Current and Future Imaging Diagnosis of Vulnerable Plaque

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Conflict of Interest Disclosure

- Akiko Maehara
  - Personal: Consultant for ACIST, Boston Scientific Corporation, Speaker fee: St Jude Medical
  - Cardiovascular Research Foundation: Boston Scientific Corporation

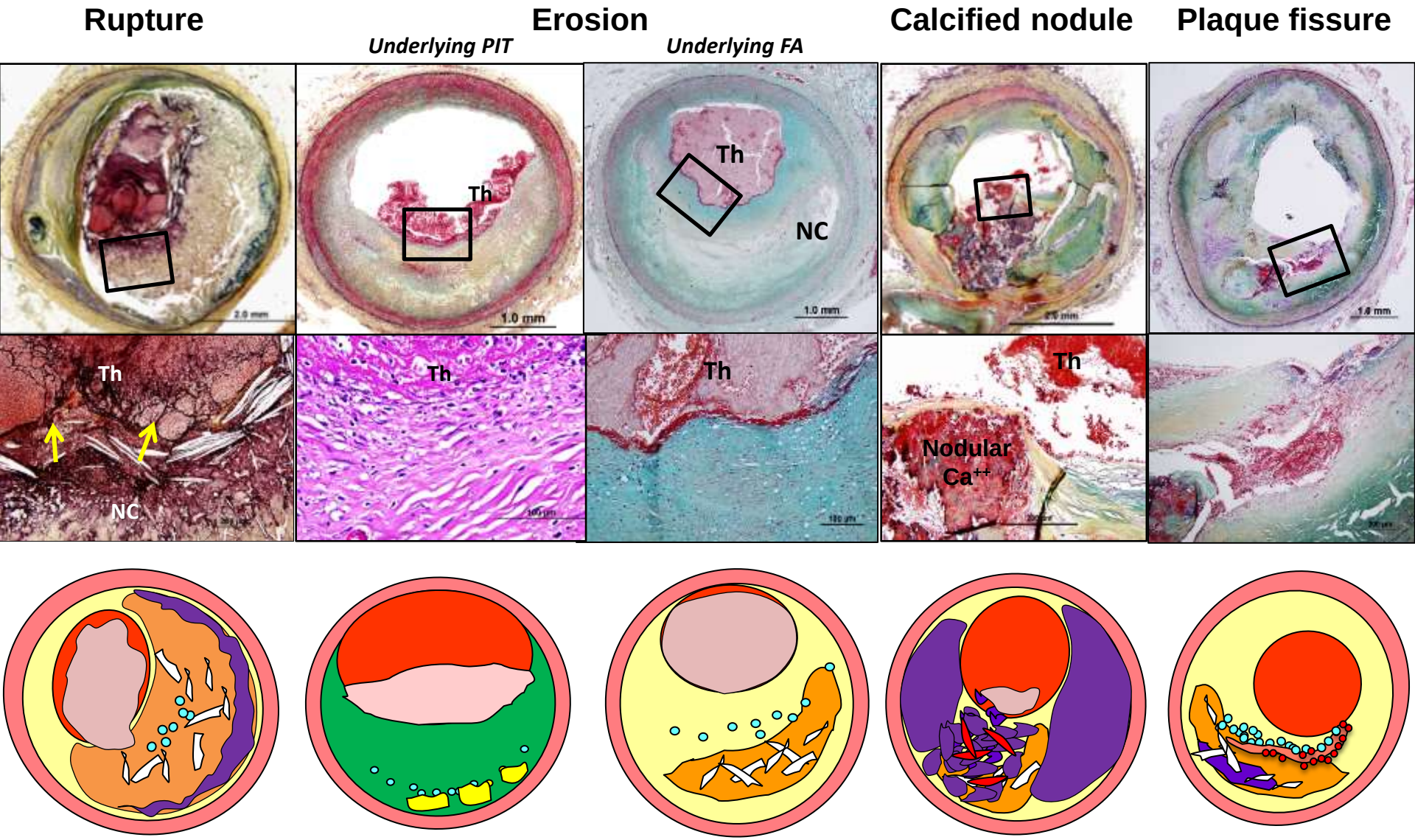
Vulnerable plaque

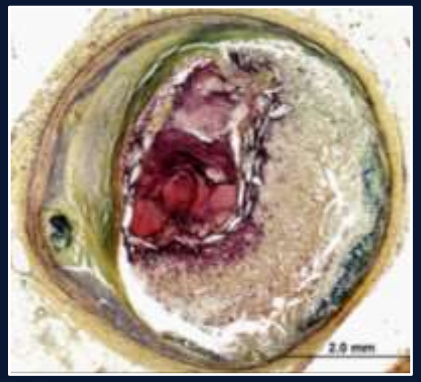
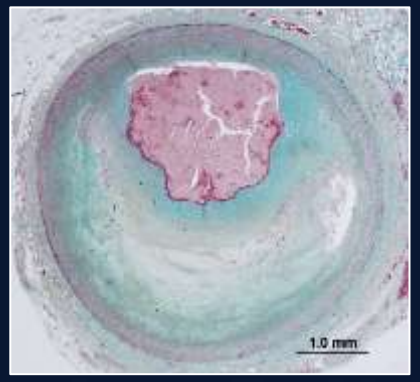
= The lesion which will cause thrombotic event (STEMI, NSTEMI, unstable AP)

Causes of Coronary Thrombosis

Lesions with acute thrombi

Joner M
CRT2015



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

Libby P. et al. Eur Heart J 2015: 36; 2984-7.

Rupture vs Erosion

	Rupture (n=65)	Erosion (n=50)	P-Value
Age	52±10	43±9	<0.0001
Male	89%	74%	0.03
Plaque burden (%)	77±14	71±15	<0.0001
% Necrotic core	38±23	18±24	<0.0001
% Macrophage	3.4±2.8	2.5±2.7	<0.0001
Thrombus age			
Early <1 day	46%	12%	
Lytic 1-3 day	26%	14%	
Infiltrating 4-7 day	19%	28%	
Healing >7day	9%	46%	

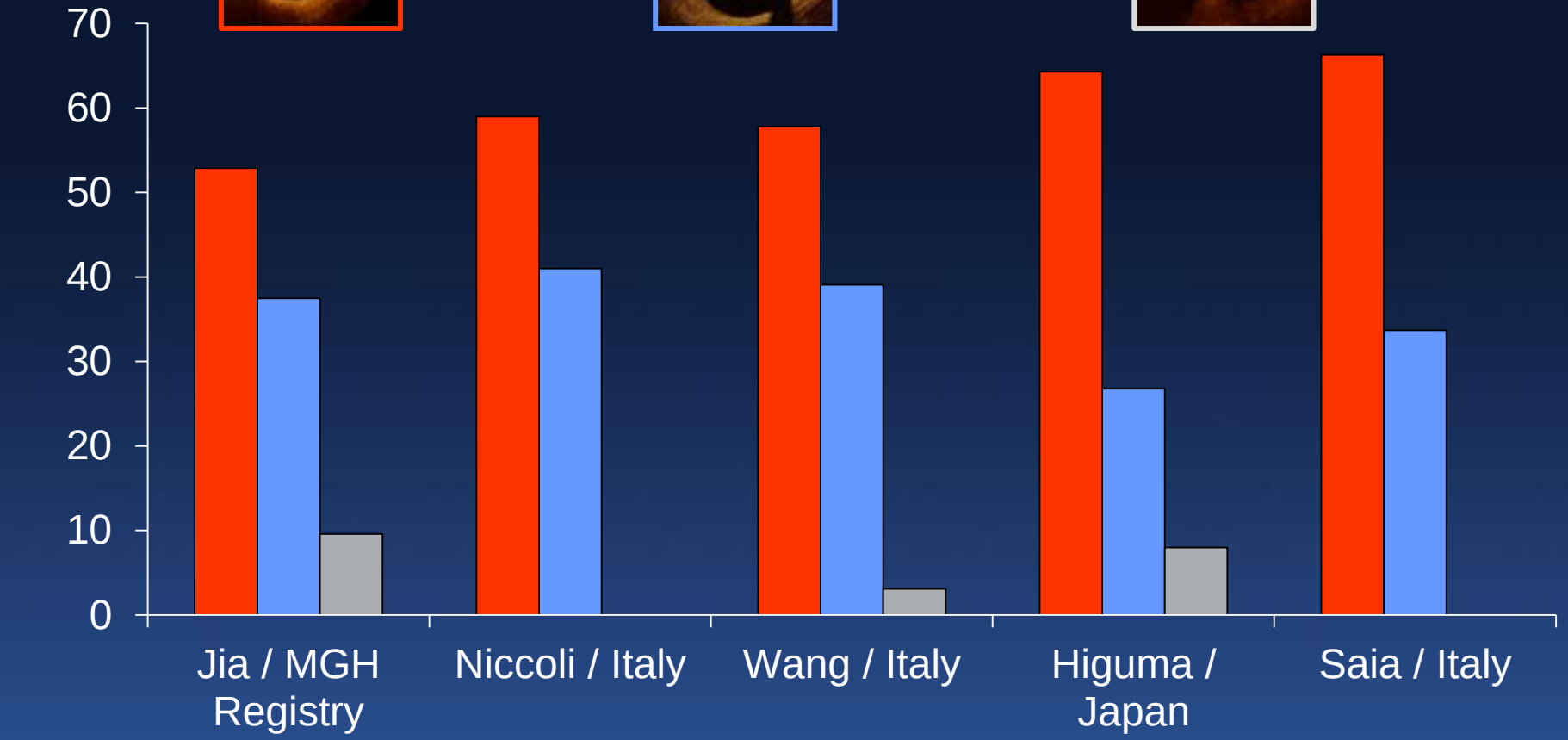
Kramer M. et al. JACC 2010: 55; 122-32.

