

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.

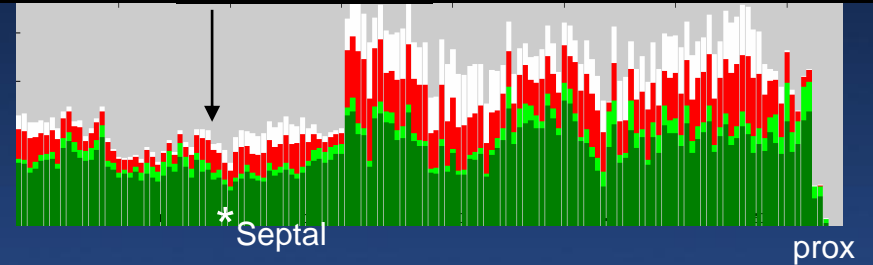
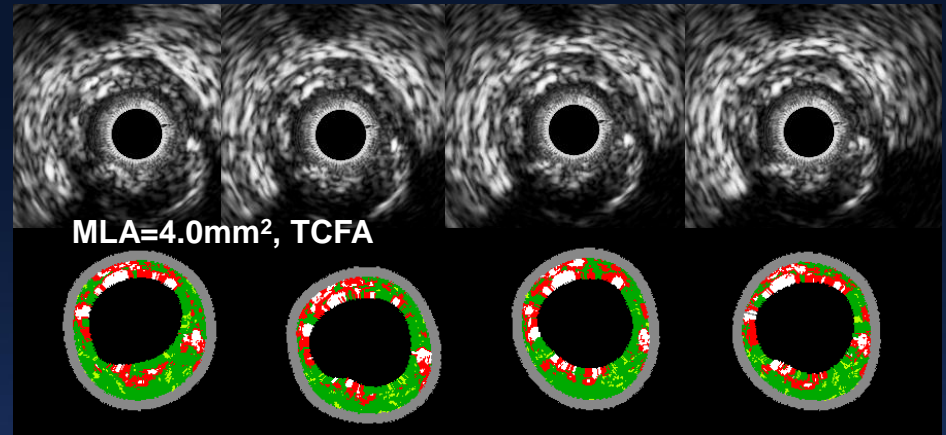
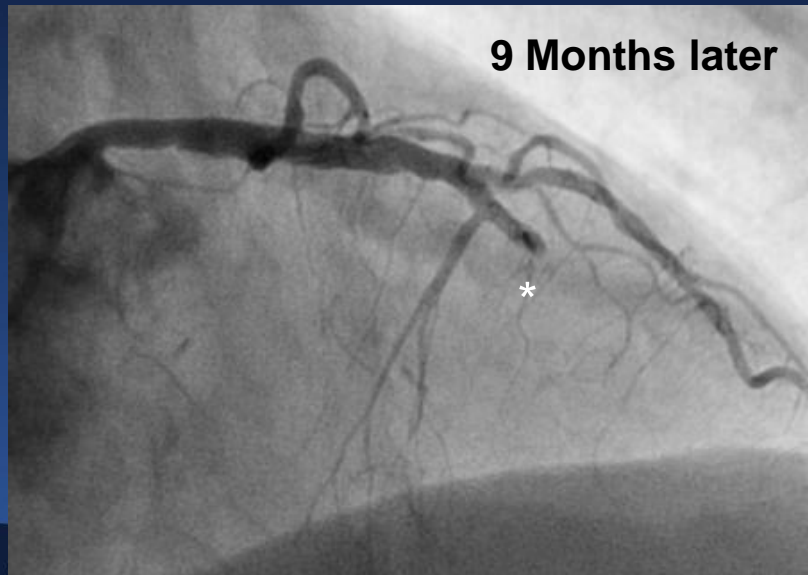
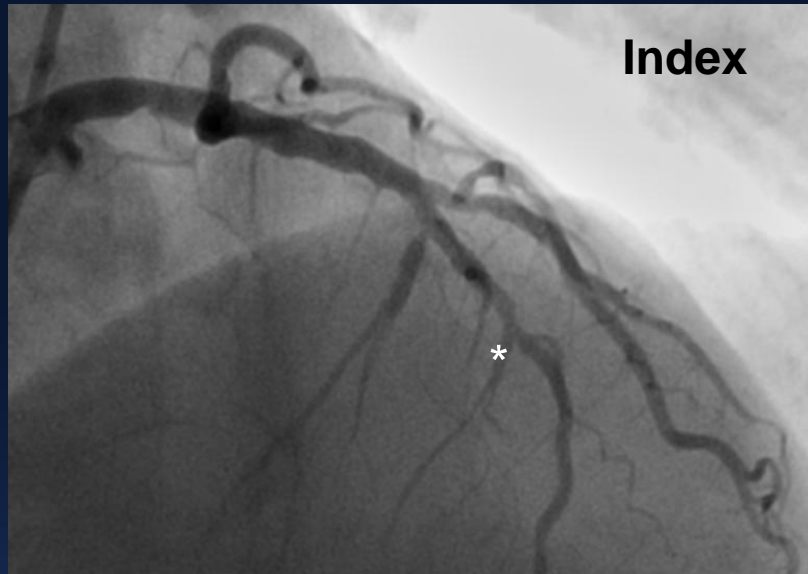
Consultant:

Boston Scientific Corp.

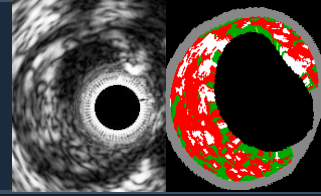
Speaker Fee:

St Jude Medical, Volcano Corporation

A PROSPECT Case



The PROSPECT Trial



700 pts with ACS

UA (with ECG Δ) or NSTEMI or STEMI >24^o
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
- TNF α
- MMP9
- Lp-PLA2
- others

PCI of culprit lesion(s)

Successful and uncomplicated

Formally enrolled

VH-IVUS Classification

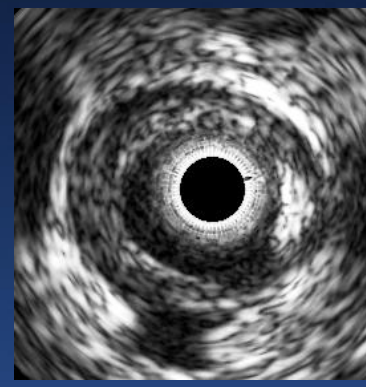
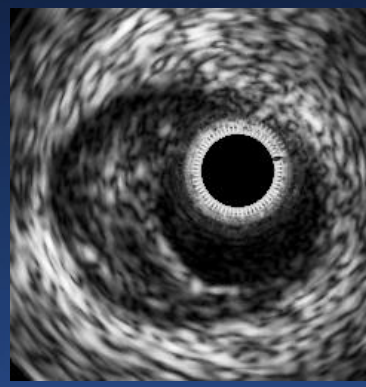
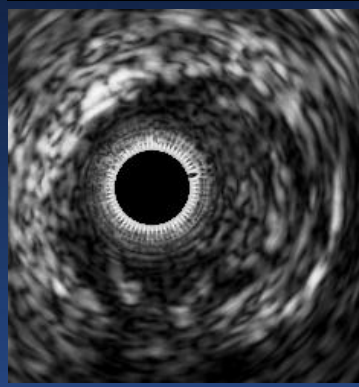
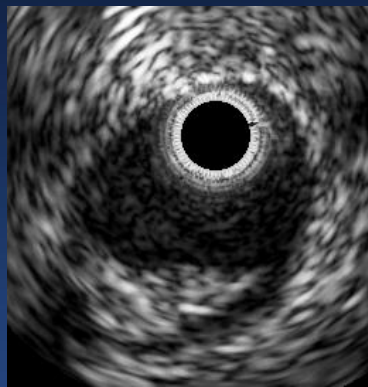
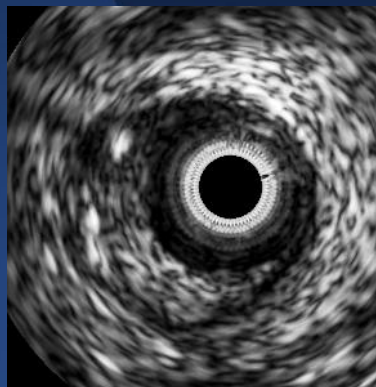
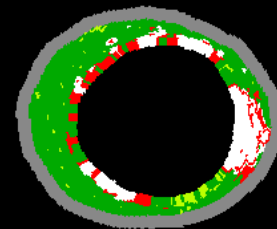
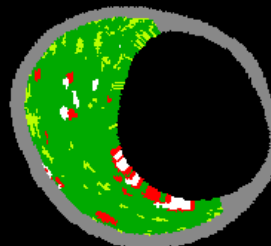
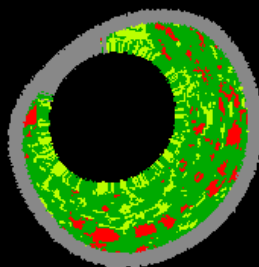
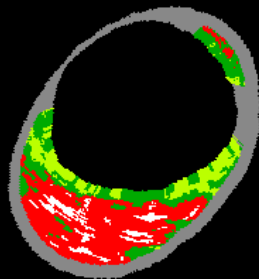
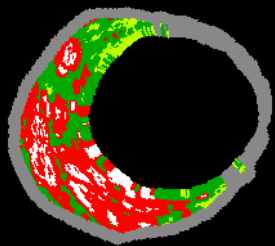
Thin-cap FA

