

Define Vulnerable Plaque: Coronary Imaging Perspective

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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

- Grant/Research Support
- Consulting Fees/Honoraria

Company

- Boston Scientific, Abbott Vascular
- Boston Scientific, OCT Medical Imaging Inc.

Rupture



Erosion



Disruption of fibrous cap

Deficiency of endothelium

Smooth muscle cell apoptosis

Endothelial cell apoptosis

Thin fibrous cap

Proteoglycan rich thick cap

Lipid rich

Lipid poor

Abundant inflammation

Few inflammation

STEMI presentation (70%)

NSTEMI presentation (60%)

Male dominant

Female dominant

High LDL

High triglycerides

OCT Defined Underlying Plaque in ACS



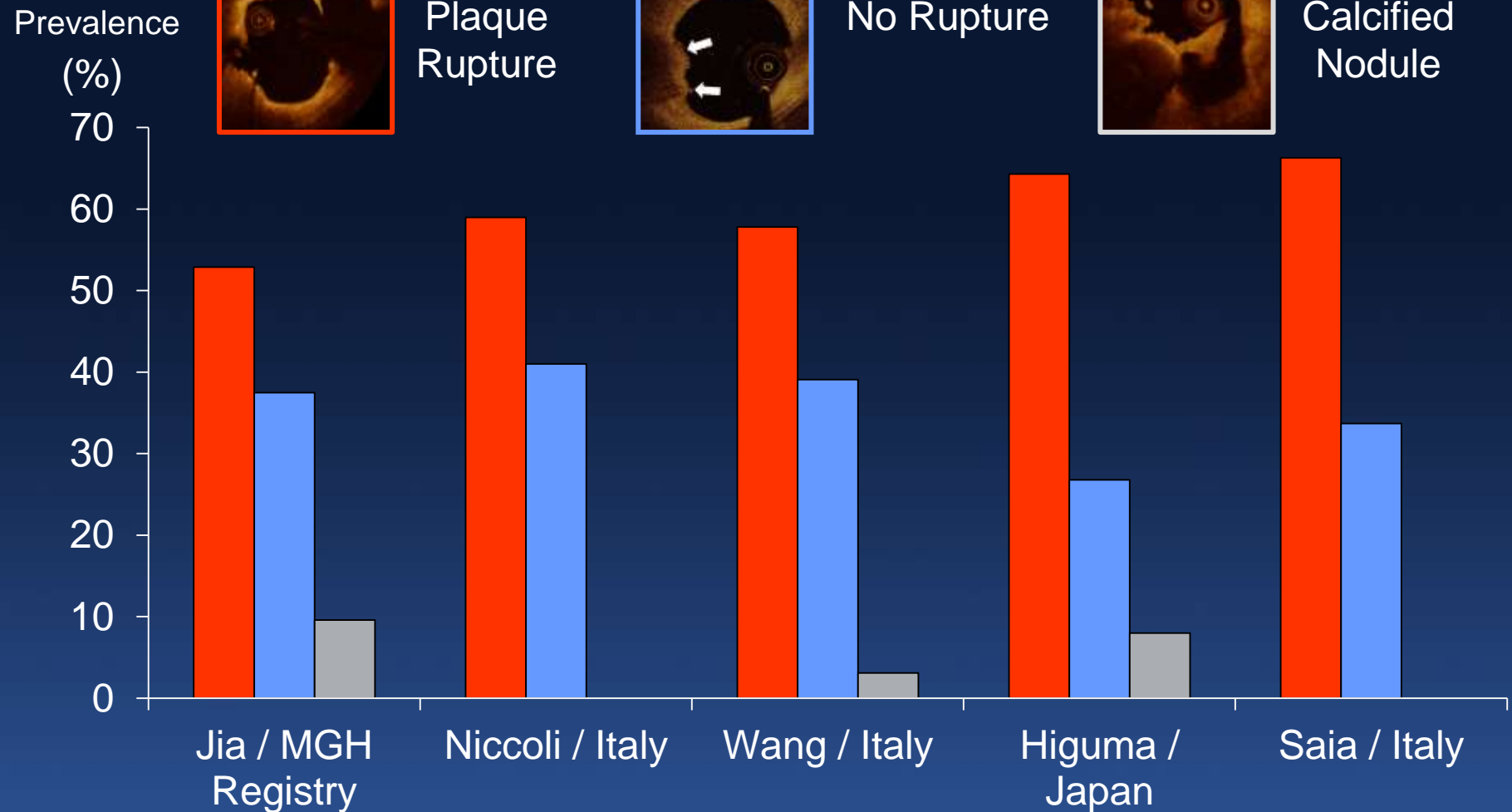
Plaque Rupture



No Rupture



Calcified Nodule



Jia H, et al. JACC 2013;62:1748-58. Niccoli G et al. EHJ 2015; 36:1377-84. Wang L et al. EHJ 2015
doi:10.1093/ehjc.jev105 Higuma T et al. JACC Interv 2015;8:1166-76. Saia JACC Img 2015; 8: 566-75.

Difference of Underlying Morphology

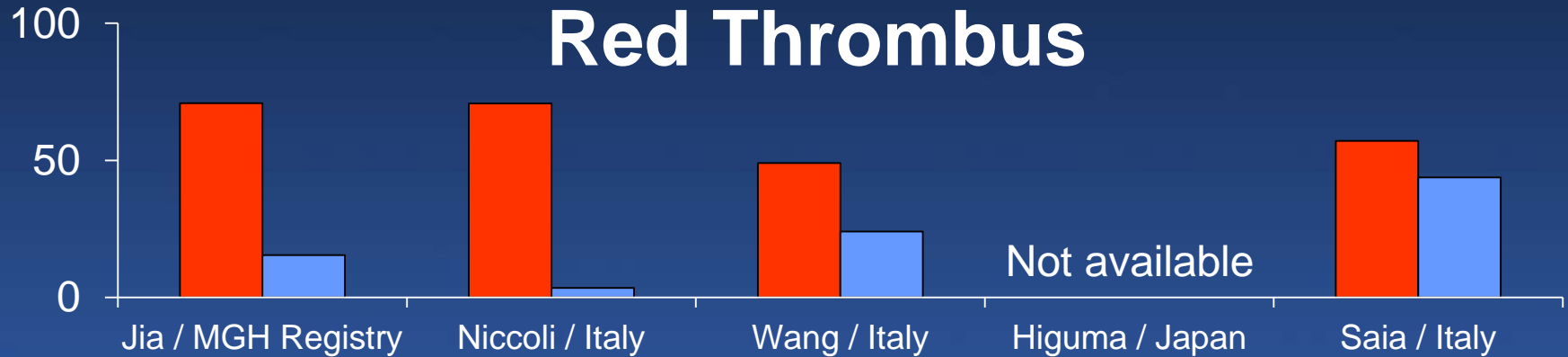
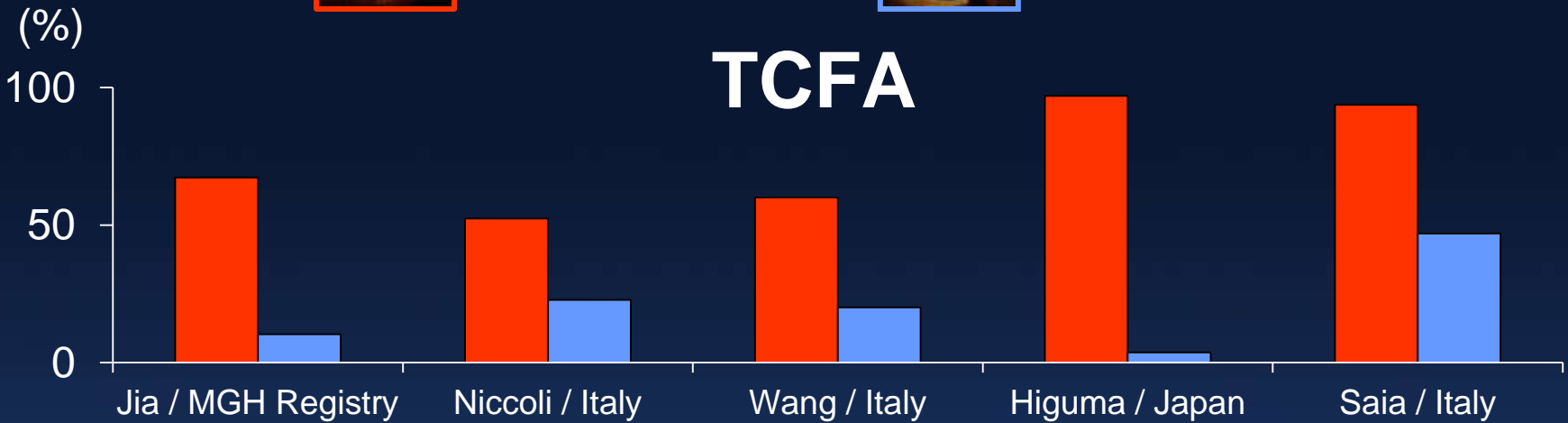


