Detection and Treatment of Vulnerable In-Stent Neointima

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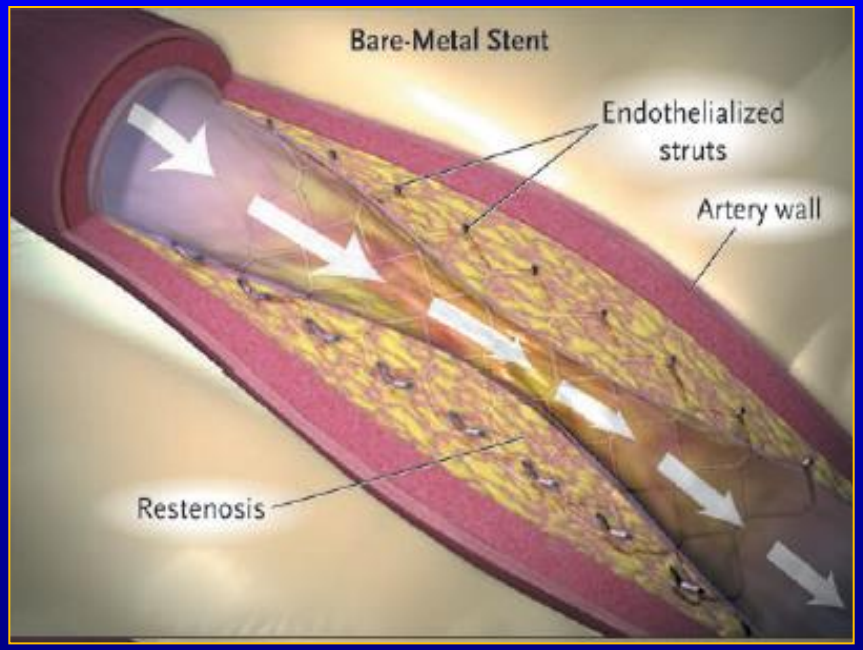
OCT Stent "Failure"

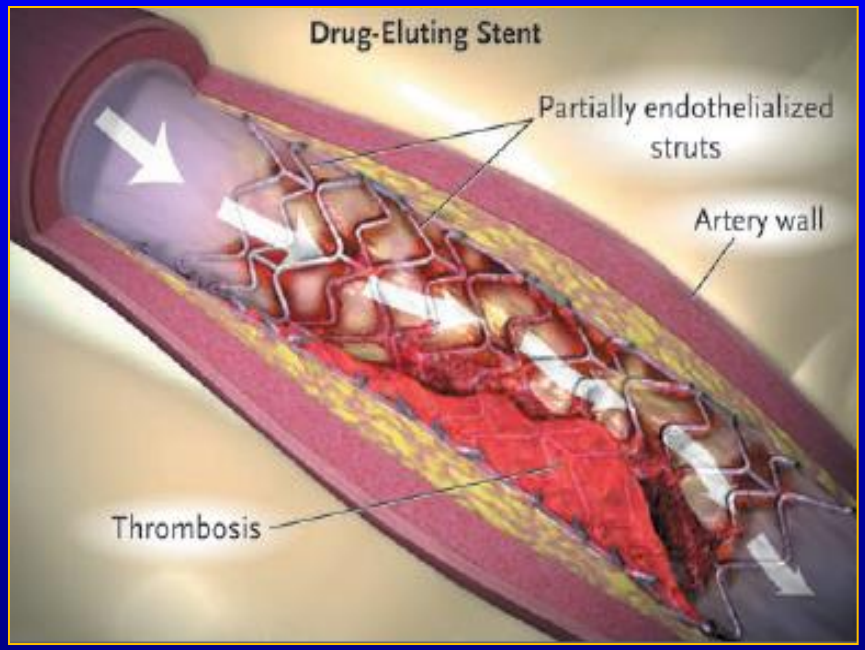
"Stent Failure"

In-Stent Restenosis



(Frequent, Benign)

Stent Thrombosis



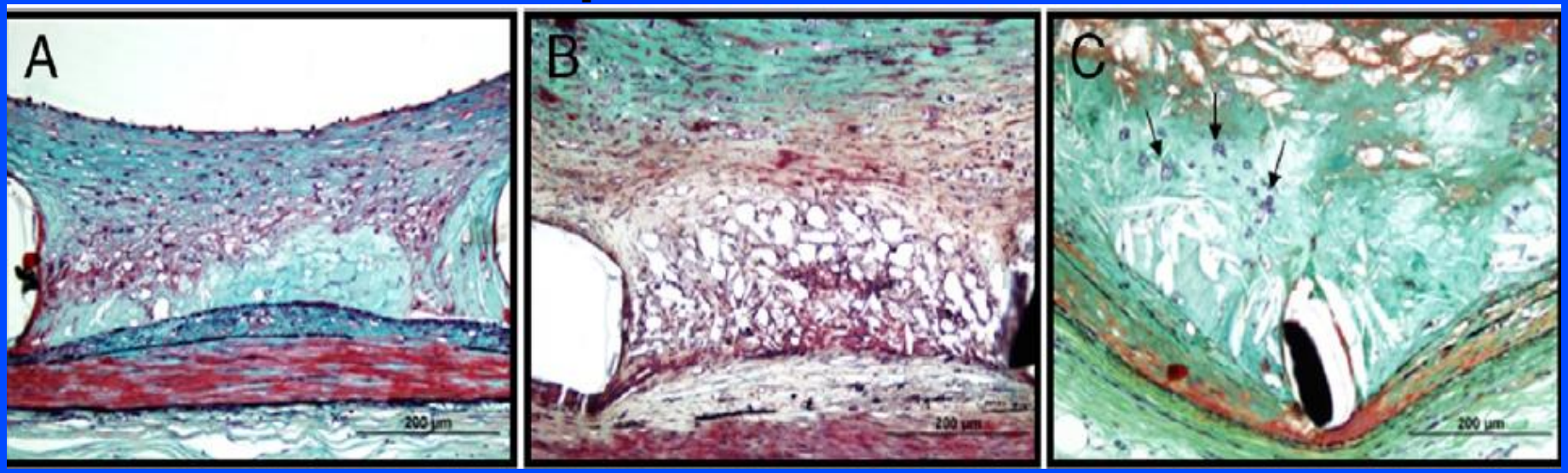
(Rare, Major Complication)

Curfman GD, Morrissey S, Jarcho JA, Drazen JM. Drug-eluting coronary stents--promise and uncertainty. N Egl J Med 2007;356(10):1059-60.

Neoatherosclerosis & ISR

Newly Formed Atherosclerotic Changes Within Neointima After Stent Implantation

SES implanted for 13 months



Foamy macrophage clusters in the peristrut region

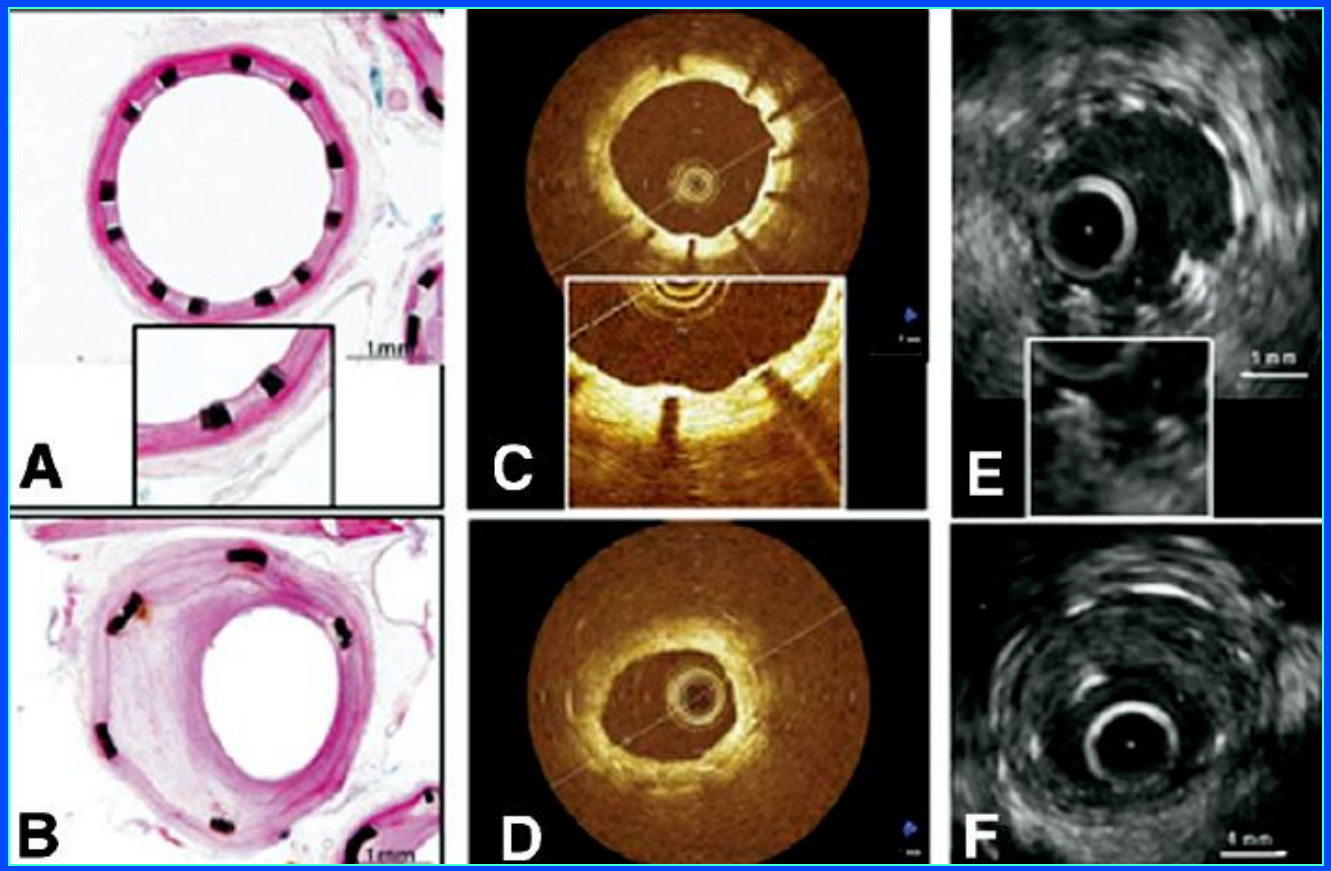
Fibroatheroma with foamy macrophage-rich lesion and early necrotic core

Fibroatheroma, peristrut early necrotic core, cholesterol clefts, surface foamy macrophages, and early calcification (arrows)

Nakazawa G, … Virmani R. J Am Coll Cardiol 2011;57:1314–22

ISR OCT vs IVUS

In Vivo Comparison Between Optical Coherence Tomography and Intravascular Ultrasound for Detecting Small Degrees of In-Stent Neointima After Stent Implantation

