# Vulnerable Plaques: Natural History and Clinical Outcomes

**Soo-Jin Kang, MD., PhD.**

Department of Cardiology, Univ. of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea

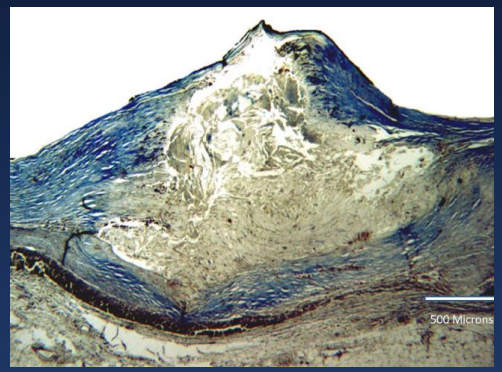
# Disclosure Statement of Financial Interest

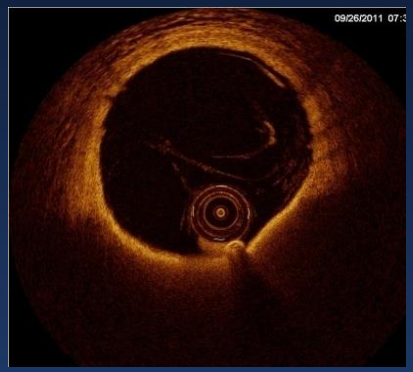
I, Soo-Jin Kang DO NOT have a financial interest /arrangement or affiliation with organizations that could be perceived as a conflict of interest in the context of the subject of this presentation

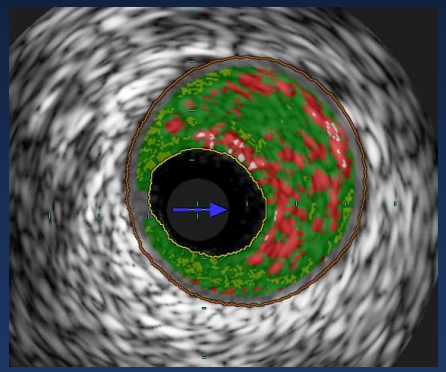
# *Thrombosis-prone plaque and plaque with a high probability of undergoing rapid progression*

| Morphological Predictors of Plaque Rupture | | | |
|---|---|---|---|
| | p | Odds Ratio | 95% CI |
| %Necrotic core | 0.02 | 2.0 | 1.1 – 3.7 |
| Cap thickness (<65 µm) | 0.005 | 0.35 | 0.2 – 0.7 |
| %Macrophage | 0.052 | 1.8 | 1.0 – 3.2 |

## Thin-cap Fibroatheroma (TCFA)

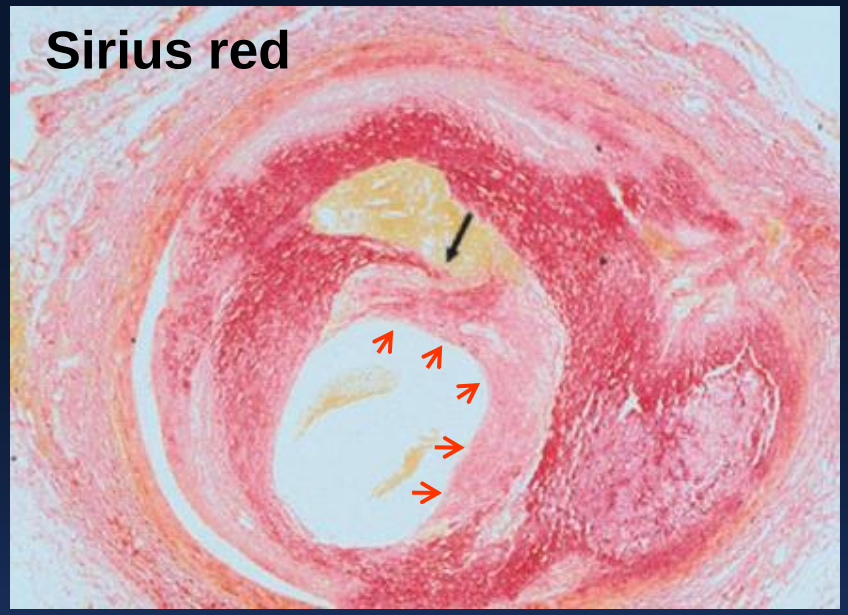


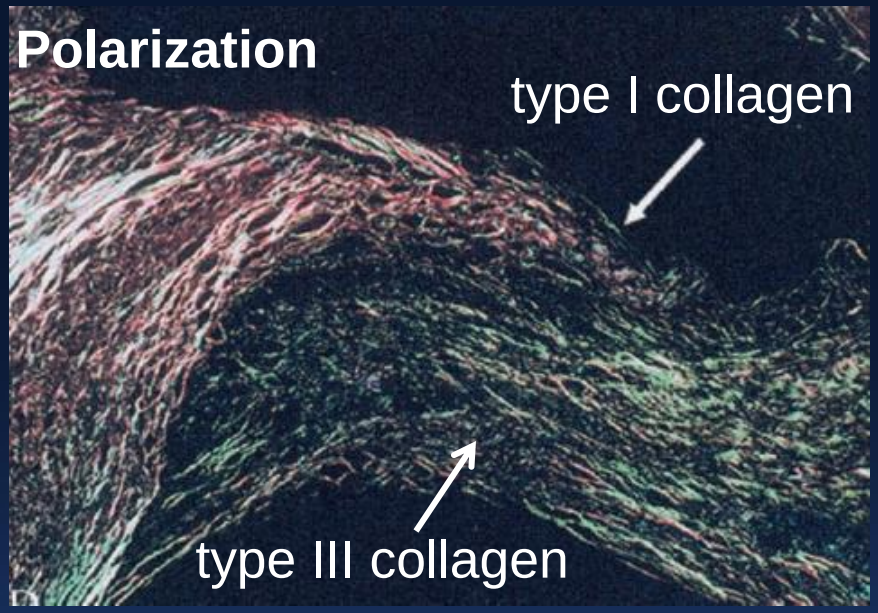



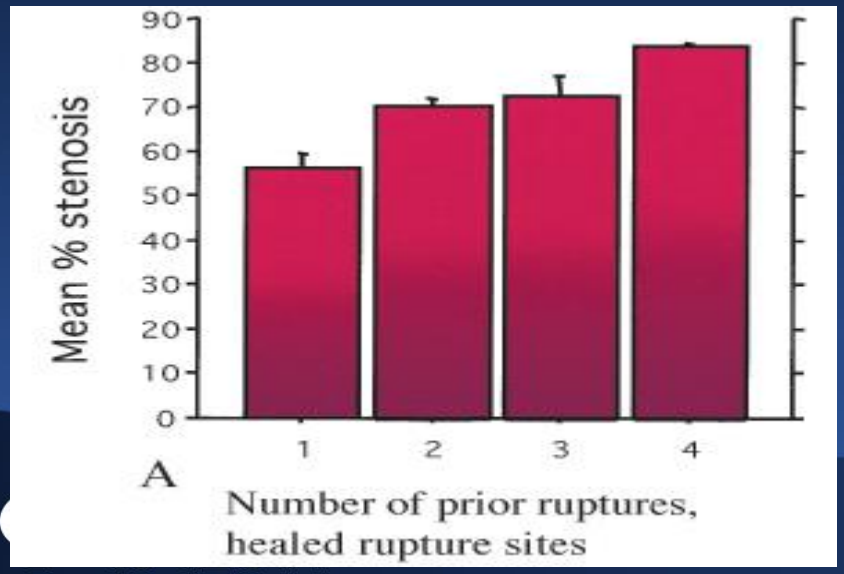


*Rodriguez-Granillo et al. JACC 2005;46:2038-42*
*Naghavi et al. Circulation 2003;108:1664-72*

