Detection of VP & Natural Course by OCT

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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.

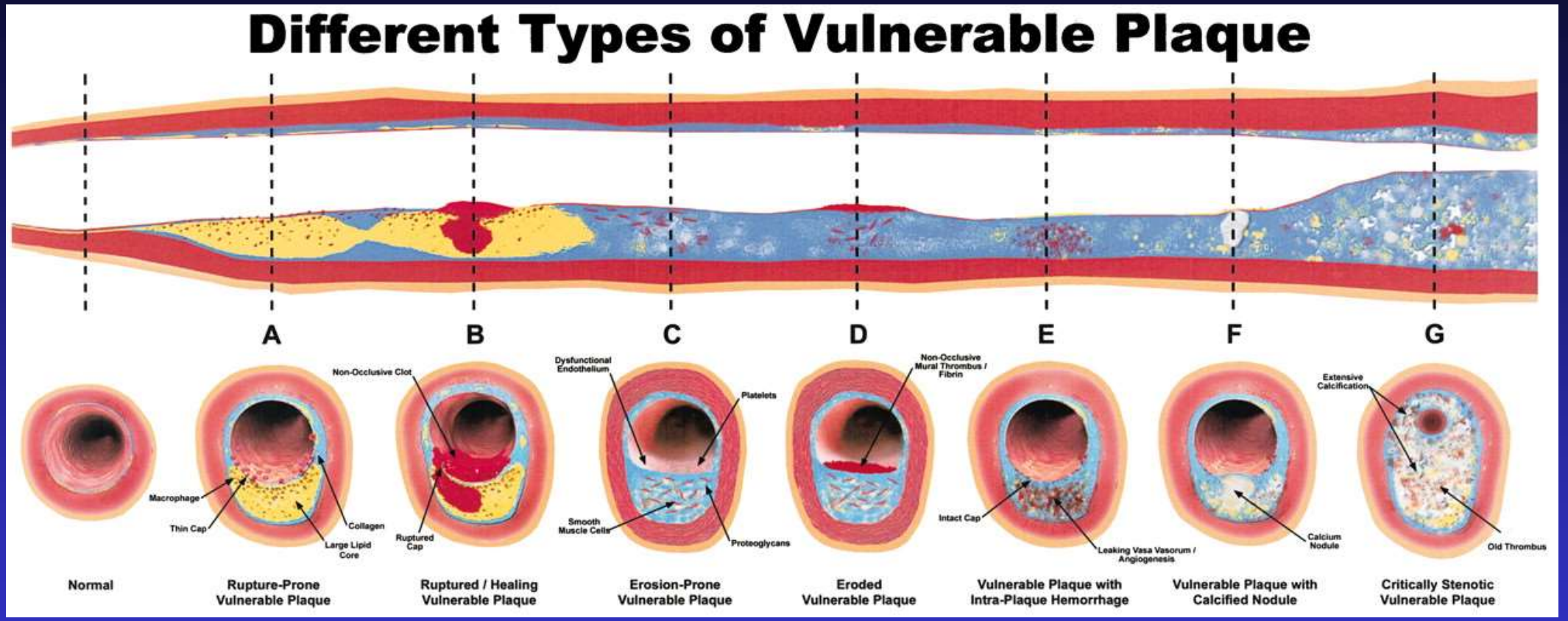
Affiliation/Financial Relationship

- **Grant/Research Support** : **Abbott Vascular Japan**
  Boston Scientific Japan
  Goodman Inc.
  St. Jude Medical Japan
  Terumo Inc.

- **Consulting Fees/Honoraria** : **Astellas Pharmaceutical Inc.**
  Daiichi-Sankyo Pharmaceutical Inc.
  Goodman Inc.
  St. Jude Medical Japan
  Terumo Inc.

Progression of atherosclerotic plaque

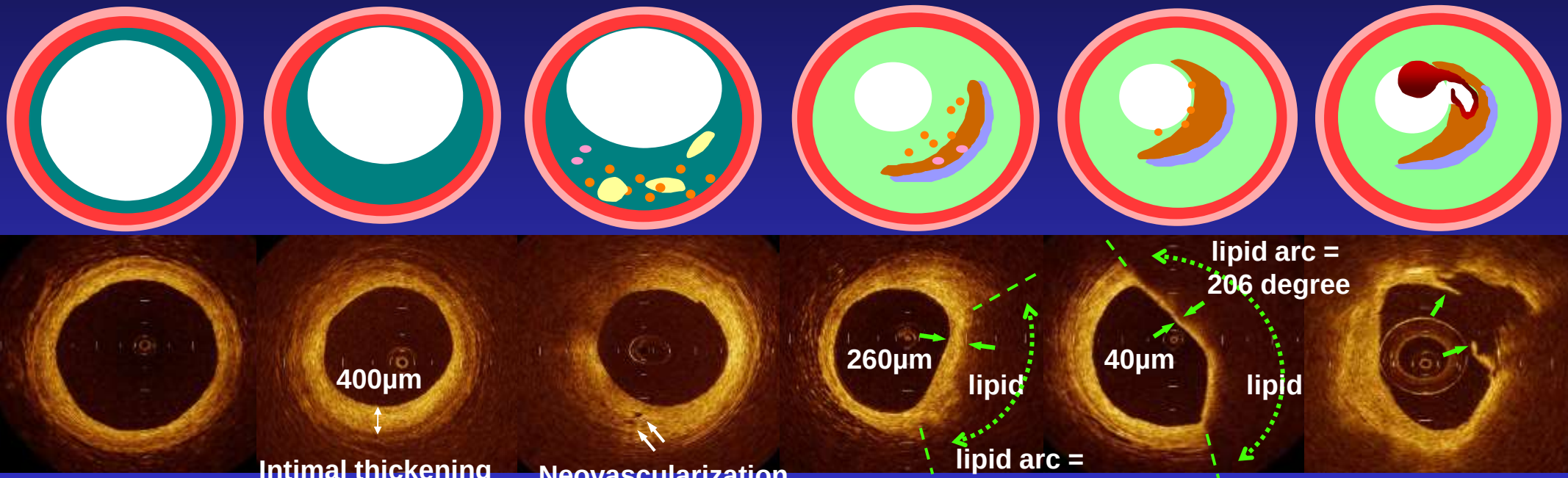
(Naghavi M, et al. Circulation 2003;108:1664-1672)



Positive remodeling can be identified in the early stage and this is thought to be an initial adaption for atherosclerotic change. Finally, vessel become narrowing significantly according to atheroscrelosis. ACS may occur even in insignificant stenosis.

Progression of atherosclerosis & corresponding OCT Images

A	B	C	D	E	F
Normal	Intimal thickening	Early plaque formation with neovascularization	Fibrous cap atheroma	Thin-cap fiboratheroma	Plaque rupture



- Extracelluler lipid
- Machrophage form cells
- Smooth muscle cells
- Neovascular vessel
- Necrotic core
- Calcified plaque
- Thrombus
- Collagen

Identification of vulnerable plaque

- Plaque prone to disruption

Rupture
Erosion
Calcified nodule
Intraplaque hemorrhage

Disruption (-)　Disruption (+)

Event (-)　　Event (+)

=

Silent plaque rupture

MACE

UAP　AMI　Sudden cardiac death

Demonstration of various causes in ACS

Plaque rupture

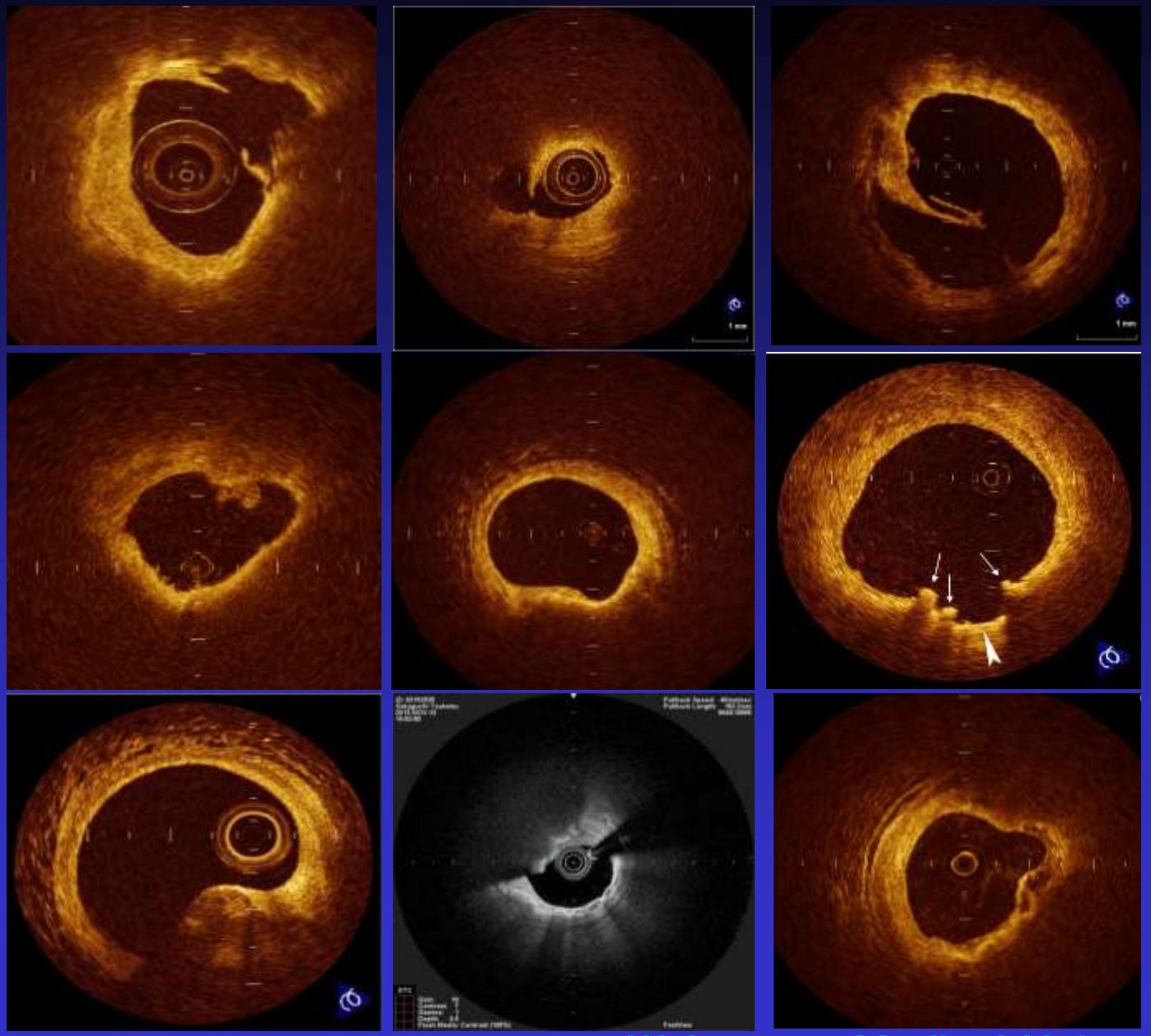
60 – 70 %

Plaque erosion

20 – 30 %

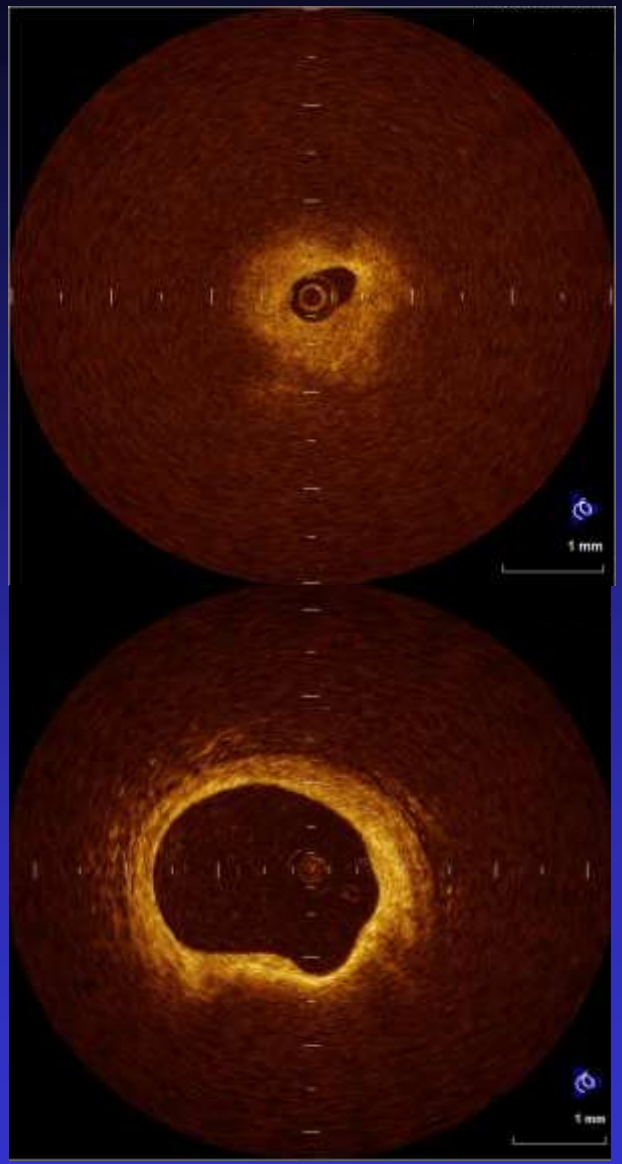
Calcified nodule

5 – 6 %

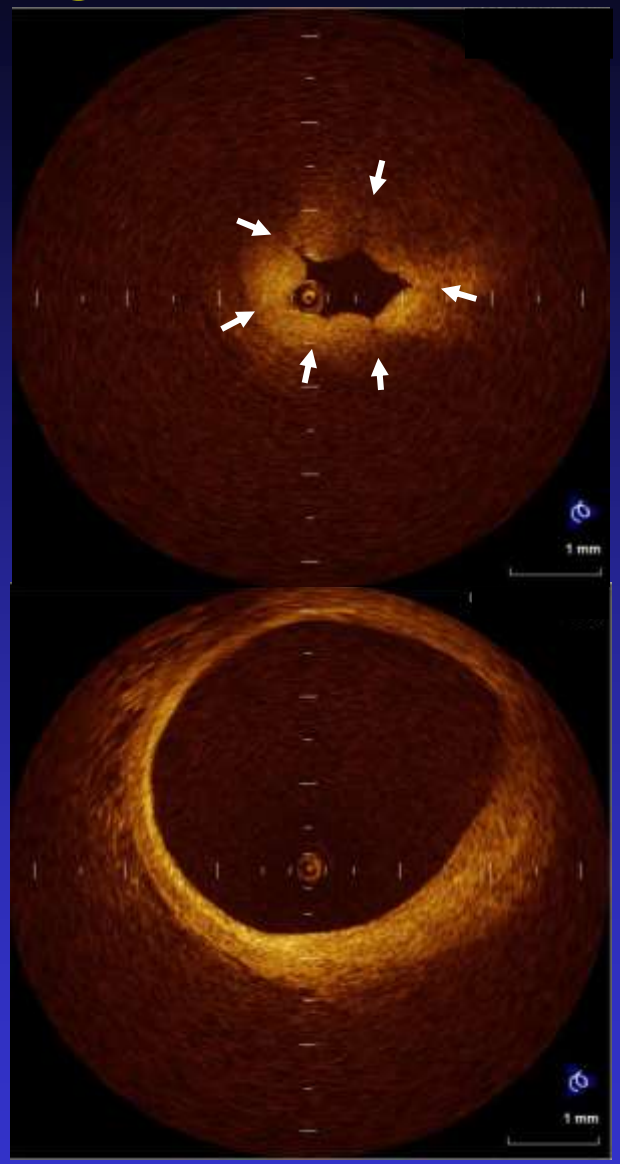


Kubo T, Akasaka T, et al. (J Am Coll Cardiol 50:933-939,2007)

