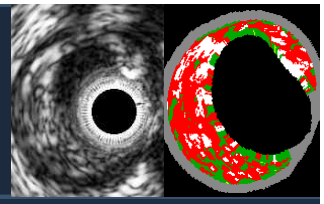
The PROSPECT Trial



***P**roviding **R**egional **O**bservations to **S**tudy **P**redictors of **E**vents in the **C**oronary **T**ree*

Does PROSPECT Support the Use of Invasive Imaging to Diagnose and Treat Vulnerable Plaque with DES?

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CARDIOVASCULAR RESEARCH FOUNDATION

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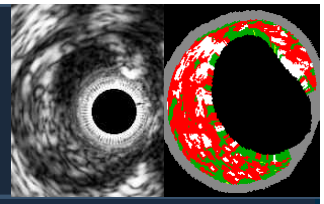
NewYork-Presbyterian

The University Hospital of Columbia and Cornell

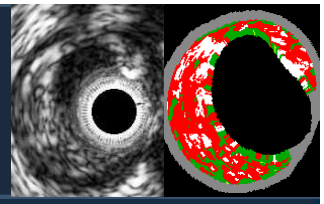
The PROSPECT Trial



Background

- PROSPECT was a prospective, multicenter natural history study using 3 vessel multimodality intracoronary imaging to identify those lesions which place pts at risk for unexpected adverse cardiovascular events

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)

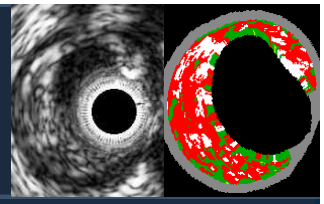
Successful and uncomplicated

Formally enrolled

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

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

The PROSPECT Trial



3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n=~350)

Proximal 6-8 cm of each coronary artery

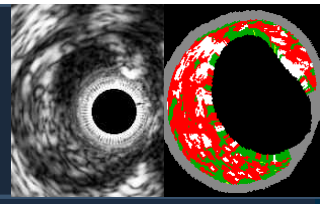
Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: 1 mo, 6 mo, 1 yr, 2 yr, ±3-5 yrs

MSCT Substudy
N=50-100

Repeat imaging in pts with events

PROSPECT: Primary Endpoint



MACE attributable to non-culprit lesions*

- Cardiac death
- Cardiac arrest
- Myocardial infarction
- Rehospitalization due to
  - Unstable angina
  - Progressive angina

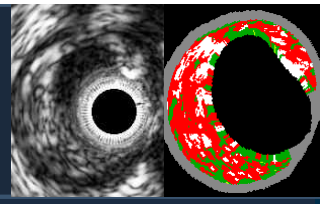
Most severe

Hierarchical

Least severe

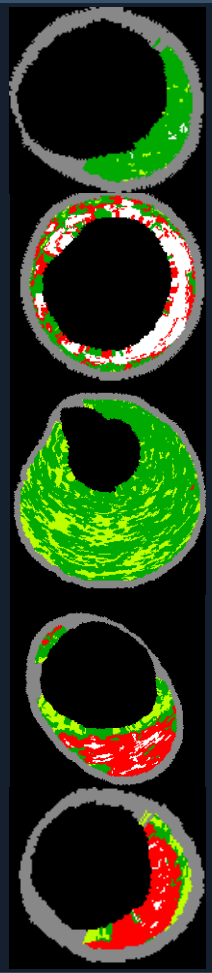
MACE during FU were adjudicated by the CEC as attributable to culprit lesions (those treated during or before the index hospitalization) or non culprit lesions (untreated areas of the coronary tree) based on angiography (+ECGs, etc.) at the time of the event; events occurring in pts without angiographic follow-up were considered indeterminate in origin.

PROSPECT: Methodology



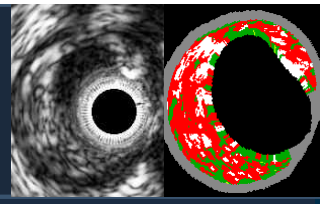
Virtual histology lesion classification

Lesions are classified into 5 main types



1. Fibrotic
2. Fibrocalcific
3. Pathological intimal thickening (PIT)
4. Thick cap fibroatheroma (ThCFA)
5. VH-thin cap fibroatheroma (VH-TCFA)
   (presumed high risk)