Plaque Rupture



No Rupture

Prevalence



Comparison between OCT defined Erosion vs Plaque Rupture in 773 STEMI

	Erosion (n=209)	Plaque rupture (n=564)
Age	55±11	59±10
Current smoker	64%	52%
Dyslipidemia	50%	71%
LAD location	61%	47%
Nearby bifurcation	59%	35%
TCFA	14%	90%

Longitudinal Distribution of Erosion and Rupture

Prevalence (%)



Plaque Rupture

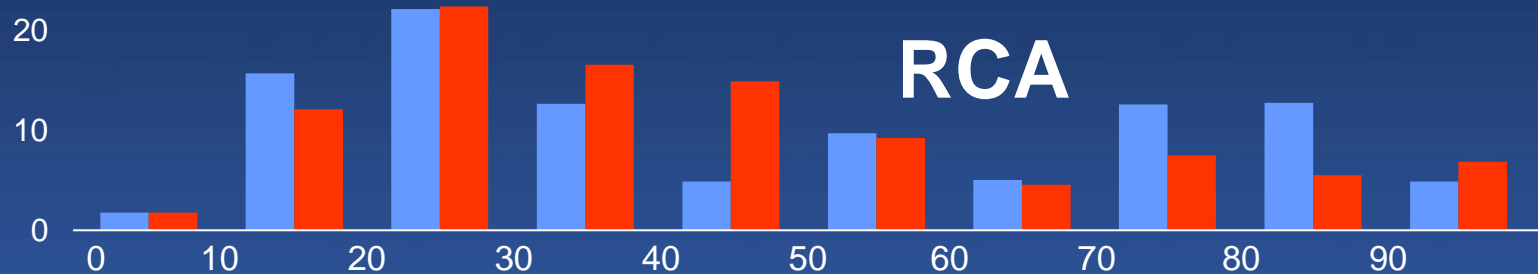
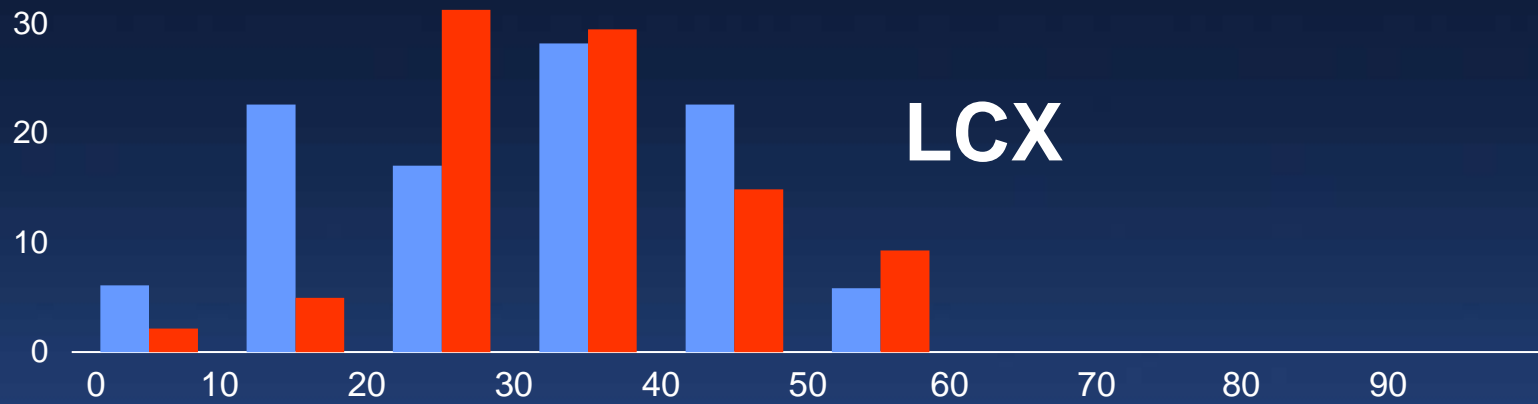
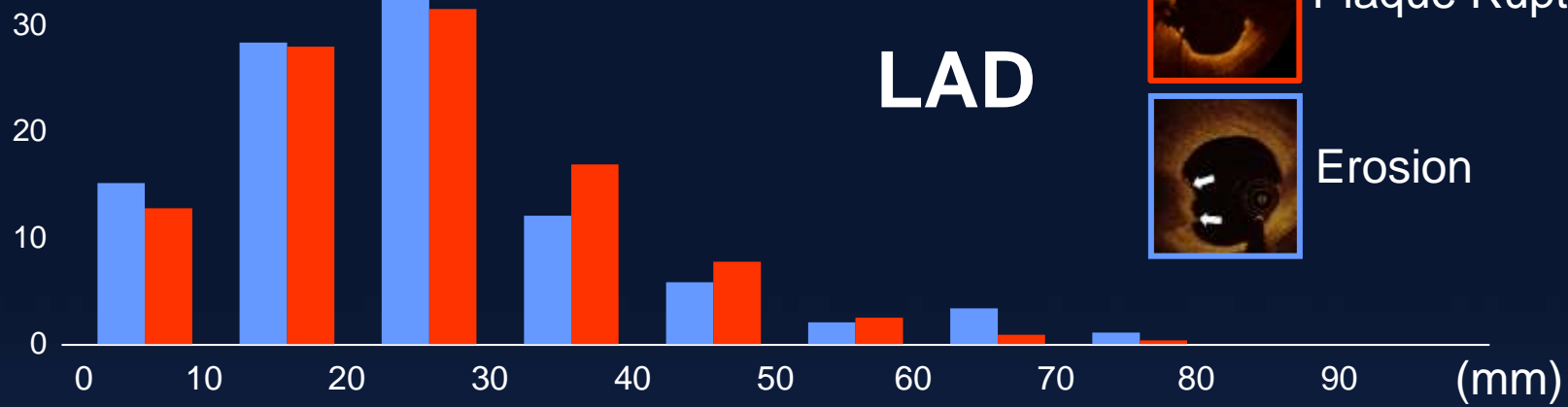


Erosion

LAD

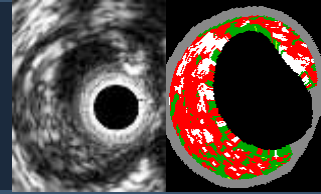
LCX

RCA



Distance from the ostium

PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

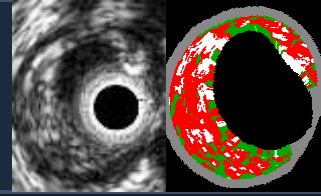


Independent predictors of lesion level events by Cox Proportional Hazards regression

<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

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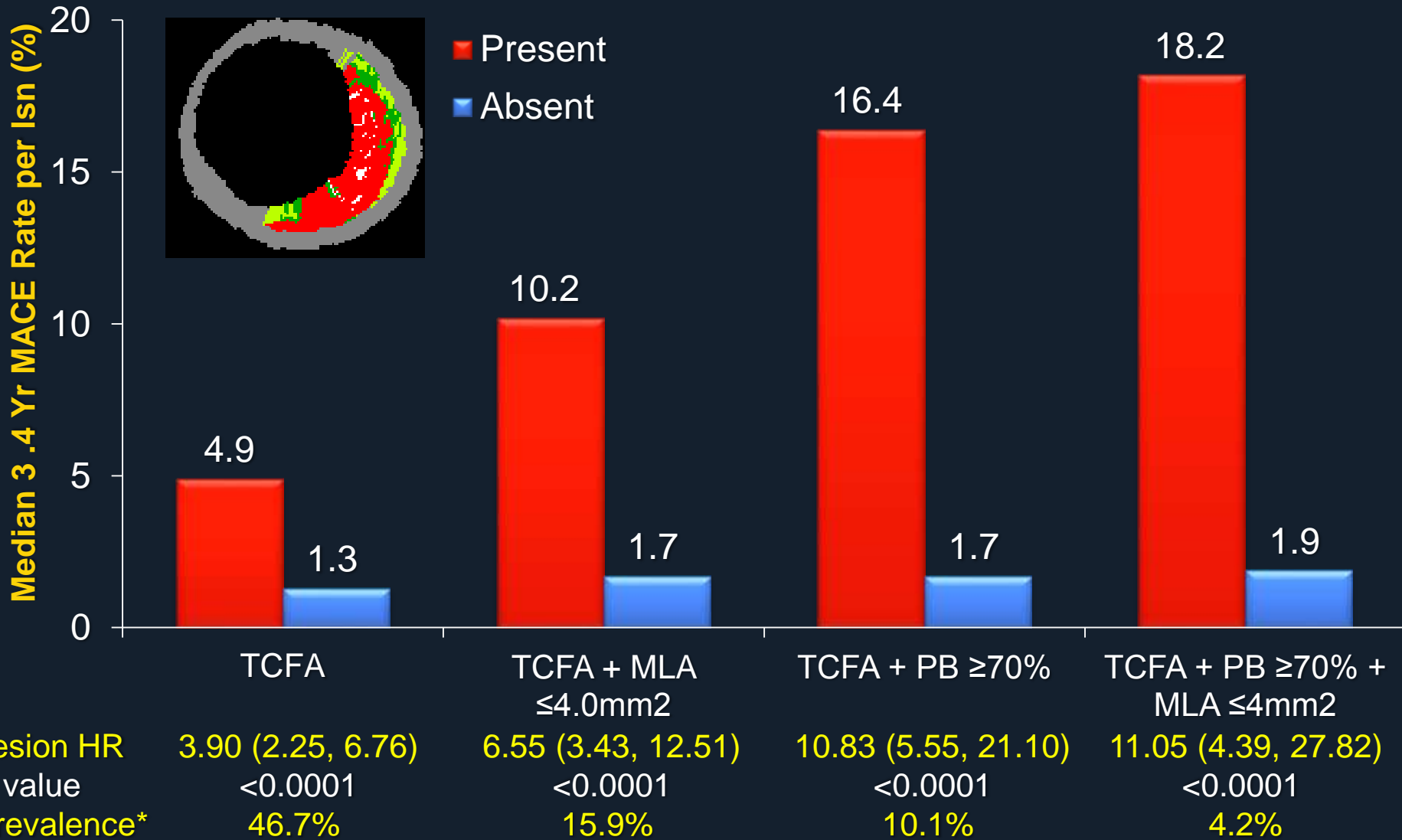
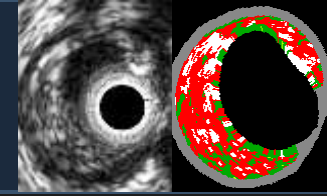


