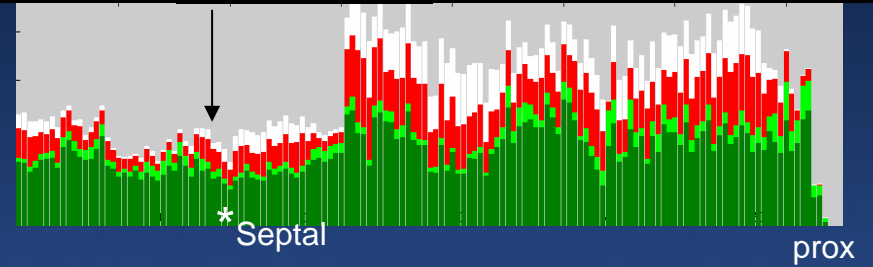
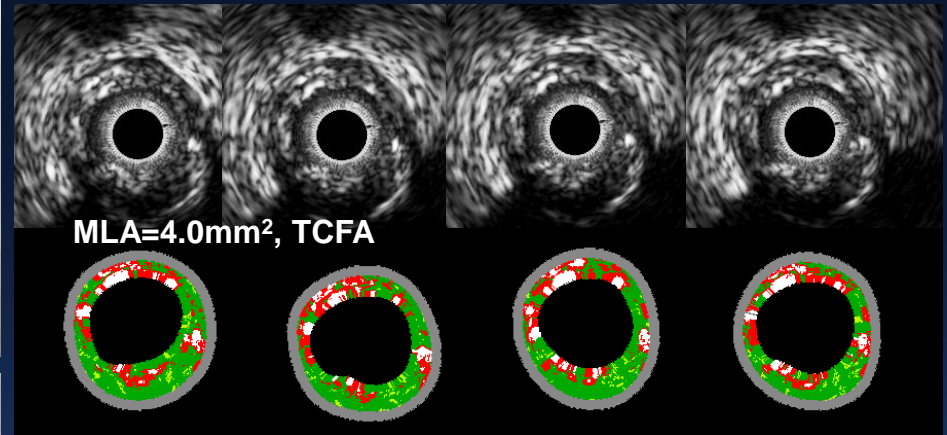
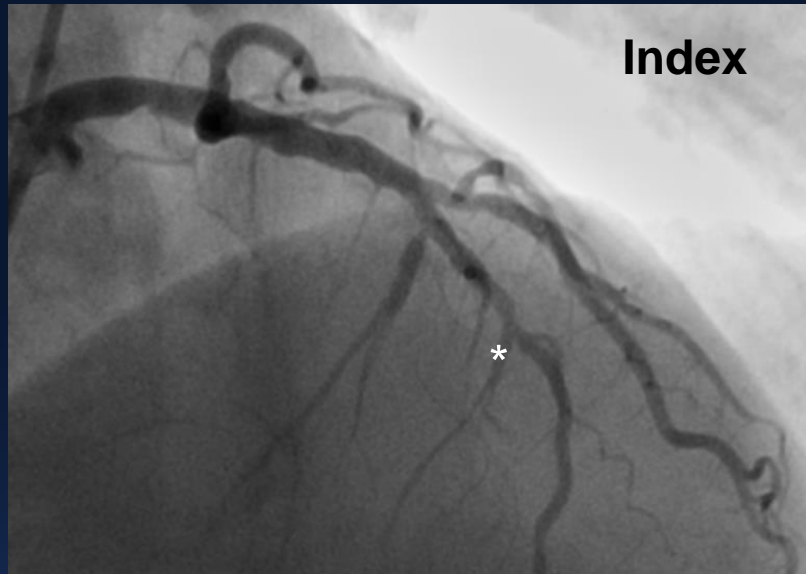


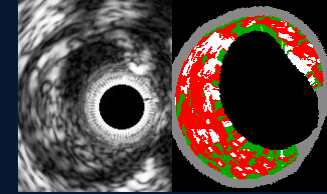
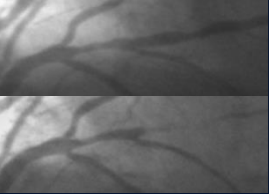
# **NIRS: PROPSCT II and PROSPECT ABSORB Trial**

***Akiko Maehara, MD***

**Cardiovascular Research Foundation  
Columbia University Medical Center  
New York City, NY**

# A PROSPECT Case





# PROSPECT Study

700 pts with ACS

3-vessel imaging post PCI

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n= $\sim$ 350)

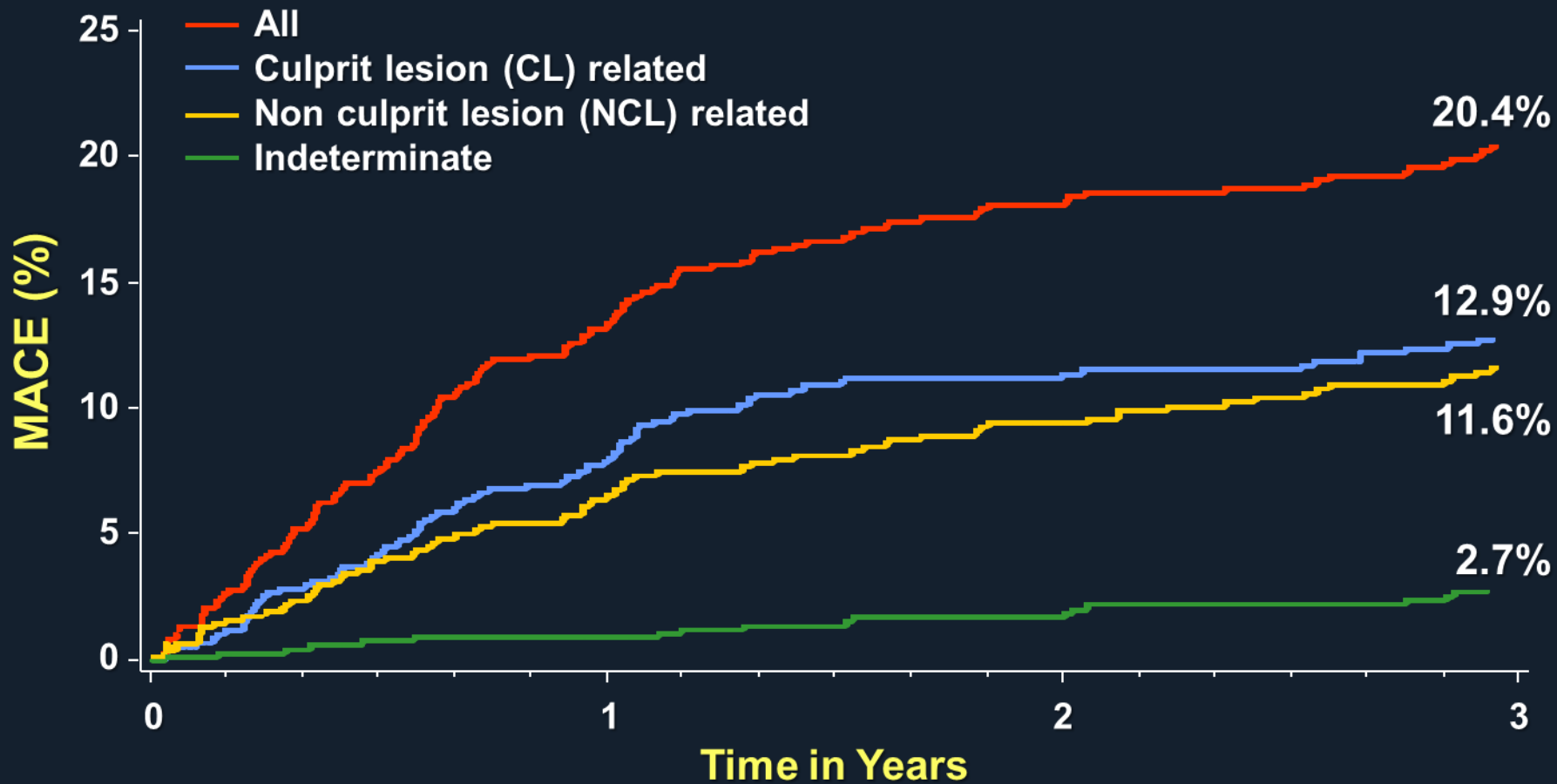
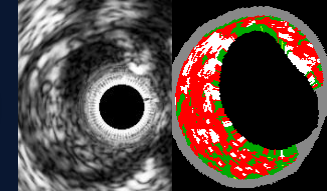
Proximal 6-8 cm of each coronary artery

Meds rec  
Aspirin  
Plavix 1yr  
Statin  
Repeat biomarkers  
@ 30 days, 6 months