PROSPECT 82910-012: 52 yo♂



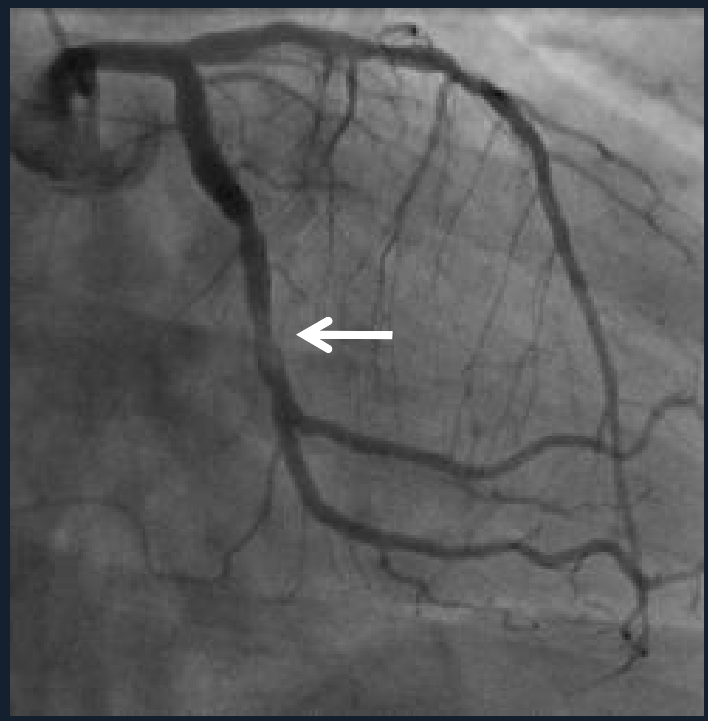
2/13/06: NSTEMI, PCI of MLAD

2/6/07 (51 weeks later): NSTEMI attributed to LCX

Index 2/13/06

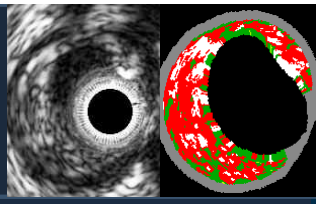
QCA PLCX DS 28.6%

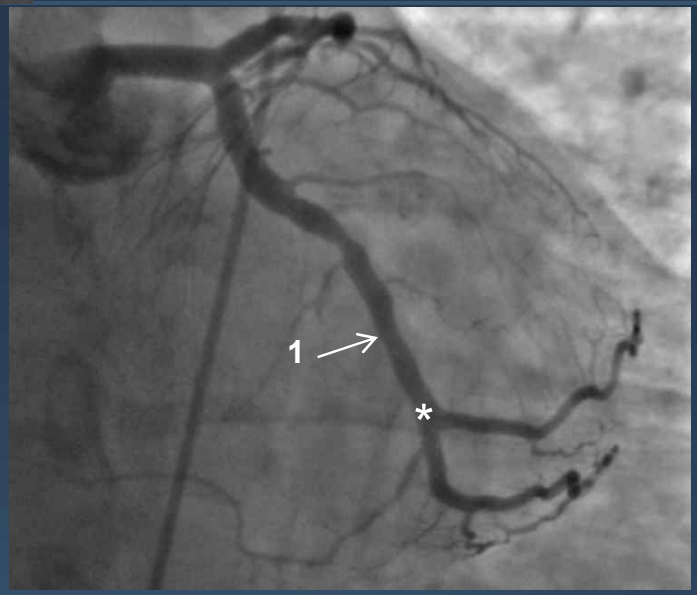
Event 2/6/07



QCA PLCX DS 71.3%

PROSPECT 82910-012: Index 2/13/06





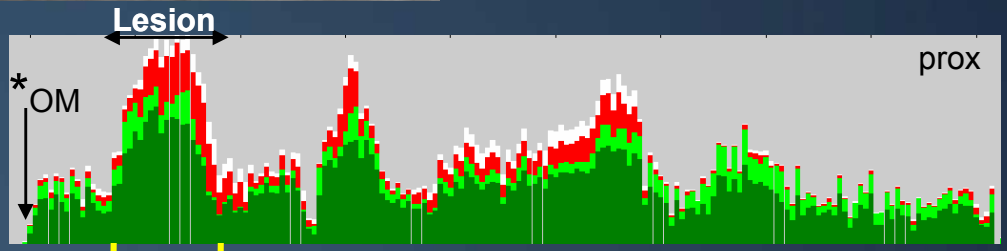
Baseline PLCX

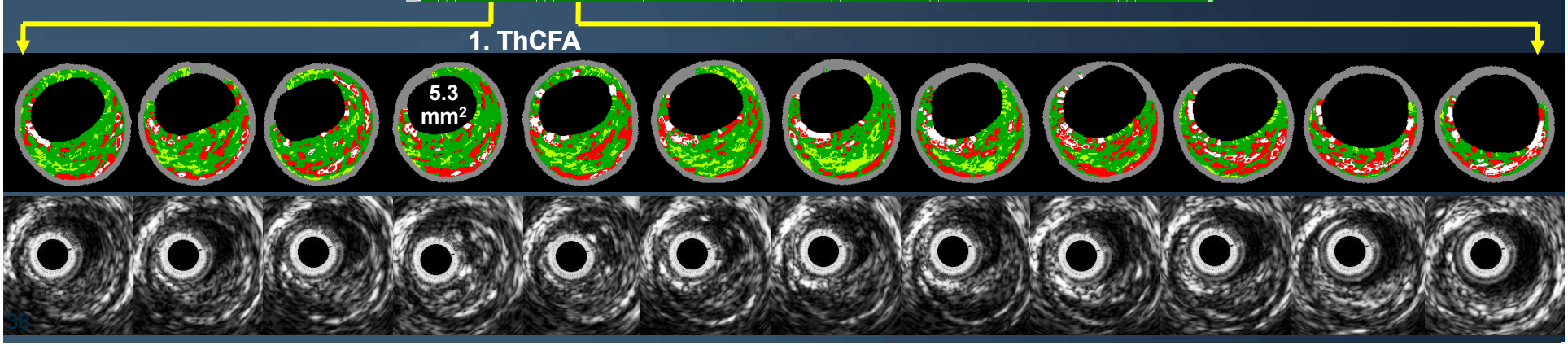
QCA: RVD 2.82 mm,

