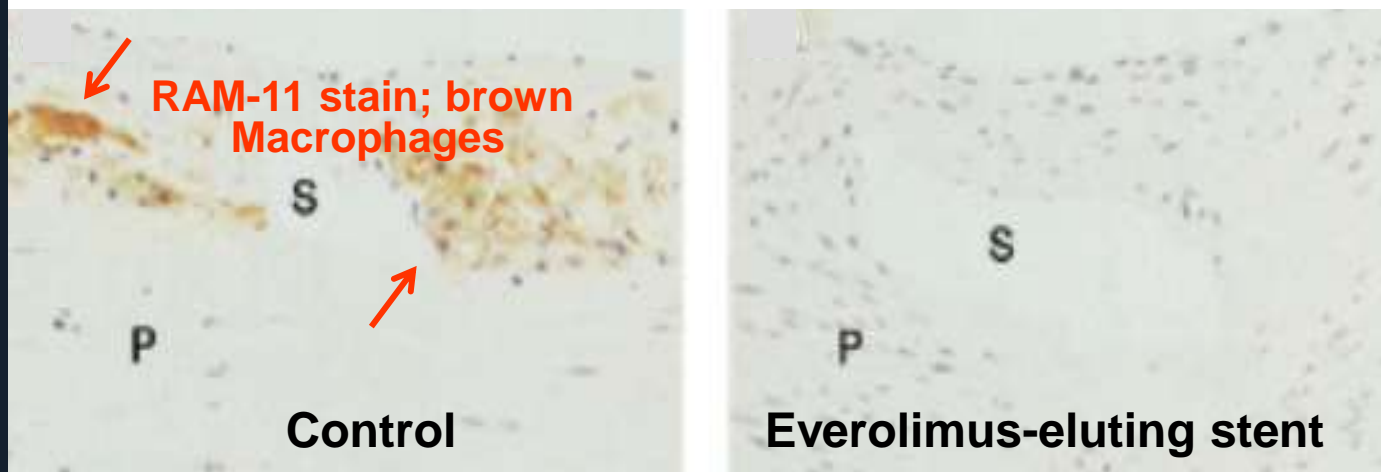


Metallic &
Polymer Strut

Everolimus Strut

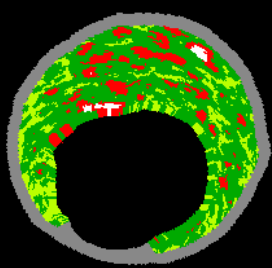
Everolimus Induced, Reduction of Macrophage

Atherosclerotic arteries of cholesterol-fed rabbits

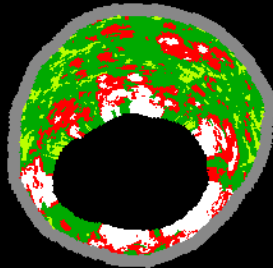


EES resulted in marked reduction of macrophage content, with preservation of SMC, *which can stabilize the plaque vulnerability*

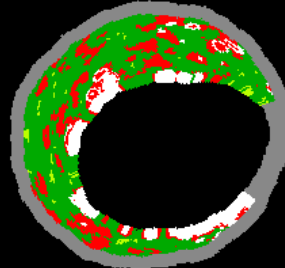
BVS on Vulnerable Plaque, Plaque Stabilization and Lumen Enlargement