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PROSPECT: VH-TCFA and Non Culprit Lesion Related Events

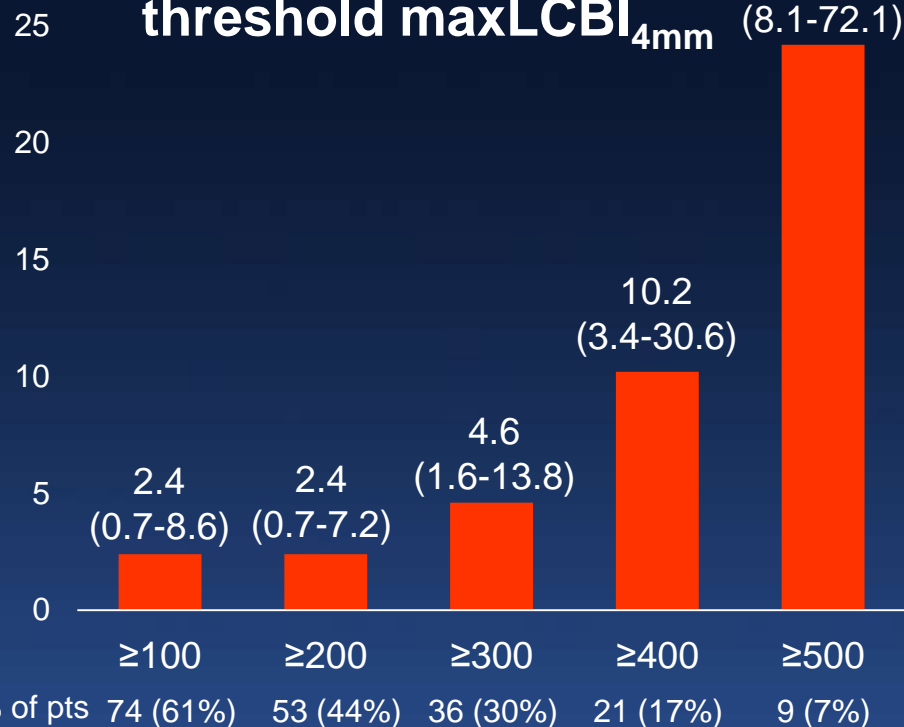
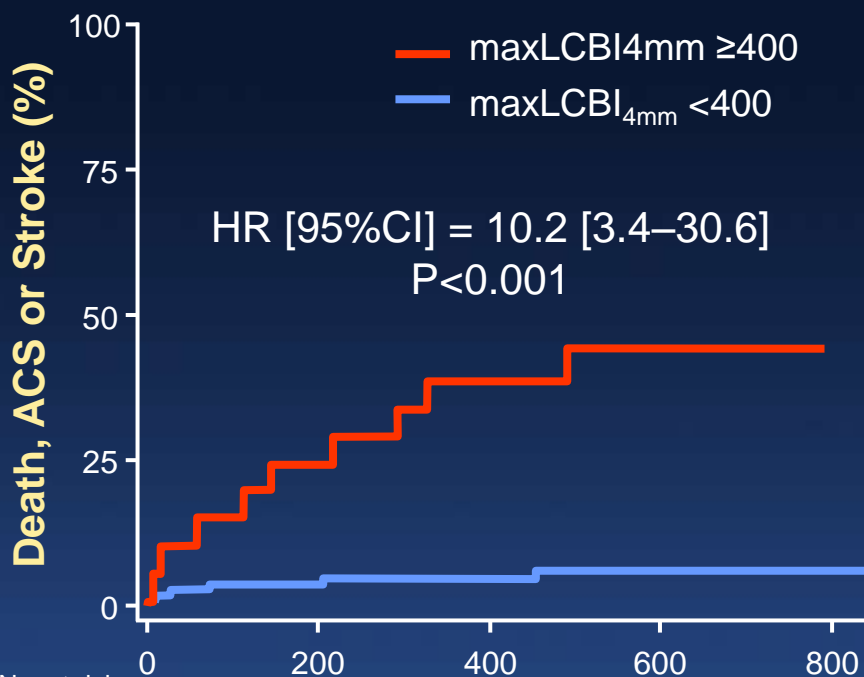


*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA

Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

- Non-target segment in culprit vessel in 121 patients, >1 year follow-up
- 14 MACCE: 5 all-cause mortality, 8 non-fatal ACS, 1 acute cerebrovascular events

Hazard ratios for various threshold maxLCBI_{4mm}

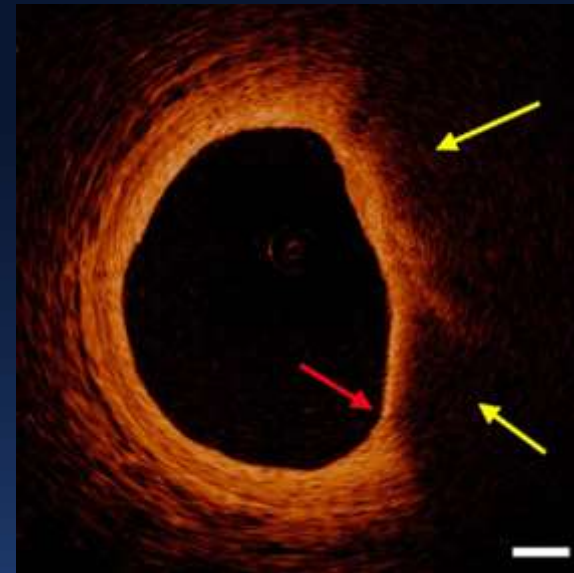
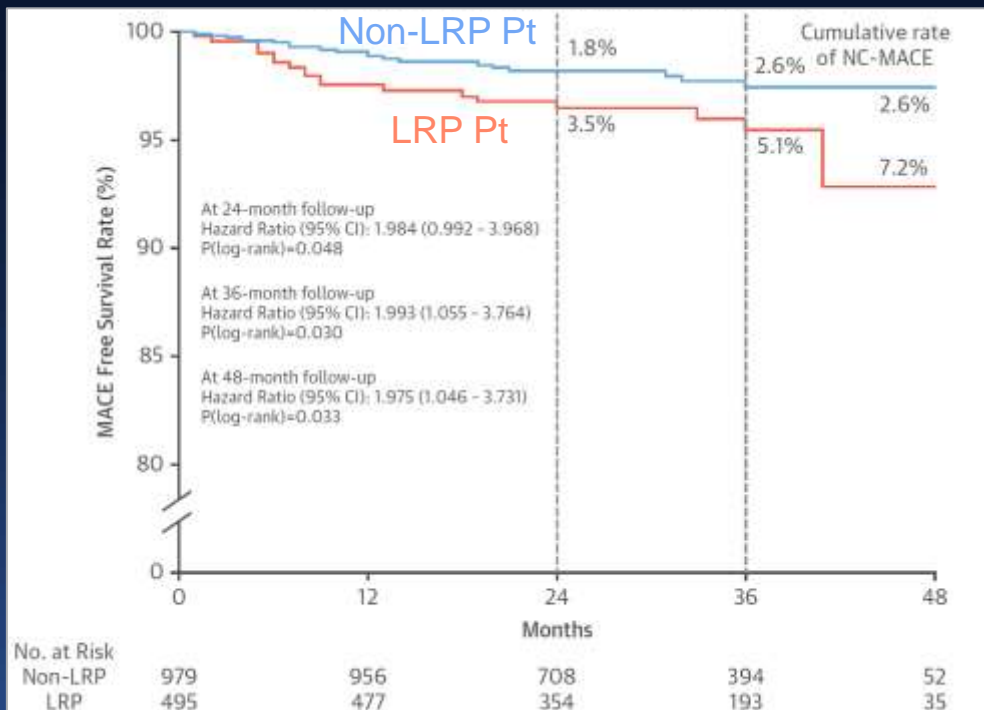


