

Functionally Insignificant, Vulnerable Plaque: Do You Want to Treat? - YES! I DO! -

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial Interest /arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship

Company

Grant/ Research Support:

Boston Scientific Corp.

Consultant:

Boston Scientific Corp.

Speaker Fee:

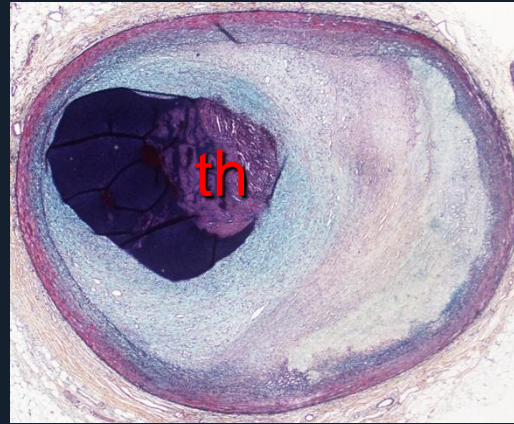
St Jude Medical, Volcano Corporation

Unstable Plaque=Causing Thrombosis

Plaque Rupture



Plaque Erosion



Calcified Nodule



Stable Plaque=Not Causing Thrombosis

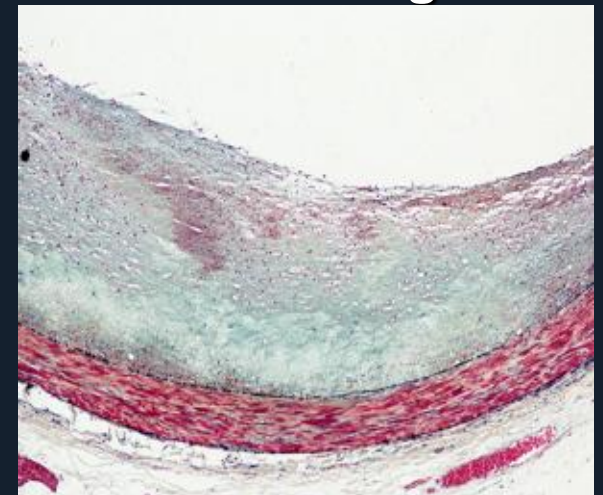
Fibrocalcific Plaque



Healed Rupture



Pathological Intimal Thickening

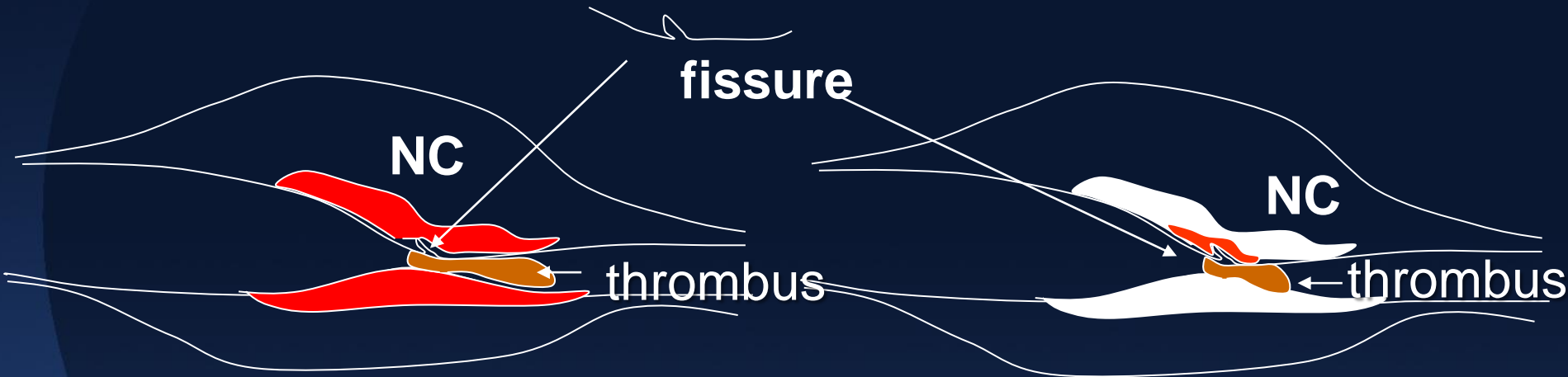


IVUS

	Age>80	Age<65	p-value
Thrombus	1 (2%)	7 (14%)	0.04
Calcified Plaque	57%	10%	0.009
Calcified Length, mm	5.5±2.9	3.5±2.8	0.006
Lesion Max Calcified Arc, °	199±91	115±71	<0.0001
Prox Ref Calcified Arc, °	90±50	65±23	0.2
Distal Ref Calcified Arc, °	68±30	49±18	0.4
MLA, mm²	2.6±1.2	2.8±1.8	0.5
Remodeling Index, mm²	0.85±0.2	1.03±0.2	0.0004

