Fate of Vulnerable Plaque and Neointimal Tissue Characterization Using VH-IVUS

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Contents

- ✓Fate of Vulnerable Plaque
- ✓VH neointimal tissue characteristics

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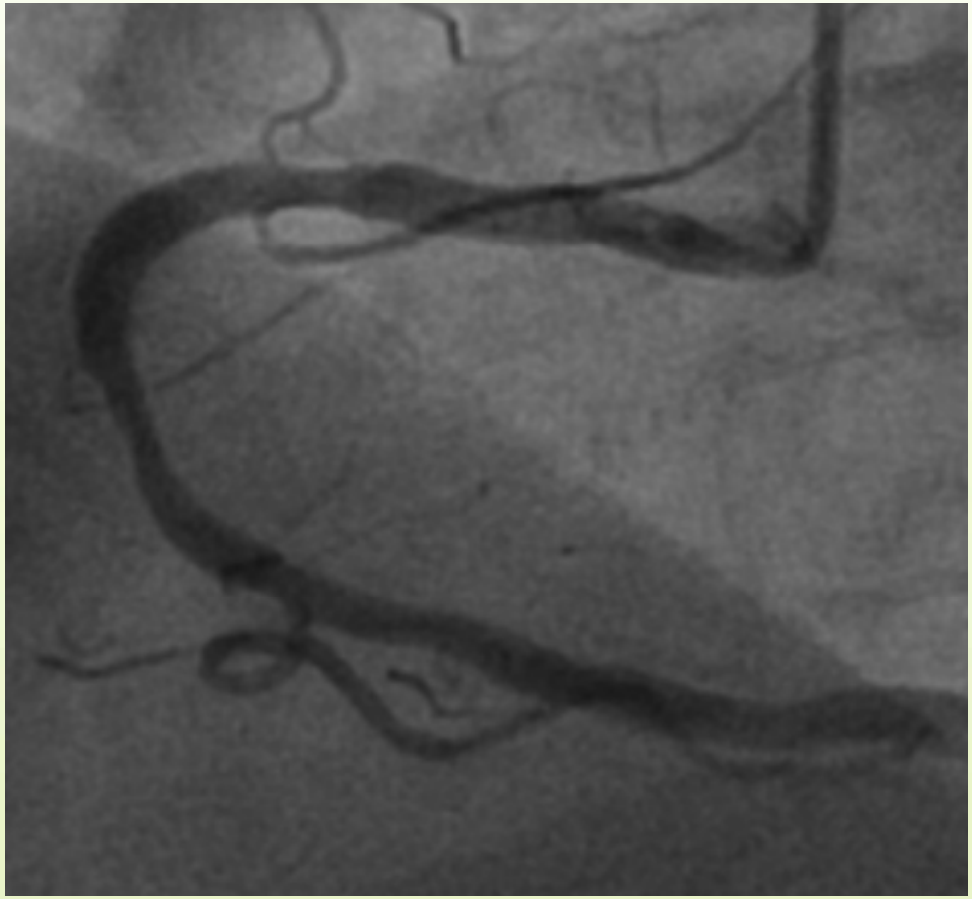
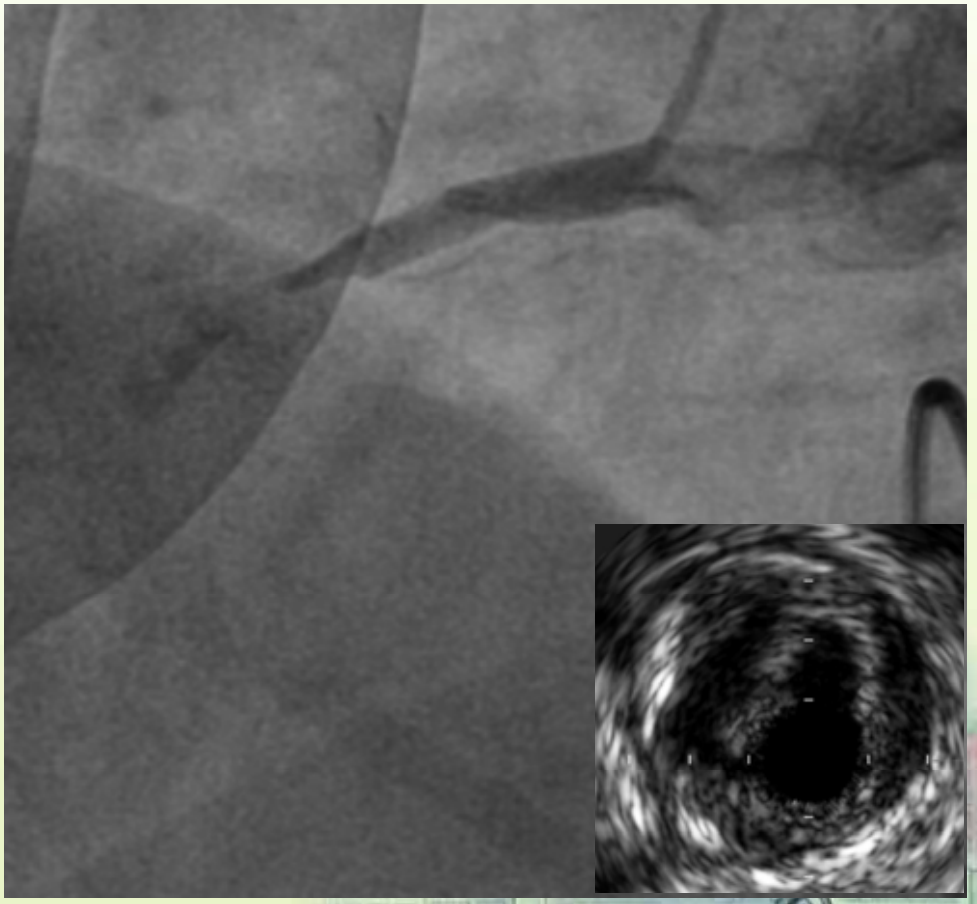
- ✓**Fate of Vulnerable Plaque**
- ✓**VH neointimal tissue characteristics**

62 years old gentleman

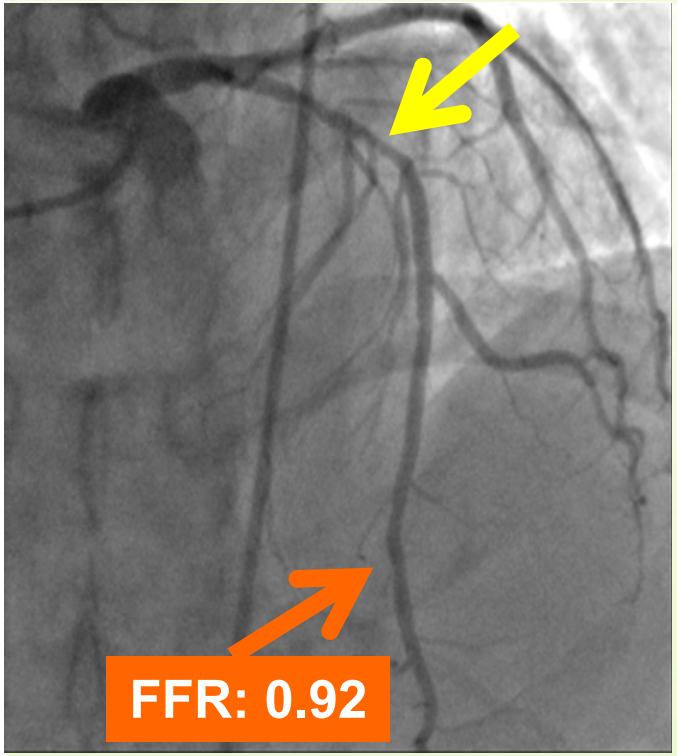
SAP **10 months later** STEMI

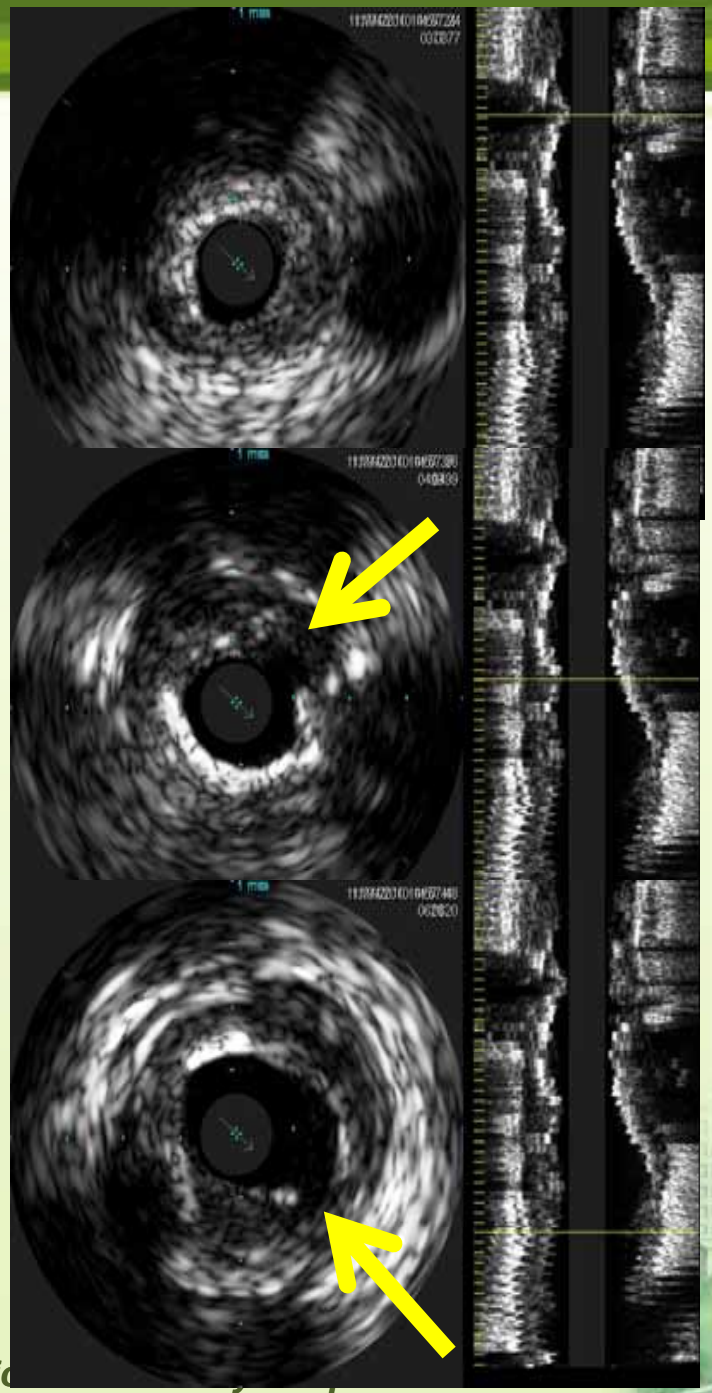




Courtesy of Dr. Bae JH

64Y/Male Unstable angina, DM, HT





MLA 2.04 mm²

1 year later

NSTEMI

Heavily calcified lesion with multiple plaque rupture

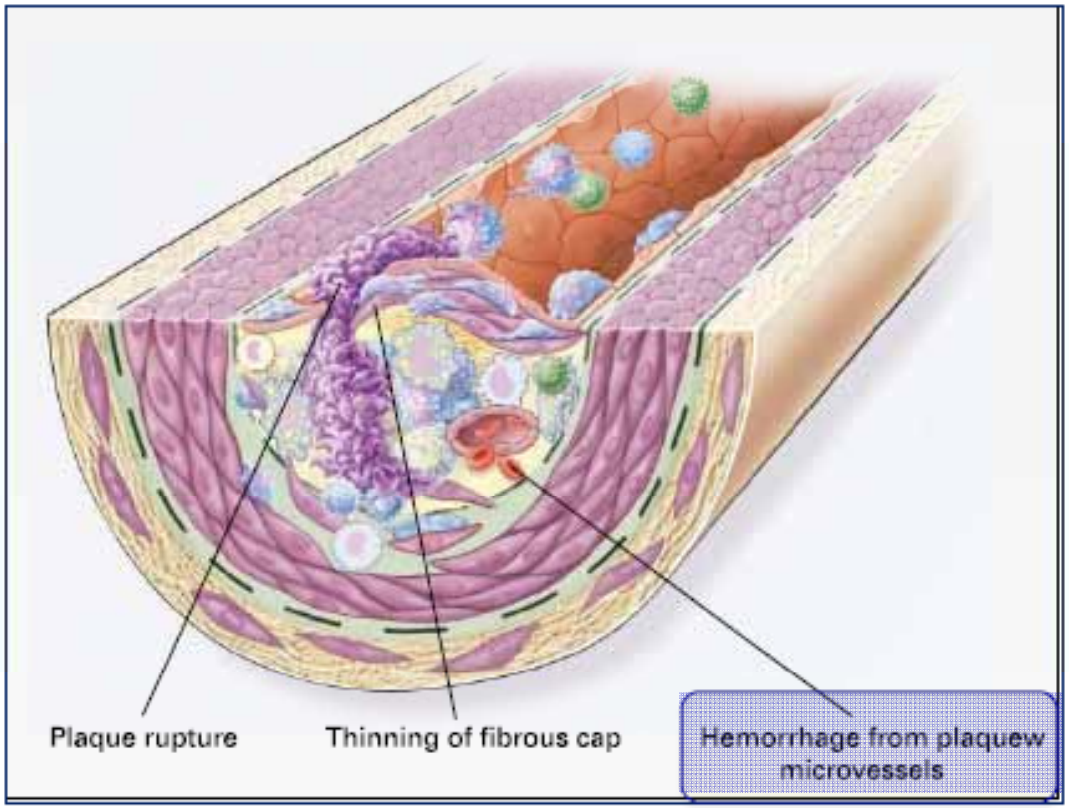
Courtesy of Dr. Kim SW

The Vulnerable Plaque

A vulnerable plaque is an atherosclerotic plaque in a coronary artery that is likely to rupture or fissure, leading to thrombosis, and then acute coronary syndrome or sudden cardiac death.

The Fate of Vulnerable Plaque – Additional Factors (I)

Intraplaque hemorrhage

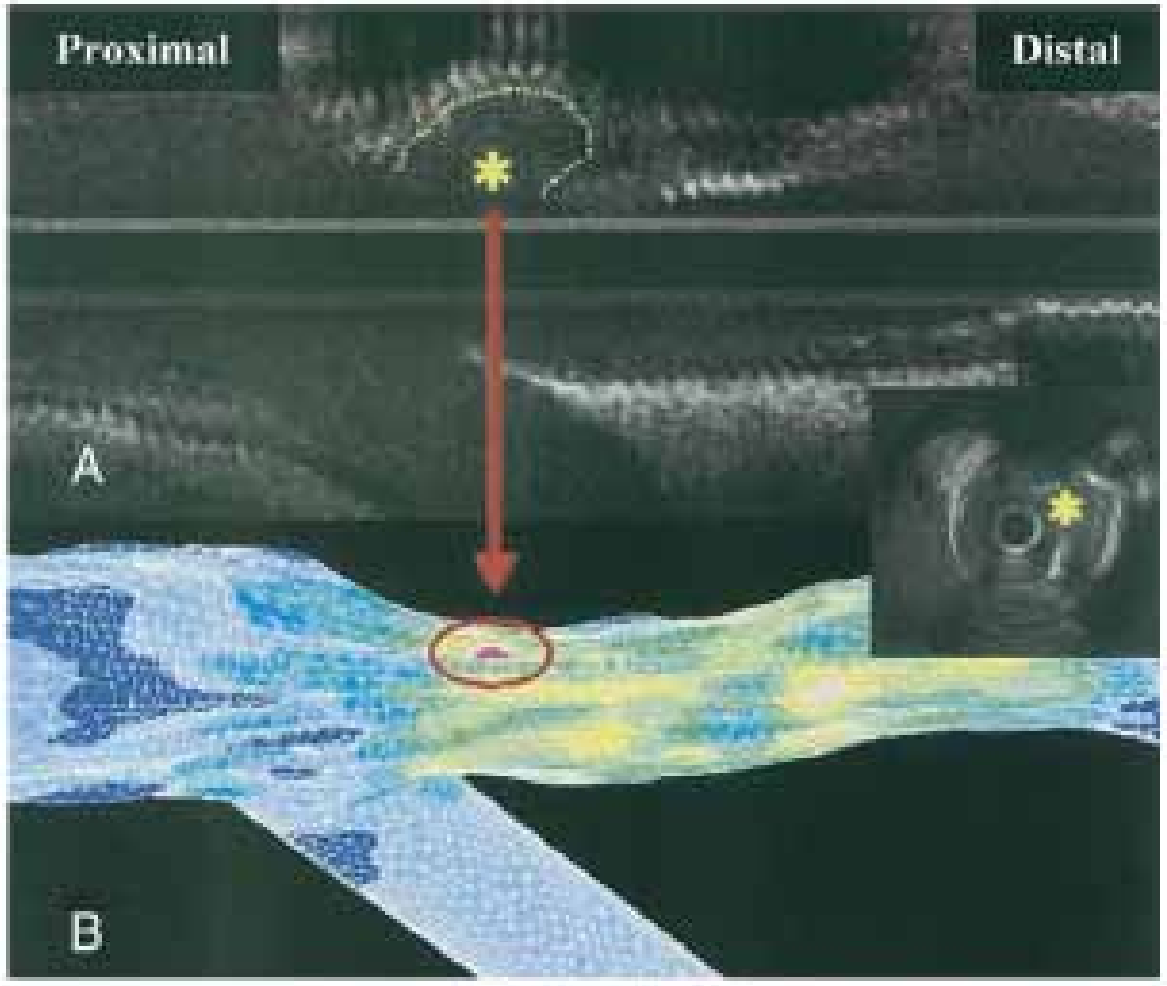


Metallo- proteinases and other proteolytic enzymes cause degradation of the matrix, which can lead to hemorrhage from the vasa vasorum or from the lumen of the artery and can result in thrombus formation and occlusion of the artery.

Ross, NEJM, 2005:340:115

The Fate of Vulnerable Plaque – Additional Factors (II)

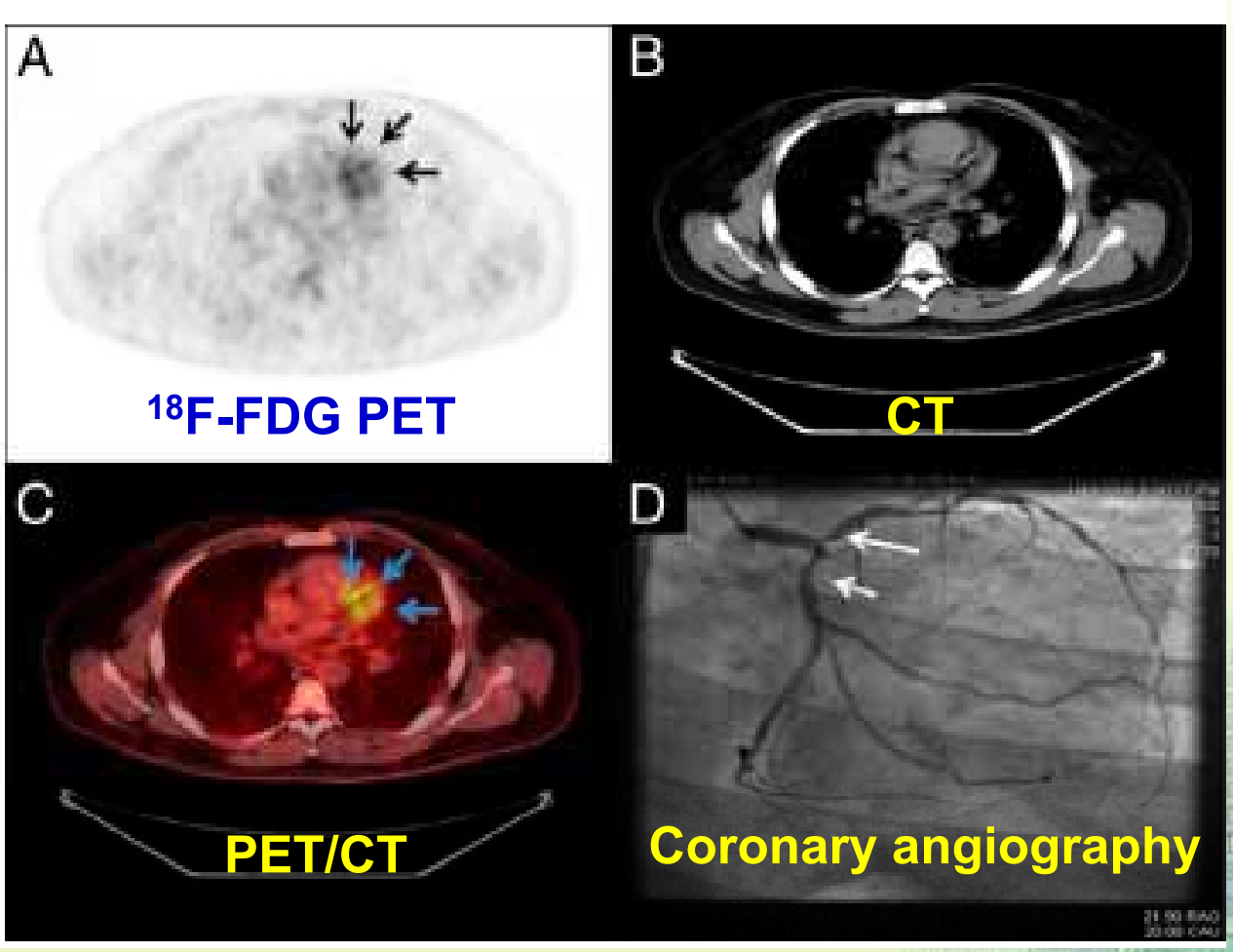
Shear Stress



Shear stress contributes to local endothelial dysfunction and eccentric plaque build up, and transform the lesion into a rupture-prone vulnerable plaque.