F/U: 1 mo, 6 mo,  
1 yr, 2 yr,  
 $\pm$ 3-5 yrs

MSCT  
Substudy  
N=50-100  
Repeat imaging  
in pts with events

# PROSPECT: MACE (N=697)



## 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

Stone GW et al. NEJM 2011;364:226-35

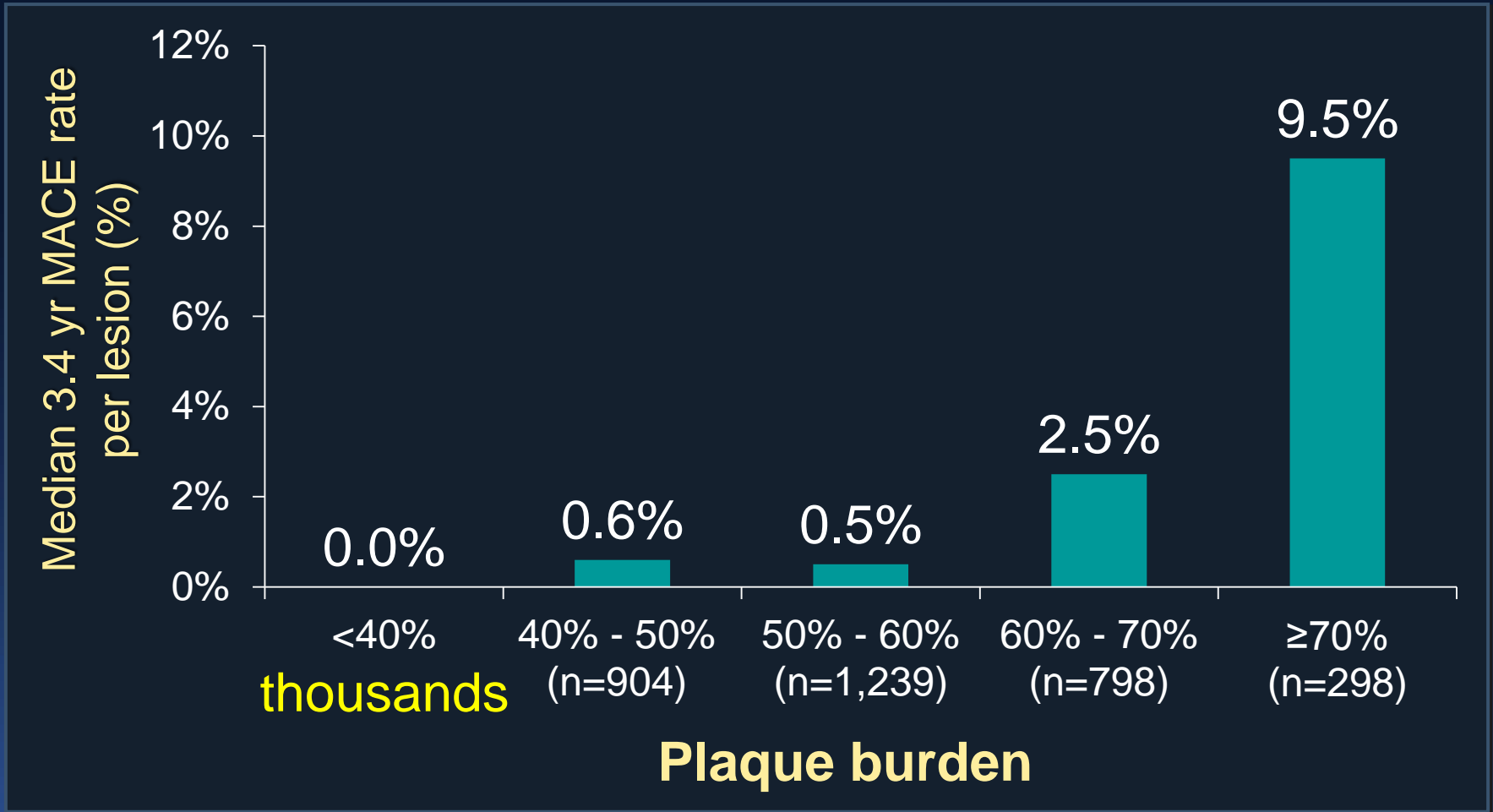
# PROSPECT: Multivariable Correlates of Non-Culprit Lesion Related Events

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:** minimal lumen area (MLA), plaque burden at the MLA, external elastic membrane at the MLA, lesion length, distance from the coronary ostium to the MLA, remodeling index, thin-cap fibroatheroma, insulin-requiring diabetes and prior percutaneous coronary intervention

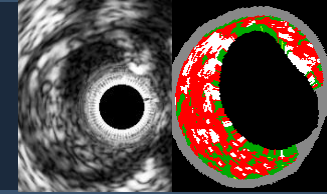
# PROSPECT: Correlates of Non-culprit Lesion Related Events: Impact of plaque burden



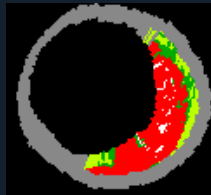
➔ 31.3% of patients had  $\geq 1$  lesion with PB  $\geq 70\%$



# PROSPECT: NCL events arising from stenoses with PB $\geq 70\%$

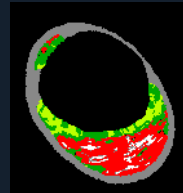


Thin-cap fibroatheroma



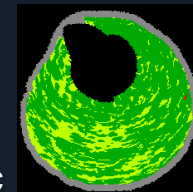
HR (95%CI) =  
10.83 (5.55, 21.10)  
 $P < 0.0001$

Thick-cap fibroatheroma



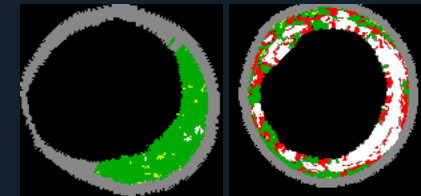
HR (95%CI) =  
5.17 (2.59, 10.32)  
 $P < 0.0001$

Pathologic intimal thickening



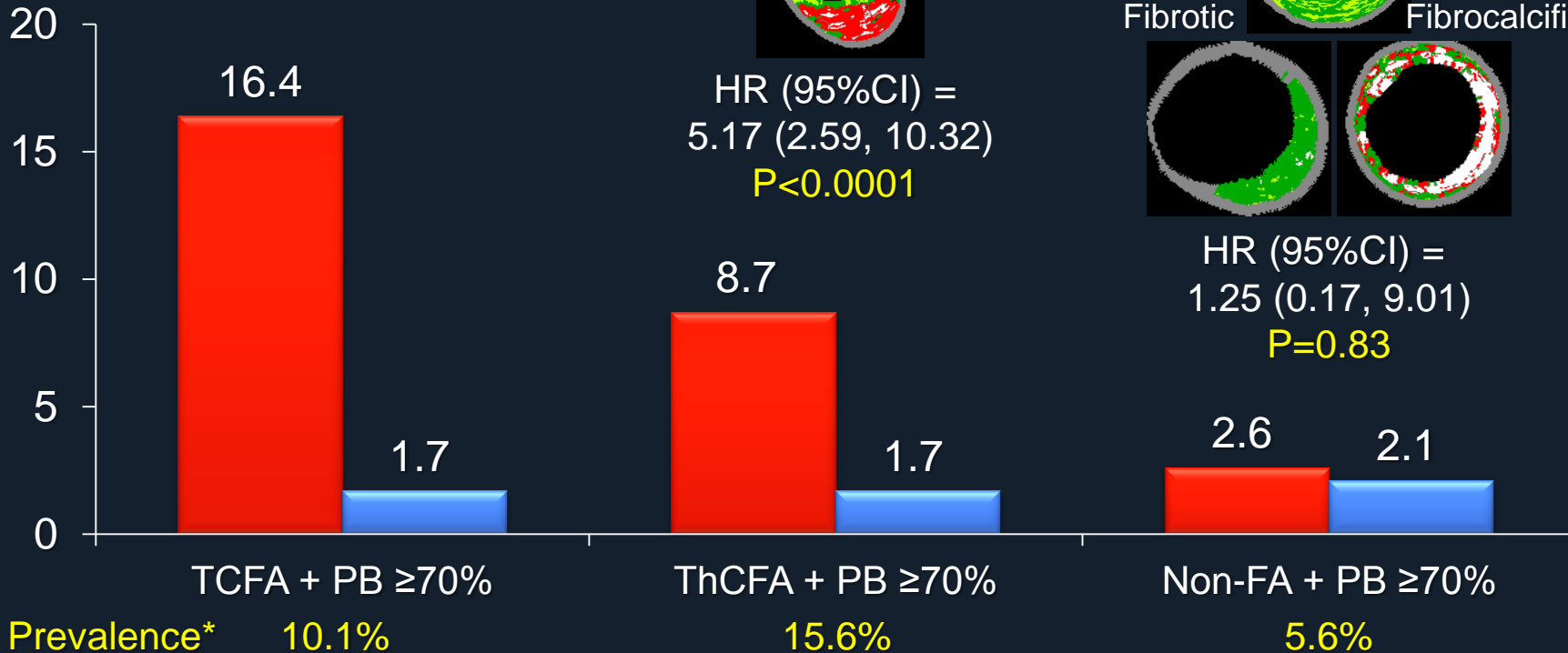
Fibrotic

Fibrocalcific



HR (95%CI) =  
1.25 (0.17, 9.01)  
 $P = 0.83$

Median 3 .4 Yr MACE Rate  
per Isn (%)



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

# PRAMI - Enrollment -

2428 STEMI pts screened

1922 not eligible  
1122 single vessel disease  
269 non-infarct artery unsuitable for PCI  
118 left main disease  
Others