Hassani et al. *JACC* 2006;47; 2413-9

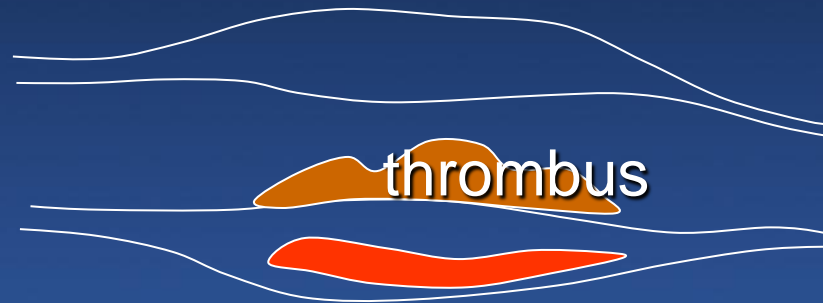
Small rupture with small thrombus



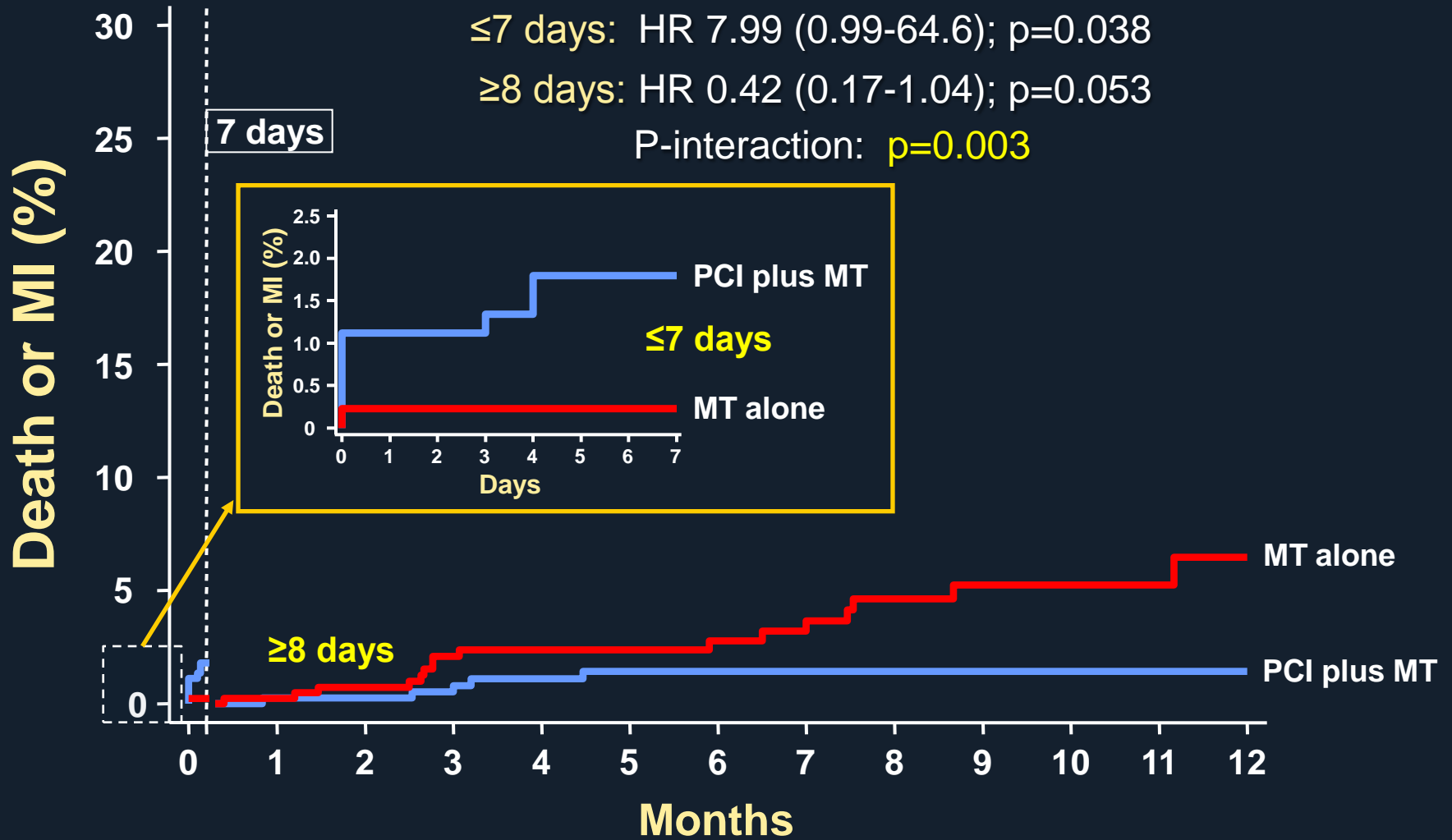
Large rupture with large thrombus



Erosion with thrombus



FAME 2: Landmark Analysis of Death or MI

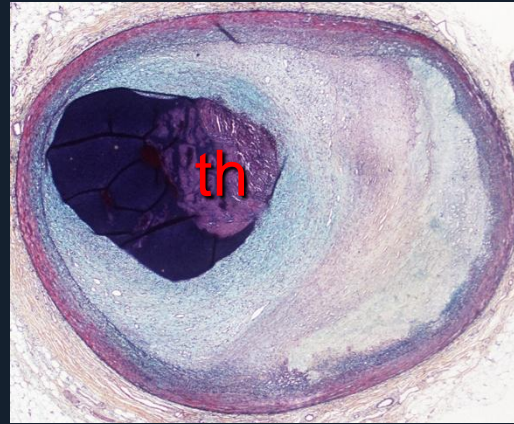


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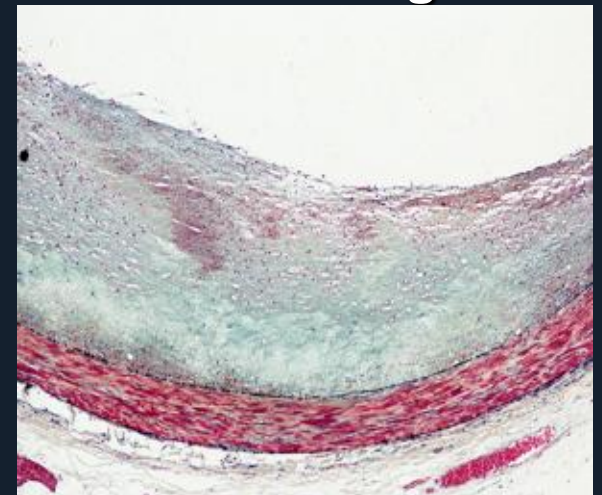
Fibrocalcific Plaque



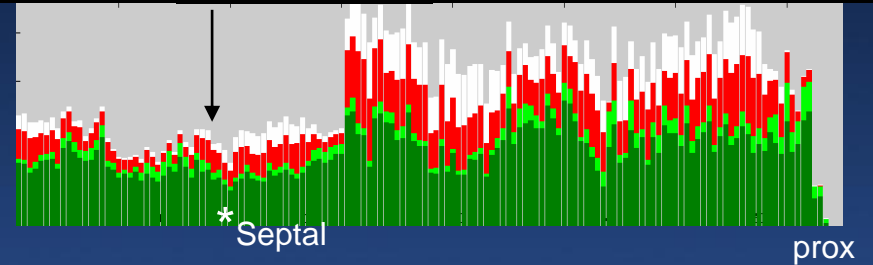
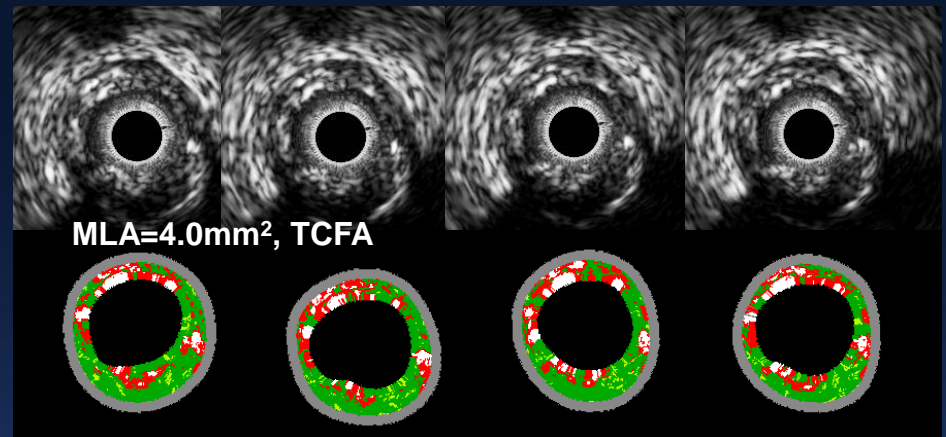
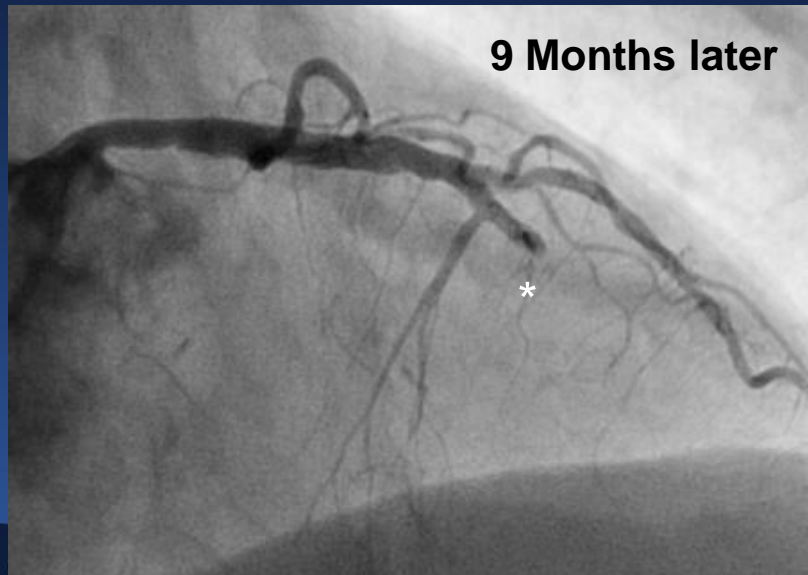
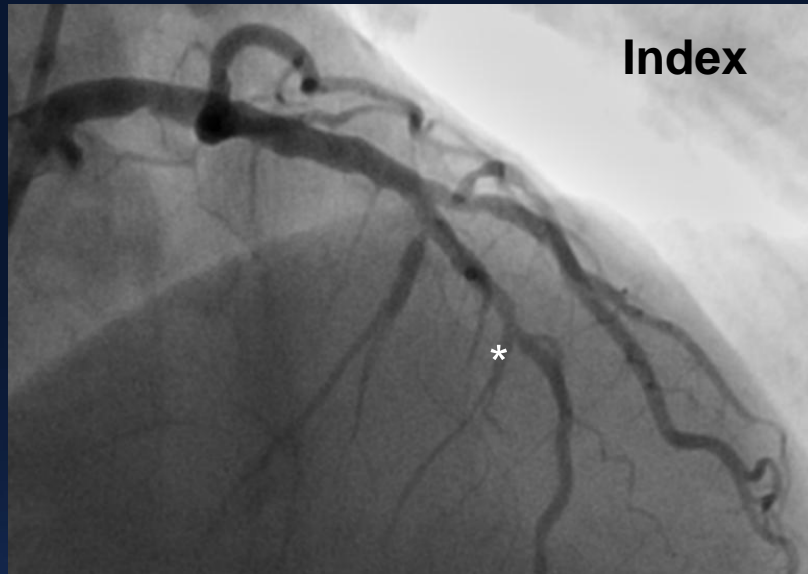
Healed Rupture



