

VH-IVUS: Native Vessel and Neointima

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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
- Speaker Fee

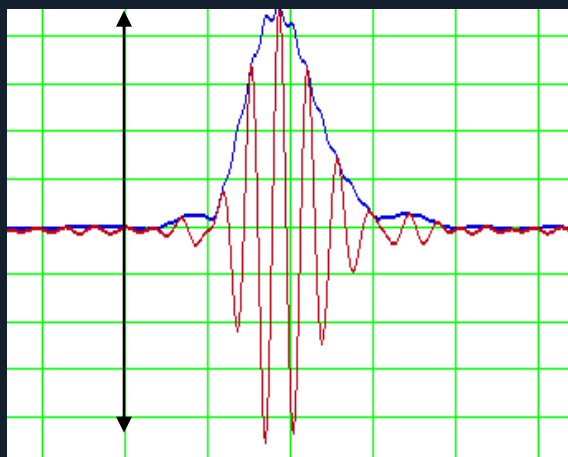
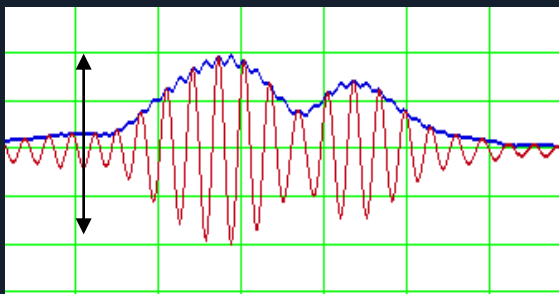
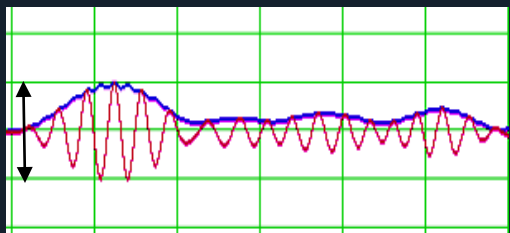
Company

- Boston Scientific Corporation
- Boston Scientific Corporation, ACIST
- Volcano Corporation, St Jude Medical

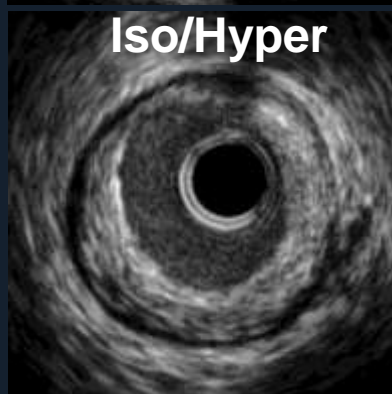
Basic of Virtual Histology

Gray Scale IVUS Tissue Characterization

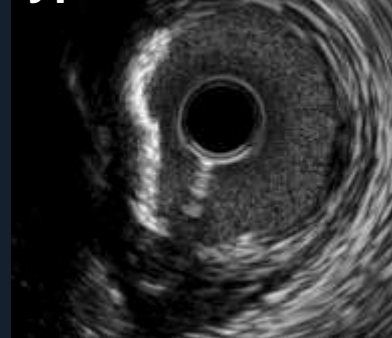
Ultrasound Wave



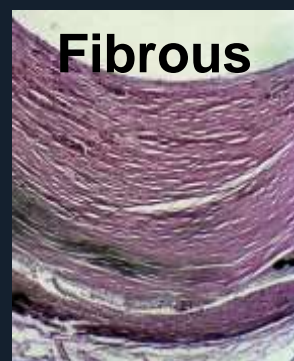
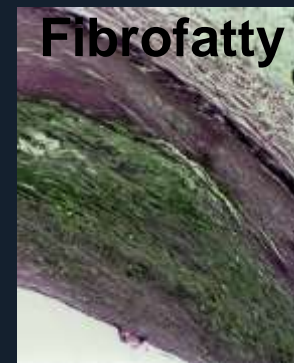
Gray Scale



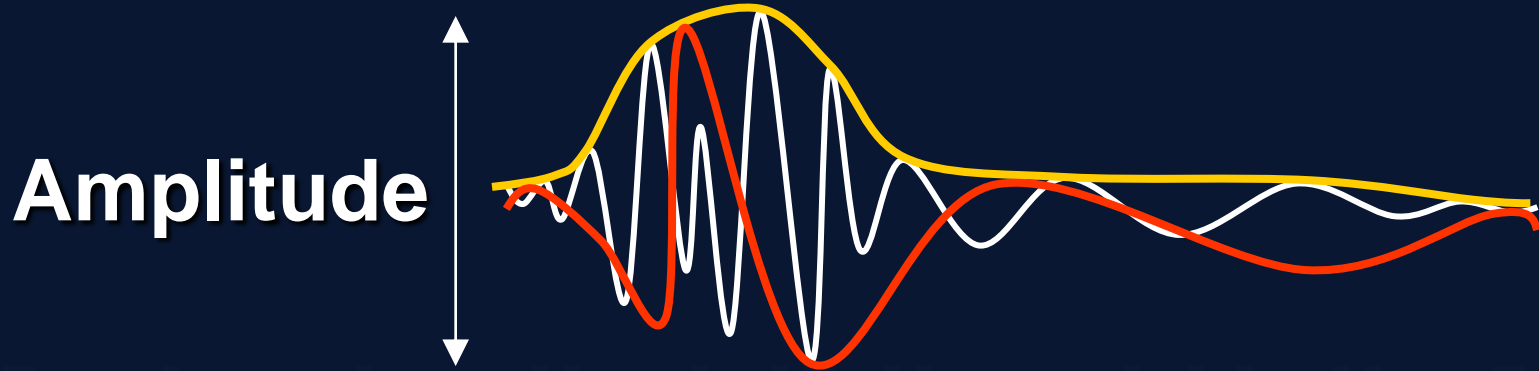
Hyper with Shadow



Pathology

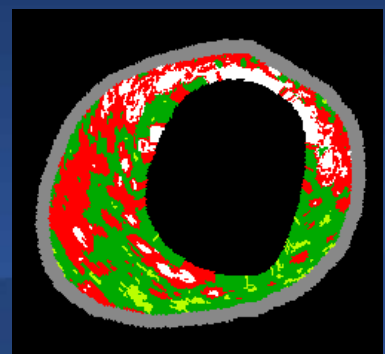


Virtual Histology

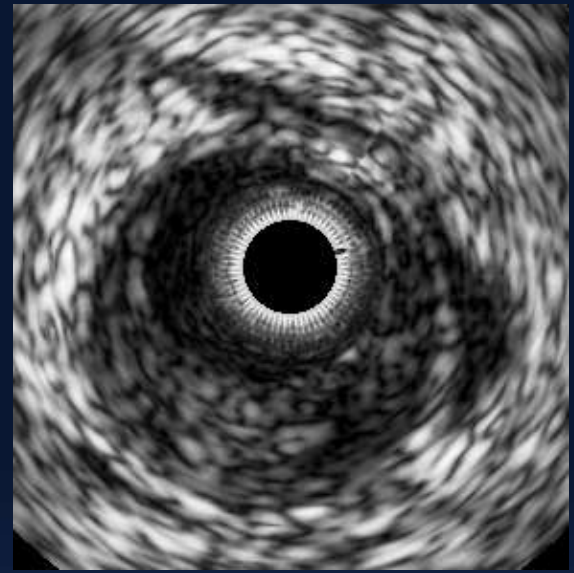
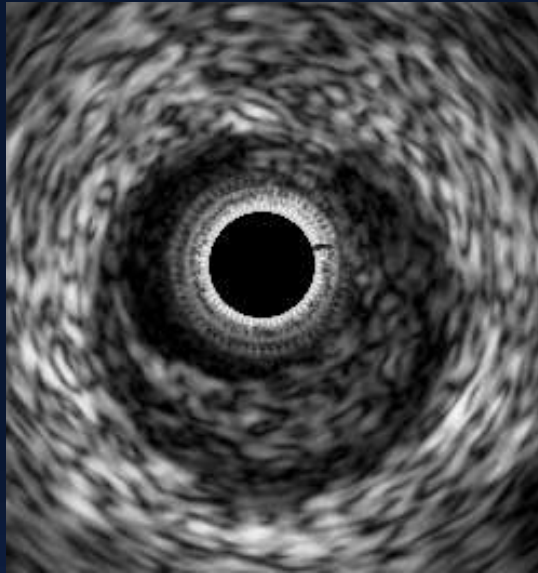


Algorithm

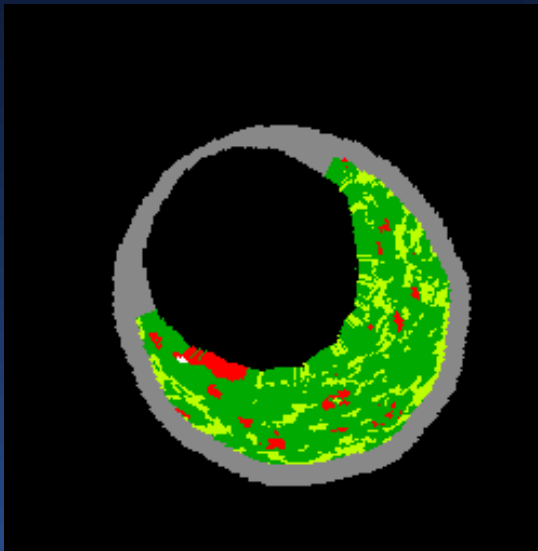
- Dense Calcium
- Necrotic Core
- Fibrous Tissue
- Fibrofatty Plaque



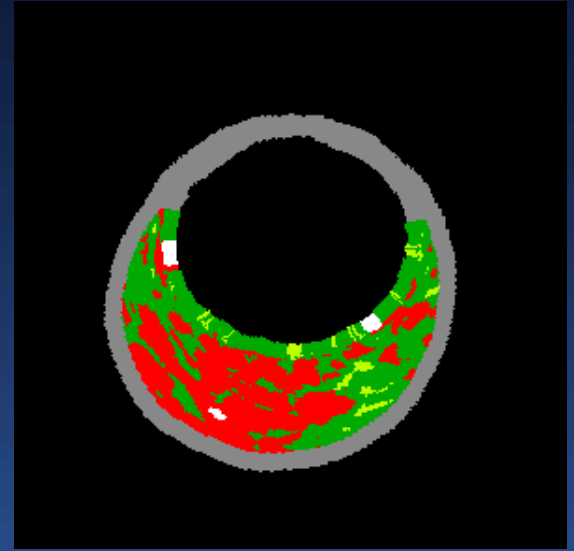
Gray Scale IVUS



VH-IVUS



Pathological Intimal
Thickening (PIT)



Thick Cap
Fibroatheroma

VH-IVUS Classification

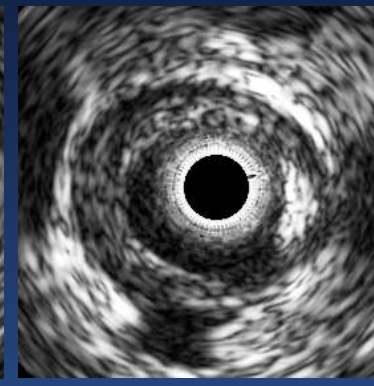
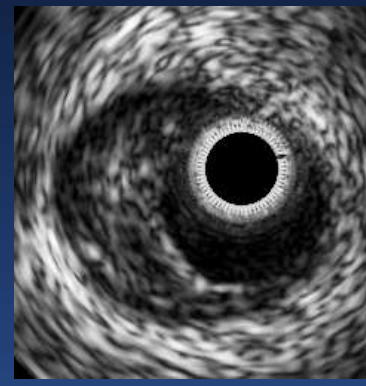
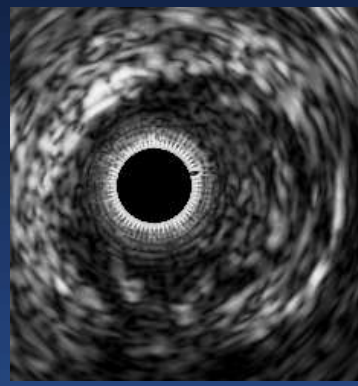
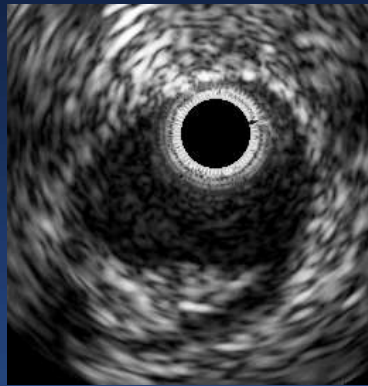
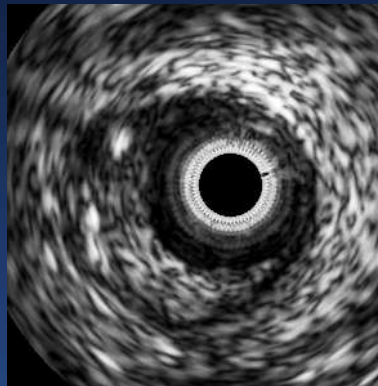
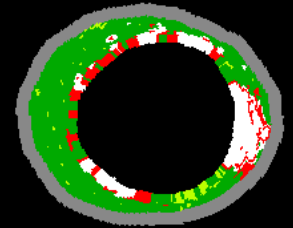
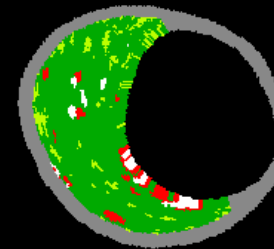
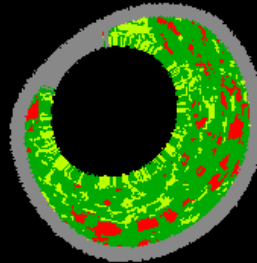
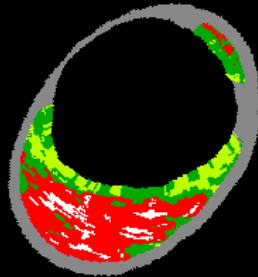
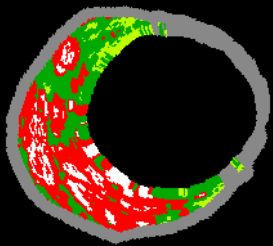
Thin-cap FA