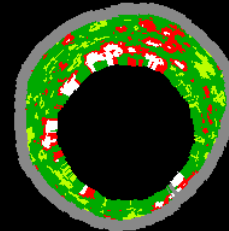
Pre-PCI



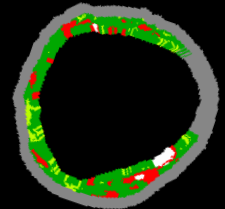
Post-PCI



6 months



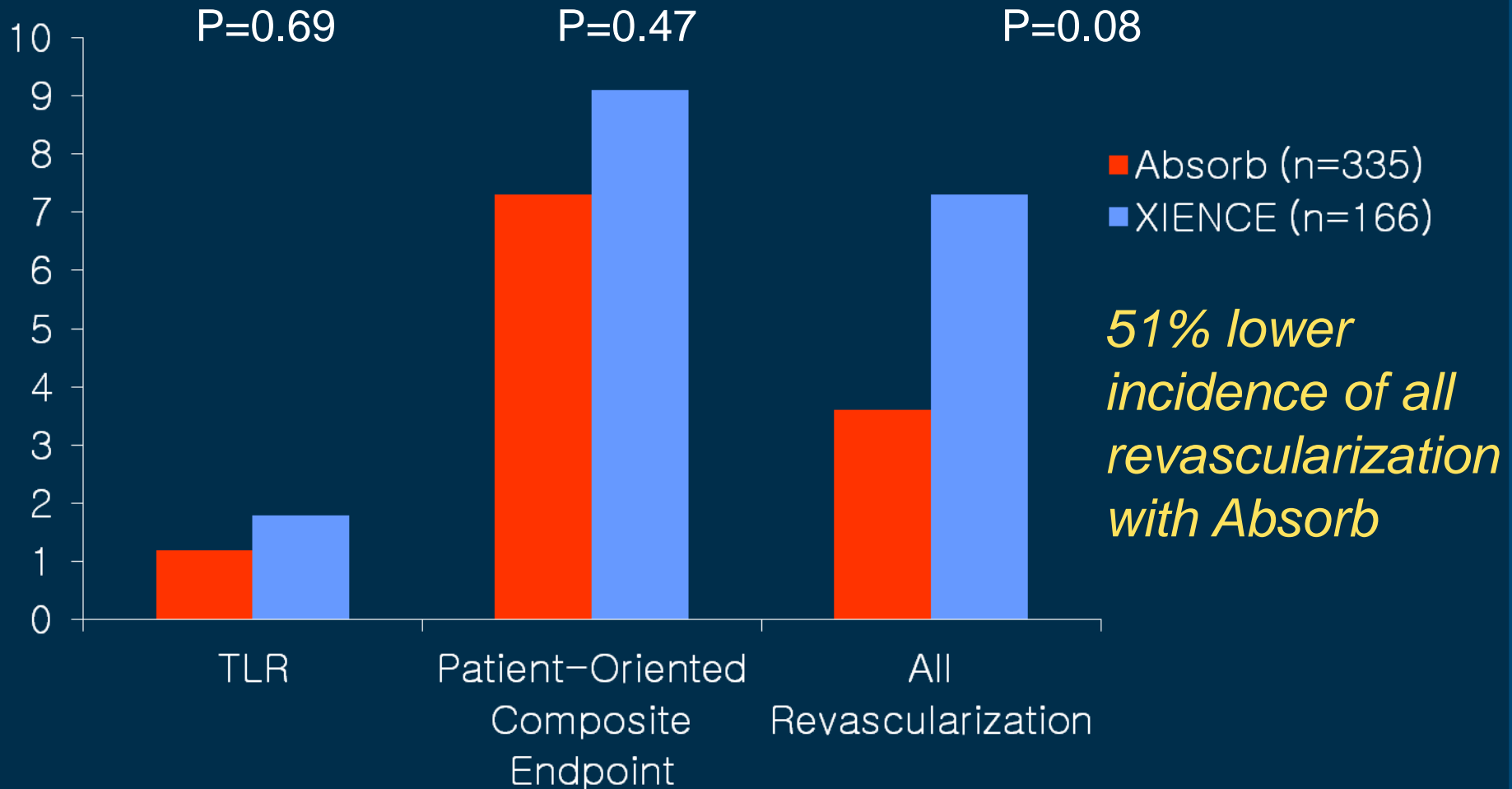
2 years



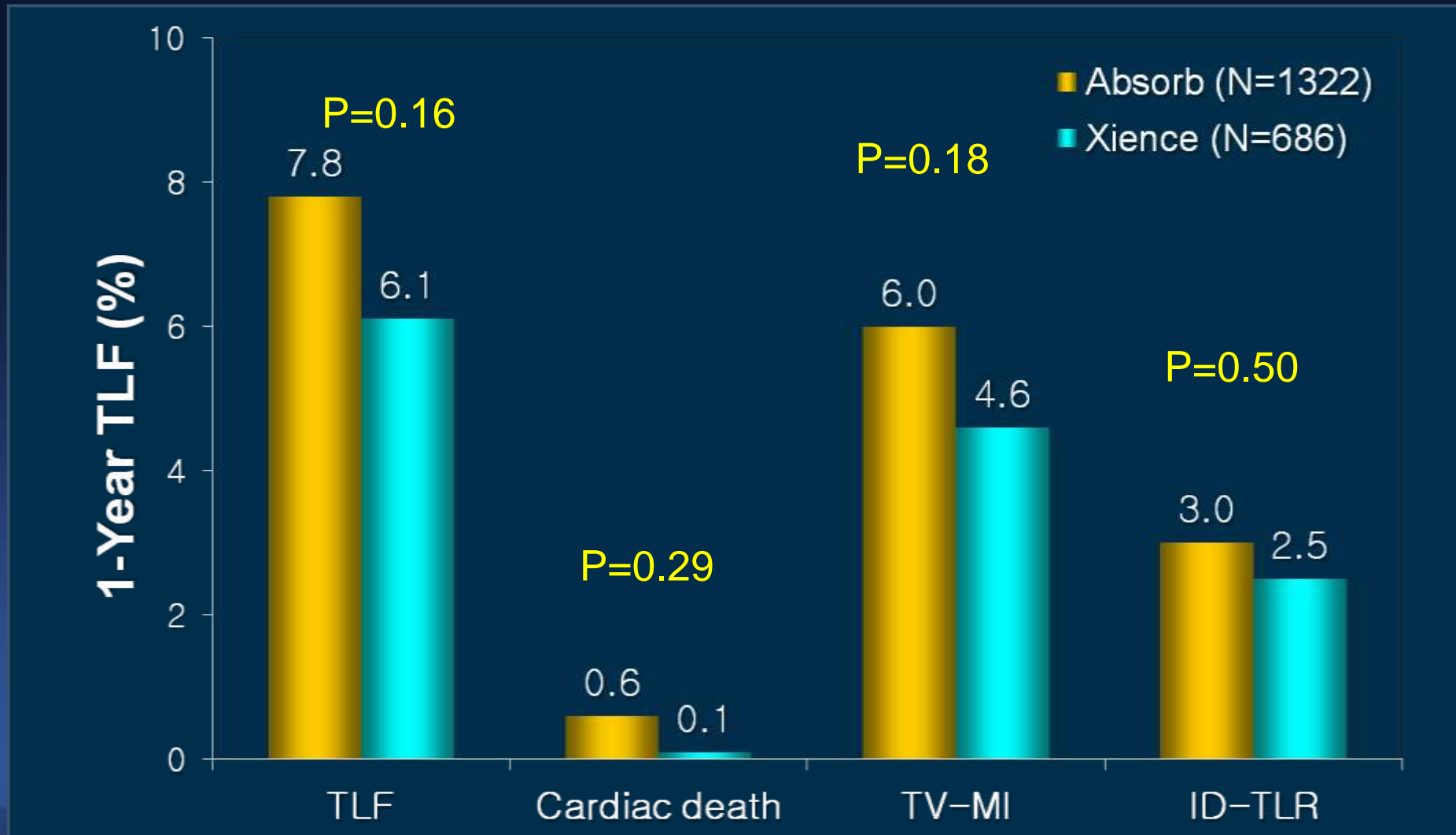
5 years

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 lumen area (mm ²)	6.95	6.17 (11%)	6.56 (5.6%)	8.09 (16%) ↑

ABSORB II, 1-year Results



ABSORB III, 1-year Results

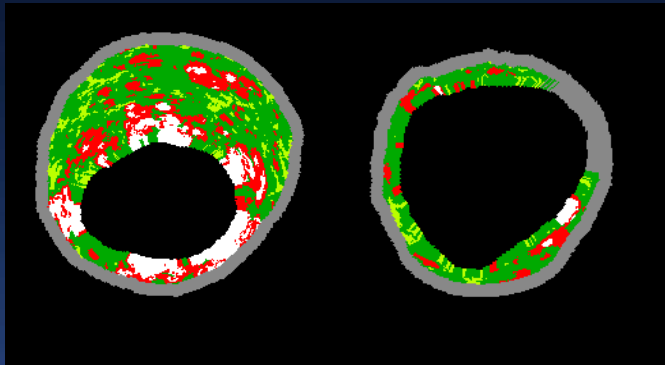


Hypothesis,

BVS Implantation Can Stabilize Plaque Vulnerability Which May Prevent Future Events of Vulnerable Plaque.

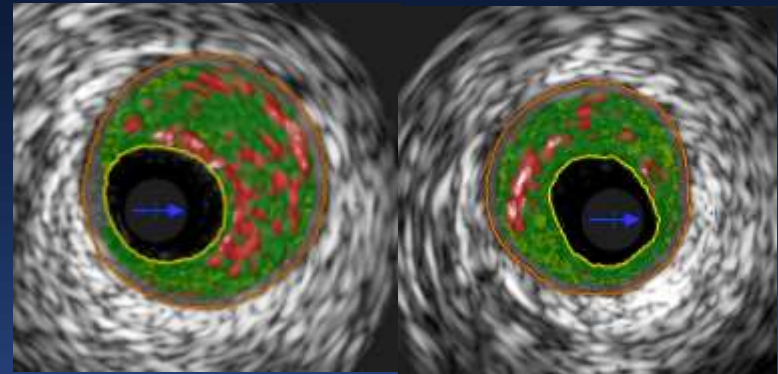
What's the Difference ?

BVS



Stabilized Plaque
Decreased Plaque
Decrease Vessel Size
Increased Lumen

Optimal Medical
Treatment



Stabilized Plaque
Decreased Plaque
Decrease Vessel Size
Decreased Lumen

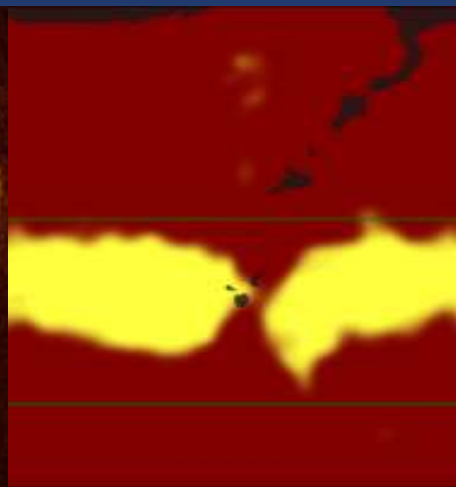
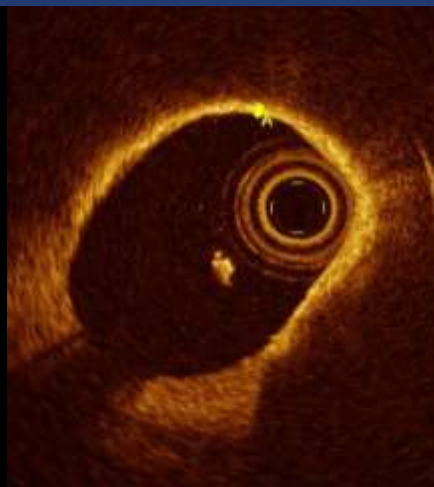
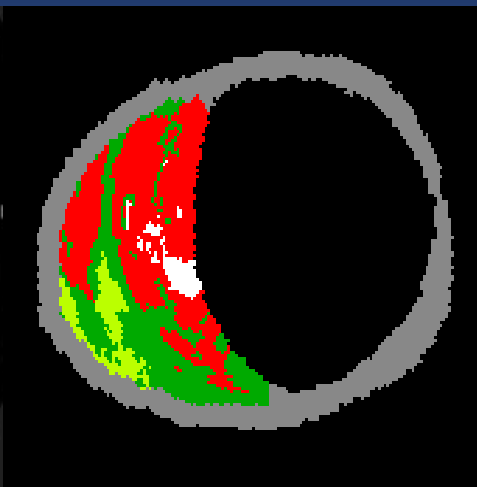
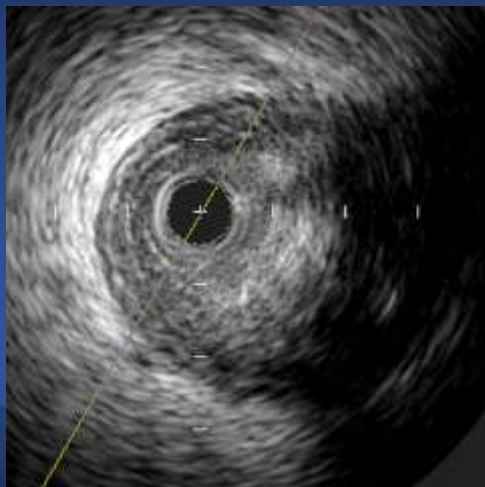
PREVENT Study,

