

Detection and Treatment of Vulnerable Plaque: **PROSPECT II** and **PROSPECT ABSORB**

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Focus on Non-Culprit Lesions

NHLBI Dynamic Registry 1997 – 1999

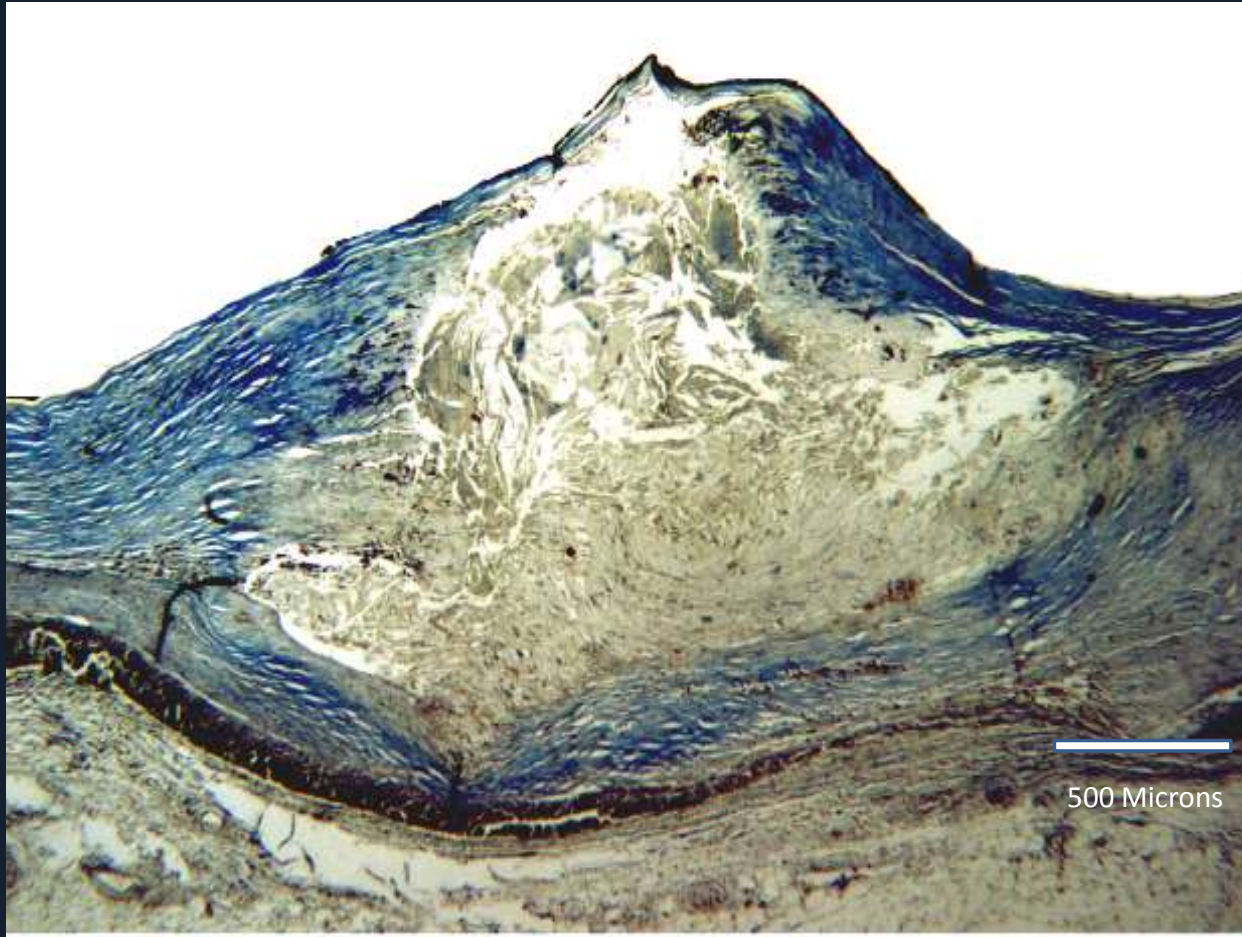
5.8% of 3,747 pts undergoing PCI developed clinical plaque progression within 1 yr requiring unplanned PCI (62% w/ACS)

Plaque progr. from $42 \pm 21\%$ to $84 \pm 14\%$ @ mean of 5.2 mos



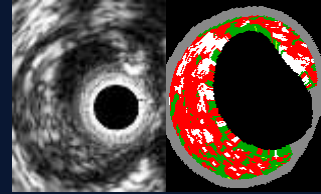
RCA at the time of LAD PCI Unstable angina 133 days later

Thin Cap Fibroatheroma (TCFA) is the Precursor Lesion of Plaque Rupture



- TCFA =
- Lipid rich necrotic core
 - Thin fibrous cap (<65 um)
 - Cap = type 1 coll with few SMC
 - Cap infiltrated by mp and lym

PROSPECT Study



700 pts with ACS

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

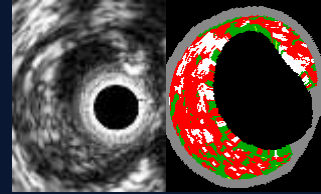
Biomarkers

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

PCI of culprit lesion(s)
Successful and uncomplicated

Formally enrolled

PROSPECT Study



3-vessel imaging post PCI

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

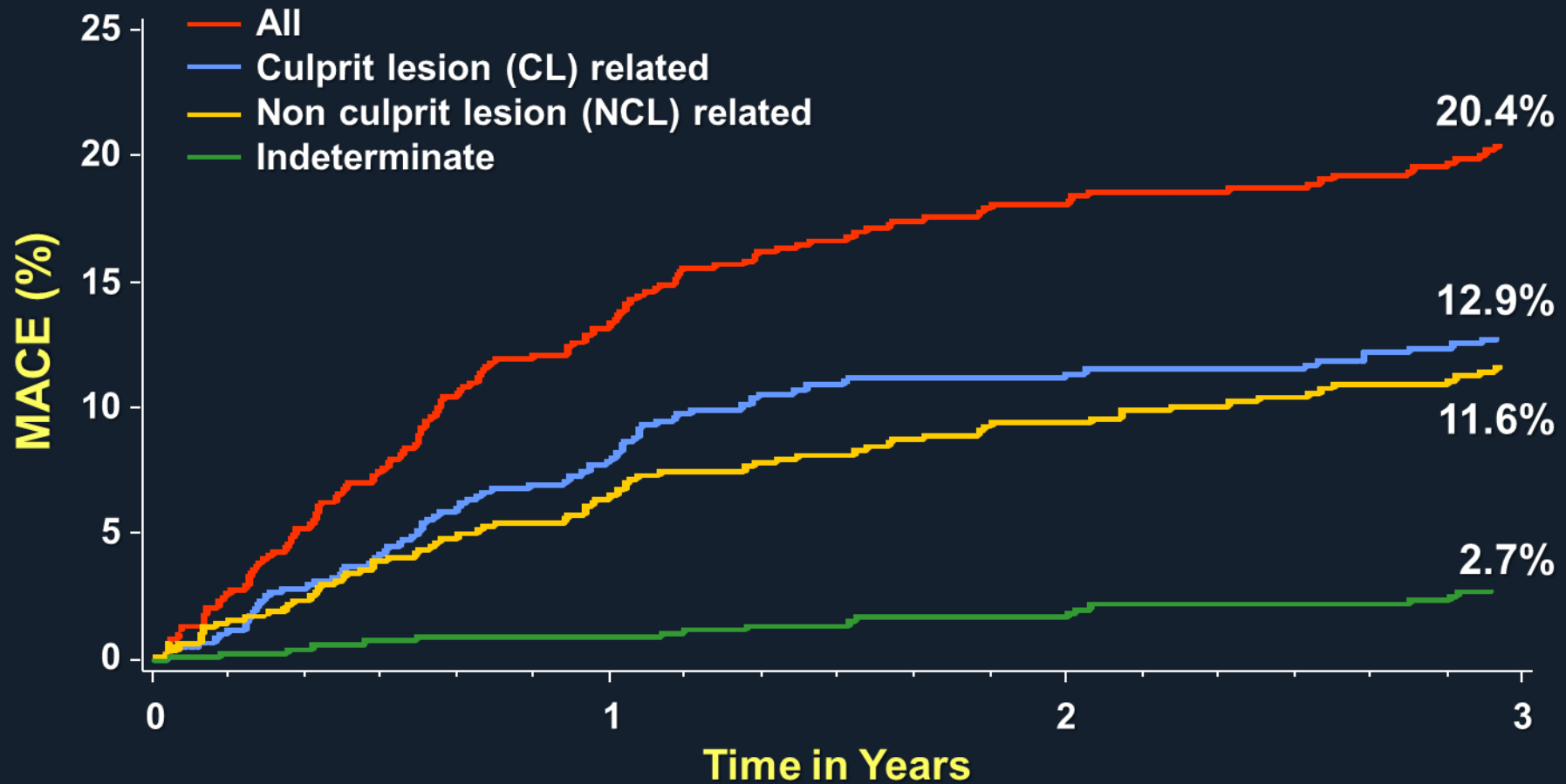
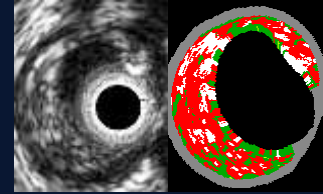
MSCT