Thick-cap FA

PIT

Fibrous

Fibrocalcific



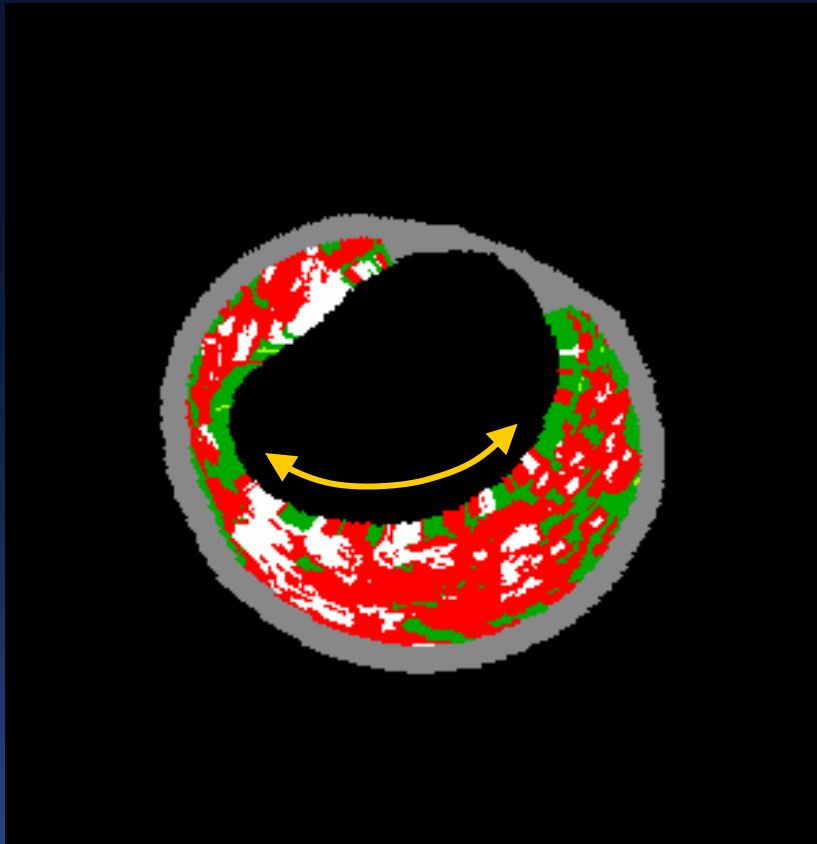
More than 10%
Confluent
Necrotic Core

More than 15%
Fibrofatty

NO more than 10%
Confluent Necrotic
Core

More than 10%
confluent
calcium

VH Thin Cap Fibroatheroma (TCFA)

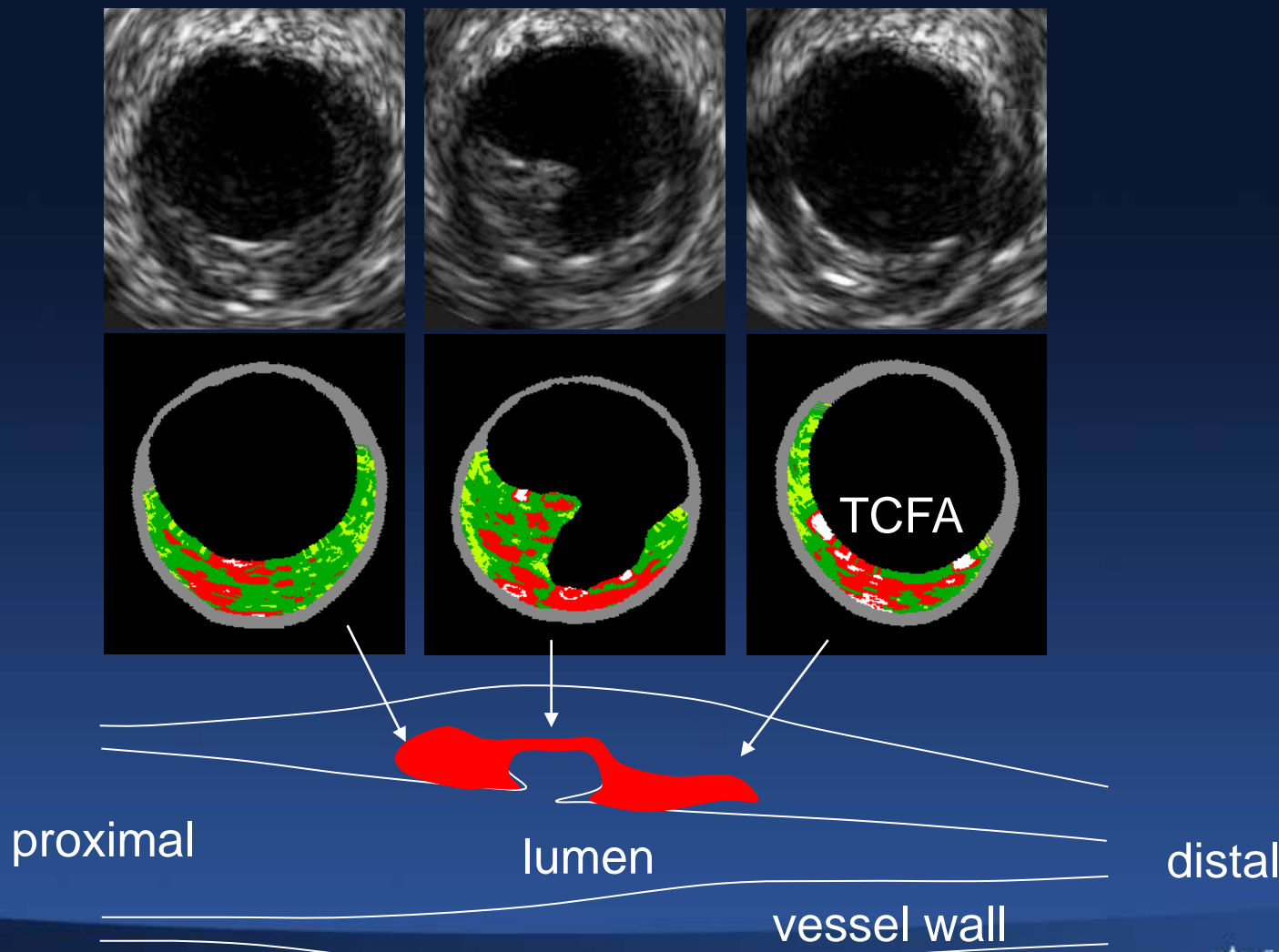


1. Confluent NC > 10%
2. 30° NC abutting the lumen
3. 3 consecutive frames
(= 1.5 mm in length)

Thin cap < 65 μm (less than the 200 μm resolution of IVUS)

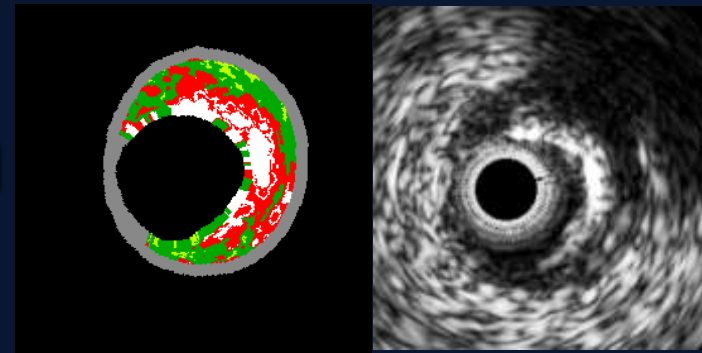
VH Morphology at Rupture Site

In 128 ruptured plaque sites, 63% showed necrotic core at bottom/shoulder of cavity, and 46% showed TCFA at proximal or distal adjacent sites.



Pitfall of Virtual Histology

Plaque behind Calcium

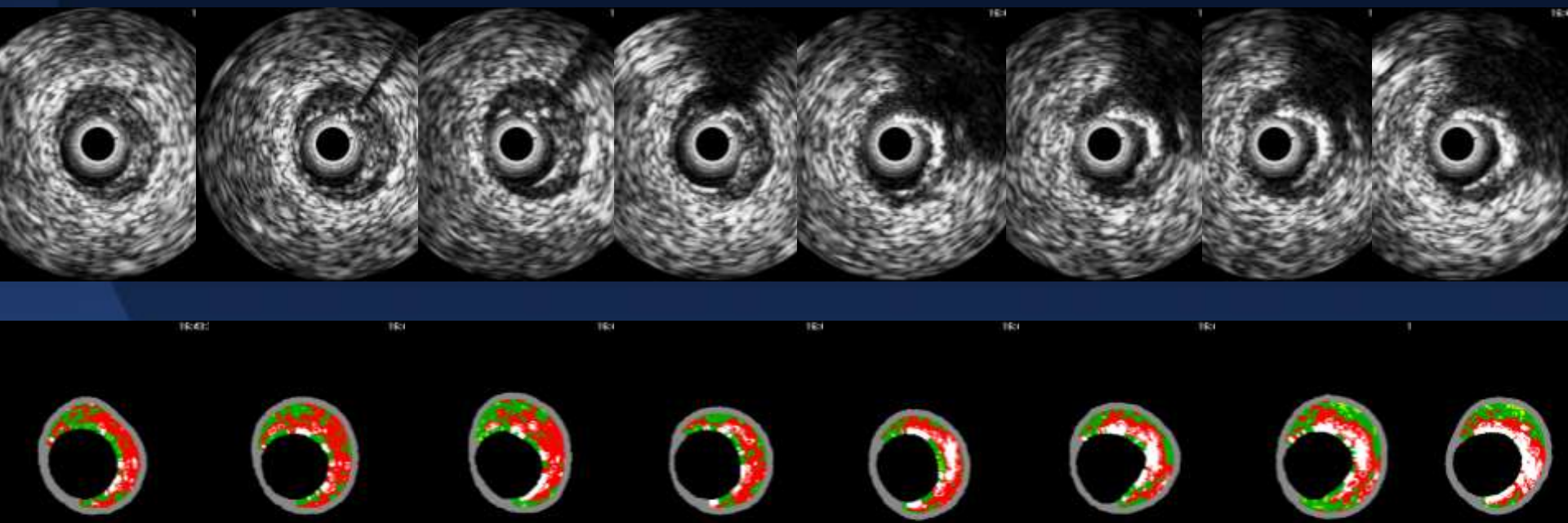


		Correct	Incorrect	ROIs	Accuracy
Mild microcalcium	IVG	2	0	2	100%
	S5	1	1	2	50%
Heavy microcalcium	IVG	3	6	9	33.3%
	S5	18	9	27	66.7%
Dense calcium	IVG	27	10	37	73%
	S5	27	16	43	62.8%
Overall	IVG	32	16	48	66.7%
	S5	46	26	72	63.9%

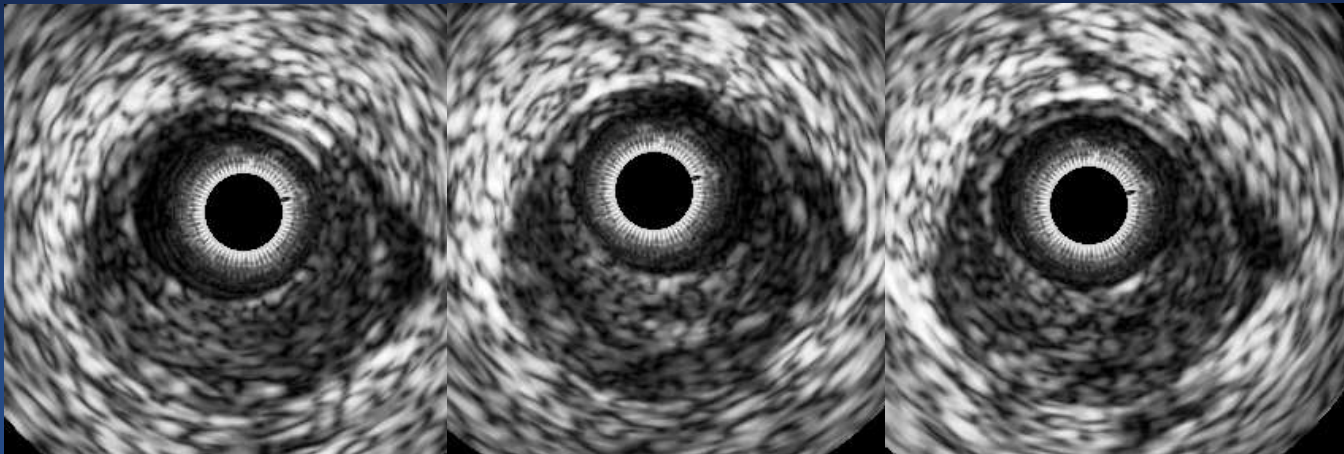
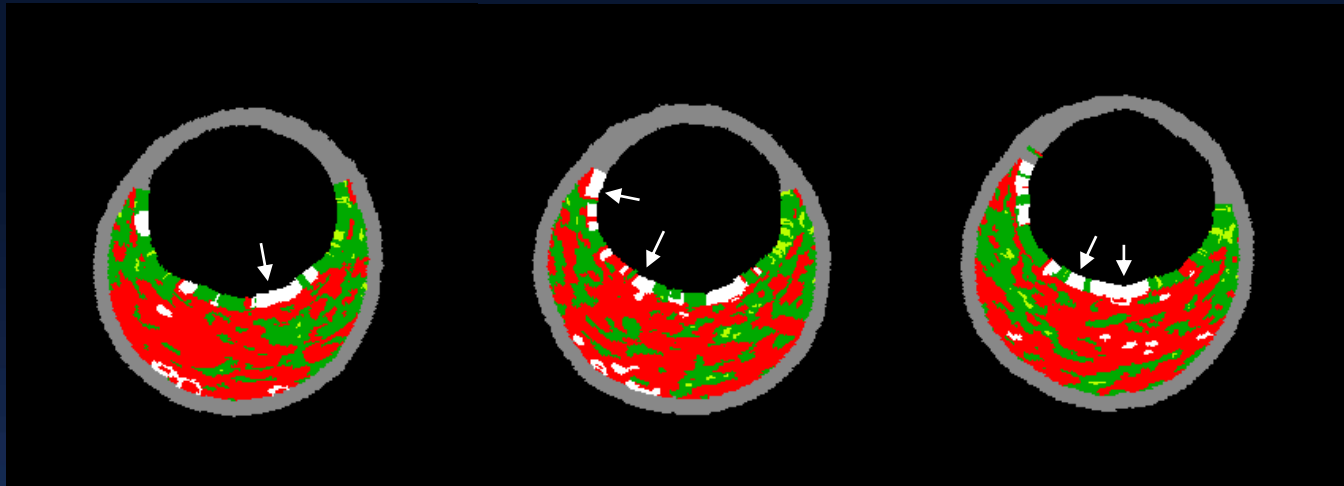
Overall Accuracy: 65.0 %

When inaccurate, tissue is classified as NC (65% of the time), as FT (18% of the time), as FF (14% of the time)