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

*Defining, Functionally Insignificant **Vulnerable** Plaque*



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



PREVENT Trial

Any Epicardial Coronary Stenosis with FFR ≥ 0.80 and with Two of the following

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

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)

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.

Inclusion Criteria

Age 18 years or older,
Symptomatic or asymptomatic coronary stenosis,
Eligible for PCI, with
FFR >0.80 and met the two of the following

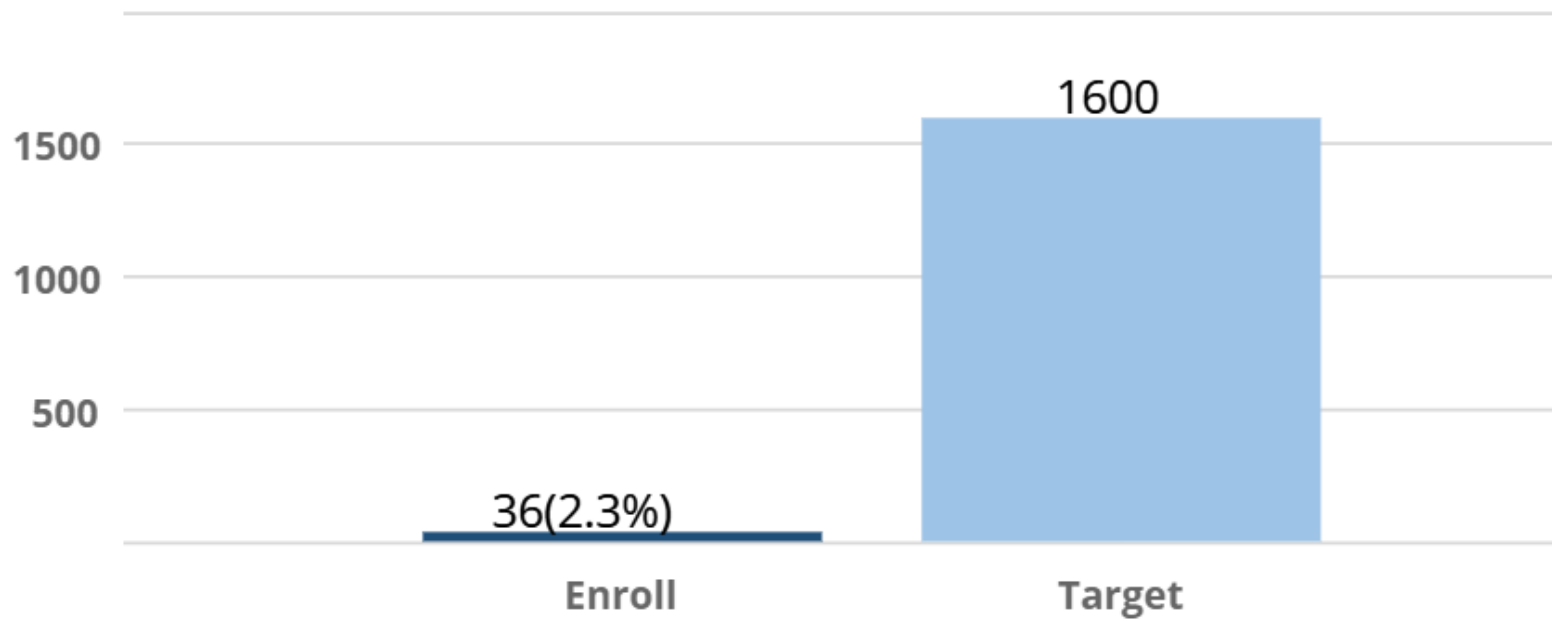
1. TCFA by OCT or VH-IVUS
2. IVUS MLA < 4mm²
3. IVUS plaque burden > 70%
4. Lipid-rich plaque on NIRS ($_{\max} \text{LCBI}_{4\text{mm}} > 315$)

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.

Just Started at Oct, 2015
36 Patients Enrolled

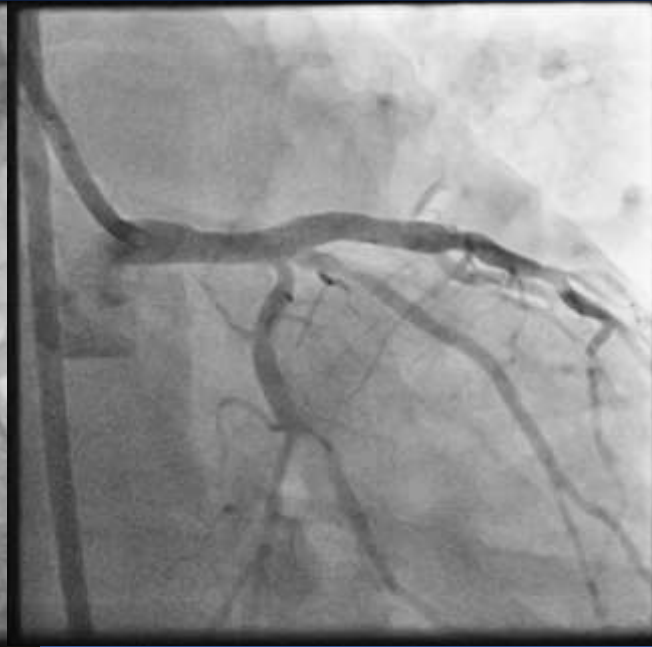
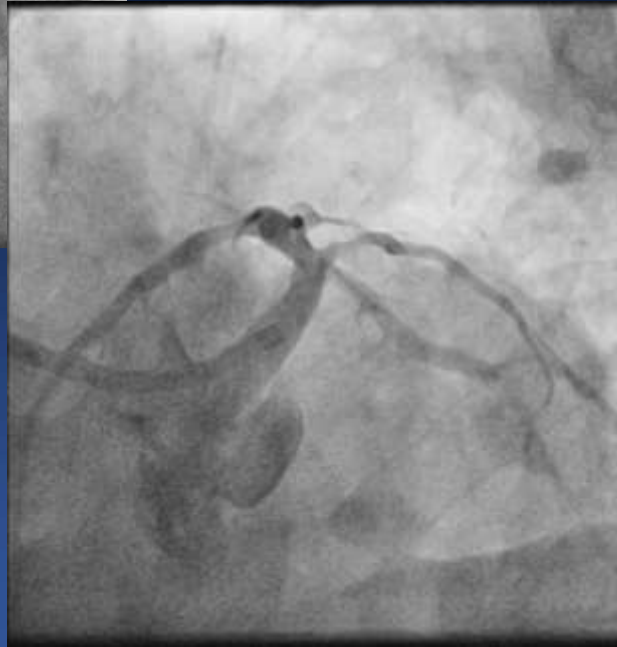
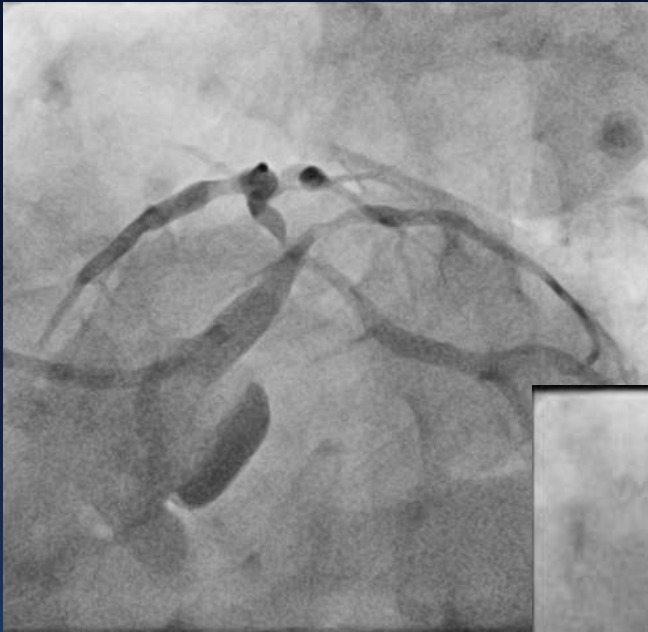