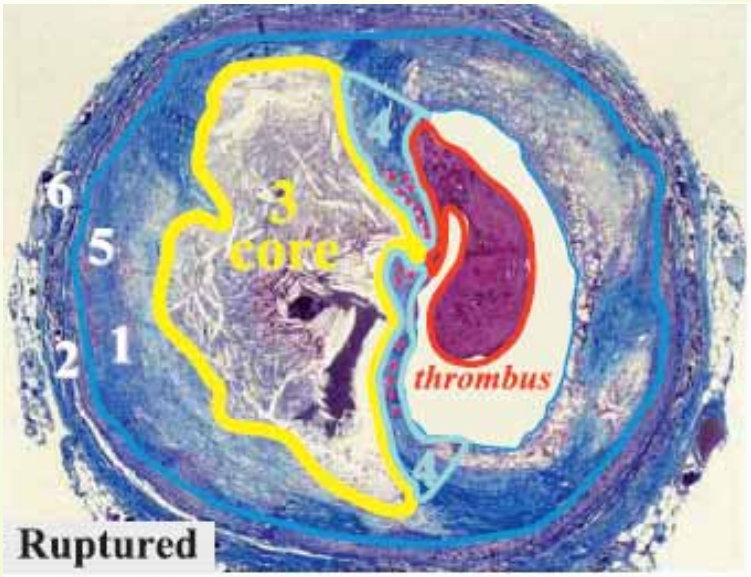
The Fate of Vulnerable Plaque – Additional Factors (III)

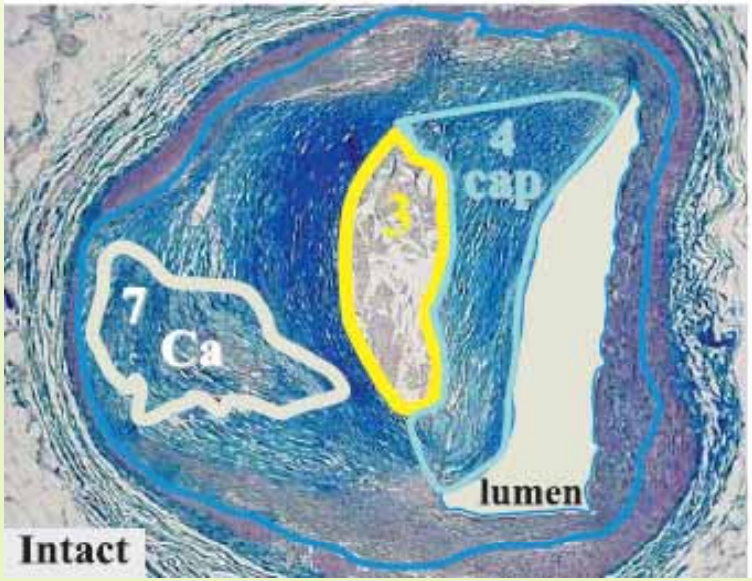
FDG Imaging of Coronary Inflammation



Vancraeynest, JACC 2011;57:1961

Coronary plaque rupture and rupture-prone vulnerable plaques



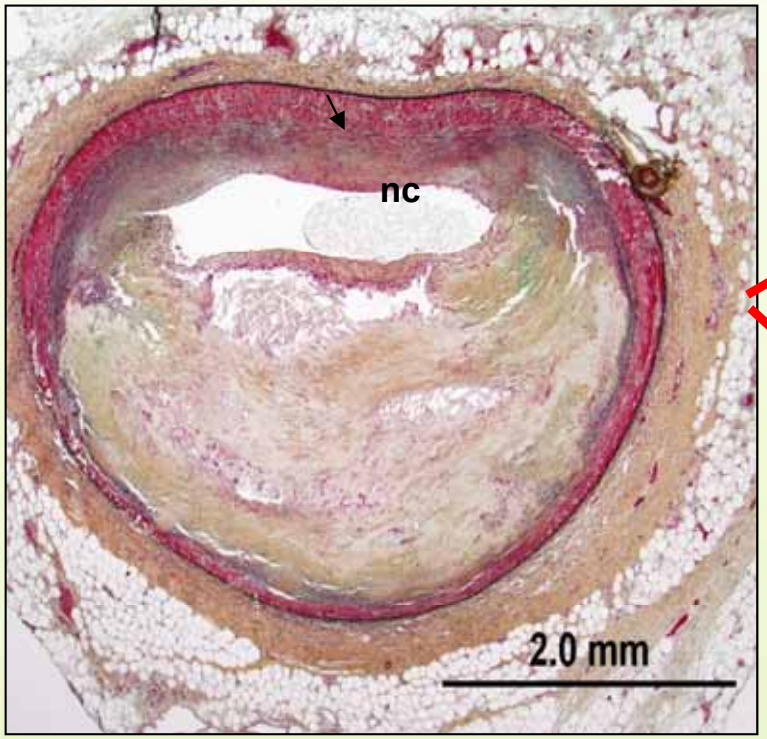


Coronary Plaque Rupture

1. Plaque size↑
2. Expansive remodelling
3. Necrotic core↑
   - ~34% of plaque area
   - ~3.8 mm², ~9 mm long
4. Fibrous cap
   - thickness↓, ~23 µm (95% <65 µm)
   - macrophages (●)↑, ~26% of cap
   - smooth muscle cells↓ (apoptosis)
   - thrombus
5. Angiogenesis↑
   - intraplaque haemorrhage
6. Perivascular inflammation
7. Calcification↓ - *spotty*

Thrombosis and Haemostasis 106.1/2011

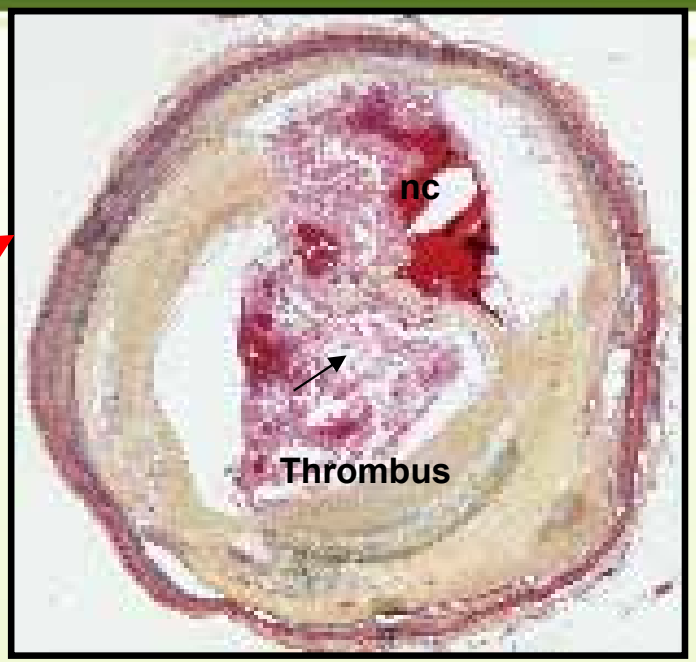
Do thin cap fibroatheromas (vulnerable plaques) go on and Rupture?



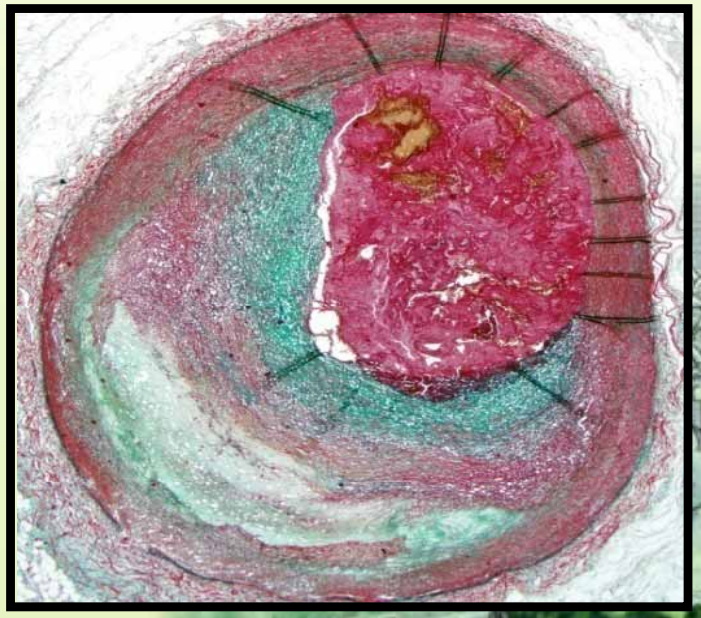
Thin cap fibroatheroma

Plaque Rupture

?

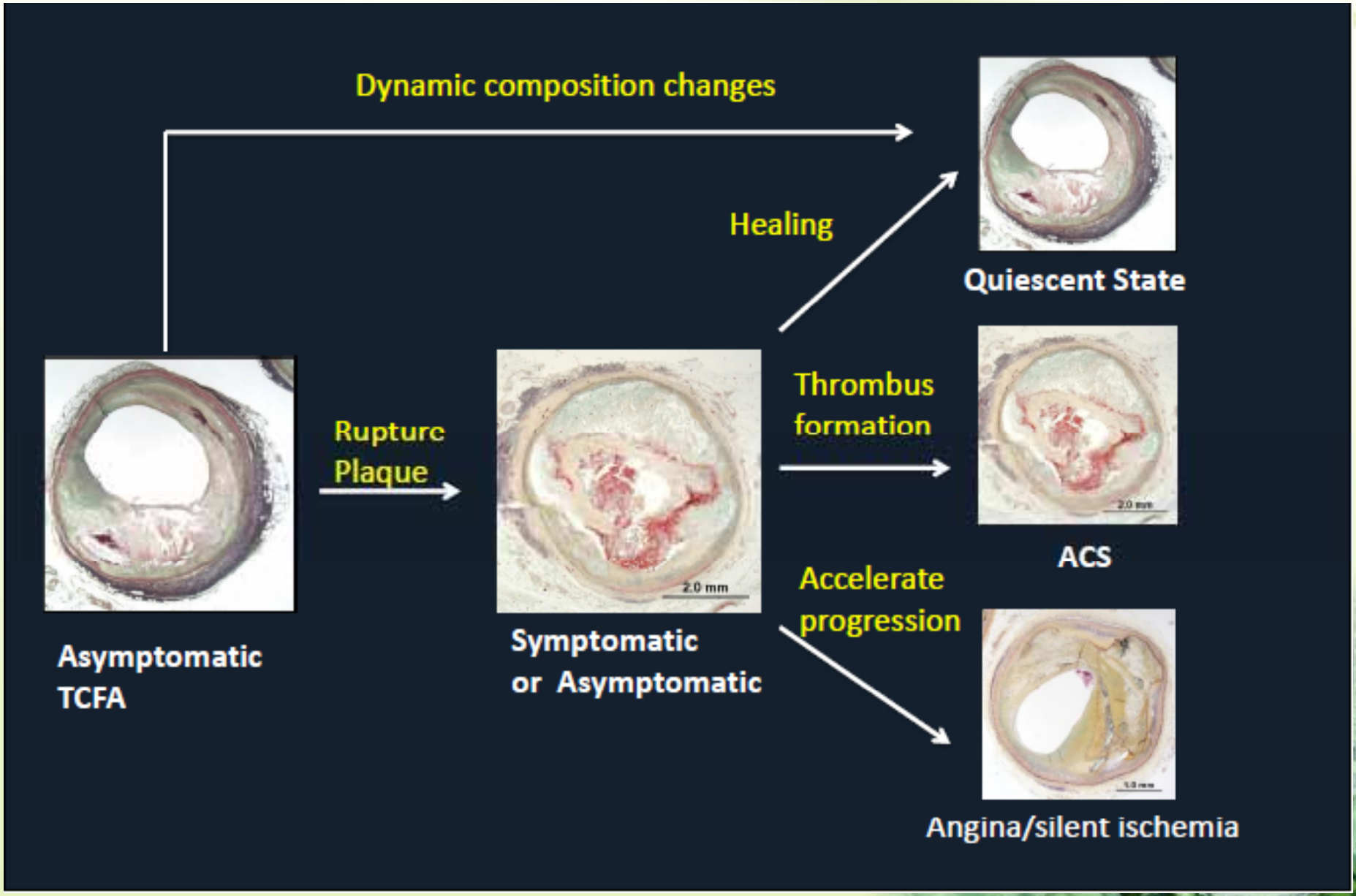


Plaque Erosion

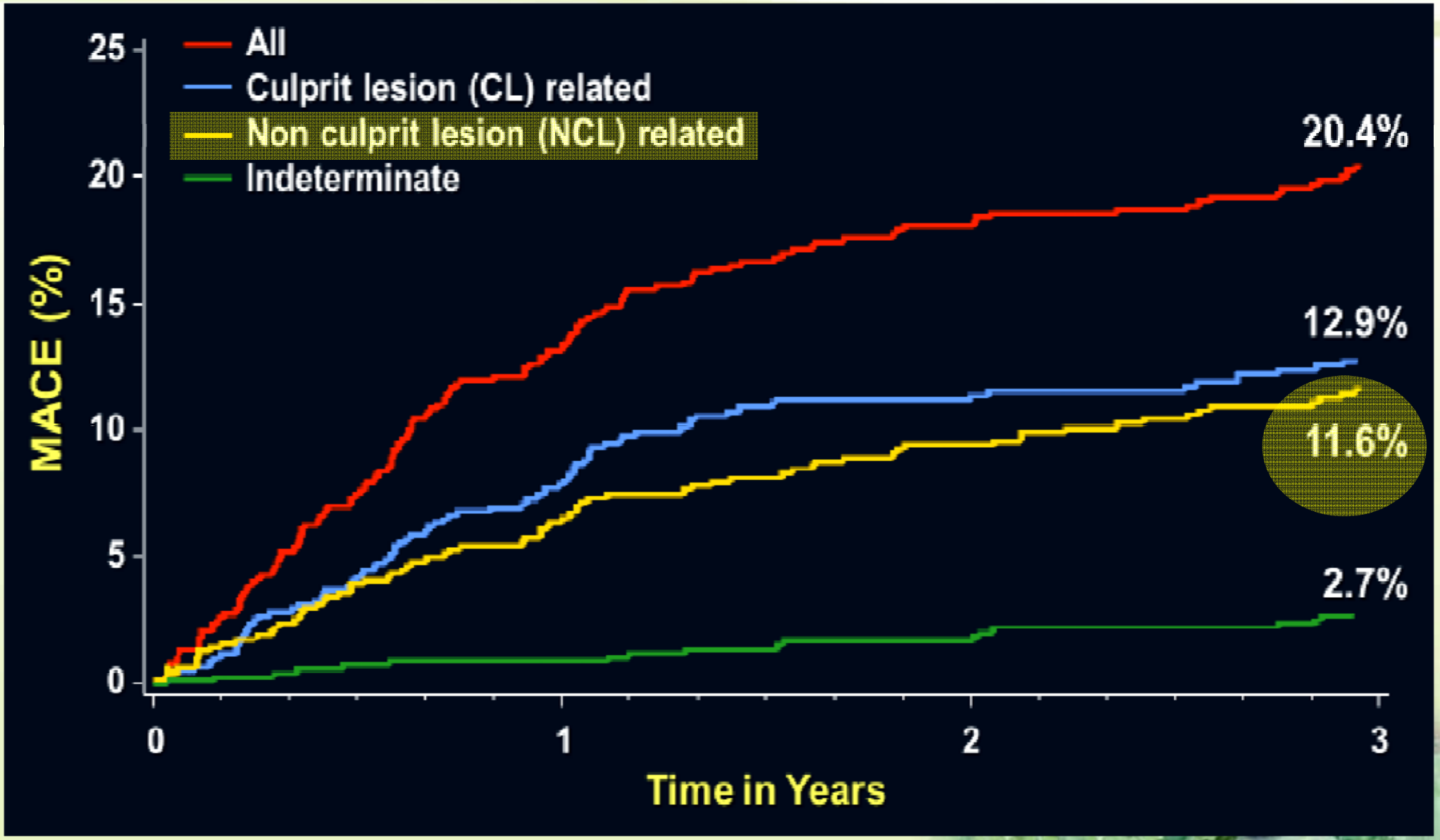


The Fate of Vulnerable Plaque

Plaque changes is dynamic process.



PROSPECT: MACE (n=697)



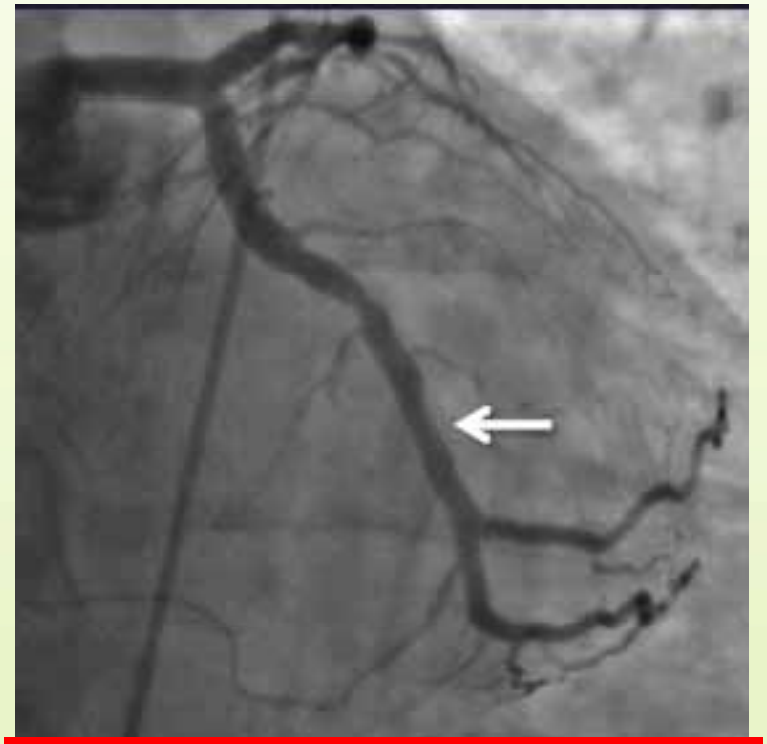
Stone GW et al. NEJM 2011;364:226-35

PROSPECT 52Y Male

2/13/06: NSTEMI, PCI of MLAD

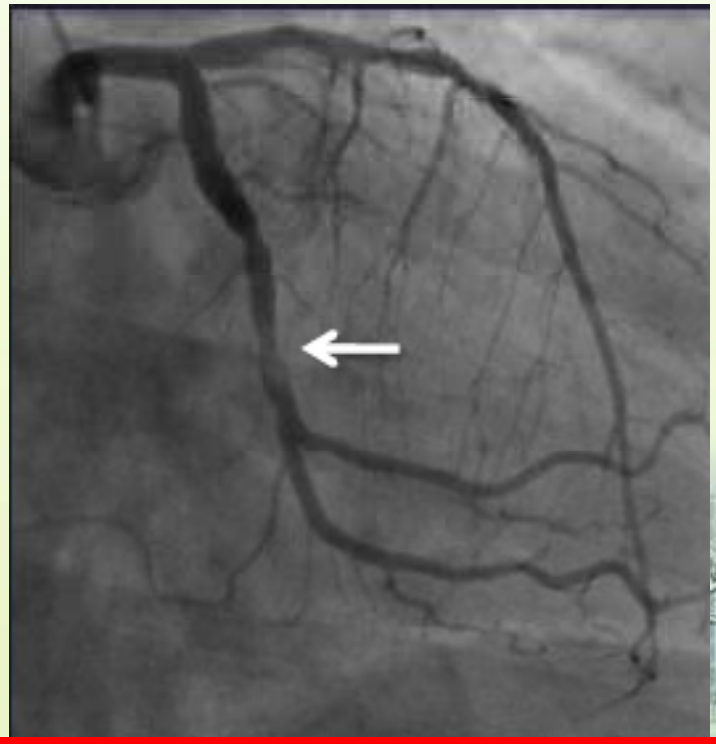
2/6/07 (51 weeks later): NSTEMI attributed to LCX