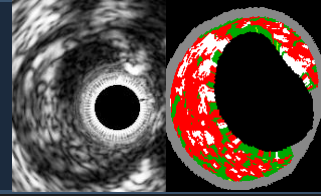
Pathological Intimal Thickening



A PROSPECT Case



The PROSPECT Trial



700 pts with ACS

UA (with ECGΔ) or NSTEMI or STEMI >24°
undergoing PCI of 1 or 2 major coronary arteries
at up to 40 sites in the U.S. and Europe

Metabolic S.

- Waist circum
- Fast lipids
- Fast glu
- HgbA1C
- Fast insulin
- Creatinine

Biomarkers

- Hs CRP
- IL-6
- sCD40L
- MPO
- TNFα
- MMP9
- Lp-PLA2
- others

PCI of culprit lesion(s)

Successful and uncomplicated

Formally enrolled

PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

Independent predictors of lesion level events by Cox Proportional Hazards regression

<u>Variable</u>	<u>HR [95% CI]</u>	<u>P value</u>
$PB_{MLA} \geq 70\%$	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
$MLA \leq 4.0 \text{ mm}^2$	3.21 [1.61, 6.42]	0.001

Variables entered into the model: minimal luminal area ($MLA \leq 4.0 \text{ mm}^2$); plaque burden at the MLA ($PB_{MLA} \geq 70\%$); external elastic membrane at the MLA ($EEM_{MLA} < \text{median} (14.1 \text{ mm}^2)$); lesion length $\geq \text{median} (11.2 \text{ mm})$; distance from ostium to MLA $\geq \text{median} (30.4 \text{ mm})$; remodeling index $\geq \text{median} (0.94)$; VH-TCFA;

VIVA Study (VH-IVUS in Vulnerable Atherosclerosis)

167 pts with stable CAD or ACS underwent 3-vessel VH-IVUS imaging;

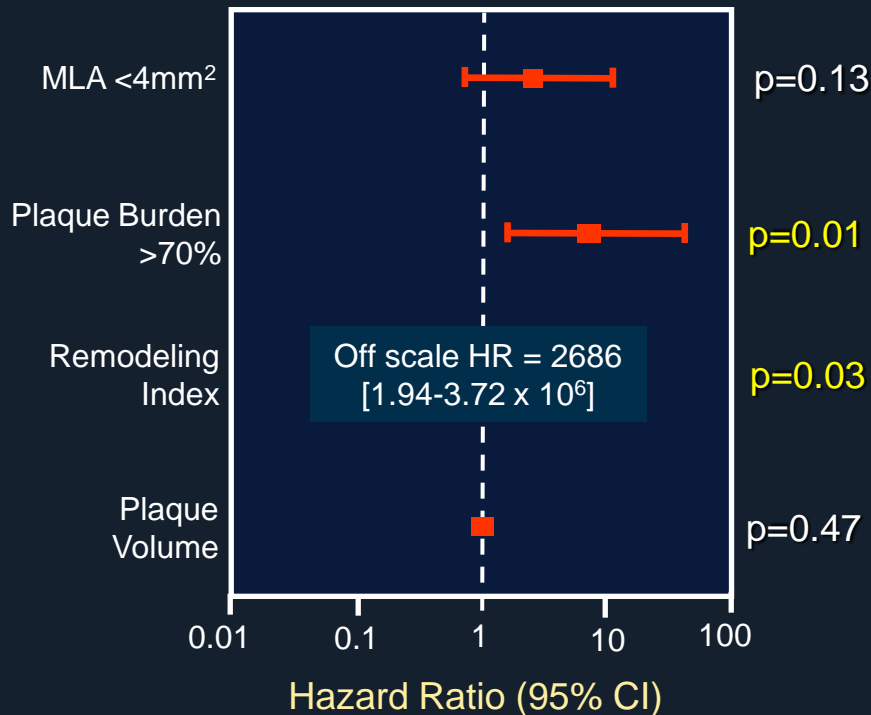
1,096 plaques were classified; median follow-up 625 days

18 MACE (death [2], MI [2] or revasc [14]) occurred in 16 pts from

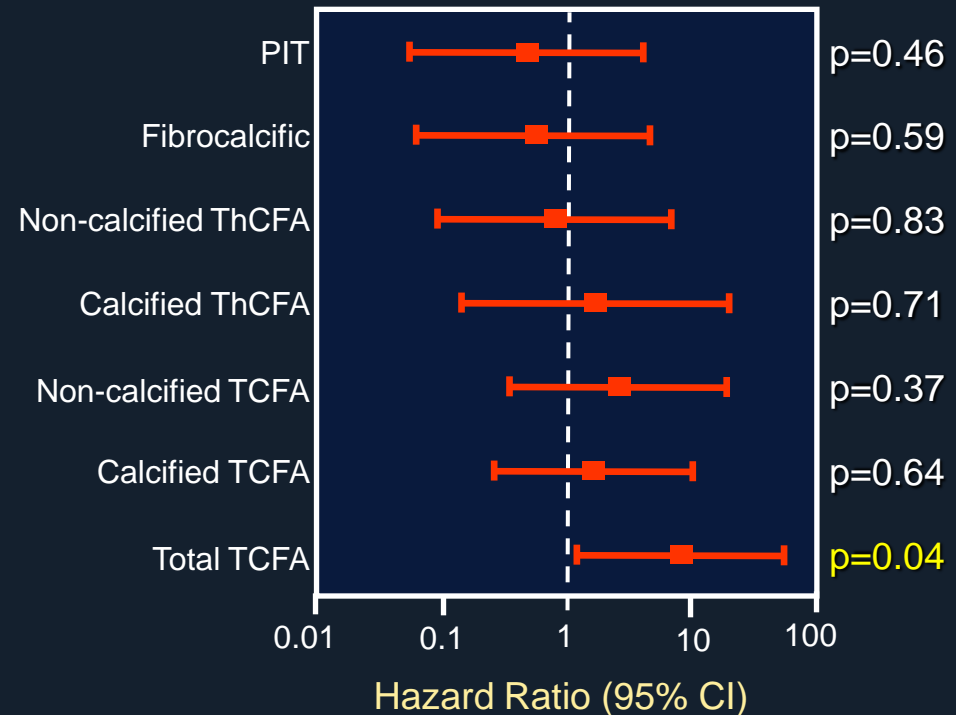
19 lesions (13 nonculprit lesions and 6 culprit lesions)