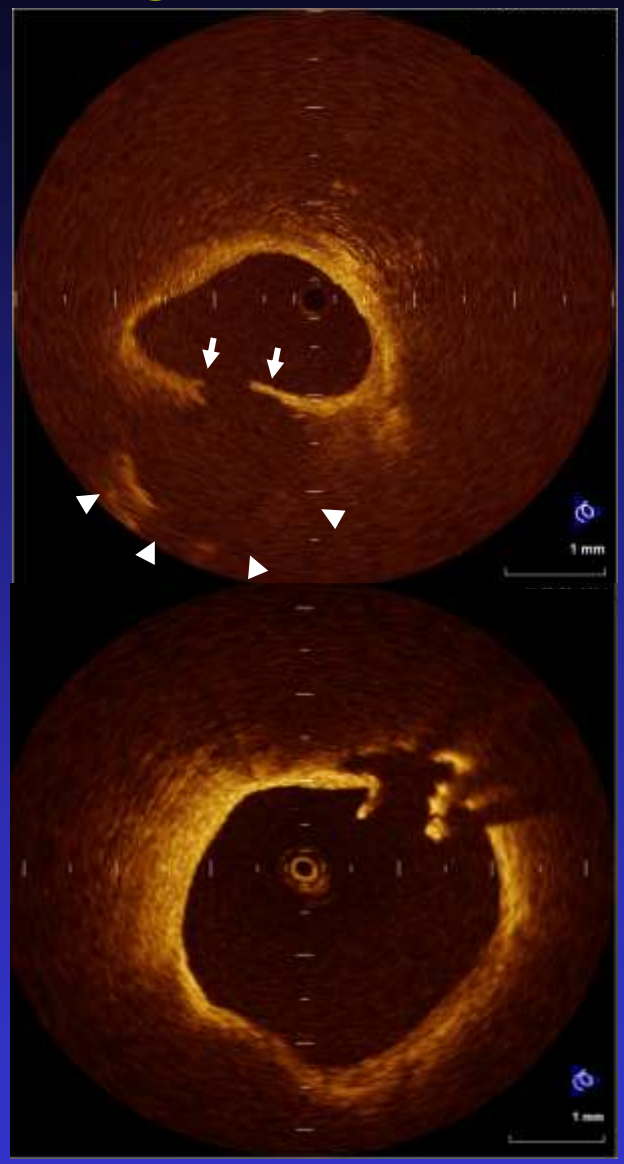
OCT findings in unstable angina



Class I



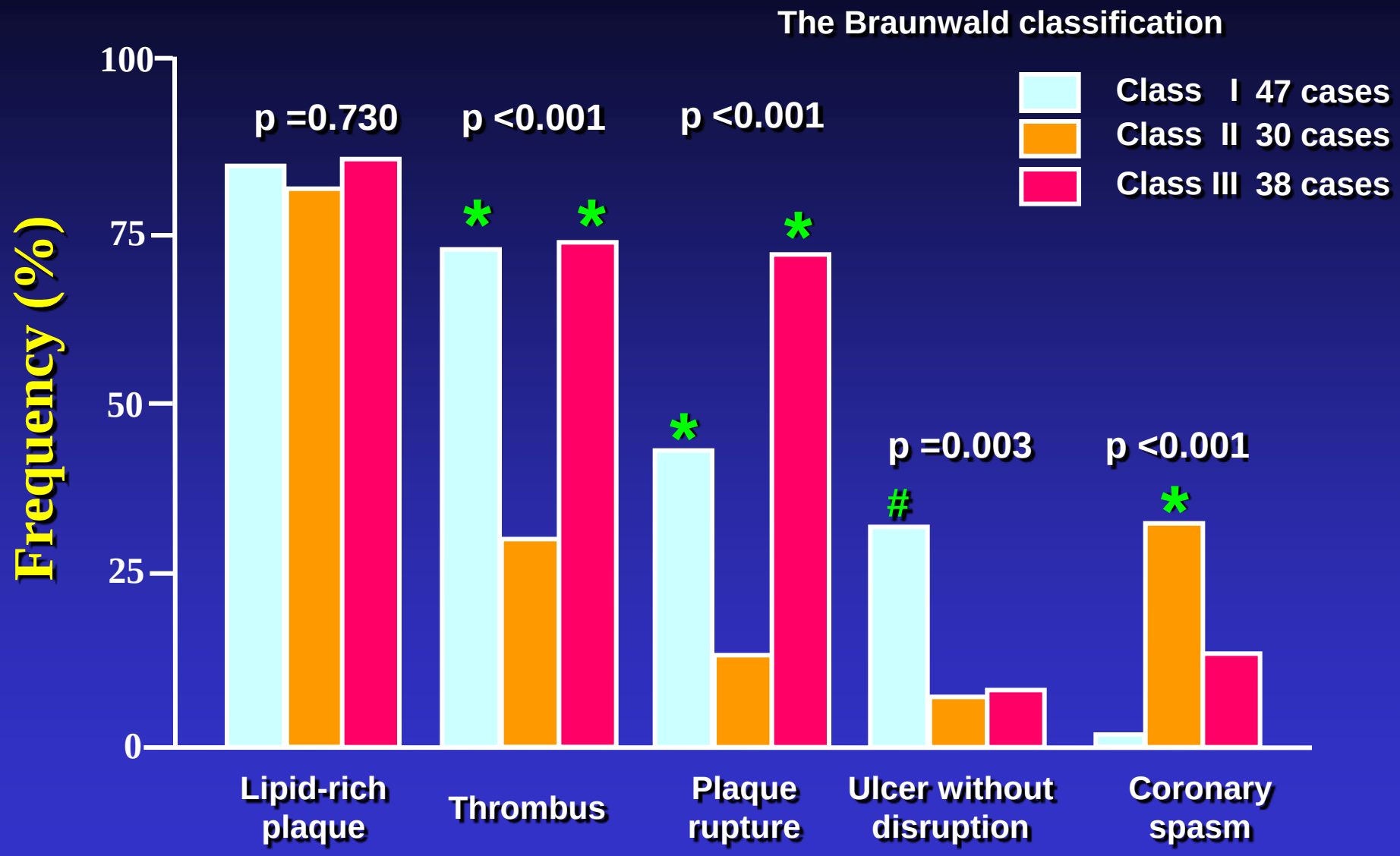
Class II



Class III

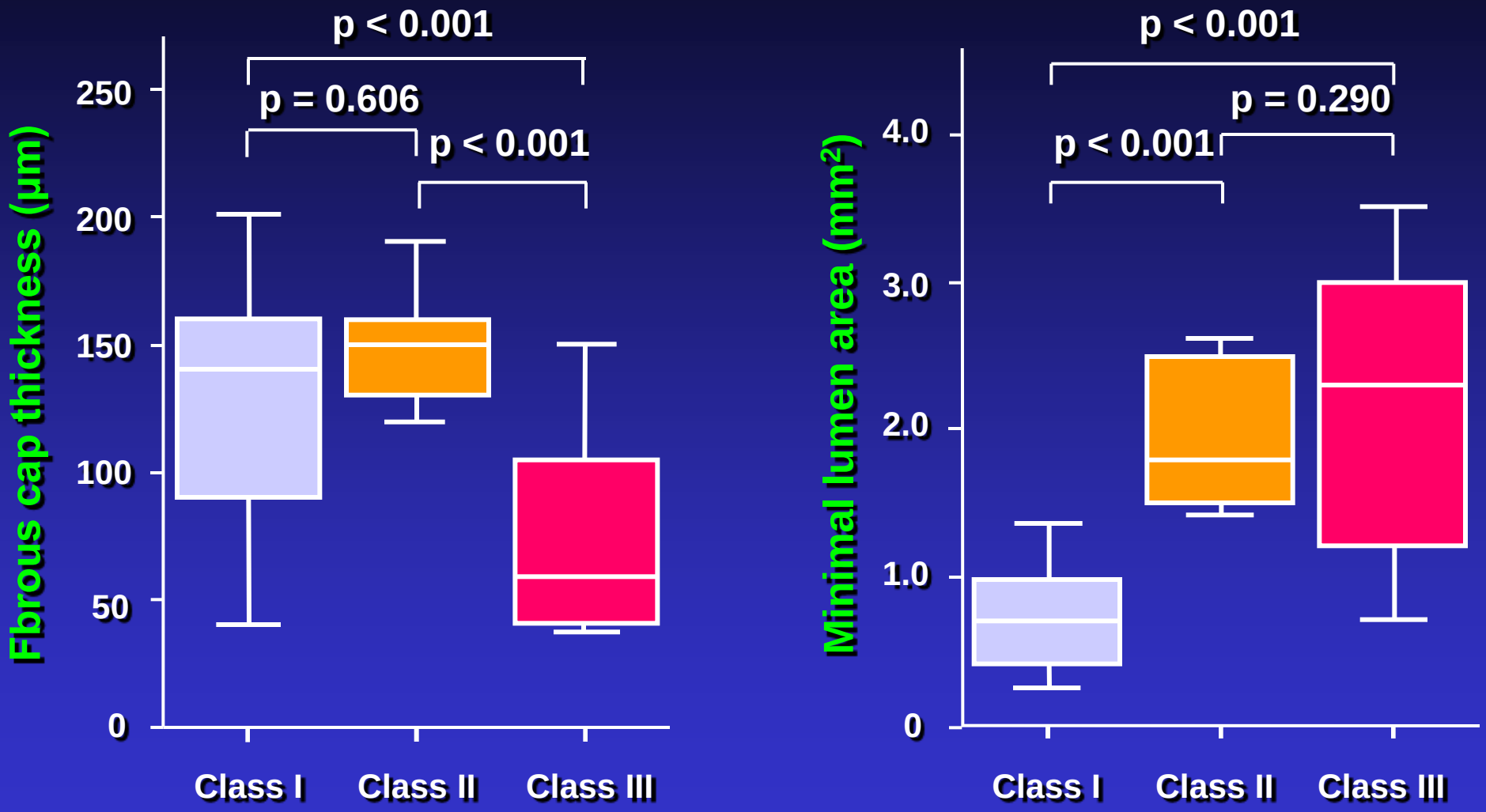
（Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328 ）

OCT findings in 115 cases with unstable AP



（Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328）

Clinical manifestation & Fibrous cap thickness, MLA of the culprit lesion

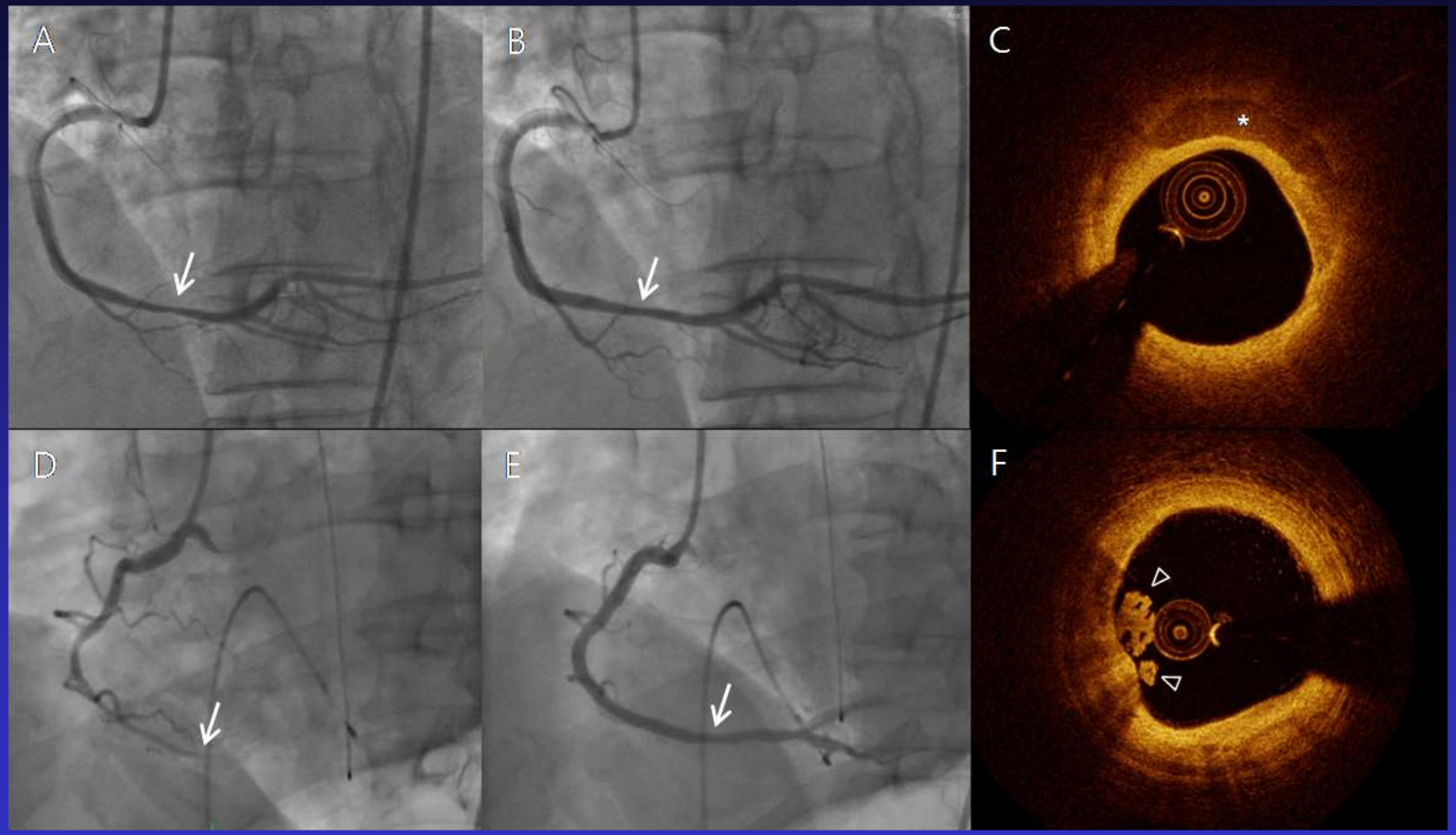


（Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328）

OCT findings at the target lesions in cases with & without vasospasm

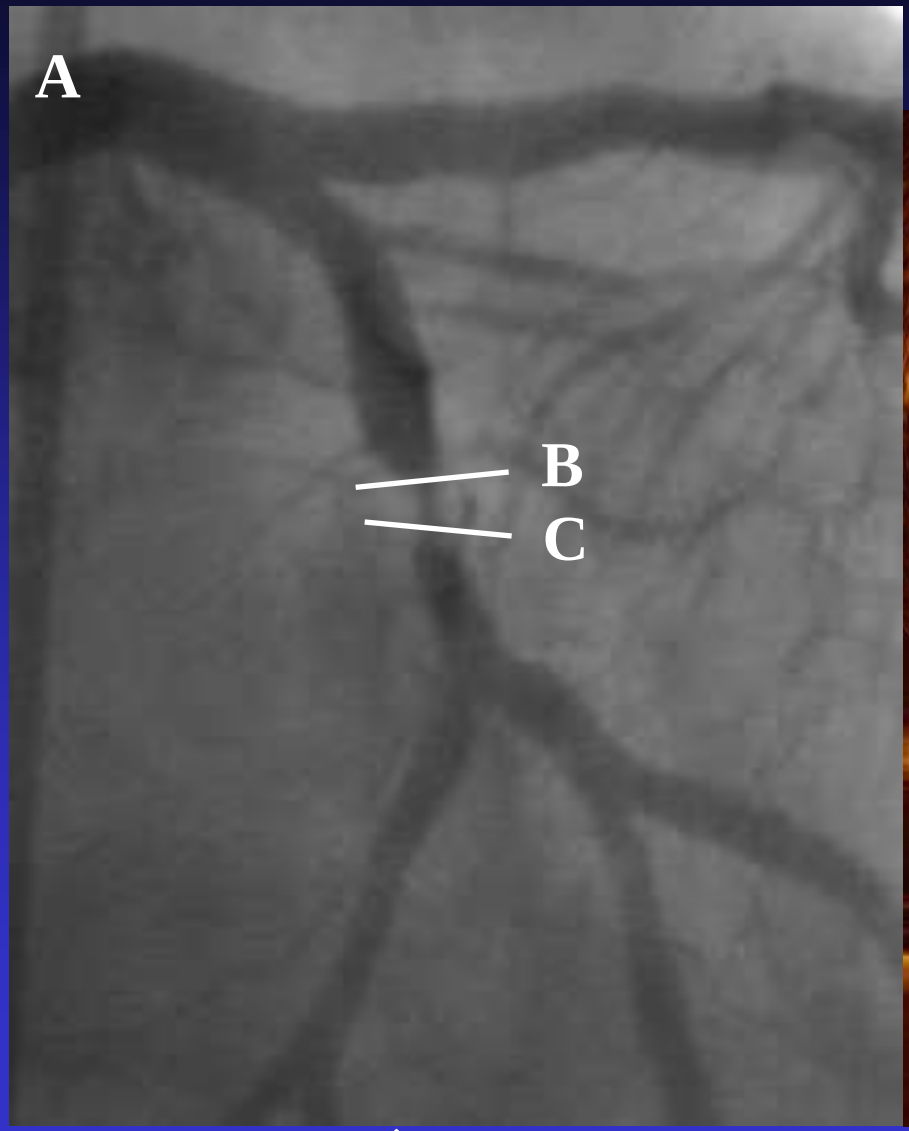
Vasospasm (-)

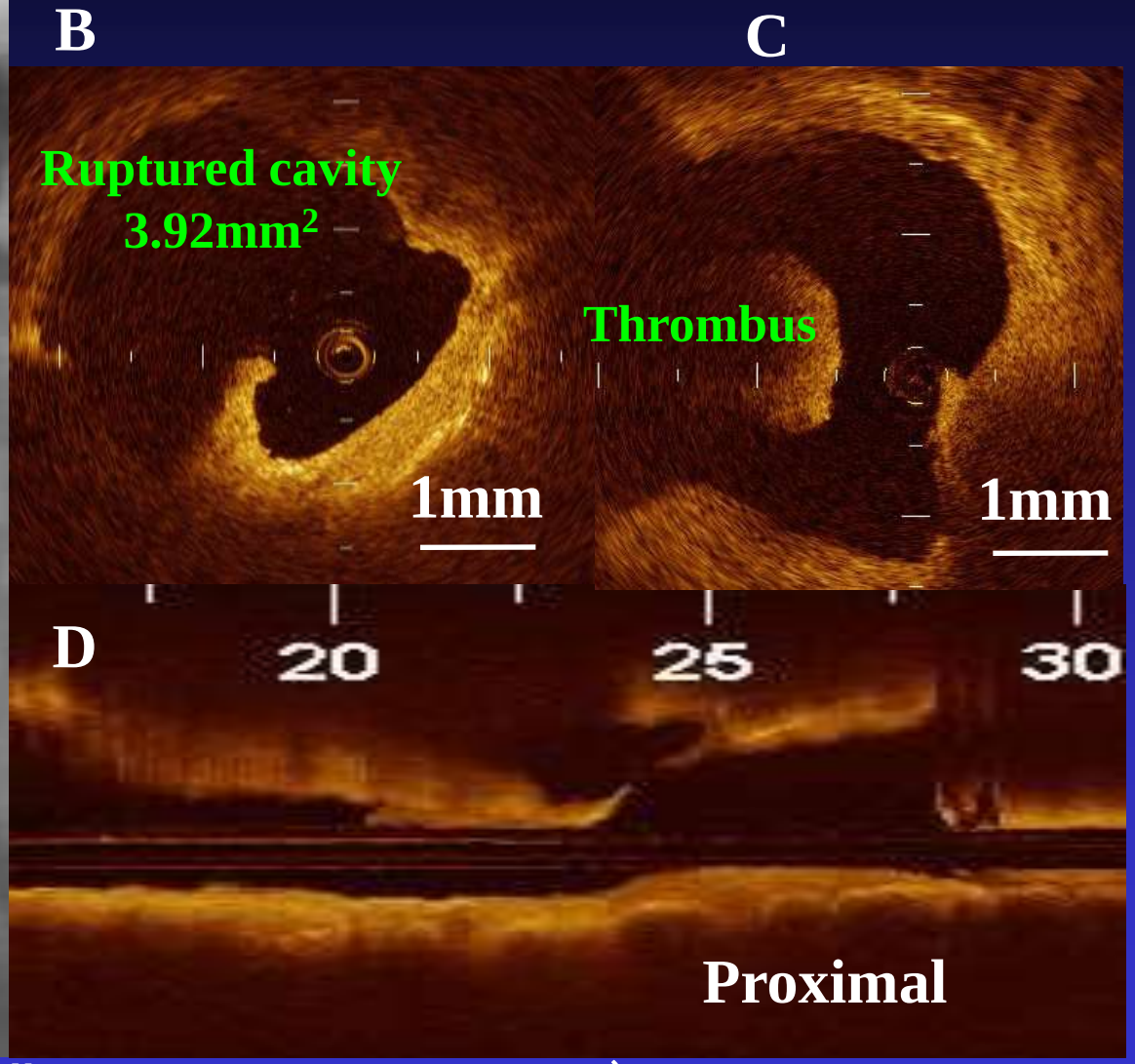
Vasospasm (+)