# Healed Plaque Rupture
## A Role in Lesion Progression

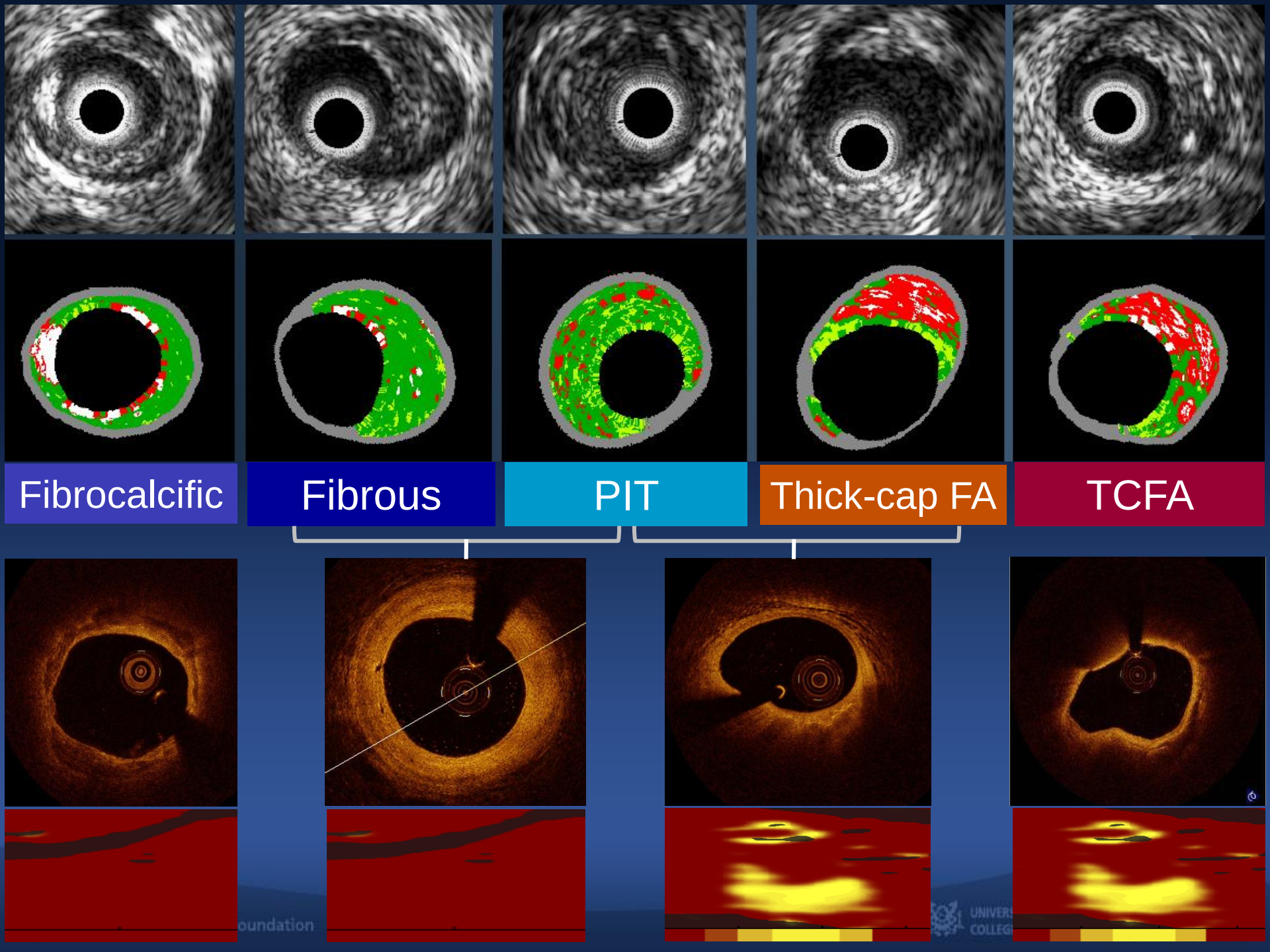



Inner layer, newly formed neointima composed of type III collagen, loose-SMC and proteoglycan-rich ECM

*Burke et al. Circulation 2001;103:934–40*


Fibrocalcific
Fibrous
PIT
Thick-cap FA
TCFA

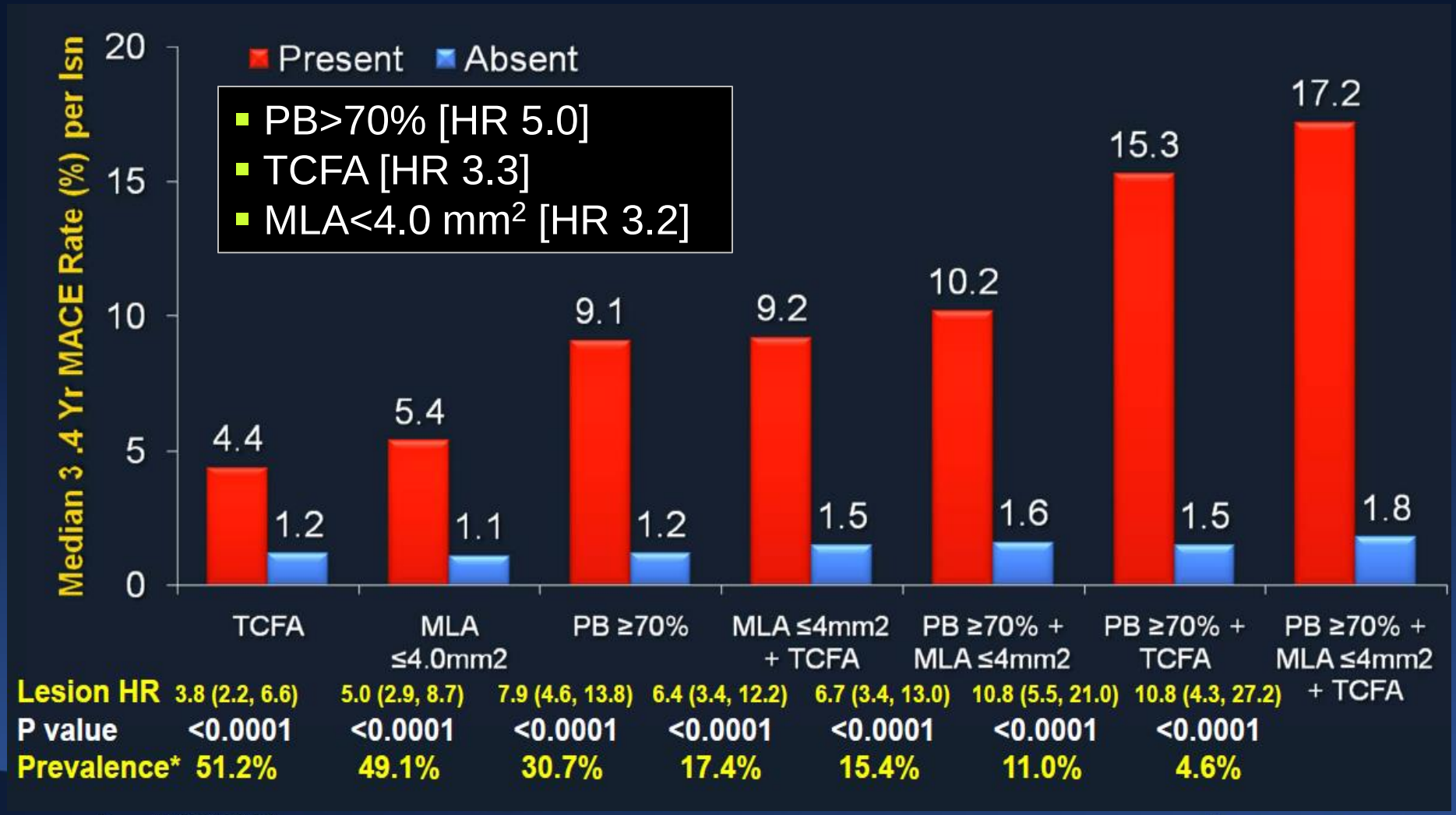
# PROSPECT

- Culprit-related MACE at 3 years= 12.9%
- NC-related MACE at 3 years = 11.6%
- Prevalence of NC-TCFA per patient = 46.7%

| | Culprit -related | Nonculprit -related | All events |
|---|---|---|---|
| Composite end point | 12.9% | 11.6% | 20.4% |
| Re-hospitalization *for unstable/ progressive angina* | 11.5% | 10.8% | 17.5% |
| Cardiac death | 0.2% | **0%** | 1.9% |
| Cardiac arrest | 0.3% | **0%** | 0.5% |
| Myocardial infarction | 2.0% | **1.0%** | 3.3% |