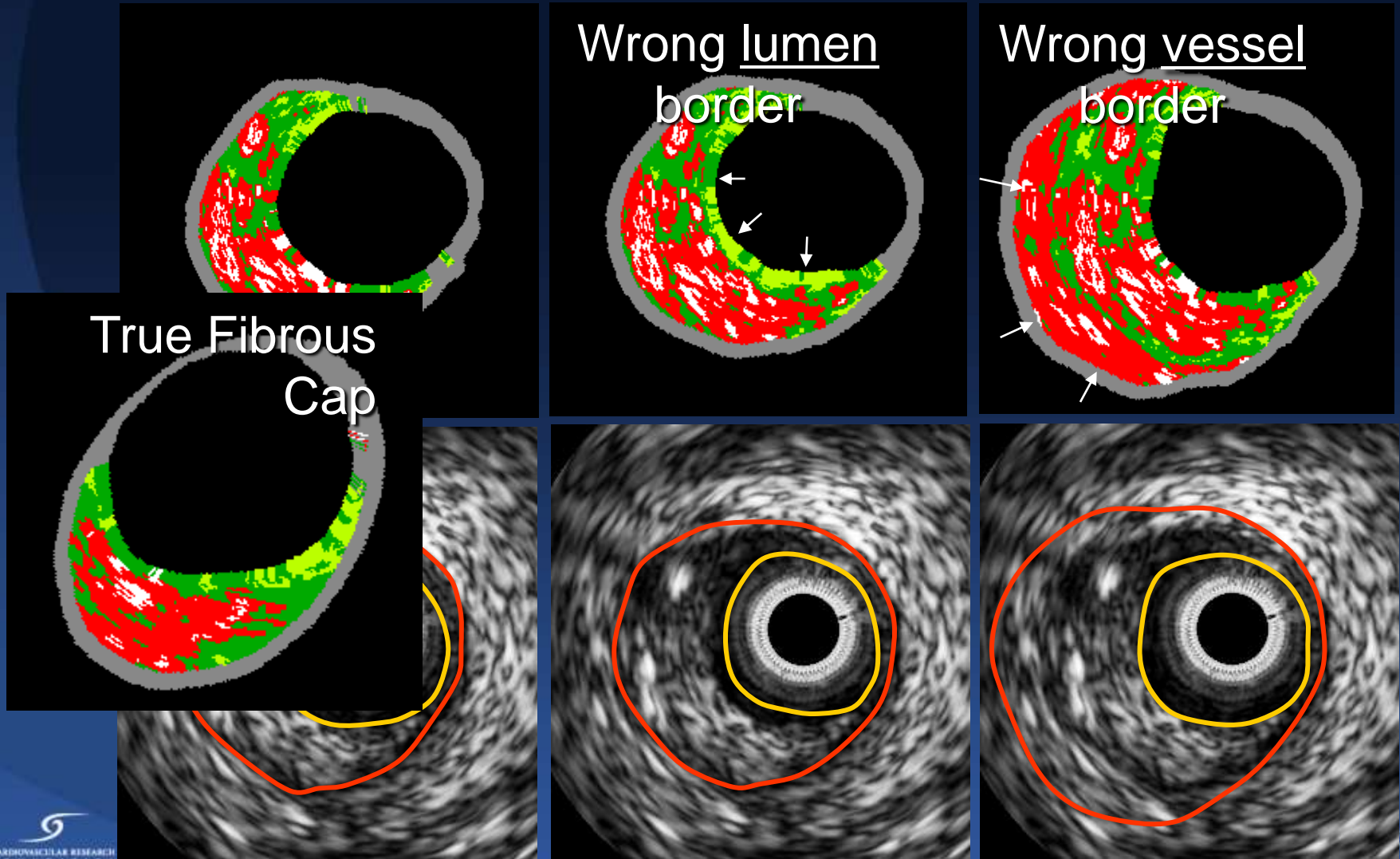
Necrotic Core Behind Calcium



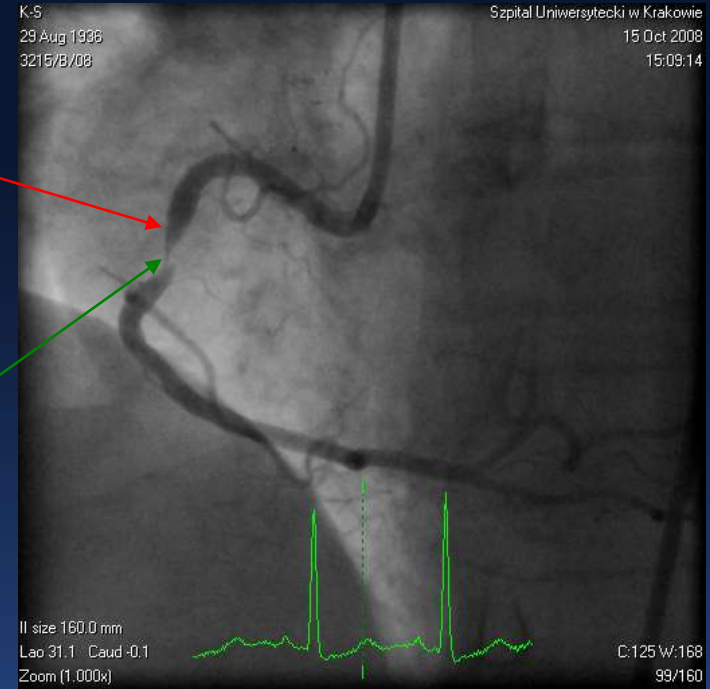
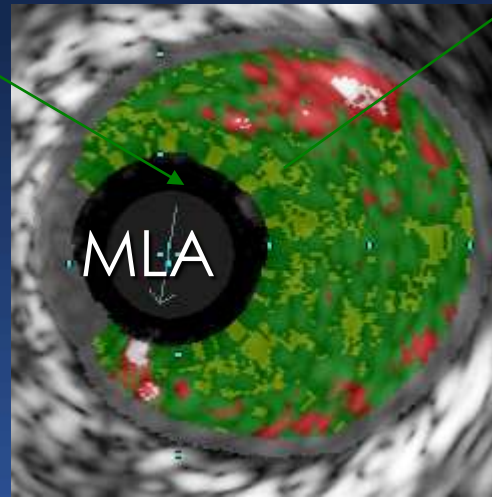
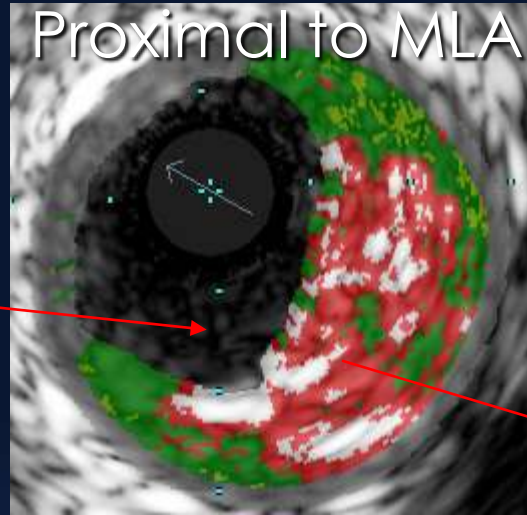
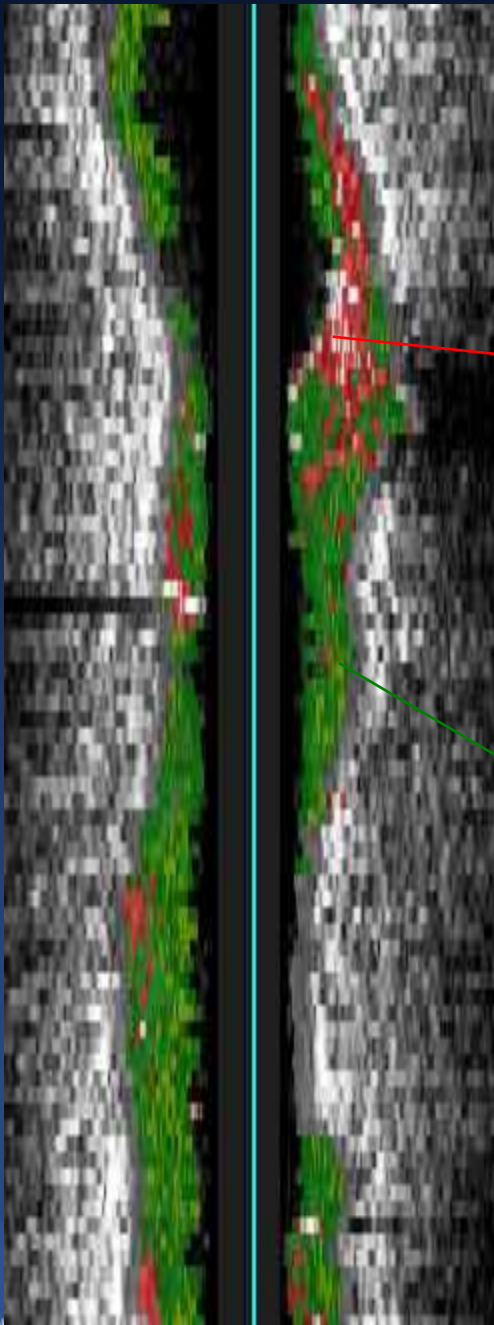
One Pixel White Border on the Surface



Wrong Lumen/Vessel Border

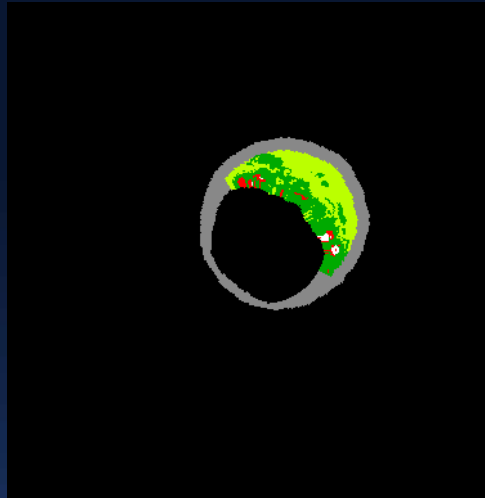


Thrombus

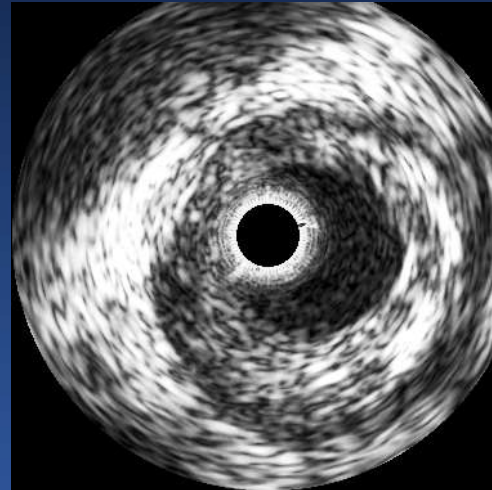
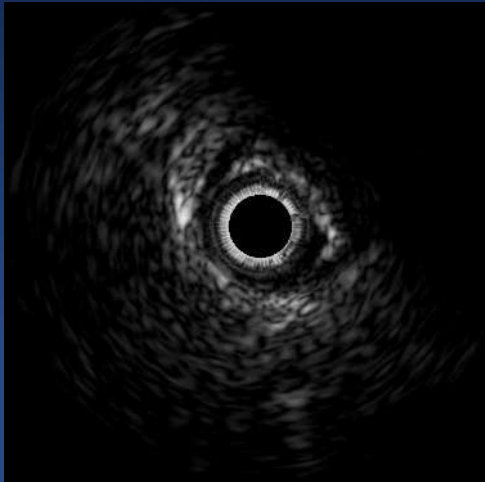
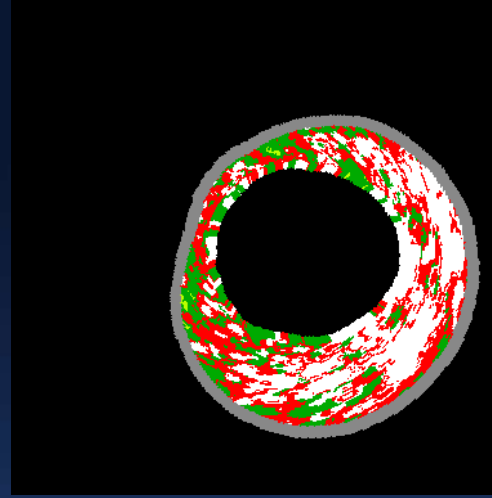


Variation of Sensitivity of Catheter

Weak Power

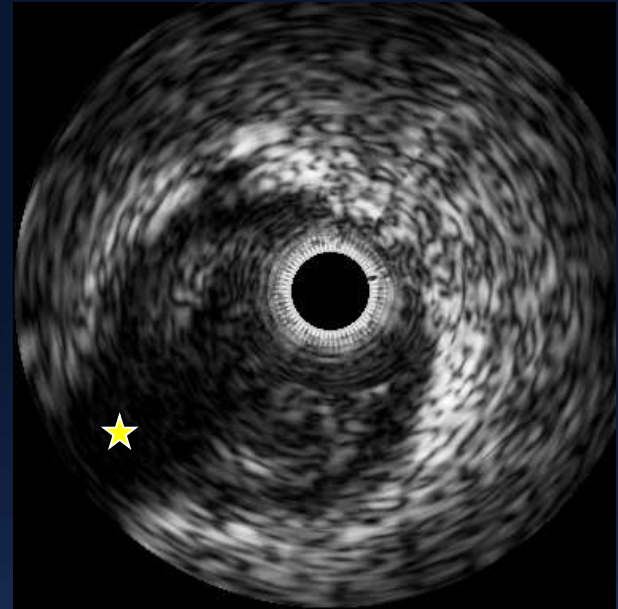
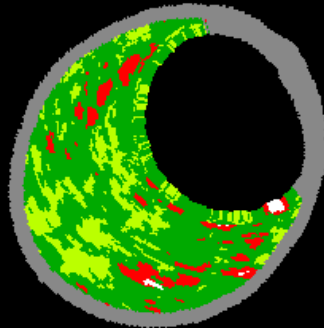


Strong Power

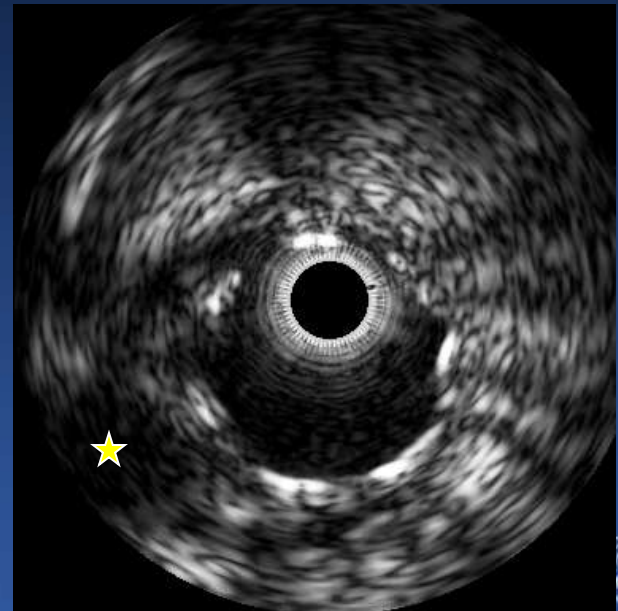
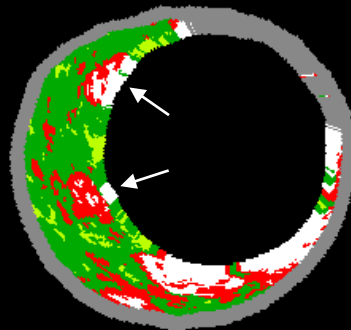