Shin ES, et al. J Am Coll Cardiol Cardiovasc Imag 2015 (in press)

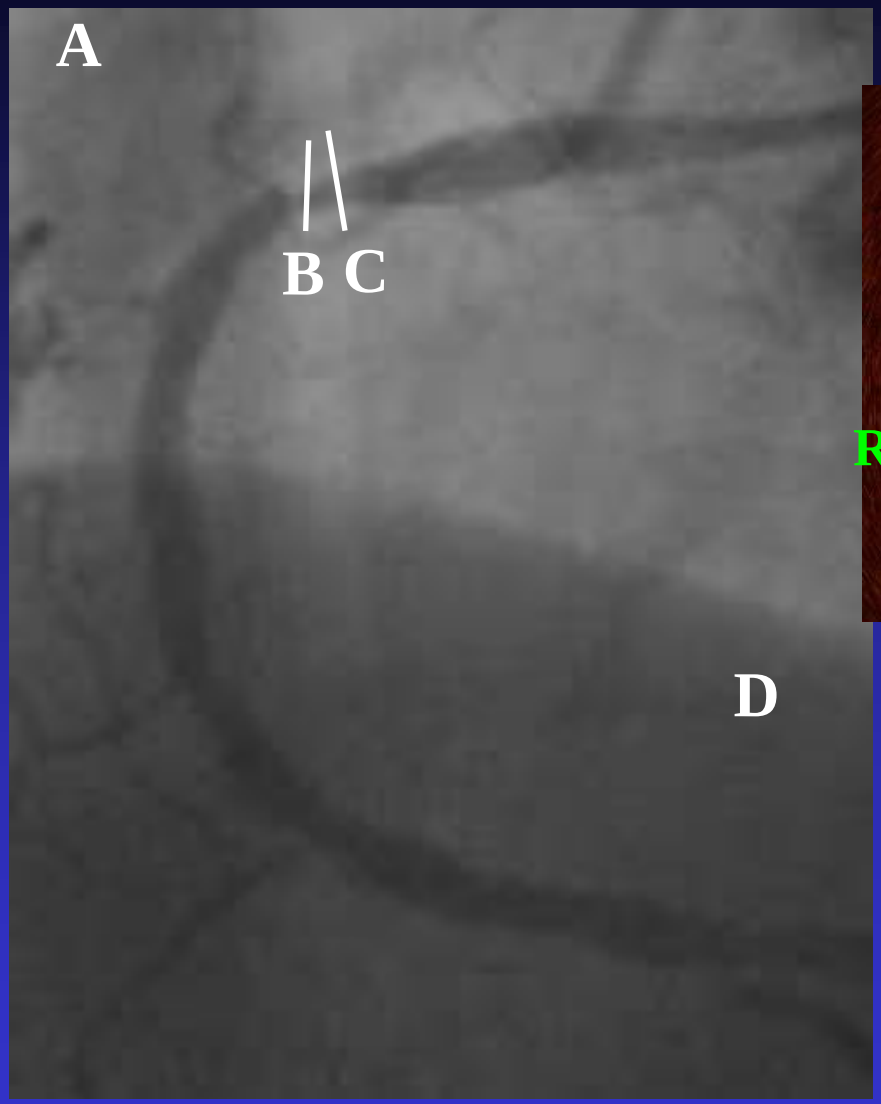
OCT Findings of Ruptured Plaque in STEMI

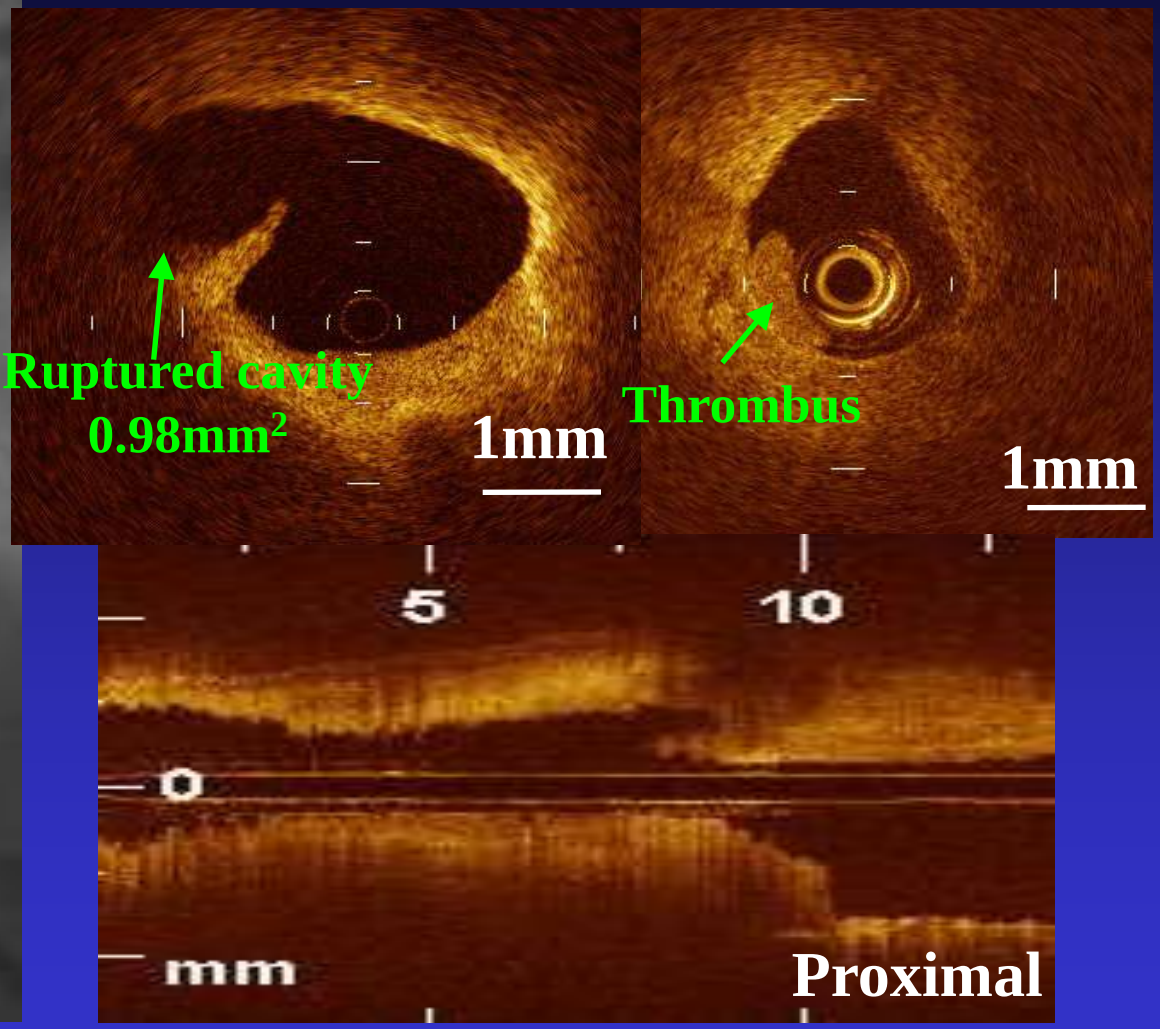




（Ino Y, et al. JACC Cardiovasc Interv. 2011;4:76-82）

OCT Findings of Ruptured Plaque in NSTEMI (UAP)





（Ino Y, et al. JACC Cardiovasc Interv. 2011;4:76-82）

OCT Findings of Culprit Lesions

	STEMI (n=40)	NSTEACS (n=49)	p value
Plaque rupture, n(%)	28(70)	23(47)	0.033
Lipid-rich plaque (>=2 quadrants), n(%)	36(90)	35(71)	0.036
Fibrous cap thickness, μm	55±20	109±55	<0.0001
TCFA, n(%)	31(78)	24(49)	0.008
Thrombus, n(%)			<0.0001
Red thrombus	31(78)	13(27)	
White thrombus	9(22)	20(41)	
None	0(0)	16(32)	

（Ino Y, et al. JACC Cardiovasc Interv. 2011;4:76-82）

OCT Findings of Ruptured Plaque

	STEMI (n=28)	NSTEACS (n=23)	P value
Maximum ruptured cavity CSA, mm^2	2.52±1.36	1.67±1.37	0.034
Lumen CSA at maximum ruptured cavity site, mm^2	2.44±1.34	2.96±1.91	0.250
Minimum lumen CSA, mm^2	1.95±0.80	1.88±0.86	0.756
Longitudinal morphological features of plaque rupture, n(%)			0.036
Proximal-type	13(46)	4(17)	
Mid-type	12(43)	11(48)	
Distal-type	3(11)	8(35)	

（Ino Y, et al. JACC Cardiovasc Interv. 2011;4:76-82）

Difference of ruptured plaque morphology between asymptomatic coronary artery disease and non-ST elevation acute coronary syndrome patients: An optical coherence tomography study

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Non-ST elevation acute coronary syndrome

ABSTRACT

Background: Autopsy studies have reported that rupture of a thin-cap fibroatheroma and subsequent thrombus formation is the major mechanism leading to acute coronary syndrome (ACS). However, it is not clear why only some plaque ruptures lead to ACS. Optical coherence tomography (OCT) is a high-resolution imaging modality which is capable of investigating detailed coronary plaque morphology in vivo. The objective of this study was to determine whether ruptured plaque morphology assessed by OCT differs between asymptomatic coronary artery disease (CAD) and non-ST elevation acute coronary syndrome (NSTEACS).

Methods: We examined ruptured plaque morphology using OCT in 80 patients, 33 with asymptomatic CAD and 47 with NSTEACS.

Results: The frequency of lipid-rich plaque and intracoronary thrombus was significantly lower in asymptomatic CAD than in NSTEACS (61% vs. 85%, $p = 0.013$ and 9% vs. 83%, $p < 0.001$, respectively). Although maximal ruptured cavity cross-sectional area (CSA) was similar in both groups, lumen area at the rupture site and minimal lumen area were significantly larger in asymptomatic CAD than in NSTEACS (3.78 ± 1.50 mm^2 vs. 2.70 ± 1.55 mm^2, $p = 0.003$ and 2.75 ± 0.99 mm^2 vs. 1.72 ± 0.90 mm^2, $p < 0.001$, respectively).

Conclusions: OCT revealed that the morphology of ruptured plaques differs between asymptomatic CAD and NSTEACS in terms of lumen area and the frequency of lipid-rich plaques and thrombi. These morphological features may be associated with the clinical presentation of CAD.

Table 3

OCT findings of target lesions.

	Asymptomatic CAD ($n = 33$)	NSTEACS ($n = 47$)	p-Value
Lipid-rich plaque, n (%)	22 (67)	40 (85)	0.013
Lipid arc, degree	133 ± 71	169 ± 71	0.031
Thrombus, n (%)	3 (9)	39 (83)	<0.001
Red thrombus, n (%)	0 (0)	15 (32)	<0.001
White thrombus, n (%)	3 (9)	24 (51)	<0.001
Ruptured cap thickness, μm	69 ± 24	62 ± 22	0.165
Maximal ruptured cavity area, mm^2	1.63 ± 0.86	1.66 ± 1.35	0.884
Lumen area at rupture site, mm^2	3.78 ± 1.50	2.70 ± 1.55	0.003
MLA, mm^2	2.75 ± 0.99	1.72 ± 0.90	<0.001
Location of maximum ruptured cavity			0.380
Proximal to the MLA site, n (%)	9 (27)	10 (21)	
MLA site, n (%)	11 (33)	23 (49)	
Distal to the MLA site, n (%)	13 (40)	14 (30)	

Values are given as n (%) or mean ± standard deviation. CAD = coronary artery disease; MLA = minimal lumen area; NSTEACS = non-ST elevation acute coronary syndrome.

Table 4

OCT findings of target lesions after excluding patients with thrombus aspiration.

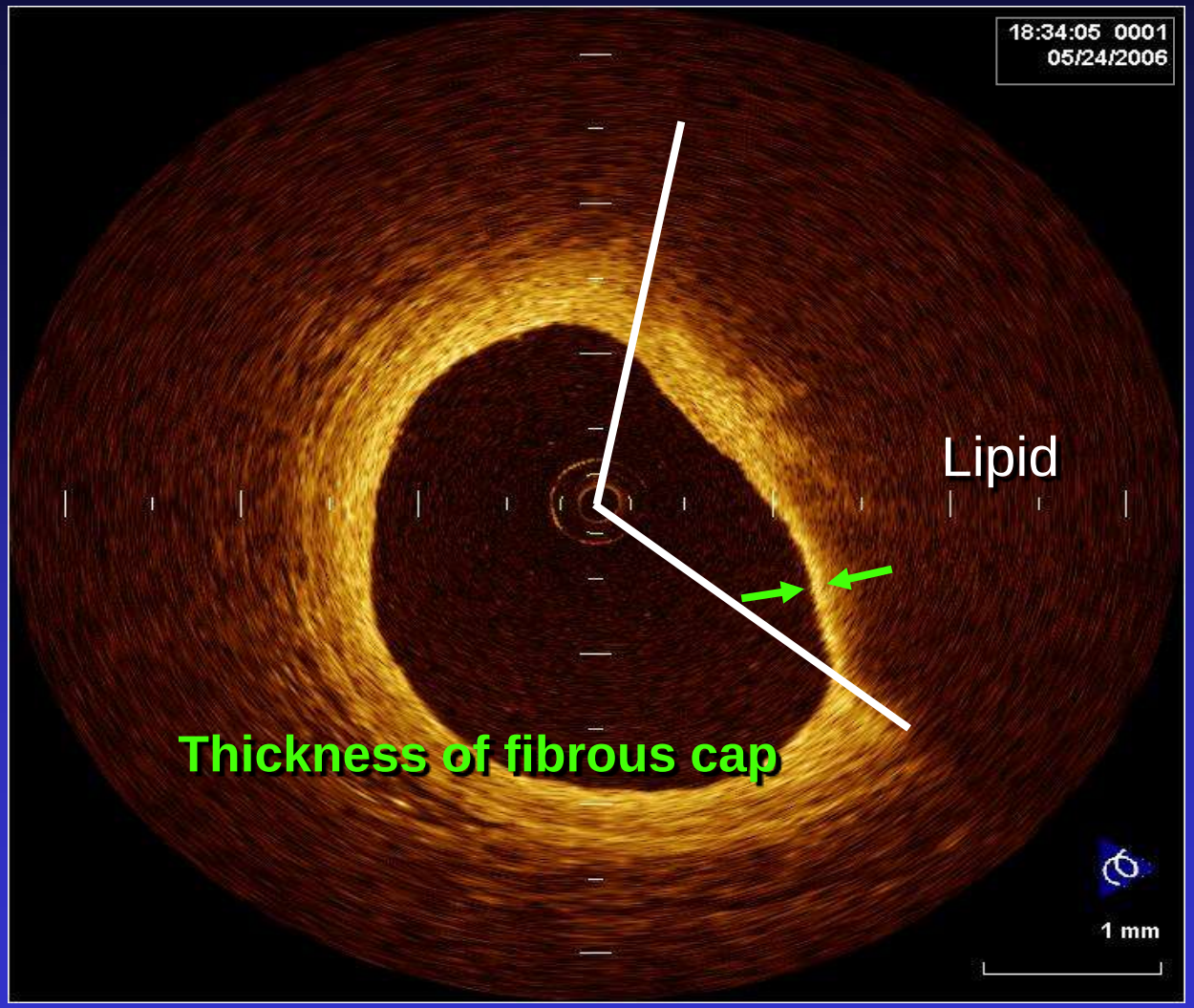
	Asymptomatic CAD ($n = 33$)	NSTEACS ($n = 32$)	p-Value
Lipid-rich plaque, n (%)	22 (67)	28 (88)	0.046
Lipid arc, degree	133 ± 71	171 ± 71	0.037
Thrombus, n (%)	3 (9)	25 (78)	<0.001
Red thrombus, n (%)	0 (0)	9 (28)	<0.001
White thrombus, n (%)	3 (9)	16 (50)	<0.001
Ruptured cap thickness, μm	69 ± 24	60 ± 23	0.142
Maximal ruptured cavity area, mm^2	1.63 ± 0.86	1.79 ± 1.43	0.573
Lumen area at rupture site, mm^2	3.78 ± 1.50	2.76 ± 1.58	0.009
MLA, mm^2	2.75 ± 0.99	1.79 ± 0.92	<0.001
Location of maximum ruptured cavity			0.538
Proximal to the MLA site, n (%)	9 (27)	7 (22)	
MLA site, n (%)	11 (33)	15 (47)	
Distal to the MLA site, n (%)	13 (40)	10 (31)	

Values are given as n (%) or mean ± standard deviation. CAD = coronary artery disease; MLA = minimal lumen area; NSTEACS = non-ST elevation acute coronary syndrome.