Thick-cap FA

PIT

Fibrous

Fibrocalcific



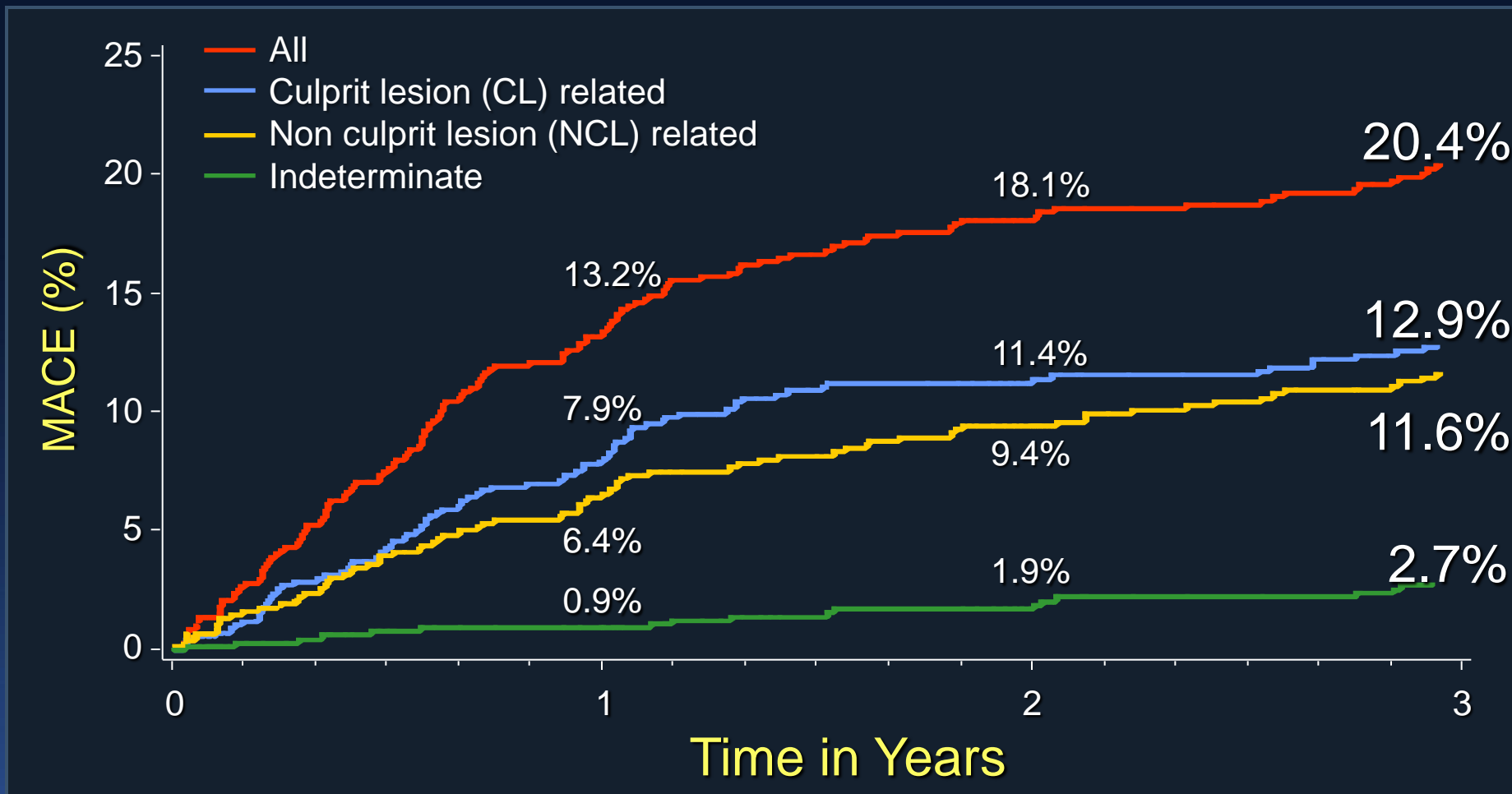
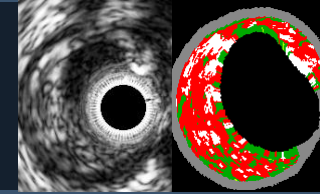
More than 10%
Confluent
Necrotic Core

More than 15%
Fibrofatty

NO more than 10%
Confluent Necrotic
Core

More than 10%
confluent
calcium

PROSPECT: MACE



Number at risk

	0	1	2	3
ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

PROSPECT: MACE

3-year follow-up, non hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeterminate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.8% (11)
Cardiac arrest	0.5% (3)	0.3% (2)	0% (0)	0.2% (1)
MI (STEMI or NSTEMI)	3.3% (21)	2.0% (13)	1.0% (6)	0.3% (2)
Unstable angina	8.0% (51)	4.5% (29)	3.3% (21)	0.5% (3)
Increasing angina	14.5% (93)	9.2% (59)	8.5% (54)	0.3% (2)
Composite MACE	20.4% (132)	12.9% (83)	11.6% (74)	2.7% (17)
Cardiac death, arrest or MI	4.9% (31)	2.2% (14)	1.0% (6)	1.9% (12)

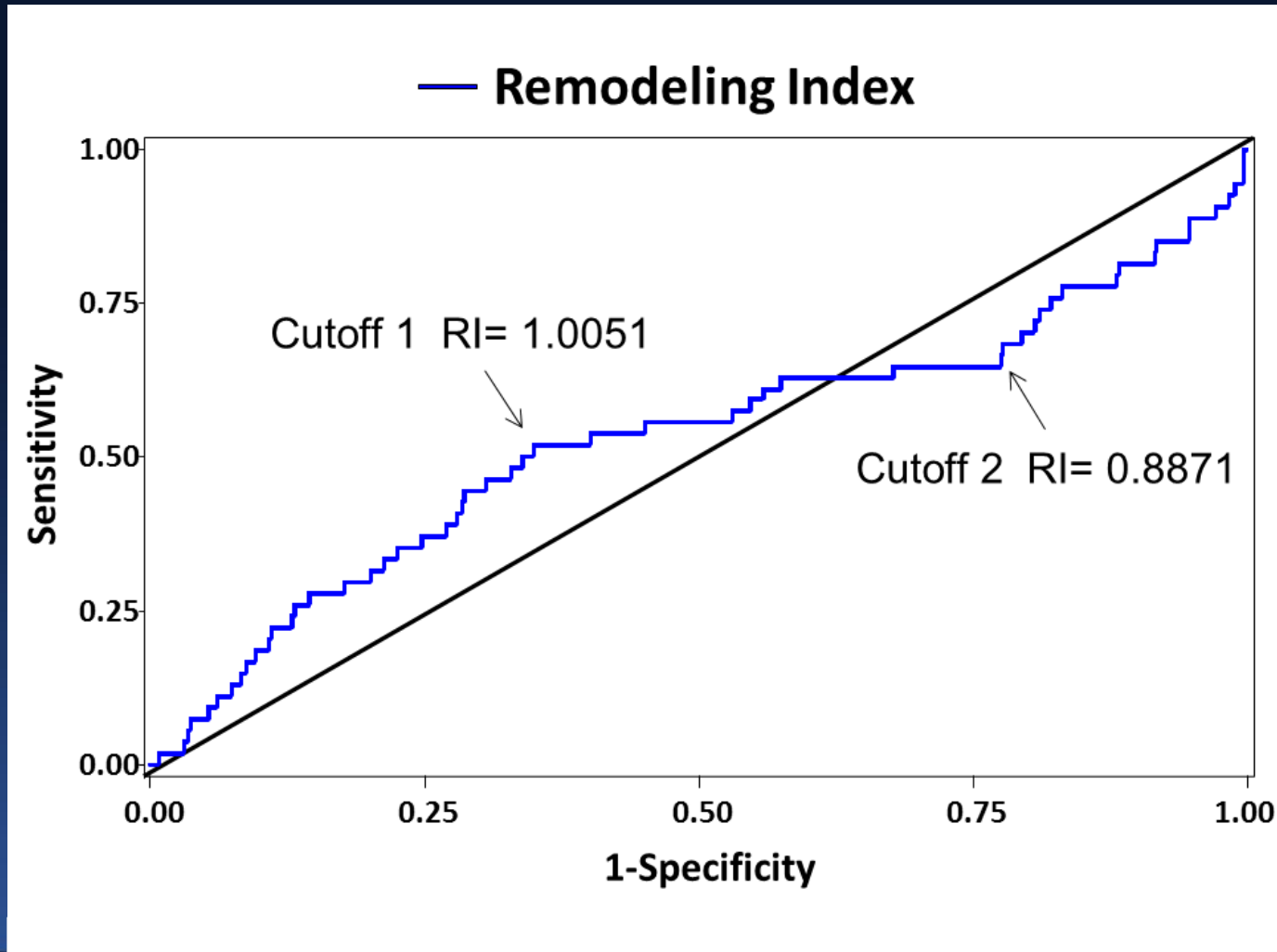
PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