Substudy

N=50-100

**Repeat imaging
in pts with events**

PROSPECT: MACE (N=697)



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

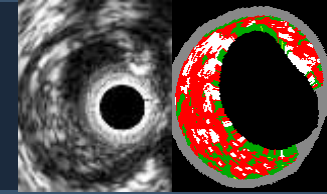
PROSPECT: Multivariable Correlates of Non-Culprit Lesion Related Events

Independent predictors of lesion level events by Cox Proportional Hazards regression

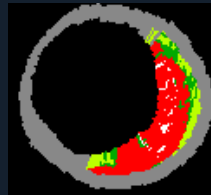
<u>Variable</u>	<u>HR [95% CI]</u>	<u>P value</u>
PB _{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm ²	3.21 [1.61, 6.42]	0.001

Variables entered: 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: NCL events arising from stenoses with PB $\geq 70\%$



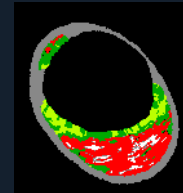
Thin-cap fibroatheroma



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

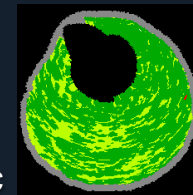
■ Present ■ Absent

Thick-cap fibroatheroma



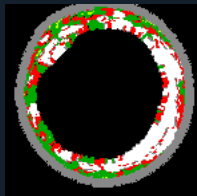
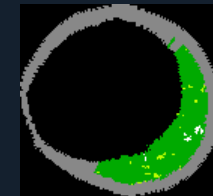
HR (95%CI) =
5.17 (2.59, 10.32)
P<0.0001