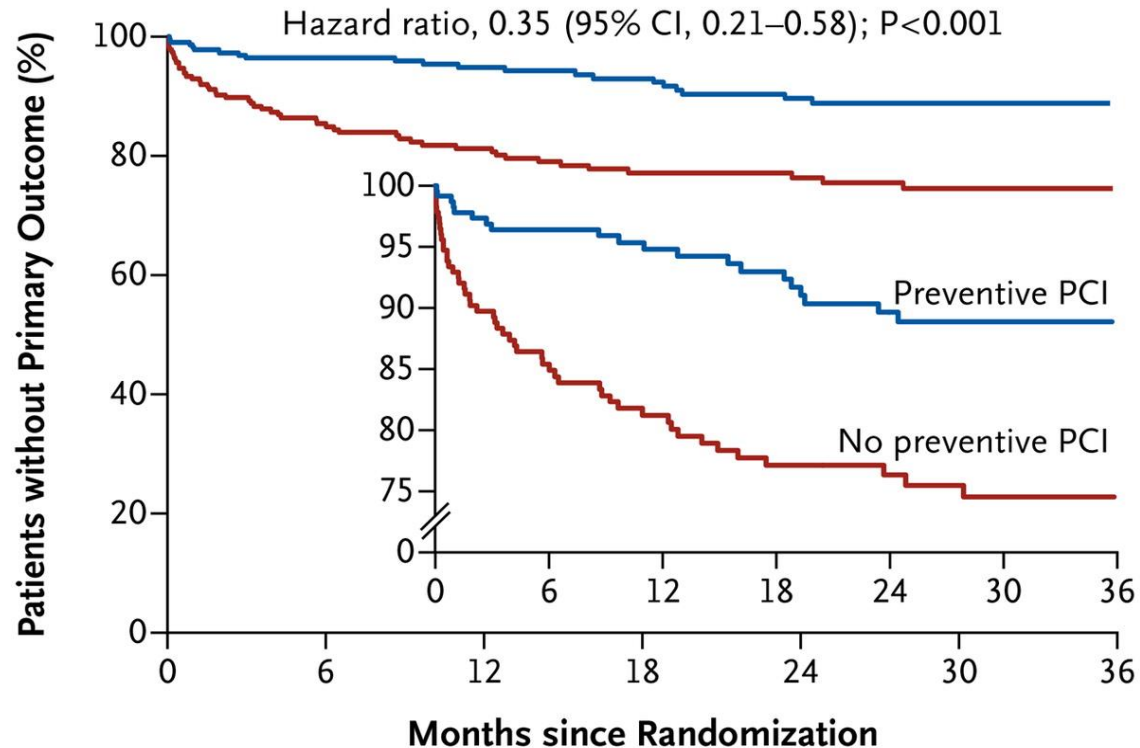
465 randomization

234 Prevention PCI

231 Non-Prevention PCI



# Kaplan–Meier Curves for the Primary Outcome (Cardiac Death, MI, Refractory Angina)

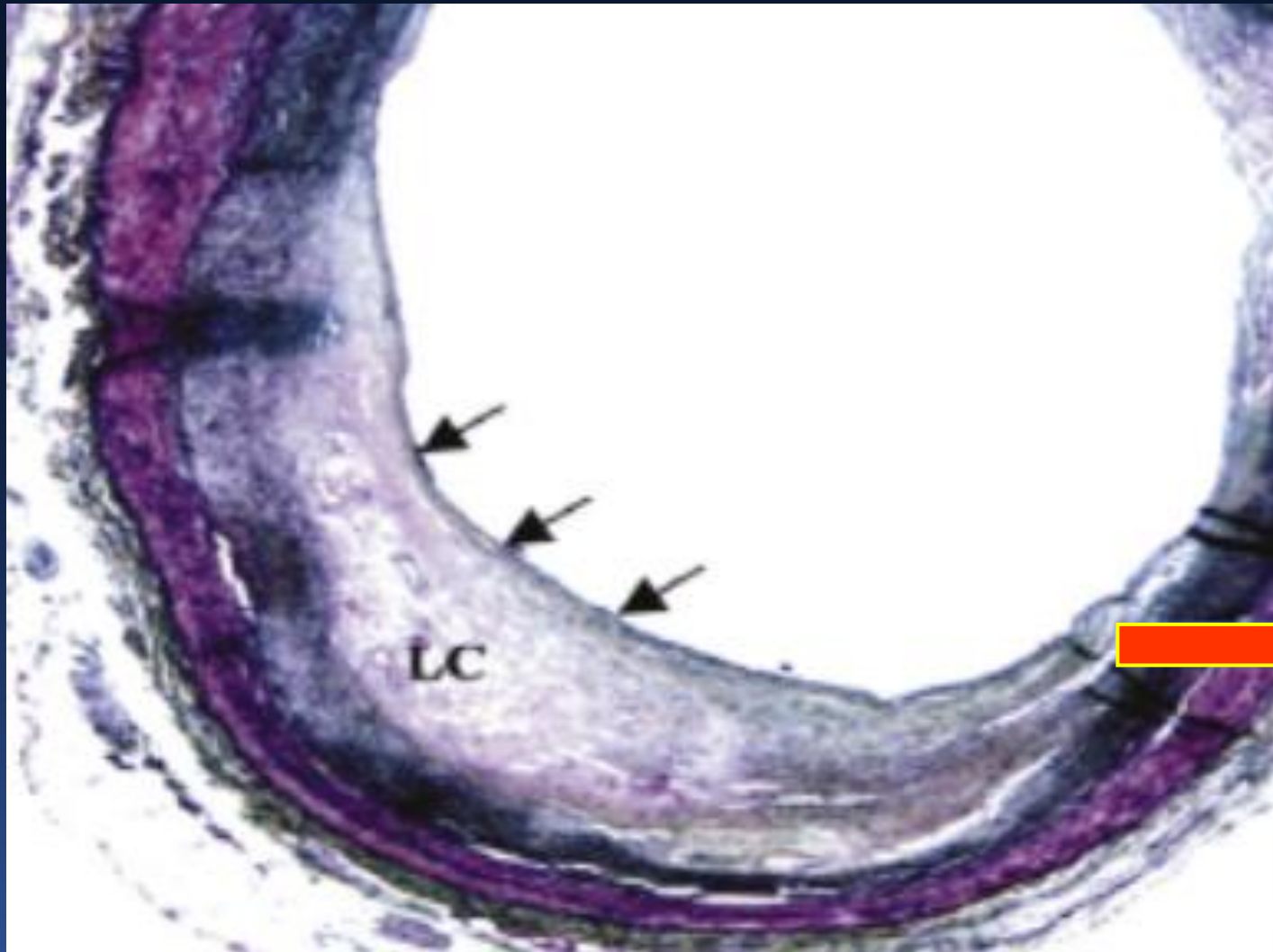


## No. at Risk

Preventive PCI	234	196	166	146	118	89	67
No preventive PCI	231	168	144	122	96	74	50

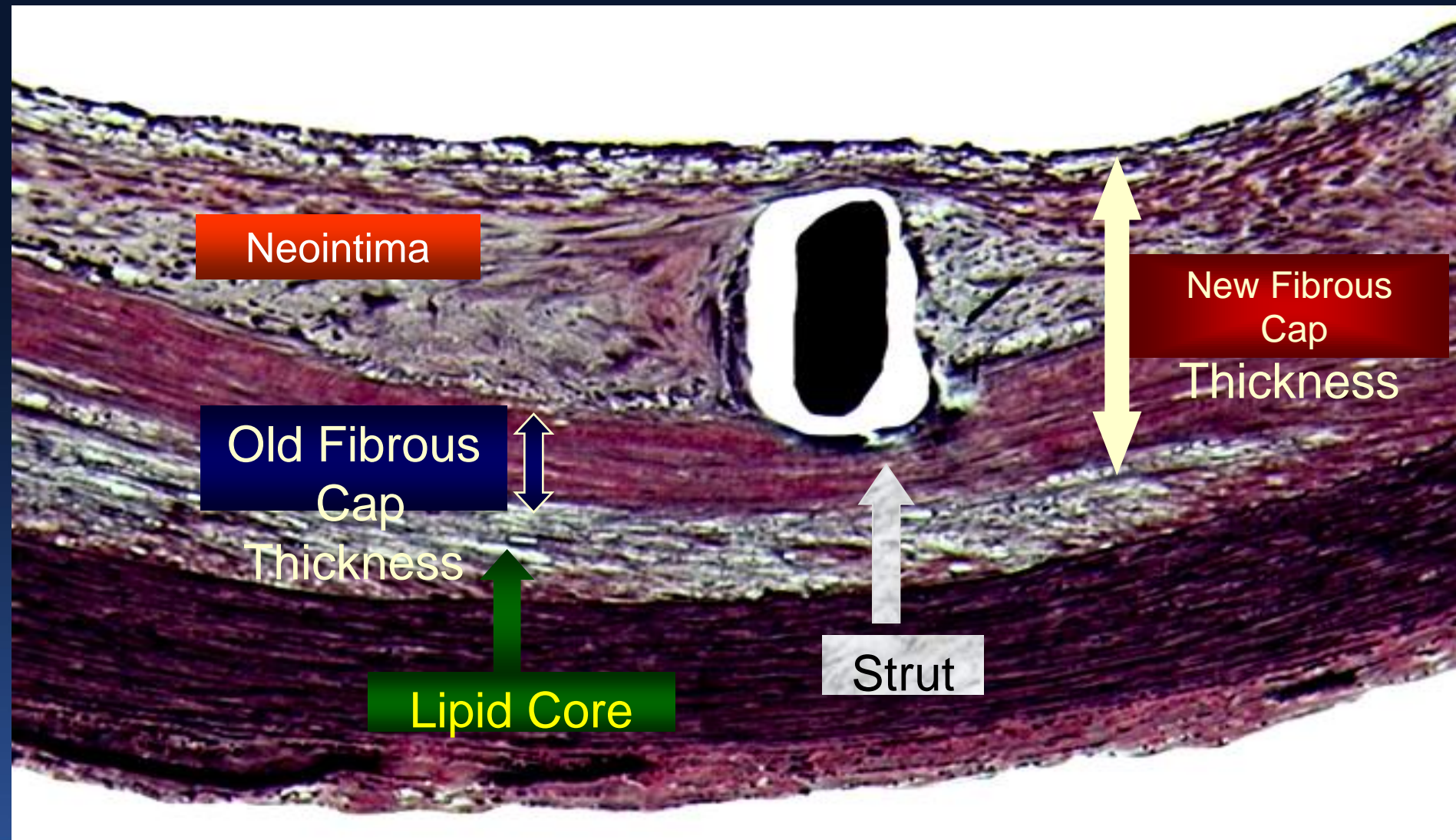
Wald DS et al. N Engl J Med 2013;369:1115-1123.

# Hypercholesterolemic rabbit aorta TCFAs



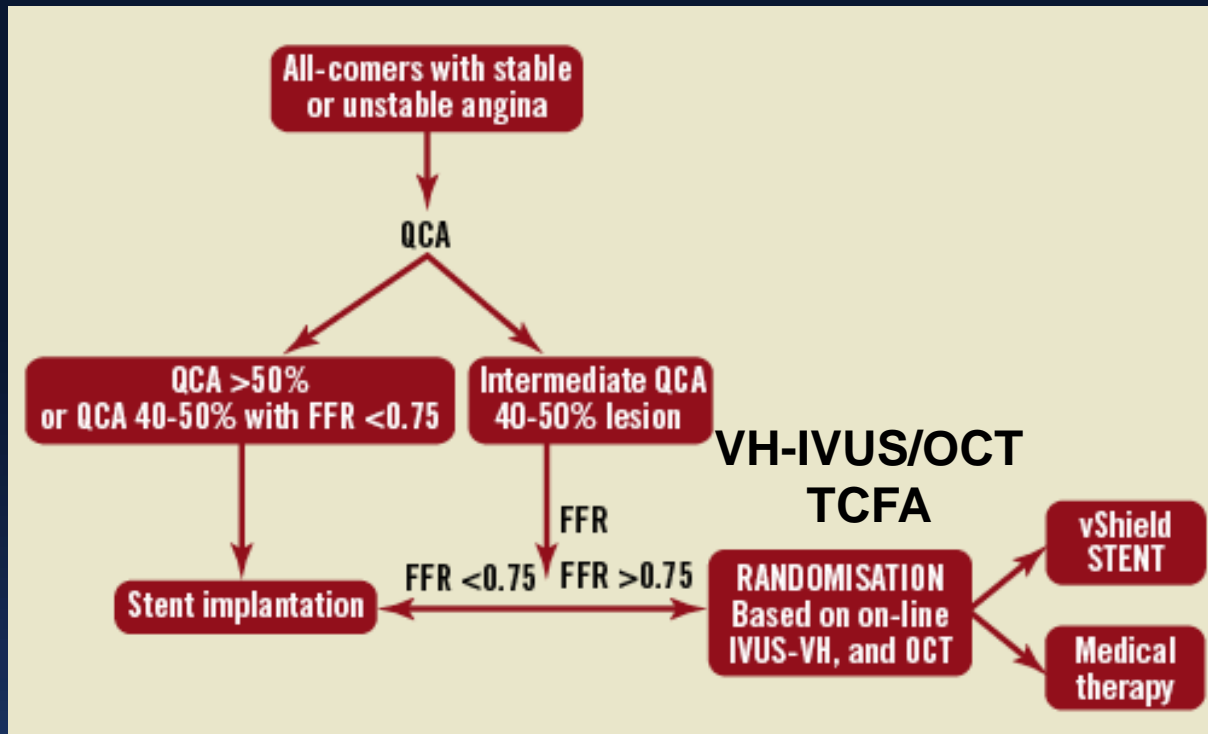
Stent

# Hypercholesterolemic rabbit aorta TCFAs





# SECRITT: Plaque Sealing



48 patients were evaluated.