OCT Defined Underlying Plaque in ACS

Plaque Rupture

No Rupture

Calcified Nodule

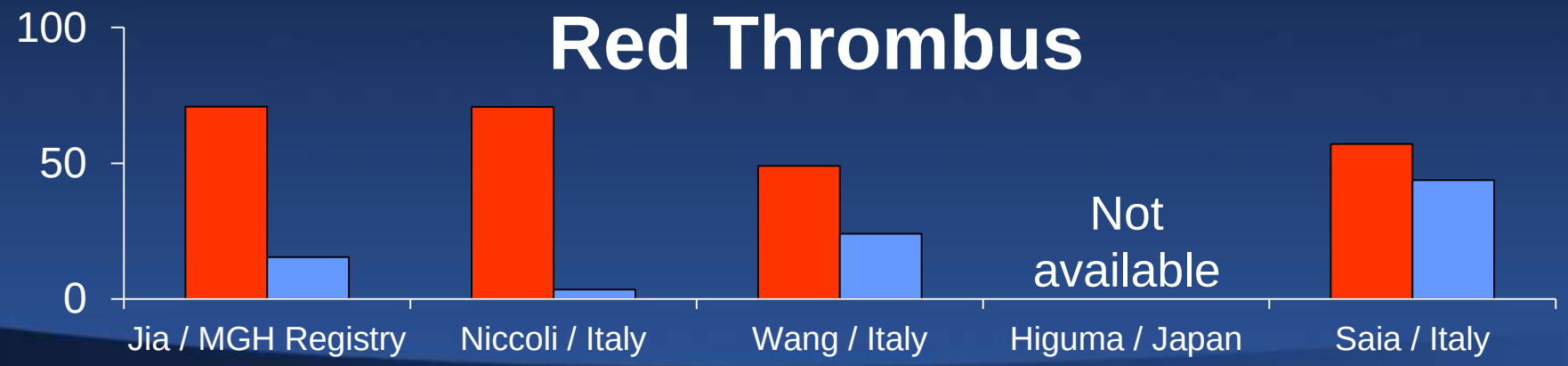


Jia H, et al. JACC 2013;62:1748-58. Niccoli G et al. EHJ 2015; 36:1377-84.Wang L et al. EHJI 2015 doi:10.1093/ehjc.jev105 Higuma T et al. JACC Interv 2015;8:1166-76. Saia JACC Img 2015; 8: 566-75.

Difference of Morphology

Plaque Rupture

No Rupture



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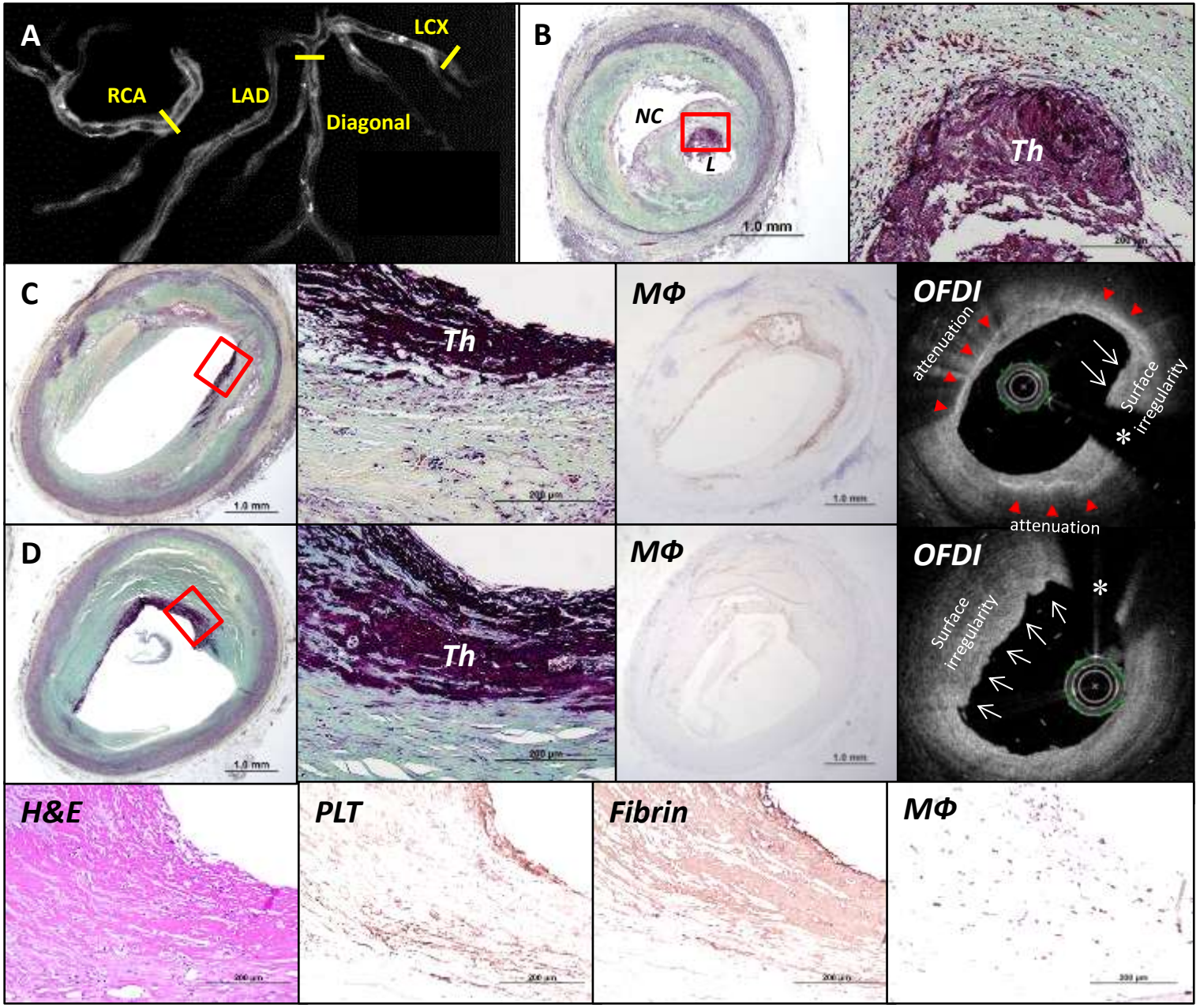
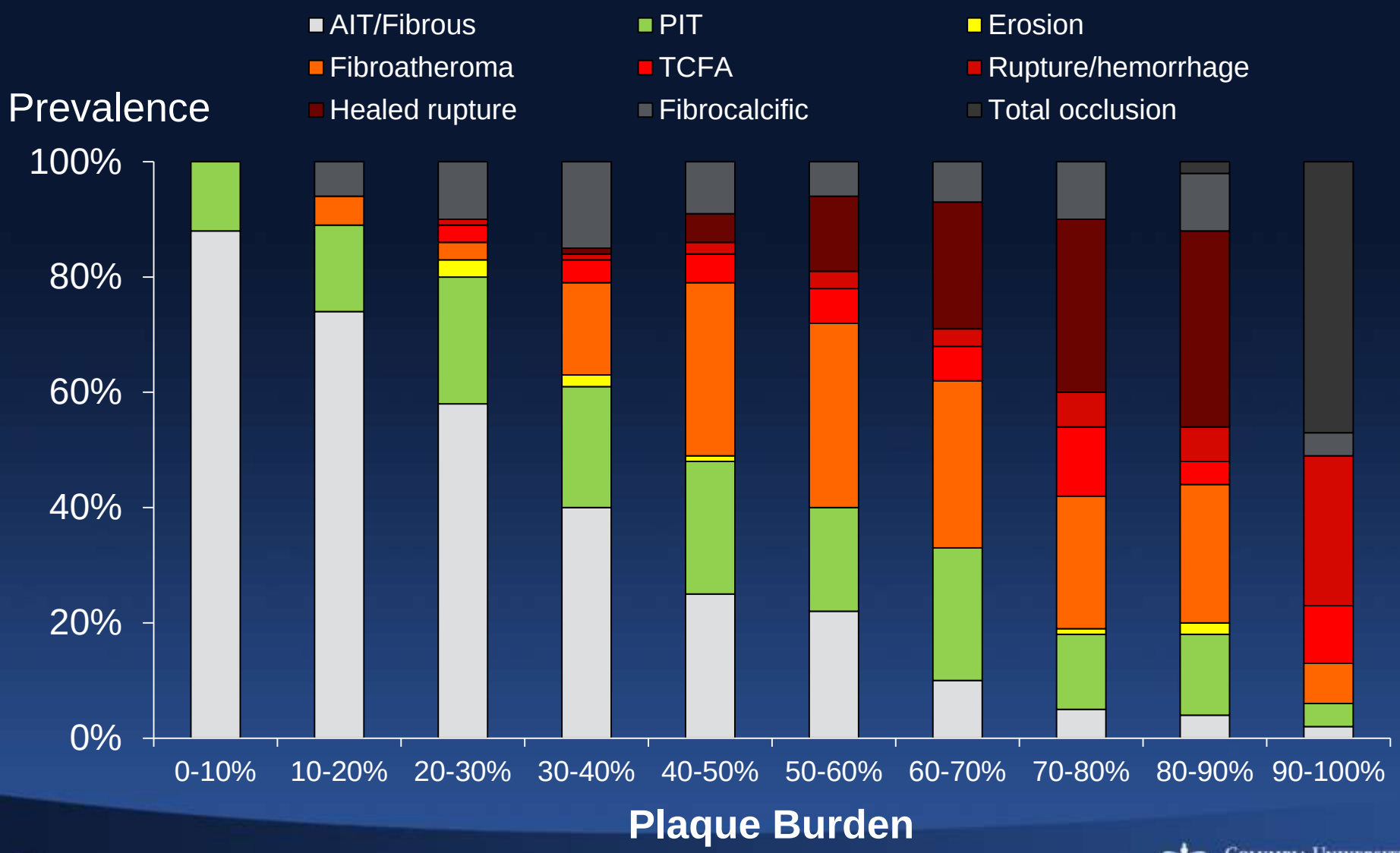
Erosion - Thrombus in the Absence of Rupture -