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

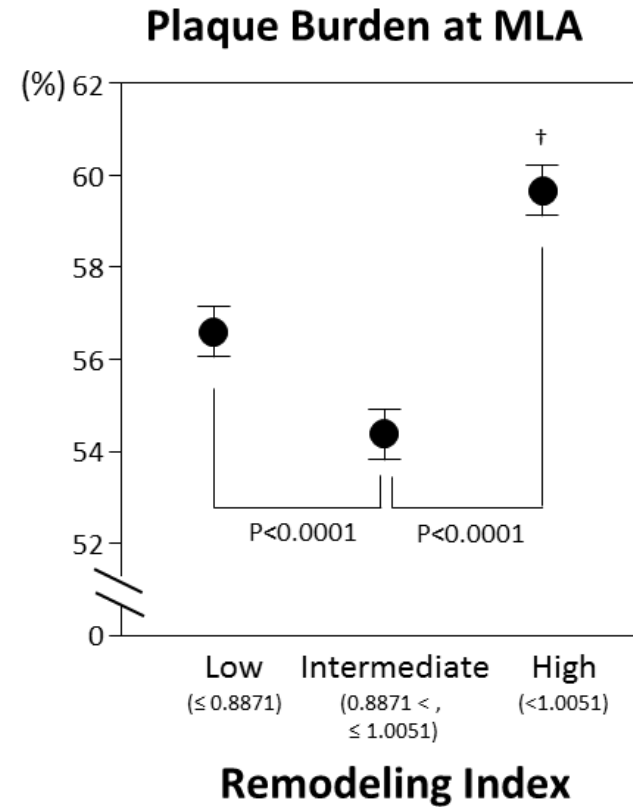
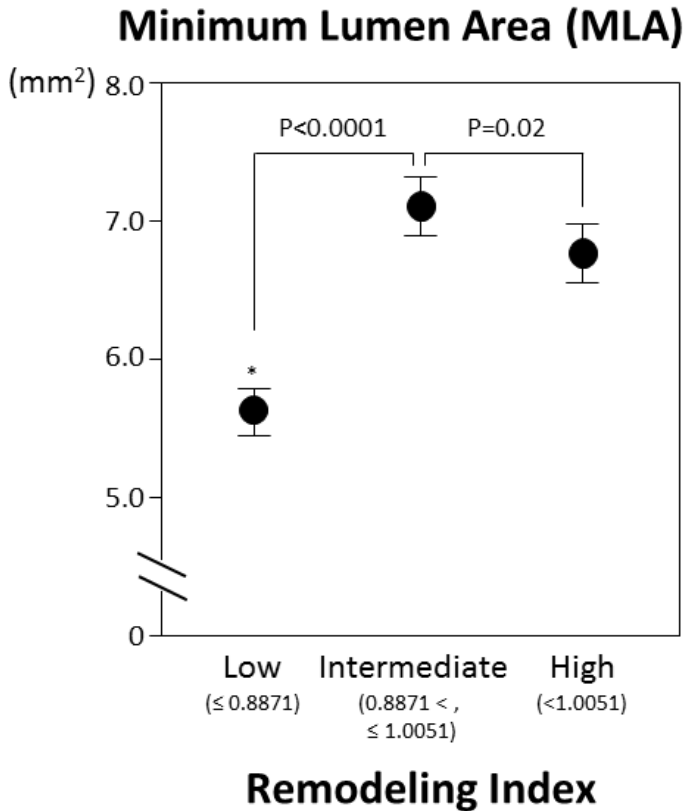
Variables entered into the model: minimal luminal area ($MLA \leq 4.0 \text{ mm}^2$); plaque burden at the MLA ($PB_{MLA} \geq 70\%$); external elastic membrane at the MLA ($EEM_{MLA} < \text{median} (14.1 \text{ mm}^2)$); lesion length $\geq \text{median} (11.2 \text{ mm})$; distance from ostium to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

Remodeling Index to predict MACE

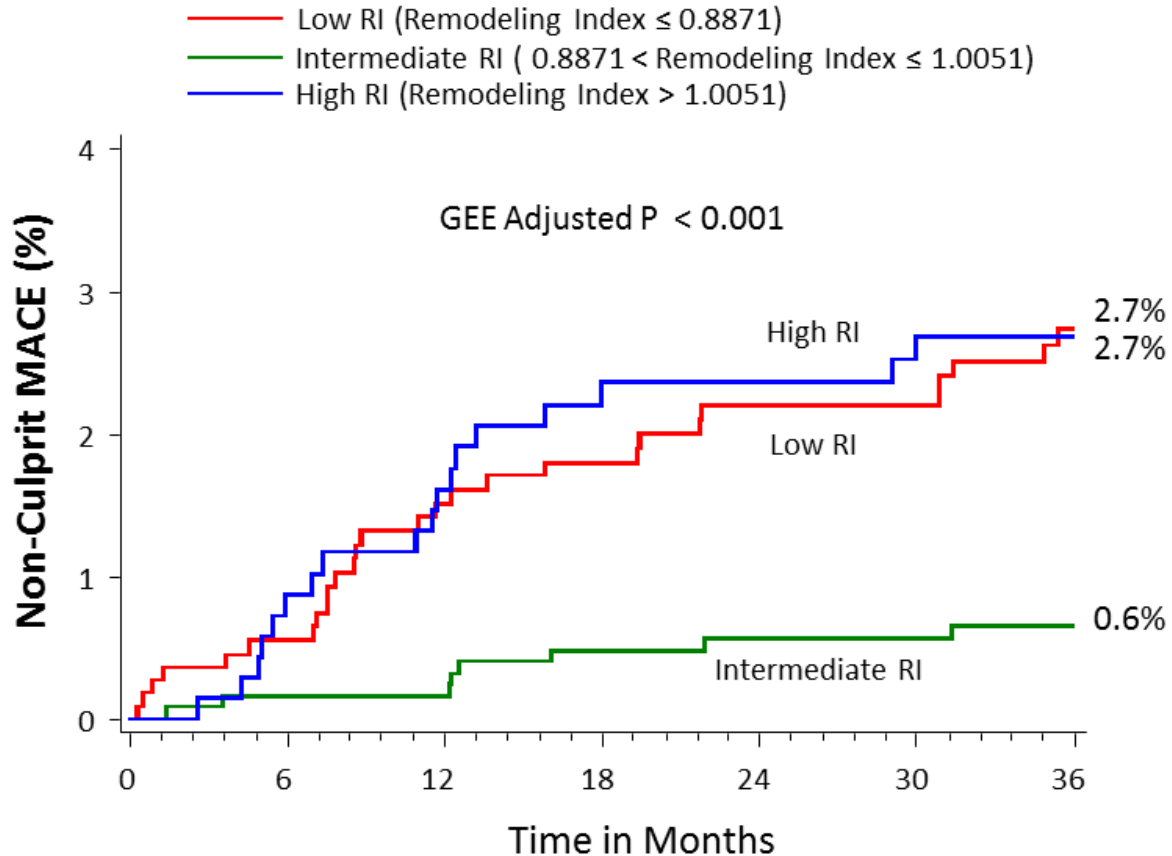


Inaba S, et al, JACC Img in press

Relationship between remodeling index and MLA



Remodeling Index and MACE



Number at risk

Low RI	1137	1041	1019	996	970	940	598
Intermediate RI	1355	1262	1244	1209	1186	1154	712
High RI	731	675	666	640	622	601	385

VIVA Study (VH-IVUS in Vulnerable Atherosclerosis)

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

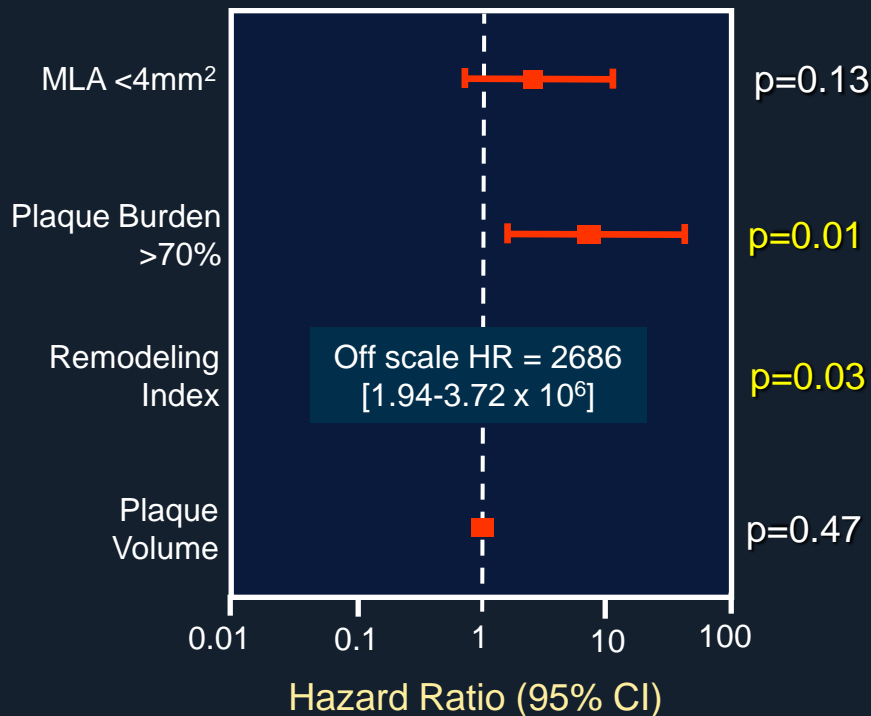
1,096 plaques were classified; median follow-up 625 days