DS 28.6%, length 6.8 mm

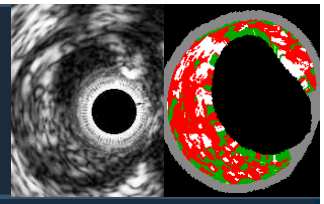
IVUS: MLA 5.3 mm²

VH: ThCFA

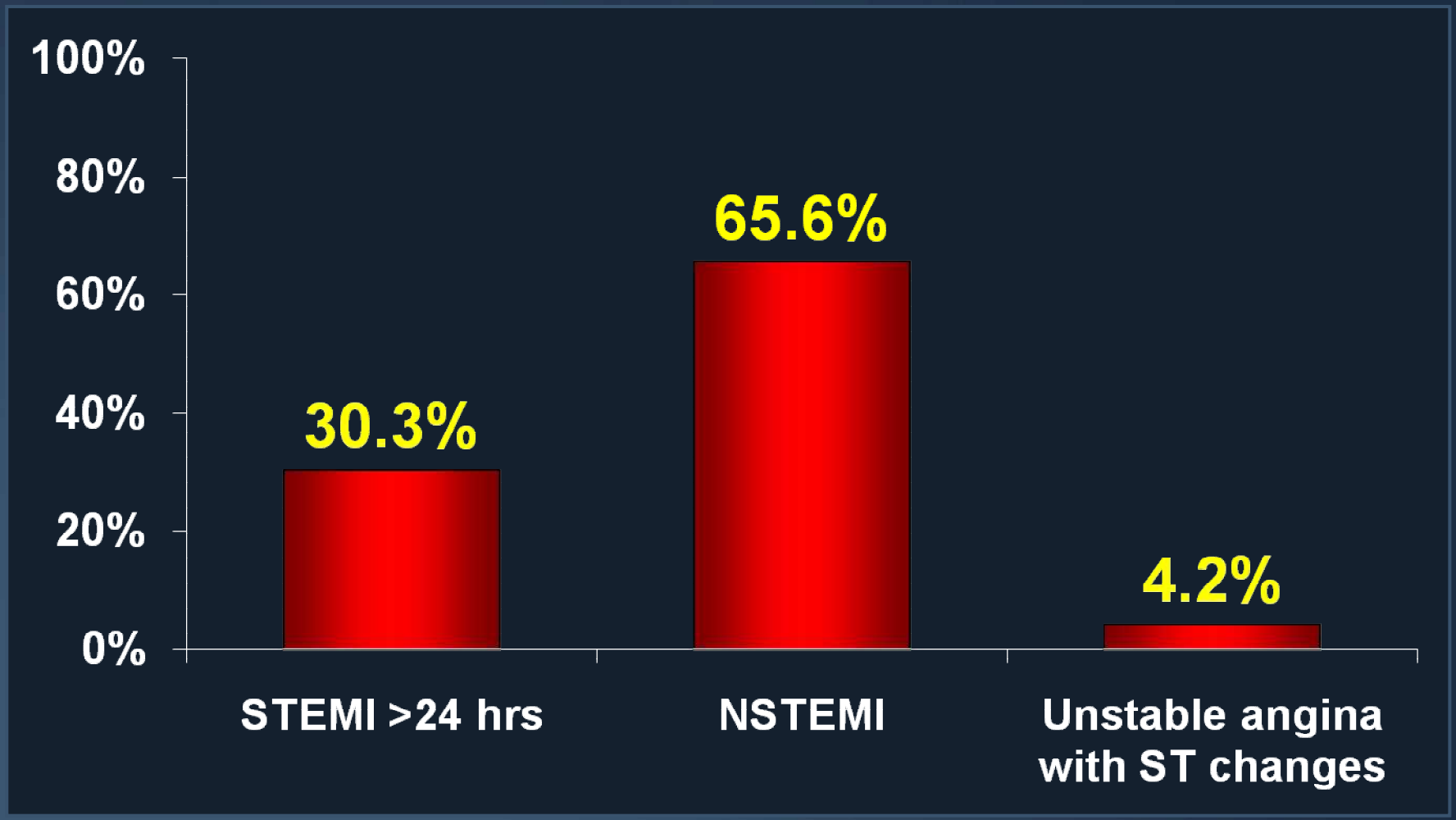




PROSPECT: Baseline Features

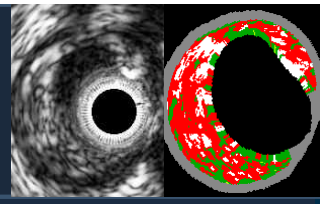


N = 697*



*3 patients who were never consented were de-registered

PROSPECT: Imaging Summary

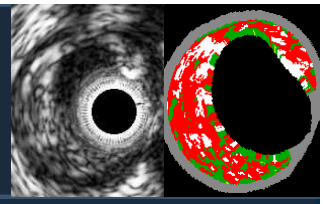


Length of coronary arteries analyzed (core lab)

Mean (mm)	Angiography (N=697)	IVUS (N=673)	VH data* (N=623)