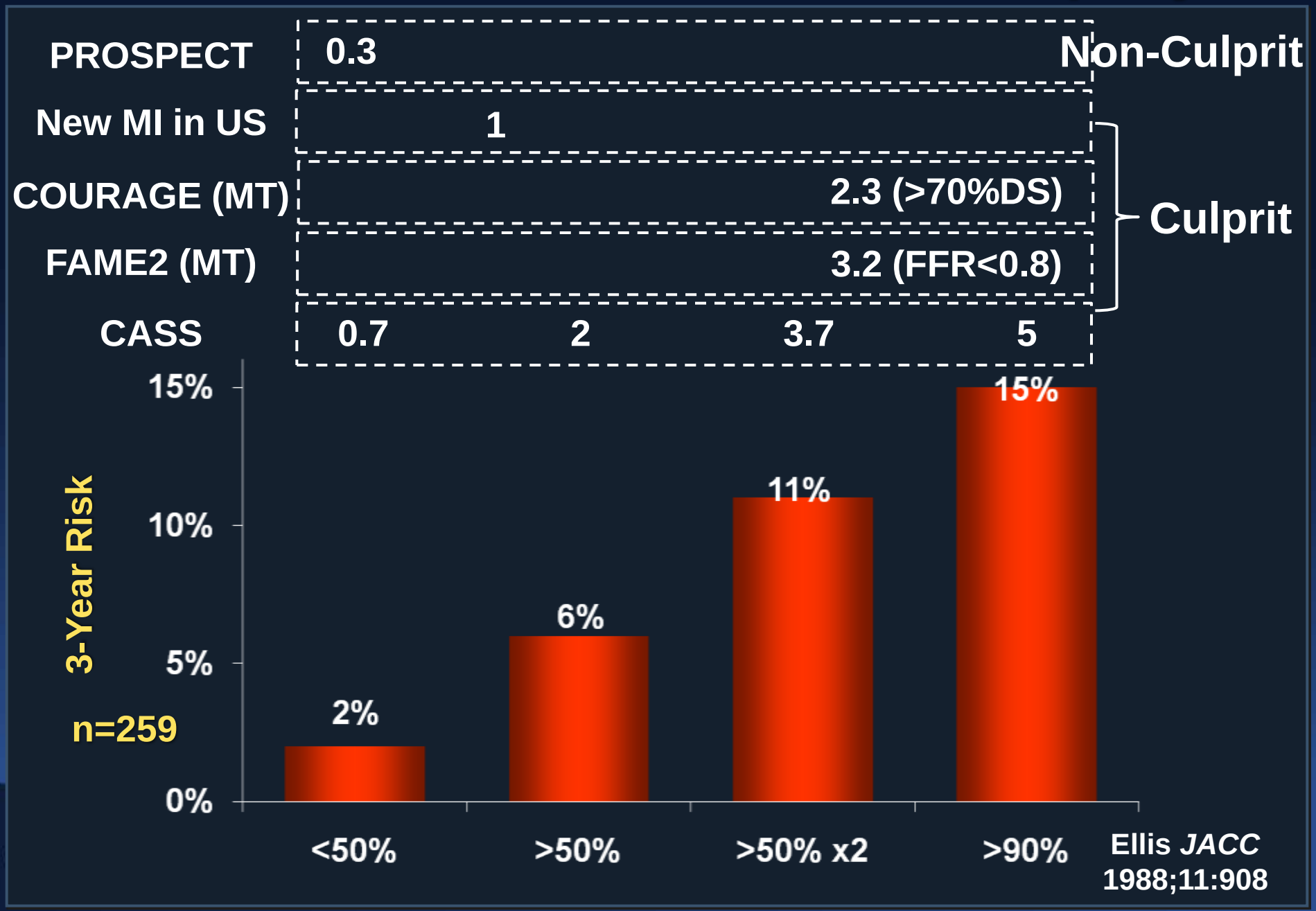
Joner M
CRT2015

Lesion Morphology and Plaque Burden in Pathology

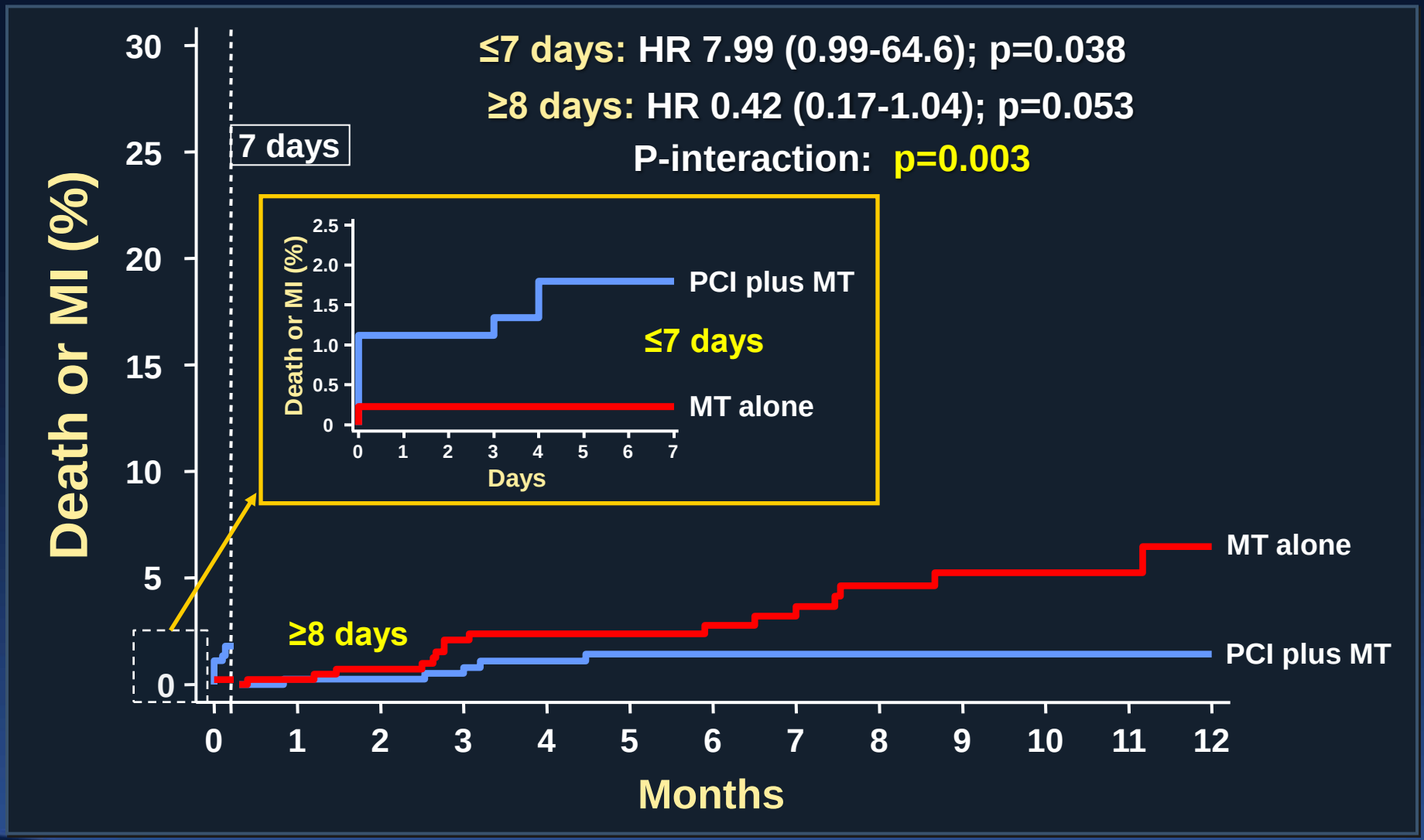


Otsuka F, et al. ATVB 2014; 34:724-36.