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

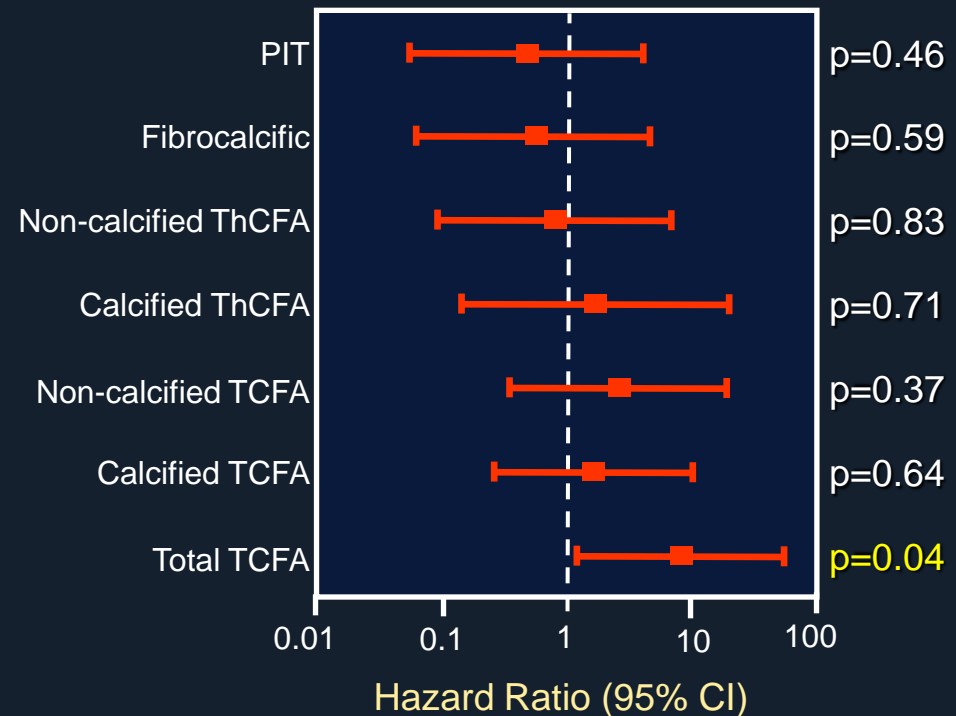
19 lesions (13 nonculprit lesions and 6 culprit lesions)

Univariate predictors of non-culprit MACE

Grayscale IVUS characteristics

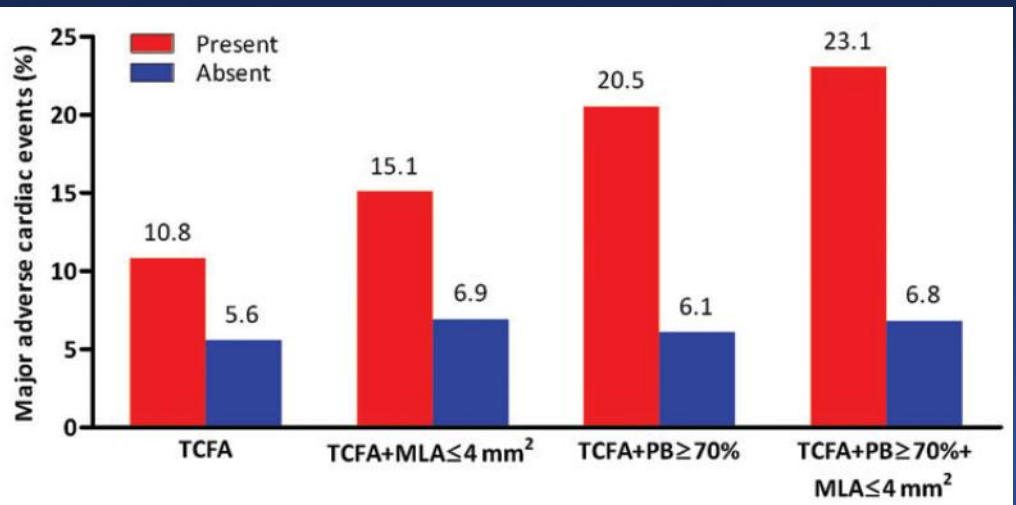
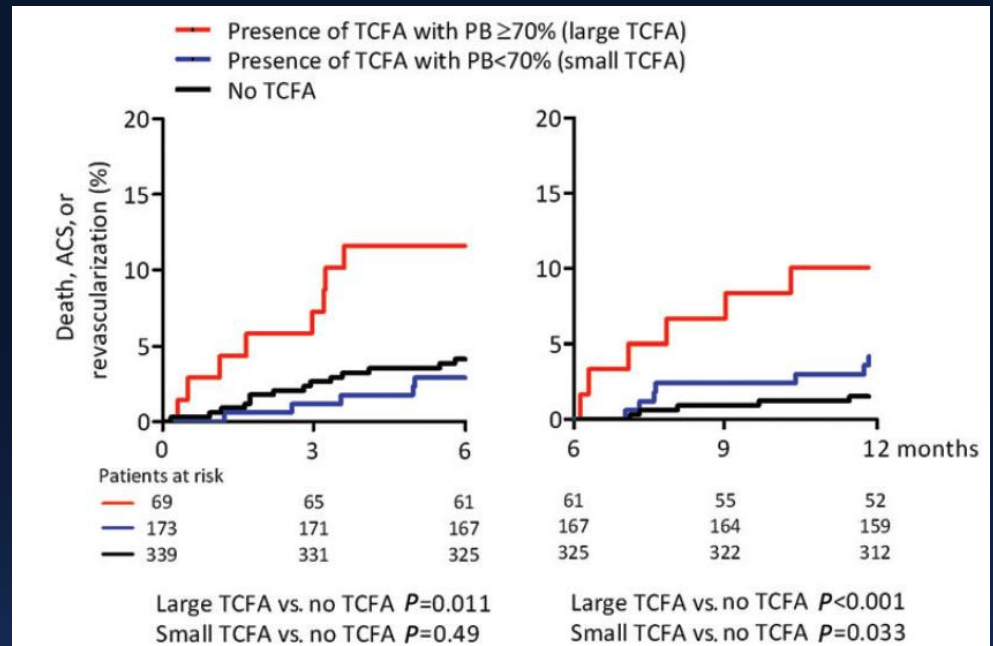


VH-IVUS lesion classification



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



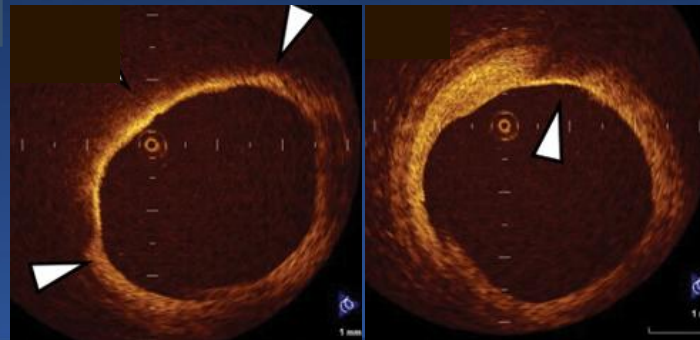
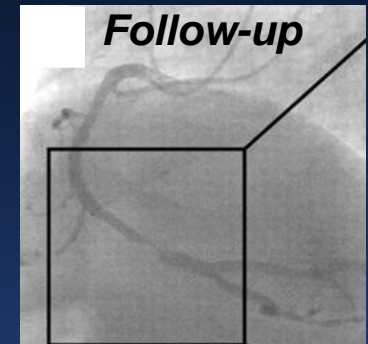
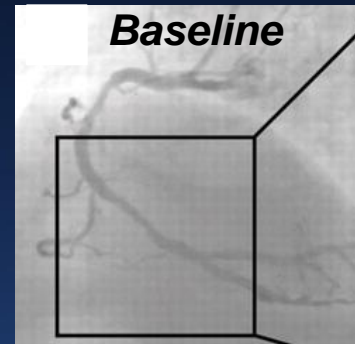
OCT Predictor for Progression

- **DESIGN:** Prospective, Single Center, Observational Study
- **OBJECTIVE:** To evaluate OCT predictor for disease progression in non-culprit lesions
- **METHODS:**
 1. 3 vessel OCT after successful PCI of culprit lesions
 2. 6-9 month follow-up
 3. Progression: Late loss > 0.4mm