LM	9.3 ± 4.3	12.8 ± 9.8	12.8 ± 9.7
LAD	153.5 ± 41.1	73.3 ± 34.1	73.8 ± 33.7
LCX	132.7 ± 49.9	63.3 ± 36.1	63.6 ± 36.0
RCA	148.3 ± 45.1	85.2 ± 39.6	85.5 ± 39.4
Total per pt	437.9 ± 86.4	192.0 ± 97.7	206.7 ± 85.4
Total all pts	305,228.3	129,216.8	128,757.9

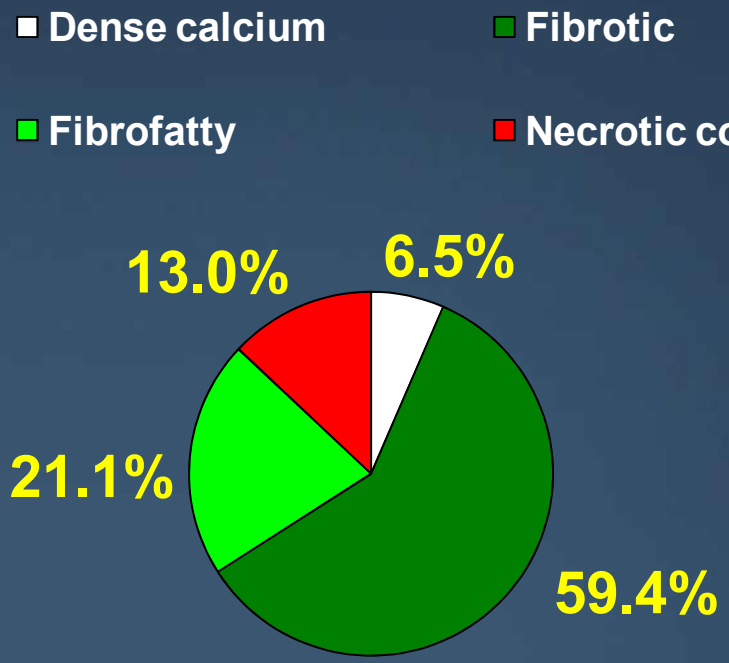
*** Note: VH data doesn't register if there is no plaque**

PROSPECT: Imaging Summary



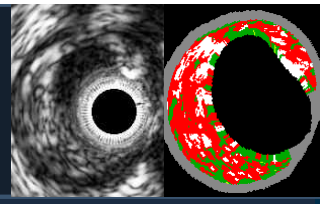
Virtual histology (N=2811 lesions in 611 pts)