Stent Struts

Before-Stent

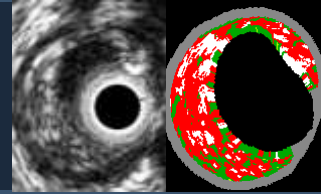


Post-Stent



Evidence of Virtual Histology

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= \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

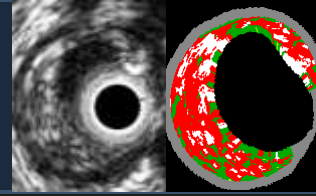
MSCT

Substudy

N=50-100

Repeat imaging
in pts with events

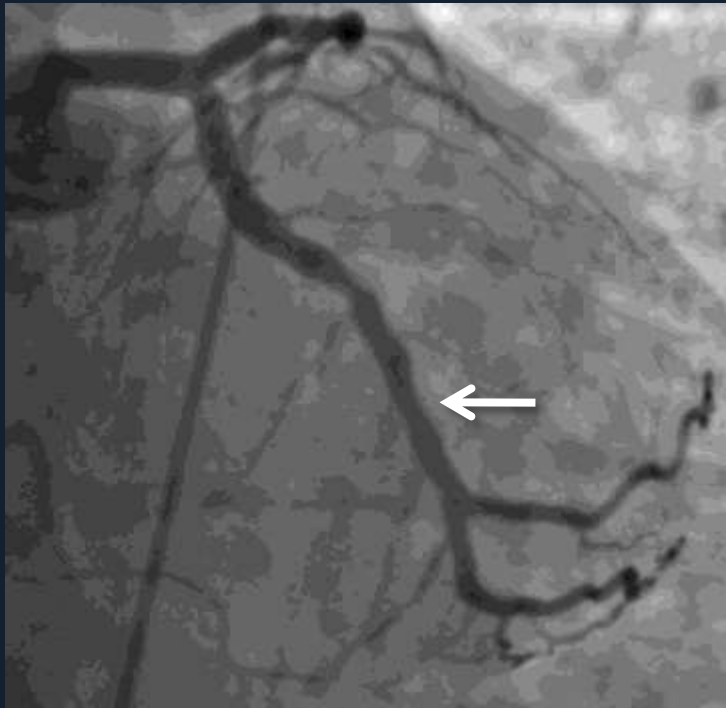
PROSPECT 82910-012: 52 yo ♂



2/13/06: NSTEMI, PCI of MLAD

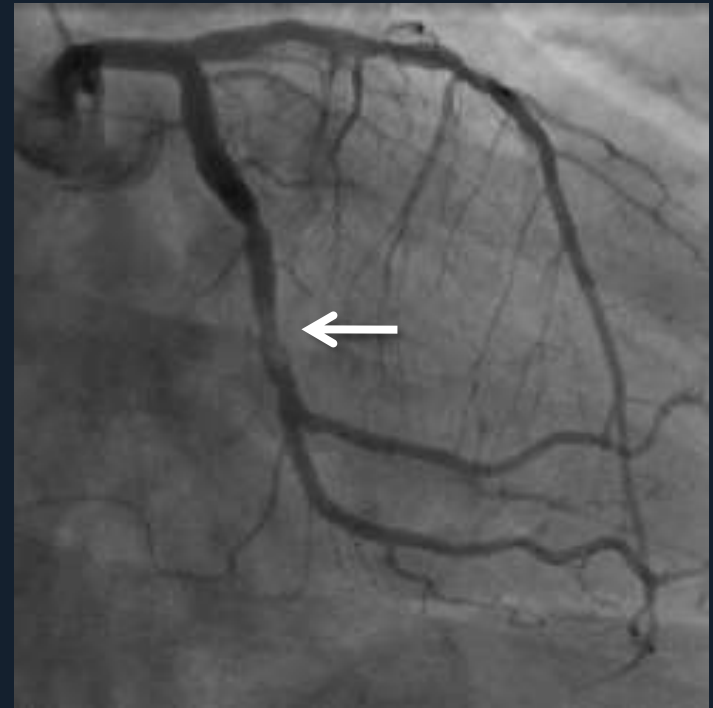
2/6/07 (51 weeks later): NSTEMI attributed to LCX

Index 2/13/06

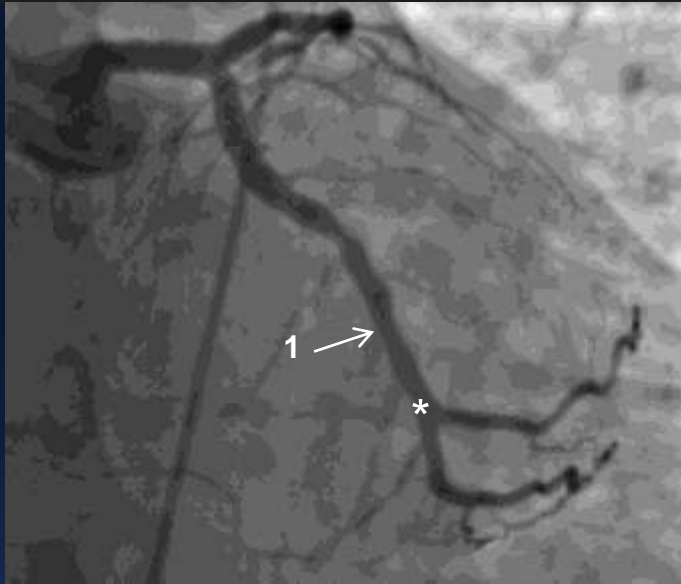
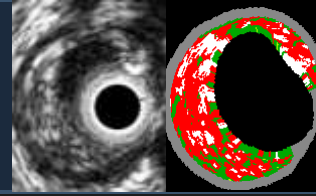


QCA PLCX DS 28.6%

Event 2/6/07

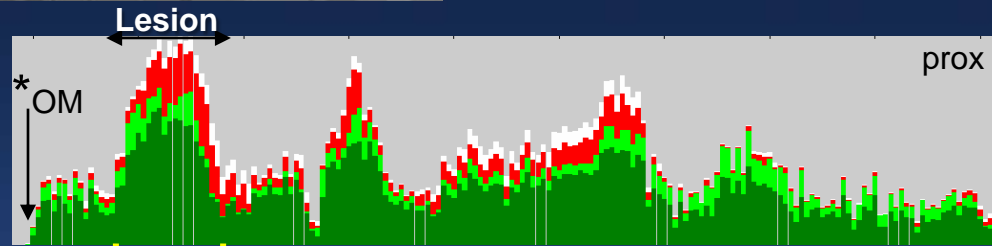


QCA PLCX DS 71.3%

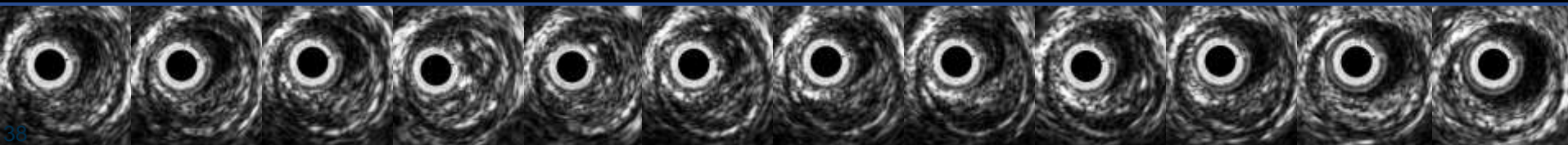
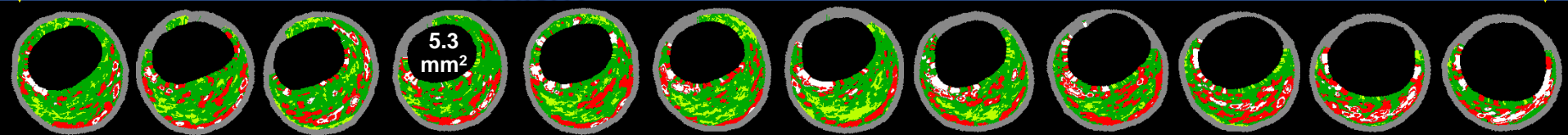


Baseline PLCX

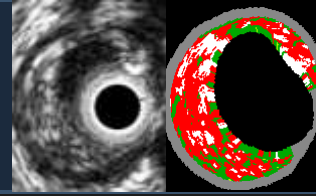
**QCA: RVD 2.82 mm,
DS 28.6%, length 6.8 mm**
IVUS: MLA 5.3 mm²
VH: ThCFA



1. ThCFA

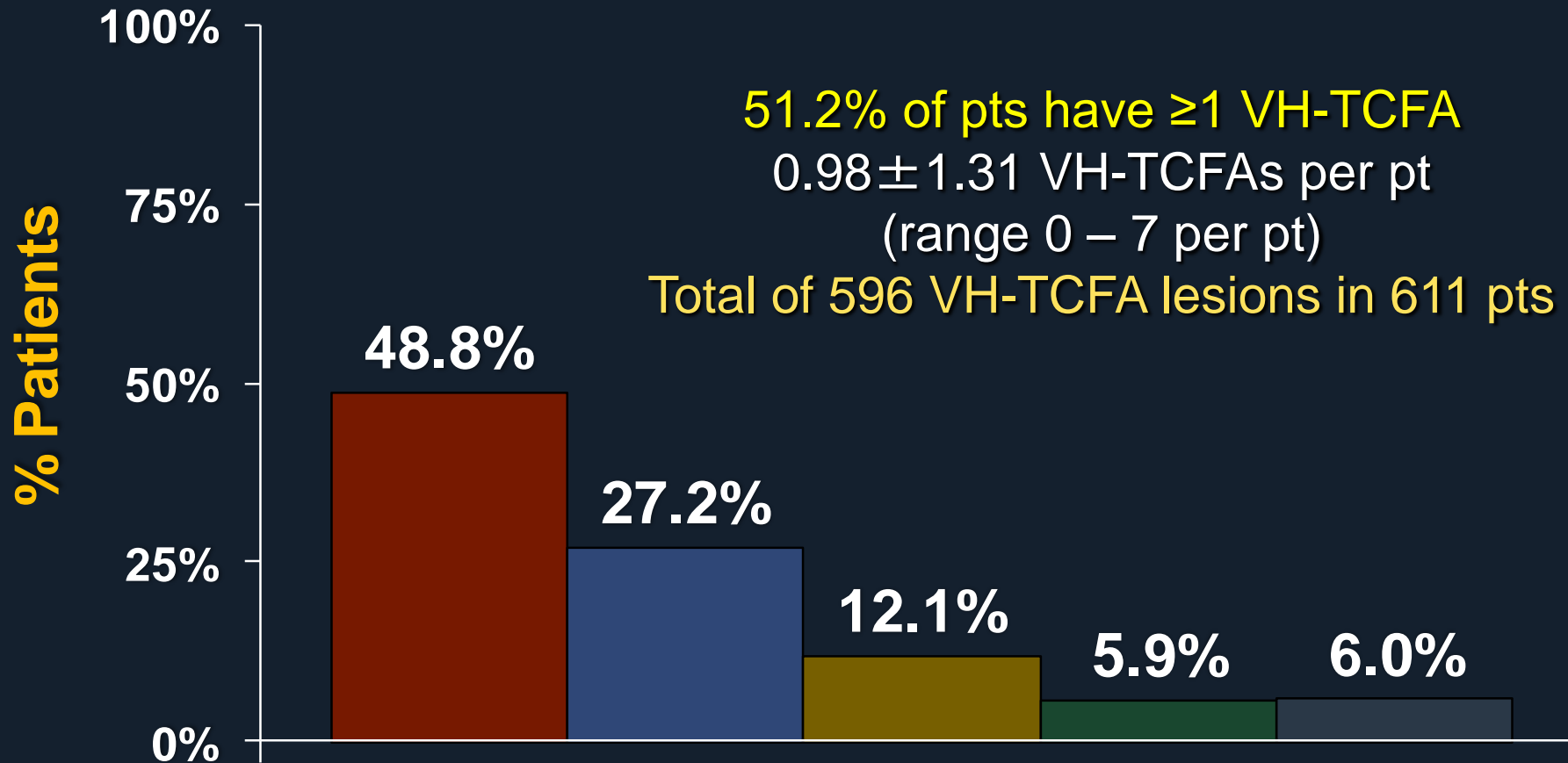


PROSPECT: Imaging Summary

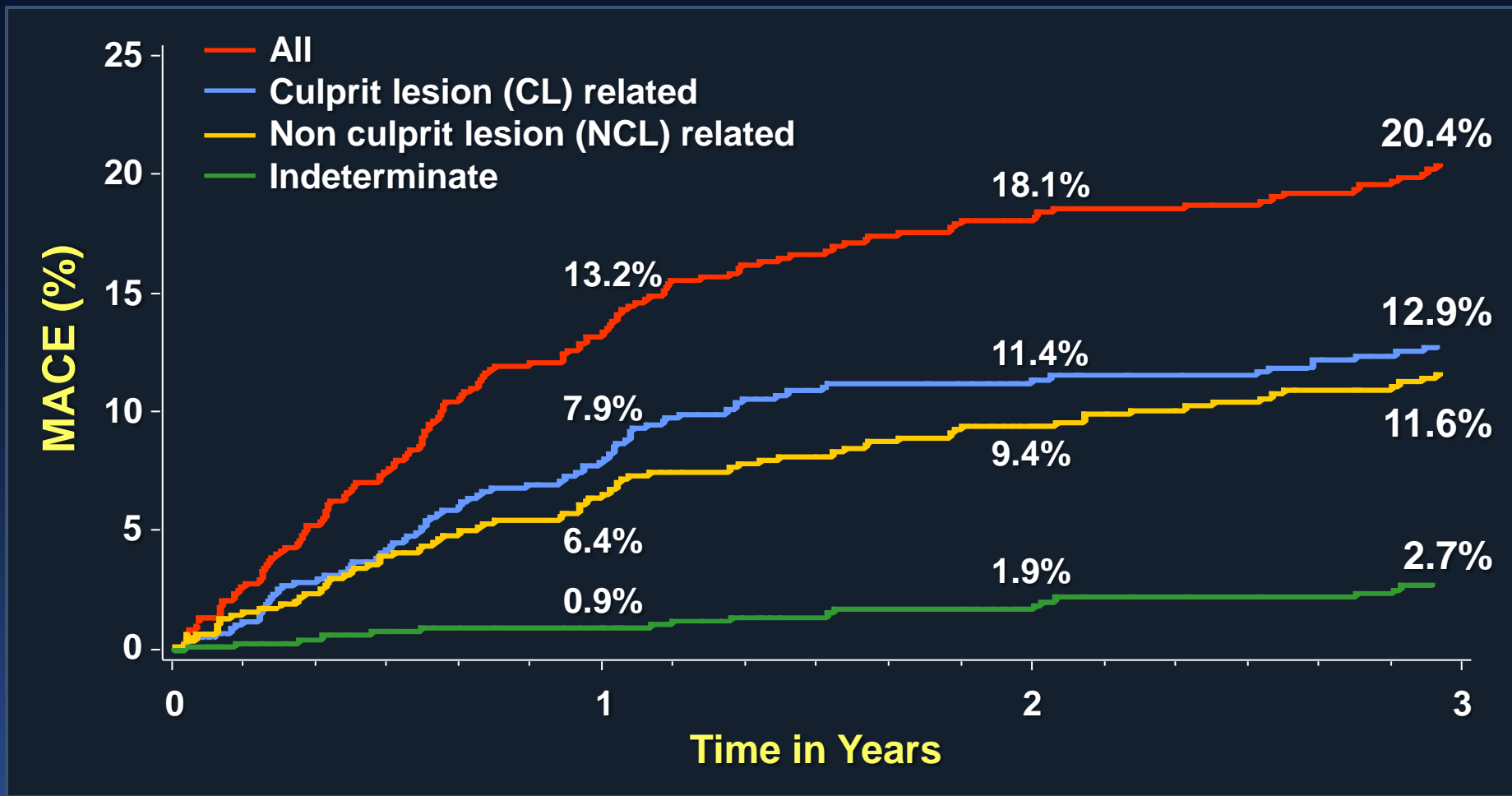
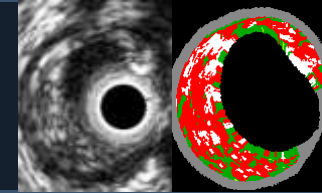