Univariate predictors of non-culprit MACE

Grayscale IVUS characteristics

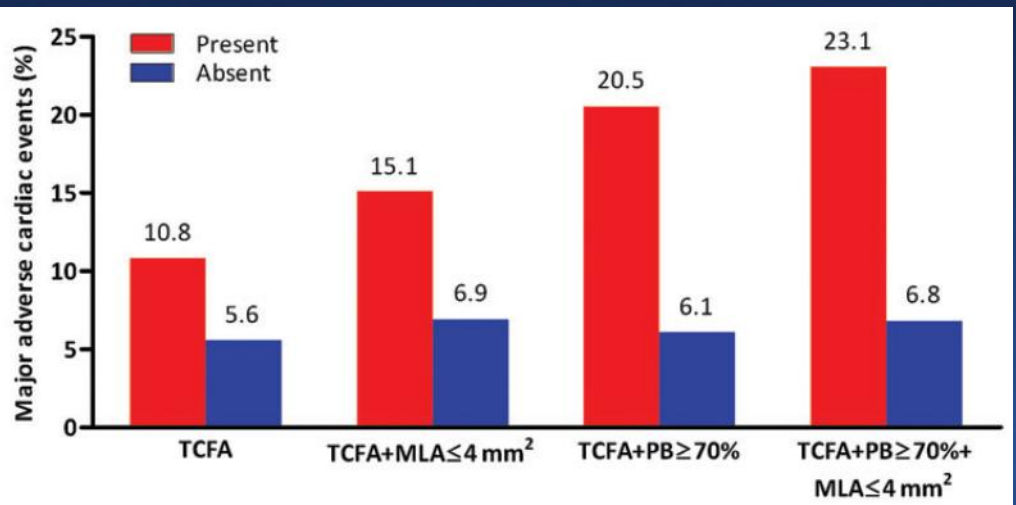
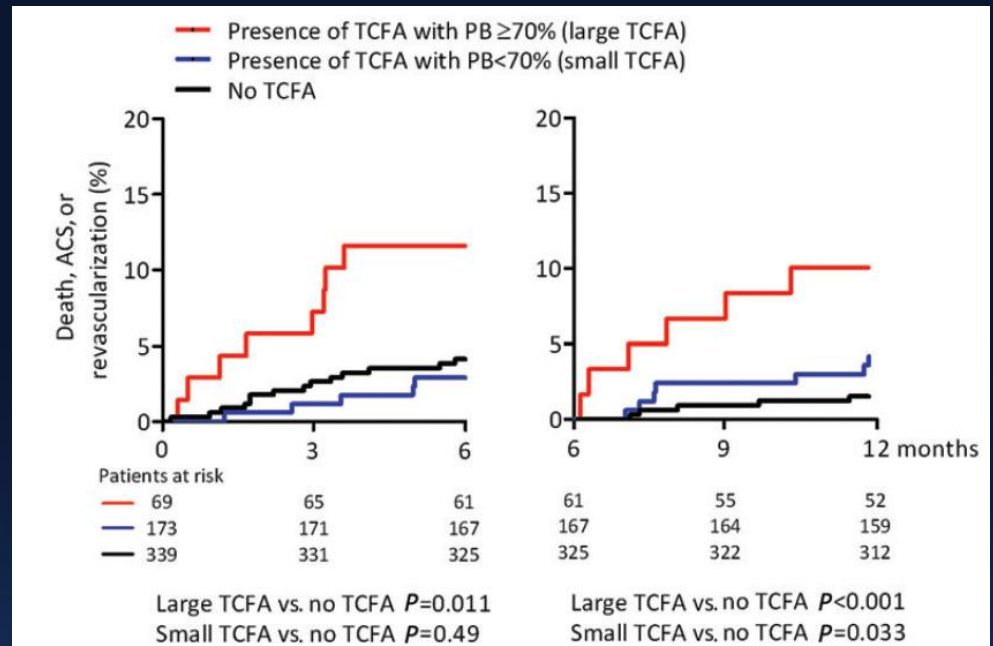


VH-IVUS lesion classification

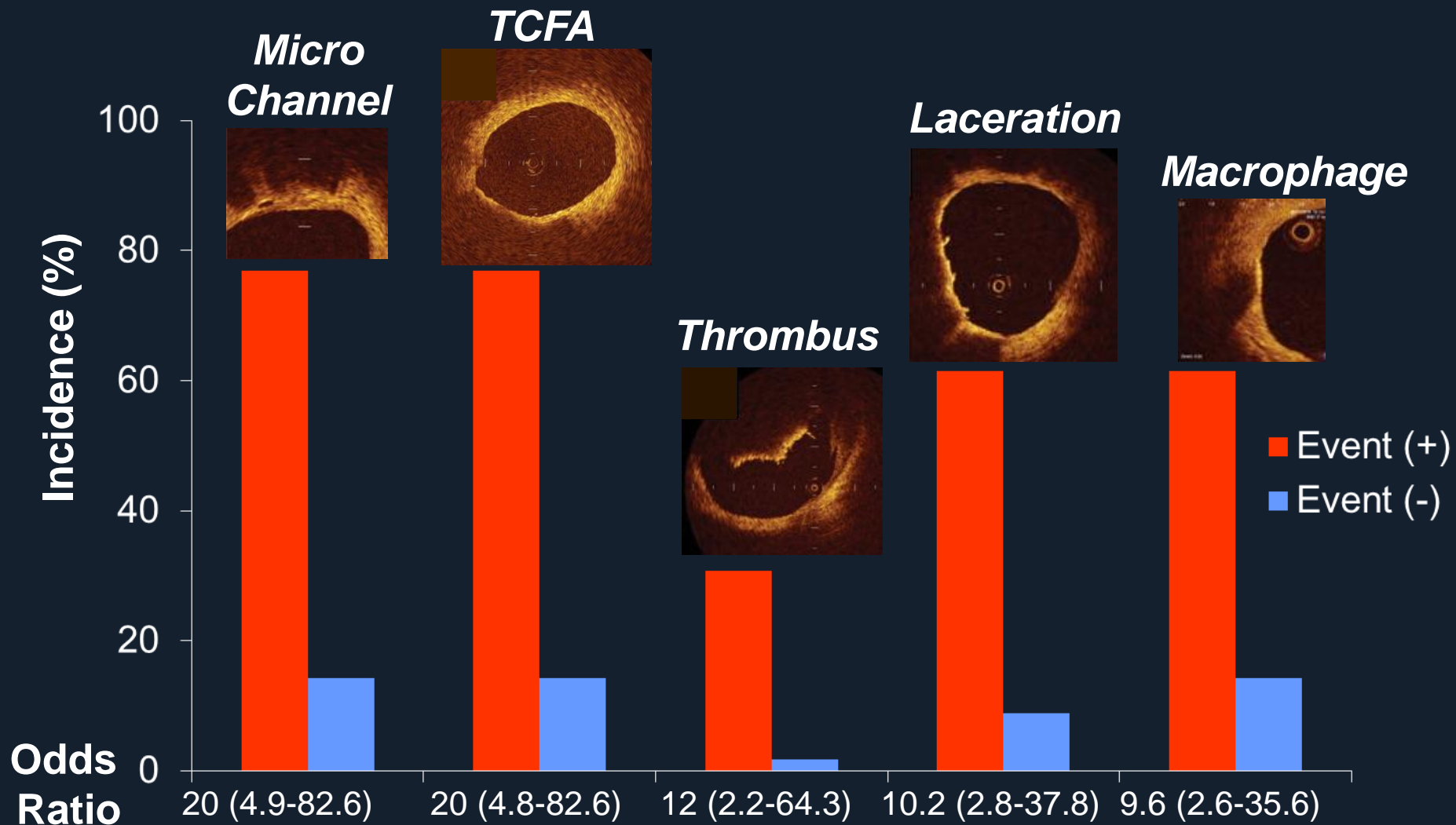


ATHEROREMO-IVUS Study

- 581 patients in 2008-2011
- 1 year follow-up
- MACE (non-culprit related ACS, unplanned coronary revascularization or indeterminate mortality)
- Single center, prospective