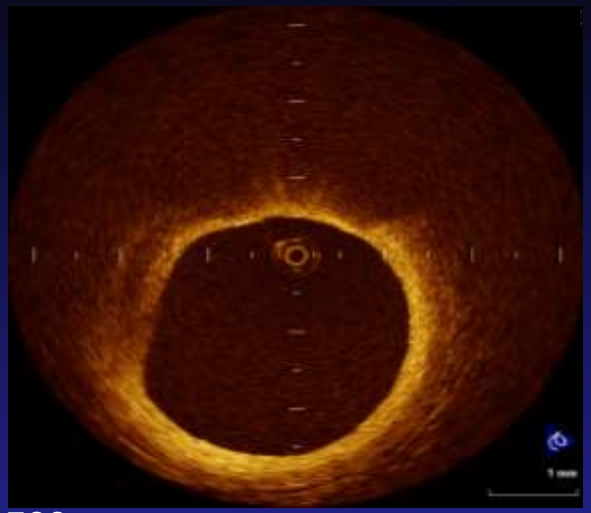
Thin-capped Fibroatheroma (TCFA)

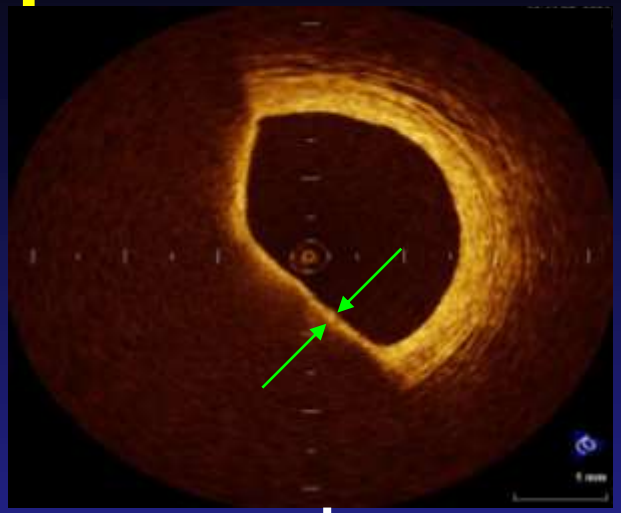
The TCFA was defined as a plaque with lipid content in more than 2 quadrants and the thinnest part of a fibrous cap measuring less than 65 μm by histology.

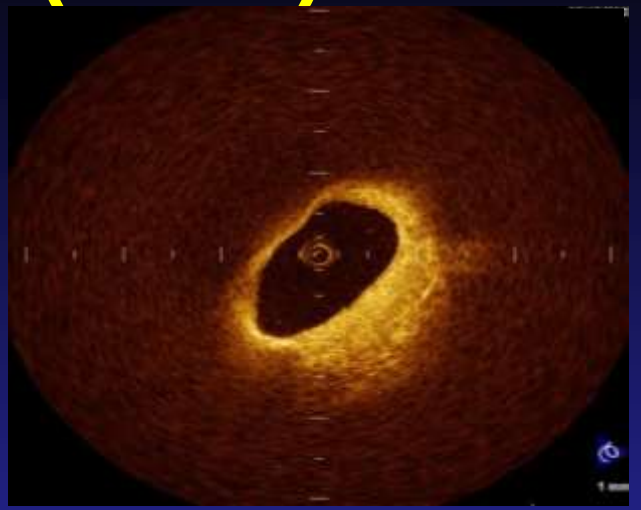
The cap thickness is measured from the surface of the lumen to the portion just starting the attenuation

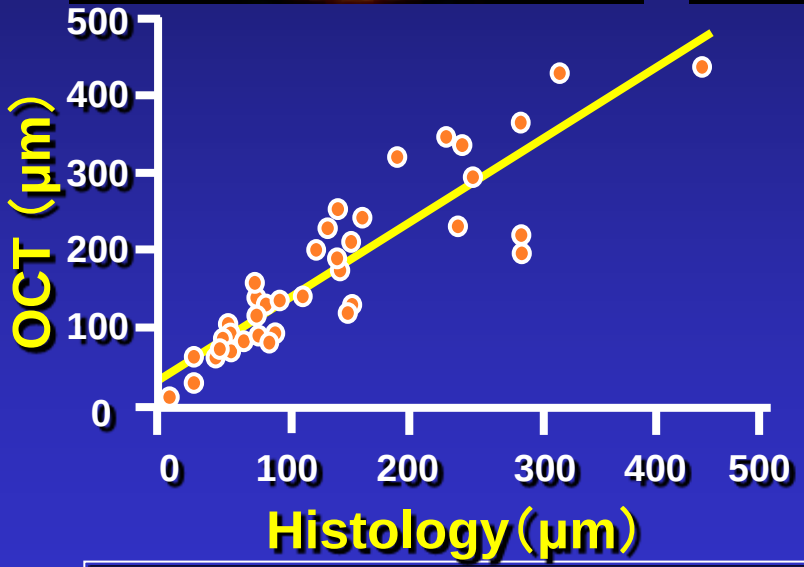


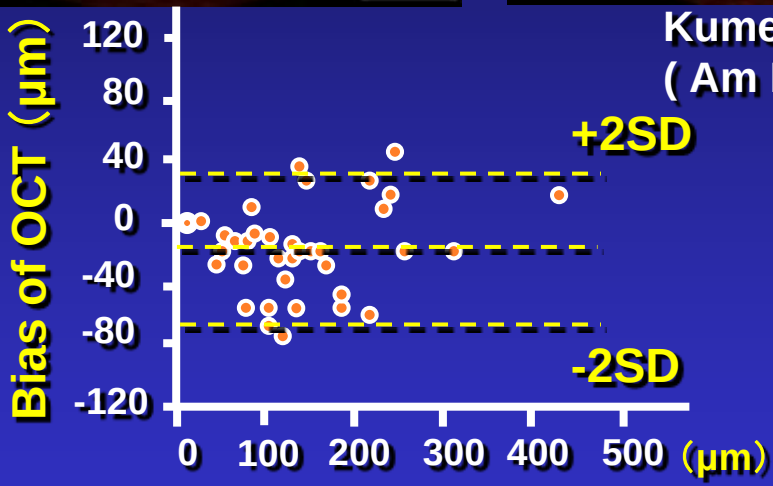
Thin-cap fibroatheroma (TCFA)









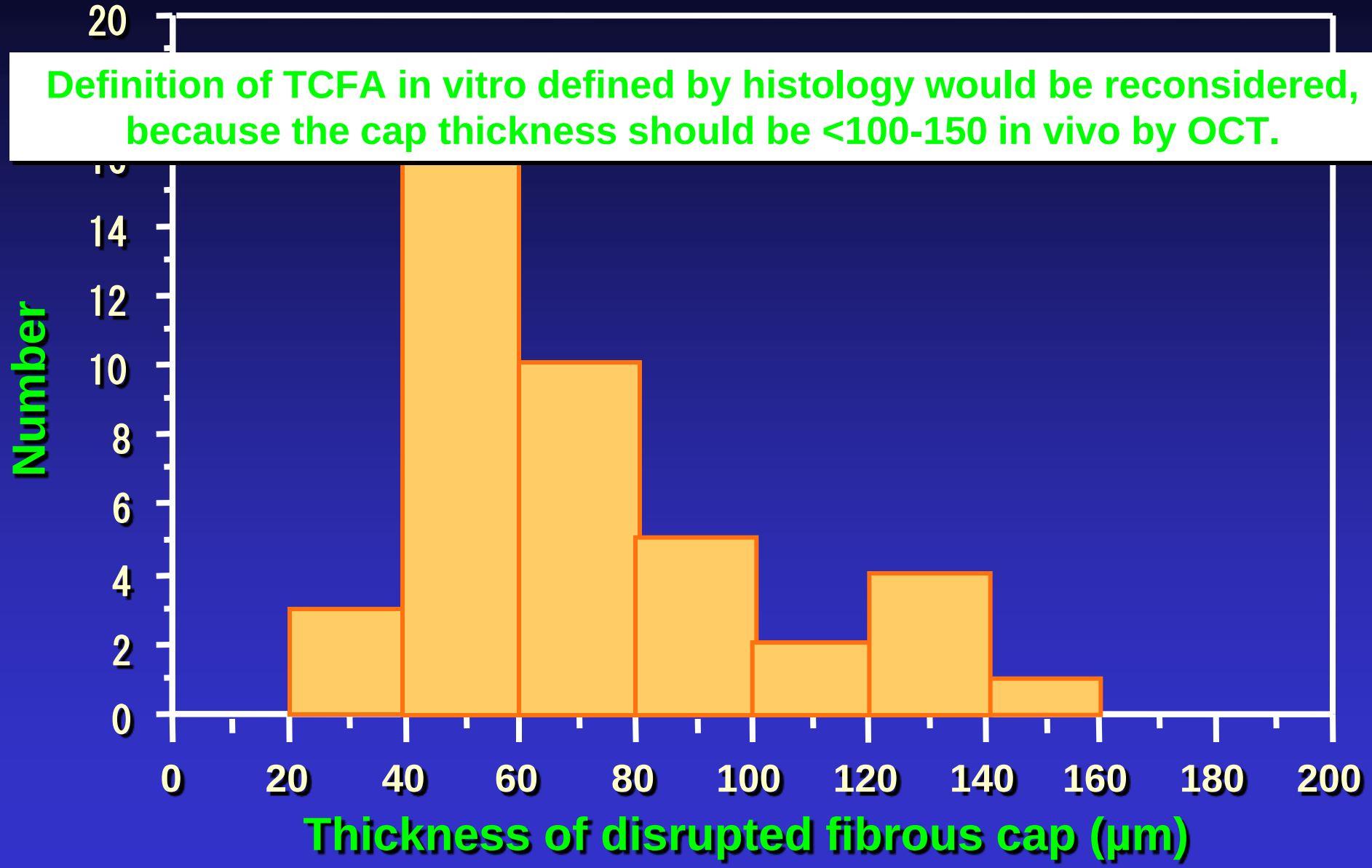


Kume T, Akasaka T, et al
(Am Heart J.152:755, 2006)

TCFA is demonstrated by the thin high intensity layer with rapid attenuation of the signals, and the cap thickness is measured by the thickness from the surface of the lumen to the portion just starting the attenuation.

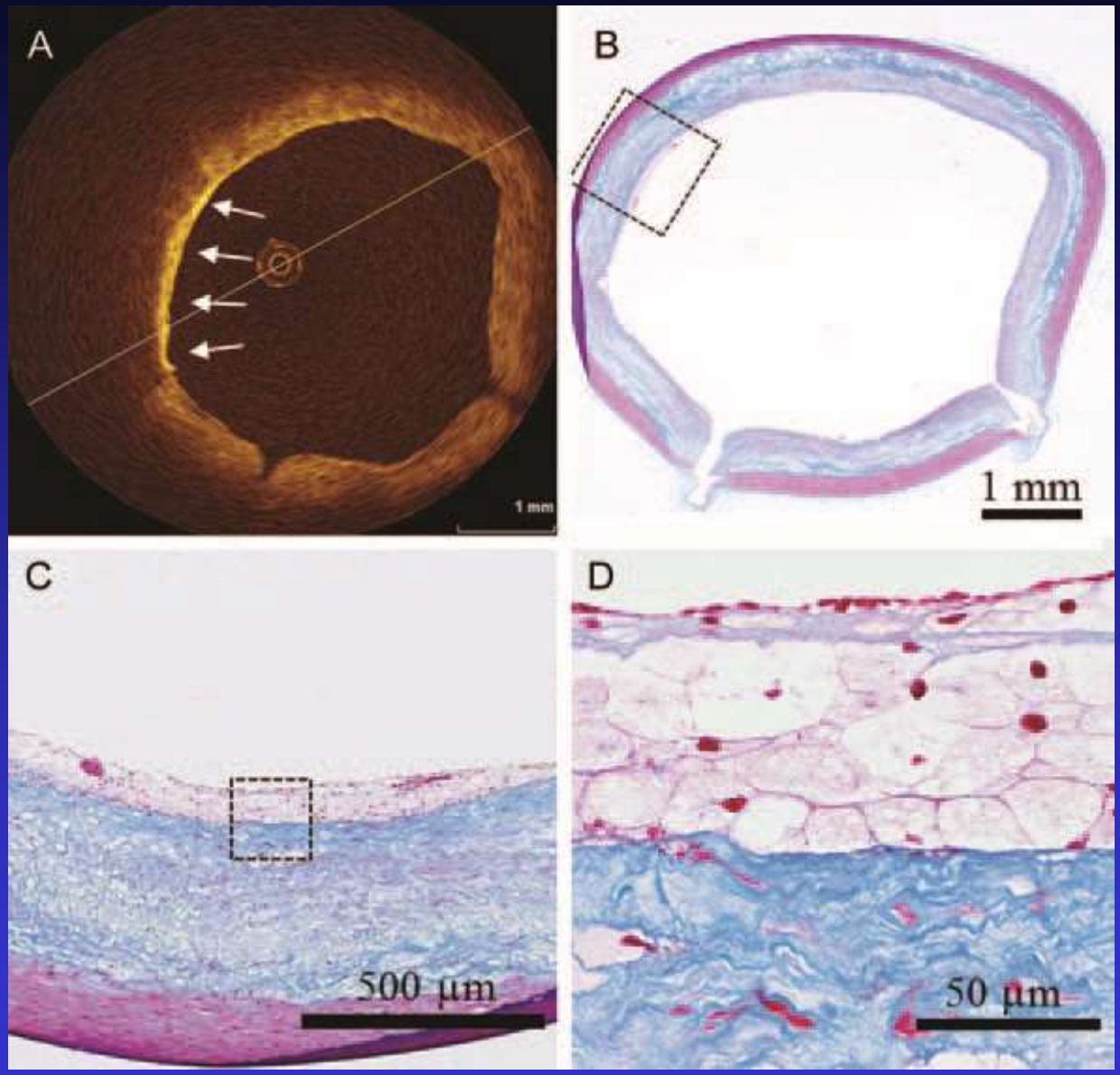
Distribution of disrupted fibrous-cap thickness

Definition of TCFA in vitro defined by histology would be reconsidered, because the cap thickness should be <100-150 in vivo by OCT.



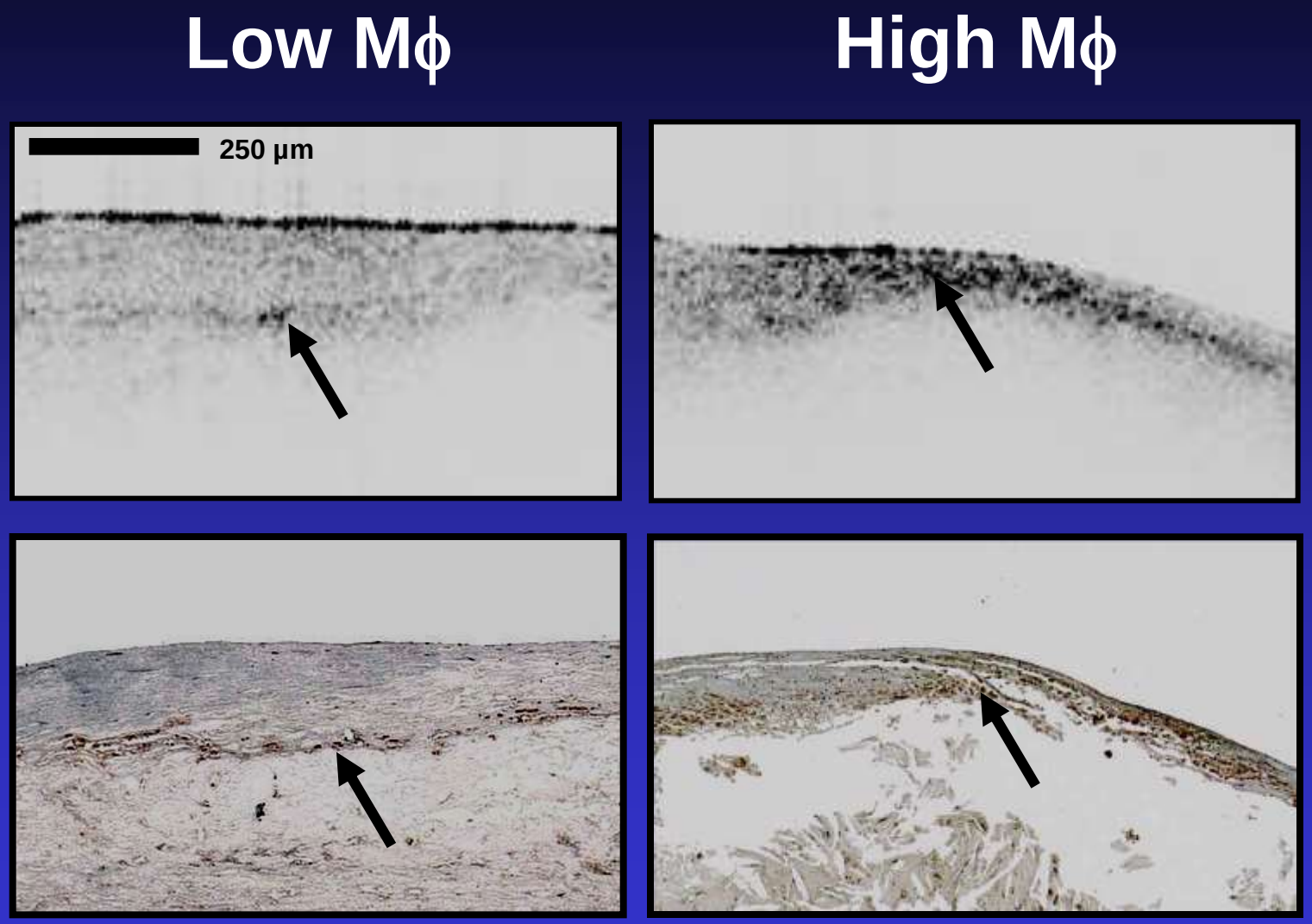
Tanaka A, et al. Circulation. 2008,118: 2368-2373

Identification of macrophage (fatty streak)