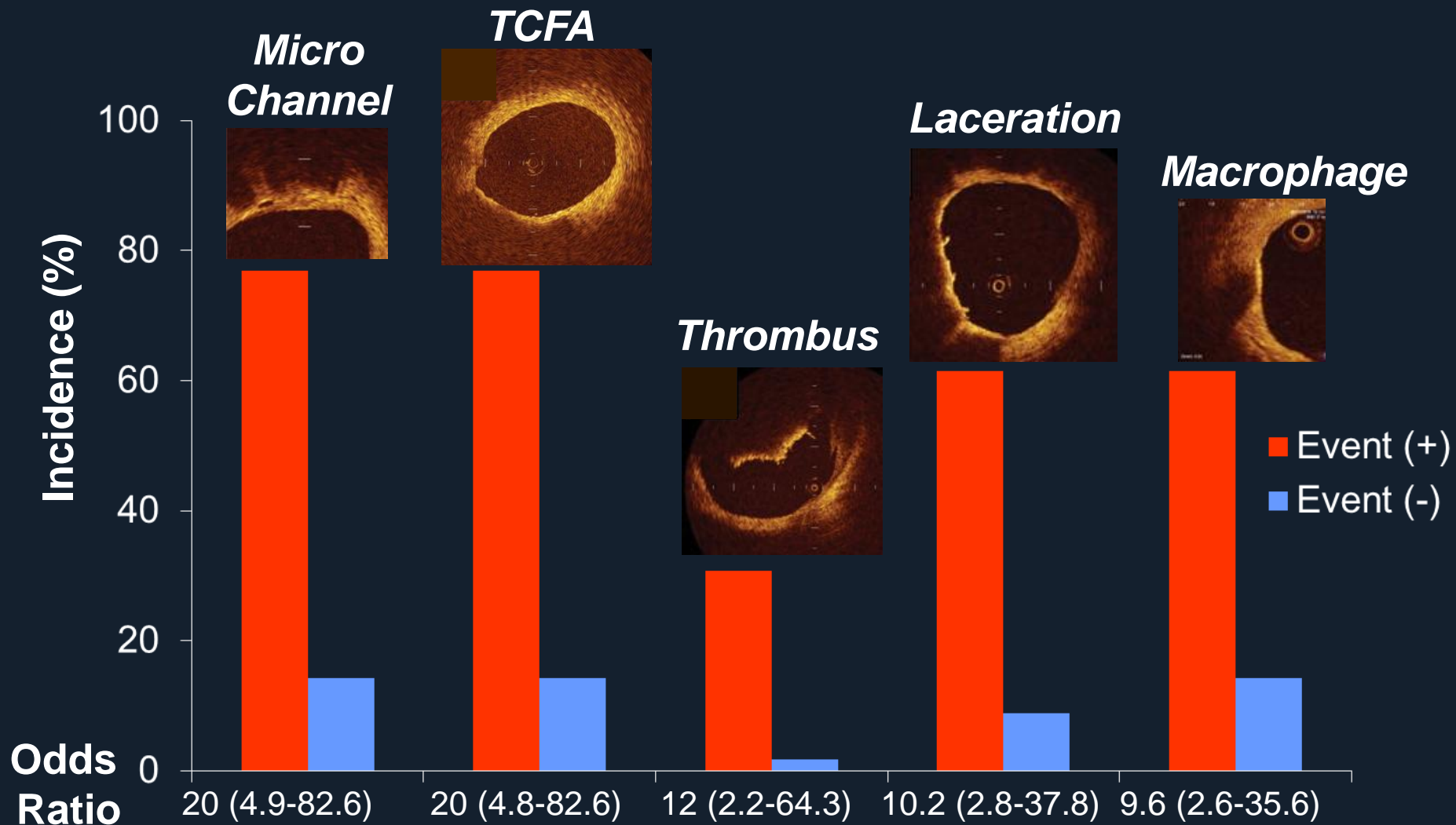
69 Non-culprit lesion in 69 vessels in 53 pts

- 3 ACS events in 3pts
- 10 progression without event in 10 pts

- 56 non-culprit lesion in 40 pts



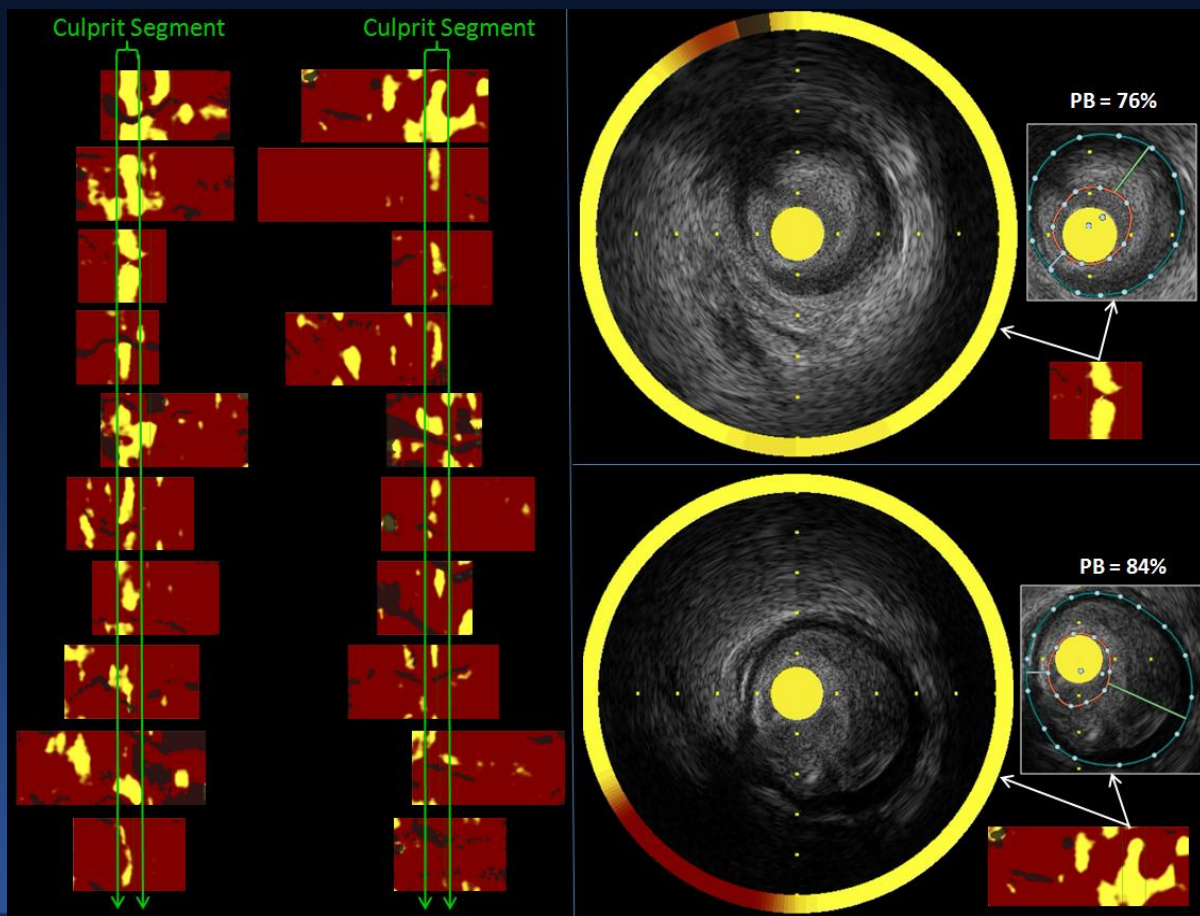
OCT Predictors for Progression of Non-Culprit Lesions



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.

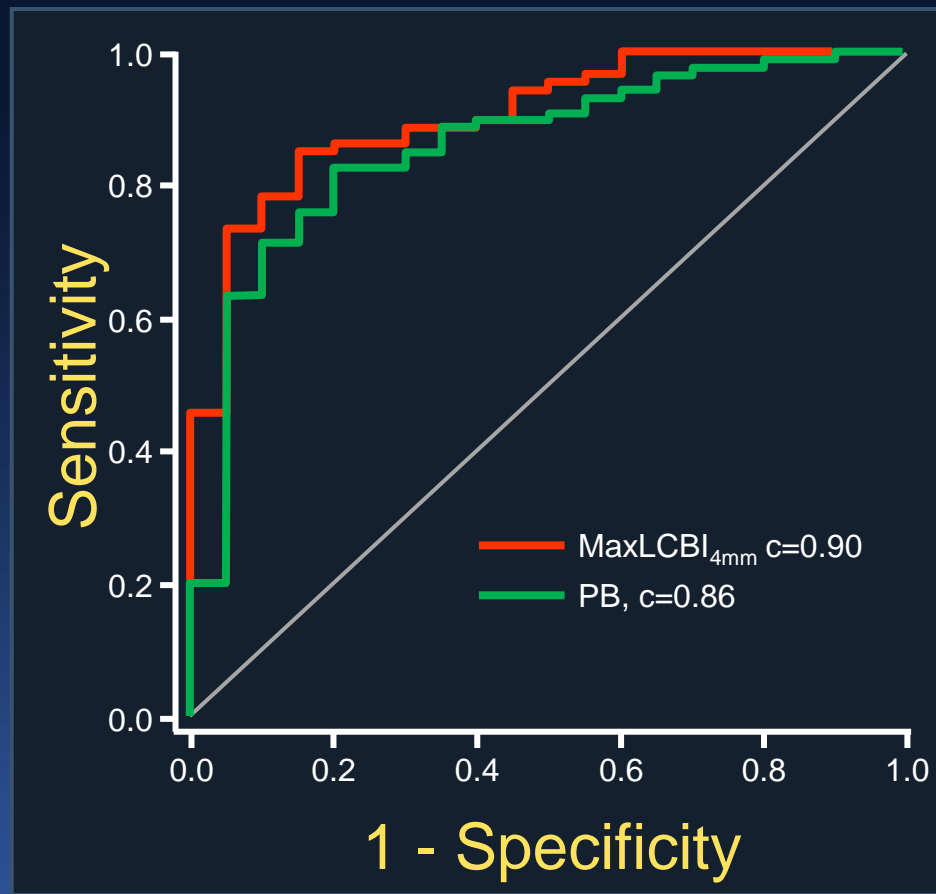


Is there a characteristic signal of lesions that cause STEMI?