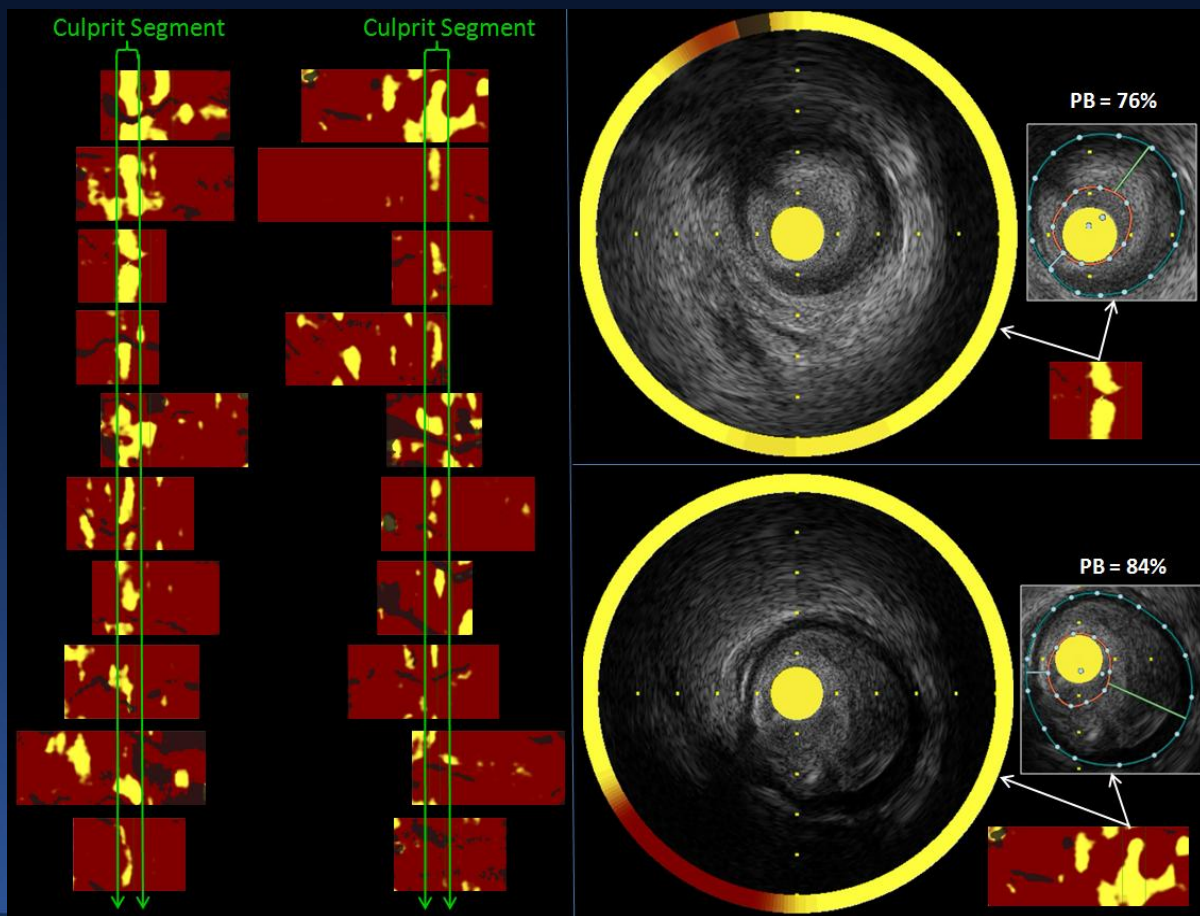
OCT Predictors for Progression of Non-Culprit Lesions



Is there a characteristic signal of lesions that cause STEMI?

Near infrared spectroscopy (InfraReDx) was performed immediately after infarct artery recanalization in 20 pts with STEMI

The NIRS chemograms of all 20 STEMI pts. The culprit segments contain LCP in 19 cases (95%), all with large plaque burden.