Per patient incidence of VH-TCFAs

N lesions/pt per coronary tree: ■ 0 ■ 1 ■ 2 ■ 3 ■ ≥4



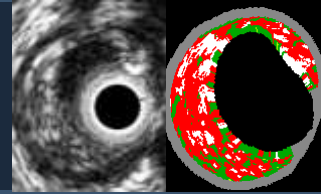
PROSPECT: MACE



Number at risk

Group	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

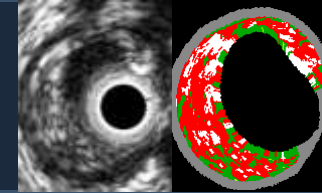
PROSPECT: MACE



3-year follow-up, non hierarchical

	All	Culprit lesion related	Non culprit lesion related	Indeter- minate
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

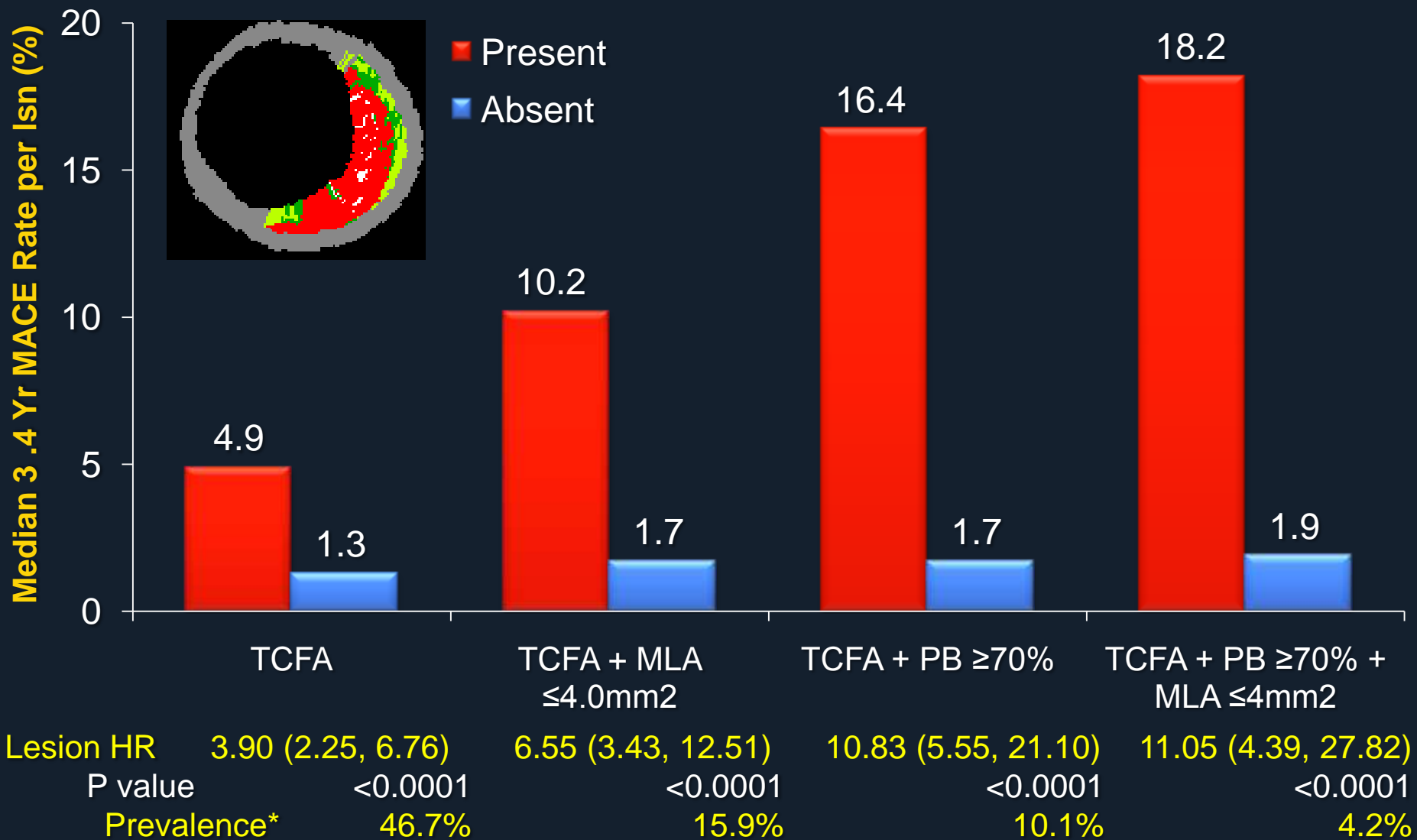
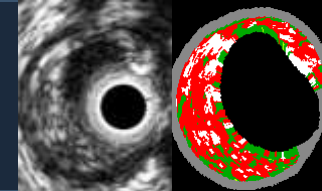


Independent predictors of lesion level events by Cox Proportional Hazards regression

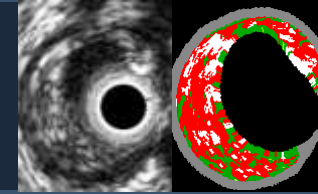
<u>Variable</u>	<u>HR [95% CI]</u>	<u>P value</u>
$PB_{MLA} \geq 70\%$	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
$MLA \leq 4.0 \text{ mm}^2$	3.21 [1.61, 6.42]	0.001

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.

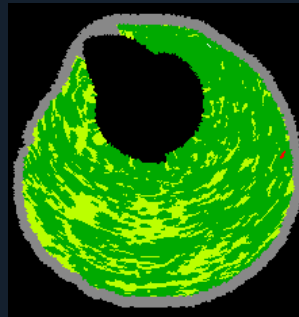
PROSPECT: VH-TCFA and Non Culprit Lesion Related Events



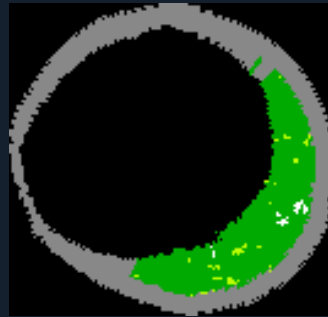
PROSPECT: Non Fibroatheromas and Non Culprit Lesion Events



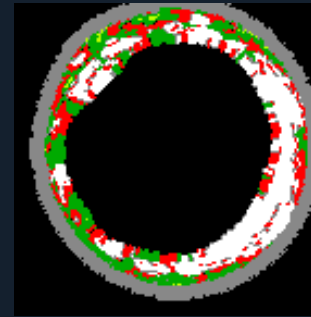
Median 3.4 year MACE rate per lesion (%)



Pathological Intimal thickening

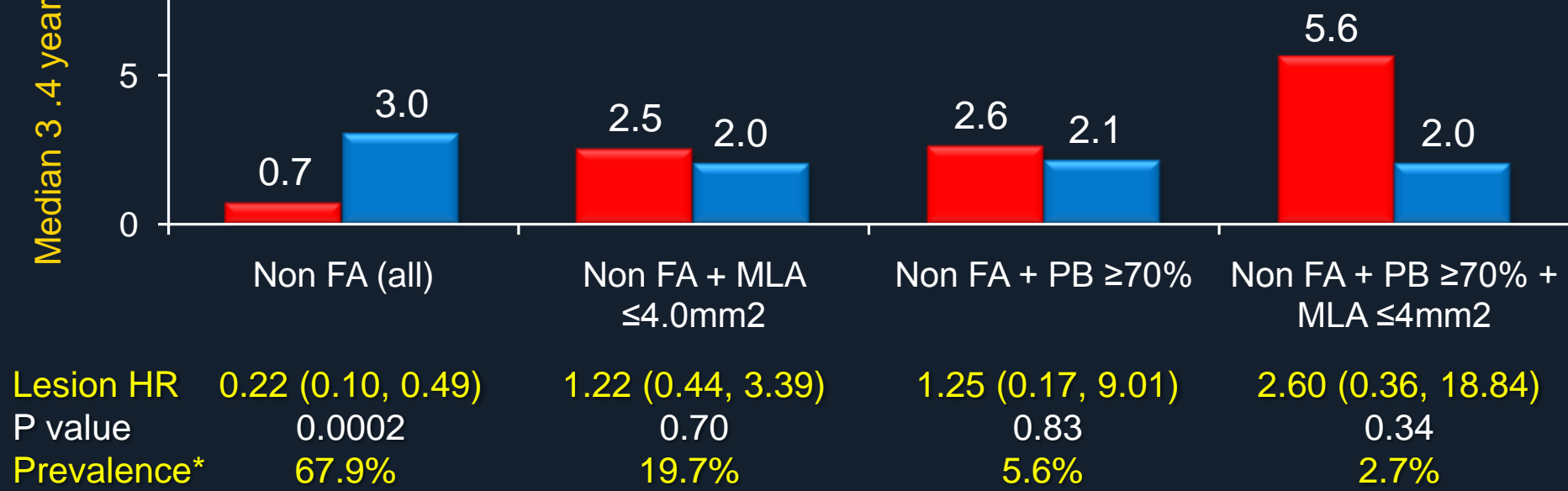


Fibrotic



Fibrocalcific

■ Present
■ Absent



VIVA Study (VH-IVUS in Vulnerable Atherosclerosis)

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

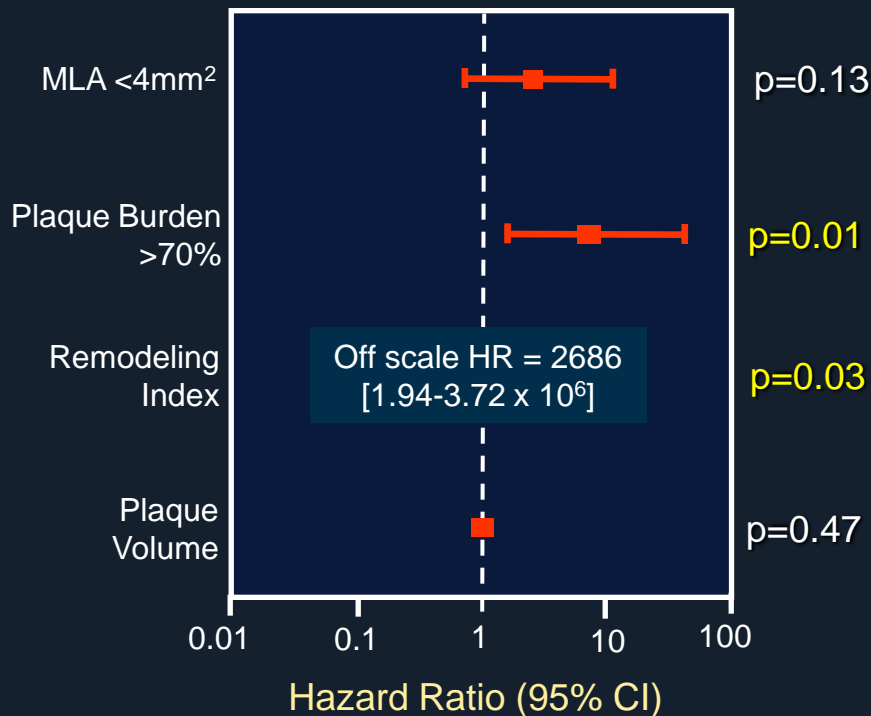
1,096 plaques were classified; median follow-up 625 days

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

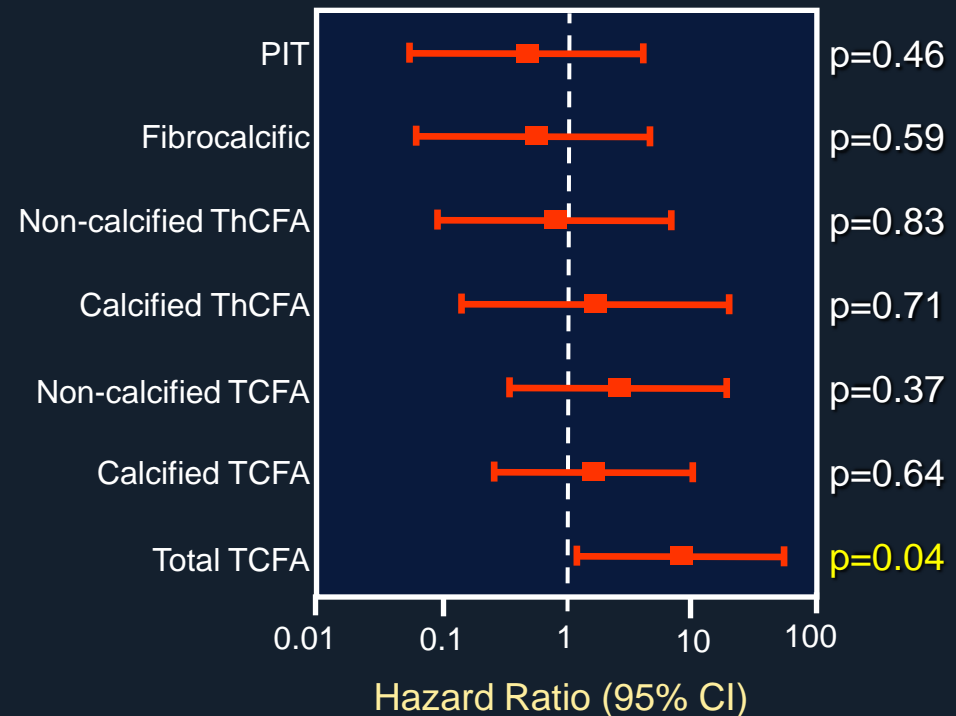
19 lesions (13 nonculprit lesions and 6 culprit lesions)