*Stone G et al. N Engl J med 2011;364:226-35*

# PROSPECT
## Predictors of Non-Culprit MACE

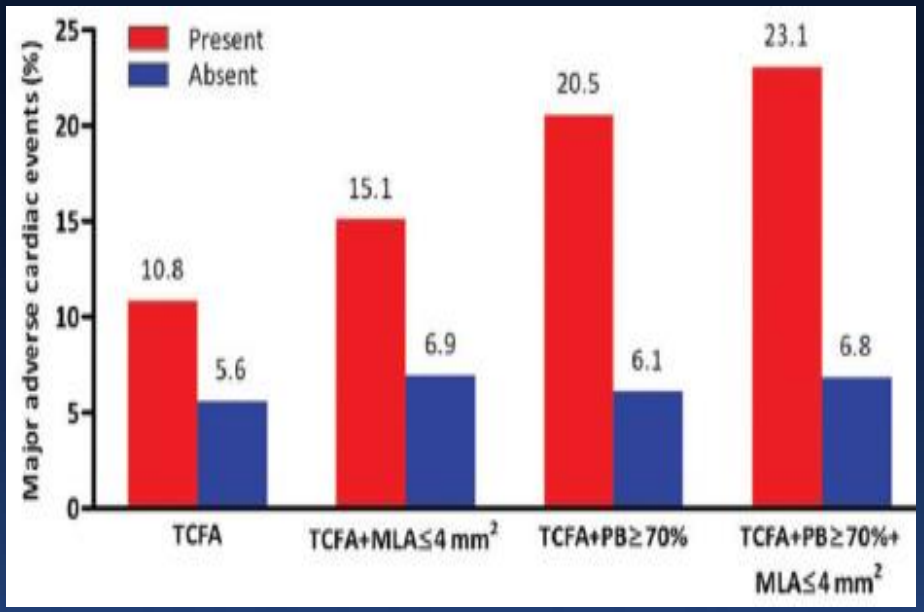


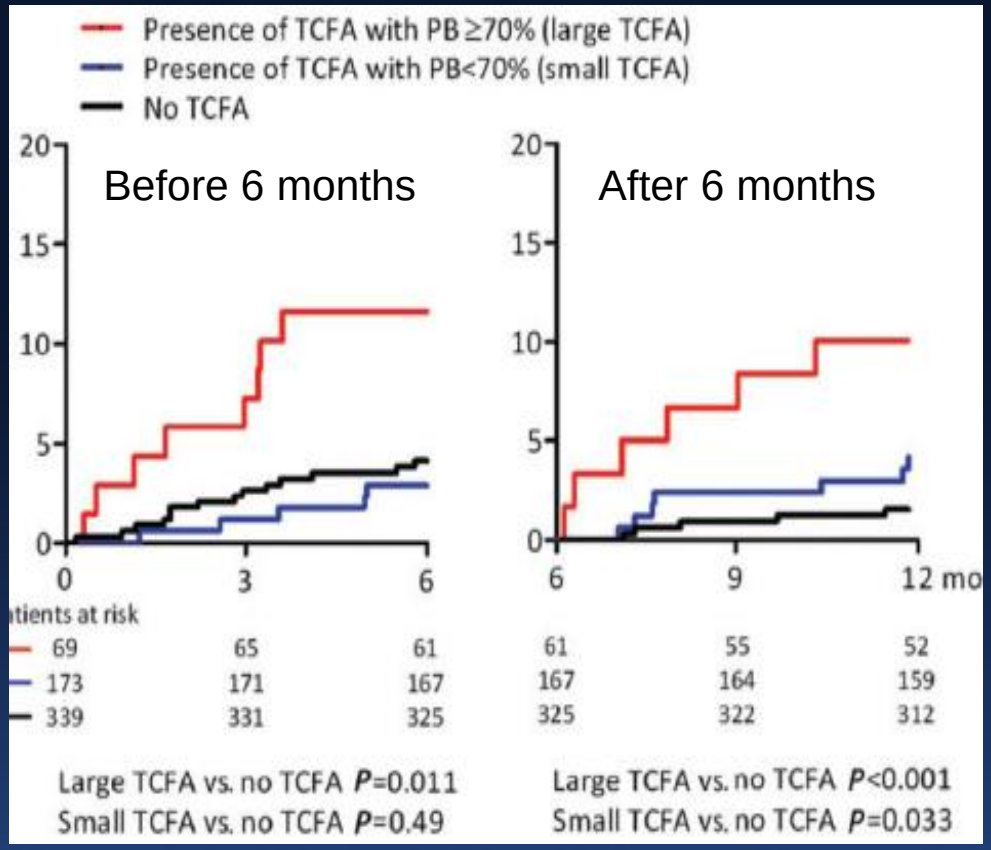



*Stone G et al. NEJM 2011;364:226-35*

# Predictors of Non-Culprit MACE

## ATHEROREMO



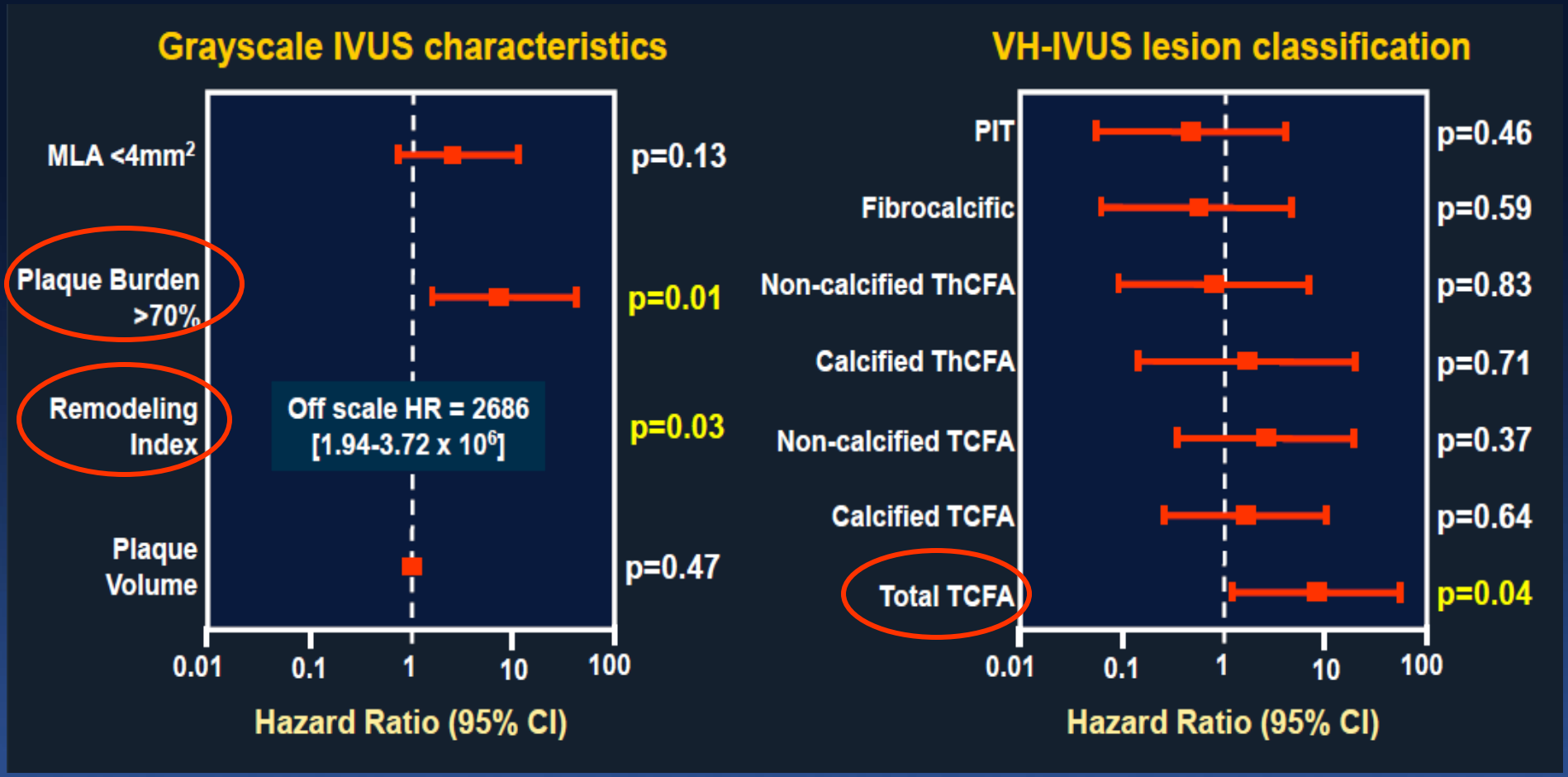

*Cheng et al. EHJ 2014;35:639-47*

- PB>70% [HR 2.9]
- TCFA [HR 1.9]