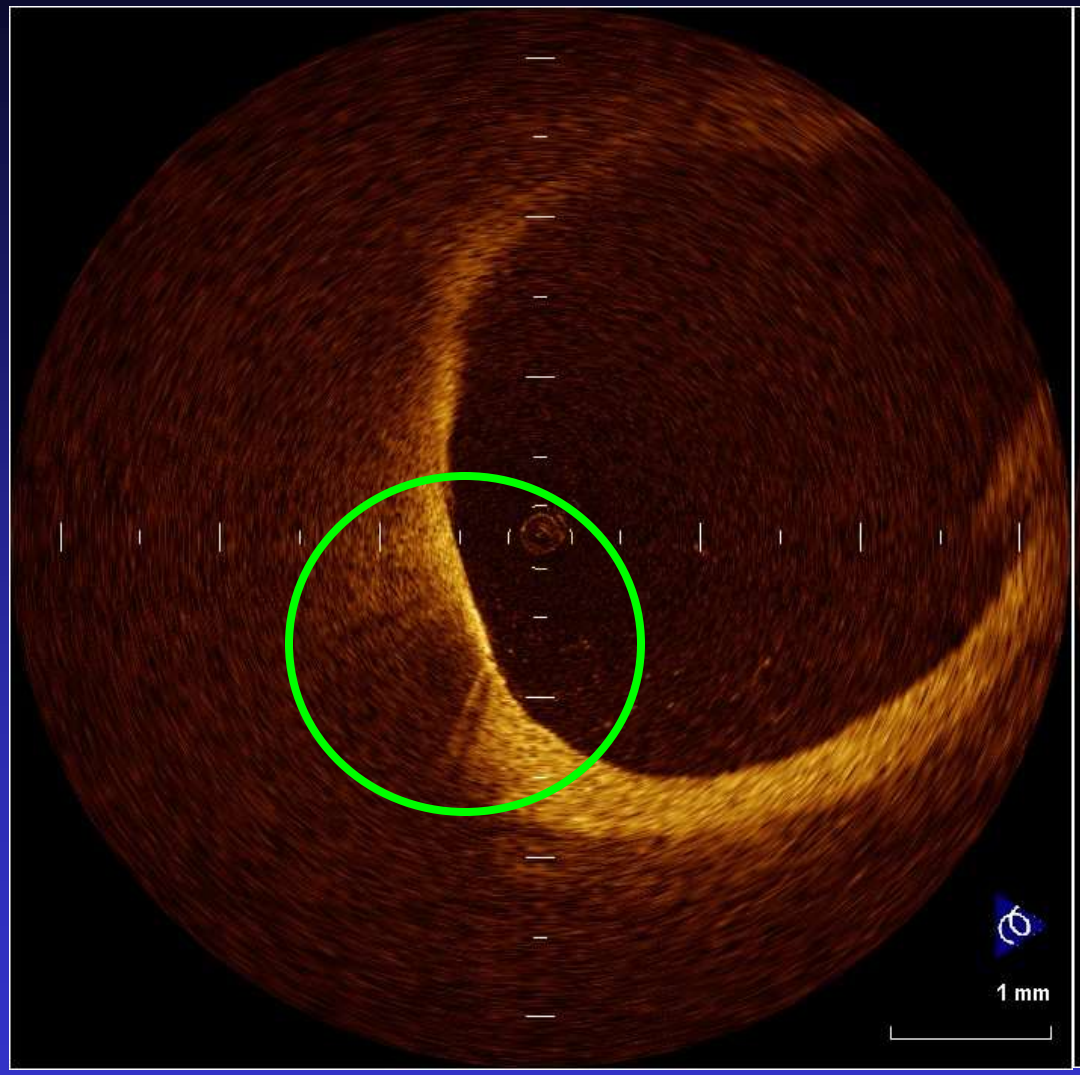
Kashiwagi M, et al. EHJ Cardiovasc Imag 2012

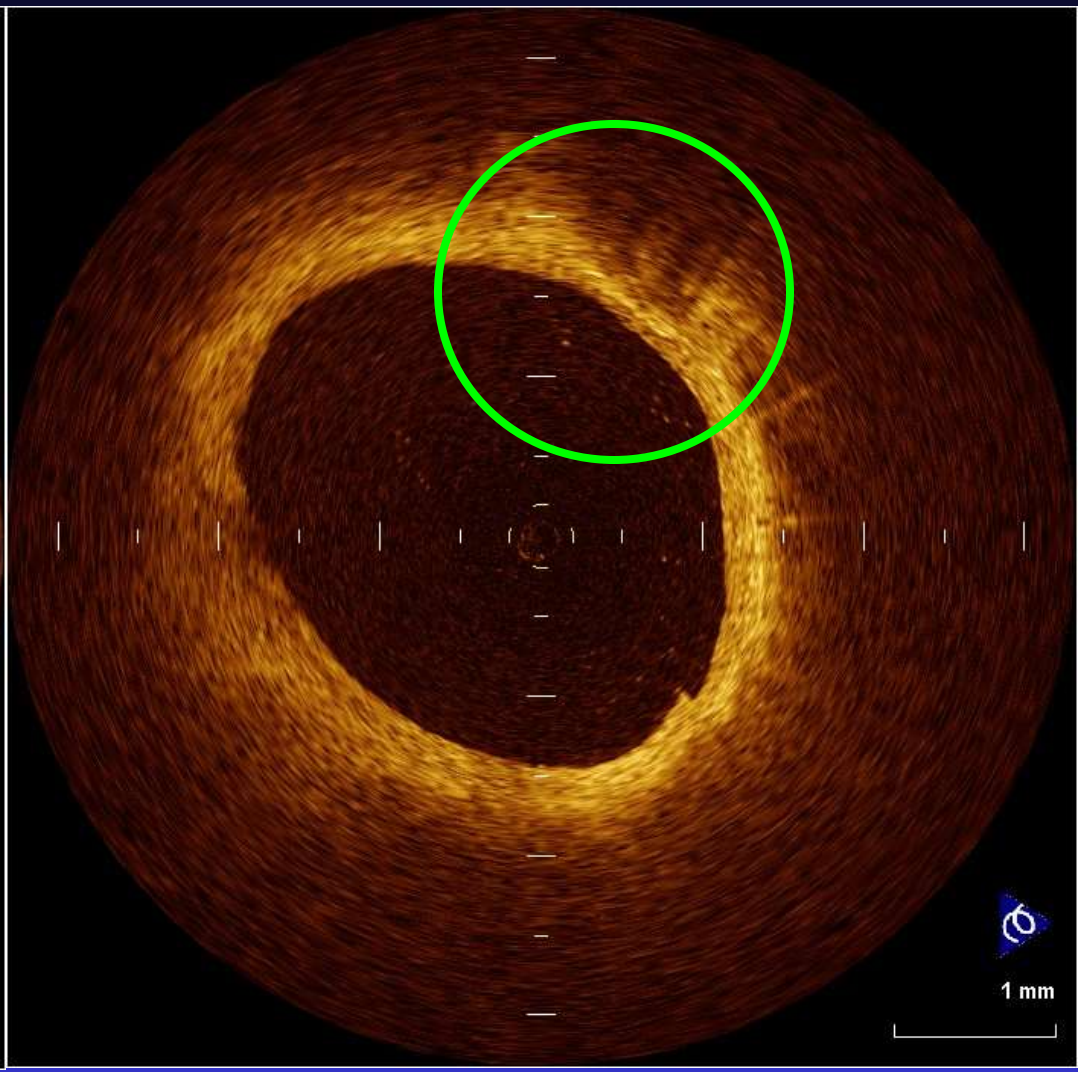
OCT findings of macrophages



Tearney GJ et al. Circulation, 107:113-119, 2003

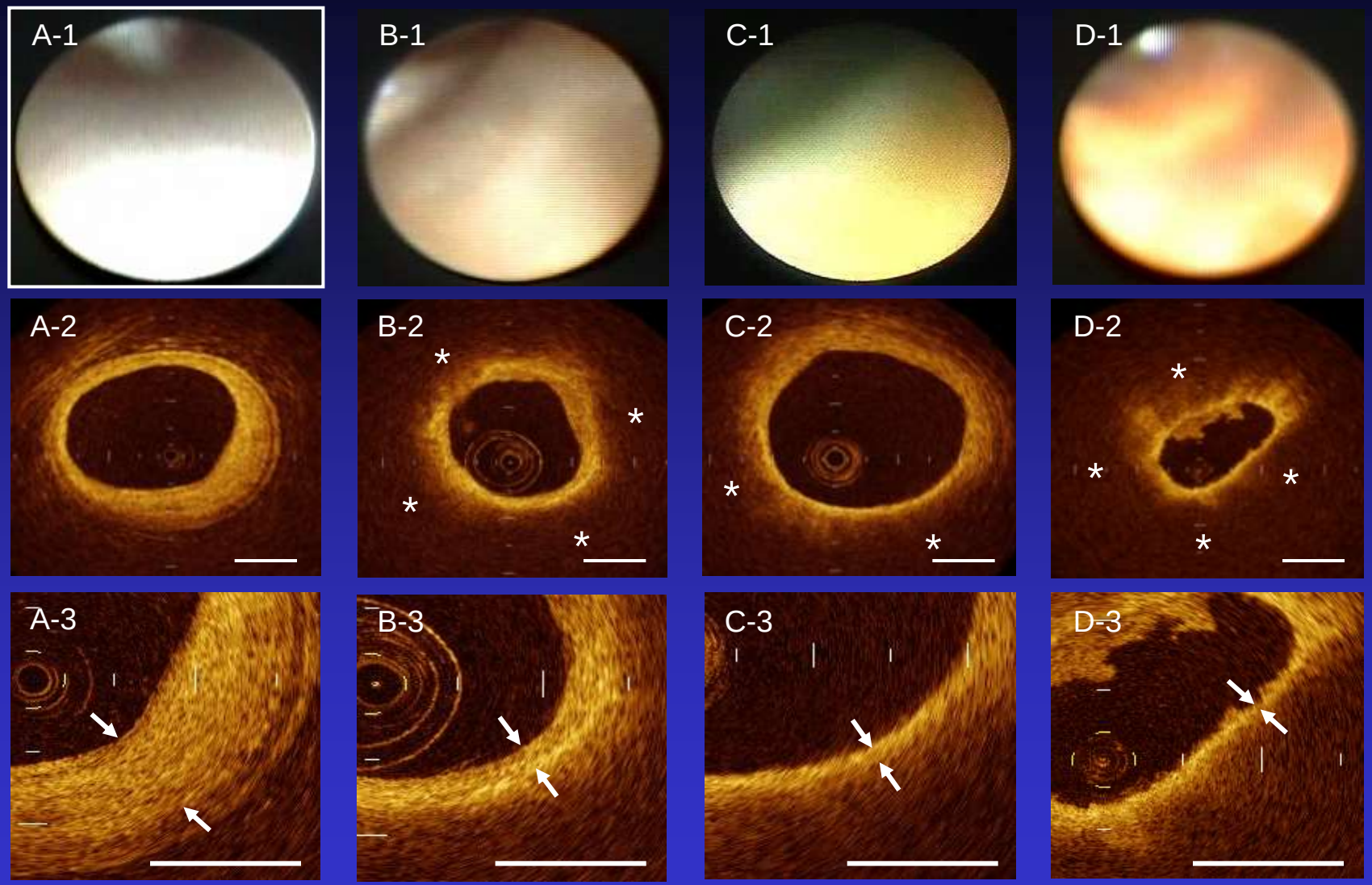
Identification of macrophage





Extremely high signal with rapid attenuation on the surface of the vessel wall or within fibrous tissue might demonstrate macrophage accumuration.

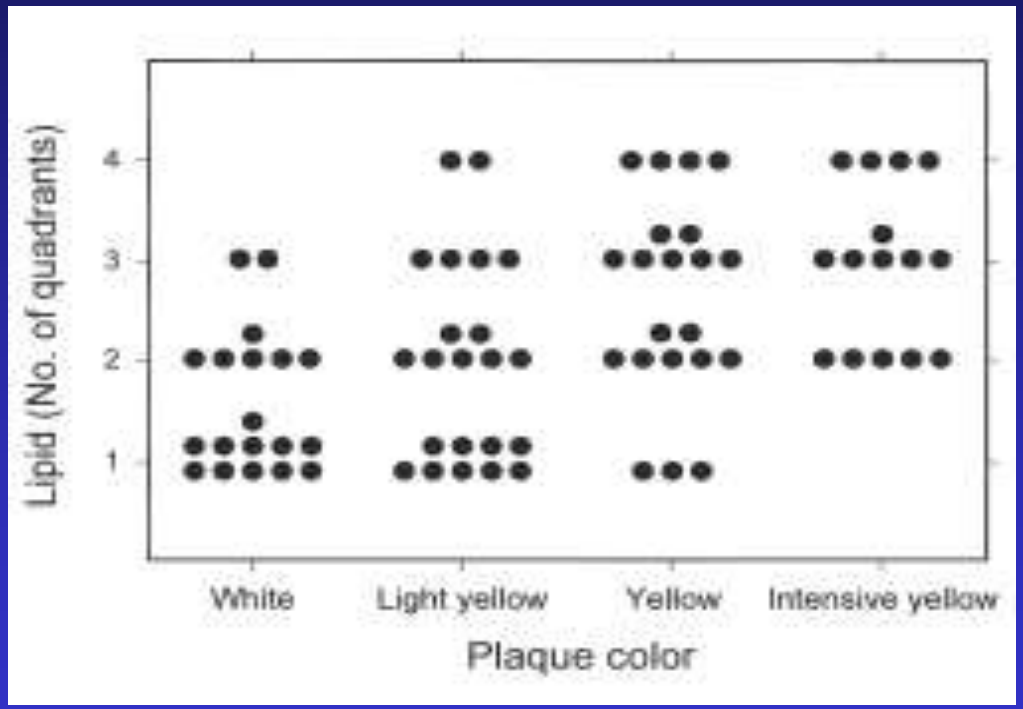
Corresponding Images of OCT and Angioscopy



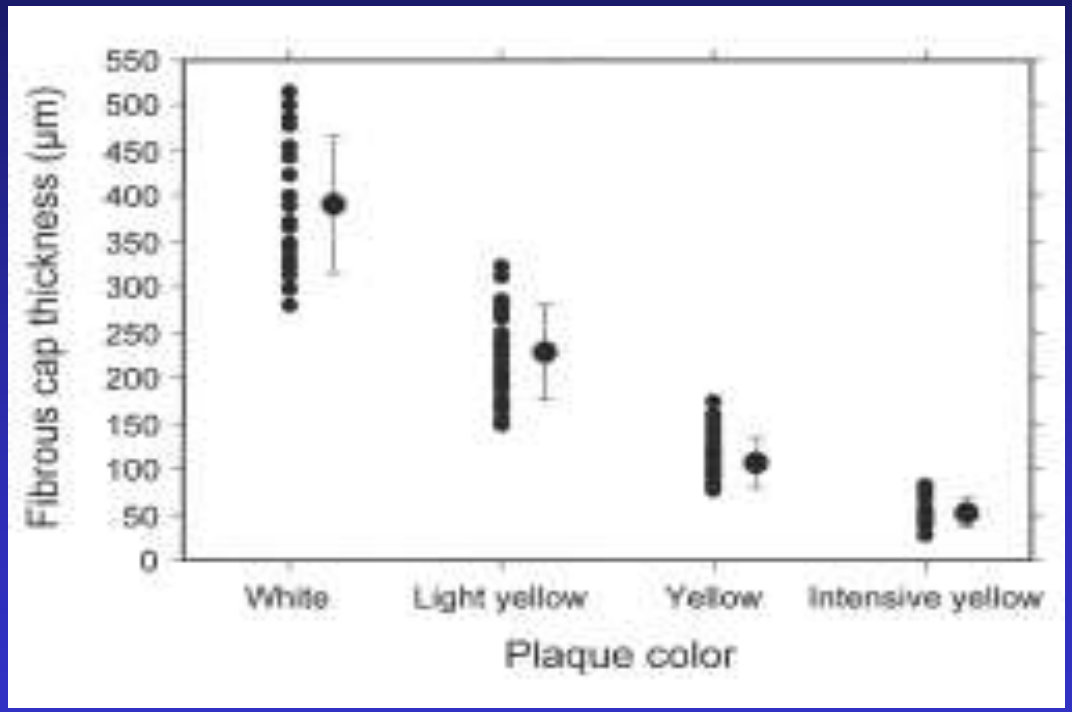
（Kubo T, et al. J Am Coll Cardiol Intv 1:74-80,2008）

Angioscopy vs OCT

Plaque color vs lipid size



Plaque color vs fibrous cap thickness



(Kubo T, et al. J Am Coll Cardiol Intv 1:74-80,2008)

Criteria for defining vulnerable plaque

(Naghavi M, et al. Circulation 2003;108:1664-1672)

Major criteria

- **Active inflammation (monocyte/macrophage and sometimes T-cell infiltration)**
- **Thin cap (< 65 μm) with large lipid core**
- **Endotherial denudation with superficial platelet aggregation**
- **Fissued plaque**
- **Stenosis > 90%**

Minor criteria

- **Superficial calcified nodule**
- **Glistening yellow**
- **Intraplaque hemorrhage**
- **Endotherial dysfunction**
- **Outward (positive) remodering**