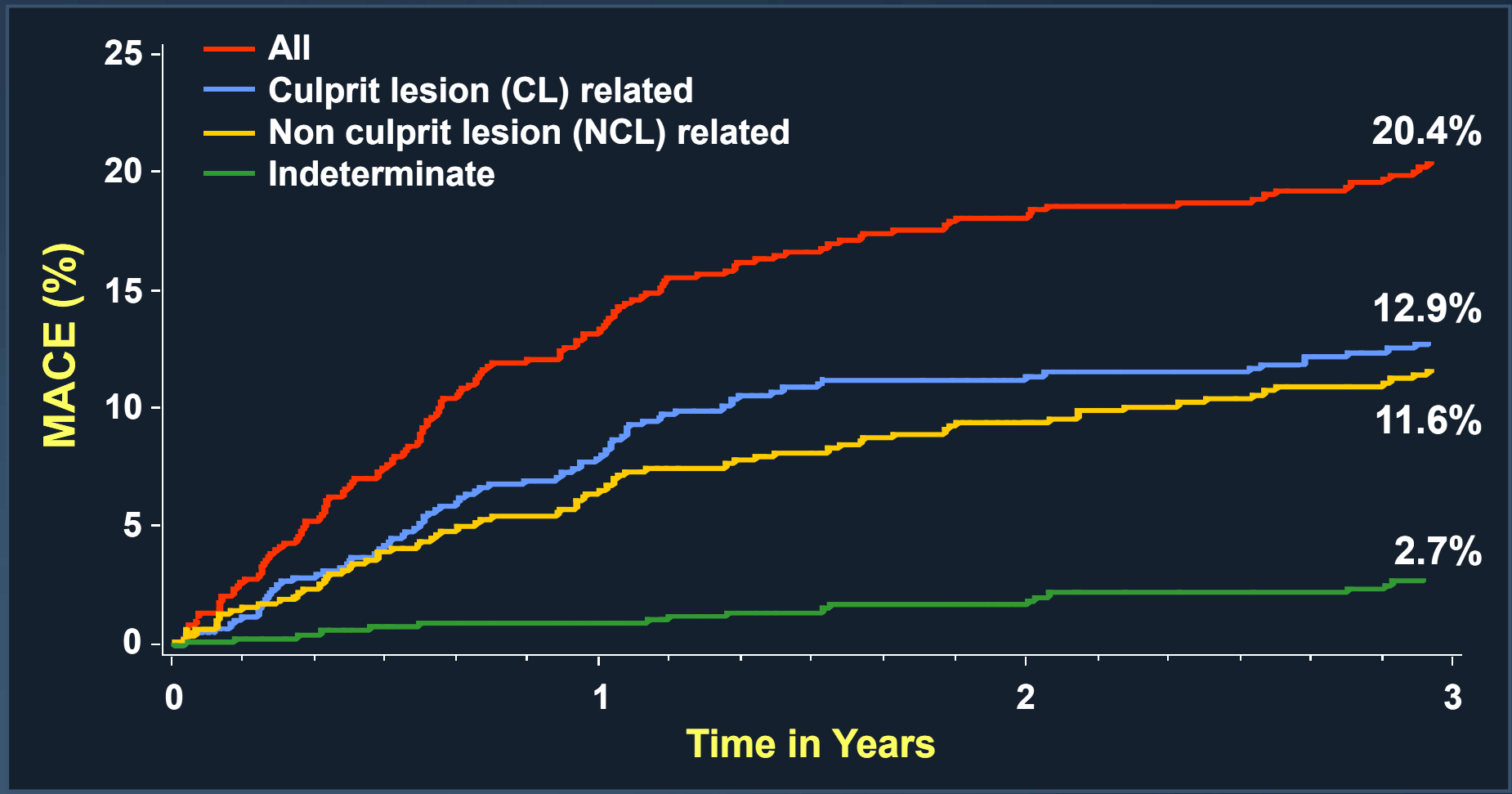
- Mean plaque composition-



Plaque subtype	N=2811
Fibrotic	2.5%
Fibrocalcific	1.2%
PIT	35.9%
Fibroatheroma	57.4%
- Thick cap	36.2%
- VH-TCFA	18.9%
- Single, - Ca	5.2%
- Single, + Ca	0.5%
- Multiple, - Ca	9.5%
- Multiple, + Ca	6.1%

PROSPECT: MACE

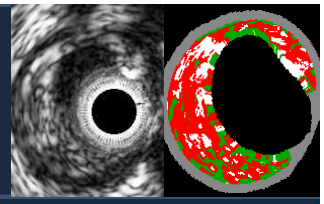




Number at risk

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

PROSPECT: MACE

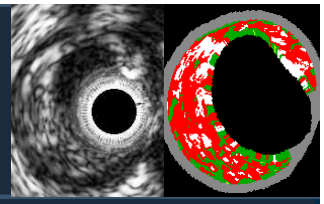


3-year follow-up, hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter-minate
Cardiac death	1.9% (12)	0.2% (1)	0% (0)	1.7% (11)
Cardiac arrest	0.3% (2)	0.3% (2)	0% (0)	0% (0)
MI (STEMI or NSTEMI)	2.7% (17)	1.7% (11)	1.0% (6)	0.2% (1)
Rehospitalization for unstable or progressive angina	15.4% (101)	10.4% (69)	10.7% (68)	0.8% (5)
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)

Rates are 3-yr Kaplan-Meier estimates (n of events)

PROSPECT: MACE



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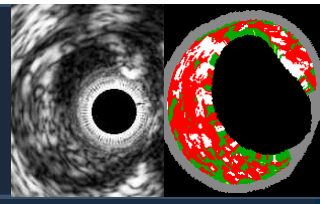
Rates are 3-yr Kaplan-Meier estimates (n of events)

PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

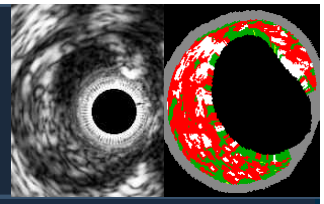


Independent predictors of lesion level events by Cox Proportional Hazards regression