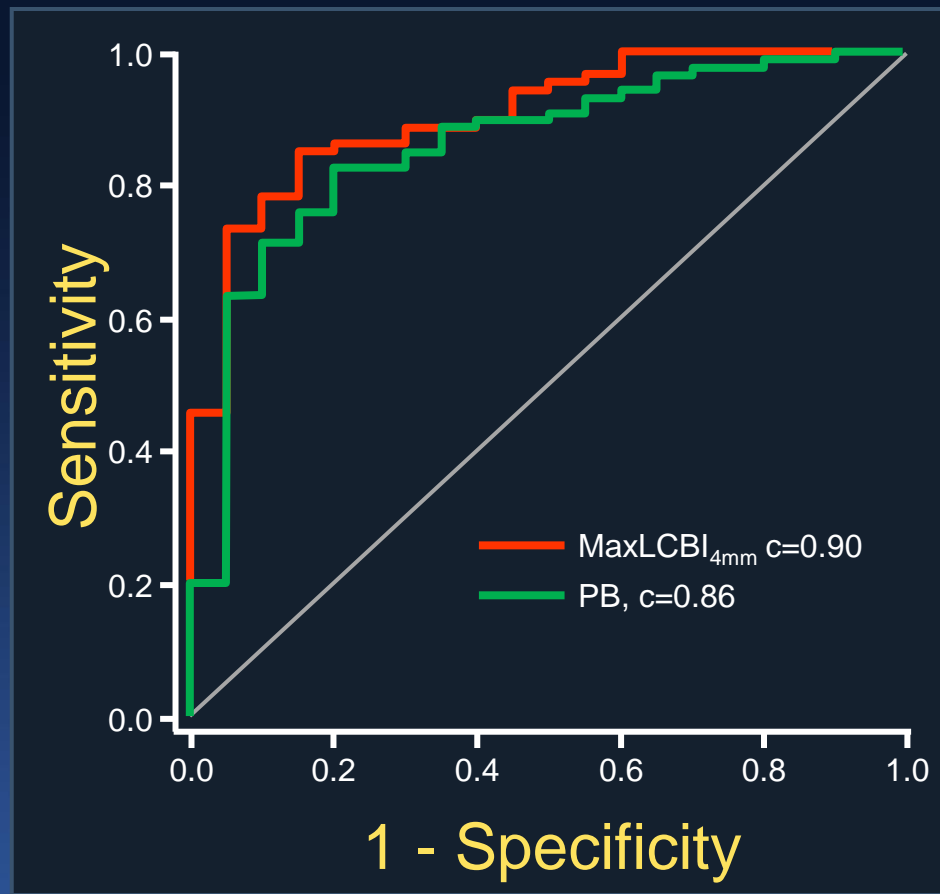


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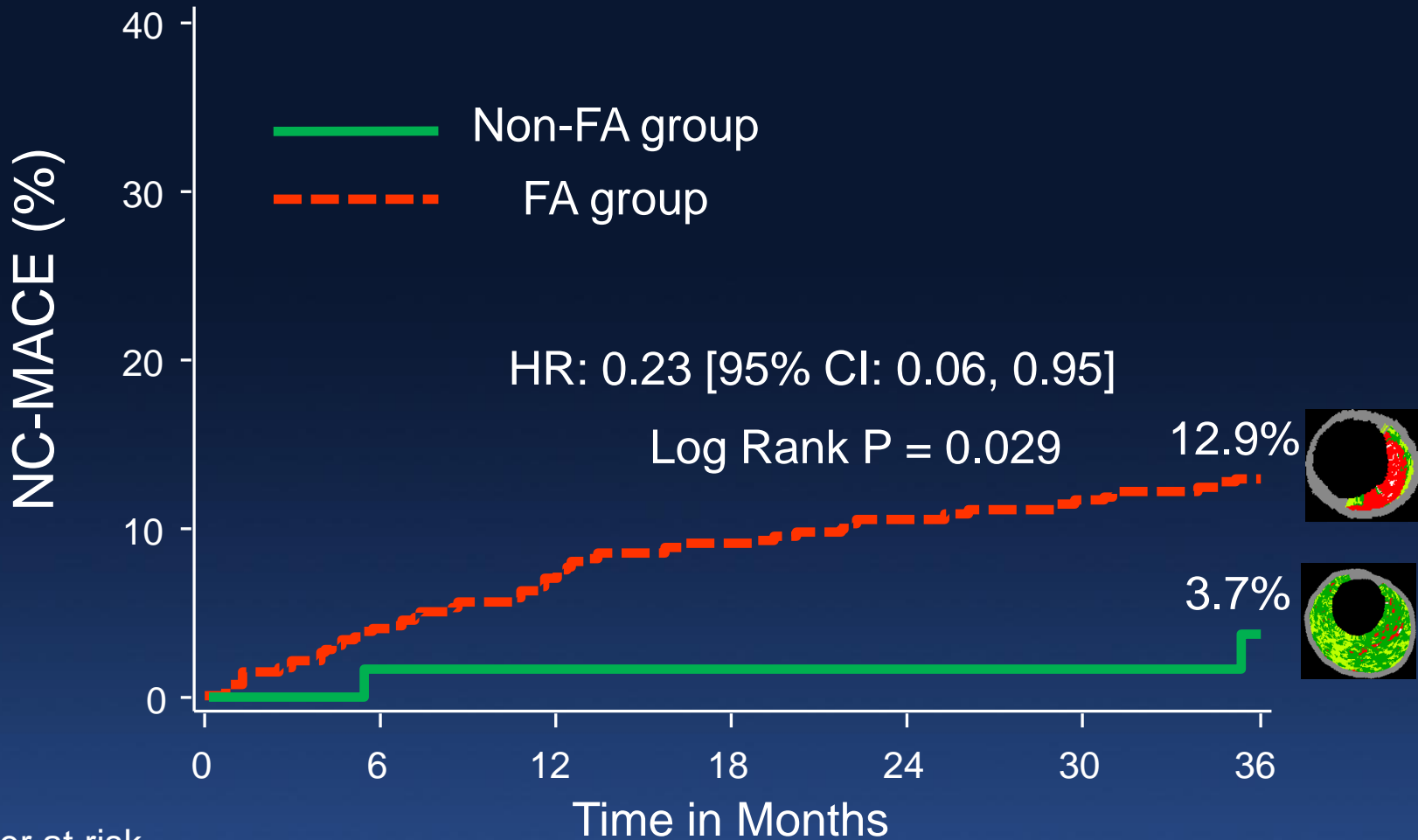
Near infrared spectroscopy (InfraReDx) was performed immediately after infarct artery recanalization in 20 pts with STEMI

Ability of NIRS (maxLCBI_{4mm}) and IVUS (plaque burden and calcification) to distinguish the culprit segment from non-culprit segments of the STEMI culprit vessel:

- AUC for maxLCBI_{4mm} = 0.90
- AUC for plaque burden = 0.86



PROSPECT: Non-FA Lesions

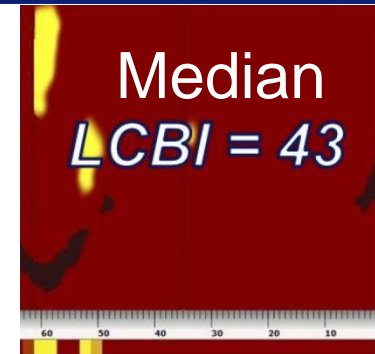
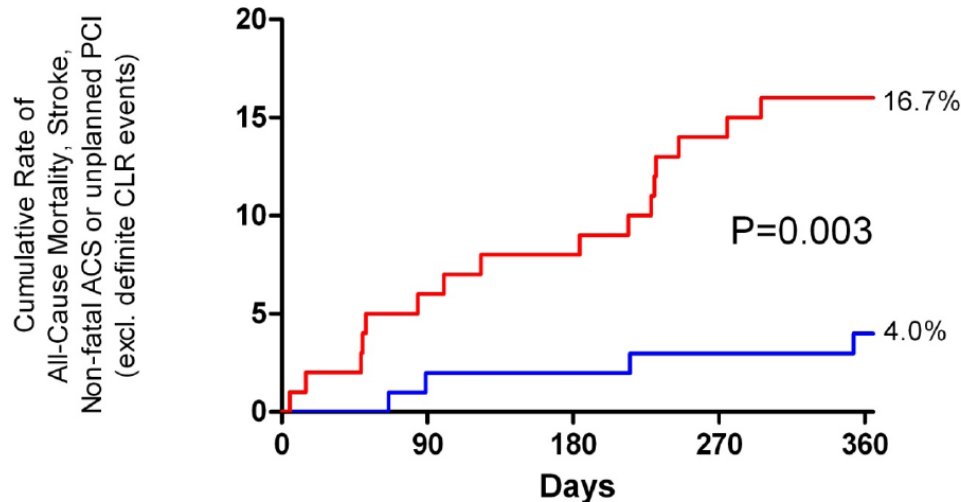


Number at risk

Non-FA group	67	62	61	61	60	57	29
FA group	542	485	463	443	424	406	248

Relationship between Lipidic Plaque detected by NIRS and Outcomes

Primary endpoint



- LCBI ≥ median
- LCBI < median

No. at Risk

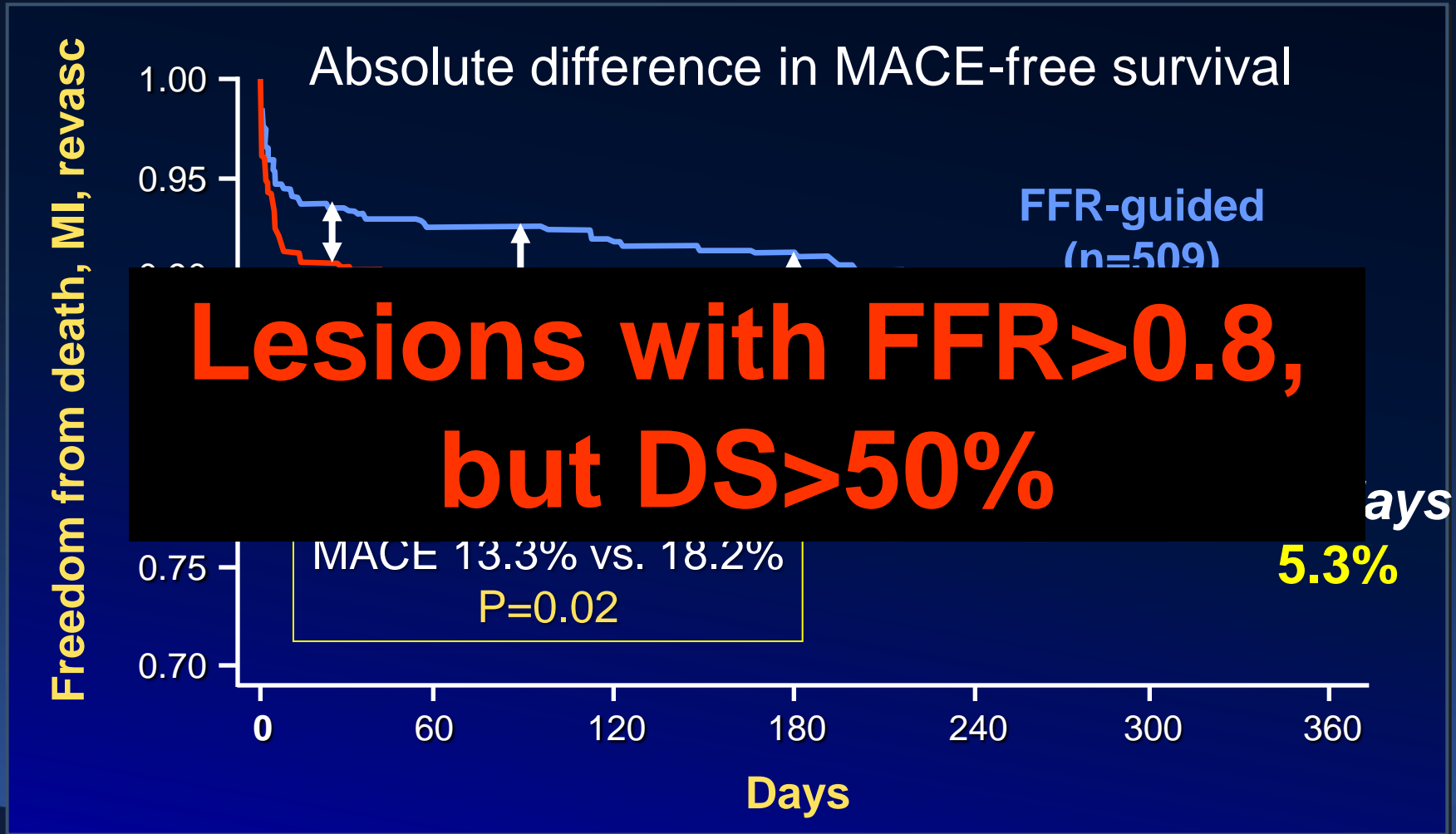
LCBI < Median	101	99	99	97	91
LCBI ≥ Median	102	94	92	86	83