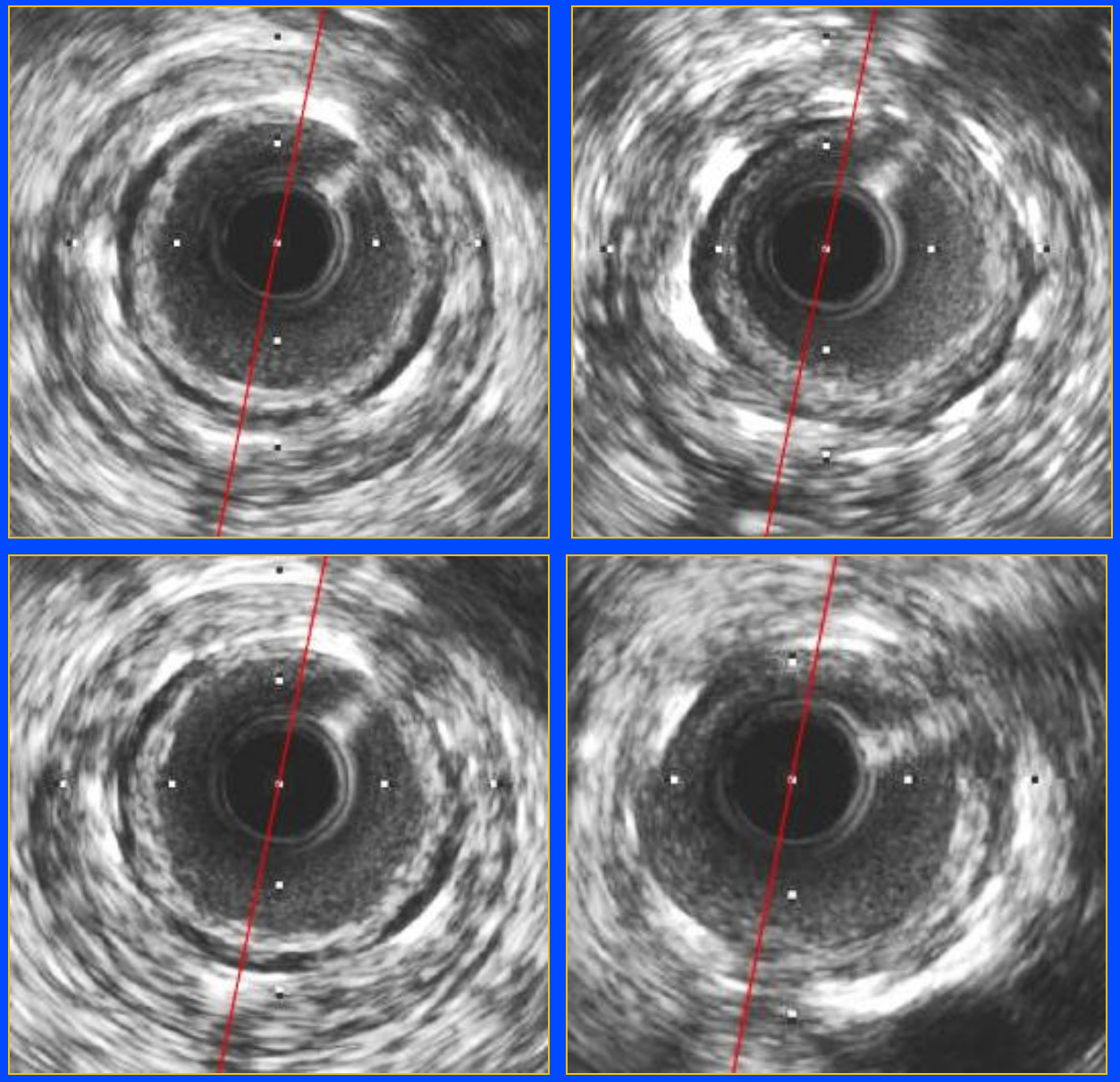


"Neointima"

As compared with histology, the diagnostic accuracy of OCT (AUC 0.967) was higher than that of IVUS (AUC 0.781)

Suzuki Y … Fearon WF. J Am Coll Cardiol Intv 2008;1:168 –73)

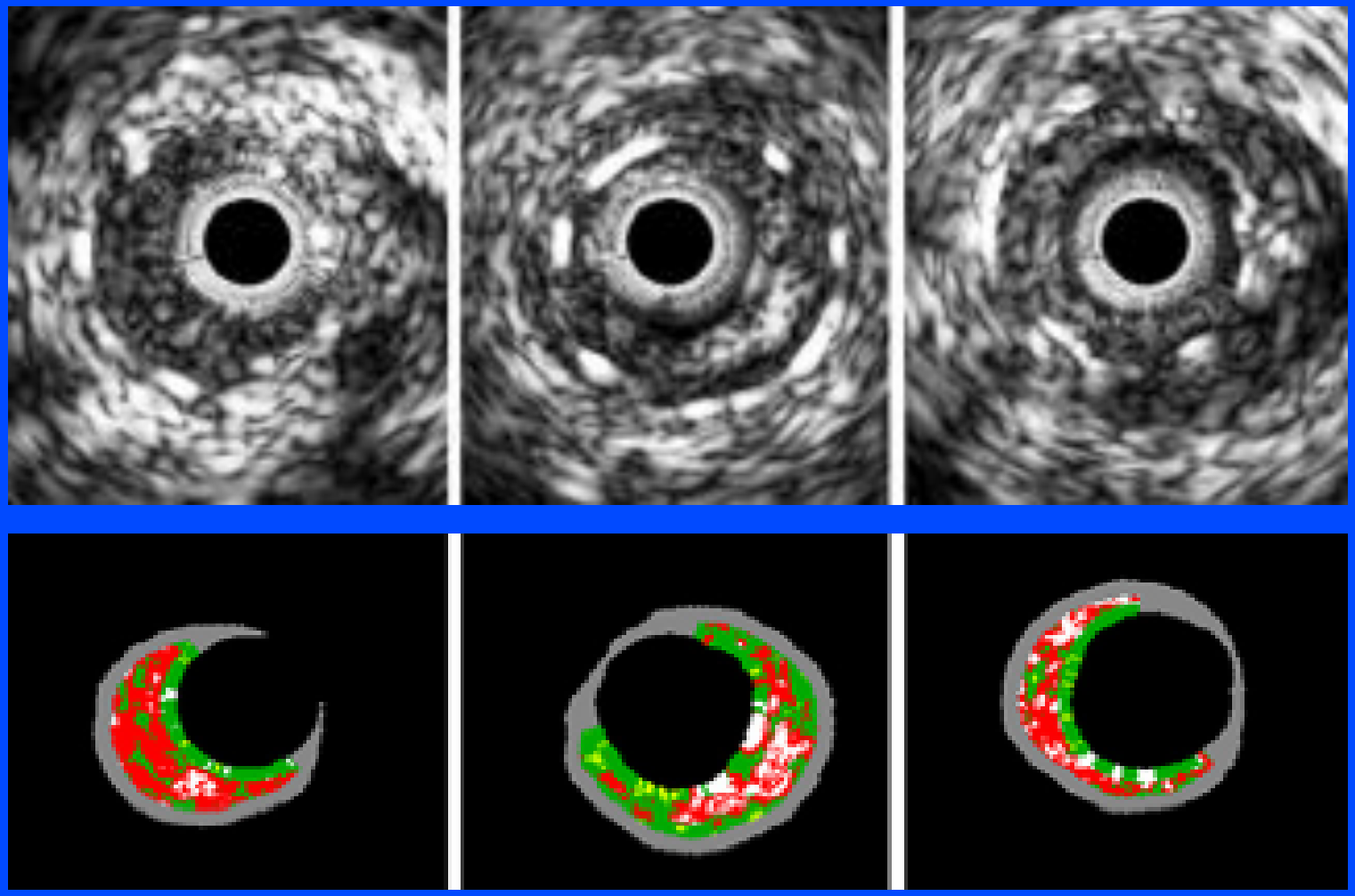
“Layered” ISR



VCP DB #1941474 (9M FU RIBS 4)

OCT-ST

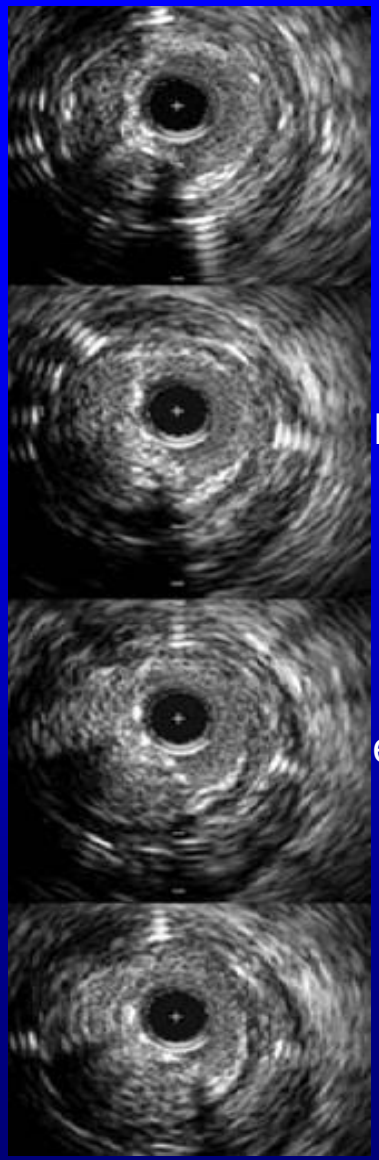
Virtual Histology Composition of Neointima at Maximal Percent Intimal Hyperplasia Sites



Park SJ, et al. J Am Coll Cardiol 2012;59:2051–7

ISR & VLST

Intravascular Ultrasound Findings in Patients With Very Late Stent Thrombosis After Either Drug-Eluting or Bare-Metal Stent Implantation