Pathologic intimal thickening



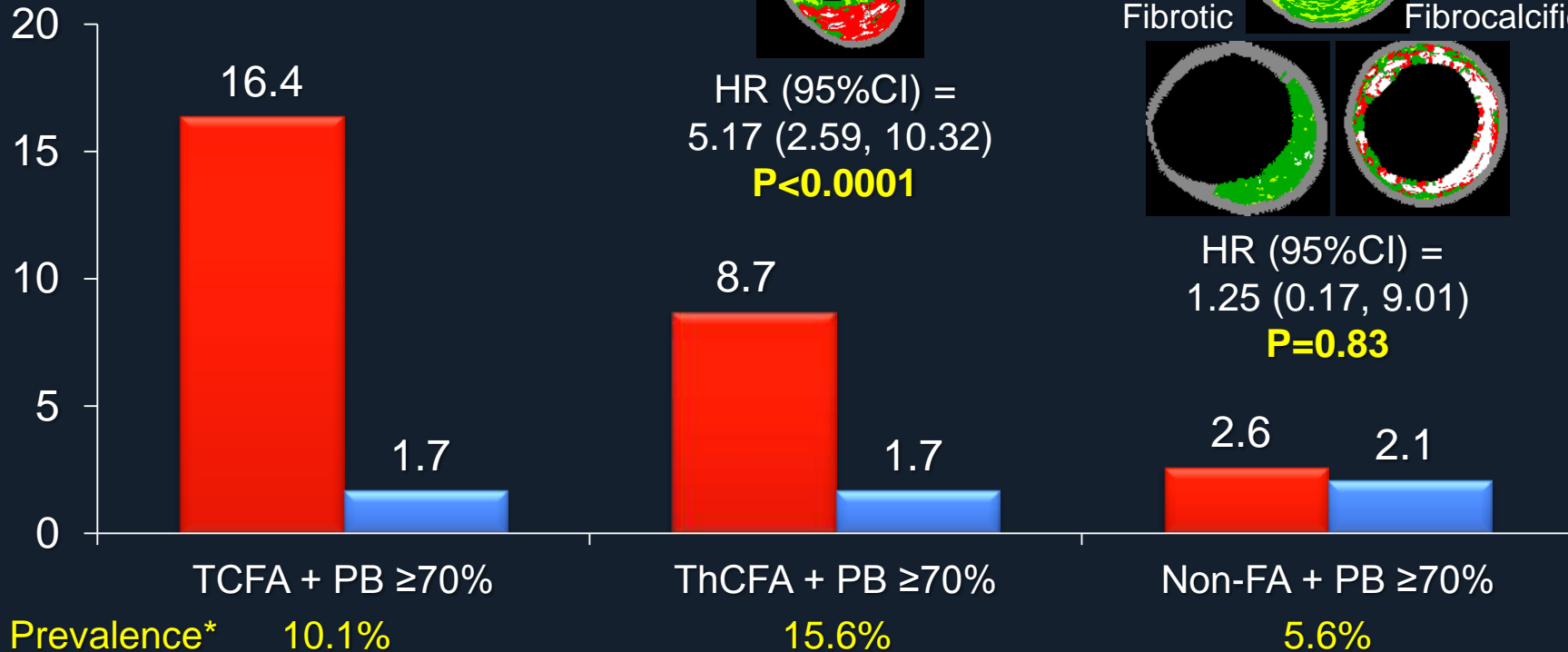
Fibrotic

Fibrocalcific



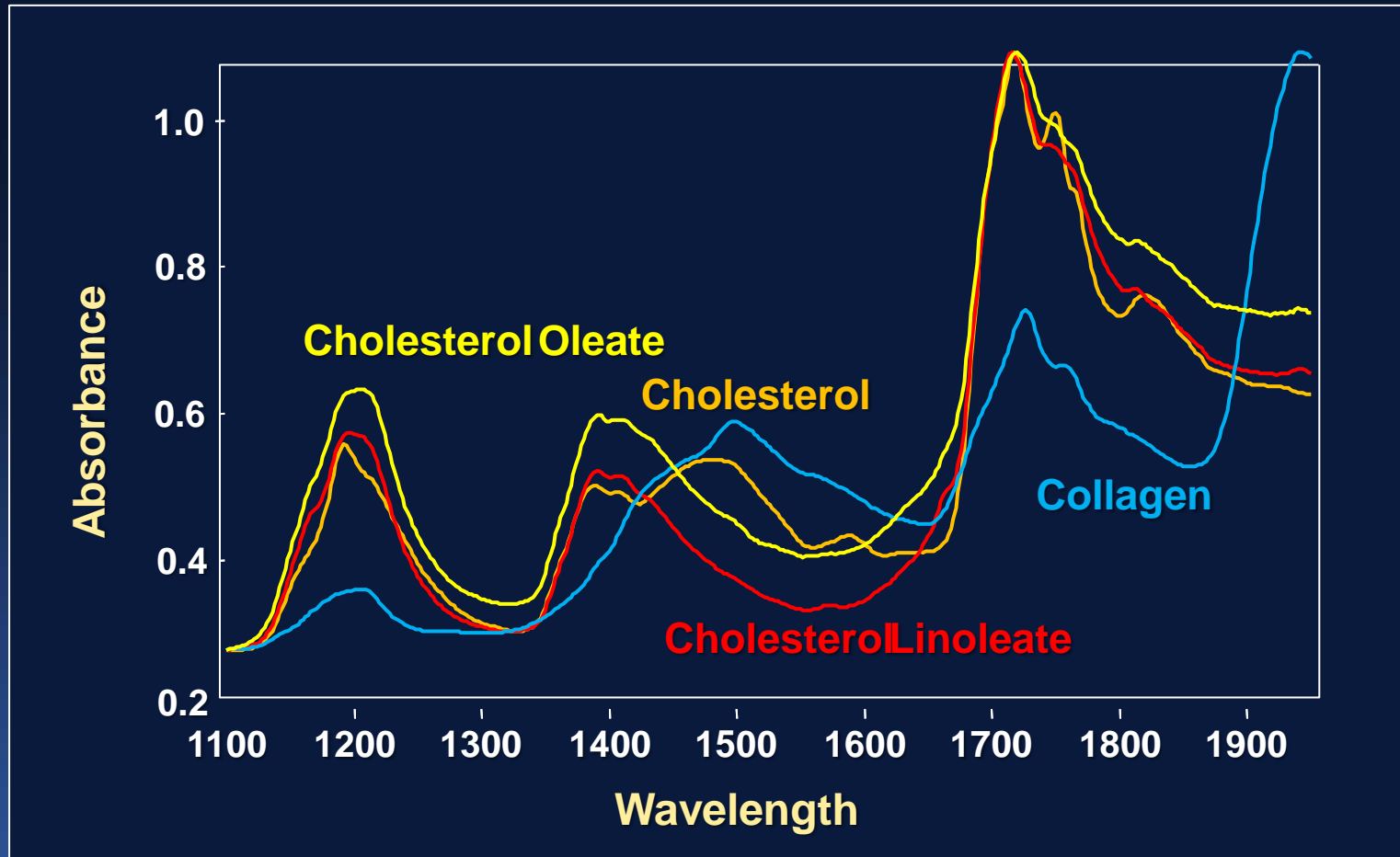
HR (95%CI) =
1.25 (0.17, 9.01)
P=0.83

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

Diffuse Reflectance NIR Spectroscopy to Identify Chemical Composition of Unknown Substances



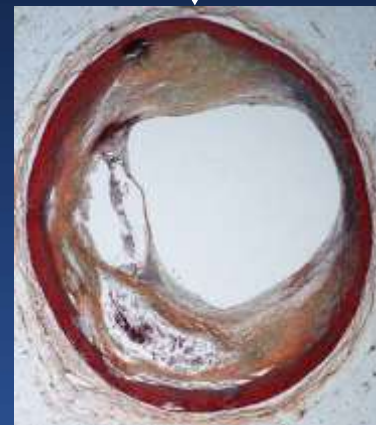
Chemogram Findings in a Coronary Autopsy Specimen: **Comparison with Histology**



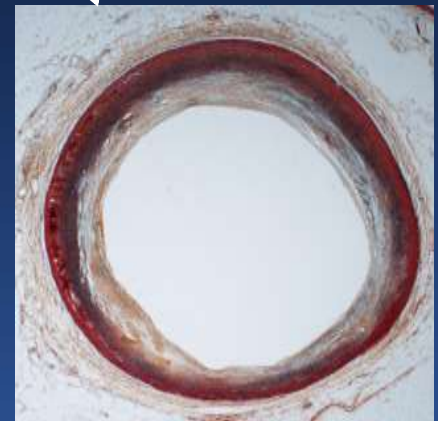
40 mm



36 mm



26 mm

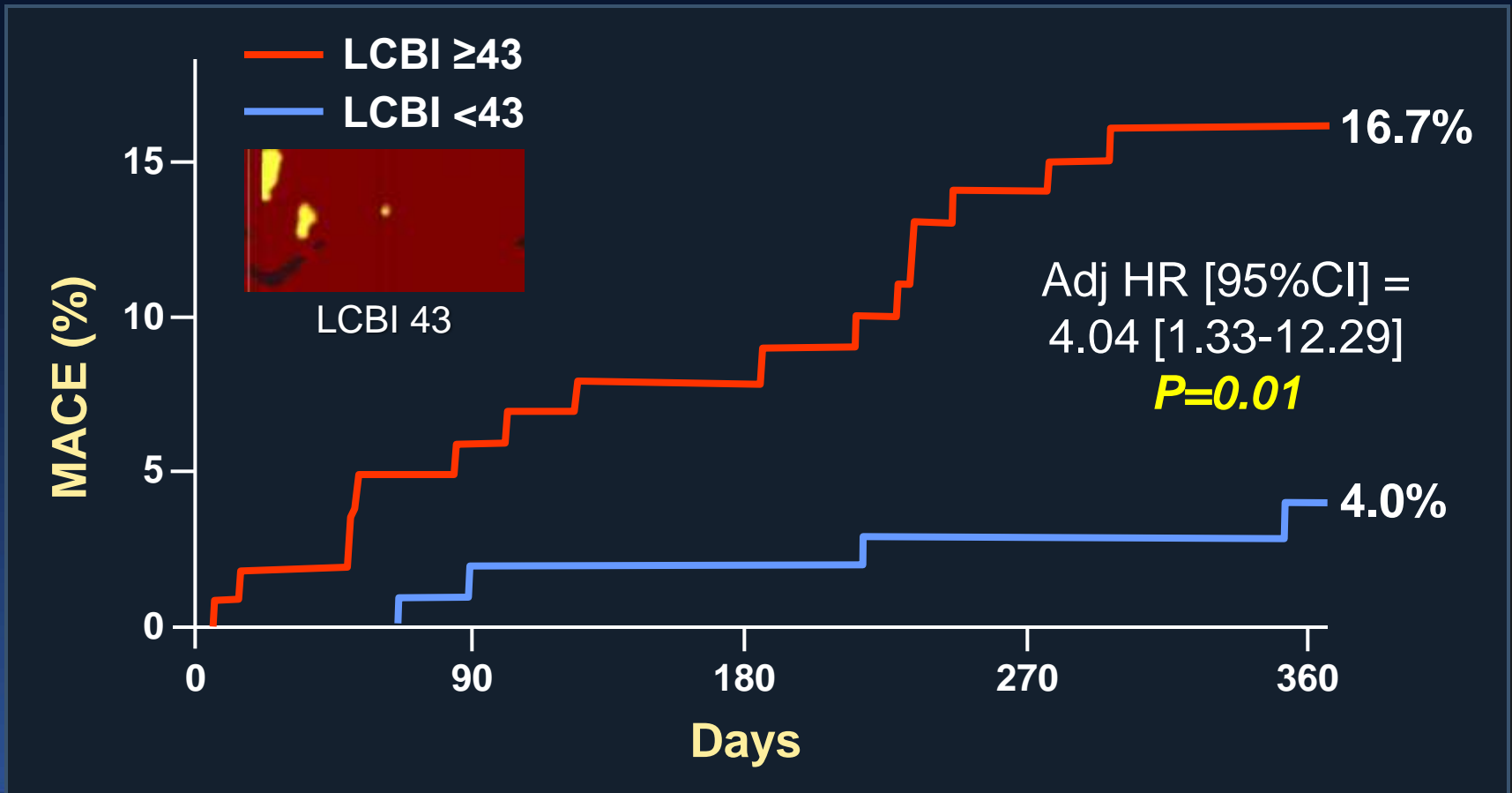


20 mm

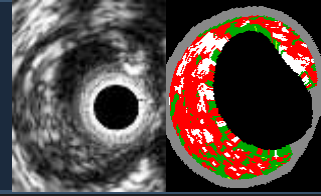
InfraReDx TVC

Predictive Value of NIRS

NIRS was performed in a non-culprit vessel in 203 pts with stable angina or ACS. MACE (death, ACS, stroke or unplanned coronary revasc) was examined in pts with LCBI above vs. below median of 43.