23 patients met inclusion criteria.

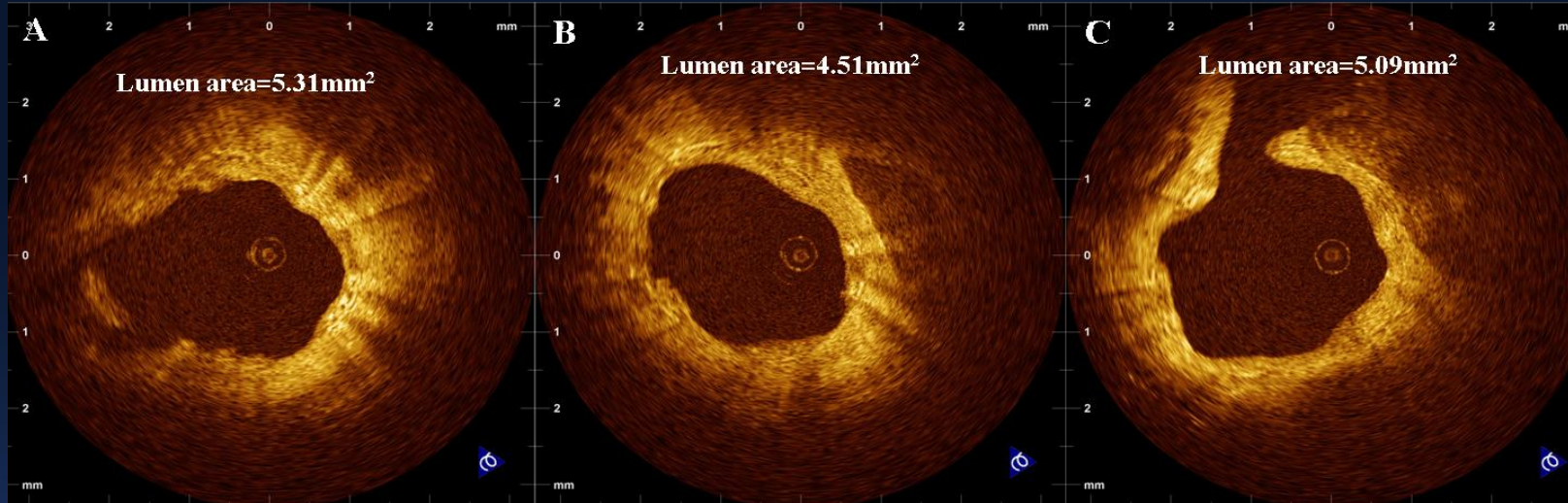
vShield: Ultra thin (56µm) self-expanding Nitinol stent

## Serial Angiographic and FFR assessment in Shielded and Control Groups

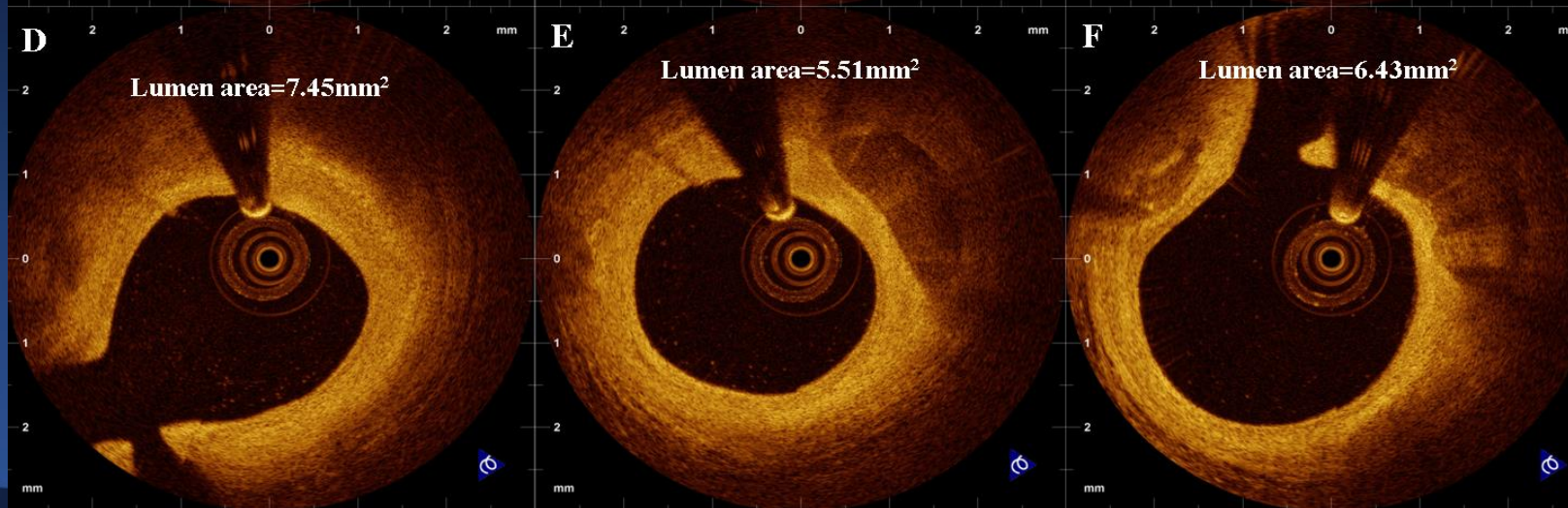
QCA	Baseline			6-month follow-up	
	Shielded group		Control group (n=5)	Control group (n=5)	Shielded group (n=11)
	Pre-stenting (n=11)	Post-stenting (n=11)			
MLD (mm)	<u>2.01±0.39</u>	<u>2.43±0.44</u>	<u>1.87±0.54</u>	<u>1.78±0.49</u>	<u>2.19±0.33</u>
RVD (mm)	2.95±0.39		2.93±0.44	3.08±0.50	2.72±0.46
% diameter stenosis	33.2±13.5%	21.0±10.7%	35.4±16.3%	39.0±19.3%	18.7±16.9%
Late loss (mm)				0.22±0.12	0.24±0.13
FFR	0.93±0.06		0.93±0.05	0.82±0.29	0.93±0.05

# Treatment of a TCFA with BVS: Substantial lumen enlargement due to plaque regression with adaptive remodeling (cohort A pt)

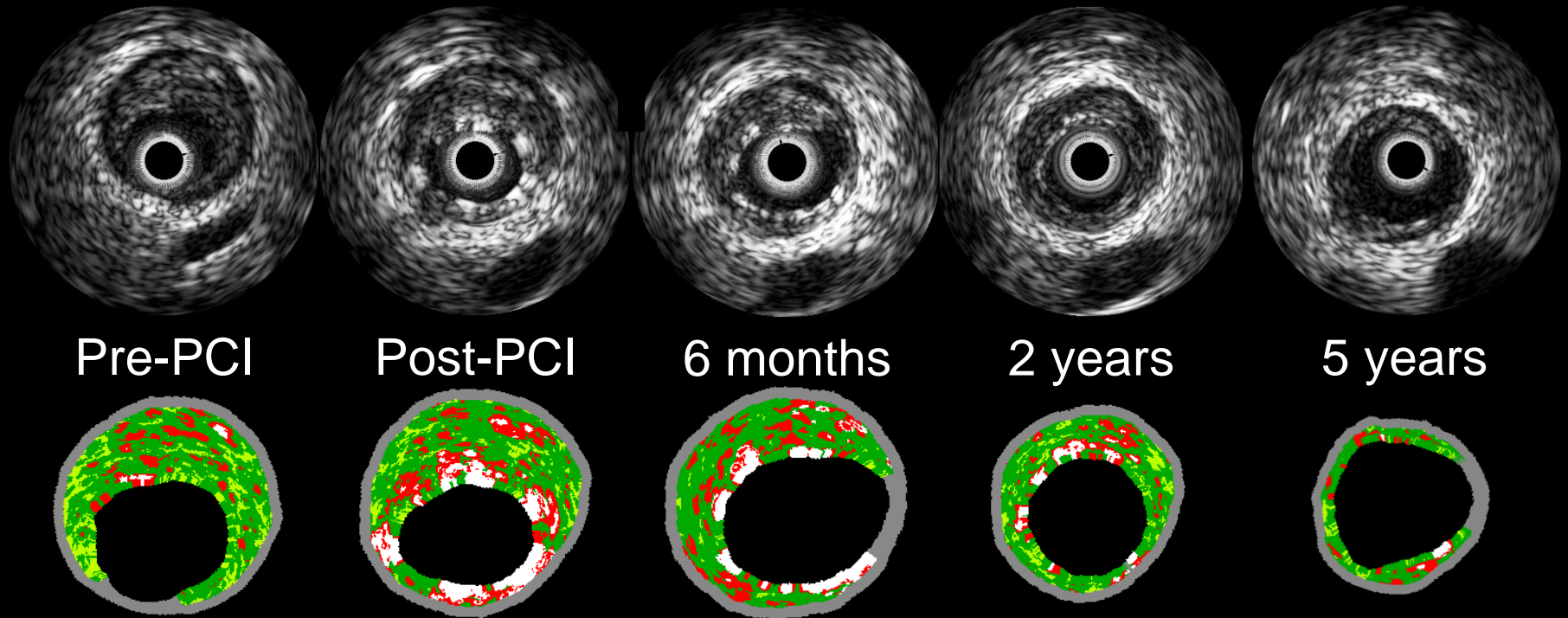
6 months



5 years



# Interventional Plaque Regression by BVS: Substantial lumen enlargement due to plaque regression with adaptive remodeling (cohort A pt)