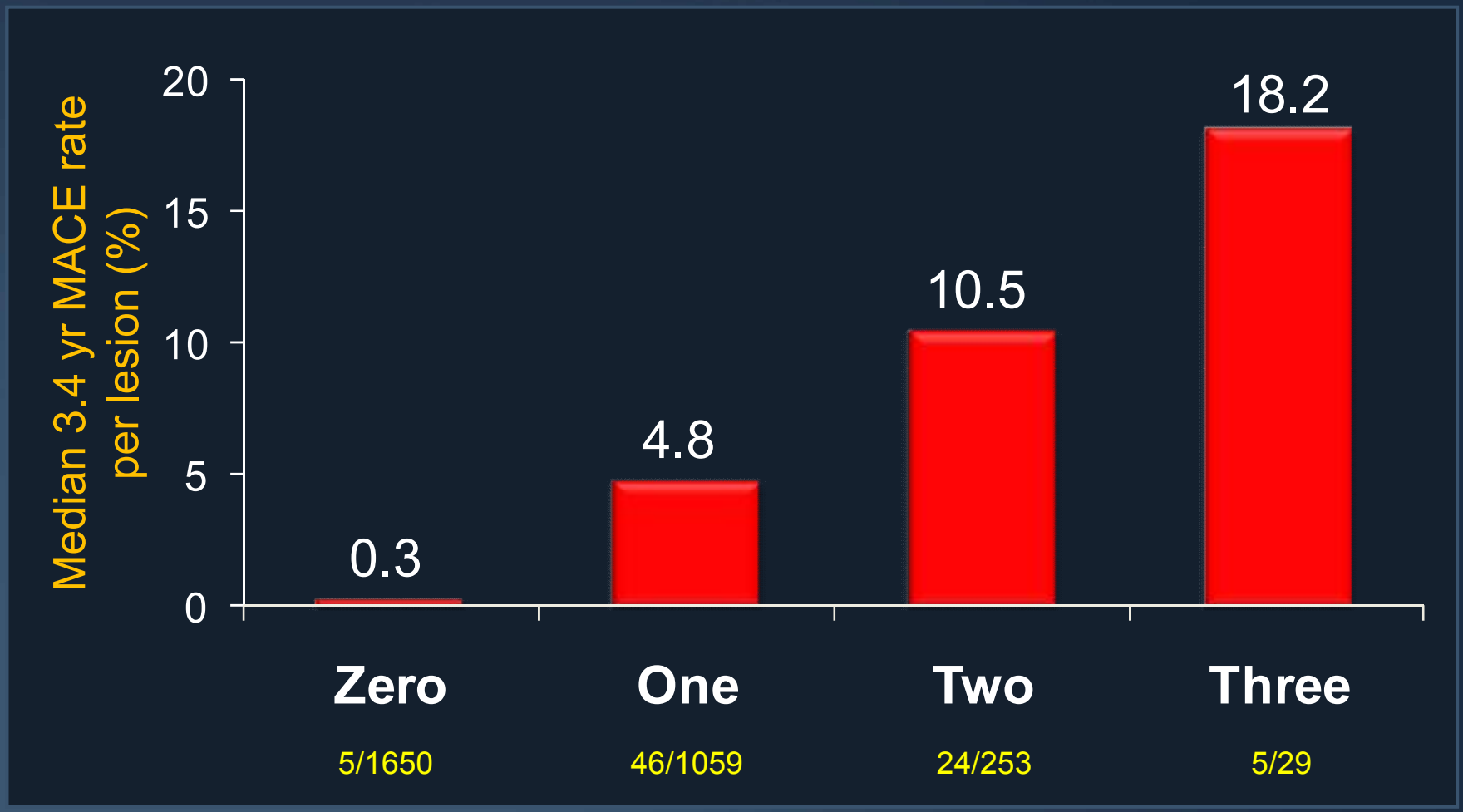
Variable	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

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.