Index 2/13/06



QCA PLCX DS 28.6%

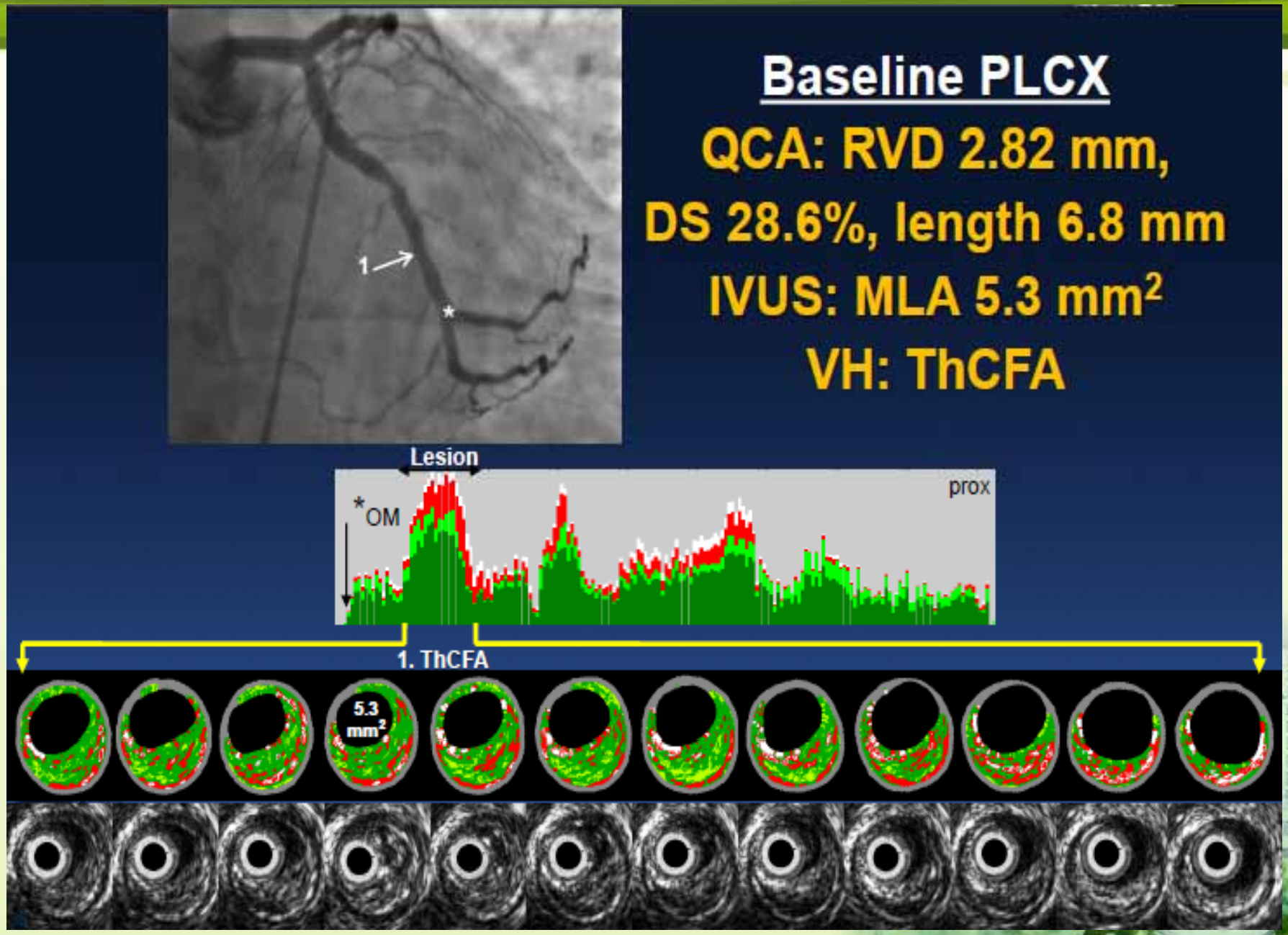
Event 2/06/07



QCA PLCX DS 71.3%

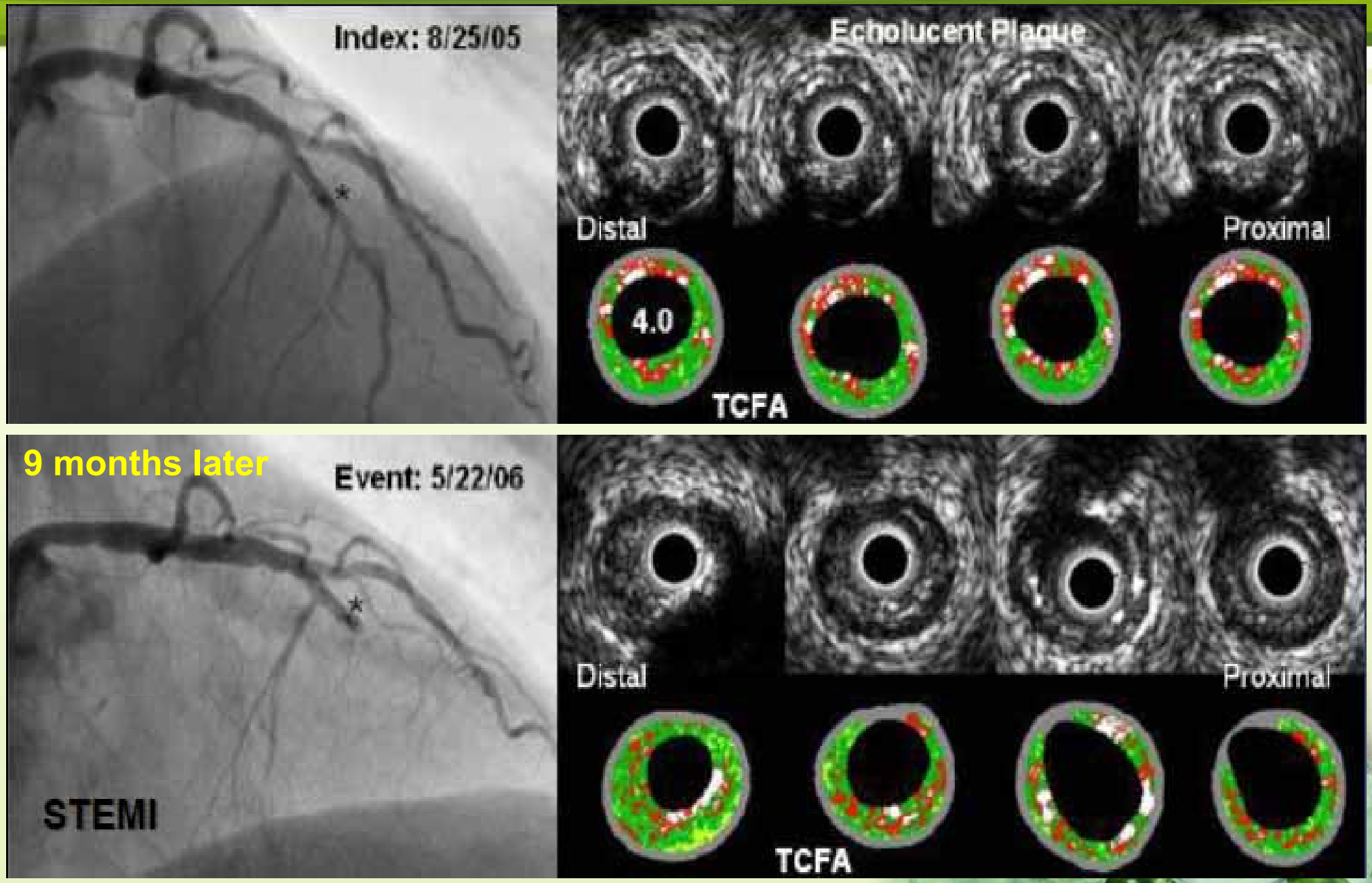
Gregg W. Stone, TCT 2011

PROSPECT 52Y Male



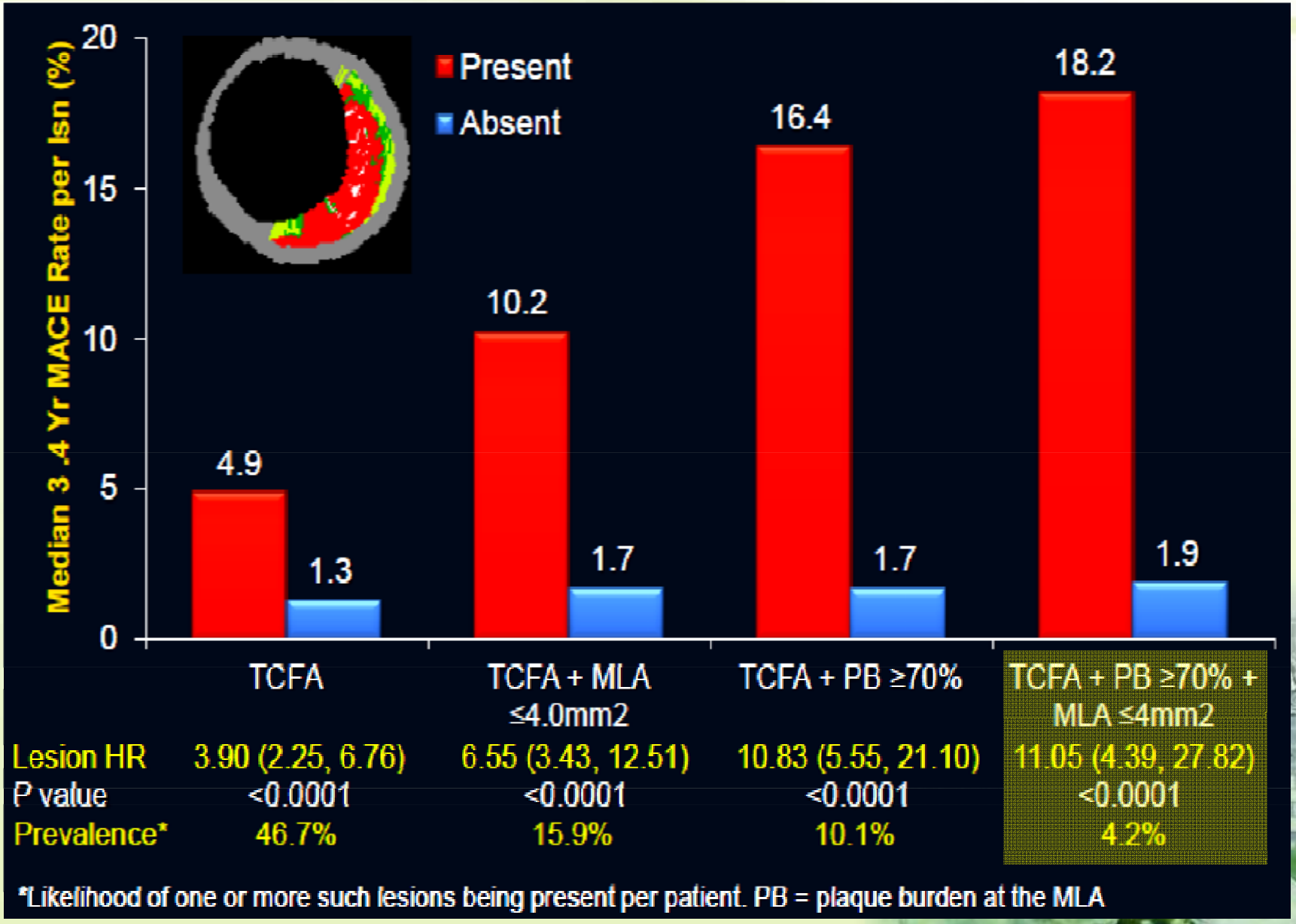
Gregg W. Stone, TCT 2011

MLA 4.0 mm^2; plaque burden 62%; TCFA



Gregg W. Stone, TCT 2011

PROSPECT: VH-TCFA and Non-culprit lesion related events



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

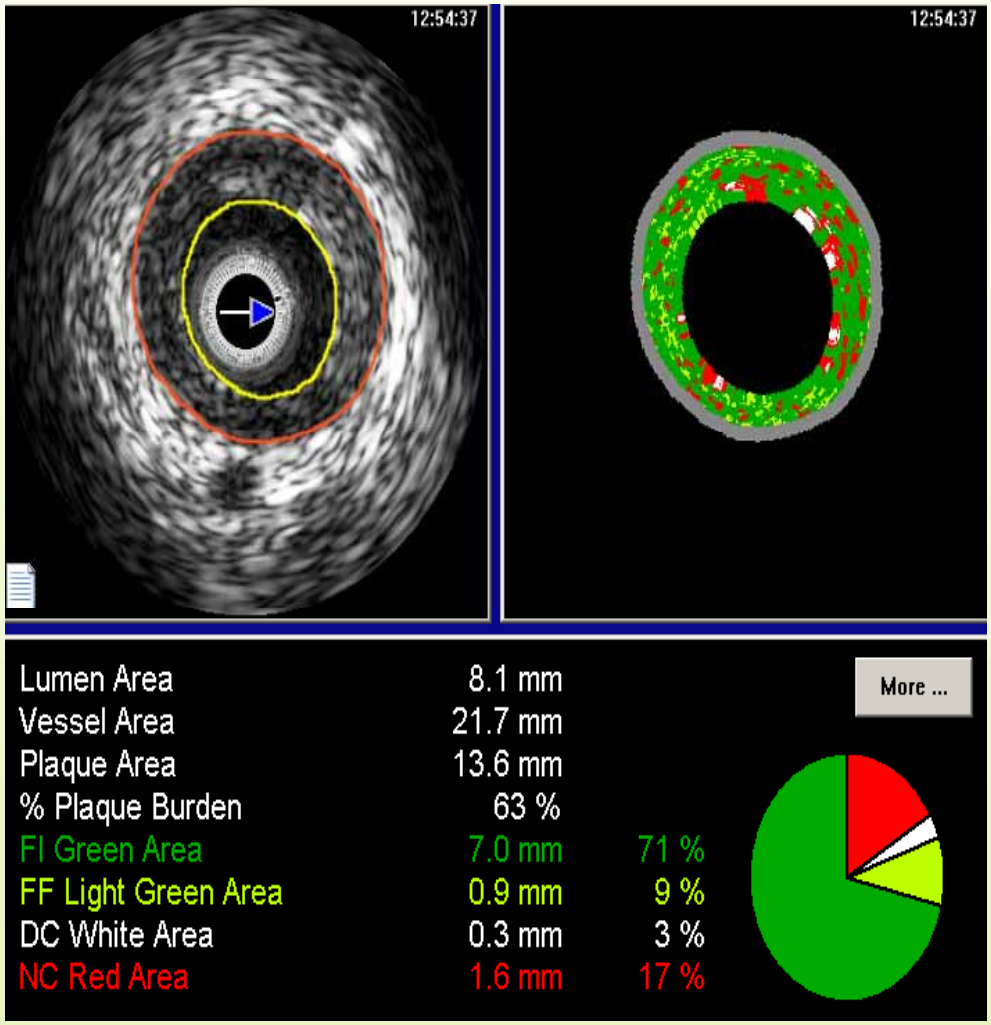
Impact of Baseline Plaque Components on Plaque Progression in Nonintervened Coronary Segments in Patients With Angina Pectoris on *Rosuvastatin* 10 mg/day

Young Joon Hong, MD, Myung Ho Jeong, MD*, Yun Ha Choi, RN, Eun Hye Ma, RN, Jum Suk Ko, MD, Min Goo Lee, MD, Keun Ho Park, MD, Doo Sun Sim, MD, Nam Sik Yoon, MD, Hyun Ju Youn, MD, Kye Hun Kim, MD, Hyung Wook Park, MD, Ju Han Kim, MD, Youngkeun Ahn, MD, Jeong Gwan Cho, MD, Jong Chun Park, MD, and Jung Chaee Kang, MD

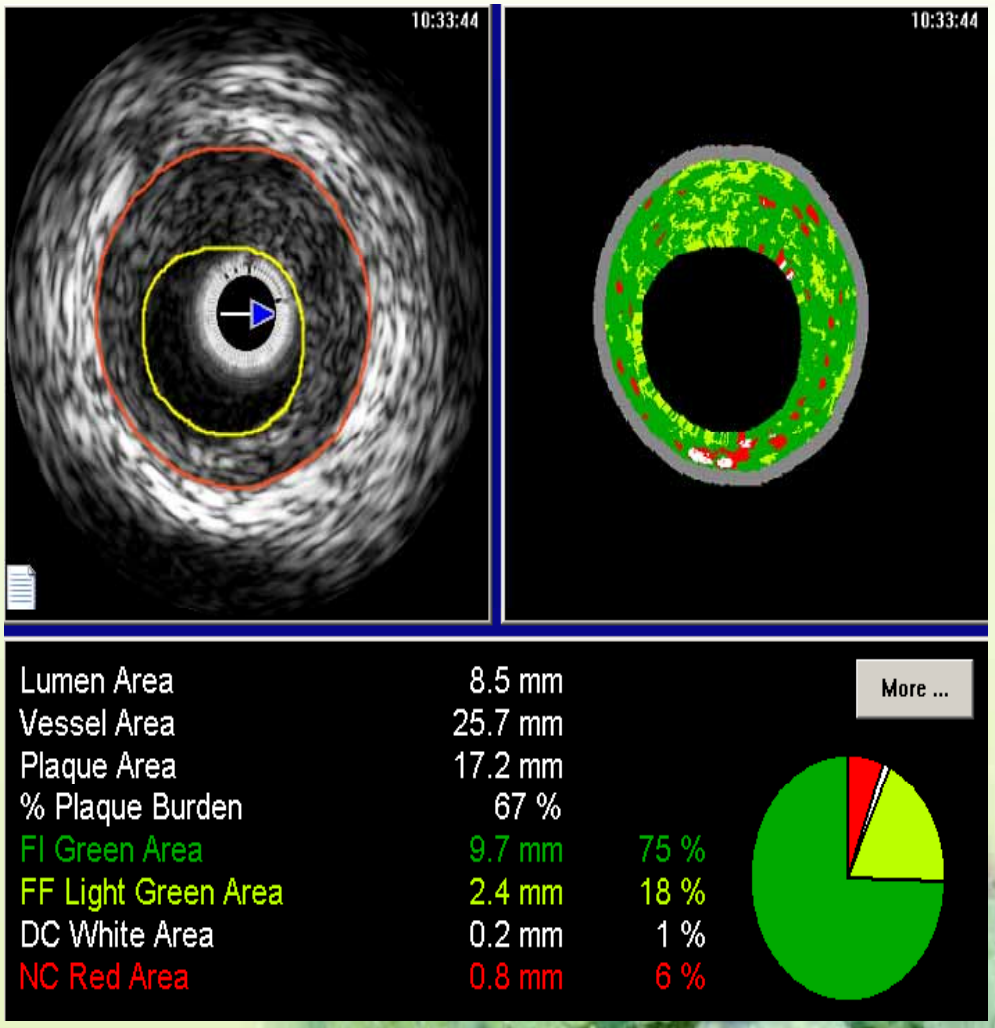
It is not well known which lesions are progressed or regressed in patients with angina pectoris who use statins. We assessed the impact of plaque components on plaque progression in patients with angina pectoris who used rosuvastatin 10 mg/day using virtual histology plus intravascular ultrasound. Sixty-six patients who underwent baseline and 9-month follow-up virtual histology plus intravascular ultrasound for nonintervened intermediate coronary stenosis were grouped according to plaque progression (increase of plaque plus media area, n = 22) or plaque regression (decrease of plaque plus media area, n = 44) at baseline minimum lumen area (MLA) site at follow-up and compared the various parameters including baseline plaque components between the 2 groups. Follow-up low-density lipoprotein cholesterol was not significantly different between the progression and regression groups (85 ± 30 vs 82 ± 24 mg/dl, p = 0.6). Baseline percent necrotic core (NC) area was significantly larger (26.1 ± 10.9% vs 17.6 ± 10.8%, p = 0.004) and baseline percent fibrofatty area was significantly smaller (8.1 ± 6.2% vs 14.2 ± 12.1%, p = 0.008) at the MLA site in the progression group compared to the regression group. Thin-cap fibroatheroma was observed more frequently in the progression group compared to the regression group (32% vs 9%, p = 0.020). Change of plaque plus media area from baseline to follow-up at the MLA site correlated with baseline percent NC area (r = 0.375, p = 0.002), baseline percent fibrofatty area (r = −0.388, p = 0.001), and baseline percent fibrotic area (r = −0.242, p = 0.050). Baseline percent NC area at the MLA site was an independent predictor of plaque progression at follow-up (odds ratio 1.265, 95% confidence interval 1.069 to 1.497, p = 0.006). In conclusion, NC is associated with plaque progression in patients when low-density lipoprotein cholesterol level is around 80 mg/dl at 9-month follow-up in patients with angina pectoris on rosuvastatin 10 mg/day. (Am J Cardiol 2010;106:1241–1247)

Plaque Progression at 9-Month Follow-Up

Baseline

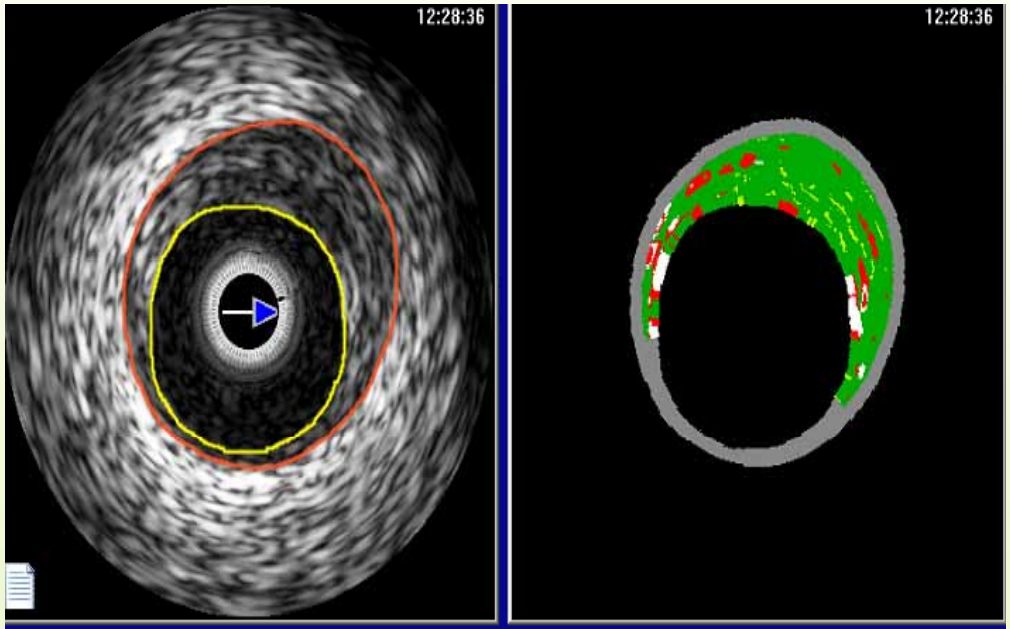


Follow-up



Plaque Regression at 9-Month Follow-Up

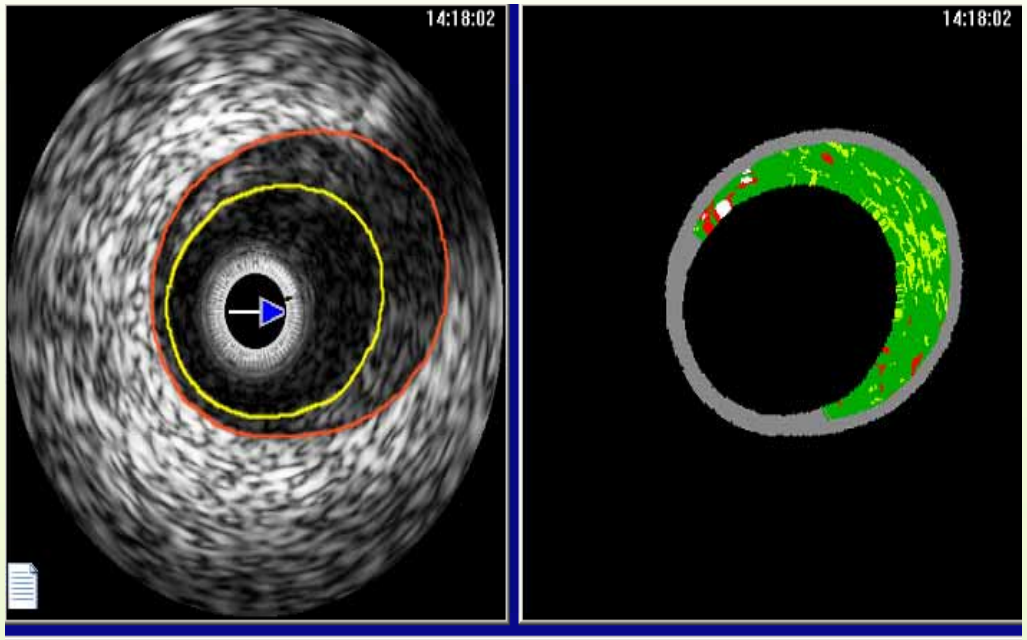
Baseline



Lumen Area	13.1 mm	
Vessel Area	25.3 mm	
Plaque Area	12.2 mm	
% Plaque Burden	48 %	
FI Green Area	6.1 mm	80 %
FF Light Green Area	0.3 mm	3 %
DC White Area	0.5 mm	6 %
NC Red Area	0.8 mm	10 %

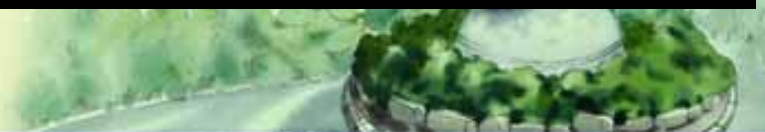
More ...