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

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:

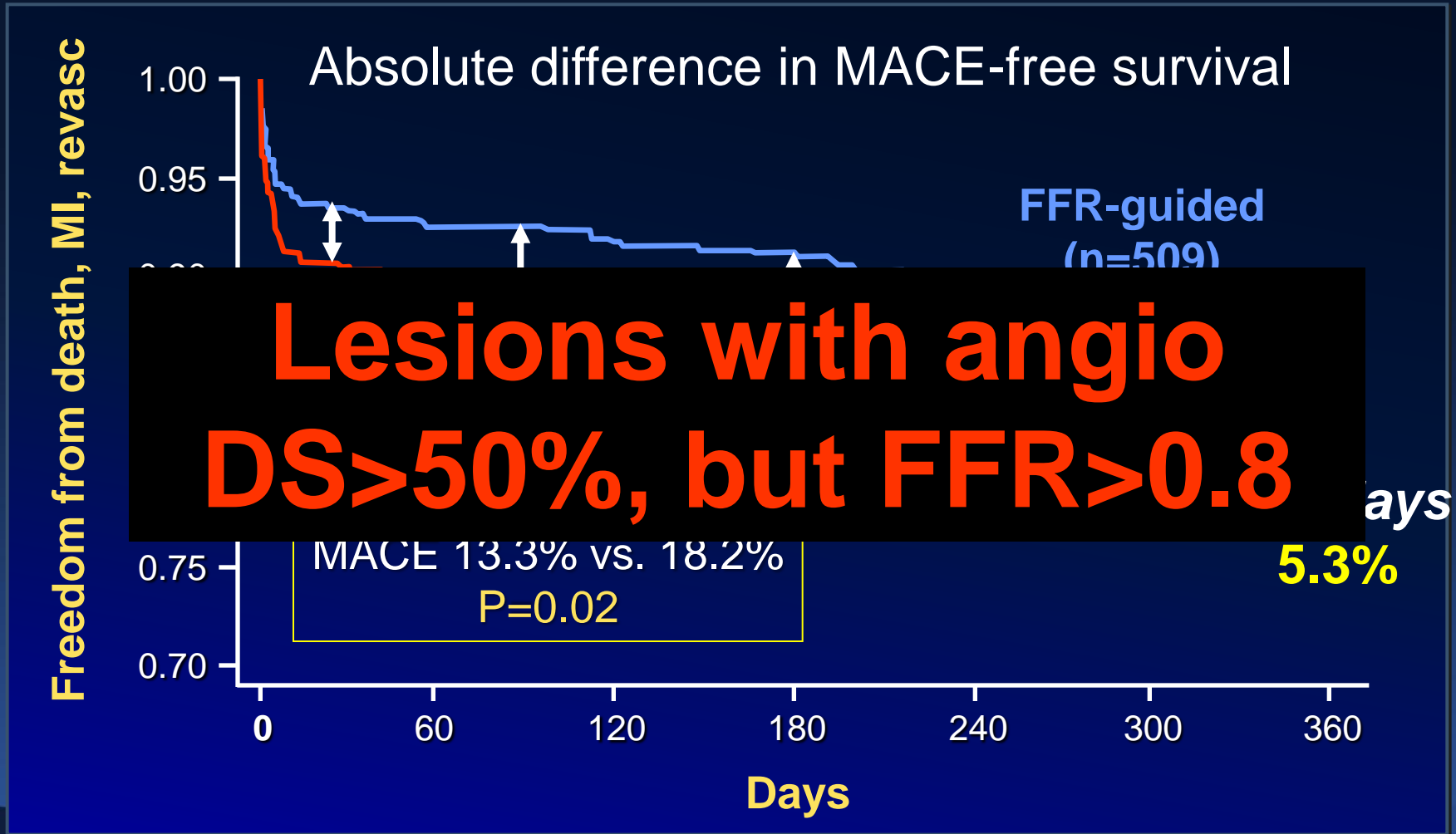
- AUC for maxLCBI_{4mm} = 0.90
- AUC for plaque burden = 0.86