# Predictors of Non-Culprit MACE

## VIVA

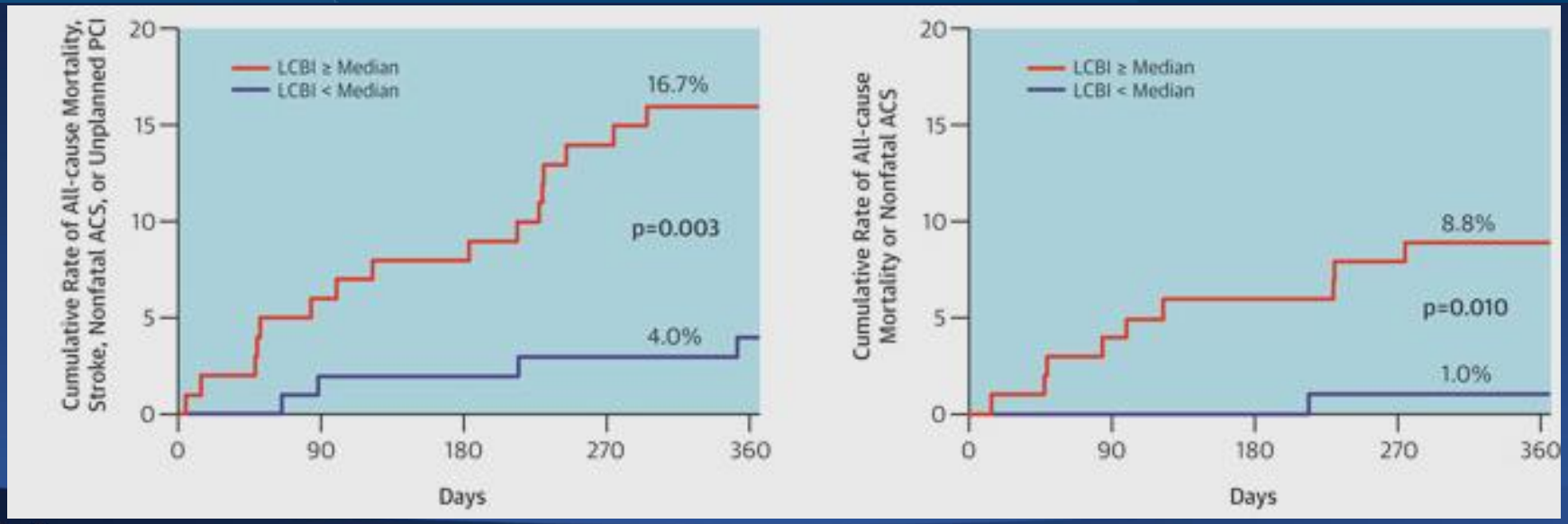
Univariable analysis




*Calvert et al. JACC Cardiovasc Imaging 2011;4:894–901*

# ATHEROREMO-NIRS: 203 patients referred to a single center for angiography/PCI underwent NIRS in a nonculprit vessel.

- The median lipid core burden index (LCBI) was 43.0 (IQR 15.0-90.0)
- Patients with an LCBI ≥ 43 had a fourfold higher rate of 1-year MACCE (excluding culprit lesion–related events) than those with an LCBI < 43
- No interaction between LCBI prediction of MACCE and presentation with stable CAD vs ACS

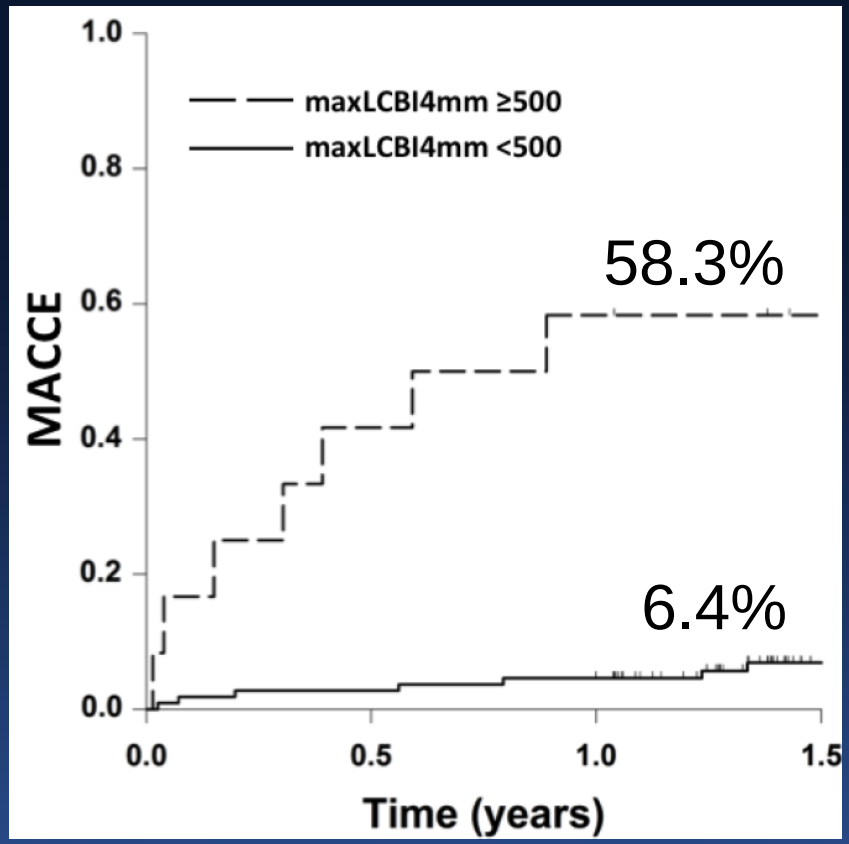





*Oemrawsingh et al. JACC 2014;64:2510-8*

# Prospective NIRS-IVUS Registry

Frederik Meijer Heart & Vascular Institute




all-cause mortality, recurrent ACS requiring revasc, or acute cerebrovascular events

**LRP (Max $LCBI_{4mm}$≥500)** in non-culprit segment independently predicted MACCE (HR 13.3, 95% CI 4.6–38.3, p<0.001

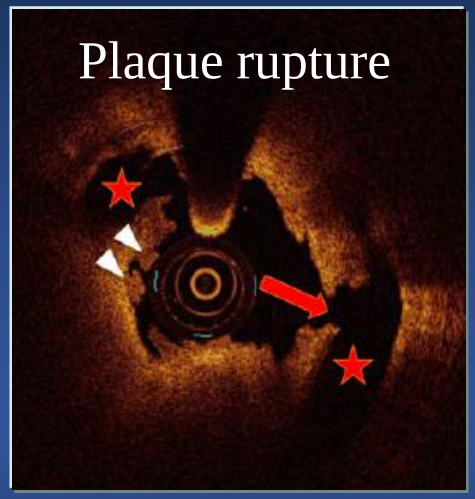
But, the best LCBI cut-off needs to be clarified

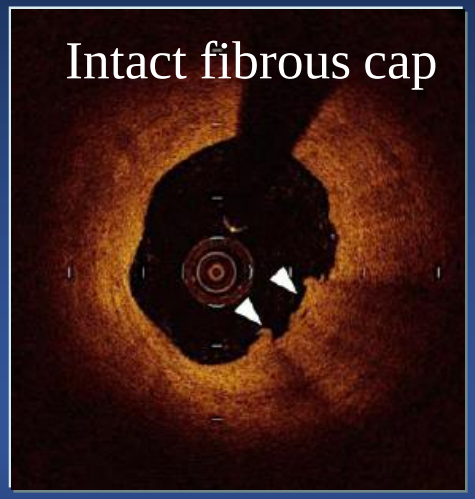
*Madder et al. presented in 2014 TCT*

# Plaque rupture and intact fibrous cap assessed by optical coherence tomography portend different outcomes in patients with acute coronary syndrome

Giampaolo Niccoli[1*], Rocco A. Montone[1], Luca Di Vito[2,3], Mario Gramegna[1], Hesham Refaat[1,4], Giancarla Scalone[1], Antonio M. Leone[1], Carlo Trani[1], Francesco Burzotta[1], Italo Porto[1], Cristina Aurigemma[1], Francesco Prati[2,3], and Filippo Crea[1]

- To evaluate the prognostic value of plaque rupture vs. intact fibrous cap in 139 ACS patients undergoing PCI
- No differences in clinical, angiographic, or procedural data