Should VP be Treated?

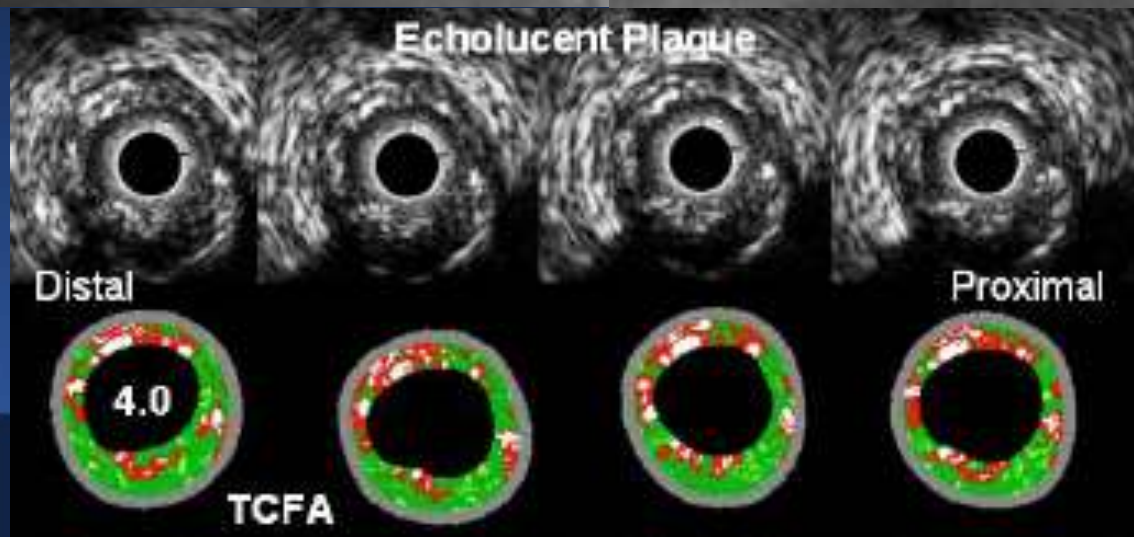
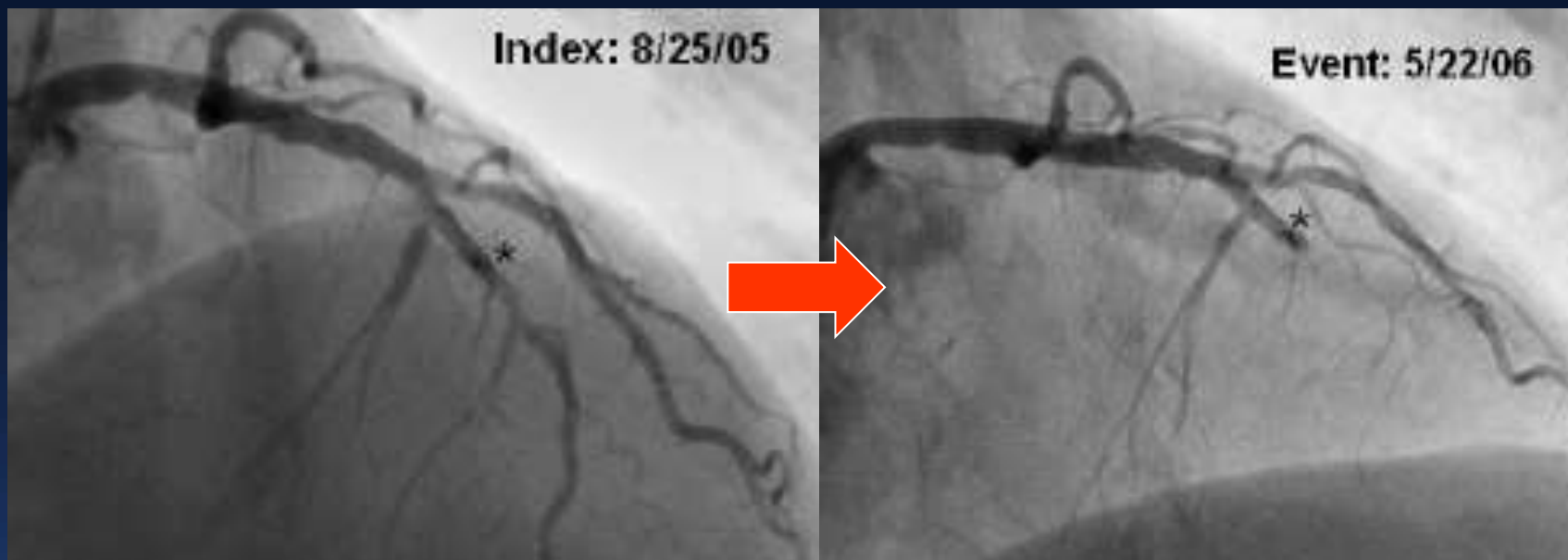


PROSPECT case example



Should VP be Treated?

MLA 4.0 mm²; plaque burden 72%; TCFA



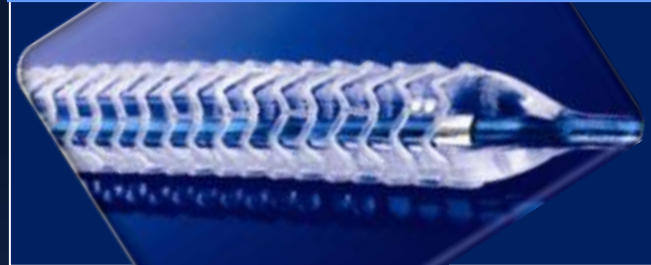
Bioresorbable Vascular Scaffolds (BRS)

Igaki-Tamai



PLLA

Abbott Absorb



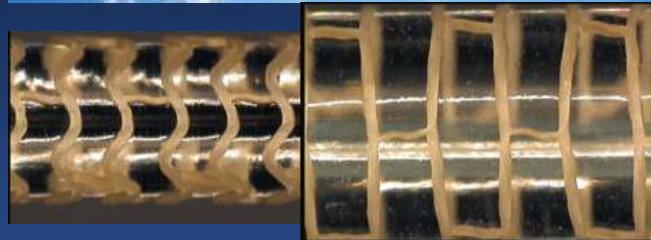
PLLA
(eluting everolimus)

Elixir DESolve



PLLA
(eluting novolimus)