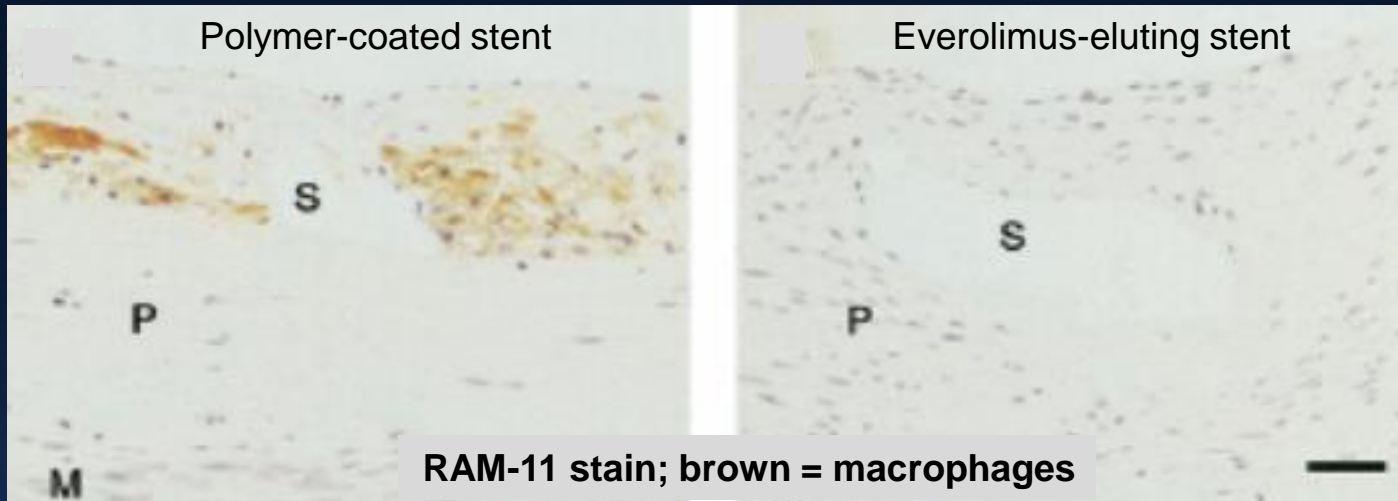


<b>Vessel area (mm<sup>2</sup>)</b>	<b>15.72</b>	<b>15.34</b>	<b>14.09</b>	<b>13.76</b>
<b>Mean lumen area (mm<sup>2</sup>)</b>	<b>6.95</b>	<b>6.17</b>	<b>6.56</b>	<b>8.09</b>
<b>Plaque area (mm<sup>2</sup>)</b>	<b>8.78</b>	<b>9.17</b>	<b>7.54</b>	<b>7.07</b>

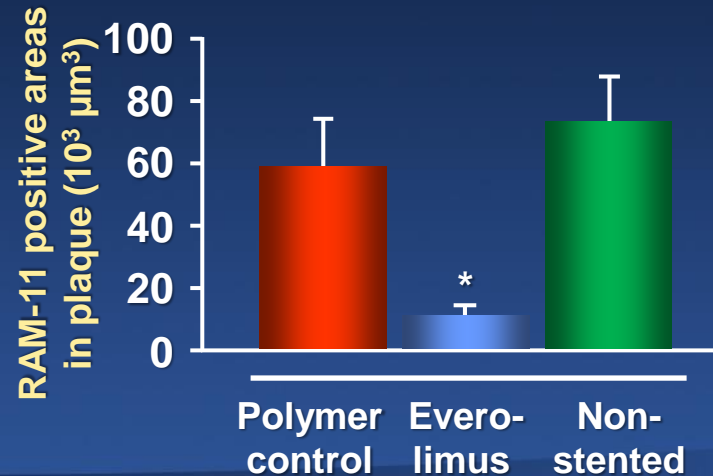
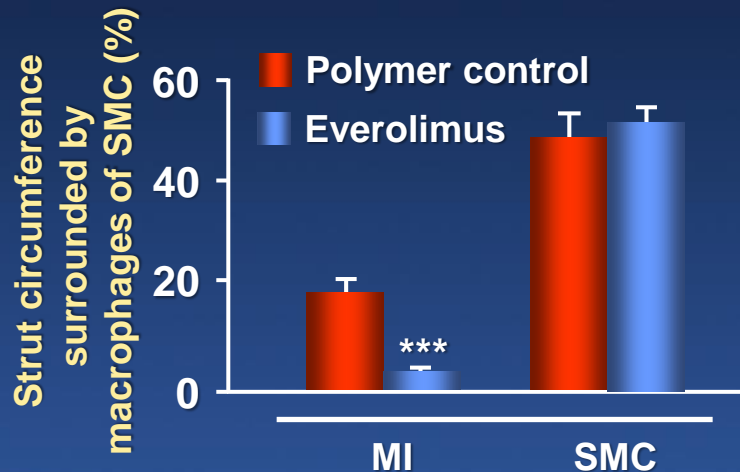


# Everolimus Induced Autophagy of Macrophages

EES and polymer only coated metallic stents implanted in atherosclerotic arteries of cholesterol-fed rabbits



EES resulted in marked reduction of macrophage content, with preservation of SMC content





# PROSPECT II Study

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

NSTEMI or STEMI  $>12^{\circ}$

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

Successful PCI of all intended lesions (by angio  $\pm$  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)



# 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)

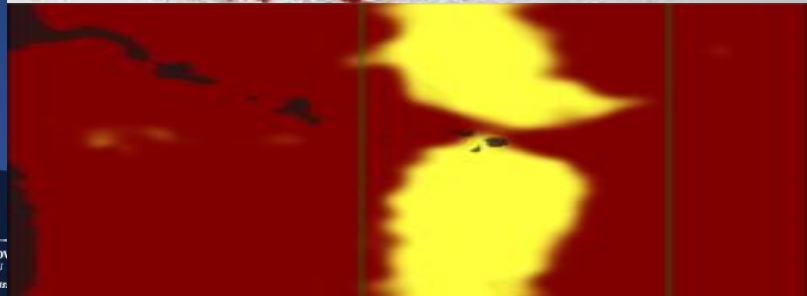
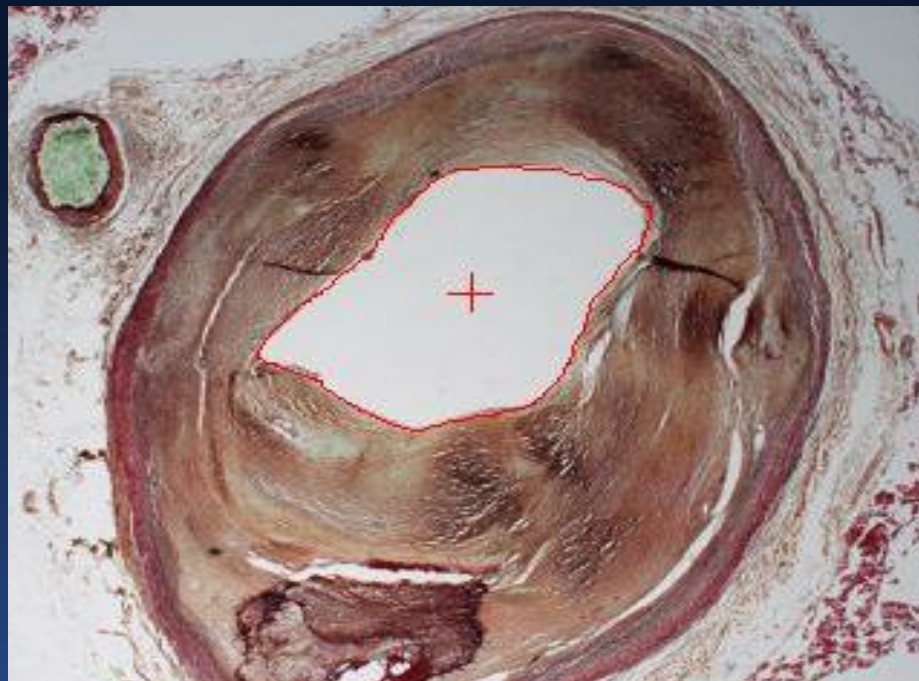
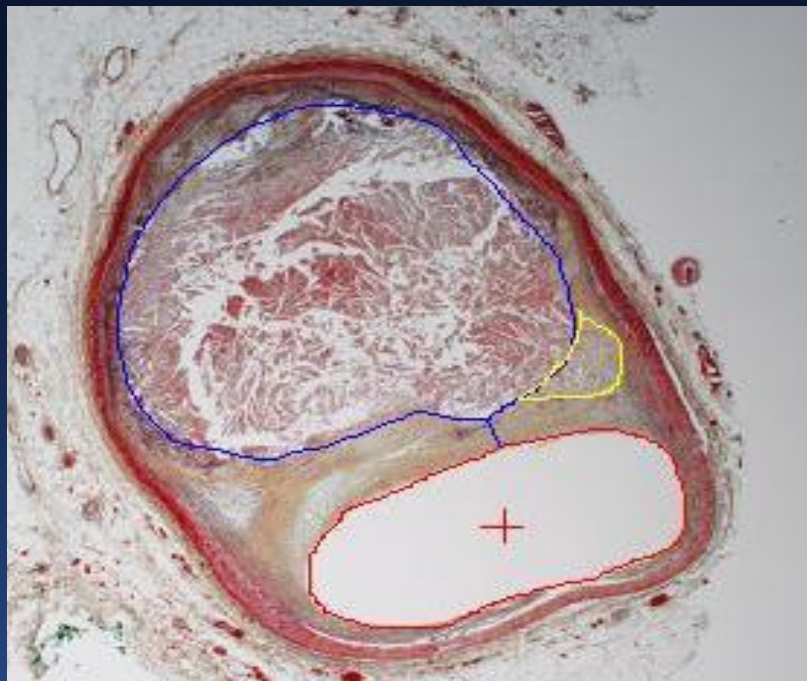
Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for up to 15 years