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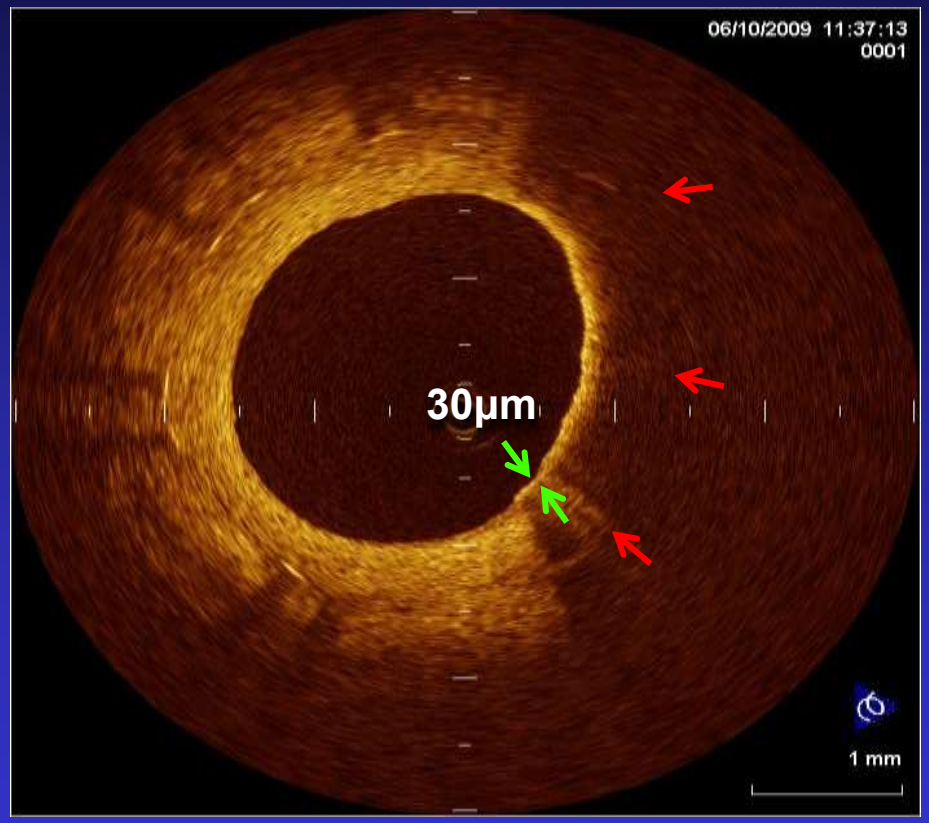
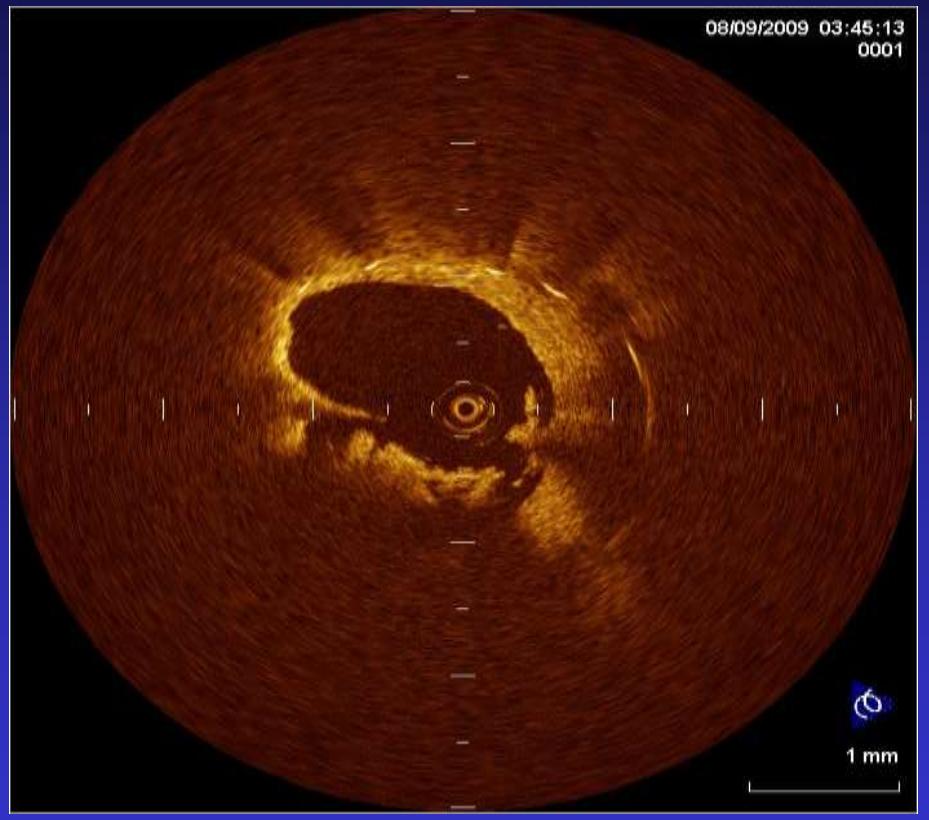
Representative OCT images of neoatherosclerosis within BMS

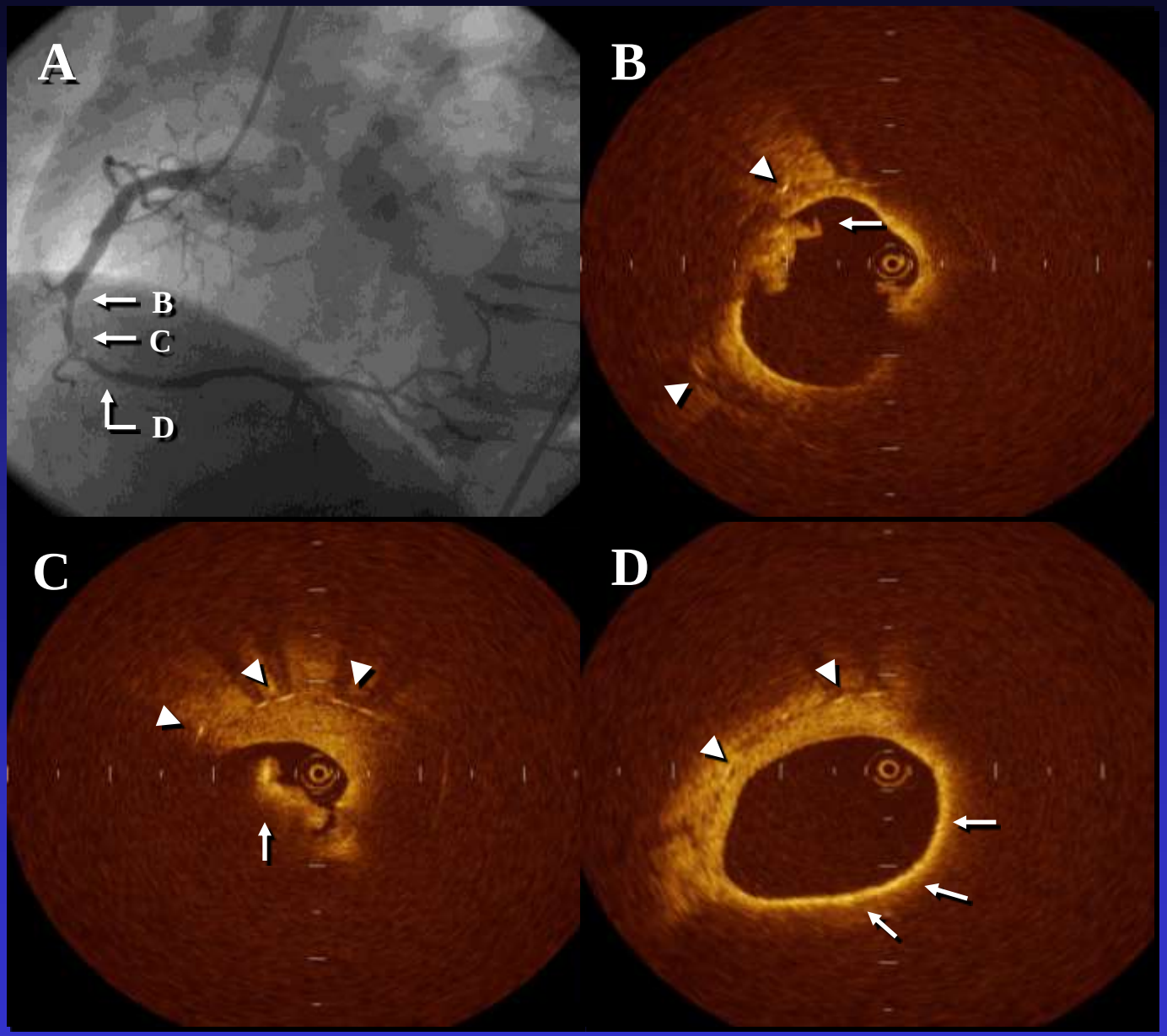


TCFA-like intima



Intimal disruption with thrombus

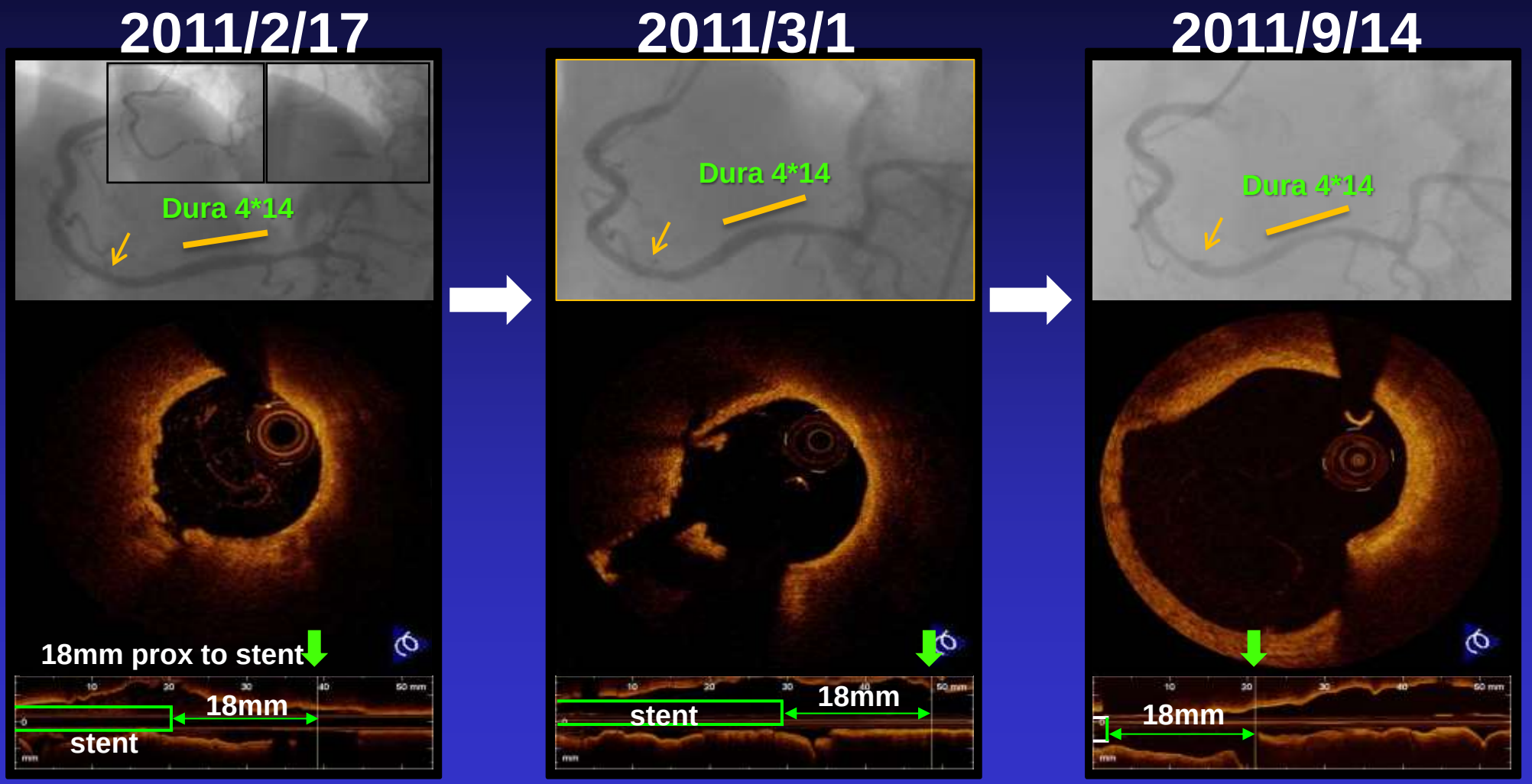
VLT in BMS (58 y.o. man)



- STEMI 7 yrs ago
- BMS to RCA. (3.0 × 18mm)
- Recurrent CP (NSTEMI)

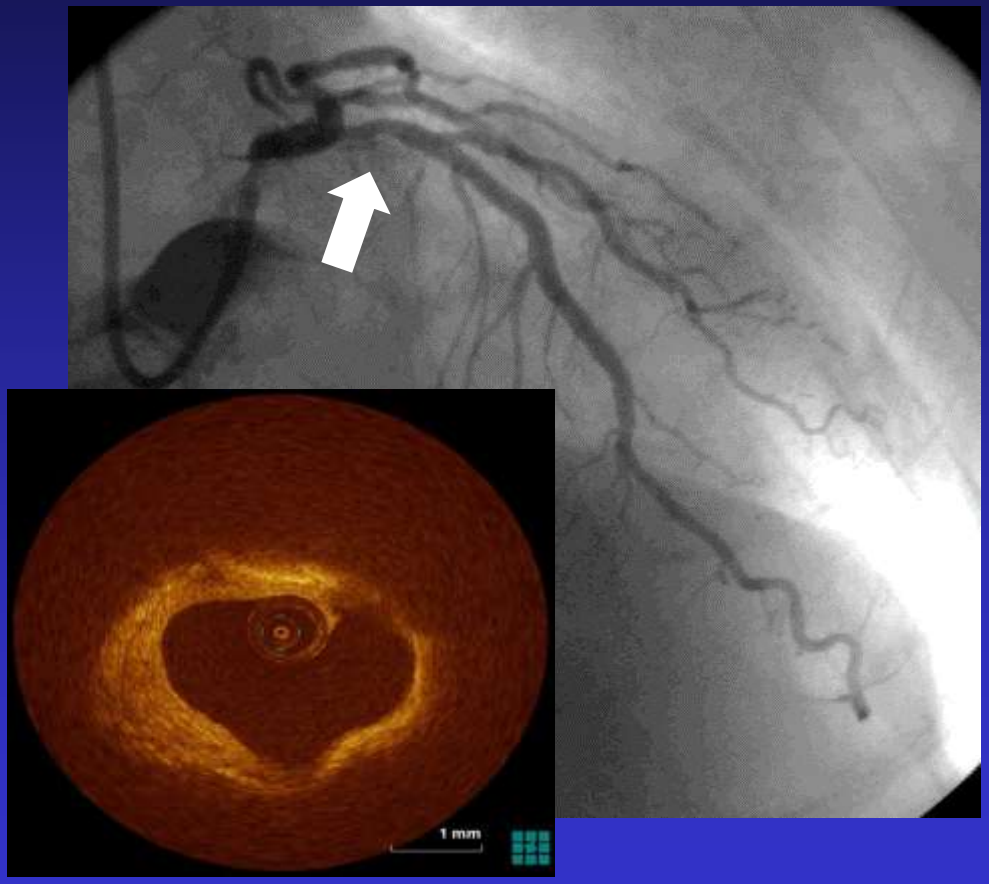
(Kashiwagi M, et al. JACC Imaging 2010;3: 525-527)