residual fibrous cap remnant

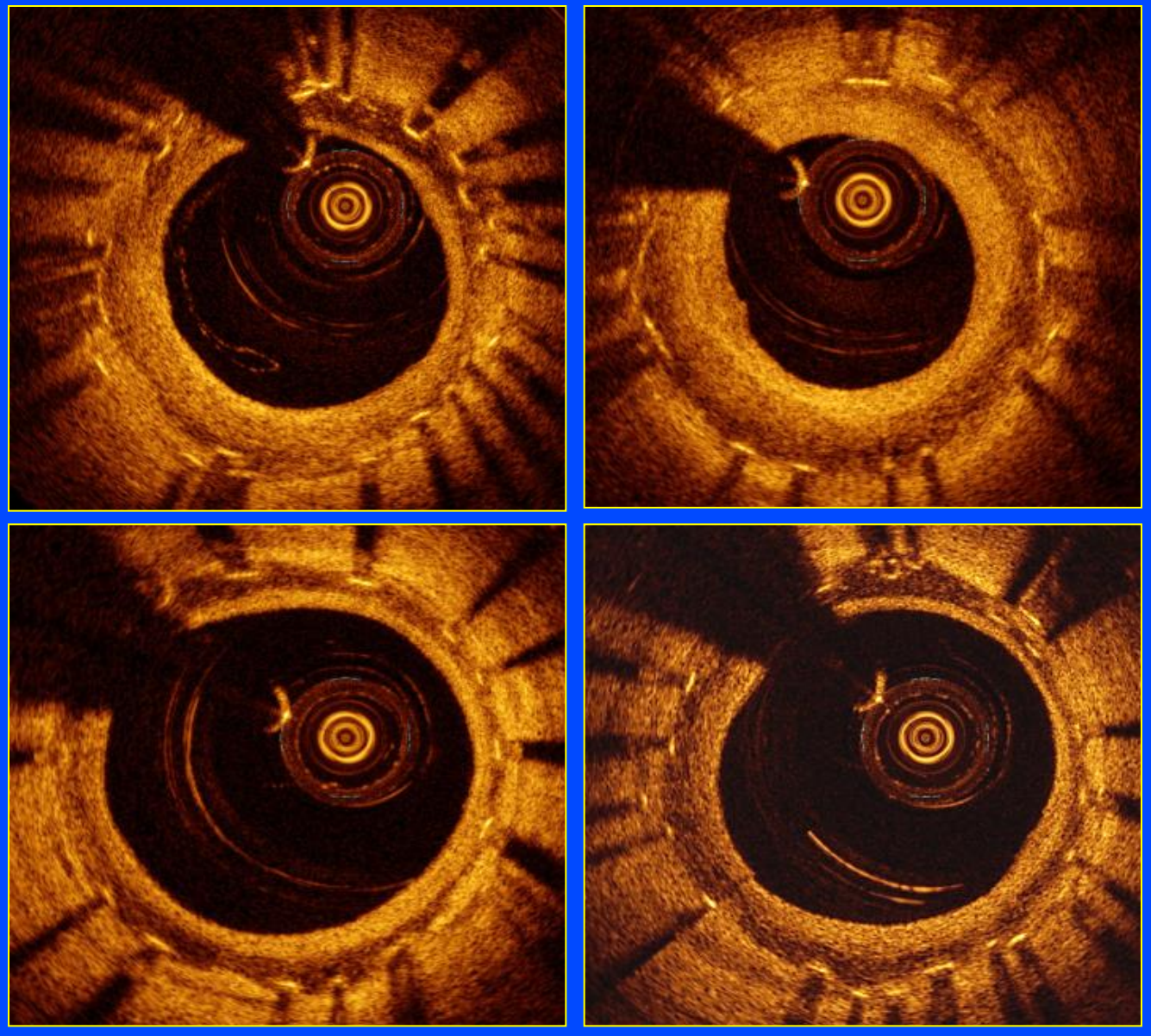
highly eccentric intrastent plaque

echolucent zone

intraluminal thrombus

Lee CW, et al. J Am Coll Cardiol 2010;55:1936-44

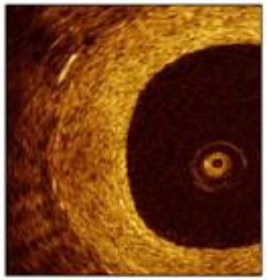
“Layered” ISR



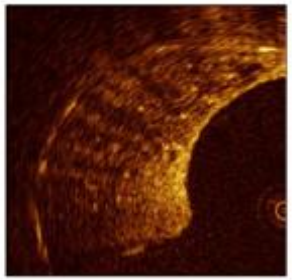
VCP DB #1941474 (9M FU RIBS 4)

OCT-ISR

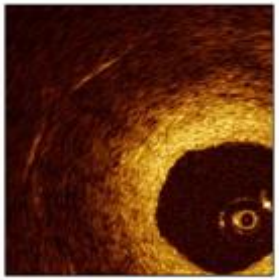
Restenotic tissue structure



Homogeneous: restenotic tissue has uniform optical properties and does not show focal variations in backscattering pattern.

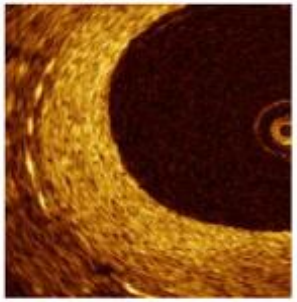


Heterogeneous: restenotic tissue has focally changing optical properties and shows various backscattering patterns

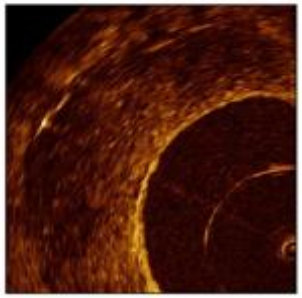


Layered: restenotic tissue consists of concentric layers with different optical properties: an adluminal high scattering layer and an abluminal low scattering layer

Restenotic tissue backscatter

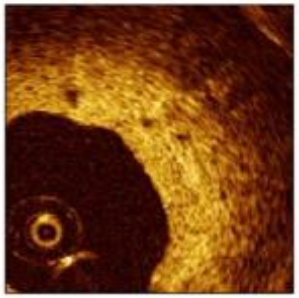


High: the majority of the tissue shows high backscatter and appears bright

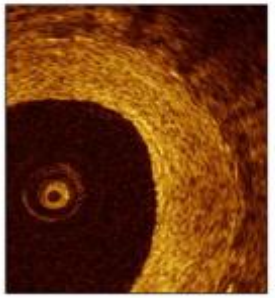


Low: the majority of the tissue shows low backscatter and appears dark or black

Microvessels visible



Yes: microvessels appear as well delineated low backscattering structures less than 200 micron in diameter that show a trajectory within the vessel

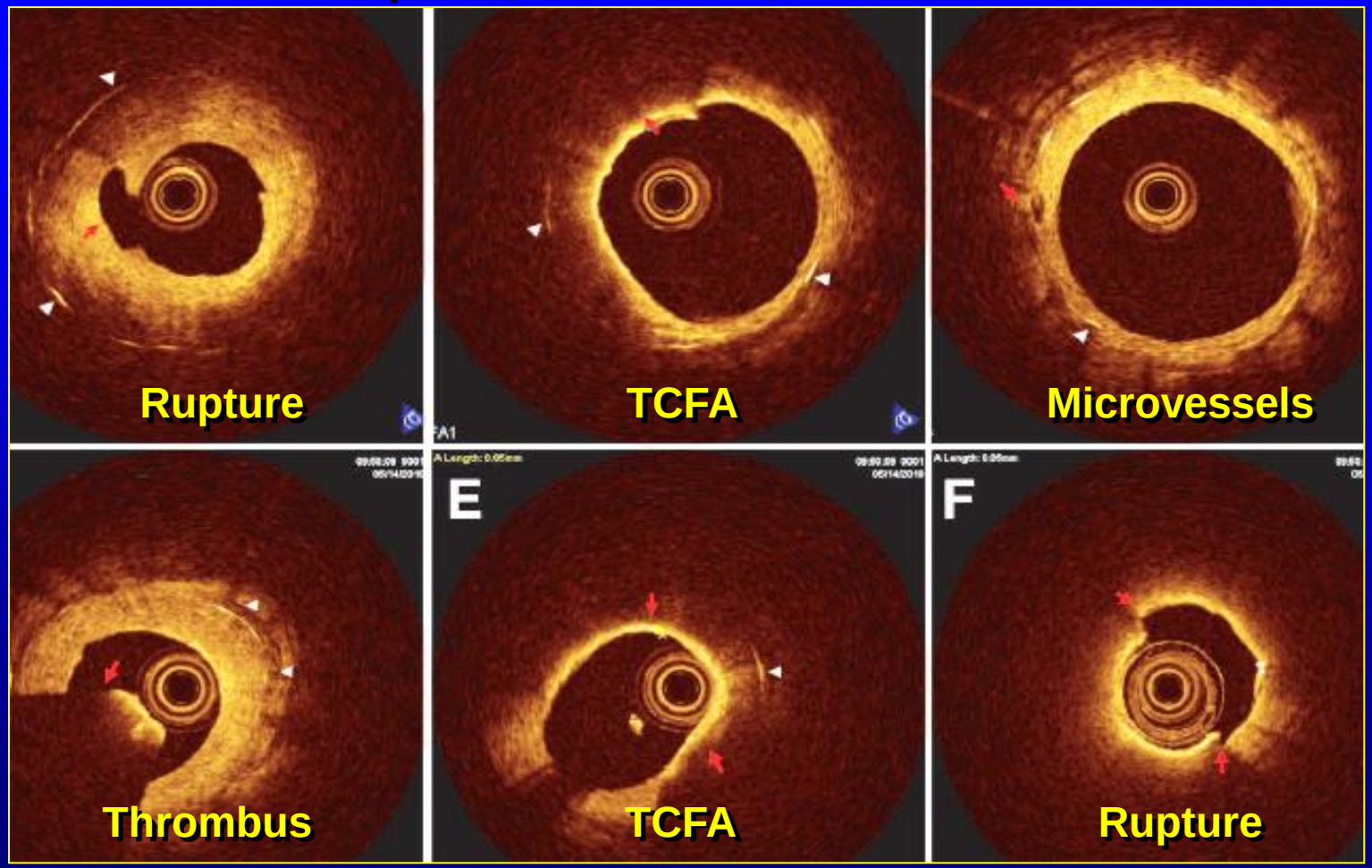


No

Gonzalo N, et al. Am Heart J 2009;158:284-93

OCT DES ISR: Pathophysiology

- **OCT in 50 Pts with DES ISR**
  58% Rupture, 52% TCFA, 58% Thrombus



Kang SJ, Mintz GS. Circulation. 2011;123:2954-2963

OCT-ISR (Microvessels)

J Invasive Cardiol. 2012 Mar;24(3):116-20.

Optical coherence tomography evaluation of in-stent restenotic lesions with visible microvessels.

Kim BK, Kim JS, Shin DH, Ko YG, Choi D, Jang Y, Hong MK.

Division of Cardiology, Yonsei Cardiovascular Center, and Severance Biomedical Science Institute, Yonsei University College of Medicine, 250 Seongsanno, Seodaemun-gu, Seoul 120-752, Korea. mkhong61@yuhs.ac.

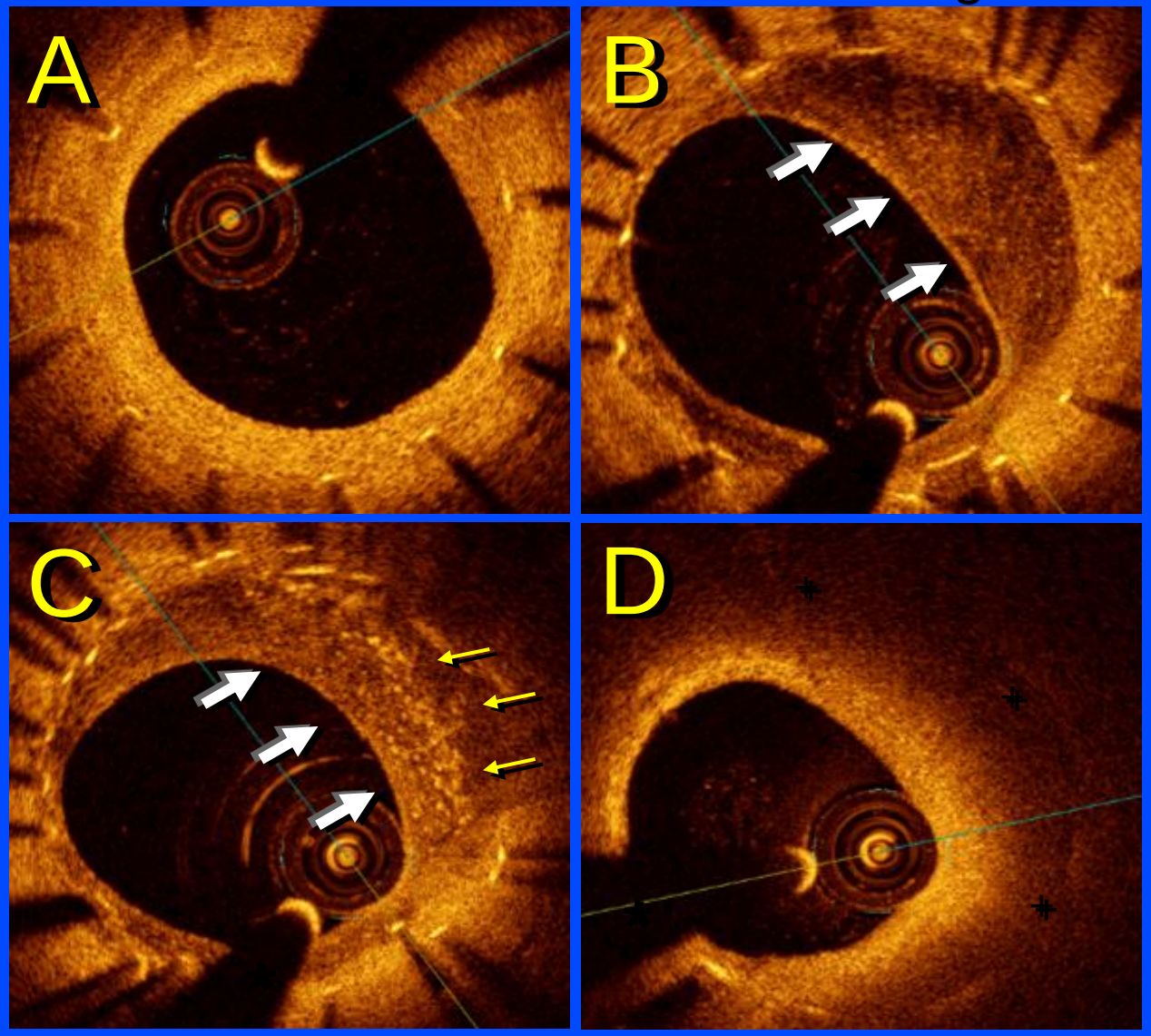
78 ISR lesions (72 DES, 6 BMS) 21 (27%) had microvessels .