Difference of the Incidence of MI/100 pts/year

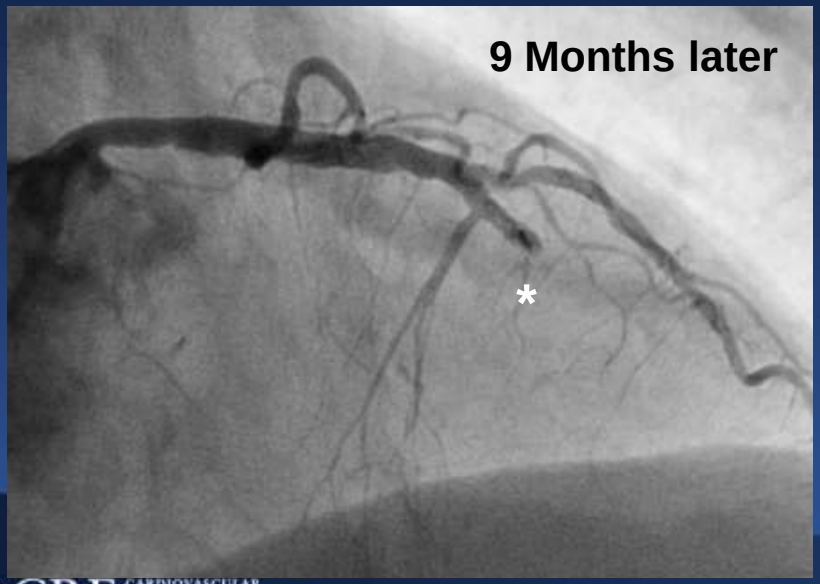


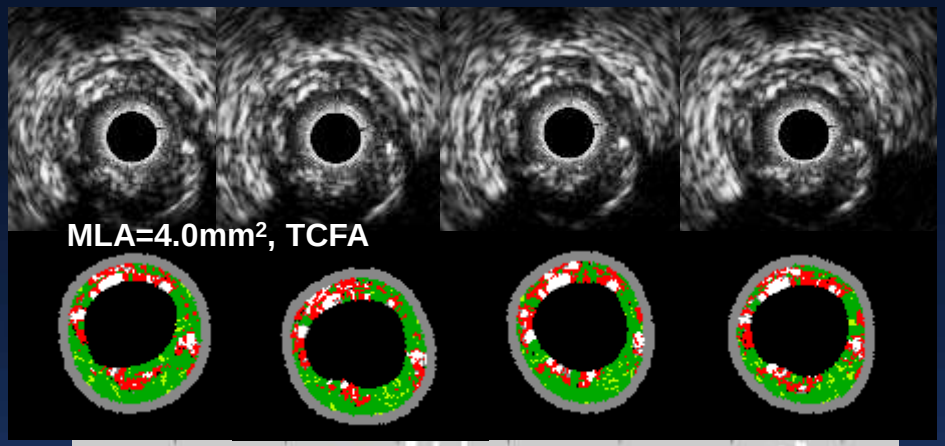
FAME 2: Landmark Analysis of Death or MI

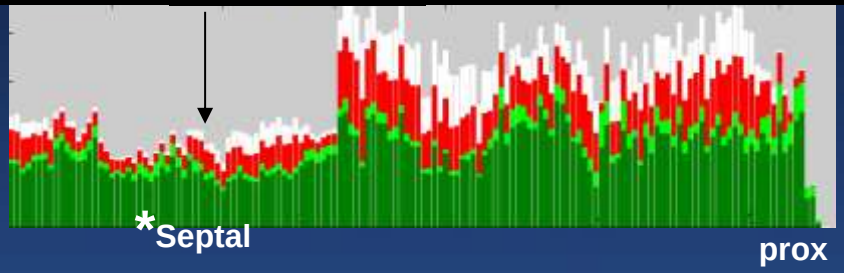


De Bruyne B et al. NEJM 2012:367:991-1001

A PROSPECT Case







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The PROSPECT Trial

700 pts with ACS

UA (with ECGΔ) or NSTEMI or STEMI >24º 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

PCI of culprit lesion(s)

Successful and uncomplicated

Formally enrolled

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

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PI: Gregg W. Stone
Sponsor: Abbott Vascular; Partner: Volcano

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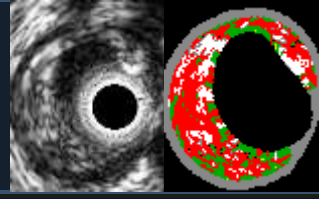
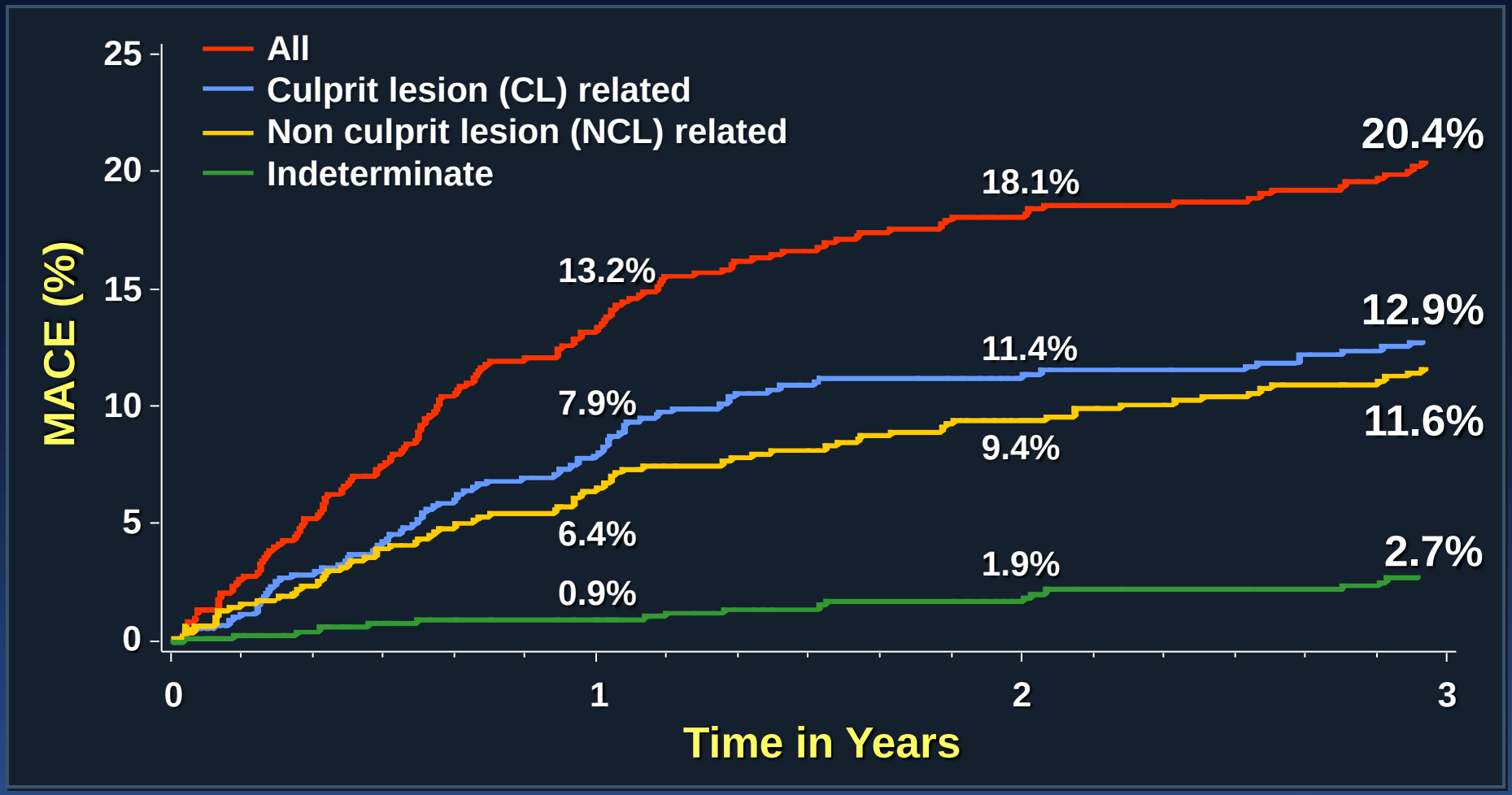
PROSPECT: MACE