No. at risk:	0	200	400	600	800
maxLCBI _{4mm} ≥400	21	16	12	5	0
maxLCBI _{4mm} <400	100	97	87	47	13

Neither plaque burden ≥70% by IVUS (HR 1.30 [0.41-4.16], P=0.65) nor MLA ≤4.0 mm² (HR 0.80 [0.28-2.38], P=0.69) was significantly associated with MACCE

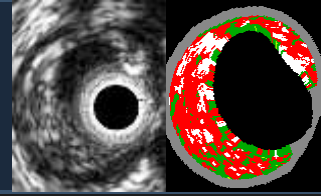
Non-culprit Lipid Rich Plaque detected by OCT and Non-culprit lesion related MACE

- Non-target segment in culprit vessel in 1,474 patients, ≥1 year follow-up
- MACE: composite of cardiac death, MI, or ischemic driven revascularization (IDR)
- 38 MACE events (4.3%) including 9 MI (0.7%) and 38 (4.3%) IDR at 4 yrs
- No information between LRP and event



Predictor of 4-yr NC MACE	RR (95%CI)
LRP in non-culprit segment	2.1 (1.1-4.0)
ACS presentation at index	2.5 (1.2-5.2)
Interruption of statin ≥1 yr	4.5 (1.9-10.6)

PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

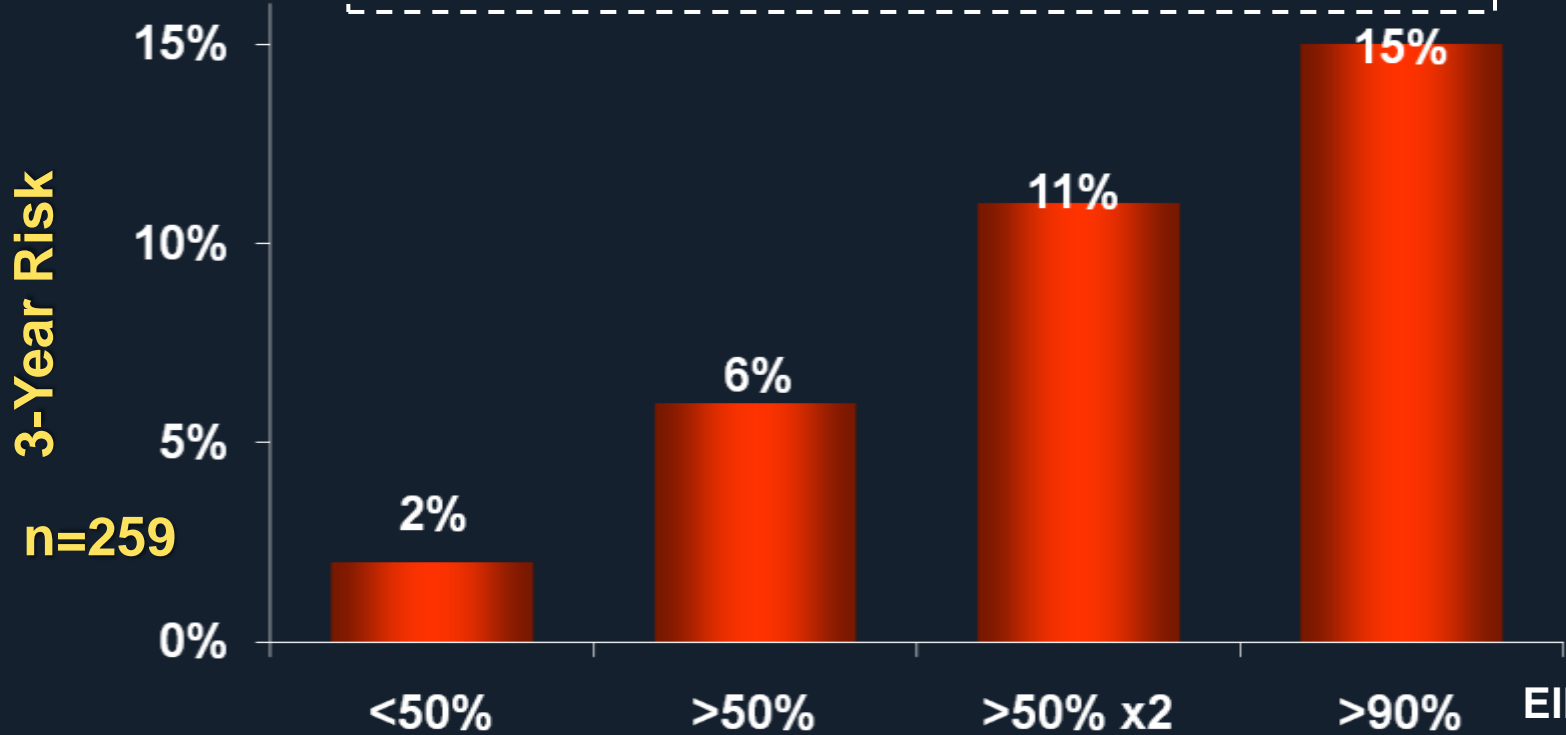
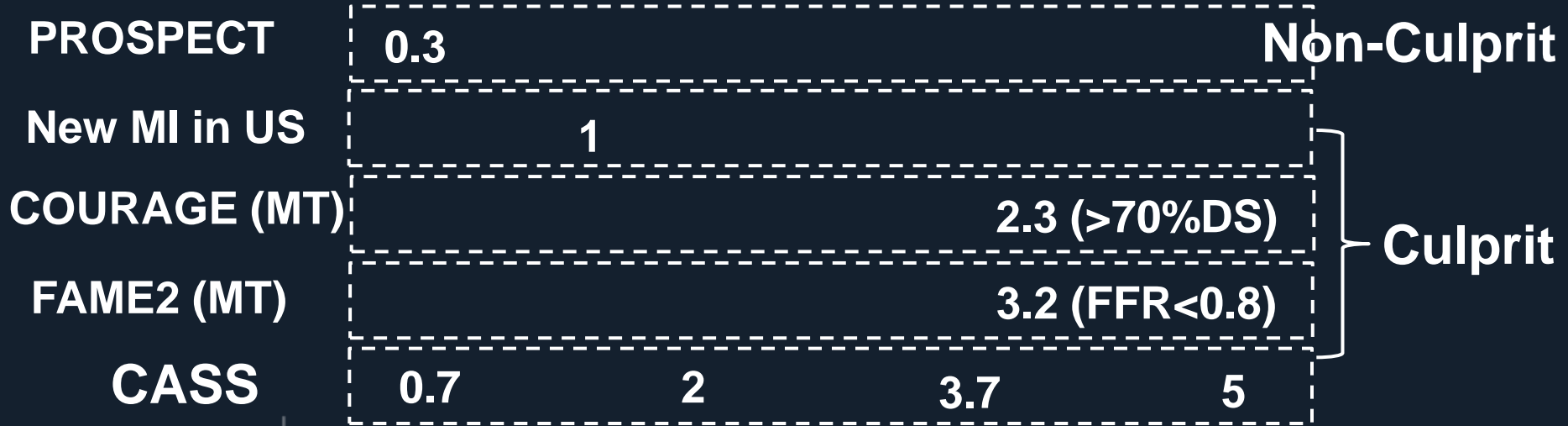


Independent predictors of lesion level events by Cox Proportional Hazards regression