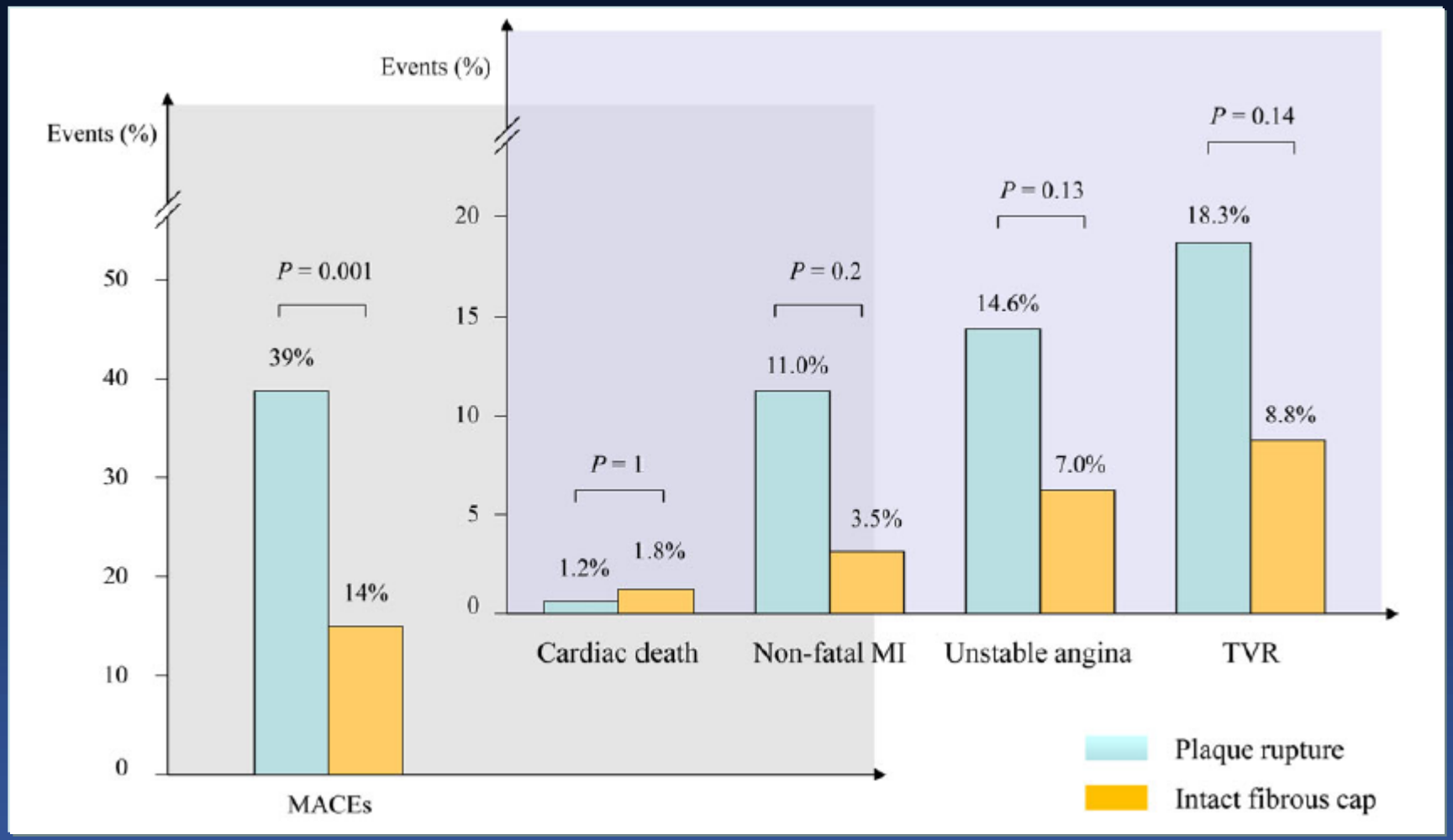



*Niccoli et al. Eur Heart J 2015;36:1377-84*

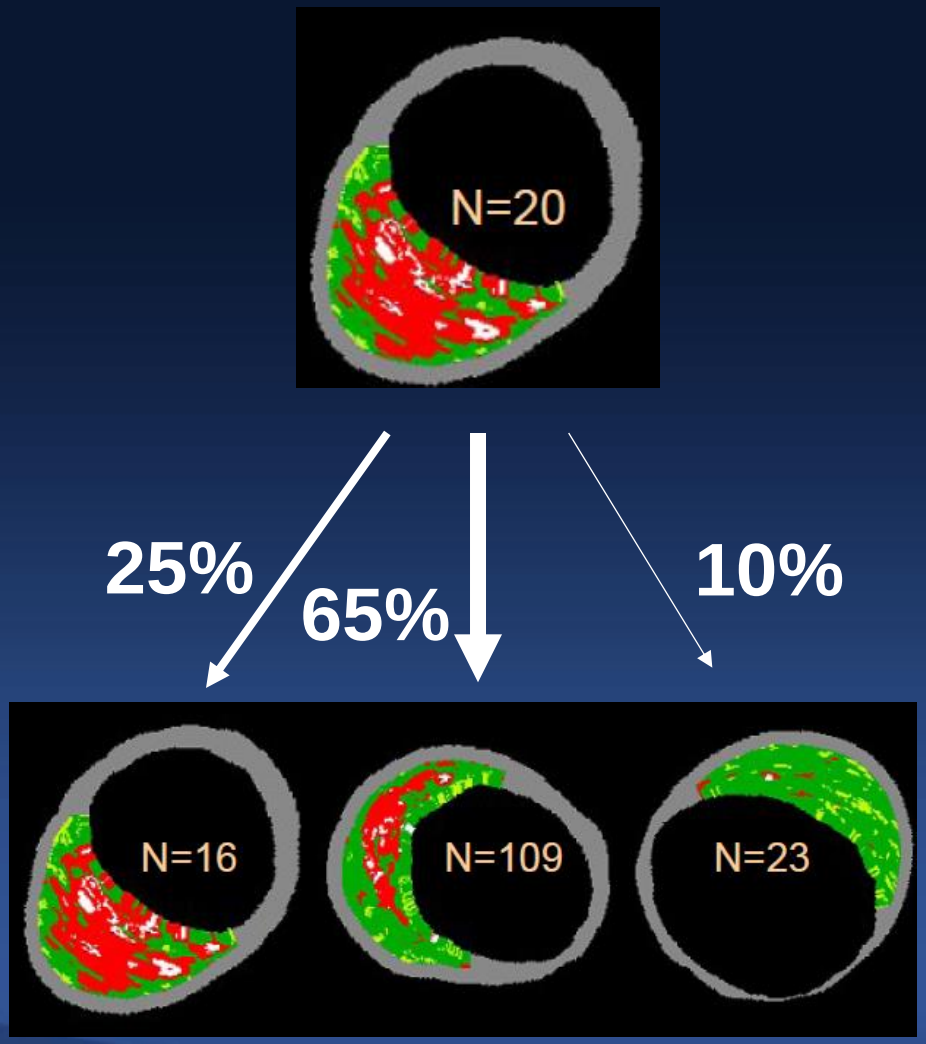
# MACE rates

## Patients with plaque rupture vs. with intact fibrous cap




*Niccoli et al. Eur Heart J 2015;36:1377-84*

# Dynamic Change in TCFA Over Time



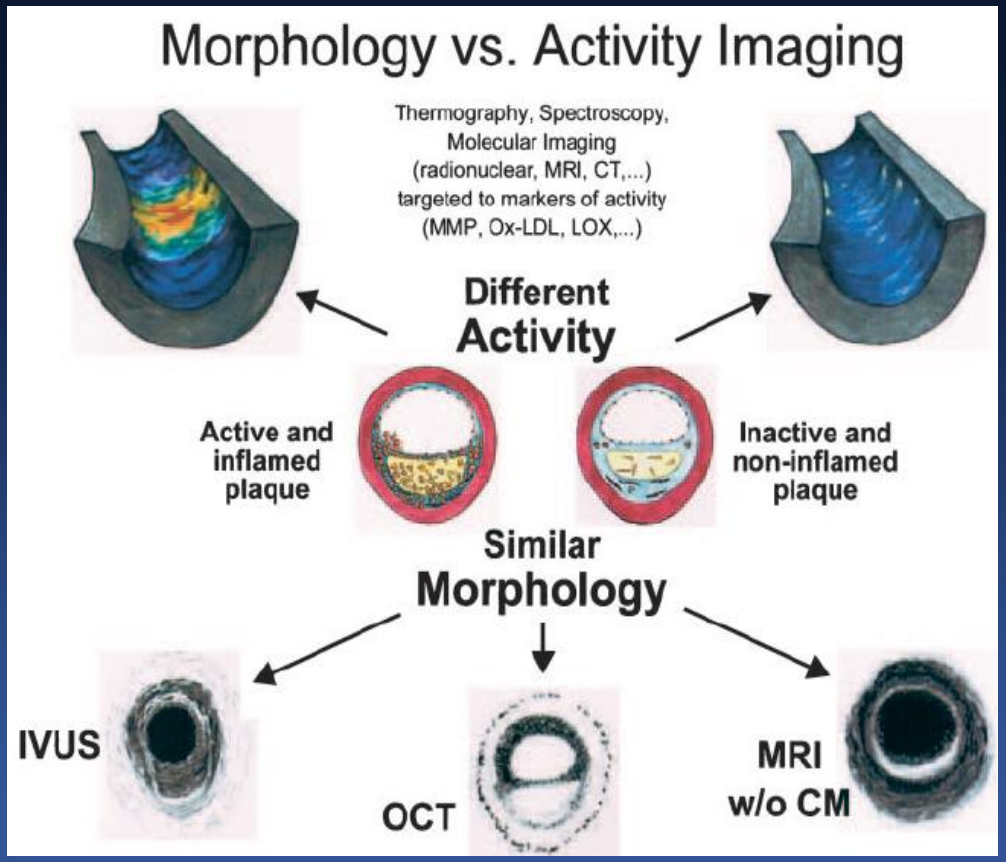

- Plaque morphology
- Clinical factors
- Inducible ischemia
- Biological activities
- Mechanical shear stress
- Thrombogenecity
- Responsiveness to Rx