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

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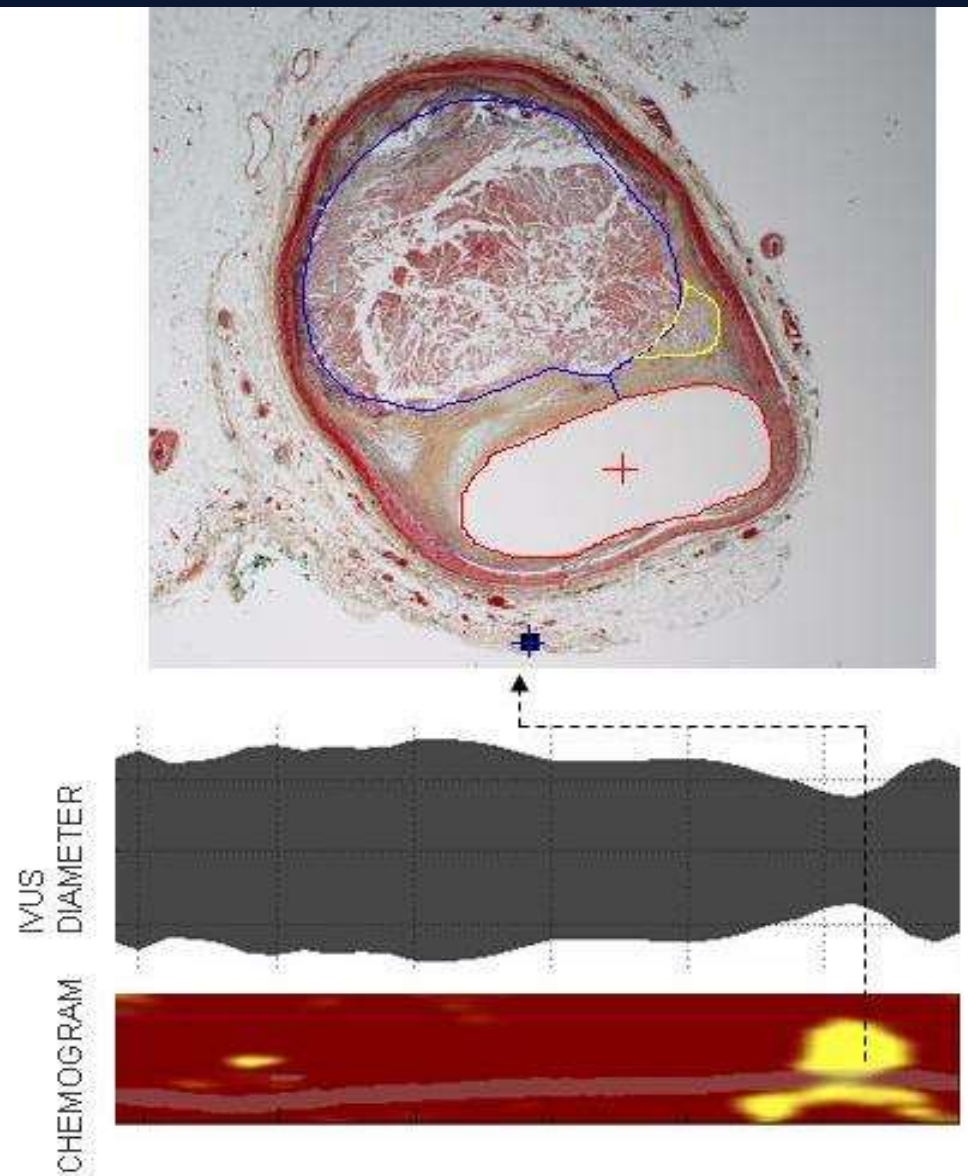
PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

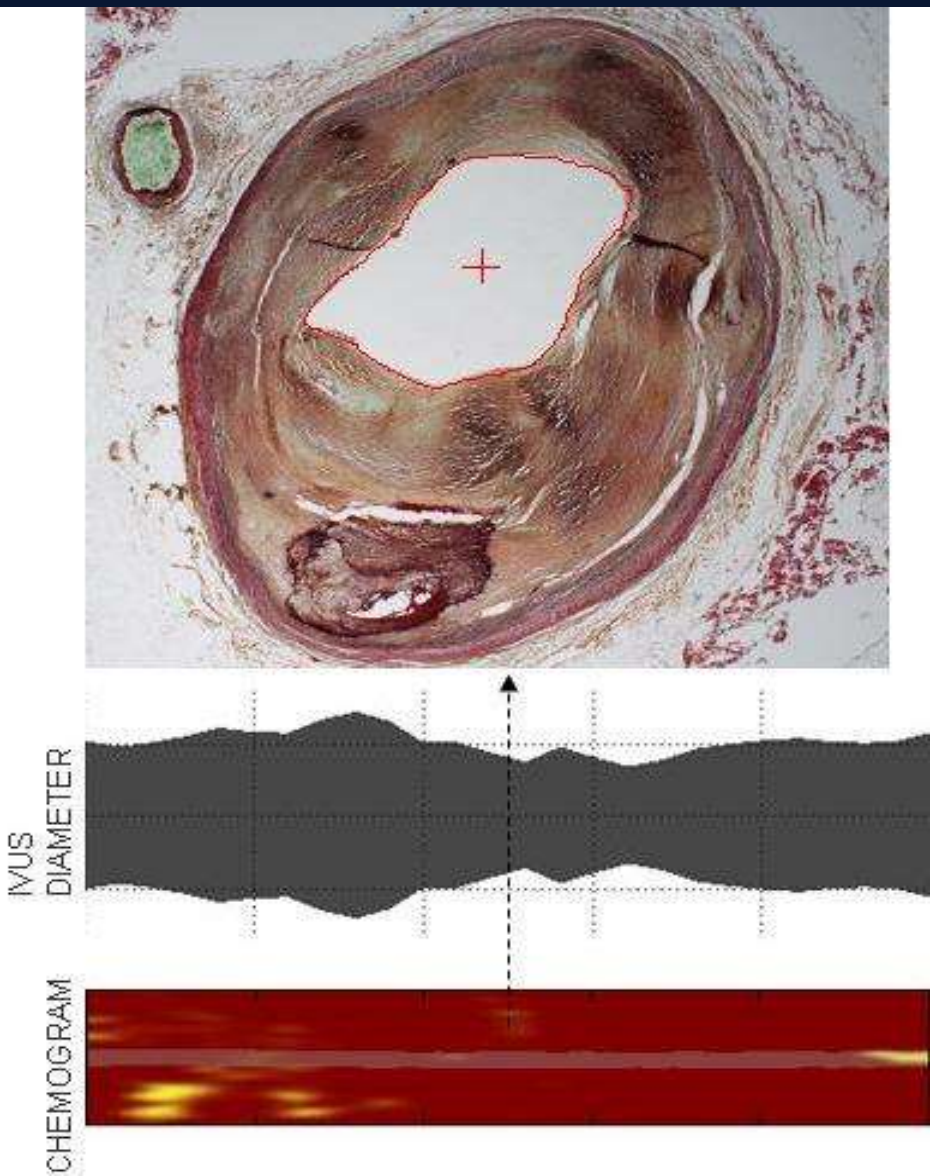
Independent predictors of lesion level events by Cox Proportional Hazards regression

Variable	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

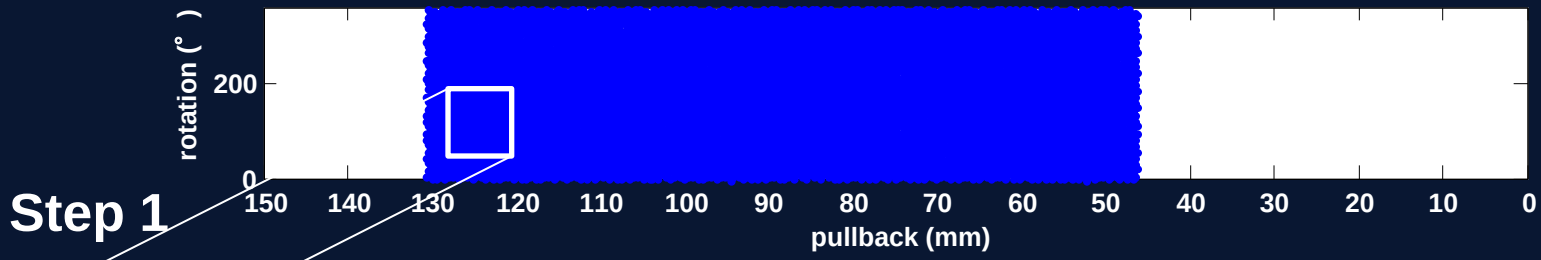
Variables entered into the model: minimal luminal area (MLA) ≤4.0 mm^2; plaque burden at the MLA (PB_{MLA}) ≥70%; external elastic membrane at the MLA (EEM_{MLA}) <median (14.1 mm^2); lesion length ≥median (11.2 mm); distance from ostium to MLA ≥median (30.4 mm); remodeling index ≥median (0.94); VH-TCFA.