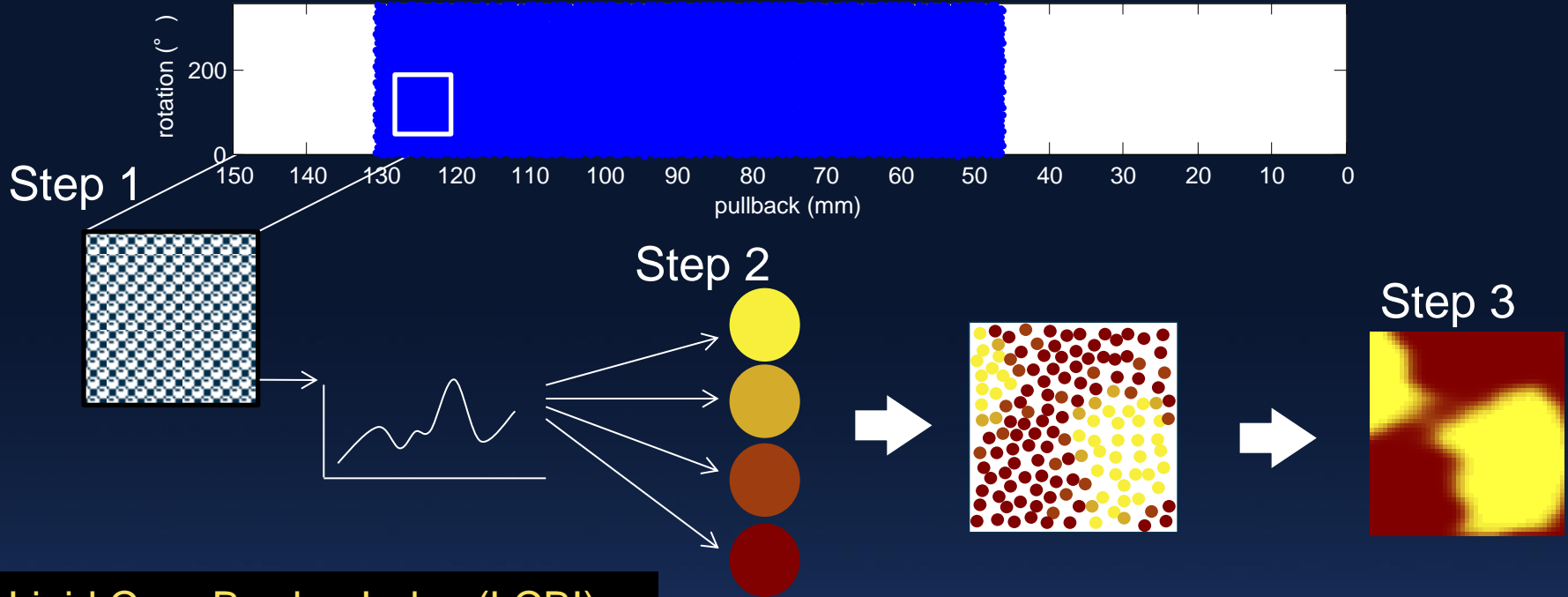
# PROSPECT ABSORB RCT

- Secondary endpoint -

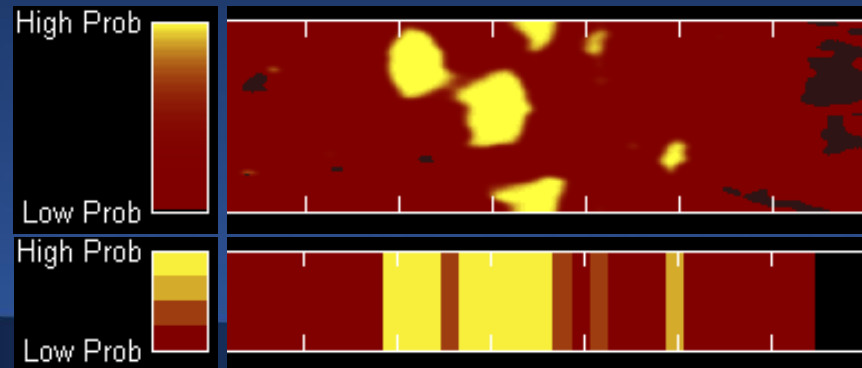
Safety and efficacy of BVS in lesions with large plaque burden which are LRP+ vs LRP-



# Near Infrared Spectroscopy

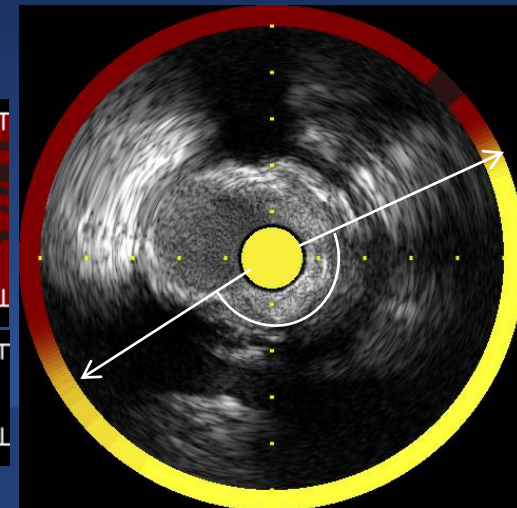


**Lipid Core Burden Index (LCBI)**  
 = Yellow pixel / All variable pixel  
 × 1000



Proximal

Distal

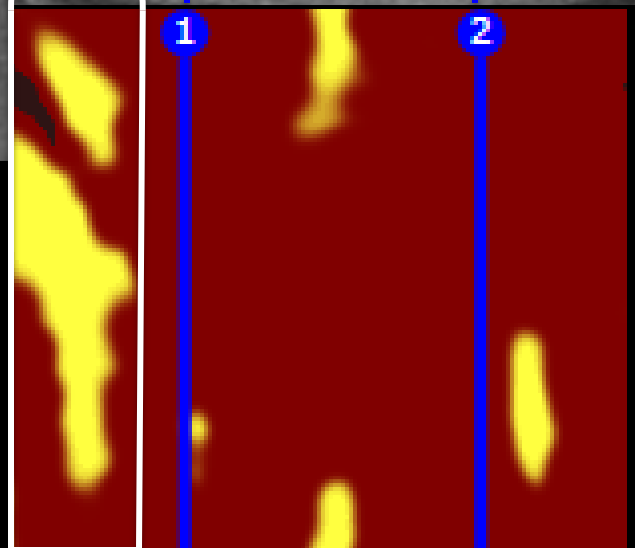
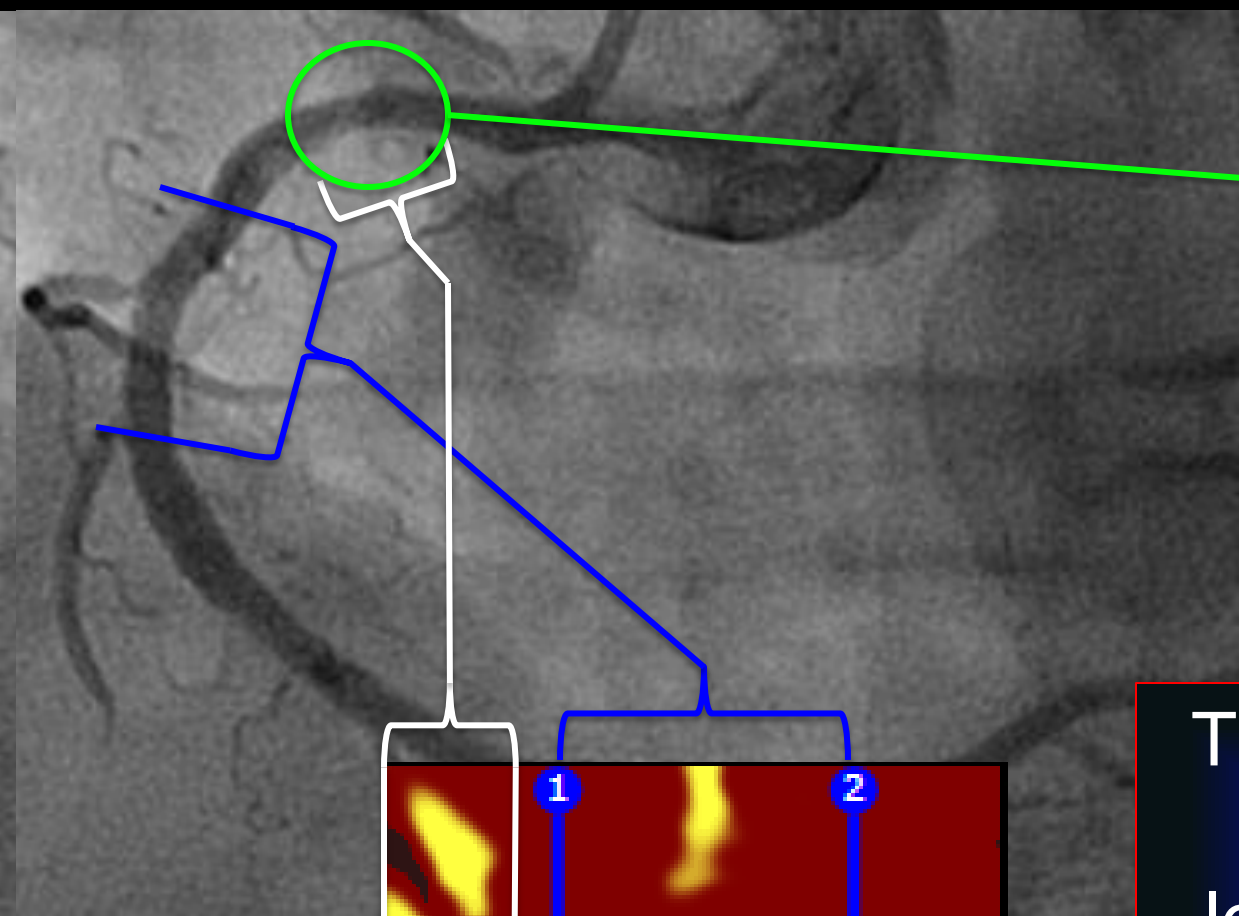




64 year old presents with STEMI in March 2012



Unstable angina October 2012



maxLCBI<sub>4mm</sub>  
694

This was the only de novo culprit lesion to emerge from the 462 coronary segments imaged at baseline