PROSPECT: Correlates of Non Culprit Lesion Related Events

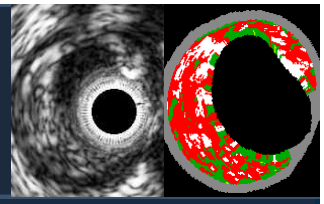


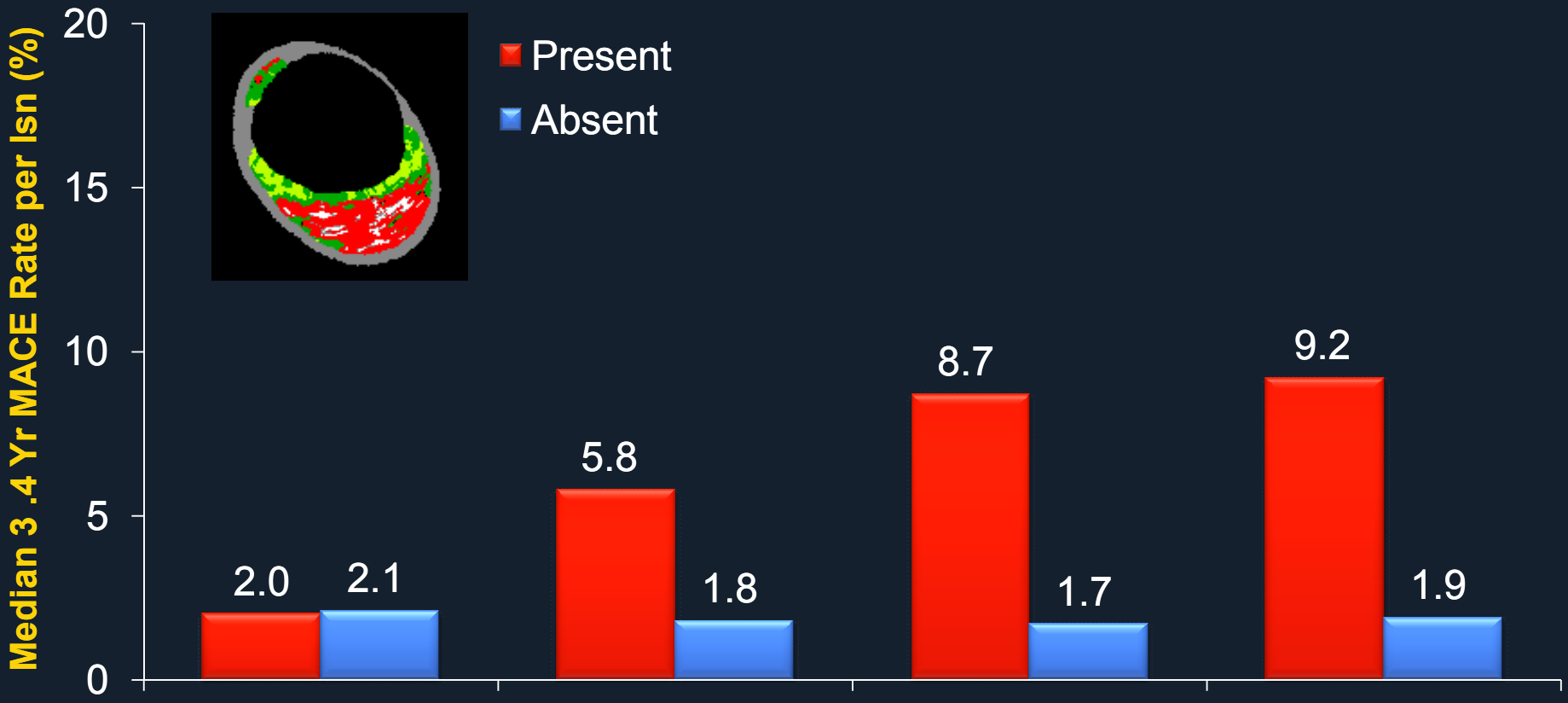
Number of factors present: PB_{MLA} ≥70%, MLA ≤4.0mm^2 or TCFA



PB = plaque burden at the MLA

PROSPECT: Thick CFA and Non Culprit Lesion Related Events

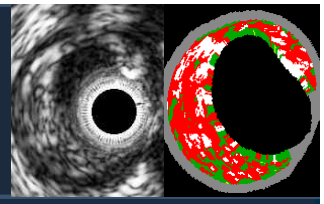




	ThCFA	ThCFA + MLA ≤4.0mm2	ThCFA + PB ≥70%	ThCFA + PB ≥70% + MLA ≤4mm2
Lesion HR	0.92 (0.52, 1.63)	3.41 (1.75, 6.65)	5.17 (2.59, 10.32)	5.02 (1.99, 12.63)
P value	0.77	0.0003	<0.0001	<0.0001
Prevalence*	67.6%	22.7%	15.6%	8.3%