A Case

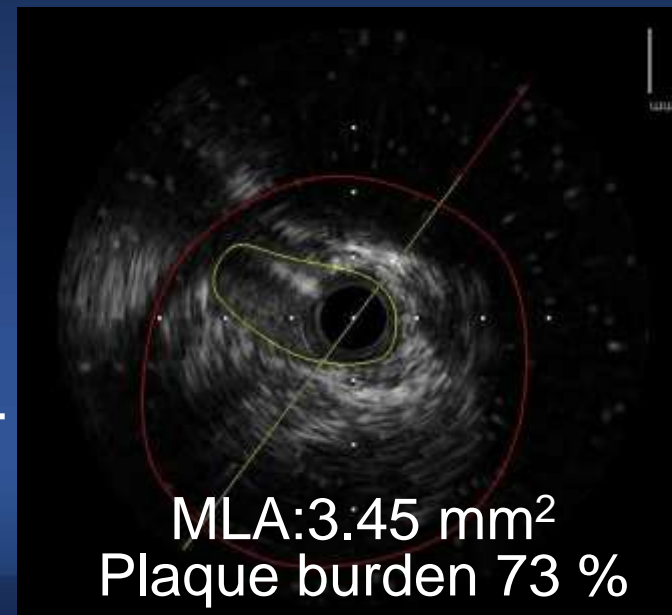
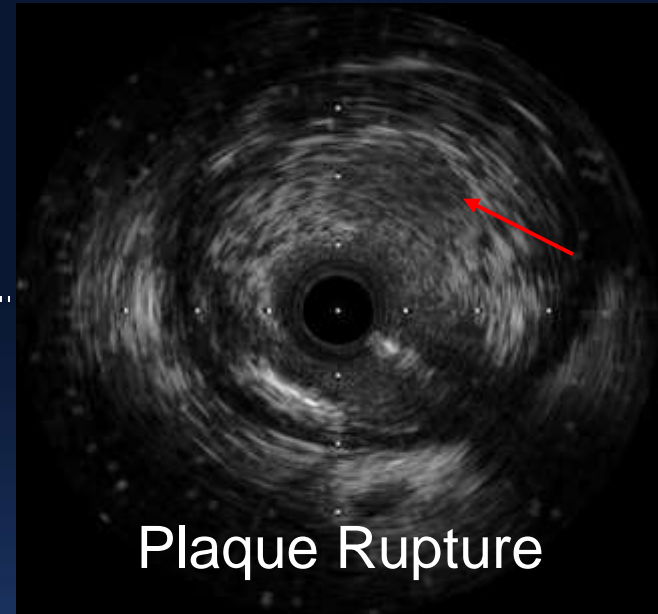
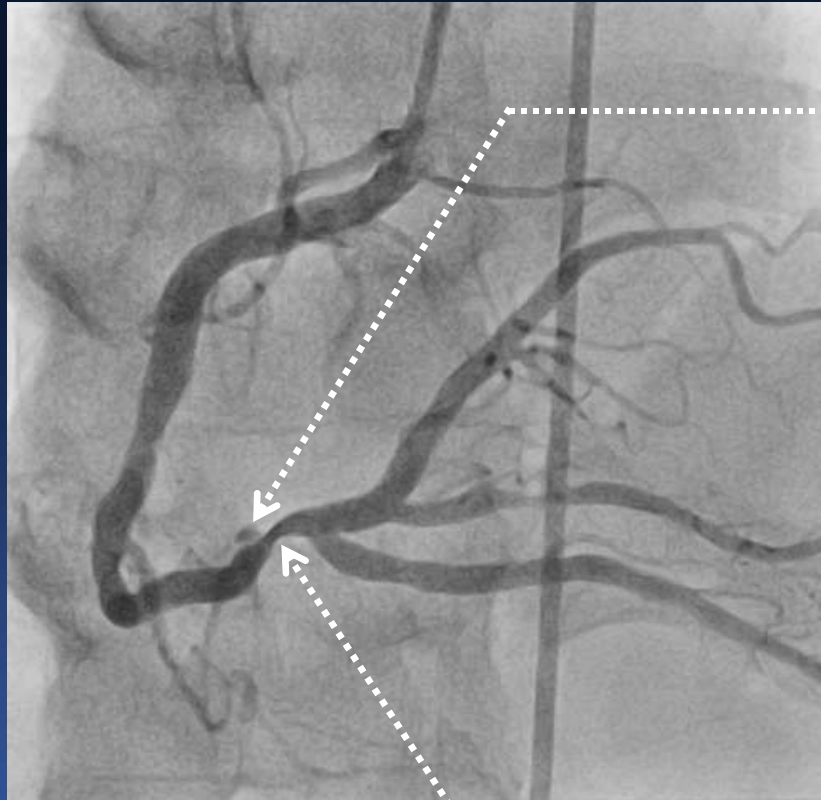
55 y/o male, Effort Chest Pain, *Stable Angina*