NIR can Distinguish Lipid-rich from Fibrotic Plaques

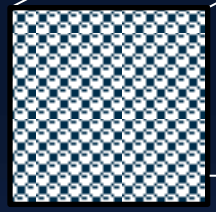




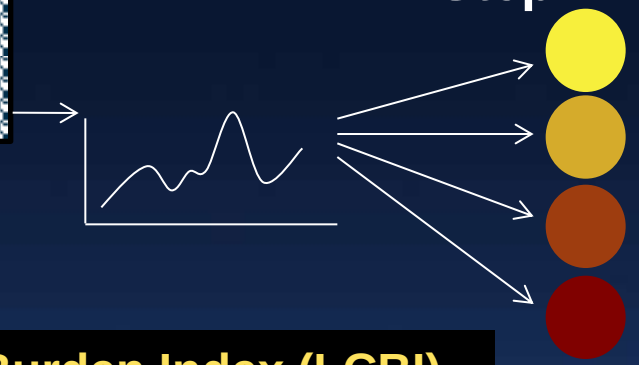
Near Infrared Spectroscopy

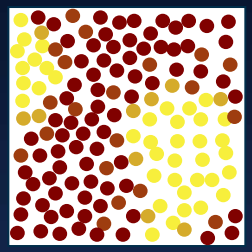


Step 1

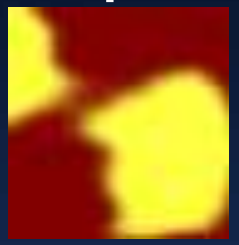


Step 2





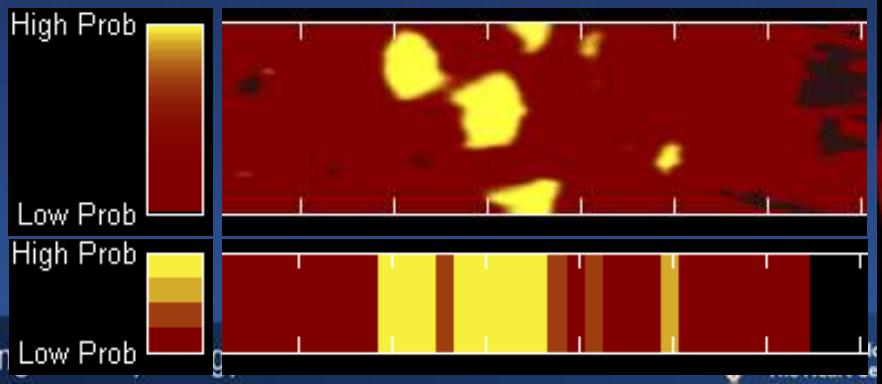
Step 3

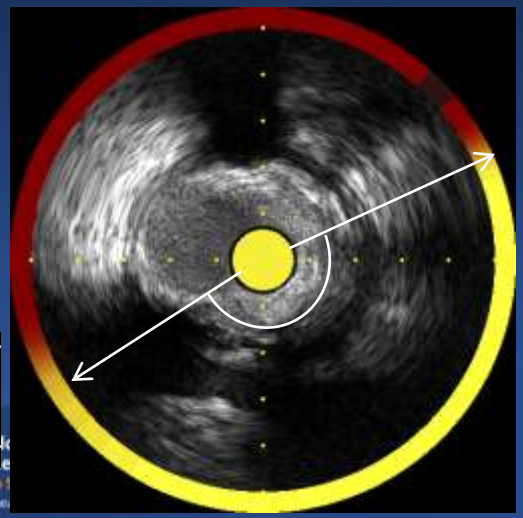


Lipid Core Burden Index (LCBI)
=Yellow pixel /All variable pixel
×1000

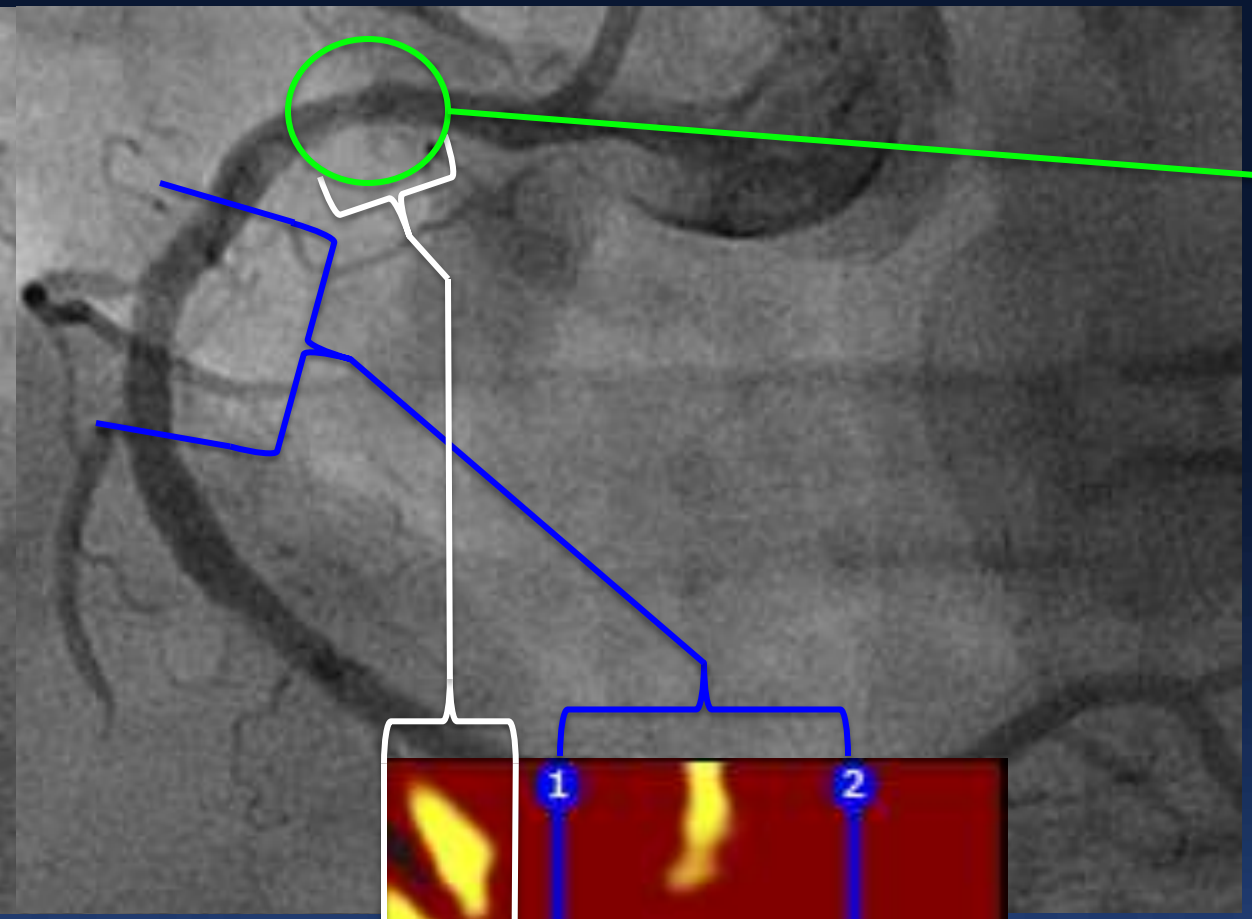
Lesion

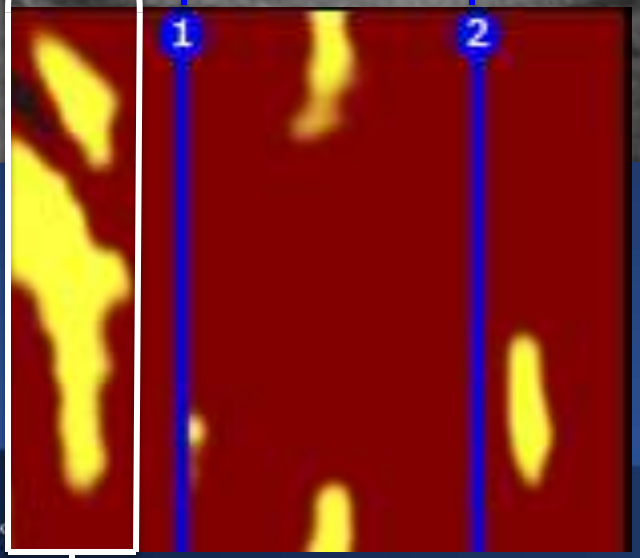
LCBI Max$_{4mm}$





64 year old presents with STEMI in March 2012 → Unstable angina October 2012





maxLCBI$_{4mm}$
694

Madder R et al. Eur Heart J Img; 2016, doi:10,1093/ehjci/jev340

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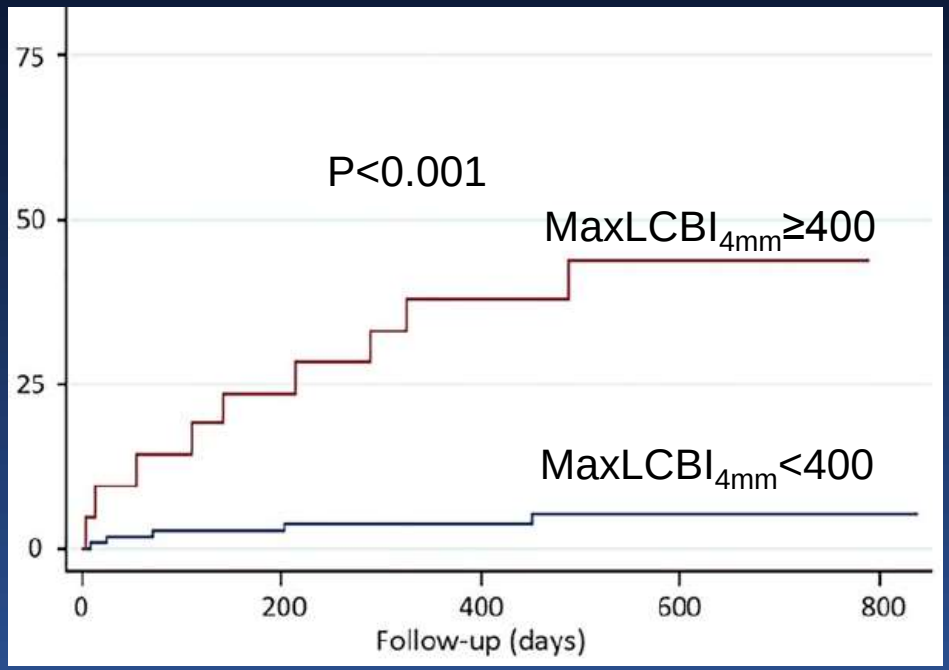
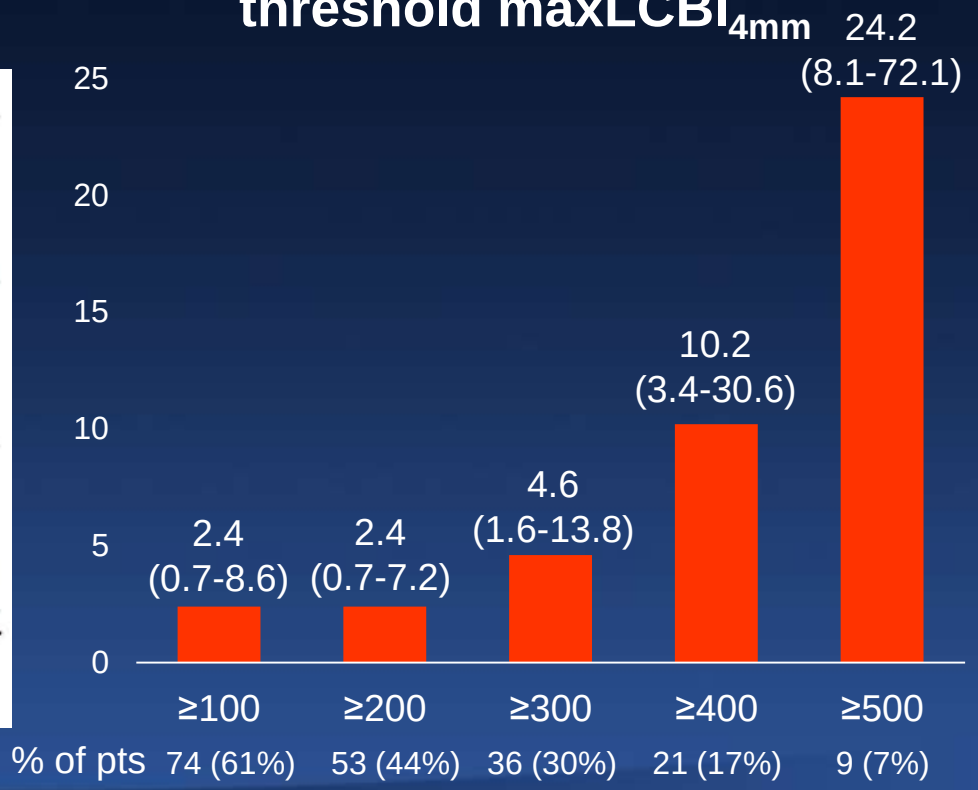
Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

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

MACCE in 2 years



Hazard ratios for various threshold maxLCBI$_{4mm}$