Plaque rupture; serial OCT

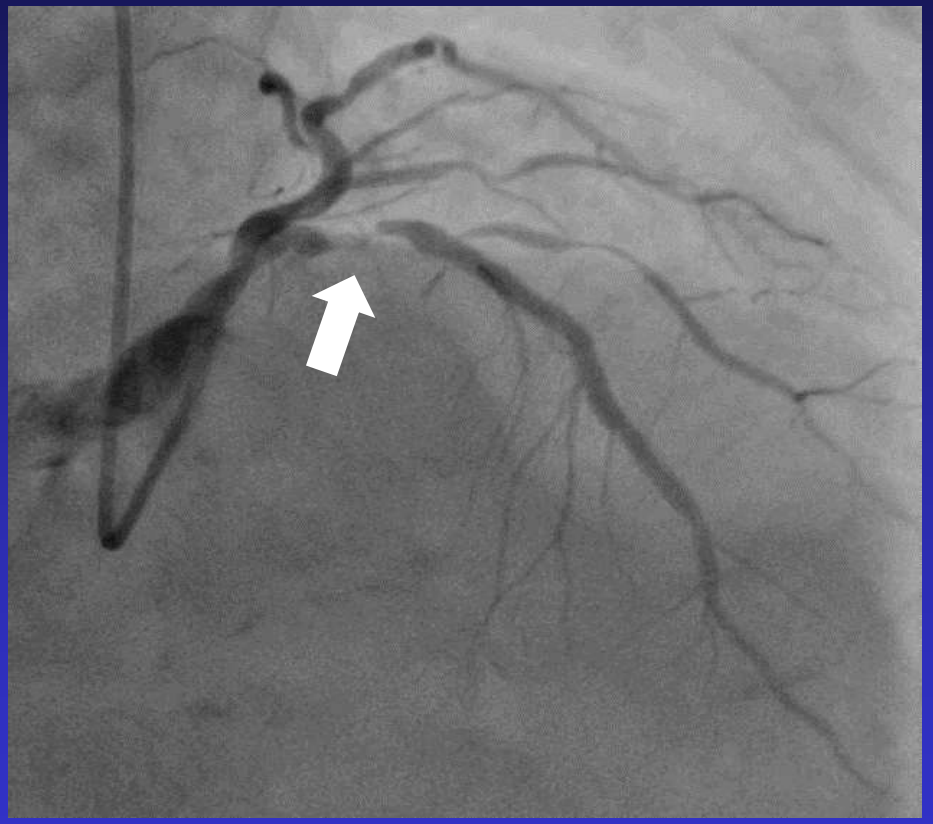


A Case developing NSTEMI during f/u of TCFA

2011/3/14



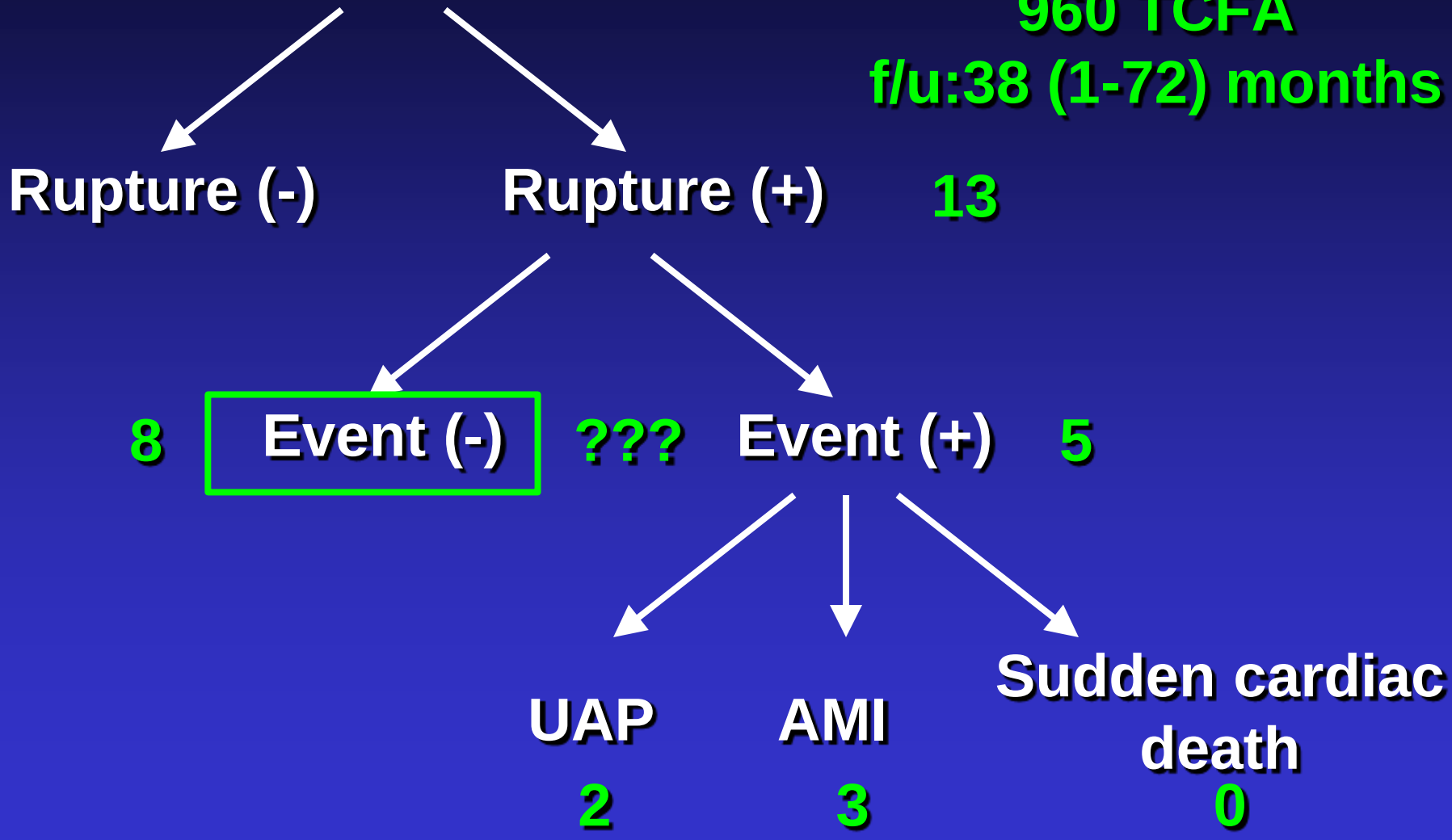
2013/6/7 *(2 years later)* ***NSTEMI***



Identification of vulnerable plaque

- Plaque prone to disruption

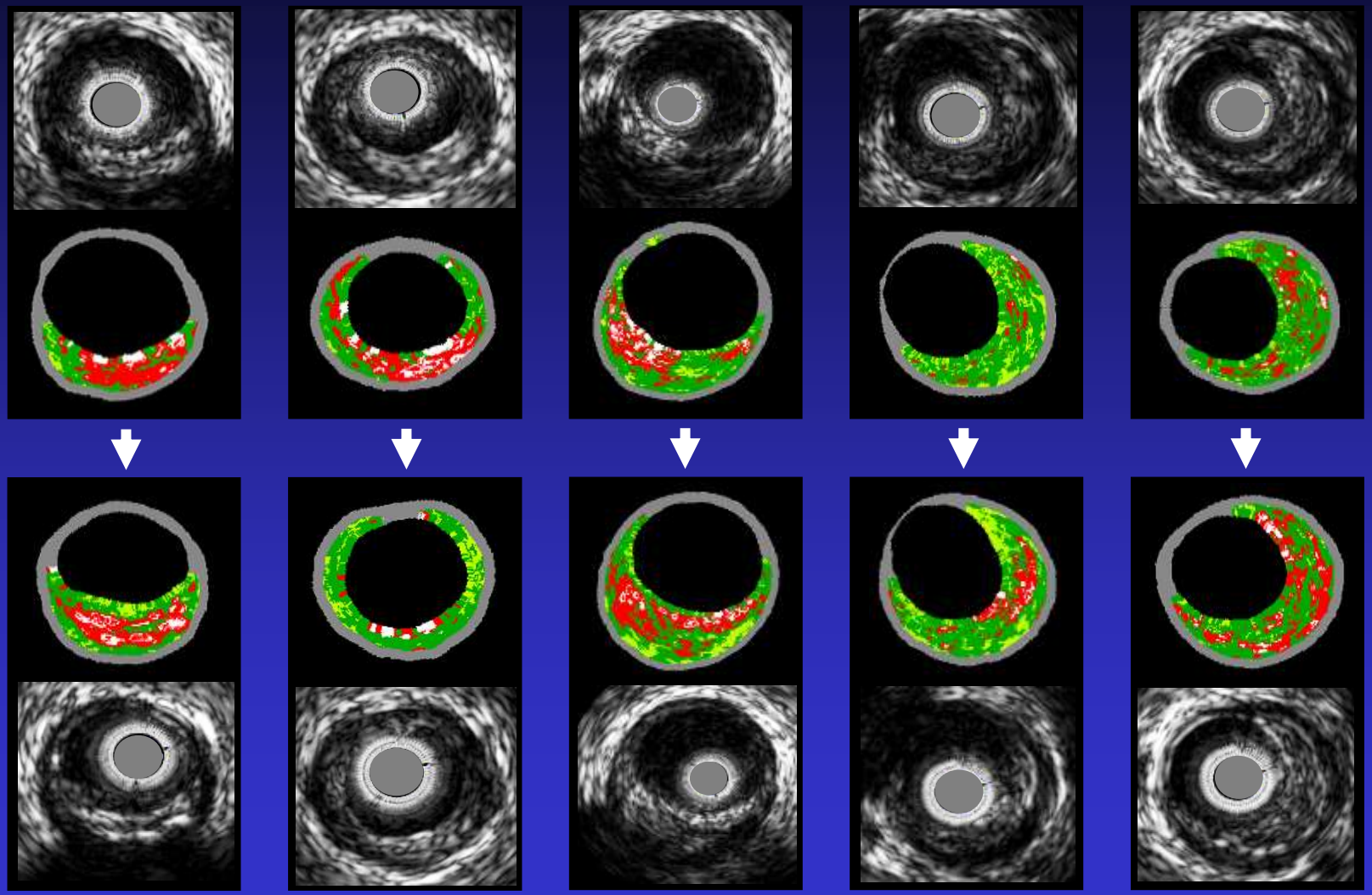
960 TCFA
f/u:38 (1-72) months



13 lesions assessed by OCT before plaque rupture

	1st OCT (Baseline)					2nd OCT (Follow-up)	
Case	Vessels	TCFA	Fibrous-cap thickness (μm)	Lipid-arc (degree)	Macro phages	Duration (M)	Clinical presentation
1	RCA	+	60	360	-	7	subclinical
2	LCX	+	60	360	+	11	subclinical
3	RCA	-	140	210	+	8	subclinical
4	LCX	+	50	330	+	7	UAP
5	LCX	-	110	270	-	3	AMI
6	LAD	+	40	270	+	8	UAP
7	RCA	+	50	170	+	9	subclinical
8	RCA	+	40	210	+	10	subclinical
9	RCA	-	80	150	-	9	subclinical
10	RCA	+	40	340	+	1	subclinical
11	RCA	-	100	360	-	27	AMI
12	RCA	+	60	270	+	5	NSTEMI
13	LAD	+	80	360	+	27	NSTEMI

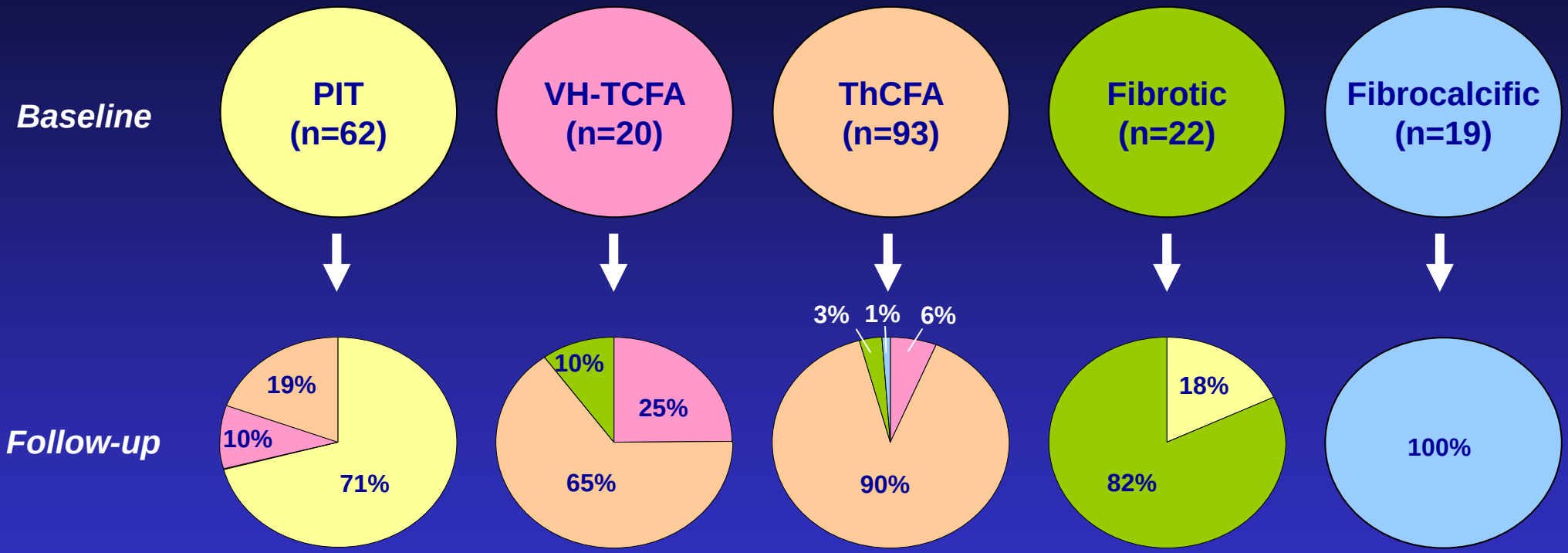
Representative images of serial VH-IVUS



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

Wakayama Medical University

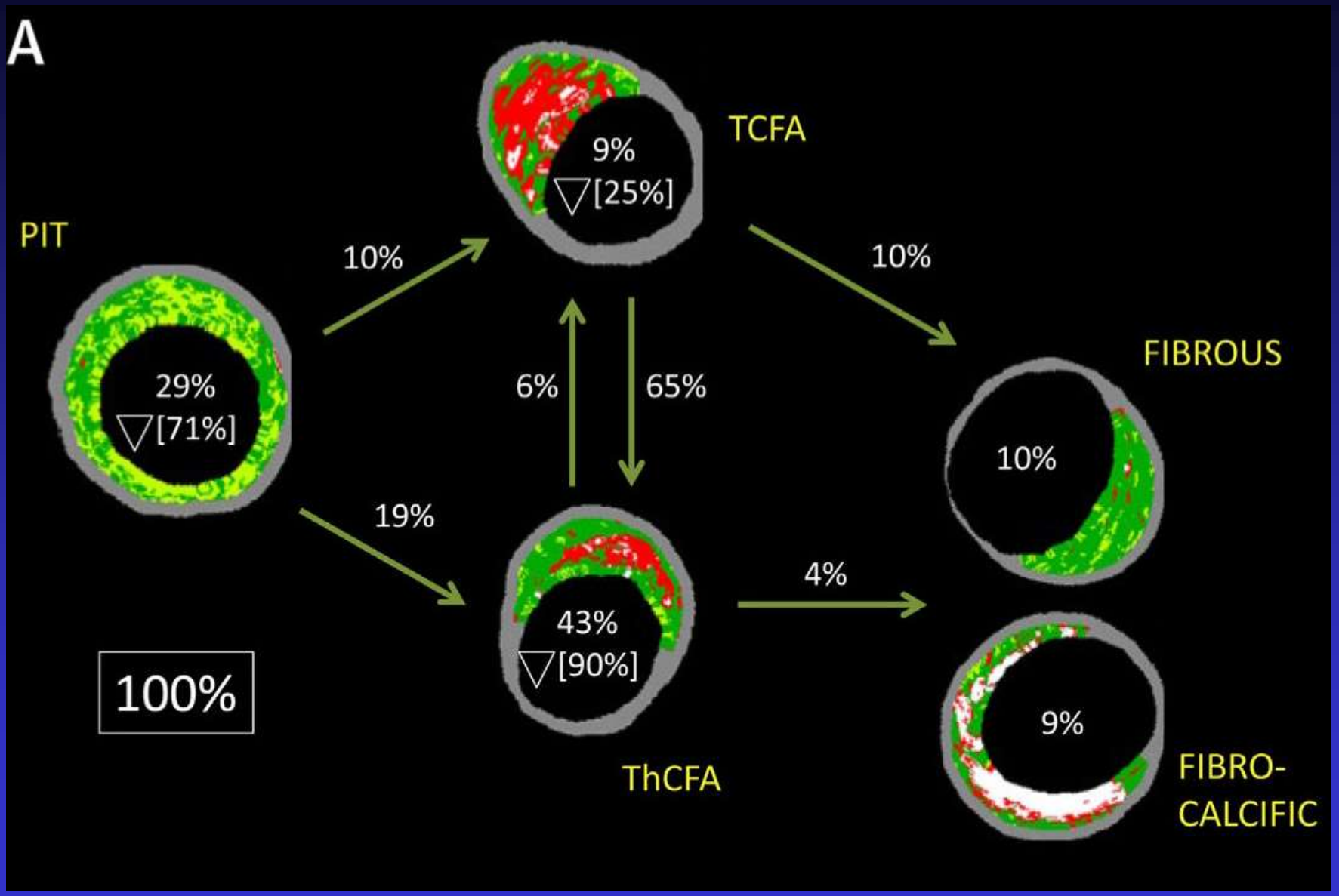
Changes in plaque characteristics



During follow-up, 75% of VH-TCFA evolved into a ThCFA or fibrotic plaque, and 25% remain unchanged. Conversely, 10% of PIT and 6% of ThCFA evolved into VH-TCFAs. No fibrotic plaque and fibrocalcific plaque evolved into fibroatheromas.

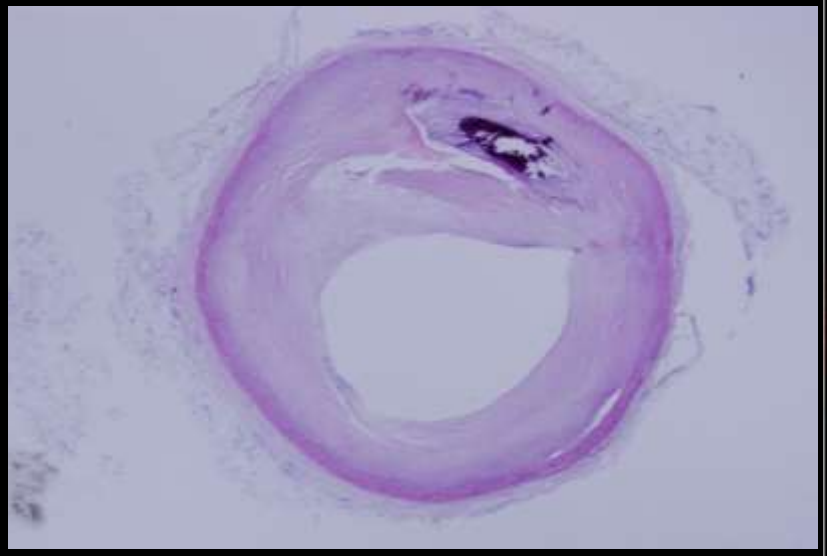
Kubo et al. J Am Coll Cardiol 2010;55:1590–7