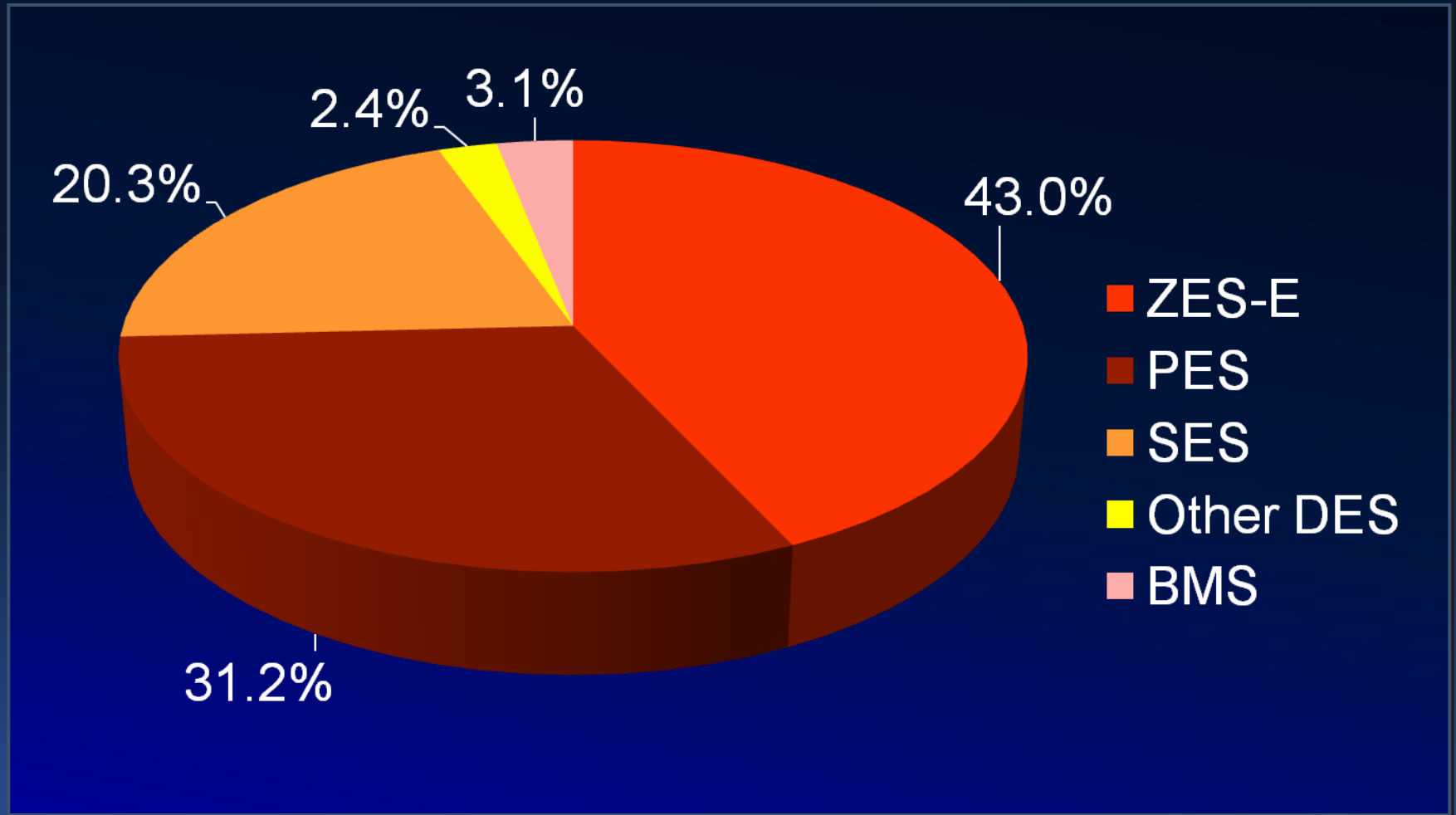
FAME: Primary Endpoint



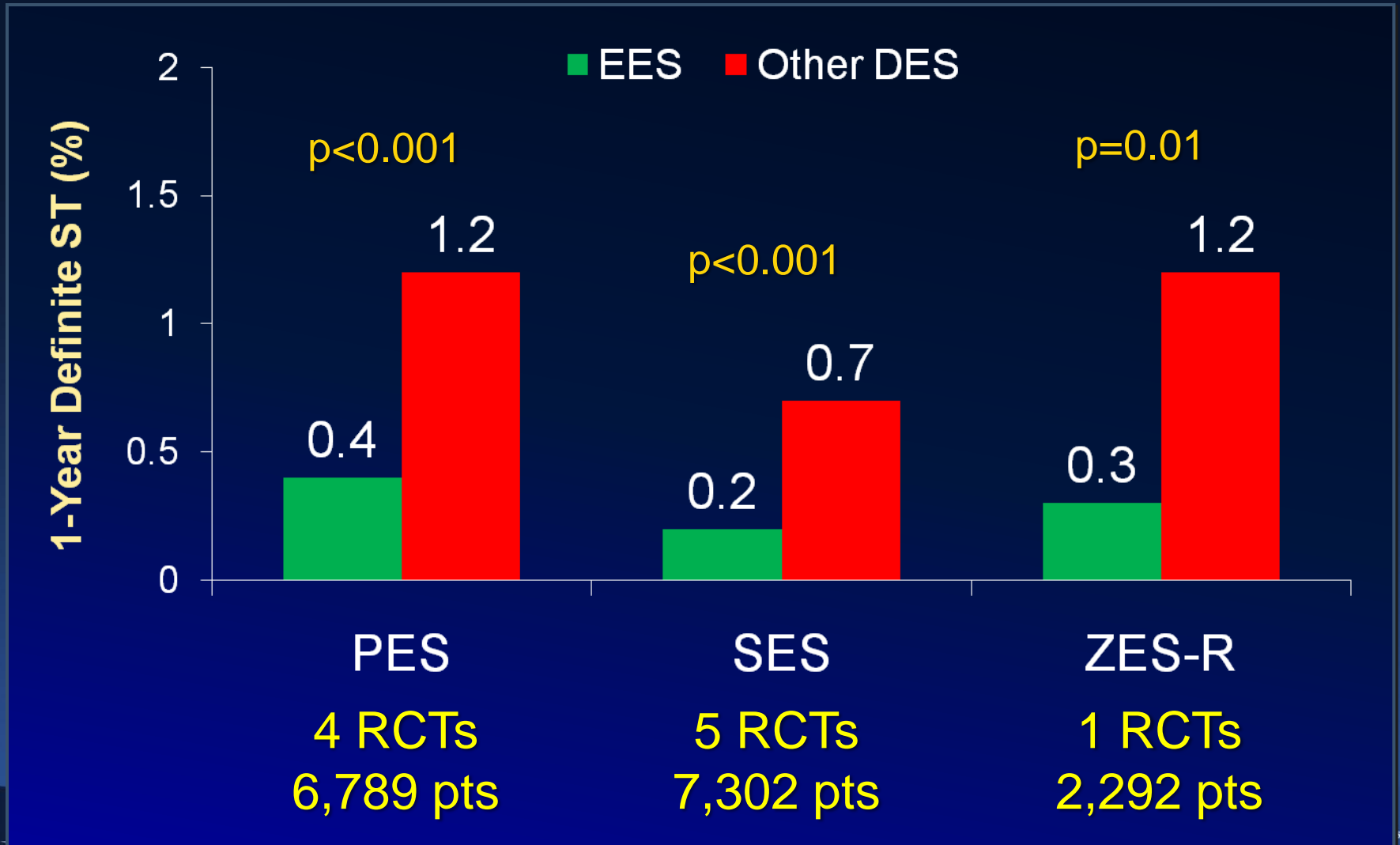
1005 pts with MVD (83% CSA) undergoing PCI with DES were randomized to FFR-guided vs. angio-guided intervention



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. angio-guided intervention

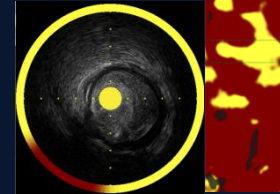
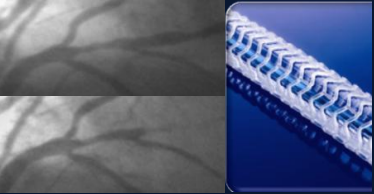
Death, MI, revasc

NO longer significant difference

30 days

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

Days



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)

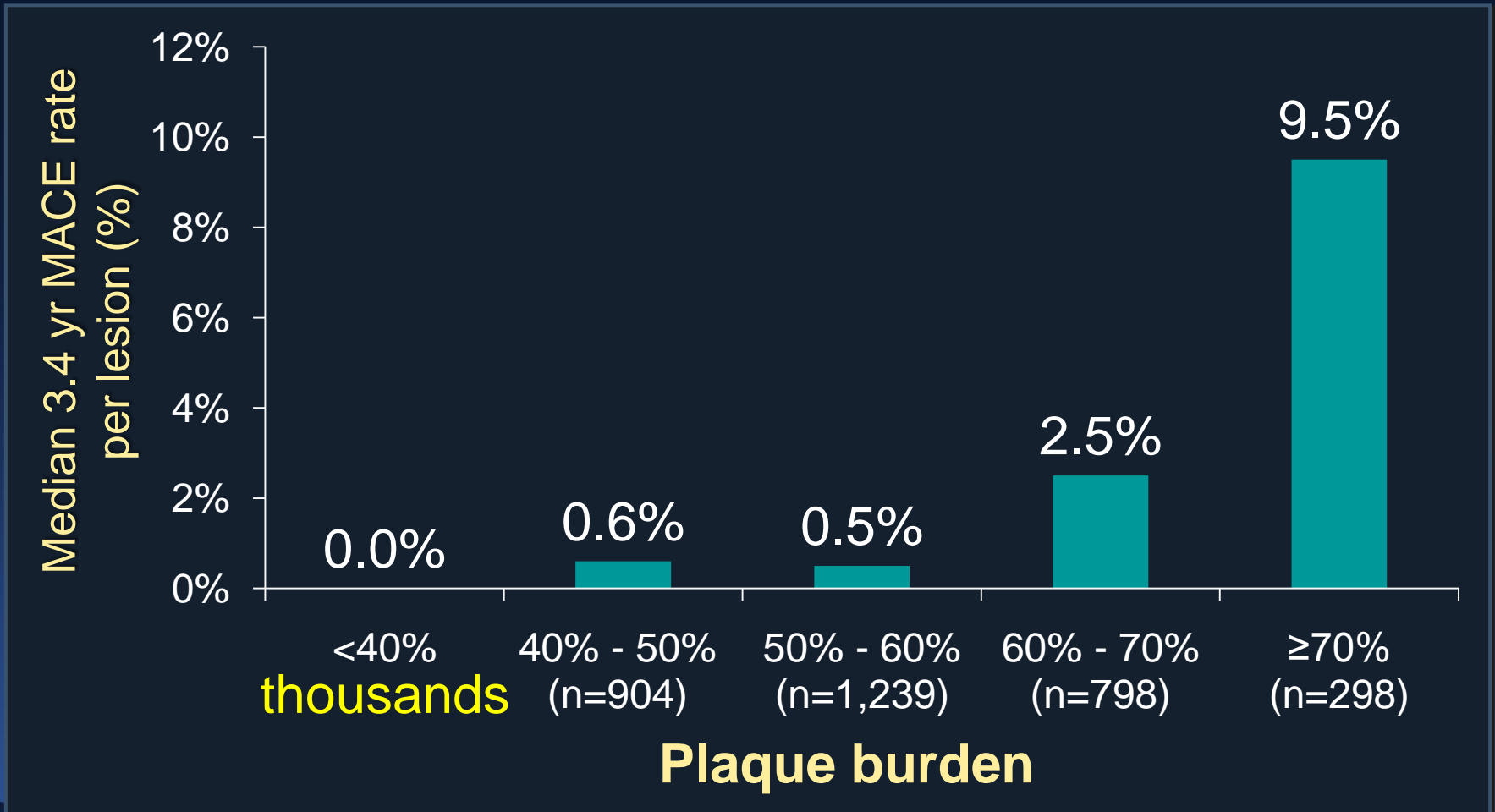
GDMT
(N=100)

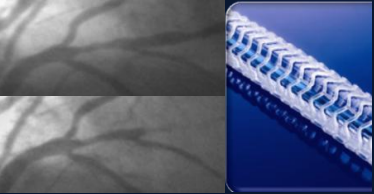
Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for ≥3 years

PROSPECT: Correlates of Non-Culprit Lesion Related Events

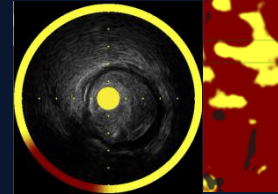
Impact of plaque burden





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

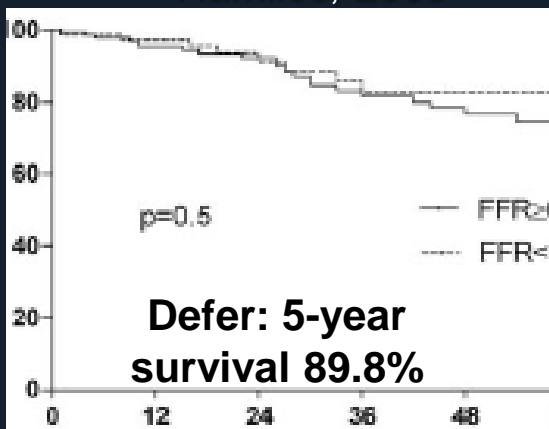
Endpoints and analysis: IVUS MLA at 2 years (superiority, powered); Death, TV-MI, TLR (noninferiority, not powered)

LMCA Defer by FFR

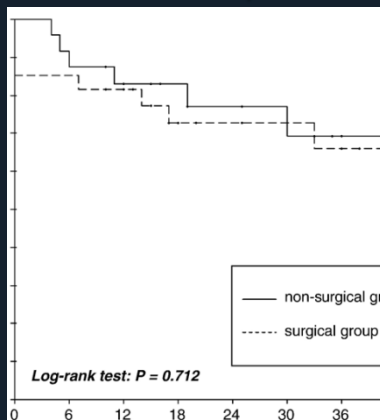
- Any Death
- LMCA revasc
- Other revasc