Univariate predictors of non-culprit MACE

Grayscale IVUS characteristics

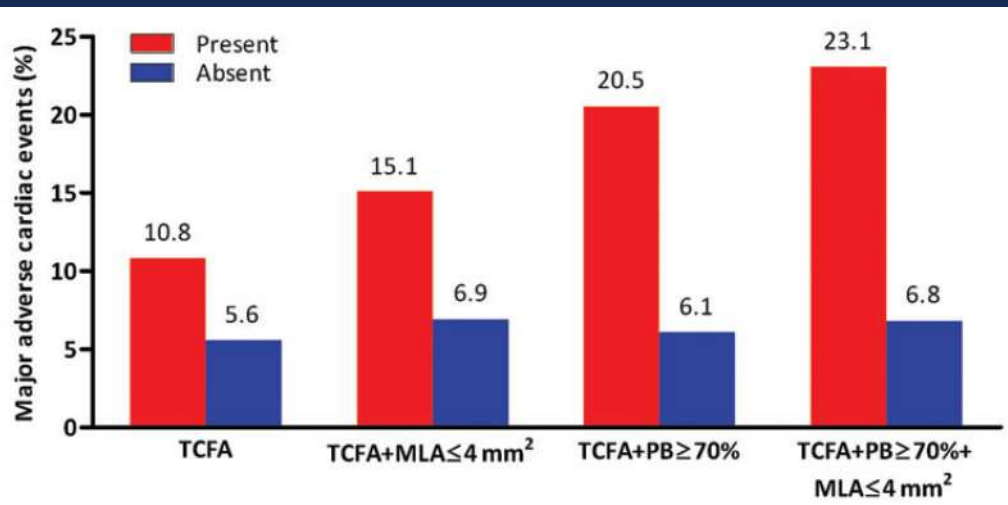
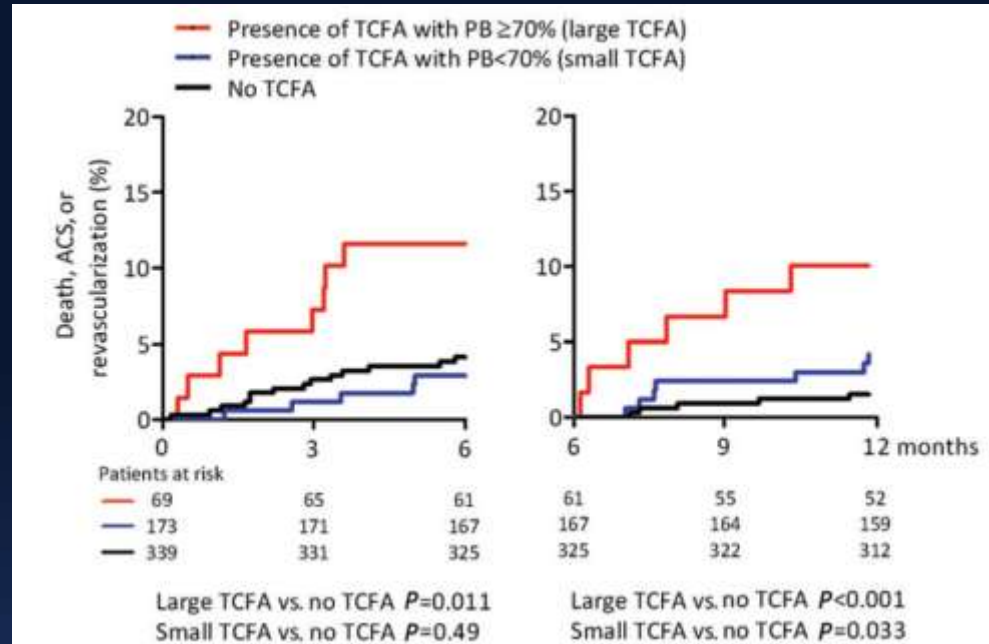


VH-IVUS lesion classification



ATHEROREMO-IVUS Study

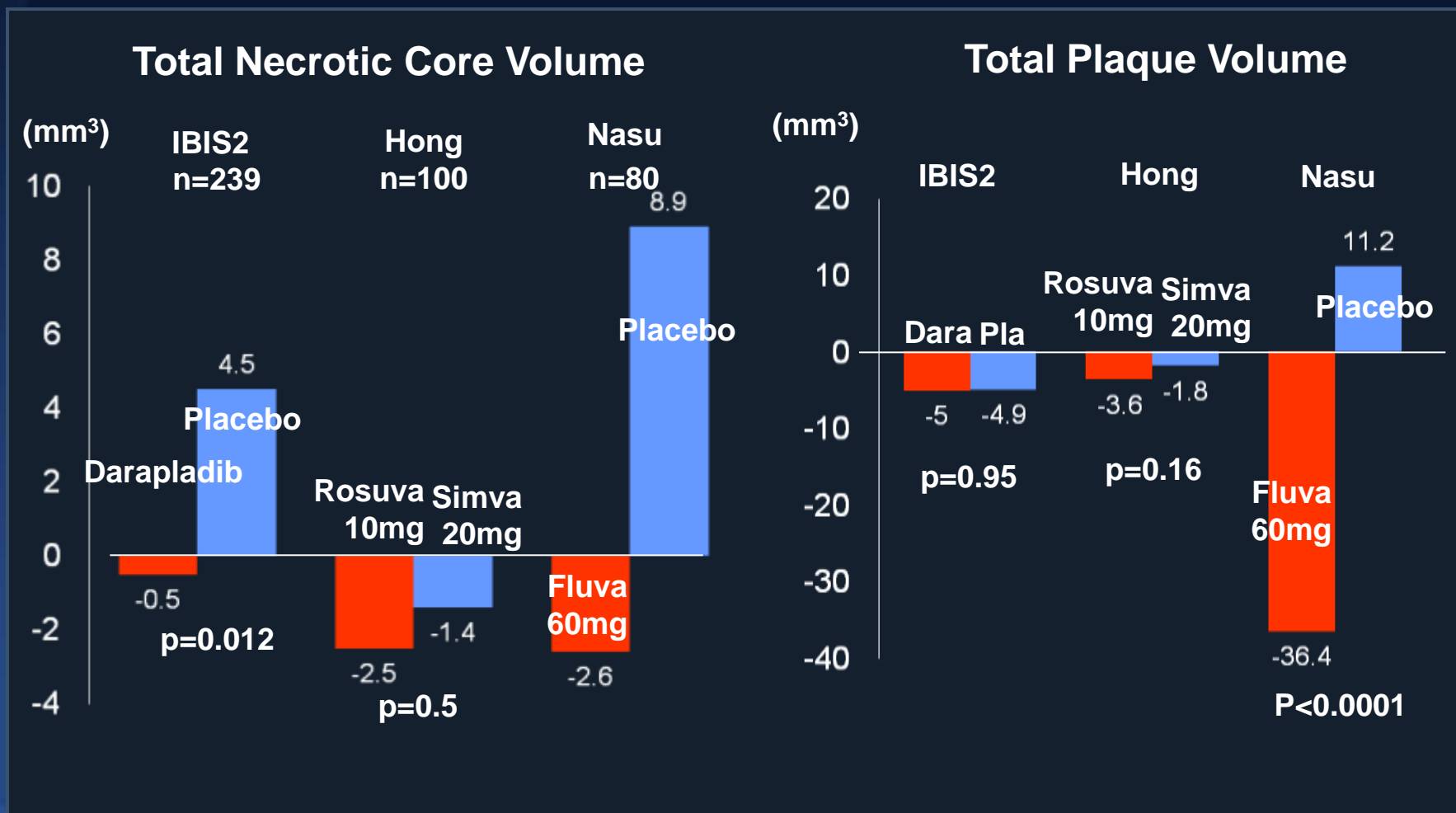
- 581 patients in 2008-2011
- 1 year follow-up
- MACE (non-culprit related ACS, unplanned coronary revascularization or indeterminate mortality)
- Single center, prospective



Serial (Multiple Time Points) Evaluation of Virtual Histology

Regression/Stabilization Trials by VH-IVUS

Darapladib (oral Lp-PLA₂ inhibitor), 1 yr FU



Serruys P, Circulation 2009;118:1172, Hong M, JACC Int 2009;2:679, Nasu K, JACC Int 2009;2:686

Change of Plaque Type in 216 Non-Culprit Lesions in 99 pts - Stable Cohort-

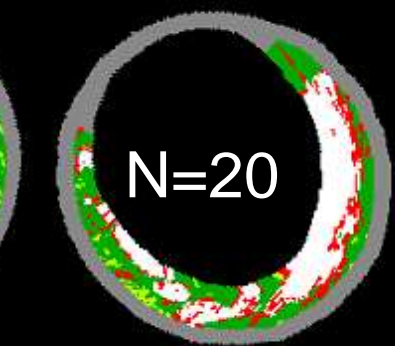
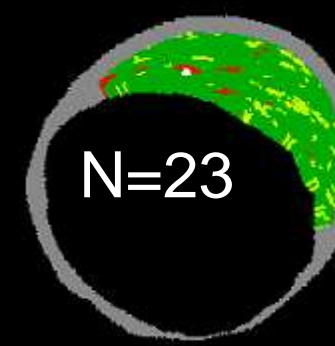
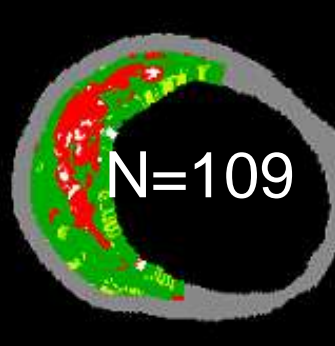
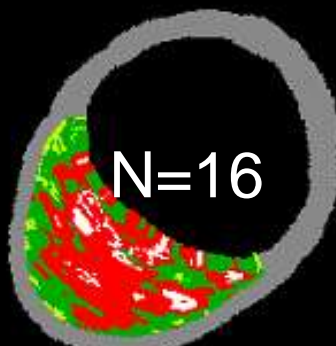
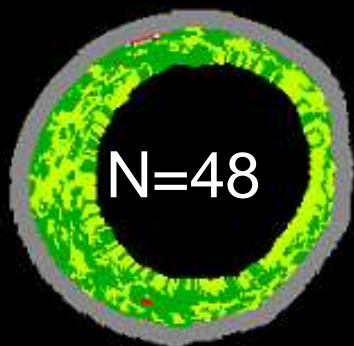
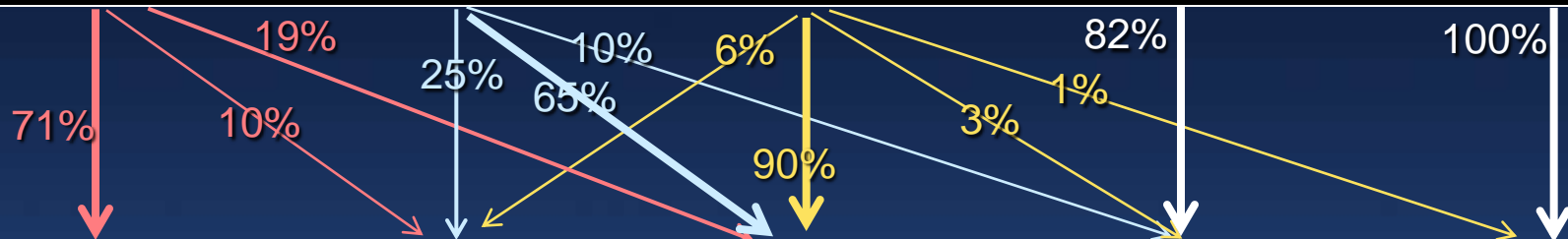
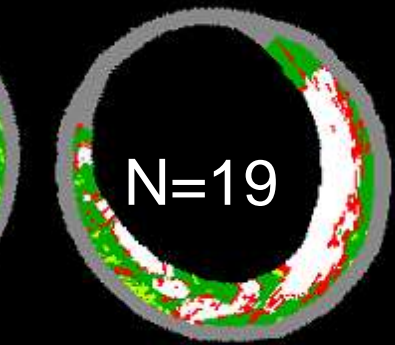
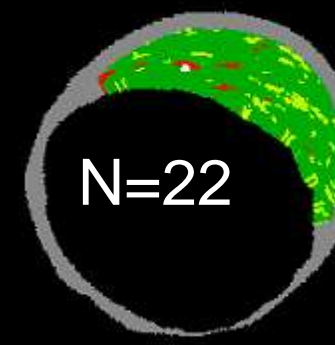
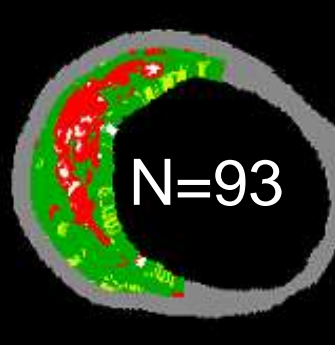
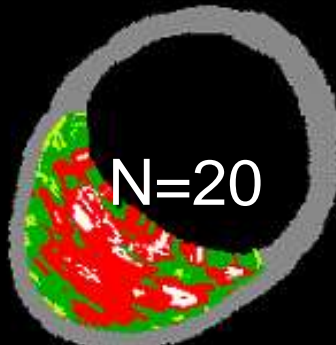
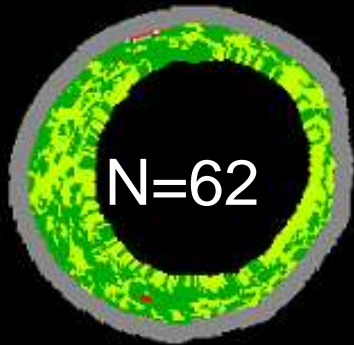
PIT