LM disease, Treated with *Single Stent Cross-Over*



RCA, IVUS



RCA, FFR

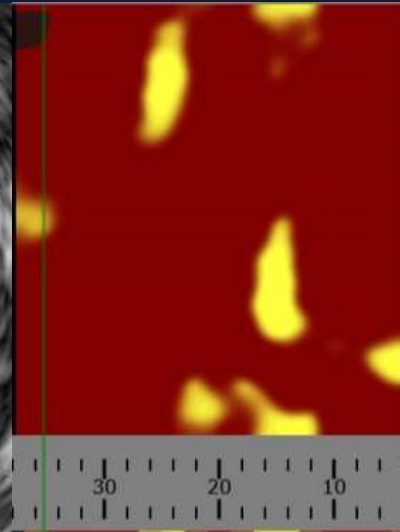
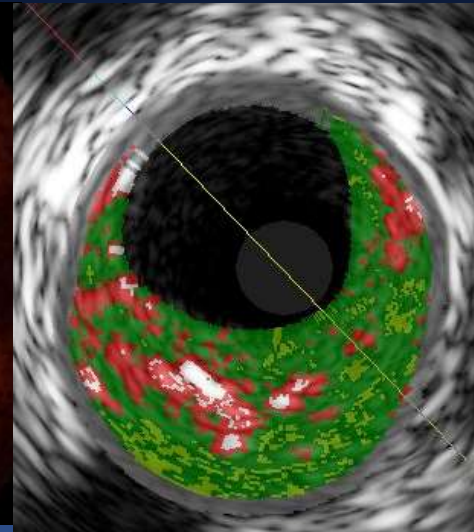
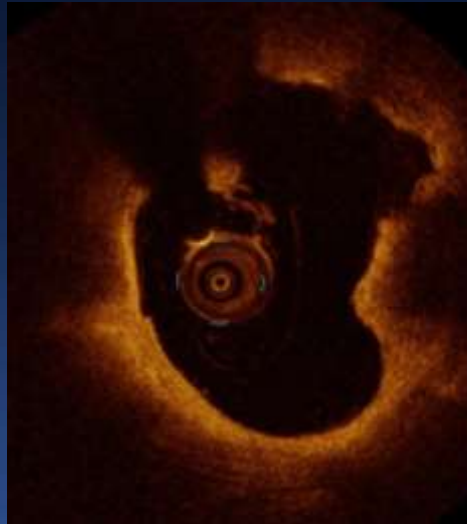
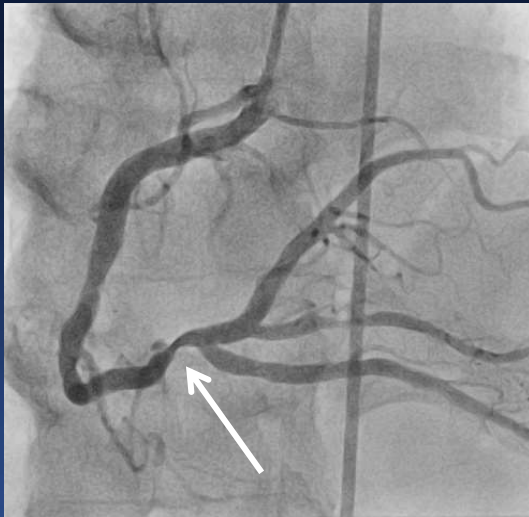
Intravenous adenosine, 200 µg/kg/min



Clinically Stable Angina, Imaging

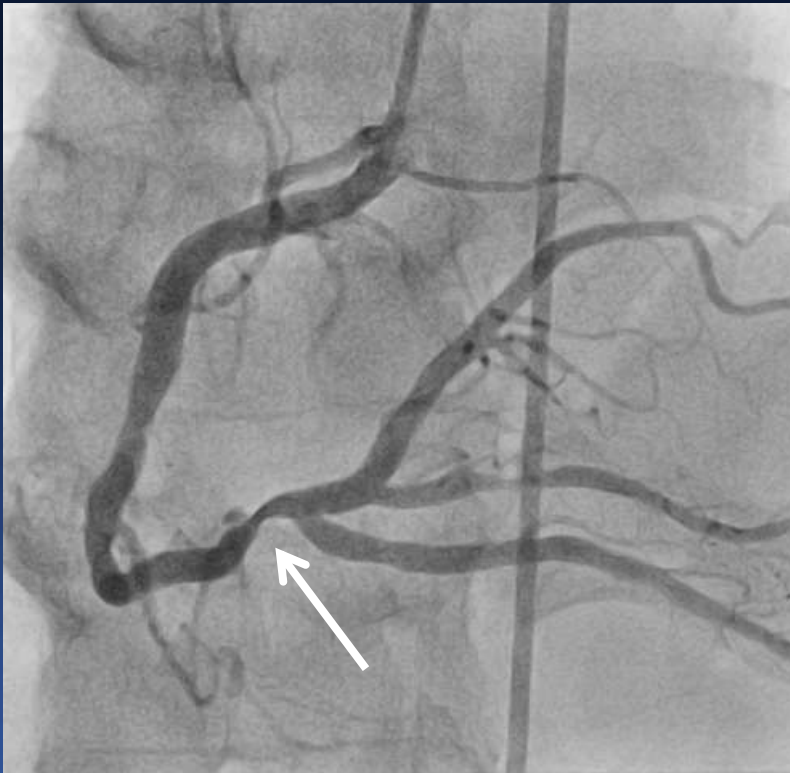
Rupture, TCFA

$\max \text{LCBI}_{4\text{mm}} = 404$



Necrotic Core 25%

Randomized with OMT



FFR : 0.89

Angiographic DS : 70%

IVUS MLA : 3.45 mm²

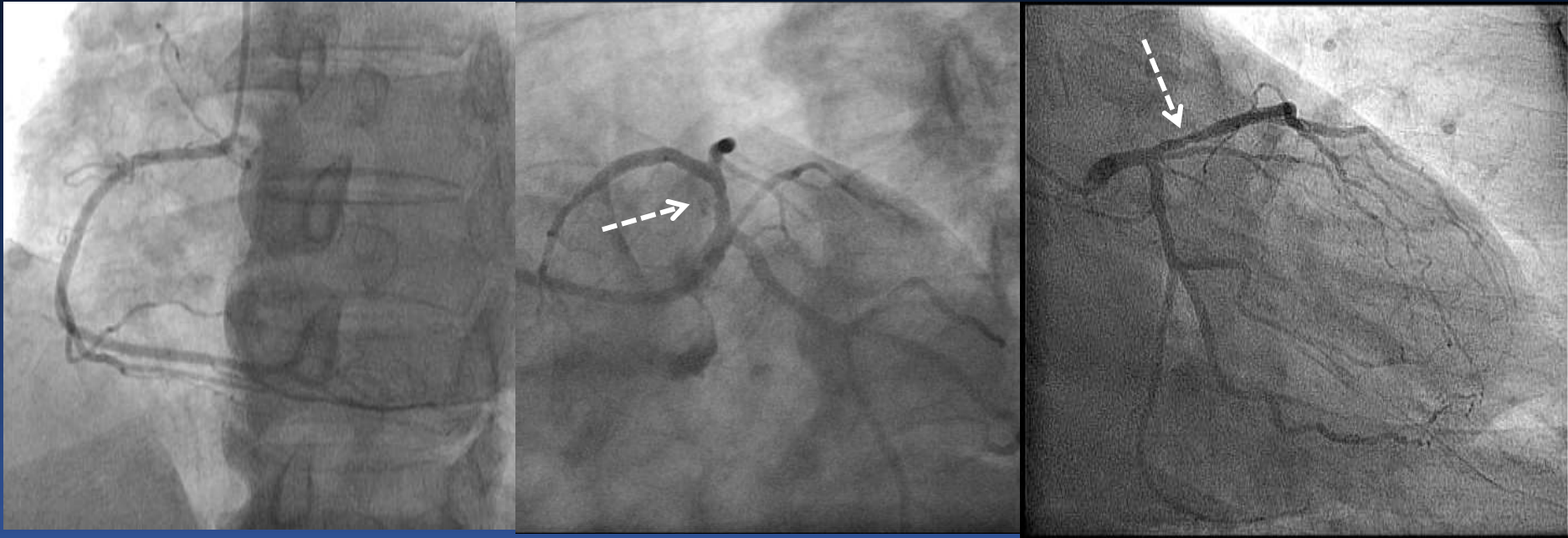
Plaque burden : 73%

max LCBI_{4mm} : 404

TCFA (+)