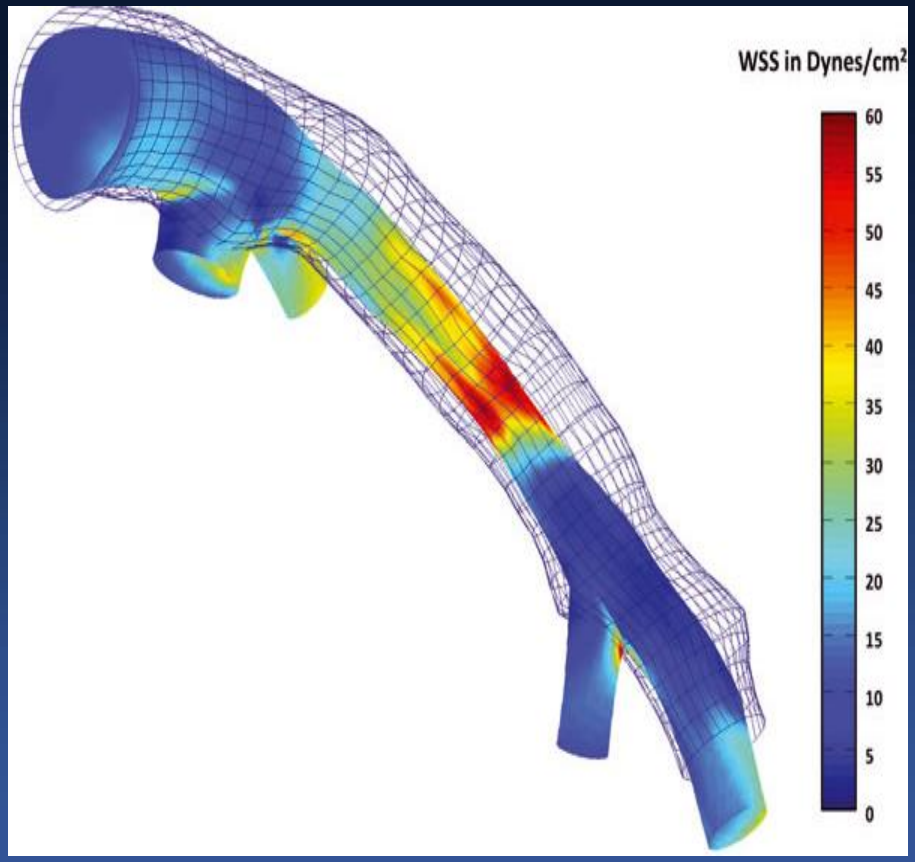
Although TCFA is a substrate of plaque rupture and a predictor of MACE, it may undergo dynamic change over time

*Kubo et al. J Am Coll Cardiol 2010;55:1590-7*

# What Affect Dynamic Changes?
## Offensive Factors

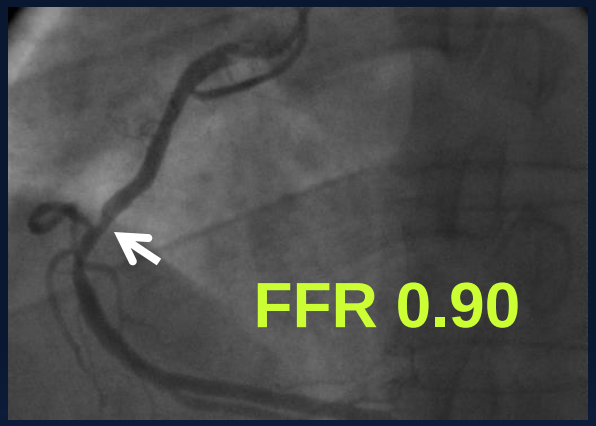
**Biological Activity** | **Wall Shear Stress**



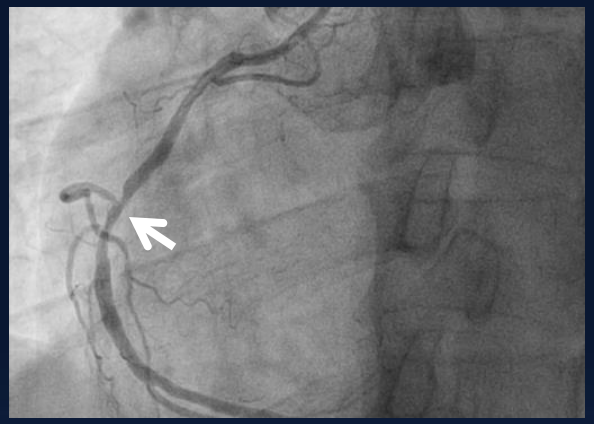



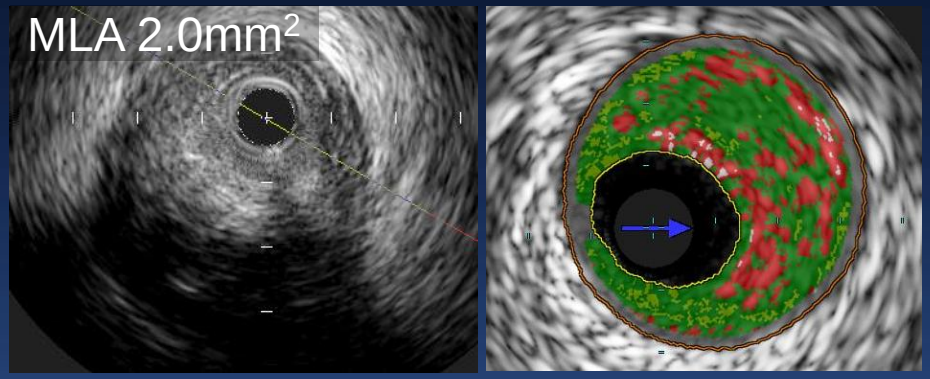

*Circulation 2003;108:1664-72* *Eshtehardi et al. J Am Heart Assoc 2012;1:e002543*