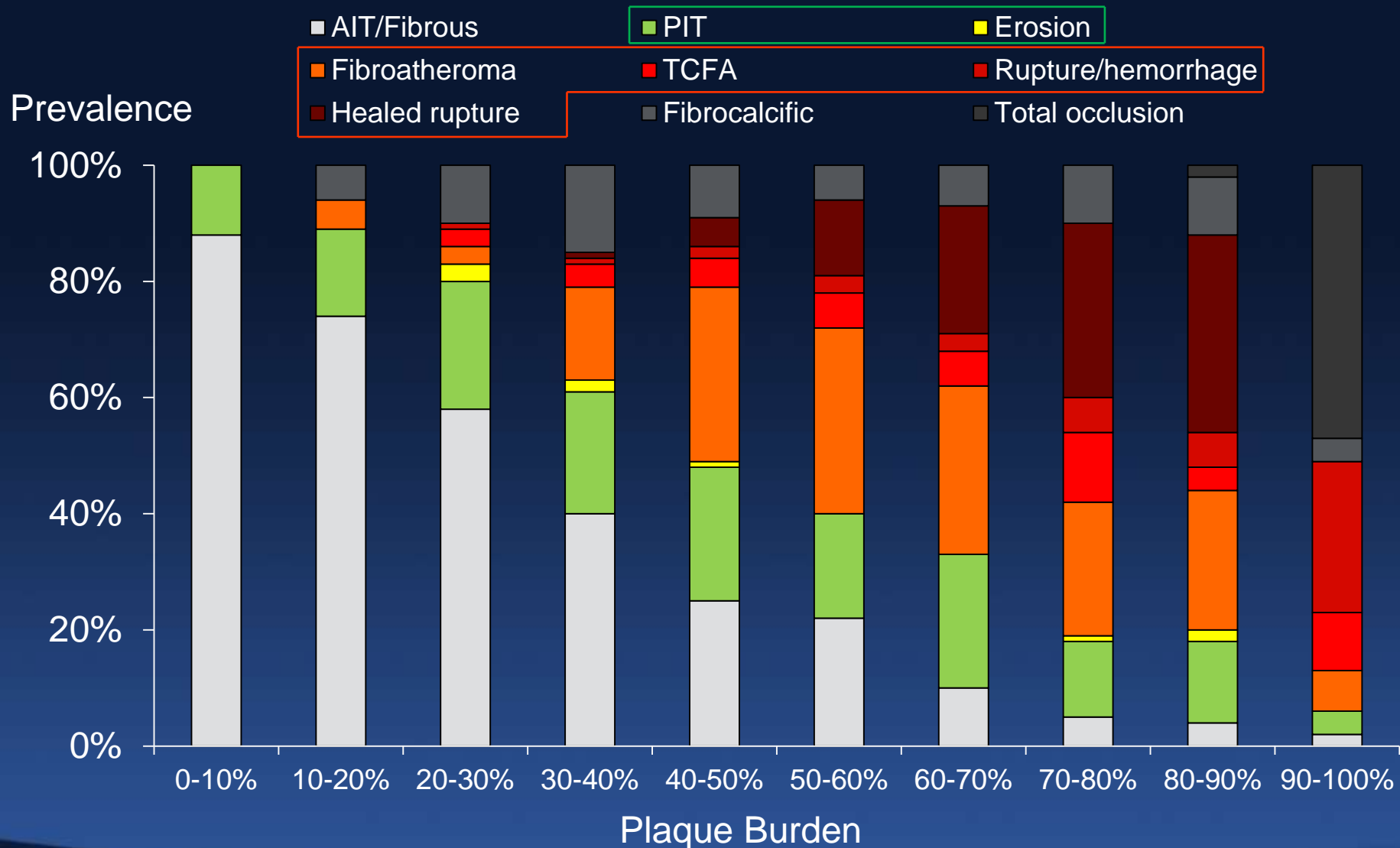
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Difference of the Incidence of MI/100 pts/year



Lesion Morphology and Plaque Burden in Pathology



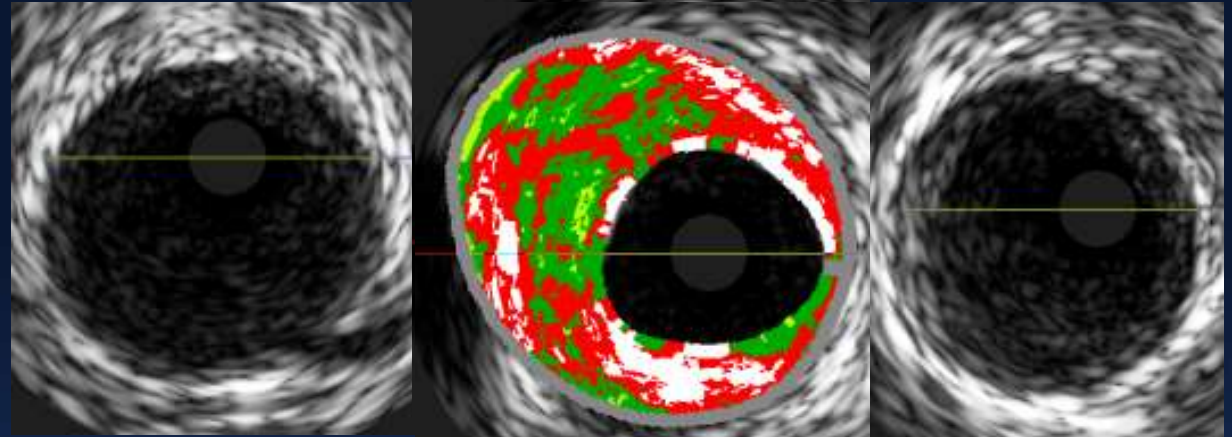
Otsuka F, et al. ATVB 2014; 34:724-36.

TCFA morphology with angiographic DS>30% by OCT/IVUS

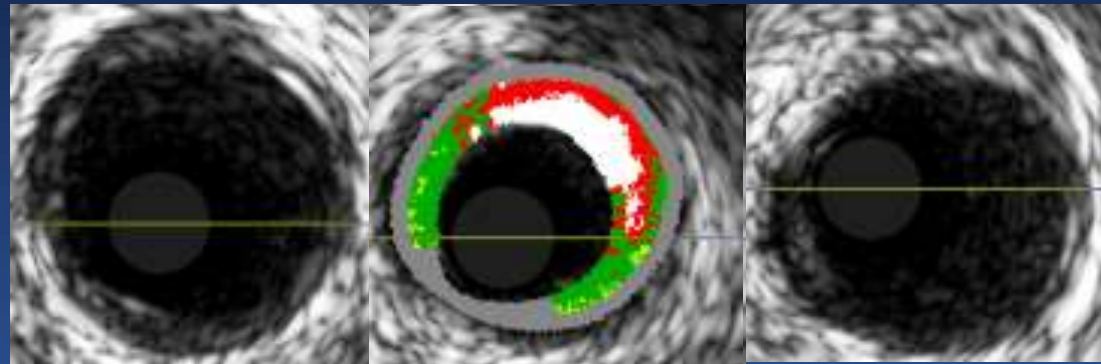
Angio DS	30-49%	50-69%	>70%
OCT			
Prevalence of TCFA	18% (58/325)	18% (40/227)	36% (33/91)
Fibrous cap thickness (µm)	57.0±6.6	56.0±7.5	49.0±9.2
Lipid arc (°)	214±56	209±55	204±59
Lipid length (mm)	9.4±4.6	10.5±5.5	9.6±4.5
IVUS			
Lumen area (mm ²)	5.8±2.4	4.5±2.1	3.2±2.3
Plaque burden (%)	58.1±8.4	67.5±9.4	80.1±7.4
Remodeling index	0.98±0.10	1.02±0.13	1.09±0.13