Follow-up



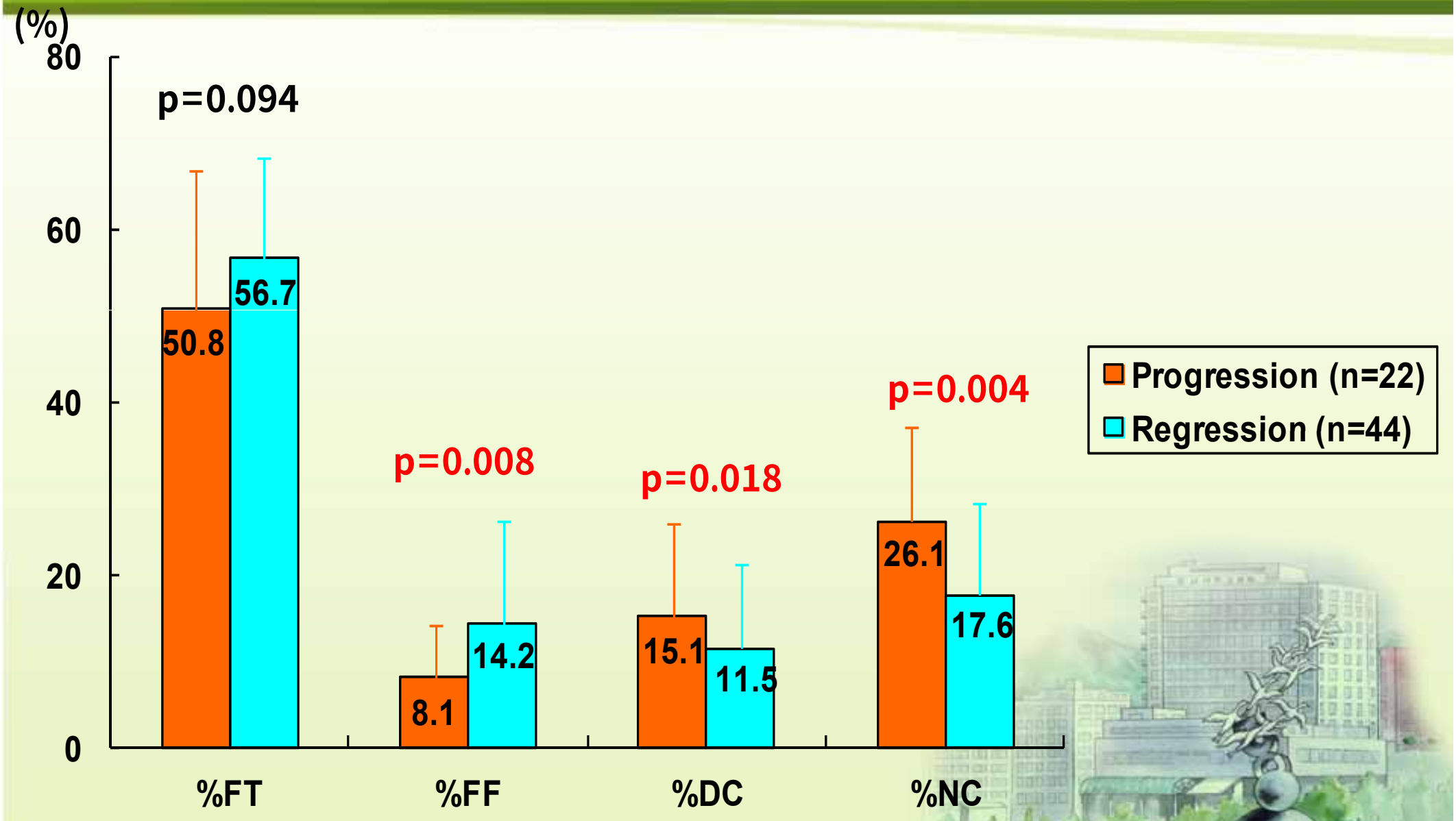
Lumen Area	13.1 mm	
Vessel Area	24.5 mm	
Plaque Area	11.4 mm	
% Plaque Burden	46 %	
FI Green Area	5.5 mm	81 %
FF Light Green Area	0.9 mm	14 %
DC White Area	0.1 mm	1 %
NC Red Area	0.3 mm	4 %

More ...



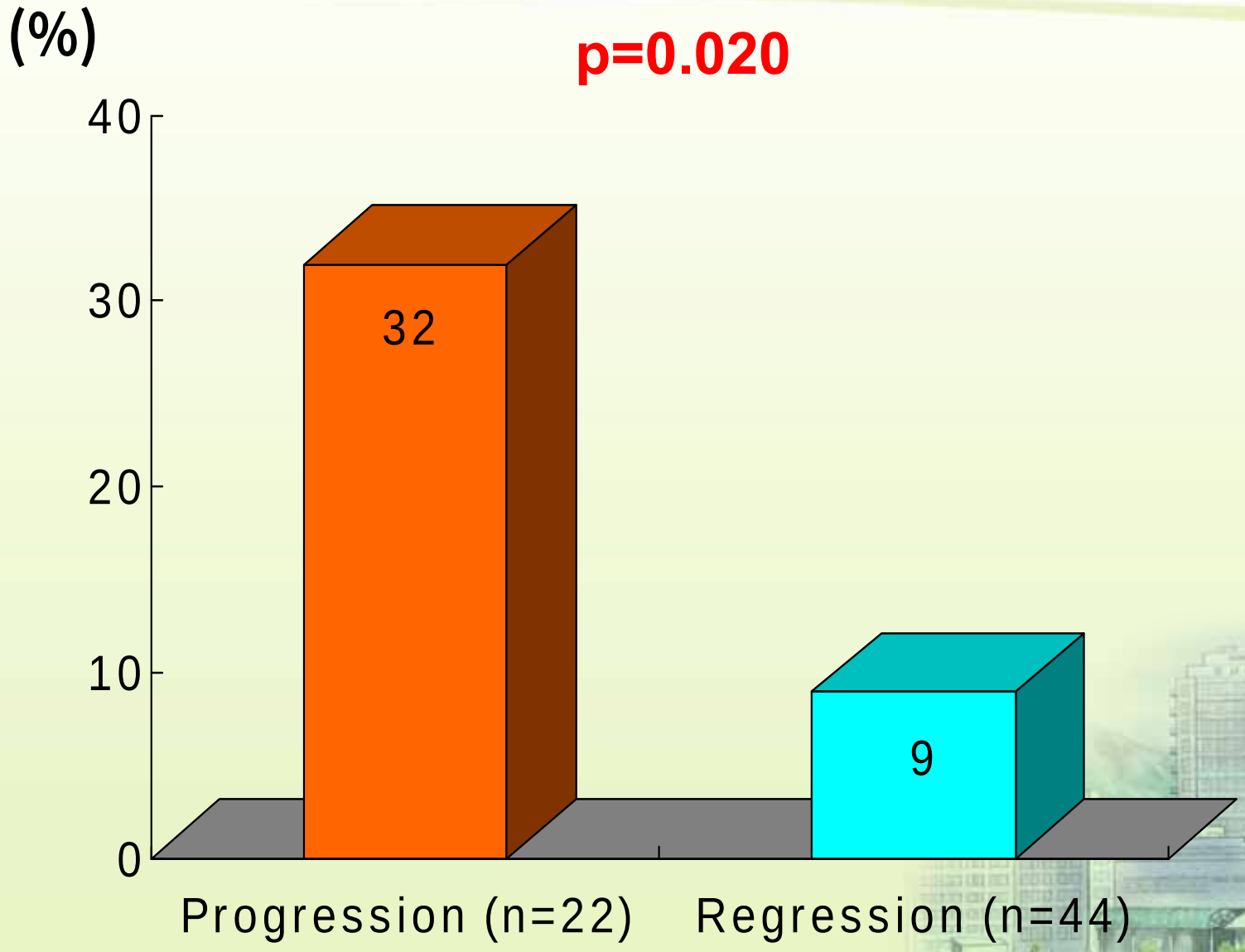
The Heart Center of Chonnam National University Hospital

Baseline Minimum lumen site Relative plaque area

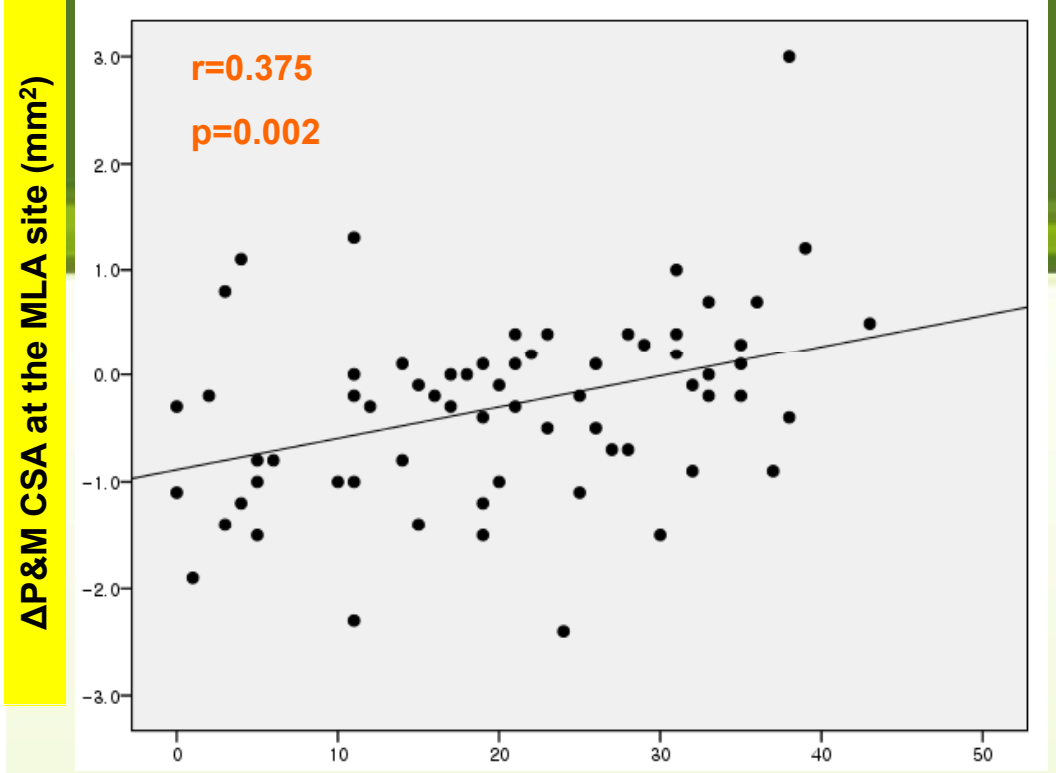


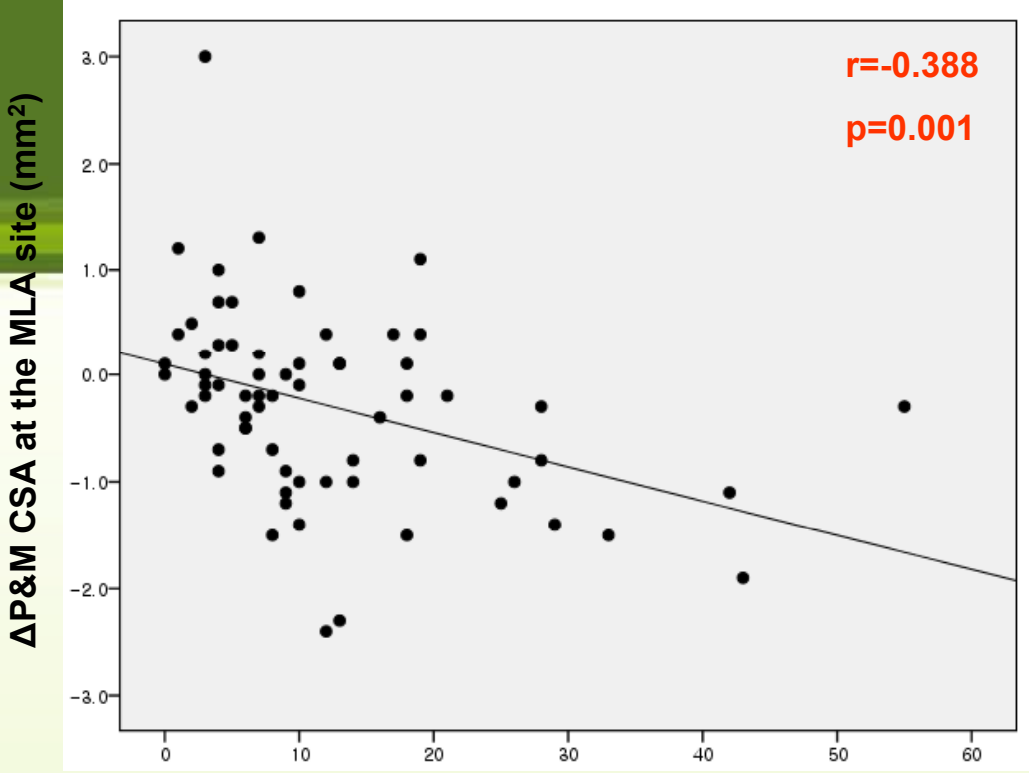
Hong YJ et al., Am J Cardiol 2010:106;1241-1247.

Thin-Cap Fibroatheroma



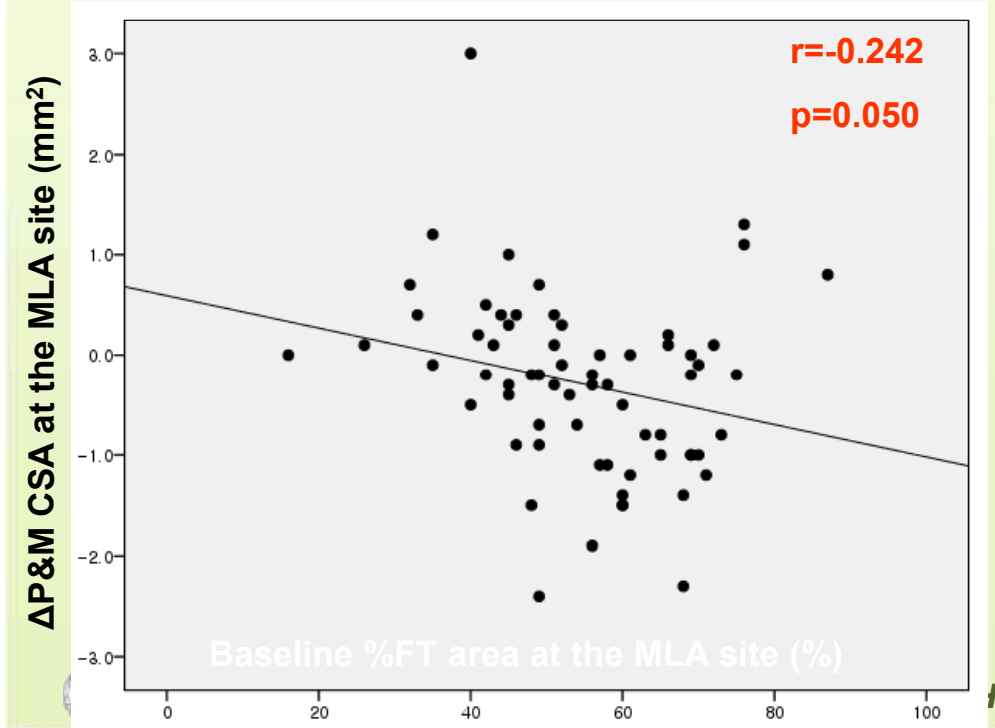
Hong YJ et al., Am J Cardiol 2010:106;1241-1247.





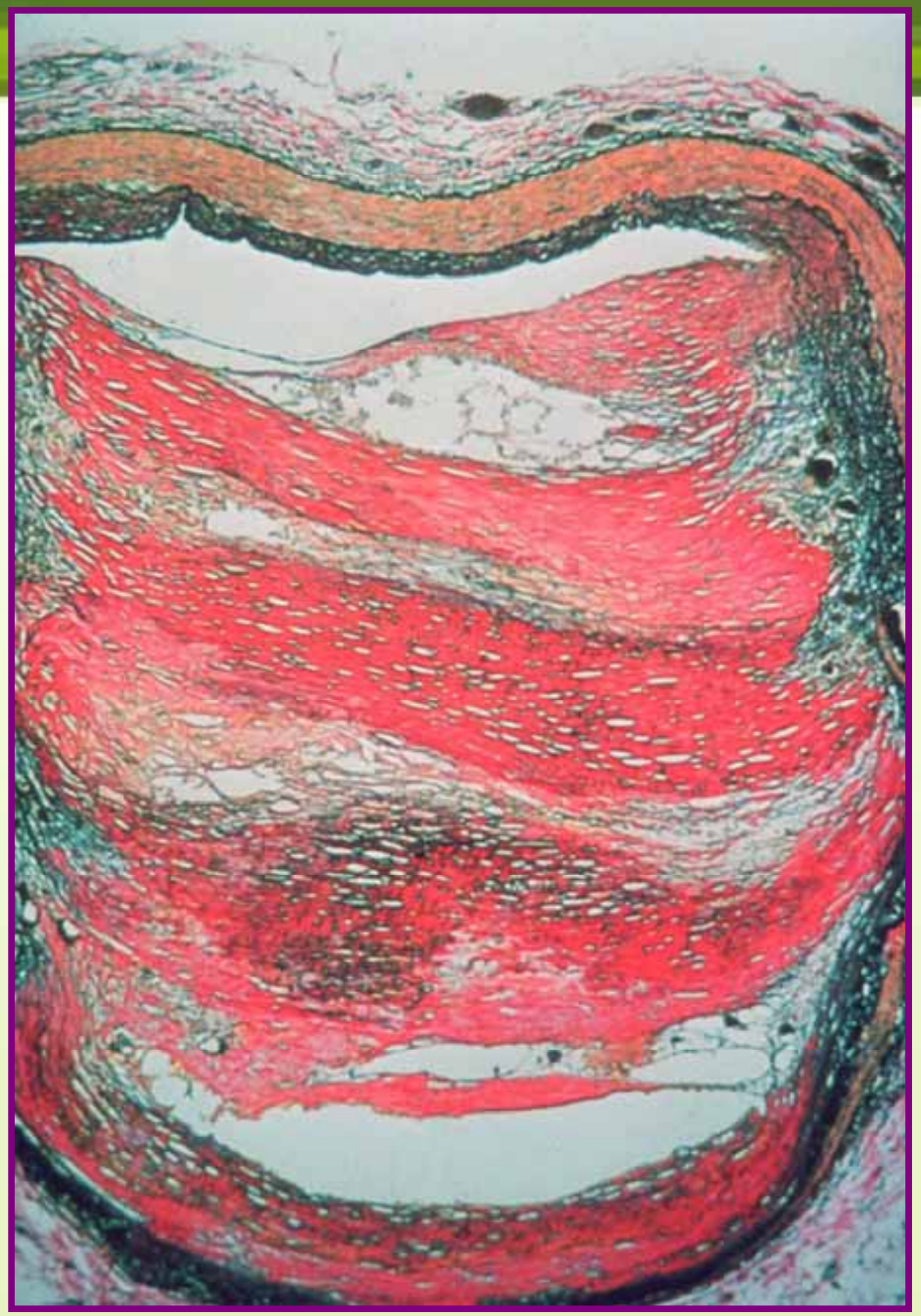
Baseline %NC area at the MLA site (%)