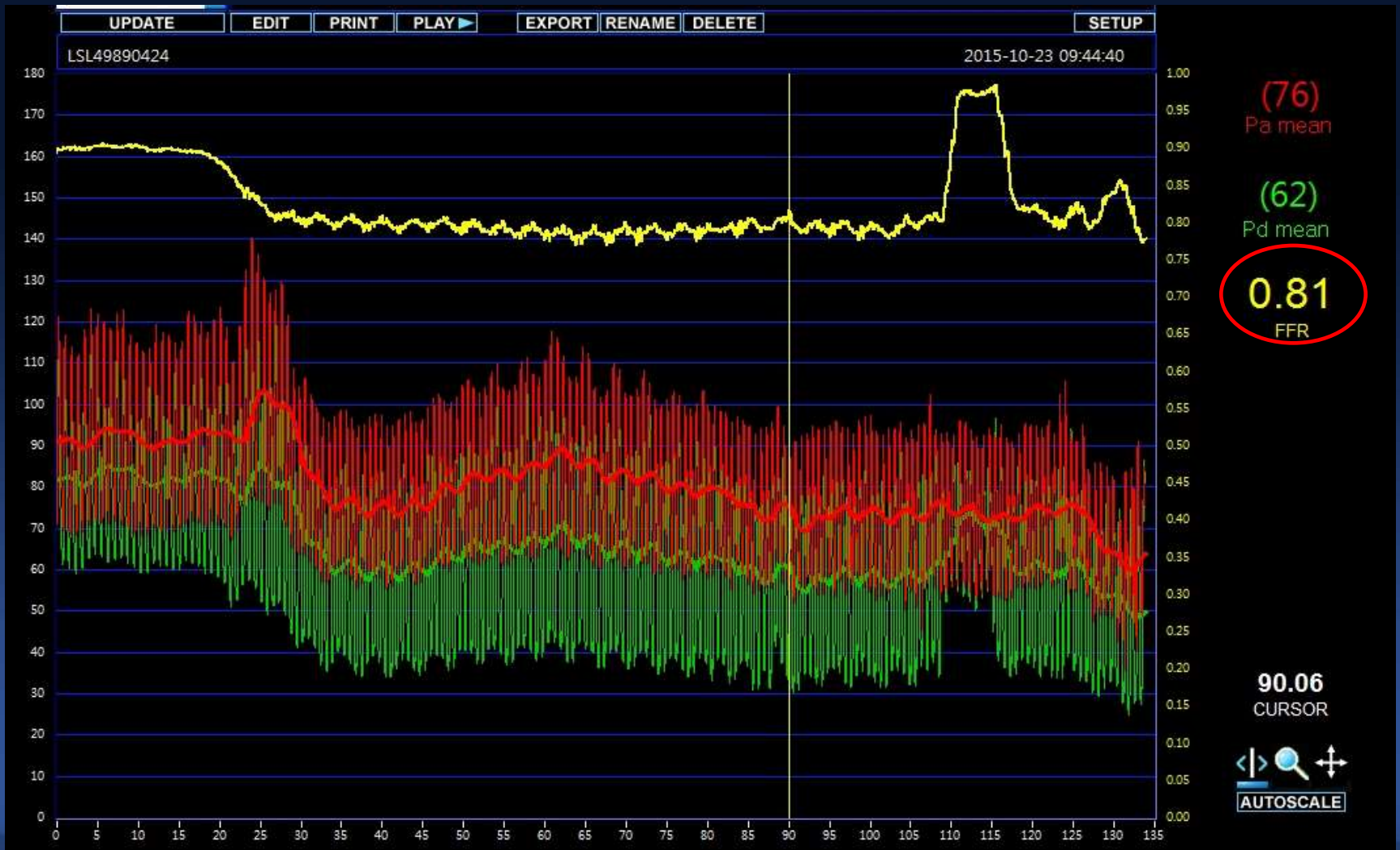
A Case

58 y/o male, *Unstable Angina*

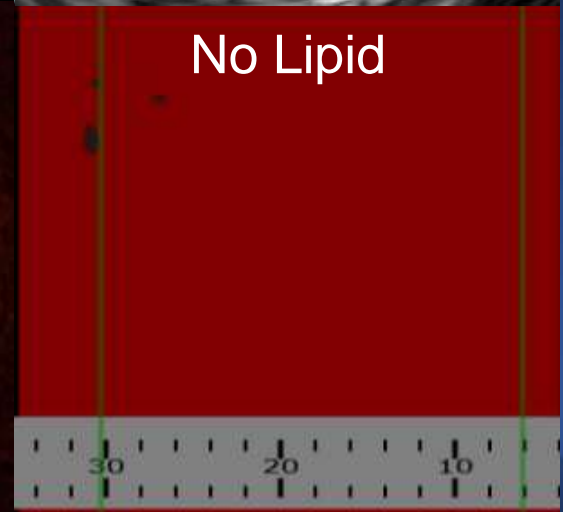
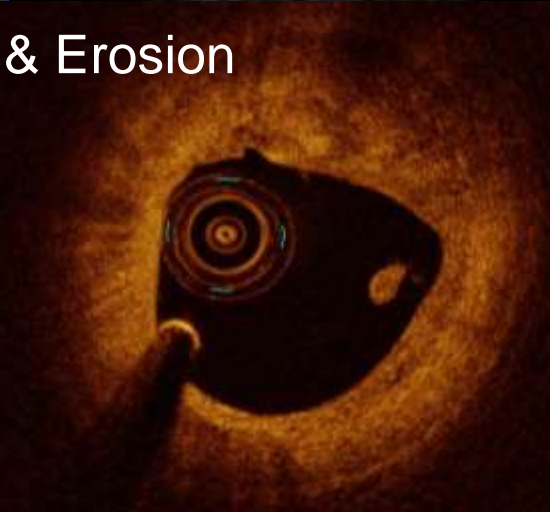
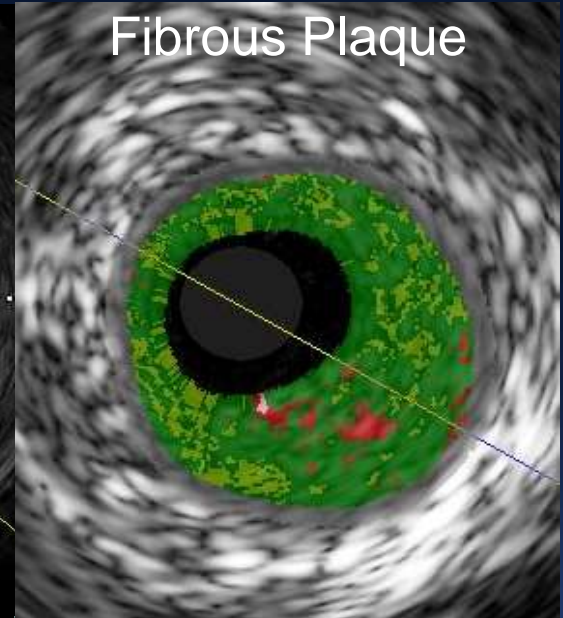
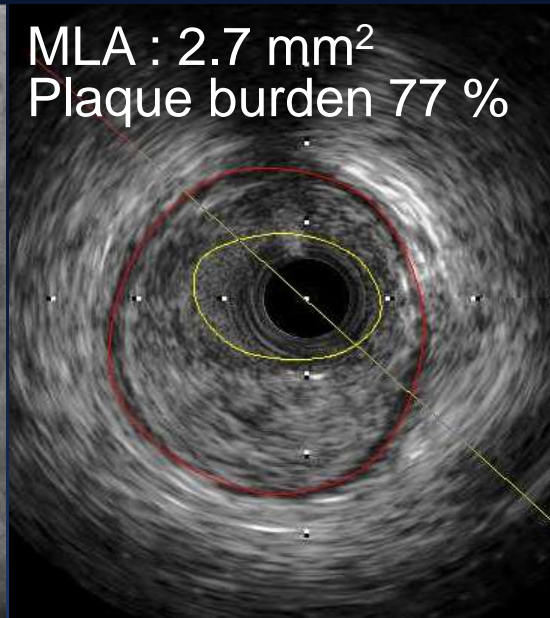
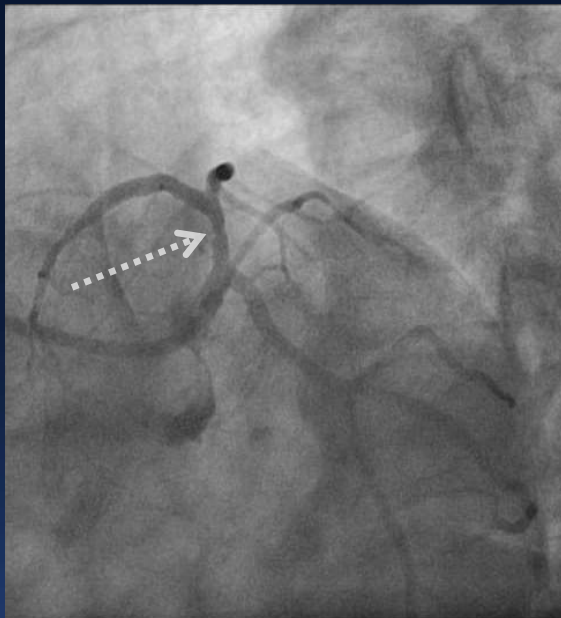