Vessel Remodeling

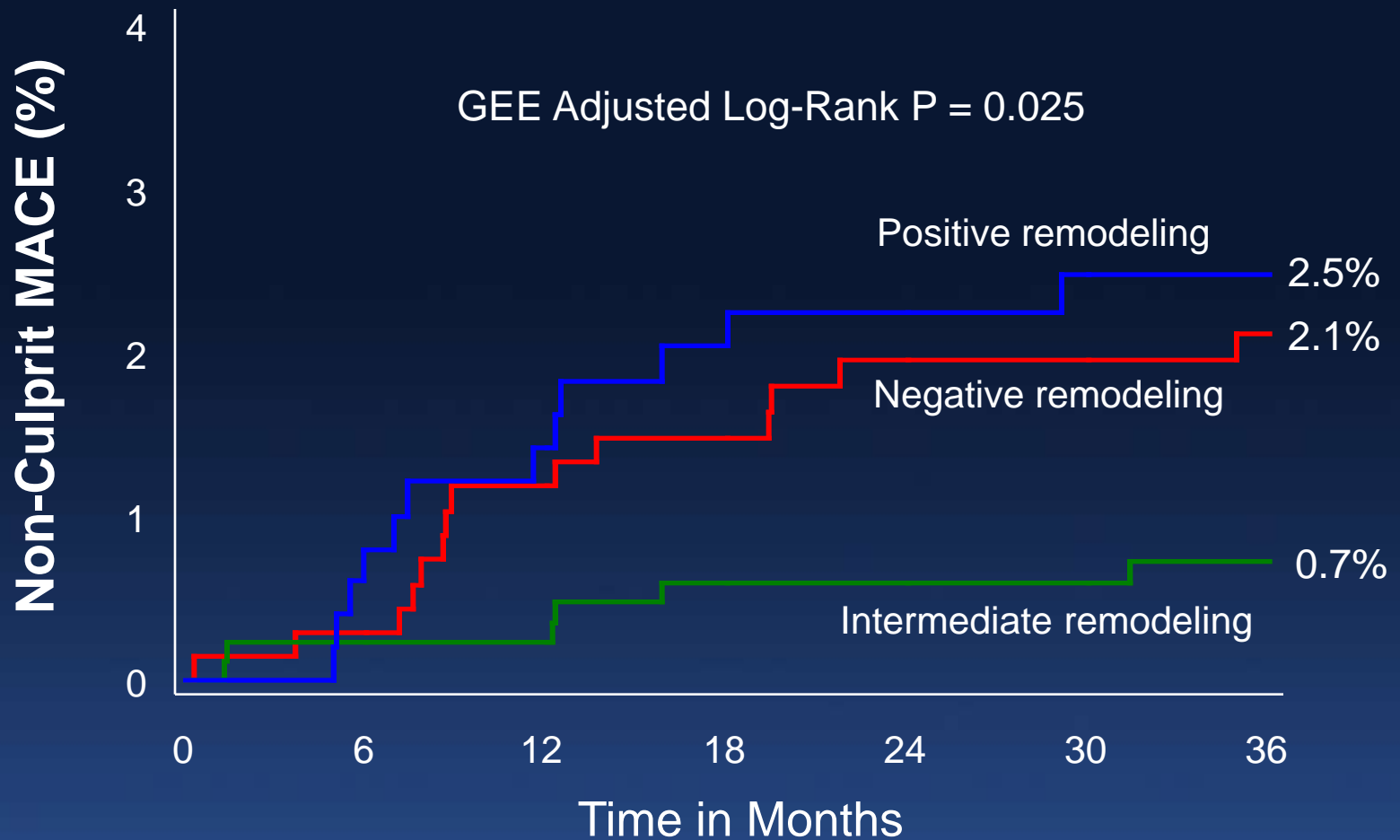
**Positive
Remodeling
($RI > 1.00$)**



**Negative
Remodeling
($RI < 0.88$)**



Remodeling Pattern and Subsequent Outcome



Number at risk

Negative R.	734	671	657	643	629	607	391
Intermediate R.	911	841	832	807	798	775	482
Positive R.	537	488	484	460	451	435	286

Inaba et al. JACC img 2014; 7; 70-8.

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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} ≥70%	5.03 [2.44, 10.35]	<0.01
VH-TCFA	3.05 [1.63, 5.71]	<0.01
MLA ≤4.0 mm ²	3.04 [1.51, 6.13]	<0.01
Negative Rem	2.39 [1.07, 5.34]	0.03
Positive Rem	2.34 [1.00, 5.44]	0.05

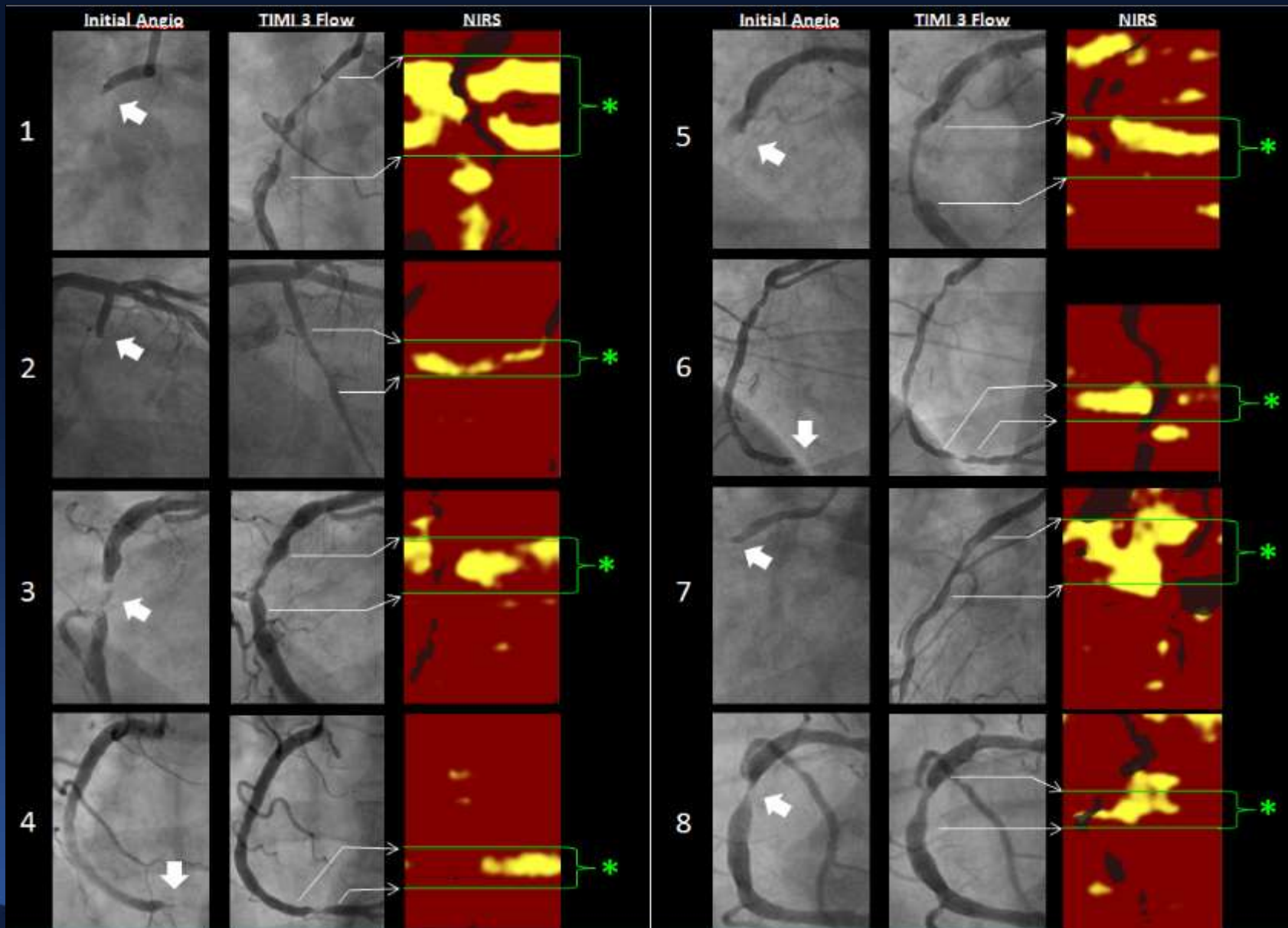
Rem=Remodeling compared to intermediate remodeling

48 yo Male, Sudden Coronary Death



Image is courtesy of Dr. James Muller.

NIRS Findings in STEMI Cases

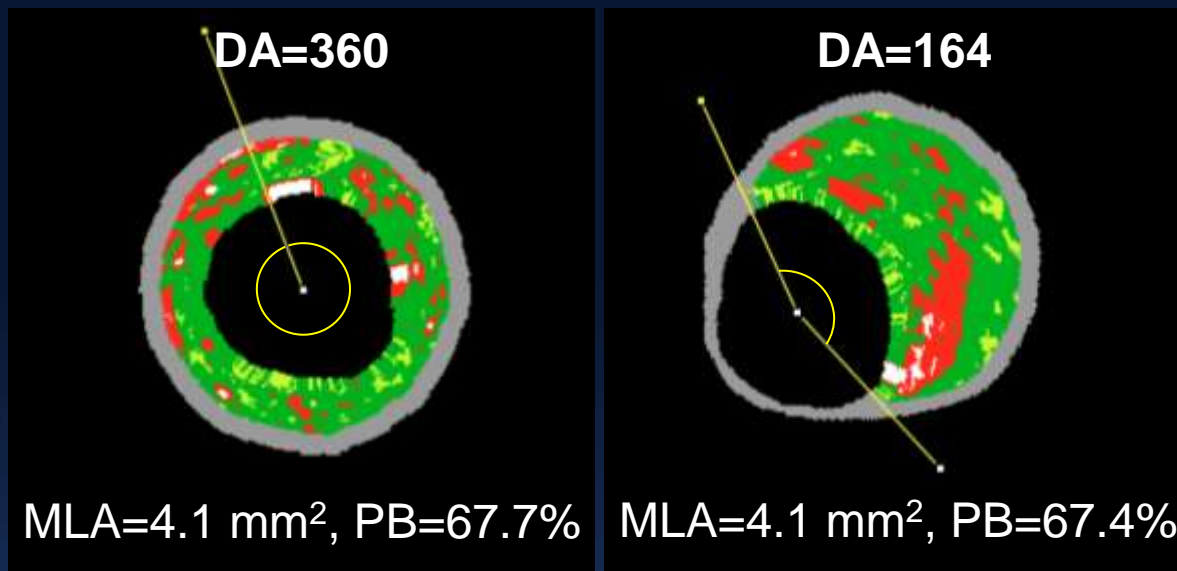


Madder RD. JACC Interv 2013, 6: 838-46.