(Microvessels: low backscattering structures <200 μm in diameter)

- Microvessels associated with:
  - Neointimal hyperplasia (NIH) CSA (5.4 vs 4.2 mm^2; p=0.024)
  - % NIH CSA (79 vs 67%; p=0.001).

Kim BK et al. J Invasive Cardiol 2012 Mar;24(3):116-20.

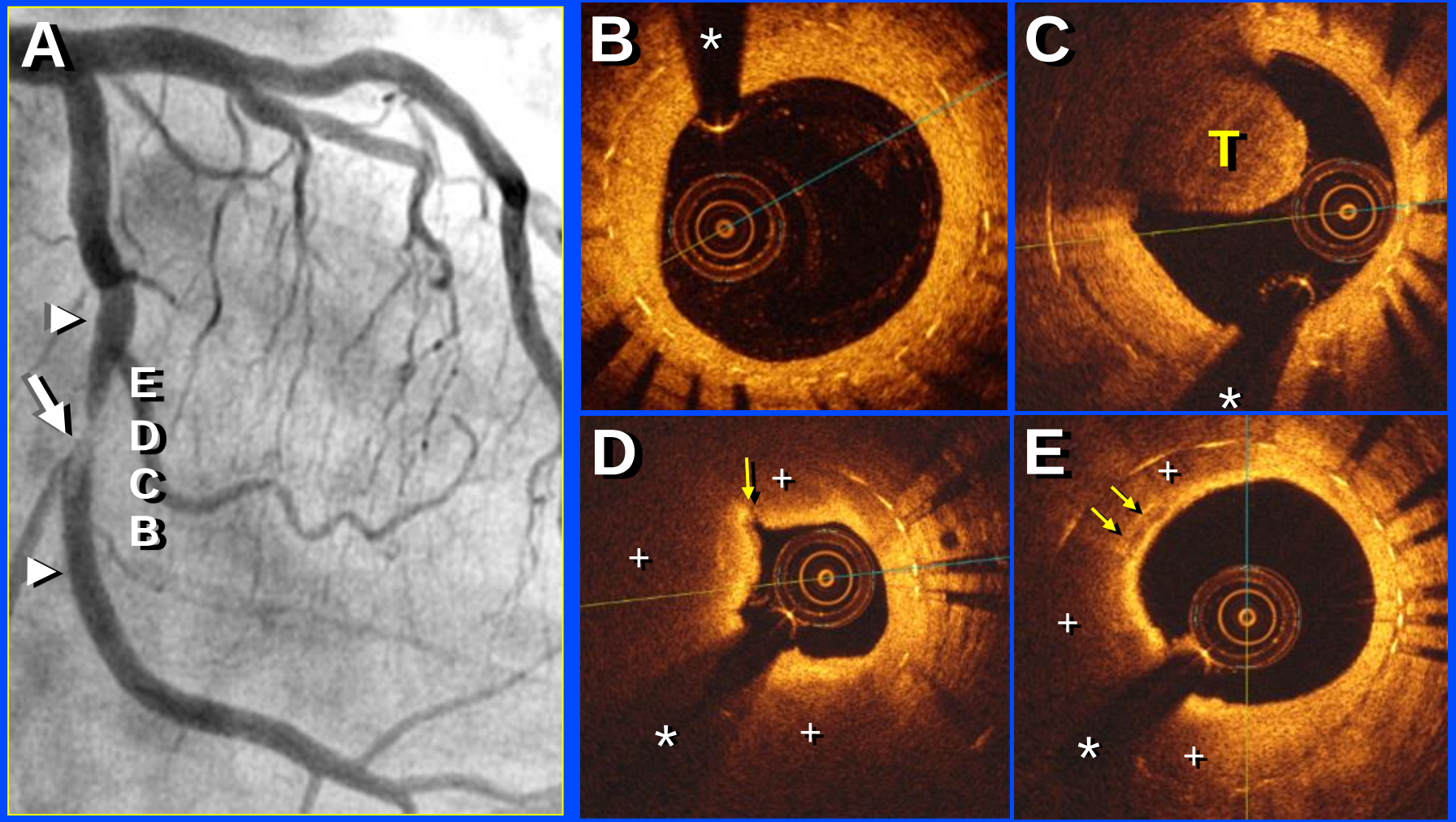
Neoatherosclerois After Paclitaxel-Eluting Balloon



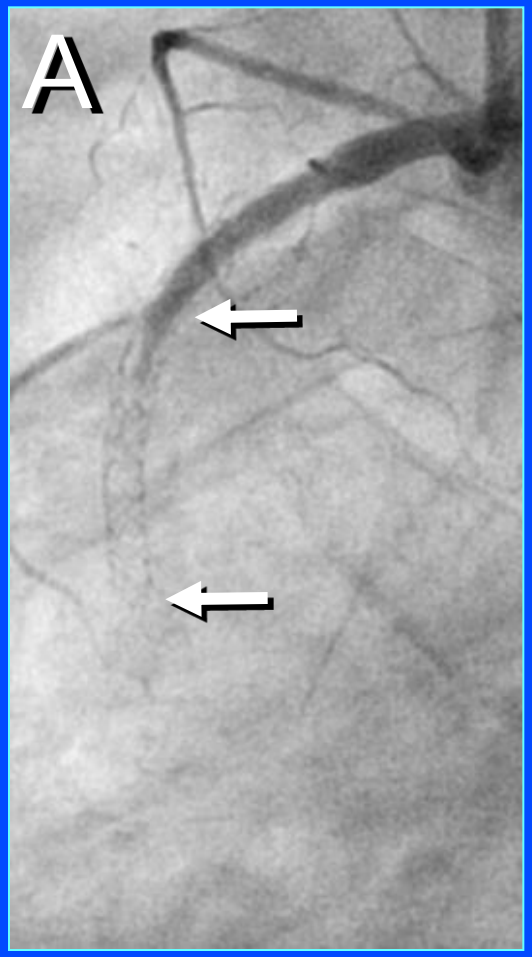
Alfonso F. Circulation 2013

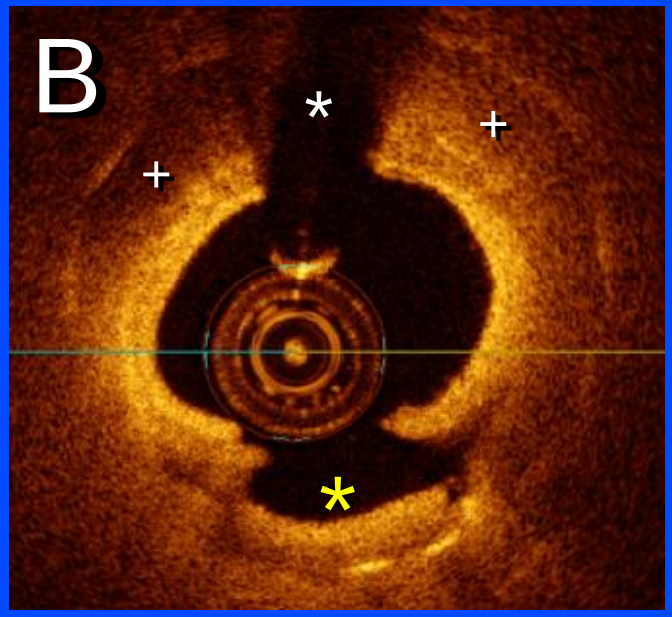
Ruptured Neoatherosclerosis

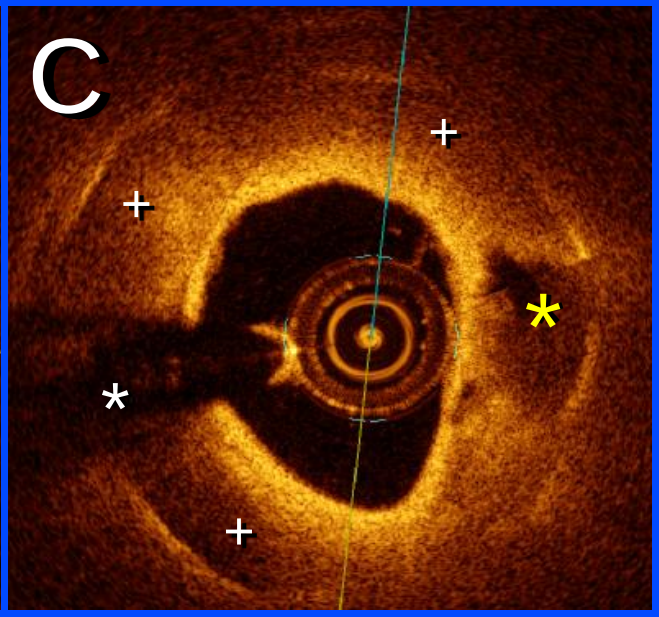
"The elusive link between very late ISR and ST"