Reva Fantom



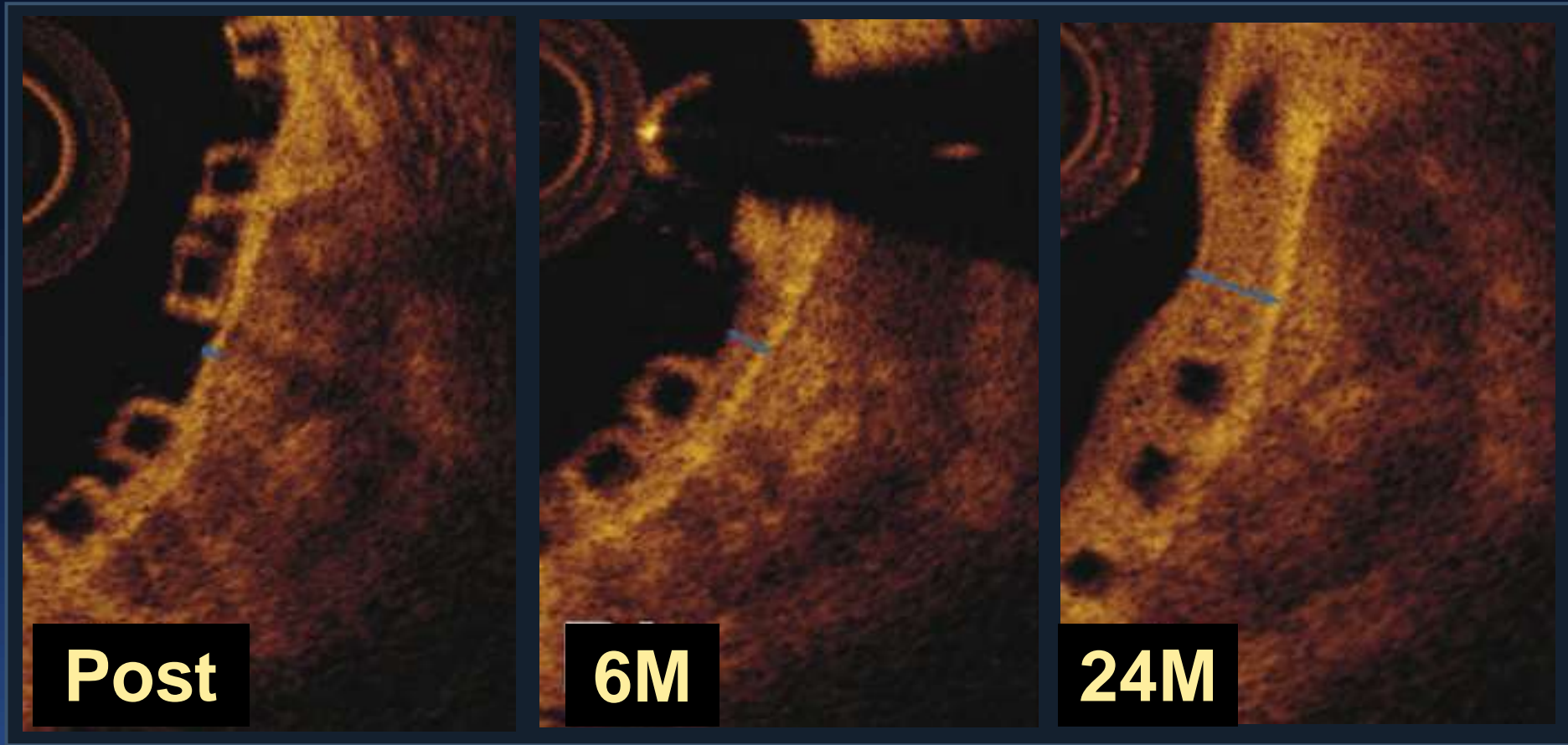
Iodinated tyrosine-
derivative
(eluting sirolimus)

Biotronik Dreams



Magnesium
(eluting sirolimus)

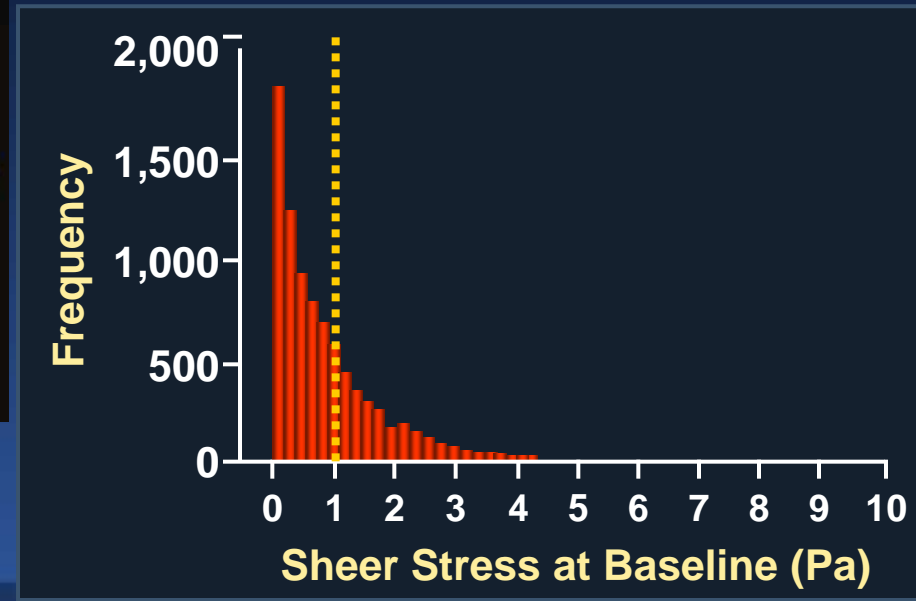
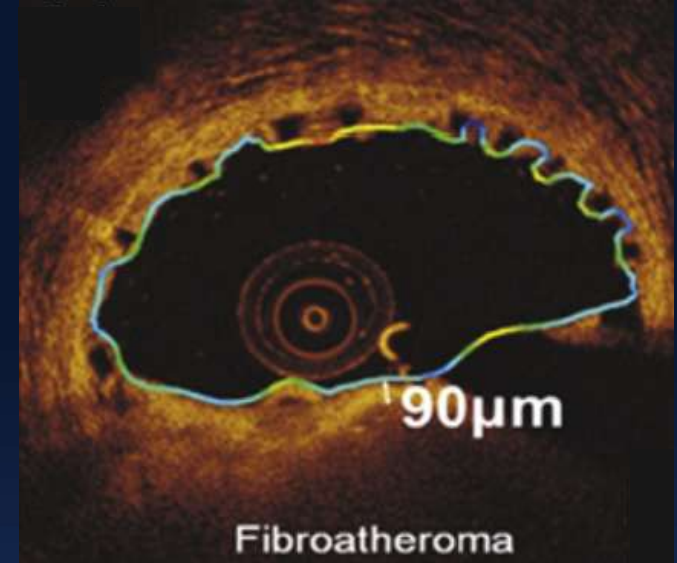
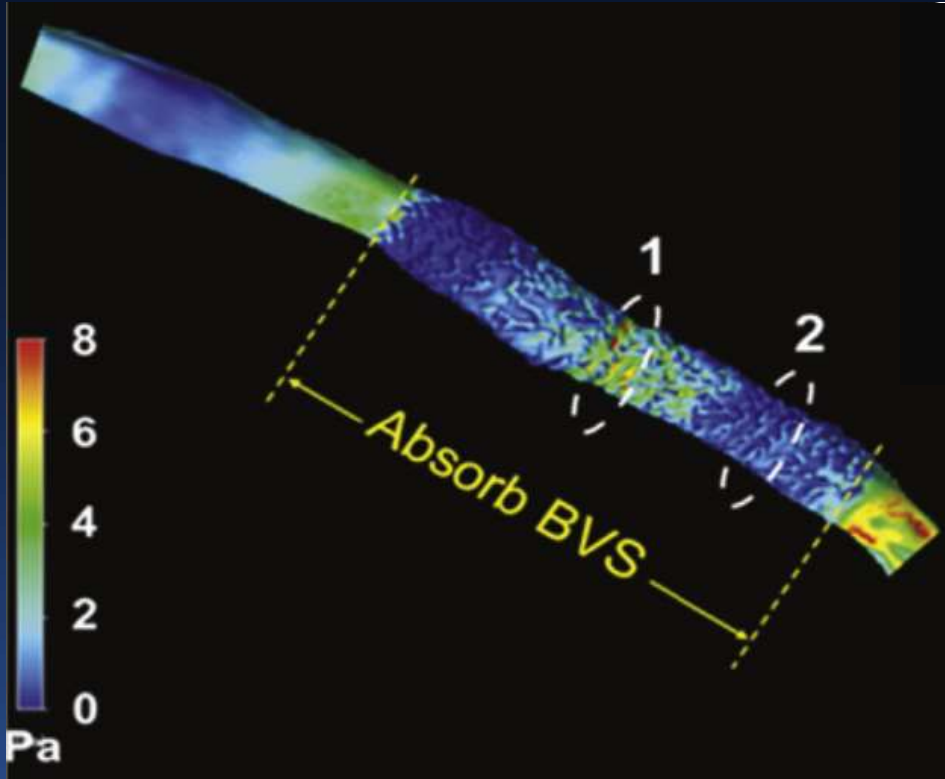
Sealing and Shielding of Plaques After Scaffold Implantation