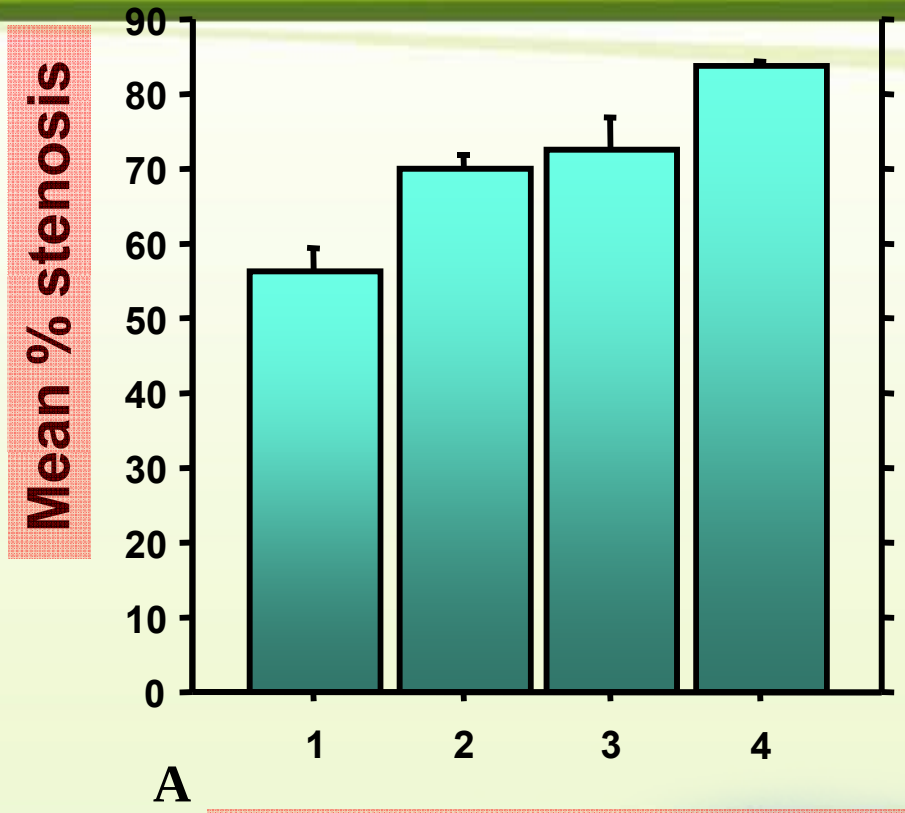
Baseline %FF area at the MLA site (%)



Hong YJ et al., Am J Cardiol 2010;106:1241-1247

Silent Ruptures and Erosions lead to Plaque Progression



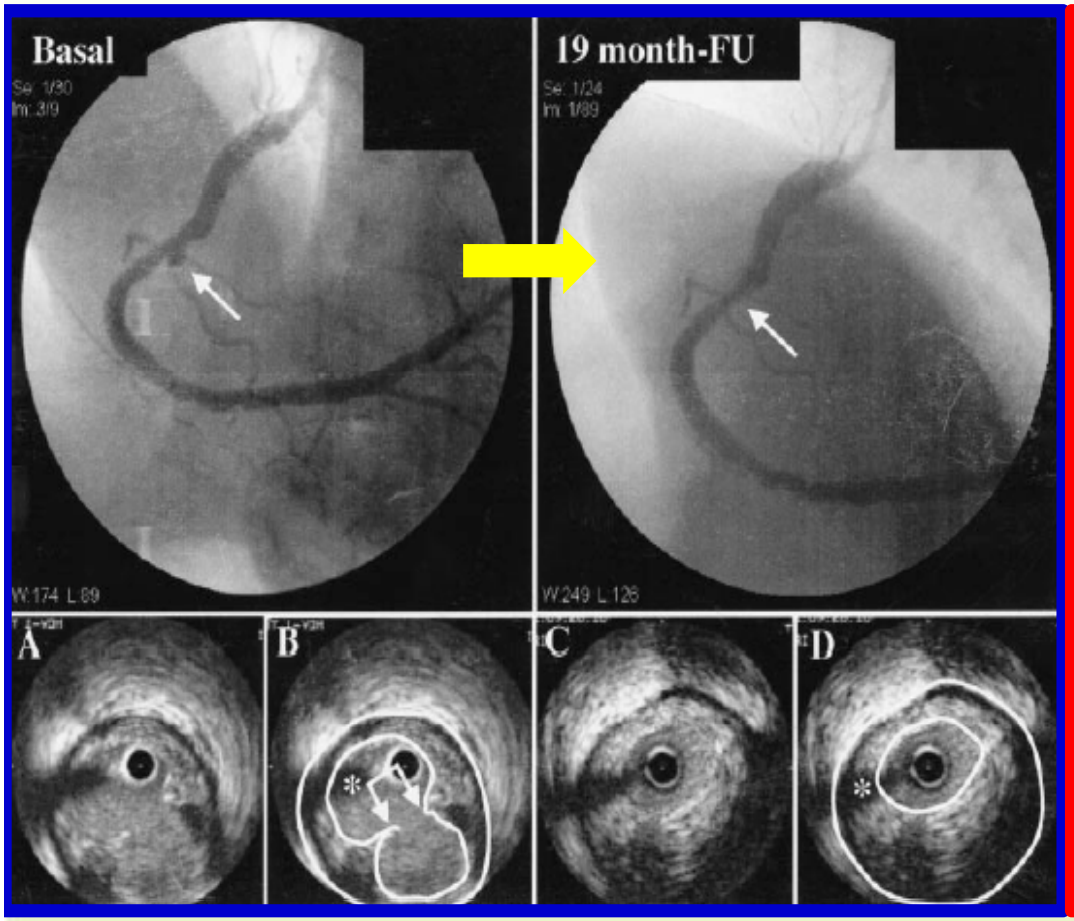


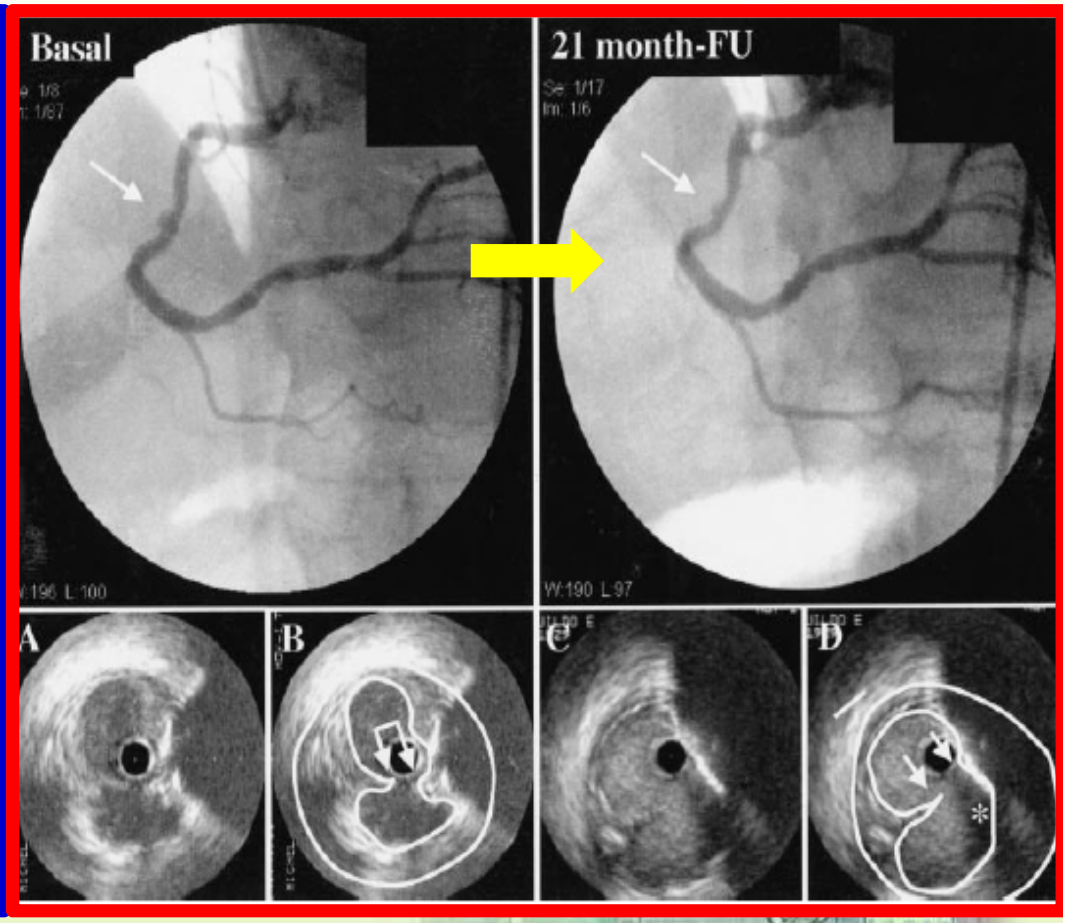
Number of prior ruptures, healed rupture sites

11% of plaque rupture are virgin

Evolution of Spontaneous Atherosclerotic Plaque Rupture With Medical Therapy in ACS

In 14 Pts with 28 plaque ruptures, 22 months FU



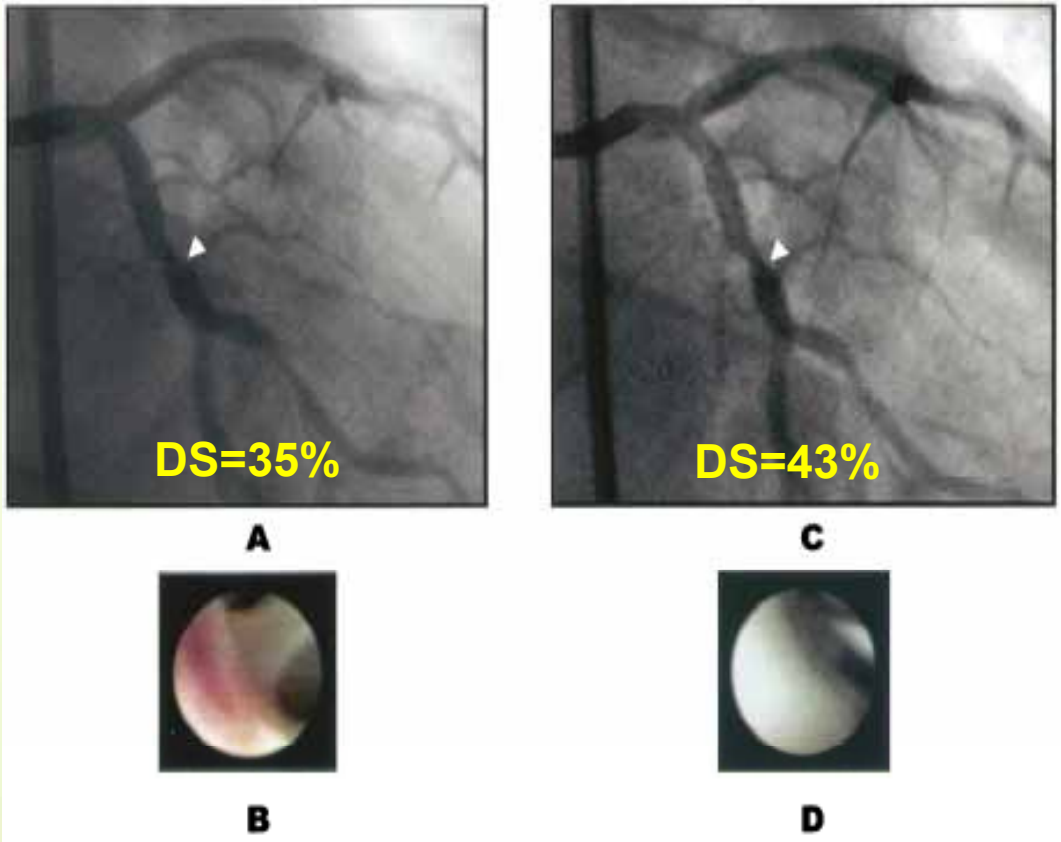


50% healed without significant plaque modification.

Rioufol G. et al. *Circulation* 2004;110:2875-80

Healing of nonculprit plaques in ACS (30 pts) in Non-culprit Lesions; 13±9 Mo FU

- Overall healing; 30%
- Remaining of thrombi in 35 (70%)
- Thrombus color change from red (56%) at baseline to pinkish-white (83%) at follow-up
- %DS at the healed plaque (12.3% to 22.7%, p<0.05)
- 1 pt need PCI



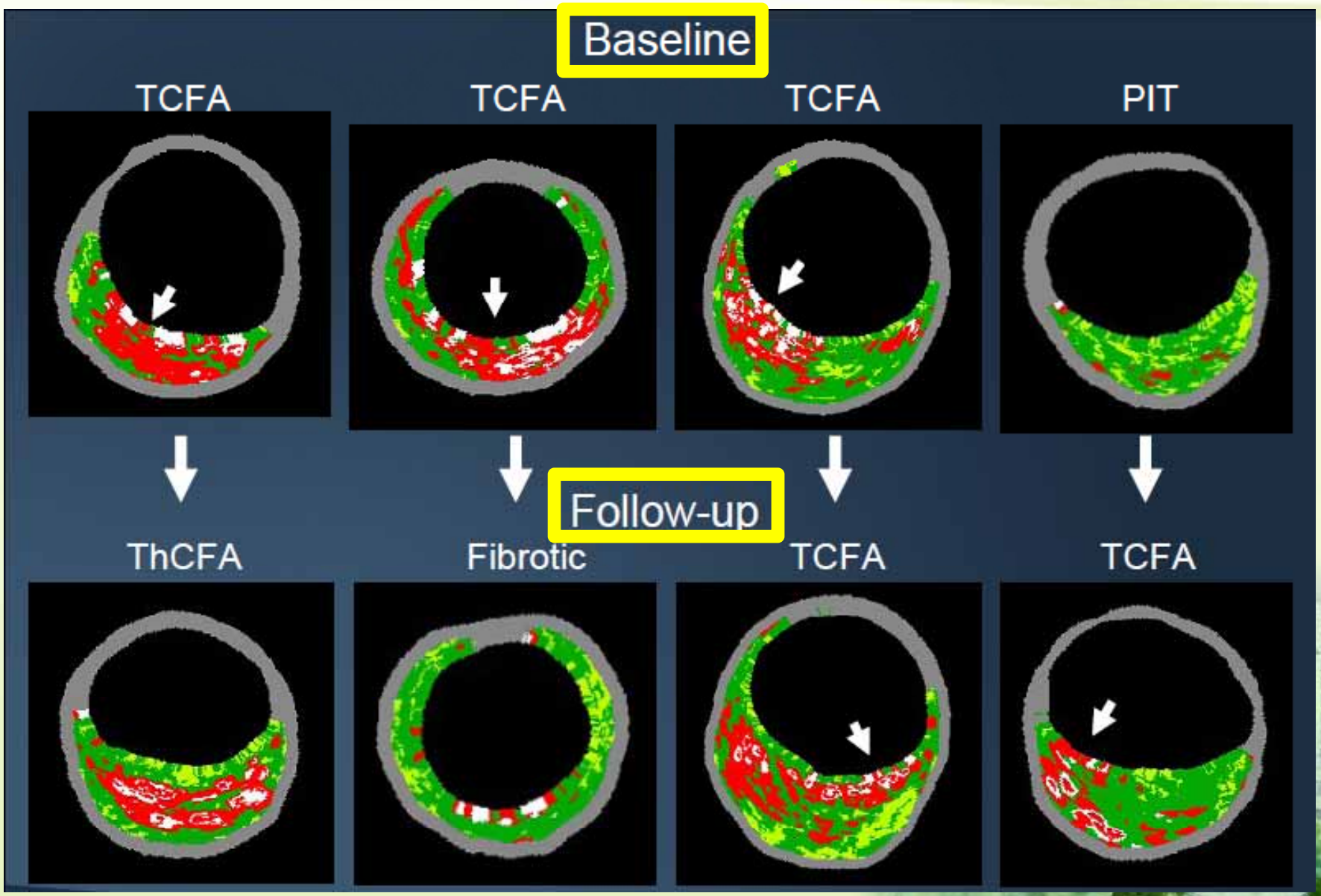
Pinkish-white thrombus on the yellow plaque

Smooth white intima without thrombus

Ruptured plaques in nonculprit lesions tend to heal slowly with a progression of angiographic stenosis.

Takano M et al, J Am Coll Cardiol 2005;45:652–8

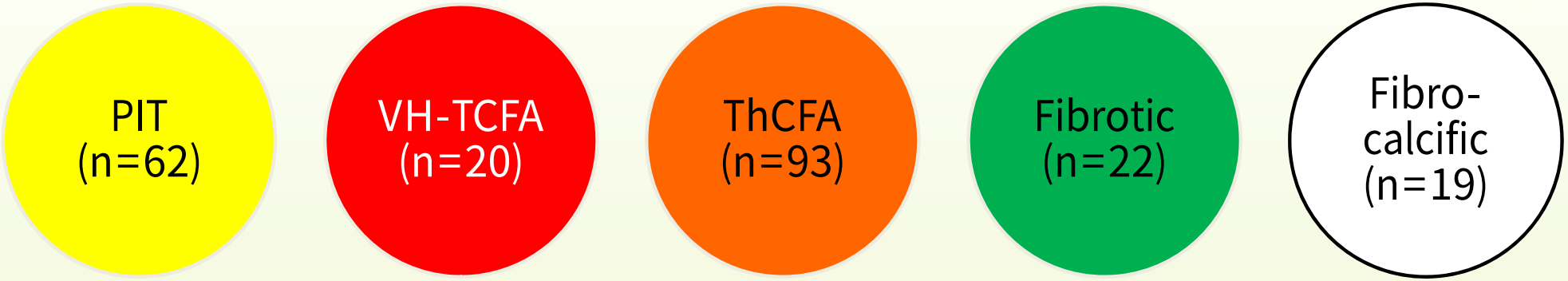
Changes in Plaque Characteristics Assessed by VH-IVUS Between Baseline and Follow-Up



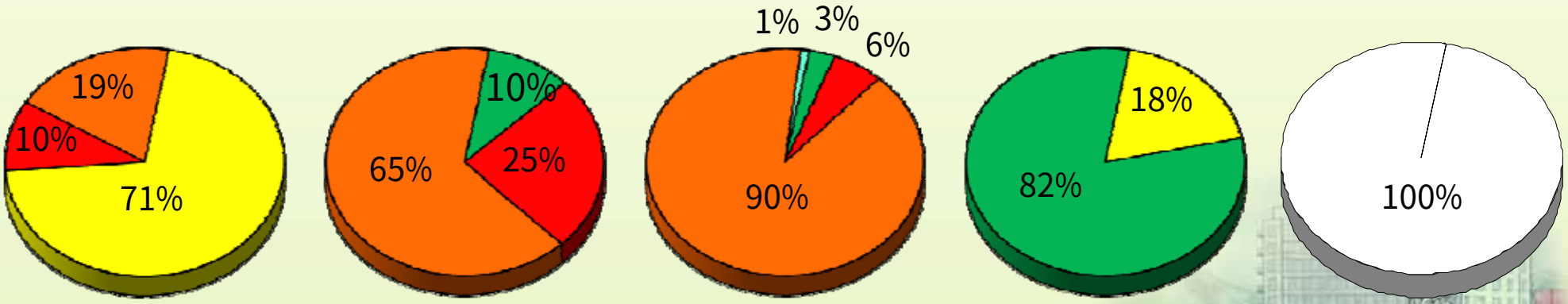
Kubo T et al: JACC 55:1890, 2010

Changes in Plaque Characteristics Assessed by VH-IVUS Between Baseline and Follow-Up

Baseline



Follow-up

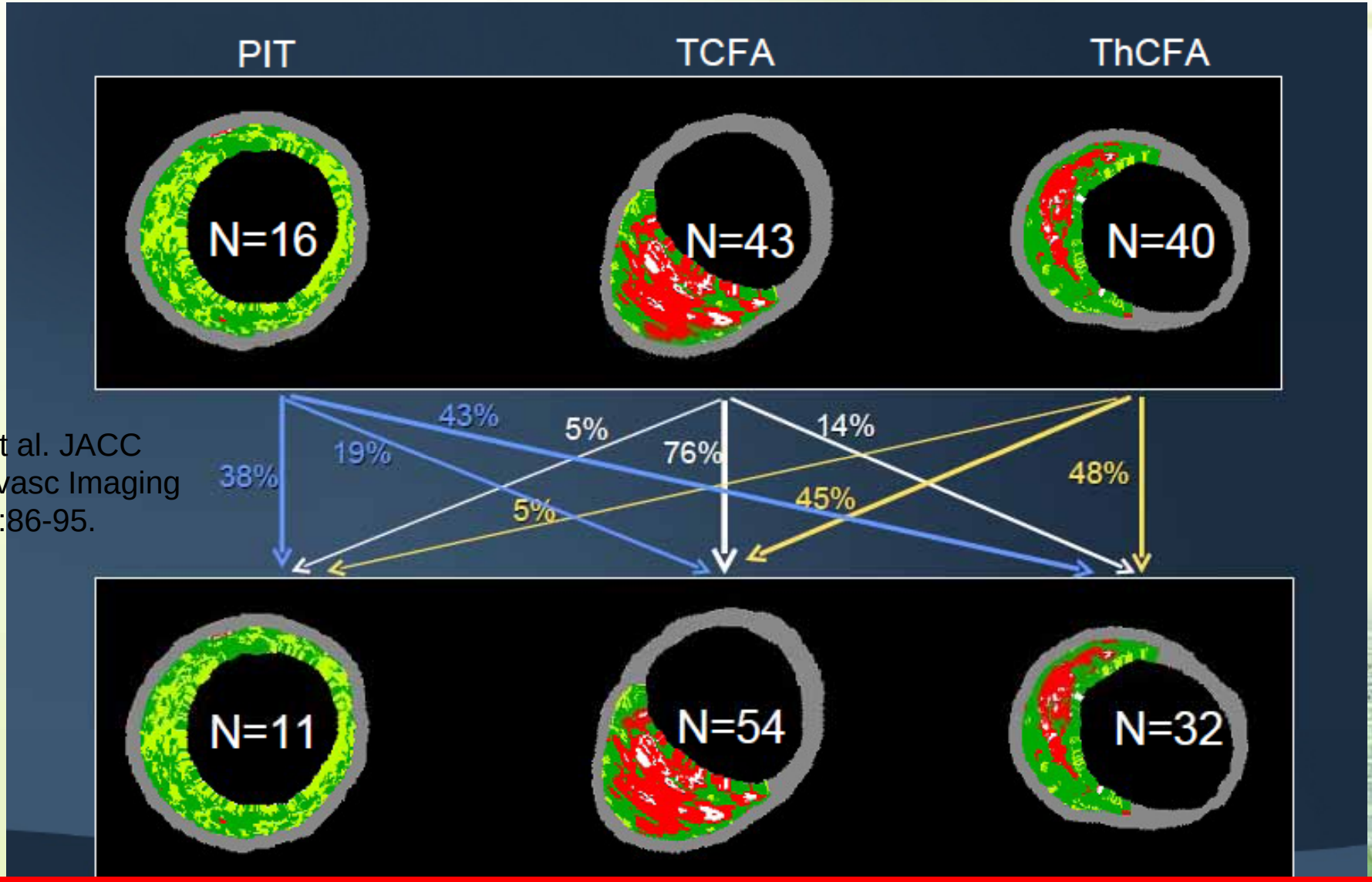


Most VH-TCFAs healed during 12-month follow-up, whereas new VH-TCFAs also developed. This is a dynamic process!