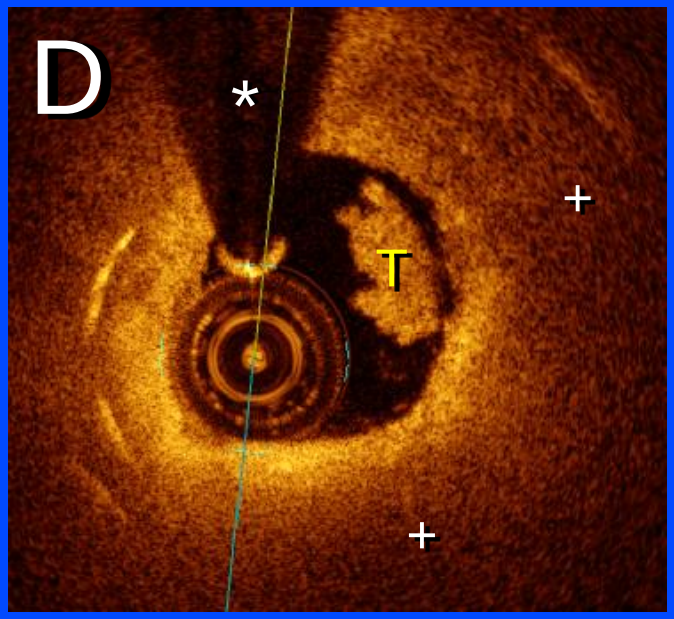


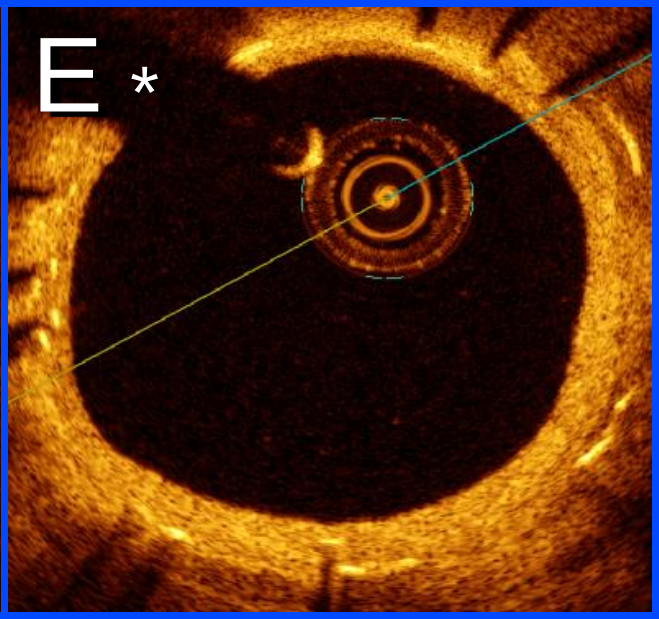
Neoatherosclerosis Causing Late ST





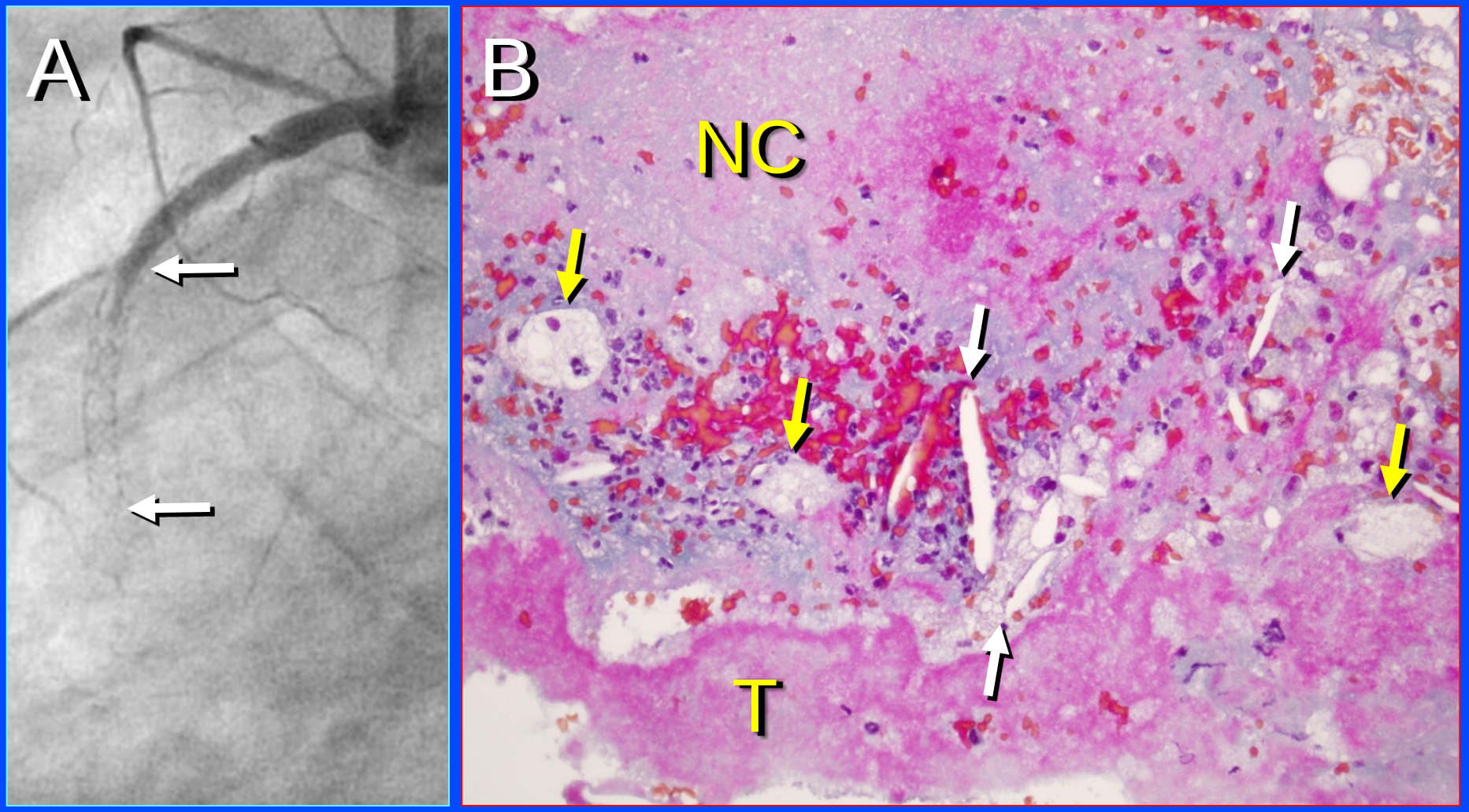






Neoatherosclerosis Causing Late ST

«Thromboaspiration»

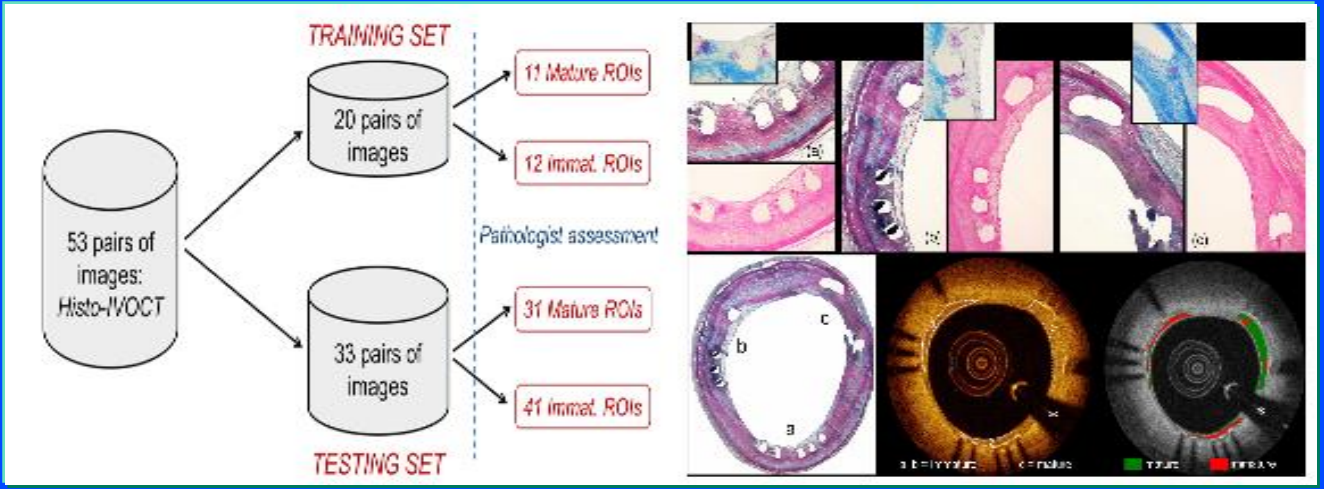


Detection & Treatment: Vulnerable In-Stent Neointima

Automatic Characterization of Neointimal Tissue by OCT

Previous OCT studies indicated that well-organized mature neointimal tissue appears as a high-intensity, smooth, and homogeneous regions, while lower-intensity signal areas might correspond to immature tissue mainly composed of acellular material.

New Zealand White rabbits:
Pixel-wise classification accuracy of 87%
Two-dimensional region-based analysis accuracy of 92%
(with sensitivity and specificity of 91% and 93%, respectively)

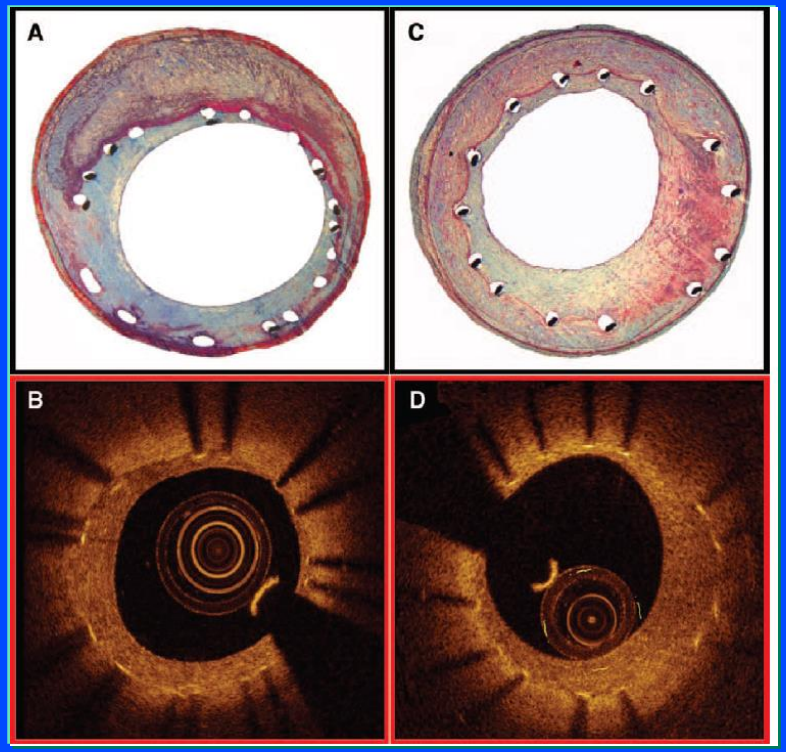


J. Biomed. Opt. 19(2), 021104 (Jul 24, 2013).

Detection & Treatment: Vulnerable In-Stent Neointima

Tissue Characterization After Drug-Eluting Stent Implantation Using Optical Coherence Tomography