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Madder R et al. Eur Heart J Img; 2016, doi:10,1093/ehjci/jev340

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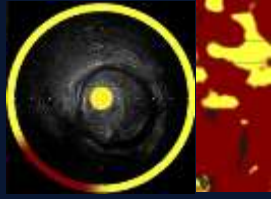
PROSPECT II Study



900 pts with ACS at up to 20 hospitals in Sweden, Denmark and Norway (SCAAR)

NSTEMI or STEMI >12º

IVUS + NIRS (blinded) performed in culprit vessel(s)

Successful PCI of all intended lesions (by angio ±FFR/iFR)

↓

Formally enrolled

↓

3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS + NIRS (blinded) (prox 6-8 cm of each coronary artery)

↓

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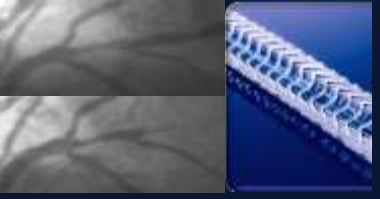
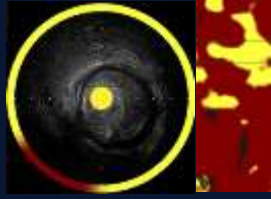


PROSPECT II Study
PROSPECT ABSORB RCT



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 1:1

ABSORB BVS + GDMT (N~150)

GDMT (N=150)

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

Clinical FU for ≥3 years

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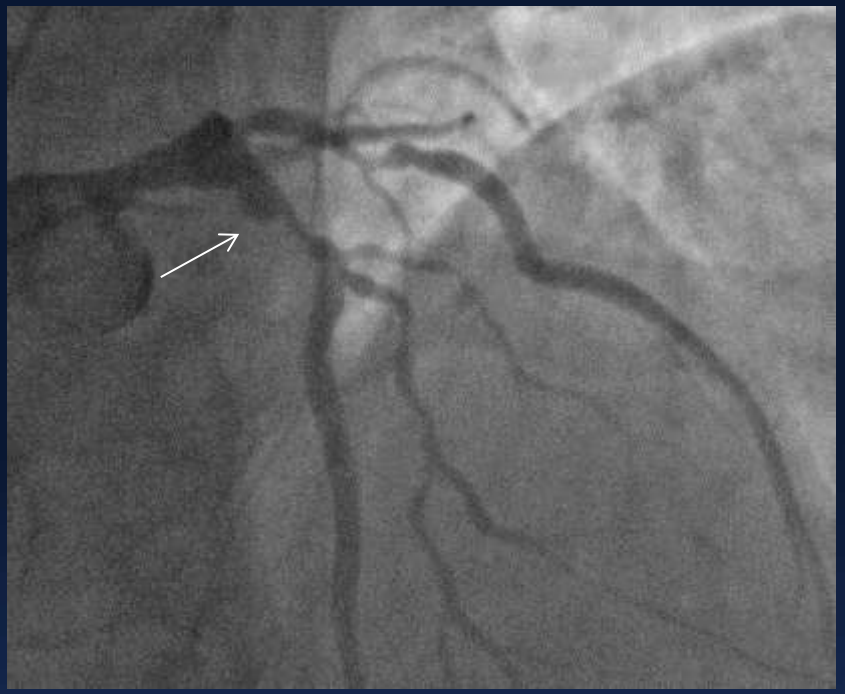
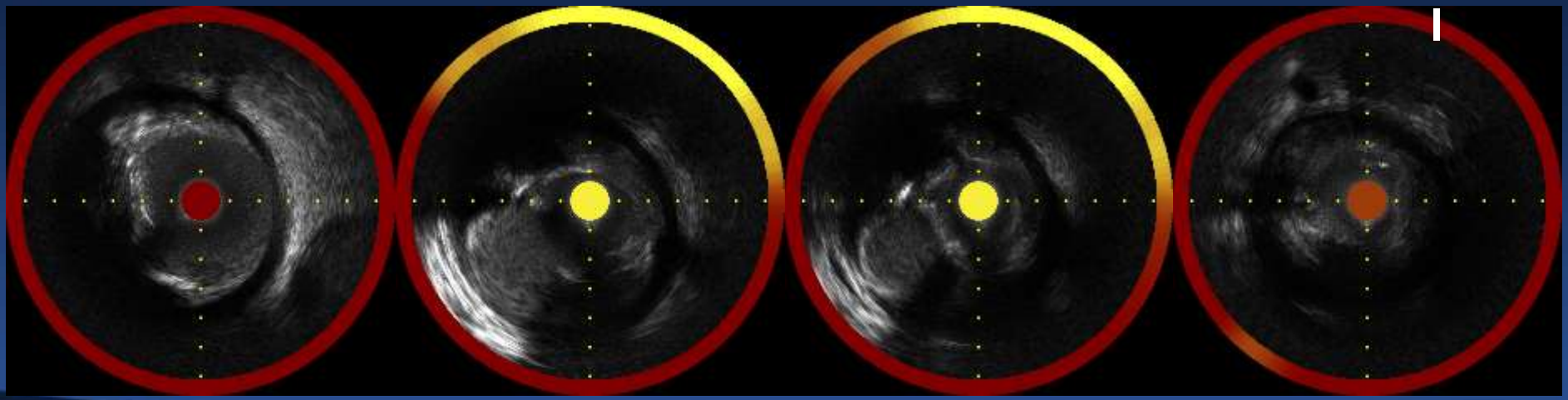
High definition IVUS