TCFA

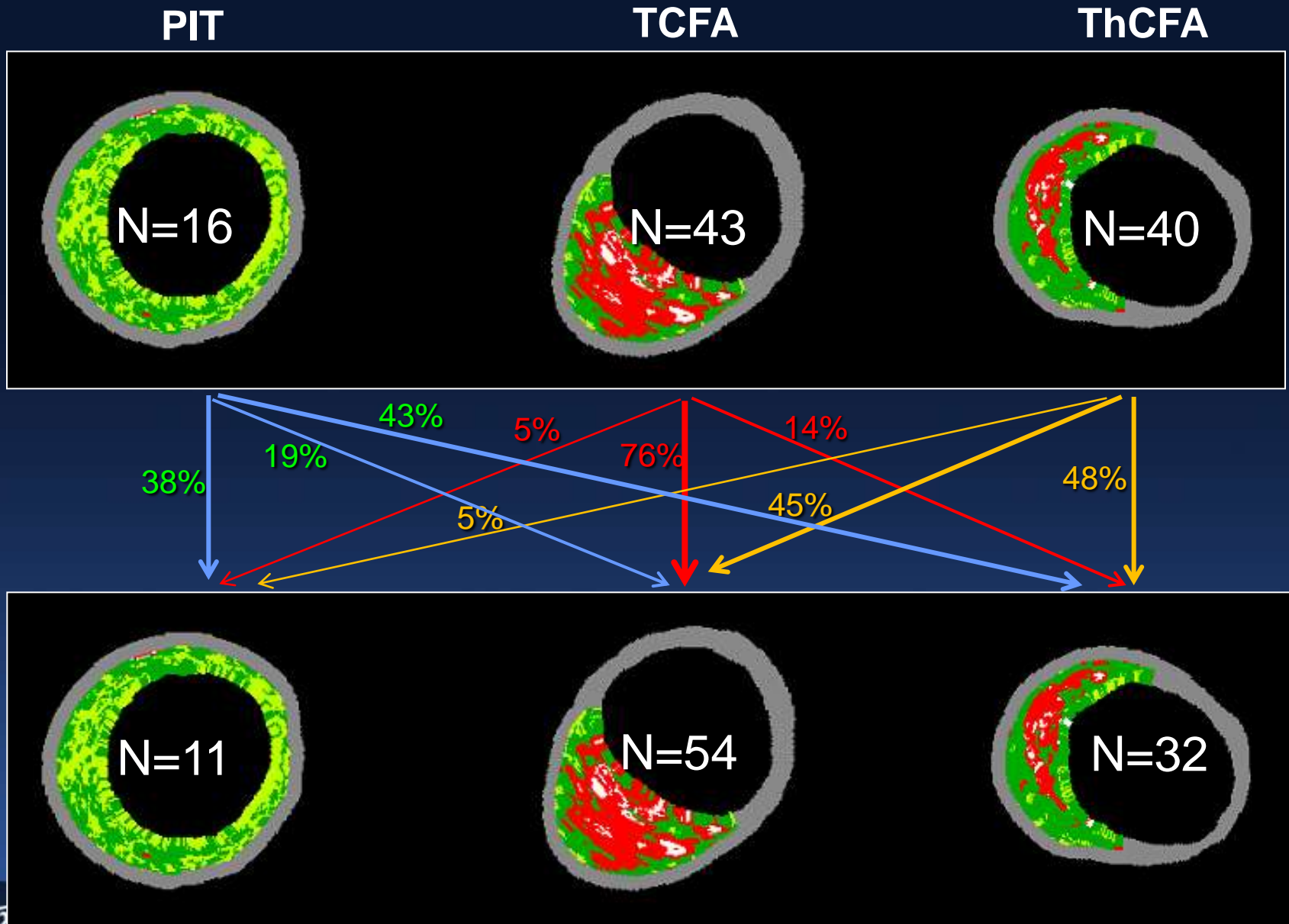
ThCFA

Fibrotic

Fibrocalcific



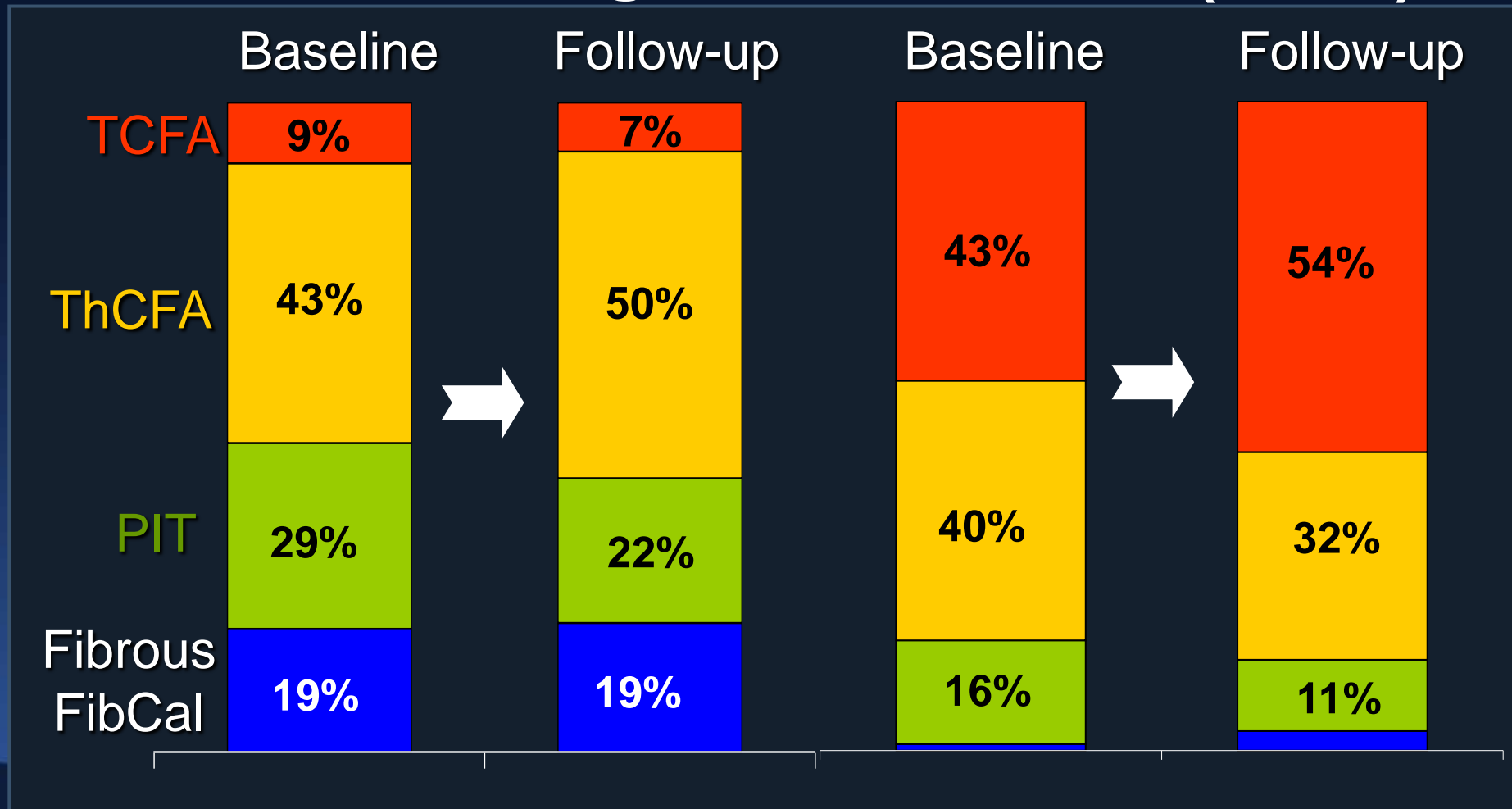
HORIZONS-AMI in 101 non-culprit lesions in 63 pts



Differences in Temporal Changes of Non-Culprit Lesions

Stable Angina

STEMI (100%)



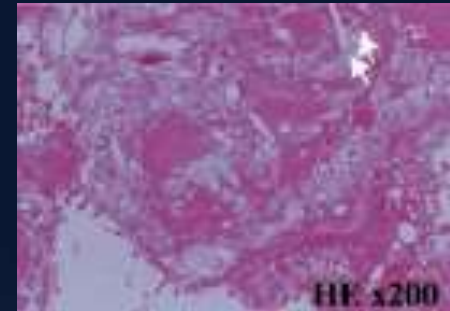
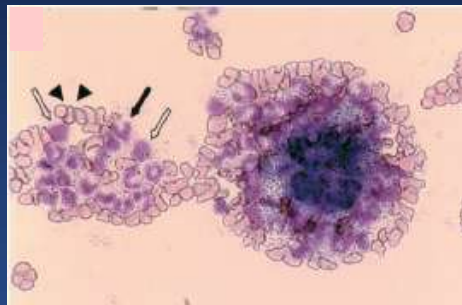
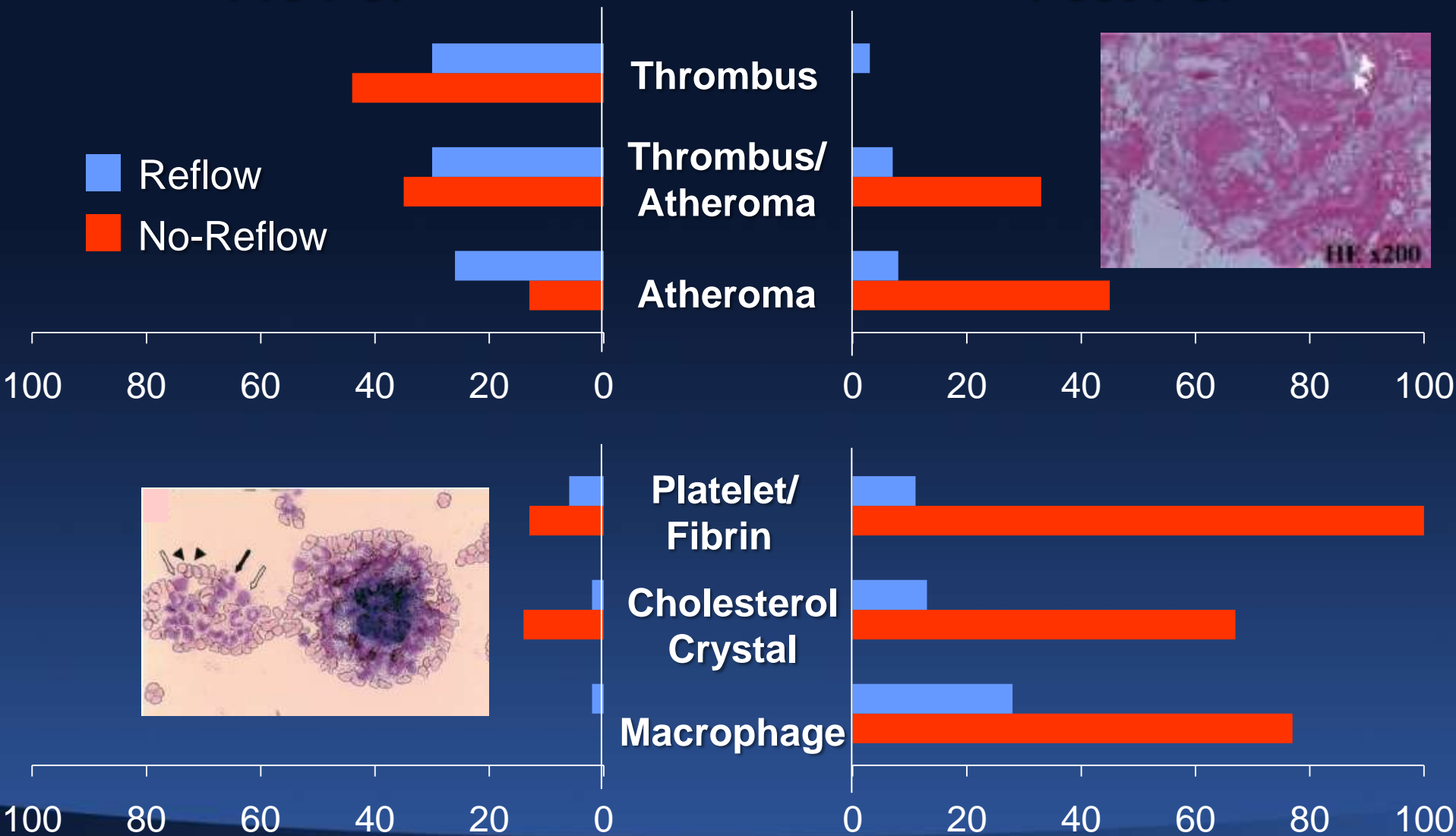
Prediction of Distal Embolization