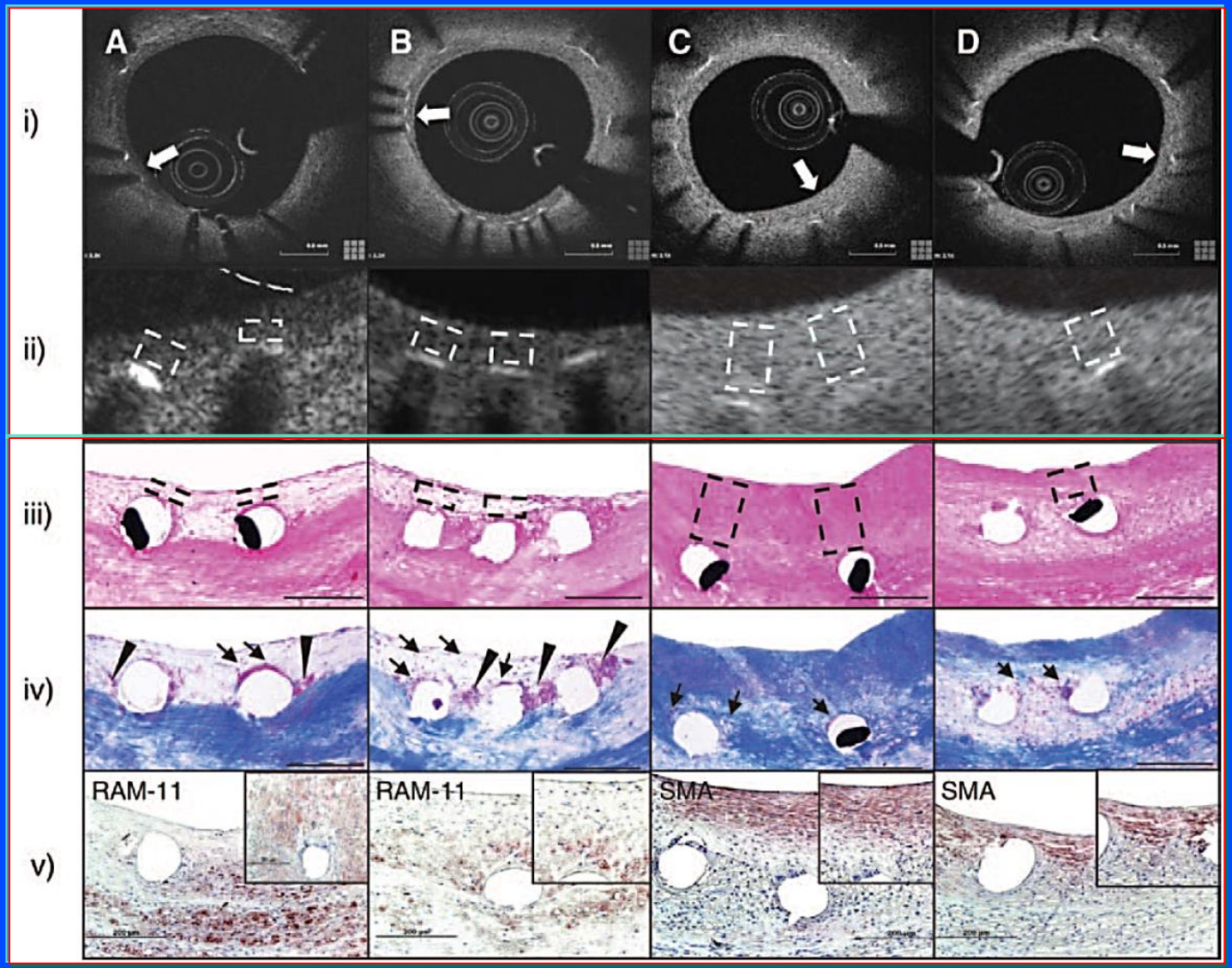
Caroline Malle, Tomohisa Tada, Kristin Steigerwald, Giovanni J. Ughi, Tibor Schuster, Masataka Nakano, Steffen Massberg, Johannes Jehle, Giulio Guagliumi, Adnan Kastrati, Renu Virmani, Robert A. Byrne, Michael Joner



After coregistration with histology, gray-scale signal intensity (**GSI**) was measured for identified "mature" or "immature" neointimal tissue.

Malle C, et al Arterioscler Thromb Vasc Biol. 2013;33:1376-1383

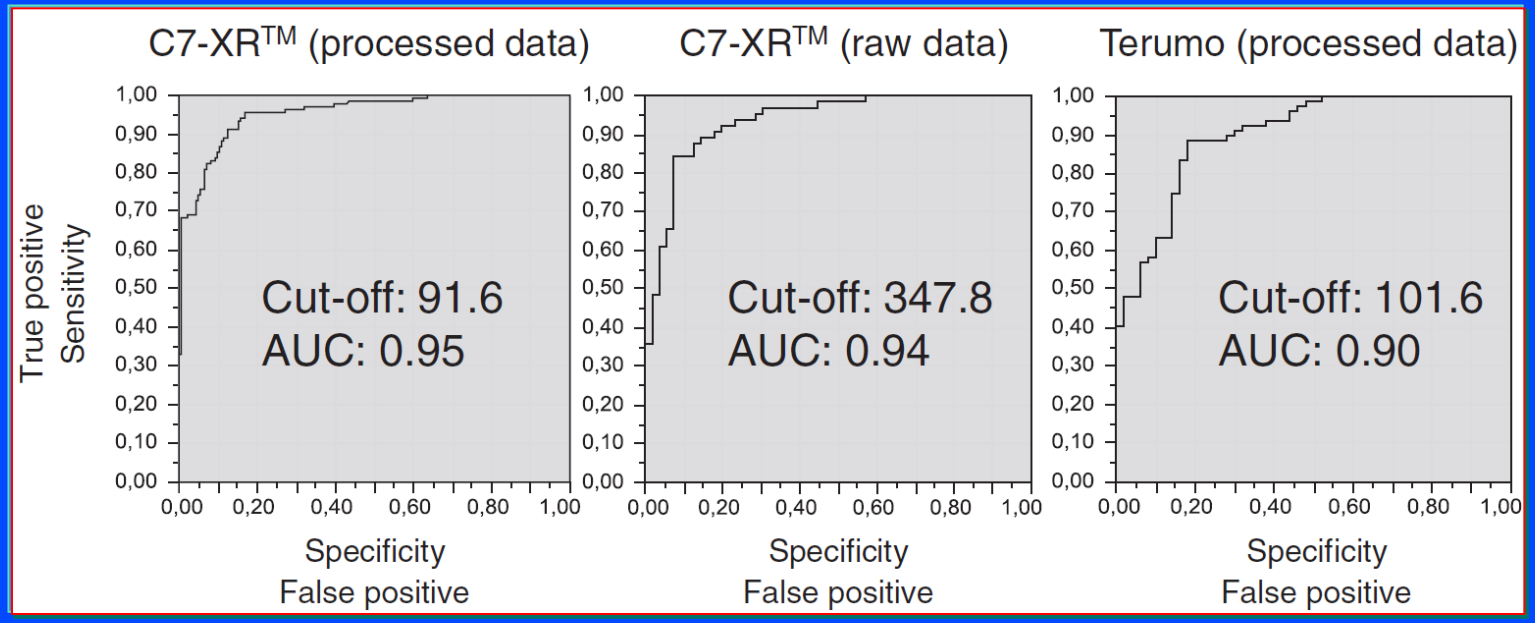
Detection & Treatment: Vulnerable In-Stent Neointima



Malle C, et al Arterioscler Thromb Vasc Biol. 2013;33:1376-1383

Detection & Treatment: Vulnerable In-Stent Neointima

Detection of «Mature Neointimal Tissue" by gray-scale signal intensity (GSI) analysis



ROC analysis displayed high sensitivity and specificity for detection of mature neointima in animal (96% and 79%, respectively) and human autopsy (89% and 71%, respectively) data.

In patients undergoing OCT follow-up 6 months after DES, prospective GSI analysis revealed that a minimum of 27.7% of areas above stent struts represented mature neointima.

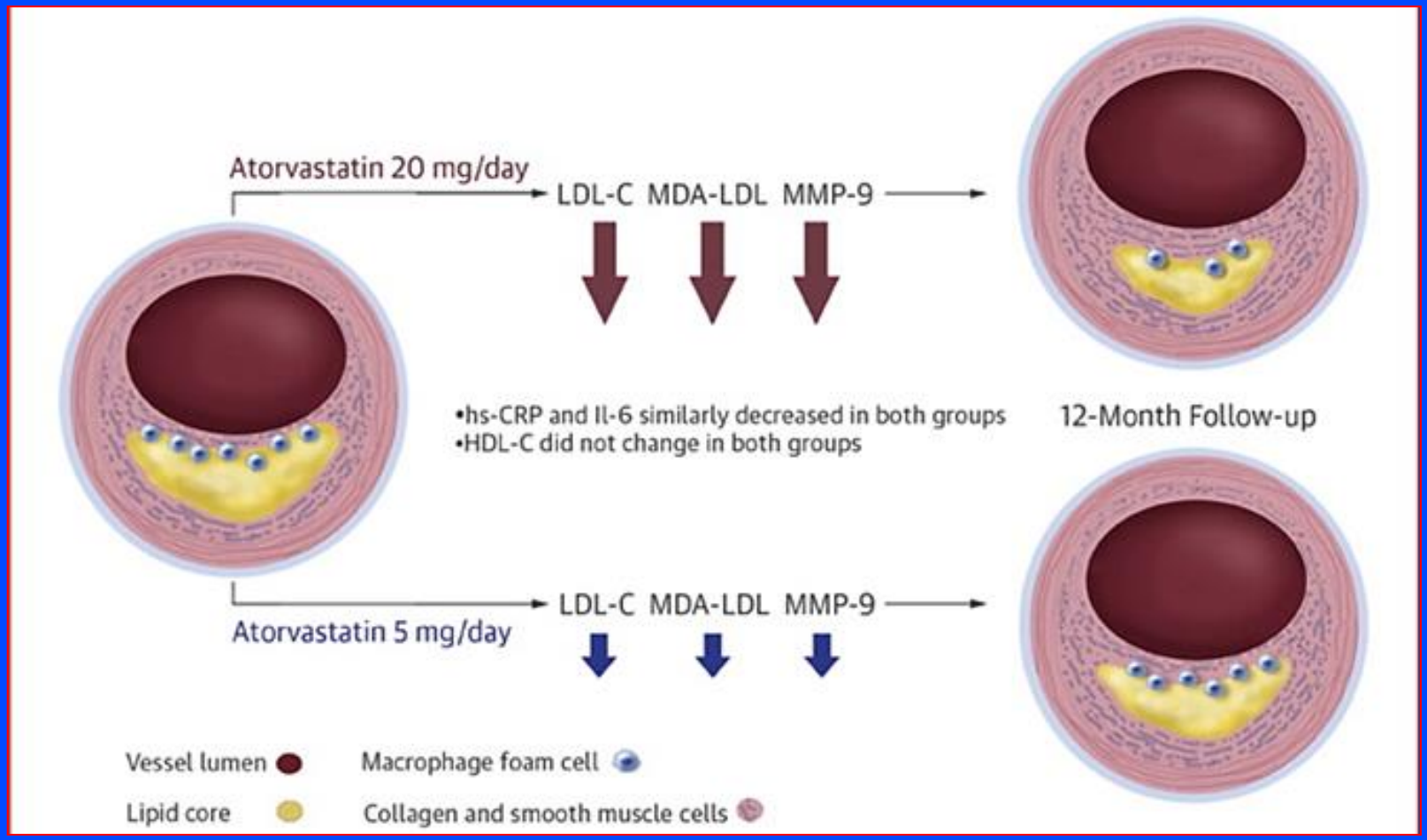
Malle C, et al Arterioscler Thromb Vasc Biol. 2013;33:1376-1383

Treatment of Vulnerable Neointima

Detection & Treatment: Vulnerable In-Stent Neointima

The EASY-FIT Study (RCT)

Effect of Atorvastatin Therapy on Fibrous Cap Thickness in Coronary Atherosclerotic Plaque as Assessed by Optical Coherence Tomography



Komukai K et al. J Am Coll Cardiol. 2014;64(21):2207-2217.