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

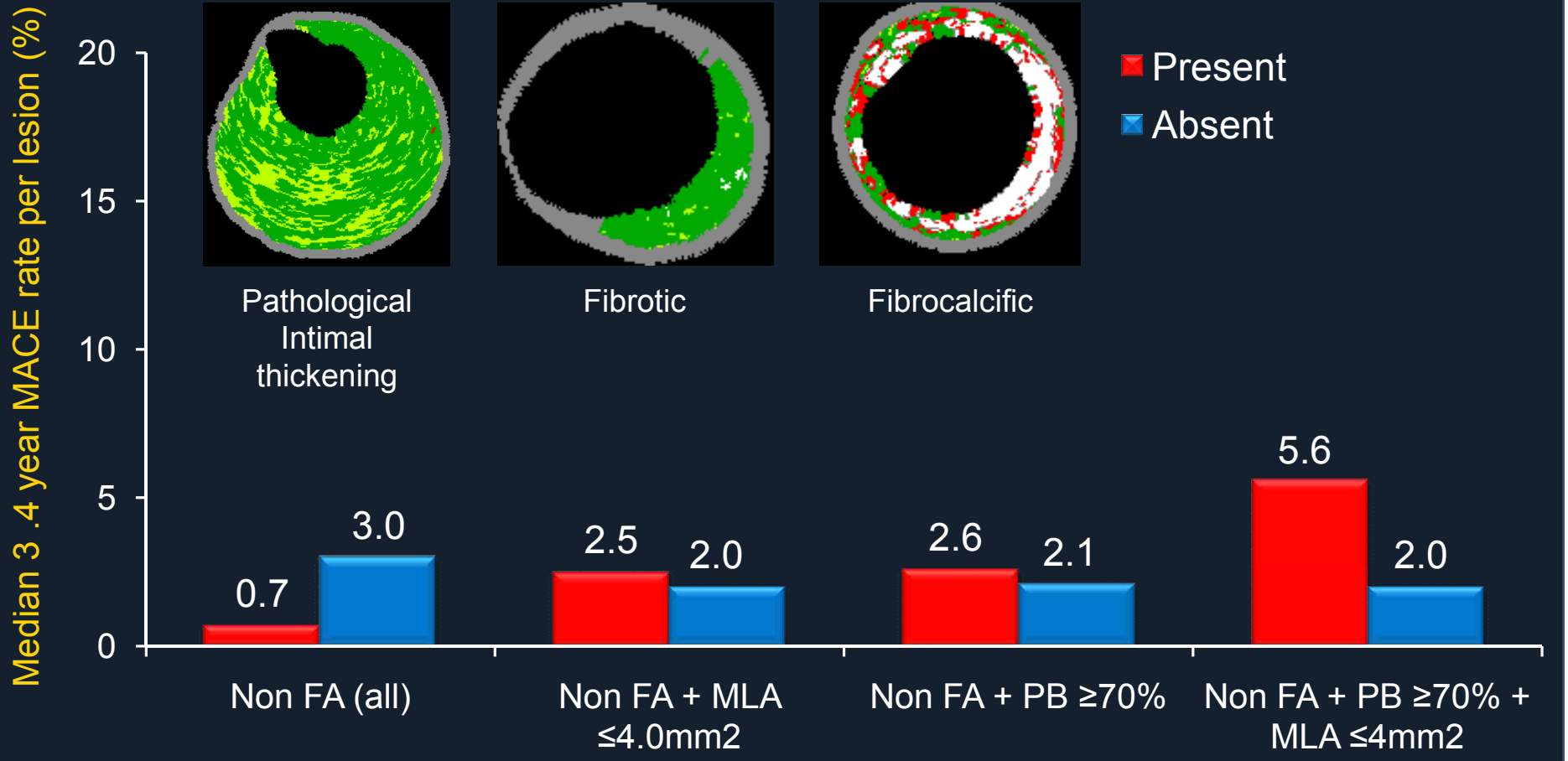
PROSPECT: Non Fibroatheromas and Non Culprit Lesion Events



Pathological Intimal thickening

Fibrotic

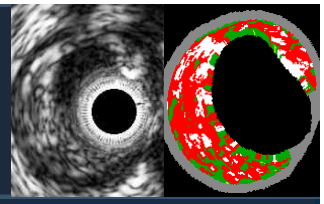
Fibrocalcific



	Non FA (all)	Non FA + MLA ≤4.0mm2	Non FA + PB ≥70%	Non FA + PB ≥70% + MLA ≤4mm2
Lesion HR	0.22 (0.10, 0.49)	1.22 (0.44, 3.39)	1.25 (0.17, 9.01)	2.60 (0.36, 18.84)
P value	0.0002	0.70	0.83	0.34
Prevalence*	67.9%	19.7%	5.6%	2.7%

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

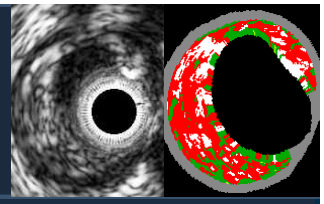
PROSPECT



- The Big Question -

Does PROSPECT Support the Use of Invasive Imaging to Diagnose and Treat Vulnerable Plaque with DES?

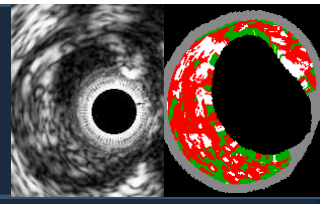
PROSPECT: Implications



- The relatively low prevalence of high-risk lesions (~1 in 5 pts), coupled with the fact that when they become symptomatic they usually present with angina and not death or MI, suggests that 3-vessel imaging to identify and prophylactically stent these lesions is not warranted in ACS patients who are revascularized and treated with optimal medical therapy.

- Similarly, if a high risk non ischemia-producing lesion happens to be found (e.g. 3 year event rate >10%), since most patients present with angina, prophylactic DES cannot be recommended absent a large, randomized trial.

PROSPECT: Implications



- However, millions of persons per year who have not been diagnosed with CAD and are not receiving optimal medical therapy die, arrest or develop MI every year.
- This suggests that future investigation should focus on identifying asymptomatic or minimally symptomatic pts with large plaque burden, small MLA and TCFAs through noninvasive screening (e.g. MSCT), for consideration of enhanced medical therapy and possible angiography.