Kubo T et al: JACC 55:1890, 2010

HORIZONS-AMI

Dynamic nature of nonculprit coronary artery lesion morphology in STEMI



Zhao et al. JACC Cardiovasc Imaging 2013;6:86-95.

Untreated nonculprit lesions in STEMI patients frequently have TCFA morphology that does not change during 13-month follow-up.

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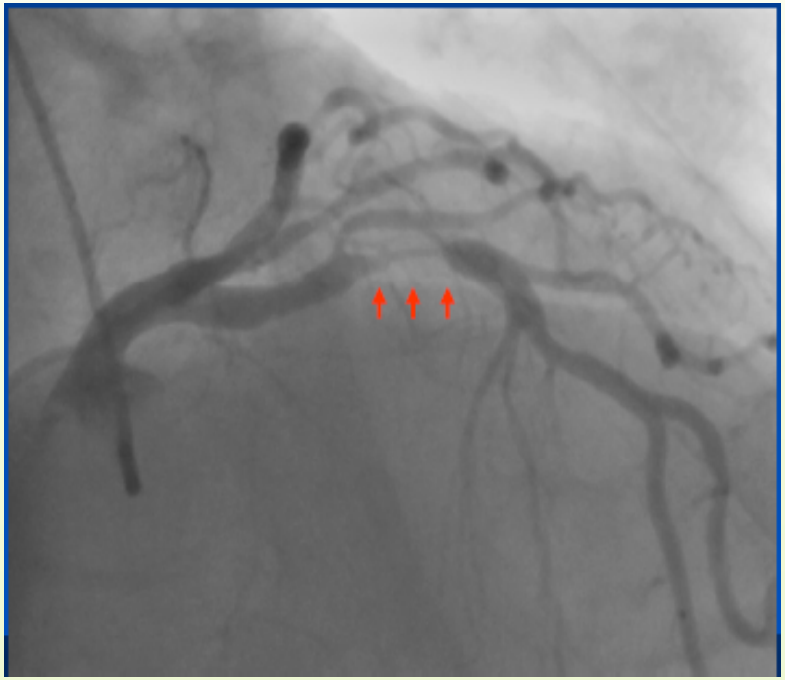
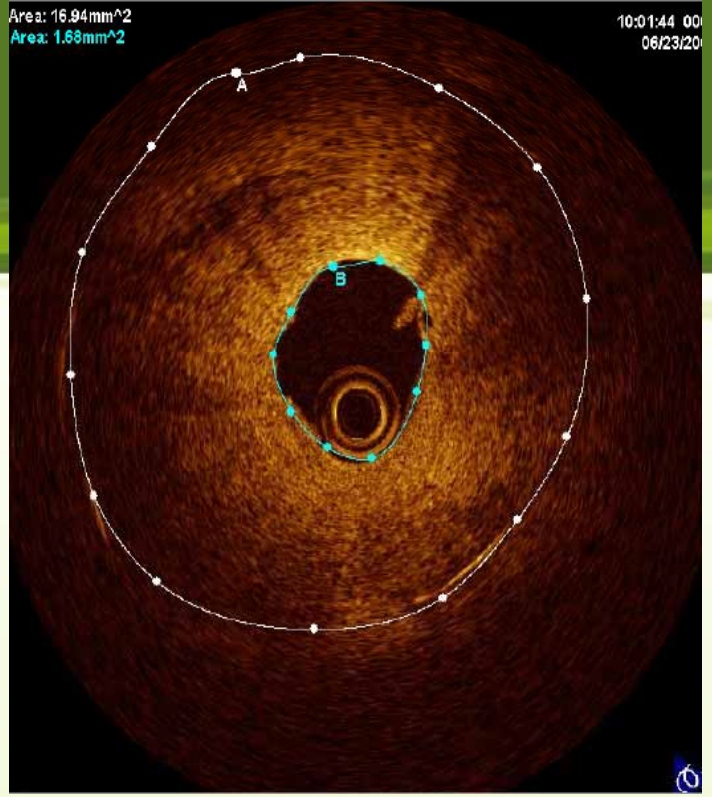
✓Fate of Vulnerable Plaque

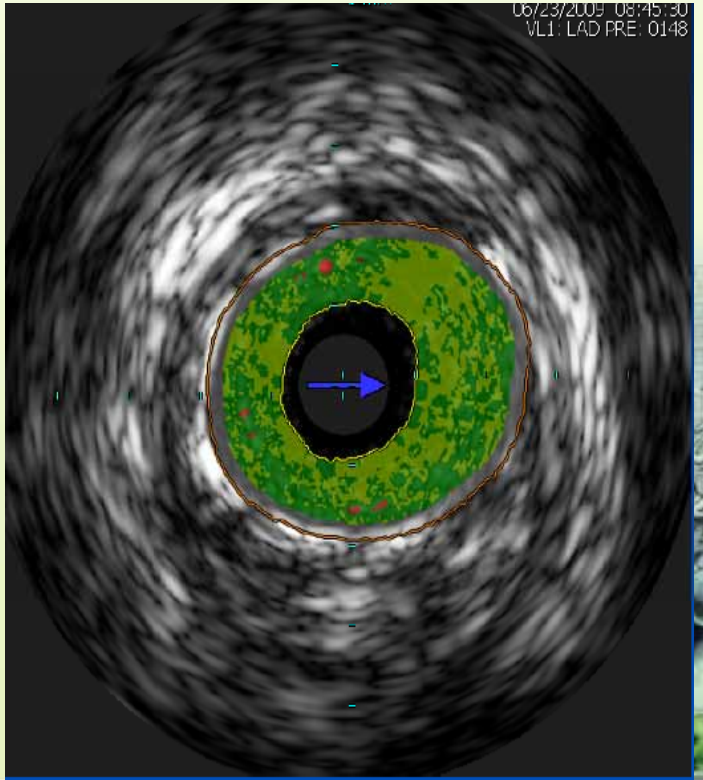
✓**VH neointimal tissue characteristics**