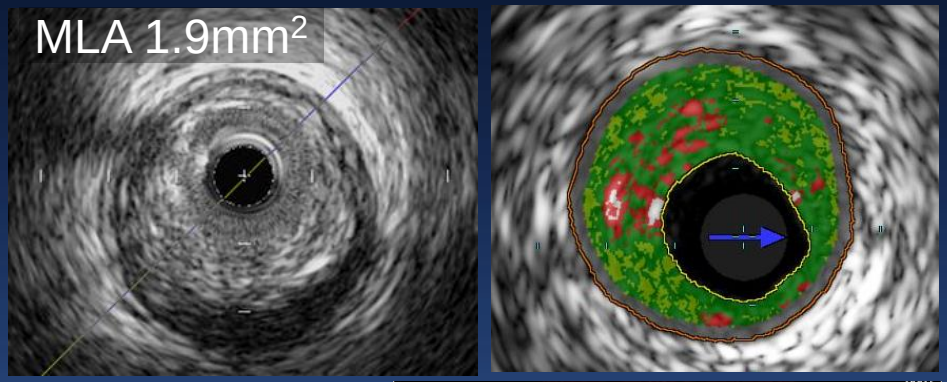
# Baseline

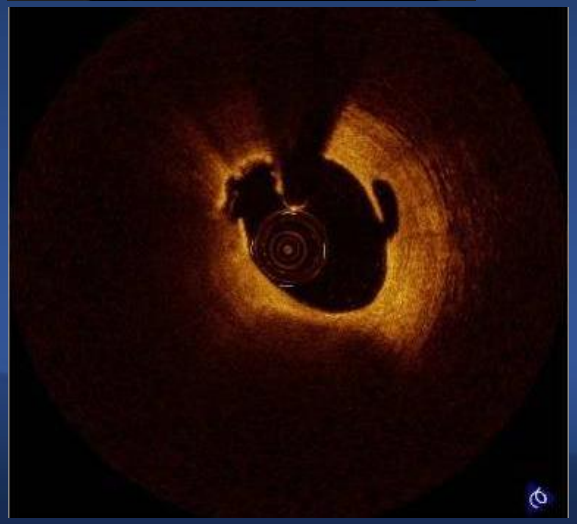



# 1-year F/U

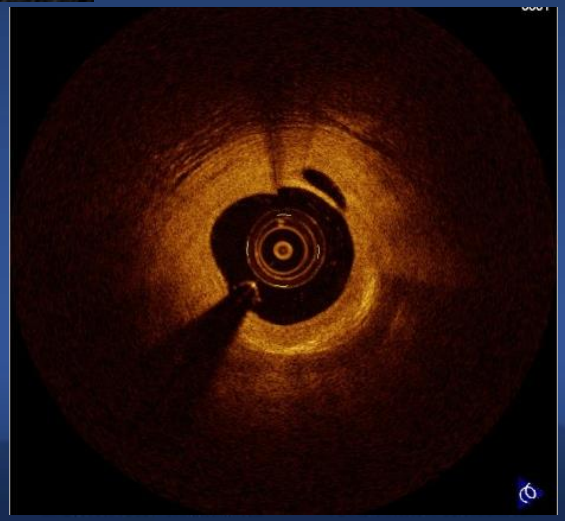




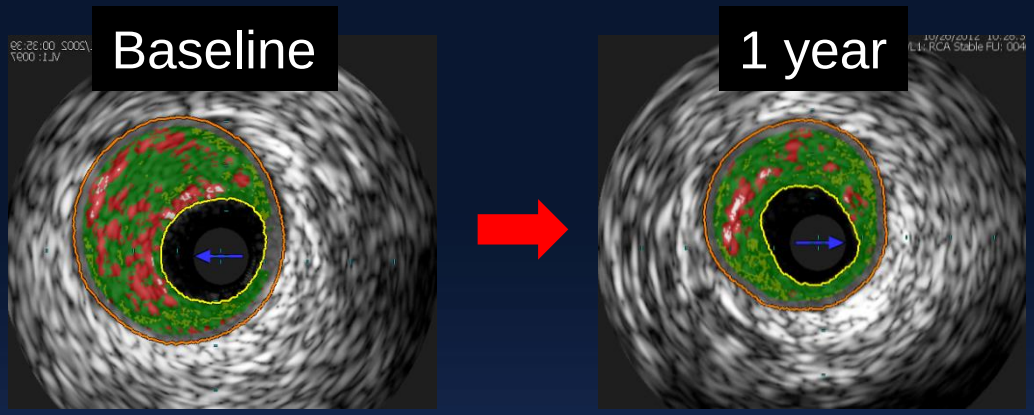



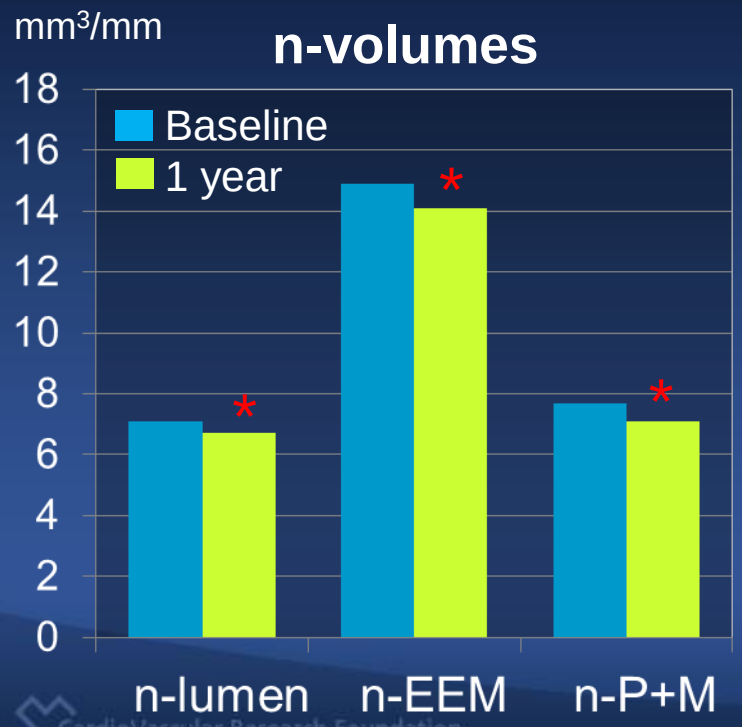
Plaque burden ↓
IVUS-attenuation ↓
Necrotic core ↓
Constrictive remodeling
Disappeared TCFA



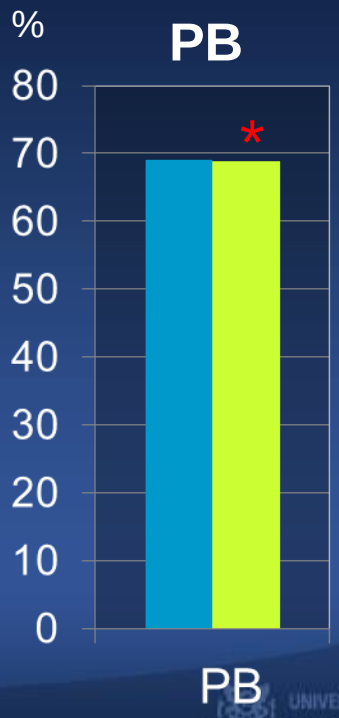
# STABLE Vascular Change after 1-year Statin

## *Fibroatheroma*-containing non-culprit lesions



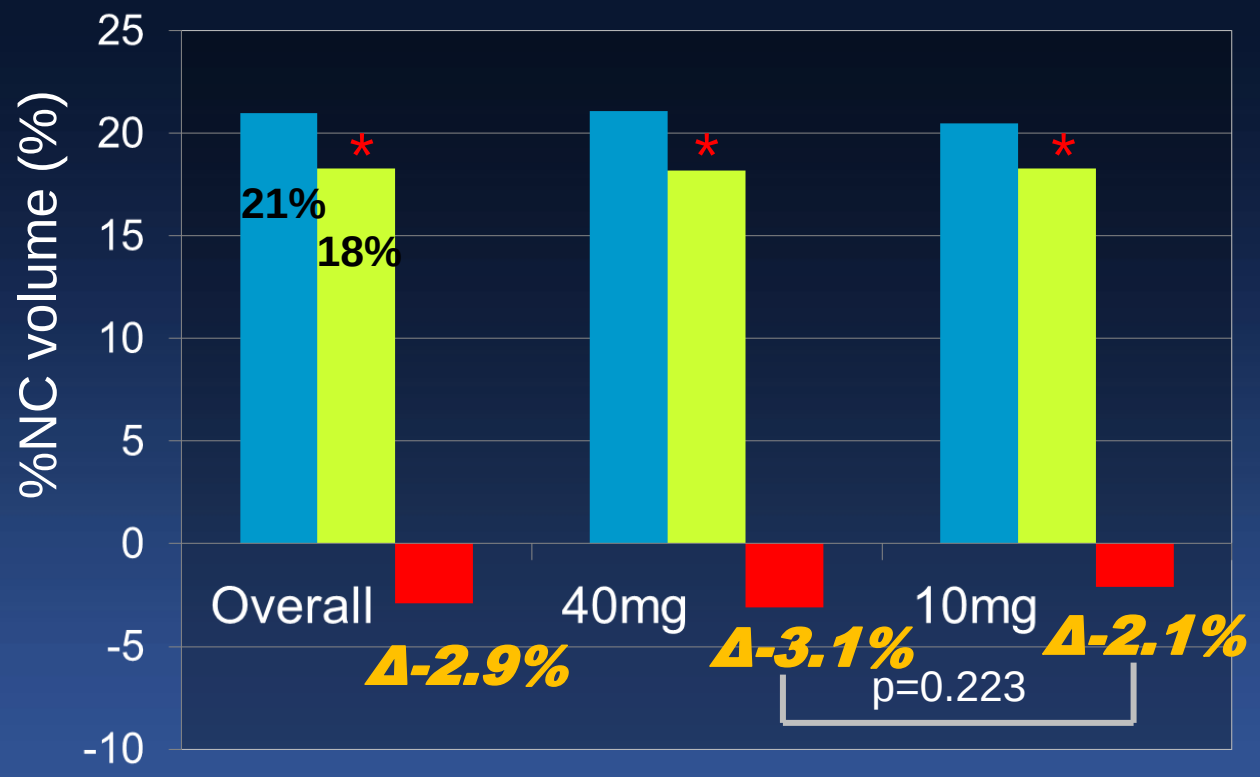



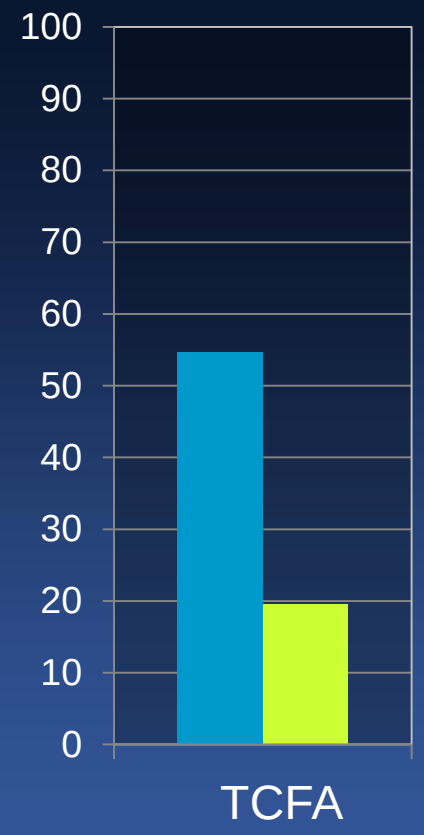





# STABLE: Endpoints

Primary: change in %NC volume within target segment
Secondary: change in %NC volume in rosuvastatin 40 vs. 10mg