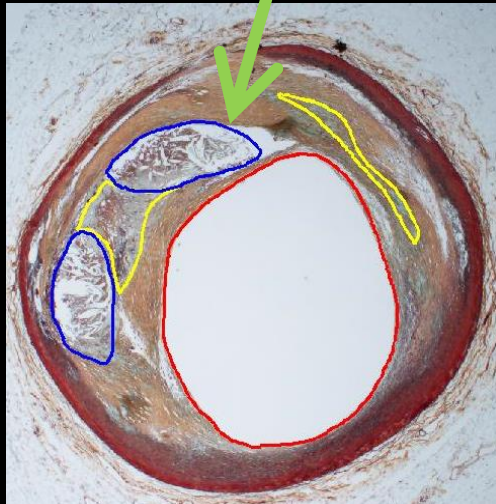
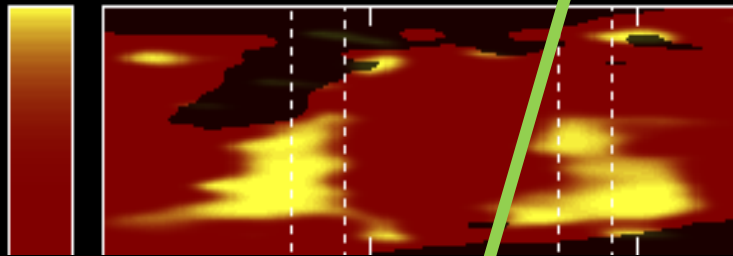
# NIRS Collagen-deficient LCP Preliminary Algorithm:

Detection of Thin cap in an Autopsy Specimen

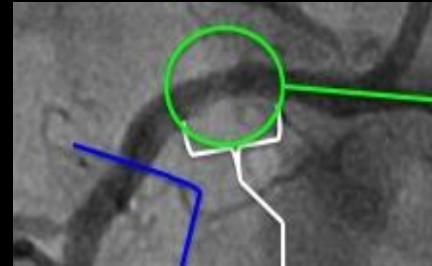
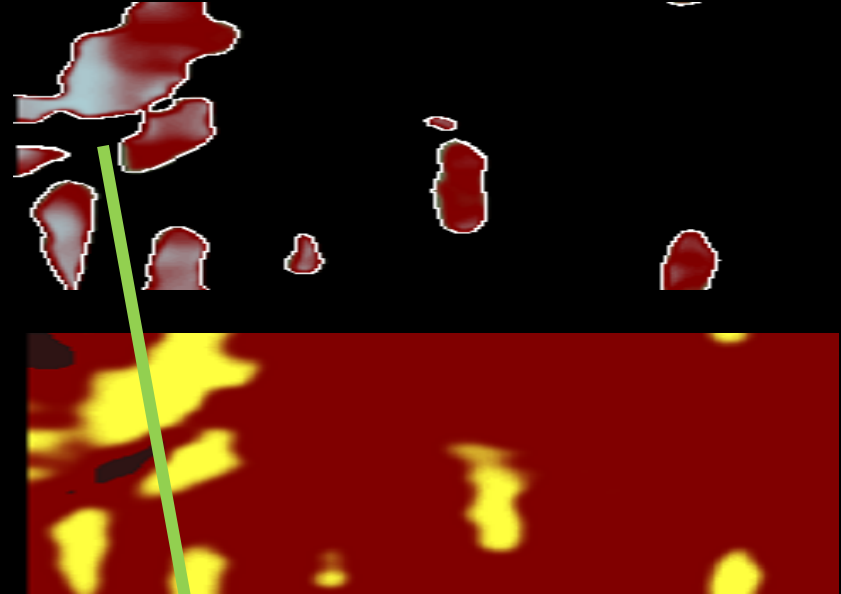
Blue signal indicates collagen-deficient signal over LCP



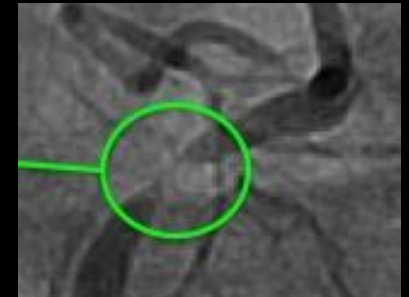
NIR CHEMOGRAM



Detection of Collagen Deficient Signal Over LCP in a Patient Followed by a Coronary Event

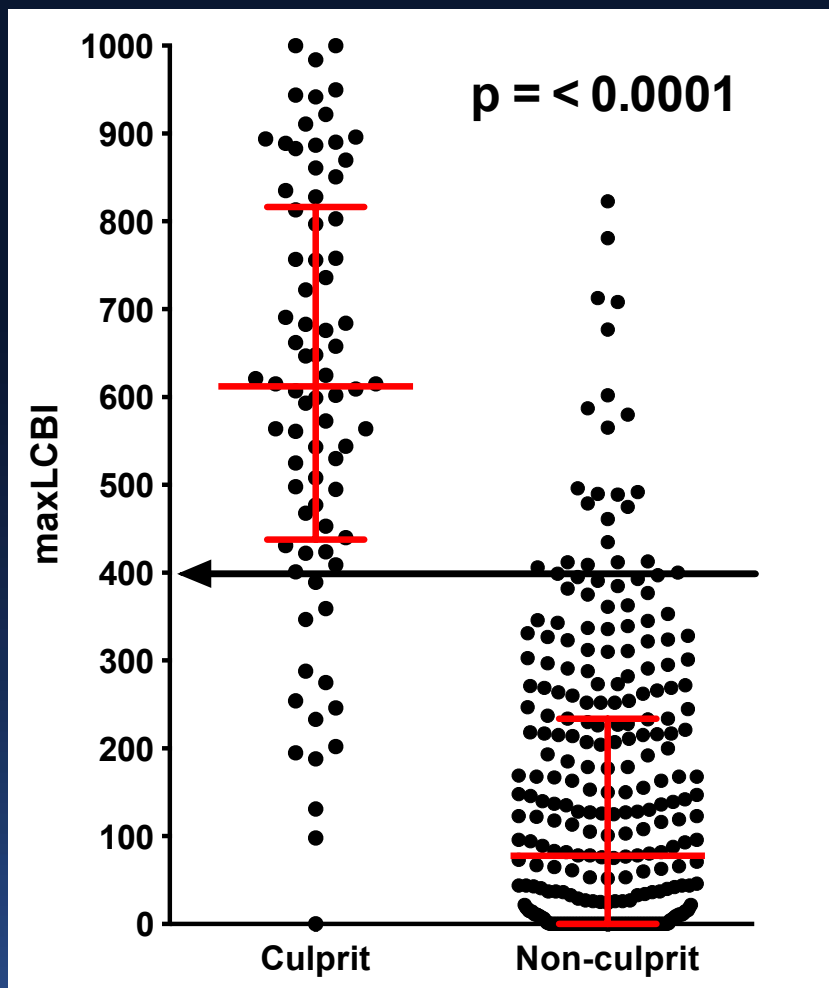


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Courtesy of Ryan Madder, MD  
Sean Madden Ph.D and Joel Raichlen, MD

# STEMI culprit vs. non-culprit segments



*STEMI culprit lesions:*  
 $maxLCBI_{4mm} = 612 (438-817)$

*Non-culprit lesions:*  
 $maxLCBI_{4mm} = 78 (0-234)$

*MaxLCBI<sub>4mm</sub> >400 was present at the STEMI culprit site in 63 of the 78 cases*

*MaxLCBI<sub>4mm</sub> >400 was present at the non-culprit site in 22 of the 304 segments*

Mann-Whitney U test  
Median  $\pm$  interquartile range





# Methods

## Spectrum NIRS-IVUS Registry

- Single center, observational
- Prospectively enrolled patients undergoing NIRS-IVUS

## Inclusion criteria

- Patients completing  $\geq 1$  year of follow-up

## Exclusion criteria

- Prior CABG/referred for CABG
- Uninterpretable NIRS
- NIRS imaging performed only within a stented segment

January 2012 to April 2013

**167 patients**  
NIRS-IVUS imaging  
&  
 $\geq 1$  year of follow-up

→ Excluded

Prior CABG (7)

Referred for CABG (17)

Uninterpretable NIRS (15)

NIRS only in stent (7)

**121 patients**  
included in this analysis

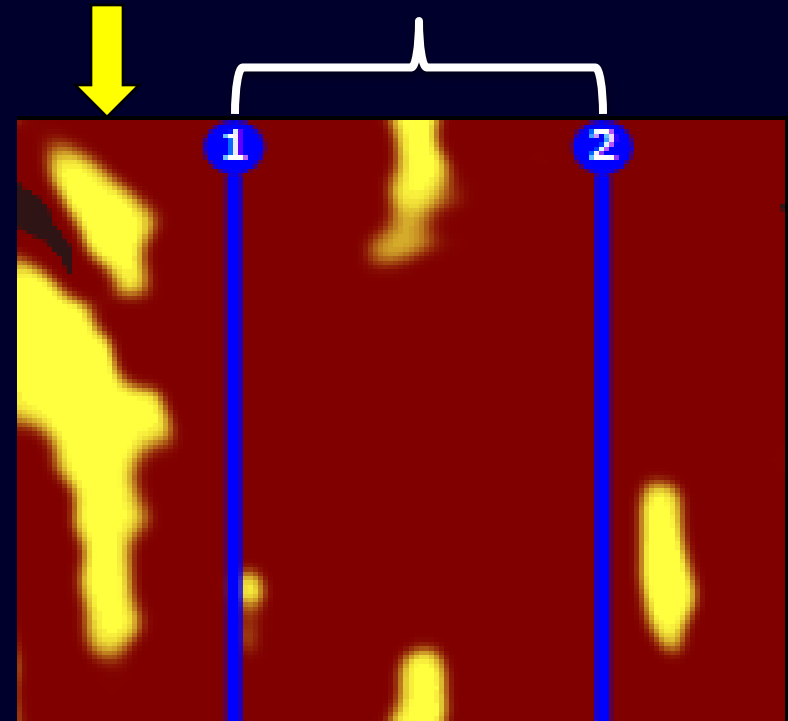


# Methods

- Evaluated non-stented coronary segments for large LRP
  - defined as a  $\max\text{LCBI}_{4\text{mm}} \geq 500$
- Patients followed for MACCE
  - Composite of all-cause mortality, recurrent ACS requiring revascularization, or acute cerebrovascular events
- Events related to previously stented segments were excluded
- All events adjudicated blinded to the NIRS-IVUS imaging