68/M
Asymptomatic ISR



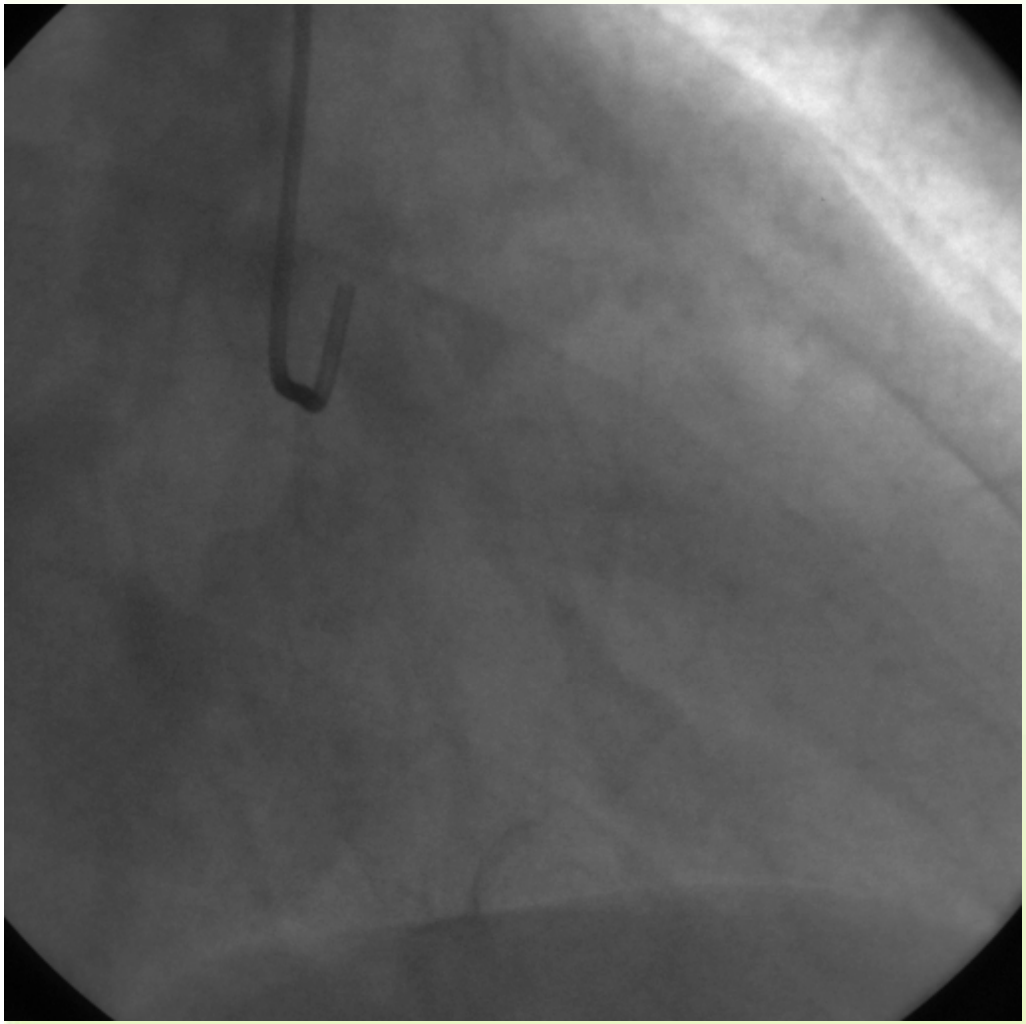
Taxus 4.0*20mm at mLAD

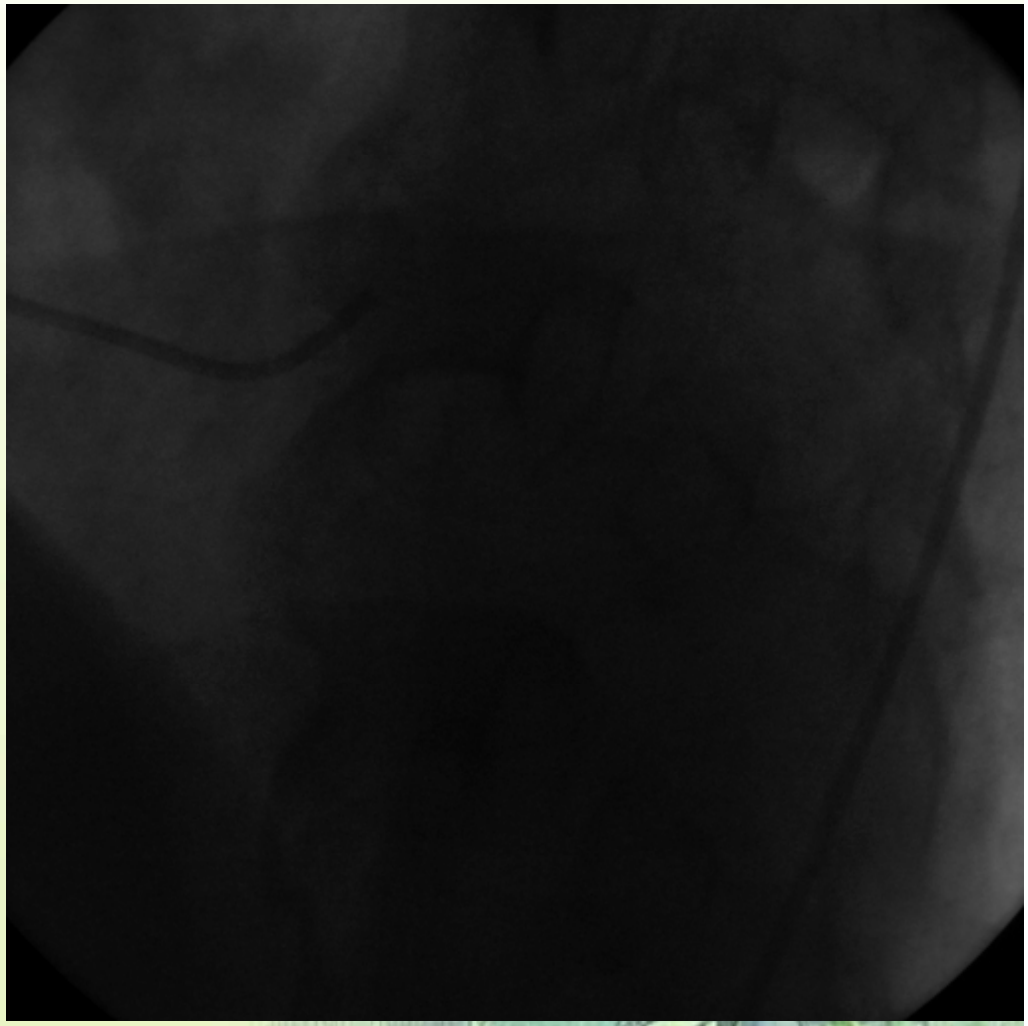




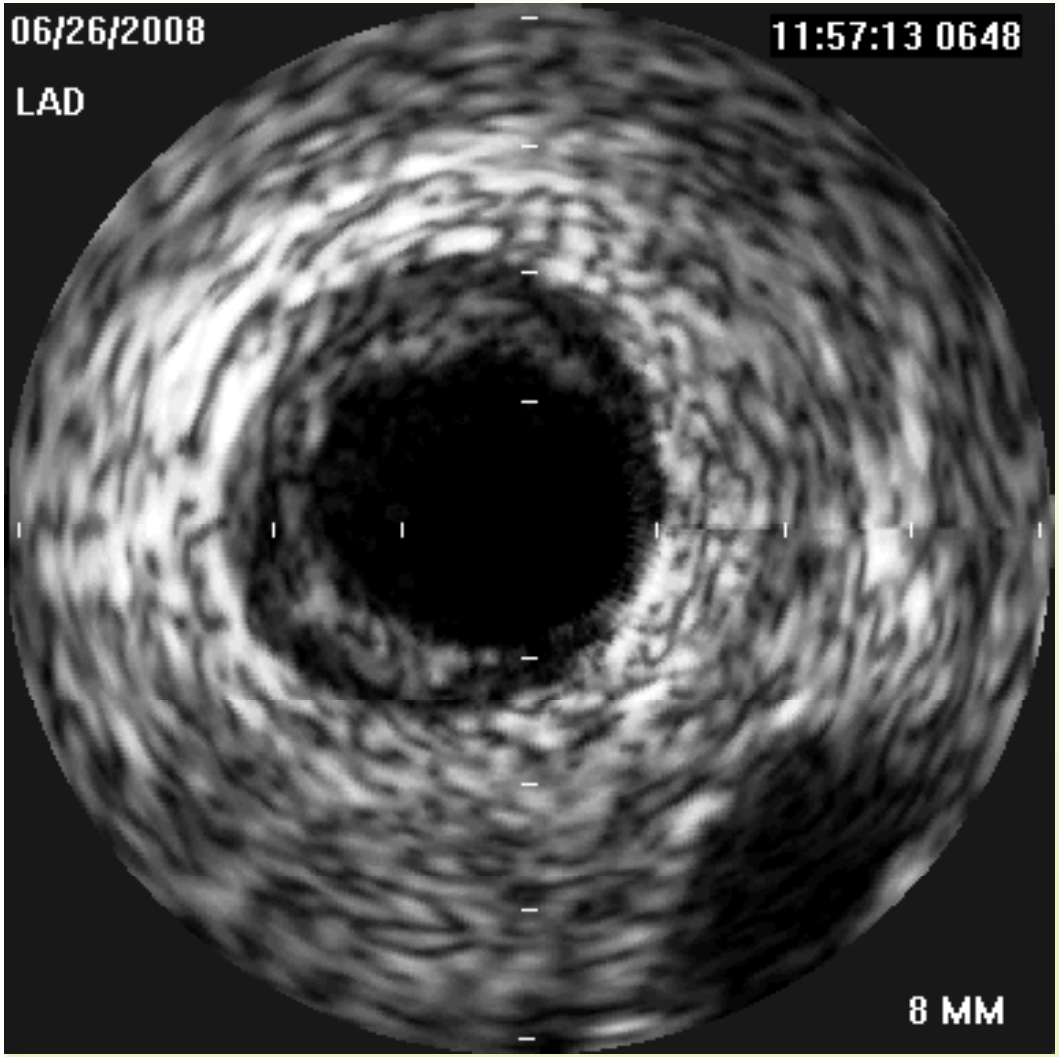
Courtesy of Dr. Kang SJ

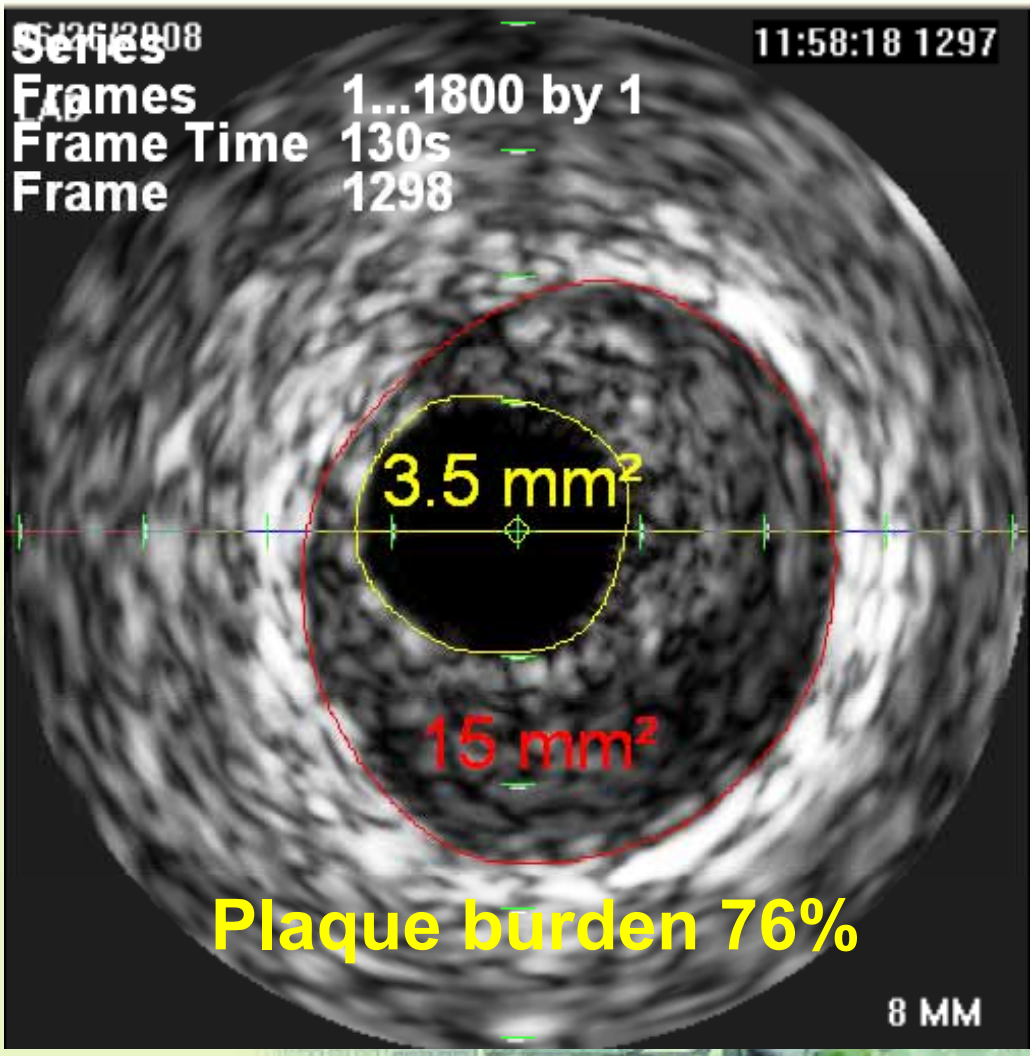
77/M, SAP, DM, HT, DL



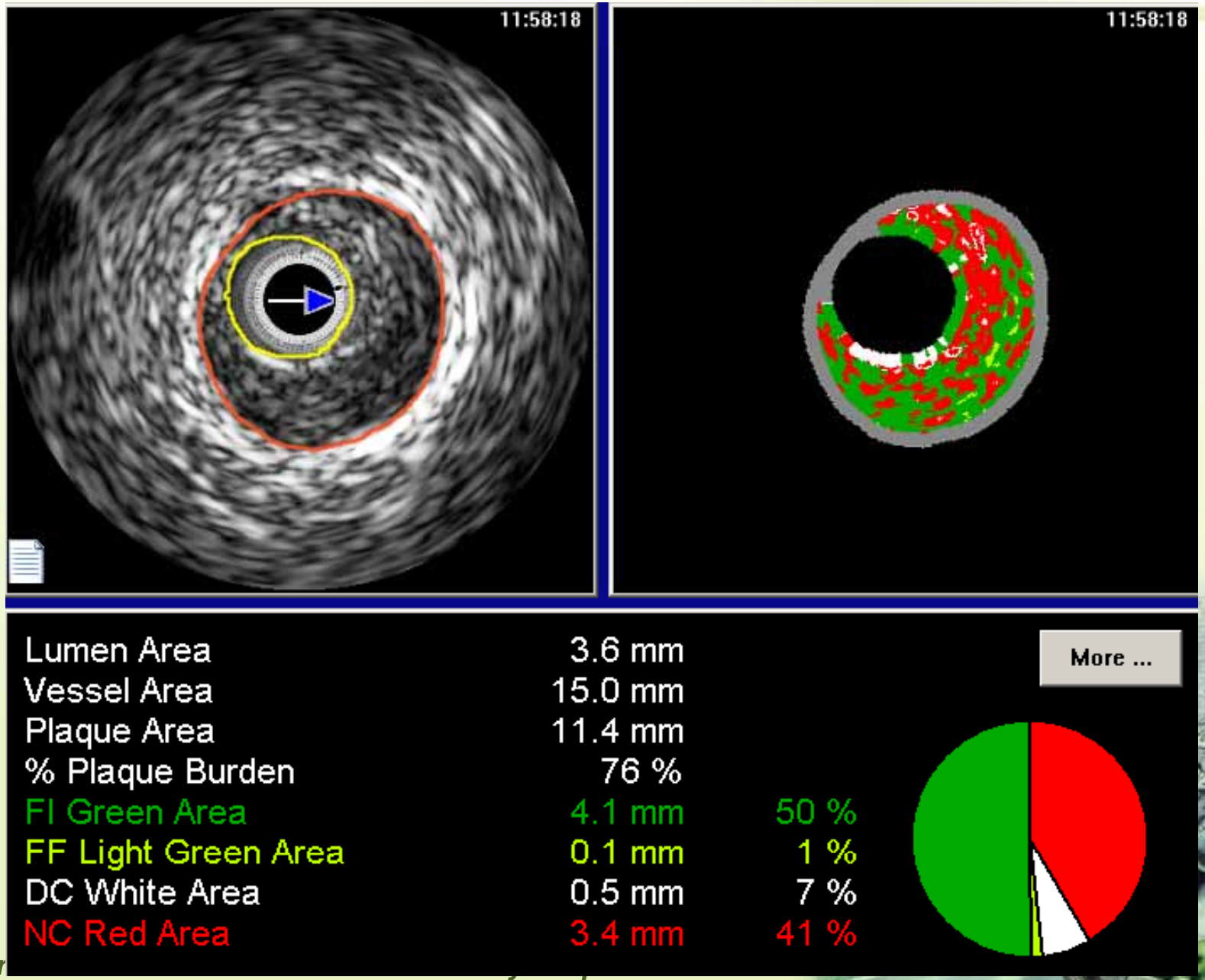


IVUS

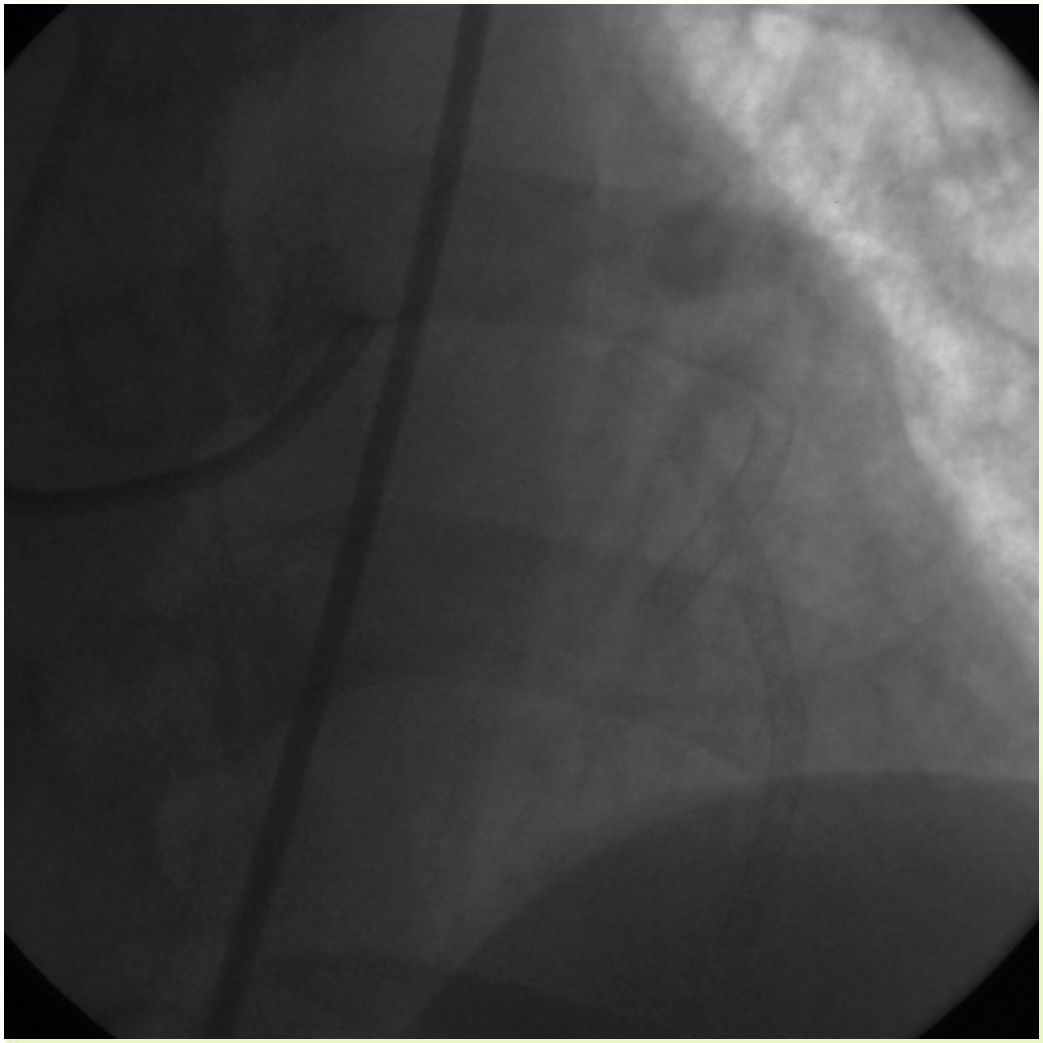

06/26/2008
11:57:13 0648
LAD
8 MM

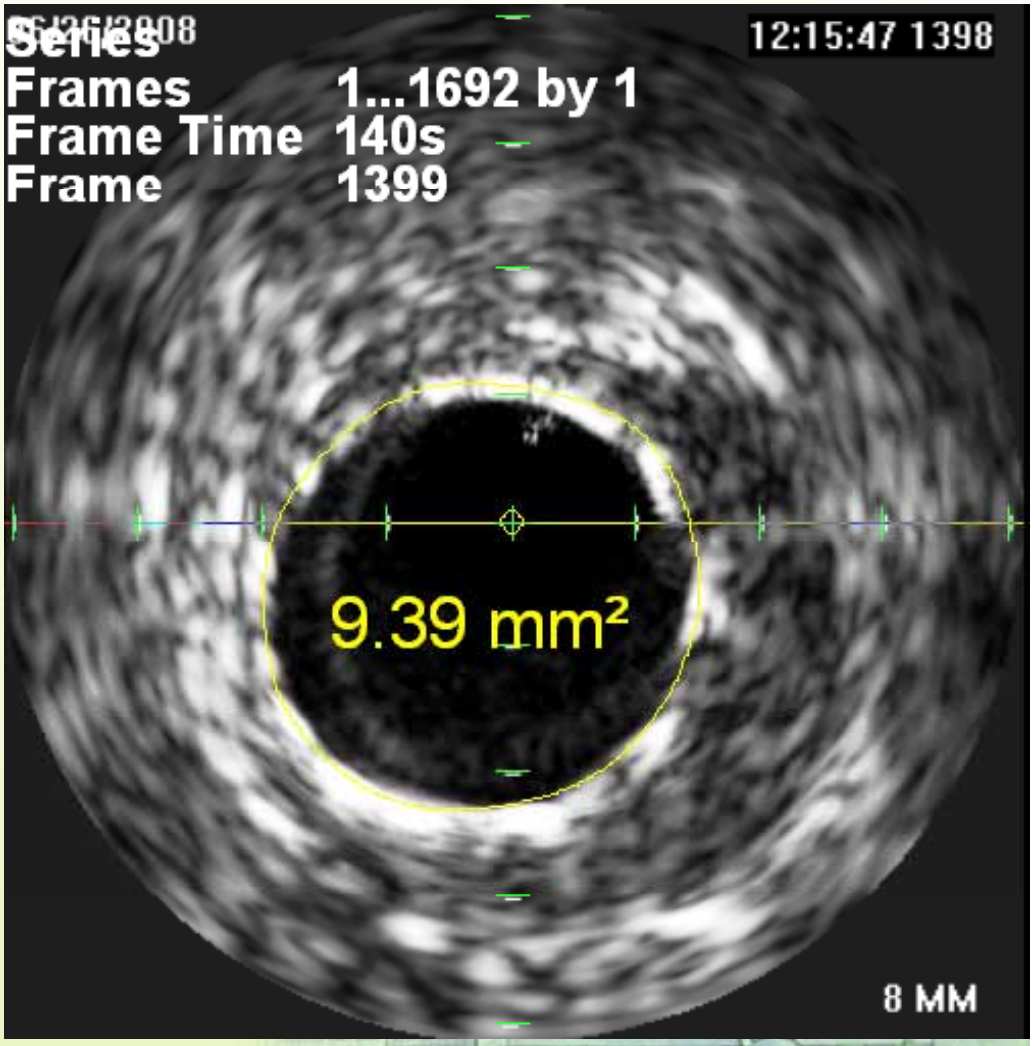

11:58:18 1297
Series
Frames 1...1800 by 1
Frame Time 130s
Frame 1298
3.5 mm²
15 mm²
Plaque burden 76%
8 MM

VH-IVUS

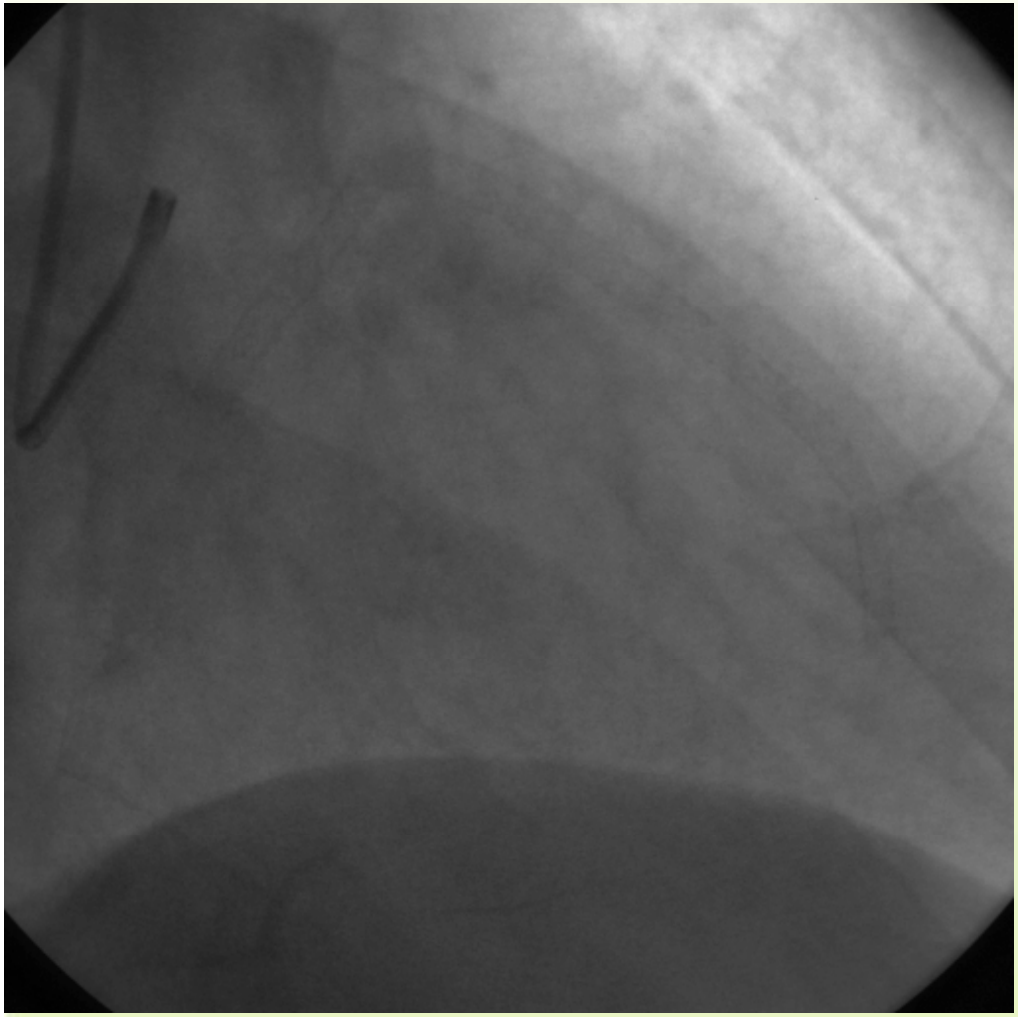

11:58:18
11:58:18
Lumen Area 3.6 mm
Vessel Area 15.0 mm
Plaque Area 11.4 mm
% Plaque Burden 76 %
FI Green Area 4.1 mm 50 %
FF Light Green Area 0.1 mm 1 %
DC White Area 0.5 mm 7 %
NC Red Area 3.4 mm 41 %
More ...