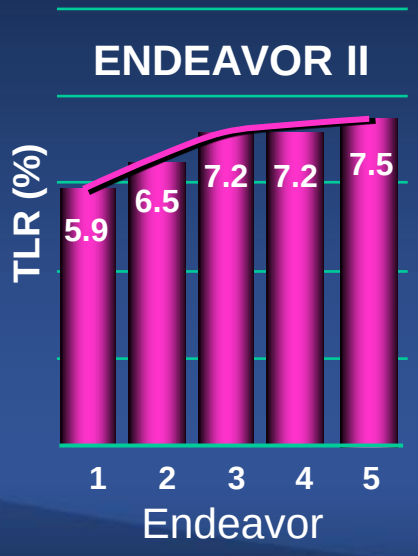

Baseline
12 months

* *p value <0.05*

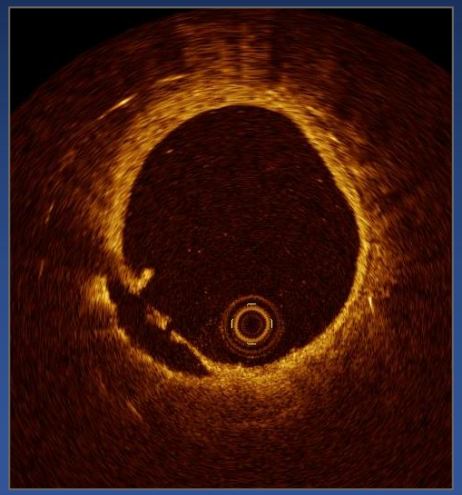
# Non-ischemic, Vulnerable Lesion

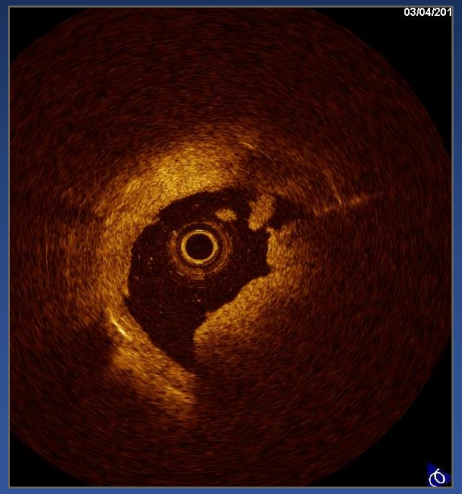
# Systemic vs. Local

- Numerous TCFAs, but hard event is rare
- Ischemia-based revascularization
- Drugs alter natural history
- Late stent failure (neoatherosclerosis…)



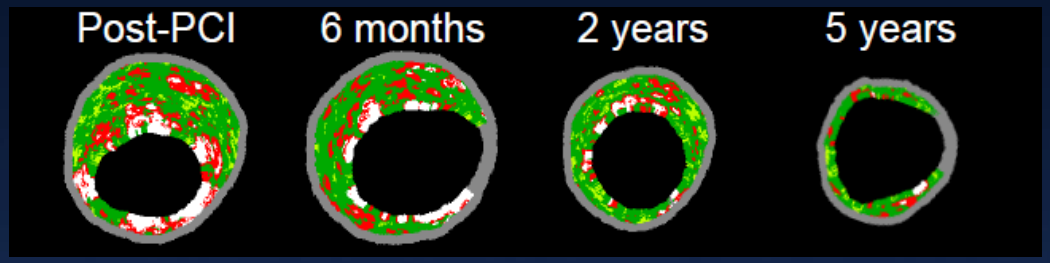


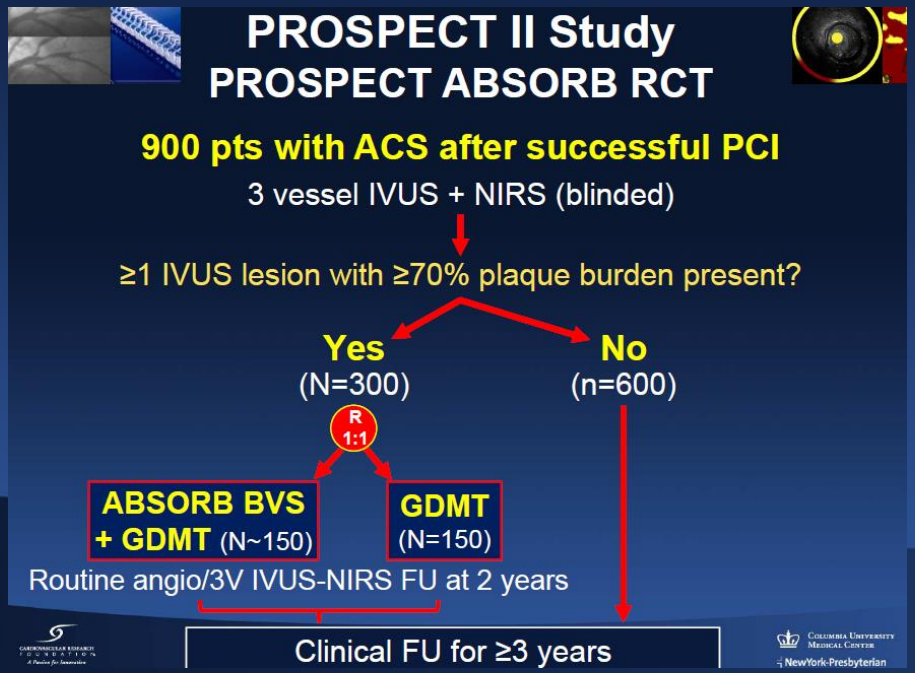


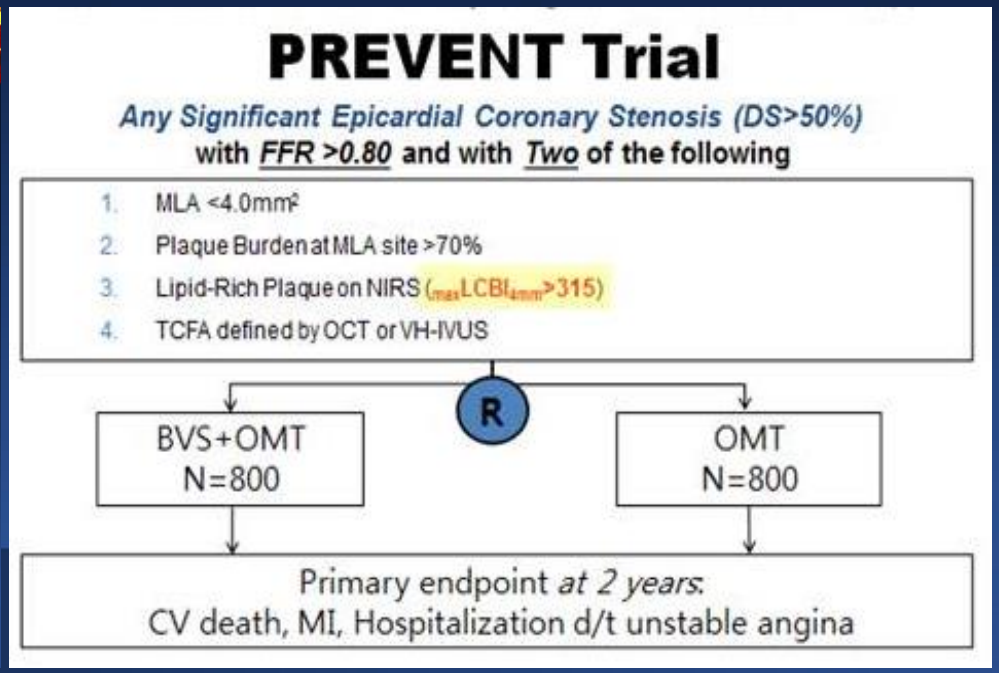


# Interventional Plaque Regression

## Bioresorbable Vascular Scaffolds

# SUMMARY

- Lesion morphology and plaque composition can be assessed by in vivo imaging modalities
- Natural history studies have shown that plaque burden, MLA and VH-TCFA predicted non-culprit MACE
- Although vulnerable plaque morphology is a substrate, determinants of the dynamic changes are multifactorial
- Statin is effective in plaque regression and stabilization
- Appropriate treatment of non-ischemic vulnerable lesion (systemic vs. local) needs to be determined in future trial