FFR=0.8

Hamilos, 2009

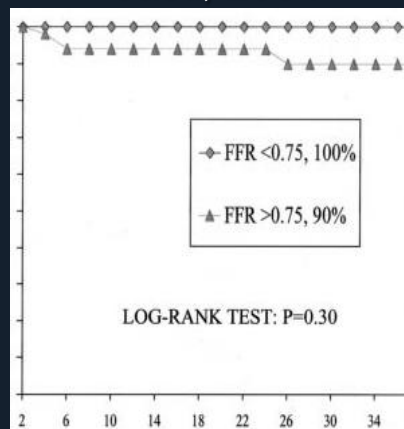


Lindstaedt, 2006

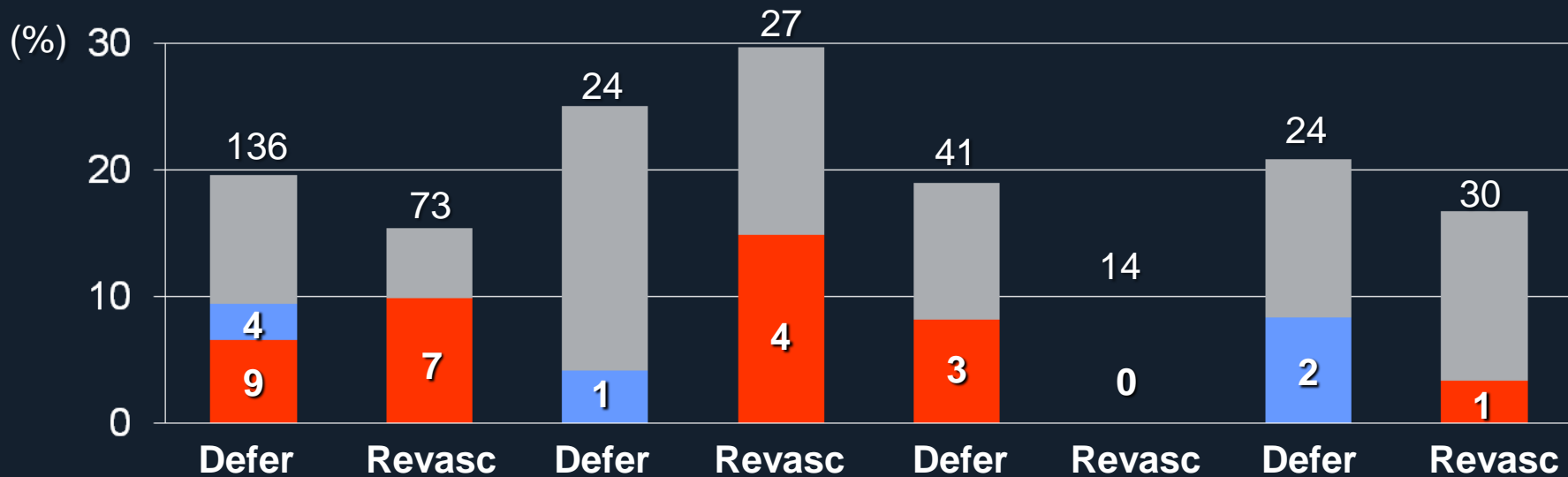
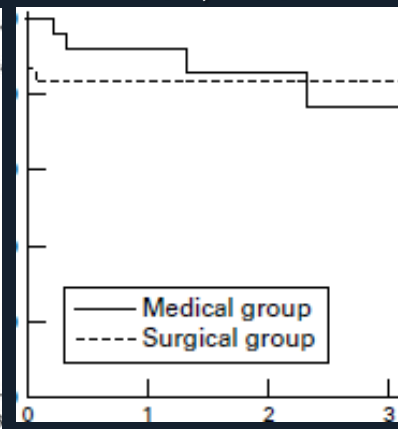


FFR=0.75

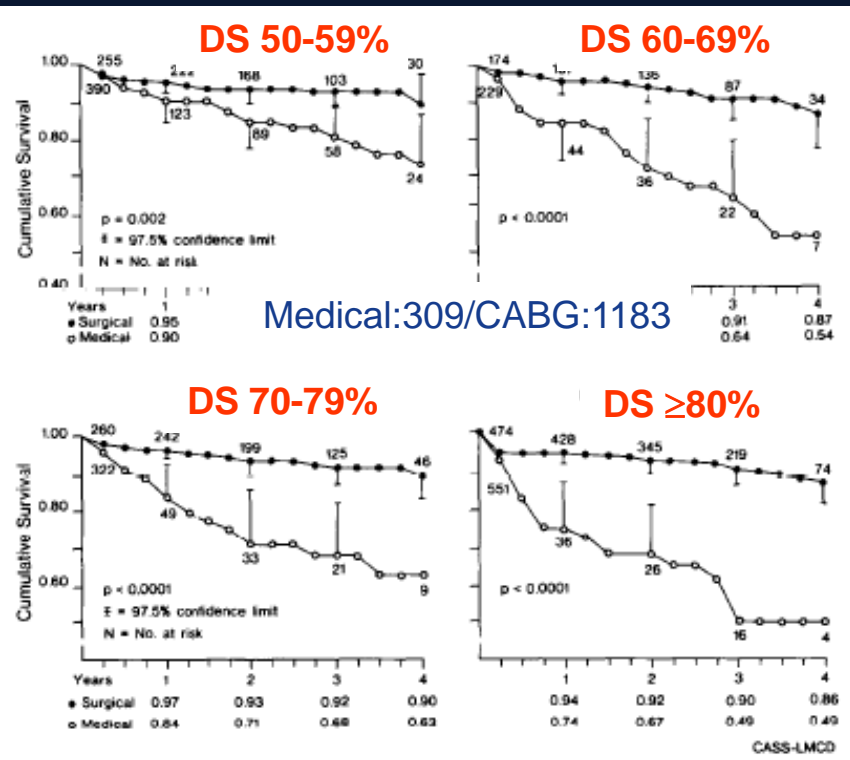
Jasti, 2004



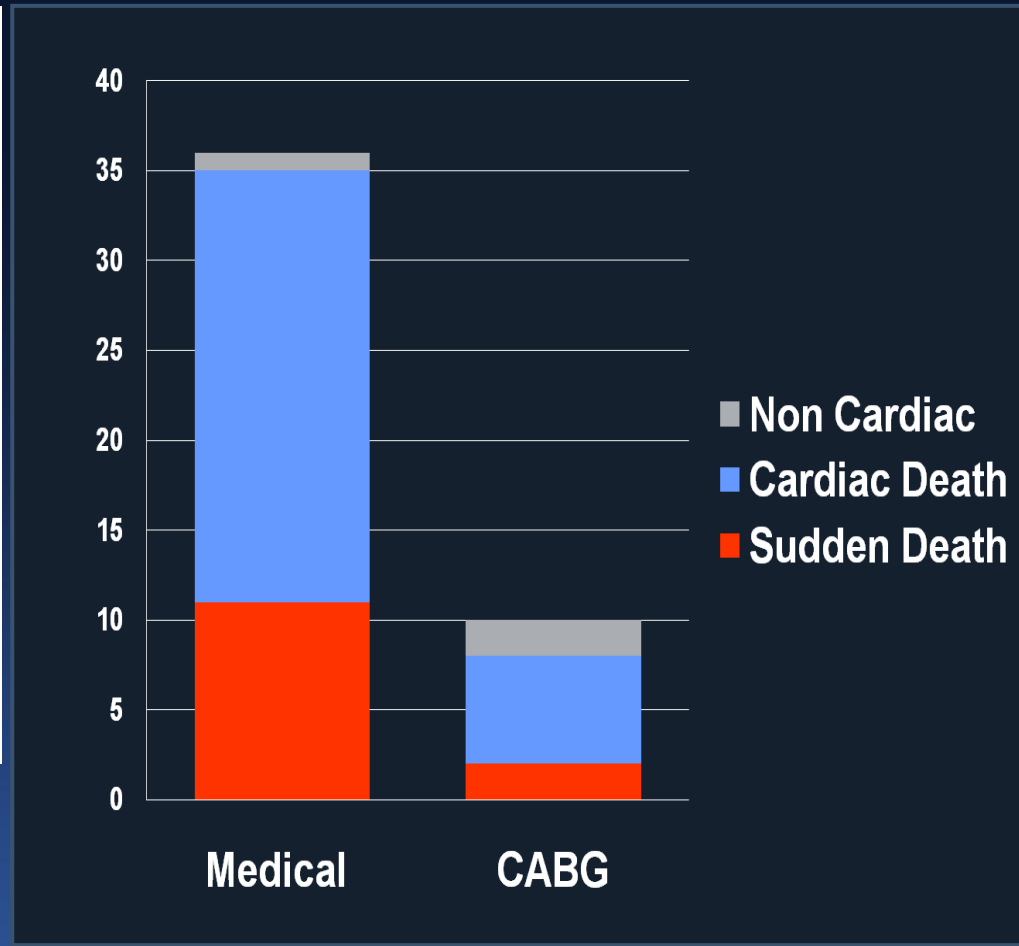
Bech, 2001



Natural History of Left Main Disease



Chaitman et al, *AJC* 1981;48: 765-777



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!