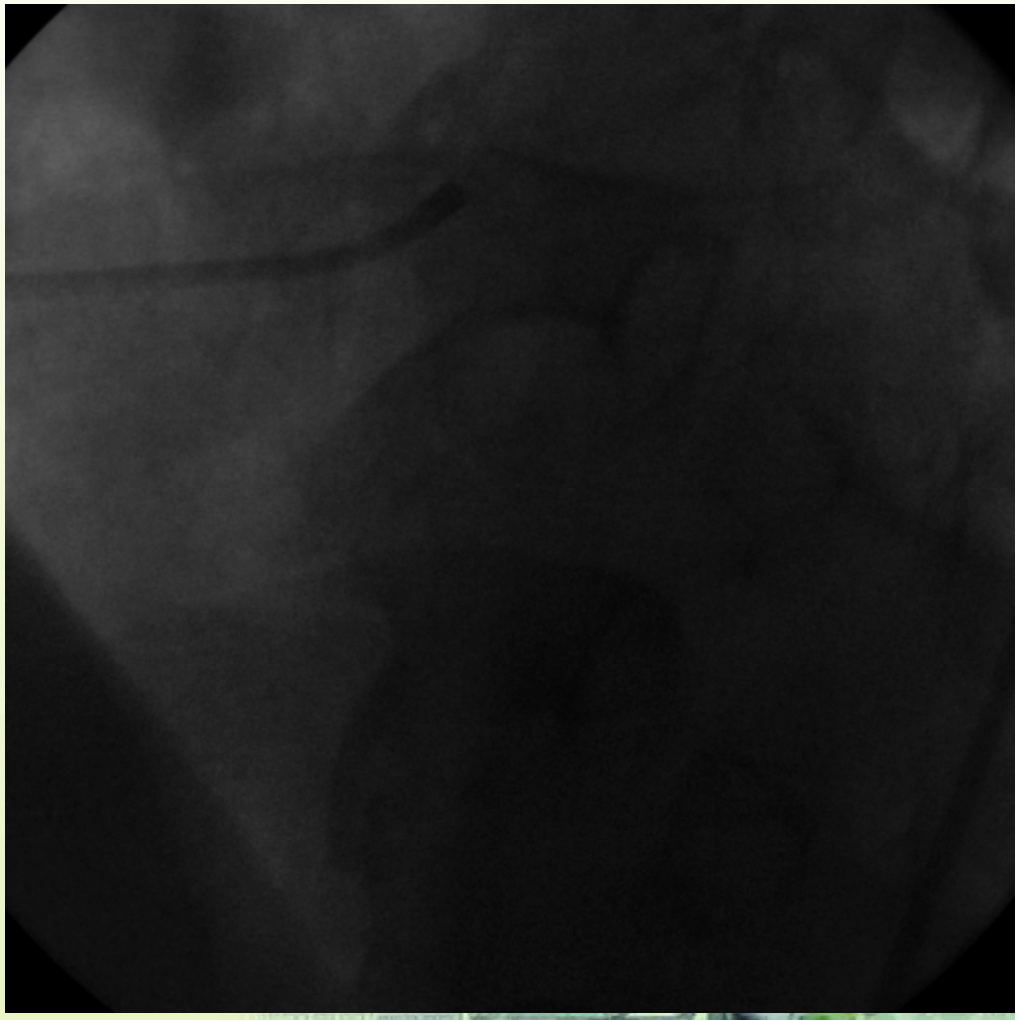
Two-DES with Overlapping



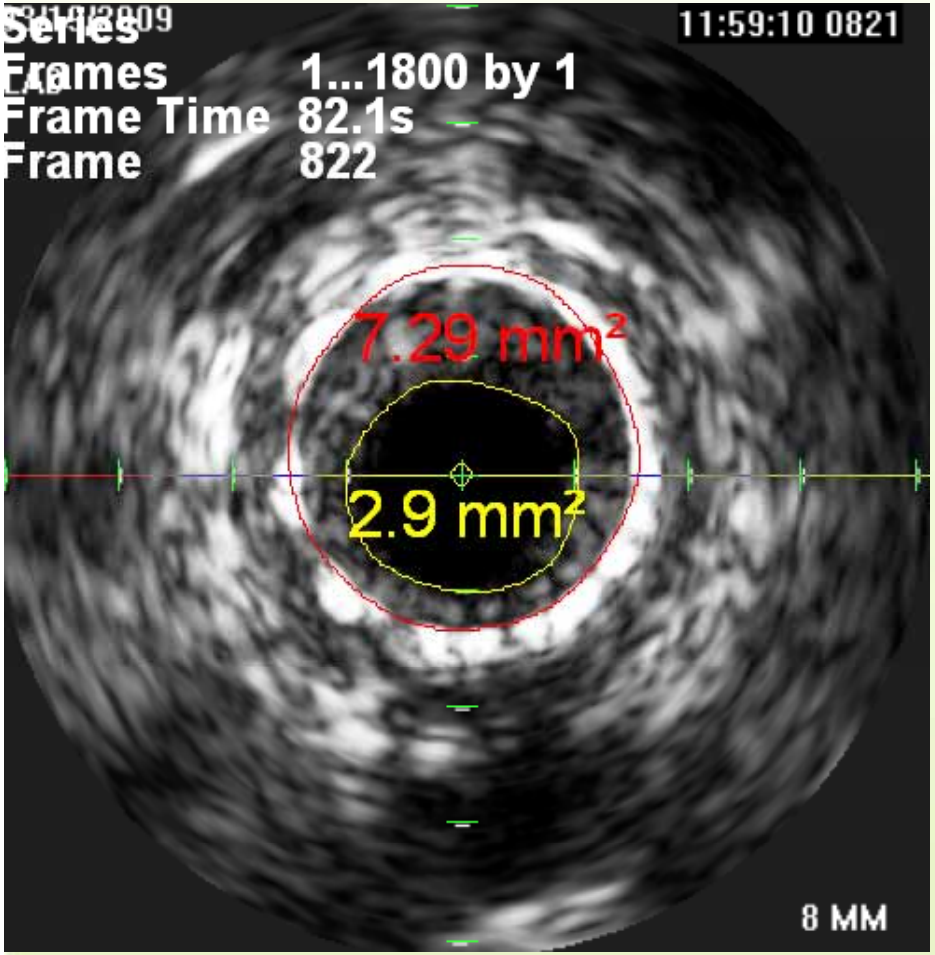


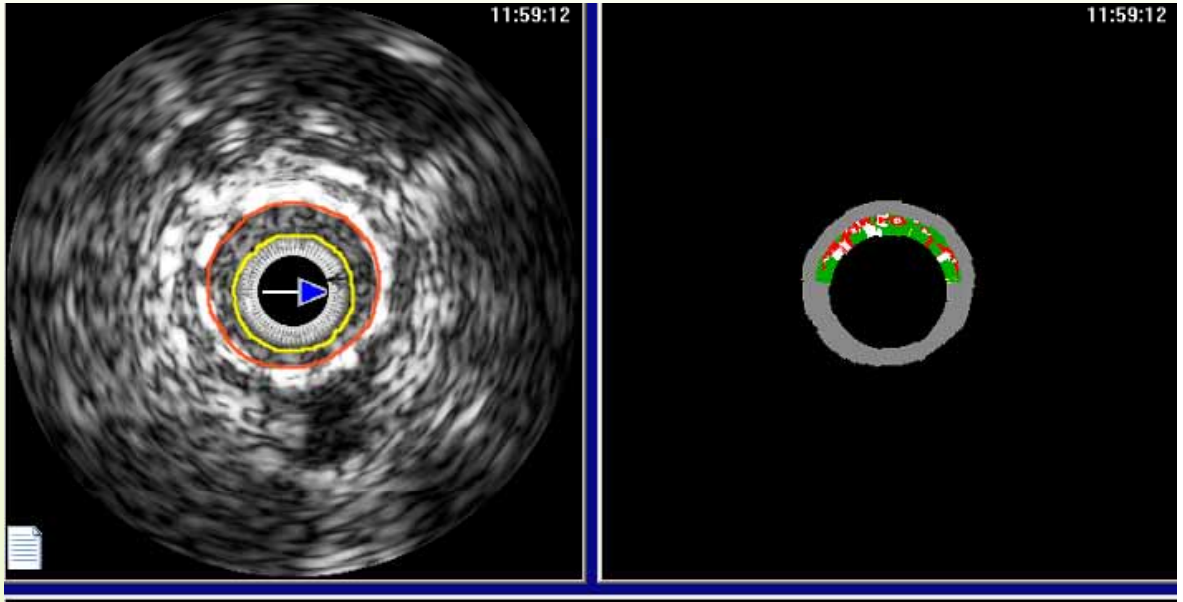
Unstable angina
9-Month FU CAG





9-Month FU IVUS



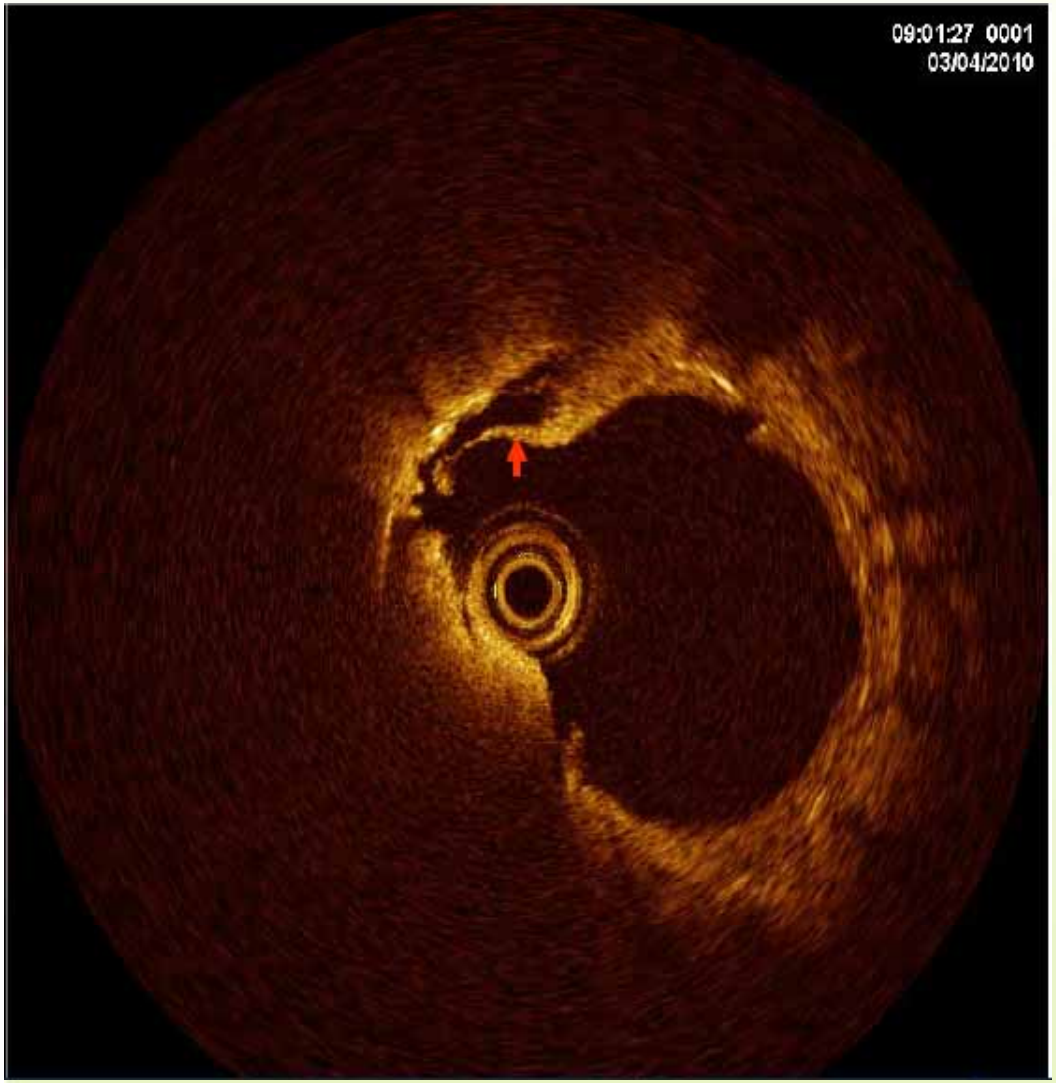


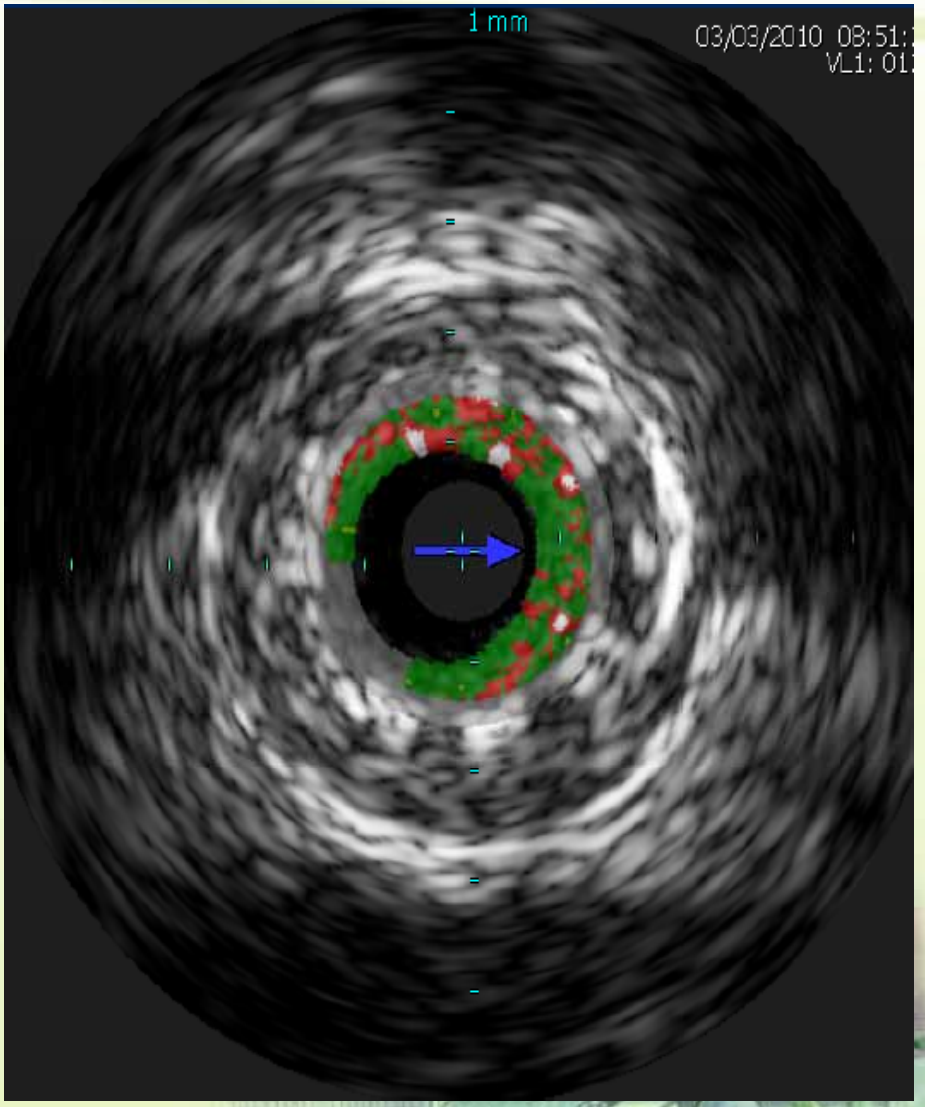
Lumen Area	3.3 mm	
Vessel Area	7.0 mm	
Plaque Area	3.7 mm	
% Plaque Burden	53 %	
FI Green Area	0.6 mm	56 %
FF Light Green Area	0.0 mm	1 %
DC White Area	0.2 mm	19 %
NC Red Area	0.3 mm	24 %

More ...

59/M, NSTEMI d/t VLST

Cypher 3.0*23mm, 3.5*8mm at p~mLAD





In-Stent Neo-atherosclerosis with Vulnerable Intima

%NC=30%

The Heart Center of Chonnam National University Hospital

Courtesy of Dr. Kang SJ

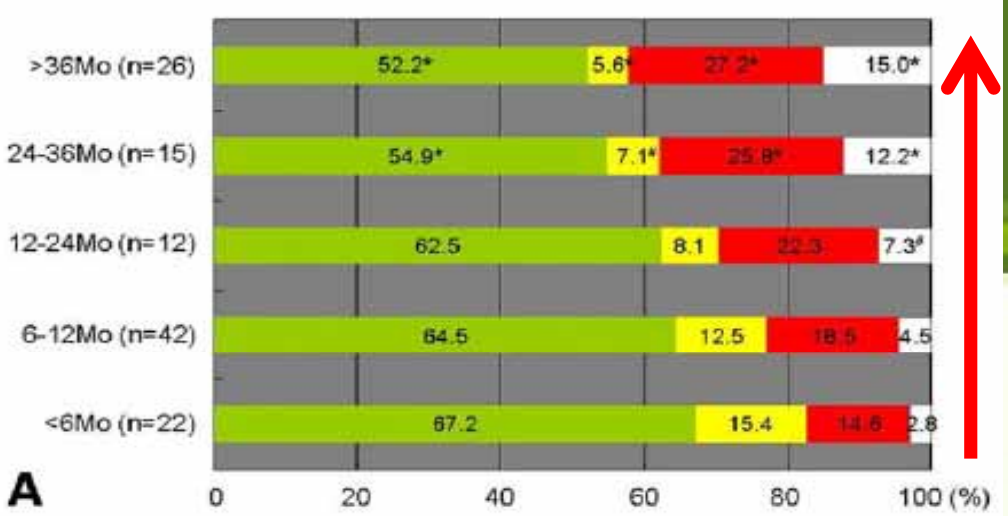
Tissue Characterization of In-Stent Neointima Using Intravascular Ultrasound Radiofrequency Data Analysis

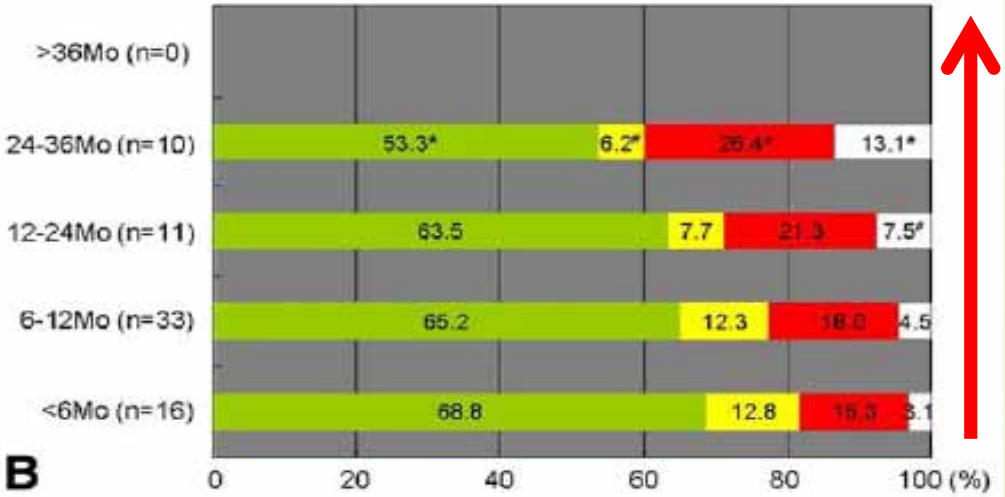
Soo-Jin Kang, MD[a], Gary S. Mintz, MD[b], Duk-Woo Park, MD[a], Seung-Whan Lee, MD[a], Young-Hak Kim, MD[a], Cheol Whan Lee, MD[a], Ki-Hoon Han, MD[a], Jae-Joong Kim, MD[a], Seong-Wook Park, MD[a], and Seung-Jung Park, MD[a,*]

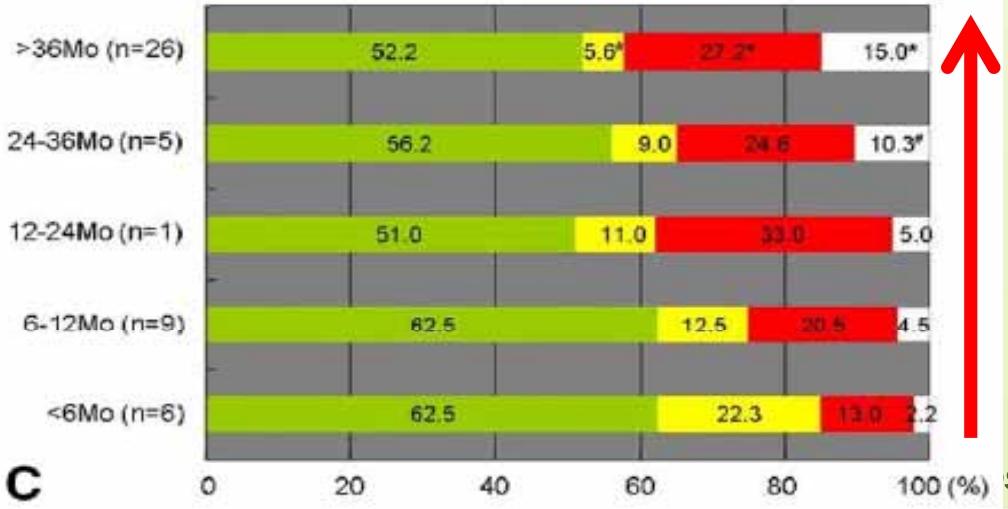
Using virtual histology and intravascular ultrasound (VH-IVUS), tissue characterization of restenotic in-stent neointima after drug-eluting stent (DES) and bare metal stent (BMS) implantation was assessed. VH-IVUS was performed in 117 lesions (70 treated with DESs and 47 treated with BMSs) with angiographic in-stent restenosis and intimal hyperplasia (IH) >50% of the stent area. The region of interest was placed between the luminal border and the inner border of the struts and tissue composition was reported as percentages of IH area (percent fibrous, percent fibrofatty, percent necrotic core, percent dense calcium) at the 2 sites of maximal percent IH and maximal percent necrotic core. Mean follow-up times between stent implantation and VH-IVUS study were 43.5 ± 33.8 months for BMS-treated lesions and 11.1 ± 7.8 months for DES-treated lesions ($p < 0.001$). The 2 groups had greater percent necrotic core and percent dense calcium at maximal percent IH and maximal percent necrotic core sites, especially in stents that had been implanted for longer periods. In conclusion, this VH-IVUS analysis showed that BMS- and DES-treated lesions develop in-stent necrotic core and dense calcium, suggesting the development of in-stent neoatherosclerosis. (Am J Cardiol 2010;106:1561–1565)

Kang SJ et al., Am J Cardiol 2010;106:1561-1565

Differences in VH-IVUS Composition of In-Stent Neointimal Tissue at Various Follow-up Periods







(A) Overall, 117 lesions **combining bare metal and drug-eluting stents**

(B) 70 lesions treated with **drug-eluting stents**

(C) 47 lesions treated with bare metal stents

Necrotic core and dense calcium within the neointima increased over time after both DES and BMS Implantation.

Kang SJ et al., Am J Cardiol 2010;106:1561-1565

spital

Neointima between DES vs. BMS

J Invasive Cardiol. 2011 Jul;23(7):262-8.

In vivo virtual histology intravascular ultrasound comparison of neointimal hyperplasia within drug -eluting- versus bare metal stents.

Wakabayashi K, Mintz G, Delhaye C, Choi YJ, Doh JH, Ben-Dor I, Gaglia M Jr, Pakala R, Suddath W, Satler L, Kent K, Pichard A, Weissman N, Waksman R.
Washington Hospital Center, Division of Cardiology, Washington, DC 20010, USA.

Abstract

BACKGROUND: The process of in-stent neointimal hyperplasia (NIH) between drug-eluting stents (DES) and bare metal stents (BMS) might be different. We compared in vivo composition of in-stent NIH between DES and BMS using virtual histology-intravascular ultrasound (VH-IVUS).

METHODS AND RESULTS: Volumetric VH-IVUS was used to compare in-stent NIH between 23 DES and 15 BMS in 30 patients who underwent coronary angiography because of angina. The inner and outer VH-IVUS contours were drawn in a way to avoid the stent strut artifacts. Cross-sectional analysis was done at every VH-IVUS frame within the stent, thereby allowing volumetric measurement of stent, lumen, and NIH and its components. Baseline characteristics and IVUS measurements were similar between DES and BMS groups. The duration of follow-up was similar between DES (median 38 months [interquartile range, 7-59]) vs. BMS (median 40 months [interquartile range, 7-99]), (p=0.26). % necrotic core (NC) volume was significantly higher in DES than BMS: 19.5 [16.3, 25.6] vs. 12.1 [8.2, 18.5] (p=0.006). %NC volume significantly increased with time in BMS (p=0.007), but not in DES (p=0.24) so that at any given time point, %NC in DES was greater than in BMS. After adjustment for baseline differences, only DES (p=0.003) and stent age (p=0.043) were independent predictors of %NC volume. VH-IVUS in-stent thin-cap fibroatheromas were detected only in the DES group: 34.8% vs. 0%, p=0.013.

CONCLUSION: In vivo composition of in-stent NIH between DES and BMS was different, suggesting that the process of in-stent NIH in DES and BMS is diverse.

Long-term Effects of DES on Coronary Morphology

Am Heart J. 2010 Feb;159(2):271-7.

Analysis of the long-term effects of drug-eluting stents on coronary arterial wall morphology as assessed by virtual histology intravascular ultrasound.

Kubo T, Maehara A, Mintz GS, Garcia-Garcia HM, Serruys PW, Suzuki T, Klauss V, Sumitsuji S, Lerman A, Marso SP, Margolis MP, Margolis JR, Foster MC, De Bruyne B, Leon MB, Stone GW.

Cardiovascular Research Foundation, 111 East 59th Street, New York, NY 10022, USA.

Abstract

BACKGROUND: Animal models show impairment of arterial healing after drug-eluting stents (DES) compared with bare-metal stents (BMS). Virtual histology intravascular ultrasound (VH-IVUS) offers an opportunity to assess lesion morphology in vivo.

METHODS: We used VH-IVUS in 80 patients to assess long-term (median = 10 months) native artery vascular responses after 76 implantations of DES compared with 32 BMS. The presence of "necrotic core abutting the lumen" was evaluated at baseline and follow-up.

RESULTS: At baseline, necrotic core abutting the lumen through the stent struts was observed in 76% of DES and 75% of BMS. Although the percentage of necrotic core within the plaque behind the stents did not change during follow-up in DES (23% [18%, 28%] to 22% [17%, 27%], P = .57) or BMS (22% [19%, 27%] to 20% [12%, 26%], P = .29), necrotic core abutting the lumen through the stent struts decreased more in BMS (75% to 19%, P < .001) than DES (76% to 61%, P = .036) because of the lack of an overlying, protective neointima in DES-treated lesions. Furthermore, within the adjacent reference segments, the incidence of necrotic core abutting the lumen decreased in BMS-treated lesions (proximal 23% to 0%, P = .023; distal 21% to 0%, P = .023), but not in DES (proximal 22% to 17%, P = .48; distal 23% to 21%, P = .82).

CONCLUSIONS: Serial VH-IVUS analysis of DES-treated lesions showed a greater frequency of unstable lesion morphometry at follow-up compared with BMS. The apparent mechanism was a suppression of the protective neointimal hyperplasia layer coupled with a lack of vulnerable plaque resolution at reference segments in DES compared with BMS.

Conclusion (I)

Fate of Vulnerable Plaque

- Some vulnerable plaques rupture asymptomatically and are detected incidentally.
- TCFAs can heal or rupture asymptomatically, and new TCFAs can develop.
- Lesions with vulnerable plaque can evoke acute coronary syndrome.
- A combination of large plaque burden, compromised lumen, and the presence of a TCFA increase the risk of silent plaque progression to become a clinical event.
- Changes in plaque characteristics are dynamic process.

Conclusion (II)

Neointimal Tissue Characteristics

- Tissue characteristics of neointima varied in the lesions with DES failure.
- Stents that have been implanted for longer periods and develop late DES ISR have in-stent tissue composition that includes necrotic core and dense calcium suggestive of in-stent neoatherosclerosis.
- Large necrotic core containing DES ISR lesions can also rupture and thrombose to cause very late stent thrombosis.