InfraReDx: 50MHz

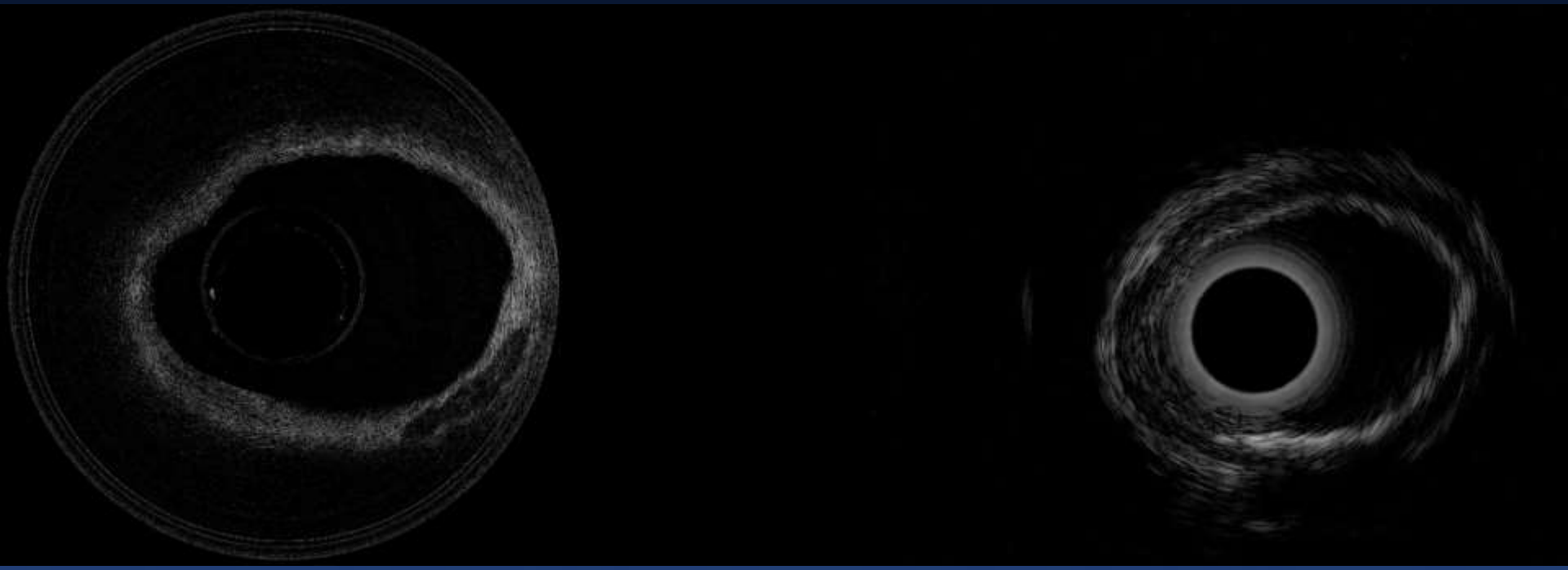


proximal

dista



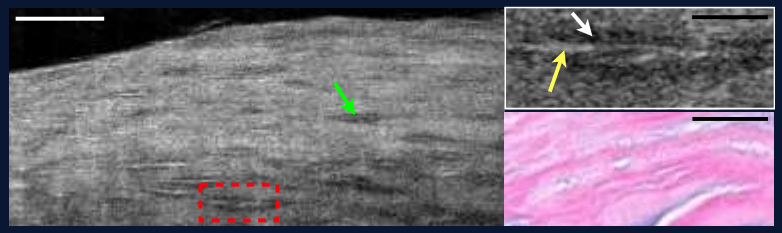
OCT/IVUS Combined Catheter



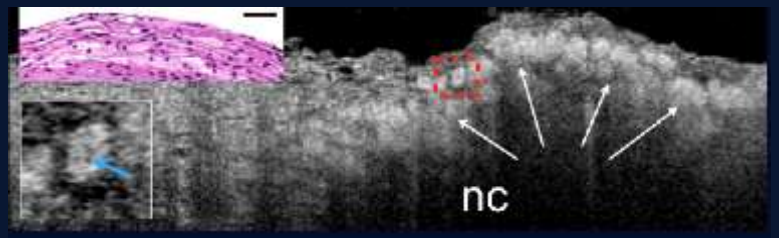
Courtesy for Pranav Patel & Zhongping Chen University of California, Irvine; Ram Ramalingam OCT Medical Imaging Inc.

μOCT with <1-2 Micron Resolution

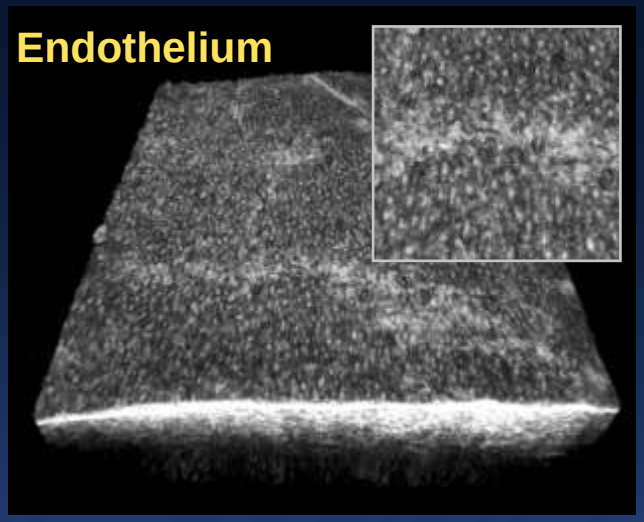
Smooth Muscle Cells



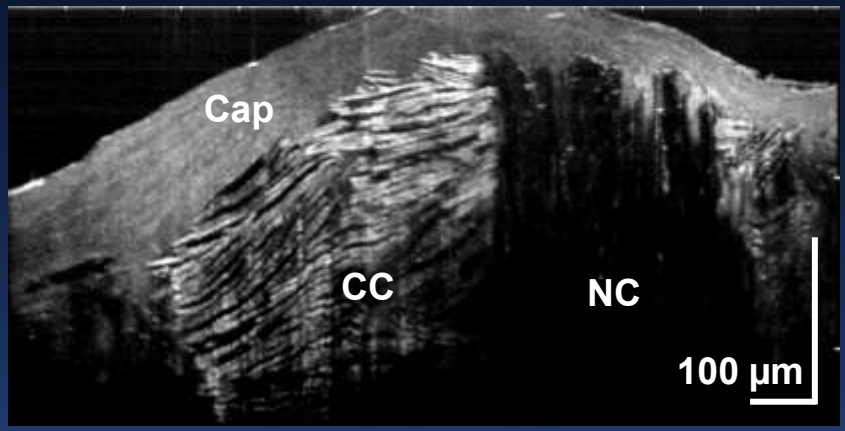
Macrophages



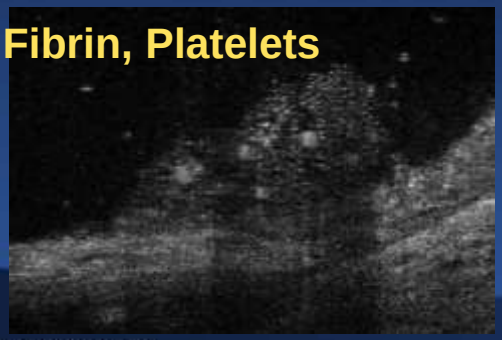
Endothelium



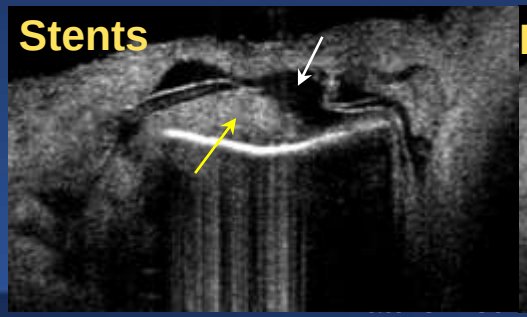
Necrotic Core Cholesterol Crystals



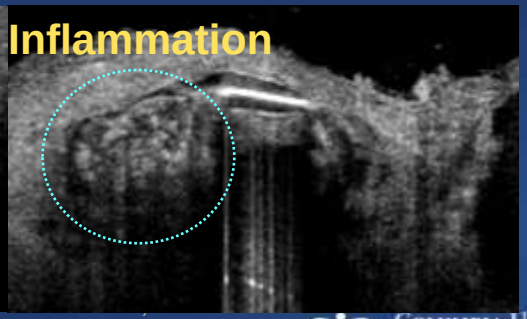
Fibrin, Platelets



Stents



Inflammation



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Tearney, G Nat Med 17: 1010-14, 2012

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Summary

1. Vulnerable plaque can be defined as a lesion with large plaque burden, severe stenosis, and thin cap fibroatheroma.
2. Further understanding is needed for prediction of erosive thrombosis and natural history of vulnerable plaque.
3. High definition IVUS, OCT (micro OCT) and OCT/IVUS combined catheter may contribute the better detection of vulnerable plaque.