Adjusted HR: **4.04** 95% CI: 1.3-12.3 P=0.01

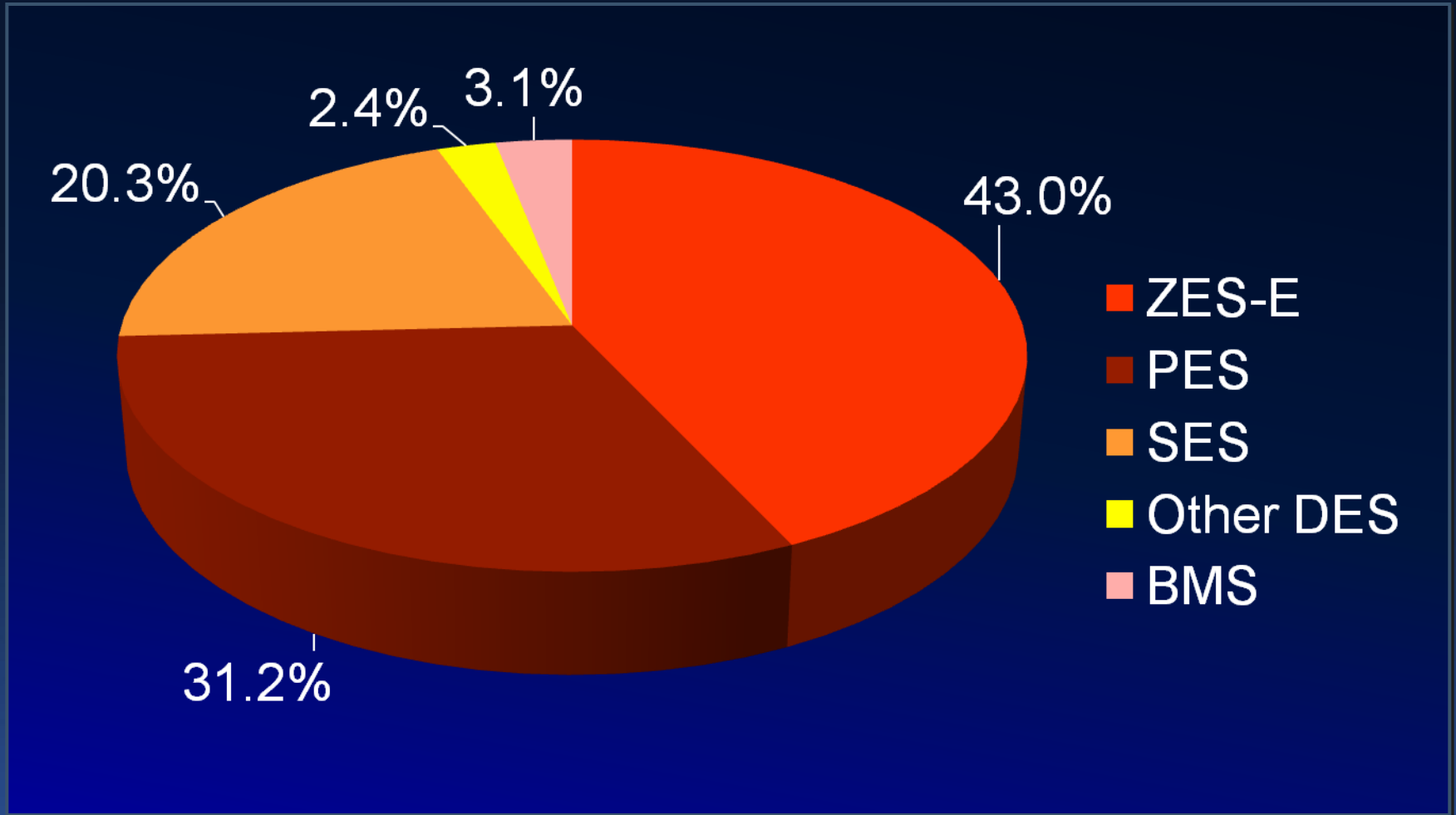
FAME: Primary Endpoint



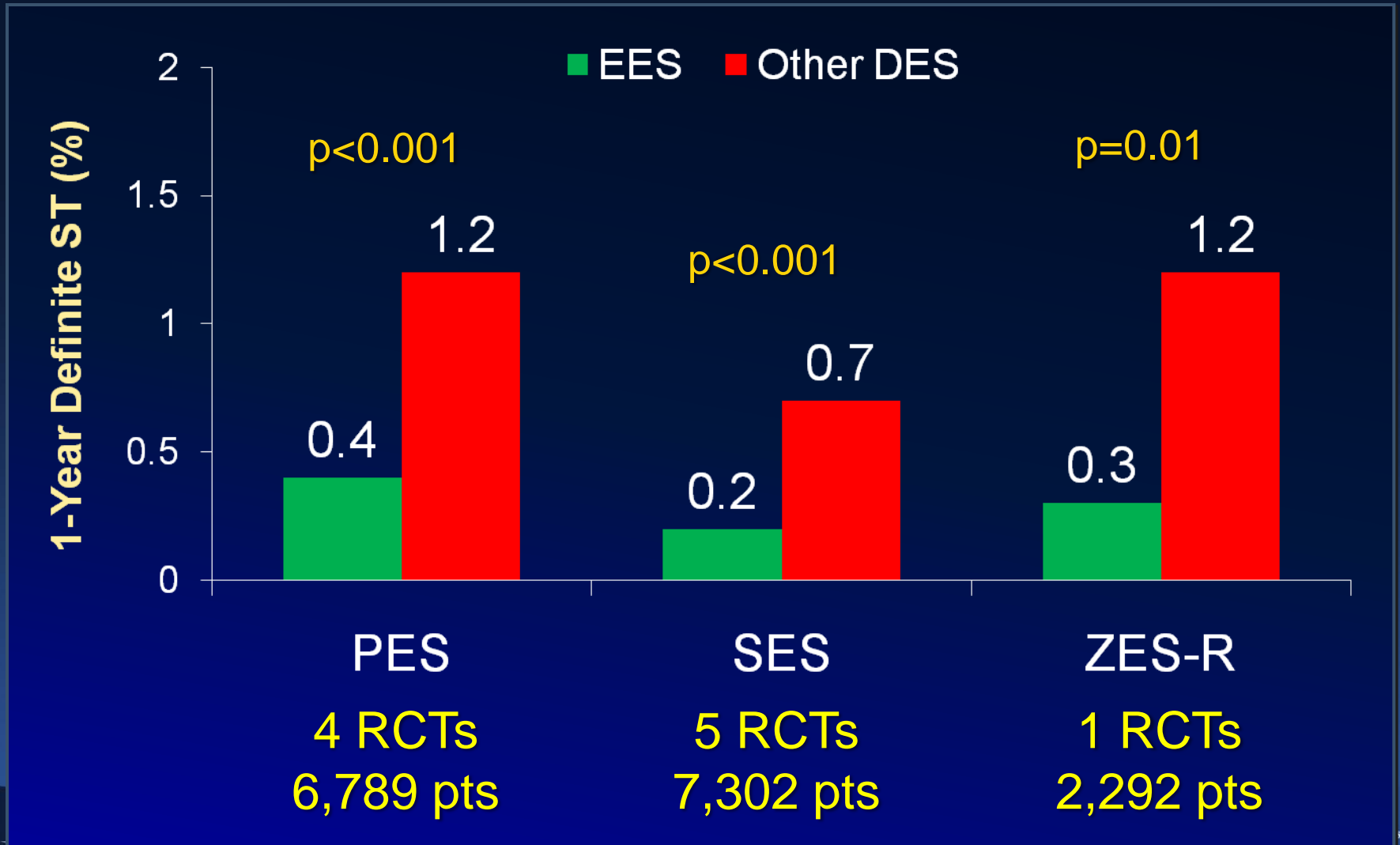
1005 pts with MVD (83% CSA) undergoing PCI with DES were randomized to FFR-guided vs. angio-guided intervention