Example of capping a calcified plaque

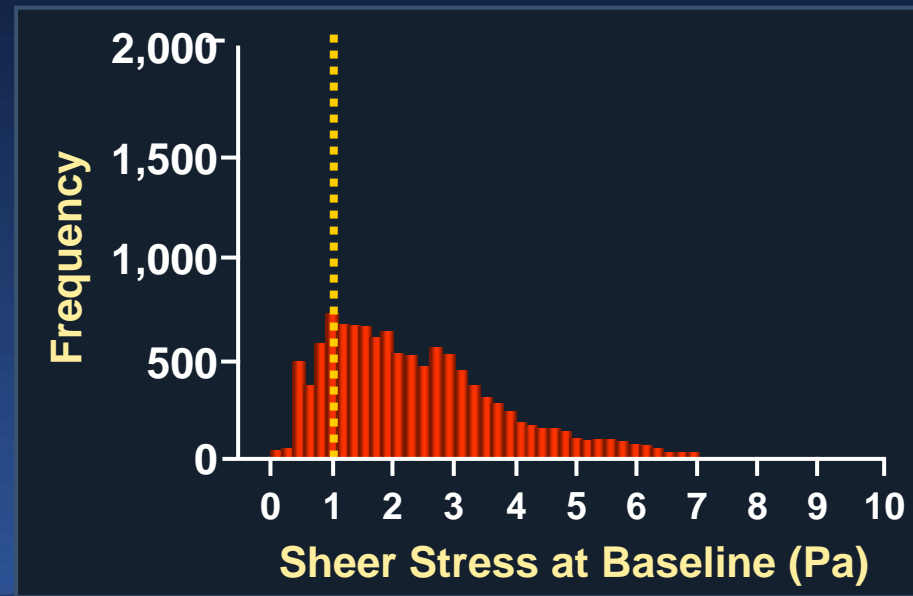
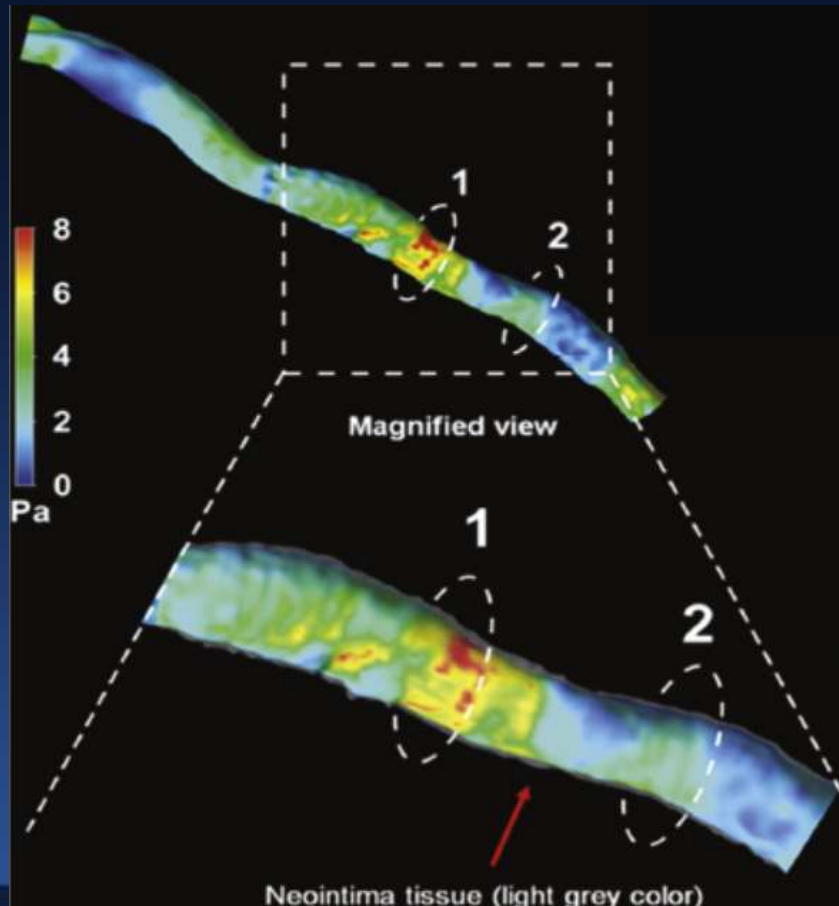
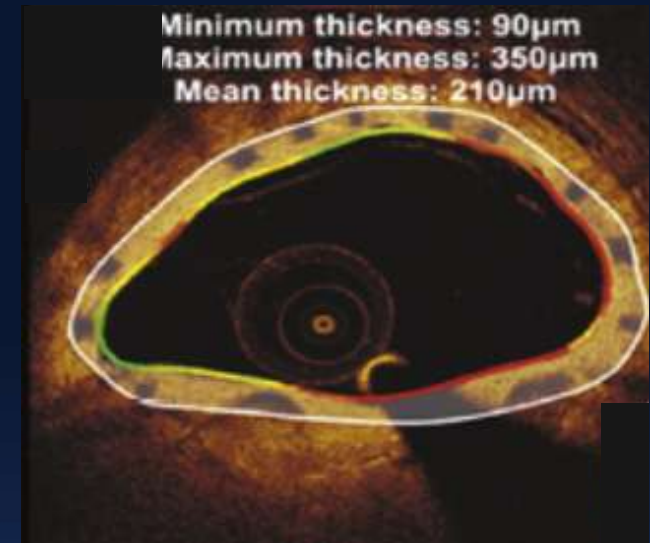
BVS Implantation Over a Fibroatheroma