Large LRP  
in  
non-  
stented  
segment

Stented  
segment  
excluded  
from  
analysis

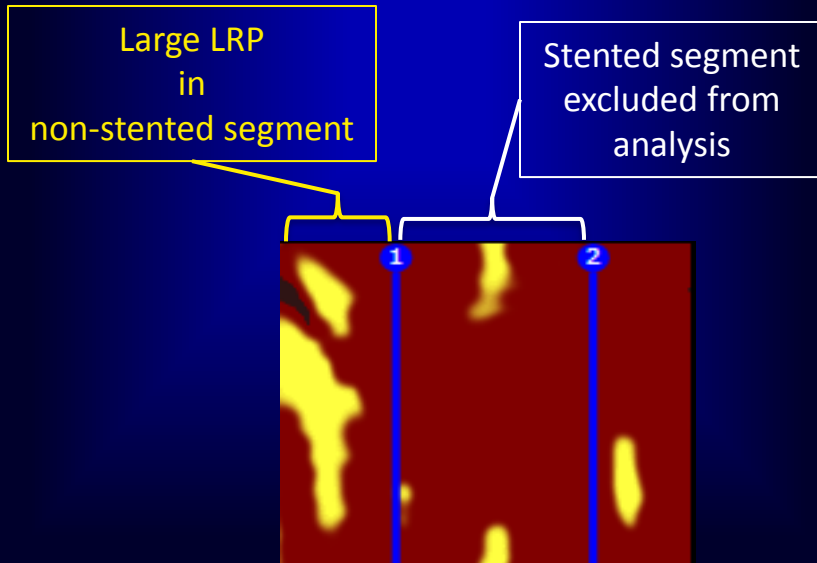




# Results

## Baseline NIRS Findings

- 462 non-overlapping 10-mm coronary segments analyzed
- A large LRP was detected in 15 (3.2%) segments & in 12 (9.9%) patients

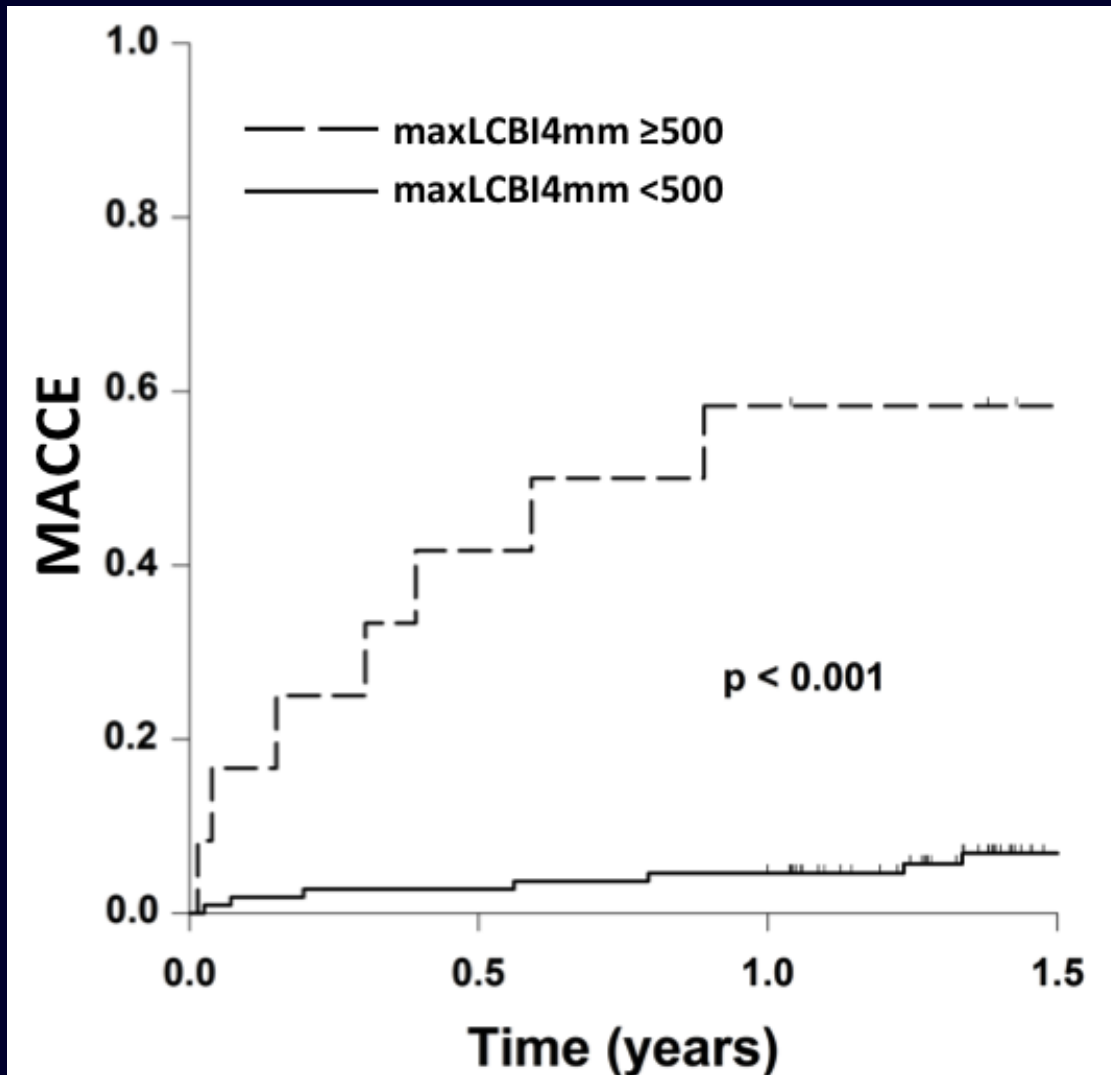


## Follow Up Events

- Average follow-up duration was  $603 \pm 145$  days (1.7 years)
- MACCE (unrelated to previously stented segments) occurred in **11.6%** of patients during follow up
  - ➔ All-cause death 4.1%
  - ➔ ACS requiring revascularization 6.6%
  - ➔ CVA 0.8%



# Large LRP by NIRS and MACCE



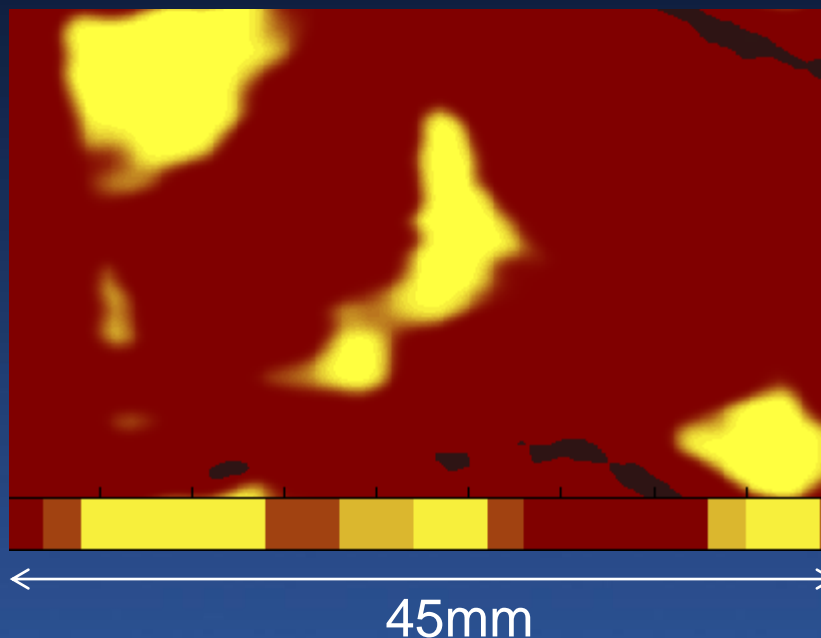
**MACCE Rate**  
Large LRP 58.3%  
vs  
No large LRP 6.4%  
( $p < 0.001$ )

**ACS Requiring Revascularization**  
Large LRP 25.0%  
vs  
No large LRP 4.6%  
( $p < 0.001$ )

# Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

- Prospective Single Center Study, 206 patients (ACS47%)
- Primary Endpoint: Composite of all-cause mortality, non-fatal ACS, stroke and unplanned PCI during one-year FU
- >40mm non culprit segment of NIRS

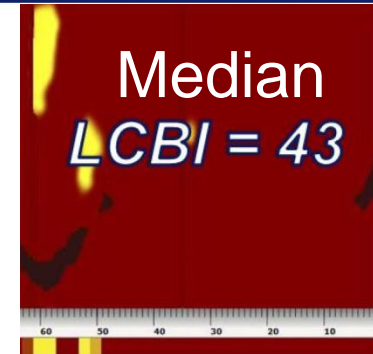
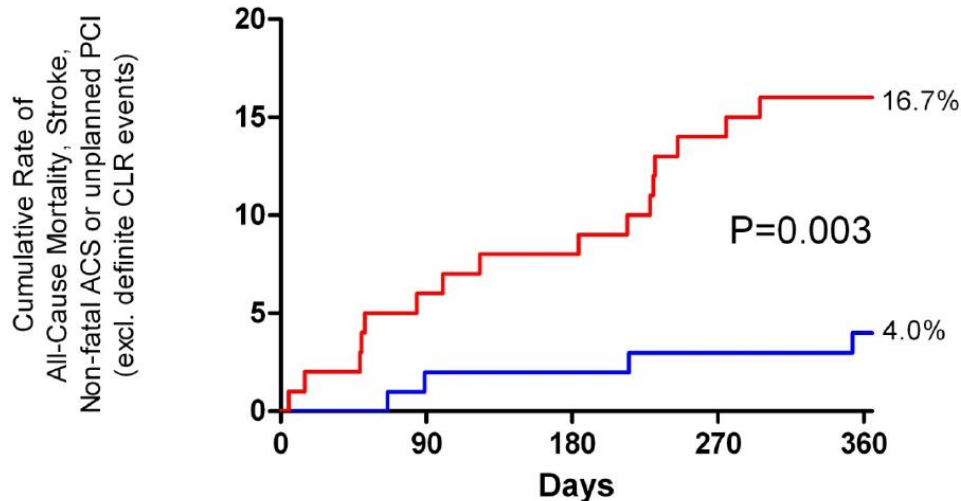
Lipid Core  
Burden Index  
(LCBI)=188



# Relationship between Lipidic Plaque detected by NIRS and Outcomes

Primary endpoint

Erasmus MC



- 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

# Summary

1. PROSPECT I study showed 1) plaque burden >70%, 2) MLA <4mm<sup>2</sup>, and 3) TCFA were the lesion morphology to predict future event.
2. Using plaque burden >70% as the most robust criteria of vulnerable plaque, PROSPECT ABSORB will randomize these lesions into BRS versus optimal medical therapy.
3. NIRS/IVUS defined vulnerable plaque will be evaluated in natural history PROSPECT2 study.