Plaque Concentricity

Event-NCL

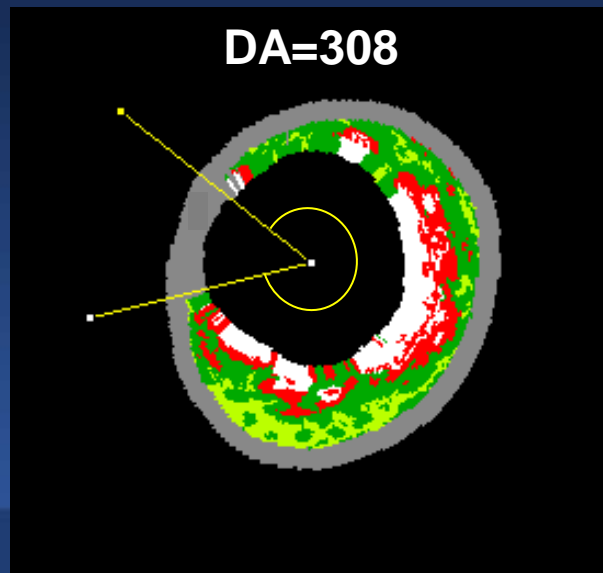
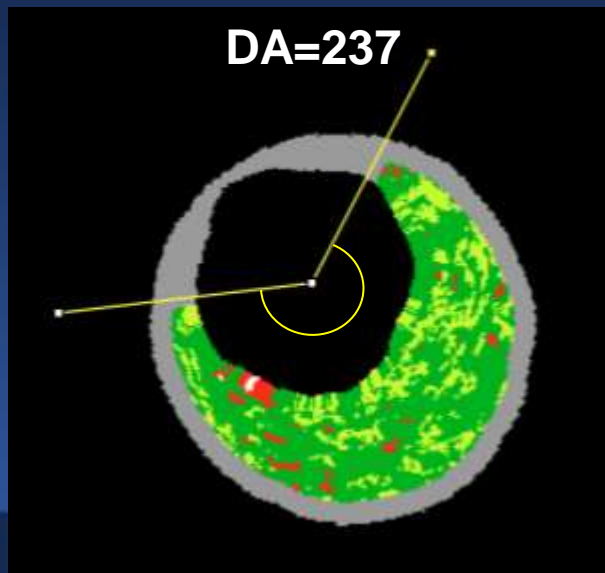
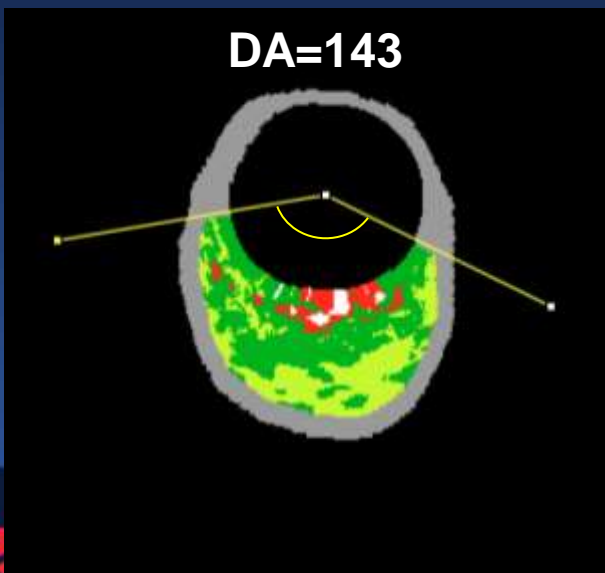
No Event-NCL



DA=143

DA=237

DA=308

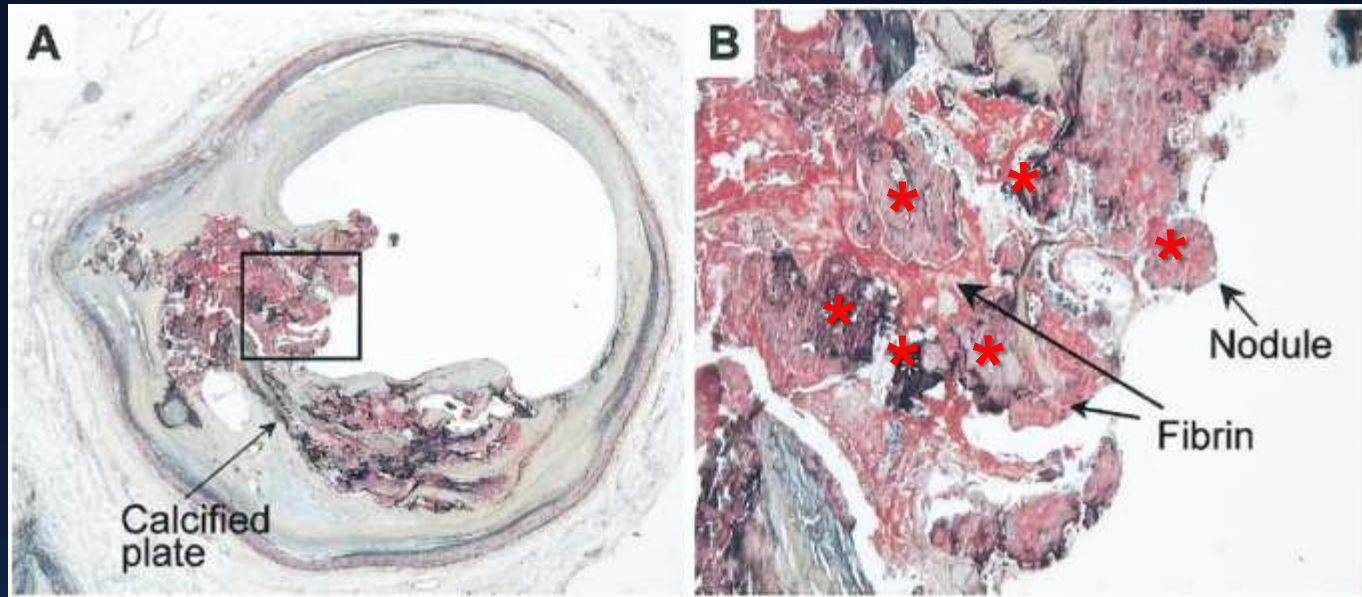


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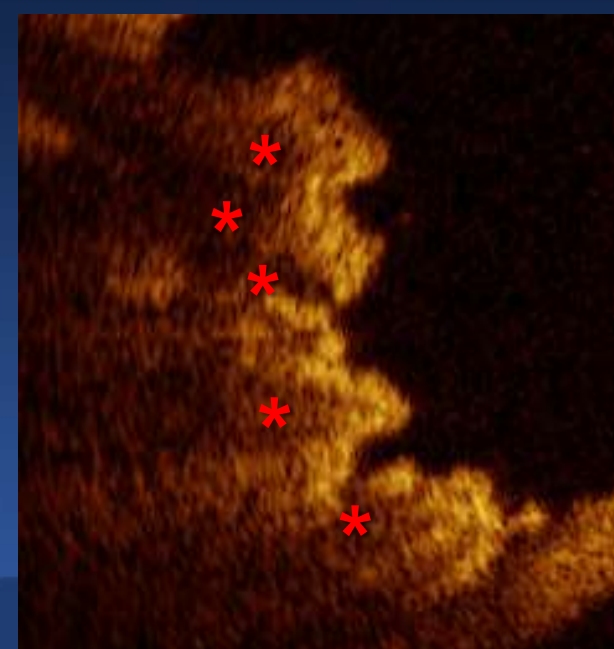
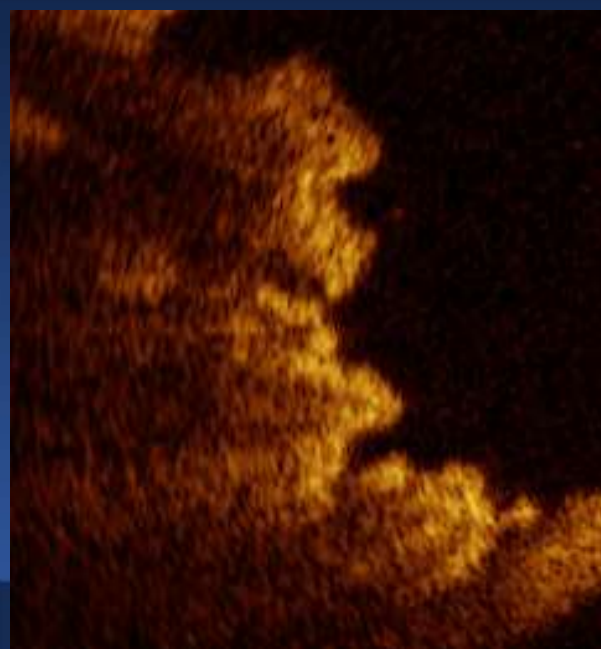
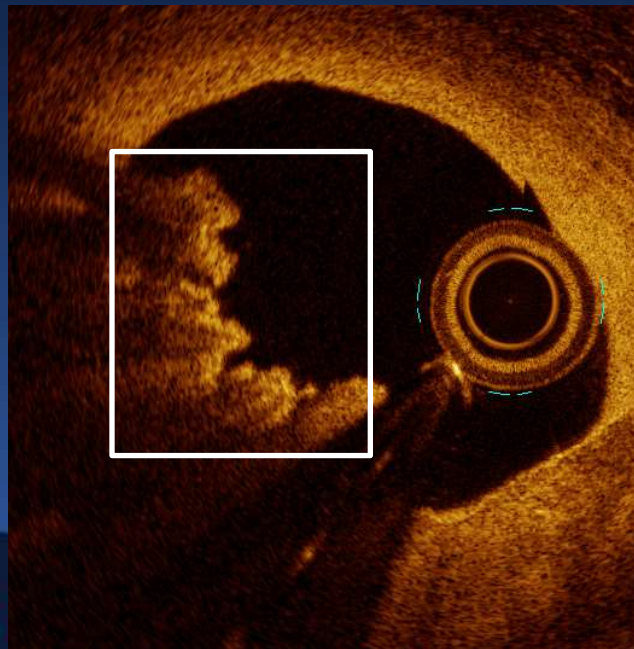
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PB _{MLA} $\geq 70\%$	3.78 [1.92, 7.46]	0.0001
VH-TCFA	3.03 [1.67, 5.49]	0.0001
MLA ≤ 4.0 mm ²	3.78 [1.91, 7.45]	0.0001
Disease arc $\geq 330^\circ$	2.19 [1.29, 3.72]	0.004

Calcified Nodule



Virmani R et al. J Am Coll Cardiol 18;47:C13-8.