LAD reconstruction showing low shear stress throughout the BVS



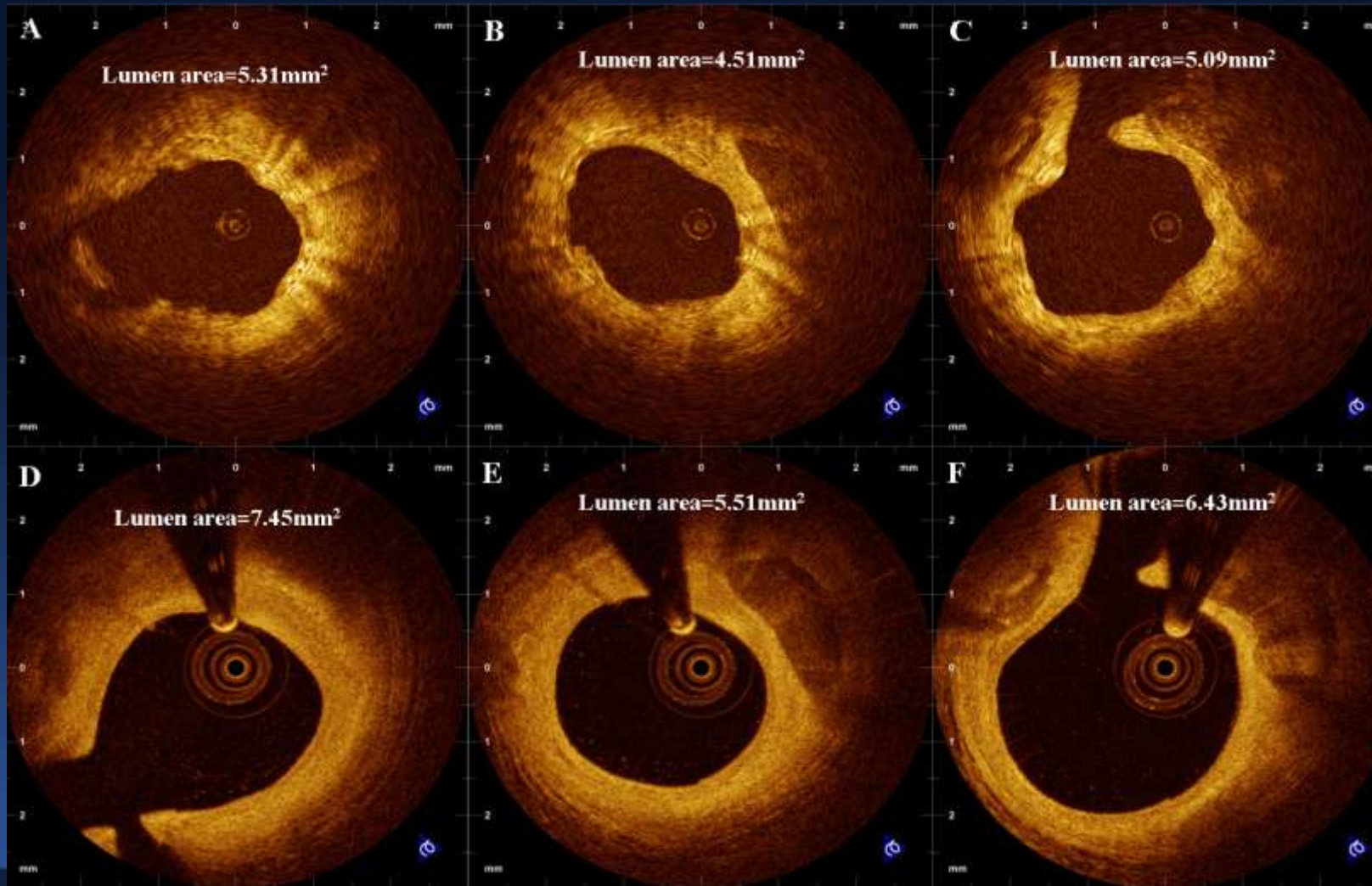
BVS Implantation Over a Fibroatheroma

2 years later: ESS has normalized over the scaffold, and a 210 μm layer of neointima has developed



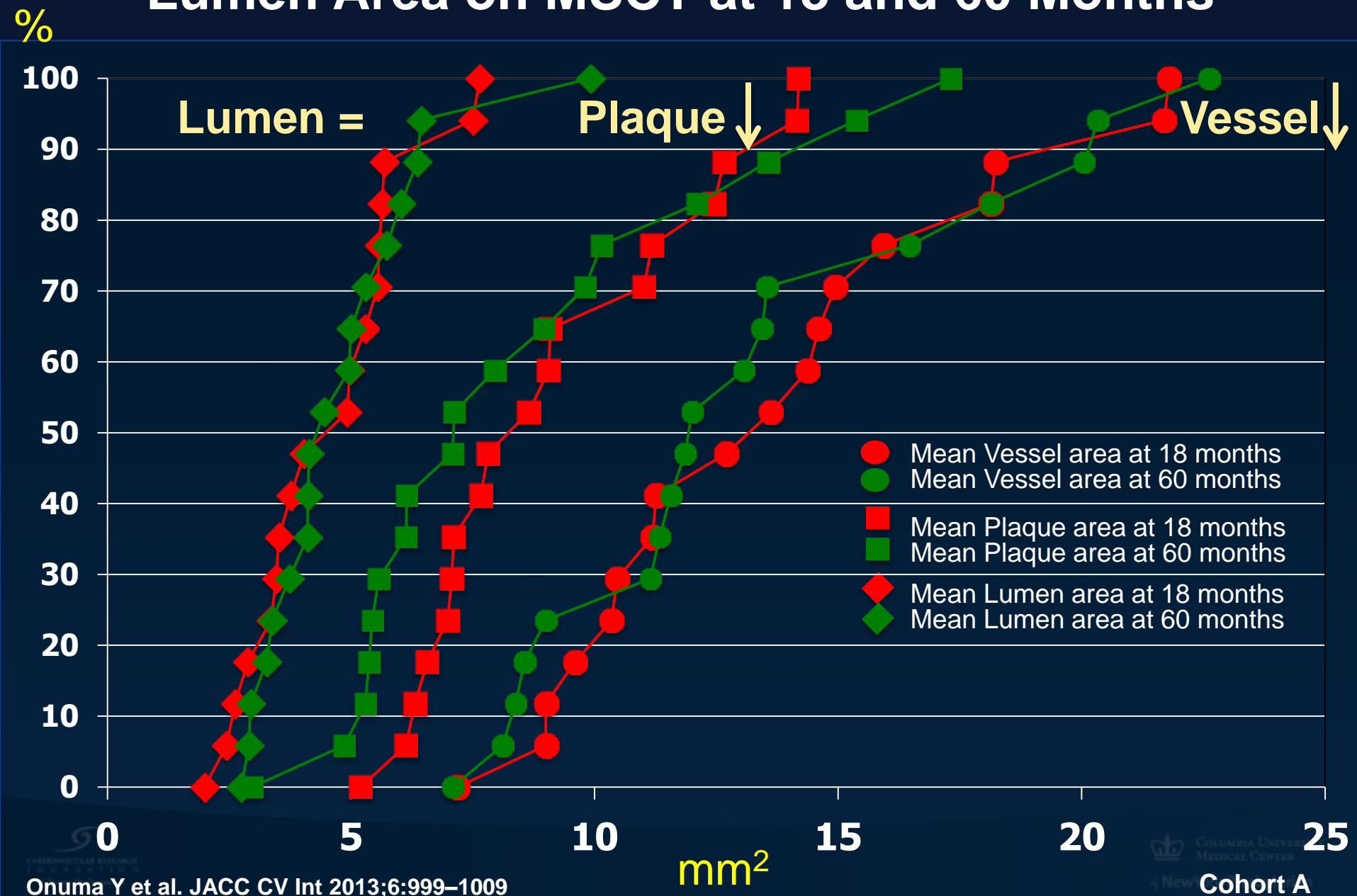
Treatment of a TCFA with BVS: Substantial lumen enlargement due to plaque regression with adaptive remodeling (cohort A pt)