FAME Trial: Stent Use



RCTs of EES vs. Other DES (n-16,383): 1-year definite stent thrombosis



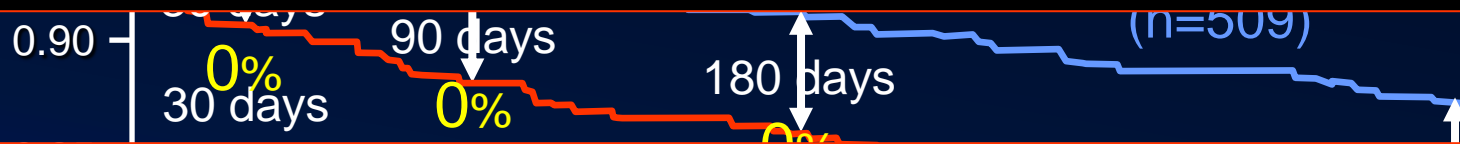
FAME: With better stents????



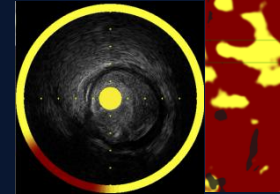
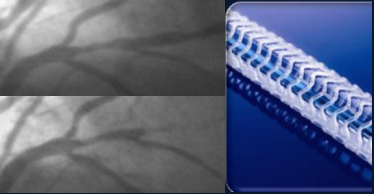
1005 pts with MVD (83% CSA) undergoing PCI with DES were randomized to FFR-guided vs. angiography-guided intervention

NO longer significant difference

Death, MI, revasc



Treatment of lesions with FFR > 0.8, DS > 50% will not make difference.



PROSPECT II Study PROSPECT ABSORB RCT

900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥70% plaque burden present?

Yes

(N=300)

No

(n=600)

R

2:1

**ABSORB BVS
+ GDMT** (N~200)

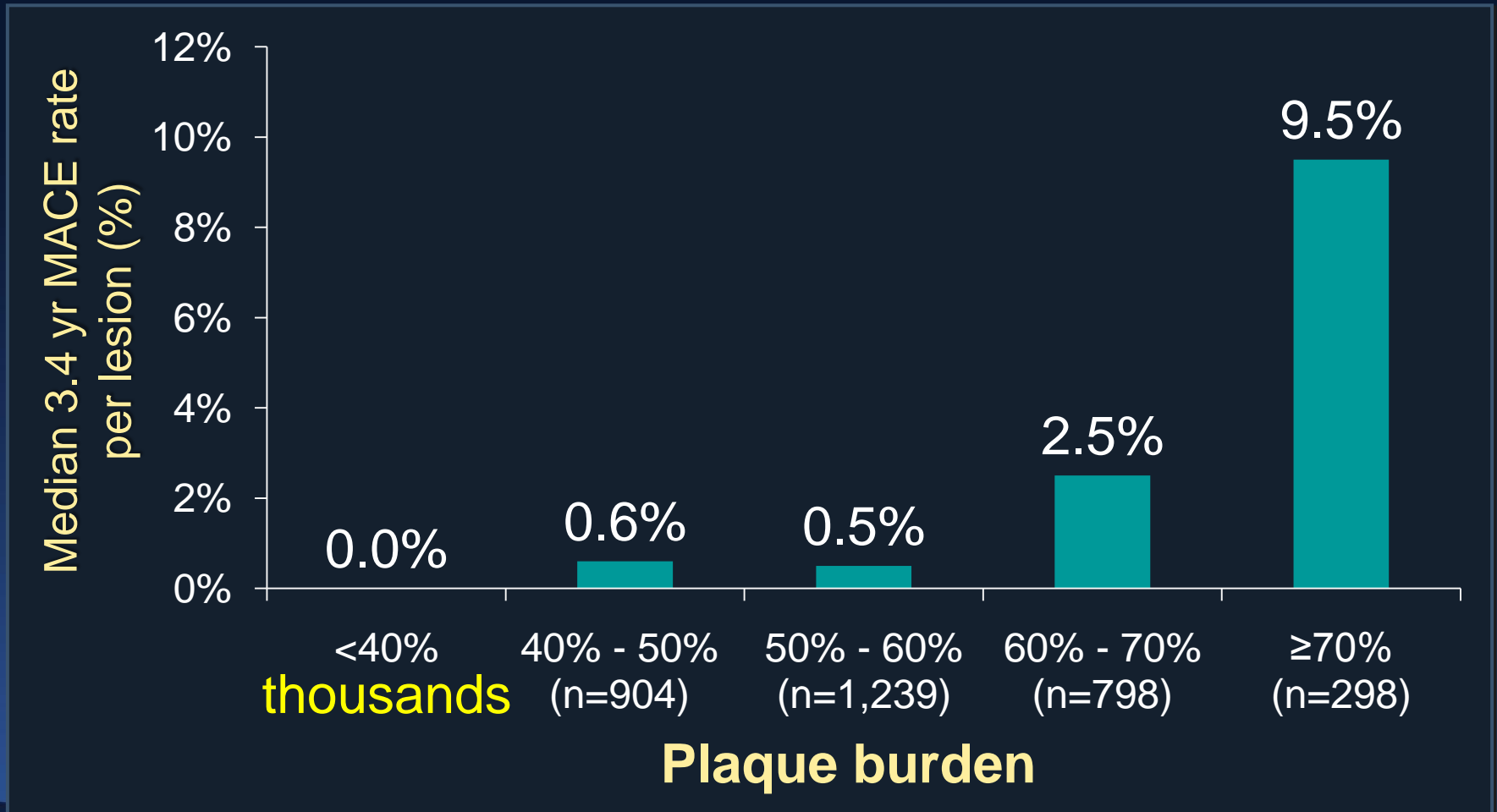
GDMT
(N=100)

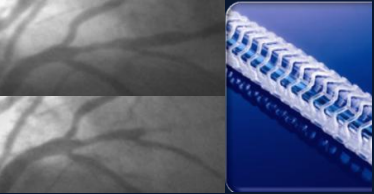
Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for ≥3 years

PROSPECT: Correlates of Non-Culprit Lesion Related Events

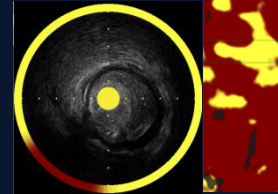
Impact of plaque burden





PROSPECT II Study

PROSPECT ABSORB RCT



- Primary endpoints and analysis -

PROSPECT II

Endpoints: Composite MACE (cardiac death, cardiac arrest, MI, or unstable or progressive angina requiring rehospitalization or revascularization) adjudicated to non-culprit lesions

Analysis: Multivariable predictors, including clinical, QCA, IVUS and NIRS (patient and lesion level)

PROSPECT ABSORB

Endpoints and analysis: IVUS MLA at 2 years (superiority, powered); Death, TV-MI, TLR (noninferiority, not powered)

Summary

- Does morphology predict future event?

YES!

- Does physiology predict future event?

YES!

- Is only physiology enough?

I believe NO...

- Should we treat vulnerable plaque in physiologically non-significant lesion?

We will answer in PROSPECT2!