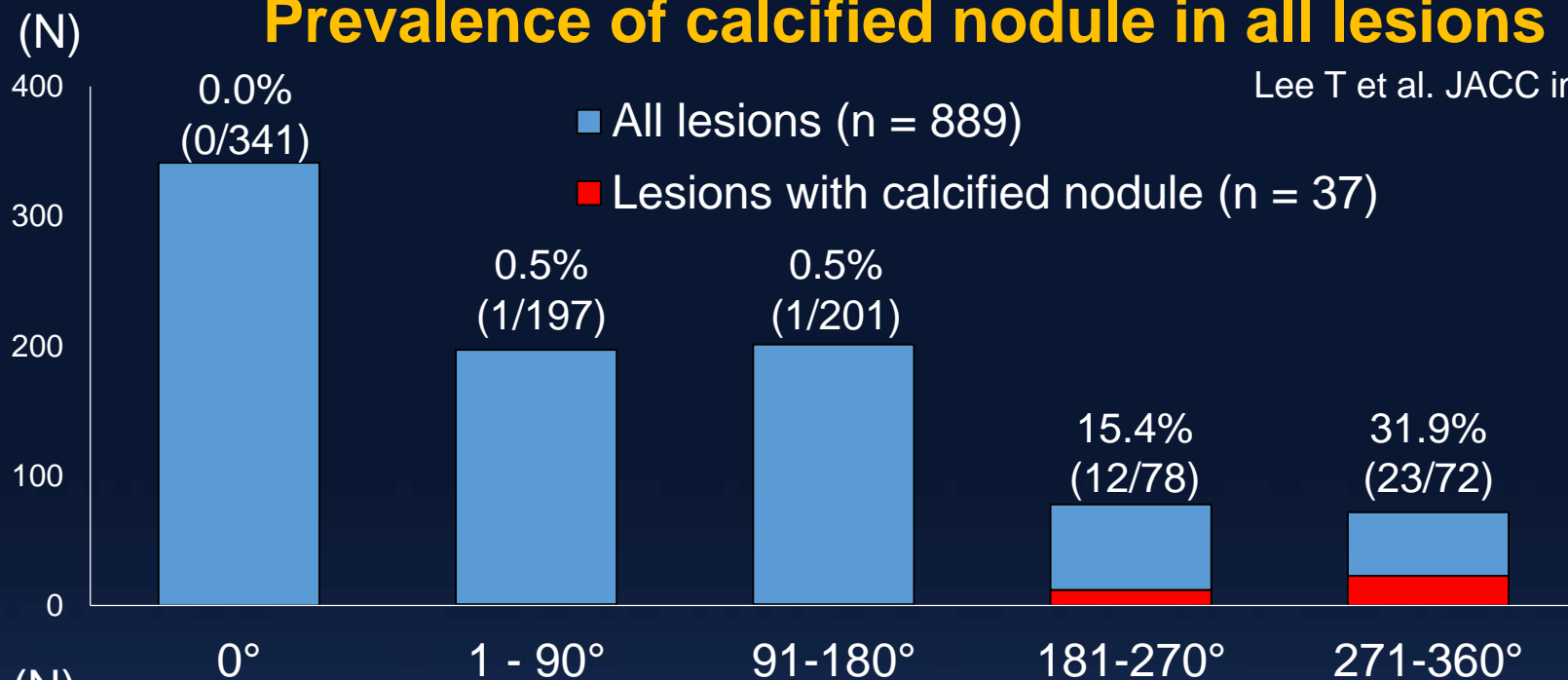
Clinical and Morphological Difference

	Calcified Nodule (n=37)	No Calcified Nodule (n=852)	P Value
Age, yrs	73 (65, 79)	66 (58, 73)	0.001
ACS presentation	45.9%	48.2%	0.79
DM	51.4%	33.3%	0.02
Hemodialysis	18.9%	2.6%	<0.001
Δ Angle in lesion	16 (14, 21)	9 (6, 14)	<0.001
OCT Max Ca angle, °	301 (247, 347)	64 (0, 123)	<0.001
Mean Ca angle, °	166 (134, 202)	48 (0, 81)	<0.001
Max Ca thickness, mm	1.18 (0.94, 1.3)	0.21 (0, 0.75)	<0.001

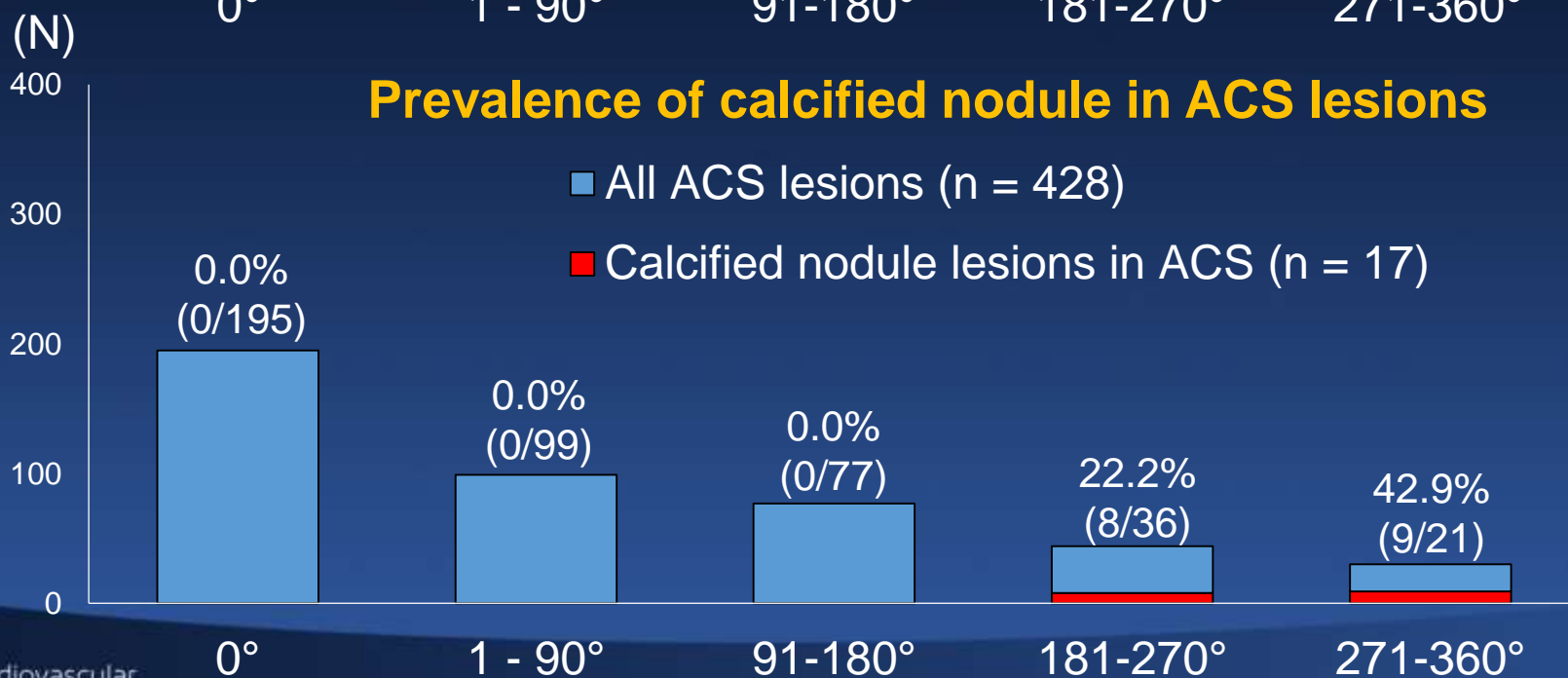
Lee T et al. JACC img 2017;10:833-91.

Prevalence of calcified nodule in all lesions

Lee T et al. JACC img 2017



Prevalence of calcified nodule in ACS lesions



Define Vulnerable Plaque by Imaging

- 1.** The predictors of plaque rupture are large necrotic core with severe stenosis (large plaque burden, positive remodeling).
- 2.** Clinical or anatomical predictors of plaque erosion could be young female, smoking, LAD, and bifurcation. However, the morphological predictors of plaque erosion is unknown.
- 3.** In the very calcified lesions, calcified nodule was found in 43% of ACS lesions.