FFR

Intravenous adenosine, 140 $\mu\text{g}/\text{kg}/\text{min}$

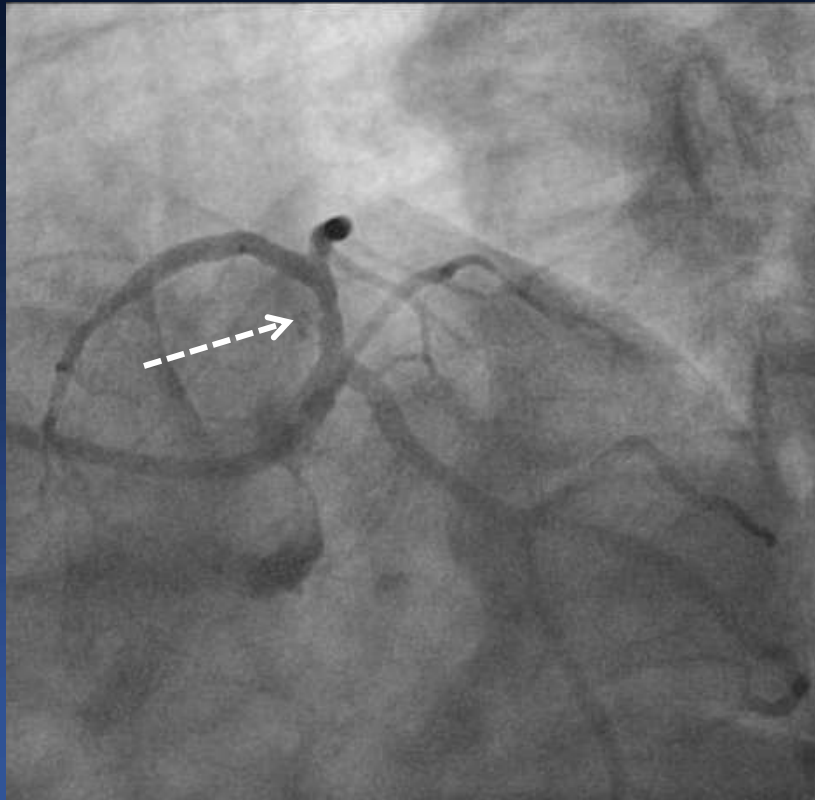


Clinically Unstable Angina, Imaging



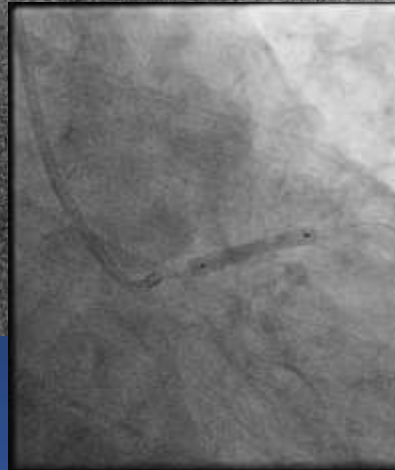
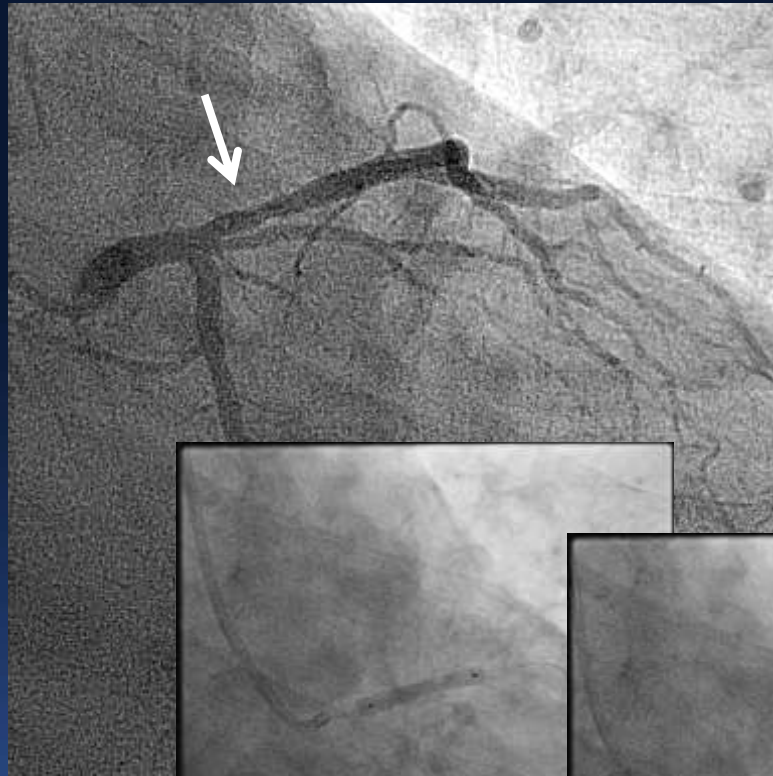
Randomized with BVS

58 y/o male, *Unstable Angina*

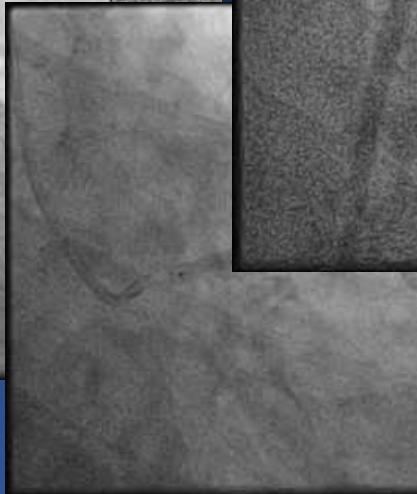


- Angiographic DS : 50%
- FFR : 0.81
- IVUS MLA : 2.7 mm²
- Plaque burden : 77 %
- $\max \text{LCBI}_{4\text{mm}}$: 0

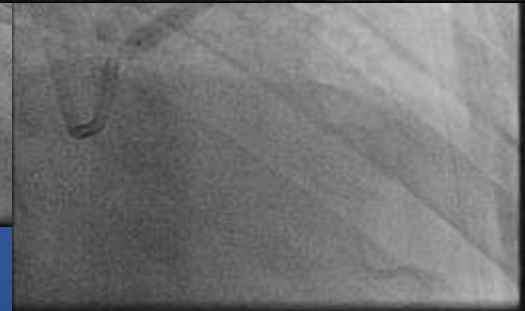
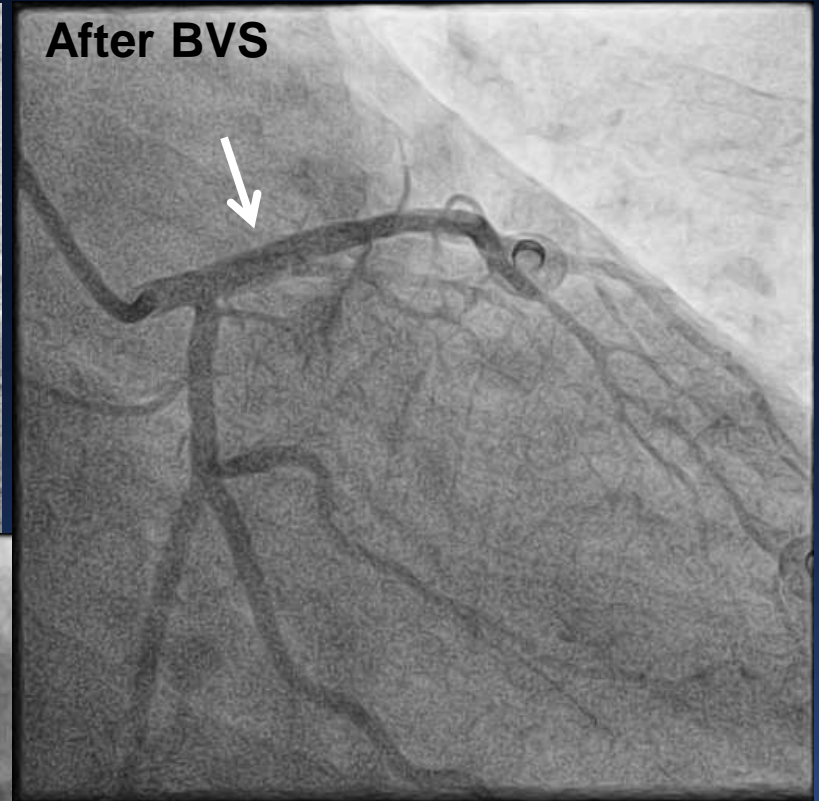
BVS, Absorb