Detection & Treatment: Vulnerable In-Stent Neointima

The EASY-FIT Study (RCT)

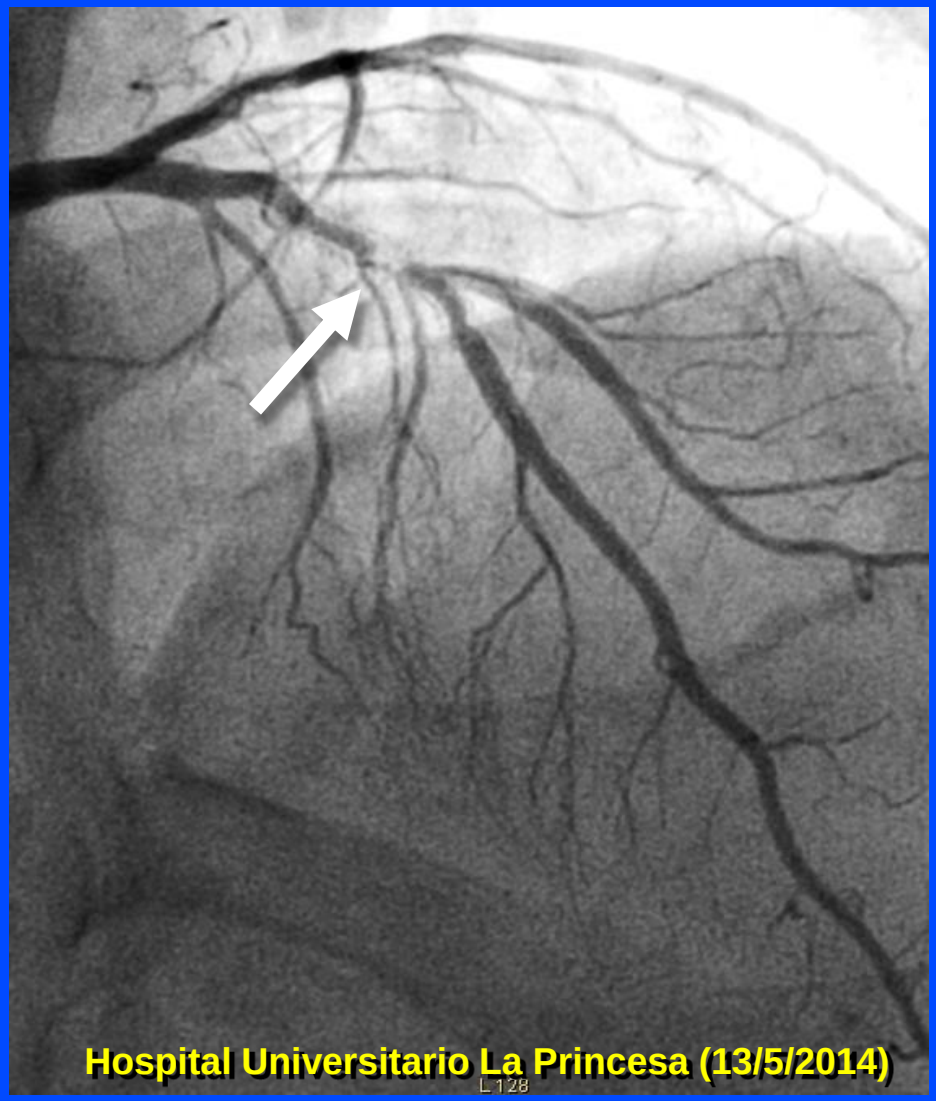
Effect of Atorvastatin Therapy on Fibrous Cap Thickness in Coronary Atherosclerotic Plaque as Assessed by Optical Coherence Tomography

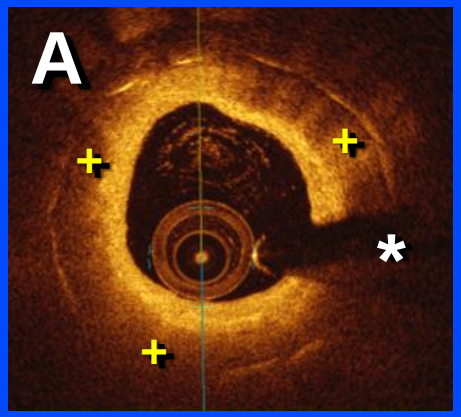
- **Atorvastatin 20 mg/d vs 5 mg/d:**
  - **Reduced LDL cholesterol levels**
    - (69 mg/dl vs. 78 mg/dl; p = 0.039).
  - **Increased fibrous cap thickness**
    - (69% vs. 17%; p < 0.001).
- The **increase in fibrous cap thickness** correlated with the ***decrease*** in serum levels of:
  - LDL cholesterol (R = −0.450; p < 0.001),
  - High-sensitivity C-reactive protein (R = −0.276; p = 0.033),
  - Matrix metalloproteinase-9 (R = −0.502; p < 0.001)
  - OCT-derived macrophages (R = −0.415; p = 0.003).

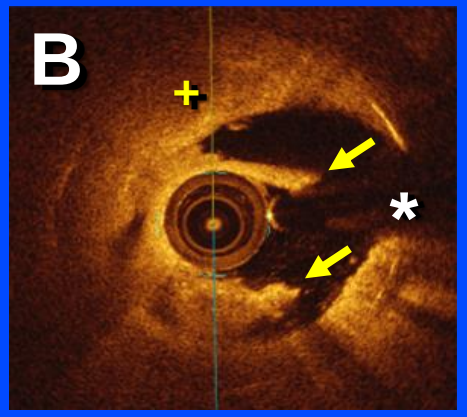
Komukai K et al. J Am Coll Cardiol. 2014;64(21):2207-2217.

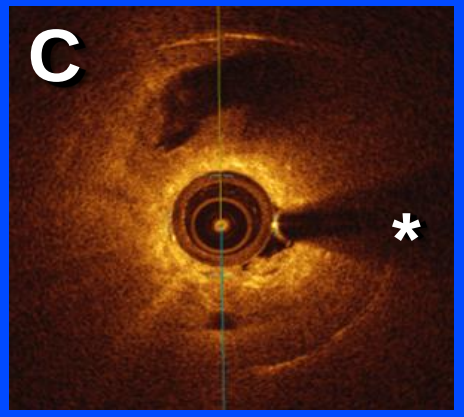
Detection & Treatment: Vulnerable In-Stent Neointima

64 yo. PES in LAD 10 years ago
Prologed Chest Pain, (-) T waves, Troponin (++)