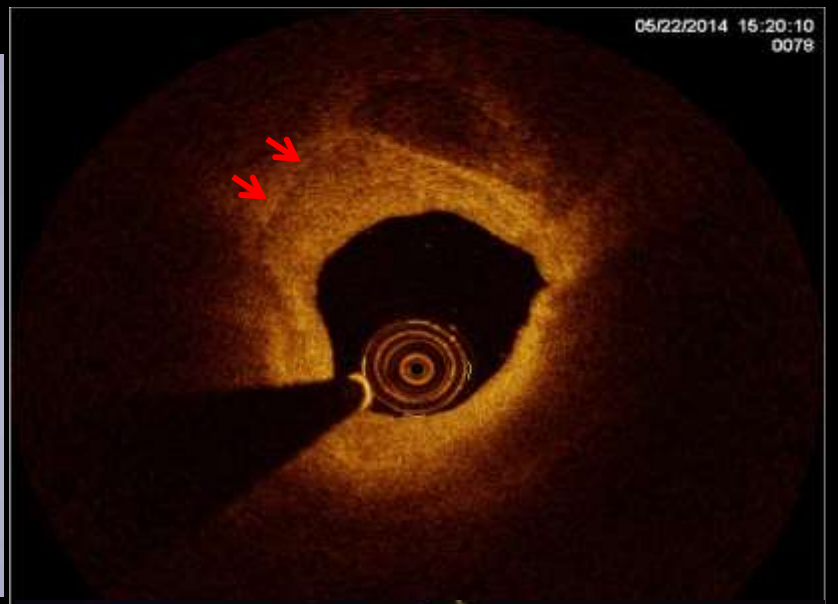
Changes in plaque characteristics

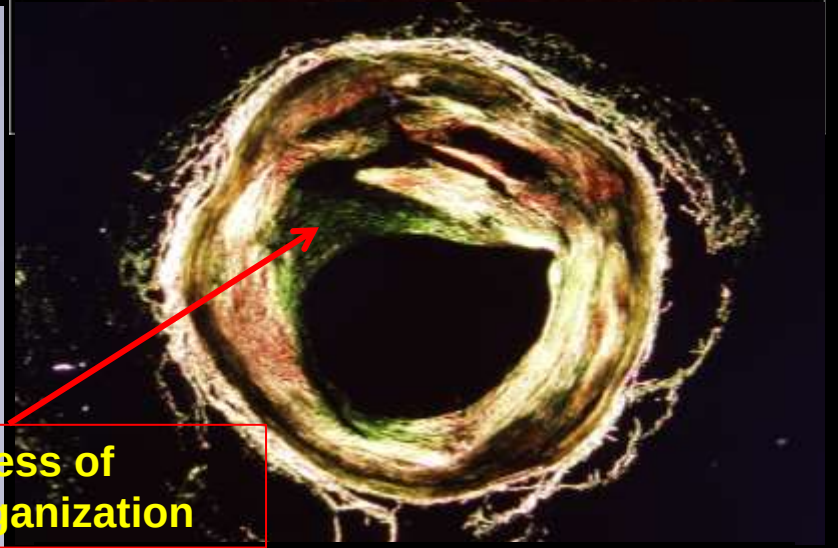


An Example of layered structure within a plaque

HE







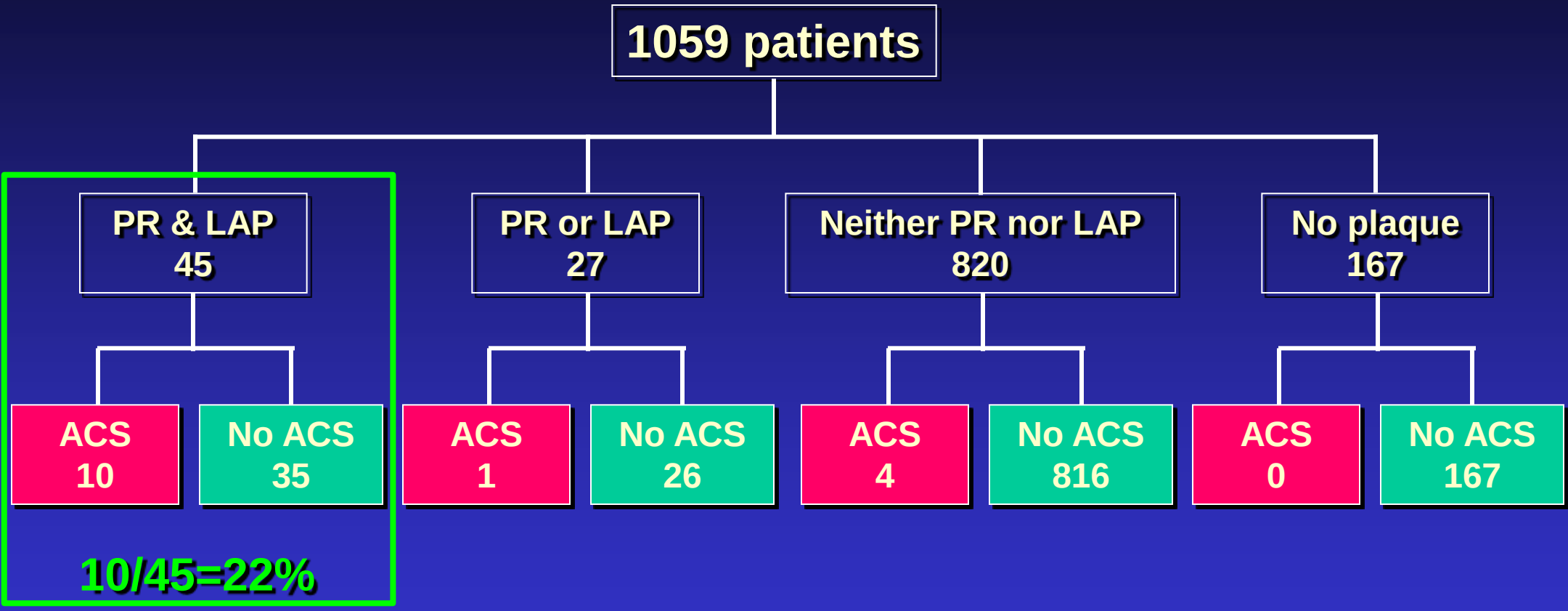
S/O process of thrombus organization

Sirius red stain
(Collagen : red)

Sirius red stain with polarized
Type Ⅲ (immature) collagen : green
Type Ⅰ (mature) collagen: orange

Patient population & event

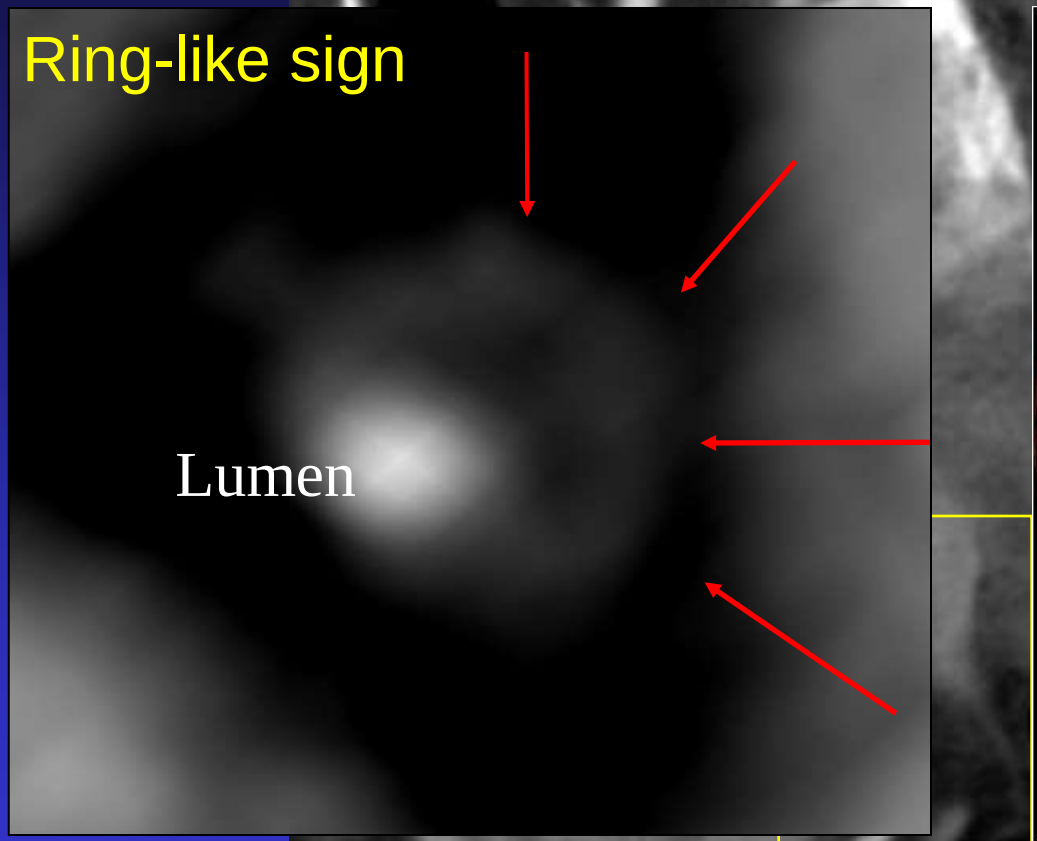
Motoyama S, et al. J Am Coll Cardiol 54: 49-57, 2009

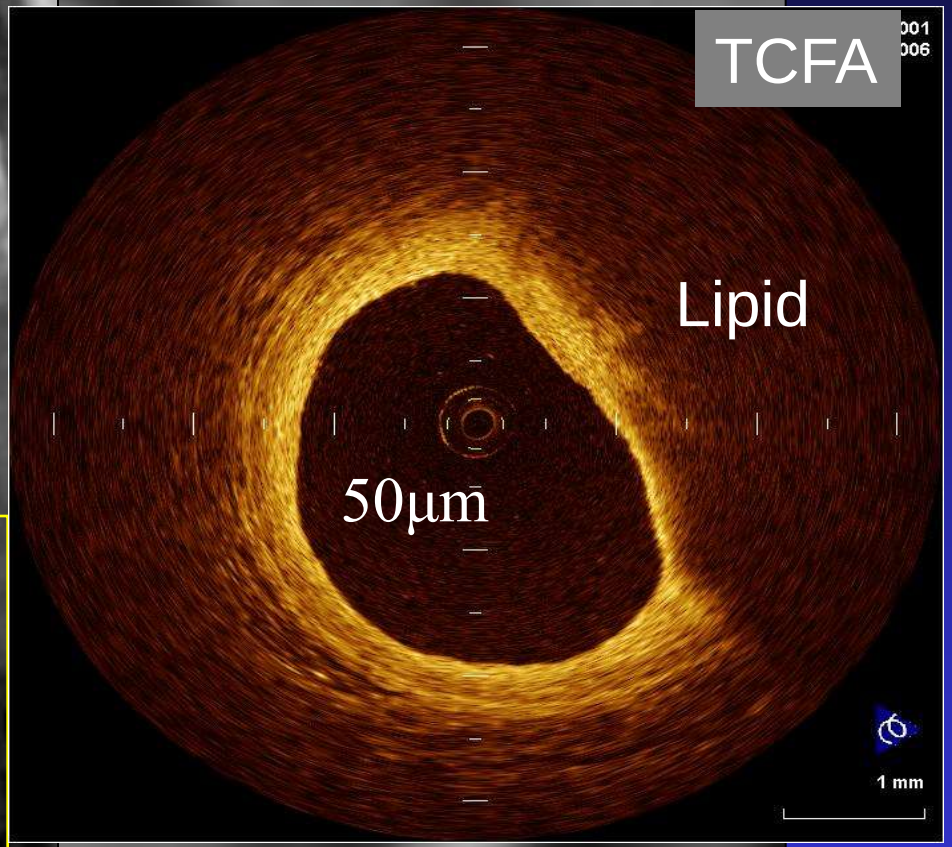


PR: positive remodeling
LAP: low-attenuation plaque

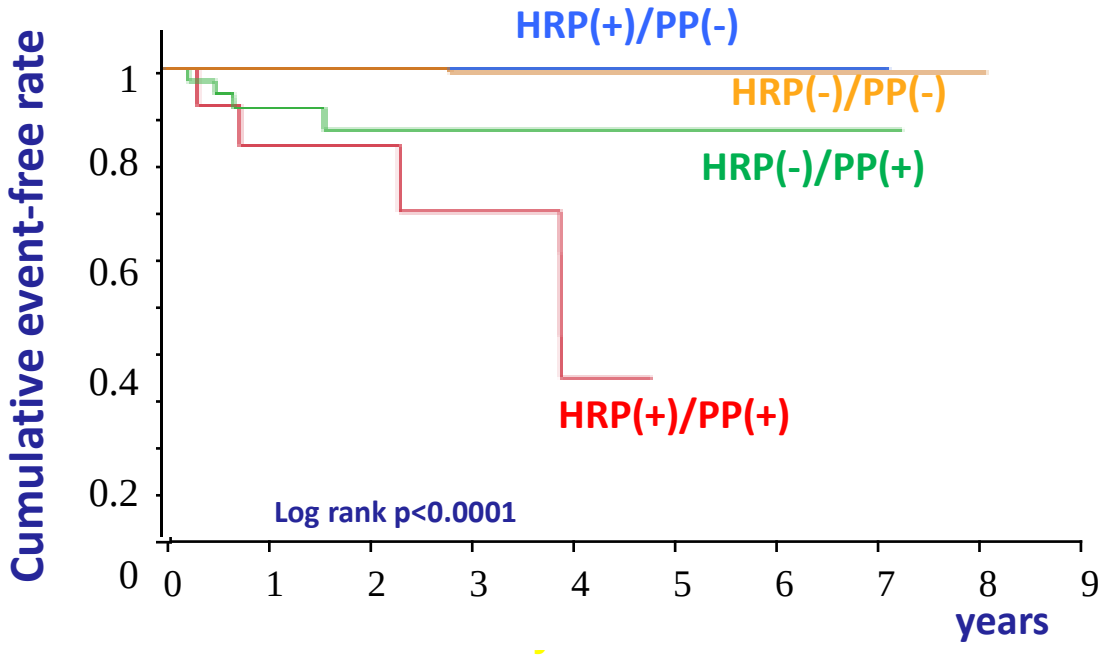
PR & LAP with Ring-like Sign by MSCT

Kashiwagi M, et al. JACC Cardiovasc Imaging 2: 1412-1419, 2009

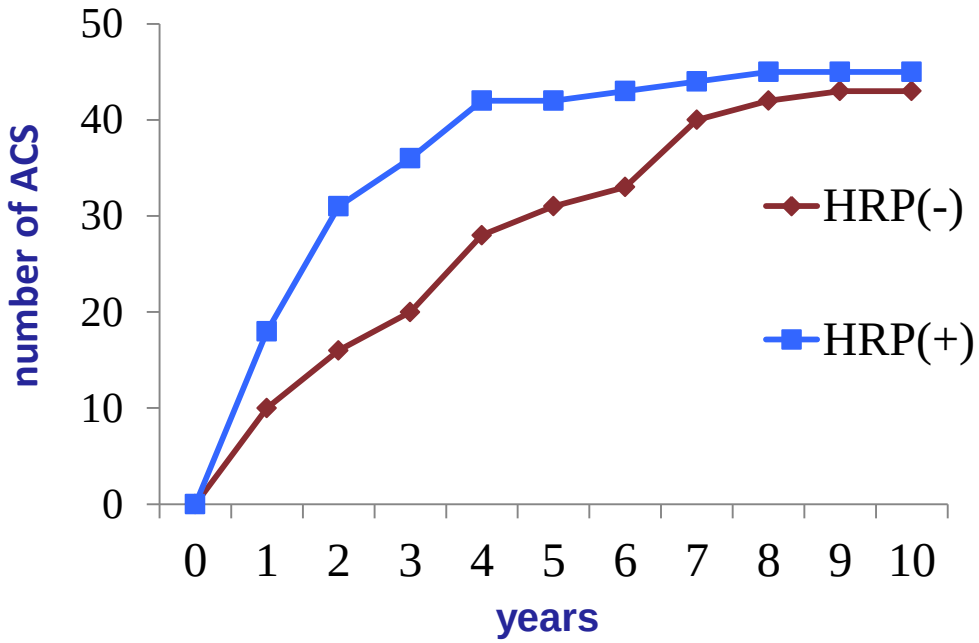




Kaplan-Meier Curve for ACS based on CTA-1 and CTA-2

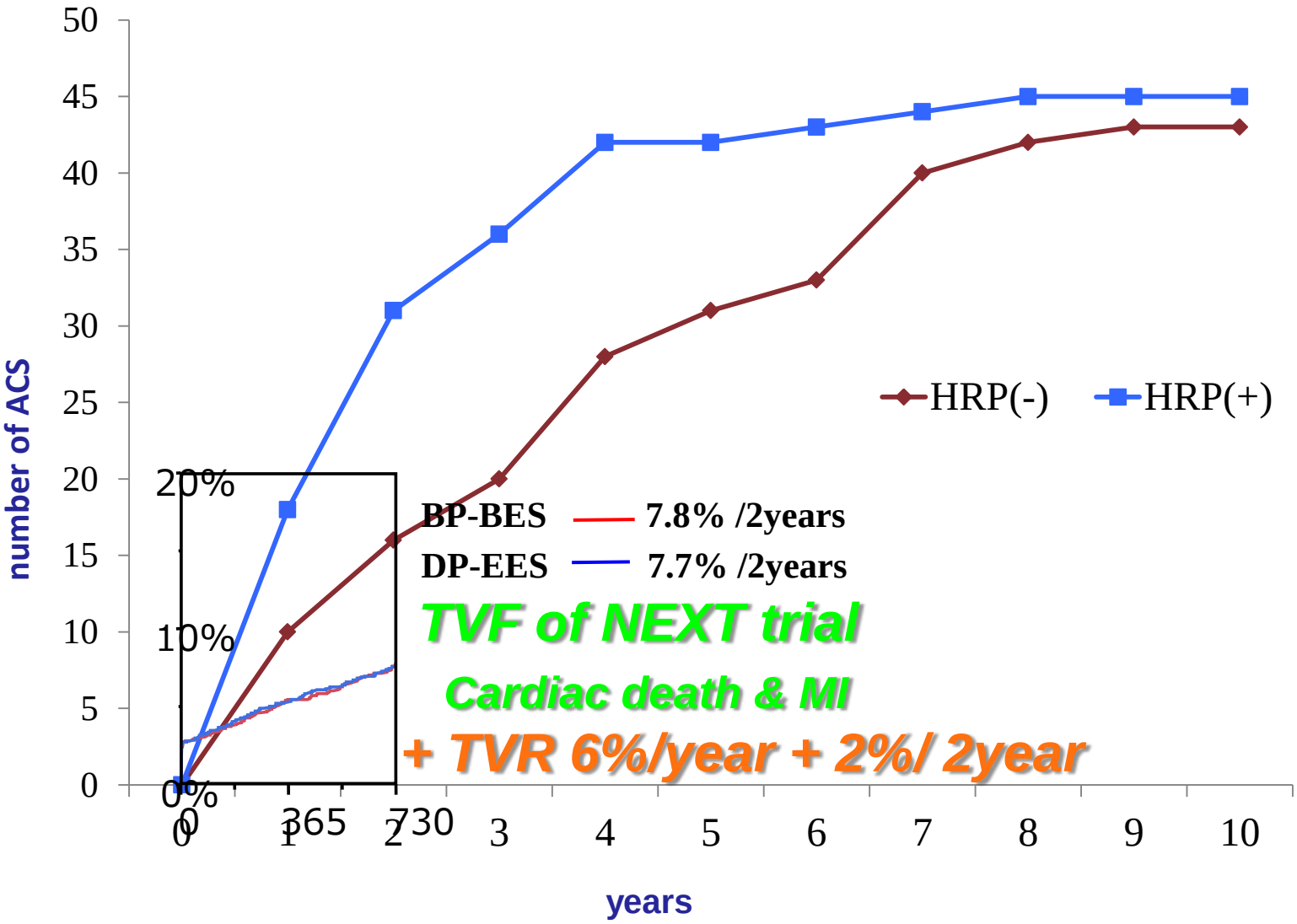


Lesion based analysis: number of ACS based on plaque characteristics



Motoyama, Narula et al. JACC [submitted for publication]
TCT 2014, Washington DC

Lesion based analysis: number of ACS based on plaque characteristics



Motoyama, Narula et al. JACC [submitted for publication]

TCT 2014, Washington DC

Wakayama Medical University

Summary (1)
Detection of VP & Natural Course by OCT

- Similar morphology can be demonstrated at the culprit lesions in ACS including plaque disruption, such as rupture, erosion & calcified nodule, thrombus, TCFA, lipid rich plaques, etc.
- Several differences could be identified at the culprit sites among different types of ACS and silent plaque disruption showing types of disruption and thrombus, size of MLA and ruptured cavity, position of disruption, etc.
- Although TCFA is thought to be a precursor of plaque disruption, further prospective study would be requested to predict future MACE as a vulnerable plaque (VP) relating to future events.
- OCT may be the most useful modality to demonstrate VP, further prospective study would be required to confirm its ability in the assessment of VP.

Summary (2)

Detection of VP & Natural Course by OCT

- Although development of various imaging modalities may allow us to demonstrate vulnerable plaques in some degree, prediction of future ACS might be difficult at the moment.
- According to the natural course of plaque morphology, it would be better to treat patients with coronary artery disease by stabilizing plaque vulnerabilities for ever.
- There are still possibilities of plaque sealing by intervention if the event rate of the interventions would be lower than MACE rate of VP.