Pre-Dilate, NC
3.0 mm x 15 mm

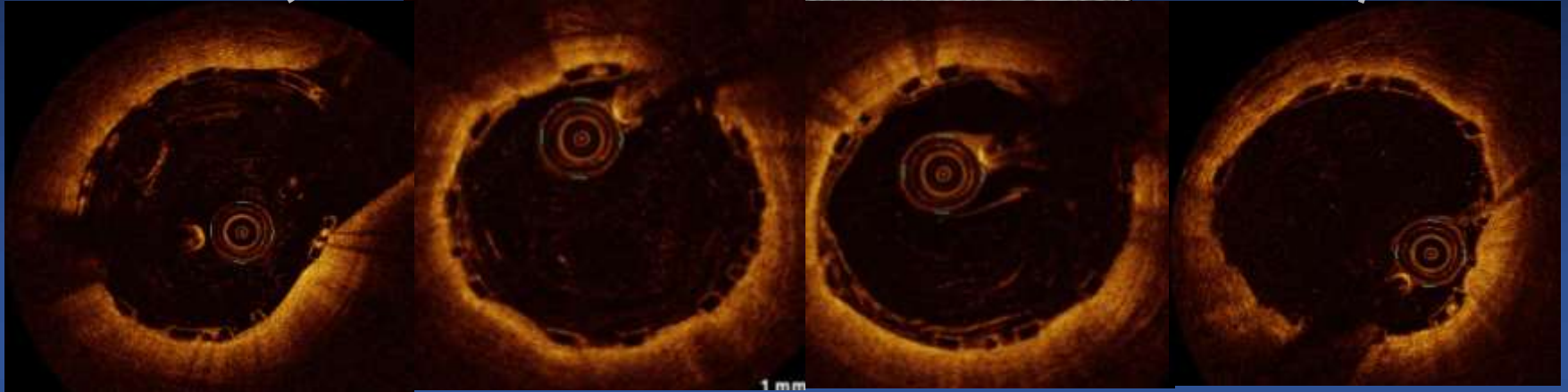


Absorb BVS
3.5 mm x 18 mm

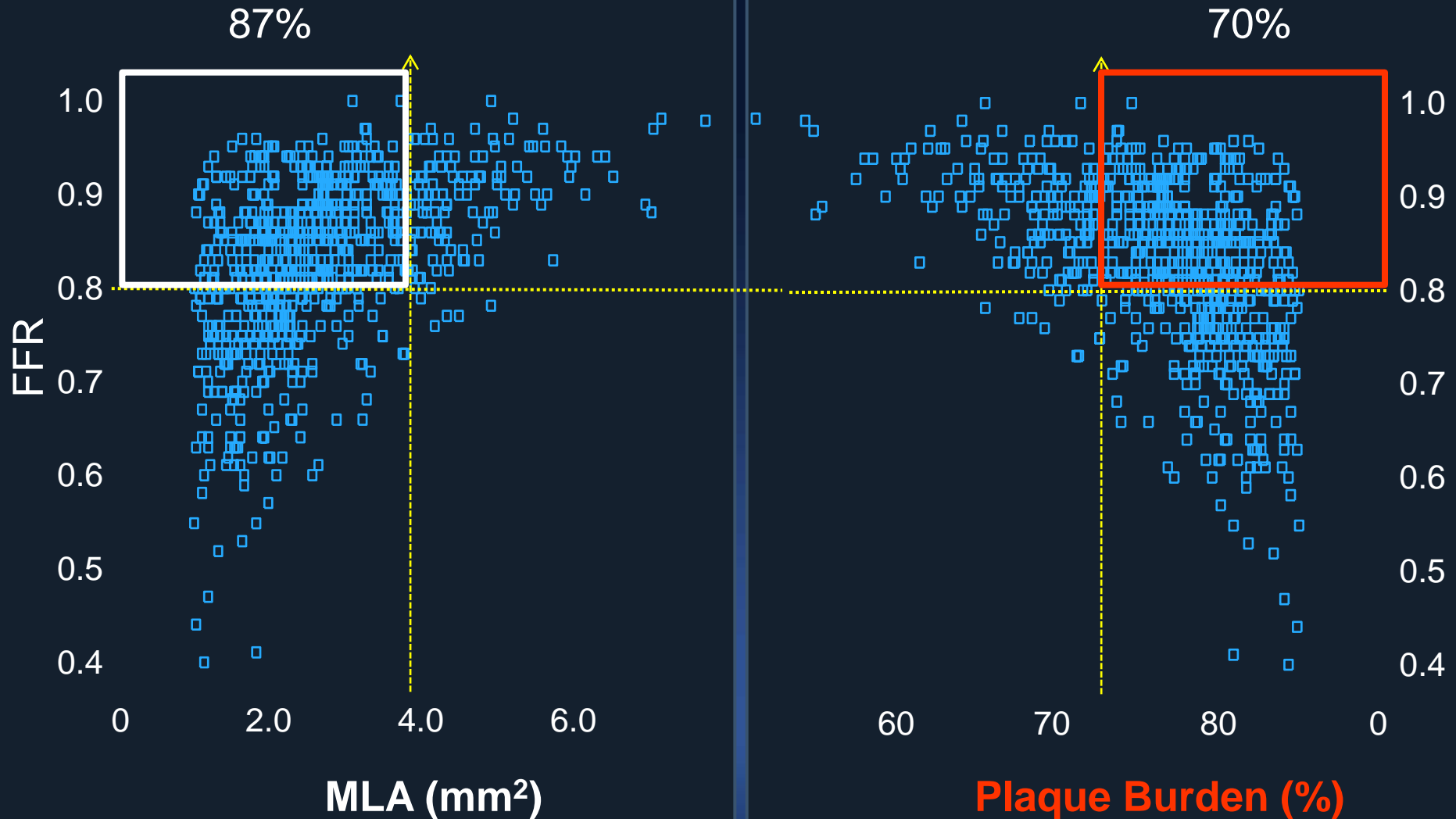


NC Balloon,
4.0 mm x 13 mm

1st BVS Randomized Case



Study Candidate in Real Practice



PREVENT Trial,

8 Countries, 30 Centers

Principal Investigators

Seung-Jung Park, MD, PhD.
Korea

Co-Principal Investigator

Gregg Stone, MD, PhD.
USA

Active Participants

Korea, Japan, Taiwan,
Hong-Kong, New Zealand,
Australia, Italy and USA

Drs. Akasaka, Kao, Michael Lee,
Nepson, Alan Young, Ron
Waksman, David Cohen,
Antonio Colombo.

The background of the slide is a monochromatic blue image of a mountainous landscape. In the foreground, there are dark, silhouetted hills covered in dense evergreen trees. Beyond these, several layers of lighter blue mountain ranges recede into the distance, creating a sense of depth. The sky is a pale, clear blue with a few wispy clouds near the horizon.

Thank You !!

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