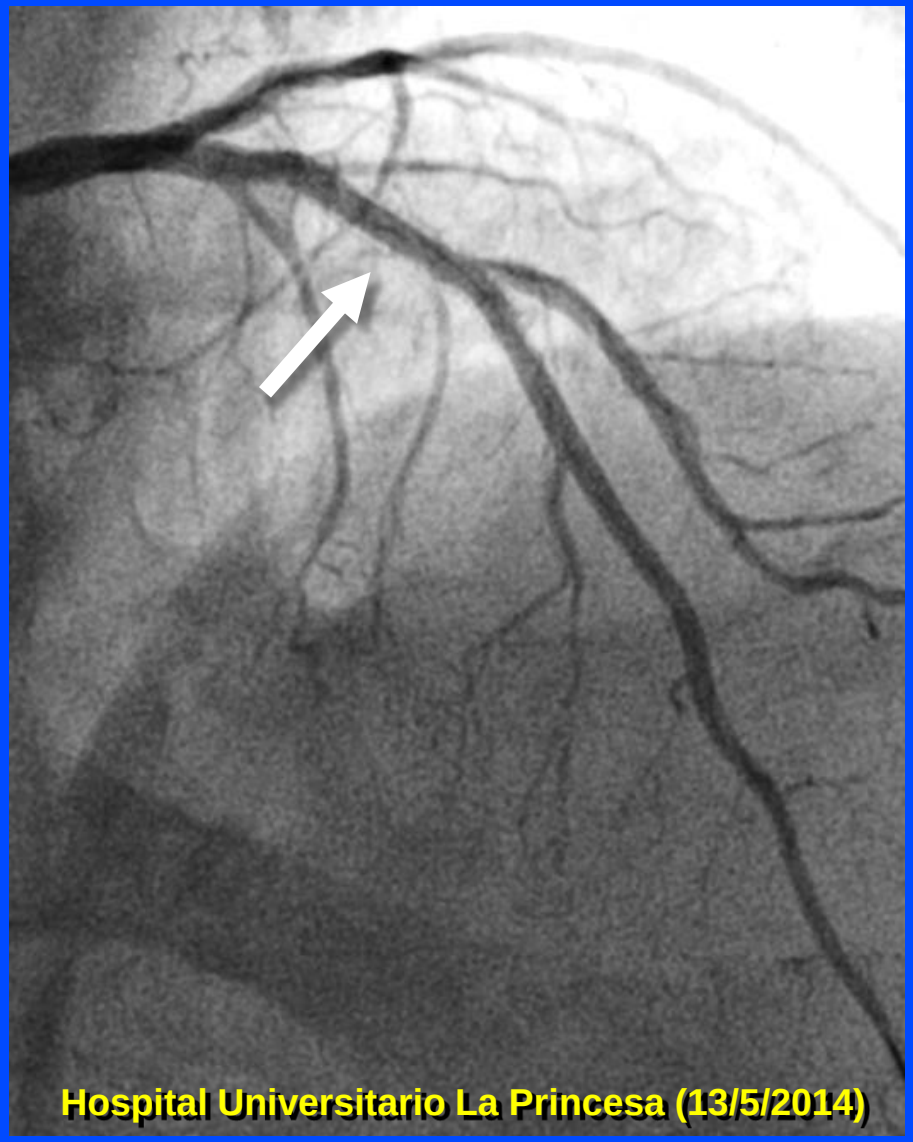


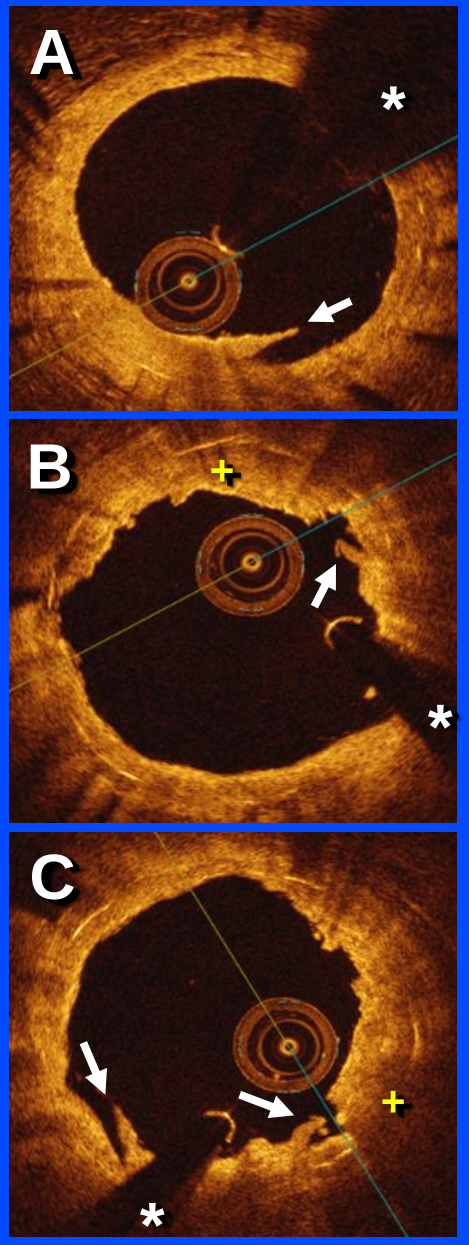




Detection & Treatment: Vulnerable In-Stent Neointima

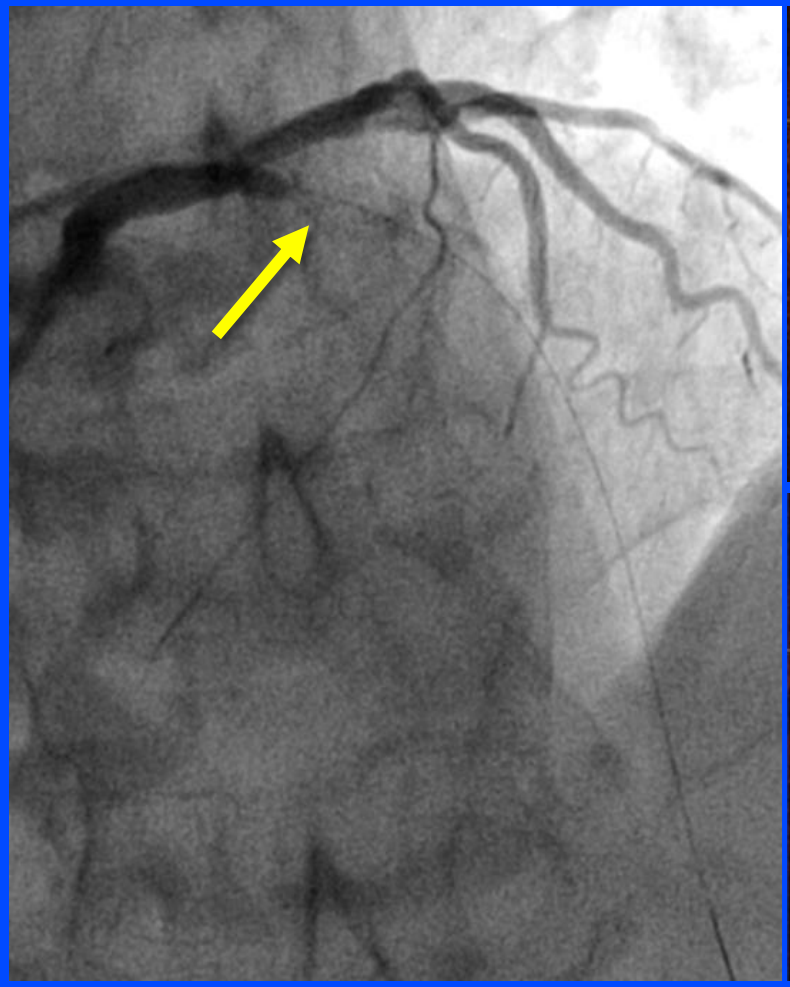
High-Pressure Predilation and DCB

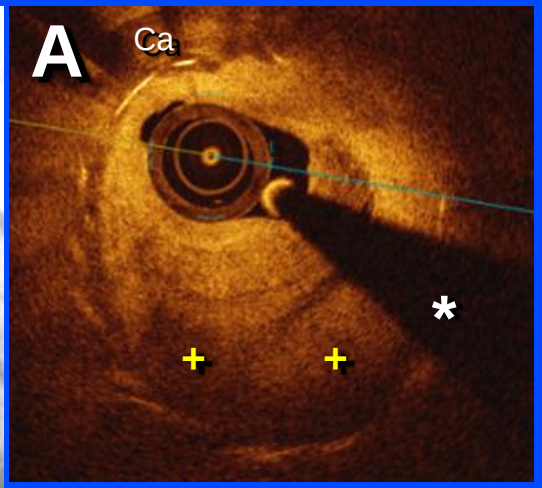


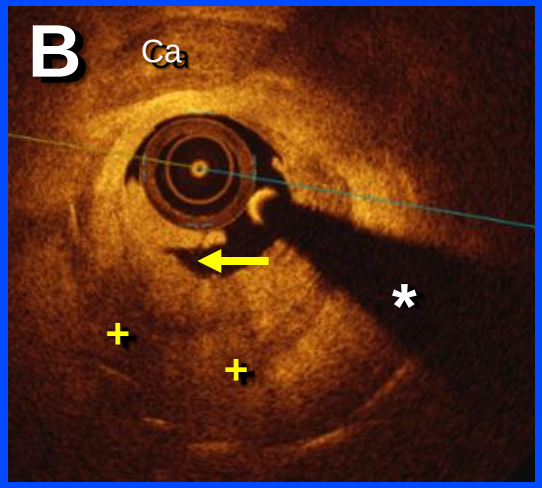


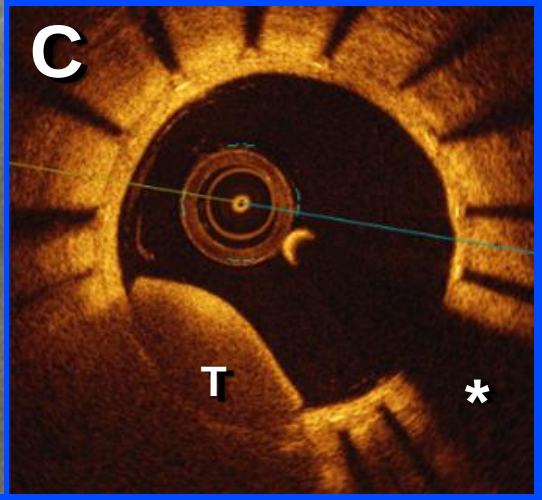
Detection & Treatment: Vulnerable In-Stent Neointima

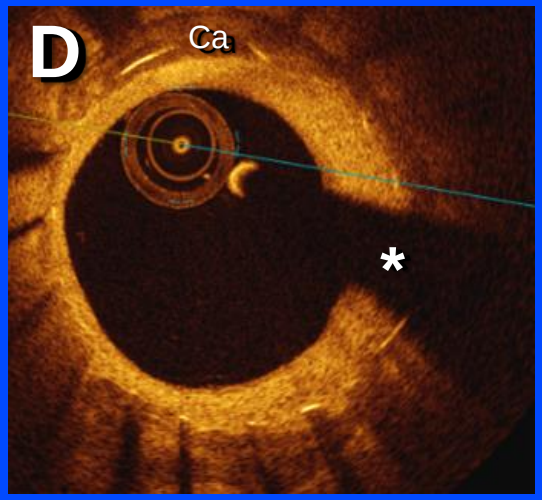
52 yo. PES in LAD 8 years ago
Anterior STEMI







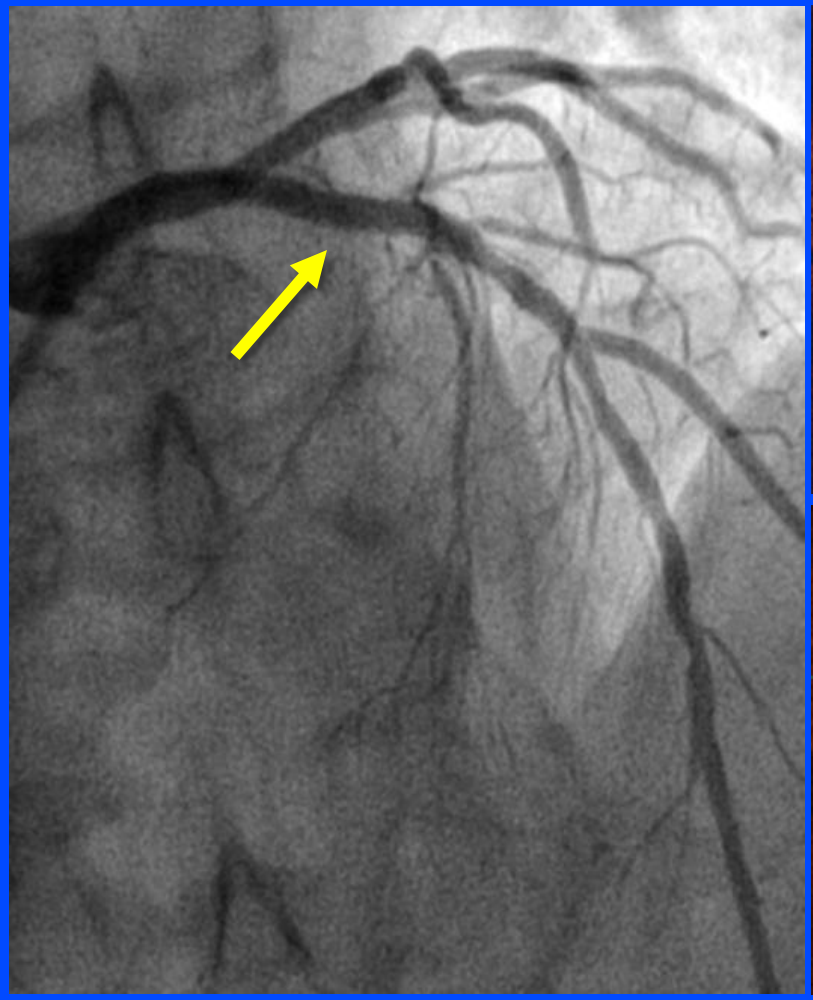


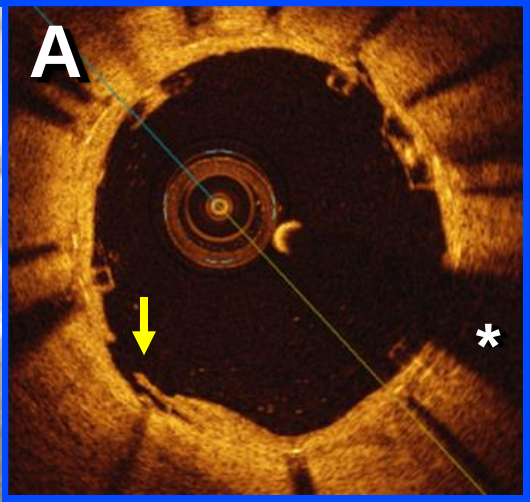


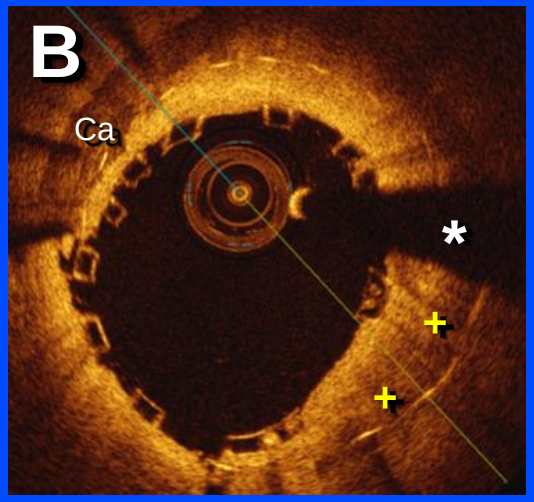
Hospital Universitario La Princesa (13/5/2014)

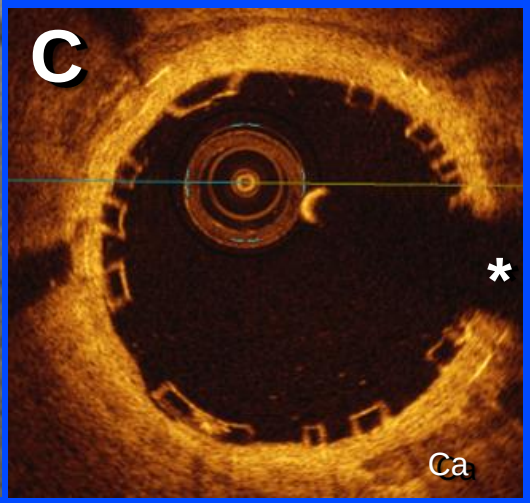
Detection & Treatment: Vulnerable In-Stent Neointima

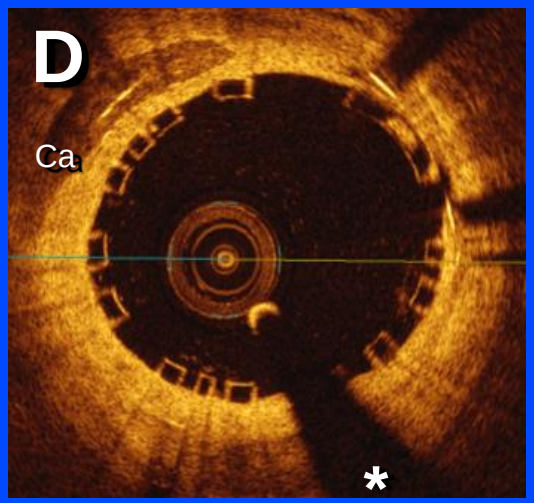
BVS











Hospital Universitario La Princesa (13/5/2014)

Detection and Treatment of Vulnerable In-Stent Neointima

- We can detect morphological features suggestive of «high-risk» potentially «vulnerable» neointima
- Further studies are required to establish adequate therapies to prevent complications in asymptomatic patients.
- The treatment of choice for patients with ISR as a result of neoatherosclerosis remains unsettled