6
months



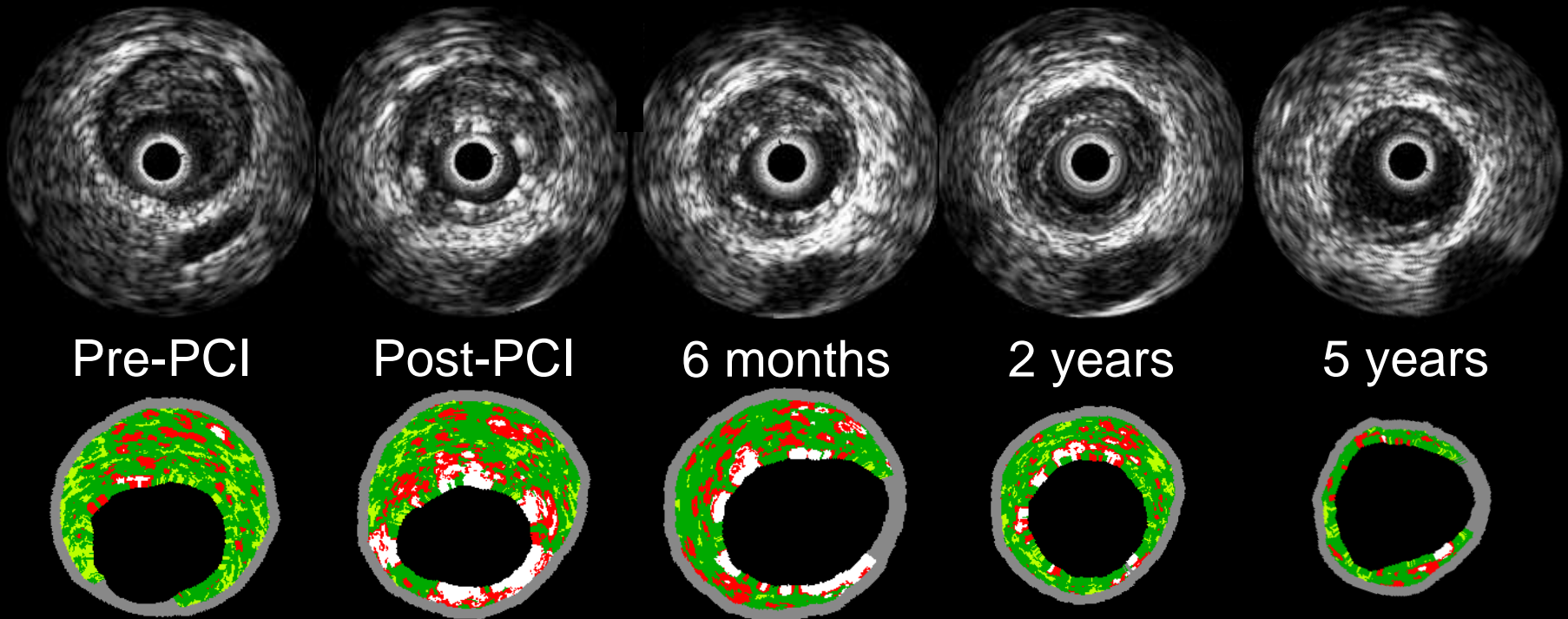
5 years

CFD Curves of Vessel Area, Plaque Area and Lumen Area on MSCT at 18 and 60 Months



Interventional Plaque Regression by BVS:

Substantial lumen enlargement due to plaque regression with adaptive remodeling (cohort A pt)



Vessel area (mm²)	15.72	15.34	14.09	13.76
Mean lumen area (mm²)	6.95	6.17	6.56	8.09
Plaque area (mm²)	8.78	9.17	7.54	7.07

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 ≥65% plaque burden present?

Yes

(N=300)

No

(n=600)

R
1:1

**ABSORB BVS
+ GDMT** (N~150)

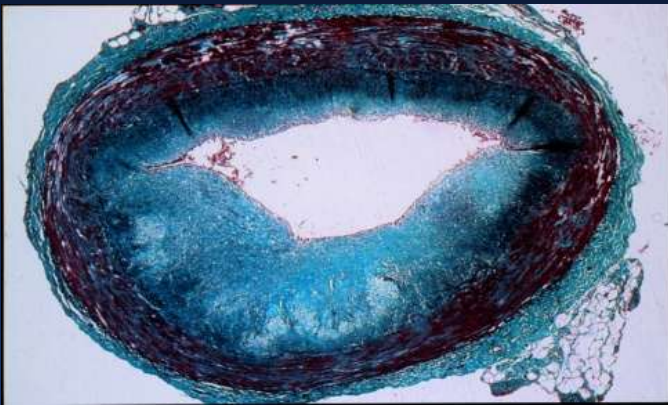
GDMT
(N=150)

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

Clinical FU for up to 15 years

Searching for Vulnerable Plaque Requires Seeing Beyond the Angiogram

The “stable”
atherosclerotic
plaque

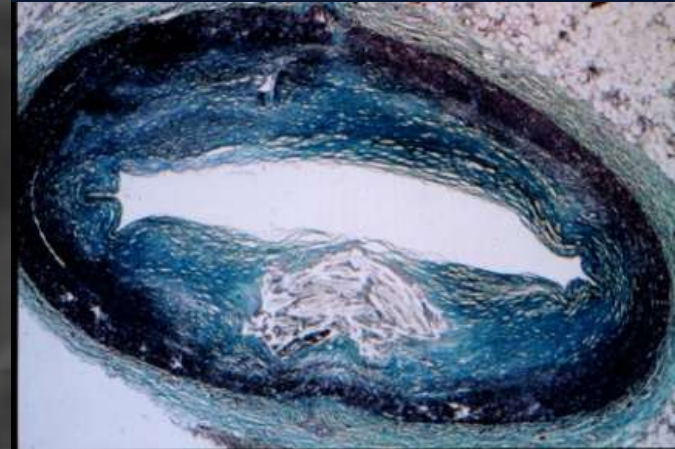


Inactive and
non-inflamed plaque
Pathologic intimal
thickening



VS.

The “vulnerable”
atherosclerotic
plaque

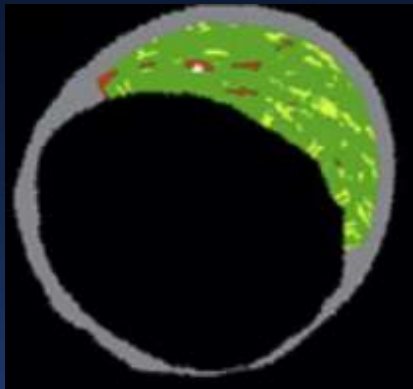


Active and
inflamed plaque
Thin-cap
fibroatheroma

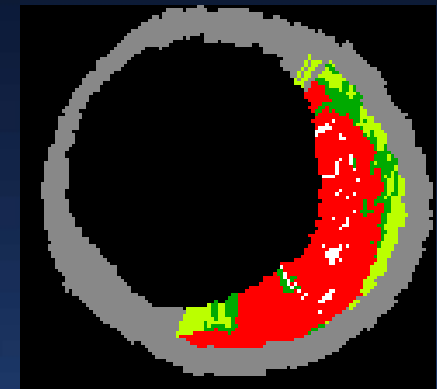
Searching for Vulnerable Plaque

Requires Seeing Beyond the Angiogram

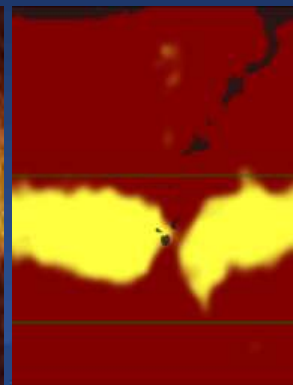
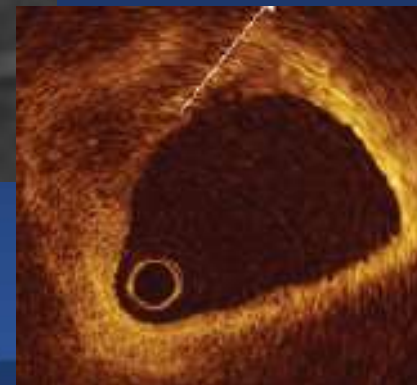
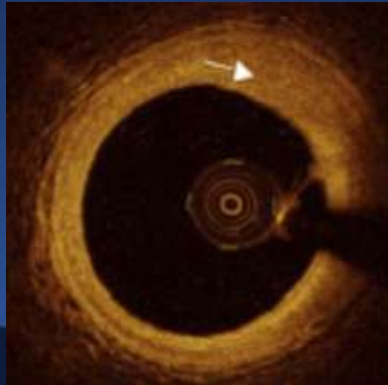
The “stable”
atherosclerotic
plaque



The “vulnerable”
atherosclerotic
plaque



VS.



Braunwald Algorithm for Vulnerable Plaque Screening and Treatment