Flow and Retrieved Material

Pre-PCI

Post-PCI

Reflow
No-Reflow



Necrotic Core /TCFA

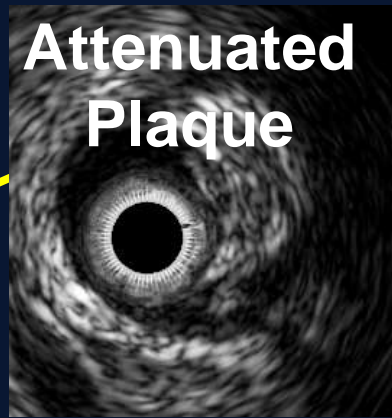
Near Infrared Spectroscopy



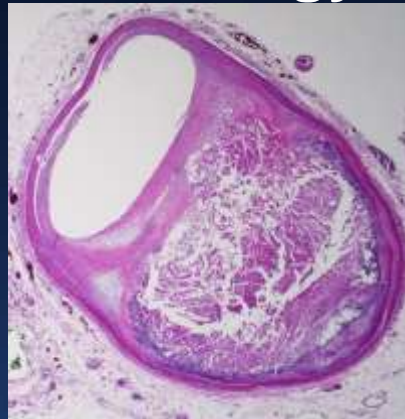
MDCT



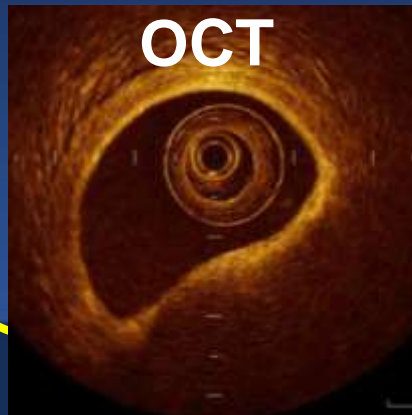
Attenuated Plaque



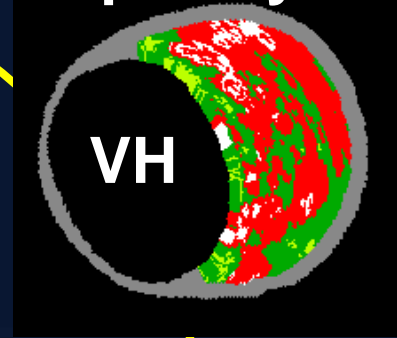
Pathology



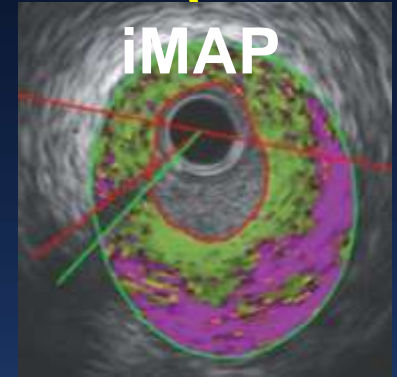
OCT



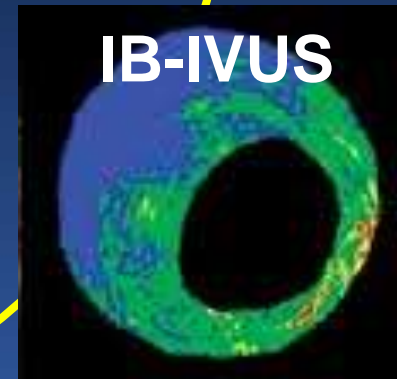
Radio-Frequency IVUS



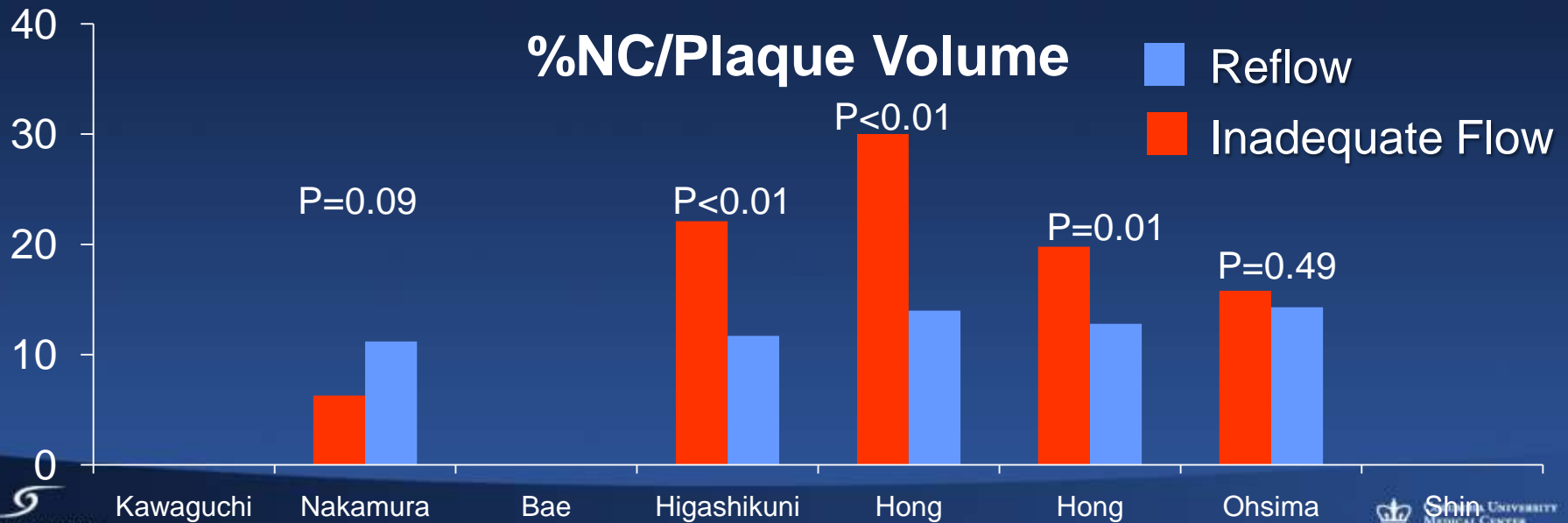
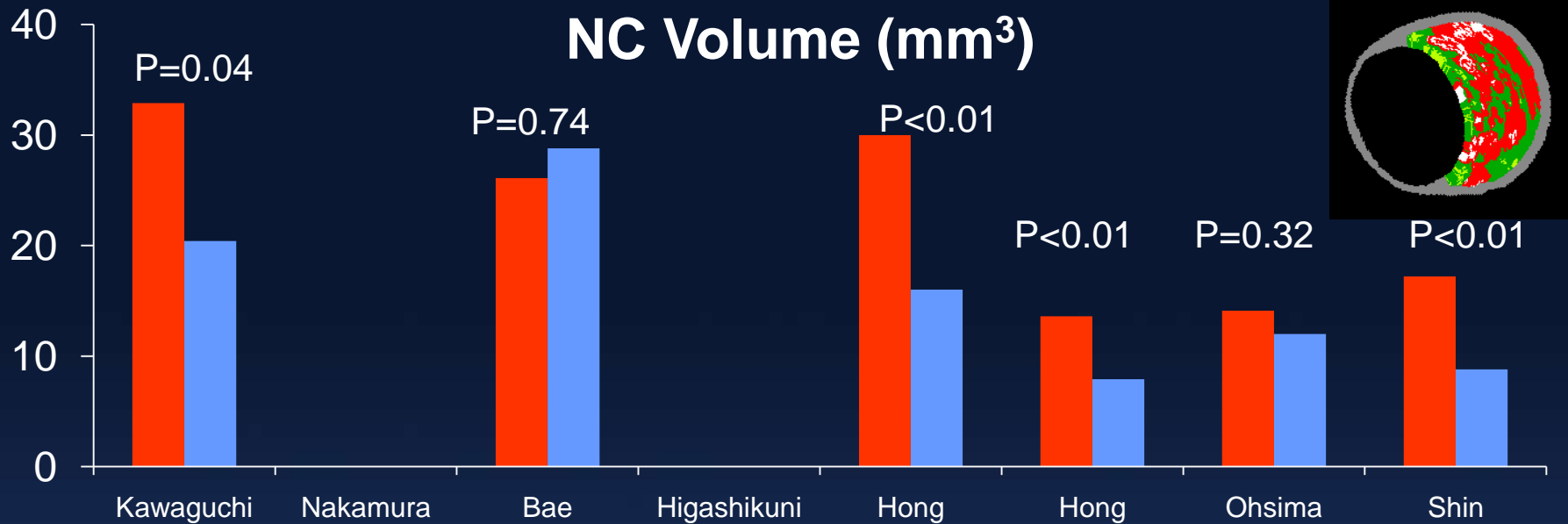
iMAP



IB-IVUS



VH Necrotic Core and Inadequate Flow



Neoatherosclerosis Evaluation

Various Neointimal VH Composition at the Maximal %IH Sites

6-mo Taxus

%NC 8%
%DC 2%

9-mo Taxus

%NC 28%
%DC 8%

22-mo Taxus

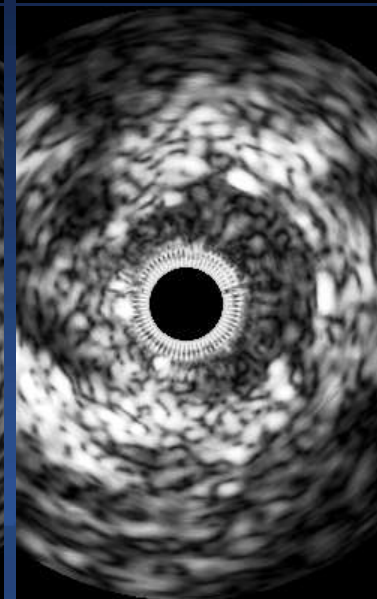
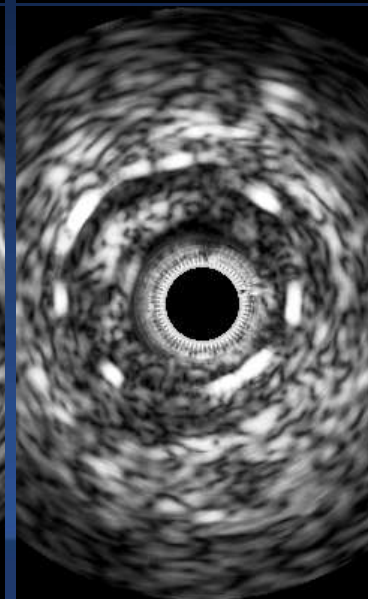
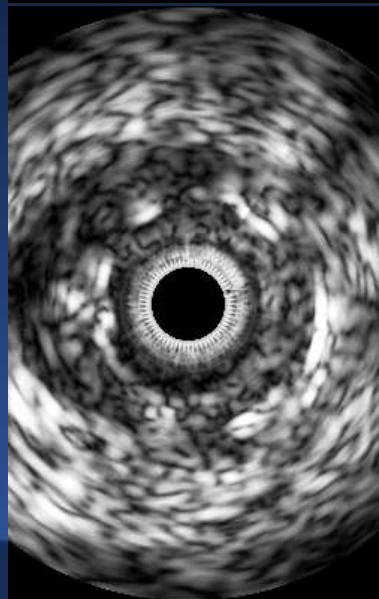
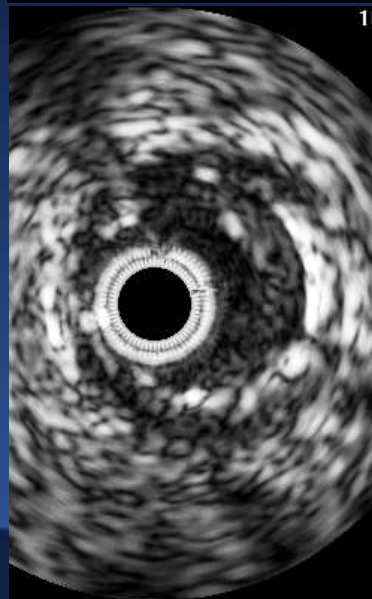
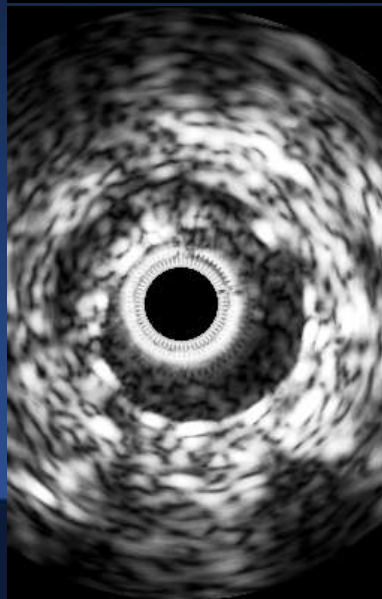
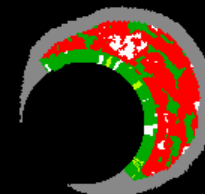
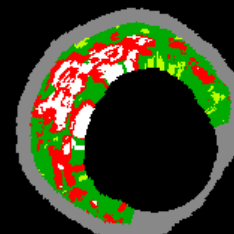
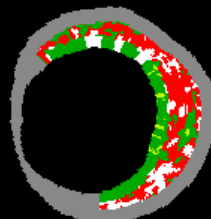
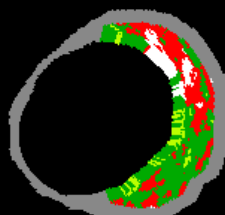
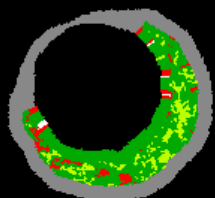
%NC 39%
%DC 20%

48-mo BMS

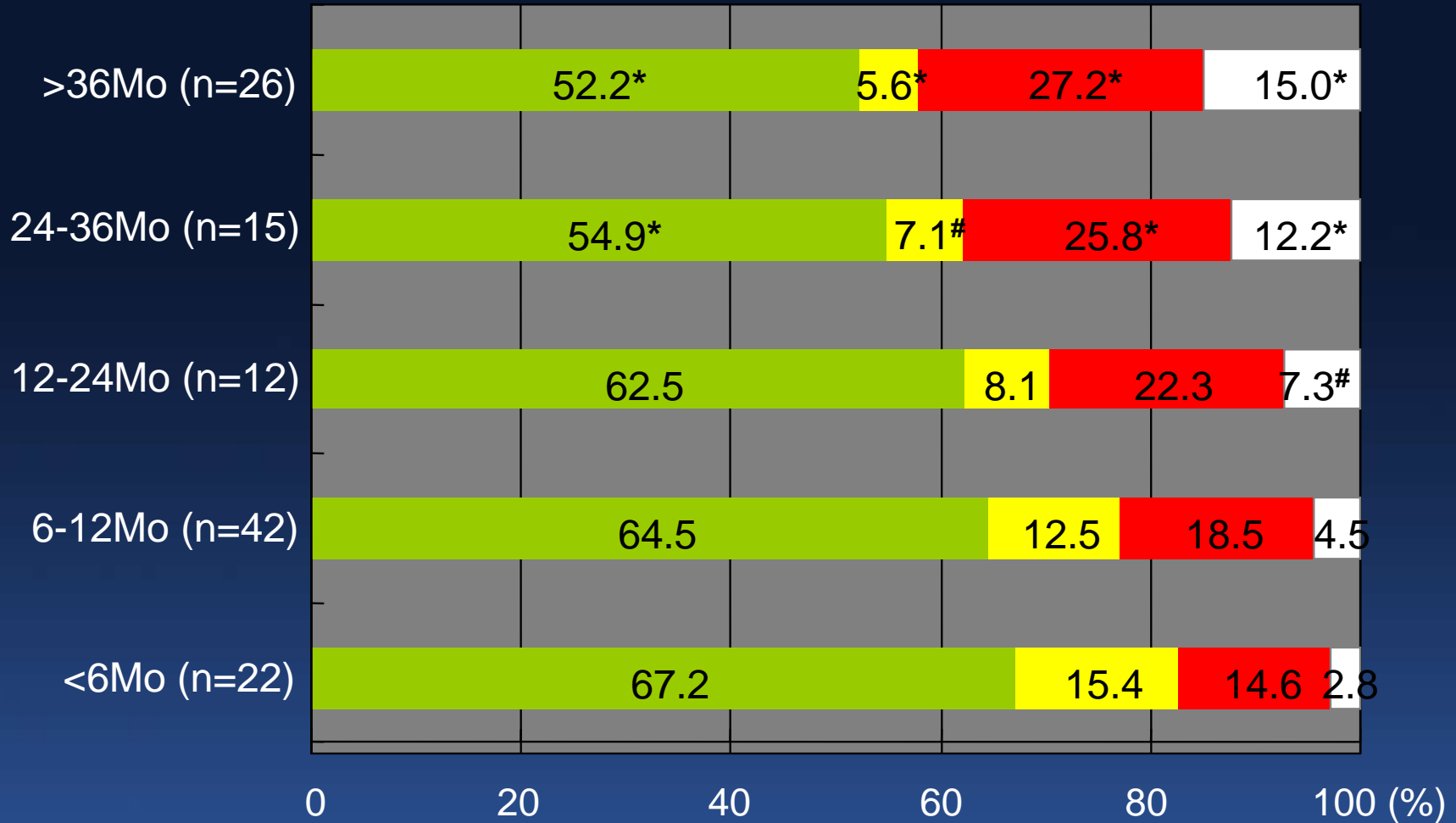
%NC 40%
%DC 25%

57-mo BMS

%NC 57%
%DC 15%



VH Composition of Neointima at Various Follow-Up Times in 117 ISR Lesions Combining 47 BMS and 70 DES



*p<0.01 and #p<0.05, vs. lesions at follow-up time <6 months

Take Home Message

- 1. VH-IVUS is an algorithm using both frequency and amplitude information to characterize tissue components quantitatively.**
- 2. PROSPECT and other studies confirmed the ability of VH components to predict future event in the prospective manner.**
- 3. VH-IVUS can be used for serial change of tissue components in natural history and effect of drug stabilization.**
- 4. VH can also evaluate neotherosclerosis in the stent.**